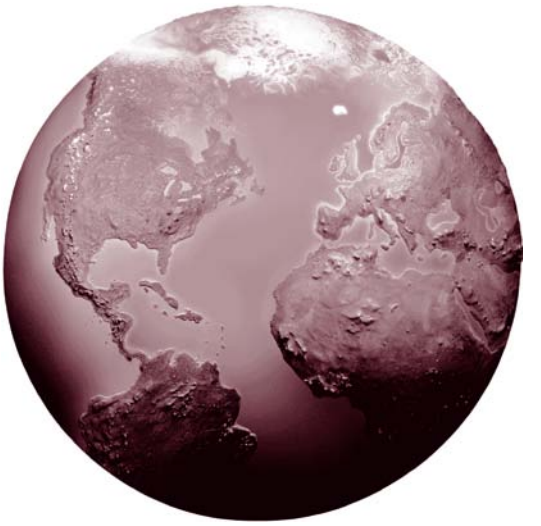

HEALTH EFFECTS INSTITUTE

# ANNUAL CONFERENCE 2016

## Program and Abstracts

May 1–3, 2016

**Brown Palace Hotel**

321 17th Street
Denver, Colorado 80202

1-303-297-3111

*Trusted Science • Cleaner Air • Better Health*

## Conference Coordinators

### Scientific Program
Annemoon M.M. van Erp

### Administration
Jacqueline C. Rutledge
Robert A. Shavers
Anny Luu
Sarah Benckart

### Publications
Hope Green
Hilary Selby Polk
Ruth E. Shaw

# HEALTH EFFECTS INSTITUTE

## 2016 Annual Conference

May 1–3, 2016
Brown Palace Hotel
Denver, Colorado



**Please Note:** With the speaker's permission, presentation slides will be posted at *www.healtheffects.org* after the conference.

# AT A GLANCE

## Sunday May 1

8:00 Registration Opens

9–11 Preconference Workshop: Demystifying Causal Inference in Air Pollution Epidemiology

11:30 Lunch

1:00 The Heat Is On: Climate, Air Pollution, and Health

4:00 Poster Session 1

6:00 Reception and Dinner

8:00 Keynote Speaker

## Monday May 2

7:00 Breakfast

8:30 HEI Update

10:30 How Low Should We Go? New Research on Low-Level Air Pollution

12:30 Lunch

1:45 Poster Session 2

3:15 The Global Burden of Disease from Air Pollution and Its Major Sources

5:30 Adjourn for Free Evening

## Tuesday May 3

7:00 Breakfast

8:30 Ozone and Cardiovascular Effects: Where Is "MOSES" Leading Us?

11:30 Lunch

12:30 Traffic and Health: Air Pollution, Noise, and Interactions with Socioeconomic Status

2:30 Conference Adjourns

# HEI Annual Conference Program

May 1–3, 2016

Denver, Colorado

## Sunday, May 1, 2016

**9–11 AM** **Preconference Workshop: Demystifying Causal Inference in Air Pollution Epidemiology**

Leaders: *Corwin Zigler* and *Francesca Dominici,* Harvard T.H. Chan School of Public Health

Causal modeling techniques have been proposed as alternatives to conventional epidemiological methods for making inferences about the relationships between air pollution exposures and public health outcomes. This workshop aims to provide attendees with a basic introduction to causal modeling methods and, drawing on details from recent HEI-funded research, with useful insights into the conceptual benefits and practical challenges in their application and interpretation. This preconference workshop is open to all conference attendees.

11:30 AM Lunch

**1:00 PM** **The Heat Is On: Climate, Air Pollution, and Health**

Chairs: *Warren Washington,* National Center for Atmospheric Research and HEI Board of Directors, and *Jana Milford,* University of Colorado–Boulder and HEI Review Committee

Air pollution and climate are intricately linked. Changes in global climate may alter temperature, precipitation, wildfire, and dust storm patterns, all of which may affect air pollution and public health. Correspondingly, air pollutant levels may affect climate. Regulations aimed at reducing specific air pollutants could either work in concert with or counteract efforts to reduce potential climate-forcing agents. This session will explore recent developments in climate research, including health effects from heat, droughts, and forest fires, and how air pollution and climate interact.

1:05 Introduction
*Warren Washington*

1:15 Modeling Climate and Air Quality
*Christine Wiedinmyer,* National Center for Atmospheric Research

1:45 U.S. Global Change Research Program on Climate Change and Human Health
*Allison Crimmins*, U.S. Environmental Protection Agency

2:15 Health Effects of Temperature and Its Interaction with Air Pollution: Methodological Issues and Preliminary Results from a Multicountry Study
*Antonio Gasparrini,* London School of Hygiene & Tropical Medicine, United Kingdom

2:45 Implications of Climate Change for Pollen and Allergic Diseases
*Kate Weinberger,* Brown University

3:15 Conclusions
*Jana Milford*

3:25 General Discussion

3:45 PM Break

**4:00 PM** **Poster Session 1**

**6:00 PM** **Opening Reception and Dinner**

**8:00 PM** **Keynote Speaker**

*Christopher Murray,* Director, Institute for Health Metrics and Evaluation, University of Washington–Seattle

## Monday, May 2, 2016

7:00 AM Breakfast

**8:30 AM** **HEI Update**

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

HEI will present progress of its research programs and publications. Highlights will include updates of HEI's recent work on diesel exhaust and plans for new research on 21st century oil and gas development. We will also introduce the recipient of the 2015 Walter A. Rosenblith New Investigator Award.

8:30 Introduction of the Committees
*David Eaton* and *James Merchant*

8:45 Presentation of the 2015 Walter A. Rosenblith Award
*David Eaton*

8:50 Upcoming Scientific Activities at HEI
*Rashid Shaikh*, Health Effects Institute

9:00 HEI's 21st Century Oil and Natural Gas Development Project
*Donna Vorhees,* Health Effects Institute

9:20 Progress on Diesel — and Looking Ahead
*Dan Greenbaum,* Health Effects Institute

9:40 Discussion

10:00 AM Break

**10:30 AM** **How Low Should We Go? New Research on Low-Level Air Pollution**

Chairs: *Amy Herring,* University of North Carolina–Chapel Hill and HEI Research Committee, and *Roger Peng,* Johns Hopkins Bloomberg School of Public Health and HEI Review Committee

Although levels are declining in high-income regions, epidemiological studies continue to report associations of air pollution with adverse health effects in the general population even at levels below current air quality standards, providing a continuing impetus for lower standards. This session will review those epidemiological studies, highlight HEI's new efforts on this topic, and discuss critical study design considerations and challenges that the studies will need to confront.

10:30 Overview of RFA 14-3: Assessing Health Effects of Low Levels of Air Pollution
*Jonathan Samet,* University of Southern California

10:40 New HEI Studies Assessing Health Effects of Low Levels of Air Pollution
*Hanna Boogaard,* Health Effects Institute

10:50 What Do Policy Makers and Risk Assessors Need to Know About Adverse Air Pollution Effects at Low Levels?
*Bryan Hubbell*, U.S. Environmental Protection Agency

11:05 The Current Knowledge on Adverse Effects of Low-Level Air Pollution
*Antonella Zanobetti,* Harvard T.H. Chan School of Public Health

11:30 Critical Methodologic Issues in Planning for Studies Assessing Low Levels of Air Pollution
*Arden Pope,* Brigham Young University

11:55 Panel Discussion
Panelists: *Mark Utell,* University of Rochester, *Jonathan Samet, Bryan Hubbell, Antonella Zanobetti,* and *Arden Pope*

12:30 PM Lunch

**1:45 PM Poster Session 2**

3:00 PM Break

**3:15 PM The Global Burden of Disease from Air Pollution and Its Major Sources**

Chairs: *Michal Krzyzanowski,* King's College London, and *Terry Keating,* U.S. Environmental Protection Agency

The Global Burden of Disease (GBD) 2013 study estimated that exposure to fine particulate air pollution contributed to some 2.9 million premature deaths in 2013, with nearly two-thirds of those deaths occurring in China, India, and other developing Asian countries. This session will present the most recent estimates of the burden due to air pollution in 2013 and trends from 1990 to 2013, as well as new estimates of the current and future projected burden of disease from coal-burning and other major pollutant sources in China and India from HEI's GBD MAPS project.

3:15 Introduction
*Michal Krzyzanowski* and *Terry Keating*

3:25 The Global Burden of Disease Due to Air Pollution and Its Major Sources: Estimates from the GBD 2013 Study
*Aaron Cohen,* Health Effects Institute

3:45 Estimates of Emissions and $PM_{2.5}$ Levels from Major Air Pollution Sources in China
*Ma Qiao,* Tsinghua University, China

4:05 Estimates of Emissions and $PM_{2.5}$ Levels from Major Air Pollution Sources in India
*Sarath Guttikunda,* Indian Institute of Technology Bombay, India

4:25 Current and Future Burden of Disease from Major Air Pollution Sources in China and India
*Michael Brauer,* University of British Columbia, Canada

5:05 Panel and General Discussion
Panelists: *Jonathan Samet* and *Kalpana Balakrishnan,* Sri Ramachandra University, India

**5:30 PM Adjourn for Free Evening**

## Tuesday, May 3, 2016

7:00 AM Breakfast

**8:30 AM Ozone and Cardiovascular Effects: Where Is "MOSES" Leading Us?**

Chairs: *David Christiani,* Harvard T.H. Chan School of Public Health and HEI Research Committee; and *Lianne Sheppard,* University of Washington–Seattle and HEI Review Committee

Many areas struggle to meet the ozone standard, and changing climate and emissions profiles for ozone precursors paint a complicated picture. HEI recently completed the Multicenter Ozone Study in Elderly Subjects (MOSES) of cardiovascular effects at low exposures of ozone. We will discuss the science behind the 2015 ozone regulations in the United States and the current knowledge base linking ozone to cardiovascular and respiratory effects, based on the results of MOSES and other human clinical studies. The session will conclude with comments from the MOSES Review Panel and the public.

8:30 Introduction
*David Christiani*

8:35 The Science Behind the Recent Ozone Standards
*Molini Patel*, U.S. Environmental Protection Agency

9:05 Cardiovascular Effects of Ozone: Evidence from Clinical Studies
*Nicholas Mills*, University of Edinburgh, United Kingdom

9:35 AM Break

10:00 Cardiovascular Effects at Low Ozone Levels: Results of the MOSES Study
*John Balmes,* University of California–San Francisco

10:30 Review Panel Response on MOSES Results and Interpretation
*James Merchant,* University of Iowa and Chair, HEI Review Committee

11:15 General Discussion

11:30 AM Lunch

**12:30 PM Traffic and Health: Air Pollution, Noise, and Interactions with Socioeconomic Status**

Chairs: *Barbara Hoffmann,* University of Düsseldorf, Germany; and *Jeffrey Brook,* Environment Canada; both on HEI Research Committee

This session will explore important factors related to the design and interpretation of health studies of traffic-related air pollution. It is intended to build on the findings of HEI's previous work and to lay the groundwork for upcoming deliberations on research needs in this area. Speakers will discuss differences in traffic and vehicle mixes around the world and the complex interactions between socioeconomic status (SES) and traffic noise in health studies of traffic-related air pollution.

12:30 Motor Vehicle Emissions: Worldwide Achievements and Challenges for Exposure Assessment
*Michael Walsh,* International Council on Clean Transportation

1:00 The Complex Interactions Between SES and Traffic-Related Air Pollution Effects
*Marie O'Neill,* University of Michigan

1:30 Is It Traffic-Related Air Pollution or Traffic Noise, or Both?
*Barbara Hoffmann*

2:00 Key Policy Questions on Traffic and Health
*Chad Bailey,* U.S. Environmental Protection Agency

2:15 General Discussion

**2:30 PM Conference Adjourns**

# POSTER SESSION 1

**Sunday, May 1, 4:00–6:00 PM**

## ACCOUNTABILITY

HEI's accountability, or 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. The Plan is targeted at a complex mix of sources, including marine shipping, long-haul trucking, non-road harbor equipment, and rail transport. After completion of Phase 1 to assess changes in air quality, Phase 2 will assess changes in health outcomes. **Dr. Russell** is studying changes in air quality in the Southeastern United States that have resulted from regulatory programs to reduce emissions from stationary and mobile sources: 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. Dr. Russell is estimating the number of emergency department visits and hospital admissions for cardiovascular and respiratory diseases that have been avoided due to each regulation in Atlanta, Georgia.

**Improvements in Air Quality and Health Outcomes Among California Medicaid Enrollees Due to Goods Movement Actions (Phase II Health Effect 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, Jim Mulholland, Yongtao Hu, Talat Odman, Lucas Henneman, Cong Liu, Mitch Klein, Joe Abrams, Stefanie Sarnat, Howard Chang, and Matt Strickland

## EMISSIONS AND EXPOSURE NEAR URBAN ROADWAYS AND IN TUNNELS

In 2014 HEI funded two studies under RFPA 14-1, *Enhancing Near-Road Exposure Assessment Through Characterization of Non-Tailpipe and Tailpipe Emissions Near Urban Roads and in Tunnels*. **Dr. Koutrakis** will develop sampling and statistical analysis methods to characterize contributions to ambient particles released directly (tailpipe and non-tailpipe emissions) and indirectly (resuspended road dust) and will identify variables that may influence the measurements. He will construct a mobile sampling platform equipped with coarse and fine particle concentrators to collect particle samples at 100 locations near major roads in the Greater Boston area. **Dr. Wang** is measuring concentrations of air pollutants in the Shing Mun Tunnel in Hong Kong and in the Fort McHenry Tunnel in Maryland (USA) to characterize current real-world vehicle emissions and to track changes in emissions over time due to regulations. Funded under RFA 13-1, *Improving Assessment of Near-Road Exposure to Traffic Related Pollution*, **Dr. Seto** is evaluating the sensitivity of exposure assessment methods that employ land-use regression models of various complexities compared with real-time pollutant concentrations measured using low-cost sensors. A team at U.S. EPA led by **Dr. Evans** is evaluating 1-minute sensor data on $O_3$ and $PM_{2.5}$ concentrations and developing guidance for users and manufacturers on how to interpret such short-term data. **Dr. Karperos** and colleagues present a literature review of strategies to reduce near-roadway air pollution, including urban design, roadside features, street design and traffic management, and pollutant removal from buildings. **Dr. Yuhnke**

evaluated a planned expansion of interstate highway I-70 through north Denver, and estimated neighborhood $PM_{10}$ concentrations projected for the planned highway and an alternative route.

