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

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Conflict of Interest Statement

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*

Air Pollution: A Leading Cause of the Global Burden of Disease

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

Global Burden of Disease, Injuries, and Risk Factors Study 2015. Cohen AJ, et al. *Lancet* 2017; 389: 1907–18

Despite Phenomenal Progress U.S. Air Pollution Continues to Impact Population Health

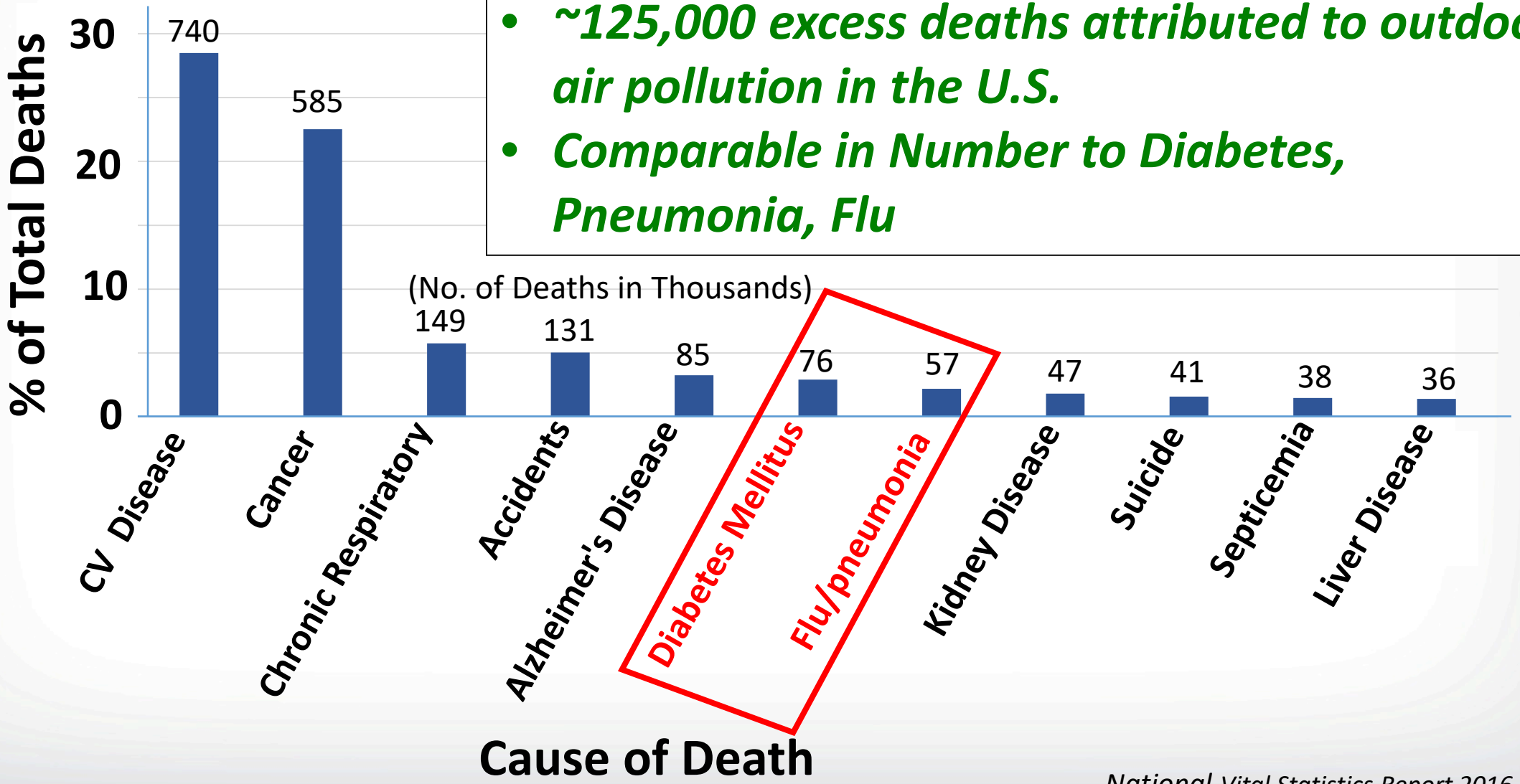
Air pollution remains a significant U.S. Public Health Concern

- 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**

Fann N. et al. Risk Anal 2012; Fann et al. *Environ Sci Tech* 2013; US EPA

Causes of Deaths in U.S.

- ***~125,000 excess deaths attributed to outdoor air pollution in the U.S.***
- ***Comparable in Number to Diabetes, Pneumonia, Flu***



National Vital Statistics Report 2016

Environmental Health Scientists Continue to Study Air Pollution and Human Health

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

Topic Area	# of Publications	Maturity of Field
Central Nervous System	119	New
Birth Outcomes	287	Growing
Cardiovascular	432	Growing
Cancer	407	Stable
Respiratory	727	Stable
Other	922	

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

Fall in Air Pollution Related Deaths Over Time

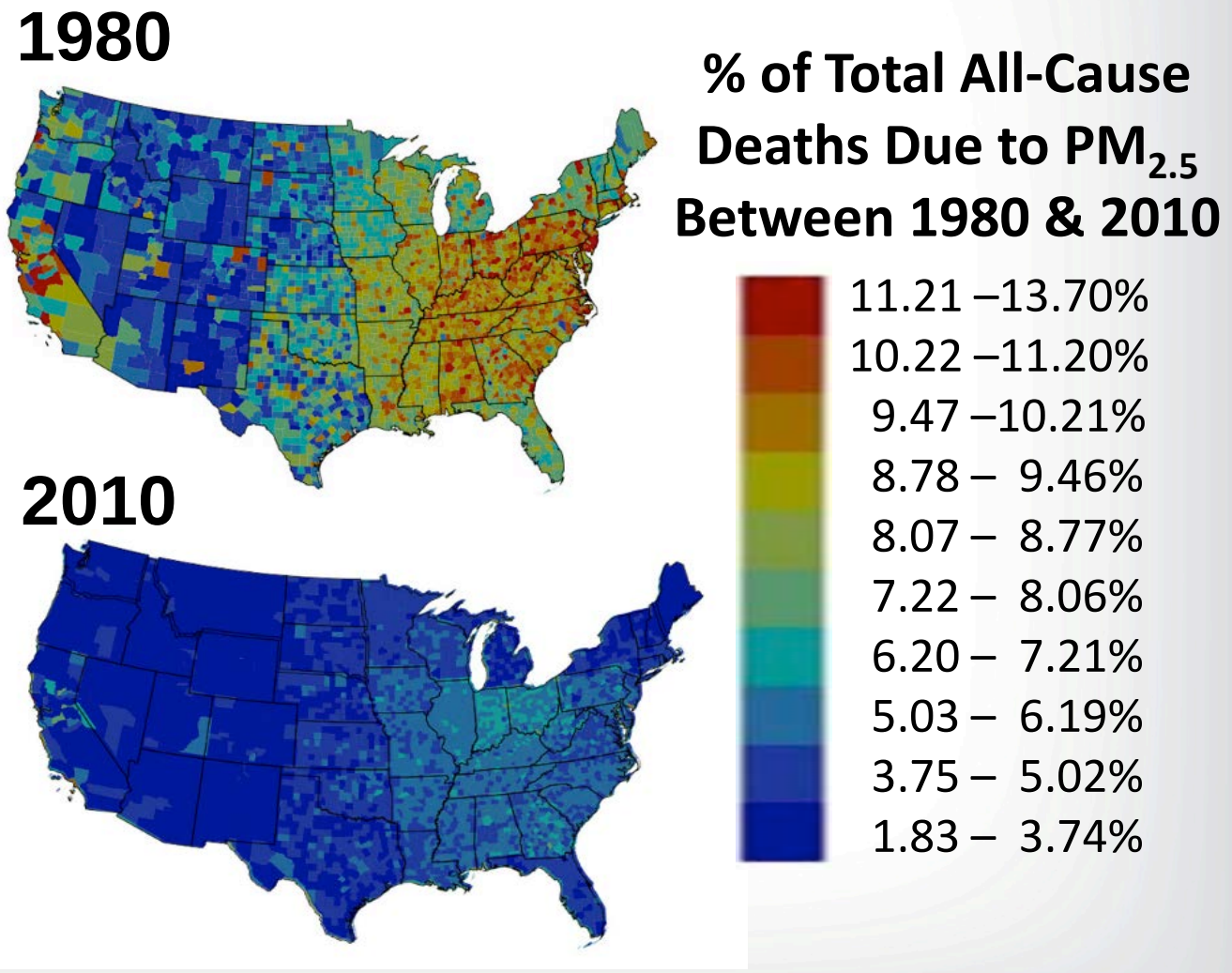
Fraction of Total All-Cause Deaths Attributed to $PM_{2.5}$

