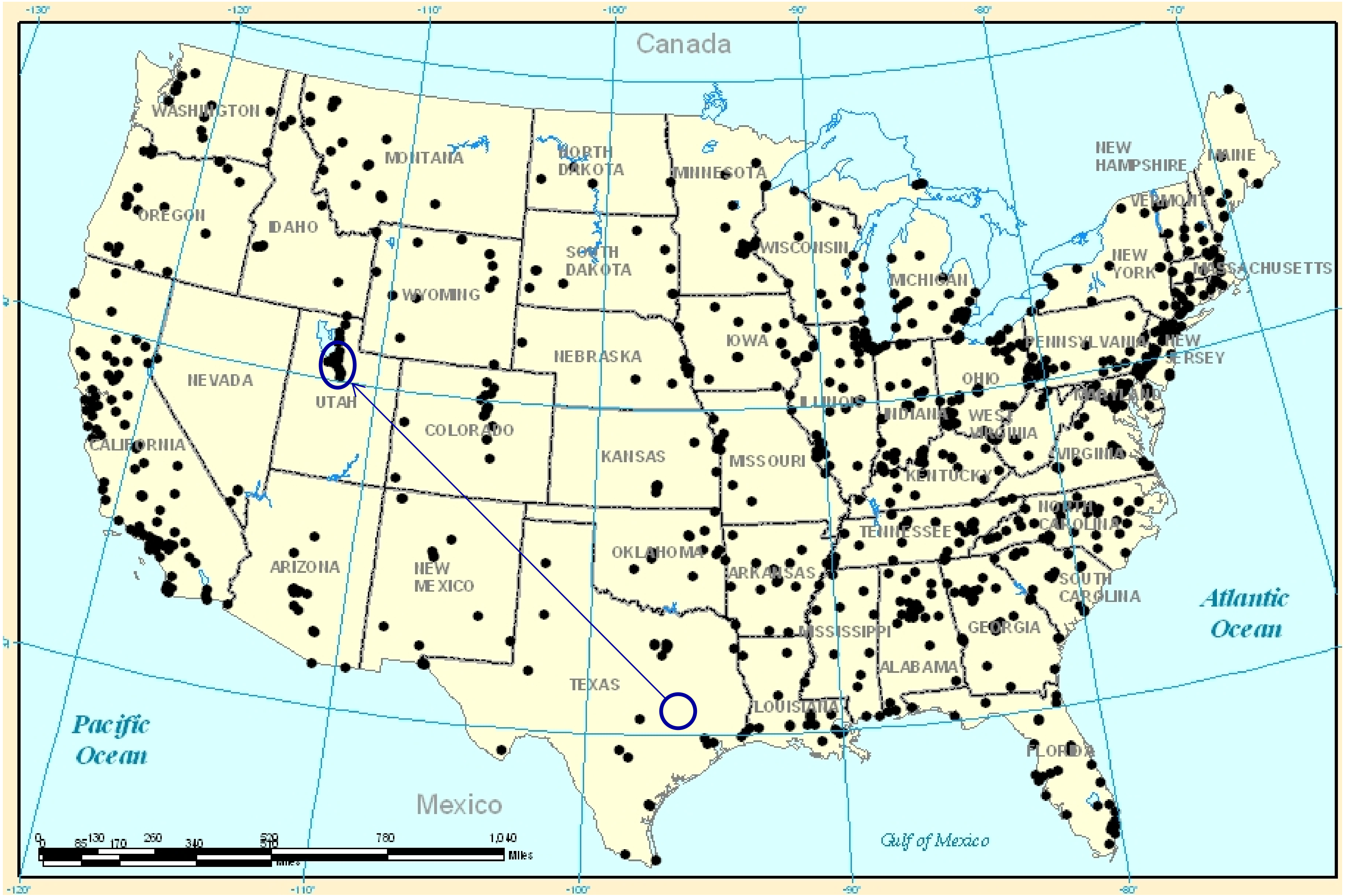
Evaluating the Human Health Costs Air Pollution: Critical Joint Roles of Air Monitoring and Epidemiology

C. Arden Pope III, Mary Lou Fulton Professor

Brigham Young University

Presented at: 2009 National Ambient Air Monitoring Conference

November 2-5, 2009

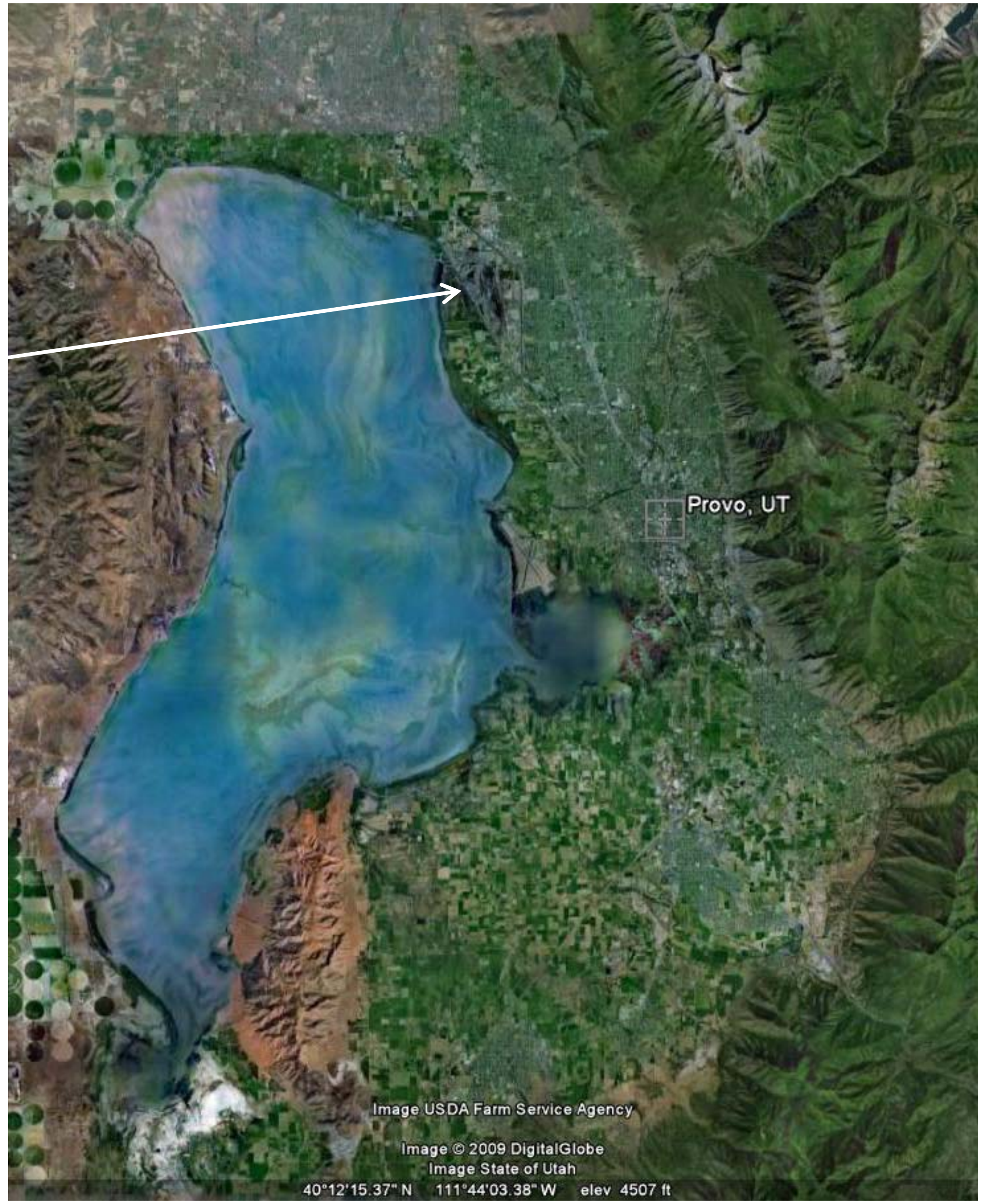


PM$_{2.5}$ FRMs Reporting to AQS—**thanks to Joann Rice for slide**

Utah Valley, 1980s

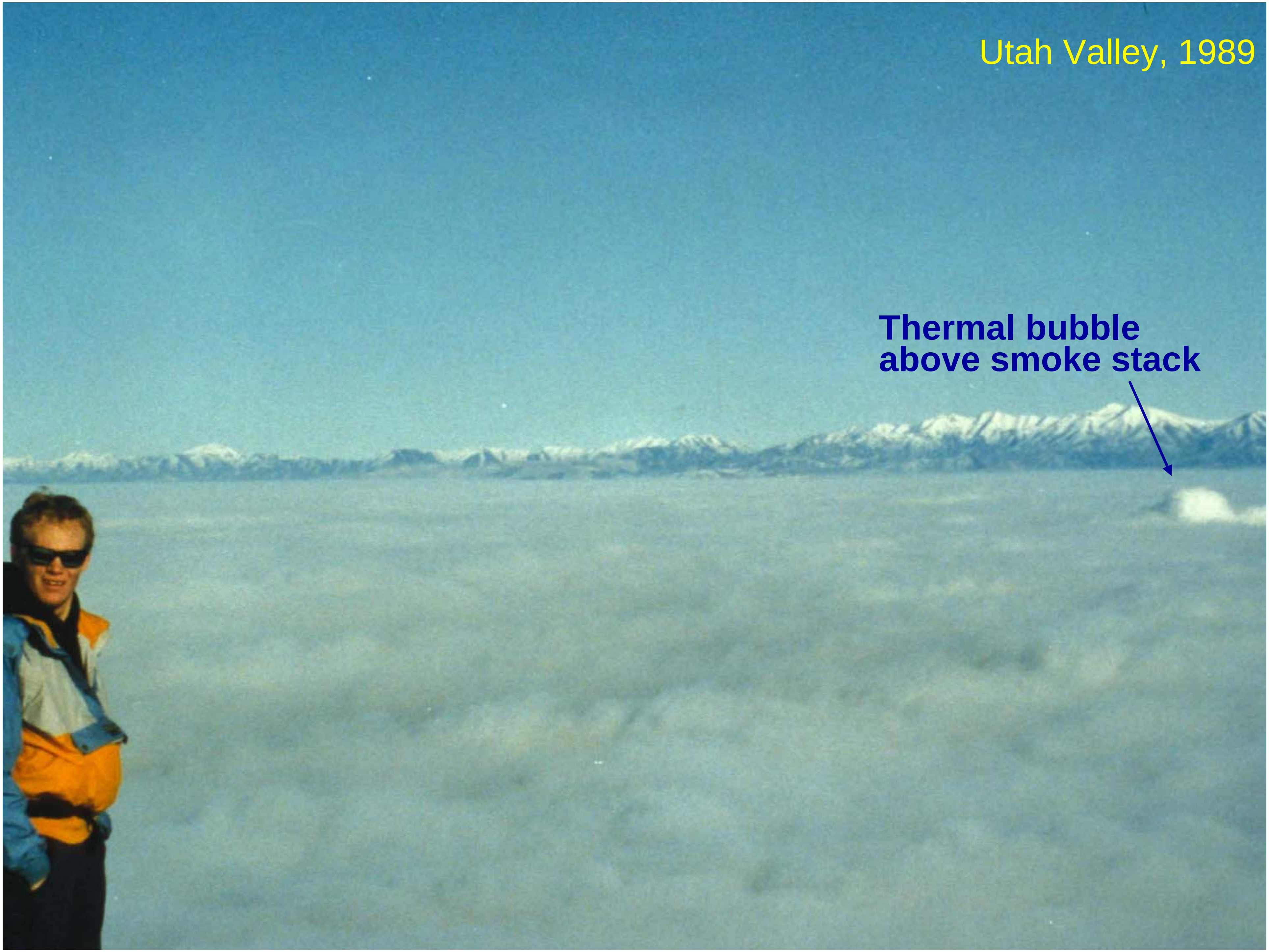
- Winter inversions trap local pollution
- Natural test chamber

