



What Will We Learn from Epidemiology Studies of Long Term Exposure to Particulate Matter?

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Science Question

1. Does long-term exposure to ambient particulate matter increase the risk of mortality or chronic disease in population-based epidemiology studies?
2. Is annual change in measures of subclinical disease or increased incidence of clinical disease associated with long-term exposure to particulate matter?
3. Are these adverse health endpoints differentially associated with specific chemical constituents, size fractions, or sources of ambient particulate matter?
4. Does the presence of gaseous co-pollutants alter the estimated risk of PM-related disease?
5. Is the estimated risk higher in potentially susceptible subgroups?

Research Goals

1. Examine the role of long-term exposure to PM and copollutants in the development of respiratory disease, cardiovascular disease, and mortality in the general population, and in potentially susceptible subpopulations by conducting retrospective epidemiologic studies that make use of existing information on health and air quality.
2. Conduct a multi-site, prospective, population-based observational study of adults designed to determine the long-term effects of PM constituents and co-pollutants on the natural history of cardiovascular disease, including indicators of sub-clinical disease, clinical disease incidence, mortality and the assessment of physiological parameters indicative of the progression of disease.

Retrospective Exposure Assessment in Existing Studies

The EPA is supporting several epidemiology studies to address uncertainties regarding the health effects of chronic PM exposure. The studies are developing a retrospective exposure assessment of long-term PM₁₀, estimated PM_{2.5} and other pollutants using a common dataset retrieved from the EPA Air Quality System and will model individual exposure to PM₁₀ and PM_{2.5}.

Long-term Exposure to Ambient Particulate Matter and Subclinical Atherosclerosis (R830543),
Ana Diex-Roux, University of Michigan

- * **Multiethnic Study of Atherosclerosis (MESA) (NIH)**
Risk factors for subclinical atherosclerosis and its progression using three state-of-the-art measures (ultrasound carotid intima-medial wall thickness, coronary calcium, and ankle-brachial blood pressure index) in 6500 subjects enrolled in 1999 at six areas in the U.S. These measures, plasma markers of health status, and clinical health, are assessed every 2 years.

Relating Cardiovascular Disease Risk to Ambient Air Pollutants using Geographic Information Systems Technology and Bayesian Neural Networks: The AHSMOG Study. (R830547),
Synnové F. Knutsen, Loma Linda University

- * **Adventist Health Study of SMOG**
A study of risk factors for mortality among 6338 non-smoking California Seventh-day Adventists followed for 22 years.

Chronic Exposure to Particulate Matter and Cardiopulmonary Disease (R830545),
Francine Laden, Brigham and Women's Hospital

- * **Nurses Health Study (NIH)**
Risk factors for incident disease and mortality among 121,000 women residing in the United States, 30 to 55 years of age at enrollment in 1976.

Characteristics of Epidemiology Studies Using Established Cohorts

Cohort	Location	Exposure	Health Outcomes	Sensitive Subgroups
MESA	Baltimore, MD, Chicago, IL, Forsyth County, NC, Los Angeles, CA, New York, NY, St. Paul, MN	Individual level PM 1987-2003 mean linked to residence & days prior to exam date	Subclinical atherosclerosis Inflammatory markers	Subjects with cardiovascular risk factors Race/Ethnicity
NHS	National	Individual level PM 1986-2000 mean linked to residence	Incident coronary and respiratory disease & mortality	Pre-existing disease including diabetes Antioxidant consumption
AHSMOG	California	Individual level PM 1977-2000 mean linked to residence & work	Fatal and nonfatal coronary heart disease and cerebrovascular disease	Pre-existing disease including diabetes, hypertension, elderly, previous smokers
Medicare Veterans	National	County level PM 1987-2005 annual mean & daily	Cause-specific mortality & hospitalizations	Pre-existing disease
WHI-OS	National	Individual level PM Year 2000 mean at closest monitor to residence (median distance 6 mi.)	Incident fatal and nonfatal coronary heart disease and cerebrovascular disease events	Subjects with cardiovascular risk factors Socioeconomic status

Chronic and Acute Exposure to Ambient Fine Particulate Matter and Other Air Pollutants: National Cohort Studies of Mortality and Morbidity (RD830548),
Jonathan M. Samet, Johns Hopkins Bloomberg School of Public Health

- * **National Medicare Cohort and Veterans Health Study Cohort**
A medical care system comprising over 27 million Medicare participants living within 10 miles of a PM_{2.5} monitor. Data on doctors' visits were obtained for 1999- 2002, with about 800,000 deaths annually.

