Air Pollution and Heart Health: Making the Connection

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• Why should communities care about ambient air pollutants?
• Why should healthcare systems care about ambient air pollutants?
• Why should health care providers care about ambient air pollutants?
• Why should their patients care about ambient air pollutants?
EPA:

“Epidemiologic evidence is sufficient to conclude that a causal relationship exists between: short-term and long-term exposure to PM$_{2.5}$ and mortality.”

Integrated Science Assessment (ISA) for Particulate Matter 2009
“Air pollution should be viewed as one of several major modifiable risk factors in the prevention and management of cardiovascular disease.”

“Health professionals, including cardiologists, have an important role to play in supporting educational and policy initiatives as well as counseling their patients.”
Air Pollution Deaths
Comparable to Alzheimer’s, Diabetes, Flu

~130,000 excess deaths attributed to outdoor air pollution in the U.S.

(No. of Deaths in Thousands)
CV Disease: 740
Cancer: 585
Chronic Respiratory: 149
Accidents: 131
Alzheimer's Disease: 85
Diabetes Mellitus: 76
Flu/pneumonia: 57
Kidney Disease: 47
Suicide: 41
Septicemia: 38
Liver Disease: 36

Cause of Death

Estimated Excess Mortality
Burden of Air Pollution Deaths by County

PM$_{2.5}$ and O$_3$-related Mortality by County based on 2005 air pollution levels

US EPA’s BENMAP
http://www.epa.gov/airquality/benmap/index.html

Fann et al. Risk Analysis 2012
PM Causes Both Short- and Long-term Health Impacts

Short-term clinical events
- Associated with daily transient changes (BLUE arrows)

Long-term clinical events
- Associated with annual average (YELLOW line)
Population studies and cardiovascular health effects of particle air pollution
### Epidemiological Evidence

PM$_{2.5}$-Related Air Pollution Effects

**Clinical cardiovascular endpoints from epidemiological studies at ambient concentrations**

<table>
<thead>
<tr>
<th>Health Outcomes</th>
<th>Short-Term Exposure (Days)</th>
<th>Longer-Term Exposure (Months to Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-cause mortality</td>
<td>↑ ↑ ↑ ↑</td>
<td>↑ ↑ ↑</td>
</tr>
<tr>
<td>Cardiovascular mortality</td>
<td>↑ ↑ ↑ ↑</td>
<td>↑ ↑ ↑</td>
</tr>
<tr>
<td>Cardiovascular hospitalizations</td>
<td>↑ ↑ ↑ ↑</td>
<td>↑</td>
</tr>
<tr>
<td>Ischemic heart disease*</td>
<td>↑ ↑ ↑ ↑</td>
<td>↑ ↑ ↑</td>
</tr>
<tr>
<td>Heart failure*</td>
<td>↑ ↑ ↑</td>
<td>↑</td>
</tr>
<tr>
<td>Ischemic stroke*</td>
<td>↑ ↑</td>
<td>↑</td>
</tr>
<tr>
<td>Vascular diseases</td>
<td>↑</td>
<td>↑ †</td>
</tr>
<tr>
<td>Cardiac arrhythmia/cardiac arrest</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

*Brook et al. Circulation 2010*
**PM$_{2.5}$ Increases Risk in Women**

First Cardiovascular Event or Death

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**A Overall Effect**

Annual NAAQS

PM$_{2.5}$ = 12µg/m$^3$

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**Outcome**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Hazard Ratio $\uparrow$</th>
</tr>
</thead>
<tbody>
<tr>
<td>First cardiovascular event</td>
<td></td>
</tr>
<tr>
<td>Any cardiovascular event†</td>
<td>1.24 (1.09–1.41)</td>
</tr>
<tr>
<td>Coronary heart disease‡</td>
<td>1.21 (1.04–1.42)</td>
</tr>
<tr>
<td>Cerebrovascular disease§</td>
<td>1.35 (1.08–1.68)</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>1.06 (0.85–1.34)</td>
</tr>
<tr>
<td>Coronary revascularization</td>
<td>1.20 (1.00–1.43)</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.28 (1.02–1.61)</td>
</tr>
<tr>
<td>Death from cardiovascular cause</td>
<td></td>
</tr>
<tr>
<td>Any death from cardiovascular cause</td>
<td>1.76 (1.25–2.47)</td>
</tr>
<tr>
<td>Coronary heart disease</td>
<td></td>
</tr>
<tr>
<td>Definite diagnosis</td>
<td>2.21 (1.17–4.16)</td>
</tr>
<tr>
<td>Possible diagnosis</td>
<td>1.26 (0.62–2.56)</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>1.83 (1.11–3.00)</td>
</tr>
</tbody>
</table>

*Miller et al. NEJM 2007*
Air Pollution Triggers Heart Attacks

Low PM exposure associated with lower risk

Population Attributable Fractions (PAF)

Related to: the strength of the association between exposure to a risk factor and the prevalence of this risk factor within the population

Modified from Nawrot et al. Lancet 2011
Air Particle Pollution and Stroke
Short-term Exposure & Ischemic Stroke

Within a population: low levels of PM are associated with ischemia stroke

Does Air Pollution Increase Atherosclerosis?
Long-term PM$_{2.5}$ and NO$_2$ exposure increases coronary artery calcium, an indicator of atherosclerosis.