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



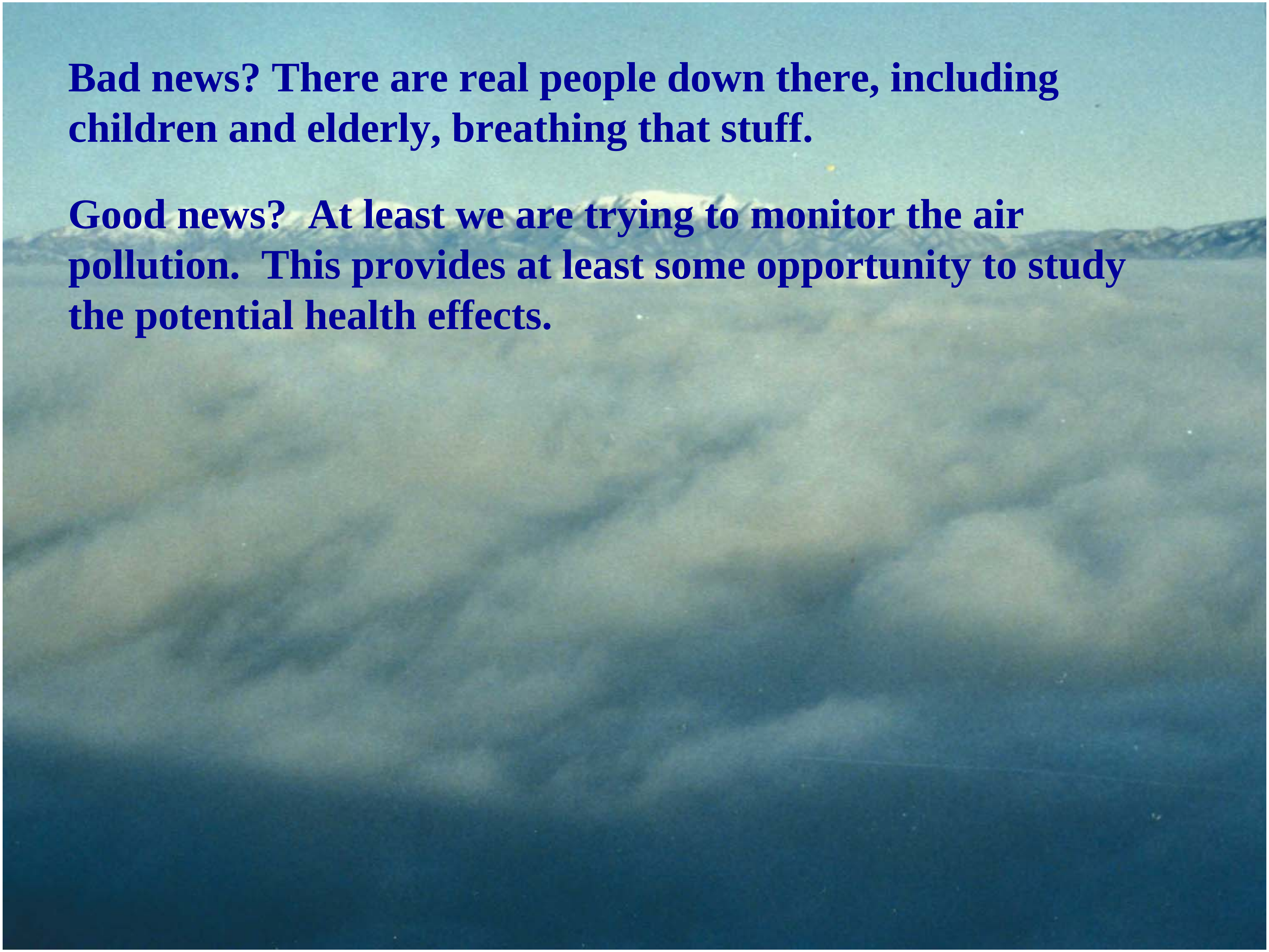
Local Steel Mill, Utah Valley, 1989


Utah Valley,
11 11 '89

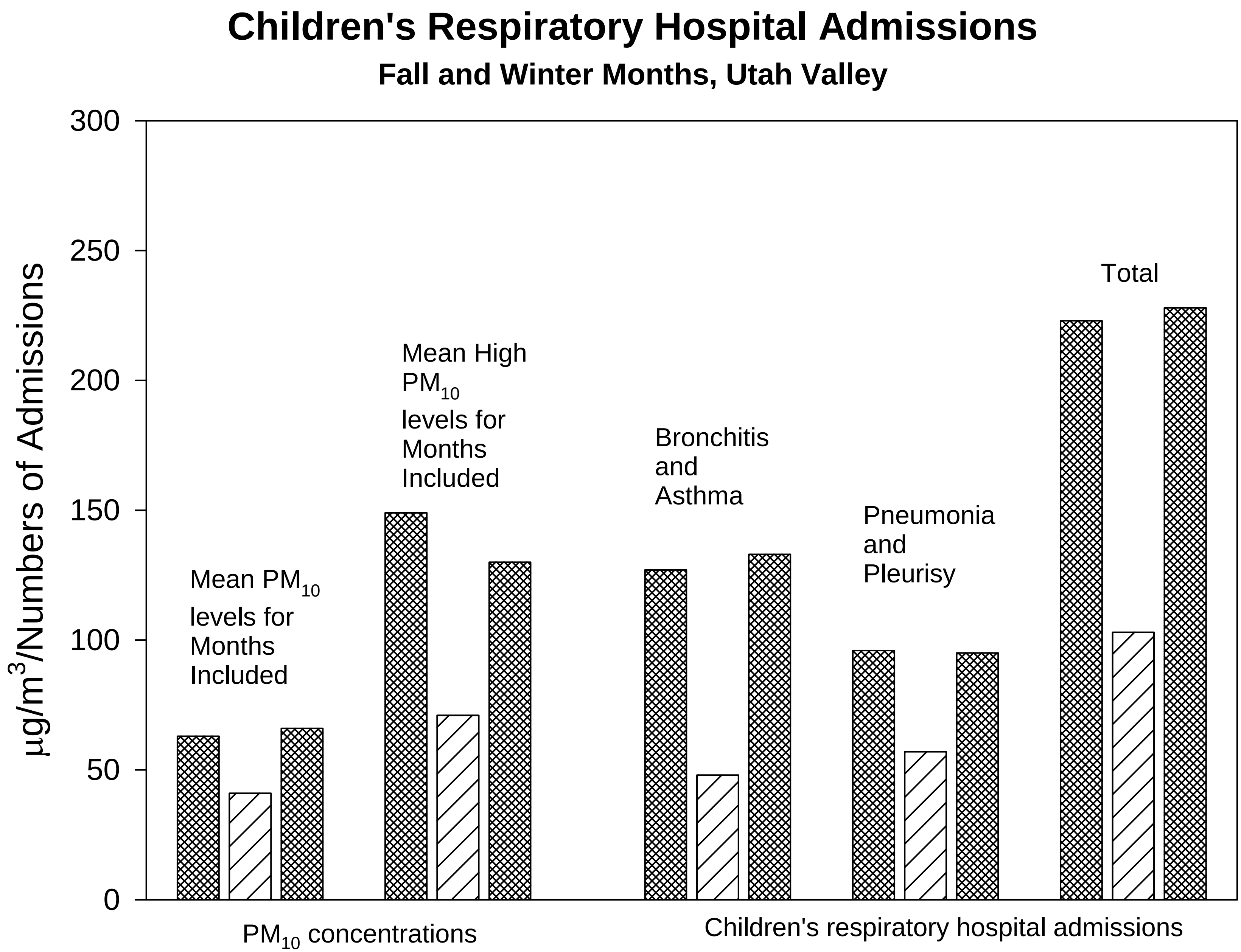

Utah Valley, 1989
Thermal bubble
above smoke stack

Bad news? There are real people down there, including children and elderly, breathing that stuff.

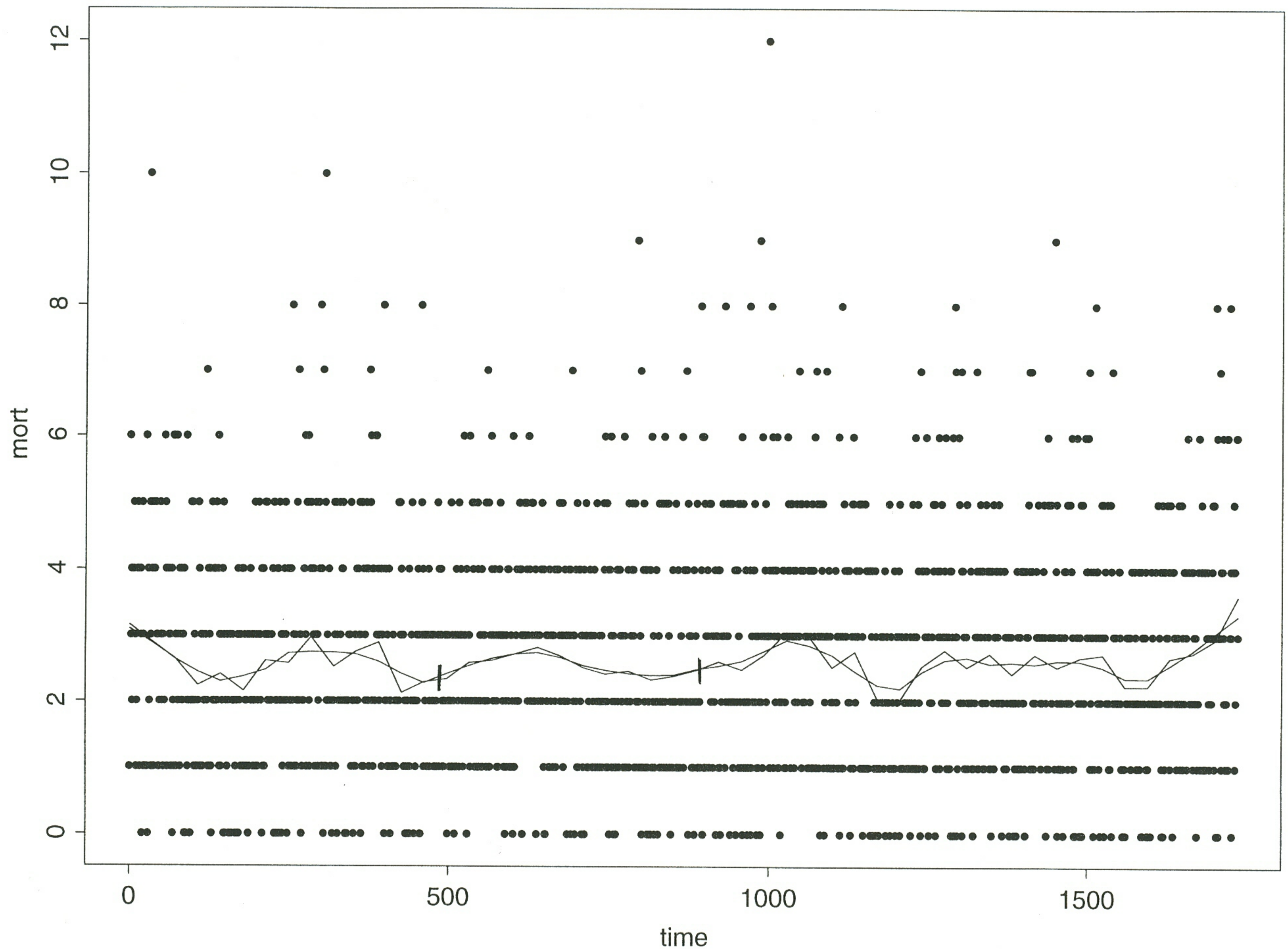
Good news? At least we are trying to monitor the air pollution. This provides at least some opportunity to study the potential health effects.




Long-term high-quality monitoring sites.
American Fork
Pleasant Grove
Saratoga Springs
Lindon
Vineyard
Orem
Provo, UT
Springville
Bird Island
State St
E State
N State St
N Redwood Rd
Westlake Rd
Redwood Rd
N 100 E
E 800 N
Geneva Rd
W 1300 S
E 1300 S
N 2050 W Geneva Rd
W Center St
S University Av
Veterans Memorial Hwy
S State St
E 1400 N
E 3900 S
W 400 S
W 4000 S
189
114
265
68
89
© 2009 Google
© 2009 Europa Technologies
Image © 2009 DigitalGlobe
Image State of Utah



Sources: Pope. Am J Pub Health.1989; Pope. Arch Environ Health. 1991

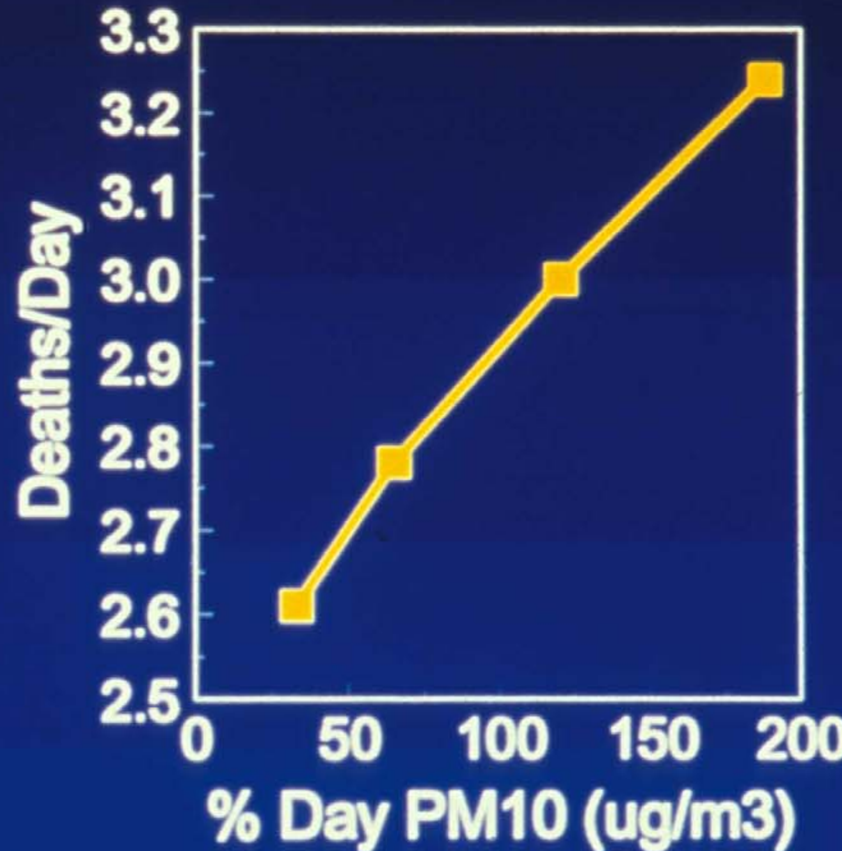


12
10
8
6
4
2
0
mort
0
500
1000
1500
time

Utah Valley Mortality

Pope et al, Arch Env Hlth, 1992

- Daily deaths 1985-90 for Utah Valley
  - Mean 2.7 per day
- Daily PM10 measures
  - Mean 47 ug/m3
  - Max 365 ug/m3
  - Lo SO_2, O_3, NO_2
- Poisson Regression
  - 1.5% per 10ug/m3



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

Increased hospital admissions:
Pope (1989) Am. J. Public Health
Pope (1991) Arch. Environ. Health

Increased respiratory symptoms:
Pope, Dockery, Spengler, Raizenne (1991) Am. Rev. Resp. Dis.

Reduced lung function:
Pope, Dockery (1992) Am. Rev. Resp. Dis.
Pope, Kanner (1993) Am. Rev. Resp. Dis.

Increased school absences:
Ransom, Pope (1992) Environ. Res

Increased respiratory and cardiovascular deaths:
Pope, Schwartz, Ransom (1992) Arch. Environ. Health
Pope, Kalkstein (1996) Environ. Health Perspect.
Pope, Hill, Villegas (1999) Environ. Health Perspect.

What was the critical aspect of this valley that allowed us to conduct this research in Utah Valley?

- Well-defined mountain valley study area
- Well-defined very low-smoking population
- Intermittent operation of primary pollution source (natural exp.)
- Minimal occupational exposure (Univ/educ, high tech, etc)
- Large local university and excellent collaborators
- Intermountain Health Care hospitals with excellent data
- etc.

Ambient Air Monitoring.

Excellent, regular monitoring of air pollution had been (and continues to be) conducted along Utah's Wasatch Front, including at multiple sites in Utah Valley, for many years.

