Understanding the Relationship of Particulate Matter (PM) and Premature Mortality

An Historical Perspective

The Air Resources Board PM Symposium
Sacramento, CA
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Health Effects Institute

# *Particulate Matter (PM)*

- Historically, high levels of PM (> 500 μg/m^3) known to cause premature death

- 1990s:
  - Studies in US, Europe, elsewhere found association of PM with premature mortality at much lower levels (<50 μg/m^3)

- Substantial work by HEI, others to test and extend short term and long-term results

HEI

"Fly the city, shun its turbid air
Breathe not it's chaos of eternal smoke"

British medical poet John Armstrong, the *Art of Preserving Health*, **1744**

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Key Air Pollution Events of the Mid-20ᵗʰ Century
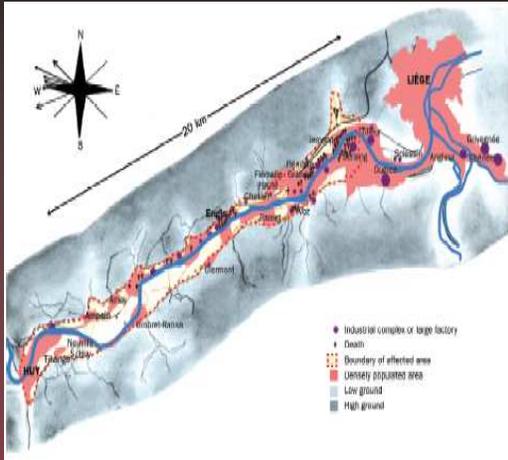
The Fog Disaster in the **Meuse Valley, 1930**...led to the first scientific proof of the potential for atmospheric pollution to cause deaths and disease, and it clearly identified the most likely causes. 60 deaths that were attributed to the fog occurred on Dec 4 and 5. *Nemery et al. Lancet 2001*

Public Health

MORTALITY IN THE LONDON FOG
INCIDENT, 1952

W. P. D. LOGAN
M.D. Glasg., Ph.D. Lond.

CHIEF MEDICAL STATISTICIAN, GENERAL REGISTER OFFICE

THE Meuse Valley fog episode in 1930 caused 64 deaths, and the Donora (Pennsylvania) episode in 1948 caused 20 deaths. In December, 1952, a four-day fog in London caused about 4000 deaths. This paper gives a short account of when and where these deaths occurred, the age-distribution, and the reported medical causes. No attempt is made here to present detailed meteorological data or to discuss clinical aspects; these and other features of the incident, including additional details about mortality, will no doubt be discussed in a report which, it is understood, will be made to the Minister of Health when investigations have been completed. Two papers have already been published concerning the

TABLE I—DEATHS REGISTERED IN GREATER LONDON FROM WEEK ENDED NOV. 15, 1952, TO JAN. 10, 1953, COMPARED

1952 London Fog
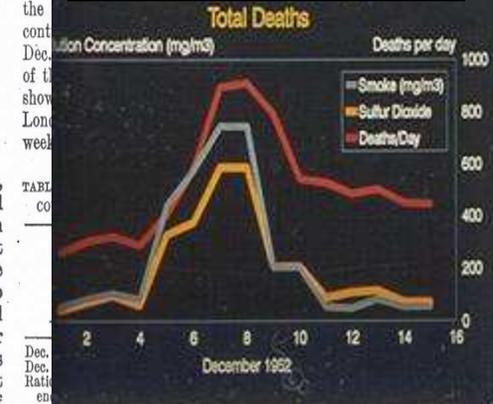
Beginning on October 26, 1948, sparse air movement contributed to a temperature inversion in the atmosphere over western Pennsylvania, Ohio, and areas of neighboring states. A fog laden with particulates and other industrial contaminants saturated the air of

Donora, a small industrial town on the banks of the Monongahela River, some 30 miles south of Pittsburgh. Visibility was so poor that even locals lost their sense of direction. An estimated 5000 to 7000 persons in a town of 14000 residents became ill, some 400 required hospitalization, and 20 died before rain dispersed the killing smog on October 30 and 31, 1948. *Helfand et al. AJPH 2001*