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

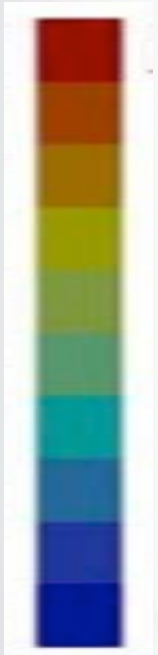


Fann N, et al. Environmental Health Perspectives 2017

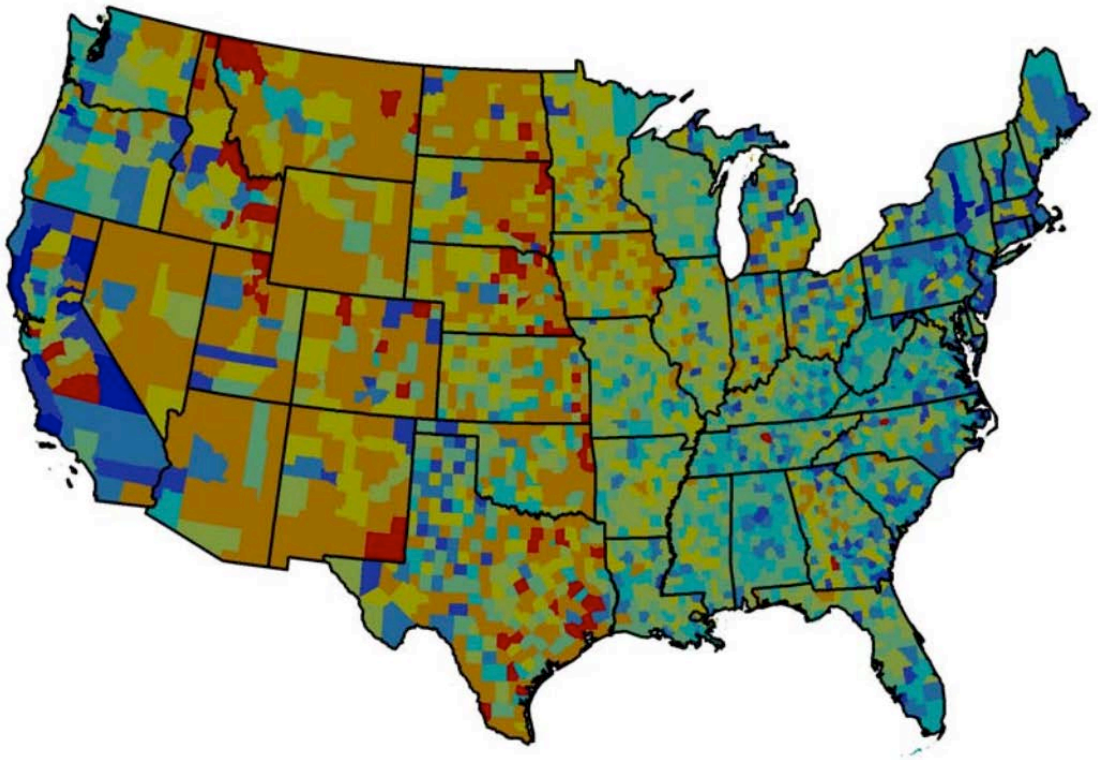
Air Pollution

Public Health Benefits of Decreasing $PM_{2.5}$ 1980-2010

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

Fann N, et al. Environmental Health Perspectives 2017

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

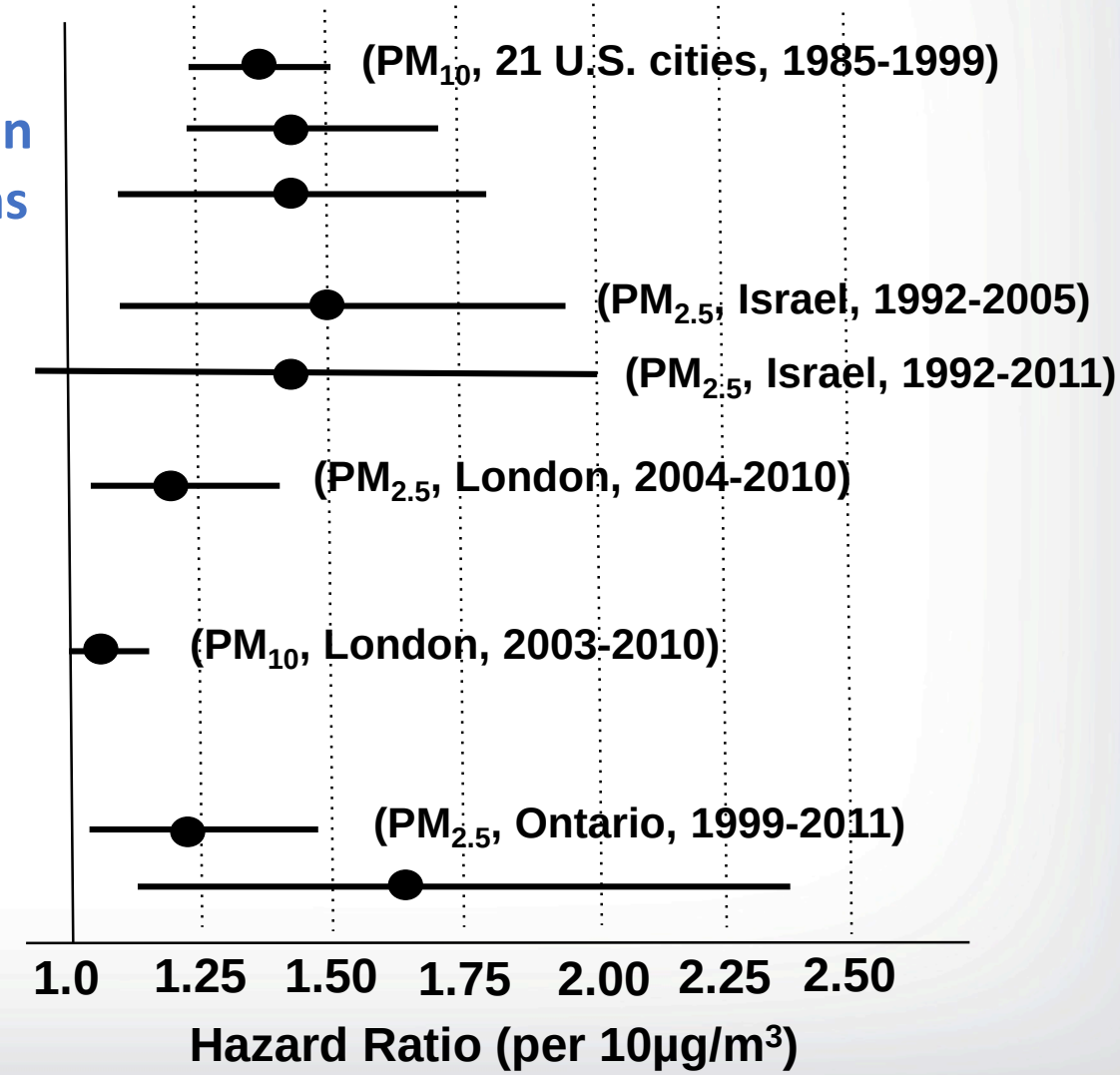
Chen H, et al. *Environ Health Perspect*, 2016

Maheswaran et al. *Stroke* 2010

Air Pollution and Mortality

Effect of PM on Survival and Subsequent Clinical Events

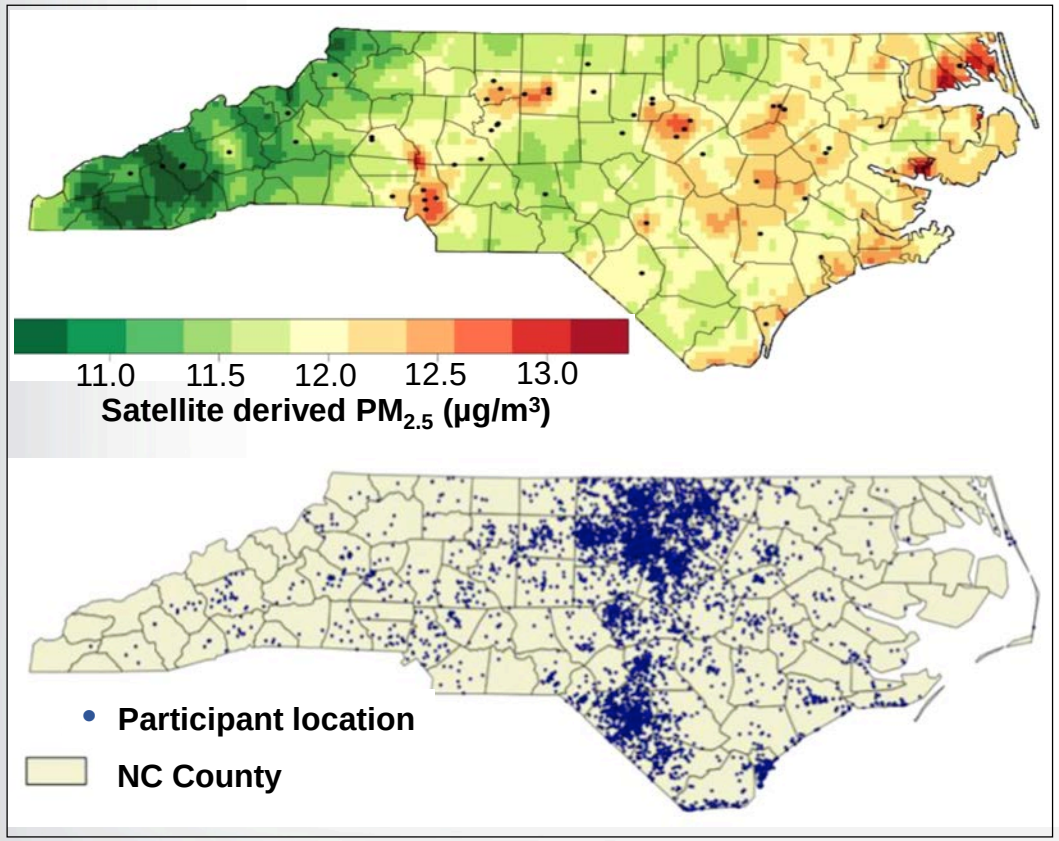
Zanobetti A & Schwartz J. *Environ Health Perspect* 2007	Mortality	(PM_{10}, 21 U.S. cities, 1985-1999)
	CHF hospitalization	
	MI hospitalizations	
Koton *et al.* *Prev Med* 2013	MI, CHF, Stroke	($PM_{2.5}$, Israel, 1992-2005)
	Mortality	($PM_{2.5}$, Israel, 1992-2011)
Tonne et al. *Eur Heart J* 2013	Mortality	($PM_{2.5}$, London, 2004-2010)
Tonne et al. *Int J Hyg Envir Health* 2016	Mortality	(PM_{10}, London, 2003-2010)
Chen et al. *EHP* 2016 *Environ Health Perspect 2016*	Mortality	($PM_{2.5}$, Ontario, 1999-2011)
	MI Mortality	



