The Ever Expanding Knowledge-Base of Air Pollution’s Health Effects

Wayne Cascio, MD, FACC
Acting Director, National Health and Environmental Effects Research Laboratory
Office of Research & Development, US EPA
Research Triangle Park, NC
Wayne Cascio, MD

• No conflicts of interest
• The presentation represents the opinions of the speaker and does not necessarily represent the policies of the US EPA
In 2015 ambient PM$_{2.5}$ was the fifth-ranking global mortality risk factor -

**Exposure to PM$_{2.5}$ caused:**
- 4.2 million deaths (7.6% of total deaths)
- 103.1 million disability-adjusted life-years (4.2% of DALYs)

**Between 1990 and 2015 deaths increased in association with PM$_{2.5}$ exposure from:**
- 3.5 million to 4.2 million

**Ozone exposure contributed to morbidity and mortality -**

**In 2015 ozone exposure is estimated to have accounted for:**
- 254,000 deaths
- 4.1 million DALYs from chronic obstructive pulmonary disease
Despite Phenomenal Progress U.S. Air Pollution Continues to Impact Population Health

Air pollution remains a significant U.S. Public Health Concern

- Estimated excess mortality 125,000 deaths/year
- Over 20 million school days and work days lost
- Over 1 million life-years lost
- 122.5 million people living in counties with one or more pollutants exceeding the NAAQS in 2016

• ~125,000 excess deaths attributed to outdoor air pollution in the U.S.
• Comparable in Number to Diabetes, Pneumonia, Flu
Environmental Health Scientists Continue to Study Air Pollution and Human Health

2,894 Publications on “Air Pollution and Human Health” in PubMed since 2016

<table>
<thead>
<tr>
<th>Topic Area</th>
<th># of Publications</th>
<th>Maturity of Field</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Nervous System</td>
<td>119</td>
<td>New</td>
</tr>
<tr>
<td>Birth Outcomes</td>
<td>287</td>
<td>Growing</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>432</td>
<td>Growing</td>
</tr>
<tr>
<td>Cancer</td>
<td>407</td>
<td>Stable</td>
</tr>
<tr>
<td>Respiratory</td>
<td>727</td>
<td>Stable</td>
</tr>
<tr>
<td>Other</td>
<td>922</td>
<td></td>
</tr>
</tbody>
</table>
Overview of Presentation

- **Benefits of NAAQS on Mortality in the U.S.**
- **Health Effects of Air Pollution**
  - Cardiovascular
  - Central Nervous System
  - Human Development
- **Emerging Issues, Technology & Opportunities**
  - Wildfire Smoke
  - Sensors and Citizen Science
  - Public Health and Clinical Interventions
After the implementation of local, state, and federal air quality policies

- PM$_{2.5}$ precursor emissions declined over the course of several decades

Between 1980 - 2010, PM$_{2.5}$ exposures fell by about half, and estimated excess deaths decreased by about a third

- California, Virginia, New Jersey, and Georgia had some of the largest estimated reductions in PM$_{2.5}$-attributable deaths
Change in the % of Death Due to PM$_{2.5}$ Between 1980 - 2010

-2.85 – -0.04%
-0.03 – -0.01%
0.02 – 2.18%
2.19 – 3.01%
3.02 – 3.71%
3.72 – 4.37%
4.38 – 5.09%
5.10 – 6.07%
6.08 – 8.11%
8.12 – 11.7%

Relative to a hypothetical population with exposures held constant at 1980 levels

- people born in 2050 would live about 1 year longer
- there would be a cumulative gain of 4.4 million life years among adults ≥30 years of age
Health Effects of Air Pollution
Cardiovascular
**Long-term Health Effects of Air Pollution**

**PM$_{2.5}$ Exposure and Post-MI Survival in Ontario, Canada**

**Post-Myocardial Infarction Survival**

**Ontario, Canada 1999-2011**

- 8,873 patients with 4,016 non-accidental deaths
- Mortality follow-up through 2011
- Cumulative time-weighted exposures to PM$_{2.5}$ were derived from satellite observations
- For each 10-µg/m$^3$ increase in PM$_{2.5}$ non-accidental mortality increased by 22%