****A Moment of Science: Interpreting and Communicating Short-Term Sensor Data**
Kristen Benedict, Alison Davis, Ron Evans, Bryan Hubbell, Scott Jenkins (Presenter), Martha Keating, Tom Long, Tom Luben, Elizabeth Mannshardt, Liz Naess, Jason Sacks, Michael Stewart, Susan Stone, and Karen Wesson

****Strategies to Reduce Near-Roadway Pollution Exposure**
Kurt Karperos, Bart Croes, Maggie Witt, and Annalisa Schilla

**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

**Evaluation of Alternative Sensor-Based Exposure Assessment Methods**
Elena Austin, Surakshya Dhakal, Jeffery Shirai, Katharine Hammond, Michael Jerrett, Alan Hubbard, Ying-Ying Meng, Ronald Cohen, and Edmund Seto

**On-road Vehicle Emission 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

****I-70 Hot Spot Analysis for $PM_{10}$ and Alternatives to Avoid PM NAAQS Violations and Reduce Population Exposures**
Robert E. Yuhnke and Lisa A. Warren

## EXPERIMENTAL STUDIES — NEW INVESTIGATOR AWARDS

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, will investigate 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. This will be tested in normal mice and in mice genetically lacking the Scavenger Receptor B1 that binds 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. **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 Baldridge, and Juan C. Gonzalez-Rivera

**Scavenger Receptor B1 Regulates Oxidized Lipid Driven Pulmonary and Vascular Inflammation After Ozone Exposure**
Kymberly M. Gowdy, Myles Hodge, Nate Holland, Michael B. Fessler, Robert M. Tighe, Sean Davies, and Christopher J. Wingard

** Study not funded by HEI.

**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

## MODELING POPULATION EXPOSURE

Even when good air quality information exists, it remains challenging to estimate exposures of populations at a regional, local, or individual level. Often, obtaining good air quality information is the first hurdle. **Dr. Guttikunda** presents challenges in forecasting air quality in India due to the limited number of available monitors. **Dr. Henze** and colleagues used a combination of modeling and remote sensing information to improve understanding of the relationship between exposure and emissions from particular sectors and locations around the globe, using data from the Global Burden of Disease project. **Dr. Milford** and colleagues are examining the air pollution co-benefits of imposing greenhouse gas emissions fees in the U.S. energy system. Fees are applied to $CO_2$ and $CH_4$ emissions, over the range of values developed by Interagency Working Group on the Social Cost of Carbon. **Dr. Palma** and colleagues are presenting the fifth version of the National Air Toxics Assessment (NATA), a screening tool that provides information on the potential risks from breathing air toxics. **Dr. Simon** and colleagues are examining ozone changes in response to large reductions in nitrogen oxides in 3 urban areas: Philadelphia, Atlanta, and Chicago. They are also examining sensitivity to reductions in VOCs during 2006–2008. **Dr. Vicars** and colleagues used a geographic information system (GIS) based model for estimating population served in mountainous terrain and will discuss the application of this technique to an assessment of Colorado's air quality monitoring network, specifically as it relates to environmental justice and public health goals.

****Forecasting Air Pollution in India**
Sarath Guttikunda

****Modeled Current and Future $PM_{2.5}$ Health Impacts of Location and Sector-Specific Emissions Using GBD Exposure Estimates, Satellite-Based Downscaling, and Global Source-Receptor Modeling**
Forrest Lacey (Presenter), Daven Henze, Colin Lee, Randall Martin, and Aaron van Donkelaar

****Air Quality Co-Benefits of Greenhouse Gas Emissions Fees in the U.S. Energy System**
Kristen E. Brown, Daven Henze, and Jana Milford

****Using the National Air Toxics Assessment to Screen for Potential Health Impacts in Communities**
Ted Palma, Mark Morris, and Madeleine Strum (Presented by Karen Wesson)

****Assessing Changes to Spatial and Temporal Patterns of Ozone in Three Urban Areas Due to Large $NO_x$ Reductions**
Heather Simon, Benjamin Wells, Kirk R. Baker, and Bryan Hubbell

****The "Population Served" Concept and Its Role in Examining the Efficiency and Equity of Colorado's Air Quality Monitoring Network**
William Vicars, Cindy Wike, and Gordon Pierce

** Study not funded by HEI.

# POSTER SESSION 2

**Monday, May 2, 1:45–3:15 PM**

## TRAFFIC-RELATED AIR POLLUTION: EXPOSURE AND ENVIRONMENTAL JUSTICE

Several ongoing studies funded under RFA 13-1, *Improving Assessment of Near-Road Exposure to Traffic Related Pollution*, are improving the assessment of near-road exposure to traffic-related air pollution. **Dr. Barratt** is performing an extensive spatial measurement campaign, and is collecting additional indoor and outdoor measurements at different building heights (both outdoors and indoors) in canyon streets with high, adjoining buildings in Hong Kong. He will develop a three-dimensional land-use regression model for residents that will be applicable to other Asian megacities. **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 through extensive fixed and mobile sampling campaigns. **Dr. Sarnat** is evaluating 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 will explore the use of metabolomics (the study of chemical processes involving metabolites) to identify possible exposure-related metabolites. **Dr. Marshall** and colleagues are using three approaches to understanding environmental justice aspects of transportation-related air pollution in the United States (i.e., national-scale longitudinal analyses, case studies, and life cycle assessment). **Dr. Wong** and colleagues investigated the effectiveness of regulations to reduce emissions from mobile and stationary sources by determining diesel particulate mater concentrations and emission trends. They also conducted in vitro toxicologic studies of PM samples collected from a heavy-duty vehicle equipped with advanced retrofit technologies to screen for the inadvertent production of novel, more toxic compounds.

**The Hong Kong D3D Study: A Dynamic Three-Dimensional Exposure Model for Hong Kong**
Benjamin Barratt, Poh-Chin Lai, Linwei Tien, Thuan-Quoc Thach, Robert Tang, Martha Lee, Paulina Wong, Jenny Cheng, Anthony Tsui, Ryan Allen, and Michael Brauer

**Enhancing Models and Measurements of Traffic-Related Air Pollutants for Health Studies Using Bayesian Fusion: Analysis of Near-Road Concentration Gradients From Repeated Transect Measurements**
Stuart Batterman, Owais Gilani, Veronica Berrocal, 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**
H. Christopher Frey, Andrew Grieshop, Nagui Rouphail, Montse Fuentes, Andrey Khlystov, John Bangs, and Daniel Rodriquez

****Environmental Justice Aspects of Transportation-Related Air Pollution in the U.S.: Evidence from National-Scale Longitudinal Analyses, Case Studies, and Life Cycle Assessment**
Julian D. Marshall, Lara P. Clark, Matthew J. Bechle, Nam P. Nguyen, Kathryn R. Swor, Christopher W. Tessum, Jason D. Hill, and Dylan B. Millet

** Study not funded by HEI.

**Multipollutant and Biological Indicators of Primary Traffic Exposures in the Dorm Room Inhalation to Vehicle Emissions (DRIVE) Study**
Jeremy A. Sarnat, Armistead G. Russell, Donghai Liang, Jennifer Moutinho, Rachel Golan, Rodney J. Weber, Stefanie E. Sarnat, Roby Greenwald, Dong Gao, Vishal Verma, Howard Chang, and Dean P. Jones

****Diesel Particulate Matter in California: Ambient Trends and in Vitro Toxicity Screening of Engine Emissions**
Patrick Wong, Jeff Austin, Will Vance, Christoph Vogel, Norman Y. Kado, Jorn Herner, Martin Shafer, Reiko Kobayashi, Alvaro Alvarado, Linda Tombras Smith, Bart Croes (Presenter)

## HEALTH EFFECTS AT LOW AMBIENT CONCENTRATIONS

Three new studies, funded under RFA 14-3, *Assessing Health Effects of Long-term Exposure to Low Levels of Ambient Air Pollution*, will investigate 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 epidemiologic 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** will investigate mortality effects of low levels of air pollution in Canada using Canadian census data from about 6 million people. **Dr. Brunekreef** will investigate health effects of low levels of air pollution in Europe using pooled data from 10 cohorts analyzed in the European Study of Cohorts for Air Pollution Effects (ESCAPE) and 6 large administrative cohorts, resulting in a study population of about 25 million people. **Drs. Dominici** and **Zanobetti** will examine health effects of low levels of air pollution in the U.S. using data from ~56 million people enrolled in Medicare and Medicaid; in addition, they will develop new causal modeling methods to characterize the shape of the exposure–response function.

**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, Randall V. Martin, Michael Tjepkema, and Scott Weichenthal

**Mortality and Morbidity Effects of Long-Term Exposure to Low-Level $PM_{2.5}$, Black Carbon, $NO_2$, and $O_3$: An Analysis of European Cohorts**
Bert Brunekreef and collaborating institutions

**Assessing Adverse Health Effects of Long-Term Exposure to Low Levels of Ambient Pollution**
Francesca Dominici, Antonella Zanobetti, Brent Coull, Joel Schwartz, Petros Koutrakis, Cory Zigler, and Christine Choirat

## CONTROLLED EXPOSURE, PANEL, AND COHORT STUDIES

The HEI-funded Multicenter Ozone Study in Elderly Subjects (MOSES) aims to assess the effects of exposure to ambient concentrations of ozone on the human respiratory and cardiovascular systems. The funded investigators at three clinical research centers are **Drs. Balmes, Bromberg, and Frampton**. The biostatistical and data management team is led by **Dr. Stark**. The study subjects are healthy older persons 55 to 75 years of age and are being exposed to ozone while intermittently exercising. The endpoints being measured (before and after exposure) include cardiac function, blood pressure, prothrombotic and systemic inflammatory biomarkers, endothelial function, lung inflammation and injury, and pulmonary function.

** Study not funded by HEI.

A team in Belgium led by **Dr. Int Panis** conducted a one-week panel study performed in 55 healthy adult nurses to document cardiovascular effects of exposure to black carbon. **Dr. Kraus** is investigating the effects of short- and long-term exposure to particulate matter in a cohort of individuals with clinically evident heart disease who have undergone cardiac catheterization in North Carolina. He is examining the effect of exposure to air pollution on acute cardiovascular outcomes and chronic cardiovascular disease, and on biomarkers of cardiovascular metabolic risk and blood-borne whole genome gene expression profiles. **Drs. Yinping Zhang** and **Junfeng Zhang** and colleagues conducted a panel study among office workers living together on a work campus in China to examine whether and how ozone and $PM_{2.5}$ may differentially affect mechanisms of cardiopulmonary pathophysiology. In their study, they used different indoor filtration systems to manipulate indoor levels of $PM_{2.5}$ and ozone.

**Multicenter Ozone Study in Elderly Subjects (MOSES): Design and Preliminary Results**
John Balmes, Mehrdad Arjomandi, and Peter Ganz; Philip Bromberg, Milan Hazucha, Alan Hinderliter, Neil Alexis, and Nigel Mackman; Mark Frampton, David Rich, and Wojciech Zareba; Paul Stark and Danielle Hollenbeck-Pringle; and Maria Costantini

****Personal Black Carbon Exposure Is Associated with Microcirculatory and Macrocirculatory Changes**
Luc Int Panis, Tijs Louwies, Eline Provost, Bianca Cox, Tim Nawrot, and Patrick De Boever

**Gene–Environment Interactions in a Cardiovascular Disease Cohort**
Akihiko Nichimura, Cavin Ward-Caviness, Susanne Breitner, Regina Hempel, Alexandra Schneider, Annette Peters, Laura McGuinn, Robert B. Devlin, Lucas M. Neas, David Diaz-Sanchez, Wayne E. Cascio, Petros Koutrakis, David Dunson, Elizabeth R. Hauser, Svati H. Shah, and William E. Kraus

****Ozone and $PM_{2.5}$ in Pollution Mixture Differentially Impact Cardiopulmonary Pathophysiologic Mechanisms**
Drew B. Day (Presenter), Jianbang Xiang, Jinhan Mo, Feng Li, Mingkei Chung, Jicheng Gong, Jan Sundell, Charles J. Weschler, Pamela A. Ohman-Strickland, Yinping Zhang, and Junfeng (Jim) Zhang

## EXPLORING CAUSAL ASSOCIATIONS IN TIME-SERIES DATA

There is growing interest in the role that statistical methods can play in understanding the causal relationships between air pollution and adverse health outcomes. The HEI Annual Conference workshop "Demystifying Causal Inference Methods for Air Pollution Research" (Sunday, May 1) discussed examples involving long-term exposures to air pollution. The two posters in this group examine short-term, daily exposures. **Dr. Cox** presents his work on a Causal Analysis Toolkit that brings together multivariate regression, directed acyclic graph learning algorithms, Granger causality tests, and transfer entropy algorithms. He applied it to three data sets of daily mortality and air pollution in the LA basin to assess how well its algorithms can complement and support causal interpretations of exposure–response associations. **Dr. Young** and colleagues conducted extensive time-series analyses of $PM_{2.5}$ and ozone levels and mortality counts in the 8 most populous air basins of Southern California to investigate whether air pollution and health effects are causally related.

****A Causal Analysis Toolkit for Assessing Air Pollution Health Effects: Applications to Mortality Time Series, Medicare Data, and Survey Data**
Louis Anthony (Tony) Cox, Jr.

****Air Quality and Acute Deaths in California, 2000–2012**
S. Stanley Young, Richard L. Smith, and Kenneth K. Lopiano

** Study not funded by HEI.

# ABSTRACTS

## Multicenter Ozone Study in Elderly Subjects (MOSES): Design and Preliminary Results

J. Balmes, M. Arjomandi, and P. Ganz, *University of California–San Francisco, USA*; P. Bromberg, M. Hazucha, A. Hinderliter, N. Alexis, and N. Mackman, *University of North Carolina–Chapel Hill, USA*; M. Frampton, D. Rich, and W. Zareba, *University of Rochester Medical Center, Rochester, NY, USA*; P. Stark and D. Hollenbeck-Pringle, *New England Research Institutes, Watertown, MA, USA*; M. Costantini, *Health Effects Institute, Boston, MA, 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 ($O_3$), in part due to the notion that $O_3$ causes primarily local effects on lung function, which are the basis for the current $O_3$ National Ambient Air Quality Standards (NAAQS). However, several recent epidemiological studies that included assessment of associations with specific causes of death have reported stronger associations of ambient exposures to $O_3$ 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** This multi-center study investigated whether short-term exposure of elderly, healthy volunteers to ambient levels of $O_3$ in a controlled exposure setting induces acute cardiovascular responses. The study was conducted at three clinical centers and a Data Coordinating and Analysis Center using a common protocol. All procedures were approved by the IRB's of the participating centers. Healthy volunteers 55 to 70 years of age were recruited. They signed an IRB-approved informed consent form and those who successfully completed the screening and training sessions were enrolled in the study. The subjects were exposed for 3 hours in random order to clean air, 70 ppb $O_3$ (near the current NAAQS), and 120 ppm $O_3$ (a level measured in several outdoor locations in the US), alternating 15 min of moderate exercise with 15 min of rest. A suite of cardiovascular and pulmonary endpoints was measured on the day before, the day of, and up to 22 hours after, each exposure. 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** Subject recruitment started in June 2012 and the first subject was randomized on July 25, 2012. Subject recruitment ended on December 31, 2014, and testing of all subjects was completed by April 30, 2015. A total of 87 subjects completed all three exposures. The data analyses have been completed and the final report will be submitted to HEI by the end of February. Preliminary results indicate no significant ozone effects on any of the primary cardiovascular endpoints. Exposure to ozone caused small but statistically significant changes in lung function and increases in some markers of lung inflammation and injury.

