

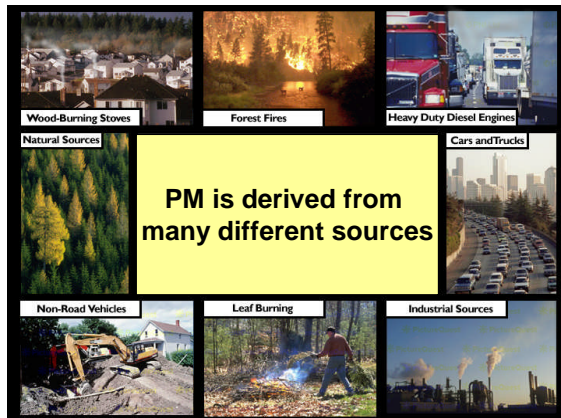


www.epa.gov/airscience

CLEAN AIR RESEARCH PROGRAM

BUILDING A SCIENTIFIC FOUNDATION FOR SOUND ENVIRONMENTAL DECISIONS

Session 1: Health and Exposure



Robert Devlin

Office of Research and Development

US EPA



State of the Science in 1999

- **More than 50 epidemiology studies from around the world report similar associations between ambient PM and cardiac mortality and morbidity.**
But chemical make-up of PM differs in different cities and different times of the year
- **Very little information about PM attributes.**
Size
Components
- **No widely accepted pathophysiological process or mechanism that could explain how a person could die following an acute exposure to such low levels of air pollution particles.**

At the Time of the Last BOSC Review

- **A larger and more robust epidemiology database**
Chronic effects, size fractions, components, susceptibility
- **Mechanisms**
Begin to understand how PM can cause acute mortality and morbidity
- **PM Physical and Chemical Attributes**
Ultrafine, and coarse PM effects
Focus on transition metals and organics as causative agents
- **Susceptibility**
Clinical and toxicology studies provide biological plausibility to epidemiology findings

What Progress Has Been Made?

Since the last BOSC review there has been significant progress in many areas, including:

- Ability of ultrafine particles to cause CV changes
- Coarse particles can cause not only respiratory but also CV changes
- Better understanding of the contribution of specific PM components to adverse health effects

And transition from components to sources (Session 3 – Multipollutant Research)

- Critical role played by vascular endothelium in PM-induced CV effects
- PM effects on the nervous system
- Molecular approaches to strengthen biological plausibility
- Identification of additional susceptibility factors
- Association between ozone exposure and mortality
- Better exposure assessment models for epidemiology studies

This Session is Organized Around 3 Themes

- **What Are the Physical/chemical Attributes of PM that Are Associated with Adverse Health Effects?**
- **How and to What Extent Does PM Cause Adverse Health Effects?**
- **Who is Susceptible to PM?**

Health and exposure data are also found in Session 3 (Multi-pollutant Research)
sources, near road

What Are the Physical/chemical Attributes of PM that Are Associated with Adverse Health Effects?

- **PM is a complex mixture that exists over a wide range of sizes and contains different classes of components comprised of dozens of different compounds.**
- **At the time of the last BOSC review there was an intense effort to study health effects of different sized particles, transition metals, and selected organic species.**
- **These areas remain a primary focus of ORD's PM program but, as the posters presented in this session demonstrate, considerable progress has been made in understanding health effects associated with PM size and components.**
- **Additional progress has been made in linking health effects with PM sources, which is described in Session 3 (Multipollutant Research).**

PM Size

- Different size fractions are distinguished by chemistry but also feature differential deposition patterns based upon aerodynamic properties.
- EPA currently regulates PM on the basis of mass in specific size ranges.

Is the current coarse standard adequately protective of human health?

Is there a need for a dual coarse standard (urban, rural)?

Is a number-based standard needed to protect humans from exposure to ultrafine particles?

