

US EPA ARCHIVE DOCUMENT

Health Effects of Particulate Matter Air Pollution

C. Arden Pope III

Mary Lou Fulton Professor of Economics



Presented at
EPA Wood Smoke Health Effects Webinar
July 28, 2011

What we breath impacts our health

- Pure Air--nitrogen (78%),Oxygen (21%), Argon, CO₂. . .

+

- Various gaseous pollutants including:
 - SO₂, NO₂, CO, O₃ . . .

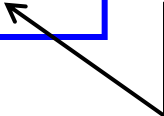
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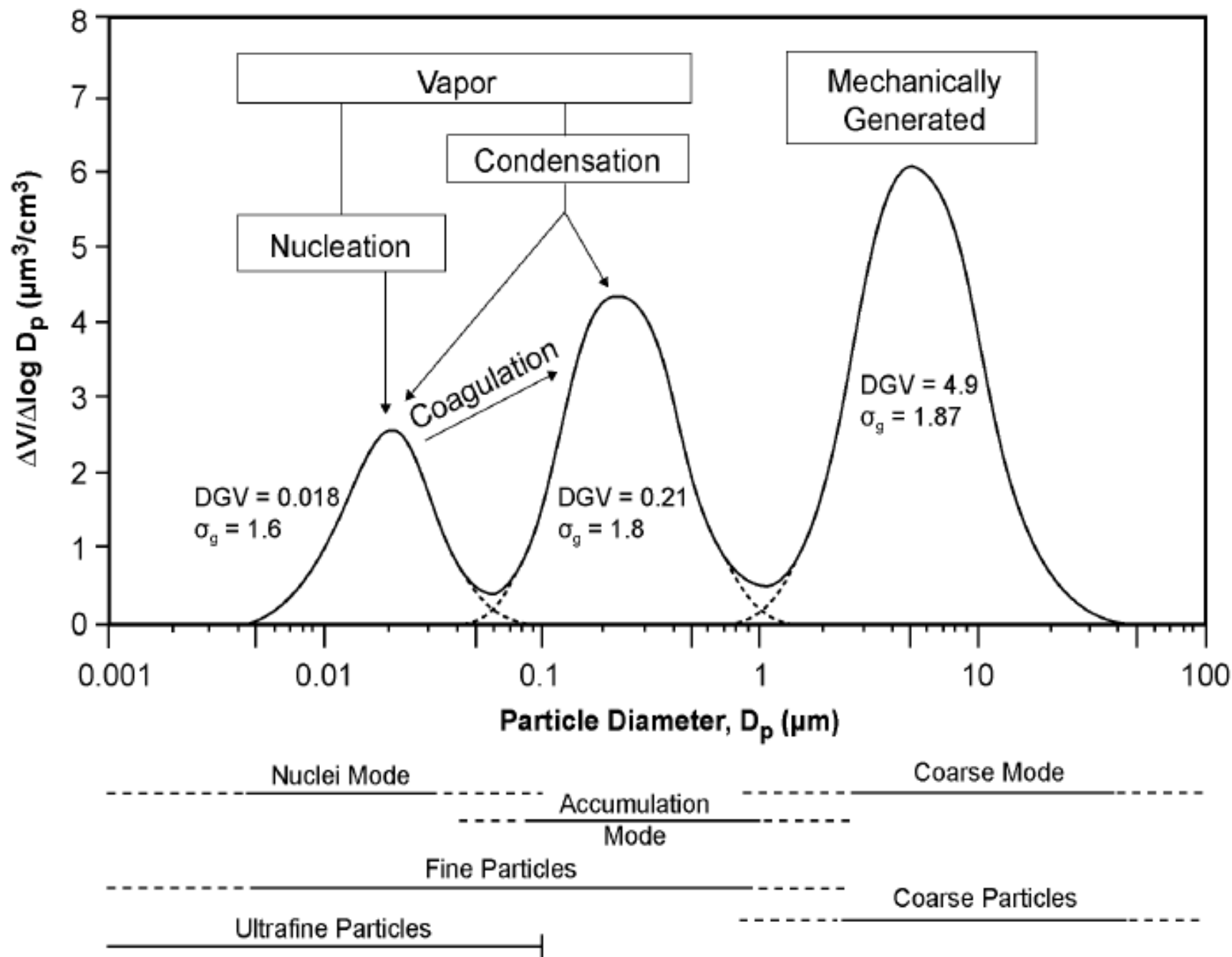
- **Particulate matter:**
 - Course particles (> 2.5 μm in diameter)
 - **Fine particles (< 2.5 μm in diameter)**

+

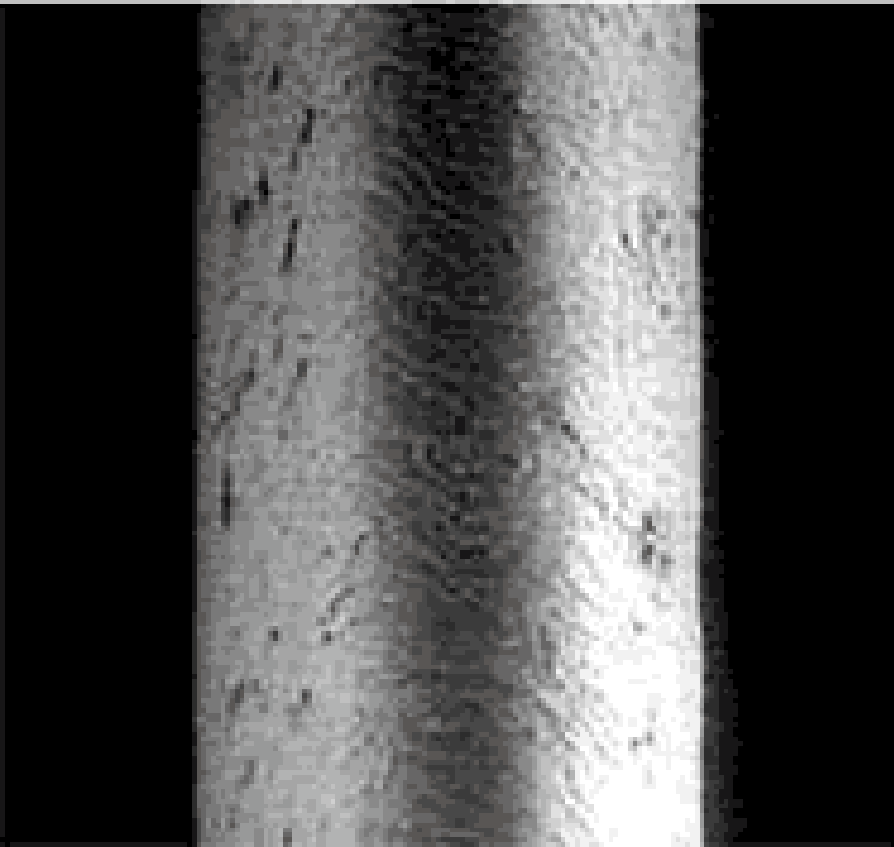
- Other air toxics

Wood
Smoke

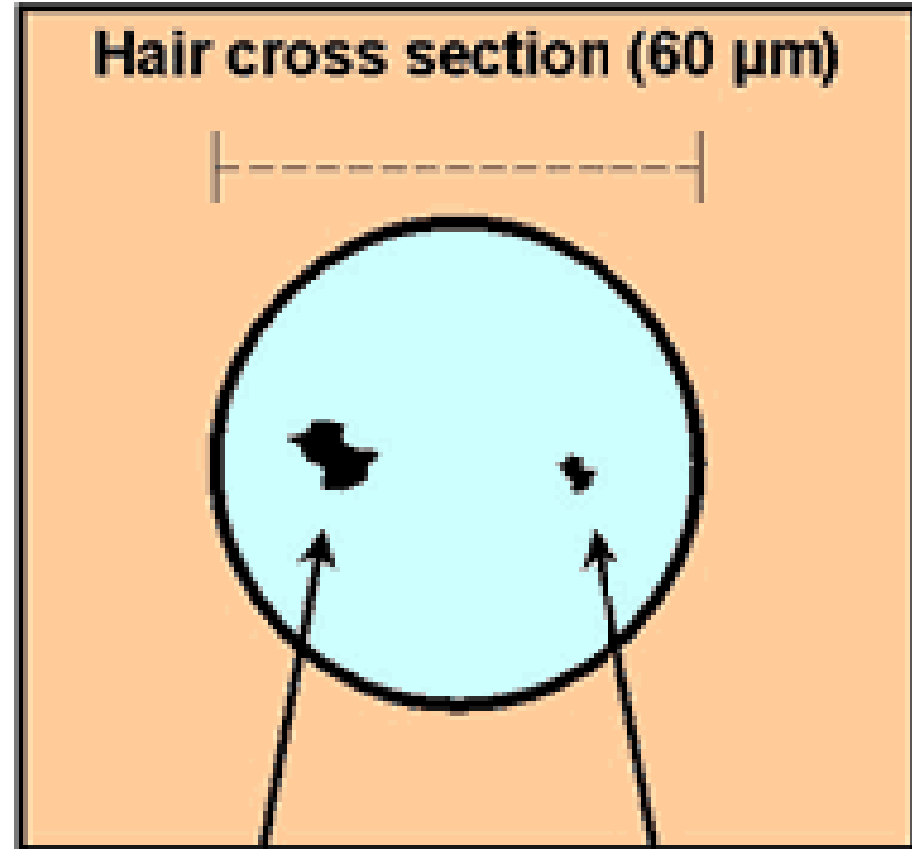




How small are fine particles?

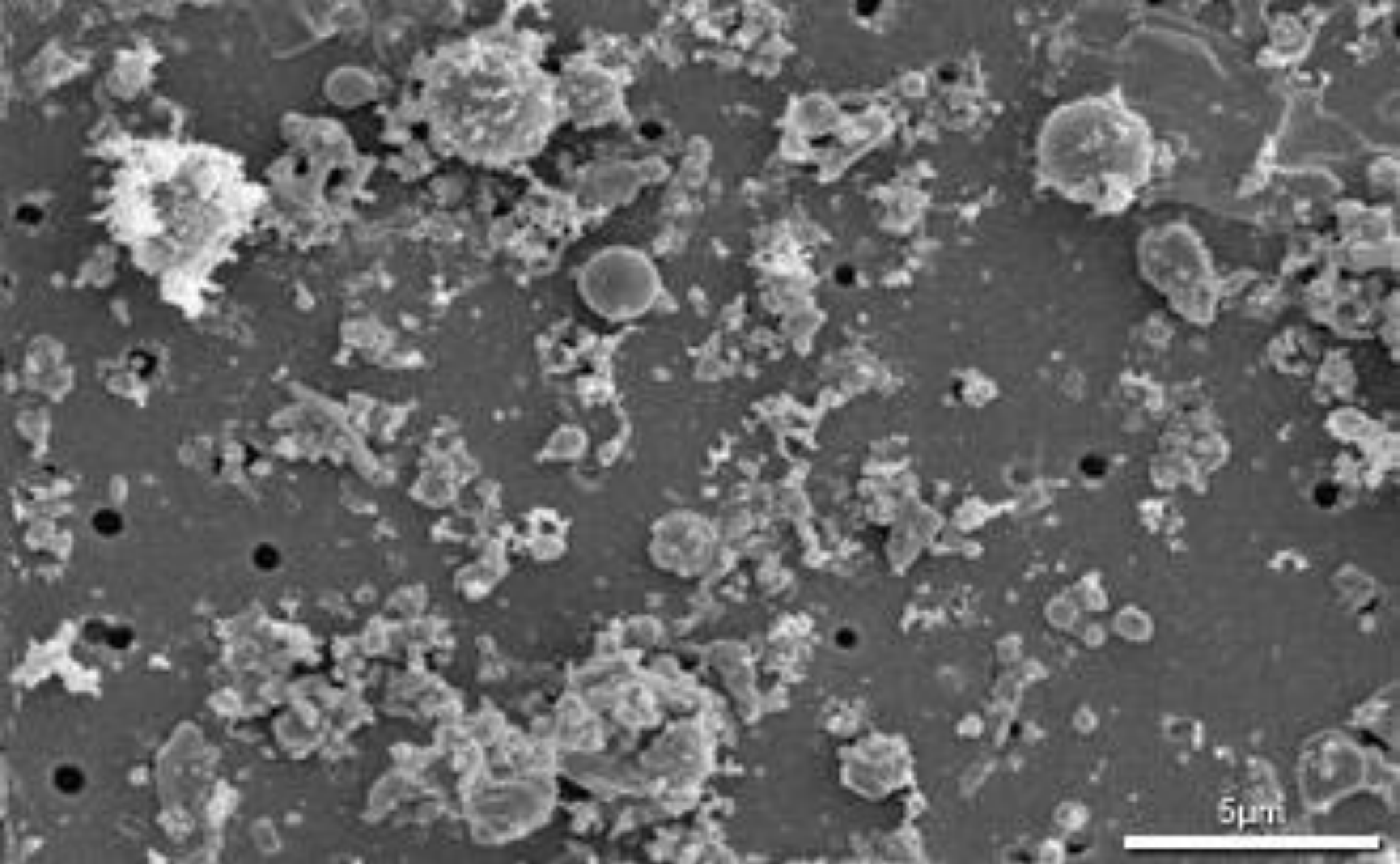


Human Hair
(60 μm diameter)



PM₁₀
(10 μm)

PM_{2.5}
(2.5 μm)



Magnified ambient particles (www.nasa.gov/vision/earth/environment)



This presentation not organized chronologically, but methodologically

Studies of short-term exposure (hours-days)

- Episode
- Population-based daily time-series
- Panel-based acute exposure
- Case-crossover

Studies of long-term exposure (years-decades)

- Population-based cross-sectional
- Cohort-based mortality
- Cohort- and panel-based morbidity
- Case-control studies

Intervention/natural experiment (months-years)

Controlled experimental human and animal

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Q
&
A

The diagram consists of a vertical box on the right containing the text 'Q & A' in red. Three red arrows originate from this box and point to specific parts of the text on the left. The first arrow points from the 'Q' to the 'Case-crossover' study type. The second arrow points from the '&' to the 'Cohort- and panel-based morbidity' study type. The third arrow points from the 'A' to the 'Controlled experimental human and animal' study type.

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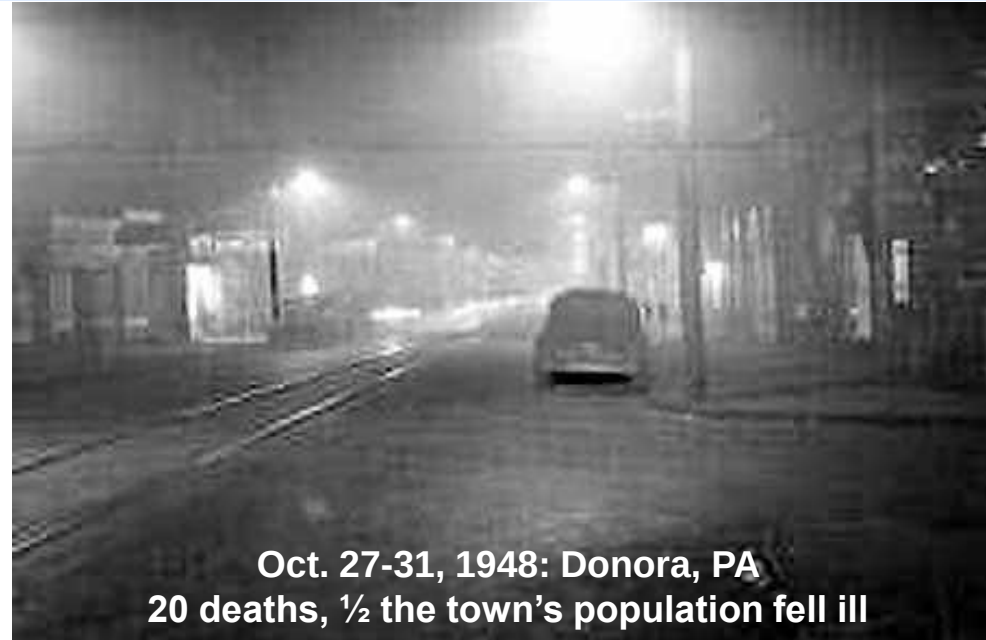
Studies of long-term exposure (years-decades)

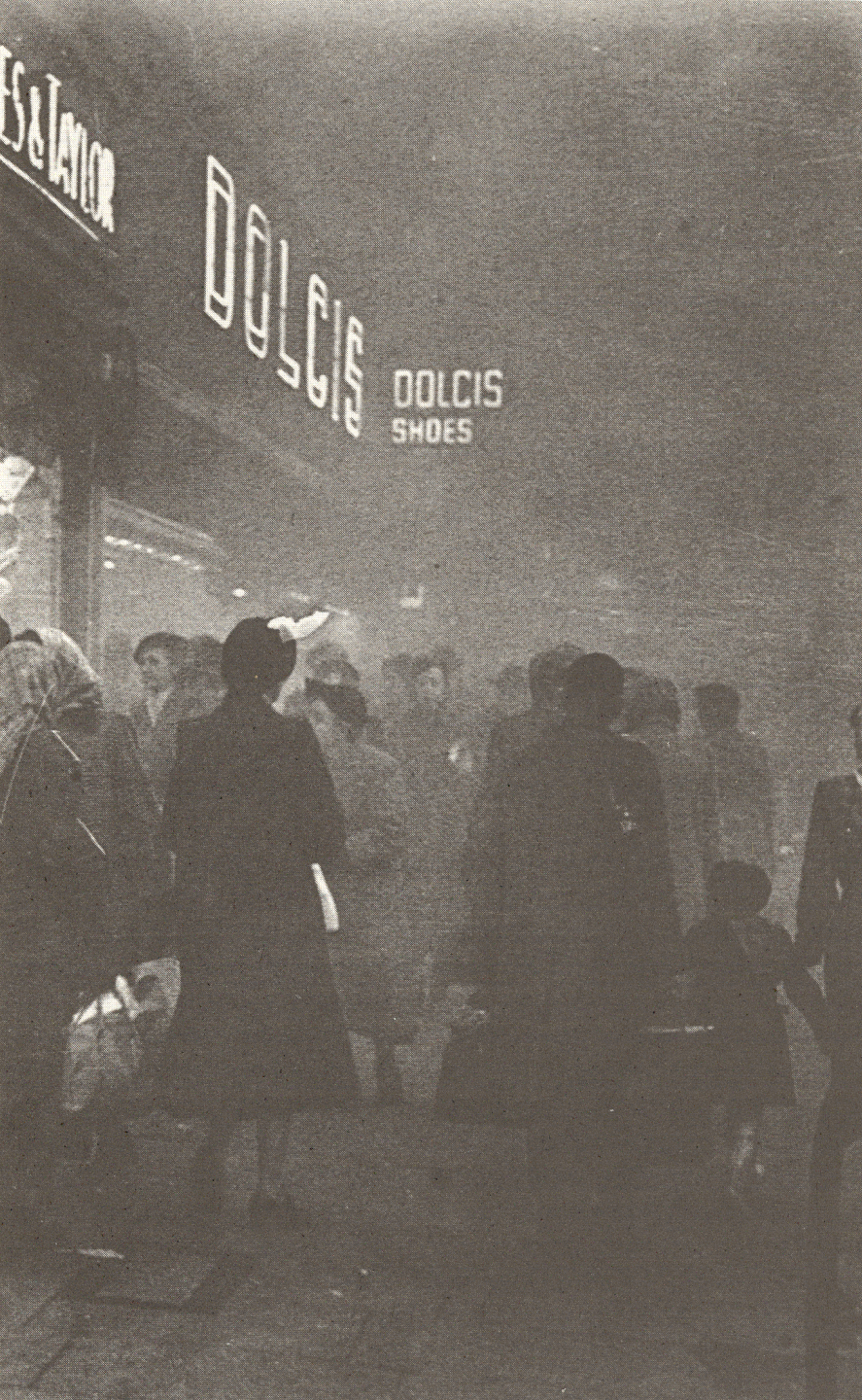
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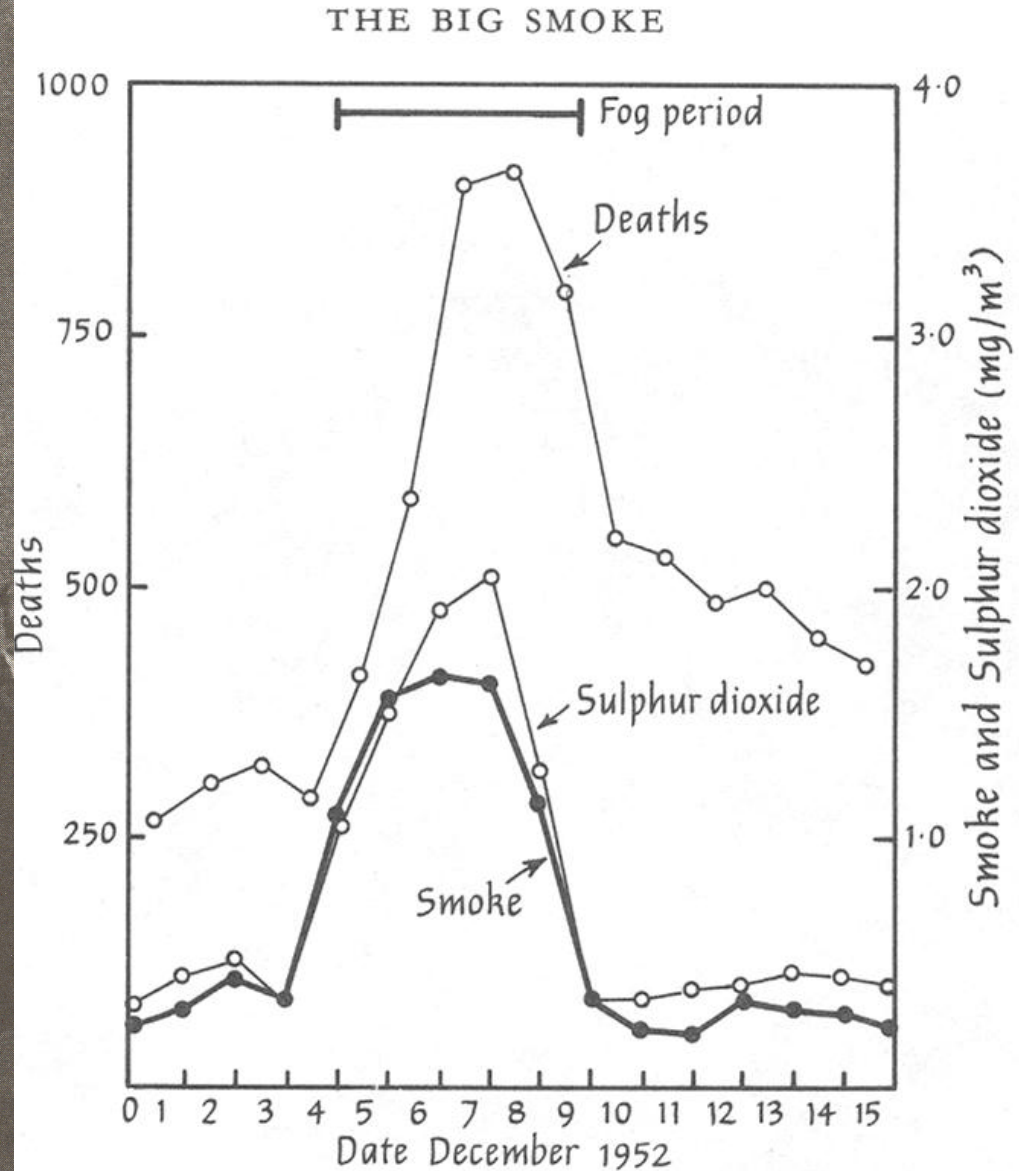
Controlled experimental human and animal

