The current knowledge on adverse effects of low-level air pollution

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Recent Air Pollution Facts
Top Risk Factors Ranked by Attributable Burden of Disease in 2013 (disability adjusted life years)

#5: Ambient particulate matter pollution

As air pollution levels continue to decrease
  – Regulatory actions become more costly
  – Steps taken to quantify the public health benefits of cleaner air will be subject to intense scrutiny.

The current dilemma is how to reconcile the increasing challenges and costs of further reducing air pollution levels with the mounting evidence of public health benefits of cleaner air.
Background

• Epidemiological studies provide:
  – strong evidence of the adverse health effects of air pollution
  – the main evidence for setting the National Ambient Air Quality Standards (NAAQS)

• New studies have included increasingly larger populations and more sophisticated analytical methods

• Many gaps of knowledge remain:
  – Health effects of short and long-term exposure to lower levels of air pollution
  – Uncertainty about the shape of the exposure response relationship
Current knowledge on adverse effects of low-level air pollution

Studies around the world:

• Examined associations between short-term and long-term exposure to air pollution and mortality or morbidity

• Health effects below NAAQS using:
  – The concentration-response relationship as a way to show health effect at low concentrations
  – Threshold

• Focus on improving exposure assessment
  – Accurate exposure (LUR, Spatio-temporally resolved predictions with AOD) could reduce uncertainty and measurement error
Short term exposure studies
PM10 and mortality (EPA PM ISA 2009)

- Schwartz (2004) analysis of PM$_{10}$ and mortality in 14 U.S. cities using thresholds
- Samoli et al (2005)
- Exposure–response curves of PM10 and total, cardiovascular, and respiratory mortality in 22 European cities in the APHEA project
### Study Reference

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Study population</th>
<th>Mean PM2.5</th>
<th>Method</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PM2.5</strong></td>
<td></td>
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<tr>
<td>Samoli et al., 2013</td>
<td>10 European cities</td>
<td>13.6-27.7</td>
<td>threshold</td>
<td>No threshold, linear</td>
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<tr>
<td>Cao et al. 2011</td>
<td>Xi’an, China</td>
<td>182</td>
<td>splines</td>
<td>No threshold, linear</td>
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<tr>
<td>Yorifuji et al. 2015</td>
<td>Tokyo, Japan</td>
<td>17</td>
<td>threshold</td>
<td>Linear</td>
</tr>
<tr>
<td>Li et al., 2013</td>
<td>Beijing</td>
<td>75</td>
<td>threshold</td>
<td>Linear at low concentrations, plateaued &gt; 150 μg/m3.</td>
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<tr>
<td><strong>PM10</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Samoli et al., 2013</td>
<td>10 European cities</td>
<td>25.0-44.4</td>
<td>threshold</td>
<td>No threshold, linear</td>
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<tr>
<td>Zeng et al., 2015</td>
<td>7 Chinese cities</td>
<td>72-130</td>
<td>penalized spline</td>
<td>Linear, but varied across cities</td>
</tr>
<tr>
<td>Lu et al., 2015</td>
<td>Nanjing, China</td>
<td>109</td>
<td>penalized spline</td>
<td>Linear at low concentrations, plateaued &gt; 150 μg/m3.</td>
</tr>
<tr>
<td>Shuang et al., 2013</td>
<td>Urumqi, China</td>
<td>144</td>
<td>spline</td>
<td>almost linear or J-shaped</td>
</tr>
<tr>
<td>Kan et al., 2010</td>
<td>Shanghai, China</td>
<td>102</td>
<td>penalized spline</td>
<td>Linear at low concentrations, plateaued &gt; 150 μg/m3.</td>
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<tr>
<td>Wong et al, 2010</td>
<td>Hong-Kong</td>
<td>51.6</td>
<td>penalized spline</td>
<td>Linear at low concentrations, plateaued &gt; 150 μg/m3.</td>
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<tr>
<td>Balakrishnan et al., 2011</td>
<td>Chennai, India</td>
<td>48-108</td>
<td>penalized spline</td>
<td>No threshold, linear</td>
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<tr>
<td>Rajarathnam et al., 2011</td>
<td>Delhi, India</td>
<td>221</td>
<td>penalized spline</td>
<td>Linear at low concentrations, plateaued &gt; 150 μg/m3.</td>
</tr>
</tbody>
</table>
Acute effect of fine particulate matter on mortality in 3 Southeastern states

- Evaluate the acute effect of PM$_{2.5}$ on mortality, stratified by EPA standards, rural/urban, individual characteristics
- 848,270 non-accidental death
- PM$_{2.5}$: zip code predictions from satellite, mean 11.1 $\mu$g/m$^3$