Air Pollution and Cardiovascular Disease Events in the Women's Health Initiative Observational (WHI-OS) Study (R827355),
Joel Kaufman, The University of Washington

- * **Women's Health Initiative Observational Study (WHI-OS) (NIH)**
Began in 1991 to identify risk factors and track the health of over 93,000 post-menopausal women in the U.S. for heart disease, cancers, fractures and other disease. Evaluation of 70,966 women without a prior history of cardiovascular disease at baseline with a median follow-up of 6 years through August, 2003. After adjustment for confounding factors, each 10 µg/m³ of PM_{2.5} was associated with a 20% increased risk of incident nonfatal and fatal CVD events, relative hazard (RH) 1.20 (95% CI: 1.09, 1.33) per 10 µg/m³.

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

Prospective Study of Atherosclerosis, Clinical Cardiovascular Disease, and Long-Term Exposure to Ambient Particulate Matter and Other Air Pollutants in a Multi-Ethnic Cohort (RD831697),
Joel Kaufman, The University of Washington



Primary Aims

In a multi-city, multi-ethnic cohort, prospectively examine the relation between an individual level assessment of long-term ambient air pollution exposures and:

- Progression of Subclinical Cardiovascular Disease (n = 3600)
- Incidence of Clinical Cardiovascular Disease (n=8700)

Secondary Aims

- Assess Effect Modification and Identify Susceptible Populations
- Assess Health Effects Using Exposure Measures Other Than Particulate Mass
- Air Pollutants and Plasma Markers of Inflammation, Fibrinolysis, Oxidative Stress, and Endothelial Activation
- Consider Acute and Chronic Time Scales of Exposure

The MESA Study

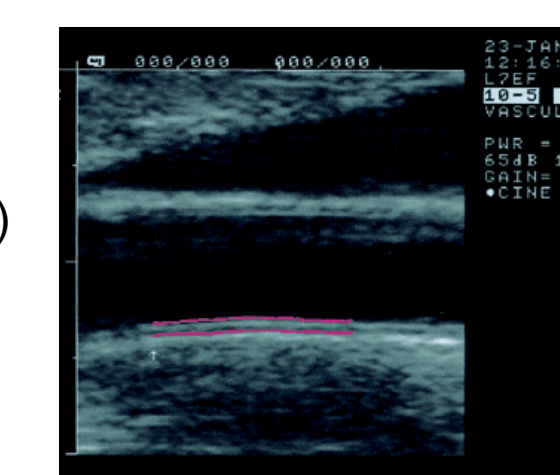
This project is built on the framework of the NIH/NHLBI Multi-Ethnic Study of Atherosclerosis (MESA). MESA is a study of the characteristics of subclinical cardiovascular disease (disease detected non-invasively before it has produced clinical signs and symptoms) and the risk factors that predict progression to clinically overt cardiovascular disease or progression of the subclinical disease. MESA researchers study a diverse, population-based sample of men and women who were 45-84 years of age in 1999. Subjects were free of clinical cardiovascular disease at recruitment. Approximately 40 percent of the recruited participants are white, 30 percent African-American, 20 percent Hispanic, and 10 percent Asian, predominantly of Chinese descent. The MESA Air Pollution Study augments the existing MESA by adding subjects, air pollution exposure assessment, and additional health testing and follow-up.

Outcomes:

- Subclinical Atherosclerosis**
Coronary Artery Calcification (CAC)
Carotid Intima-Media Thickness (IMT)
- Clinical Cardiovascular Disease Events**



CAC: This electron beam CT scan demonstrates calcification in the left anterior descending coronary artery