Three posters focus on health effects associated with PM size

Gordon: comparative potency

Carraway: coarse PM

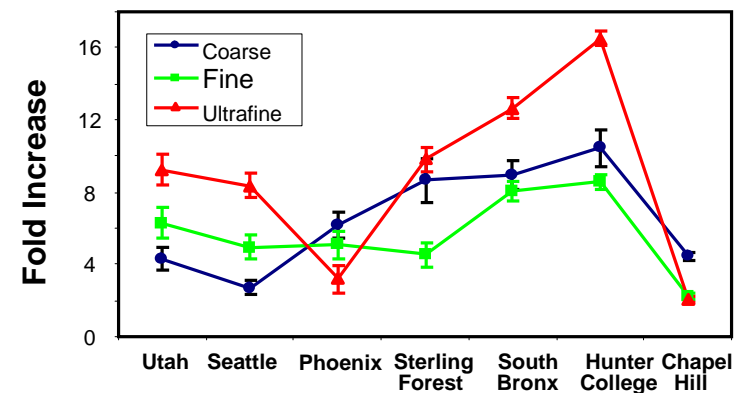
Oberdorster: ultrafine particles

Comparative Potency of Different Size PM Fractions

Understanding the ability of different size PM to cause health effects is critical in providing information that can be used to set a PM standard most protective of human health.

Exposure of Healthy Volunteers to Coarse, Fine, and Ultrafine CAPS: Summary of Effects

	Pulmonary Function	Lung Lavage	Cardiac	Vascular
Fine	No Effect	↑ PMNs ↑ Monocytes ↓ IL-8 ↓ Fibrinogen		↑ Fibrinogen ↓ WBCs ↓ RBCs
Coarse	No Effect	↑ PMNs ↓ Protein	↓SDNN	↓tPA
Ultrafine	No Effect	↑ IL-8	↑ HF, LF ↑ Norm QT var	↑ D-Dimer ↓ triglycerides

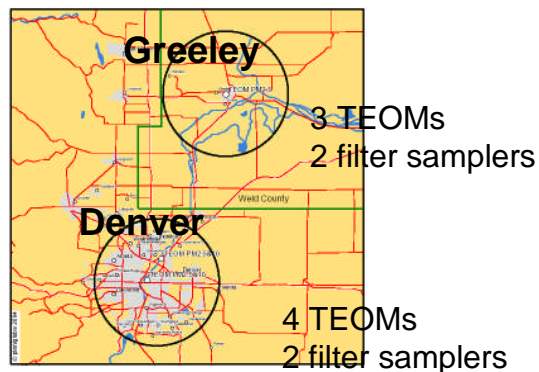


Gordon Poster

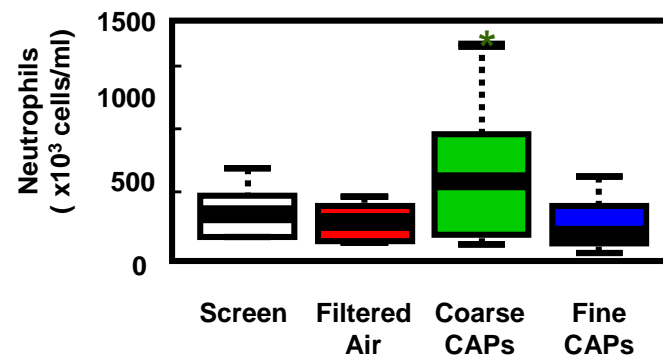
Coarse PM Health Effects?

- Epidemiology studies do not consistently find associations between coarse PM and adverse health effects (but toxicology studies do).
- But coarse and fine PM have different physical characteristics and lung deposition patterns, and likely have different potency, toxicity, and biologic effects.

Urban (Denver) and rural (Greeley) study areas in north central Colorado



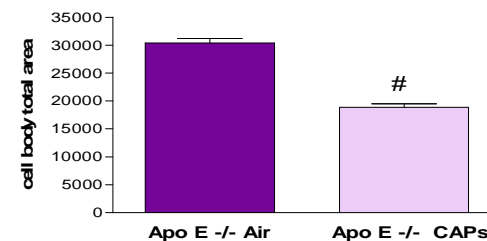
Neutrophils in induced sputum 24 hours Post Exposure to CAPS



Carraway Poster

Ultrafine PM Health Effects

- UFP have large surface area per unit mass, can be important for adsorption of gases and vapors and condensation of volatile co-pollutants
- Following deposition in the upper and lower respiratory tract, it is possible that UFP can translocate to extra-pulmonary (secondary) organs via blood circulation and sensory neurons.
- There are only a handful of epidemiology studies that link exposure to UFP with adverse health effects
 - **Difficulty in measuring exposure**
- Numerous clinical and toxicology studies, however, demonstrate that UFP can cause significant cardiovascular and neurological effects.