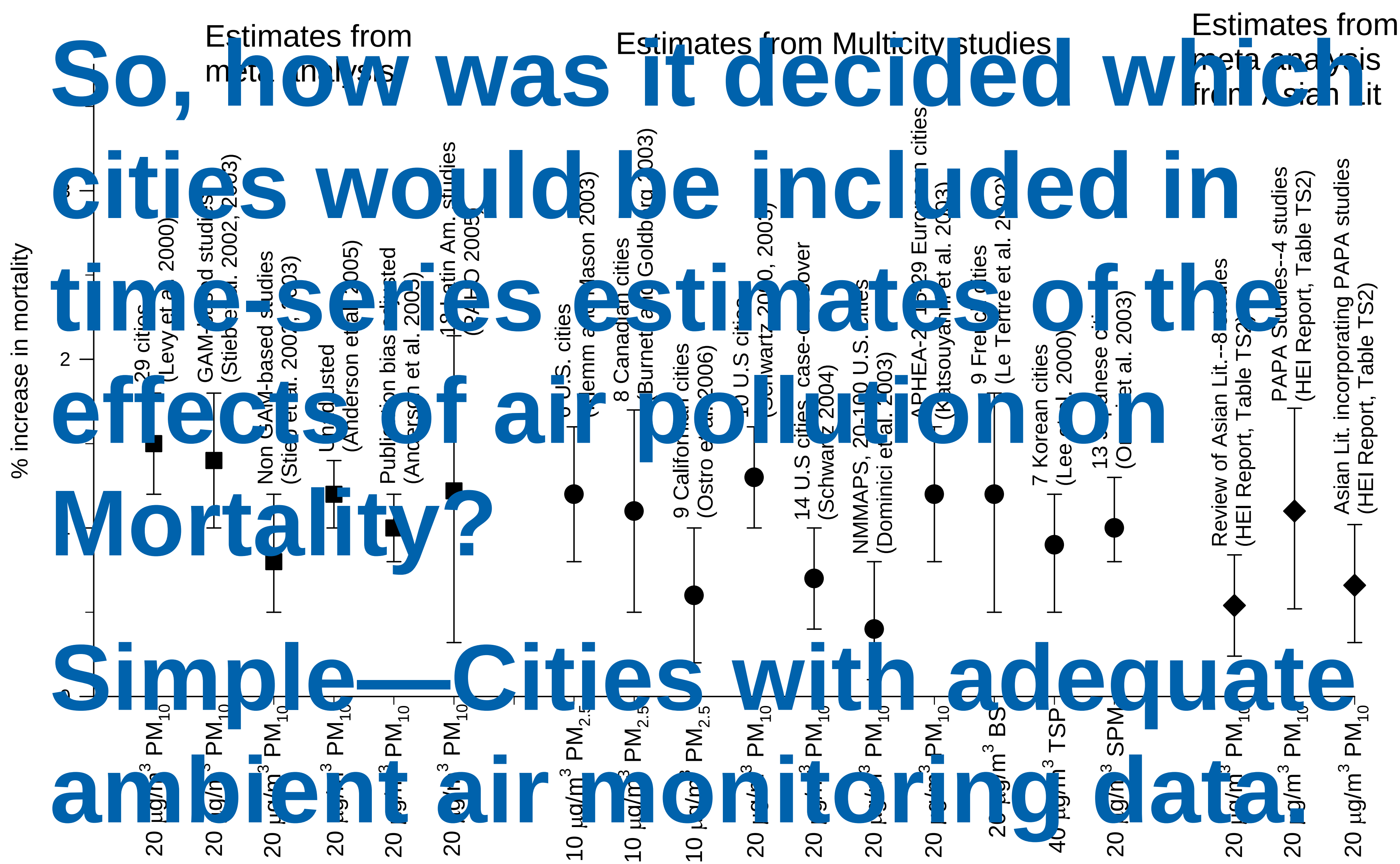
 

Experimental evidence of biological effects of PM extracted from filters
(Ghio, Kennedy, Frampton, Costa, Dye, Devlin et al. 1998-2004)

- 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?)

So, how was it decided which cities would be included in time-series estimates of the effects of air pollution on Mortality?

Simple—Cities with adequate ambient air monitoring data.

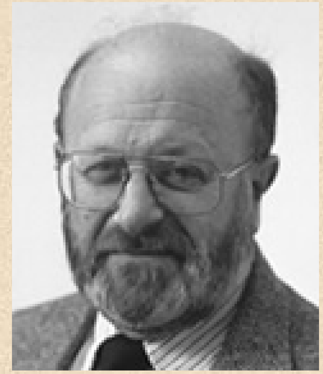


Now daily time-series mortality studies from 100s of cities.

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

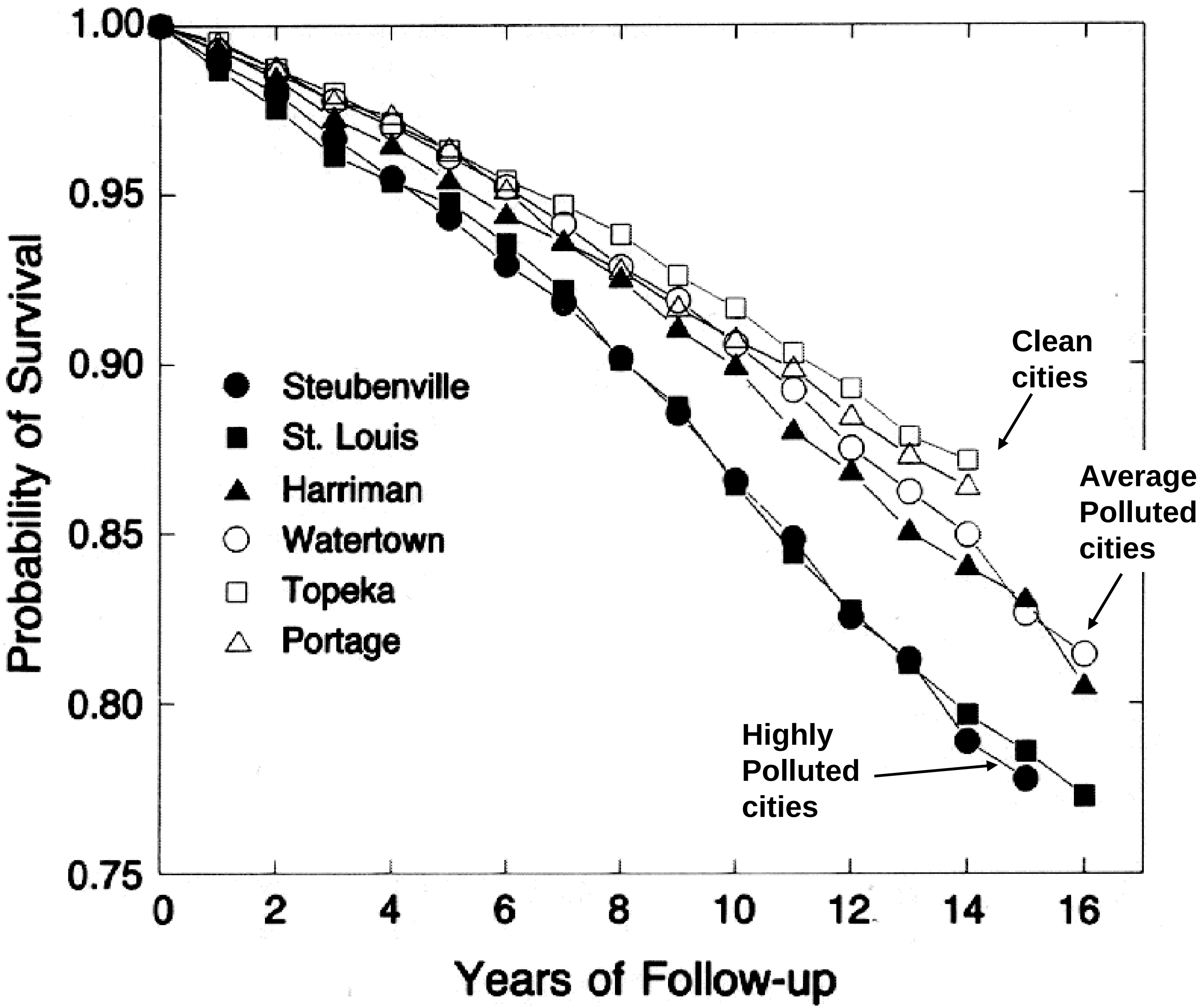
The NEW ENGLAND JOURNAL of MEDICINE 1993

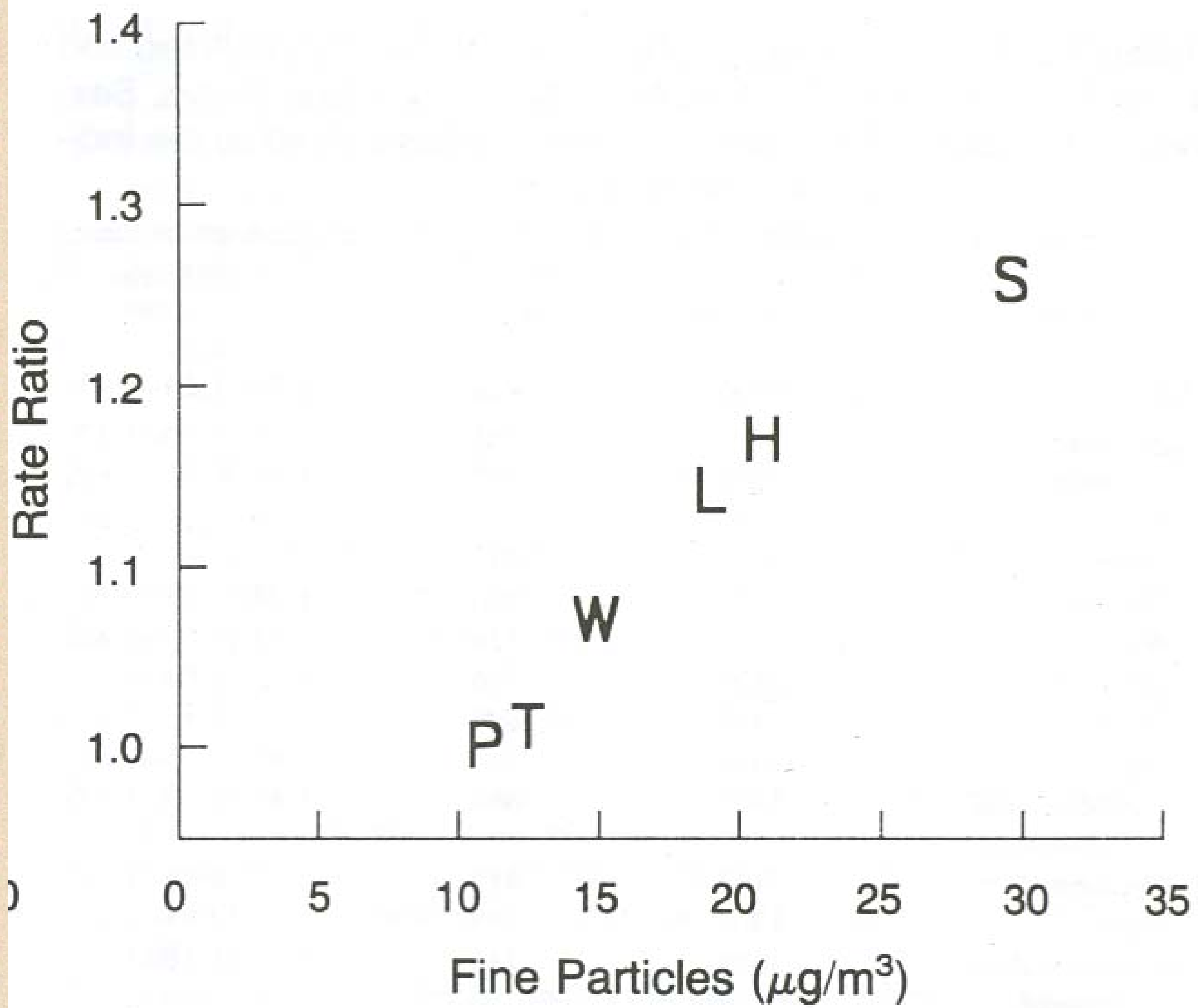
Dockery DW, Pope CA III, Xu X, Spengler JD, Ware JH, Fay ME, Ferris BG Jr, Speizer FE.



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.


1.00
0.95
0.90
0.85
0.80
0.75
Probability of Survival
0
2
4
6
8
10
12
14
16
Years of Follow-up
Steubenville
St. Louis
Harriman
Watertown
Topeka
Portage
Clean cities
Average Polluted cities
Highly Polluted cities



Rate Ratio
1.4
1.3
1.2
1.1
1.0
S
H
L
W
P
T
0
5
10
15
20
25
30
35
Fine Particles (μg/m³)

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

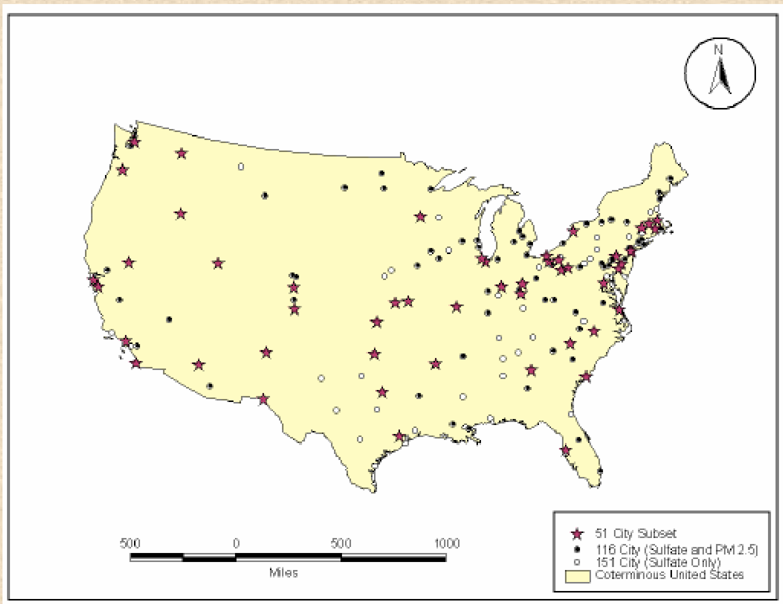
Michael Thun

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

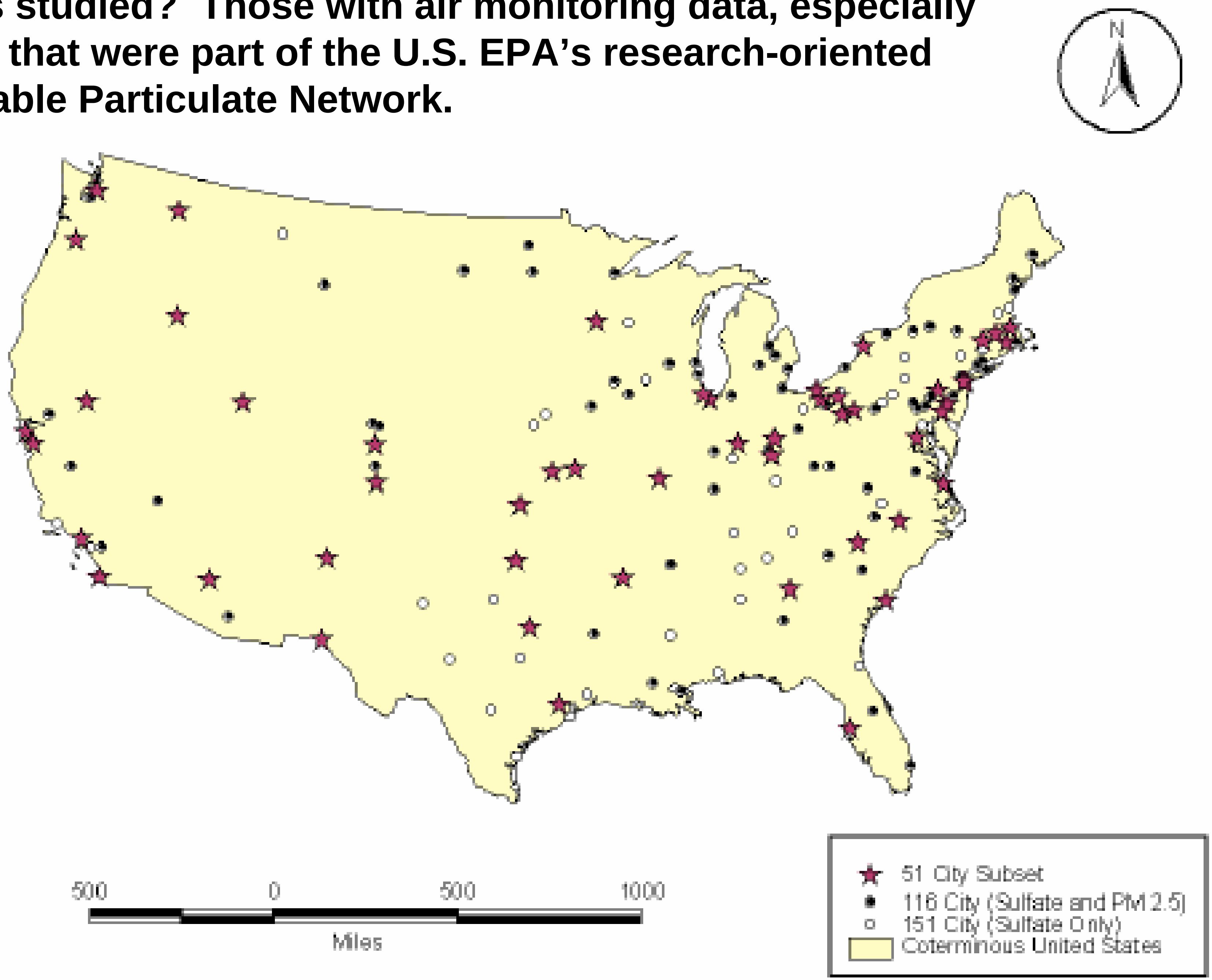
AMERICAN JOURNAL OF Respiratory and Critical Care Medicine® **1995**

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.