Early “**Killer smog**” episodes demonstrated that air pollution at extreme levels can contribute to respiratory and cardiovascular disease and death





London Fog Episode, Dec. 1952



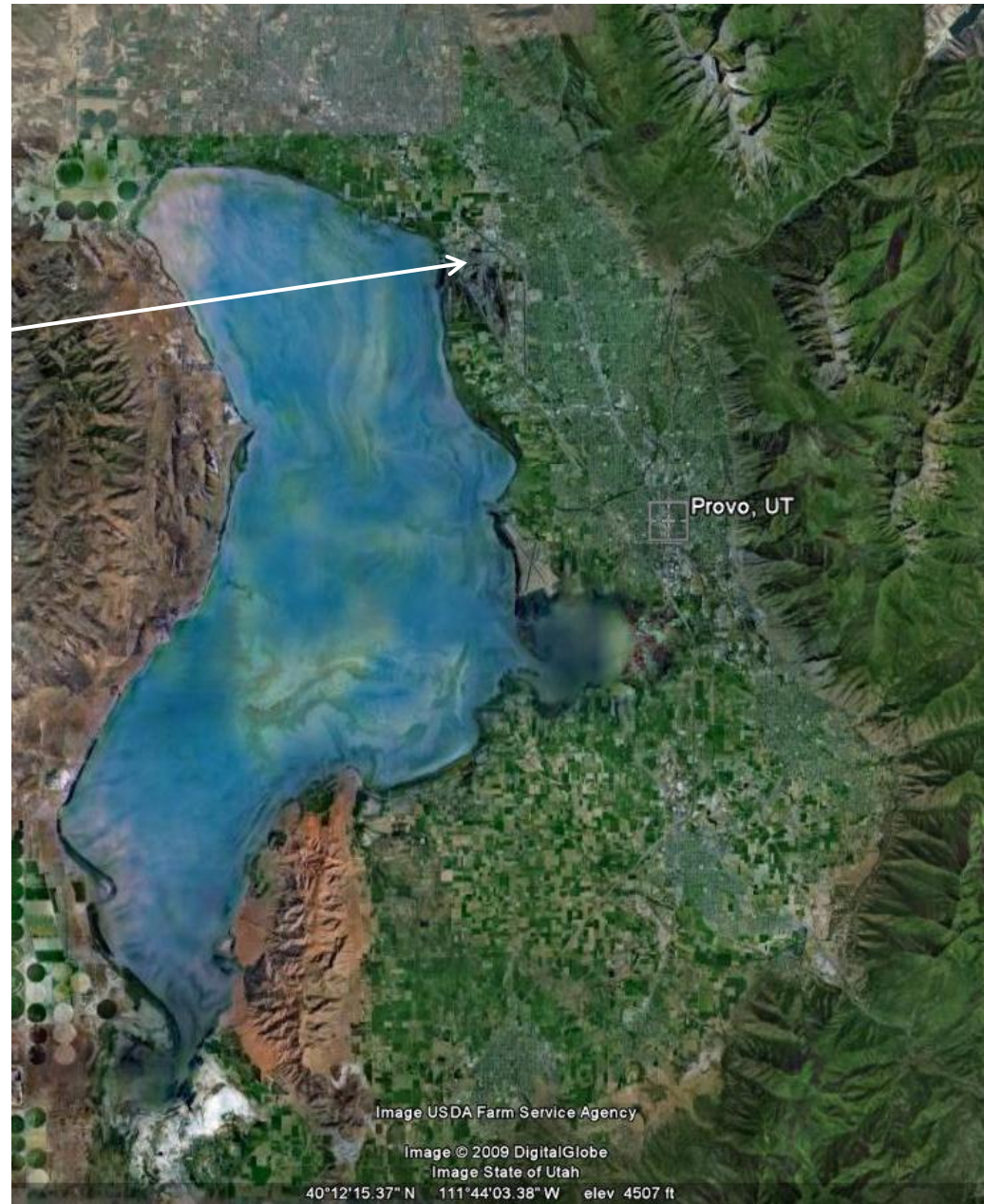
From: Brimblecombe P. The Big Smoke, Methu

Utah Valley, 1980s

- Winter **inversions** trap local pollution
- Natural test chamber



- Local Steel mill contributed ~50% $PM_{2.5}$
- Shut down July 1986-August 1987
- Natural Experiment



Large difference in air quality when inversions trap air pollution in valley

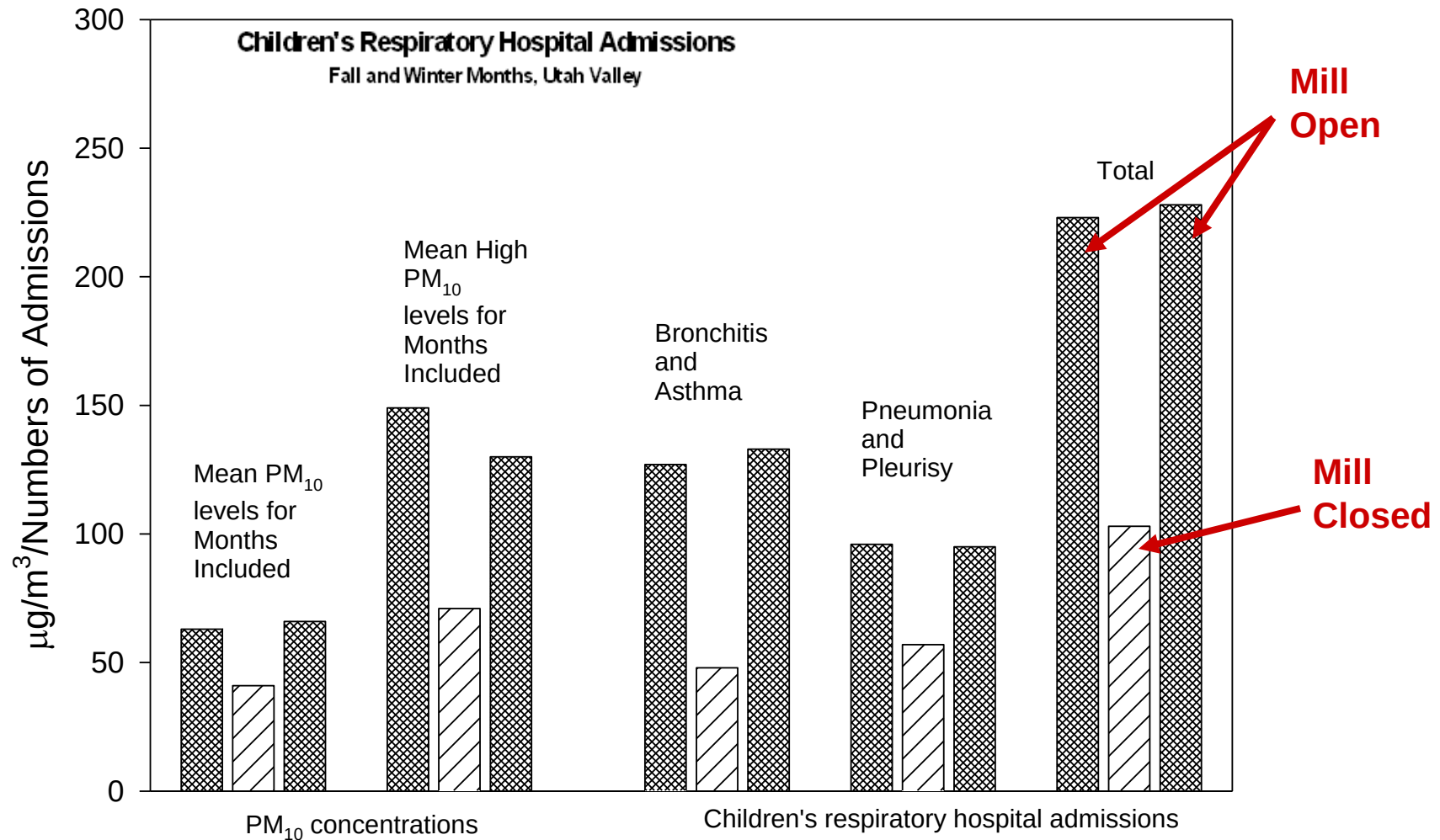
Utah Valley: Clean day



Utah Valley: Dirty day
($\text{PM}_{10} = 220 \mu\text{g}/\text{m}^3$)



When the steel mill was open, total children's hospital admissions for respiratory conditions **approx. doubled.**



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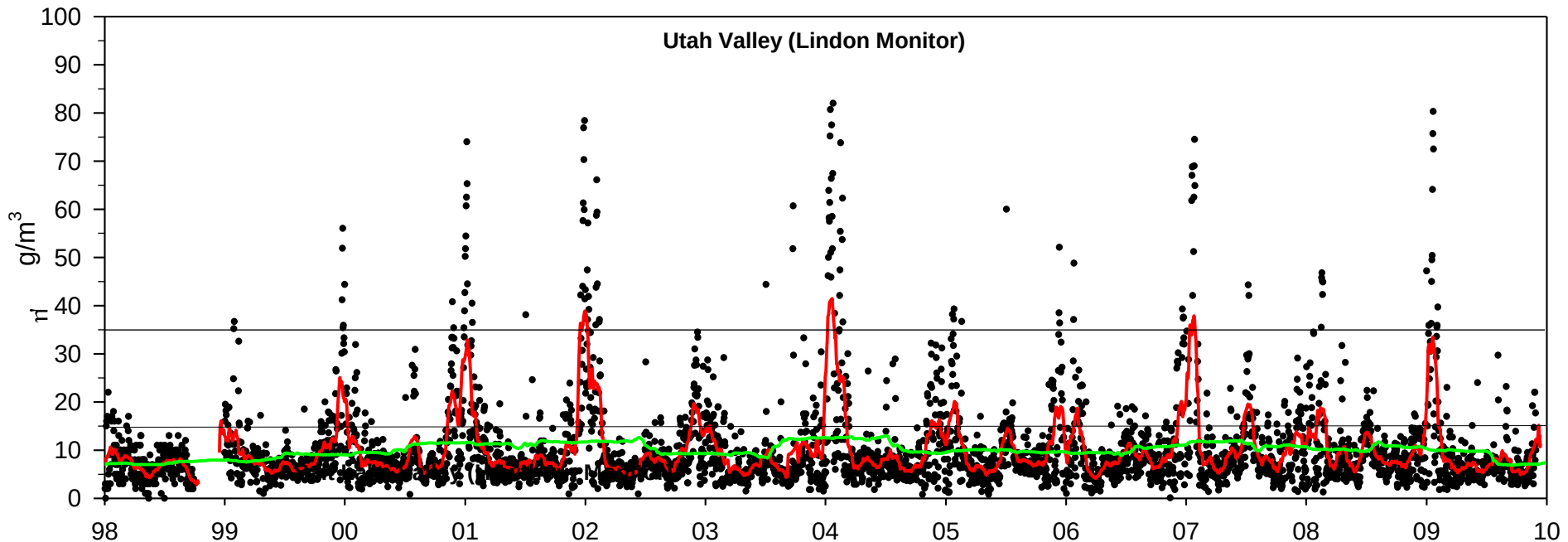
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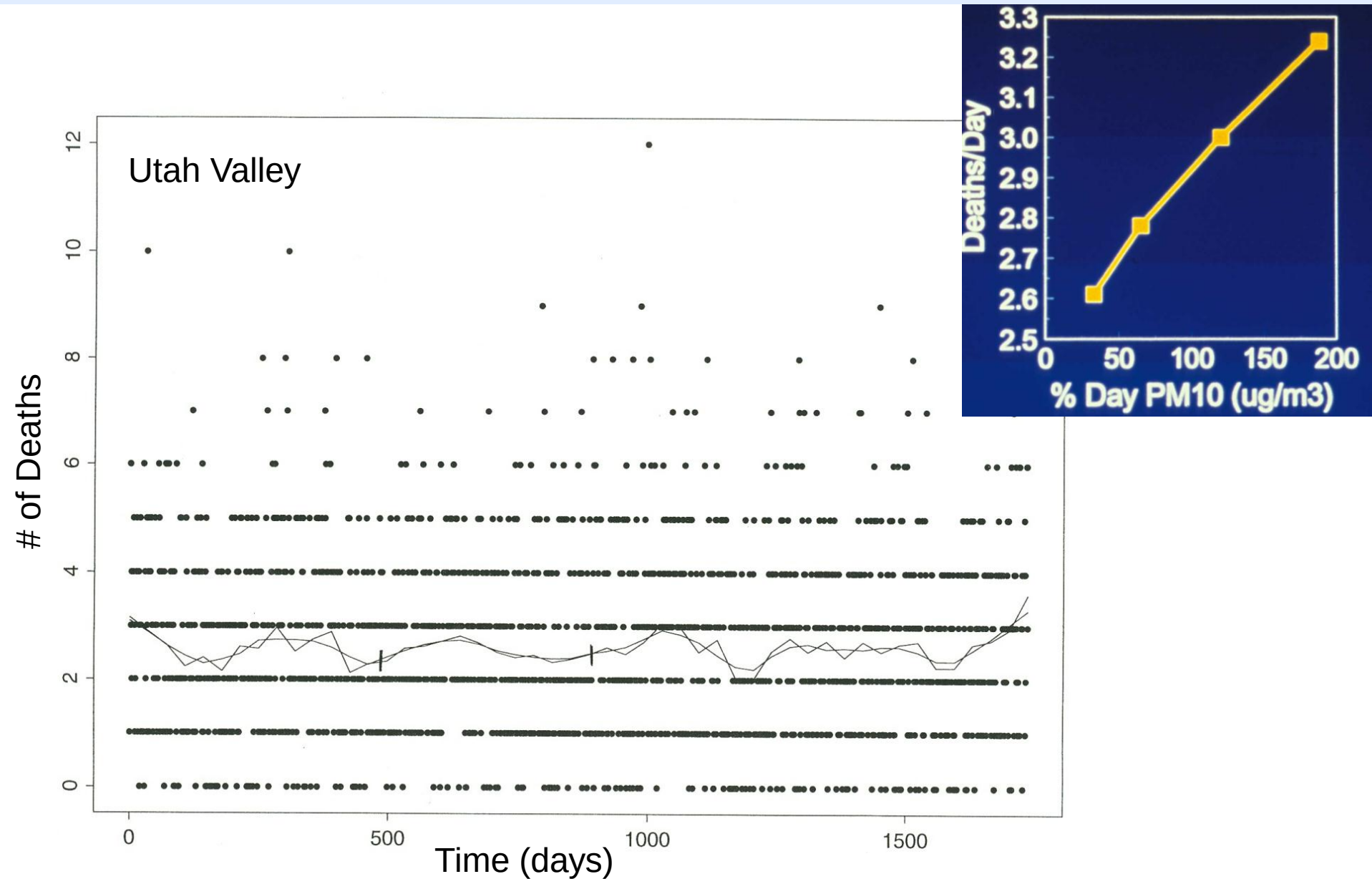
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Health studies take advantage of **highly variable** air pollution levels that result from inversions.



PM_{2.5} concentrations January 1 1998-December 12 2009. Black dots, 24-hr PM_{2.5}; Red line, 30-day moving average PM_{2.5}; Green line, 1-yr moving average PM_{2.5}.

Daily changes in air pollution $\longrightarrow$ daily death counts



Poisson Regression

Count data (non-negative integer values). Counts of independent and random occurrences classically modeled as being generated by a Poisson process with a Poisson distribution:

$$\text{Prob}(Y = r) = e^{(-\lambda)} \frac{\lambda^r}{r!}$$

Note: λ = mean and variance. If λ is constant across time, we have a stationary Poisson process. If λ changes over time due to changes in pollution (P), time trends, temperature, etc., this non-stationary Poisson process can model as:

$$\ln \lambda_t = \alpha + \beta(w_0 P_t + w_1 P_{t-1} + w_2 P_{t-2} + \dots) + s^1(t) + s^2(\text{temp}_t) + \dots$$

Modeling controversies

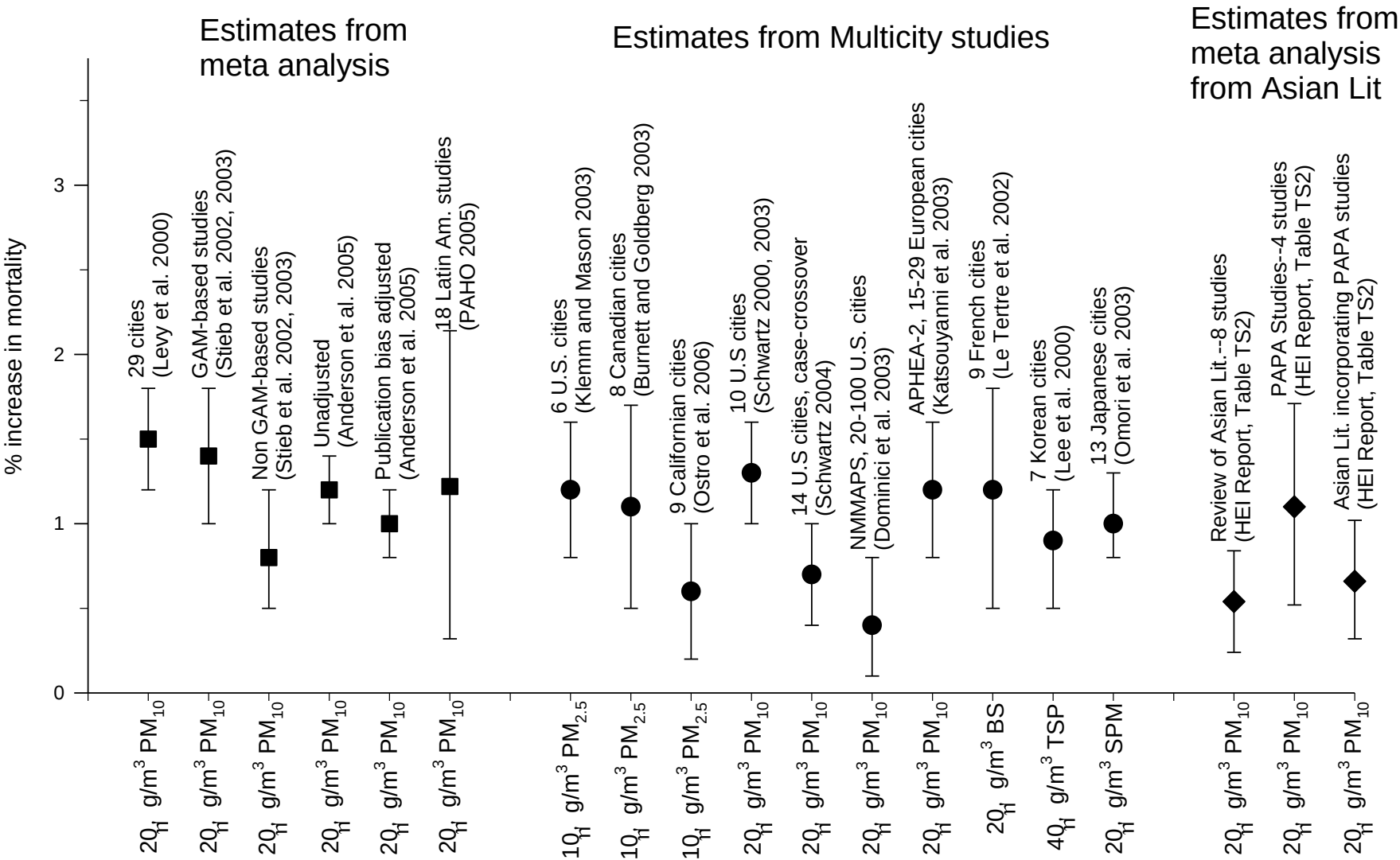
How to construct the lag structure? (MA, PDL, etc.)