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

Benjamin Barratt[1], Poh-Chin Lai[2], Linwei Tien[2], Thuan-Quoc Thach[2], Robert Tang[2], Martha Lee[4], Paulina Wong[2], Jenny Cheng[2], Anthony Tsui[2], Ryan Allen[3], and Michael Brauer[4]

*[1]King's College London, UK; [2]The University of Hong Kong, Hong Kong SAR, China; [3]Simon Fraser University, Vancouver, Canada; [4]University of British Columbia, Vancouver, Canada*

**Background** An increasing proportion of the world's population lives in densely populated three dimensional (3D) urban landscapes. Despite this, current traffic-related air pollution (TRAP) exposure estimates are strictly two dimensional (2D).

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

**Experimental Design** A 2D land use regression (LUR) model is being created and validated against data from two extensive spatial monitoring campaigns. Arrays of pollution sensors measuring black carbon (BC), $PM_{2.5}$, $NO_2$, NO, and CO have been deployed on the facing façades of buildings at four heights above street level within six selected street canyons to establish canyon decay rates. Sensors were paired inside and outside the building to assess infiltration efficiencies. A canyon typology will next be applied across the city using an existing 3D cityscape model of HK, thereby creating a 3D LUR model capable of producing exposure estimates that distinguish residential height above street level.

**Results** The preferred 2D LUR models have low $R^2$ values ($NO_2$ $R^2 = 0.46$; NO $R^2 = 0.53$; $PM_{2.5}$ $R^2 = 0.59$; BC $R^2 = 0.50$) relative to many models built for European and North American cities, but similar to existing LUR models for other East Asian cities, which may be indicative of a typically more complex urban morphology. Median Infiltration efficiency across the 28 homes monitored was lower in the warm season ($PM_{2.5}$: 0.81, BC: 0.88) than in the cool season ($PM_{2.5}$: 0.91, BC: 0.91), reflecting the increased use of in-window air conditioning and window closure during heavy monsoon rainfall. Preliminary results suggest that the majority of TRAP decay from vehicle emissions within the canyons occurs in the distance between street level and floor 3, i.e., below residential levels, resulting in a minor or flat decay above that level (mean BC 5% above background at floor 3). This evidence appears to hold across a range of canyon types and meteorological conditions. In all but one case prevailing wind direction during the monitoring campaigns was comparable with the 10 year mean.

**Conclusion** The rapid vertical decay rates found in this study, even within street canyons, highlights the importance of exposure estimates that incorporate residential height above street level in high rise Asian cities. Infiltration efficiency in Hong Kong is high in comparison with US cities.

## Enhancing Models and Measurements of Traffic-Related Air Pollutants for Health Studies Using Bayesian Fusion: Analysis of Near-Road Concentration Gradients From Repeated Transect Measurements

Stuart Batterman[1], Owais Gilani[1], Veronica Berrocal[1], Chad Milandro[1], Sarav Arunachalam[2], and Max Zhang[3]

*[1]University of Michigan–Ann Arbor, USA; [2]University of North Carolina–Chapel Hill, USA; [3] Cornell University, Ithaca, NY, USA*

**Background** An improved understanding of traffic-related air pollutants 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 of black carbon (BC), nitrogen oxides ($NO_x$), particulate matter (PM), ultrafine particles (UFP), and other pollutants. 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 objectives. First, we seek to improve the modeling of NO to $NO_2$ conversion in the "tailpipe-to-road" and "near-road" environments. Second, recognizing the need in epidemiological studies to estimate exposures at locations that are not monitored, we predict air pollution exposures at unsampled locations using spatial models that can more accurately capture the spatial correlation in the data.

**Methods** For the first analysis, we analyze data collected at the curbside of a major highway to evaluate conversion mechanisms and a turbulent reacting flow model (Comprehensive Turbulent Aerosol Dynamics and Gas Chemistry or CTAG model) for the tailpipe-to-road environment. The same data are used to evaluate several NO to $NO_2$ algorithms incorporated into the R-LINE dispersion model, which is designed for the near-road environment. For the second analysis, non-stationary spatio-temporal models are developed and evaluated for three traffic-related pollutants (NO, $NO_x$, and BC) sampled on transects across major highways. These models consider mixtures of two independent spatial processes, each using non-stationary covariance function with covariates driving the non-stationarity and the mixture weights.

**Results** A large fraction of $NO_2$ is produced through chemical reactions with $O_3$ during the "tailpipe-to-road" stage, even with a relatively short residence time. Further, results challenge the validity of the commonly assumed well-mixed zone above the road that has a constant $NO_2/NO_x$ ratio. Models simulating dispersion and conversion processes beyond the road edge, including an (empirical) polynomial method, a simplified 2-reaction scheme, and a 7-reaction scheme, could each represent diurnal patterns and major features of observed data, and preliminary results suggest that empirical schemes can provide comparable performed to the more detailed and physically based models.

In the spatial-temporal analysis, wind speed and direction proved to be important drivers of observed non-stationarity in the spatial dependence of the pollutant concentrations. For example, pollutant concentrations dispersed quickly at even low wind speeds at downwind sites, while concentrations at upwind sites had different covariance functions and the wind speed relationship differed. Accounting for wind speed and direction in the spatial covariance function was shown to improve predictions (at unsampled locations) compared to other stationary and non-stationary models.

**Conclusions** Predictions of traffic-related air pollutants in the near-road environment can be improved by accounting for NO to $NO_2$ conversion processes occurring in the tailpipe-to-road and near-road environments, and by using spatial-temporal analyses to estimate concentrations at sites of interest from monitoring data.

# 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[1], Jeffrey R. Brook[2], Richard T. Burnett[3], Daniel L. Crouse[4], Randall V. Martin[5], Michael Tjepkema[6], and Scott Weichenthal[7]

*[1]The University of British Columbia, Vancouver, British Columbia, Canada; [2]Environment Canada, Toronto, Ontario, Canada; [3]Health Canada, Ottawa, Ontario, Canada; [4]University of New Brunswick, Fredericton, New Brunswick, Canada; [5]Dalhousie University, Halifax, Nova Scotia, Canada; [6]Statistics Canada, Ottawa, Ontario, Canada; [7]McGill University, Montreal, Quebec, Canada*

**Background** Fine particulate matter ($PM_{2.5}$) 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$^3$, and studies repeatedly demonstrate associations with mortality this population, it is an ideal environment to study the relationship between mortality and low concentrations of $PM_{2.5}$.

**Objectives** To apply novel estimates of exposure to $PM_{2.5}$ to several large population-based cohorts, to characterize the relationship between $PM_{2.5}$ exposure with all cause and cause-specific mortality and to characterize the shape of the concentration-mortality association in those subjects whose average past 3 or 20 years of exposure did not exceed specified concentrations.

**Methods** We will develop novel satellite-based $PM_{2.5}$ exposure estimates at 1 km by 1 km resolution for each year from 1981 to 2012 across Canada. The estimates will be based on a combination of remote sensing based aerosol optical depth (AOD), translation of AOD to surface $PM_{2.5}$ concentrations using the chemical transport model (CTM) GEOS-Chem, and integration of these concentrations with land use and ground monitoring data. Further refinements will be made after incorporating new information on the relationship between AOD and $PM_{2.5}$ based on measurements of $PM_{2.5}$ at 5 sites across Canada where AOD is measured with sun photometers. Exposure to ozone will be assessed with a CTM, while $NO_2$ exposure will be characterized with a land use regression model incorporating satellite retrievals.

Building upon prior work, we will apply these exposure estimates to three large, population-based, cohorts: 1) ~2.5 million subjects who completed the 1991 census long form; 2) ~3.5 million subjects who completed the 2001 census long-form; 3) 350,000 subjects who participated in the Canadian Community Health Survey (CCHS) 2001, 2003, 2005, and 2007/2008 panels. All subjects are linked to annual mortality and tax records until 2011, to establish residential histories. The census cohorts include extensive information on socio-economic position such as income, occupation, education, marital status, immigrant status, and visible minority status. In addition, the CCHS includes information on behavioral risk factors such as smoking habits, obesity, diet, and alcohol consumption. The potential confounding influence on the $PM_{2.5}$-mortality association due to behavioral risk factors not recorded in the census/tax cohorts will be examined using the CCHS and indirect adjustment methods.

Using several exposure-time windows, we will characterize the shape of the concentration-mortality association using newly developed variable coefficient hazard regression models. We will also restrict our analysis to those subjects whose average past 3 or 20 years of exposure did not exceed specified concentrations (<12, 10, 8, and 6 μg/m$^3$). We will examine the sensitivity of the shape of the association to age, sex, socio-economic position (income, education occupation), ozone and $NO_2$ exposure, and behavioral (smoking, obesity, diet, alcohol) and contextual (% recent immigrants, % <high school, % low income) risk factors. Both relative and additive risk models will be examined.

## Mortality and Morbidity Effects of Long-Term Exposure to Low-Level $PM_{2.5}$, Black Carbon, $NO_2$, and $O_3$: An Analysis of European Cohorts

Bert Brunekreef

*University of Utrecht, Netherlands, with collaborating institutions: Karolinska Institute, Stockholm, Sweden; Helmholtz Zentrum München, Munich, Germany; Danish Cancer Society, Copenhagen, Denmark; IUF and University of Düsseldorf, Germany; ASL, Rome, Italy; Imperial College, London, United Kingdom; RIVM, Bilthoven, Netherlands; University of Athens, Greece; Swiss TPH, Basel, Switzerland; University of Ulm, Germany; University of Aarhus, Denmark; University of London, United Kingdom; NIPH, Oslo, Norway; and INSERM, France*

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 ends of the concentration distribution, which is partly related to the scarcity of observations, particularly in the low range. In this proposal 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 2.5 μm ($PM_{2.5}$), nitrogen dioxide ($NO_2$), and ozone ($O_3$). Studies have focused especially on $PM_{2.5}$, but increasingly associations with $NO_2$ are reported, particularly in studies that accounted for the fine spatial scale variation of $NO_2$. Very few studies have evaluated long-term morbidity and mortality effects of ozone.

We propose to 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 with detailed individual data (~340,000 subjects) and in 6 very large European administrative cohorts (> 25 million subjects). The analysis will focus on the pollutants $PM_{2.5}$, $NO_2$, and $O_3$, but will also exploit the rich monitoring data of black carbon (BC) available from the ESCAPE study with high spatial resolution. Our exposure assessment will characterize fine-scale intra-urban as well as between-urban air pollution contrasts using novel combinations of land use regression and dispersion models, routine monitoring data, and satellite observations. By combining ESCAPE cohorts and large administrative cohorts in one proposal, we will substantially increase sample size while utilizing in-depth individual characterization. Thereby, we leverage the strengths and overcome the weaknesses of each approach.

The proposal addresses the first overall aim of the call (assess health effects of long-term exposure to low levels of ambient air pollution). The proposal especially addresses specific objective 1 (different methods to characterize the exposure response function), and also contributes to objectives 2 and 3 (exploring variability across populations and different exposure assessment methods), and to objectives 4, 5, and 6 (investigating correction methods for exposure measurement error, co-occurring pollutants, and indirect approaches for confounder control).

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

Lydia M. Contreras, Kevin Baldridge, and Juan C. Gonzalez-Rivera
*University of Texas–Austin, USA*

**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 and studying how these perturbations affect normal patterns of cellular regulation. Given increasing findings that changes in expression of key regulatory proteins at the mRNA level characterize lung inflammatory responses, two important fundamental questions are: (1) what molecular mechanisms lead to the breakdown of normal (healthy) expression levels of these mRNAs in their respective pathways? And, (2) how is the breakdown of biological function at the molecular level caused by various environmental exposures? Our ability to address these questions is limited by our lack of basic knowledge of the interplay that likely exists between air chemistry and the chemistry of biological molecules. In this work, we are seeking to develop novel biosensors that allow characterization of RNA chemistry post-cellular exposures and to characterize the location of these biochemical modifications on the cellular RNAs. Ultimately, we seek to understand the implication of these biochemical changes on cellular function and overall health.

**New Results** During our first year of funding, we have conducted ozone/carbonyl exposures of BEAS-2B model lung cells and have analyzed their transcriptome for changes in 8-OG modifications upon exposures relative to clean air control. Patterns that we have seen in our data will be presented, with special focus on chemical changes (or "marks") that occur in mRNAs and regulatory miRNAs that have been implicated in lung inflammation responses. For these experiments, we have established exposure facilities on our own campus that have allowed us to conduct our experiments with higher efficiency; to validate this newly established setup we have also repeated previously obtained results to validate our current work. We have also established robust protocol for modRIP-seq analysis using commercially available antibodies that can selectively isolate 8-OG, $m^6A$, and $m^5C$ modifications. In this processed, we have now fully optimized binding times, concentrations of antibodies used, and RNA extraction protocols to be compatible with the RNA sequencing experiments. We have also established a bioinformatics pipeline to analyze our results and their statistical significance. As a way to complement our work with BEAS-2B cells, we have also established a new collaboration to allow us to analyze lung tissues of mice that have been exposed to cigarette smoke. We have developed protocols to successfully extract RNAs from these systems for comparisons with results obtained from ozone/carbonyl exposures of our BEAS-2B cells. Lastly, a major component of our work is to engineer novel sensors that can detect a wider range of RNA modifications. We have identified an initial *E.coli* protein (PNPase) and have biochemically characterize the natural binding of all of its domains to a wide range of RNAs that display chemical modifications that include (-OG, 5-OH-dC and 8-OdA). We have been able to isolate 6 major domains of this protein, after expressing them from plasmids and purifying them for in vitro gel-shift binding assays (to test affinity to the various RNAs).

**Experimental design** Air mixtures explored in these initial experiments include a concentration range of: **(i)** ozone/carbonyl mixture of ~4 ppm $O_3$, 2 $\mu g/m^3$ carbonyls, 1 hr.

## ** A Causal Analysis Toolkit for Assessing Air Pollution Health Effects: Applications to Mortality Time Series, Medicare Data, and Survey Data

Louis Anthony (Tony) Cox, Jr.

