Latest Findings Regarding Health Effects from Fine PM and Associated Components

Environmental Monitoring, Evaluation, and Protection in New York: Linking Science and Policy

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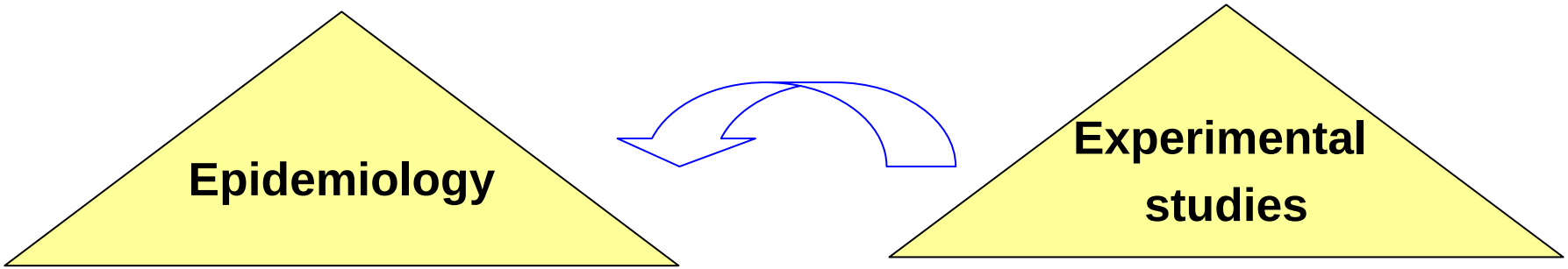
Drivers of Health Effects Research

- New $PM_{2.5}$ ambient standards set in 1997
- Time series studies and cohort studies showed increased cardiopulmonary mortality and morbidity with increased levels of $PM_{2.5}$
  - Subsequent HEI and other analyses have confirmed though some questions remain
- Questions:
  - Who is at risk? Who are the most susceptible individuals?
  - What are the mechanisms of PM effects?
  - Which particles are most toxic? How can we ensure we control components and sources with the highest effects?

Answering the Questions



- Focus on specific diseases and subgroups
- Effects of long-term exposure
- Effects of short-term exposure

- To test mechanistic hypotheses
- To test animal models of human diseases

e.g. HEI's Godleski study in "susceptible" dogs exposed to CAP showed changes in cardiac function (2000)

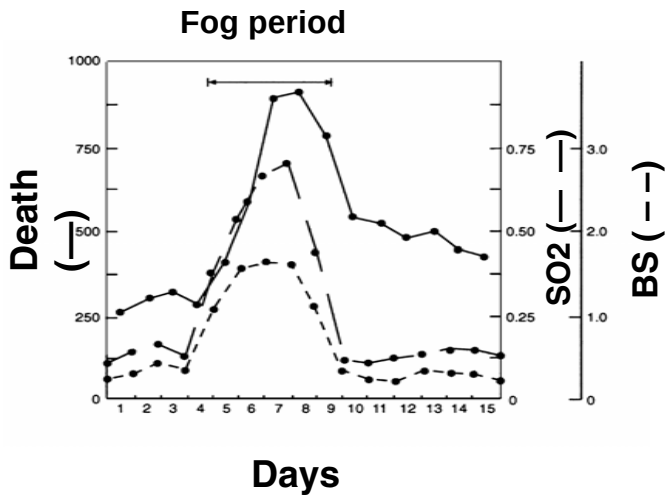
Cohort Versus Time-Series Studies

Cohort Studies

Estimate effects of *long-term exposure* by collecting health data at the individual level. Exposure to air pollution is assessed at either the community level or the individual level.