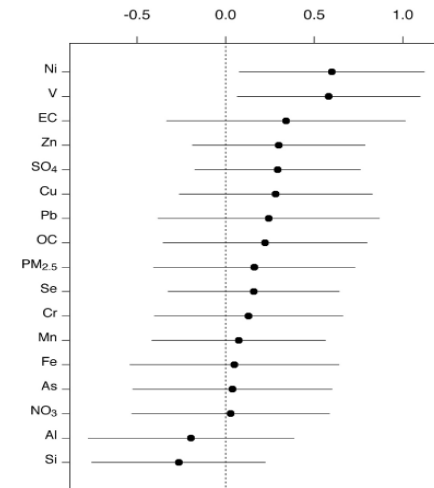
Oberdorster Poster

PM Components

- **At the time of the last review, most epidemiological work focused on mass based causation**
Few sites provided daily speciation data
- **The increased availability of speciation data have led to newer studies which associate risk of mortality with PM components**
Poster presented by Dominici in Session 3.
- **At the time of the last review, most toxicology studies focused on transition metals present in oil fly ash, or soluble metal salts.**
- **These studies have evolved to include metals present on ambient particles and an increased emphasis on organic PM constituents.**

In addition to studies examining transition metals and organics, the **HEI funded NPACT study** is a major initiative to investigate both the short and long term health effects of multiple PM components.

Ni and V were the only PM_{2.5} components significantly associated with daily mortality



Differences in mortality risk coefficients per the 5th to 95th percentile difference in FPM and FPM component concentrations across NMMAP MSAs (for the 60 MSAs for which FPM speciation data were available). (Lippmann et al. 2009, in press).

Kodavanti and Cho Posters

How and to What Extent does Air Pollution Cause Adverse Health Effects?

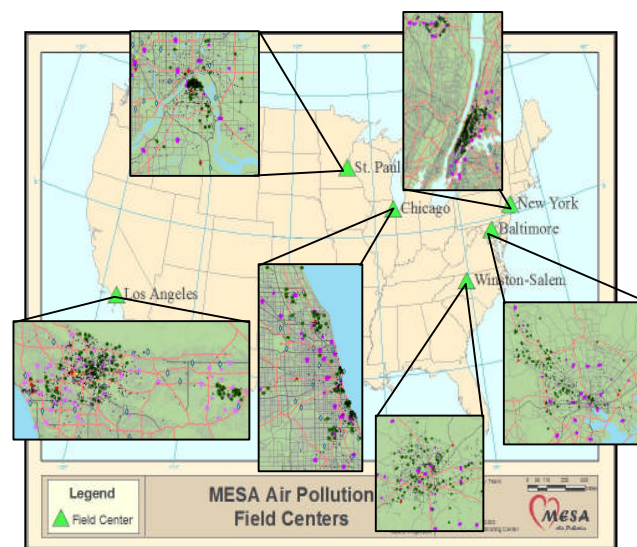
- The current PM standard rests primarily on a large and coherent epidemiological database.
- At the time of the last BOSC review there were a number of human and animal toxicology studies underway that addressed the biological plausibility of how exposure to very small levels of particles could cause rapid mortality.
 - Primary focus on cardiac and soluble vascular factors
- During the past four years, significant progress has been made in describing the pathophysiological process which underlie PM-induced adverse health effects.
 - newer studies have examined effect of PM on vascular cells and nervous tissue
- Mechanisms responsible for chronic PM effects are also underway.
- Newer epidemiology studies have demonstrated mortality associated with exposure to ozone.

Health effects of Long Term PM Exposure

The centerpiece of ORD's chronic PM research program is the 10 year MESA Air study.