*Cox Associates and University of Colorado–Denver, USA*

**Background** Drawing valid causal conclusions from observational data is challenging, yet crucial for predicting how changes in ambient air pollution would affect public health. Computer-aided methods have been proposed to help discover, test, and validate causal models and predictions. Some rely on untestable assumptions or judgments to interpret associations causally, but others use data to test implications of causal hypotheses. Current data science algorithms available in R packages can be used to test the following implications of "Exposure X is a cause of effect Y" in a population: (1) Y is not conditionally independent of X after conditioning on other variables. 2. Changes in X help to predict and explain subsequent changes in Y. 3. Information flows from changes in X to changes in Y over time.

**Methods and Data** We developed a Causal Analysis Toolkit (CAT) that allows Excel users without R knowledge to apply advanced R packages to epidemiological data sets. CAT quantifies multivariate associations among predictors (exposure and covariate variables) and response variables using traditional regression models, and offers visualizations of descriptive statistics and bivariate associations. It augments these with directed acylic graph (DAG) learning algorithms to reveal statistical dependence and conditional independence relations among variables; Granger causality tests and generalizations to determine whether changes in exposures help to predict subsequent changes in responses; and transfer entropy (TE) algorithms for determining whether information flows from exposure variables to response variables over time. We apply CAT to three data sets to assess how well its algorithms can complement and support causal interpretations of exposure-response associations: (1) Daily $PM_{2.5}$, temperature, and mortality counts in the Los Angeles (LA) air basin for 2007-2010; (2) Coronary hospitalization and mortality data from the CMS (Centers for Medicare & Medicaid Services) MEDPAR database for health providers, joined to local air quality data from the U.S. EPA "AirData" database for FY 2011-13; and (3) Survey data on asthma, heart attack, strokes, and socioeconomic variables from the CDC Behavioral Risk Factor Surveillance System (BRFSS), joined to U.S. EPA ambient $PM_{2.5}$ and $O_3$ concentration data at the county level for 2008-2012.

**Results** CAT algorithms proved valuable for identifying potential causes and confounders of health effects and detecting regression model specification errors. They found that temperatures for the past 14 days or more affect daily elderly mortality rates in LA; that historical exposure-response associations between $PM_{2.5}$, $O_3$, and elderly coronary mortality rates do not predict *changes* in mortality rates following changes in pollution levels in the Medicare data; and that income powerfully confounds the association between $PM_{2.5}$ and heart attack risk in the BRFSS data.

**Conclusions** Data science tools for computer-aided exploration and testing of causal hypotheses can help users propose causal hypotheses that are consistent with observed statistical dependencies and independence relations among variables; identify potential confounders and pathways of association; and detect where parametric regression models do not adequately describe exposure-response relations. They are ready for practical use in helping investigators test and refine causal hypotheses for exposure-response relations.

** Study not funded by HEI.

## 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

*Harvard TH Chan School of Public Health, Boston, MA, USA*

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 casual inference to estimate exposure response that adjusts for confounding factors and accounts for exposure error.

Aim 3. 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.

## **A Moment of Science: Interpreting and Communicating Short-Term Sensor Data

Kristen Benedict, James Brown, Alison Davis, Ron Evans, Bryan Hubbell, Scott Jenkins (Presenter), Martha Keating, Tom Long, Tom Luben, Elizabeth Mannshardt, Liz Naess, Jason Sacks, Michael Stewart, Susan Stone, and Karen Wesson

*US Environmental Protection Agency*

With the development of portable pollution sensors, highly time resolved (i.e., 1-minute) information on local concentrations of $O_3$ and $PM_{2.5}$ is becoming increasingly available. However, the available scientific evidence does not support the development of health messages for such short-term pollutant exposures. Thus, there is a need for the EPA to provide guidance to both the public and to sensor manufacturers on the appropriate interpretation and communication of 1-minute sensor data. Staff and managers from the EPA's Office of Air and Radiation and Office of Research and Development have been working to provide this guidance by developing 1-minute sensor breakpoints for $O_3$ and $PM_{2.5}$, and to develop corresponding sensor messages. Breakpoints and messages are informed by our understanding of: (1) the broad body of health evidence for short-term $O_3$ and $PM_{2.5}$ exposures; (2) available information on air quality relationships for various averaging periods, including relationships between potential sensor categories and air quality index categories; (3) near-source pollutant concentrations and exposures; and (4) potential limitations in sensor technology. Our goals in identifying sensor category breakpoints and in developing sensor messages are to guide the interpretation of sensor data, and to encourage this interpretation to be consistent with available health effects evidence and air quality information. Future efforts will include evaluation of initial interpretation guidance and will potentially expand to the development of sensor breakpoints and messages for additional pollutants, including other criteria pollutants and some hazardous air pollutants.

This abstract does not necessarily reflect EPA policy.

** Study not funded by HEI.

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

H. Christopher Frey, Andrew Grieshop, Nagui Rouphail, Montse Fuentes, Andrey Khlystov, John Bangs, and Daniel Rodriquez

*North Carolina State University, Raleigh, NC, USA; Desert Research Institute, Reno, NV, USA; North Carolina Central University, Durham, NC, USA; University of North Carolina–Chapel Hill, USA*

**Background** The objectives are to: (1) determine the most important variables that explain spatial and temporal variance of near road traffic-related pollutant concentrations; (2) demonstrate novel surrogates of near-road traffic-related pollution: and (3) improve inputs for exposure models for traffic-related health. We focus on key factors that influence the source-to-exposure continuum: 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 are leveraging 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 will be quantified and used as potential explanatory variables for near road air quality as part of quantile regression. We are monitoring traffic 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. We will introduce a spatial-temporal statistical framework to characterize the association between concentrations of multi-pollutants measured sparsely across space and time and different metrics and surrogates for exposure, such as land use attributes and traffic activity, while characterizing and accounting for distance from the roadway, wind speed and direction, temperature, building density, and foliage. Our tiered approach will include land use regression (LUR) and spatio-temporal statistical estimation.

**Results** We have conducted summer 2015 and winter 2016 field measurements at each of the I-40 freeway and Durham intersection sites. At the I-40 site, measurements of aerosol size distributions, $NO/NO_2$, black carbon (BC) and aerosol mass concentration and volatility were conducted. Measurements of $NO/NO_2$, BC and aerosol size distribution were collected at a background site. Furthermore, transects perpendicular to I-40 in the downwind direction were conducted including measurements of aerosol size distributions, $NO/NO_2$, black carbon (BC), and aerosol volatility at 4-5 locations (15, 50, 100, 150, 220 m from highway edge). Vehicle emission tracers ($NO_x$, NO, BC) decay to background levels within 200-300 m of the highway edge. Vehicle emission related pollutants (e.g., $NO_x$, NO, BC, sub-micron particle number) concentrations were consistently higher during the morning compared to mid-day and afternoon measurements. This trend is likely linked with both a lower morning mixing-height and high traffic volume during morning rush hour. Observed trends for aerosol mass concentrations were likely driven by several factors, including traffic emissions, regional background levels, meteorology and chemical and photo-chemical transformation process. 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. In related work, we have conducted field measurements at the Durham site, we have completed a characterization of the height of the natural and built environment for 5 m by 5 m grid cells within 2,000 feet of each monitoring site, and we have obtained and evaluated traffic count data for each site.

**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.

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

Kymberly M. Gowdy[1], Myles Hodge[1], Nate Holland[1], Michael B. Fessler[2], Robert M. Tighe[3], Sean Davies[4], and Christopher J. Wingard[1]

*[1]East Carolina University, Greenville, NC, USA; [2]National Institutes of Environmental Health Sciences, Research Triangle Park, NC, USA; [3]Duke University Medical Center, Durham, NC, USA; [4]Vanderbilt University, Nashville, TN, USA*

**Background** Ozone ($O_3$) exposure is associated with increased cardiopulmonary-induced morbidity and mortality. $O_3$ exposure not only causes lung injury and inflammation but also induces vascular inflammation and dysfunction, two hallmarks of cardiovascular disease (CVD). However, the mechanisms of how $O_3$ pulmonary exposure leads to systemic effects and cardiovascular complications are still unknown. $O_3$ does not have direct effects on the cardiovascular system; rather it reacts with lipids, sugars, and proteins to generate modified products that direct immune responses in the lung. One of these products are oxidized phospholipids (oxPLs), which have been reported to bind and stimulate pattern recognition receptors (PRRs) such as toll-like receptors, lectin-like oxidized low-density lipoprotein receptor-1, cluster of differentiation receptor 36 (CD36) and scavenger receptor B1 (SR-B1). Therefore, we hypothesize that the clearance of oxPLs generated in the lung during $O_3$ exposure is mediated by SR-B1 and the lack of oxPLs clearance will lead to systemic translocation, vascular inflammation and dysfunction. The studies proposed here will define: 1) if oxPLs produced in the lung after $O_3$ exposure alters vascular function; and 2) the role of SR-B1 in the oxPL-dependent pulmonary inflammation and vascular dysfunction.

**Methods** C57Bl/6J (WT) mice were exposed to 2 ppm of $O_3$ or filtered air for 3 hours to determine pulmonary injury and immune responses. Bronchoalveolar lavage (BAL) and serum cytokines, as well as cellular differentials were quantified 0, 3, 6, 12, and 24 hrs after exposure. In WT mice, SR-B1 gene expression was also assessed in whole lung and pulmonary macrophages isolated from the airspace at 0, 3, 6, 12, and 24 hrs post exposure.

**Results** Real time PCR analysis of SR-B1 expression in WT lung tissue revealed that SR-B1 is significantly induced about 3-6 hours post $O_3$ exposure but returns to baseline levels by 24 hrs post $O_3$ exposure. A similar trend for SR-B1 expression was seen in pulmonary macrophages. Current ongoing studies are determining oxPL species in the BAL and serum by liquid chromatography–mass spectrometry (LC-MS) after $O_3$ exposure. Future studies will determine if oxPLs are increased in the BAL and serum of SR-B1 deficient mice as well as determine the role of $O_3$ induced oxPLs in aortic and mesenteric contractile and relaxation responses by wire myography.

**Conclusions** This study observed that SR-B1 expression is induced in the lung and pulmonary macrophages after $O_3$ exposure and will correlate these findings with oxPL production and clearance. Findings from this research will lead to a better understanding of how $O_3$ alters cardiopulmonary inflammation and will also identify a novel receptor for the clearance of oxPLs created during $O_3$ exposure.

## **Forecasting Air Pollution in India

Sarath Guttikunda

*Indian Institute of Technology Bombay, India*

That the quality of air in Delhi is worse than that of Beijing has been the subject of several op-eds and policy discussions. As the capital, Delhi does in fact fall in the spotlight in discussions related to air pollution. With rapid urbanisation and growth, the rest of India is also subject to poor air quality but is not studied and with this lack of information, especially for tier-two cities, it makes it hard to make informed policy choices.

The Central Pollution Control Board operates 60 monitors across the country. This is far below the number of monitors that are needed (approximately 3000) for a country of this size, with a billion plus population. Data from even these 60 stations is very hard to access, as monitors are often not working and archived data unavailable. Given this vacuum of information, the only option we have is to estimate emissions and resulting concentrations. There are limitations to forecasting - overlooked sectors, acute events such as landfill flares, accurate updates of emission inventories. In developing the system for India, we have tried to address these concerns. Apart from updated inventories for the transport, power, industrial, and residential sector, we are also using the most up to date information on estimating the natural dust, open fire, and biogenic emissions, covering all the criteria pollutants linked to health.

All this is available on our *www.indiaairquality.info* site, disseminating the pollution forecasts and hindcast assessments for 640 districts in India and *www.delhiairquality.info* site, disseminating the pollution forecasts at high resolution for the national capital region of Delhi. An added feature in the dispersion model results is the delivery of forecasts disaggregated by source, providing a short-term prognosis for policy makers.

** Study not funded by HEI.

## **Modeled Current and Future $PM_{2.5}$ Health Impacts of Location and Sector-Specific Emissions Using GBD Exposure Estimates, Satellite-Based Downscaling, and Global Source-Receptor Modeling

Forrest Lacey[1] (Presenter), Daven Henze[1], Colin Lee[2], Randall Martin[2], and Aaron van Donkelaar[2]

*[1]University of Colorado–Boulder, USA; [2]Dalhousie University, Halifax, Nova Scotia, Canada*

**Background** Estimates of the health impacts of ambient $PM_{2.5}$ from the Global Burden of Disease (GBD) have been recently updated using global model calculations and remote sensing information. Understanding how these impacts may change in the future, and designing strategies for mitigating these impacts, requires improved understanding of the relationship between exposure and emissions from particular sectors and locations. A combination of modeling and remote sensing information can be used to refine these relationships throughout the globe.

**Methods** For this study, $PM_{2.5}$ exposure is estimated based on population projections and satellite-derived 0.1° by 0.1° products. We consider both the GBD 2013 estimates (Brauer et al., 2016) as well as more recent products that include a geographically weighted regression (van Donkelaar et al., submitted). Chronic health impacts associated with aerosol exposure are calculated using the World Health Organization (WHO) integrated exposure response functions. The response of these health impacts to grid-scale emissions perturbations are calculated for all species and sectors simultaneously with the GEOS-Chem adjoint model at the global $2° \times 2.5°$ resolution. These adjoint response coefficients are calculated at different decadal intervals using future emissions scenarios following Representative Concentration Pathways (RCPs).

**Results** This research represents the first use of the newest GBD $PM_{2.5}$ products in conjunction with adjoint modeling to generate source-receptor relationships between aerosol health impacts and emissions throughout the globe. Overall, we see a reduction in global mortality due to the reduction in aerosol and aerosol precursor emissions following RCP 4.5, although the reduction is not as severe as the change in emissions due to increasing population. By aggregating the global impact to each emissions sector and country we identify regions that behave counter to the global trend, particularly throughout India, West Africa, and parts of South America. The behavior in these regions is driven by both regional emissions and population trends. This work highlights regions that have higher potential for benefits from emissions targets due to the efficiency at which emissions result in premature deaths. The use of different satellite products for downscaling also allows us to generate measurement-based uncertainties associated with the results presented here.

**Conclusions** Variability in population projections, emissions, and $PM_{2.5}$ exposure all impact projections of future aerosol health impacts. By providing national-scale sector specific contributions to global mortality we have identified transportation as one of the most important sectors for human health following future emissions and population scenarios. This work will aid policy makers in identifying target sectors and species within a country in order to maximize the human health benefits of air quality control strategies.

** Study not funded by HEI.

## **Personal Black Carbon Exposure Is Associated with Microcirculatory and Macrocirculatory Changes

Luc Int Panis[1,2], Tijs Louwies[1], Eline Provost[1,2], Bianca Cox[2],Tim Nawrot[2], and Patrick De Boever[1,2]

*[1]VITO, Mol, Belgium; [2]Hasselt University, Hasselt, Belgium*

**Background** Ambient air pollution is associated with cardiovascular morbidity and mortality. Altered cardiac autonomic function, atherosclerosis and changes in vascular function and structure are potential pathways via which air pollution can influence the cardiovascular system. A detailed analysis of the cardiovascular phenotype is warranted to characterize early changes and better understand the sequential steps on the trajectory towards disease. In addition, such early changes may still be reversible and homeostatic processes can be restored (e.g., by increased physical activity).