Health and Long-term Air Pollution Exposure

Association between PM and Coronary Artery Disease

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



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

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

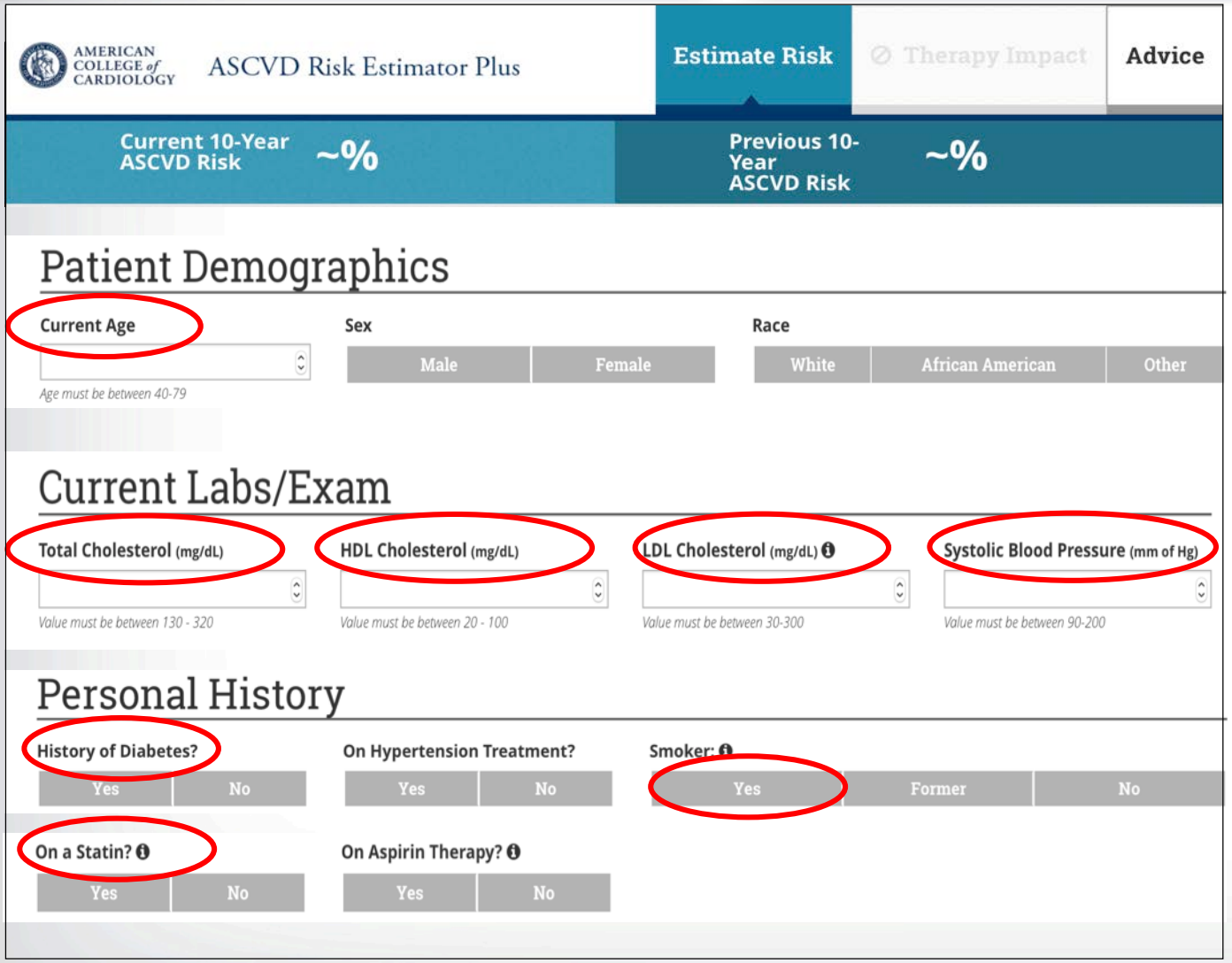
1 µg/m³ increase in annual average $PM_{2.5}$ was associated with an:

- 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

*McGuinn LA, et al. *Environ Res* 2016 **Hartiala J, et al. J *Am Heart Assoc* 2016

Cardiovascular Disease Risk Calculators

Predictive Models for Cardiovascular Outcomes



http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

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

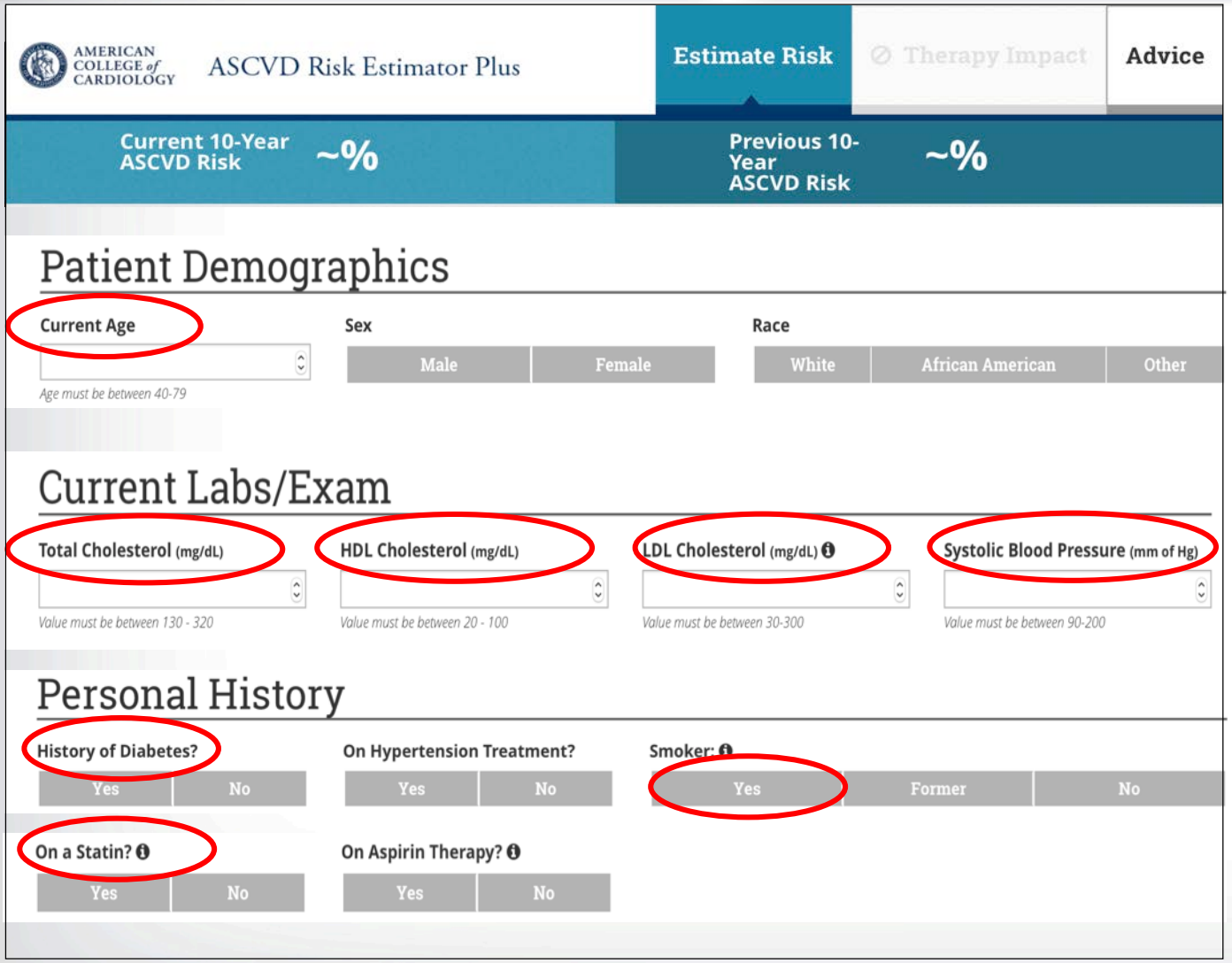
MESA Cardiovascular Risk Calculator

- Calcium Score

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

Air Pollution Worsens Vascular Risk Factors

Risk Factors for Atherosclerosis and Air Quality



http://tools.acc.org/ASCVD-Risk-Estimator-Plus/#!/calculate/estimate/

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

Giorgini et al. Curr Pharm Des. 2016

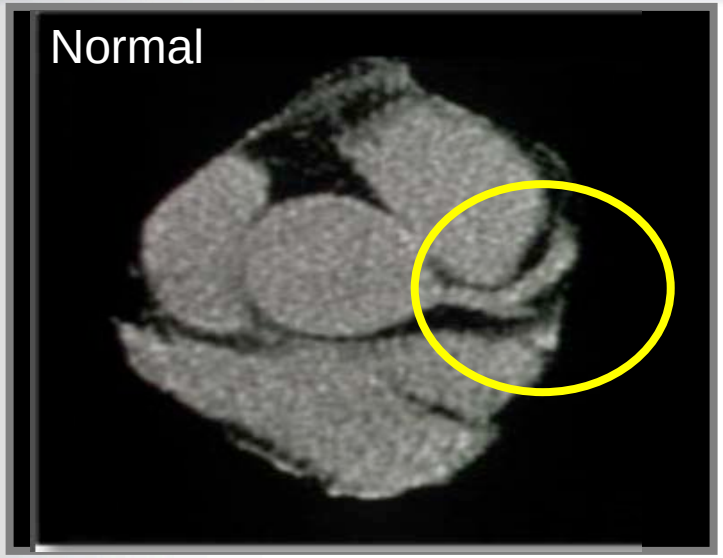
Diabetes – associated with type II diabetes

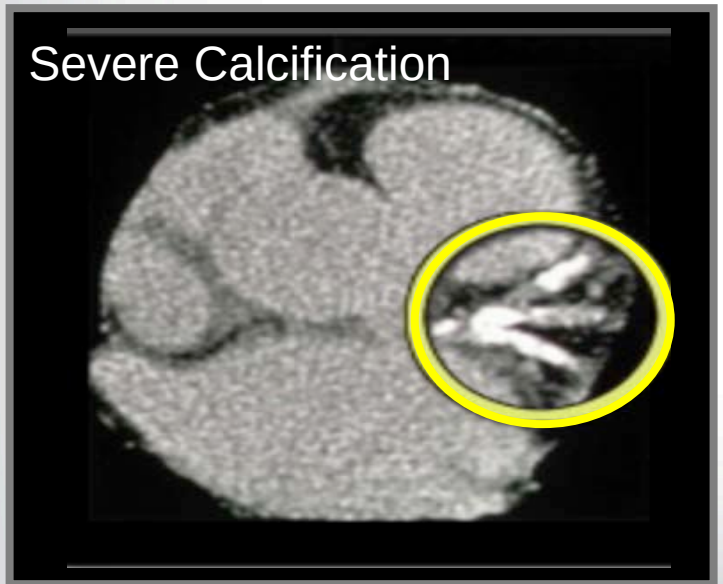
Renzi et al. Environ Int 2017

Statin Therapy – protective

O'Neill et al. Occup Environ Med 2007
Alexeeff et al. Environ Health Perspect 2011