**Conclusions:**
- Long-term air pollution exposure adversely affects the survival of Heart Attack patients

**Post-Stroke Survival**

**London, England 1995-2006**

- 3,320 patients with 1,856 deaths
- Stroke follow-up to mid-2006
- Outdoor NO$_2$ and PM$_{10}$ modeled for 2002
- HRs were adjusted for relevant factors
- 10-µg/m$^3$ increase in NO$_2$ and PM$_{10}$ was associated with a 28% and 52% increase in risk of death, respectively

**Conclusions:**
- Improvements in outdoor air quality might contribute to better survival after stroke
- A 10 µg/m$^3$ reduction in NO$_2$ exposure is expected to reduce mortality comparable to that for stroke units
Air Pollution and Mortality
Effect of PM on Survival and Subsequent Clinical Events

Zanobetti A & Schwartz J.
Environ Health Perspect 2007

Mortality
CHF hospitalization
MI hospitalizations

Koton et al.
Prev Med 2013

MI, CHF, Stroke
Mortality

Tonne et al.
Eur Heart J 2013

Mortality

Tonne et al.
Int J Hyg Envir Health 2016

Mortality

Chen et al. EHP 2016
Environ Health Perspect 2016

Mortality
MI Mortality

Hazard Ratio (per 10µg/m³)

1.0 1.25 1.50 1.75 2.00 2.25 2.50

(PM$_{10}$, 21 U.S. cities, 1985-1999)
(PM$_{2.5}$, Israel, 1992-2005)
(PM$_{2.5}$, Israel, 1992-2011)
(PM$_{2.5}$, London, 2004-2010)
(PM$_{10}$, London, 2003-2010)
(PM$_{2.5}$, Ontario, 1999-2011)
1 μg/m³ increase in annual average PM$_{2.5}$ was associated with an:

- 11.1% relative increase in the odds of significant coronary artery disease
- 14.2% increase in the odds of having had a heart attack during the previous year

5,679 patients who underwent coronary angiography at Duke University between 2002–2009 and resided in North Carolina*

6,575 Ohio residents undergoing elective diagnostic coronary angiography**

1 μg/m³ increase in annual average PM$_{2.5}$ was associated with an:

- 17% relative increase in the odds of 1-2 vessel, and a 24% increase in ≥ 3 vessel coronary artery disease
- 14% increase in the odds of having a heart attack within 3 years

# Cardiovascular Disease Risk Calculators

## Predictive Models for Cardiovascular Outcomes

---

### ACC AHA 10-Year ASCVD Risk

- Age
- Gender
- Race
- Smoker
- HDL cholesterol
- Systolic blood pressure
- Diastolic blood pressure
- Treatment for high blood pressure
- Diabetes
- Statin therapy
- Aspirin therapy
- Total cholesterol

### Reynolds Risk Calculator

- CRP: Inflammation

http://www.reynoldsriskscore.org

### MESA Cardiovascular Risk Calculator

- Calcium Score

https://www.mesa-nhlbi.org/MESACHDRisk/MesaRiskScore/RiskScore.aspx

---

**EPA**

**ASCVD Risk Estimator Plus**

<table>
<thead>
<tr>
<th>Current 10-Year ASCVD Risk ~%</th>
<th>Previous 10-Year ASCVD Risk ~%</th>
</tr>
</thead>
</table>

**Patient Demographics**

- **Current Age**
- **Sex**
  - Male
  - Female
- **Race**
  - White
  - African American
  - Other

**Current Labs/Exam**

- **Total Cholesterol (mg/dL)**
- **HDL Cholesterol (mg/dL)**
- **LDL Cholesterol (mg/dL)**
- **Systolic Blood Pressure (mm of Hg)**

**Personal History**

- **History of Diabetes**
- **On Hypertension Treatment?**
- **Smoker**
- **On a Statin?**
- **On Aspirin Therapy?**

---

http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/
Air Pollution Worsens Vascular Risk Factors
Risk Factors for Atherosclerosis and Air Quality

Poor Air Quality:

**Age** – might accelerate aging
- Ward-Caviness et al. Octotarget 2016
- McCracken et al. EHP 2010

**Total Cholesterol** – increases cholesterol
- Shanley et al. Epidemiology 2016

**HDL** – decreases HDL particle number
- Bell et al. Arterioscler Thromb Vasc Biol 2017

**LDL** – oxidizes LDL and ox-LDL receptor
- Gong et al. Genome Biol. 2007
- Wu et al. Chemosphere 2015

**Systolic BP** – increases blood pressure

**Diabetes** – associated with type II diabetes
- Renzi et al. Environ Int 2017

**Statin Therapy** – protective
- Alexeeff et al. Environ Health Perspect 2011

[Image: ASCVD Risk Estimator Plus]

http://tools.acc.org/ASCVD-Risk-Estimator-Plus#!/calculate/estimate/
**Coronary Artery Calcium Confers Increased Cardiovascular Risk**