**Methods** A 1 week panel study was performed in 55 healthy adult nurses to document cardiovascular effects of exposure to black carbon (BC, an important component of particulate air pollution used as a general measure of exposure to traffic). BC was measured with a portable μ-aethalometer to estimate personal exposure. Urinary t,t-MA, a metabolite of benzene, was analysed as an additional biomarker for traffic exposure. Four measurements of blood pressure (BP) and the microcirculation were obtained during this week. The status of the microcirculation was assessed with retinal vessel analysis in fundus photographs. Functional and structural properties of the carotid artery were examined ultrasonographically on two separate days; as a measure of the macrocirculation. Global DNA-methylation was studied using HPLC. Effects of personal BC exposure windows on BP, retinal vessel widths, carotid artery stiffness and DNA-methylation were estimated using mixed models adjusted for appropriate confounders.

**Results** Subchronic BC exposure averaged 1334 ng/m$^3$ and ranged from 338 to 3889 ng/m$^3$. An increased exposure of 631 ng/m$^3$ BC was associated with a 2.77 mmHg (95% CI: 0.39 to 5.15, P=0.027) increase in systolic BP, a 2.35 mmHg (95% CI: 0.52 to 4.19, p=0.016) increase in diastolic BP and a 5.65 μm (95% CI: 1.33 to 9.96, p=0.014) increase in Central Retinal Venular Equivalent. Increases in BC exposure 1 to 8 hours before the ultrasound measurement were significantly associated with increased carotid arterial stiffness. Increases in Young's Elastic Modulus ranged from 1.20% (95% CI: 0.48 to 1.95; P=0.0016) to 2.38% (95% CI: 0.81 to 3.97; P=0.0033) associated with a 100 ng BC/m$^3$ increase, 1 to 8 hours before the clinical examination, respectively. Increases in Pulse Wave Velocity ranged from 0.51% (95% CI: 0.19 to 0.83, P=0.0025) to 1.18% (95% CI: 0.51 to 1.88; P=0.0008). DNA methylation levels were also associated with all BC exposure windows as well as with t,t-MA. Each 0.135 mg/l increase in t,t-MA was associated with a 0.0021% (P=0.0019) decrease in global DNA methylation.

**Conclusions** Our study identified several micro- and macrovascular responses associated with personal BC exposure as well as global DNA hypomethylation. These responses may reflect different pathways via which air pollution triggers an increased risk of cardiovascular events. We advocate the combined application of several physiological measures to understand the complex response of the cardiovascular system and an accurate exposure assessment using portable devices.

** Study not funded by HEI.

## **Strategies to Reduce Near-Roadway Pollution Exposure

Kurt Karperos, Bart Croes, Maggie Witt, and Annalisa Schilla
*California Air Resources Board, Sacramento, CA, USA*

**Background** Compact and infill development exists in many parts of California and will become more prevalent in the future as a result of local, regional, and statewide efforts to achieve a variety of environmental and public health goals. This pattern of development has many public health benefits, including promoting physical activity, shortening and reducing vehicle trips and associated greenhouse gas emissions, and even improving quality of life. However, it may also mean that Californians are increasingly likely to spend time in near-roadway environments, where exposure to traffic pollution can lead to worsening of asthma and other respiratory health impacts. Therefore, identifying robust strategies that can reduce exposure to near-roadway pollution could lead to additional health benefits.

**Methods** ARB staff conducted a review of published, peer-reviewed literature and ARB-sponsored research to identify strategies that reduce near-roadway pollution exposure. Staff then narrowed the list of strategies to those that are scientifically robust, meaning that they meet the following criteria:

1. Consistent findings from multiple studies support the strategy as a means for reducing pollution concentrations, or emissions rates, or improving air flow to disperse pollutants.

2. Significant evidence of effective emissions reductions is documented in the scientific literature.

3. Diversity in the study methods supports consistent findings (such that strategies do not exclusively rely on one method of investigation).

**Results** ARB staff identified eight strategies that meet the abovementioned criteria. These strategies fall into four key categories: (1) urban design (e.g., designs that promote ventilation), (2) roadside features (e.g., sound walls and vegetation), (3) street design and traffic management (e.g., roundabouts), and (4) pollutant removal (e.g., in-building filtration). ARB staff is compiling these strategies into a Technical Advisory that also outlines their appropriate application, potential co-benefits and drawbacks, based on the literature and input from various stakeholders, including scientific experts; other state, federal, regional, and local agencies; planners, and non-profit representatives.

**Conclusions** The identification of these strategies and their compilation by ARB staff is intended to provide stakeholders involved in public health, air quality, and land use planning efforts with options for reducing exposure to traffic pollution in near-roadway environments, both for existing and new developments. ARB envisions that this document will be used as a resource to (1) identify strategies that can be employed on a site-specific basis to reduce exposure to traffic emissions at existing developments and (2) help shape local policies aimed at reducing exposure to traffic emissions and therefore associated public health impacts.

** Study not funded by HEI.

## 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

*Harvard TH Chan School of Public Health, Boston, MA, USA*

**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 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 have developed a device to collect $PM_{2.5}$ and $PM_{10}$ samples of aerosolized surface road dust *in situ*. Using this device, we will collect road dust samples at three distance ranges (including background) from each of the 100 major (A1, A2, and busy A3) roads to be included in this study. We will collect from this aerosolized dust a total of 600 $PM_{2.5}$ and $PM_{10}$ samples.

**Results** We have built a road dust aerosolization (RDA) sampler, and are validating this new device. Road dust is essentially vacuumed off the road surface. The RDA inlet is similar to the hose of a canister vacuum cleaner, connected to a wheeled vacuum head. The hose is connected to a small chamber containing mesh that prevents large debris from entering the size selective inlet (SSI). The SSI consists of a slit nozzle impactor with polyurethane foam (PUF) substrate, which provides a 15 μm size cut at 300 LPM. The purpose of the SSI is to prevent overloading of the $PM_{10}$ and $PM_{2.5}$ impactor substrates. After the SSI, the flow is split at a 15° angle Y, maintaining a constant velocity. Two identical branches off the Y are equipped with lateral unions, which branch at 120° and 180°. $PM_{10}$ samplers (30 LPM $PM_{10}$ impactor with PUF substrate and downstream filter) sample isokinetically from the 180° branch of each union. The 120° branches are diverted to a second lateral union, where similar $PM_{2.5}$ samplers collect isokinetically from the 180° branch. The 120° branches are connected to a custom housing which contains HEPA filter and a Minijammer blower. The blower on the RDA is currently powered using an extension cord that is connected to building electrical service; the field model, which will be deployed outside of the mobile platform, will be equipped with its own generator. Laboratory validation of the RDA components showed good cut curves for the $PM_{2.5}$, $PM_{10}$, and $PM_{15}$ impactors with PUF substrates. Field testing of the RDA is being conducted.

**Conclusions** Our RDA sampler effectively aerosolizes particles from road surfaces and collects both $PM_{10}$ and $PM_{2.5}$ with acceptable size cut and particle losses. We are still evaluating the sampling duration required to provide acceptable loadings for analysis under all sampling conditions and at all types of sampling sites.

## Gene–Environment Interactions in a Cardiovascular Disease Cohort

Akihiko Nichimura[1], Cavin Ward-Caviness[3], Susanne Breitner[3], Regina Hempel[3], Alexandra Schneider[3], Annette Peters[3], Laura McGuinn[2], Robert B. Devlin[2], Lucas M. Neas[2], David Diaz-Sanchez[2], Wayne E. Cascio[2], Petros Koutrakis[4], David Dunson[1], Elizabeth R. Hauser[1], Svati H. Shah[1], and William E. Kraus[1]

*[1]Duke University, Durham, NC, USA; [2]US Environmental Protection Agency, Chapel Hill, NC, USA; [3]Helmholtz Zentrum München, Neuherberg, Germany; [4]Harvard University, Boston, MA, USA*

**Background** Our project is designed to investigate the effects of acute and chronic air pollution on acute and chronic cardiovascular disease (CVD). In part, we are examining gene-by-air quality effects on newly identified cardiovascular risk biomarkers and blood-based whole genome gene expression profiles as *biological mediators* of acute cardiovascular events (myocardial infarction) and cardiovascular disease (CVD) in individuals undergoing coronary artery catheterization (collected 2001–2011). The 9323-member Duke CATHGEN cohort includes individuals with and without coronary atherosclerosis. We are addressing *three hypotheses in three Aims:* 1) Air quality — $PM_{2.5}$ and ozone — are related to chronic CVD (coronary and peripheral) and incidence of acute cardiovascular events; 2) Genetic variants mediate the interaction of air quality with CVD and incident events; 3) The interaction of genetic variants and air quality on CVD and incidence events are mediated by air quality-induced modifications of intermediate biological mediators: DNA methylation, peripheral blood gene expression, and circulating metabolic intermediates.

**Methods and Results** For Aim 1, we investigated the association between long-term exposure levels to ambient ozone levels and the incidence of myocardial infarction. We used a non-linear distributed lag model to estimate the long-term effects of daily ozone exposure on myocardial infarction (MI). For 7113 individuals from 2001–2009, the odds of incident MI increased by 11.9% for every 10% increase in mean ozone concentration. There was also strong evidence that ozone exposure has long-term effects: we estimate that it is 294 days until ozone association with MI incidence is reduced by 50%.

For Aim 2, we performed genome-wide gene-environment interaction association studies (GWIS) on European-American (N=1623) and African-American (N=554) cohorts to investigate the joint influence of common single nucleotide polymorphisms (SNPs) and traffic-related air pollution (TRAP) on peripheral arterial disease (PAD). We observed a SNP rs755249-TRAP interaction associated with PAD at a genome-wide significance level ($P=2.29 \times 10^{-8}$). This SNP is located in the 3′-untranslated region of *BMP8A*, a member of the bone morphogenic protein (BMP) family of genes. BMP genes have face validity for atherosclerosis: genes in the BMP family are regulators of muscle mass; affect vascular smooth muscle cell progression; promote vascular, aortic, and smooth muscle cell calcification; and are associated with atherosclerosis and angiogenesis.

For Aim 3, we examined associations between plasma small molecule metabolites and short-term exposure to $PM_{2.5}$, ozone and ambient temperature. We observed delayed associations between $PM_{2.5}$ and ozone with changes in plasma metabolite levels: an increase of 8.1 $\mu g/m^3$ in $PM_{2.5}$ with a lag of one day was associated with a −2.5% change in mean glycine concentration; 1-day lag ozone exposure had an effect in the same direction. A 5°C increase in temperature was associated with a 1.8% increase in glycine.

**Conclusions** Ozone exposure has long-term effects on CVD event risk; traffic-related air pollution interacts with bone morphogenic protein to increase risk for lower limb atherosclerosis; $PM_{2.5}$, ozone and ambient air temperature have measureable effects on small molecular metabolites associated with coronary risk.

Note: This abstract does not necessarily represent EPA policy.

## **Environmental Justice Aspects of Transportation-Related Air Pollution in the U.S.: Evidence from National-Scale Longitudinal Analyses, Case Studies, and Life-Cycle Assessment

Julian D. Marshall[1], Lara P. Clark[2], Matthew J. Bechle[1], Nam P. Nguyen[2], Kathryn R. Swor[2], Christopher W. Tessum[1], Jason D. Hill[2], and Dylan B. Millet[2]

*[1]University of Washington–Seattle, USA; [2]University of Minnesota–Minneapolis, USA*

**Background** Environmental injustice in air pollution exposure in the United States is widely documented (>130 studies): low-income communities and communities of color are often more exposed to air pollution and more vulnerable to air pollution health impacts (e.g., because of differential access to health care). Our research contributes to environmental justice (EJ) knowledge gaps by focusing on transportation-related air pollution, by employing a national-scale longitudinal approach, and by evaluating strategies to improve EJ outcomes.

**Methods** This poster incorporates findings from three approaches to understanding EJ aspects of transportation-related air pollution in the U.S.: (1) national-scale longitudinal analyses; (2) case studies; and (3) life cycle assessment. The national longitudinal analyses combine data from a nitrogen dioxide ($NO_2$) land use regression with Census data to measure changes in exposures by race-ethnicity and by socioeconomic status over time (years 2000-2010), based on residential and (separately) school locations. The case studies explore EJ impacts of targeting fine diesel particulate matter ($DPM_{2.5}$) emission reductions based on spatial location (e.g., reducing emissions in a specific neighborhood) or based on source type (e.g., ships vs. trains) in Southern California. Life cycle assessment explores EJ impacts of alternative transportation fuel scenarios (e.g., gasoline, biofuel, electricity) based on fine particulate matter ($PM_{2.5}$) and ozone ($O_3$) exposures.

**Results** Nationally, from 2000-2010, environmental injustice in $NO_2$ exposure decreased substantially on an absolute basis (mean change in absolute nonwhite/white exposure difference: −2.3 ppb, which is a change associated with significant public health impacts) but persisted on a relative basis (mean change in relative nonwhite/white exposure difference: −2%). In Southern California, spatially targeted $DPM_{2.5}$ emission reductions of 2.5% are associated with a 19% reduction in environmental injustice (exposure disparity between high-income whites and low-income nonwhites), and source targeted emissions reductions of 1 tonne $day^{-1}$ from trains are associated with a 1.6% reduction in environmental injustice, a larger reduction than for other transportation sources. From national life cycle assessment of alternative vehicle fuel scenarios, replacing gasoline vehicles with electric vehicles powered by clean-energy technologies (e.g., renewables) can reduce both total mortality and disparities in mortality (between lower-income nonwhites and higher-income whites) attributable to $PM_{2.5}$ exposure.

**Conclusions** Taken together, these approaches show that, on a national basis, environmental injustice due to transportation-related air pollution has decreased substantially in recent years (2000-2010), but exposure disparities, particularly by race-ethnicity, persist. Targeted emissions-reductions strategies (by spatial location or by source) and fuel switching strategies can help reduce these transportation-related exposure disparities.