Coronary Artery Calcium Confers Increased Cardiovascular Risk



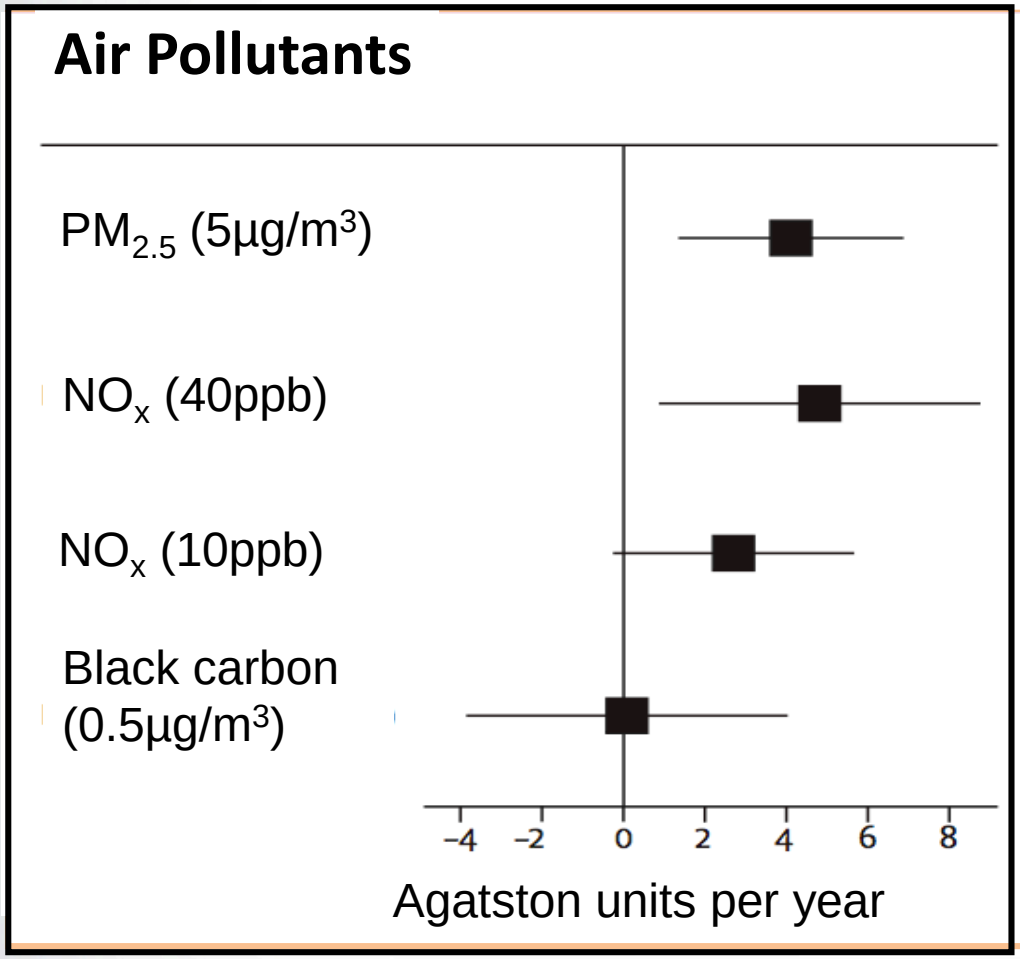


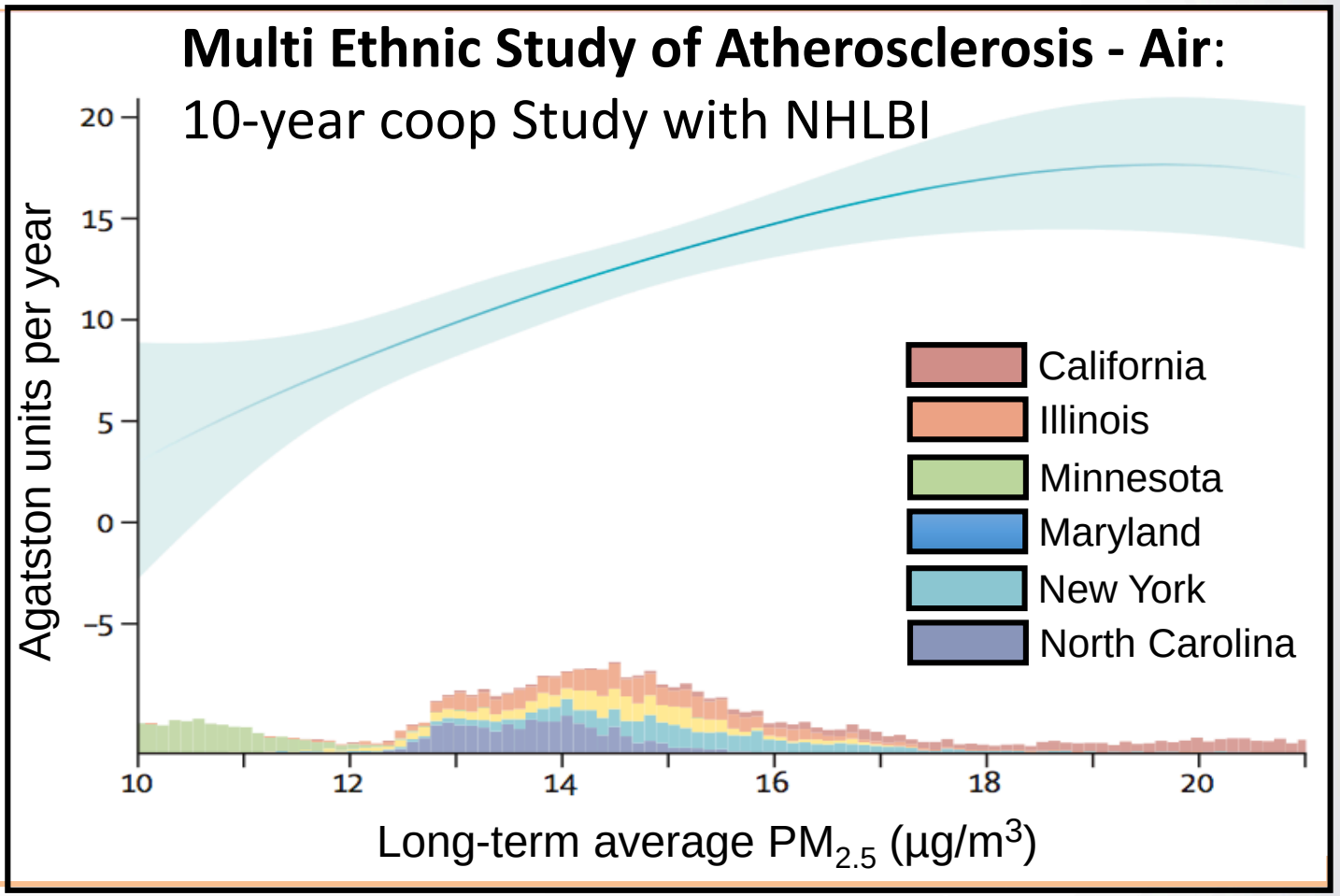
Summary of the Coronary Artery Calcium (CAC) and absolute long-term Cardiovascular Risk

CAC Score	FRS Equivalent	10-Year Event Rate, %
0	Very low	1.1 - 17
1 - 100	Low	2.3 – 5.9
101 - 400	Intermediate	12.8 – 16.4
> 400	High	22.5 – 28.6
> 1,000	Very high	37.0

Hecht HS. JACC Cardiovasc Imaging 2015;8:579-96

Long-Term $PM_{2.5}$ & NO_2 Exposure
Increases Coronary Artery Calcium



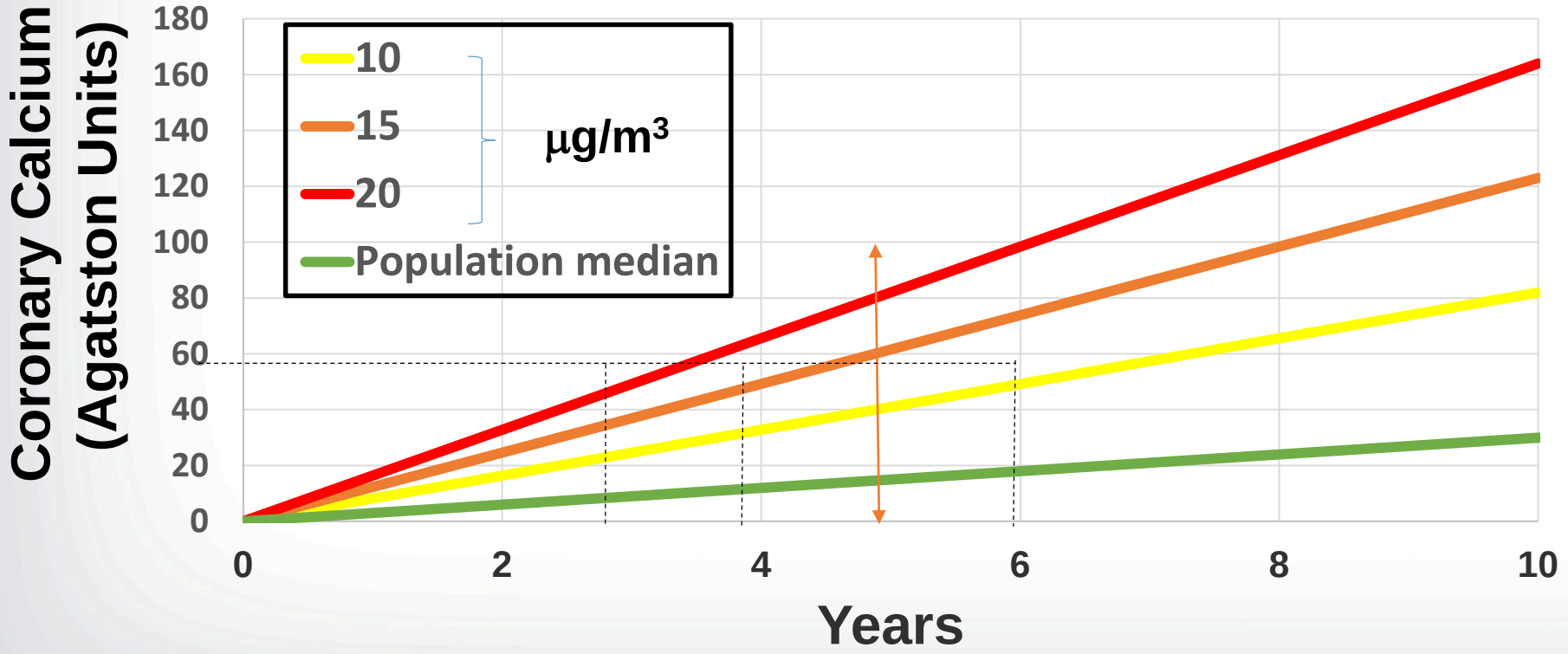


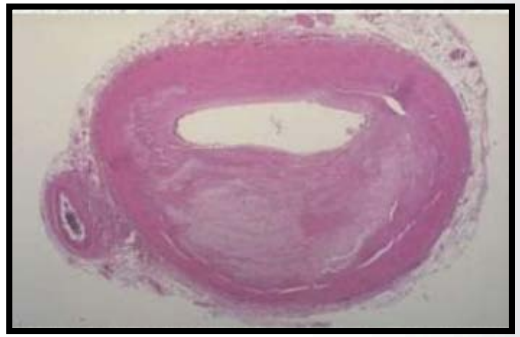
Long-term $PM_{2.5}$ and NO_2 increased coronary calcium, an indictor of atherosclerosis

Kaufman JD et al. Lancet 2016

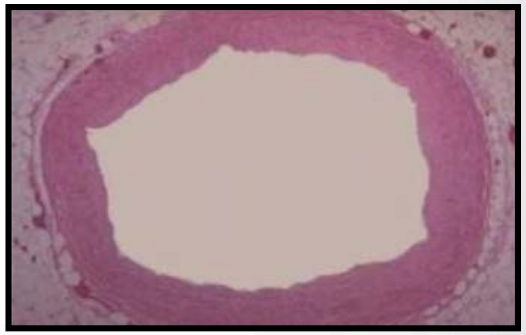
Long-term $PM_{2.5}$ & Nox Exposure
Associated Atherosclerosis Progression

MESA Air Study – Led by University of Washington





Uncertainty for 15 µg/m³ case



Kaufman JD, et al. *Lancet* 2016

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 µg/m³ $PM_{2.5}$ for 10 years = 120 Agatston Units