Time-series studies

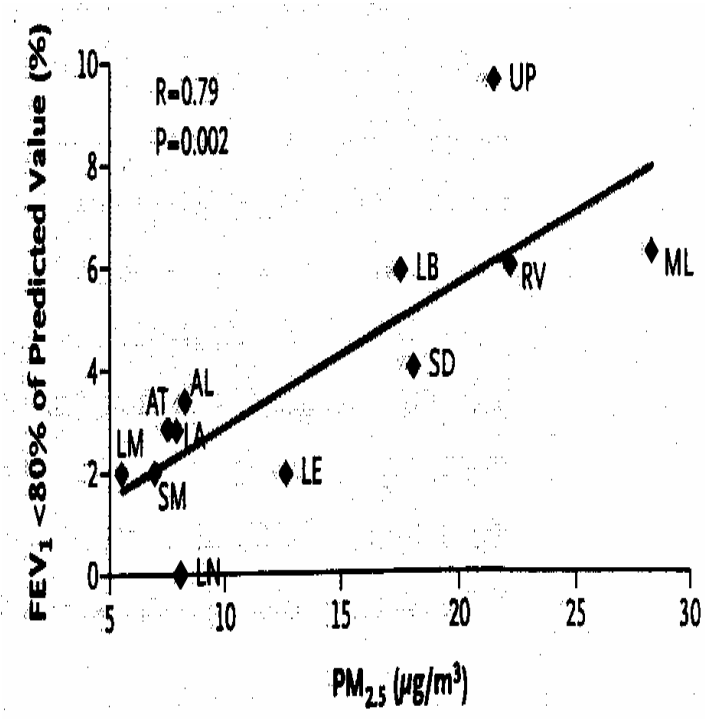
Estimate effects of *short-term exposure* by investigating the association between day-to-day variation in both air pollution and health outcome.



Long-Term Respiratory Effects CA Children Study

Gauderman et al. 2004. New Engl J Med 351:1057-1067

- Followed children (aged 10-18) in 12 Southern CA communities with different mix of pollutants for 8 years.
- Assessed exposure to $PM_{2.5}$ and other pollutants based on annual community averages.
- Measured respiratory function yearly.
- Results: Decreased growth in lung function was associated with EC, $PM_{2.5}$, acidity, and NO_2 (originating primarily from motor vehicles)
  - Is a predictor of risk of mortality and myocardial infarction



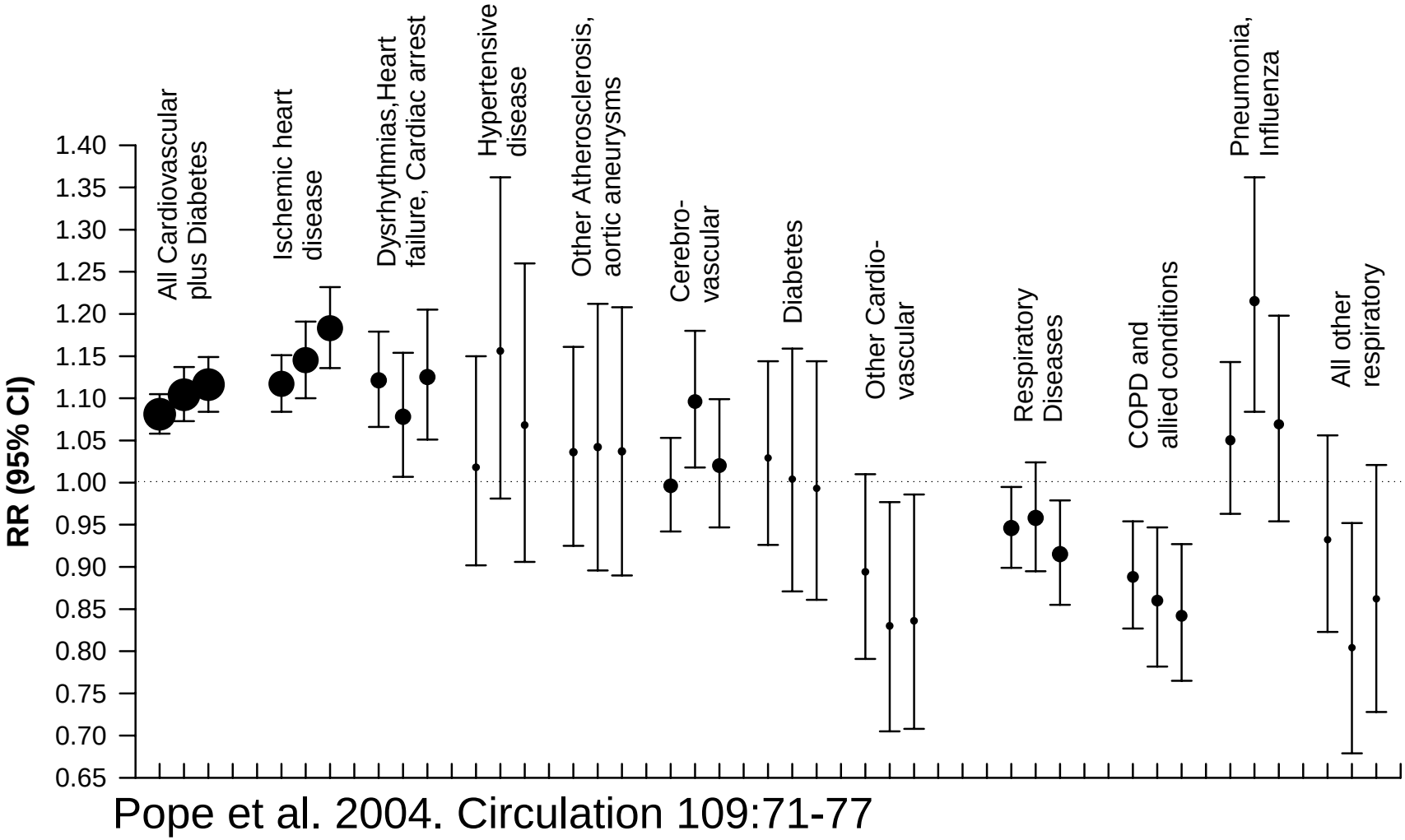
Community-specific proportion of 18-year olds with FEV1 below 80% predicted as function of average levels of PM2.5 from 1994-2000