Cities studied? Those with air monitoring data, especially cities that were part of the U.S. EPA's research-oriented Inhalable Particulate Network.



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)

Dan Krewski
Rick Burnett
Mark Goldberg
and 28 others

HEI

SPECIAL REPORT

HEALTH
EFFECTS
INSTITUTE

July 2000

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

JAMA®
The Journal of the American Medical Association
March 6, 2002—Vol 287, No. 9

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 ai and increased risk of various adverse health outcomes, including cardiopulmc tality. However, studies of health effects of long-term particulate air pollu been less conclusive.

Objective To assess the relationship between long-term exposure to fir late air pollution and all-cause, lung cancer, and cardiopulmonary mortalit

Design, Setting, and Participants Vital status and cause of death data lected by the American Cancer Society as part of the Cancer Prevention II stu going prospective mortality study, which enrolled approximately 1.2 million adu







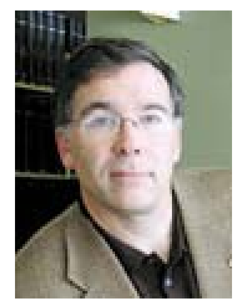
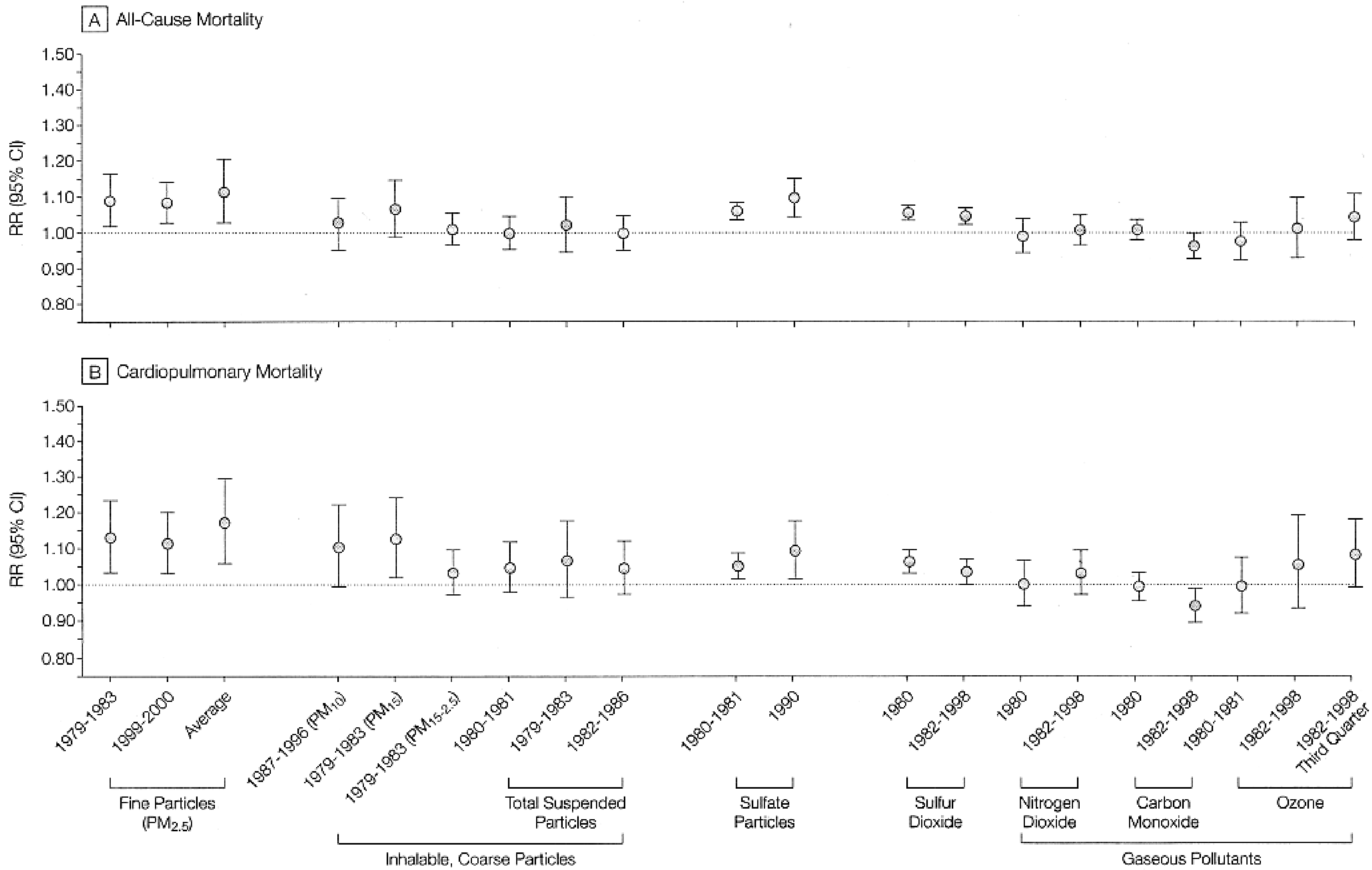
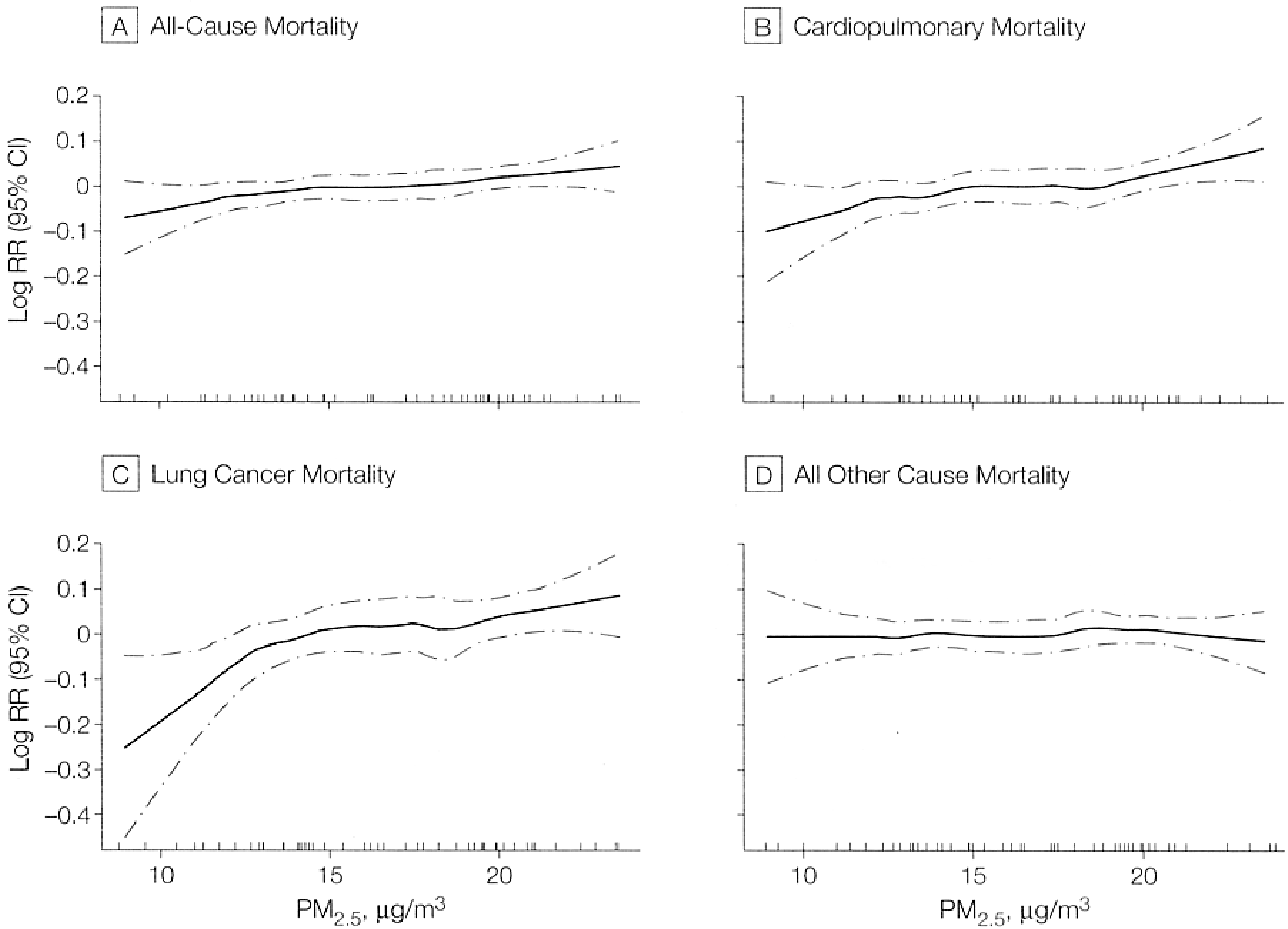


Figure 5. Adjusted Mortality Relative Risk (RR) Ratio Evaluated at Subject-Weighted Mean Concentrations



$PM_{2.5}$ indicates particles measuring less than 2.5 μm in diameter; PM_{10}, particles measuring less than 10 μm in diameter; PM_{15}, particles measuring less than 15 μm in diameter; $PM_{15\text{-}2.5}$, particles measuring between 2.5 and 15 μm in diameter; and CI, confidence interval.

Figure 2. Nonparametric Smoothed Exposure Response Relationship



Spatial analysis of air pollution and mortality in Los Angeles.
(Jerrett, Burnett, Ma, Pope, et al. Epidemiology 2005)

This research was facilitated by the substantial intra-metro air pollution monitoring network available in the greater LA metro area.

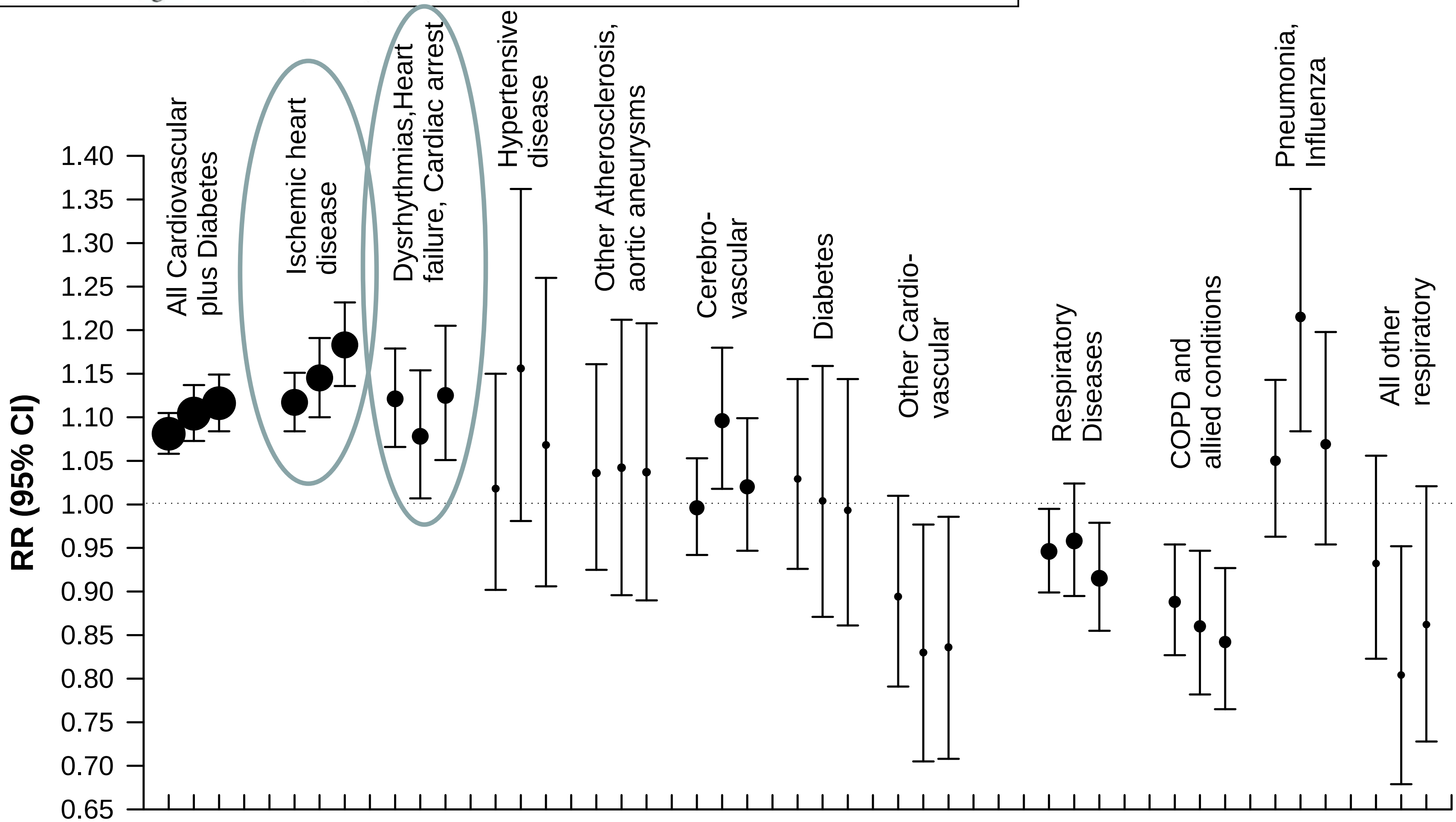
Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
2004;109:71-77