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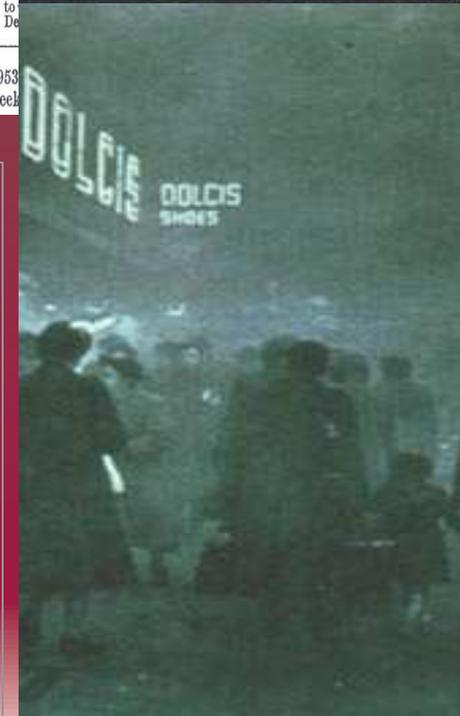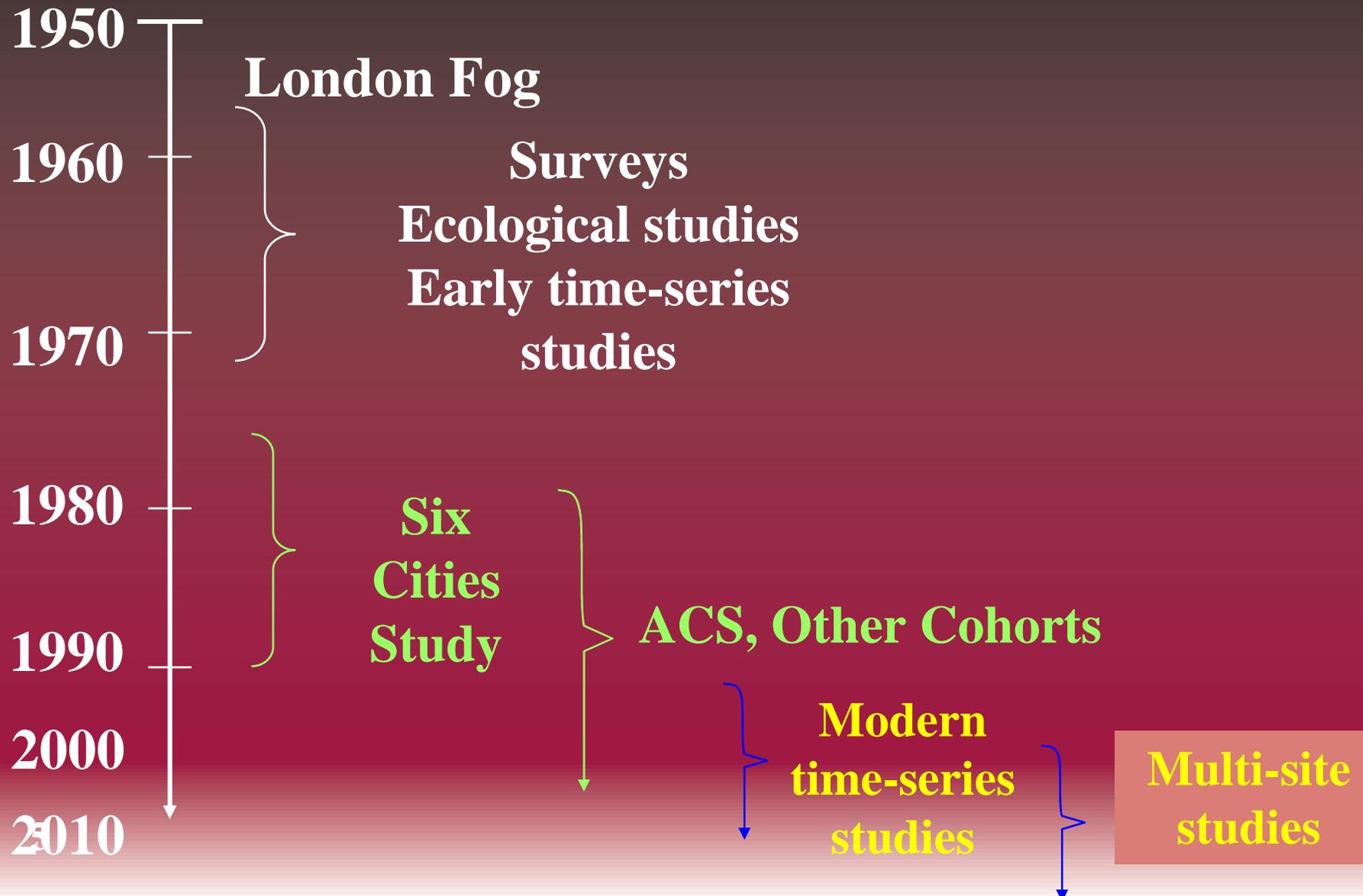
The 1990s:
New Studies of Short Term (Daily) Associations

- Daily variation in PM and health
- Some 40 studies in Europe and U.S.
- Consistent small increase in mortality, hospitalization: 0.5 - 1.0% per 10 µg/m^3
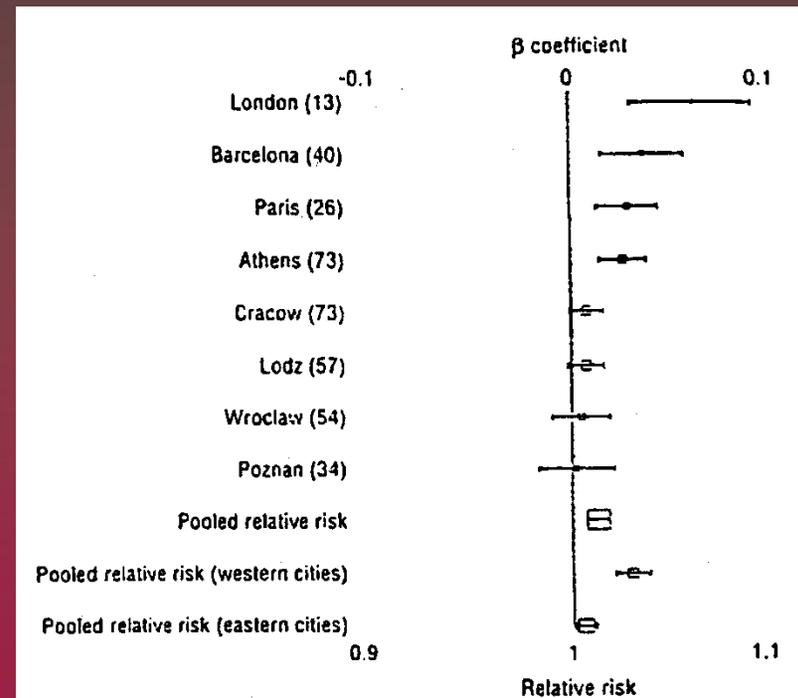- *But*, significant questions:
  - selection of cities
  - publication bias