** Study not funded by HEI.

# Improvements in Air Quality and Health Outcomes Among California Medicaid Enrollees Due to Goods Movement Actions (Phase II Health Effect Study)

Ying-Ying Meng[1], Jason G. Su[2], Michael Jerrett[3,4], Edmund Seto[5], John Molitor[6], and Xiao Chen[1]

*[1] UCLA Center for Health Policy Research, University of California–Los Angeles, USA; [2]Division of Environmental Health Sciences, School of Public Health, University of California–Berkeley, USA; [3] Department of Environmental Health Sciences, Fielding School of Public Health, University of California–Los Angeles, USA; [4] Center for Occupational and Environmental Health (COEH), Fielding School of Public Health, University of California–Los Angeles, USA; [5]Environmental & Occupational Health Sciences, University of Washington– Seattle, USA; [6] School of Biological and Population Health Sciences, Oregon State University, Corvallis, OR, USA*

**Background** In 2006, the California Air Resources Board and local air quality management districts implemented an "Emission Reduction Plan for Ports and Goods Movement." This project is conducted in two phases. In Phase I, we evaluated the effect of goods movement emission reduction actions on improvements in ambient air quality in the goods movement corridors (GMCs, locations within 500 m of truck-permitted freeways, ports, or railways), the non-goods movement corridors (NGMCs, locations within 500 m of truck-prohibited freeways or 300 m of a connecting roadway), and the control areas (CTRLs, areas outside of the above two corridors) in 10 major California counties between the 2003-2007 pre-policy and 2008-2012 post-policy periods. In Phase II, we will investigate whether regulatory actions had contributed to improvements in long-term (i.e., pre- and post-policy period) and intermediate-term (e.g., seasonal and annual) health outcomes in about 20,000 California Medicaid fee-for-service (FFS) beneficiaries with chronic conditions.

**Methods** We will first develop and evaluate measures of health effects (e.g., asthma hospitalization) and time-varying confounding factors (e.g., change in disease severity) to support our proposed research. Second, we will assess reductions in exposure to pollutants among Medicaid enrollees living in GMCs, NGMCs and CTRLs by assigning the multi-year, long-term pollutant concentration measures developed through the LUR modeling and comparing the degrees of reduction in pollutant concentrations from the pre- to the post-policy period. Third, we will use generalized linear multilevel models through difference-in-difference techniques to identify whether reductions in pollutant concentrations resulted in improvements in health outcomes, and whether the improvements were greatest in GMCs, followed by NGMCs and CTRLs. We will assess reductions in the number of emergency department (ED) visits, hospitalizations, and doctor visits among Medicaid beneficiaries with asthma, cardiovascular disease (CVD), chronic obstructive pulmonary disease (COPD) and diabetes.

**Results** In Phase I, we found that the reductions of nitrogen dioxide ($NO_2$) and nitrogen oxides ($NO_x$) in GMCs were 6.4 ppb and 21.7 ppb from the pre-policy to the post-policy period. These reductions were 5.9 ppb and 16.3 ppb in NGMCs and 4.6 ppb and 12.1 ppb in CTRLs, respectively. The mixed models demonstrated that reductions in $NO_2$ and $NO_x$ were significantly greater in GMCs than in CTRLs; there were no statistically significant differences between NGMCs and CTRLs. These results indicate that policies regulating goods movement have achieved the desired outcomes in improving air quality for California, particularly in the goods movement corridors where most disadvantaged communities live. The findings also support the Phase II study, which is to examine subsequent improvements in health outcomes that may have resulted from exposure reductions.

**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 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.

## **Air Quality Co-Benefits of Greenhouse Gas Emissions Fees in the U.S. Energy System

Kristen E. Brown, Daven Henze, and Jana B. Milford

*University of Colorado, Department of Mechanical Engineering, Boulder, CO, USA*

A critical challenge in gaining acceptance for policies to reduce greenhouse gas emissions is that the benefits of such actions are realized globally and over time, while the cost of reductions may start immediately and be felt locally. This asymmetry can partially be addressed by accounting for the near-term and relatively local benefits of co-occurring reductions in air pollutants that affect human health. This study examines the air pollution co-benefits of imposing greenhouse gas emissions fees in the U.S. energy system. We apply fees within a modified version of the U.S. Environmental Protection Agency's MARKAL model, over the time period from 2015 to 2055. The EPA MARKAL model and accompanying nine-region database determines the least cost means of meeting demand for energy services in the commercial, residential, industrial and transportation sectors and the associated emissions of conventional air pollutants and greenhouse gases. The model accounts for constraints on emissions corresponding to existing regulations and allows users to investigate future policy scenarios such as the addition of fees or further constraints on emissions. We modified the US9R database to update cost, performance, and lifetime estimates for technologies in the electricity sector, add or refine estimates of upstream emissions, and add new control options in the industrial sector. Fees are applied to $CO_2$ and $CH_4$ emissions, over the range of values developed by Interagency Working Group on the Social Cost of Carbon. Emissions responses are reported for all fee cases. For the results with moderate GHG fees, we also use the CMAQ model to examine corresponding benefits in terms of $PM_{2.5}$ and $O_3$ reductions in the year 2045, relative to a reference case without the fees. GHG emissions fees that rise to a range of 23 to 194 2005$ per tonne $CO_2$-equivalent in 2045 reduce $CO_2$ emissions in that year by 5 to 54 percent. They also reduce $NO_x$ emissions by 3 to 13 percent, and $SO_2$ emissions by 8 to 39 percent. Most of the change is in the electricity sector. In the modified MARKAL model, very high GHG fees reduce $NO_x$ less than the second highest fees, as carbon capture and sequestration comes into use with the highest fee level. We find that moderate fees that reduce 2045 emissions of $NO_x$, $SO_2$ and direct $PM_{2.5}$ by 13, 39, and 27 percent, respectively, reduce ozone and $PM_{2.5}$ concentrations in 2045 by 2% and 13%, on average across the U.S. These air quality improvements are estimated to correspond to 23,100 avoided premature deaths for $PM_{2.5}$ using concentration-response (C-R) functions based on Krewski et al. (HEI Research Report 140, 2009) and 345 avoided premature deaths from ozone using C-R functions from Jerrett et al. (NEJM 360(11):1085-1095, 2009).

** Study not funded by HEI.

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

Nga Lee Ng, Wing Y. Tuet, Shierly Fok, Rodney J. Weber, and Julie A. Champion
*Georgia Institute of Technology, Atlanta, GA, USA*

**Background** Numerous epidemiological studies have found associations between elevated particulate matter (PM) concentrations and increased incidences of cardiopulmonary disease. PM-induced oxidant production has been suggested as a possible mechanism by which PM exposure may lead to adverse health end points. Ambient PM mixtures are often complex and specific component effects are difficult to elucidate. Few considerations have been given to the health effects of secondary organic aerosol (SOA), even though they contribute a significant fraction of fine PM. Here, we present chemical and cellular measurements of oxidant production of SOA generated from common volatile organic compounds (VOC).

**Methods** SOA from photooxidation, VOC + hydroxyl radical (OH), of six commonly emitted VOCs were generated in the Georgia Tech Environmental Chamber facility (GTEC) under low-$NO_x$ conditions. The SOA precursors were chosen to represent the main classes of hydrocarbons typically found in biogenic and anthropogenic emissions. Briefly, the laboratory chambers were flushed with pure air and desired concentrations of ammonium sulfate seed, VOC, and $H_2O_2$ (OH precursor) were injected. Photooxidation was then initiated by turning on UV lights. For these experiments, laminated Teflon filters were used to collect a gas background and SOA sample. Each filter was then sectioned for parallel chemical and cellular oxidant analysis. To characterize chemical oxidative potential, we used the dithiothreitol (DTT) assay, which measures the concentration of redox active species. Macrophages were also exposed to filter samples to measure intracellular oxidant production using carboxy-$H_2$DCFDA. Briefly, the probe diffuses into the cell and a fluorescent compound is produced upon reaction with reactive oxygen species.

**Results** We obtained dose response curves, fitted using the Hill Equation, for intracellular oxidant production resulting from SOA exposure over a wide dilution range (0.00125x to 1x) to fully capture dose-dependent oxidant production. Various response parameters (maximum response, EC50, Hill slope, threshold, and area under the dose response curve, AUC) were calculated from the fits and used to characterize cellular oxidant production. These parameters were compared with measured DTT activities for each sample to determine whether chemical assays were representative of cellular responses. Differences in oxidant production between SOA generated from different parent VOCs were also investigated.

**Conclusions** PM-induced oxidant production has been suggested as a possible mechanism by which PM exposure results in disease. We generated photooxidation SOA from six common VOCs under low $NO_x$ conditions and measured oxidant production using chemical and cellular assays. We found that cellular oxidant production did not generally correlate with chemical redox potential. Different parent VOCs also generated SOA with widely different levels of oxidant production. Results from this study highlight the importance to understand the oxidant generation potential of different types of SOA to access their overall health impacts.

## **Using the National Air Toxics Assessment to Screen for Potential Health Impacts in Communities

Ted Palma, Mark Morris, and Madeleine Strum (Presented by Karen Wesson)
*Office of Air Quality Planning and Standards, U.S. Environmental Protection Agency*

On December 17, 2015, the U.S. Environmental Protection Agency (EPA) released the fifth version of the National Air Toxics Assessment (NATA), a state-of-the-science screening tool that provides information on the potential risks from breathing air toxics.

This version of NATA is based on emissions for the 2011 calendar year, the most complete and up-to-date emissions data available at the time of the assessment. The 2011 NATA assessed 180 air toxics plus diesel particulate matter from emission sources including stationary sources, mobile sources, events (e.g., wildfires and prescribed burning), biogenics (e.g., naturally-occurring emissions), secondary formed pollutants and background from long-range transport. Output from NATA includes both chronic cancer and noncancer inhalation risk estimates at a census tract resolution nationwide. NATA is a screening tool and as such not designed as a definitive means to determine actual risk at local levels. The results are best used as a tool to prioritize pollutants, emissions sources and locations of interest for further investigation. This poster shows how NATA can be used to help risk assessors evaluate the health impacts on a community resulting from emissions of air toxics.

This abstract does not necessarily reflect EPA policy.

** Study not funded by HEI.

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

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

*Georgia Institute of Technology and Emory University, Atlanta, GA, USA*

**Background** Researchers at Georgia Tech and Emory are using air quality modeling and statistical techniques to determine the impact of regulatory policies on health outcomes in the southeastern United States. The team is investigating effects of multiple national and state rules promulgated between 1993 and 2013. The approach to assess air pollution impacts combines the ability of statistical models to analyze long periods of time and observed autocorrelation structure, and the advanced chemistry included in the Community Multiscale Air Quality Model with the Decoupled-Direct-Method (CMAQ-DDM).

**Methods** Long-term (1999-2013) records of daily concentrations of ambient air pollutants obtained from one monitoring site in Downtown Atlanta (ozone, $NO_x$, $SO_2$, CO, $PM_{2.5}$, sulfate, nitrate, ammonium, OC, and EC) are detrended to account for meteorological fluctuations. Linear statistical models are applied to determine empirical sensitivities of ambient concentrations to changes in emissions from electricity generating unit (EGU) and mobile (MOB) sources in Atlanta, GA. Empirical sensitivities are used in addition to similar sensitivities developed using the CMAQ-DDM to estimate uncertainty, and are combined with counterfactual — i.e. assuming no controls — emissions estimates to create counterfactual daily ambient air pollution concentrations. Daily contrasts of observed and counterfactual ambient concentrations are 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 the absence of changes in emissions from EGU and MOB in Atlanta from 1999-2013.

**Results** Annual average concentrations of $NO_x$, $SO_2$, and CO have all fallen by at least 50% since 1999, roughly matching estimated changes in emissions. MOB regulations have had a larger impact on $PM_{2.5}$ than EGU; MOB emissions changes were found to reduce mean $PM_{2.5}$ in 2013 by 5.3 $\mu g\ m^{-3}$ ($-1.8\ \mu g\ m^{-3}$ for EGU). MOB reductions were found to increase mean ozone by 2 ppb in 2013, and EGU regulations were found to decrease mean ozone by 1.8 ppb. Comparisons between the empirically derived and CMAQ-derived ozone sensitivities found somewhat different slopes and different crossover values from where $NO_x$ controls reduce or increase ozone levels. Preliminary health models over the period from 1999-2013 suggest that the greatest reductions in asthma ED visits in Atlanta attributable to changes in emissions from EGU and MOB occurred in 2012 and 2013, in which it was estimated that there would have been 9.5% more asthma 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. The differences between the statistical and CMAQ-simulated sensitivities suggest significant uncertainties in the two approaches for assessing impacts of specific emissions controls that can be important when assessing benefits of $NO_x$ emission reductions. While the air quality and health impact analyses are ongoing, work to date indicates the regulatory actions implemented during this period were accompanied by improvements in air quality and reduction of ED visits.

## Multipollutant and Biological Indicators of Primary Traffic Exposures in the Dorm Room Inhalation to Vehicle Emissions (DRIVE) Study

Jeremy A. Sarnat[1], Armistead G. Russell[2], Donghai Liang[1], Jennifer Moutinho[2], Rachel Golan[3], Rodney J. Weber[2], Stefanie E. Sarnat[1], Roby Greenwald[4], Dong Gao[2], Vishal Verma[5], Howard Chang[1], and Dean P. Jones[1]

*[1]Emory University, Atlanta, GA, USA; [2]Georgia Institute of Technology, Atlanta, GA, USA; [3]Ben Gurion University, Beersheba, Israel; [4]Georgia State University, Atlanta, GA, USA; [5]University of Illinois–Urbana-Champaign, USA*

**Background** Recent interest in air pollution health effects and regulatory intervention has shifted towards adopting multipollutant perspectives. For sources with highly heterogeneous mixtures, including primary traffic emissions, the multipollutant framework provides new opportunities to improve identification and characterization of biologically relevant exposures. Improving exposure assessment to traffic emissions is particularly critical given the many observational studies linking traffic exposure to adverse health.

**Methods** The DRIVE study was conducted to measure traditional and multipollutant 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 GIT students living in either dormitories near (20 m) or far (1.4 km) from the highway were recruited to participate in personal exposure sampling and weekly biomonitoring. We conducted specific analyses to assess: 1) predominant near road primary traffic pollutant components; 2) potential multipollutant primary traffic exposure indicators (e.g., particulate oxidative potential, expressed as water soluble dithiothreitol (DTT) activity, and metabolomic analyses of human plasma samples); how well these novel indicators reflect observed heterogeneity in individual pollutant components; and 4) the suitability of using these novel indicators as primary traffic exposure surrogates in epidemiological studies.

**Results** We examined the spatial distribution of the DTT activity of particulate matter samples. In contrast to single-pollutant indicators of traffic, DTT levels were more homogeneously distributed across the study domain, exhibiting a moderate, inverse gradient with respect to the highway source (median outdoor DTT/volume levels at the highway roadside, near dorm, and far dorm sites = 87, 107, and 124 pmol/min/$m^3$, respectively), trends similar to overall organic aerosol and $PM_{2.5}$ mass concentrations. Conversely, median carbon monoxide, nitric oxide, and particle number concentrations, were 109, 100, and 67% higher outside of the near road dorm compared to the dorm located away from the traffic hotspot. A total of 21,766 metabolite features were reliably extracted from the plasma samples for each student. Of these features, linear random effects models were conducted to examine associations between metabolite intensity (i.e., relative concentration) and student dorm location (near dorm vs. far dorm). In total, 220 metabolites were robustly identified as significantly different in the near dorm metabolic profiles compared to those in the far dorm ($p < 0.05$, using Benjamini–Hochberg FDR correction procedure).