Cardiovascular Mortality and Long-Term Exposure to Particulate Air Pollution

Epidemiological Evidence of General Pathophysiological Pathways of Disease

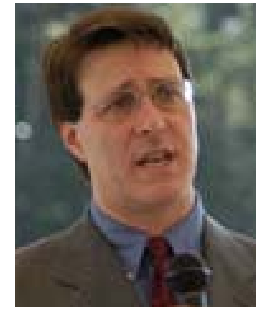
C. Arden Pope III, PhD; Richard T. Burnett, PhD; George D. Thurston, ScD; Michael J. Thun, MD; Eugenia E. Calle, PhD; Daniel Krewski, PhD; John J. Godleski, MD


John Godleski



The NEW ENGLAND JOURNAL of MEDICINE

Miller et al. Long-Term exposure to Air Pollution and Incidence of Cardiovascular Events in Women. 2007



Joel Kaufman

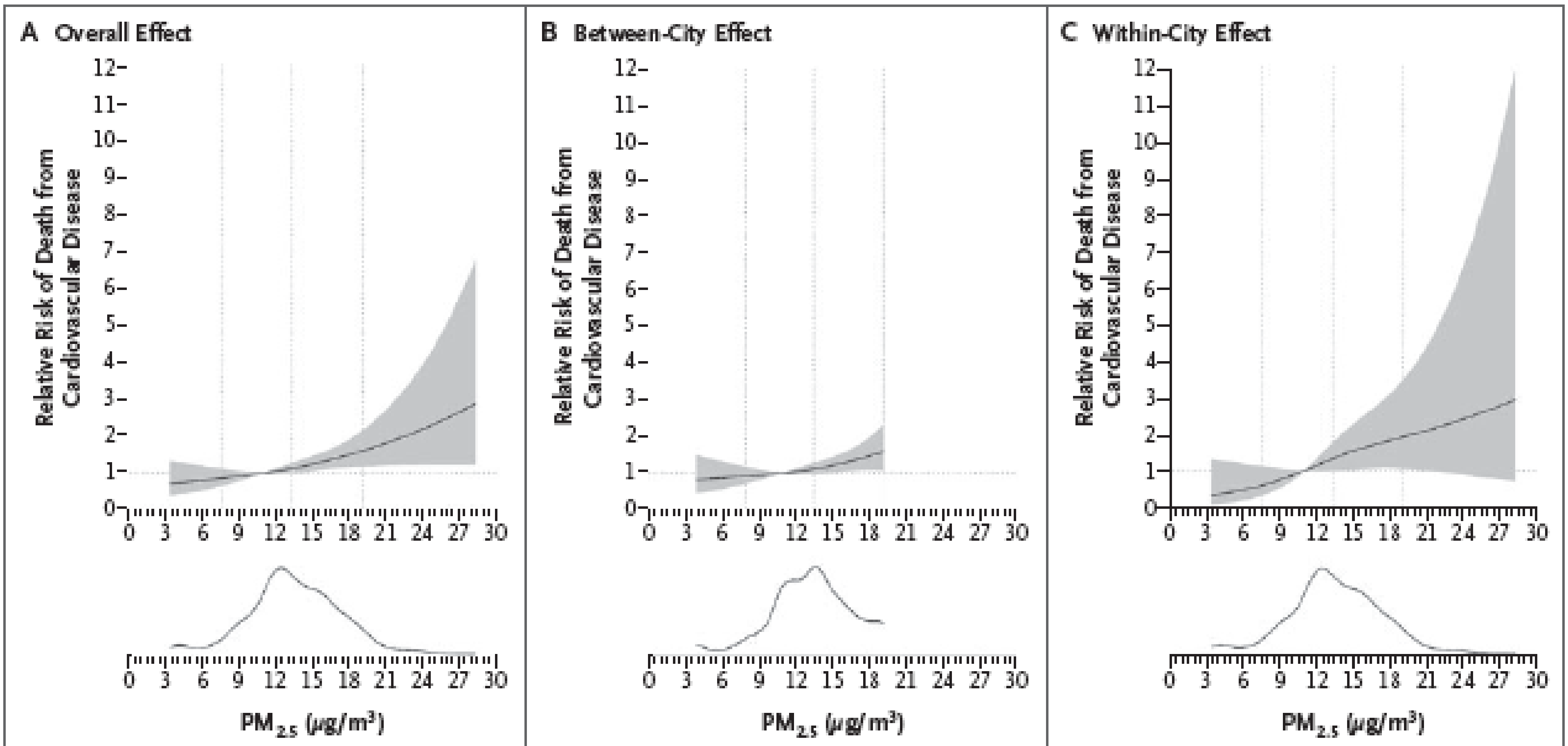


Figure 1. Level of Exposure to Fine Particulate Matter and the Risk of Death from Cardiovascular Causes in Women.

Air Pollution: Bad For Your Heart

DALLAS, Dec. 16, 2003

(AP / CBS)

(AP) Air pollution in U.S. cities causes twice as many deaths from heart disease as it does from lung cancer and other respiratory ailments, a surprising new study suggests.

QUOTE

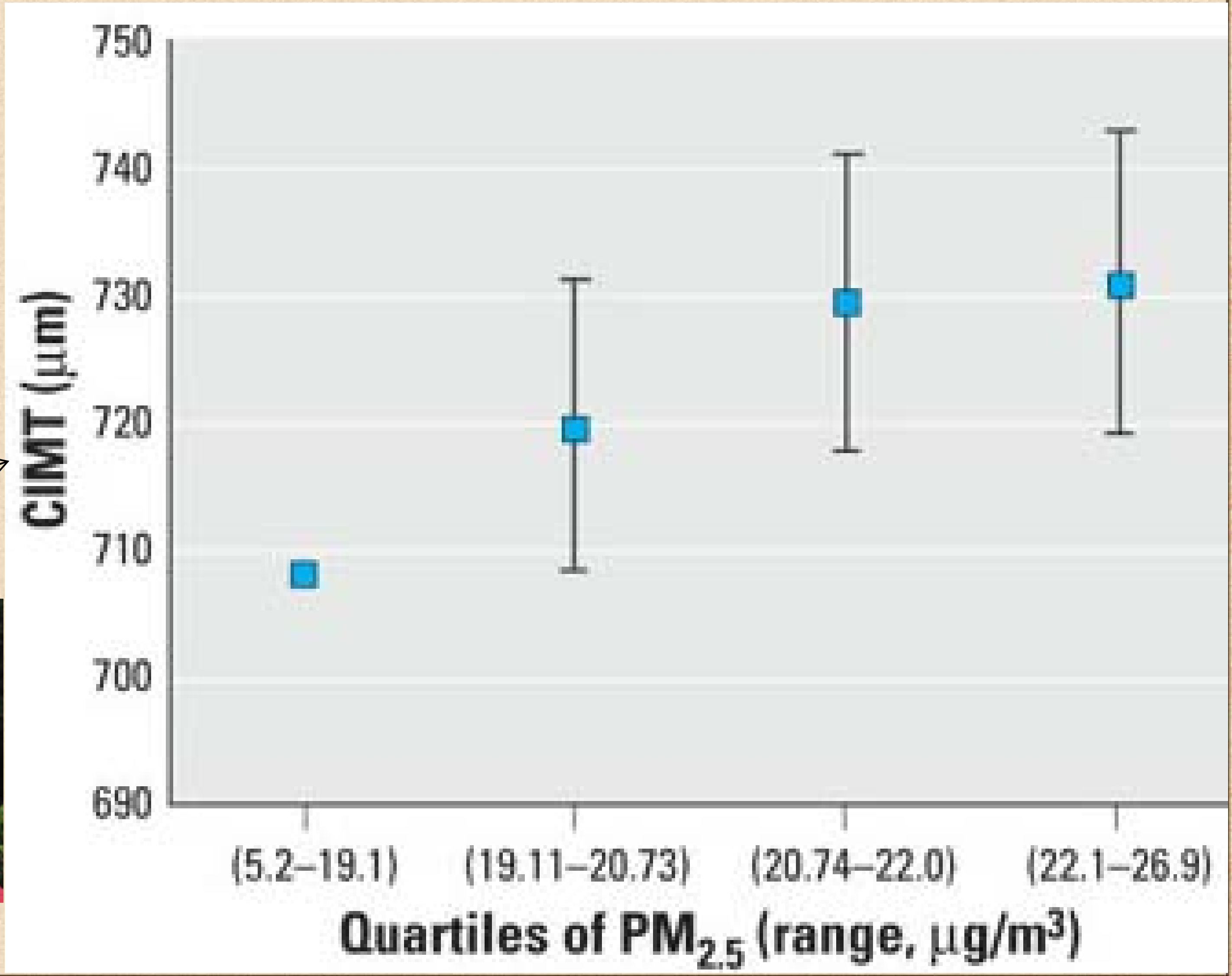
"It certainly did su
observed these r
anticipated that b
your lungs would
direct impact on y
C. Arden Pope III, B

Can this really be true?—is it biologically plausible?

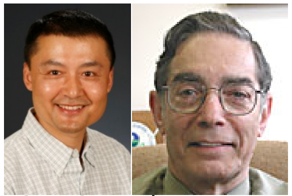
If so, how?—what are the pathopysiological pathways that link breathing air pollution and cardiovascular deaths?

Ambient Air Pollution and Atherosclerosis in Los Angeles. Kunzli et al. *EHP* 2005.

Carotid intima-media thickness



Nino Kunzli



Sun QH Lippmann M

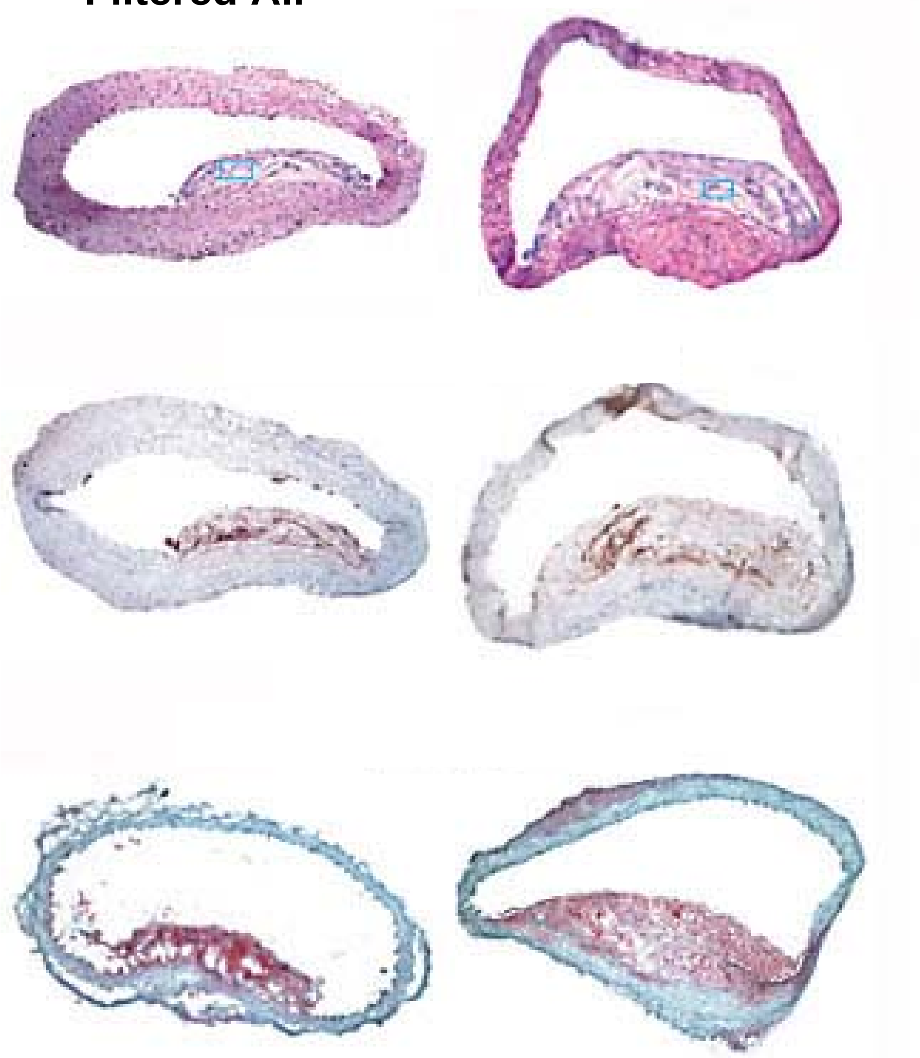
Sun et al. (*JAMA* 2005)

apoE$^{-/-}$ mouse

Representative Photomicrographs of Aortic Arch Sections

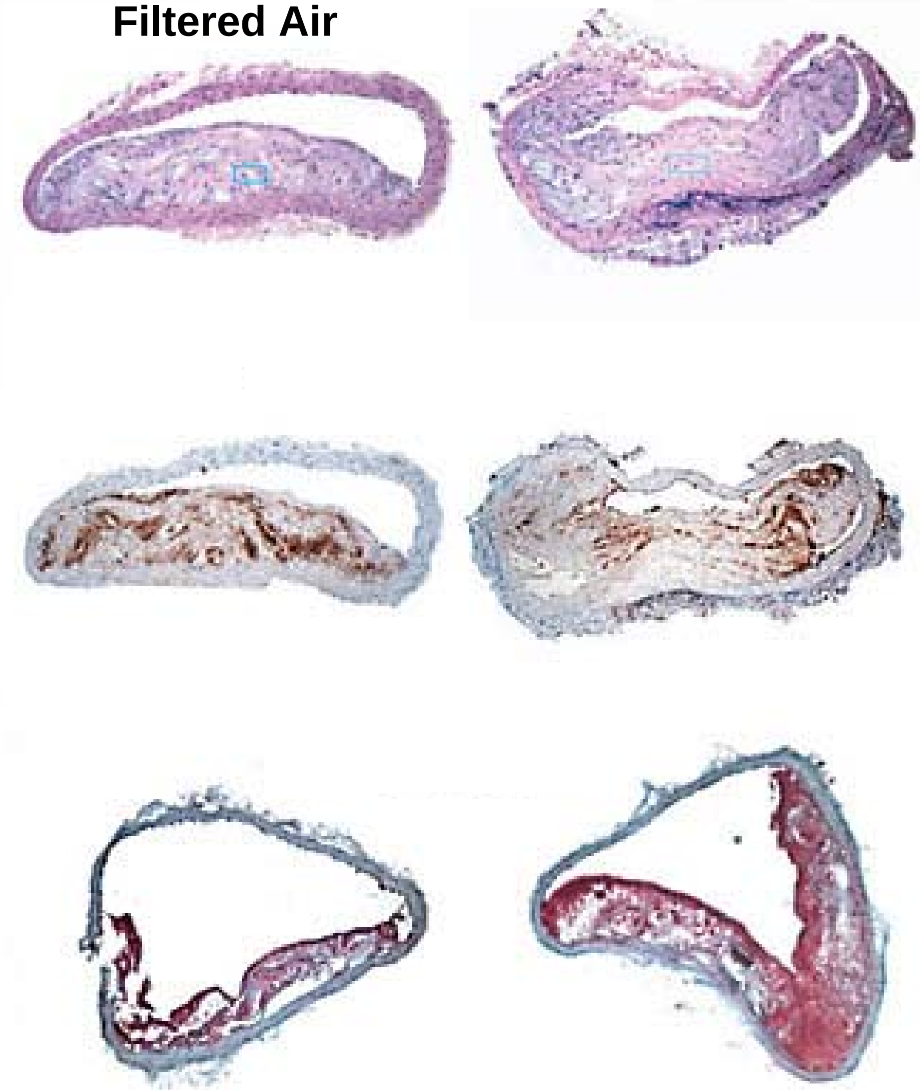
Normal Chow

Clean Filtered Air | **PM Polluted Air**



High-Fat Chow

Clean Filtered Air | **PM Polluted Air**



Deseret News

Utahns tout test for heart disease

LDS Hospital study links risks to white blood cell counts

By Lois M. Collins
Deseret Morning News
Published: Thursday, May 26, 2005 9:10 a.m. MDT
A blood test that measures white blood cell counts may provide a simple, cheap way to refine predictions of heart attacks or death, according to researchers at LDS Hospital.