Fig 2 Estimated individual city and pooled relative risks of mortality associated with increase of 50 µg/m^3 in black smoke levels. Numbers in parentheses are median value of pollutant, and the size of the point representing each relative risk is inversely proportional to its variance

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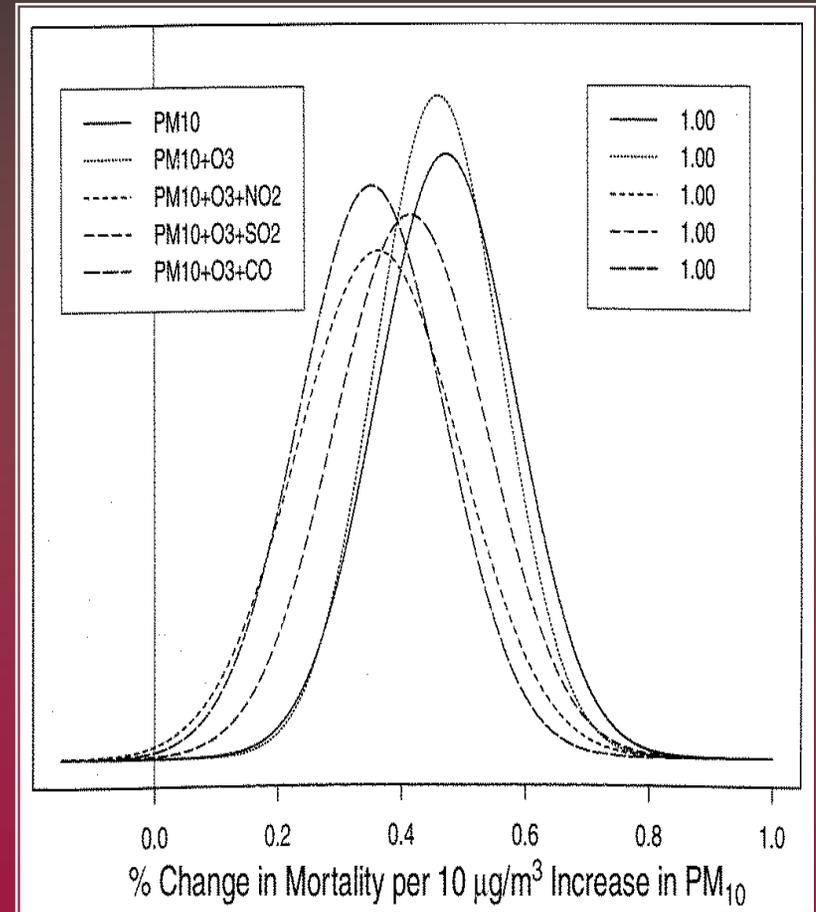# *Addressing the Questions on Short Term Effects*

- Systematic Multi-city studies
    - APHEA in Europe funded by EU (30+ cities)
    - National Morbidity, Mortality and Air Pollution (NMMAPS) funded by HEI (90 Cities)
    - Most recently APHENA (130+ Cities)
        - HEI-EU funded project bringing together European, Canadian and US investigators
        - HEI Research Report 142 October 2009

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NMMAPS *(90 US Cities - JHU)*
The Original Results (HEI 2000)

- Relatively consistent increase in premature mortality:
  - 0.4% per 10 μ/m^3 of PM$_{10}$

- Smaller results than previous U.S. analyses

- Overall, enhanced confidence in results

Legend:
PM10
PM10+O3
PM10+O3+NO2
PM10+O3+SO2
PM10+O3+CO

1.00
1.00
1.00
1.00
1.00

% Change in Mortality per 10 μg/m^3 Increase in PM$_{10}$

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Revised Analysis (2003)

- **2002:** *HEI investigators at JHU identify significant statistical issues with this and other studies*
- Over 30 studies identified by CASAC, EPA for revised analysis
- Mean estimates of effects in revised analyses generally smaller
  - 5% to 35% reduction
- *HEI Review Panel Bottom Line:*
  - Studies continue to find associations with PM
  - Revised analyses renewed questions about the role of other factors (especially weather)
  - Need for continuous improvement

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SPECIAL REPORT

HEALTH EFFECTS INSTITUTE

May 2003

Revised Analyses of Time-Series Studies of Air Pollution and Health

Revised Analyses of the National Morbidity, Mortality, and Air Pollution Study Part II *
Revised Analyses of Selected Time-Series Studies *