Increase in PM$_{2.5}$ lag 01 per 10 $\mu$g/m$^3$
- 1.56% (95% CI: 1.19, 1.94)
- In zip code with PM$_{2.5}$ $<$ 12 $\mu$g/m$^3$
  - 2.06% (1.97–2.15)
- In zip code with PM$_{2.5}$ $<$ 35 $\mu$g/m$^3$
  - 2.08% (1.99–2.17)

Short term exposure studies
PM and admissions

- The limited literature supports a no threshold, log-linear model, which is consistent with the observations made in studies that examined the PM-mortality relationship
- Pediatric asthma ED visits among children in Atlanta hospitals during 1993–2004 (Strickland et al., 2010)
- EMECAS project, cardiovascular hospital admissions in 14 Spanish and air pollutants (Ballester et al., 2006)
- PM$_{10}$ and CHF hospital admissions among Medicare beneficiaries (Wellenius et al, 2005)
- MI hospital admissions among older adults in 21 U.S. cities
- Steeper slope occurring below 50 μg/m³ (Zanobetti and Schwartz, 2005)
Short term exposure studies
NO2 and mortality

China Air Pollution and Health Effects Study: concentration-response curve for the association between total and cause-specific mortality and NO$_2$ (Chen et al 2012)

Dose–response curves for NO$_2$ concentrations. PAPA India (Rajarathnam et al. 2011)
Short term exposure studies

• Compared to the PM$_{2.5}$ studies, more studies explored the shape of the association between PM$_{10}$ and mortality.
• Most studies found a linear positive concentration-response relationship between PM$_{10}$, PM$_{2.5}$, NO$_2$ and mortality or admissions.
• Most of the new studies were conducted in Asia.
• Most studies in Asia found a linear positive association at lower concentrations that flattened at higher concentrations.
Long-term air pollution exposure and cardio-respiratory mortality: a review

The pooled effect estimate per 10 μg/m³ increase in PM$_{2.5}$ exposure:

All-cause mortality: 6% (95% CI: 4, 8%)
Cardiovascular mortality: 11% (5, 16%)

Meta-analysis of the association between PM$_{2.5}$ and all-cause mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>ES (95% CI)</th>
<th>Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS [18]</td>
<td>1.06 (1.02, 1.11)</td>
<td>12.11</td>
</tr>
<tr>
<td>NLCSAIR [23]</td>
<td>1.06 (0.97, 1.16)</td>
<td>4.31</td>
</tr>
<tr>
<td>Nurses Health [25]</td>
<td>1.26 (1.03, 1.55)</td>
<td>0.94</td>
</tr>
<tr>
<td>Health Professionals [29]</td>
<td>0.88 (0.72, 1.02)</td>
<td>1.30</td>
</tr>
<tr>
<td>US truckers [32]</td>
<td>1.10 (1.02, 1.18)</td>
<td>6.22</td>
</tr>
<tr>
<td>ACS Los Angeles [19]</td>
<td>1.17 (1.05, 1.30)</td>
<td>3.18</td>
</tr>
<tr>
<td>Canadian cohort [34]</td>
<td>1.10 (1.05, 1.15)</td>
<td>11.20</td>
</tr>
<tr>
<td>California teachers [36]</td>
<td>1.01 (0.94, 1.08)</td>
<td>6.53</td>
</tr>
<tr>
<td>Medicare cohort [26]</td>
<td>1.04 (1.03, 1.06)</td>
<td>23.27</td>
</tr>
<tr>
<td>Rome cohort [38]</td>
<td>1.04 (1.03, 1.05)</td>
<td>23.95</td>
</tr>
<tr>
<td>Six city [16]</td>
<td>1.14 (1.07, 1.22)</td>
<td>6.99</td>
</tr>
<tr>
<td>Overall (I-squared = 65.0%, p = 0.001)</td>
<td>1.06 (1.04, 1.08)</td>
<td>100.00</td>
</tr>
</tbody>
</table>

NOTE: Weights are from random effects analysis

Hoek G. et al, 2013 Environmental Health, 12:43
Early long term concentration response relationship $\text{PM}_{10}$ and mortality

- Pope CA III et al. 2002 ACS study
  - Nonparametric smoothed exposure response relationships between cause-specific mortality and $\text{PM}_{2.5}$
- Associations were not significantly different from linear

JAMA. 2002;287(9):1132-1141

- Schwartz et al 2008 follow-up of the Harvard Six Cities Study
  - penalized splines (A)
  - Bayesian model averaging (B)
- Concentration–response curve is linear and continues below NAAQS

EHP. 2008; 116(1)