A Prospective Study of Air Pollution and Cardiovascular Disease: MESA Air

- Since 2006, two additional cohort studies have been added to the epidemiological database.
 - Nurses health study
 - Women's health initiative – OS
- Chronic animal exposure studies have also reported cardiopulmonary and neurological effects.



Kaufman Poster



PM and the Vascular System

- At the time of the last BOSC review, most studies were dominated by end points which examined changes in HRV and soluble vascular markers of clotting/coagulation.
- Since that time, the critical role of the vascular endothelium in regulating PM-induced cardiovascular effects has been recognized.

The studies shown in this poster corroborate that vascular dysfunction is likely a pivotal biological mechanism explaining the increase in risk for PM-induced cardiovascular mortality.



VASCULAR DYSFUNCTION

Increased blood pressure, blunted endothelial-dependent vasodilatation

Vascular inflammation and oxidative stress

Vasoconstriction and augmented atherosclerosis

Brook Poster

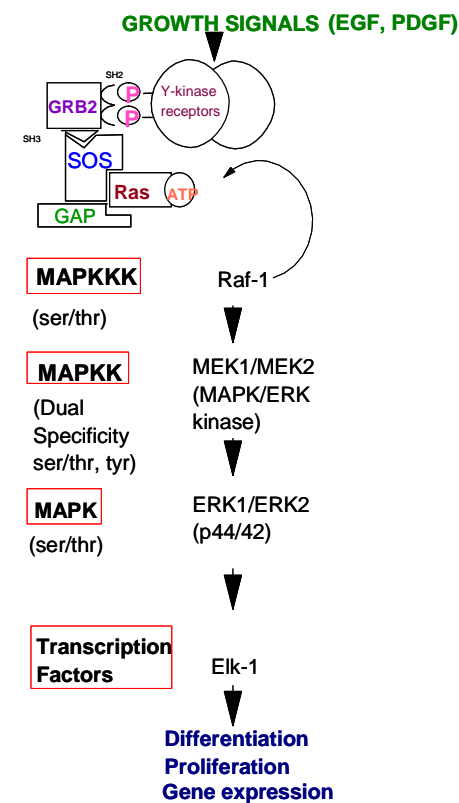
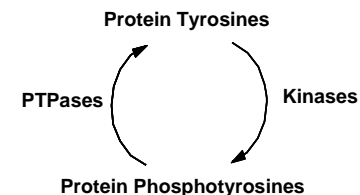
PM and Molecular Mechanisms

- Complete understanding of how PM causes adverse health effects requires knowledge of the molecular, biochemical, and cellular mechanisms which control the pathophysiological response to PM.

NAS report on toxicity testing for the 21st Century

- ORD has made significant progress in understanding what happens from the time a particle touches the outer surface of a cell until a battery of genes is activated which will trigger a cascade of events leading to an adverse health response.

Toxicity pathways

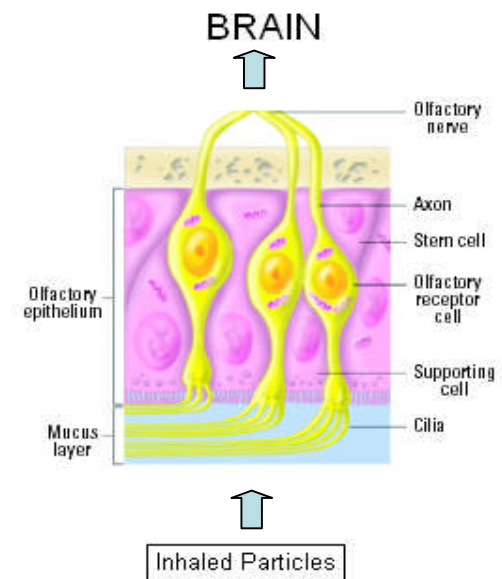


Samet and Cho Posters

PM and the Nervous System

- At the time of the last BOSC review, there was a single study suggesting that inhaled MnO_2 particles could translocate to the brain via the olfactory nerve.
- Recent studies of acute and chronic effects of PM leave little doubt that PM exposure can affect the nervous system, causing cellular and biochemical changes in the brain.
- These changes can alter downstream autonomic nervous system function which regulate a number of cardiovascular responses.