CAC Score	FRS Equivalent	10-Year Event Rate, %
0	Very low	1.1 – 1.7
1 - 100	Low	2.3 – 5.9
101 - 400	Intermediate	12.8 – 16.4
> 400	High	22.5 – 28.6
> 1,000	Very high	37.0

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

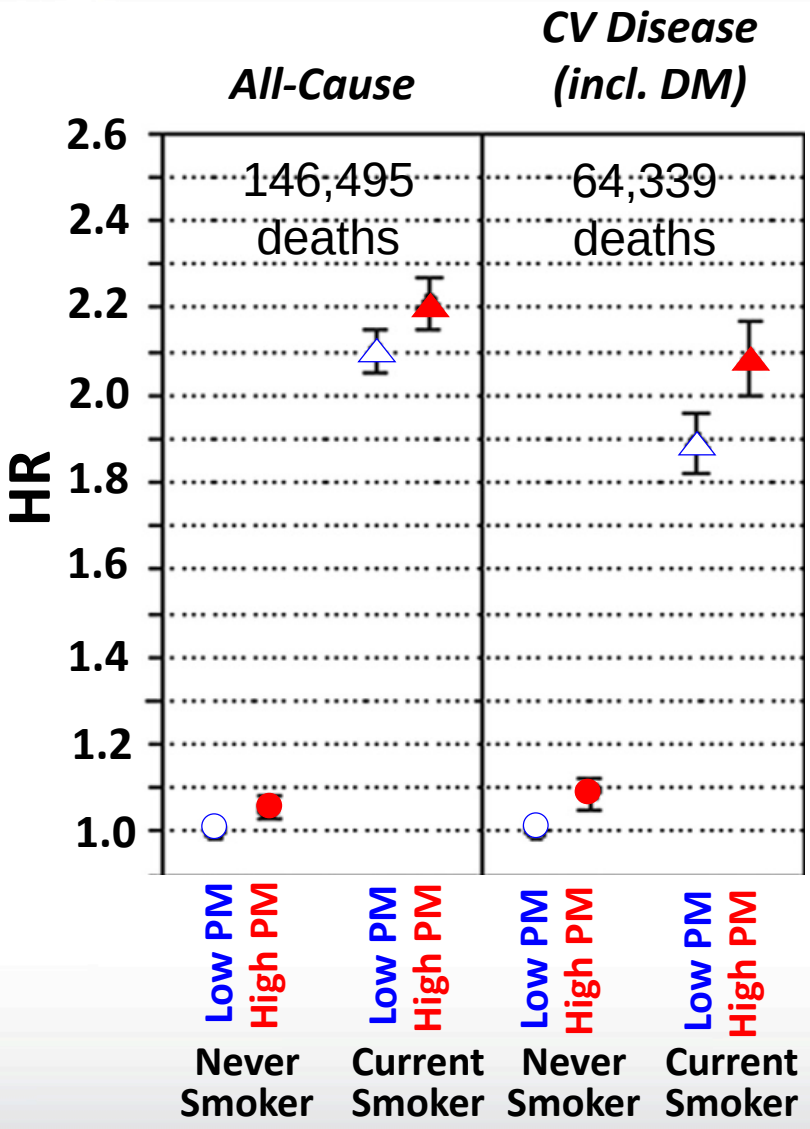
ASCVD Risk Calculators might be refined by including long-term exposure to air pollution

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/m³ exposure*



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

	All Cause	Cardiovascular Disease (plus diabetes)
High $PM_{2.5}$ vs. Low $PM_{2.5}$	44 (5, 83)	36 (9, 63)
Current vs. Never Smoker	1,080 (1,034, 1,250)	318 (288, 347)
High $PM_{2.5}$ * Current Smoker	56 (-3, 115)	32 (-6, 71)

- 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

Source: *Turner MC, et al. Environ Health Perspect 2017*

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*
    *(*Liu R et al. Environ Health Perspect 2016; Palacios et al. Rev Environ Health 2017*)*
  - *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

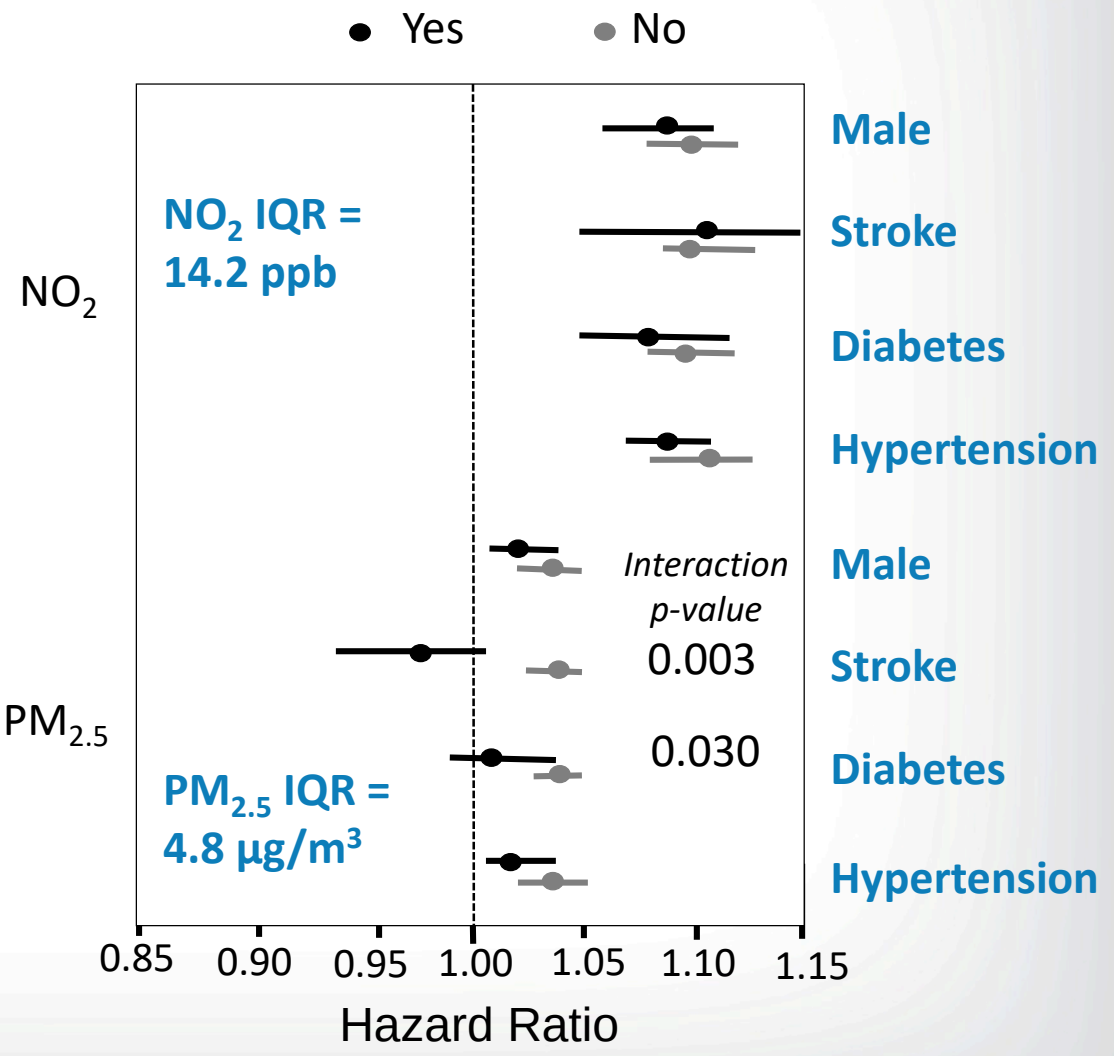
- **Effects on Child Neurodevelopment**
  - *Prenatal exposure to air pollution*
  - *Childhood exposure to air pollution*
- **Neurodevelopmental Disorders**
  - *Autism Spectrum Disorder*
  - *Attention-Deficit Hyperactivity Disorder*

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)*.

Exposure	Attributable fraction (95% uncertainty level)†	Number of dementia attributable to exposure to air pollutant (95% uncertainty level)
$PM_{2.5}$‡	2.4% (1.8–3.0%)	6278 (4738–7816)
NO_2‡	5.4% (4.4–6.6%)	13,962 (11,428–16,910)
$PM_{2.5}$ + NO_2§	6.1% (4.8–7.5%)	15,813 (12,374–19,464)



Chen H et al. *Environ Internat* 2017

Health Effects of Air Pollution

Human development

Emerging Areas of Health Effects Research
Reproductive and Developmental

Infertility

- **Menstrual cycle** (Merklinger-Gruchala et al. Internat J Environ Res Public Health 2017)
- **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

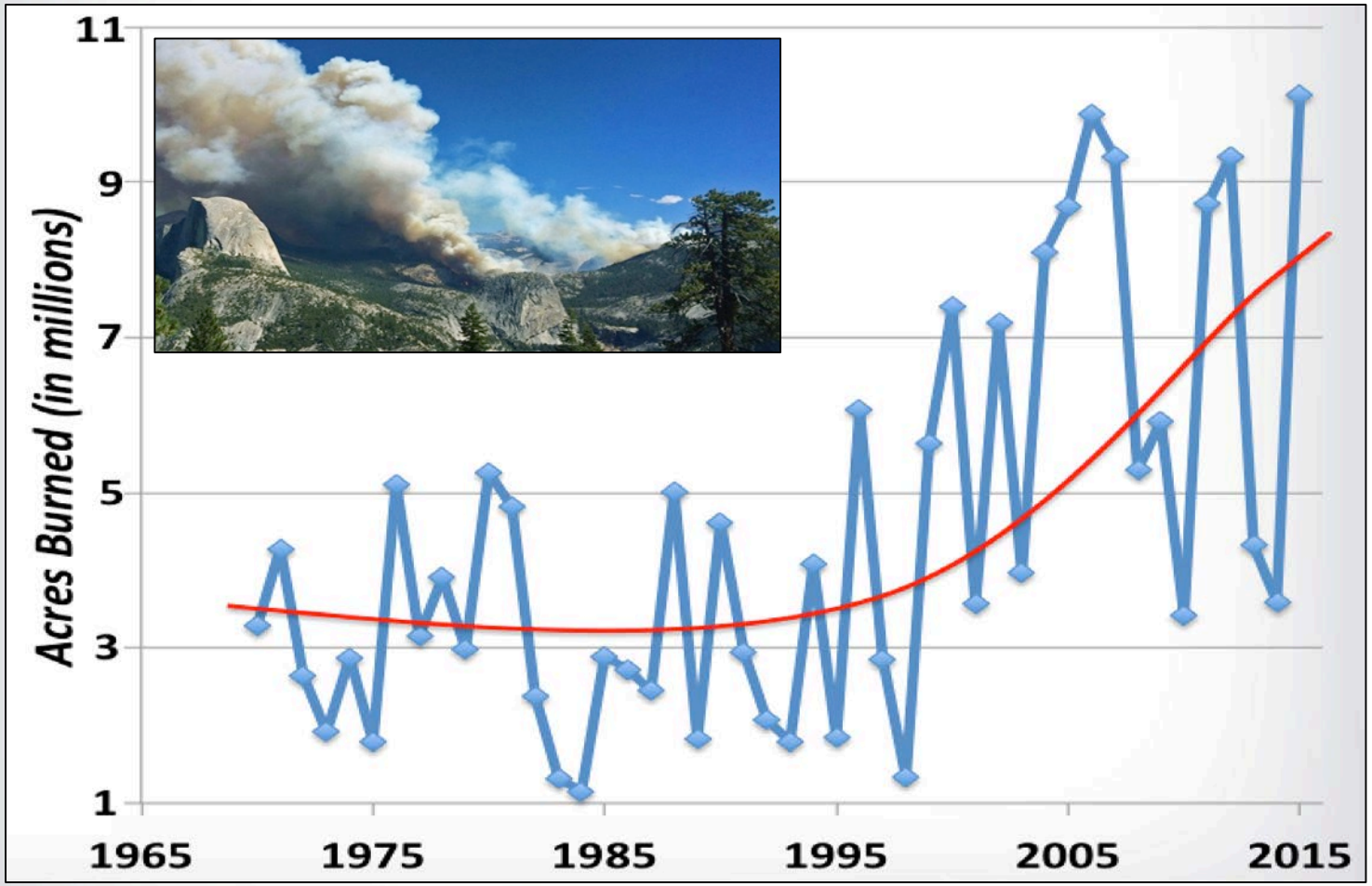
- exposure to $PM_{2.5}$ shortened telomeres measured at birth, an indicator of biological aging (*Martens DS et al. JAMA Pediatrics 2017)*