**Conclusions** Preliminary analyses of the DRIVE traditional pollutant measurements indicate dissimilar patterns of pollutant spatiotemporal variability when compared to water soluble DTT. Current analyses focus on the implications for health effects studies on the assignment of exposure to primary traffic pollution using these different metrics. In addition, metabolomics analyses in the DRIVE samples showed distinct difference in the metabolite features between the students leaving near and far from the highway source. Comprehensive pathway analysis and evaluation is currently being conducted to identify specific metabolite patterns and assess their relationship to the measured and modelled pollutant concentrations, including the measured DTT concentrations.

## Evaluation of Alternative Sensor-based Exposure Assessment Methods

Elena Austin[1], Surakshya Dhakal[1], Jeffery Shirai[1], Katharine Hammond[2], Michael Jerrett[3], Alan Hubbard[2], Ying-Ying Meng[3], Ronald Cohen[2], and Edmund Seto[1]

*[1]University of Washington–Seattle; [2]University of California–Berkeley; [3]University of California–Los Angeles*

**Background** Low-cost air pollution sensors provide an attractive option for community based non-regulatory monitoring. This approach allows for cost effective blanket sampling of a discrete geographic area and for the identification of spatial and temporal hotspots. The BANRS project aims to deploy a network of 64 sensor sites in and around Oakland, CA to identify surrogates of near-roadway air pollution.

**Methods** Four custom-built monitors, including of both gas and particle sensors, were deployed at three regulatory monitoring sites from September 29th to November 24th 2015. Gas sensors were manufactured by Alphasense (Essex, UK) and measured CO, NO, $NO_2$ and $O_3$. Particles were measured using a Shinyei (New York, NY) PPD42NS optical particle sensor (OPS). Low-cost 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 inverse regression. An iterative method was used to calibrate sensor results to regulatory instruments using the regression model.

**Results** The correlation of the sensor response to the regulatory monitor varied depending on the pollutant species measured. The electrochemical gas sensors showed a response to meteorological conditions. We confirmed the importance of accounting for meteorology on results using a likelihood ratio test. After performing the calibration of the sensor output, we find a strong correlation between sensor response and ambient concentrations of the target pollutants. We further validated our method by dividing the data into a test set and training set to examine how effectively the calibration model can be used for predicting ambient concentrations based on sensor outputs.

**Conclusions** Low-cost air pollution sensors allow for exciting new approaches to studying air pollution and its impacts on communities. We show that our deployed sensors compare well to FEM instruments, and that after calibrating our measurements and accounting for temperature and humidity we obtain good correlations with monitoring data. This provides a solid methodology by which to calibrate sensor results to nearby regulatory measurements.

## ** Assessing Changes to Spatial and Temporal Patterns of Ozone in Three Urban Areas Due to Large $NO_x$ Reductions

Heather Simon, Benjamin Wells, Kirk R. Baker, and Bryan Hubbell

*U.S. Environmental Protection Agency, Office of Air Quality Planning and Standards, Research Triangle Park, NC, USA*

**Background** Epidemiological studies often use exposure surrogates (e.g., averages of monitors in an urban area) to represent population exposures to ozone. However, these surrogates may mask important temporal and spatial variation in ozone levels and the response of ozone to changes in precursor emissions. In designing plans to reduce ozone levels, air quality planners must target reductions in $NO_x$ and VOC precursors. Ambient monitoring data show spatial gradients in ozone across urban areas and it is well known that ozone response to changes in $NO_x$ and VOC emissions can be nonlinear and depends on local atmospheric chemistry and meteorological conditions.

**Methods** In this analysis, we examine ozone changes in response to large $NO_x$ reductions in 3 urban areas: Philadelphia, Atlanta, and Chicago. We also examine sensitivity to addition of VOC reductions. We apply a photochemical air quality model to estimate temporally and spatially varying ozone response to emission reductions during 2006-2008.

**Results** We see different types of responses in these 3 cities, with both ozone increases and decreases occurring at different times, locations, and magnitudes throughout these three urban areas. Ozone increases were more frequent at times and locations where starting ozone concentrations were low (i.e., core urban areas and at night and during cooler months) and were most pronounced in Chicago. Ozone decreases were most frequent at times and locations where starting ozone concentrations were high (i.e., downwind locations, during daytime and summer) and were most pronounced in Atlanta. We demonstrate how the choice of ozone metric (i.e., 4th highest 8-hr daily max versus seasonal mean) impacts the direction and magnitude of predicted ozone response and show how these changes map to population density and total population within each of the three cities.

**Conclusion** The results from this analysis show substantial heterogeneity in ozone responses within urban areas and, thus, raise important questions about how well health studies which use surrogate exposure metrics representing spatial and temporal averages across monitors reflect three aspects of the ozone distribution (changes to high versus low ozone concentrations, spatial variability, and temporal patterns) and how they relate to total population-weighted exposure. The net impact on population exposure and associated health effects over an entire population will depend on the balance of ozone changes across high and low population density locations and across the entire ozone season as well as on the shape of the concentration-response relationship at different concentrations. Our analysis highlights the need for future epidemiology studies and health assessments to take these factors into account in the design of their analysis.

This abstract does not necessarily reflect US EPA policy.

** Study not funded by HEI.

## 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

*University of North Carolina–Chapel Hill, USA*

**Background** SOA from the atmospheric oxidation of isoprene in the presence of acidified sulfate aerosol contributes a substantial fraction of ambient fine particulate matter ($PM_{2.5}$). Whether this SOA type contributes to the adverse health effects induced by exposure to $PM_{2.5}$ reported in epidemiological studies is largely unknown. Isoprene-derived epoxides have been recently identified as key gaseous intermediates leading to SOA through heterogeneous reactions on acidic sulfate aerosol. We have evaluated the potential biological effects of the pure epoxides and selected 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 their resultant SOA constituents based on the biological pathways hypothesized to link $PM_{2.5}$ exposure to cardiopulmonary mortality, with a specific focus on cytotoxicity, oxidative stress, pulmonary inflammation, and reactive oxidant species (ROS) potential.

**Methods** Isoprene-derived epoxides, isoprene epoxydiols (IEPOX) and methacrylic acid epoxide (MAE), were synthesized and directly injected into an indoor smog chamber facility that contained acidified 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, $NO_x$ 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 using the UNC Electrostatic Aerosol Exposure System (EAVES) at the air-liquid interface. Cell viability and cytotoxicity were assessed using XTT cell proliferation assay and the release of lactate dehydrogenase (LDH). 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 RT² Profiler PCR Array with 84 oxidative stress-associated genes was performed. The dithiothreitol (DTT) assay was used to characterize the ROS generation potential of the pure epoxides and SOA.

**Results** Our findings suggest 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 epoxides induce stronger cytotoxic responses than the hydrolysis products of reactive uptake onto SOA, with MAE-derived SOA showing greater potency than IEPOX-derived SOA. We also found that isoprene SOA constituents enriched the expression of nuclear factor erythroid 2-like 2 (NRF2)-mediated oxidative stress responses in human lung cells, with MAE-derived SOA showing greater potency than IEPOX-derived SOA. Compared to other experiments with diesel exhaust PM, isoprene-derived SOA had the same or higher ROS generation.

**Conclusions** Our results could have important public health and policy implications since chamber-generated SOA have a similar chemical composition to ambient $PM_{2.5}$ and that increasing sulfate aerosol loadings enhances isoprene SOA. We are now expanding our biological analyses to more genes by applying PCR arrays.

## ** The "Population Served" Concept and its Role in Examining the Efficiency and Equity of Colorado's Air Quality Monitoring Network

William Vicars, Cindy Wike, and Gordon Pierce

*Colorado Department of Public Health and Environment, Denver, CO, USA*

It has been well established that high population densities are associated with high pollutant emissions and reduced air quality; therefore, state and local air quality monitors representing larger populations are typically thought to be of greater importance in determining regulatory compliance. Furthermore, the collection of data that is representative of the greatest possible number of people is an important public health objective. However, the population served by an individual air quality monitor is difficult to define precisely, particularly in mountainous terrain. This presents difficulties in determining how the spatial design of a network may affect protection of populations from exposure to harmful levels of air pollution.

We have developed a geographic information system (GIS) based method for estimating areas of representation and population served for air monitoring networks in mountainous terrain. This technique is based on a modified Thiessen polygon approach that accounts for both topographic barriers and pollutant-specific characteristics in assigning areas of representation to a given air quality monitor. In addition to providing an estimate of population served, this technique also provides a basis for aggregating other spatial statistics (e.g., emissions, traffic counts, etc.) within a geodatabase. We have employed this technique to an assessment of the relative value of each pollutant monitor in Colorado's ambient monitoring network.

Population served was estimated for each air quality monitor in the state of Colorado using the approach described above. Secondary pollutant networks, such as those monitoring for ozone ($O_3$) and particulate matter less than 2.5 μm in diameter ($PM_{2.5}$), were estimated to have larger areas of representation and larger population counts due to the strong spatial autocorrelation observed for these pollutants. Primary pollutant networks, such as those monitoring for $SO_2$, $NO_2$, and $PM_{10}$, yielded smaller areas of representation, typically on the order of 100–400 $km^2$. In an effort to examine the racial composition of the population represented by each APCD monitoring network, we grouped the individuals associated with each site's population served metric by race and income, then compared the expected composition (i.e., the Colorado average) with the composition observed in each site's area of representation. The results of this analysis suggest that minority and economically disadvantaged groups in Colorado are well represented by existing air pollution monitors.

** Study not funded by HEI.

## On-road Vehicle Emission Characterization from Tunnel Studies

Xiaoliang Wang[1], Andrey Khlystov[1], Judith C. Chow[1], John G. Watson[1], Barbara Zielinska[1], Lung-Wen Antony Chen[2], Kin-Fai Ho[3], and S.C. Frank Lee[4]

*[1]Desert Research Institute, Reno, NV, USA; [2]University of Nevada–Las Vegas, USA; [3]Chinese University of Hong Kong, China; [4]Hong Kong Polytechnic University, China*

**Background** Vehicle emissions have changed over the past decades due to new fuels, improved engine designs, and better exhaust aftertreatments. Detailed characterization of the current vehicle fleet emissions is useful for measuring the emission change due to regulations and new technologies, setting a baseline for future comparison, and assessing the health benefits of pollution control regulations. Roadway tunnels are widely used to measure emissions from on-road vehicles due to advantages of defined environment with isolation from other combustion sources, representative of real-world driving, and sampling a large number of vehicles. This study aims to evaluate vehicle emission changes over time through measurements in two tunnels: the Shing Mun tunnel (SMT) in Hong Kong and the Ft. McHenry tunnel (FMT) in Baltimore, MD, USA.

**Methods** Vehicle emissions were measured in SMT during winter 2015 and in FMT during winter and summer of 2015. Concentrations of gaseous and particulate pollutants were measured, including: carbon monoxide (CO), carbon dioxide ($CO_2$), volatile organic compounds (VOCs), polycyclic aromatic hydrocarbons (PAHs), carbonyls, ammonia ($NH_3$), nitrogen oxides ($NO_x$), black carbon (BC), $PM_{2.5}$ and its inorganic and organic constituents. Fleet average distance- and fuel-based emission factors (EFs) will be calculated, and their dependence on fleet composition, fuels, and ambient conditions will be evaluated. EFs will be compared to past tunnel studies to assess emission changes. Source profiles of VOCs, PAHs, carbonyls, and $PM_{2.5}$ will be developed. Potential source markers will be evaluated for their ability to separate contributions from source sub-types related to vehicle type and fuel. EFs derived from these studies will be compared with those from the EMFAC-HK and MOVES mobile source emission models to assess their performance.

**Results** The light duty (LD) vehicles in SMT showed morning and afternoon rush hour peaks on weekdays while only an afternoon peak was observed on weekends. The heavy duty (HD) vehicle flow was relatively uniform during the day. The FMT LD traffic peaked in the afternoon, and the two bores had different LD and HD mixes. CO has similar diurnal patterns as the LD flow, while $NO_x$ varies more with HD. Preliminary calculations show that the SMT fleet-average EFs for CO, $NO_x$, $SO_2$, and $PM_{2.5}$ are 1.69 ± 0.72, 1.41 ± 0.56, 0.048 ± 0.025, and 0.026 ± 0.022 g/vehicle/km, respectively. While the EFs for CO and $NO_x$ are statistically similar with those measured from SMT in 2003, $PM_{2.5}$ is only ~20% of that in 2003. Data are currently being analyzed for: 1) Fleet-averaged EFs of pollutants and their dependence on fleet composition, fuel, and ambient conditions. 2) Updated source profiles for the mixed fleets and their components, along with potential markers for different vehicle types and fuels. 3) Fleet EF and profile changes over the past 1–2 decades due to introduction of new technologies and regulations. 4) Importance of non-tailpipe emissions, including road dust to $PM_{2.5}$ and evaporative emissions to VOCs. 5) Performance evaluation of EMFAC-HK and MOVES mobile source emission models. 6) Fuel-based EFs for individual vehicle and vehicle clusters.

## **Diesel Particulate Matter in California: Ambient Trends and *in Vitro* Toxicity Screening of Engine Emissions

Patrick Wong[1], Jeff Austin[1], Will Vance[1], Christoph Vogel[2], Norman Y. Kado[1,2], Jorn Herner[1], Martin Shafer[3], Reiko Kobayashi[2], Alvaro Alvarado[1], Linda Tombras Smith[1], and Bart Croes[1] (Presenter)

*[1]California Air Resources Board, Sacramento, CA, USA; [2]Department of Environmental Toxicology, University of California–Davis, USA; [3]Department of Civil and Environmental Engineering, University of Wisconsin–Madison, USA*

**Background** Diesel Particulate Matter (DPM) is responsible for most of the known cancer risk associated with airborne exposure in California. As a result, the California Air Resources Board (CARB) identified DPM as a toxic air contaminant in 1998 and adopted the Diesel Particulate Matter Risk Reduction Plan in 1999. Since then, CARB has adopted regulations to reduce emissions from mobile and stationary source diesel engines. This study investigates the effectiveness of these regulations by determining the statewide ambient DPM concentration and emission trends for the period 1990-2012 using a novel surrogate method and calculating the cancer risks due to ambient DPM exposure. To ensure that emission control measures did not inadvertently result in novel and more toxic species, a screening protocol consisting of a panel of *in vitro* assays was applied to a set of PM emission samples from a heavy-duty vehicle equipped with advanced retrofit technologies designed to limit criteria pollutant emissions.