Journal of the American College of Cardiology
© 2005 by the American College of Cardiology Foundation
Published by Elsevier Inc.

Vol. 45, No. 10, 2005
ISSN 0735-1097/05/$30.00
doi:10.1016/j.jacc.2005.02.054

Which White Blood Cell Subtypes Predict Increased Cardiovascular Risk?

Benjamin D. Horne, PhD, MPH,* Jeffrey L. Anderson, MD, FACC,*† Jerry M. John, MD,*† Aaron Weaver, MD,*† Tami L. Bair, BS,* Kurt R. Jensen, MS,* Dale G. Renlund, MD, FACC,*† Joseph B. Muhlestein, MD, FACC,*† for the Intermountain Heart Collaborative (IHC) Study Group
Salt Lake City, Utah

OBJECTIVES We sought to determine the predictive ability of total white blood cell (WBC) count and its subtypes for risk of death or myocardial infarction (MI).

BACKGROUND An elevated WBC count has been associated with cardiovascular risk, but which leukocyte subtypes carry this risk is uncertain.

METHODS Consecutive patients without acute MI who were assessed angiographically for coronary artery disease (CAD) and were followed up long-term were studied. The predictive ability for death/MI of quartile (Q) 4 versus Q1 total WBC, neutrophil (N), lymphocyte (L), and monocyte (M) counts and N/L ratio were assessed using Cox regressions.

RESULTS A total of 3,227 patients was studied. Mean age was 63 years; 63% of patients were male, and 65% had CAD. In multivariable modeling entering standard risk factors, presentation, and CAD severity, the total WBC (hazard ratio [HR] 1.4, $p = 0.01$) and M (HR 1.3, $p < 0.02$) were weaker and N (HR 1.8, $p < 0.001$), L (HR 0.51, $p < 0.001$), and N/L ratio (HR 2.2, $p < 0.001$) were independent predictors of death/MI. When WBC variables were entered together, N/L ratio and M were retained as independent predictors. Risk associations persisted in analyses restricted to CAD patients or including acute MI patients.

CONCLUSIONS Total WBC count is confirmed to be an independent predictor of death/MI in patients with or at high risk for CAD, but greater predictive ability is provided by high N (Q4 $>6.6 \times 10^3/\mu l$) or low L counts. The greatest risk prediction is given by the N/L ratio, with Q4 versus Q1 (>4.71 versus <1.96) increasing the hazard 2.2-fold. These findings have important implications for CAD risk assessment. (J Am Coll Cardiol 2005;45:1638–43) © 2005 by the American College of Cardiology Foundation

PM$_{2.5}$ FRMs Reporting to AQS—**thanks to Joann Rice for slide**

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION
2006;114:2443-48

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

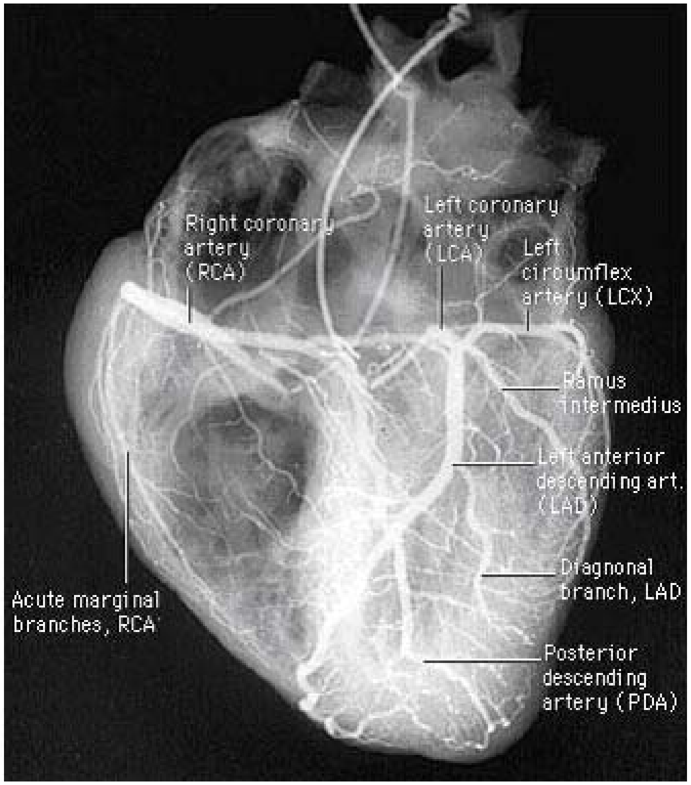
C. Arden Pope III, PhD; Joseph B. Muhlestein, MD; Heidi T. May, MSPH; Dale G. Renlund, MD; Jeffrey L. Anderson, MD; Benjamin D. Horne, PhD, MPH

Jeffrey Anderson

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



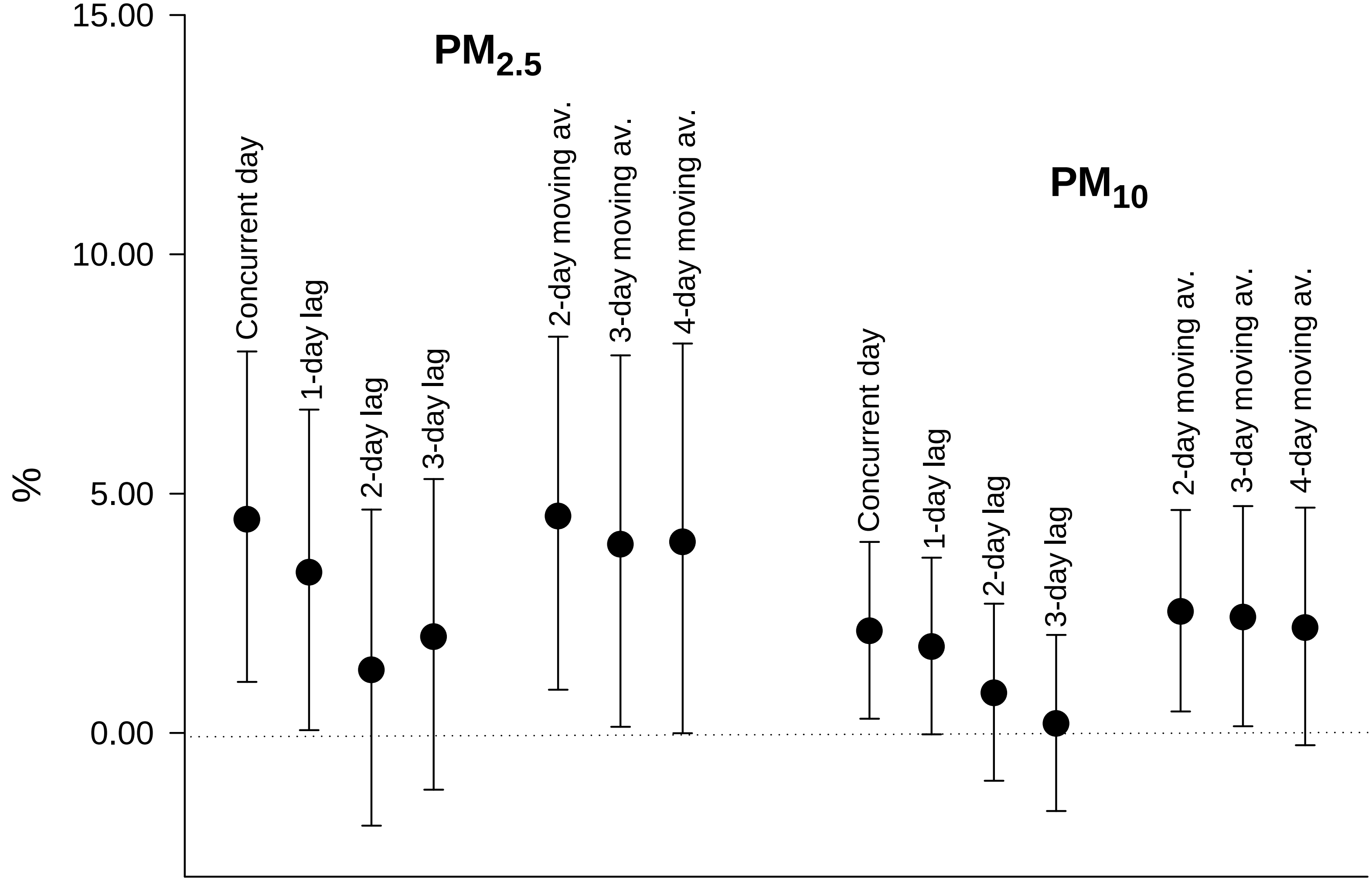


Figure 1. Percent increase in risk (and 95% CI) of acute coronary events associated with 10 $\mu g/m^3$ of $PM_{2.5}$, or PM_{10} for different lag structures.

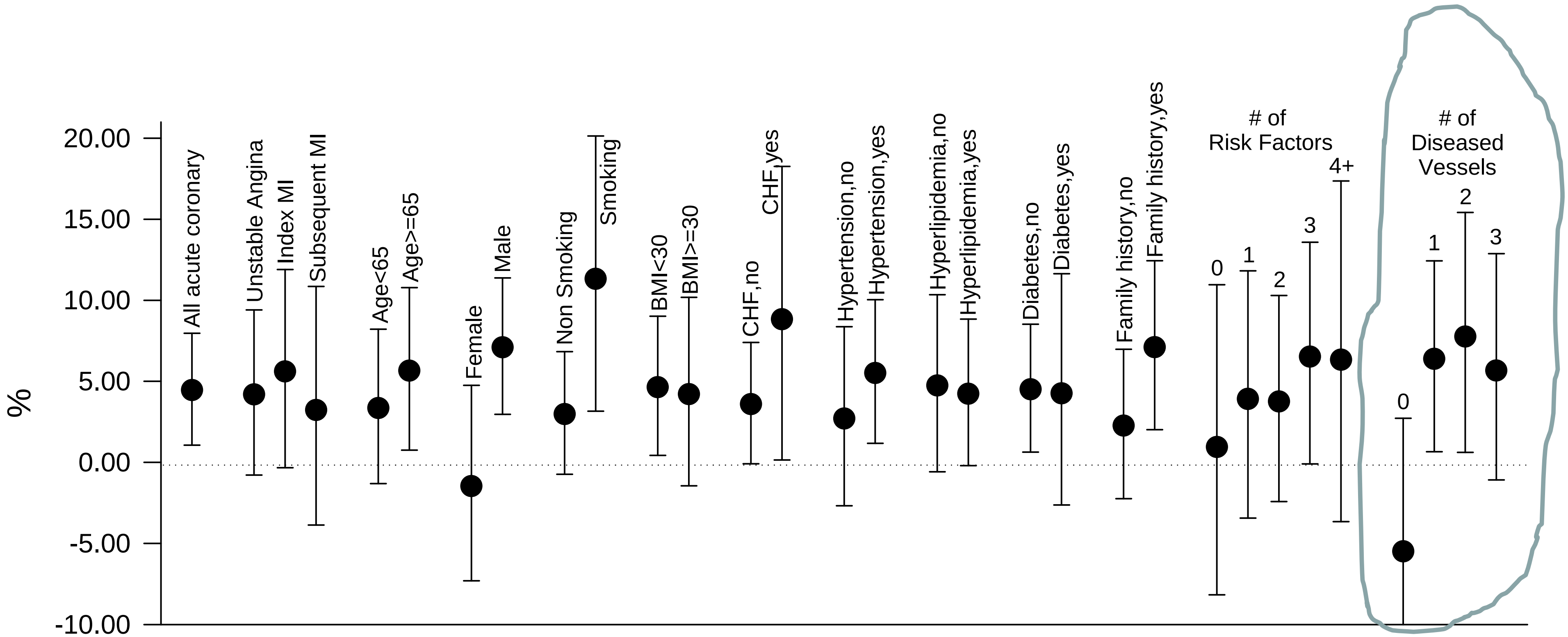
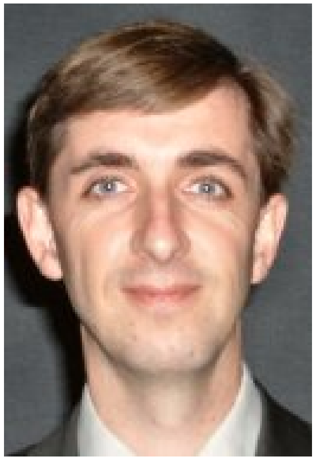


Figure 2. Percent increase in risk (and 95% CI) of acute coronary events associated with 10 $\mu g/m^3$ of $PM_{2.5}$, stratified by various characteristics.

The American Journal of Cardiology

Pope, Renlund, Kfoury, May, Horne. 2008. Relation of Heart Failure Hospitalization to Exposure to Fine Particulate Air Pollution.



Benjamin Horne

Methods:

Case-crossover study of 2,628 heart failure hospitalizations.

Conclusions:

Pollution appears to play a role in precipitating acute cardiac decompensation in otherwise well-managed patients with HF, perhaps through effects of PM on myocardial ischemia, cardiac autonomic function, and/or arrhythmic effects.