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

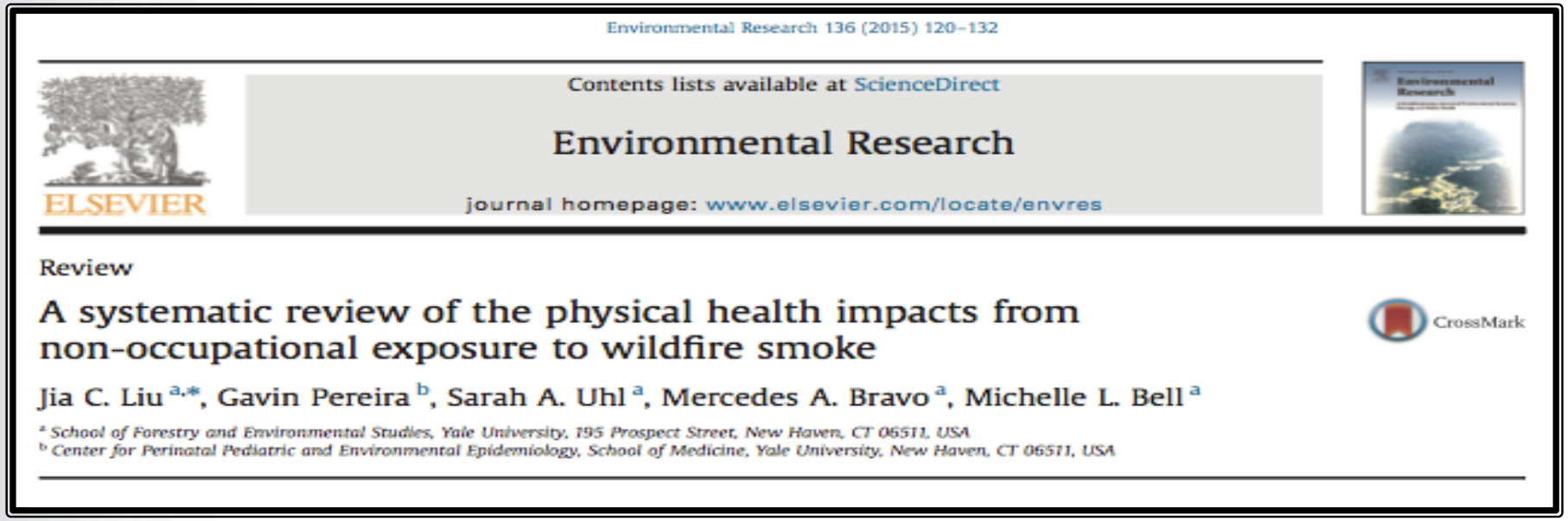


Adapted from https://www.nifc.gov/fireInfo/fireInfo_stats_totalFires.html

- ***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***

Health Effects of Wildfire Smoke

Systematic Reviews are Now Available



Environmental Research 136 (2015) 120–132

Contents lists available at ScienceDirect

Environmental Research

journal homepage: www.elsevier.com/locate/envres

Review

A systematic review of the physical health impacts from non-occupational exposure to wildfire smoke

Jia C. Liu [a,*], Gavin Pereira [b], Sarah A. Uhl [a], Mercedes A. Bravo [a], Michelle L. Bell [a]

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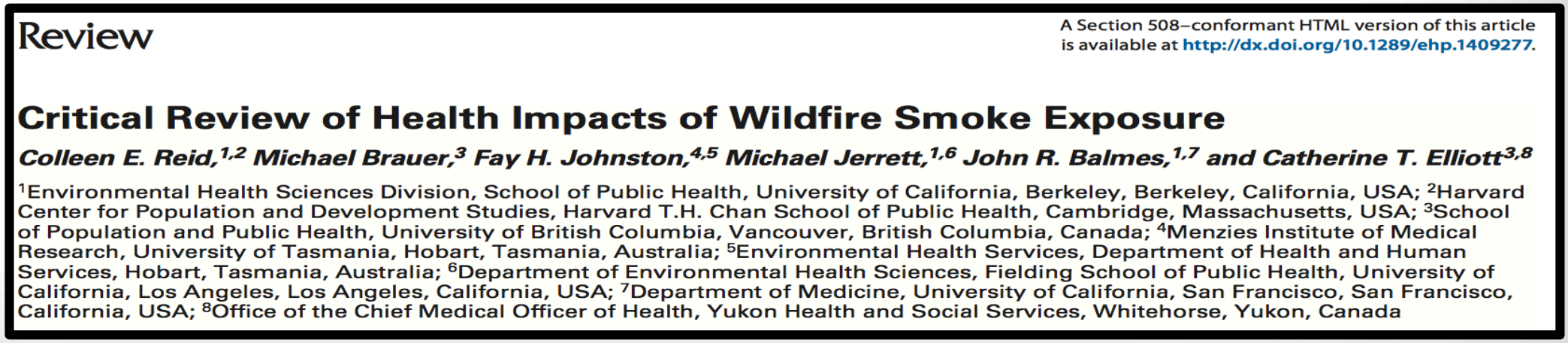
Reid et al. *Environ Res.* 2015 Jan;136:120-32

Liu et al. *Environ Health Perspect.* 2016; 124:1334–1343



Review

A Section 508–conformant HTML version of this article is available at http://dx.doi.org/10.1289/ehp.1409277.

Critical Review of Health Impacts of Wildfire Smoke Exposure

Colleen E. Reid,[1,2] Michael Brauer,[3] Fay H. Johnston,[4,5] Michael Jerrett,[1,6] John R. Balmes,[1,7] and Catherine T. Elliott[3,8]

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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

Measuring the Health Effects of Wildfire Smoke

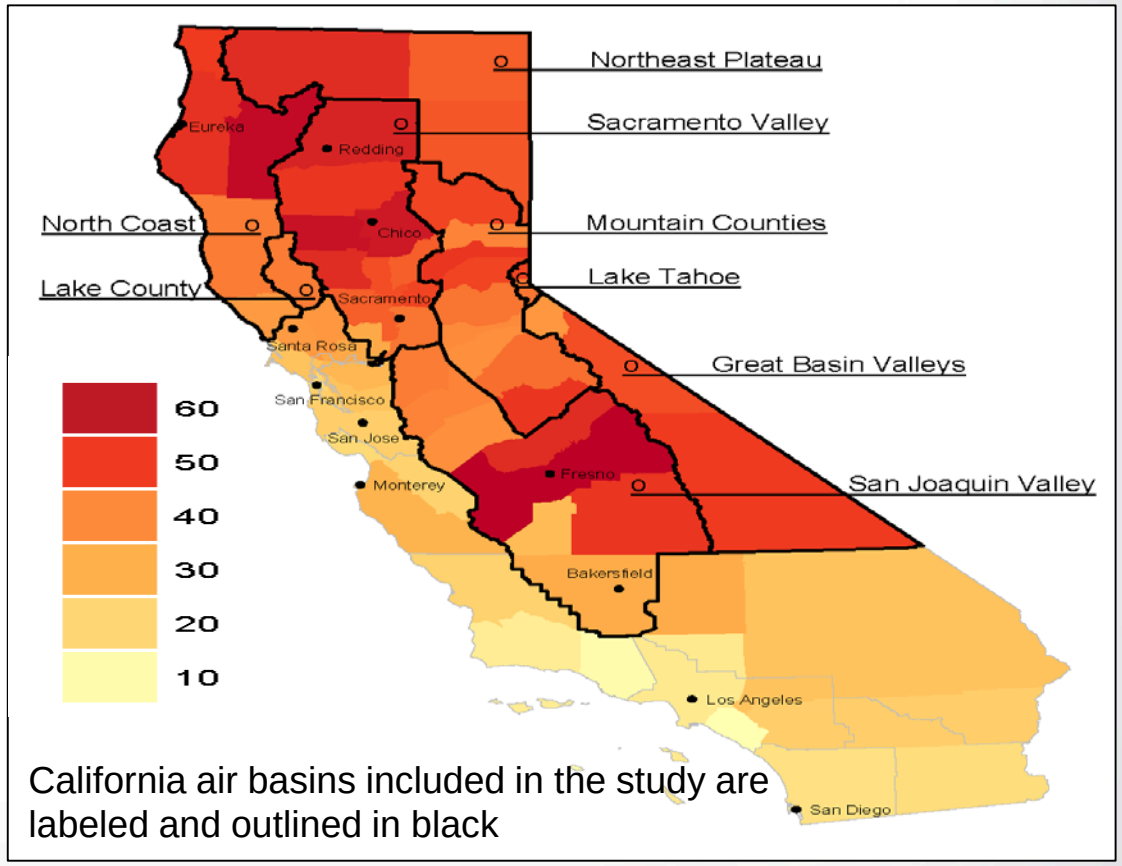
California 2015 Wildfire Study

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



California air basins included in the study are labeled and outlined in black

Wettstein Z, Hoshiko S, Cascio WE, Rappold AG et al. (in review, 2018)