How aggressive do you fit time? (harmonics vs GAMs, df, span, loess, cubic spline, etc.)

How to control for weather? (smooths of temp & RH, synoptic weather, etc.)

Also: How to combine or integrate information from multiple cities

Daily time-series studies ***of over 200 cities***



10 $\mu g/m^3$ $PM_{2.5}$ or 20 $\mu g/m^3$ PM_{10} → 0.4% to 1.5% increase in relative risk of mortality—Small but remarkably consistent across meta-analyses and multi-city studies.

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Panel studies of asthmatics and non-asthmatics



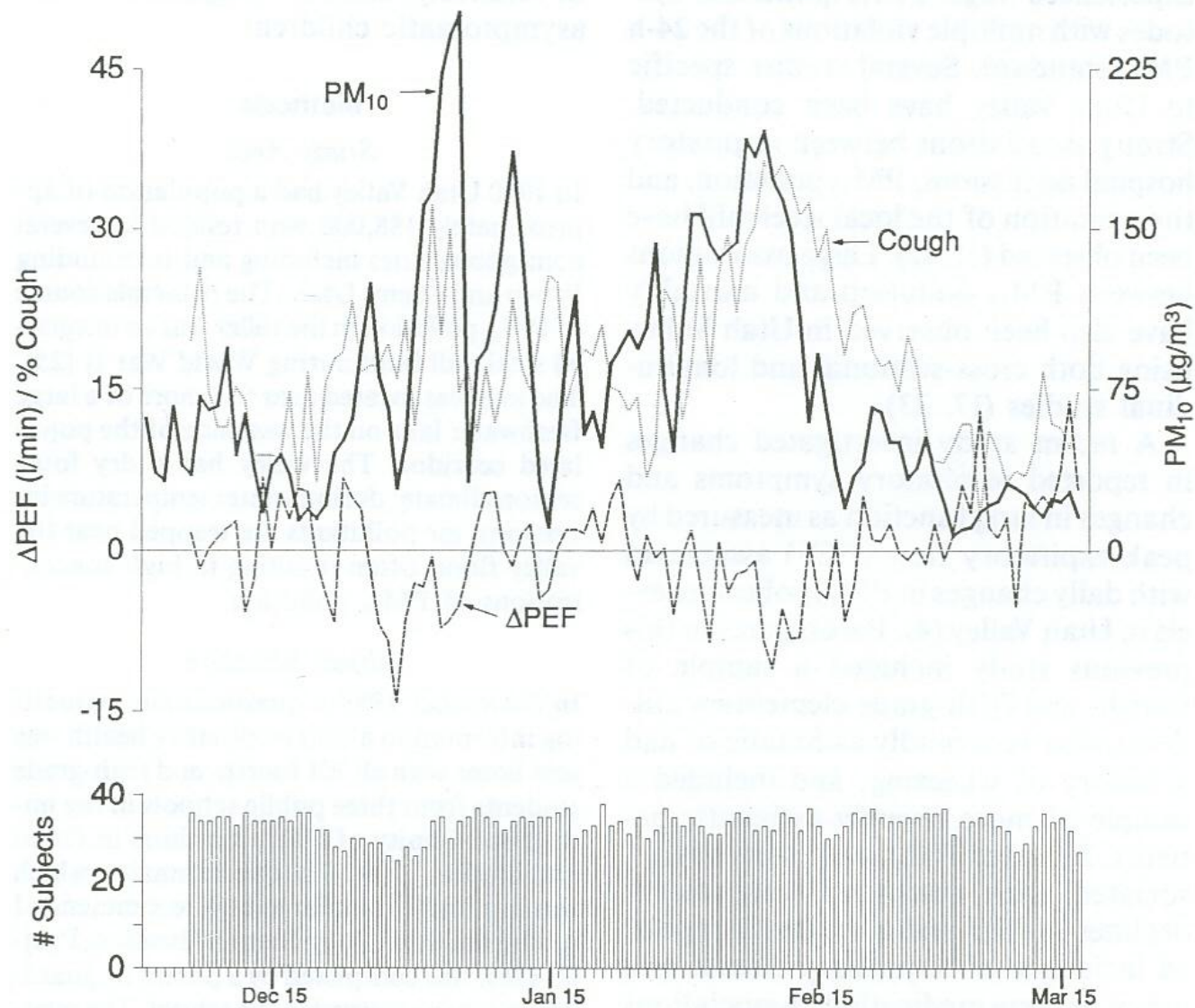


Fig. 1. Daily PM₁₀ levels, mean peak expiratory flow deviations (ΔPEF), percentage who reported cough, and number of participants for the symptomatic sample.

Summary of early Utah Valley epidemiological studies

Health effects

- **Increased hospital admissions**
- **Increased respiratory symptoms**
- **Reduced lung function**
- **Increased school absences**
- **Increased respiratory and cardiovascular deaths**

Study References

Pope (1989) Am. J. Public Health
Pope (1991) Arch. Environ. Health

Pope, Dockery, Spengler, Raizenne
(1991) Am. Rev. Resp. Dis.

Pope, Dockery (1992)
Am. Rev. Resp. Dis.

Pope, Kanner (1993)
Am. Rev. Resp. Dis.

Ransom, Pope (1992)
Environ. Res

Pope, Schwartz, Ransom (1992)
Arch. Environ. Health

Pope, Kalkstein (1996)
Environ. Health Perspect.

Pope, Hill, Villegas (1999)
Environ. Health Perspect.



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Jeffrey Anderson

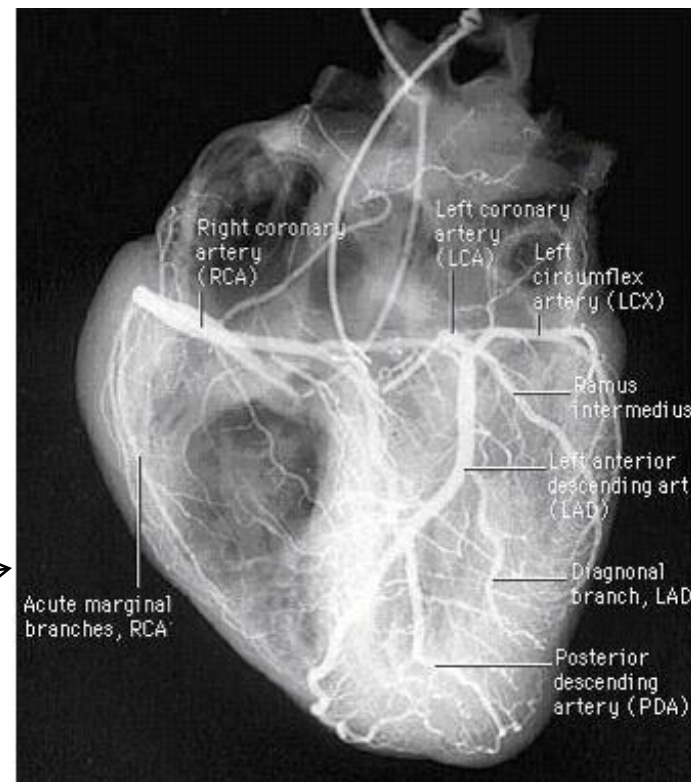
Ischemic Heart Disease Events Triggered by Short-Term Exposure to Fine Particulate Air Pollution

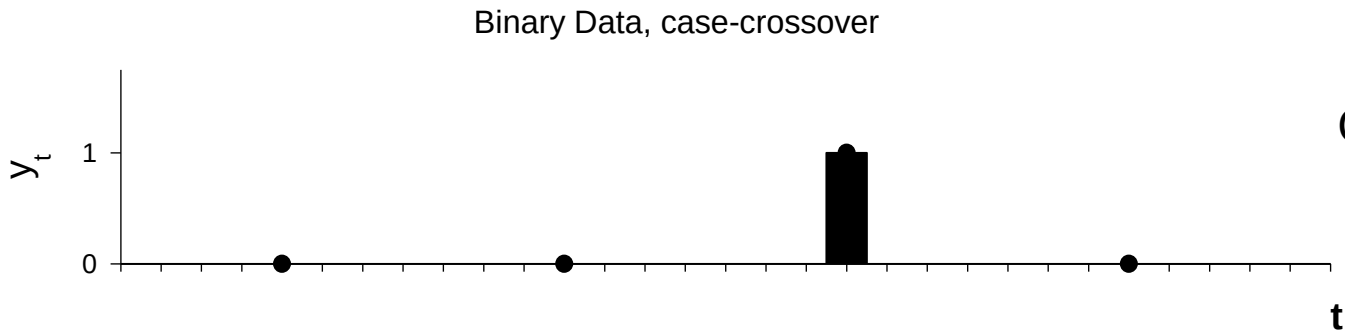
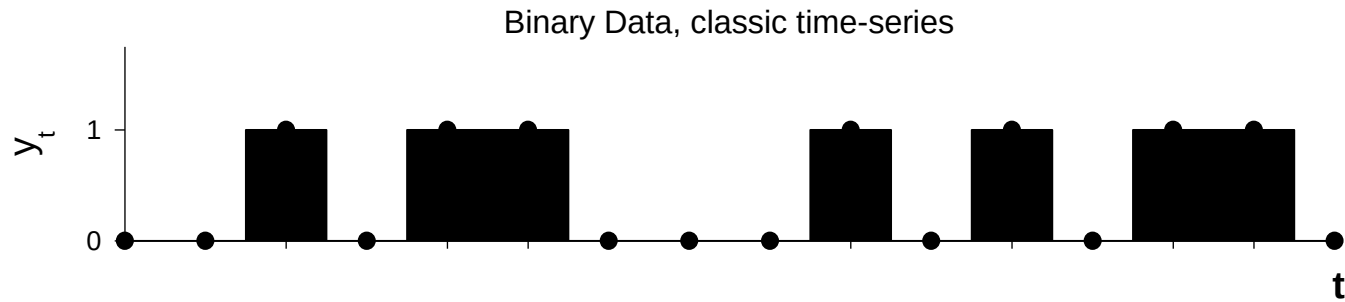
C. Arden Pope III, PhD; Joseph B. Muhlestein, MD; Heidi T. May, MSPH; Dale G. Renlund, MD; Jeffrey L. Anderson, MD; Benjamin D. Horne, PhD, MPH

Methods:

Case-crossover study of acute ischemic coronary events (heart attacks and unstable angina) in 12,865 well-defined and followed up cardiac patients who lived on Utah's Wasatch Front

...and who underwent coronary angiography





Conditional Logistic Reg.

Each subject serves as his/her own control.

Control for subject-specific effects, day of week, season, time-trends, etc.—by matching

Conditional logistic regression:

$$\ln \left(\frac{\text{Prob}(Y_t = 1)}{1 - \text{Prob}(Y_t = 1)} \right) =$$

$$\alpha_1 + \alpha_2 + \alpha_3 + \dots + \alpha_{12,865} + \beta(w_0P_t + w_1P_{t-1} + w_2P_{t-2} + \dots)$$

Control by matching for:

All cross-subject differences

(in this case, 12,865 subject-level fixed effects),

Season and/or month of year,

Time trends,

Day of week

Modeling controversies: How to select control or referent periods. Time stratified referent selection approach (avoids bias that can occur due to time trends in exposure) (**Holly Janes, Lianne Sheppard, Thomas Lumley** Statistics in Medicine and Epidemiology 2005)

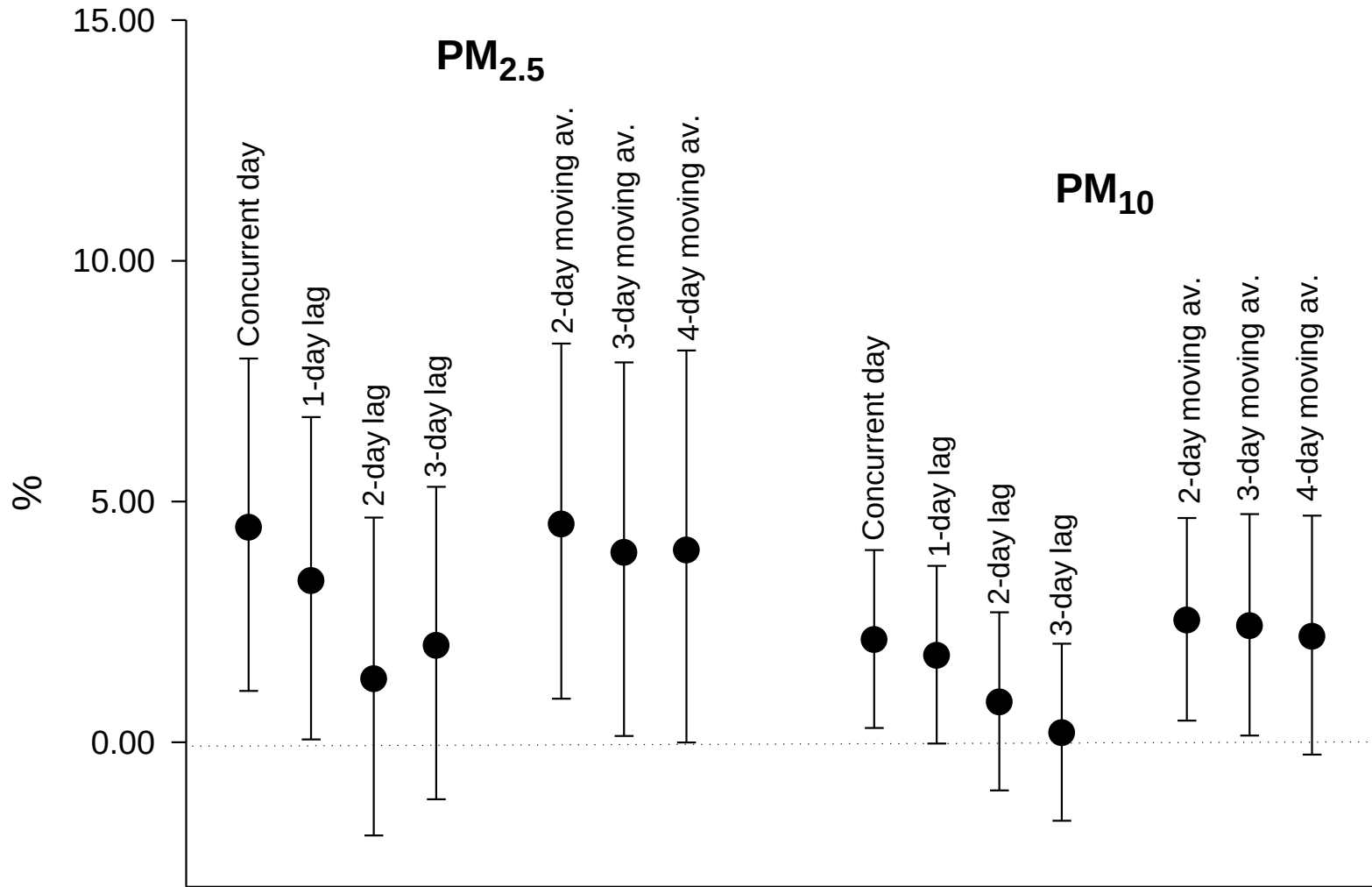


Figure 1. Percent increase in risk (and 95% CI) of acute coronary events associated with 10 $\mu\text{g}/\text{m}^3$ of $\text{PM}_{2.5}$, or PM_{10} for different lag structures.

Short-term PM exposures contributed to acute coronary events, especially among patients with underlying coronary artery disease.

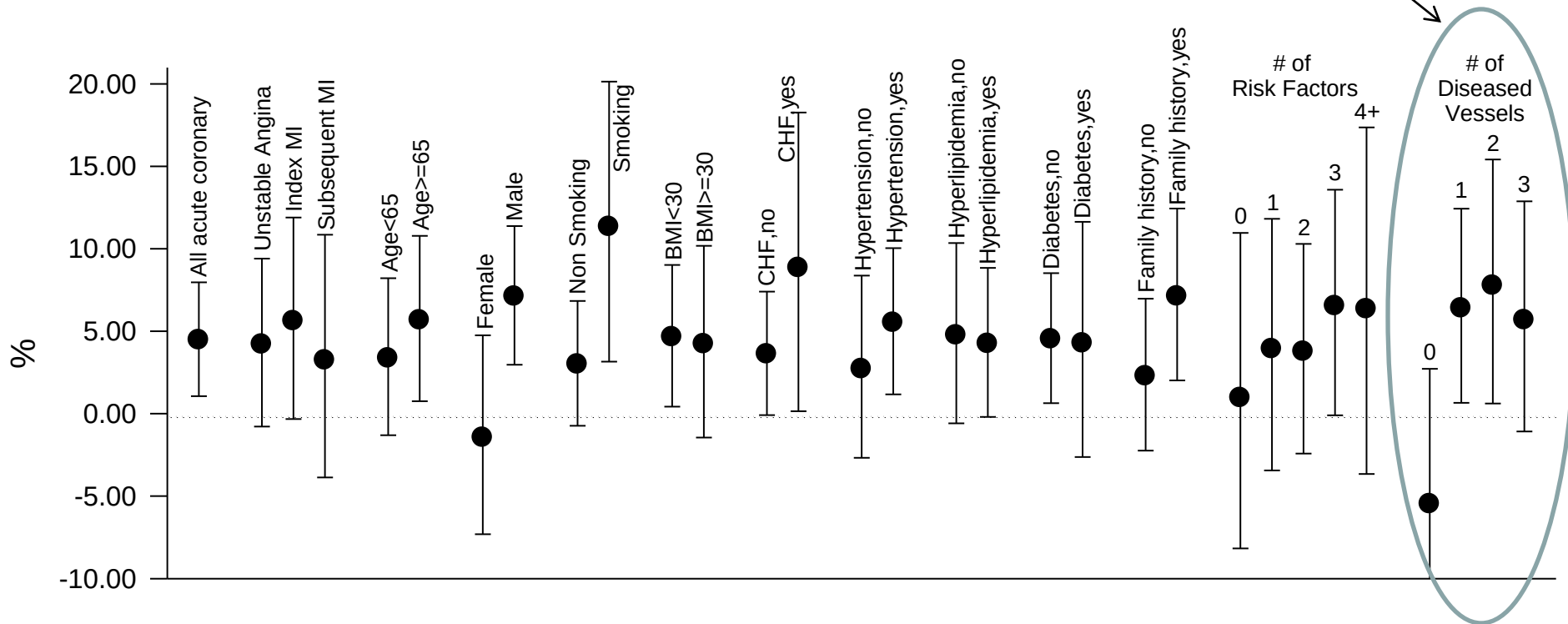


Figure 2. Percent increase in risk (and 95% CI) of acute coronary events associated with 10 µg/m³ of PM_{2.5}, stratified by various characteristics.

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Any
Questions?