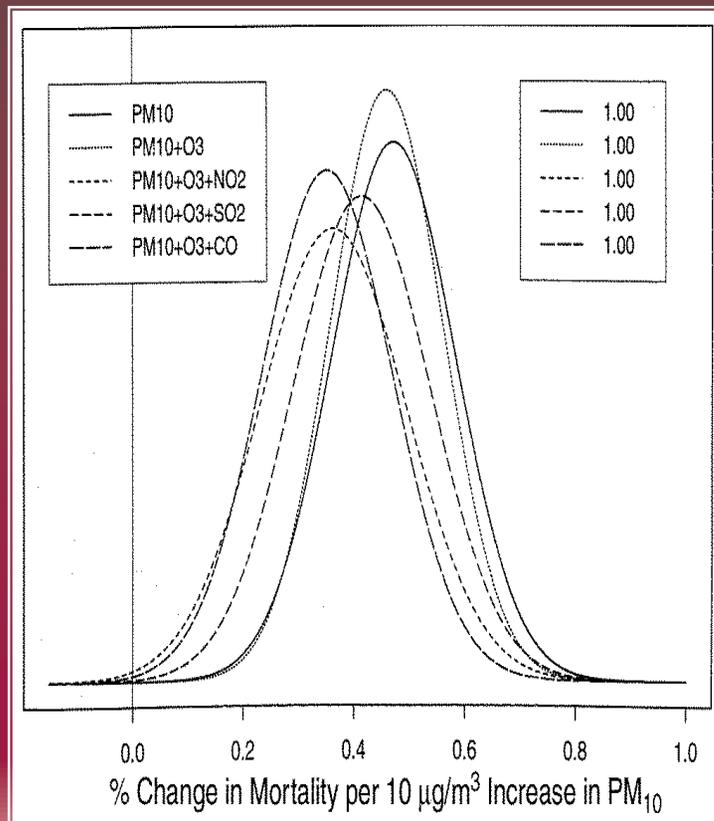* All references to Minneapolis give values for Minneapolis and St Paul.

The Time Series Models Challenge (GAM) NMMAPS: Revised Results
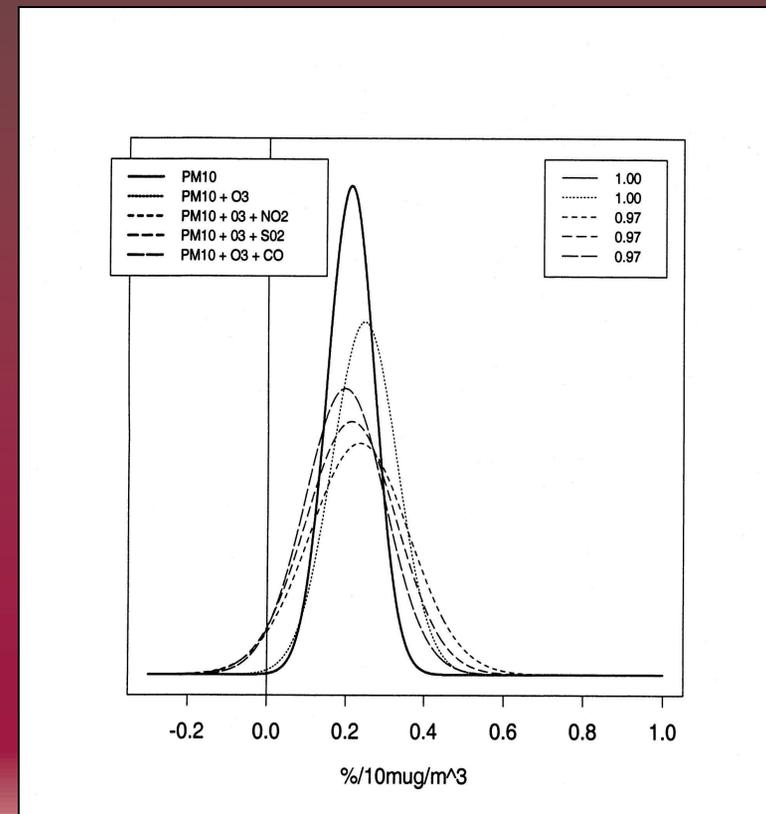
Original Results

