Particulate Matter (PM): Adverse Health Effects

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California Air Resources Board
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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. Helfand et al.
National Morbidity Mortality Air Pollution Study
National Research Council’s PM Committee
Time-series estimates to 2006: Daily all-cause mortality and PM$_{10}$ (n=314)
Integrated Science Assessment for Particulate Matter

Second External Review Draft

ISA: EPA/600/R-08/139B
ANNEXES: EPA/600/R-08/139BA

National Center for Environmental Assessment-RTP Division
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, NC
**Table 1-3. Weight of evidence for causal determination.**

<table>
<thead>
<tr>
<th>Determination</th>
<th>Health Effects</th>
<th>Ecological and Welfare Effects</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Causal relationship</strong></td>
<td>Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in health effects in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. For example: a) controlled human exposure studies that demonstrate consistent effects; or b) observational studies that cannot be explained by plausible alternatives or are supported by other lines of evidence (e.g., animal studies or mode of action information). Evidence includes replicated and consistent high-quality studies by multiple investigators.</td>
<td>Evidence is sufficient to conclude that there is a causal relationship with relevant pollutant exposures. That is, the pollutant has been shown to result in effects in studies in which chance, bias, and confounding could be ruled out with reasonable confidence. Controlled exposure studies (laboratory or small- to medium-scale field studies) provide the strongest evidence for causality, but the scope of inference may be limited. Generally, determination is based on multiple studies conducted by multiple research groups, and evidence that is considered sufficient to infer a causal relationship is usually obtained from the joint consideration of many lines of evidence that reinforce each other.</td>
</tr>
<tr>
<td><strong>Likely to be a causal relationship</strong></td>
<td>Evidence is sufficient to conclude that a causal relationship is likely to exist with relevant pollutant exposures, but important uncertainties remain. That is, the pollutant has been shown to result in health effects in studies in which chance and bias can be ruled out with reasonable confidence but potential issues remain. For example: a) observational studies show an association, but copollutant exposures are difficult to address and/or other lines of evidence (controlled human exposure, animal, or mode of action information) are limited or inconsistent; or b) animal toxicological evidence from multiple studies from different laboratories that demonstrate effects, but limited or no human data are available. Evidence generally includes replicated and high-quality studies by multiple investigators.</td>
<td>Evidence is sufficient to conclude that there is a likely causal association with relevant pollutant exposures. That is, an association has been observed between the pollutant and the outcome in studies in which chance, bias and confounding are minimized, but uncertainties remain. For example, field studies show a relationship, but suspected interacting factors cannot be controlled, and other lines of evidence are limited or inconsistent. Generally, determination is based on multiple studies in multiple research groups.</td>
</tr>
<tr>
<td><strong>Suggestive of a causal relationship</strong></td>
<td>Evidence is suggestive of a causal relationship with relevant pollutant exposures, but is limited because chance, bias and confounding cannot be ruled out. For example, at least one high-quality epidemiologic study shows an association with a given health outcome but the results of other studies are inconsistent.</td>
<td>Evidence is suggestive of a causal relationship with relevant pollutant exposures, but chance, bias and confounding cannot be ruled out. For example, at least one high-quality study shows an effect, but the results of other studies are inconsistent.</td>
</tr>
<tr>
<td><strong>Inadequate to infer a causal relationship</strong></td>
<td>Evidence is inadequate to determine that a causal relationship exists with relevant pollutant exposures. The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an effect.</td>
<td>The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an effect.</td>
</tr>
<tr>
<td><strong>Not likely to be a causal relationship</strong></td>
<td>Evidence is suggestive of no causal relationship with relevant pollutant exposures. Several adequate studies, covering the full range of levels of exposure that human beings are known to encounter and considering susceptible or vulnerable subpopulations, are mutually consistent in not showing an effect at any level of exposure.</td>
<td>Several adequate studies, examining relationships with relevant exposures, are consistent in failing to show an effect at any level of exposure.</td>
</tr>
</tbody>
</table>
Ambient Particles (Pulmonary Deposition)

- Sensory Nerves, Ganglia • Autonomic NS
- Epithelial Cell Injury • Increased ROS • Inflammation • Allergy • Infectivity
- Extra-pulmonary Tissues • Liver • Bone-marrow • Heart • Brain
- Airway Effects
- Endothelial Dysfunction
- Acute Phase Response
- Blood Coagulability

Cardiac & Respiratory Health Effects

Source: Utell, Univ. Rochester, 2003
# Short-term Exposure to PM$_{2.5}$ and Mortality