**Methods** Statewide ambient DPM measurements were calculated using $NO_x$ as a surrogate and the emission inventories of $NO_x$ and DPM. Cancer risks were calculated using risk factors developed by the State of California. The toxicology screening protocol developed for this study consisted of *in vitro* and biochemical assays which measured markers of oxidative stress, inflammation, and genotoxicity of collected DPM particles. DPM for this study was collected from pre-cleaned Teflon coated glass fiber filters from a dynamometer study of a heavy duty diesel-fueled vehicle with and without advanced retrofit technologies that comply with the 2007 and 2010 ARB heavy duty engine standards.

**Results** The study found that the DPM concentrations and cancer risks decreased 68%, even though California's population increased 31% and diesel vehicle-miles traveled increased 81% during the study period. The panel of assays targeted the major pathophysiological mechanism associated with PM exposure in humans. The results show that the toxicological responses on a per mile basis of DPM emissions from a vehicle configured with advanced retrofit technologies were substantially reduced (80-99%) over that measured in an uncontrolled vehicle. In contrast, when comparing toxicity on a per mass basis the results were mixed.

**Conclusions** Over the past two decades, CARB diesel engine regulations have led to a substantial decrease in statewide ambient DPM and its associated cancer risks. A screening panel of *in vitro* assays confirmed that the after treatment technologies used to comply with these regulations led to lower toxicological responses based on total emissions. However, this panel also revealed that some aftertreatment technologies produced DPM with enhanced responses in certain assays. These results illustrate the utility of a screening protocol and the advantage of using a panel of toxicological assays, rather than a single assay, to account for many of the currently known major physiological pathways that may be involved in engine emission toxicity.

** Study not funded by HEI.

## **Air Quality and Acute Deaths in California, 2000–2012

S. Stanley Young[1]; Richard L. Smith[2]; and Kenneth K. Lopiano[3]

*[1]CGStat, Raleigh, NC, USA; [2]University of North Carolina–Chapel Hill, USA; [3]Winterville, NC, USA*

**Background** Many studies show an association between air quality and acute deaths, and such associations are widely interpreted as causal. Several factors call causation and even association into question; for example with observational studies, multiple testing, multiple modeling, publication bias and confirmation bias can lead to false claims. Most published studies are difficult or impossible to reproduce as there is no access to the analysis data set data or analysis code used in making claims.

**Data** We obtained electronic death certificate data for California for the years 2000–2012, over two million death certificates. We also obtained daily air quality levels, $PM_{2.5}$ and ozone, daily temperature levels, minimum and maximum, and daily maximum relative humidity levels for the eight most populous California air basins. We make this analysis data set publicly available, *http://www.unc.edu/~rls/CApollution.html.*

**Methods** The data are analyzed using standard time series Poisson regression analysis. The model included terms for time lags (up to 6 days), time of year, day of week, and meteorological variables (temperature and relative humidity, again with lags). An extensive sensitivity analysis was computed holding out and predicting each year in turn, varying model parameters, locations and years. There were a total of 78,624 separate analyses.

**Results** Our analysis finds no support for an association between air quality, $PM_{2.5}$ and ozone, and acute deaths in California. The daily death variability was mostly explained by time of year or weather variables. In the sensitivity analysis neither $PM_{2.5}$ nor ozone added appreciably to the prediction of daily deaths. We also applied our analysis to the California data, 12 cities, from the NMMAPS dataset, years 1987–2000. Separately and combined over cities, we found no association of air quality with acute deaths. We have 27 years and over 99 thousand exposure days.

**Conclusions** These results, no effect of $PM_{2.5}$ or ozone on acute deaths in California, call into question the widespread belief that association between air quality and acute deaths is causal and near-universal.

** Study not funded by HEI.

## **I-70 Hot Spot Analysis for $PM_{10}$ and Alternatives to Avoid PM NAAQS Violations and Reduce Population Exposures

Robert E. Yuhnke, *Sierra Club, Gresham, OR, USA;* and Lisa A. Warren, *University of Colorado–Denver, USA*

On behalf of mostly low income, Hispanic, Spanish-speaking residents of neighborhoods in north Denver adjacent to I-70, Sierra Club volunteers reviewed the draft hot-spot analysis required by the Clean Air Act to determine whether increased traffic on the proposed 14-lane highway "will not cause or contribute to new violations of [the NAAQS]" for $PM_{10}$. Investigators found that Project emissions will likely violate the NAAQS because the emissions analysis conducted by the Colorado Department of Transportation (CDOT) predicted a future design value of 151 $\mu g/M^3$, but underestimated Project emissions by

1) not modeling the year of expected highest emissions during the time frame of the 2040 Regional Transportation Plan;

2) using historical background $PM_{10}$ concentrations rather than modeled expected future background concentrations developed for the 2025 Denver $PM_{10}$ Maintenance Plan to predict the future design value at hot-spot receptors when modeled Project emissions are added to background;

3) omitting half of expected truck emissions by using region wide truck share (4.9%) of vehicle miles traveled (VMT) rather than actual truck counts on I-70 (9.8%) to determine VMT mix on the highway segment adjacent to the highest modeled receptor locations; and

4) combining the $6^{th}$ highest modeled (AERMOD) concentration contributed by Project emissions with the $4^{th}$ highest historical background concentration to predict the expected design value at the hot-spot location, while not disclosing whether permutations of the $1^{st}$ – $5^{th}$ highest modeled concentrations when combined with the $1^{st}$ – $3^{rd}$ background concentrations, will likely cause more than three exceedances of the 24-hour $PM_{10}$ NAAQS in any 3-year period. The method applied by the agencies does not provide statistical confidence that Project emissions will not contribute to violations of the NAAQS.

A proposed alternative to re-route I-70 along the alignments of I-76 and I-270 that intersect north of the City outside of dense urban neighborhoods was investigated to compare population exposures with the current I-70 alignment. The Air Quality Technical Report prepared by CDOT estimated that $PM_{10}$ concentrations were 20-30 $\mu g/m^3$ lower along the alternative alignment. Using 2010 census block data to estimate populations within the 50 m, 150 m and 300 m health impact zones where elevated exposures to $PM_{10}$ are most likely, the Sierra Club showed that the exposed population in the I-76/I-270 alignment would be approximately 3427 compared to 9467 in the I-70 neighborhoods. Together, lower expected design values and fewer exposed residents would provide a net air quality benefit and reduce the incidence of adverse health outcomes for the diseases of air pollution in the metropolitan area.

** Study not funded by HEI.

## **Ozone and $PM_{2.5}$ in Pollution Mixture Differentially Impact Cardiopulmonary Pathophysiologic Mechanisms

Drew B. Day[1] (Presenter), Jianbang Xiang[2], Jinhan Mo[2], Feng Li[3], Mingkei Chung[4], Jicheng Gong[4], Jan Sundell[2], Charles J. Weschler[2,5], Pamela A. Ohman-Strickland[5], Yinping Zhang[2], and Junfeng (Jim) Zhang[1,4] (co-PIs)

*[1]Duke University, Durham, NC, USA; [2]Tsinghua University, Beijing, PR China; [3]Shanghai Jiao Tong University, Shanghai, PR China; [4]Duke Kunshan University, Kunshan, Jiangsu Province, PR China; [5]Rutgers University, Piscataway, NJ, USA*

**Background** The relative contributions of ozone and $PM_{2.5}$ in air pollution mixtures to cardiopulmonary outcomes remains poorly understood. In order to examine whether and how ozone and $PM_{2.5}$ may differentially impact mechanisms of cardiopulmonary pathophysiology, this study manipulated indoor levels of $PM_{2.5}$ and ozone through the use of different filtration systems.

**Methods** The present study was conducted among office workers living together on a work campus in China, where ambient $PM_{2.5}$ levels are consistently high. At baseline, workers at the field site had the air of their dorm and office environments purified by a pre-filter followed by an ozone-generating electrostatic precipitator (ESP) and a high-efficiency particulate (HEPA) filter. Eighty-six participants were split into two groups based on office location. The groups were subjected to a 4-week intervention period to modify the filtration systems by either just removing the ESP (Group I) or removing both the ESP and HEPA filter (Group II). Baseline filtration conditions were restored after the intervention period. Outdoor and indoor $PM_{2.5}$ and ozone were monitored throughout the study period to estimate 24-hour exposure concentrations. Exposure to each pollutant was characterized in detail using time-activity pattern questionnaires. Four "clinical" visits for biomarker measurement were carried out during the study period: one visit at baseline, two visits during the intervention period, and a final visit after restoring the baseline conditions. The biomarkers measured included measures of pulmonary and systemic oxidative stress and inflammation, spirometry, arterial stiffness, blood pressure, and thrombotic factors (soluble P-selectin and von Willebrand factor [VWF]).

**Results** The calculated exposure concentrations (i.e., time-weighted indoor and outdoor concentrations) for $PM_{2.5}$ and ozone showed opposing trends. Mean 24-hour exposure concentrations during the study were 37 ± 1.5 μg/m$^3$ for $PM_{2.5}$ and 6.4 ± 0.2 ppb for ozone, and they were negatively correlated. At these relatively low levels, the study design's unique manipulation of ozone and $PM_{2.5}$ exposures allowed for the observation that certain pathways are more sensitive to ozone and others are more sensitive to $PM_{2.5}$. Contrary to the findings of similar studies that show the same biomarkers trending together in response to $PM_{2.5}$ exposure, this study shows that lung inflammation, blood pressure, and soluble P-selectin were tightly associated with short-term and chronic ozone exposure, while pulmonary oxidative stress, arterial stiffness, and VWF were associated with chronic $PM_{2.5}$ exposure.

**Conclusions** These divergent patterns have not been previously reported, and they are occurring at ozone exposures thought to be below the "threshold" necessary for health effects to be observed. The unique design of this study, utilizing filtration interventions to parse the contributions of individual pollutants in mixture to pathophysiologic pathways, has provided insights into biological mechanisms by which ozone and $PM_{2.5}$ can differentially enhance cardiopulmonary disease risk.

** Study not funded by HEI.

**Session Chairs, Speakers, and Panelists**



**Principal Investigators**



** Study not funded by HEI.

† Presenter if not the principal investigator.

# HEI BOARD, COMMITTEES, and STAFF

## Board of Directors

**Richard F. Celeste, Chair** *President Emeritus, Colorado College*

**Sherwood Boehlert** *Of Counsel, Accord Group; Former Chair, U.S. House of Representatives Science Committee*

**Enriqueta Bond** *President Emerita, Burroughs Wellcome Fund*

**Purnell W. Choppin** *President Emeritus, Howard Hughes Medical Institute*

**Michael T. Clegg** *Professor of Biological Sciences, University of California–Irvine*

**Jared L. Cohon** *President Emeritus and Professor, Civil and Environmental Engineering and Engineering and Public Policy, Carnegie Mellon University*

**Stephen Corman** *President, Corman Enterprises*

**Linda Rosenstock** *Dean Emerita and Professor of Health Policy and Management, Environmental Health Sciences and Medicine, University of California–Los Angeles*

**Henry Schacht** *Managing Director, Warburg Pincus; Former Chairman and Chief Executive Officer, Lucent Technologies*

**Warren M. Washington** *Senior Scientist, National Center for Atmospheric Research; Former Chair, National Science Board*

## Health Research Committee

**David L. Eaton, Chair** *Dean and Vice Provost of the Graduate School, University of Washington–Seattle*

**Jeffrey R. Brook** *Senior Research Scientist, Air Quality Research Division, Environment Canada, and Assistant Professor, University of Toronto, Canada*

**David Christiani** *Elkan Blout Professor of Environmental Genetics, Harvard T.H. Chan School of Public Health*

**Francesca Dominici** *Professor of Biostatistics and Senior Associate Dean for Research, Harvard T.H. Chan School of Public Health*

**David E. Foster** *Phil and Jean Myers Professor Emeritus, Department of Mechanical Engineering, Engine Research Center, University of Wisconsin–Madison*

**Uwe Heinrich** *Professor, Hannover Medical School; Executive Director, Fraunhofer Institute for Toxicology and Experimental Medicine, Hanover, Germany*

**Amy H. Herring** *Carol Remmer Angle Distinguished Professor of Children's Environmental Health, and Associate Chair, Department of Biostatistics, Gillings School of Global Public Health, University of North Carolina–Chapel Hill*

**Barbara Hoffmann** *Institute of Occupational Medicine and Social Medicine, Center for Health and Society, Faculty of Medicine, University of Düsseldorf, Germany*

**Allen L. Robinson** *Raymond J. Lane Distinguished Professor and Head, Department of Mechanical Engineering, and Professor, Department of Engineering and Public Policy, Carnegie Mellon University*

**Ivan Rusyn** *Professor, Department of Veterinary Integrative Biosciences, Texas A&M University*

# HEI BOARD, COMMITTEES, and STAFF

## Health Review Committee

**James A. Merchant, Chair** *Professor and Founding Dean Emeritus, College of Public Health, University of Iowa*

**Michael Brauer** *Professor, School of Environmental Health, University of British Columbia, Canada*

**Bert Brunekreef** *Professor of Environmental Epidemiology, Institute of Risk Assessment Sciences, University of Utrecht, the Netherlands*

**Mark W. Frampton** *Professor of Medicine and Environmental Medicine, University of Rochester Medical Center*

**Jana B. Milford** *Professor, Department of Mechanical Engineering and Environmental Engineering Program, University of Colorado–Boulder*

**Roger D. Peng** *Associate Professor, Department of Biostatistics, Johns Hopkins Bloomberg School of Public Health*

**Lianne Sheppard** *Professor of Biostatistics, School of Public Health, University of Washington–Seattle*

## Officers and Staff

**Daniel S. Greenbaum** *President*

**Robert M. O'Keefe** *Vice President*

**Rashid Shaikh** *Director of Science*

**Jacqueline C. Rutledge** *Director of Finance and Administration*

**April Rieger** *Corporate Secretary*

**Zachary Abbott** *Research Assistant*

**Sarah Benckart** *Science Administration Assistant*

**Hanna Boogaard** *Staff Scientist*

**Aaron J. Cohen** *Principal Scientist*

**Maria G. Costantini** *Principal Scientist*

**Philip J. DeMarco** *Compliance Manager*

**Hope Green** *Publications Associate*

**Anny Luu** *Executive Assistant*

**Hilary Selby Polk** *Managing Editor*

**Evan Rosenberg** *Staff Accountant*

**Robert A. Shavers** *Operations Manager*

**Annemoon M.M. van Erp** *Managing Scientist*

**Donna J. Vorhees** *Senior Scientist*

**Katherine Walker** *Senior Scientist*

HEALTH
EFFECTS
INSTITUTE

75 Federal Street, Suite 1400
Boston, MA 02110, USA
+1-617-488-2300
*www.healtheffects.org*