0.4% per 10 μ/m³ of PM$_{10}$

Revised Results

0.2% per 10 μ/m³ of PM$_{10}$

NMMAPS 90 Cities PM10 and Total Mortality (Revised Analysis 2003)
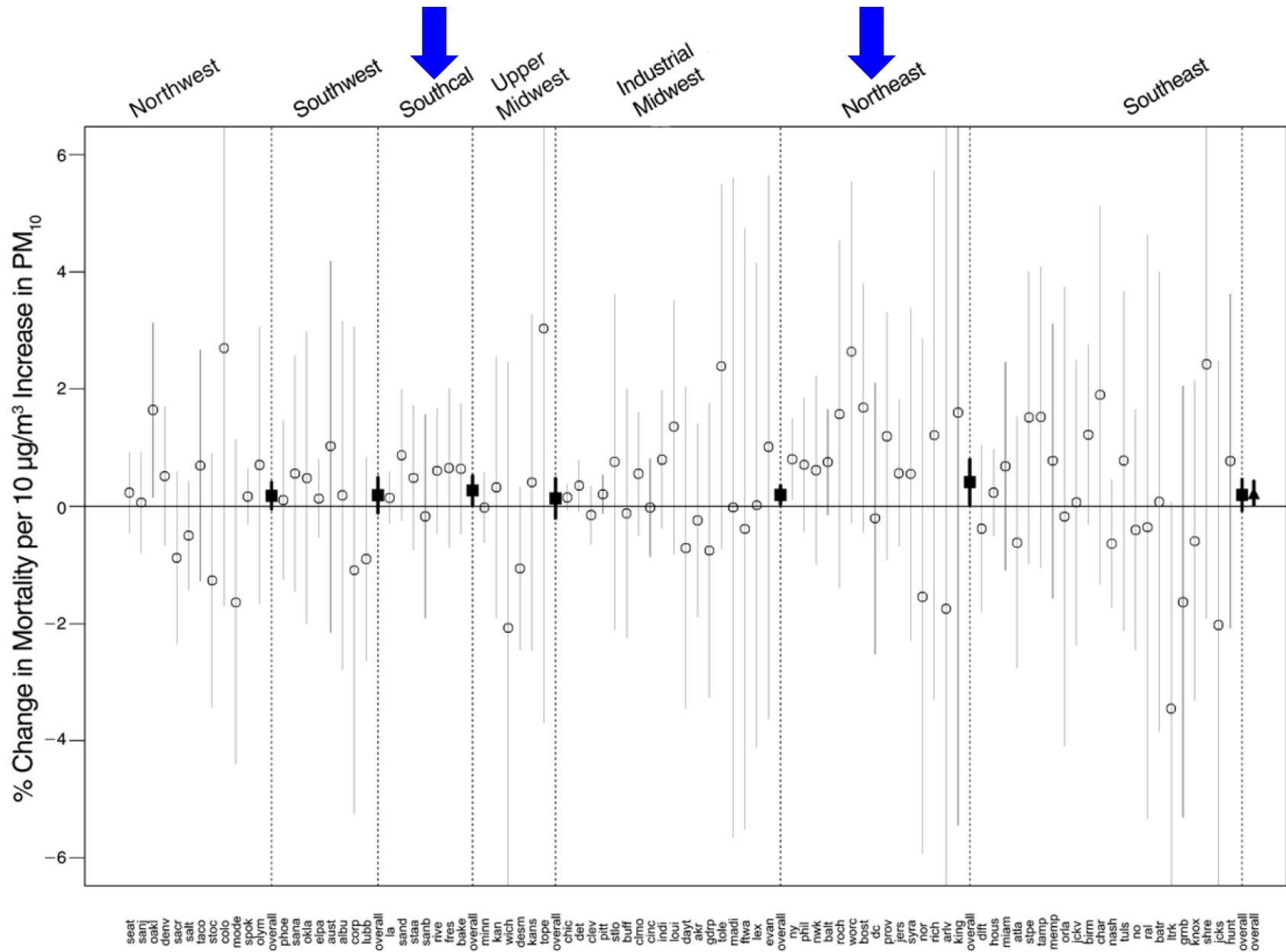
NMMAPS Regional Estimates Total Mortality (Revised Analyses 2003)

Northwest

Upper Midwest

Industrial Midwest

Northeast

Southern California

Southwest

Southeast

Effect of PM_{10}

Mean — 1, 0.5, 0.0

t-ratio — 4, 2, 0

Figure 6. Posterior means divided by posterior standard deviations (t ratios) of regional effects of PM_{10} at lag 1 for total mortality from non-external causes.