Wildfire-$PM_{2.5}$ Increases Heart Attack & Stroke

California 2015 Wildfire Study

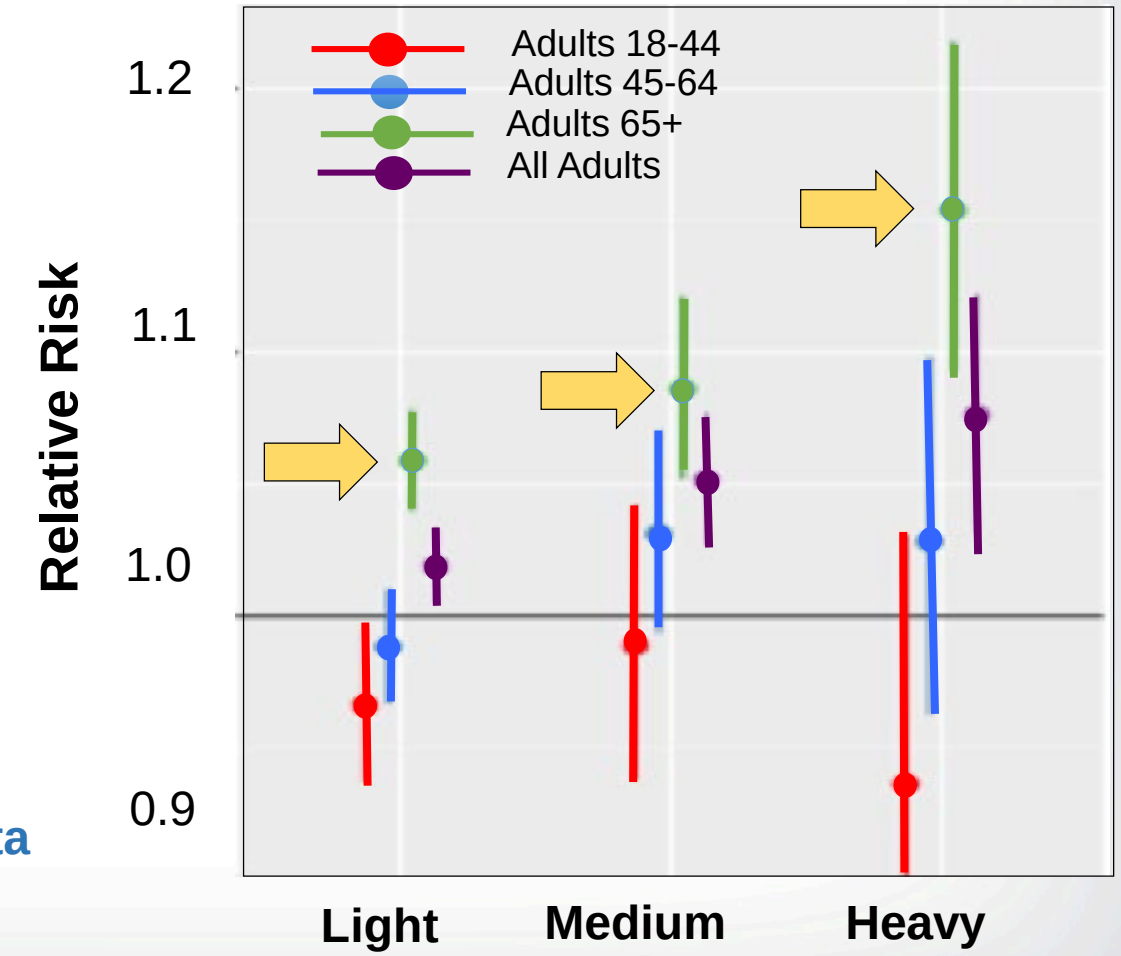
Results: Wildfire-$PM_{2.5}$ associated with heart attacks and strokes for all adults, particularly for those over 65 years old

- 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

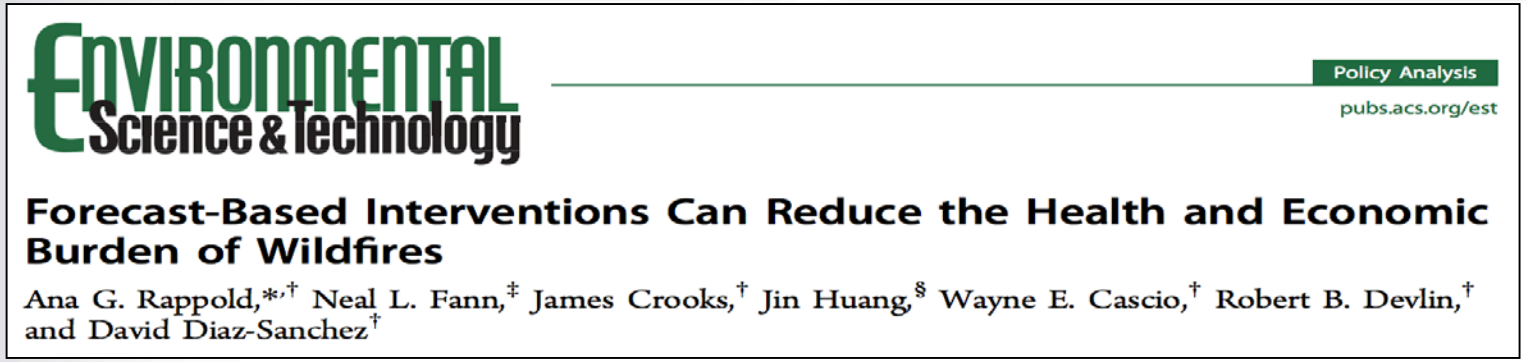
Data to be presented as a Late-Breaking Study at the *American Public Health Association* Conference in Atlanta - November 2017

All Cardiovascular Causes



Wettstein Z, Hoshiko S, Cascio WE, Rappold AG et al. (in review, 2018)

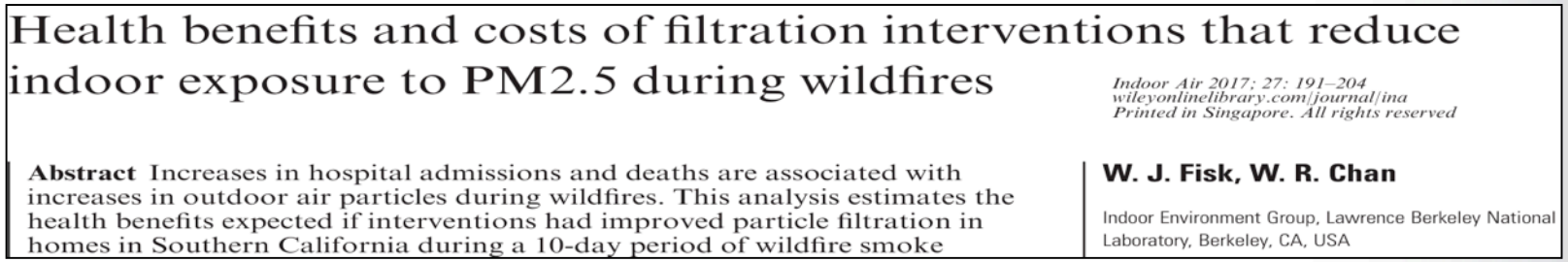
Moving to the Future



Forecast-based interventions predicted to reduce the health and economic burden of wildfires

Rappold AG, et al.
Environ Sci Technol 2014

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

Environmental Science & Technology

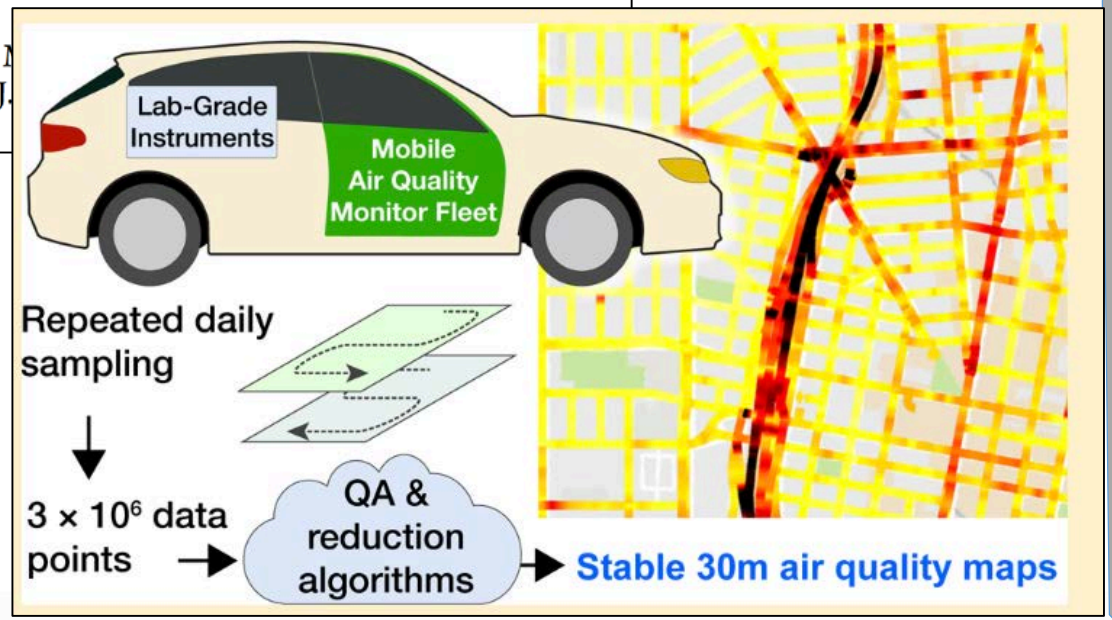
Article

pubs.acs.org/est

High-Resolution Air Pollution Mapping with Google Street View Cars: Exploiting Big Data

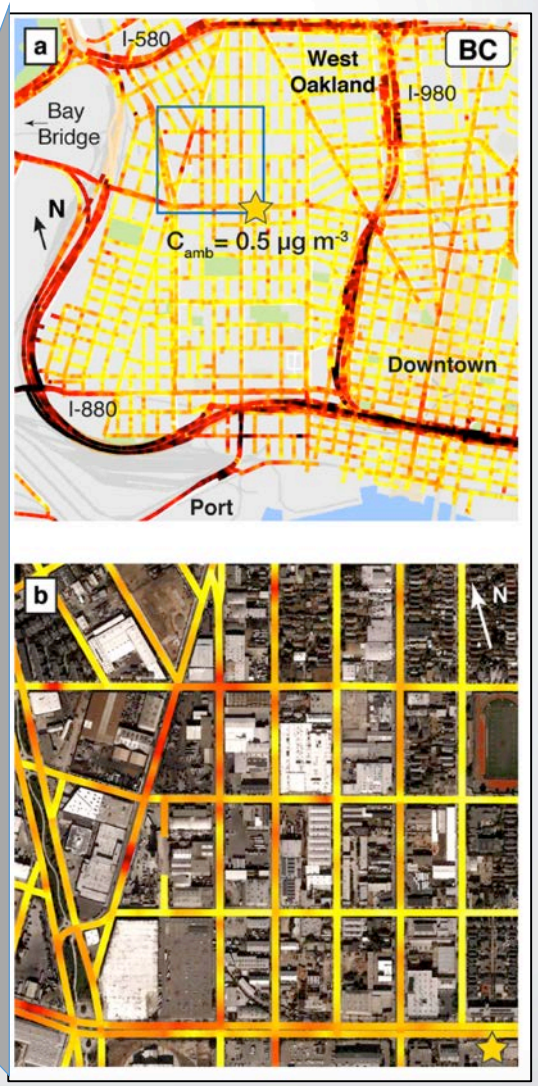
Joshua S. Apte,*,† Kyle P. Messier,†,‡ Shahzad Gani,† Melissa M. Lunden,⊥ Julian D. Marshall,# Christopher J. and Steven P. Hamburg‡