The estimated concentration–response relation between $\text{PM}2.5$ and the risk of death in the Six Cities Study
<table>
<thead>
<tr>
<th>Study reference</th>
<th>Study population</th>
<th>Unit</th>
<th>PM2.5</th>
<th>Mean PM2.5</th>
<th>Method</th>
<th>Findings</th>
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</thead>
<tbody>
<tr>
<td>Crouse DL et al 2012</td>
<td>Canadian Census</td>
<td>Zip code</td>
<td>Satellite</td>
<td>8.7</td>
<td>natural splines</td>
<td>Supralinear</td>
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<tr>
<td>Crous DL et al 2015</td>
<td>Canadian Census</td>
<td>Zip code</td>
<td>Satellite</td>
<td>8.9</td>
<td>natural splines</td>
<td>Linear</td>
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<tr>
<td>Hales et al. 2012</td>
<td>New Zealand Census Mortality Study</td>
<td>Census track</td>
<td>LUR model</td>
<td>8</td>
<td>quintiles</td>
<td>Linear</td>
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<tr>
<td>Cesaroni et al. 2013</td>
<td>Rome, 2001 Italian census</td>
<td>Address</td>
<td>Dispersion model</td>
<td>23</td>
<td>natural splines</td>
<td>Linear</td>
</tr>
<tr>
<td>Beelen R et al. 2014</td>
<td>22 European cohorts</td>
<td>Address</td>
<td>LUR model</td>
<td>6.6-31</td>
<td>Threshold</td>
<td>Linear</td>
</tr>
<tr>
<td>Fisher PH et al 2015</td>
<td>Dutch national databases on mortality</td>
<td>Address</td>
<td>LUR model</td>
<td>29</td>
<td>natural splines</td>
<td>Linear</td>
</tr>
</tbody>
</table>
Risk of Non-accidental and Cardiovascular Mortality in Relation to Long-term Exposure to Low Concentrations of Fine Particulate Matter: A Canadian National-Level Cohort

- Investigated the association between long-term exposure to ambient PM$_{2.5}$ and mortality
- CanCHEC: subset of the 1991–2001 Canadian census mortality follow-up study

- 2.1 million subjects
- 200,000 non-accidental deaths
- mean age 45.3 years.
- PM$_{2.5}$ derived from satellite
  - Zipcode
- Mean PM$_{2.5}$: 8.7 μg/m$^3$

Crouse DL et al. Environ Health Perspect, 2012; 120(5):708-14
Concentration–response curves

Natural spline models with 4 df, standard Cox models stratified by age and sex, adjusted for all individual-level covariates, urban/rural indicator, and ecological covariates.

Positive significant association between PM$_{2.5}$ and mortality

HR: 1.15 (95% CI: 1.13, 1.16)

Plots suggest that associations with mortality were present at concentrations of PM$_{2.5}$ of only a few micrograms per cubic meter.

- Non-accidental causes
- Cardiovascular disease
- Ischemic heart disease
- Cerebrovascular disease
Ambient PM$_{2.5}$, O$_3$, and NO$_2$ Exposures and Associations with Mortality over 16 Years of Follow-Up in the Canadian Census Health and Environment Cohort (CanCHEC)

- Five additional years of follow-up, 16 years total
- Tracking subjects’ annual residential histories
- Improved estimates of satellite-derived PM$_{2.5}$
  - Assigning time-varying exposures
- Added exposure estimates for ozone (O$_3$) and nitrogen dioxide (NO$_2$)
- Corrected the risk estimates for smoking using indirect methods
- Multi-pollutants models

Concentration-response for PM$_{2.5}$ and NO$_2$: Supralinear
Characterized by larger risk for low concentrations compared with higher values

Crouse DL et al. Environ Health Perspect. 2015; 123(1)
Air pollution and mortality in New Zealand: cohort study

- New Zealand Census Mortality Study:
  - 75% of the New Zealand population
  - 1.06 million adults living in urban areas
  - 17,937 total deaths
  - PM$_{10}$: census tract from LUR models, aggregated into quintiles

Average PM$_{10}$: 8 $\mu$g/m$^3$ (0.1-19)

Investigated associations between cause-specific mortality rates and average exposure to PM$_{10}$ in urban areas with relatively low levels of air pollution.

- There was an approximately linear increase in mortality with increasing average PM$_{10}$ exposure.
Long-Term Exposure to Urban Air Pollution and Mortality in a Cohort of More than a Million Adults in Rome

- Investigated the association of exposure to NO$_2$, PM$_{2.5}$, and traffic indicators on cause-specific mortality to evaluate the form of the concentration–response relationship
- Population-based cohort enrolled at the 2001 Italian census with 9 years of follow-up.

1,265,058 adults
144,441 deaths
NO$_2$ : land use regression model, annual estimate at each address
PM$_{2.5}$ : dispersion model, annual estimate at each address
Mean PM$_{2.5}$: 23 µg/m$^3$

Estimated concentration–response curves for non-accidental causes, cardiovascular disease, IHD, and lung cancer for NO$_2$ (A) and PM$_{2.5}$ (B). Cox models adjusted for sex, marital status, place of birth, education, occupation, and area-based socioeconomic position.

