# *Air Pollution and Heart Health: Making the Connection*

**Wayne Cascio, MD, FACC, FAHA**

***Director, Environmental Public Health Division***

***National Health and Environmental Effects Research Laboratory***

***Office of Research & Development, US EPA***

***Research Triangle Park and Chapel Hill, NC***

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# Ambient Air Pollution & Health

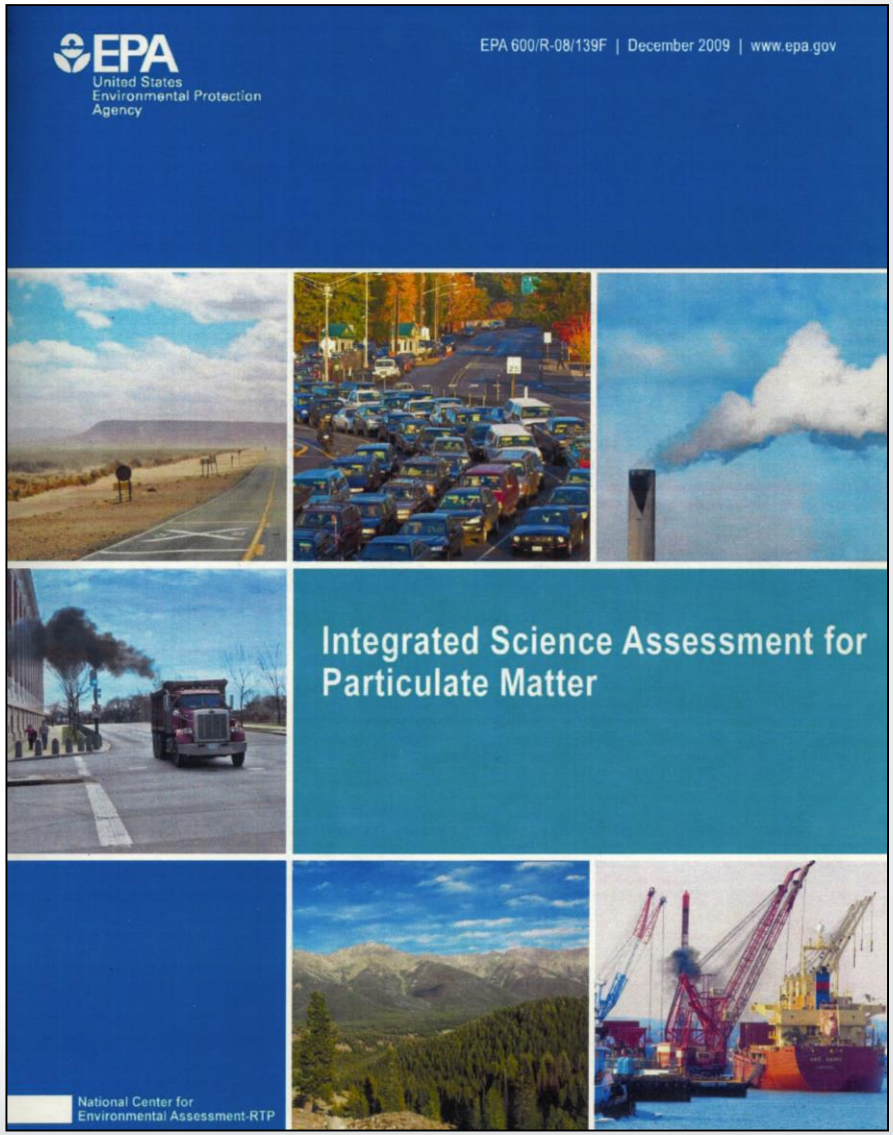
- *Why should communities care about ambient air pollutants?*
- *Why should healthcare systems care about ambient air pollutants?*
- *Why should health care providers care about ambient air pollutants?*
- *Why should their patients care about ambient air pollutants?*

