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

The Air Resources Board PM Symposium
Sacramento, CA
February 26, 2010

Dan Greenbaum, President
Health Effects Institute
Particulate Matter (PM)

- Historically, high levels of PM (> 500 µg/m³) known to cause premature death
- 1990s:
  - Studies in US, Europe, elsewhere found association of PM with premature mortality at much lower levels (<50 µg/m³)
- Substantial work by HEI, others to test and extend short term and long-term results
“Fly the city, shun its turbid air
Breathe not its chaos of eternal smoke”

British medical poet John Armstrong, the *Art of Preserving Health*, 1744
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](#)

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. [Holland et al. AJPH 2001](#)
50+ Years of Air Pollution Research

1950
London Fog

1960
Surveys
Ecological studies
Early time-series studies

1970
Six Cities Study

1980
ACS, Other Cohorts

1990
Modern time-series studies

2000

2010
Multi-site studies
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/m³
- **But**, significant questions:
  - selection of cities
  - publication bias
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
**NMMAPS (90 US Cities - JHU)**

**The Original Results (HEI 2000)**

- Relatively consistent increase in premature mortality:
  - 0.4% per 10 μg/m³ of PM$_{10}$
- Smaller results than previous U.S. analyses
- Overall, enhanced confidence in results
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
**The Time Series Models Challenge (GAM)**

**NMMAPS: Revised Results**

**Original Results**

0.4% per 10 µ/m$^3$ of PM$_{10}$

**Revised Results**

0.2% per 10 µ/m$^3$ of PM$_{10}$
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.

• Larger effects than time series:
  – 4.0 - 6.0% increase in mortality per 10 µg/m³
  – 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 *accurately conducted*?
  - Could the studies be *replicated*?
  - Would different *analytic approaches* make a difference?
  - How well did the studies control for *individual characteristics* among the population? e.g. smoking, occupation
  - Are there systematic *city level differences* between the more polluted and less polluted cities?
**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)
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
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
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
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

<table>
<thead>
<tr>
<th>Analysis</th>
<th>PM2.5</th>
<th>Sulfates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original</td>
<td>1.17 (1.08, 1.27)</td>
<td>1.15 (1.08, 1.22)</td>
</tr>
<tr>
<td>Full</td>
<td>1.18 (1.09, 1.26)</td>
<td>1.15 (1.09, 1.21)</td>
</tr>
<tr>
<td>Extended</td>
<td>1.18 (1.09, 1.26)</td>
<td>1.15 (1.09, 1.21)</td>
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</table>
Additional follow-up of the American Cancer Society (ACS) Study

Additional Mortality Follow-up (16 Years)

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**
**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$^a$

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Standard Cox Model</th>
<th>Random Effects Cox Model$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HR per 10-µg/m$^3$ Change in PM$_{2.5}$ Exposure Level (Average for 1979–1983)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td>1.03 (1.01–1.04)</td>
<td>1.04 (1.03–1.06)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1.12 (1.09–1.16)</td>
<td><strong>1.18 (1.15–1.22)</strong></td>
</tr>
<tr>
<td>Cardiopulmonary disease</td>
<td>1.06 (1.04–1.08)</td>
<td>1.09 (1.06–1.11)</td>
</tr>
<tr>
<td>Lung cancer</td>
<td>1.08 (1.03–1.14)</td>
<td>1.09 (1.03–1.15)</td>
</tr>
<tr>
<td><strong>HR per 10-µg/m$^3$ Change in PM$_{2.5}$ Exposure Level (Average for 1999–2000)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All causes</td>
<td>1.03 (1.01–1.05)</td>
<td>1.06 (1.04–1.08)</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>1.15 (1.11–1.20)</td>
<td><strong>1.24 (1.19–1.29)</strong></td>
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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,5 Yuanli Shi,1 Michelle C Turner,1 C Arden Pope III,6 George Thurston,6 Eugenia E Calle,7 Michael J Thun7

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

<table>
<thead>
<tr>
<th>Cause of Death</th>
<th>Cox Model Covariates</th>
<th>LA</th>
<th>Kriging</th>
<th>NYC</th>
<th>LUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Causes</td>
<td></td>
<td>1.20 (1.08,1.32)</td>
<td>1.24 (1.11,1.37)</td>
<td>1.01 (0.94,1.05)</td>
<td></td>
</tr>
<tr>
<td>PM2.5 only</td>
<td></td>
<td>1.14 (1.03,1.27)</td>
<td>1.17 (1.05,1.30)</td>
<td>0.98 (0.95,1.02)</td>
<td></td>
</tr>
<tr>
<td>44 Individual Covariates</td>
<td></td>
<td>1.42 (1.15,1.74)</td>
<td>1.49 (1.20,1.85)</td>
<td>1.11 (1.04,1.18)</td>
<td></td>
</tr>
<tr>
<td>IHD</td>
<td></td>
<td>1.33 (1.08,1.63)</td>
<td>1.39 (1.12,1.73)</td>
<td>1.07 (1.00,1.15)</td>
<td></td>
</tr>
<tr>
<td>PM2.5 only</td>
<td></td>
<td>1.18 (1.02,1.36)</td>
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<td></td>
</tr>
<tr>
<td>Cardiopulmonary</td>
<td></td>
<td>1.46 (1.01,2.10)</td>
<td>1.60 (1.09,2.33)</td>
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<td>1.39 (0.96,2.01)</td>
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<td>0.96 (0.84,1.09)</td>
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Table 4. A comparison of mortality HRs associated with each 10μg/m³ increase of PM$_{2.5}$ concentrations (LA) or an interdecile (P$_{10}$-P$_{90}$, 1.5 μg/m³) 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)
Thank You!

Dan Greenbaum
dgreenbaum@healtheffects.org
www.healtheffects.org