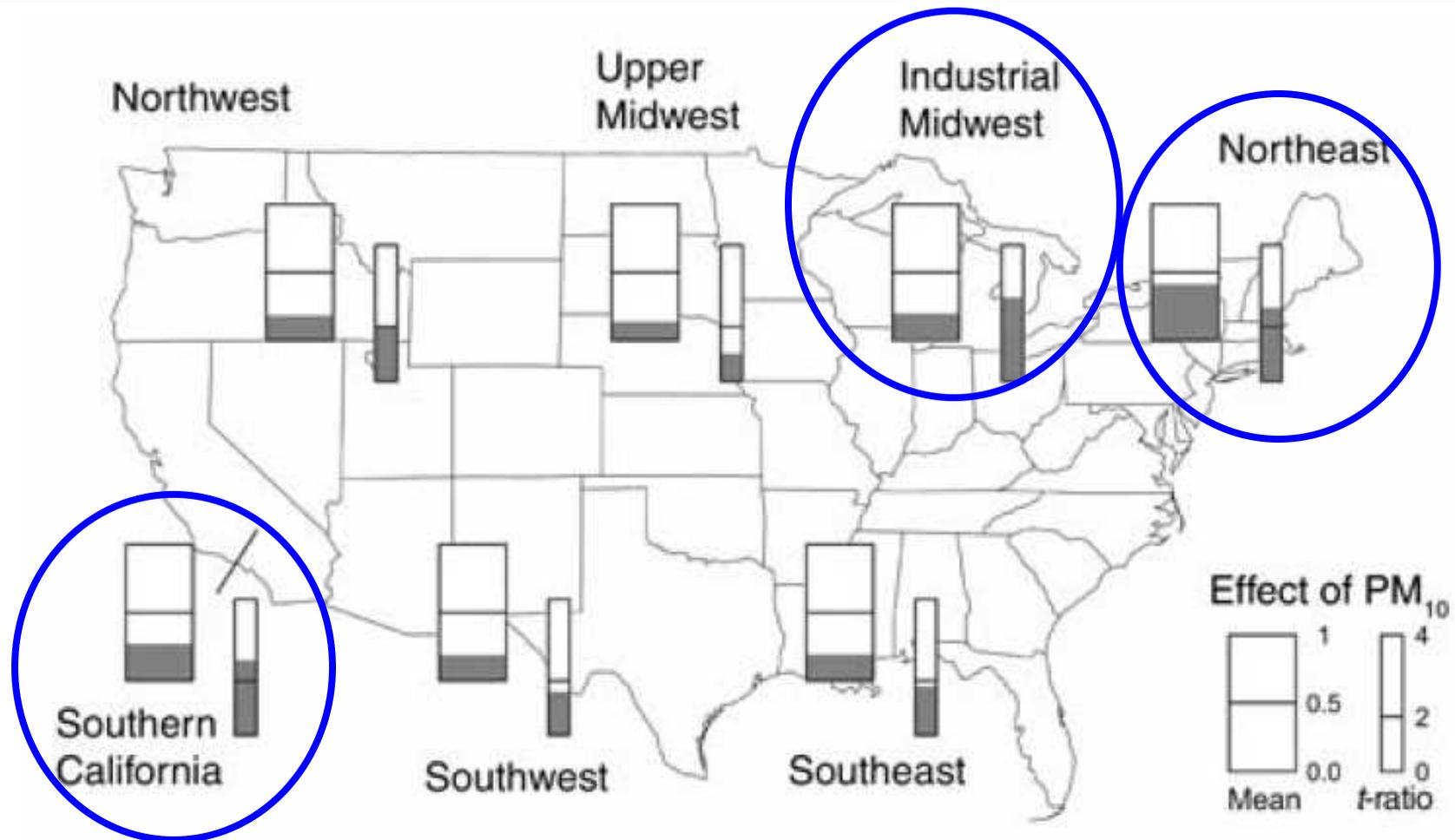# *The 1990s*
New Studies of Longer-term PM Exposure and Premature Mortality

- Two studies in U.S.
  - Harvard Six Cities (1993) →
  - Pope/American Cancer Society (ACS) (1995)
- Larger effects than time series:
  - 4.0 - 6.0% increase in mortality per 10 μg/m^3
- Became the basis of every major estimate of population effects of PM exposure
- *1996: Controversy about data access – given only two studies could they analyzed by others?*
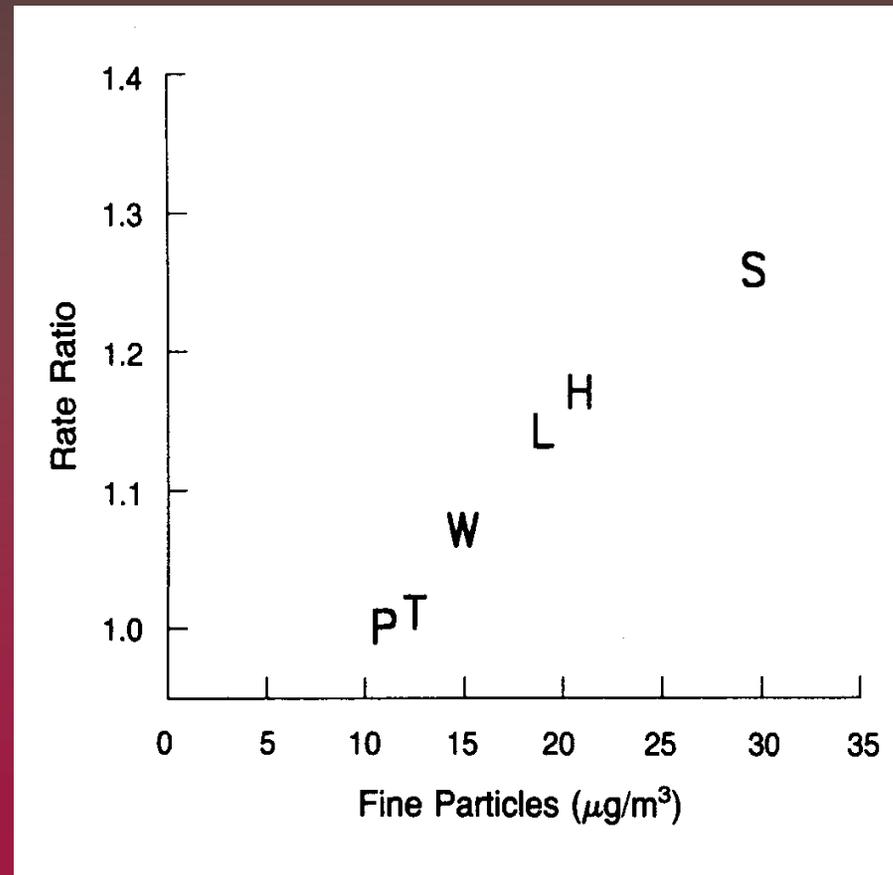
HEI asked to conduct in-depth reanalysis by all Parties;
Given Access to Data by ACS, Harvard

- *Key Questions:*
  - Were the studies <u>*accurately conducted*</u>?
  - Could the studies be <u>*replicated*</u>?
  - Would different <u>*analytic approaches*</u> make a difference?
  - How well did the studies control for <u>*individual characteristics*</u> among the population? e.g. smoking, occupation
  - Are there systematic <u>*city level differences*</u> between the more polluted and less polluted cities?