Inhaled fine and ultrafine particles can access the brain by translocation via the blood and also by passage along nerve cells. Below is an example of transport along olfactory nerves



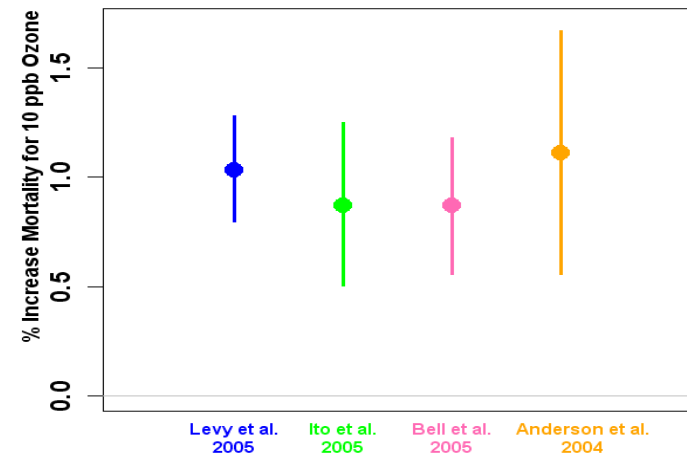
Kleinman Poster

Ozone Mortality

- At the time of the last BOSC review, epidemiology studies on ozone were inconclusive
 - Some identified an association, some did not
- However recent studies that use meta-analysis, case-crossover, and multi-city designs have reported associations between ozone exposure and increased mortality.

Meta-Analyses

Findings indicate that collectively the previously conducted time-series studies show evidence of an association between ozone and risk of mortality.

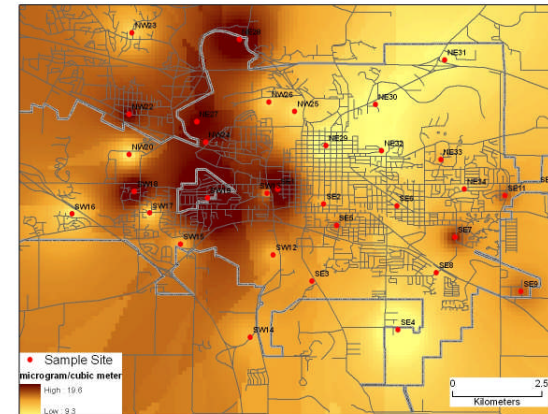


Bell Poster

Improved Exposure Characterization

- Numerous health studies have used measurements from a few central-site ambient monitors to characterize exposures to air pollution.
- However, relying on solely on central-site ambient monitors does not account for the spatial heterogeneity of ambient air pollution patterns, the temporal variability in ambient concentrations, nor the influence of infiltration and indoor sources.
- Central-site monitoring becomes even more problematic for certain PM components (e.g., metals) or size fractions (e.g, coarse, ultrafine) that exhibit significant spatial-heterogeneity.
- Since the last BOSC review, novel approaches have been developed to improve exposure assessment.
- These techniques are currently being evaluated in several health studies.

Improving Estimates of Ambient Concentrations



Distribution of mean PM_{10-2.5} concentrations in Iowa City using passive coarse particle monitors.

Baxter Poster

Who Is Susceptible to PM?