Possible Mechanisms
Exposure to PM$_{2.5}$, Traffic- and Combustion Related Air Pollution

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<th>Health Outcomes</th>
<th>Short-Term Exposure (Days)</th>
<th>Longer-Term Exposure (Months to Years)</th>
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</thead>
<tbody>
<tr>
<td>Surrogate markers of atherosclerosis</td>
<td>N/A</td>
<td>↑</td>
</tr>
<tr>
<td>Systemic inflammation</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Systemic oxidative stress</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Endothelial cell activation/blood coagulation</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Vascular/endothelial dysfunction</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>BP</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Altered HRV</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Cardiac ischemia</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Arrhythmias</td>
<td>↑</td>
<td></td>
</tr>
</tbody>
</table>

**MESA Air**

**Long-term exposure:**
- 5 µg/m$^3$ PM$_{2.5}$ associated with:
  - 6% higher IL-6
    - (95% CI = 2%, 9%)
- 40 ppb NOx associated
  - 7% higher level of D-dimer
    - (95% CI = 2%, 13%)

**Short-term exposure:**
- Daily PM$_{2.5}$ level associated with:
  - CRP
  - Fibrinogen
  - E-selectin

*Brook et al. Circulation 2010*

*Hajat et al. Epidemiology 2015*
**Pulmonary oxidative stress & inflammation**

**Blood**

PM or constituents in the circulation

- UFP, soluble metals
- Organic compounds

**Bronchioles/Alveoli**

PM and/or constituents transmitted into blood

**Systemic Oxidative stress and Inflammation**

**CELLS**: ↑ activated WBCs, platelets, myeloperoxidase, Plt-MΦ

**CYTOKINES**: ↑ IL-1β, IL-6, TNF-α

**OTHER**: ↑ ET, histamine, ? Microparticles, ox-LDL, dysFx HDL

**ANS imbalance**

- ↑SNS / ↓PSNS

**ANS**

Activation of lung ANS reflex arcs

**PM**

**Neural Response**

**SYSTEMIC “SPILL-OVER”**

**Circulating Constituents**

**Blood**

PM or constituents in the circulation

**ACUTE**: Endothelial dysfunction, Vasoconstriction, Plaque instability, Coagulation, Thrombosis, Arrhythmias

**CHRONIC**: LV hypertrophy, Atherosclerosis, Arterial Stiffness, Metabolic Syndrome: HTN, Insulin resistance, Dyslipidemia
Reducing Air Pollution Decreases Health Risk
Harvard Six-Cities Study
PM Decreased, Mortality Decreased

Adjusted CV Mortality Rate Ratios

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Person Years</td>
<td>104,243</td>
<td>54,735</td>
</tr>
<tr>
<td>On follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Deaths</td>
<td>626</td>
<td>570</td>
</tr>
</tbody>
</table>

City-specific model

<table>
<thead>
<tr>
<th>City</th>
<th>Period 1</th>
<th>Period 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portage</td>
<td>1.00</td>
<td></td>
</tr>
<tr>
<td>Topeka</td>
<td>1.03</td>
<td>1.00</td>
</tr>
<tr>
<td>Watertown</td>
<td>1.19</td>
<td>0.82</td>
</tr>
<tr>
<td>Harriman</td>
<td>1.33</td>
<td>1.23</td>
</tr>
<tr>
<td>St. Louis</td>
<td>1.21</td>
<td>0.96</td>
</tr>
<tr>
<td>Steubenville</td>
<td>1.48</td>
<td>1.21</td>
</tr>
</tbody>
</table>

Laden et al. AJRCCM 2006
Estimated adjusted rate ratios for total mortality and PM$_{2.5}$

- P - Portage, WI
- T - Topeka, KS
- W - Watertown, MA
- L - St. Louis, MO
- H - Harriman, TN
- S - Steubenville, O

Bold - Period 1
Harvard Six-Cities Study

Estimated adjusted rate ratios for total mortality and PM$_{2.5}$

- **P** - Portage, WI
- **T** - Topeka, KS
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- **S** - Steubenville, OH

**Bold** - Period 1
**Italics** - Period 2

*Laden et al. AJRCCM 2006*
• Particle pollution increases short- and long-term cardiovascular morbidity and mortality

• Aged-adults, those with pre-existing heart disease, and diabetes are at higher risk

• Mechanisms are under investigation but are likely related to effects on oxidative stress, autonomic control and inflammation

• Improvements in air pollution levels reduce health impacts and increase life expectancy

• Reductions of short-term exposures in those at higher risk are predicted to mitigated adverse health effects
Questions?