Cardiovascular and Respiratory Mortality and Long-Term Exposure

Pope et al. 2004. Circulation 109:71-77

- Previous analyses linked long-term exposure to $PM_{2.5}$ to cardiopulmonary mortality (ACS study)
- In this analysis PM individual exposure was linked to mortality for specific causes of death to help understand the pathophysiologic pathways linking PM to mortality
- Results: Statistically significant associations of $PM_{2.5}$ were observed with all cardiovascular deaths, but not for respiratory deaths.

Cardiovascular and Respiratory Mortality and Long-Term Exposure

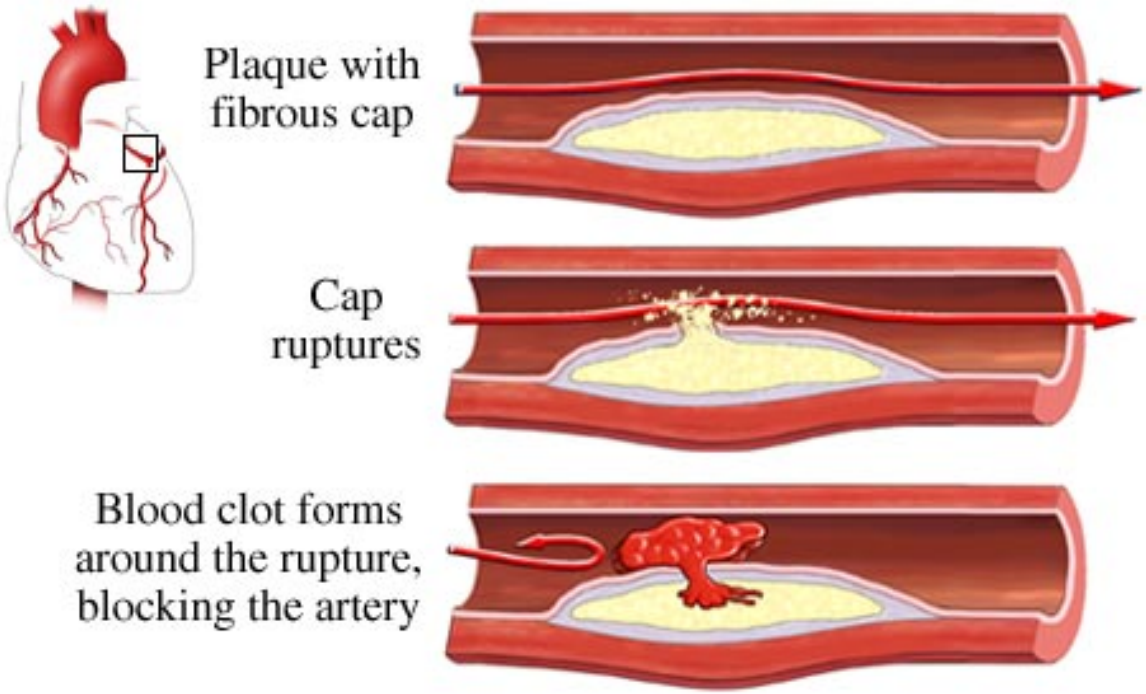


Pope et al. 2004. Circulation 109:71-77

Figure 1. Adjusted relative risk ratios for cardiovascular and respiratory mortality associated with a 10 μg/m^3 change in $PM_{2.5}$ for 1979-1983, 1999-2000, and the average of the two periods. (Relative size of the dots correspond to the relative number of deaths for each cause.)

What is Atherosclerosis?