Summary of the Coronary Artery Calcium (CAC) and absolute long-term Cardiovascular Risk

<table>
<thead>
<tr>
<th>CAC Score</th>
<th>FRS Equivalent</th>
<th>10-Year Event Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Very low</td>
<td>1.1 - 17</td>
</tr>
<tr>
<td>1 - 100</td>
<td>Low</td>
<td>2.3 – 5.9</td>
</tr>
<tr>
<td>101 - 400</td>
<td>Intermediate</td>
<td>12.8 – 16.4</td>
</tr>
<tr>
<td>&gt; 400</td>
<td>High</td>
<td>22.5 – 28.6</td>
</tr>
<tr>
<td>&gt; 1,000</td>
<td>Very high</td>
<td>37.0</td>
</tr>
</tbody>
</table>

Hecht HS. JACC Cardiovasc Imaging 2015;8:579-96
**Long-Term PM$_{2.5}$ & NO$_2$ Exposure Increases Coronary Artery Calcium**

**Long-term PM$_{2.5}$ and NO$_2$ increased coronary calcium, an indicator of atherosclerosis**

**Air Pollutants**

<table>
<thead>
<tr>
<th>Pollutant</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>5µg/m$^3$</td>
</tr>
<tr>
<td>NO$_x$</td>
<td>40ppb</td>
</tr>
<tr>
<td>NO$_x$</td>
<td>10ppb</td>
</tr>
<tr>
<td>Black carbon</td>
<td>0.5µg/m$^3$</td>
</tr>
</tbody>
</table>

**Multi Ethnic Study of Atherosclerosis - Air: 10-year coop Study with NHLBI**

**Long-term average PM$_{2.5}$ (µg/m$^3$)**

- California
- Illinois
- Minnesota
- Maryland
- New York
- North Carolina

Long-term $PM_{2.5}$ & Nox Exposure Associated Atherosclerosis Progression

MESA Air Study – Led by University of Washington

$PM_{2.5}$ and Coronary Calcium

Uncertainty for 15 $\mu$g/m$^3$ case

Coronary Artery Calcium Confers Increased Cardiovascular Risk

Possible Shift in 10-Year Event Rate due to Increases in Coronary Artery Calcium (CAC) Associated with Exposure to 15 \( \mu g/m^3 \) PM\(_{2.5} \) for 10 years = 120 Agatston Units

<table>
<thead>
<tr>
<th>CAC Score</th>
<th>FRS Equivalent</th>
<th>10-Year Event Rate, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Very low</td>
<td>1.1 – 1.7</td>
</tr>
<tr>
<td>1 - 100</td>
<td>Low</td>
<td>2.3 – 5.9</td>
</tr>
<tr>
<td>101 - 400</td>
<td>Intermediate</td>
<td>12.8 – 16.4</td>
</tr>
<tr>
<td>&gt; 400</td>
<td>High</td>
<td>22.5 – 28.6</td>
</tr>
<tr>
<td>&gt; 1,000</td>
<td>Very high</td>
<td>37.0</td>
</tr>
</tbody>
</table>

ACC AHA 10-Year ASCVD Risk Calculator does not consider environmental factors.

ASCVD Risk Calculators might be refined by including long-term exposure to air pollution.

Hecht HS. JACC Cardiovasc Imaging 2015;8:579-96
Smoking-Air Pollution Interaction & Mortality
Interaction of Smoking Cigarettes and Air Pollution

- ACS Cancer Prevention Study-II with modeled PM$_{2.5}$ levels
- Examined interactions for all-cause & cardiovascular mortality among 429,406 current or never smoking participants and PM
- High (>14.44) vs. low (≤10.59) PM$_{2.5}$ µg/m$^3$ exposure