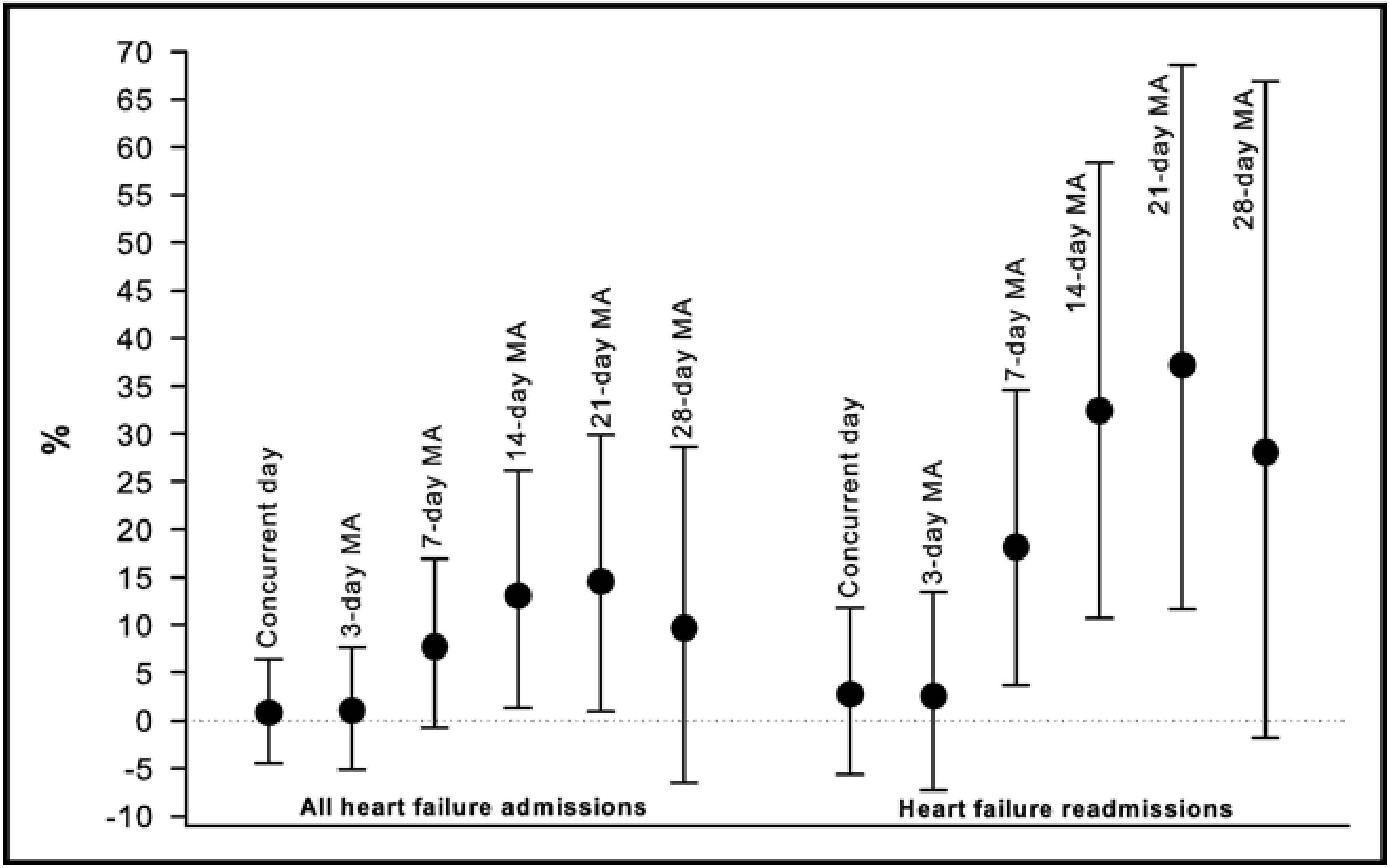


Figure 1. Percent increase in risk and 95% CIs of HF admissions and readmissions, associated with a 10 g/m3 of PM2.5 for selected lagged moving average (MA) exposures 0 to 28 days.

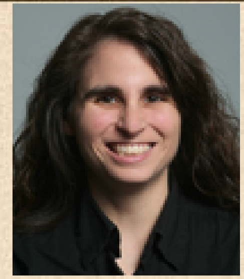
Do reductions in ambient air pollution result in reduced mortality risk/increased life expectancy?

Another job for Air Monitoring and Epidemiology.

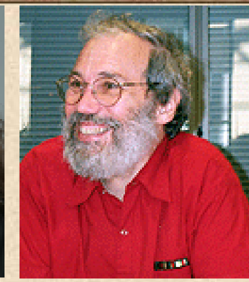
Reduction in fine particulate air pollution:

Extended follow-up of the Harvard Six Cities Study

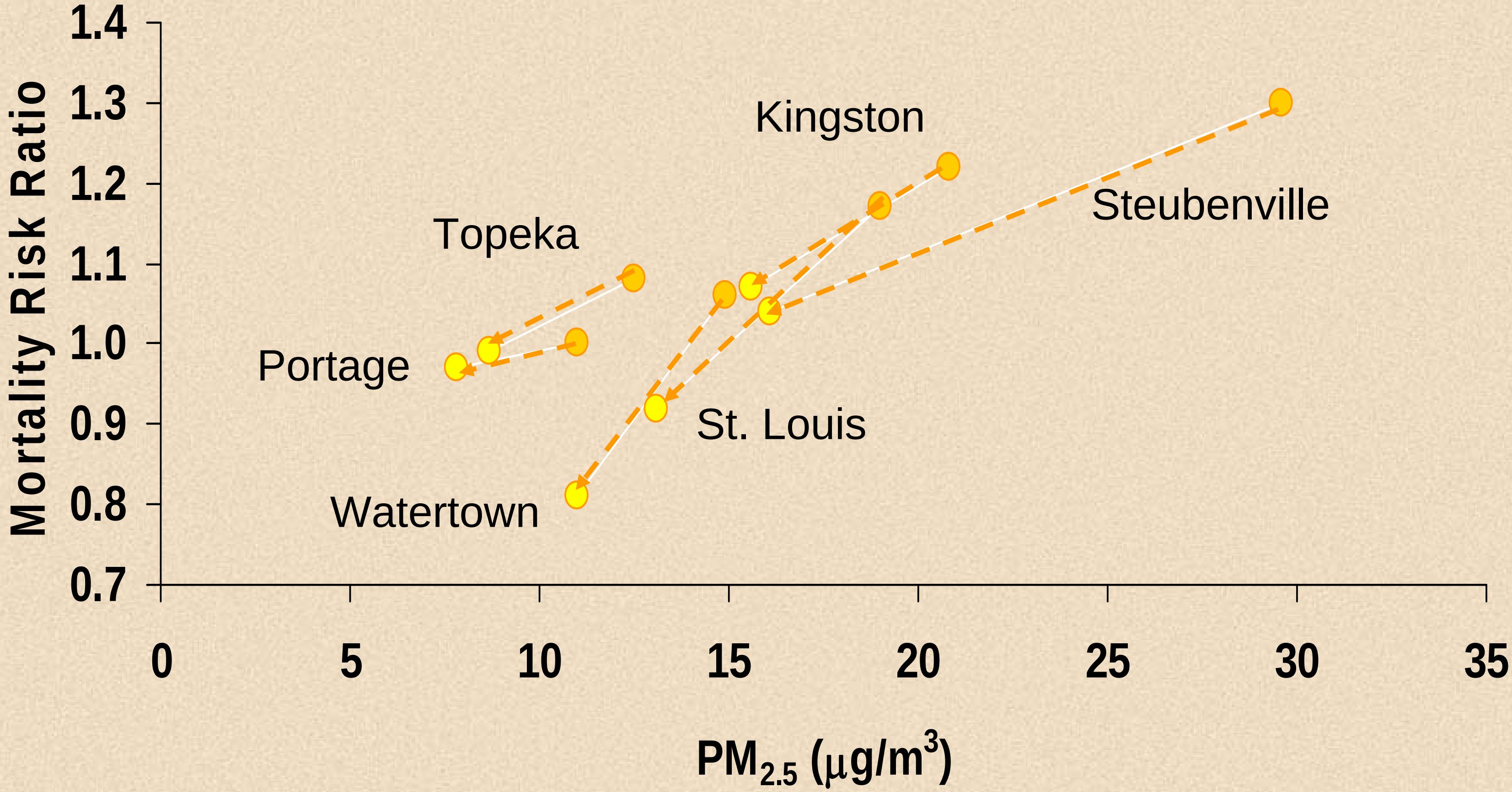
(Laden, Schwartz, Speizer, Dockery. AJRCCM 2006)

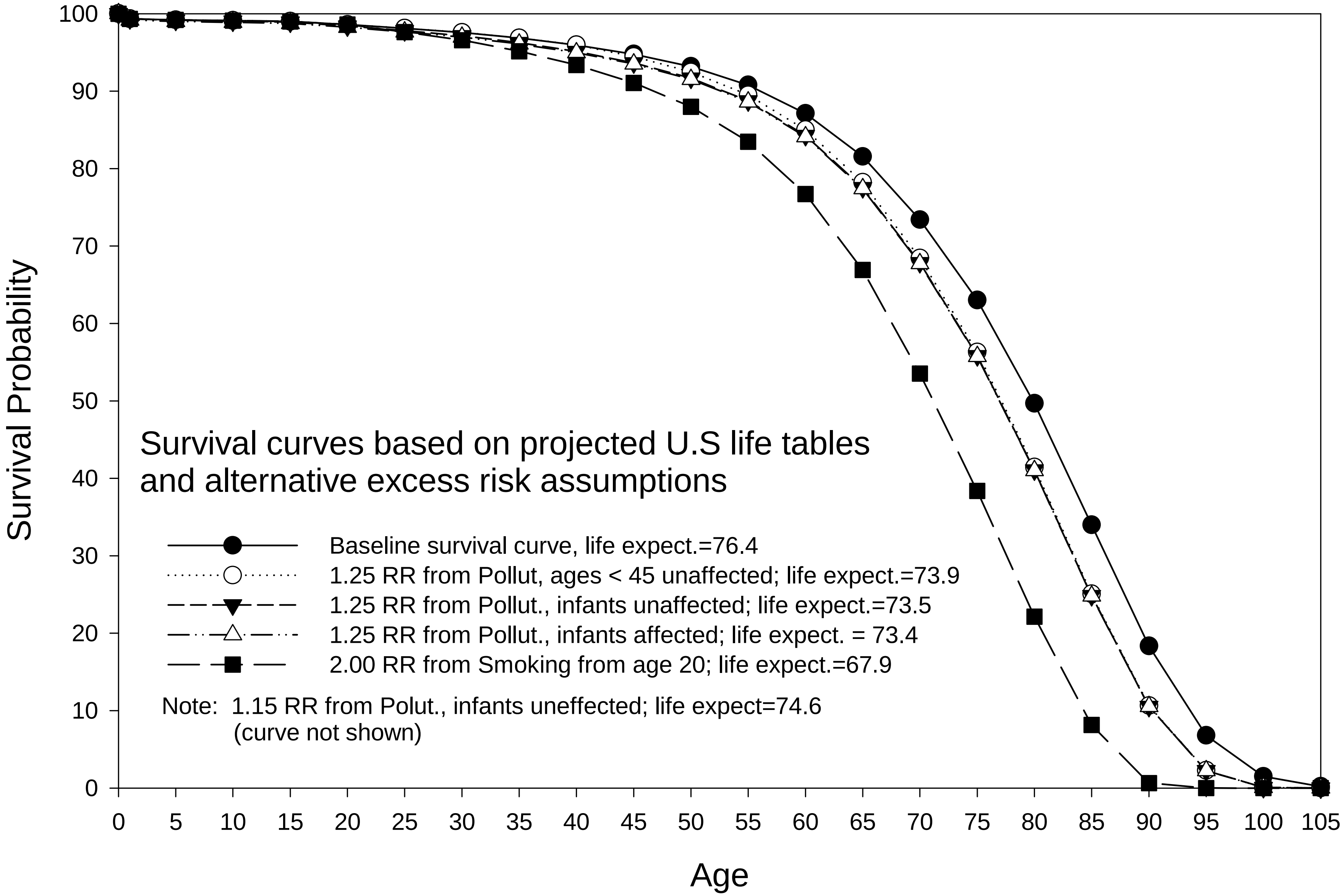


Francine Laden



Joel Schwartz





ENVIRONMENTAL HEALTH PERSPECTIVES

Pope 2000

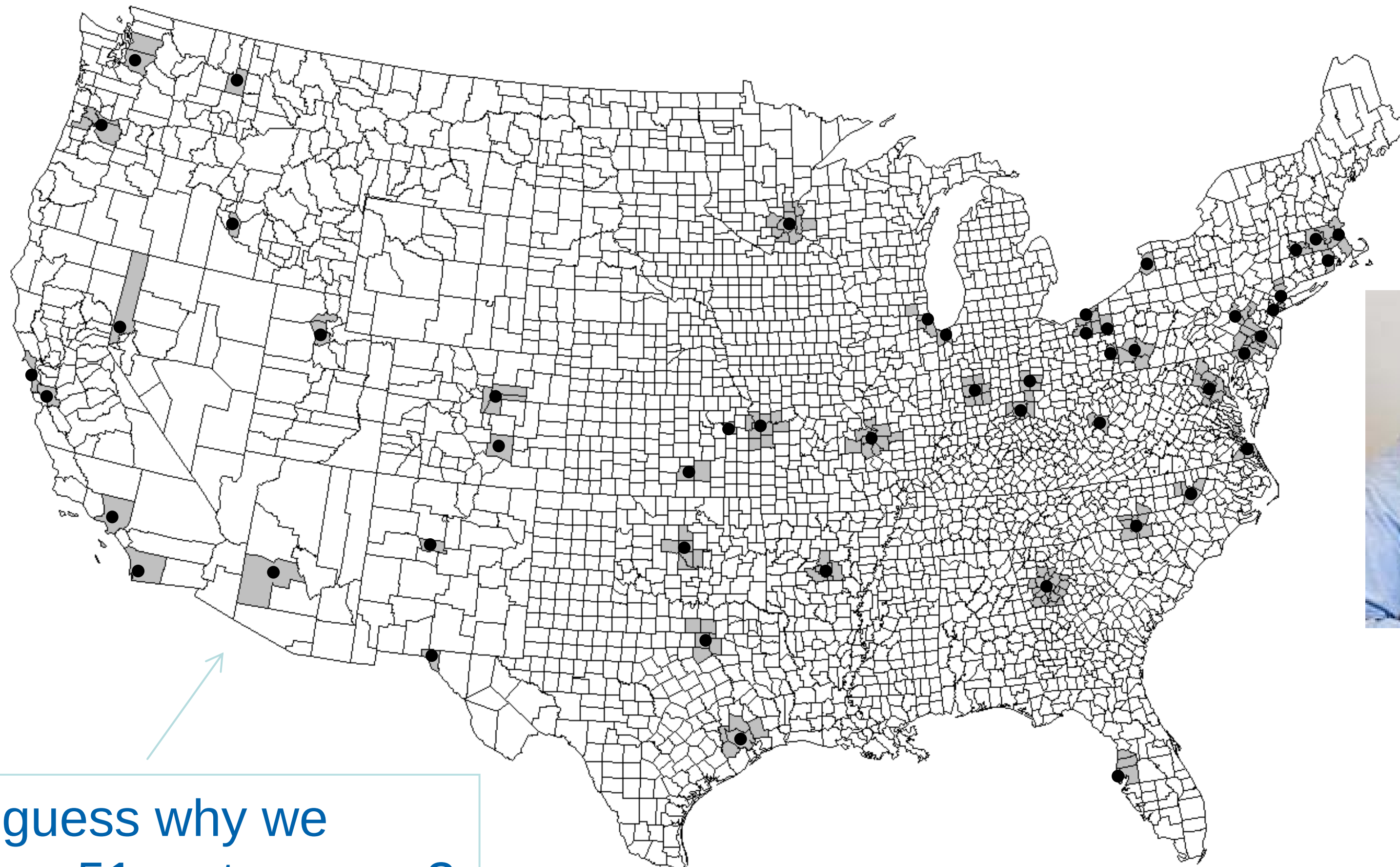
The NEW ENGLAND JOURNAL of MEDICINE

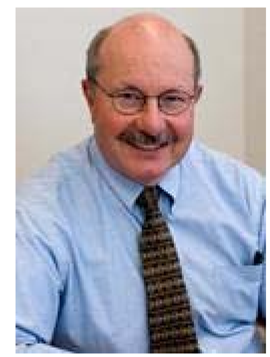
Fine-Particulate Air Pollution and Life Expectancy in the United States