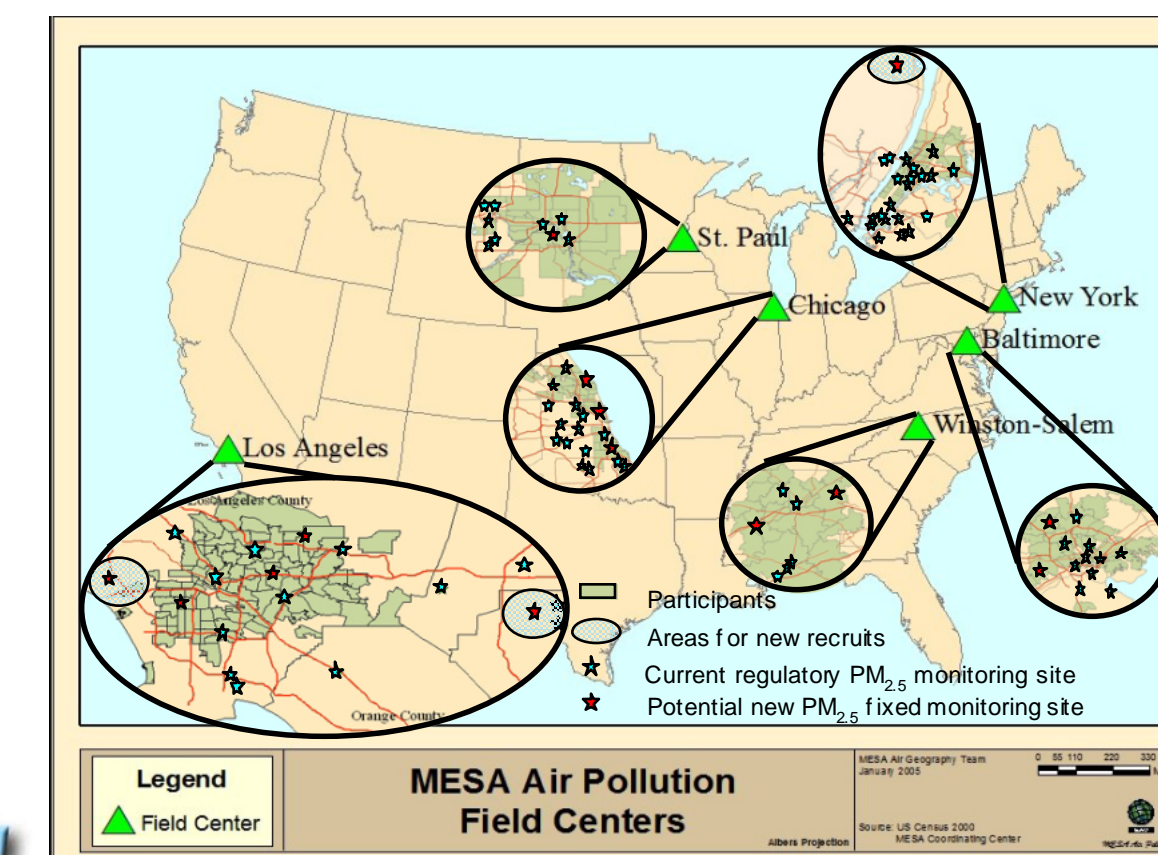


IMT: This ultrasound image of the common carotid artery and adjacent structures illustrates the lumen-intima and the media-adventitia interfaces in red.

Exposure Assessment:

Individual level exposure estimate integrating geospatial model for outdoor concentrations with participant-specific prediction of pollutant infiltration and time-location patterns. Elements include:

- Geographical Information Systems
- Fixed community-oriented monitoring
- Recurrent outdoor monitoring campaigns
- Monitoring at subjects' homes
- Questionnaires



Exposure Characteristics of Communities	Alhambra	Coastal L.A. Riverside County*	West Riverside County	St. Paul	Chicago	Manhattan/ Bronx	Rockland County	Baltimore	Winston-Salem
PM2.5	H	M	VH	L	M	M	L	M	M
PM10	H	M	VH	M	H	H	M	M	L
CO	H	M	H	M	M	H	L	L	M
NO2	H	H	VH	L	M	H	L	L	L
Ozone	H	M	VH	L	M	M	M	H	VH
SO2	L	L	L	M	M	H	H	M	M
Urban contribution	+	+	+	-	+	+	-	+	-
Long-Range Transport	-	-	-	+	+	+	+	+	+

* = Site of newly recruited subjects; other subjects already in MESA cohort
L=Low, M=Medium, H=High, VH=Very High
e.g., for PM2.5: L= (-10 µg/m³), M= (-15 µg/m³), H= (-22 µg/m³), VH= (-30 µg/m³) annual averages

Future Directions

This scientific effort will contribute to the published literature on PM health effects and exposure during the later part of this decade. Future studies will use the knowledge gained to refine individual exposure estimates using exposure models and to develop specific hypotheses regarding the role of PM sources and constituents in causing disease.

Impact and Outcomes

This body of research will:

- * Provide more precise estimates of the health risks associated with long-term exposure to ambient PM₁₀, PM_{2.5} and ultrafine particles in different regions in the U.S. and within urban areas.
- * Stimulate hypotheses regarding possible biologic mechanisms responsible for the mortality effects on cardiovascular health.
- * Provide estimates of the increased risk posed by concurrent disease, poor health status, older age and other characteristics.
- * Provide more precise estimates of long-term exposure to PM informed by variation in ambient concentration across space and time.
- * Provide comparisons of health risks resulting from long-term and short-term PM exposure.
- * Increase understanding of the effect of concurrent exposure to gaseous pollutants on the magnitude of PM-related risk.
- * Increase understanding of the role played by identified PM sources, especially mobile sources and regional influences.
- * Provide opportunities to evaluate the anticipated reduction in health risk resulting from regulatory and voluntary risk reduction actions.