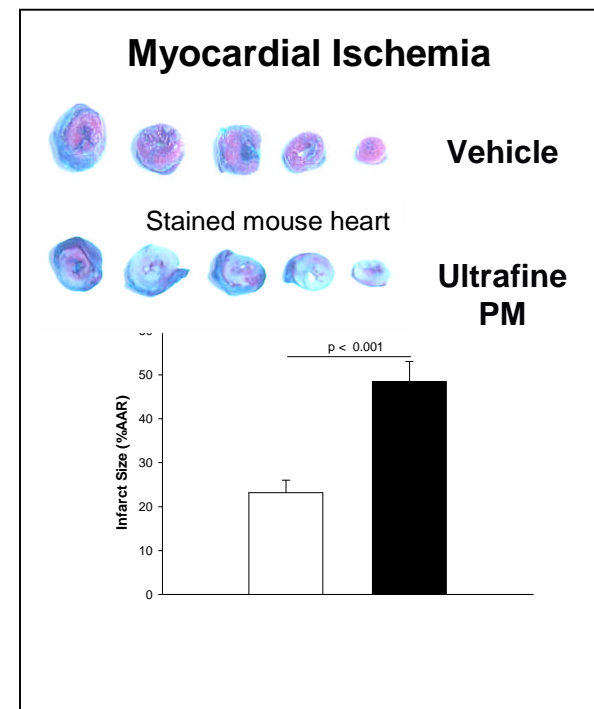
- An understanding of susceptibility is critical to achieving the public health protection called for by the 1990 amendments to the Clean Air Act.
- These amendments extended protection beyond the general population to especially susceptible subpopulations.
- These include things such as age, gender, ethnicity, presence of underlying disease, genetic susceptibility, etc.

"The moral test of a government is how it treats
those who are at the **dawn of life**,
the children;
those who are in the **twilight of life**,
the aged;
and those who are in the **shadow of life**,
the sick, the needy, and the handicapped."

Hubert Humphrey, 1976

PM and Pre-existing CV Disease

- At the time of the last BOSC review an impressive array of epidemiological, clinical, and toxicological studies left no doubt that people with pre-existing CV disease are at an increased risk from exposure to PM.
- Recent ORD studies have increased our understanding of **how** pre-existing CV disease confers enhanced susceptibility.

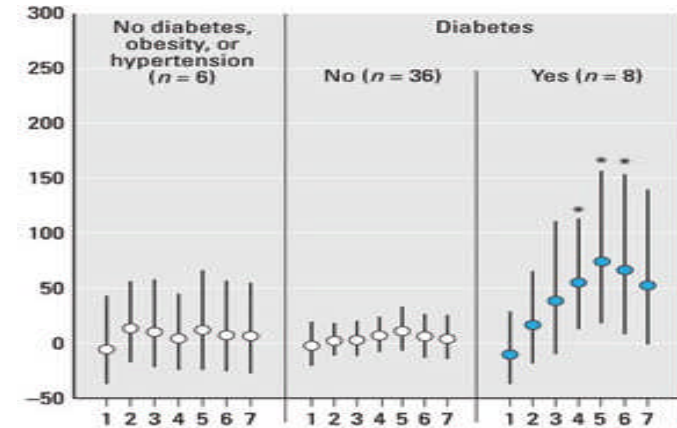


PM exposure increased infarct size in the hearts of ischemic mice.

Farraj Poster

PM and Diabetes

- 26% of U.S. adults have pre-diabetes. This at-risk population will continue to increase in coming years.
- At the time of the last BOSC review, there was preliminary evidence that diabetics were especially susceptible to PM, even compared with non-diabetics with CV disease.
- Since then, a number of epidemiology, clinical, and toxicological studies have corroborated these early studies, as well as defined some of the reasons why diabetics are a susceptible population.



C-reactive protein (CRP) increased in association with PM exposure in elderly diabetic, but not in non-diabetic, nursing home residents in St. Louis.