There was no evidence of deviation from linearity of the effects of either NO$_2$ or PM$_{2.5}$ on non-accidental, cardiovascular, and lung-cancer mortality.

Long-term exposures to both NO$_2$ and PM$_{2.5}$ were associated with an increase in non-accidental mortality.

HR = 1.03 (95% CI: 1.02, 1.03) per 10-µg/m$^3$ NO$_2$

HR = 1.04 (95% CI: 1.03, 1.05) per 10-µg/m$^3$ PM$_{2.5}$
Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multi center ESCAPE project

- 22 European cohorts
- 367,251 participants
- 29,076 deaths
- PM$_{2.5}$: LUR models
- Address
- Mean PM$_{2.5}$: 6.6 – 31 μg/m$^3$

<table>
<thead>
<tr>
<th>PM$_{2.5}$</th>
<th>HR (95% CI)</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>No threshold</td>
<td>1.07 (1.02–1.13)</td>
<td>322 159</td>
</tr>
<tr>
<td>&lt;20 μg/m$^3$</td>
<td>1.07 (1.01–1.13)</td>
<td>304 759</td>
</tr>
<tr>
<td>&lt;10 μg/m$^3$</td>
<td>1.02 (0.87–1.19)</td>
<td>68 527</td>
</tr>
</tbody>
</table>

• Long-term exposure to fine particulate air pollution was associated with natural-cause mortality across the 22 European cohorts
• Associations remained significant over concentration below the existing European annual mean limit value of 25 μg/m$^3$

Beelen R et al. The Lancet, 2014
Air Pollution and Mortality in Seven Million Adults: The Dutch Environmental Longitudinal Study (DUELS)

Evaluate the associations between long-term exposure to air pollution and non-accidental and cause-specific mortality
Dutch national databases on mortality (2004 – 2011)

✓ 7,218,363 adults
✓ 668,206 total deaths
✓ $PM_{10}$ and $NO_2$: LUR models
✓ Address

HR: 1.08 (95% CI: 1.07, 1.09)

Associations between $PM_{10}$ and non-accidental mortality did not deviate significantly from linear

Low-Concentration PM$_{2.5}$ and Mortality: Estimating Acute and Chronic Effects in a Population-Based Study

Simultaneously estimate acute and chronic health effects of PM$_{2.5}$ in a population-based cohort (≥ 65 years of age) in New England region, and at low-concentration PM$_{2.5}$ Medicare enrollees (2003-2008)

- Daily count of death for each ZIP code
- Full cohort: 551,024 deaths

PM$_{2.5}$: Spatio-temporally resolved predictions

- Short term exposure (2-day average), mean 8.2 µg/m$^3$
- Long term exposure (365-day average), mean 8.1

Restricted to:

- annual concentrations below 10 µg/m$^3$ (268,050 deaths).
- daily concentrations below 30 µg/m$^3$ (422,637 deaths).

Percent increase in mortality for a 10 µg/m$^3$ increase for PM$_{2.5}$

<table>
<thead>
<tr>
<th>PM$_{2.5}$ exposure type</th>
<th>Model</th>
<th>Percent increase</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Short-term PM$_{2.5}$ exposure</strong></td>
<td>Low daily exposure $^a$</td>
<td>2.14 (1.34,2.95)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Full cohort</td>
<td>2.14 (1.38,2.89)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td><strong>Long-term PM$_{2.5}$ exposure</strong></td>
<td>Low chronic exposure $^b$</td>
<td>9.28 (0.76,18.52)</td>
<td>0.032</td>
</tr>
<tr>
<td></td>
<td>Full cohort</td>
<td>7.52 (1.95,13.40)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

$^a$ Restricted only to person time with daily PM$_{2.5}$ less than 30 µg/m$^3$.

$^b$ Restricted only to person time with chronic PM$_{2.5}$ less than 10 µg/m$^3$.

Using a mutually adjusted model, both short- and long-term exposure to PM$_{2.5}$ were associated with all-cause mortality, even for exposure levels not exceeding the newly revised U.S. EPA standards.

Adverse health effects occur at low levels of fine particles.
Dose-response relationship for low-concentration PM$_{2.5}$ and mortality

Improving air quality below the current PM$_{2.5}$ NAAQS can still yield health benefits
Summary

- Epidemiologic studies have reported associations of air pollution with health effects in the general population even at levels below current air quality standards.

- Pollution levels in US have decreased
  - Cities have max air pollution concentration below NAAQS

- Changes in the standards require additional studies to elucidate whether health effects occur at levels below the current NAAQS levels
THANK YOU!