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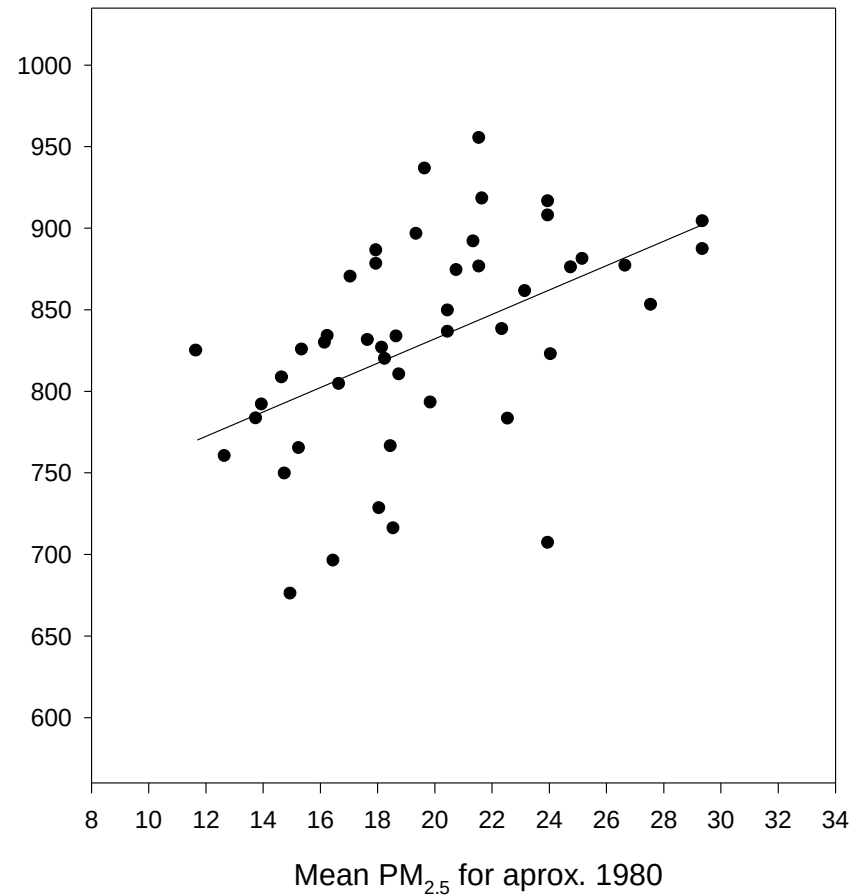
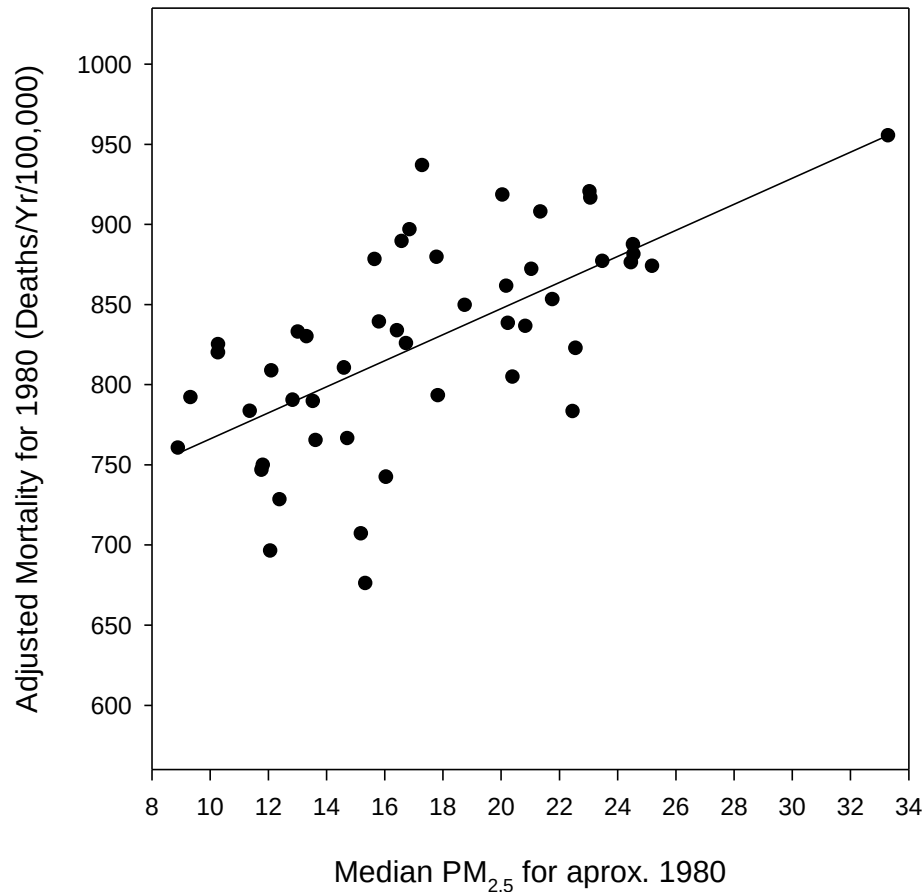
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Age-, sex-, and race- adjusted population-based mortality rates in U.S. cities for 1980 plotted over various indices of particulate air pollution (From Pope 2000).



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An Association Between Air Pollution and Mortality in Six U.S. Cities



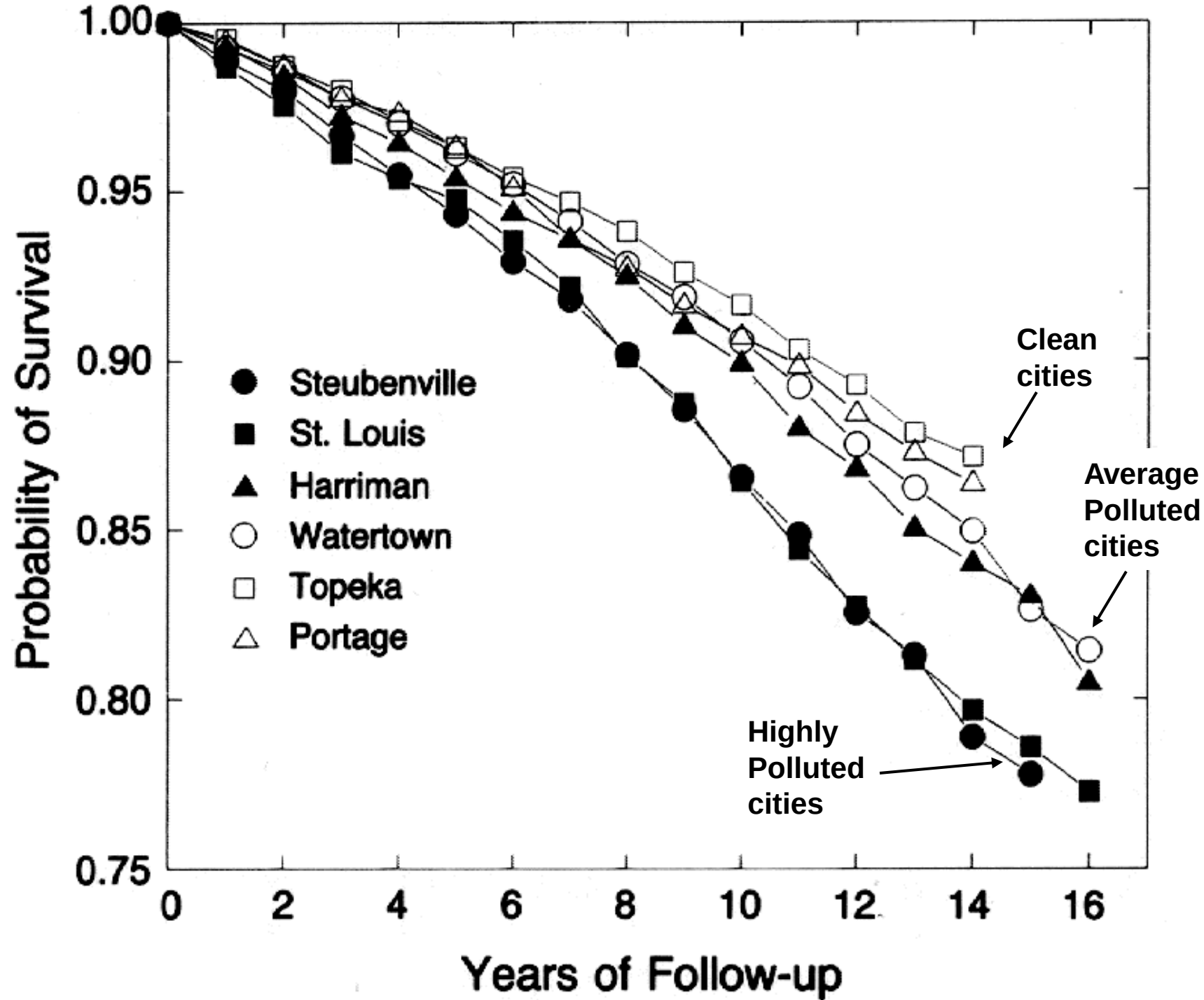
The NEW ENGLAND
JOURNAL of MEDICINE 1993

Dockery DW, Pope CA III, Xu X, Spengler JD,
Ware JH, Fay ME, Ferris BG Jr, Speizer FE.



Methods:

- 14-16 yr prospective follow-up of 8,111 adults living in six U.S. cities.
- Monitoring of TSP PM_{10} , $PM_{2.5}$, SO_4 , H^+ , SO_2 , NO_2 , O_3 .
- Data analyzed using survival analysis, including Cox Proportional Hazards Models.
- Controlled for individual differences in: age, sex, smoking, BMI, education, occupational exposure.



Cox Proportional Hazards Survival Model

Cohort studies of outdoor air pollution have commonly used the CPH Model to relate survival experience to exposure while simultaneously controlling for other well known mortality risk factors. The model has the form

$$\lambda_i^{(l)}(t) = \lambda_0^{(l)}(t) \exp(\beta^T x_i^{(l)}(t))$$

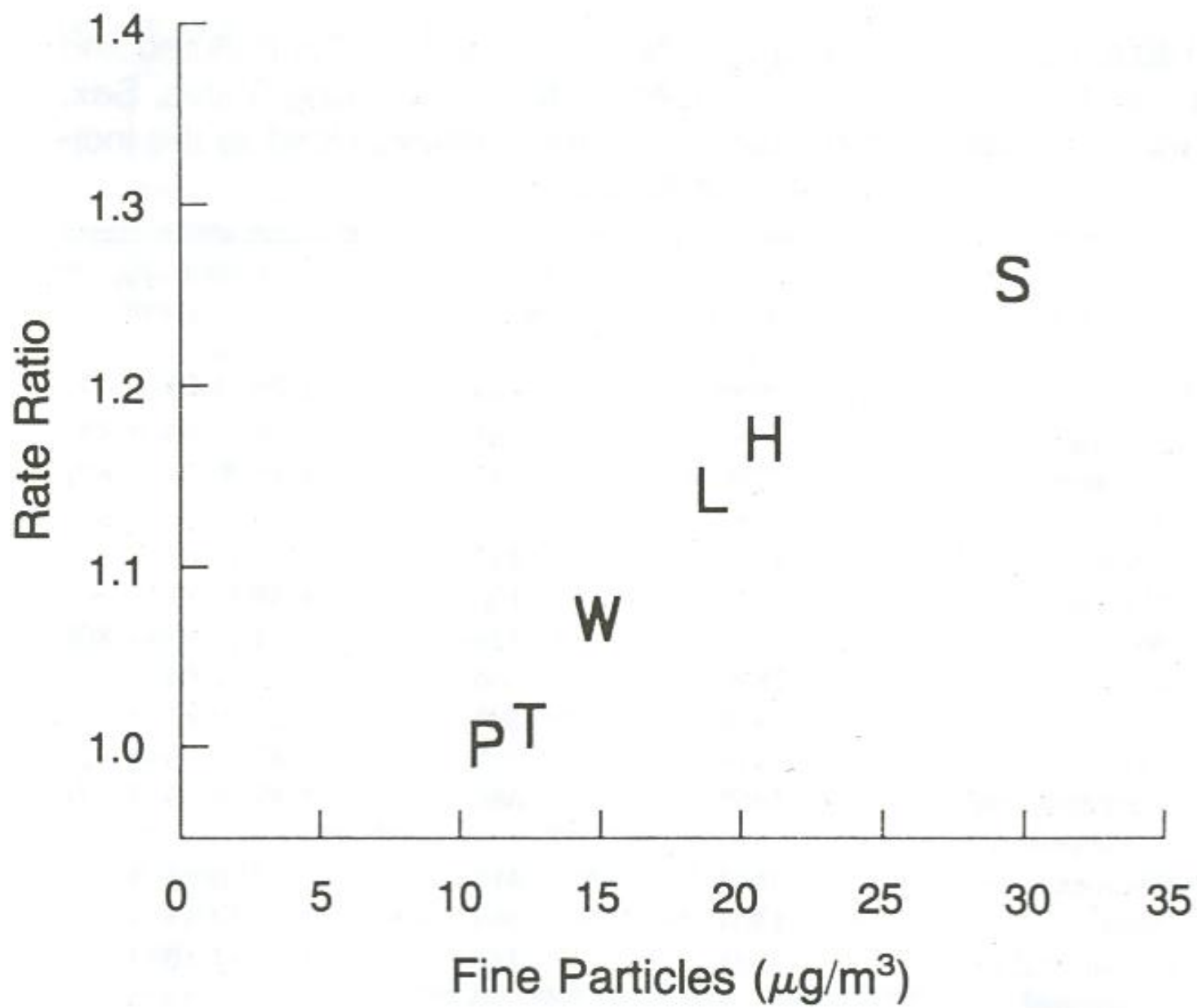
Hazard function or instantaneous probability of death for the j^{th} subject in the l^{th} strata.

Baseline hazard function, common to all subjects within a strata.

Regression equation that modulates the baseline hazard. The vector $X_i^{(l)}$ contains the risk factor information related to the hazard function by the regression vector β which can vary in time.

Adjusted risk ratios (and 95% CIs) for cigarette smoking and PM_{2.5}

Cause of Death	Current Smoker, 25 Pack years	Most vs. Least Polluted City
All	2.00 (1.51-2.65)	1.26 (1.08-1.47)
Lung Cancer	8.00 (2.97-21.6)	1.37 (0.81-2.31)
Cardio- pulmonary	2.30 (1.56-3.41)	1.37 (1.11-1.68)
All other	1.46 (0.89-2.39)	1.01 (0.79-1.30)



Particulate Air Pollution as a Predictor of Mortality in a Prospective Study of U.S. Adults



Michael Thun

Pope CA III, Thun MJ, Namboodiri MM,
Dockery DW, Evans JS, Speizer FE, Heath CW Jr.



AMERICAN JOURNAL OF

Respiratory and

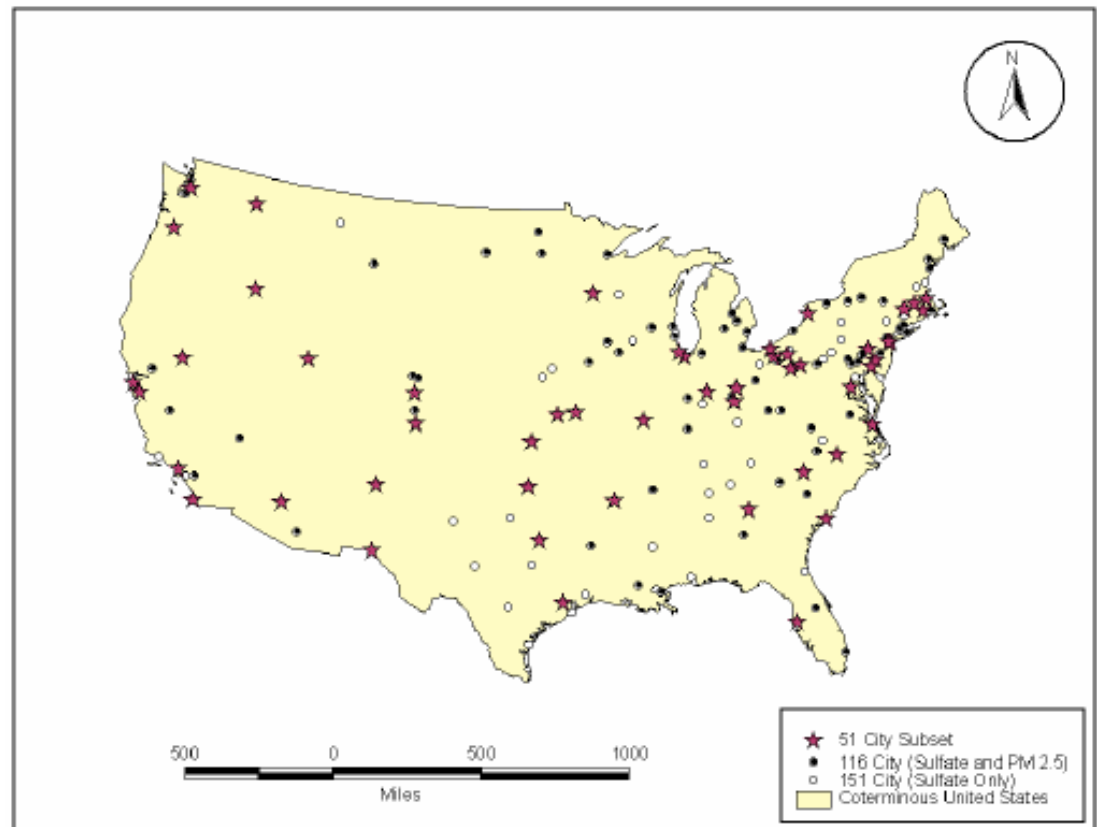
Critical Care Medicine®

1995



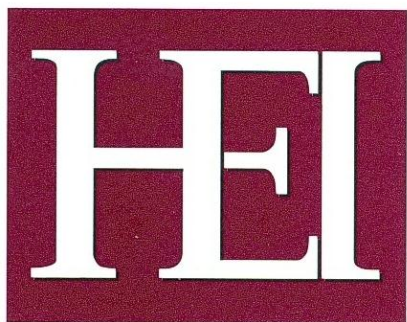
Clark Heath

Methods: Linked and analyzed ambient air pollution data from 51-151 U.S. metro areas with risk factor data for over 500,000 adults enrolled in the ACS-CPSII cohort.



Adjusted mortality risk ratios (and 95% CIs) for cigarette smoking the range of sulfates and fine particles

Cause of Death	Current Smoker	Sulfates	Fine Particles
All	2.07 (1.75-2.43)	1.15 (1.09-1.22)	1.17 (1.09-1.26)
Lung Cancer	9.73 (5.96-15.9)	1.36 (1.11-1.66)	1.03 (0.80-1.33)
Cardio-Pulmonary	2.28 (1.79-2.91)	1.26 (1.16-1.37)	1.31 (1.17-1.46)
All other	1.54 (1.19-1.99)	1.01 (0.92-1.11)	1.07 (0.92-1.24)



HEALTH
EFFECTS
INSTITUTE

July 2000



Dan Krewski
Rick Burnett
Mark Goldberg
and 28 others

SPECIAL REPORT

Reanalysis of the Harvard Six Cities Study and the American Cancer Society Study of Particulate Air Pollution and Mortality

A Special Report of the Institute's Particle
Epidemiology Reanalysis Project

Lung Cancer, Cardiopulmonary Mortality, and Long-term Exposure to Fine Particulate Air Pollution

C. Arden Pope III, PhD

Richard T. Burnett, PhD

Michael J. Thun, MD

Eugenia E. Calle, PhD

Daniel Krewski, PhD

Kazuhiko Ito, PhD

George D. Thurston, ScD

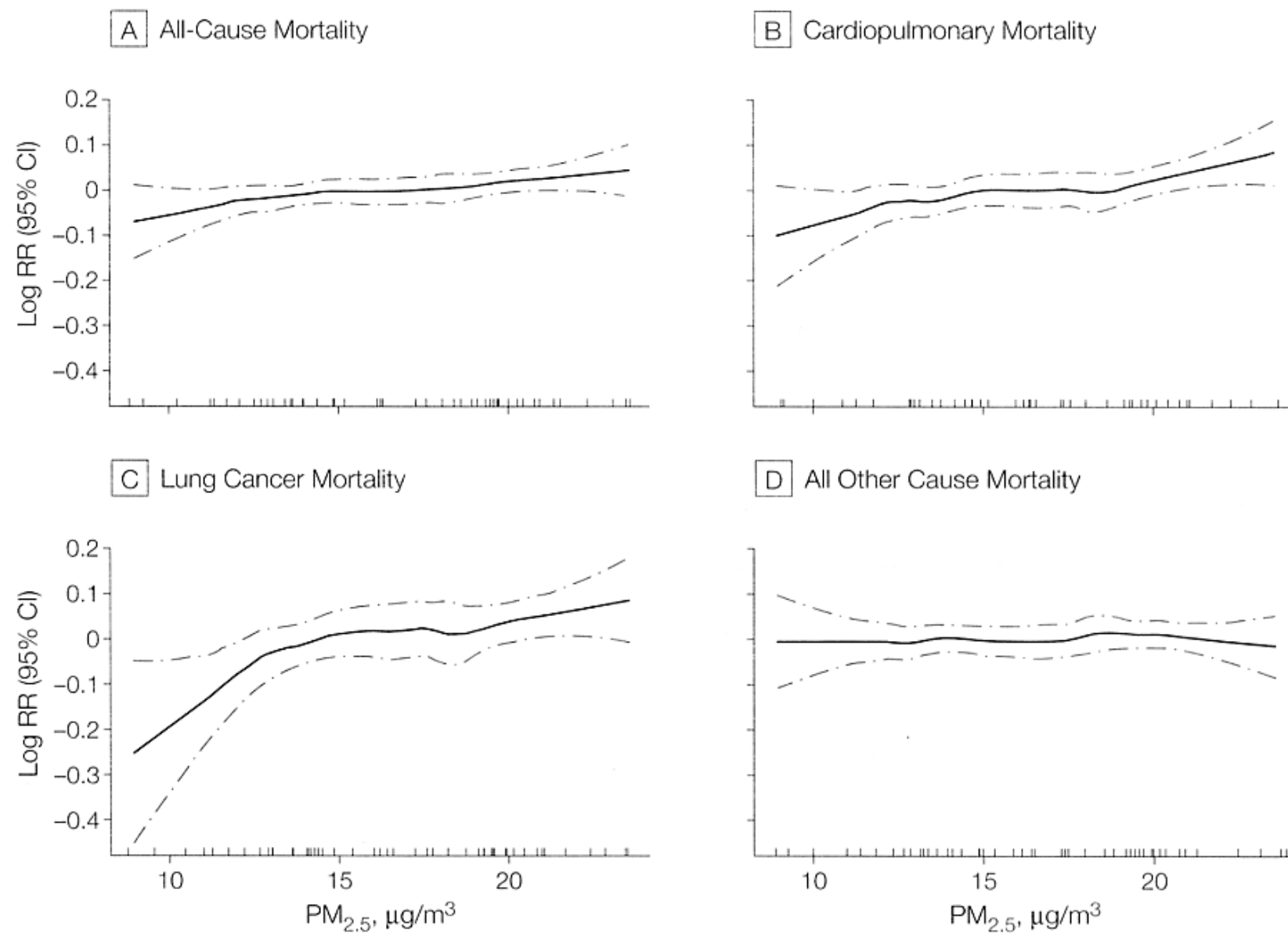
Context Associations have been found between day-to-day particulate air pollution and increased risk of various adverse health outcomes, including cardiopulmonary mortality. However, studies of health effects of long-term particulate air pollution have been less conclusive.