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HEI Reanalysis Approach
Independent Expert Oversight Panel

- Independent experts in Epidemiology, statistics, exposure assessment to:
  - select investigators competitively:
    - U. Ottawa
  - identify relevant questions
  - oversee new investigators

- Members
  - Arthur Upton, Chair
  - Steven Colome
  - Leon Gordis
  - Geoffrey Howe
  - David Jacobs
  - Suresh Moolgavkar
  - Sverre Vedal
  - Clarice Weinberg
  - Bernard Goldstein (ex officio)

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HEI Reanalysis Approach
Independent Review Panel

- Independent subject matter experts
- Not involved in reanalysis
- Rigorous peer review
  - biostatistics
  - exposure
  - health
- Prepare Commentary

- Members
  - Millicent Higgins, Chair (U. Michigan)
  - John C. Bailar III
  - Michael Brauer
  - Bert Brunekreef
  - David Clayton
  - Manning Feinleib
  - Brian Leaderer
  - Richard L. Smith

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HEI Reanalysis Approach
Advisory Committee

- Key stakeholders, prominent critics and scientists with relevant skills

- To suggest to the Expert Panel key questions and analyses with which to challenge the studies

- Members
  - Michal Krzyzanowski
  - Frederick W. Lipfert
  - Allan H. Marcus
  - Franklin E. Mirer
  - Gerhard K. Raabe
  - Ken Rothman
  - Jonathan Samet
  - Ronald H. White
  - George T. Wolff

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Extensive Re-analysis

- *Accurately Done?* Audit randomly tested 500 individual files
- *Replicable?* Team did detailed duplicate analyses
- *Analytic Approaches?* Over a dozen different models
- *Individual differences?* Nearly 30 new individual variables
- *City Differences?*
  - Assessed effect of 20 other variables (including income, health care, altitude, water hardness, other pollutants)
  - Applied new analytic techniques to assess spatial patterns

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Reanalysis Results
Sensitivity Analyses with Additional Variables

- **Overall, the reanalysis**:
  - Assured the quality of the data
  - Replicated the original results,
  - Tested those results against alternative explanations *without substantively altering the original findings of an association between indicators of particles and mortality*

- *However*, **also identified:**
  - New findings and questions on education and "effects" of SO2

Results from ACS Study Reanalysis

Analysis	PM2.5	Sulfates
Original	1.**17**(1.08,1.27)	1.**15**(1.08,1.22)
Full	1.**18**(1.09,1.26)	1.**15**(1.09,1.21)
Extended	1.**18**(1.09,1.26)	1.**15**(1.09,1.21)

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HEI

Additional follow-up of the American Cancer Society (ACS) Study

Additional Mortality Follow-up (16 Years)

- **Pope CA III, et al. 2002**. Lung cancer, cardiopulmonary mortality, and long-term exposure to fine particulate air pollution. JAMA 287:1132–1141.
- **Pope CA III, et al. 2004**. Cardiovascular mortality and long-term exposure to particulate air pollution: Epidemiological evidence of general pathophysiological pathways of disease. Circulation 109:71–77.

Most Recent HEI-funded follow-up (18 Years)

- **Krewski D, et al. 2009**. Extended Follow-Up and Spatial Analysis of the American Cancer Society Study Linking Particulate Air Pollution and Mortality. HEI Research Report 140, Health Effects Institute, Boston, MA.
- *Substantial additional statistical analysis*
- *Subjected to full HEI Review and Commentary*

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Effects of long-term PM$_{2.5}$ Exposure

(Extended Follow-Up of the American Cancer Society Study of PM and Mortality; HEI Krewski Report #140, 2009)

Nationwide Analysis

- Estimated *4 – 6 %* increase in premature mortality per 10 µg/m^3
- Larger effects for ischemic heart disease: *18 - 24%* per 10 µg/m^3

Commentary Table 3. Associations Between Various Causes of Death and Long-Term Exposure to PM$_{2.5}$ in Two Time Periods from the Nationwide Analysis[a]

Cause of Death	Standard Cox Model	Random Effects Cox Model[b]
HR per 10-µg/m^3 Change in PM$_{2.5}$ Exposure Level (Average for 1979–1983)		
All causes	1.03 (1.01–1.04)	1.04 (1.03–1.06)
Ischemic heart disease	1.12 (1.09–1.16)	1.18 (1.15–1.22)
Cardiopulmonary disease	1.06 (1.04–1.08)	1.09 (1.06–1.11)
Lung cancer	1.08 (1.03–1.14)	1.09 (1.03–1.15)
HR per 10-µg/m^3 Change in PM$_{2.5}$ Exposure Level (Average for 1999–2000)		
All causes	1.03 (1.01–1.05)	1.06 (1.04–1.08)
Ischemic heart disease	1.15 (1.11–1.20)	1.24 (1.19–1.29)
Cardiopulmonary disease	1.09 (1.06–1.12)	1.13 (1.10–1.16)
Lung cancer	1.11 (1.04–1.18)	1.14 (1.06–1.23)