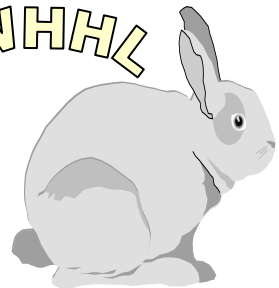
Atherosclerosis is a progressive disease characterized by the buildup of fatty plaques in artery walls. Plaques that rupture cause blood clots to form that can block blood flow or break off.



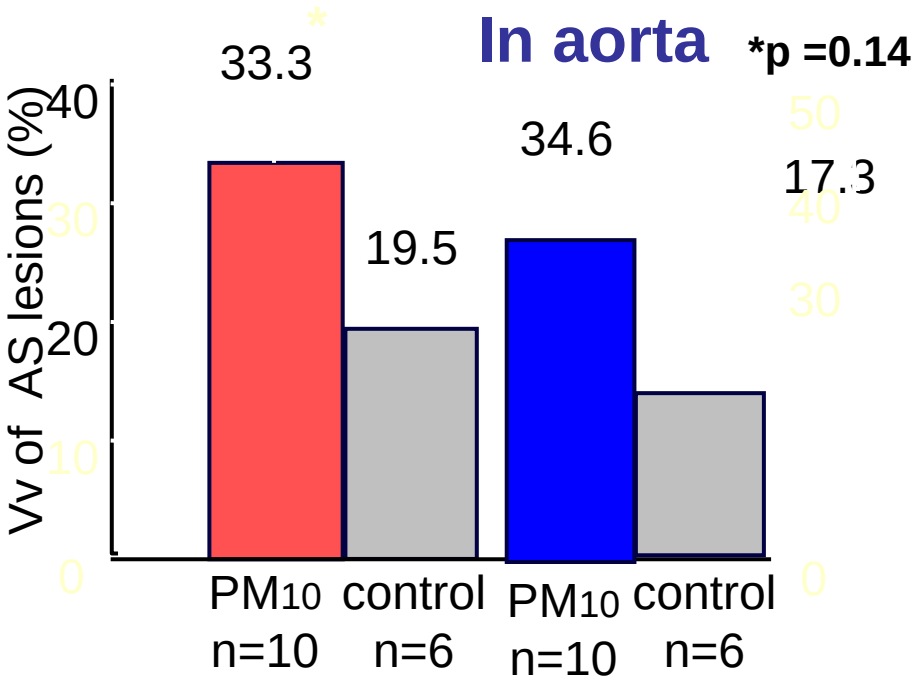
Courtesy of A Pope

Repeated Exposure to PM of Rabbits that Develop Atherosclerosis (AS)

Courtesy of James Hogg



In coronary arteries ***p<0.05**



- Hypercholesterolemia
- Rapid development of AS lesions

- 4 weeks exposure to 5 mg/ml resuspended PM_{10} from 1993;
- Measured volume fraction of vessel taken up by AS

Results: PM increased plaque size, i.e., was associated with progression of AS

Suwa et al. 2000. J Am Coll Cardiol 39:935-942

Air Pollution and Atherosclerosis

Kunzli et al. 2005. Environ Health Perspect 113:201-206

- Participants in clinical trial of atherosclerosis and vitamin B with no clinical symptoms of heart disease (N=798)
- Estimated long-term exposure to $PM_{2.5}$ based on residential address
- Measured carotid artery intima-media thickness

Results: Found an association between long-term exposure to $PM_{2.5}$ and a subclinical measure of atherosclerosis (artery thickness), especially in women >60 years of age

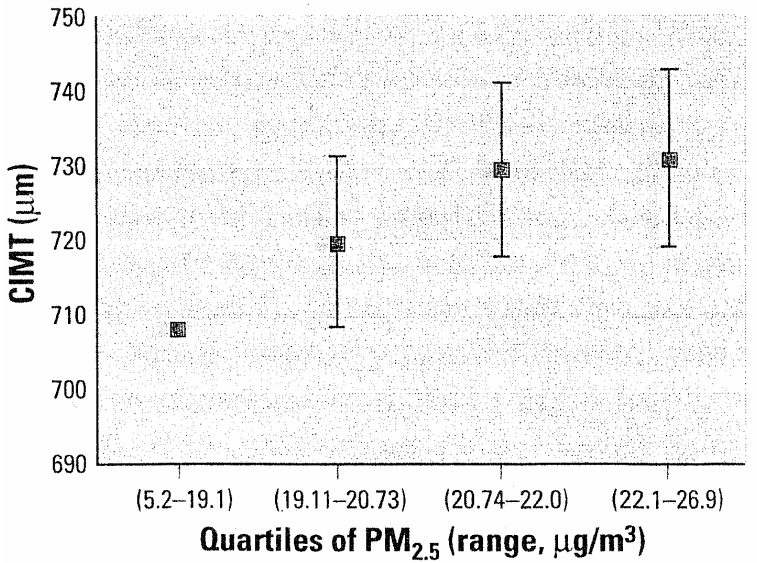


Figure 2. Mean CIMT ± 1 SE among quartiles of the $PM_{2.5}$ distribution. The *y*-axis shows mean CIMT levels at the population average of the adjustment covariates (age, sex, education, and income). The first quartile is the reference group.