### Number of Additional Deaths Per 100,000 Person Years (95% CI)

<table>
<thead>
<tr>
<th></th>
<th>All Cause</th>
<th>Cardiovascular Disease (plus diabetes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>High PM$_{2.5}$</td>
<td>44</td>
<td>36</td>
</tr>
<tr>
<td>vs. Low PM$_{2.5}$</td>
<td>(5, 83)</td>
<td>(9, 63)</td>
</tr>
<tr>
<td>Current vs. Never Smoker</td>
<td>1,080</td>
<td>318</td>
</tr>
<tr>
<td></td>
<td>(1,034, 1,250)</td>
<td>(288, 347)</td>
</tr>
<tr>
<td>High PM$_{2.5}$ *</td>
<td>56</td>
<td>32</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>(-3, 115)</td>
<td>(-6, 71)</td>
</tr>
</tbody>
</table>

- Reductions in smoking will reduce all-cause & cardiovascular death the most
- Reductions in PM$_{2.5}$ will prevent a proportion of mortality attributed to smoking

Health Effects of Air Pollution
Central Nervous System
Emerging Areas of Health Effects Research
Neurological and Neurodegenerative

Air Pollution & Neurotoxicity in Adults

- **Effects on Neurodegenerative Disorders**
  - Parkinson’s
  - Multiple sclerosis

- **Non-Specific Neurological Symptoms**
  - Cognitive Function
    (Tallon et al. Environ Internat 2017)
  - Fatigue
  - Anxiety and Depression
    (Szyszkowicz M et al. Environ Health insights 2016; Pun EHP 2016; Vert Intern J Hygiene Envir Health 2017)

Air Pollution & Neurotoxicity in Children

- **Effects on Child Neurodevelopment**
  - Prenatal exposure to air pollution
  - Childhood exposure to air pollution

- **Neurodevelopmental Disorders**
  - Autism Spectrum Disorder
  - Attention-Deficit Hyperactivity Disorder
Air Pollution: Cognition and Dementia

- 257,816 cases of dementia in 2001–2013 in Ontario
- Positive association between air pollutants and dementia incidence
- The incidence of dementia increased for every interquartile-range increase in exposure to:
  - PM$_{2.5}$ the hazard ratio (HR) was 1.04 (95% CI: 1.03–1.05)
  - NO$_2$ the HR was 1.10; (95% CI: 1.08–1.12)

### Estimated attributable fraction and the number of incident dementia attributable to exposure to PM$_{2.5}$ and NO$_2$ among a cohort in Ontario, during the follow-up period 2001–2013 (total number of incident cases = 257,816).

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Attributable fraction (95% uncertainty level)</th>
<th>Number of dementia attributable to exposure to air pollutant (95% uncertainty level)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM$_{2.5}$</td>
<td>2.4% (1.8–3.0%)</td>
<td>6278 (4738–7816)</td>
</tr>
<tr>
<td>NO$_2$</td>
<td>5.4% (4.4–6.6%)</td>
<td>13,962 (11,428–16,910)</td>
</tr>
<tr>
<td>PM$_{2.5}$ + NO$_2$</td>
<td>6.1% (4.8–7.5%)</td>
<td>15,813 (12,374–19,464)</td>
</tr>
</tbody>
</table>

Chen H et al. Environ Internat 2017
Health Effects of Air Pollution
Human development
Emerging Areas of Health Effects Research
Reproductive and Developmental

Infertility

- **Gametogenesis** (Carré J et al. Environmental Health 2017)

Fetal Growth

- exposure to PM$_{10}$, PM$_{2.5}$ and NO$_2$ was associated with reductions in measurements at birth and biparietal diameter from late second trimester onwards. (Clemens T et al. Environ Internat 2017)

Stillbirth

- ambient air pollution suspected of increasing stillbirth (Siddika et al. Occup Environ Med. 2016)

Preterm Delivery

- PM$_{2.5}$ constituents and preterm delivery were observed for Blacks and Asians, older mothers, and those with some college education compared to their reference groups (Basu R et al. Ped Perinatal Epi 2017)

Low Birth Weight

- exposure to PM$_{2.5}$ is associated with low birth weight. (Rosa MJ et al. Environ Internat 2017)

Accelerated Biological Aging

- exposure to PM$_{2.5}$ shortened telomeres measured at birth, an indicator of biological aging (Martens DS et al. JAMA Pediatrics 2017)
Emerging Issues and Opportunities

- Wildfire Smoke
- Low cost sensors
- Public health and clinical interventions
Wildfire: An Issue of Concern for the States
Impacts of Local and National Importance