Objective To assess the relationship between long-term exposure to fine particulate air pollution and all-cause, lung cancer, and cardiopulmonary mortality.

Design, Setting, and Participants Vital status and cause of death data were collected by the American Cancer Society as part of the Cancer Prevention II study, a long-running prospective mortality study, which enrolled approximately 1.2 million adults.



Figure 2. Nonparametric Smoothed Exposure Response Relationship



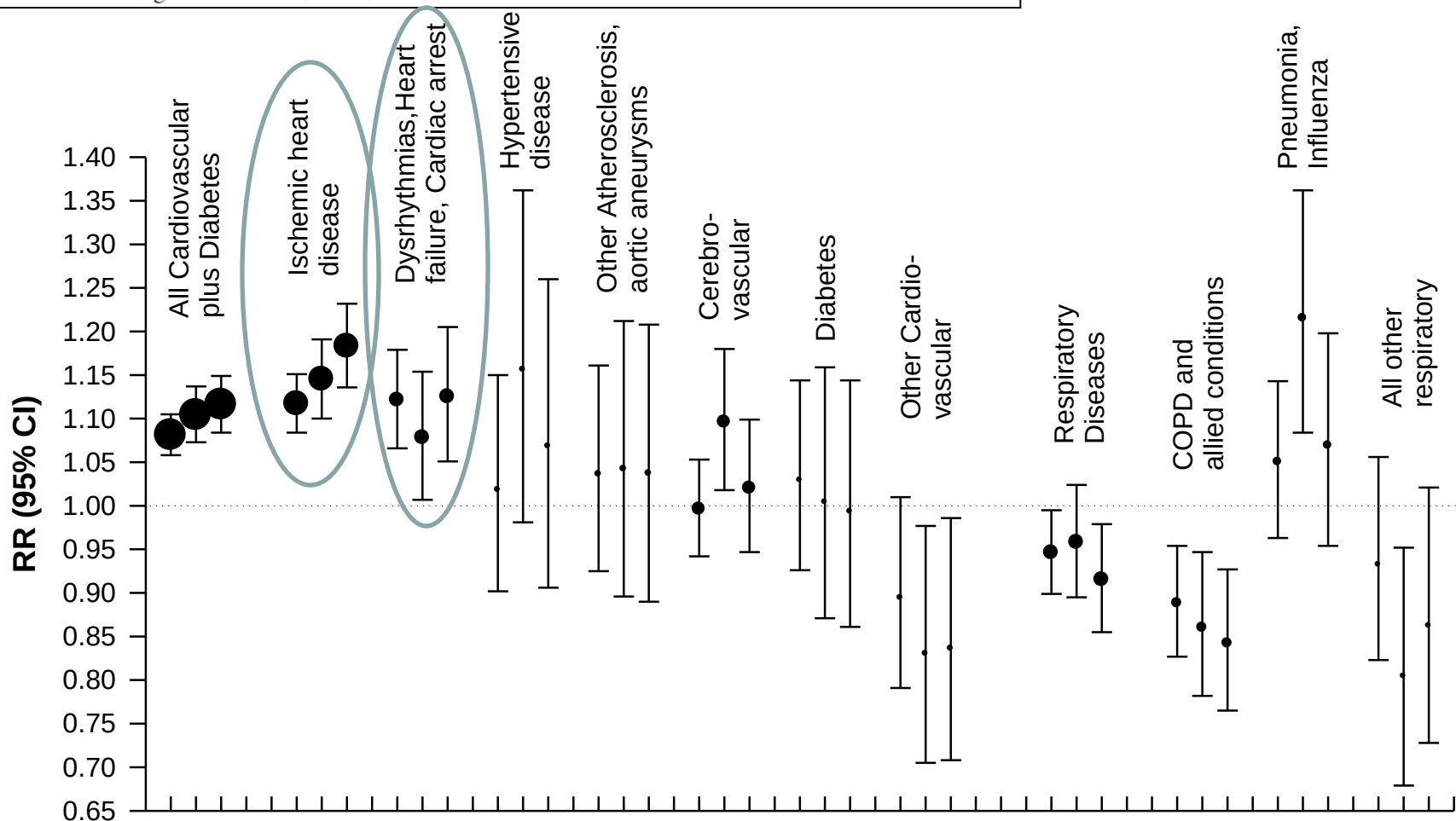
Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution

Epidemiological Evidence of General Pathophysiological Pathways of Disease

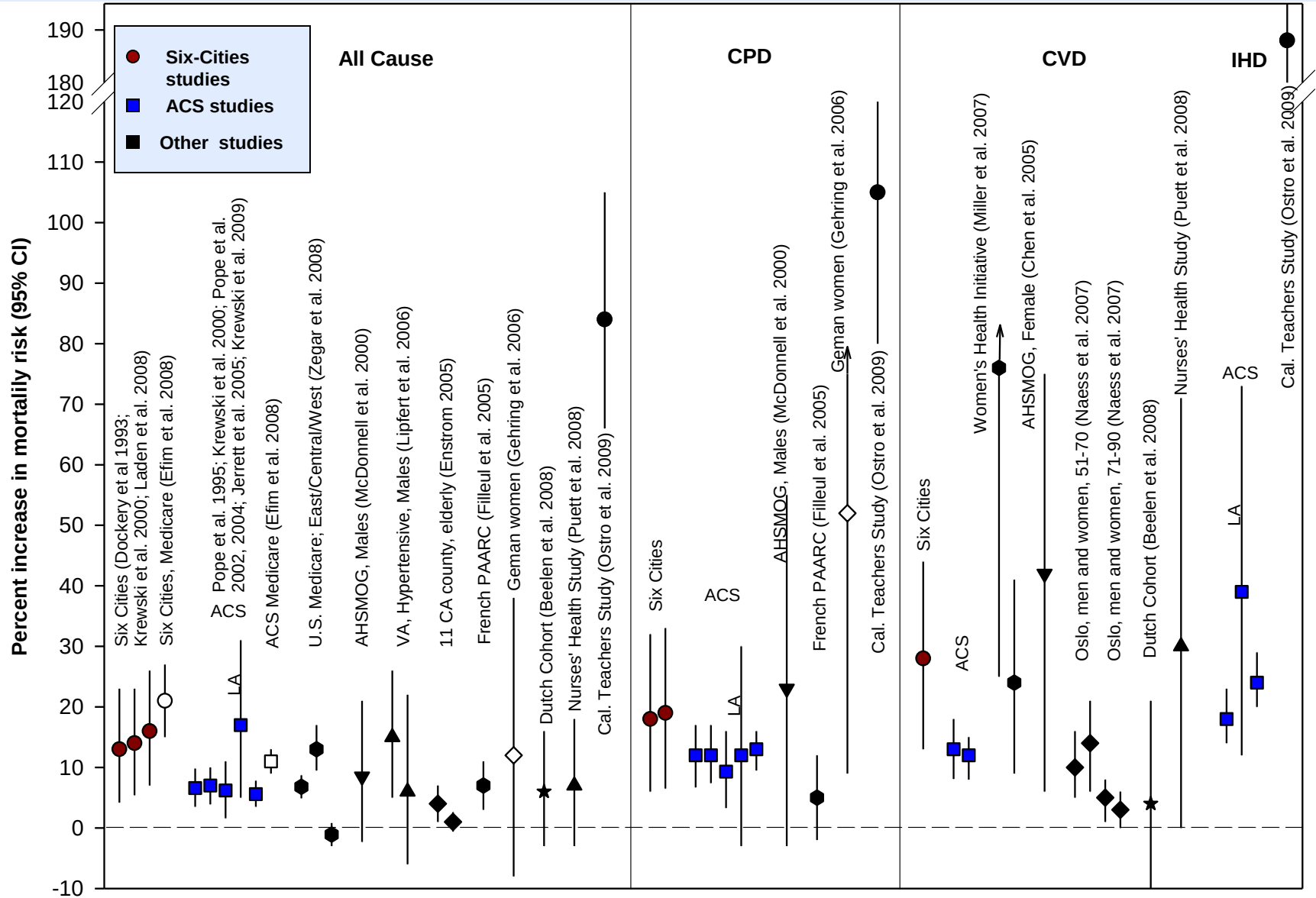
C. Arden Pope III, PhD; Richard T. Burnett, PhD; George D. Thurston, ScD; Michael J. Thun, MD; Eugenia E. Calle, PhD; Daniel Krewski, PhD; John J. Godleski, MD



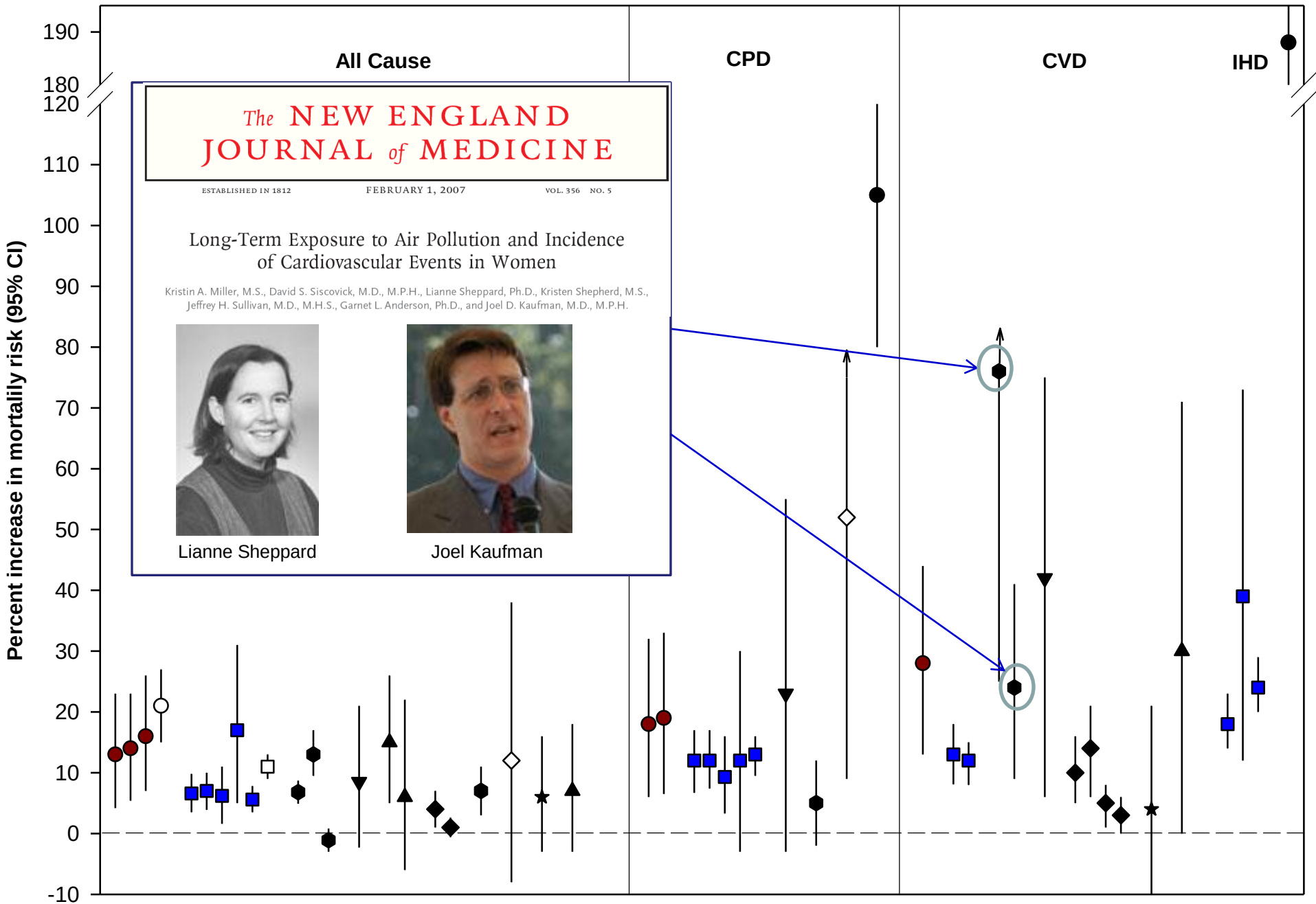
John Godleski

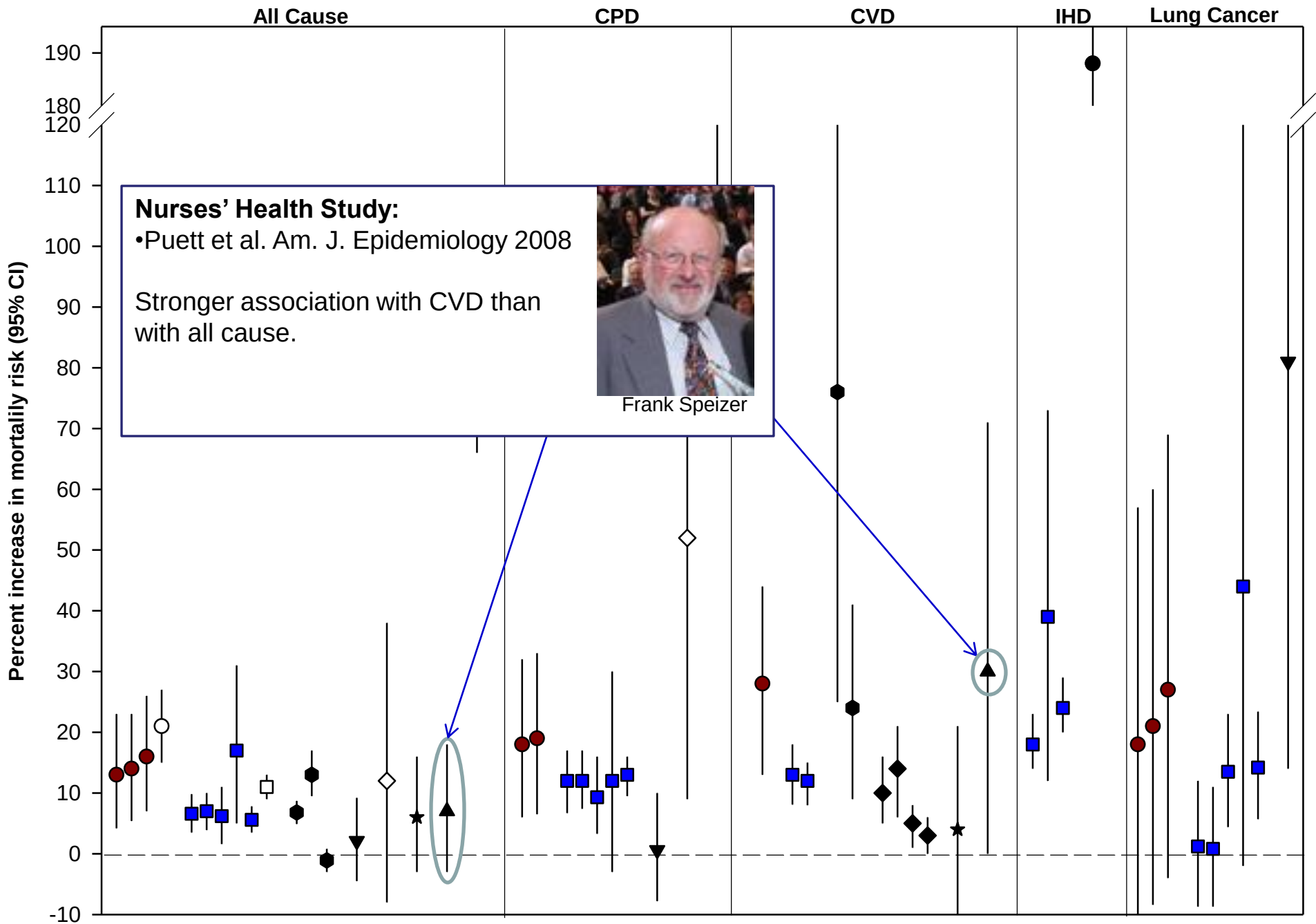


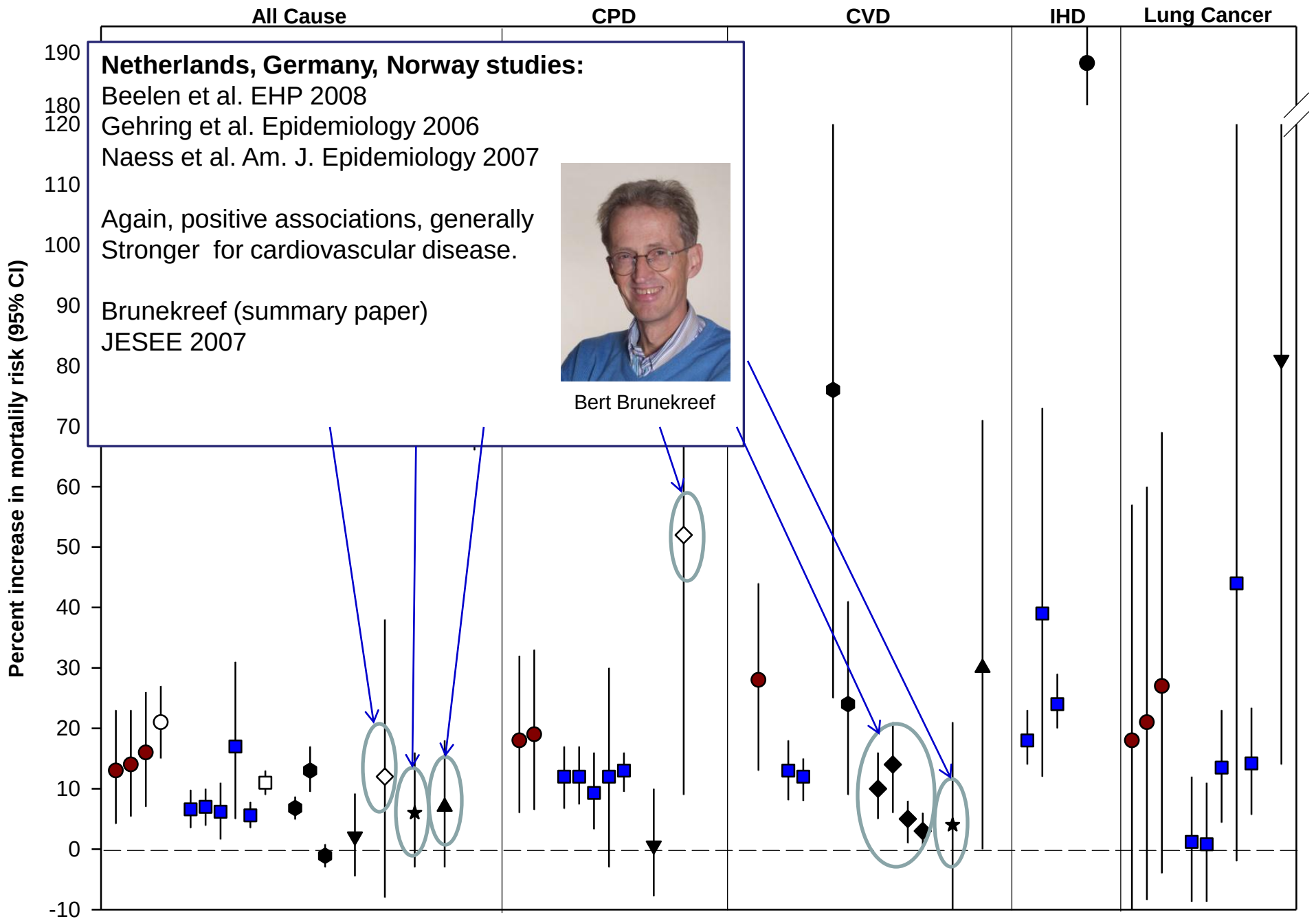
Other cohort studies have shown associations between exposure to fine PM and increased risk of cardiovascular death.