Extended Follow-up of the American Cancer Society Study
## *Linking Particulate Air Pollution & Mortality*

Daniel Krewski,[1] Michael Jerrett,[2] Richard T Burnett,[3] Renjun Ma,[4] Edward Hughes,[1] Yuanli Shi,[1] Michelle C Turner,[1] C Arden Pope III,[5] George Thurston,[6] Eugenia E Calle,[7] Michael J Thun[7]

Intra-Urban Analyses in LA and New York

Much more detailed exposure analysis

LA: Much higher risk estimates than national

NY: Elevated risk only for ischemic heart disease
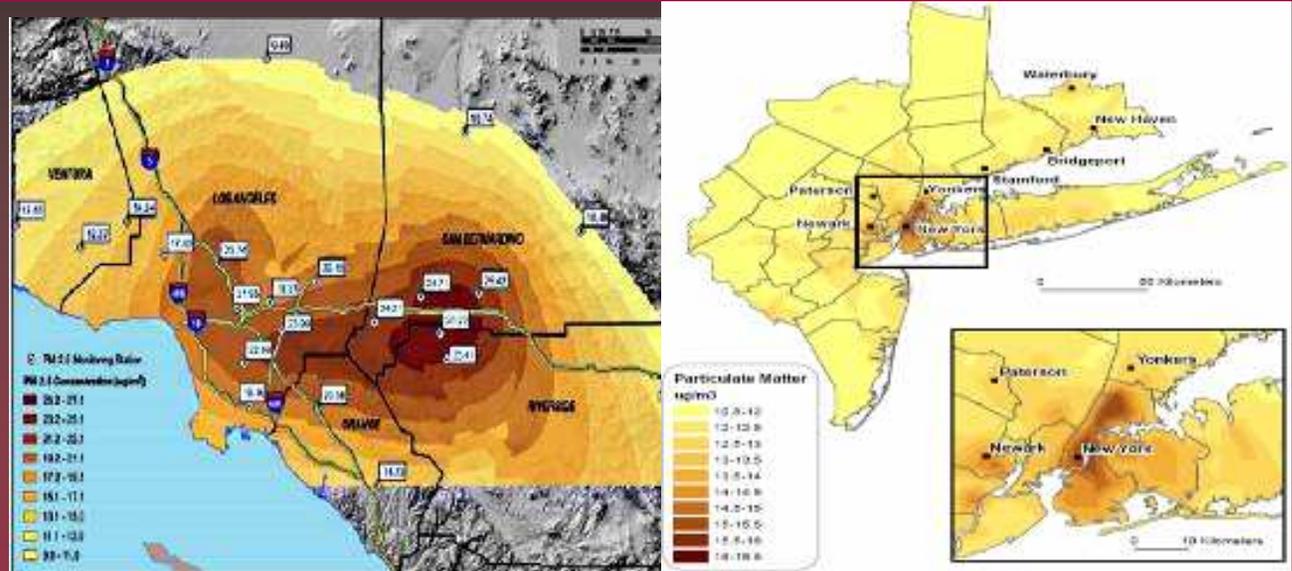
Cause of Death Cox Model Covariates	LA		NYC
	LUR	Kriging	LUR
All Causes			
PM2.5 only	1.20 (1.08,1.32)	1.24 (1.11,1.37)	1.01 (0.94,1.05)
44 Individual Covariates	1.14 (1.03,1.27)	1.17 (1.05, 1.30)	0.98 (0.95,1.02)
IHD			
PM2.5 only	1.42 (1.15,1.74)	1.49 (1.20, 1.85)	1.11 (1.04,1.18)
44 Individual Covariates	1.33 (1.08,1.63)	1.39 (1.12, 1.73)	1.07 (1.00,1.15)
Cardiopulmonary			
PM2.5 only	1.18 (1.02,1.36)	1.20 (1.04, 1.39)	0.98 (0.93,1.03)
44 Individual Covariates	1.11 (0.97,1.28)	1.12 (0.97, 1.30)	0.95 (0.90,1.01)
Lung Cancer			
PM2.5 only	1.46(1.01,2.10)	1.60 (1.09, 2.33)	1.04 (0.91,1.18)
44 Individual Covariates	1.39(0.96,2.01)	1.44 (0.98, 2.11)	0.96 (0.84,1.09)

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Table 4. A comparison of mortality HRs associated with each 10ug/m^3 increase of PM$_{2.5}$ concentrations (LA) or an interdecile (P$_{10}$-P$_{90}$, 1.5 µg/m^3) of PM$_{2.5}$ (NYC) with exposure estimated by LUR and kriging.

Summary

- 20 years of investigation, re-analysis, and extended analyses have built confidence in the basic finding of a relationship between PM exposure and premature mortality
  - Even at these relatively low ambient concentrations

- Some additional national cohorts have also been analyzed (e.g. Medicare, Veteran's, Women's Health Initiative)

- Science, of course, has further questions to answer, even as decisions are made

- *Looking forward*, we need:
  - Continuous improvement in epidemiology (model selection; regional variability; and more, younger cohorts)
  - Improved mechanistic understanding (esp. long term)
  - A systematic approach to toxicity of PM components and sources (and the gases)

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Thank You!

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