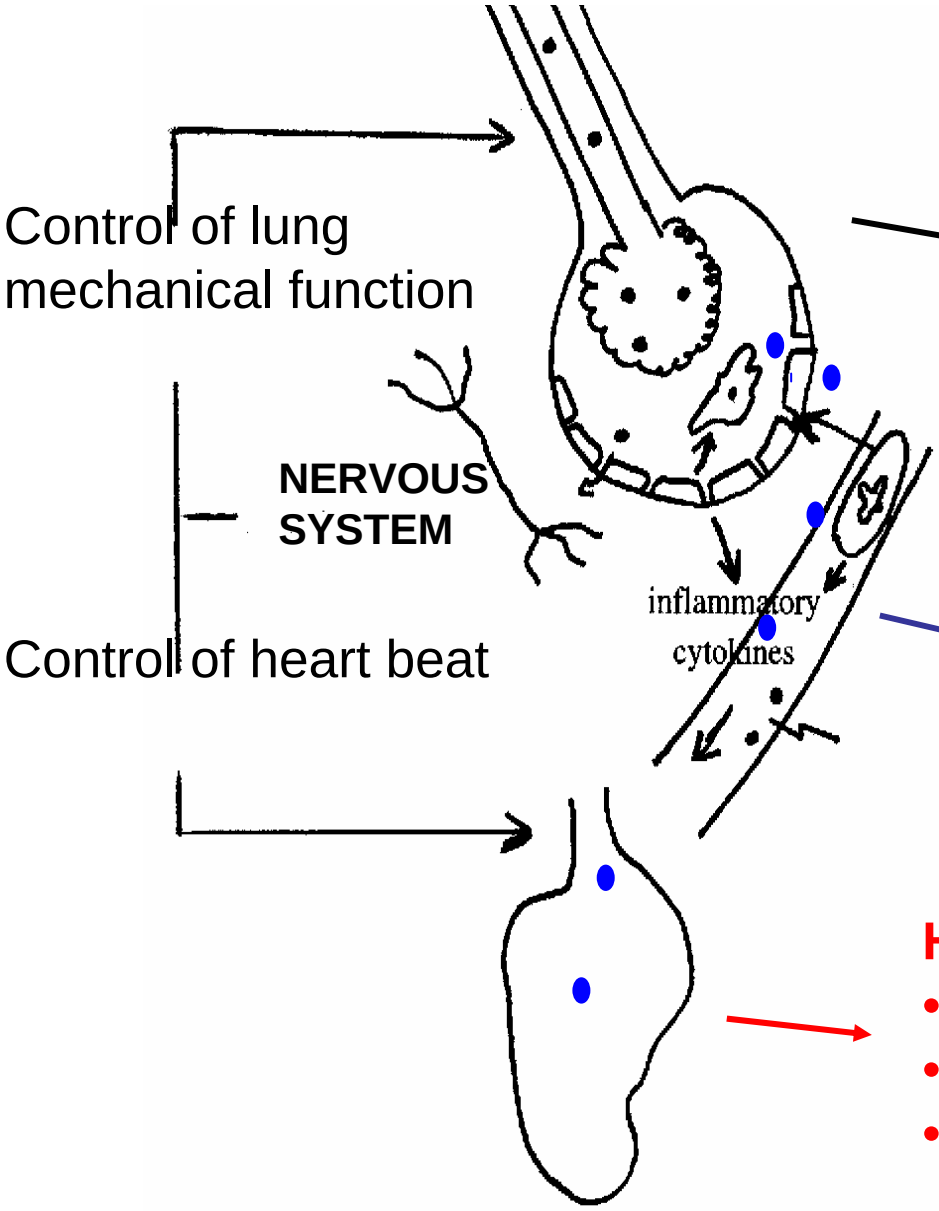
Answering the Questions
Who Is at Risk?