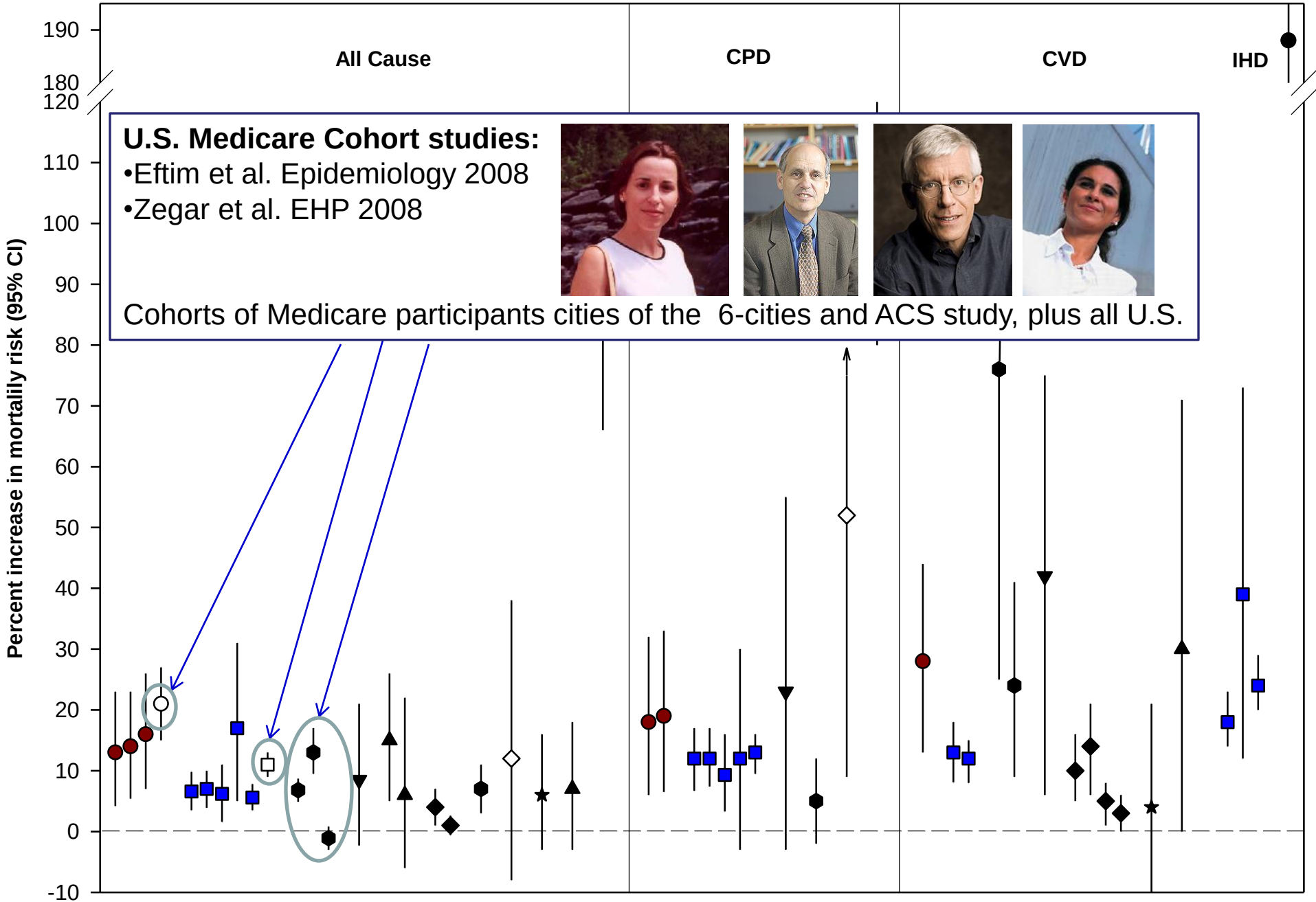
Women's Health Initiative Study







U.S. Medicare Cohort Studies



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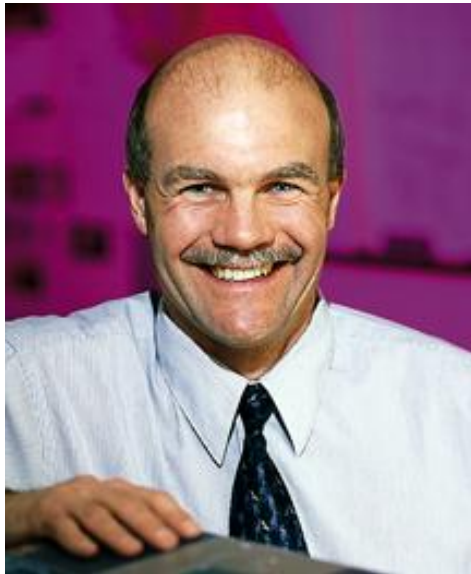
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Southern California Children's Health Study

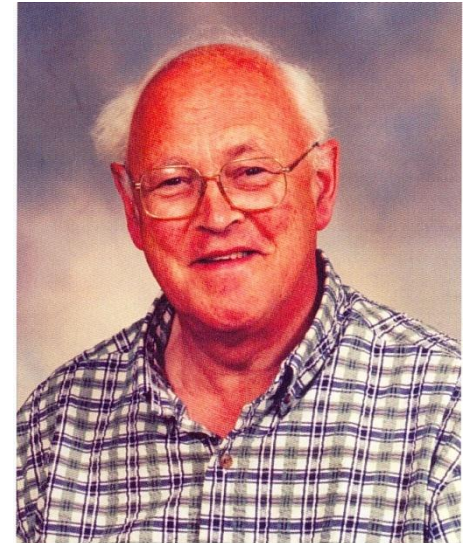
Effects of air pollution on children's health, especially lung function growth.



W. James Gauderman

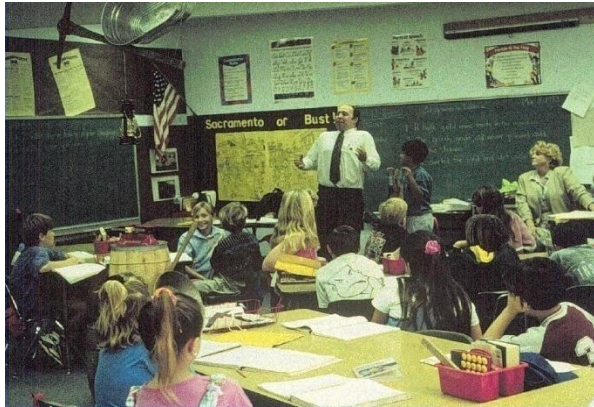


John Peters



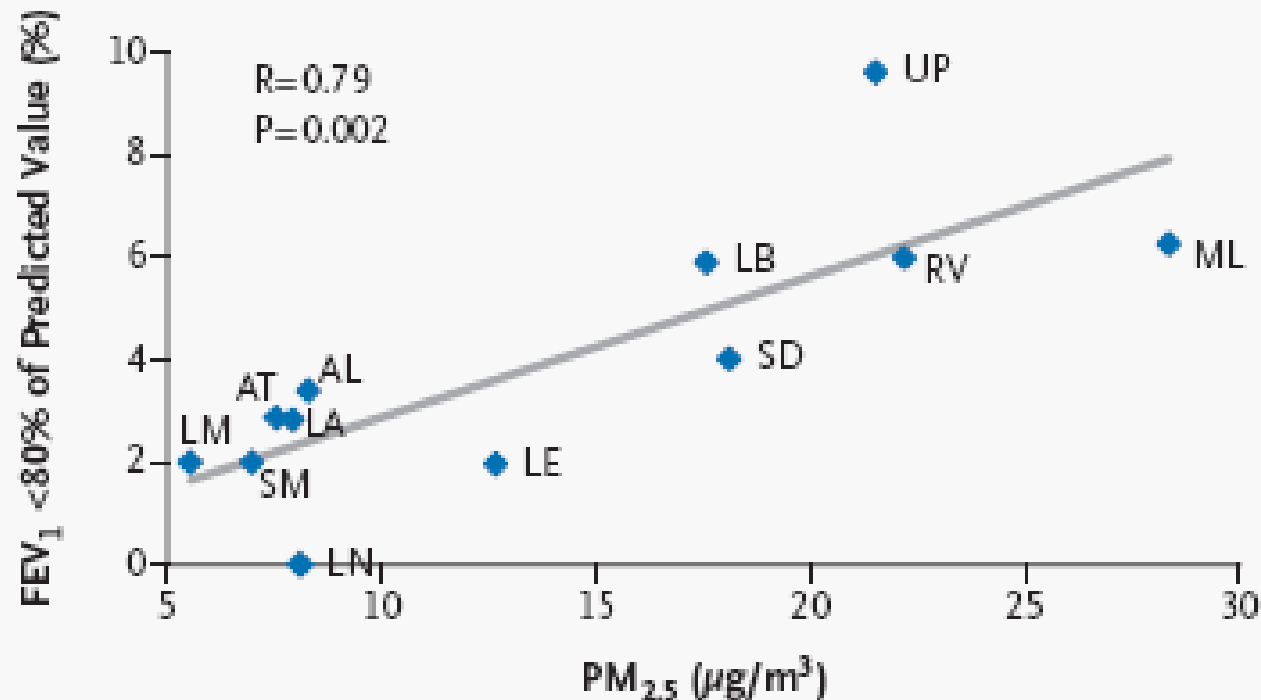
David Bates, Advisor

Southern California Children's Health Study, has shown that **air pollution impacts lung development in children.**



THE LANCET

Gauderman et al. 2007



Children living in cities with higher air pollution and living near major traffic sources showed greater deficits in lung function growth.

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Fine-Particulate Air Pollution and Life Expectancy in the United States

C. Arden Pope, III, Ph.D., Majid Ezzati, Ph.D., and Douglas W. Dockery, Sc.D.

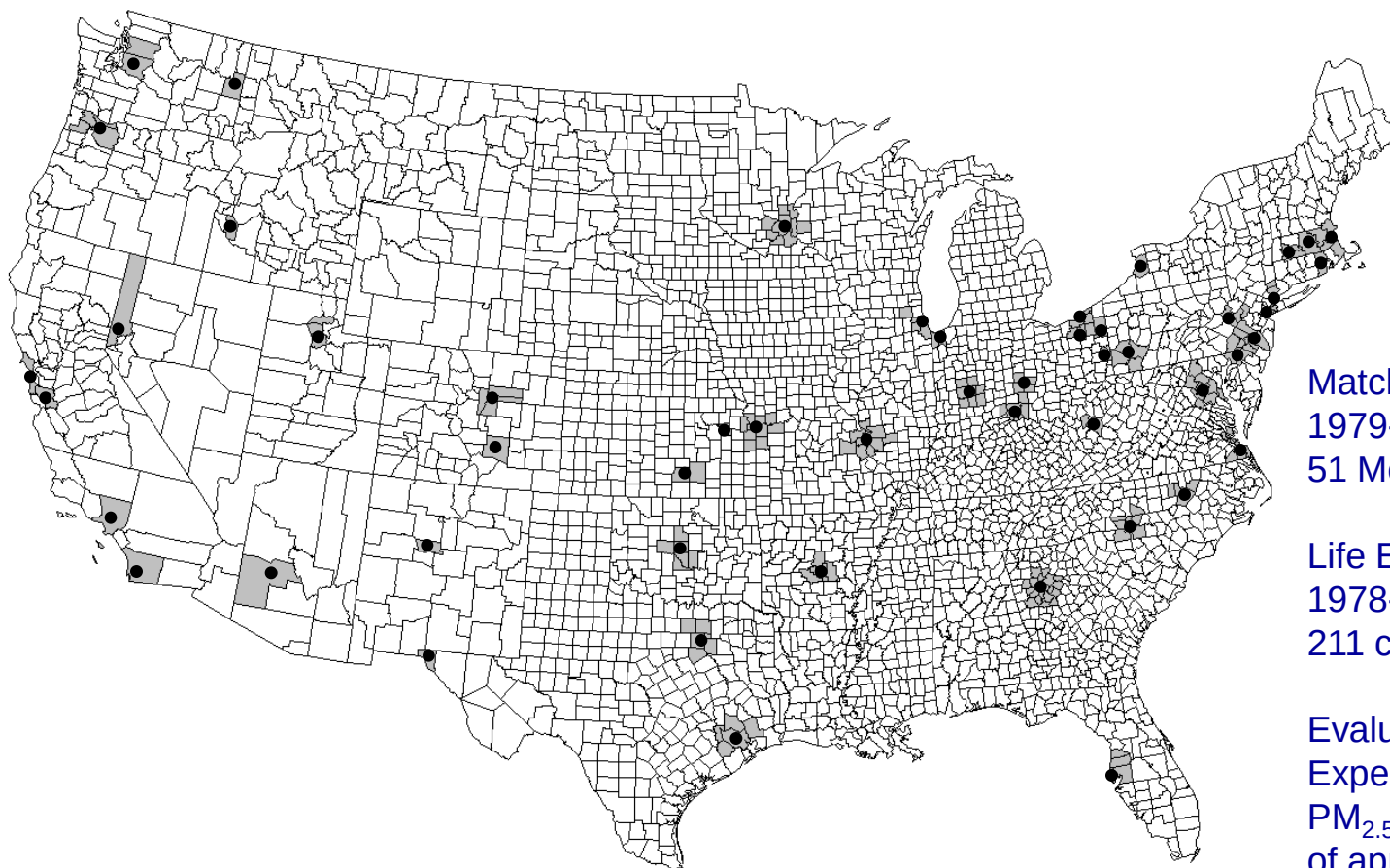
January 22, 2009



Majid Ezzati



Doug Dockery



Matching PM_{2.5} data for
1979-1983 and 1999-2000 in
51 Metro Areas

Life Expectancy data for
1978-1982 and 1997-2001 in
211 counties in 51 Metro areas

Evaluate changes in Life
Expectancy with changes in
PM_{2.5} for the 2-decade period
of approximately 1980-2000.

Covariates included in the regression models

Changes in socio-economic and demographic variables (from U.S. Census Data):

- Per capita income
- Population
- 5-yr in-migration
- High-school graduates
- Urban population
- Black proportion of population
- Hispanic proportion of population

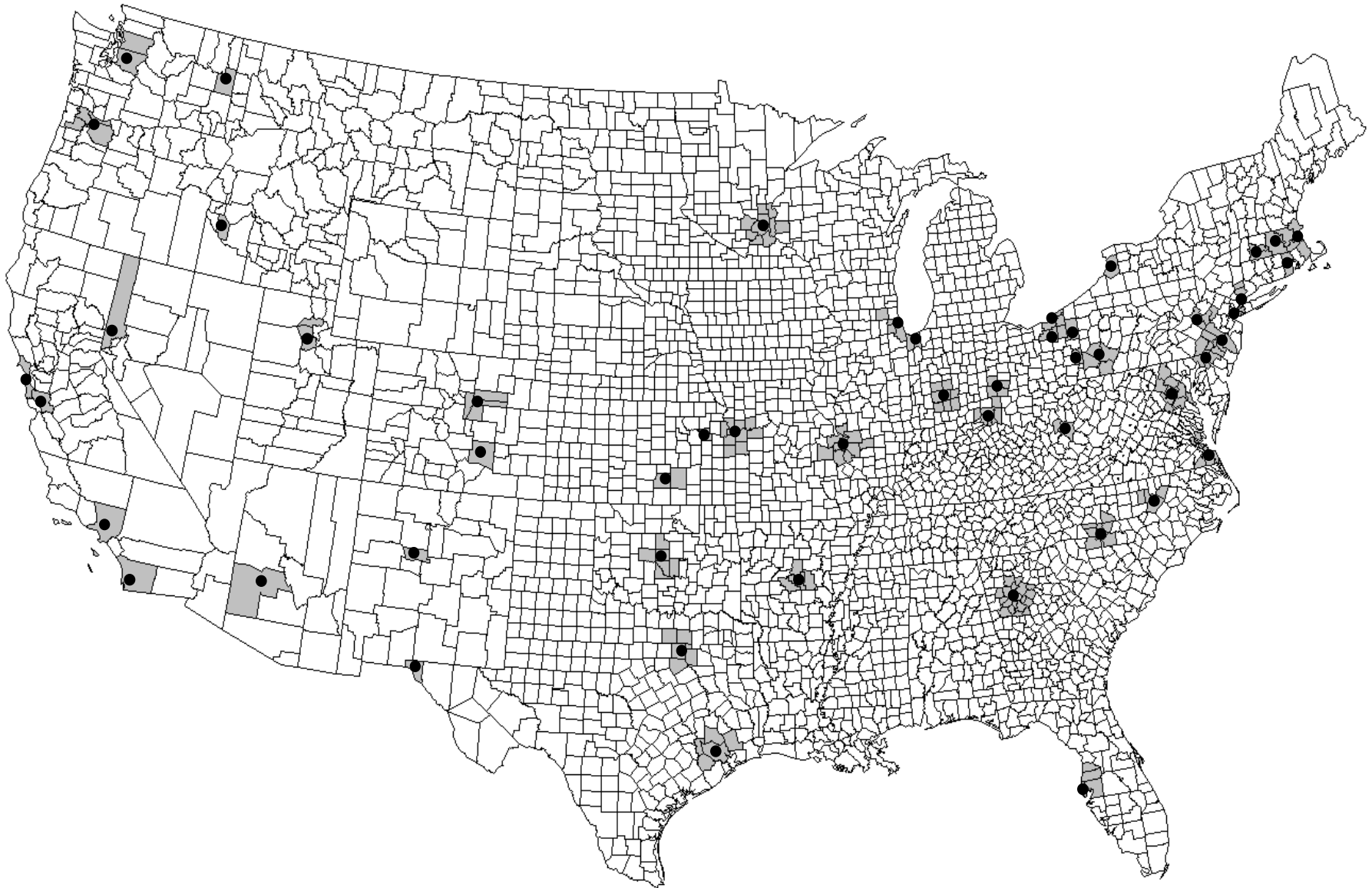
Proxy cigarette smoking variables—available for all 211 counties

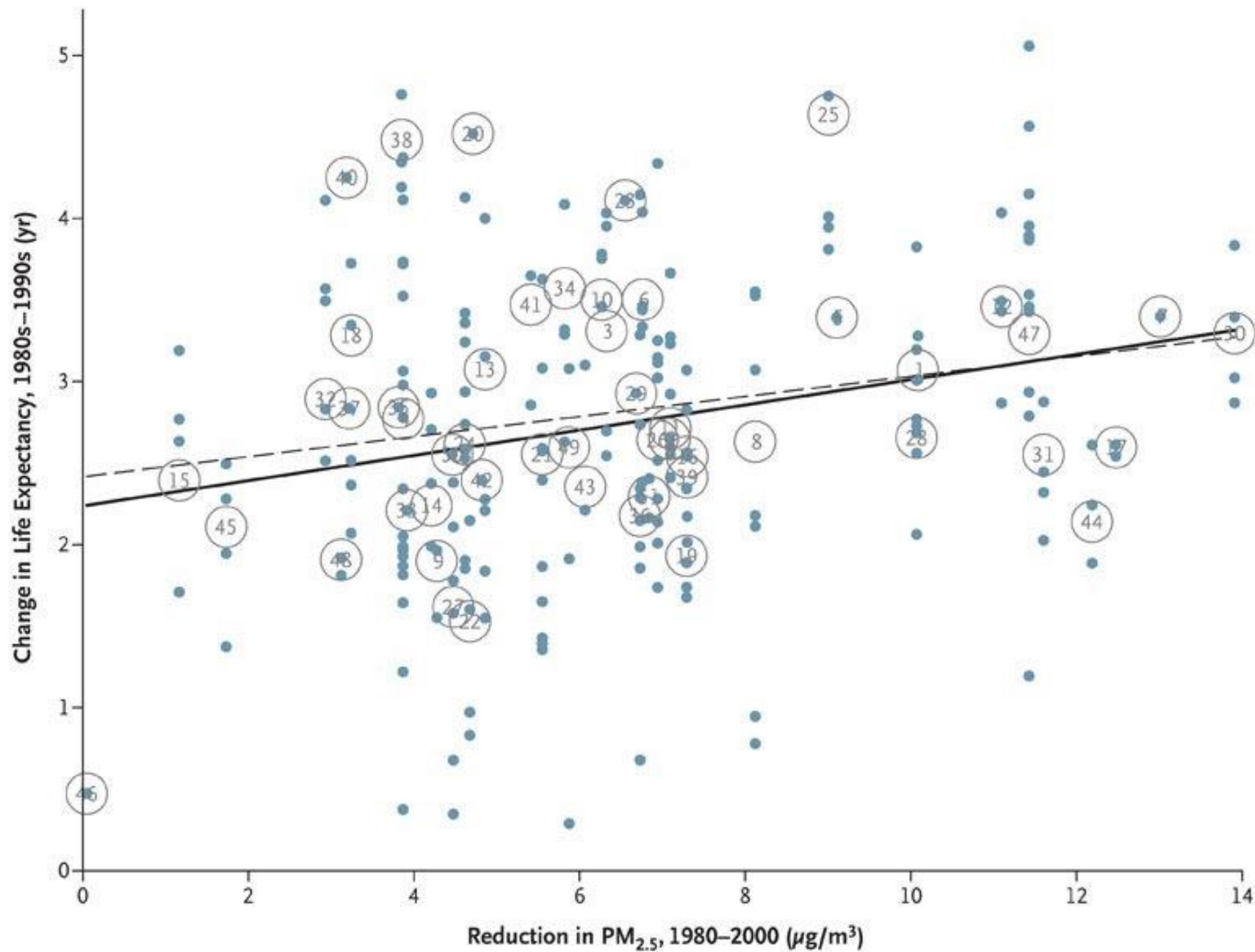
- COPD mortality rates
- Lung Cancer mortality rates

Survey-based metro-area estimates of smoking prevalence

- National Health Interview Survey (1978-1980)
- Behavioral Risk Factor Surveillance System (1998-2000)
- Matching data available for only 24 of 51 metro areas

- Clustered standard errors (clustered by the 51 metro areas) were estimated for all models except for analysis that included only the 51 largest counties in each metro area.