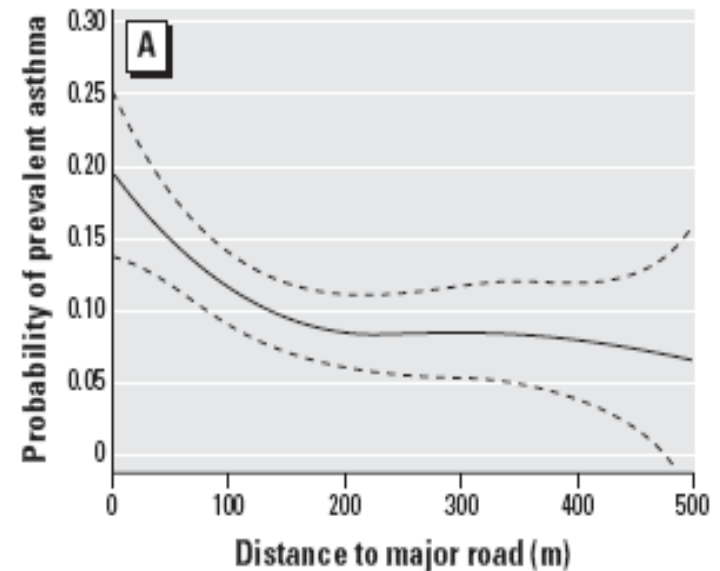
Frampton Poster

PM and Asthma

- At the time of the last BOSC review, it was accepted that air pollution is a significant cause of asthma exacerbation.
- However, the degree to which air pollution exposure influences disease progression and the potential for air pollution to contribute to the onset of asthma were not well understood.
- The studies presented in this poster show for the first time that air pollution can cause asthma.
- Somewhat counter-intuitively, they also show that PM causes more CV effects than pulmonary effects in asthmatics.
- The [poster by Neas](#) also shows that asthmatics are affected by near road exposures.

Peden Poster

Poor Air Quality Can Cause Asthma

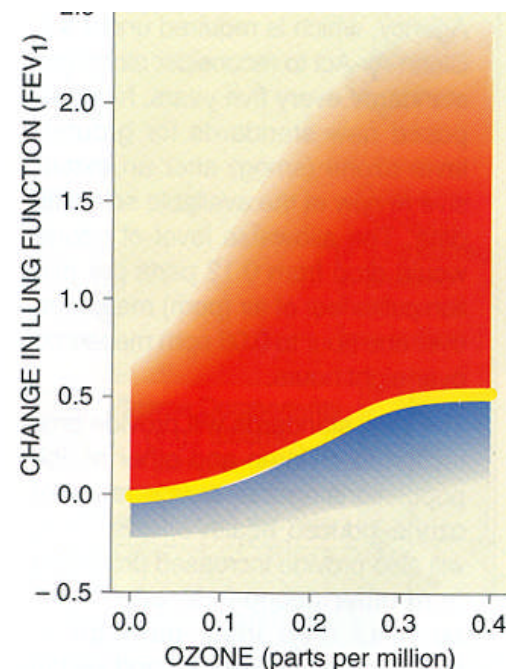


Prevalence of asthma by distance of residence to a major road

PM and Genes

- At the time of the last BOSC review, there were only a few preliminary studies which suggested that genetic polymorphisms might be associated with enhanced responsiveness to air pollution.
- The recent revolution in “omics” technology has provided the tools that can be used to address this question.
- There is now a significant body of literature showing that a number of genetic and epigenetic factors control responsiveness to air pollution.