- "Answer is not simple but is dependent on the health effects being evaluated and the level and length of exposure"
- "Chronic exposure studies suggest rather broad susceptibility to cumulative effects of repeated exposure."
  - Children, people with underlying cardiovascular or respiratory disease, people with diabetes
- "The number of those hospitalized or dying may be quite limited, but the number of those susceptible to less serious effects may be quite broad"

Pope AC. 2000. Environ Health Perspect 108 (Suppl 4):713-723

Answering the Questions

What Are the Mechanisms?



LUNG
- oxidative stress
- airway inflammation
- changes in lung function
- asthma symptoms

CIRCULATION
- blood coagulability
- systemic inflammation
- blood pressure
- vasoconstriction
- plaque size and structure

HEART
- changes in rate and rhythm (HRV)
- myocardial infarction
- arrhythmia

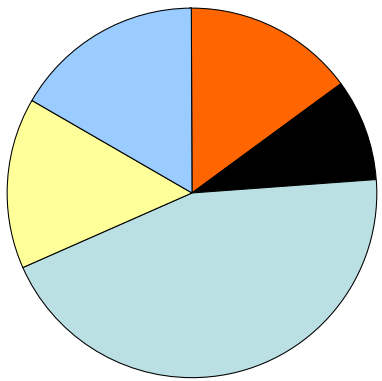
Answering the Questions

Which particles are most toxics?

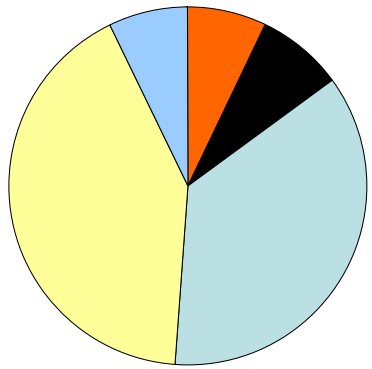
Sources of PM2.5

- **SULFATE** from SO_2 (Power Plants and Coal & Oil-fired Boilers)
- **NITRATE** from NOx (Cars, Trucks, Power Plants & Heavy Equipment)
- **CRUSTAL MATERIAL** (Roads, Construction & Field Dust)
- **ELEMENTAL CARBON** (Diesel Engines, Heavy Equipment, Highway Vehicles)
- **ORGANICS** (Wildland Fires, Waste Burning, Heavy Equipment Engines, Cars & Trucks)

Typical Western City



Typical Eastern City



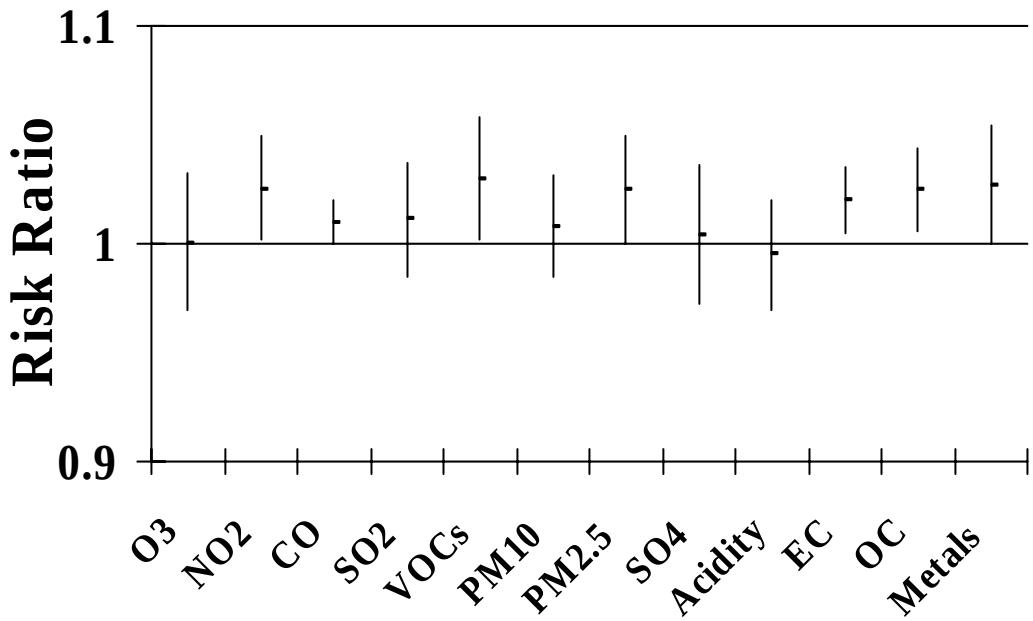
Multi-Pollutant Short Term Analyses in Different Cities Show Varying Results