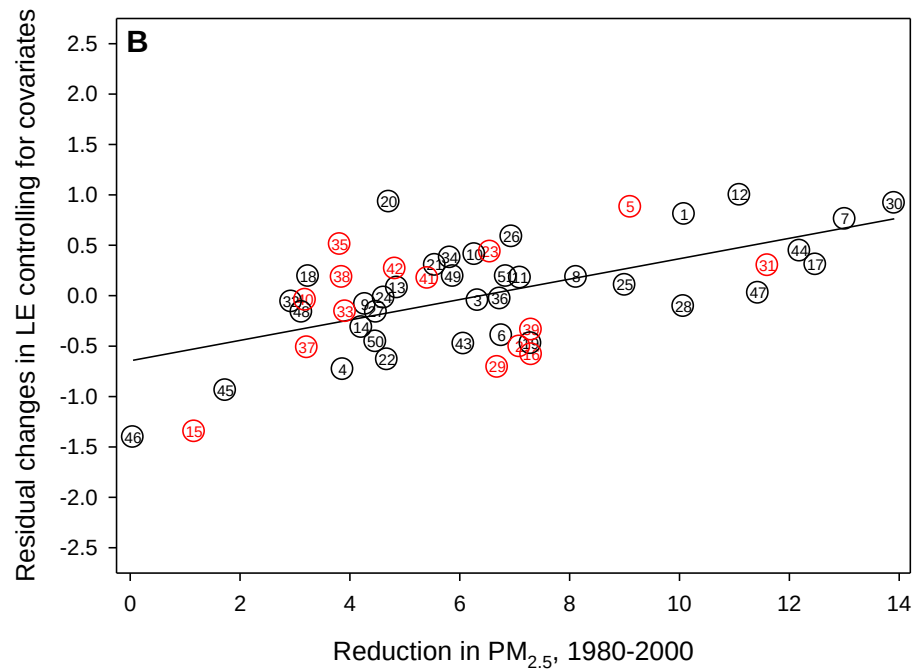
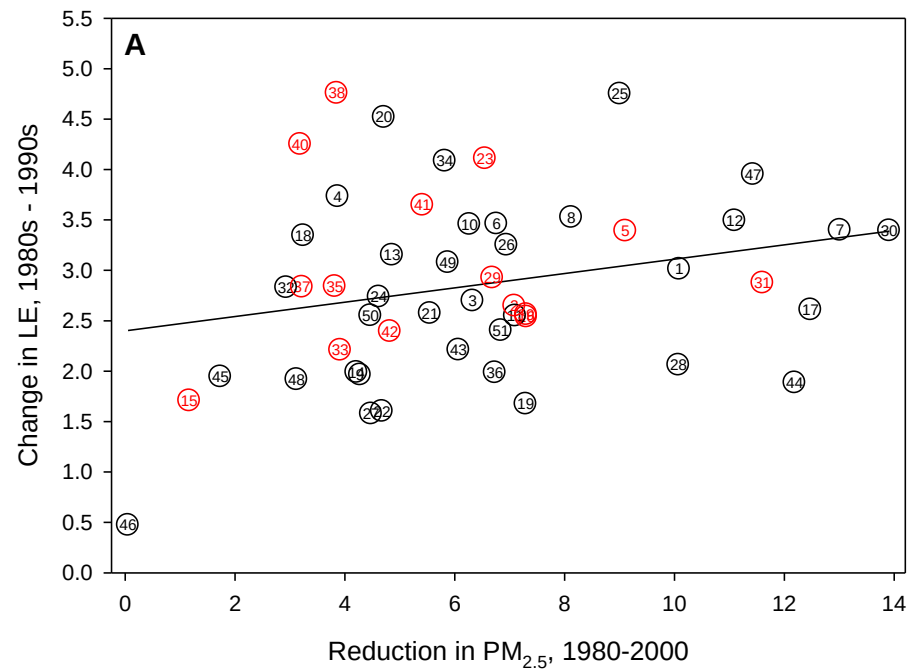


A 10 $\mu\text{g}/\text{m}^3$ decrease in $\text{PM}_{2.5}$ was associated with a **7.3 (± 2.4) month** increase in life expectancy.

Table 2. Results of Selected Regression Models, Including Estimates of the Increase in Life Expectancy Associated with a Reduction in $\text{PM}_{2.5}$ of 10 μg per Cubic Meter, Adjusted for Socioeconomic, Demographic, and Proxy Indicators for Prevalence of Smoking.*

Variable	Model 1	Model 2	Model 3	Model 4	Model 5†	Model 6‡	Model 7‡
	years						
Intercept	2.25 $\pm$ 0.21§	0.80 $\pm$ 0.19§	1.78 $\pm$ 0.27§	1.75 $\pm$ 0.27§	2.02 $\pm$ 0.34§	1.71 $\pm$ 0.51§	2.09 $\pm$ 0.36§
Reduction in $\text{PM}_{2.5}$ (10 $\mu\text{g}/\text{m}^3$)	0.72 $\pm$ 0.29¶	0.83 $\pm$ 0.20§	0.60 $\pm$ 0.20§	0.61 $\pm$ 0.20§	0.55 $\pm$ 0.24¶	1.01 $\pm$ 0.25§	0.95 $\pm$ 0.23§
Change in income (in thousands of \$)	—	0.17 $\pm$ 0.02§	0.13 $\pm$ 0.02§	0.13 $\pm$ 0.01§	0.11 $\pm$ 0.02§	0.15 $\pm$ 0.04§	0.11 $\pm$ 0.02§
Change in population (in hundreds of thousands)	—	0.08 $\pm$ 0.02§	0.05 $\pm$ 0.02§	0.06 $\pm$ 0.02§	0.05 $\pm$ 0.02§	0.04 $\pm$ 0.02	0.05 $\pm$ 0.02¶
Change in 5-yr in-migration (proportion of population) **	—	0.19 $\pm$ 0.79	1.28 $\pm$ 0.80	—	—	-0.02 $\pm$ 1.83	—
Change in high-school graduates (proportion of population)	—	0.17 $\pm$ 0.56	-0.11 $\pm$ 0.53	—	—	-0.90 $\pm$ 0.86	—
Change in urban residence (proportion of population)	—	-0.16 $\pm$ 0.32¶	-0.40 $\pm$ 0.25	—	—	0.03 $\pm$ 1.88	—
Change in black population (proportion of population) ††	—	-1.94 $\pm$ 0.58§	-2.74 $\pm$ 0.58§	-2.70 $\pm$ 0.64§	-2.95 $\pm$ 0.78§	-5.06 $\pm$ 2.12§	-5.98 $\pm$ 1.99§
Change in Hispanic population (proportion of population) ††	—	1.46 $\pm$ 1.23	1.33 $\pm$ 1.10	—	—	2.44 $\pm$ 2.22	—
Change in lung-cancer mortality rate (no./10,000 population)	—	—	-0.07 $\pm$ 0.02§	-0.06 $\pm$ 0.02§	-0.07 $\pm$ 0.03¶	0.01 $\pm$ 0.03	0.02 $\pm$ 0.03
Change in COPD mortality rate (no./10,000 population)	—	—	-0.07 $\pm$ 0.02§	-0.08 $\pm$ 0.02§	-0.09 $\pm$ 0.03§	-0.15 $\pm$ 0.06§	-0.19 $\pm$ 0.05§
No. of county units	211	211	211	211	127	51	51
R ² ‡‡	0.05	0.47	0.55	0.53	0.60	0.76	0.74

This increase in life expectancy persisted even after controlling for socio-economic, demographic, or smoking variables



This presentation not organized chronologically, but methodologically

Studies of short-term exposure (hours-days)

- Episode
- Population-based daily time-series
- Panel-based acute exposure
- Case-crossover

Studies of long-term exposure (years-decades)

- Population-based cross-sectional
- Cohort-based mortality
- Cohort- and panel-based morbidity
- Case-control studies

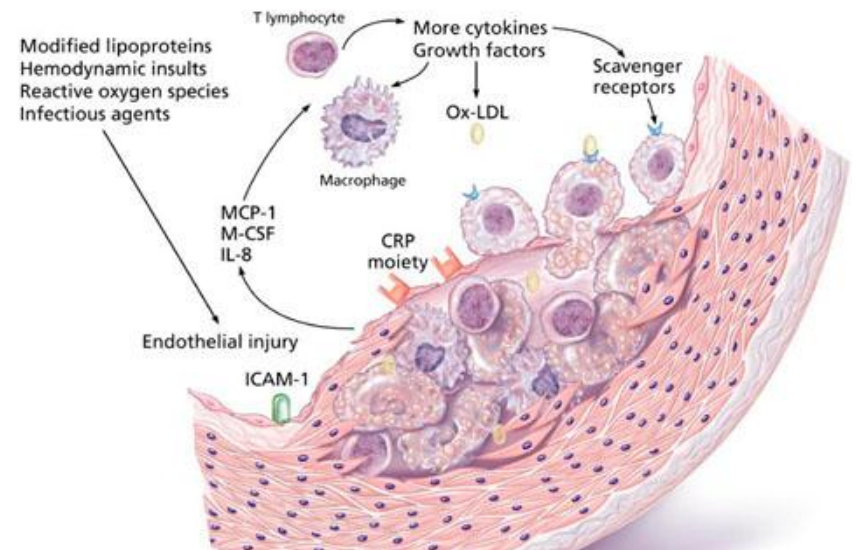
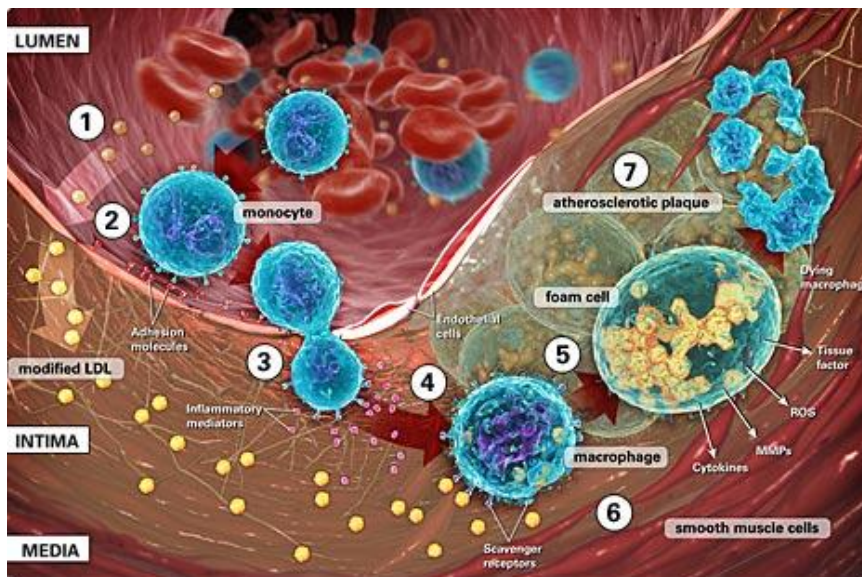
Intervention/natural experiment (months-years)

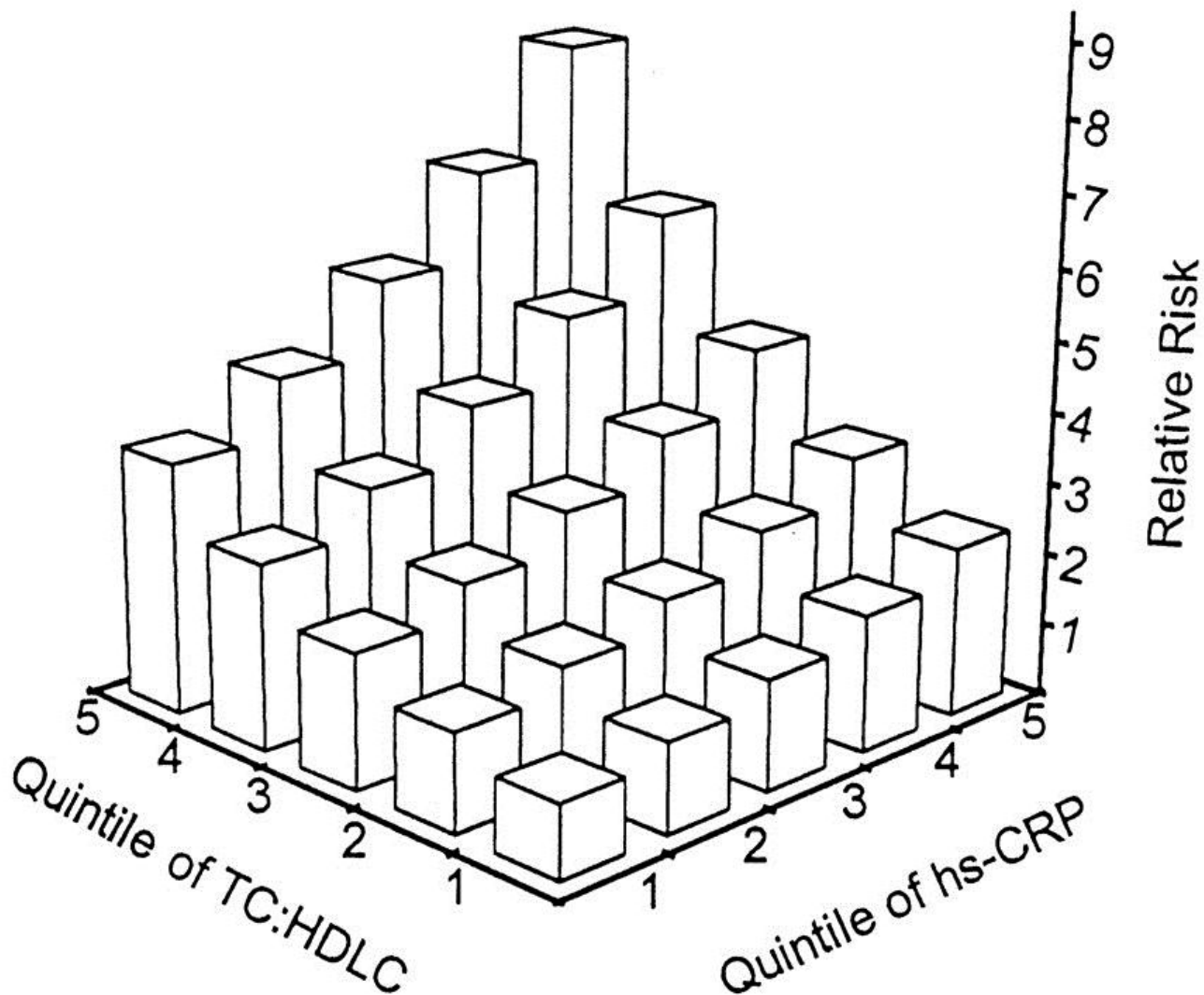
Controlled experimental human and animal

Cardiovascular disease as part of chronic and acute inflammatory processes.

By the early 2000s, there was increasingly compelling evidence that inflammation is a major accomplice with LDL cholesterol in the initiation and progression of atherosclerosis.

Furthermore, inflammation contributes to acute thrombotic complications of atherosclerosis, increasing the risk of making atherosclerotic plaques more vulnerable to rupture, clotting, and precipitating acute cardiovascular or cerebrovascular events (MI or ischemic stroke).





Paul Ridker

Interactive effects of hs-CRP (marker of inflammation) and blood lipids.

**Fine Particulate
exposure**

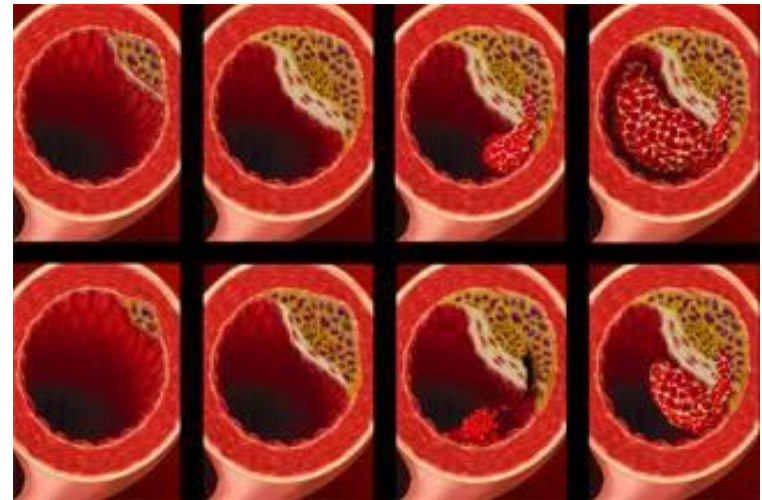
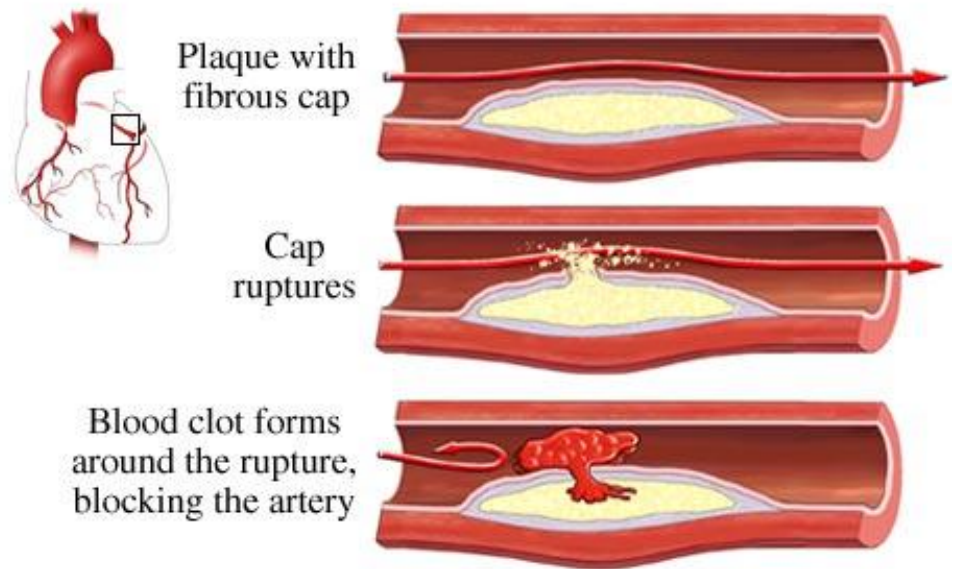


**Pulmonary and
systemic
inflammation
and oxidative stress**

(along with blood lipids)



**Progression and
destabilization of
atherosclerotic
plaques**

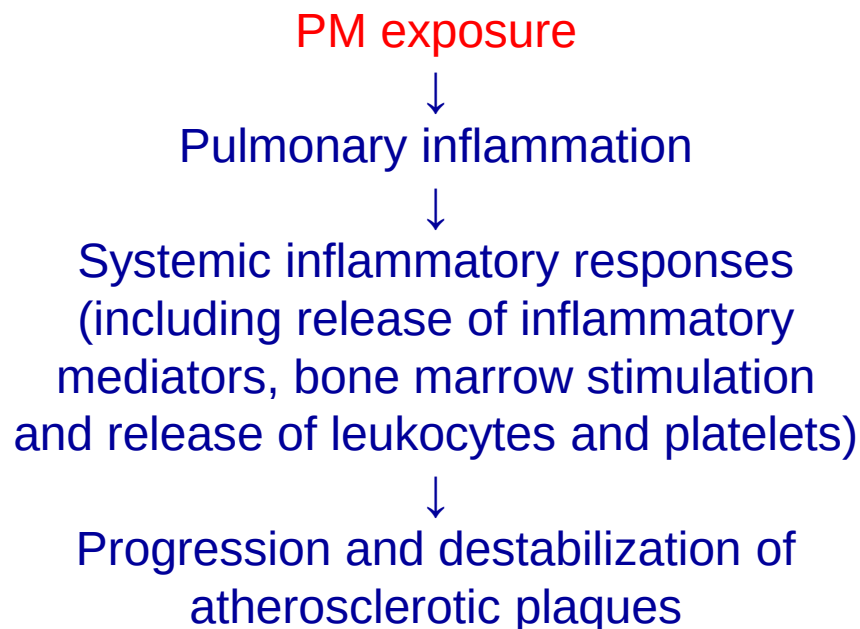




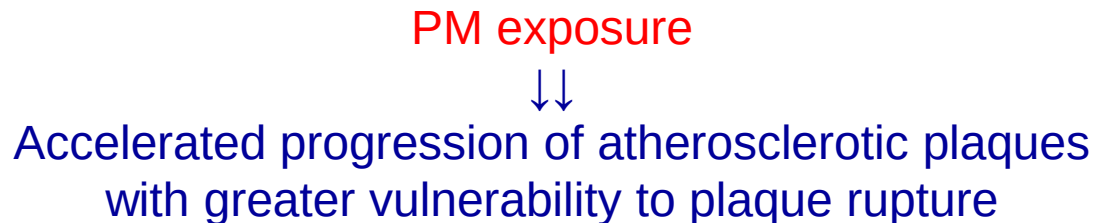
Experimental evidence of biological effects of PM extracted from filters (Ghio, Costa, Devlin, Kennedy, Frampton, Dye, et al. 1998-2004)

- Acute airway injury and inflammation in rats and humans
- *In vitro* oxidative stress and release of proinflammatory mediators by cultured respiratory epithelial cells
- Differential toxicities of PM when the mill was operating versus when it was not (metals content and mixtures?)