<table>
<thead>
<tr>
<th>Study</th>
<th>Outcome</th>
<th>Mean: 95th (μg/m$^3$)</th>
<th>Effect Estimates</th>
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<tr>
<td>Locatelli et al. (2008, 0817891)</td>
<td>Lower Respiratory Infection</td>
<td>8.1: NR</td>
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<tr>
<td>Slaughther et al. (2005, 0768514)</td>
<td>Asthma Exacerbation</td>
<td>7.3: NR</td>
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<td>Chen et al. (2004, 0898969)</td>
<td>COPD</td>
<td>7.9: NR</td>
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<tr>
<td>Chen et al. (2008, 0879433)</td>
<td>Respiratory Disease</td>
<td>7.7: NR</td>
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<td>Fong et al. (2008, 0890799)</td>
<td>Respiratory Disease</td>
<td>7.6: NR</td>
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<td>Rich et al. (2005, 0853151)</td>
<td>IHD Shock</td>
<td>8.2: NR</td>
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<td>Villeneuve et al. (2006, 0901911)</td>
<td>Hemorrhagic Stroke; Cool Seas;</td>
<td>8.5: NR</td>
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<tr>
<td>Liu et al. (2005, 087528)</td>
<td>Respiratory Disease</td>
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<td>Ma et al. (2004, 0879091)</td>
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<td>Dukkak et al. (2005, 0878905)</td>
<td>Hemorrhagic Stroke; Cool Seas;</td>
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<td>Mar et al. (2005, 0829091)</td>
<td>Respiratory Disease</td>
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<td>Page et al. (2006, 0614346)</td>
<td>Respiratory Disease</td>
<td>10.2: NR</td>
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<td>Rabenentz et al. (2006, 0857031)</td>
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<tr>
<td>Page et al. (2006, 0925490)</td>
<td>MI</td>
<td>11.1: NR</td>
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<td>Peters et al. (2001, 0165488)</td>
<td>MI</td>
<td>12.1: 29.2</td>
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<tr>
<td>Slaughther et al. (2005, 0768514)</td>
<td>MI</td>
<td>13.2: NR</td>
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<td>Sullivan et al. (2009, 0505041)</td>
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<td>Sullivan et al. (2009, 0512080)</td>
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<td>Domingo et al. (2008, 0839898)</td>
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<td>Bell et al. (2007, 1942268)</td>
<td>MI</td>
<td>13.4: 24.4</td>
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<td>Zhang et al. (2009, 1819737)</td>
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<td>O'Connor et al. (2008, 1509100)</td>
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<td>Ilb et al. et al. (2007, 0273022)</td>
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<td>13.5: 24.6</td>
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<td>Delmic et al. et al. (2007, 0268071)</td>
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<td>13.5: 24.6</td>
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<td>Znamen et al. (2006, 0501230)</td>
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<td>Rich et al. et al. (2009, 0250901)</td>
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<td>Metzner et al. (2008, 0279089)</td>
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<td>Shapard et al. (2003, 024247)</td>
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<td>Burnett et al. (2007, 0253976)</td>
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<td>Gent et al. (2009, 0131936)</td>
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<td>Tolbert et al. (2007, 090314)</td>
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<td>Metzner et al. (2004, 044222)</td>
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<td>McIlveen et al. (2008, 0208067)</td>
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<td>Lin et al. et al. (2009, 0263939)</td>
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<td>Ilb et al. et al. (2007, 0245908)</td>
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<td>Lipman et al. (2002, 0249767)</td>
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<td>Delmic et al. et al. (2007, 0268071)</td>
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<td>Metzner et al. (2008, 0279089)</td>
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<td>Throner et al. (2008, 0242912)</td>
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<td>Ostro et al. (2008, 0917101)</td>
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<td>Paul et al. (2009, 0505035)</td>
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<td>Ostro et al. (2008, 0789151)</td>
<td>MI</td>
<td>13.5: 24.6</td>
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</tr>
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</table>

**Figure 2.1.** Excess risk estimates from epidemiologic studies of PM$_{2.5}$ ordered by mean 24-h avg concentration as reported by the investigator.
<table>
<thead>
<tr>
<th>Size Fraction</th>
<th>Outcome</th>
<th>Causality Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>Cardiovascular Effects</td>
<td>Causal</td>
</tr>
<tr>
<td></td>
<td>Respiratory Effects</td>
<td>Likely to be causal</td>
</tr>
<tr>
<td></td>
<td>Mortality</td>
<td>Likely to be causal</td>
</tr>
</tbody>
</table>
### Table 2.2: Projected PM\textsubscript{2.5} Concentrations by Region