Metzger et al. 2004. Epidemiology 15:46-56

Atlanta (ARIES study)

- **Measured association between emergency visits for cardiovscaular disease and components of air pollution (1993-2000)**
- **Results:**
  - **NO_2,CO, VOC, $PM_{2.5}$, EC, and OC associated (mobile sources?)**
  - **Sulfate, acidity, and PM counts (UF) are not**

Relative risk of cardiovascular emergency visits

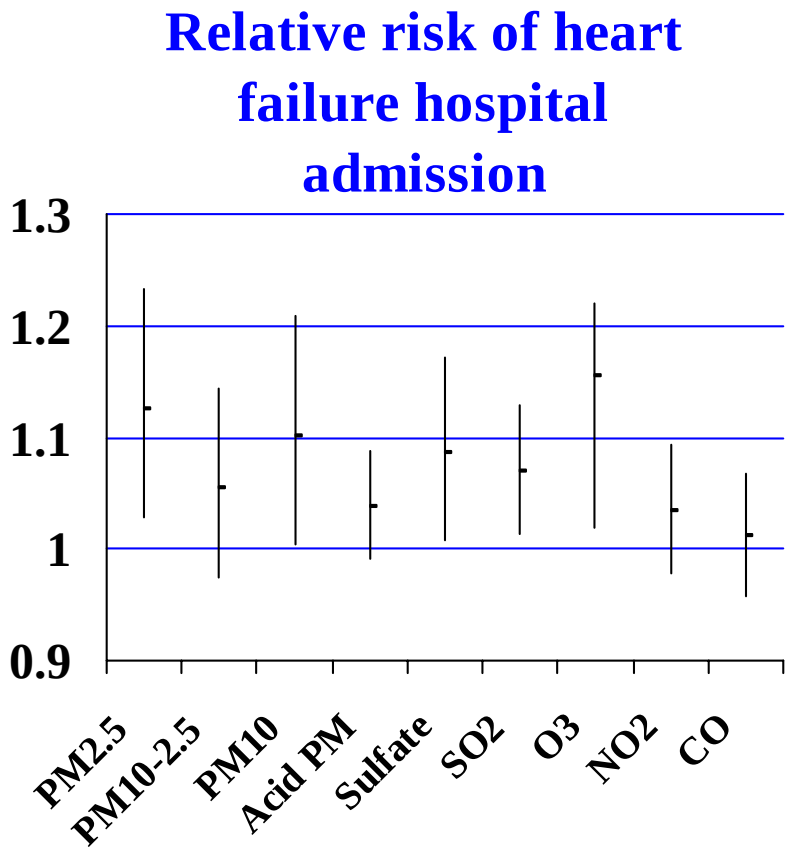


Multi-Pollutant Short Term Analyses in Different Cities Show Varying Results

Lippmann et al . 2000. HEI Report # 95

Detroit

- **Measured association between emergency visits for heart failure in the elderly and components of air pollution (1993-2000)**
- **Results:**
  - **In this study $PM_{2.5}$, sulfate, SO_2 and ozone are associated**
  - **Acid, coarse particles, NO_2, and CO are not**



Study of Utah Valley PM in Human Volunteers

Ghio and Devlin. 2001. Am J Respir Crit Care Med 164:704-708

- Volunteers exposed to aqueous extracts of PM
- Measured inflammatory response in lung lavage
- Results: Extracts from PM collected before and after reopening of steel mill provoked greater inflammatory response relative to extracts from PM collected during plant shutdown
  - Possible role of metals?

TABLE 1. NEUTROPHILS, PROTEIN, AND IL-8 IN LAVAGE FLUID AFTER INSTILLATION OF LOWER MASS (100 μg) OF EXTRACT

	1986	1987	1988
Neutrophils, %	37.0 ± 6.6	15.7 ± 2.7	31.5 ± 6.2
Protein, μg/ml	175 ± 29	76 ± 14	153 ± 32
IL-8, pg/ml	56.5 ± 17.4	18.8 ± 10.1	61.0 ± 10.5

TABLE 2. METAL CONCENTRATIONS IN THE THREE PM EXTRACTS FROM UTAH VALLEY (NG METAL/MG EXTRACT)

	1986	1987	1988
Iron	82.2	14.8	257.5
Copper	402.8	29.1	471.8
Zinc	1276.5	20.2	690.2
Lead	186.6	5.7	286.7
Nickel	17.6	3.8	11.0
Vanadium	6.0	7.4	37.7

Effects of Fine and Ultrafine PM

de Hartog et al. 2003. Am J Epidem 157:613-623

- 131 elderly subjects with coronary heart disease living in 3 European cities (1998-1999)
- Measured PM2.5 and number count (UF) at fixed monitors
- Measured cardiac and respiratory symptoms
- Results: Increase in 10 ug/m^3 $PM_{2.5}$ associated with incidence of shortness of breath. No association with UF.