A series of studies by van Eeden, Hogg, Suwa et al. (1997-2002) suggest:



In rabbits naturally prone to develop atherosclerosis they found that:



Stephan van Eeden



James Hogg



Sun et al. (*JAMA* 2005)



Representative Photomicrographs
of Aortic Arch Sections

Normal Chow

High-Fat Chow

Clean
Filtered Air

PM Polluted Air

Clean
Filtered Air

PM Polluted Air

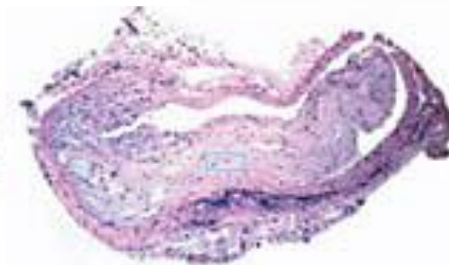


Table 1. Stylized outline of studies on air pollution and health.

General Study Designs	Examples	Time-scale	Selected Sample of Effects of Elevated Exposures	Common Statistical Modeling Approaches
Episode	Meuse Valley 1930 ⁷³ Donora 1948 ⁷⁴ London 1952 ^{75,76}	Days	↑ episode-related cardiovascular disease and respiratory illness and death	Simple Comparative Stats, Graphs
Population-based time-series	Meta analysis ²⁷ Large multi-city mortality ²⁸⁻³¹ Large multi-city hospitalizations ⁷⁷	Days	↑ daily cardiovascular disease and respiratory mortality and hospitalization counts	Poisson reg., (GAMs, smooths for time, weather etc.)
Panel-based acute exposure	Review resp. effects ¹⁹ Review CVD effects ⁵⁴ HRV/Inflammation ^{78,79}	Hours-days	↑ respiratory symptoms ↓ pulmonary function ↑ markers of inflammation ↓ heart rate variability	Linear and Logistic Reg., (fixed effects, temporal autocorr., etc.)
Case-crossover	Multi-city Ischemic heart disease			Conditional Logistic Reg.
Population-based cross-sectional	U.S. mortality			Linear regression
Cohort-based mortality	Harvard Six Cities American Women's Medical Research Council European			Survival Analyses, Cox Proportional Hazards models (random effect, spatial autocorr., etc.)
Cohort- and panel-based morbidity	Swiss Cohort Harvard So. California Atherosclerosis			Various regression modeling strategies (fixed effects, mixed models, . . .)
Case-control studies	Czech Lung Cancer Lung Cancer AMI trials Italy DVT ⁹⁴		↑ acute myocardial infarction ↑ risk of deep vein thrombosis	Conditional Logistic Reg.
Intervention/natural experiment	Utah Valley, steel mill ¹⁸ Dublin coal ban ⁶⁵ Hong Kong Sulfur ⁶⁶ Copper smelter strike ⁶⁴ Cook stove intervention ⁹⁵ U.S. Life Expectancy ⁶⁷	Months to years	Various intervention-related improvements in morbidity, mortality and/or life expectancy	Various comparative stats and regression models
Controlled experimental human studies and animal toxicology	Human instillation ⁹⁶ Human chamber ^{97,98} Tox, rabbits ⁹⁹ Tox, hamsters ^{100,101} Tox, dogs ¹⁰² Tox, mice ¹⁰³⁻¹⁰⁵	Variety, usually hours to weeks	Growing complementary evidence of adverse cardiopulmonary health effects of air pollution	Various comparative stats and regression models

Many studies using various study designs and approaches with companion statistical modeling approaches and techniques have provided remarkably coherent evidence.

Table 6. Overall Summary of Epidemiological Evidence of the Cardiovascular Effects of PM_{2.5}, Traffic-Related, or Combustion-Related Air Pollution Exposure at Ambient Levels

Health Outcomes	Short-Term Exposure (Days)	Longer-Term Exposure (Months to Years)
Clinical cardiovascular end points from epidemiological studies at ambient pollution concentrations		
Cardiovascular mortality	↑ ↑ ↑	↑ ↑ ↑
Cardiovascular hospitalizations	↑ ↑ ↑	↑
Ischemic heart disease*	↑ ↑ ↑	↑ ↑ ↑
Heart failure*	↑ ↑	↑
Ischemic stroke*	↑ ↑	↑
Vascular diseases	↑	↑ †
Cardiac arrhythmia/cardiac arrest	↑	↑
Subclinical cardiovascular end points and/or surrogate measures in human studies		
Surrogate markers of atherosclerosis	N/A	↑
Systemic inflammation	↑ ↑	↑
Systemic oxidative stress	↑	
Endothelial cell activation/ blood coagulation	↑ ↑	↑
Vascular/endothelial dysfunction	↑ ↑	
BP	↑ ↑	
Altered HRV	↑ ↑ ↑	↑
Cardiac ischemia	↑	
Arrhythmias	↑	

Table 7. Summary of Level of Evidence Supporting Global Biological Pathways and Specific Mechanisms Whereby PM_{2.5}, Traffic-Related, or Combustion-Related Air Pollution Exposure Can Affect the Cardiovascular System

	Animal Studies	Human Studies
General “intermediary” pathways whereby PM inhalation can instigate extrapulmonary effects on the cardiovascular system		
Pathway 1: Instigation of systemic proinflammatory responses	↑ ↑ ↑	↑ ↑ ↑
Pathway 2: Alterations in systemic ANS balance/activity	↑	↑ ↑
Pathway 3: PM and/or associated constituents directly reaching the systemic circulation	↑	↑
Specific biological mechanisms directly responsible for triggering cardiovascular events		
Vascular dysfunction or vasoconstriction	↑ ↑ ↑	↑ ↑
Enhanced thrombosis or coagulation potential	↑ ↑	↑ ↑
Elevated arterial BP	↑ ↑	↑ ↑
Enhanced atherosclerosis or plaque vulnerability	↑ ↑	↑
Arrhythmias	↑	↑

This presentation not organized chronologically, but methodologically

Studies of short-term exposure (hours-days)

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Studies of long-term exposure (years-decades)

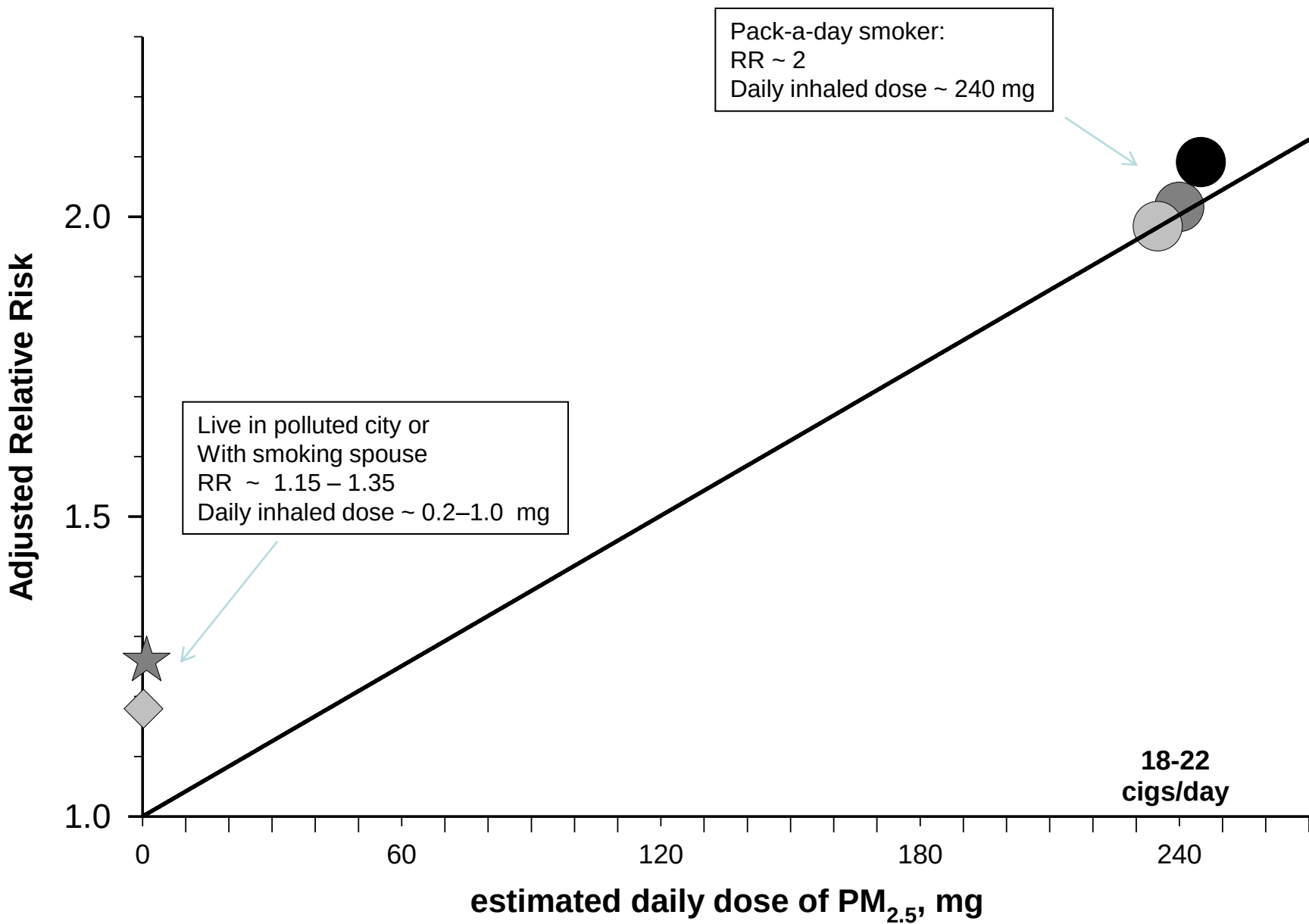
- Population-based cross-sectional
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Intervention/natural experiment (months-years)

Controlled experimental human and animal



Any
Questions?



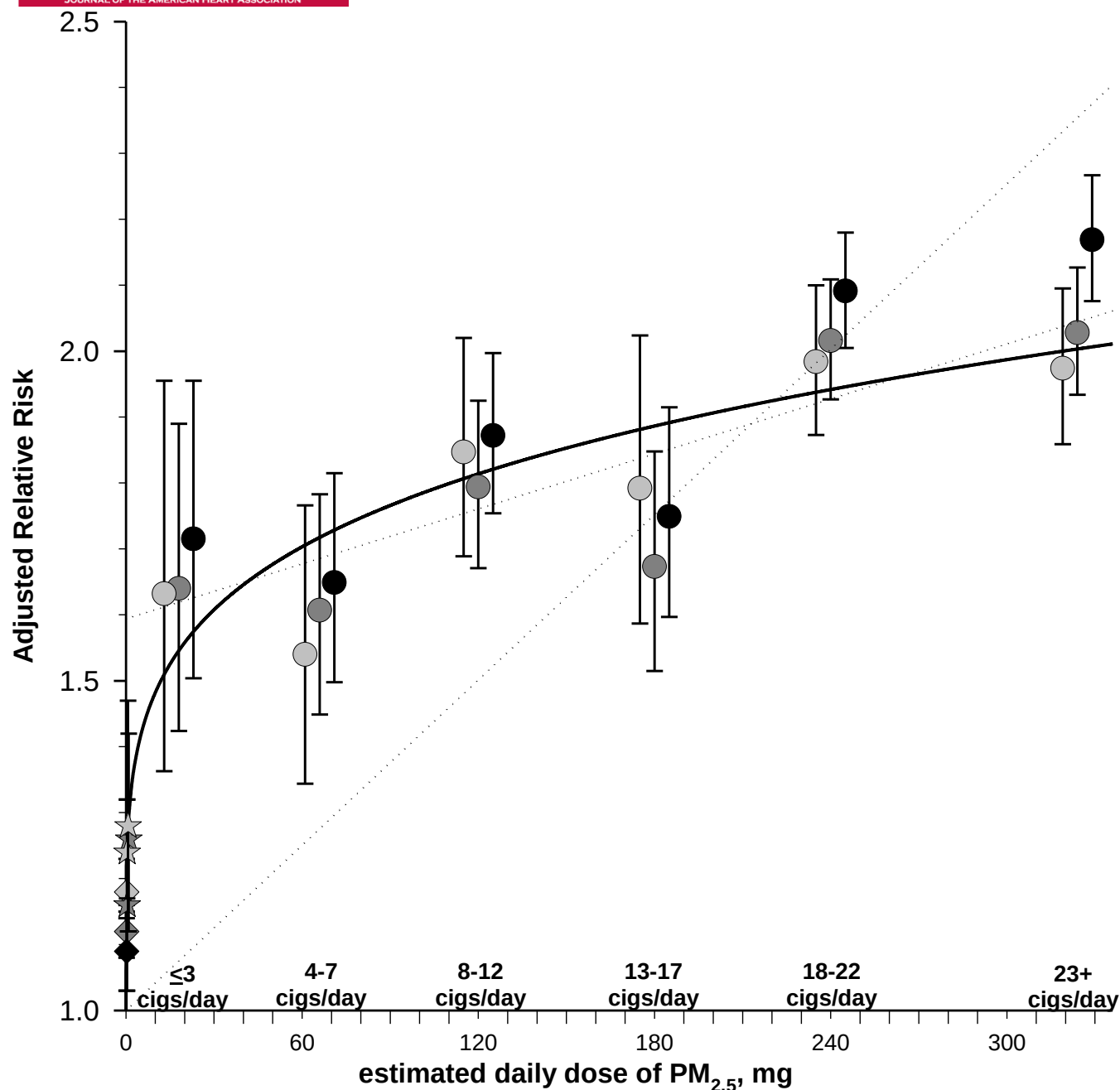


Figure 1. Adjusted relative risks (and 95% CIs) of IHD (light gray), CVD (dark gray), and CPD (black) mortality plotted over estimated daily dose of $PM_{2.5}$ from different increments of current cigarette smoking. Diamonds represent comparable mortality risk estimates for $PM_{2.5}$ from air pollution. Stars represent comparable pooled relative risk estimates associated with SHS exposure from the 2006 Surgeon General's report and from the INTERHEART study.

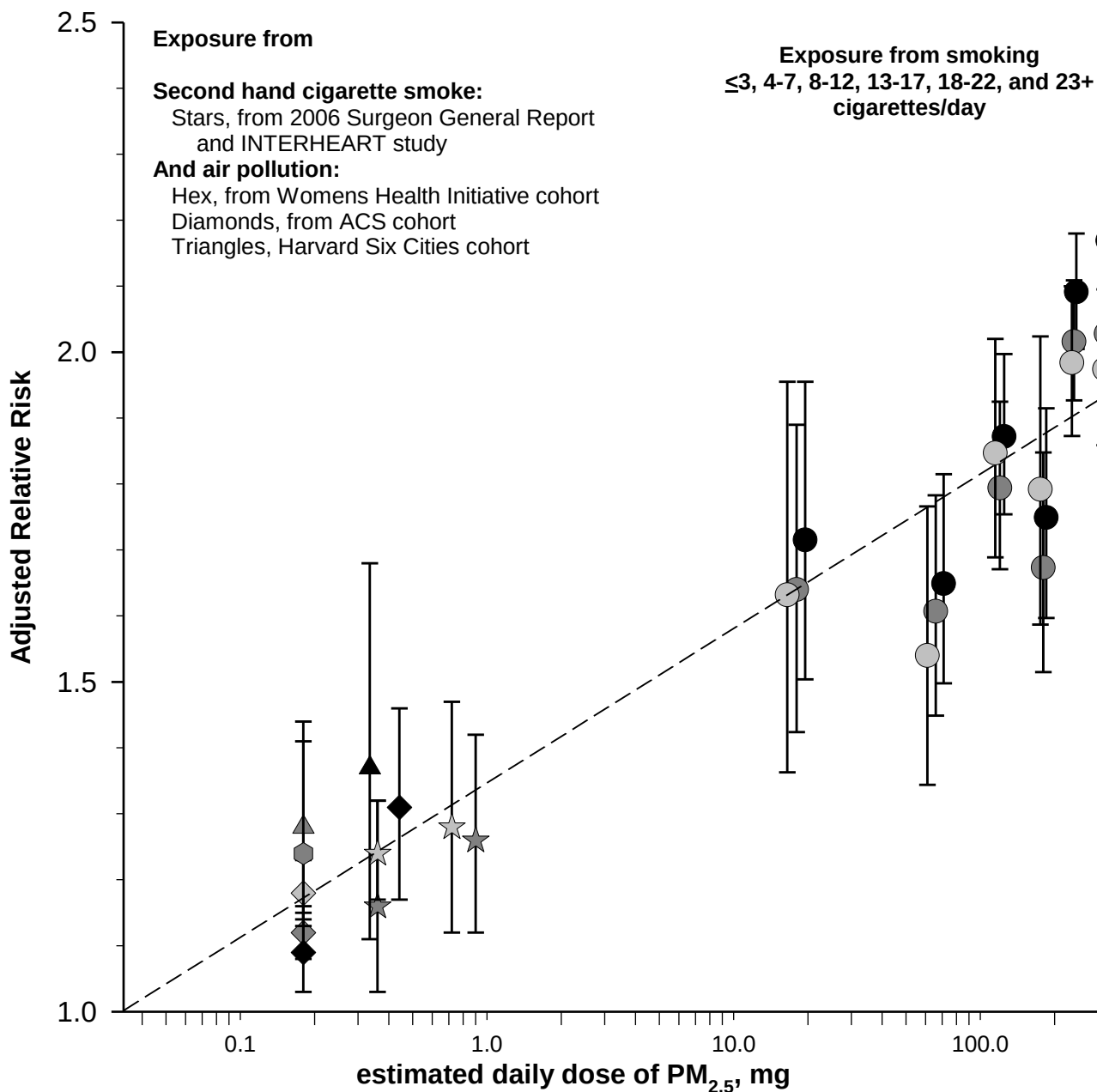


Figure 2. Adjusted relative risks (and 95% CIs) of ischemic heart disease (light gray), cardiovascular (dark gray), and cardiopulmonary (black) mortality plotted over baseline estimated daily dose (using a log scale) of PM_{2.5} from current cigarette smoking (relative to never smokers), SHS, and air pollution.