Apte JS et al. Environ Sci Technol 2017



Oakland, CA

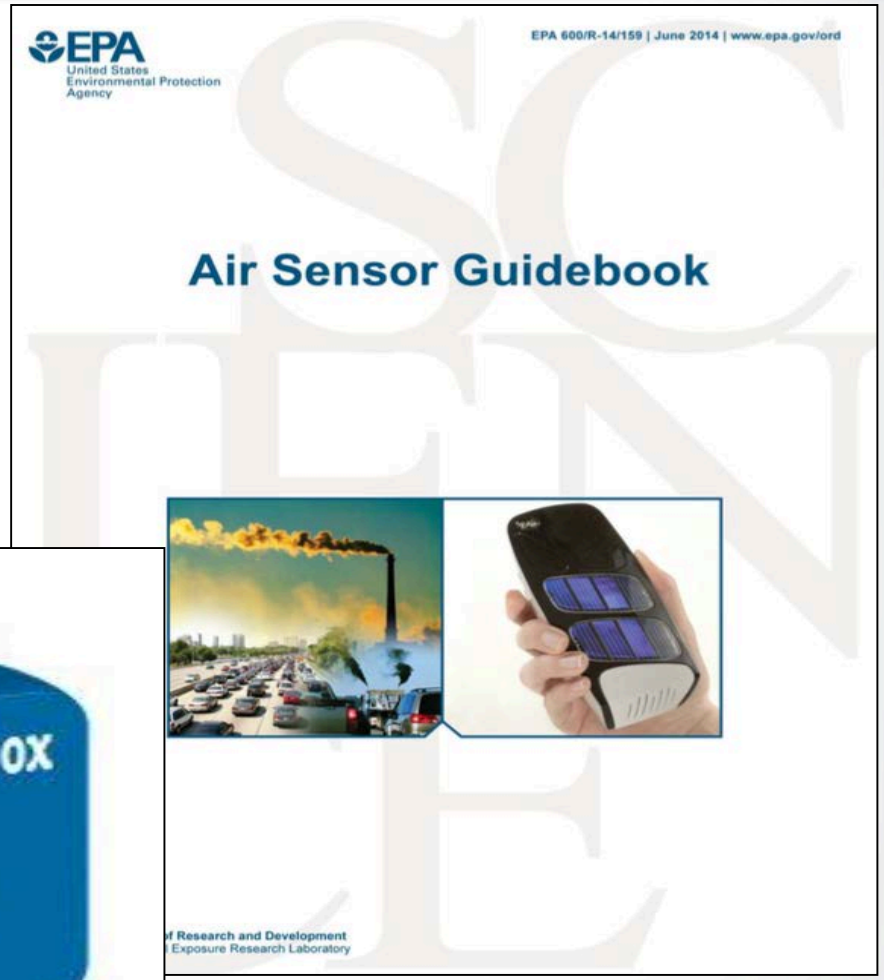
Spatial distribution of Black Carbon (BC)



Hankey S et al. Population-Level Exposure to Particulate Air Pollution during Active Travel: Planning for Low-Exposure, Health-Promoting Cities. *Environmental Health Perspectives* 125:527–534, *2017*

New Portable Technologies

- **EPA actively engaged in new sensor technologies for:**
  - *personal use*
  - *community engagement*
  - *research*

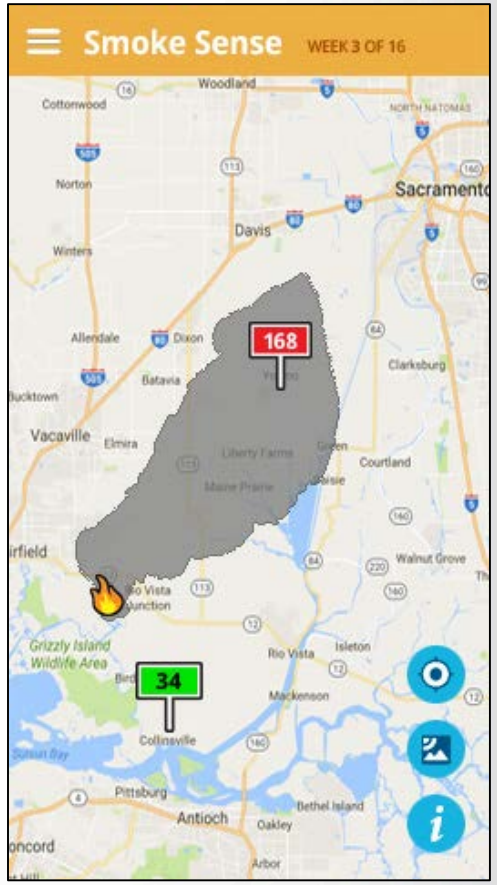


Smoke Sense Project
Improving Public Health Outcomes

- ***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

Air Quality & Smoke Plume Information

- 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

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Office of Research and Development
U.S. Environmental Protection Agency

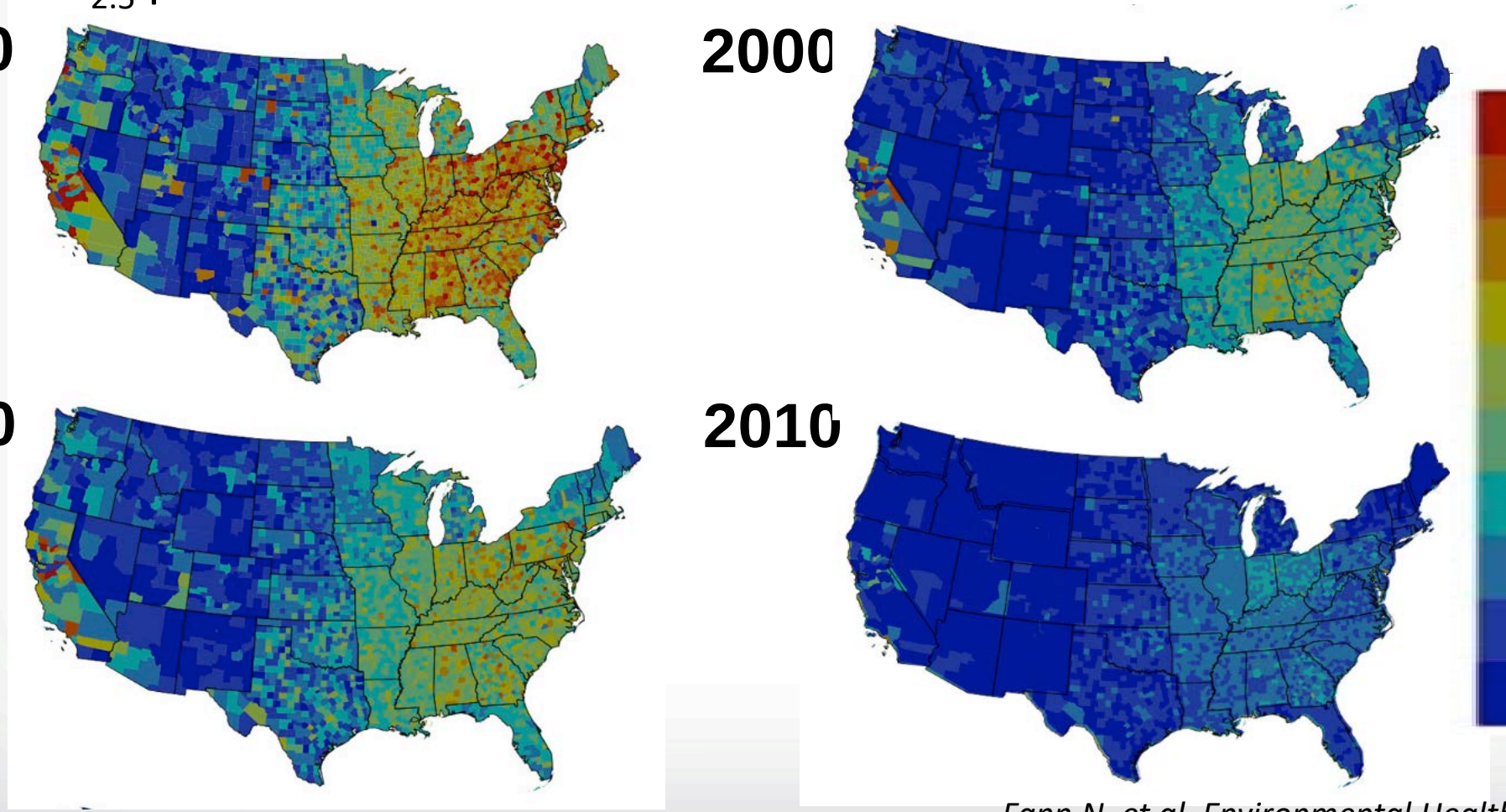
Email: cascio.wayne@epa.gov

Fall in Air Pollution Related Deaths Over Time

Fraction of Total All-Cause Deaths Attributed to $PM_{2.5}$

After the implementation of local, state, and federal air quality policies –

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



Fann N, et al. Environmental Health Perspectives 2017

Air Pollution: Miscellaneous

Lee EY et al. Traffic-Related Air Pollution and Telomere Length in Children and Adolescents Living in Fresno, CA: A Pilot Study. J Occup Environ Med. 2017 May;59(5):446-452.

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

Berhane K, et al. Association of Changes in Air Quality With Bronchitic Symptoms in Children in California, 1993-2012.JAMA. 2016 Apr 12;315(14):1491-501.

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

Keet CA, et al. Long-term Coarse PM Exposure is Associated with Asthma Among Children in Medicaid. Am J Respir Crit Care Med. 2017 Dec 15. doi: 10.1164/rccm.201706-1267OC

Exposure to higher average coarse PM levels is associated with increased asthma prevalence and morbidity.

Improving Air Quality
An Important Priority to Achieve the EPA's Mission

"…promoting and protecting a strong and healthy environment is among the lifeblood priorities for the government, and EPA is vital to that mission."

E. Scott Pruitt, Senate Confirmation Hearing January 18, 2017

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

E. Scott Pruitt, Testimony before US Senate Committee on Appropriations: Subcommittee on Interior, Environmental and Related Agencies July 17, 2017