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

January 22, 2009

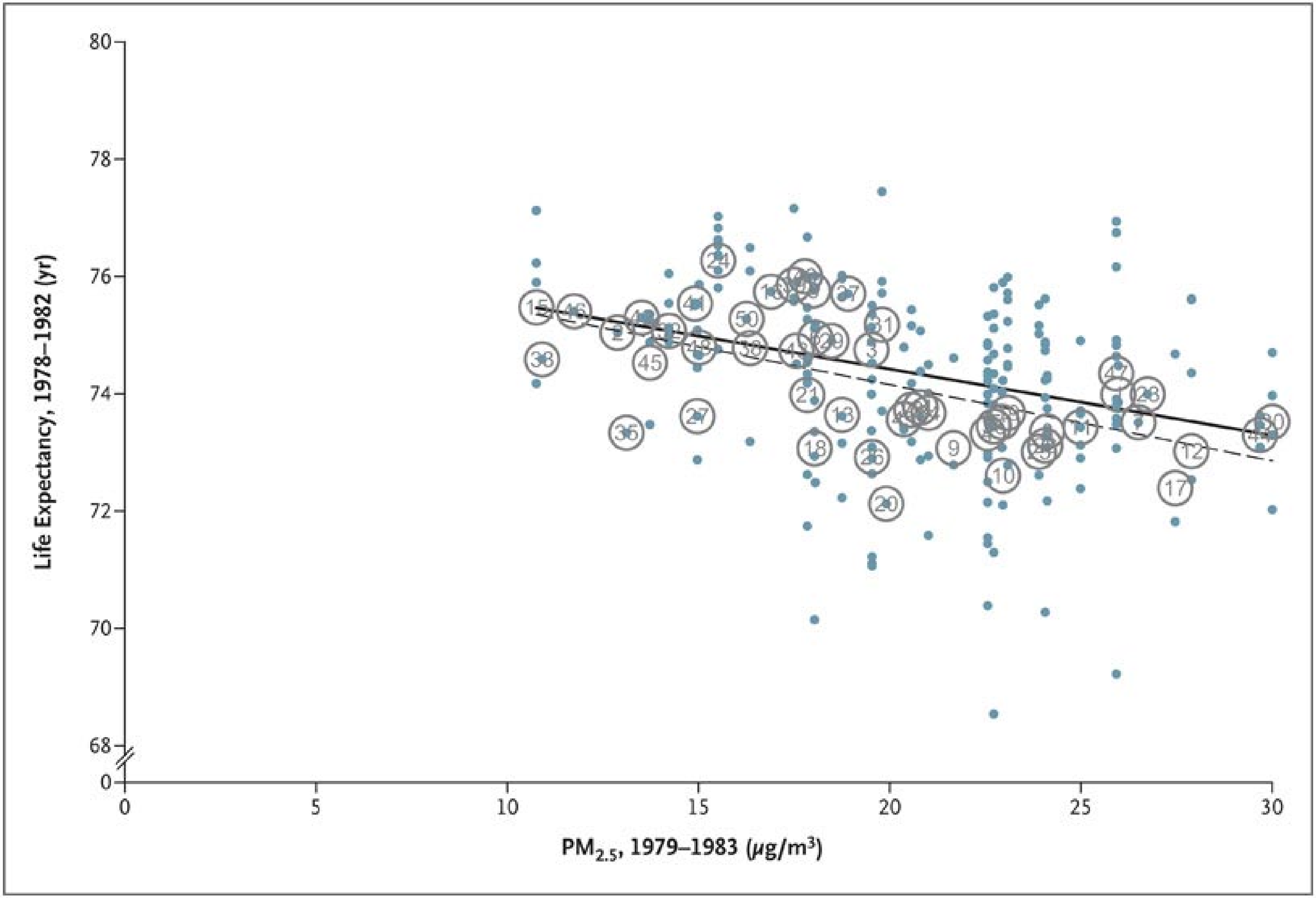
Majid Ezzati



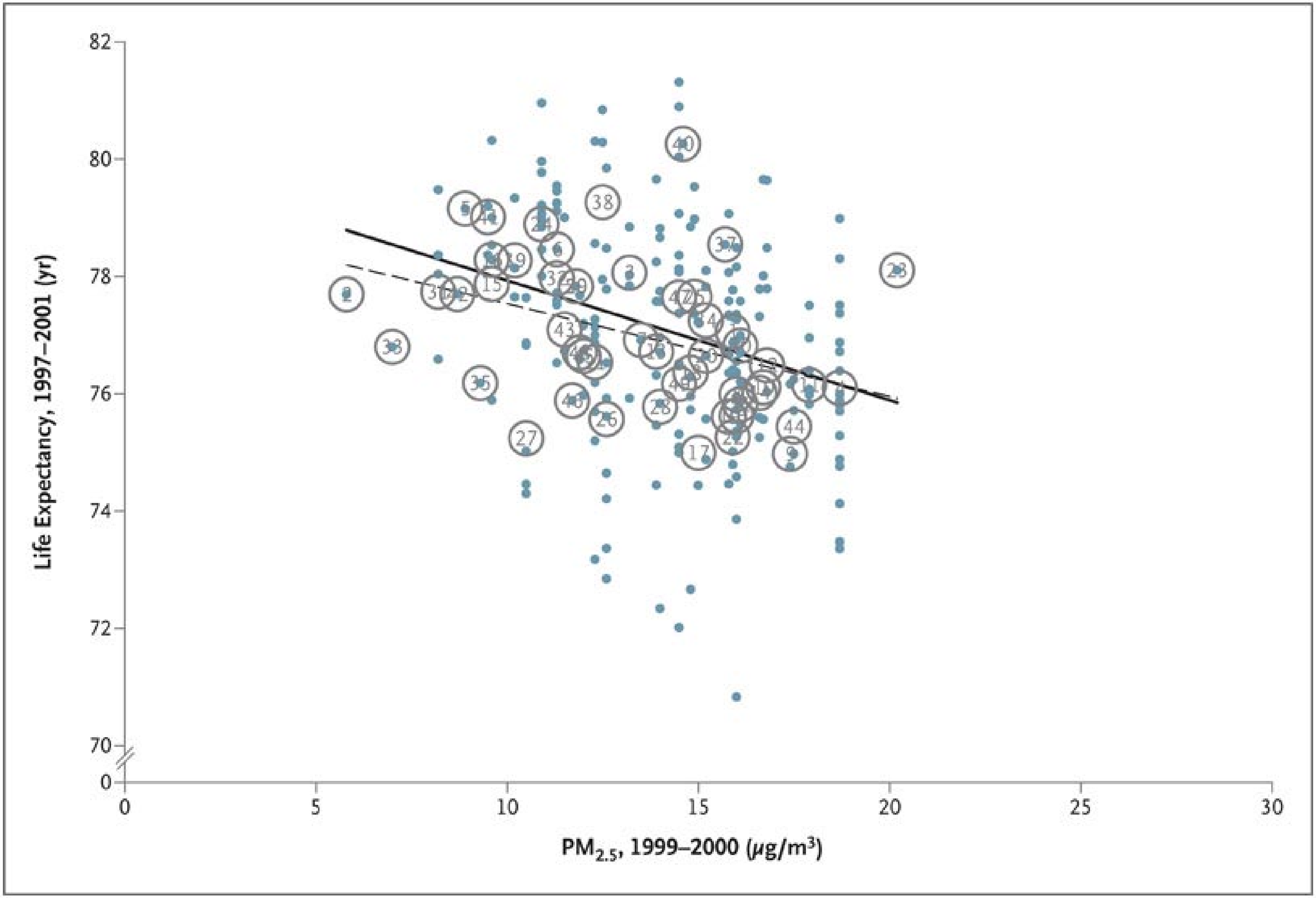


Doug Dockery

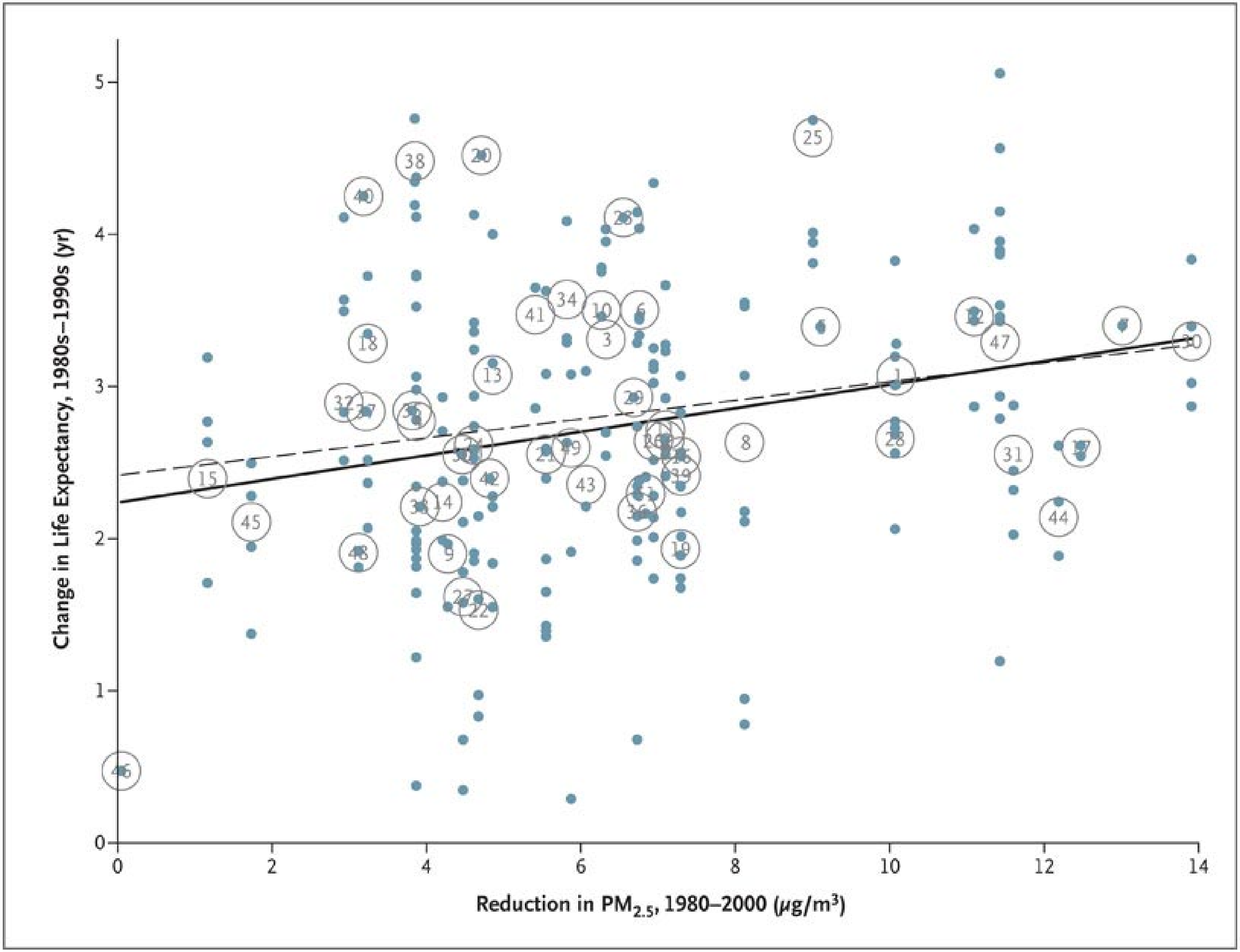
Want to guess why we used these 51 metro areas?



Life Expectancy, 1978–1982 (yr)
80
78
76
74
72
70
68
0
0
5
10
15
20
25
30
PM2.5, 1979–1983 (μg/m3)



82
80
78
76
74
72
70
0
Life Expectancy, 1997–2001 (yr)
0
5
10
15
20
25
30
PM2.5, 1999–2000 (μg/m3)



Change in Life Expectancy, 1980s–1990s (yr)
0
1
2
3
4
5
Reduction in PM2.5, 1980–2000 (μg/m3)
0
2
4
6
8
10
12
14

Table 2. Results of Selected Regression Models, Including Estimates of the Increase in Life Expectancy Associated with a Reduction in $PM_{2.5}$ 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±0.21§	0.80±0.19§	1.78±0.27§	1.75±0.27§	2.02±0.34§	1.71±0.51§	2.09±0.36§
Reduction in $PM_{2.5}$ (10 μg/m³)	0.72±0.29¶	0.83±0.20§	0.60±0.20§	0.61±0.20§	0.55±0.24¶	1.01±0.25§	0.95±0.23§
Change in income (in thousands of $)	—	0.17±0.02§	0.13±0.02§	0.13±0.01§	0.11±0.02§	0.15±0.04§	0.11±0.02§
Change in population (in hundreds of thousands)	—	0.08±0.02§	0.05±0.02§	0.06±0.02§	0.05±0.02§	0.04±0.02	0.05±0.02¶
Change in 5-yr in-migration (proportion of population)‖**	—	0.19±0.79	1.28±0.80	—	—	−0.02±1.83	—
Change in high-school graduates (proportion of population)‖	—	0.17±0.56	−0.11±0.53	—	—	−0.90±0.86	—
Change in urban residence (proportion of population)‖	—	−0.76±0.32¶	−0.40±0.25	—	—	0.03±1.88	—
Change in black population (proportion of population)‖††	—	−1.94±0.58§	−2.74±0.58§	−2.70±0.64§	−2.95±0.78§	−5.06±2.12§	−5.98±1.99§
Change in Hispanic population (proportion of population)‖††	—	1.46±1.23	1.33±1.10	—	—	2.44±2.22	—
Change in lung-cancer mortality rate (no./10,000 population)	—	—	−0.07±0.02§	−0.06±0.02§	−0.07±0.03¶	0.01±0.03	0.02±0.03
Change in COPD mortality rate (no./10,000 population)	—	—	−0.07±0.02§	−0.08±0.02§	−0.09±0.03§	−0.15±0.06§	−0.19±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

- 10 μg/m³ decrease in $PM_{2.5}$ associated with ~ 0.61 (± 0.20) years increase in life expectancy
- Not sensitive to controlling for socio-economic, demographic, or smoking variables

Conclusions

Epidemiologists, including myself, are indebted to our partners and colleagues that provide critical air monitoring data.

I am convinced that future epidemiology research (and even clinical-based and some toxicology) will be greatly enhanced by improved air quality monitoring, including more sites with daily speciation data, etc.