Range of response to ozone exposure



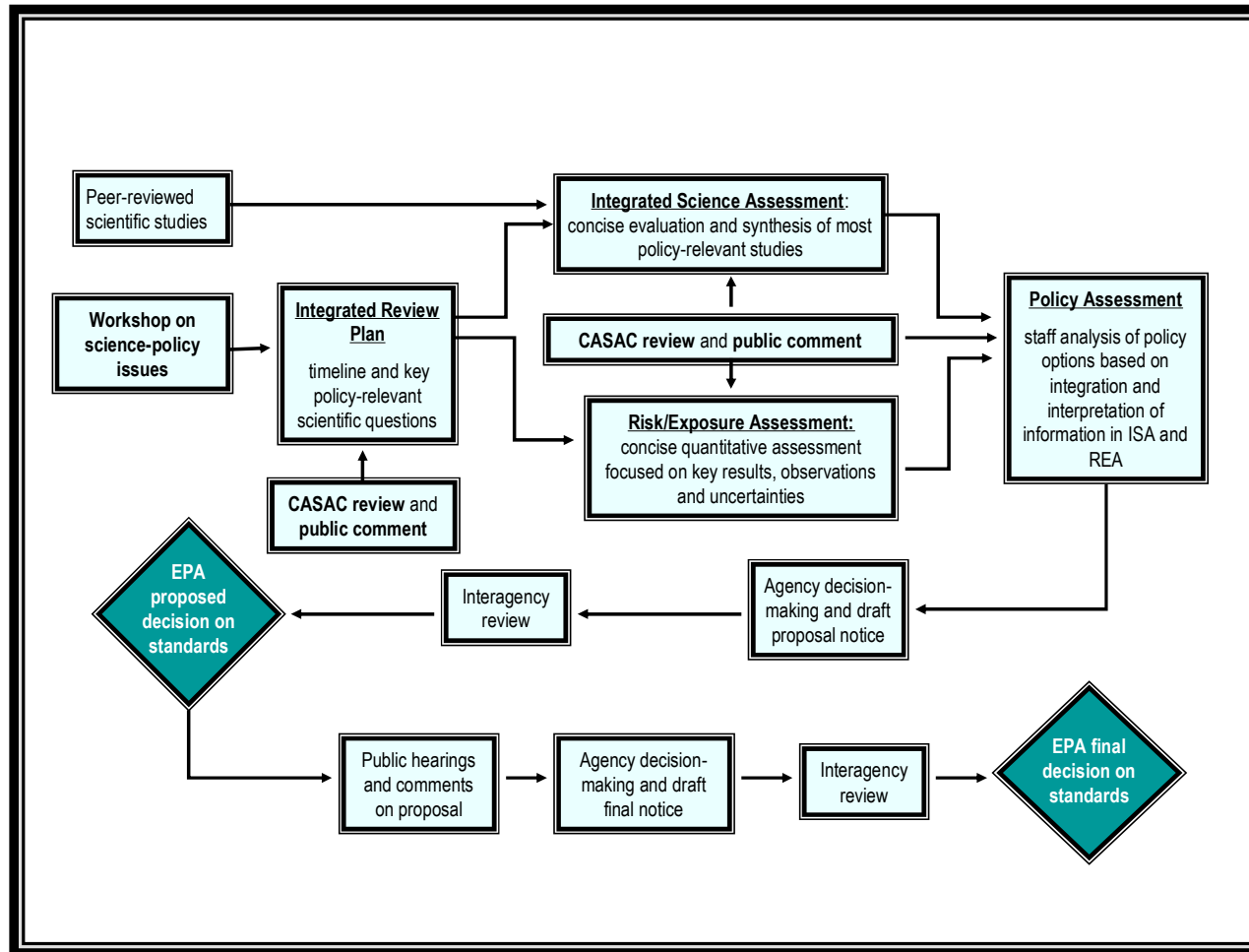
Schwartz Poster

Progress Has Been Made...

My goal is simple. It is complete understanding of the universe, why it is as it is and why it exists at all." —

Stephen Hawking.

What Is the Impact of this Research?




Hassett-Sipple and Stanek Poster


The Air Quality Index: Why Color the Days?

Reduce your risk by using the **Air Quality Index (AQI)** to plan outdoor activities.

AQI Levels of Health Concern	AQI Values	What Action Should People Take?
Good	0-50	Enjoy Activities
Moderate	51-100	People unusually sensitive to air pollution: Plan strenuous outside activities when air quality is better
Unhealthy for Sensitive Groups	101-150	Sensitive Groups: Cut back or reschedule strenuous outside activities Particle Pollution: People with heart or lung disease (including diabetics), older adults and children Ozone: Active children and adults and people with lung disease Sulfur Dioxide: Active children and adults with asthma Carbon Monoxide: People with heart disease and possibly fetuses and infants
Unhealthy	151-200	Everyone: Cut back or reschedule strenuous outside activities Sensitive Groups: Avoid strenuous outside activities
Very Unhealthy	201-300	Everyone: Significantly cut back on outside physical activities Sensitive Groups: Avoid all outside physical activities



AQI
AIR QUALITY INDEX
www.epa.gov/airnow



EPA United States
Environmental Protection
Agency

Air and Radiation
EPA-452/F-04-001
www.epa.gov
Date



Stone Poster

EPA's Health and Effects Program Provides a Science Foundation for Protecting the Air We Breathe

Air Pollution health and exposure research has significant benefits and impacts:

- **Indicates that the current standards are necessary to protect public health**
- **Strengthens confidence in the scientific basis for these standards**
- **Provides information to inform people, particularly at risk populations, of the harmful effects of air pollutants and to educate them to minimize exposure to air pollutants**