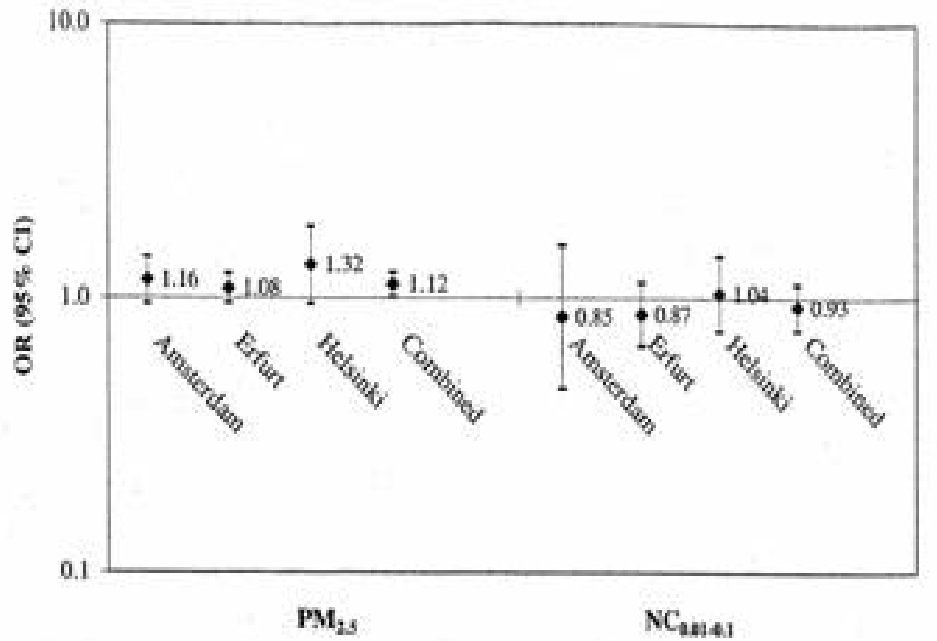


FIGURE 4. Odds ratios (OR) for the relation of incident shortness of breath to increases in particulate matter less than 2.5 μm in diameter ($PM_{2.5}$) and number concentrations of particles in the size range of 0.01–0.1 μm ($NC_{0.01-0.1}$) among elderly subjects with a history of coronary heart disease, ULTRA Study, winter 1998–1999. The odds ratios shown are for an increase of 10 μg/m^3 in $PM_{2.5}$ and an increase of 10,000 particles/cm^3 in $NC_{0.01-0.1}$ (5-day average). Bars, 95% confidence interval (CI).

Effects of Fine and Ultrafine PM

Timonen et al. 2005. J Expo Anal Environ Epidem *(on-line)*

- However,…recent results in the same elderly panels
- Reported an association between increases in UF (10,000 particles/cm^3) and NO_2 (10 µg/m^3), but not $PM_{2.5}$, with decrease in LF/HF ratio
  - LF (low frequency) and HF (high frequency) are measures of Heart Rate Variability, the normal beat to beat variability in the heart's rhythm (controlled by the autonomic nervous system).
  - Results suggest that UF PM affects the autonomic nervous system control of the heart.

Summary

Recent epidemiologic and experimental studies have suggested:

- Both the cardiovascular and the respiratory systems are affected by long-and short-term exposure to fine PM
- **Results depend on health outcomes, who is being studied, location, analysis method and other factors which have not been applied systematically.**
- Possible mechanisms by which PM can cause effects
  - Different biological processes may be involved; may depend on underlying conditions, type of particles

Summary (cont)

Studies have provided evidence that many components may have effects:

- Metals, sulfate, elemental carbon, UF have been found to be associated with some outcomes in different studies
- Particles of different composition or from different sources may act through different pathways
- Gases also may play a role (PM effects could not be distinguished from effects of gases in many studies)

Key Issues

Future studies should focus

- On using a more systematic approach to identify components of particles that are associated with different effects
  - improved assessment of exposure to PM
  - Integrated epidemiology and toxicology approaches
- on specific hypotheses that consider distinct etiologic processes
- *PM centers, NYSERDA, and others working on this*
- *HEI has major current RFA to seek systematic studies to address this*