<table>
<thead>
<tr>
<th>Study</th>
<th>Endpoint Description</th>
<th>Concentration (\mu g/m\textsuperscript{3})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zeger et al. (2008)</td>
<td>All Cause Mortality</td>
<td>10.7</td>
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<tr>
<td>Kim et al. (2004)</td>
<td>Bronchitis (Children)</td>
<td>12</td>
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<tr>
<td>Zeger et al. (2008)</td>
<td>All Cause Mortality</td>
<td>13.1</td>
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<tr>
<td>Miller et al. (2002)</td>
<td>CVD Morbidity or Mortality</td>
<td>13.5</td>
</tr>
<tr>
<td>Eftim et al. (2006)</td>
<td>All Cause Mortality</td>
<td>13.6</td>
</tr>
<tr>
<td>Goss et al. (2004)</td>
<td>All Cause Mortality</td>
<td>13.7</td>
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<tr>
<td>McConnell et al. (2003)</td>
<td>Bronchitis (Children)</td>
<td>13.8</td>
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<tr>
<td>Zeger et al. (2008)</td>
<td>All Cause Mortality</td>
<td>14.0</td>
</tr>
<tr>
<td>Krewski et al. (2000)</td>
<td>All Cause Mortality</td>
<td>14.0</td>
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<td>Krewski et al. (2008)</td>
<td>CHD Mortality</td>
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<tr>
<td>Krewski et al. (2008)</td>
<td>Lung Cancer Mortality</td>
<td>14.0</td>
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<tr>
<td>Eftim et al. (2006)</td>
<td>All Cause Mortality</td>
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<tr>
<td>Upfert et al. (2006)</td>
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<td>Dockery et al. (1996)</td>
<td>Bronchitis (Children)</td>
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<td>Woodruff et al. (2008)</td>
<td>Infant Mortality (Respiratory)</td>
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<td>Lader et al. (2008)</td>
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<td>Infant Mortality (Respiratory)</td>
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<td>Enstrom (2005)</td>
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<tr>
<td>Chen et al. (2005)</td>
<td>CHD Mortality</td>
<td>29.0</td>
</tr>
</tbody>
</table>

### Figure 2.2
Summary of U.S. studies examining the association between long-term exposure to PM\textsubscript{2.5} and CVD morbidity/mortality, respiratory morbidity/mortality, and all-cause mortality conducted in locations where the mean annual PM\textsubscript{2.5} concentration ranged from 10.7-29 \mu g/m\textsuperscript{3}. All effect estimates have been standardized to reflect a 10 \mu g/m\textsuperscript{3} increase in mean annual PM\textsubscript{2.5} concentration.
Table 2-2. Summary of causal determinations for long-term exposure to PM$_{2.5}$.

<table>
<thead>
<tr>
<th>Size Fraction</th>
<th>Outcome</th>
<th>Causality Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>Cardiovascular Effects</td>
<td>Causal</td>
</tr>
<tr>
<td></td>
<td>Respiratory Effects</td>
<td>Likely to be causal</td>
</tr>
<tr>
<td></td>
<td>Mortality</td>
<td>Likely to be causal</td>
</tr>
<tr>
<td></td>
<td>Reproductive and Developmental</td>
<td>Suggestive</td>
</tr>
<tr>
<td></td>
<td>Cancer, Mutagenicity, and Genotoxicity</td>
<td>Suggestive</td>
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</table>
Table 2.3. Summary of causal determinations for short-term exposure to $PM_{10-2.5}$.

<table>
<thead>
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<th>Size Fraction</th>
<th>Outcome</th>
<th>Causality Determination</th>
</tr>
</thead>
<tbody>
<tr>
<td>$PM_{10-2.5}$</td>
<td>Cardiovascular Effects</td>
<td>Suggestive</td>
</tr>
<tr>
<td></td>
<td>Respiratory Effects</td>
<td>Suggestive</td>
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<tr>
<td></td>
<td>Mortality</td>
<td>Suggestive</td>
</tr>
<tr>
<td>Size Fraction</td>
<td>Outcome</td>
<td>Causality Determination</td>
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<tr>
<td>Ultrafine Particles</td>
<td>Cardiovascular Effects</td>
<td>Suggestive</td>
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<td></td>
<td>Respiratory Effects</td>
<td>Suggestive</td>
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</table>