- Wildland fires accounted for 38% of PM$_{2.5}$ emissions in 2014
- 2017 was substantially worse than the average of the last 10 years
- Between 2001 - 2010 over 40% of the country's large wildfires occurred in the Southeast
- U.S. spends more than $2 billion each year to fight wildfires

Adapted from https://www.nifc.gov/fireInfo/fireInfo_stats_totalFires.html
Health Effects of Wildfire Smoke Systematic Reviews are Now Available


Health Effects Linked to Smoke from Wildland Fires

Health effects known or suspected to be caused by wildland fire smoke

- All-cause mortality
- Asthma & chronic obstructive pulmonary disease (COPD) exacerbations
- Bronchitis & pneumonia
- Cardiovascular outcomes
- Childhood respiratory disease
- Adverse birth outcomes
- Symptoms such as eye irritation, sore throat, wheeze and cough

Source: Studies reviewed in Liu et al. 2015
Problem: Cardiovascular health effects of wildfire smoke are uncertain

Approach:
- Epidemiology study during the 2015 California wildfire season
- Associate wildfire-PM$_{2.5}$ exposure with emergency department visits for cardiovascular and respiratory diagnoses
- Collaborative study partners:
  - California Dept. of Public Health
  - Univ. of California at San Francisco
  - US EPA/ORD/NHEERL

Smoky days/county during the study: May through September 2015
**Results:** Wildfire-PM$_{2.5}$ associated with heart attacks and strokes for all adults, particularly for those over 65 years old

- Increase in risk the day after exposure:
  - All cardiovascular, 12%
  - Heart attack, 42%
  - Abnormal heart rhythm, 24% (same day)
  - Heart failure 16%
  - Stroke 22%
  - All respiratory causes 18%

**Impact:** Highlights the importance of decreasing exposure in at-risk populations

Data to be presented as a Late-Breaking Study at the American Public Health Association Conference in Atlanta - November 2017

**All Cardiovascular Causes**

![Relative Risk Graph](image_url)
Forecast-based interventions predicted to reduce the health and economic burden of wildfires


Cost effectiveness is improved by intervening only in the homes of those at highest risk, e.g. older persons

Fisk WJ, Chan WR Indoor Air 2017

“... we believe that the time is ripe to definitively test the efficacy of personal-level interventions…”

Brook RD, et al. JAMA Cardiol. 2017
High Resolution Air Pollution Mapping
Small Scale Variability due to Local Sources

Oakland, CA
Spatial distribution of Black Carbon (BC)

Apte JS et al. Environ Sci Technol 2017

New Portable Technologies

- EPA actively engaged in new sensor technologies for:
  - personal use
  - community engagement
  - research
Smoke Sense Project
Improving Public Health Outcomes

• **Aims of Smoke Sense:**
  - Measure the effect of wildfire smoke exposure on health and productivity
  - Develop health risk communication strategies to improve public health outcomes

• **As part of this, researchers have developed a Smoke Sense mobile phone application to:**
  - Collect user input on how smoke events impact their health and daily activities
  - Provide information about the smoke exposure and recommended health risk messages
Smoke Sense provides current and future air quality

Forecasted smoke plumes can be visualized

Less time outside during smoke episodes to decrease exposure, and protect health

Smoke Sense helps collect information about who, when, and how frequently people are impacted by smoke

Information about smoke in the air and symptoms experienced in the past week will be logged
Thank you

Wayne E. Cascio, MD, FACC
Acting Director, National Health and Environmental Effects Research Laboratory
Office of Research and Development
U.S. Environmental Protection Agency

Email: cascio.wayne@epa.gov
After the implementation of local, state, and federal air quality policies –

- PM$_{2.5}$ precursor emissions declined over the course of several decades

1980

1990

2000

2010

Fann N, et al. Environmental Health Perspectives 2017

Exposure to ambient PAH may play a role in telomere shortening.


Decreases in ambient pollution levels were associated with statistically significant decreases in bronchitic symptoms in children.


Exposure to higher average coarse PM levels is associated with increased asthma prevalence and morbidity.
EPA Administrator’s Priorities:

- Cooperative Federalism: Environmental law, policy, and progress are all based on cooperation: cooperation between the States, cooperation between the States and EPA, and cooperation between the regulators and the public.
  - **Improving air quality**
  - Restoring the role of States in the regulation of water
  - Cleaning up contaminated land to revitalize communities
  - Ensuring the safety of chemicals in commerce