# EPA and AHA State that PM CAUSES Mortality and Morbidity

**EPA:**

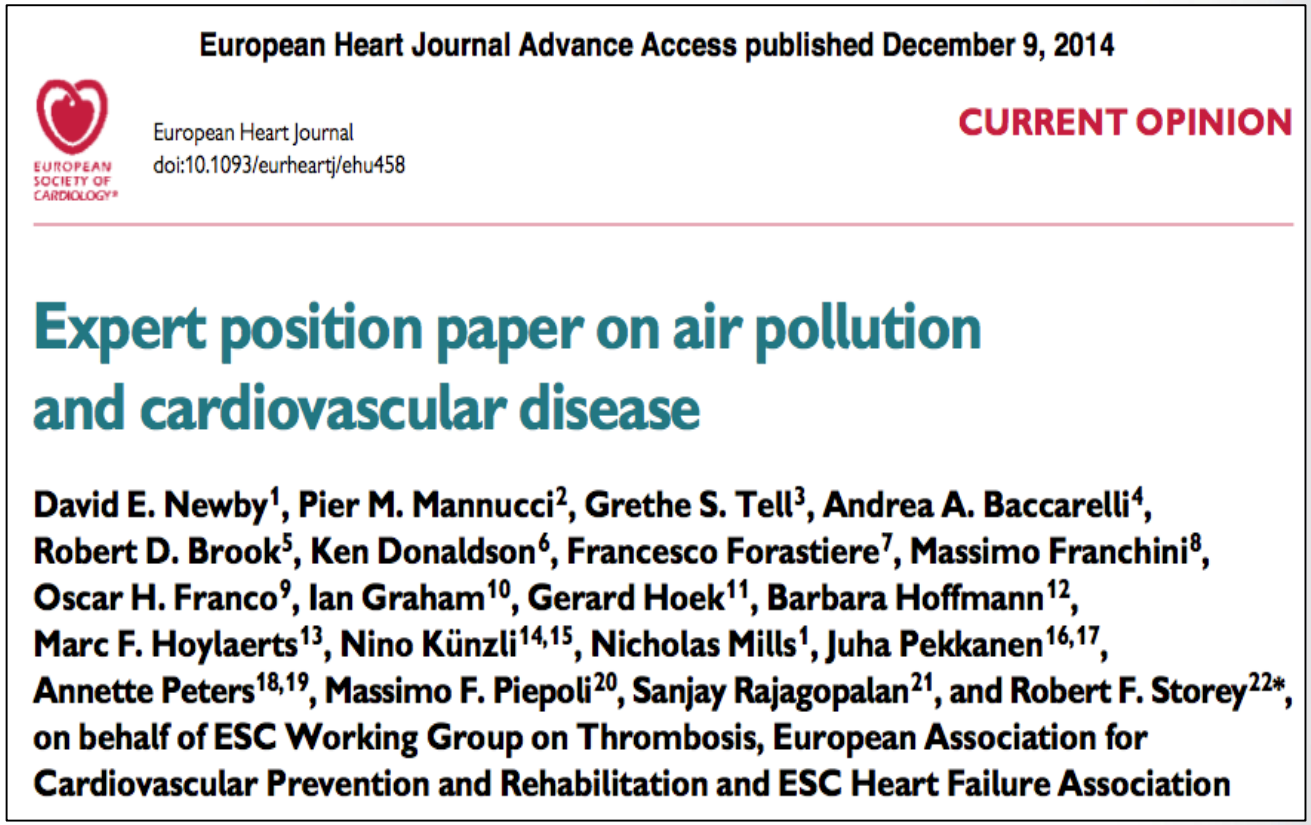
*"Epidemiologic evidence is sufficient to conclude that a causal relationship exists between:* ***short-term and long-term exposure to $PM_{2.5}$ and mortality."***

*Integrated Science Assessment (ISA) for Particulate Matter 2009*



# Call for Public Health & Healthcare Action

- *"Air pollution should be viewed as <u>one of several major modifiable risk factors</u> in the prevention and management of cardiovascular disease."*



European Heart Journal Advance Access published December 9, 2014

European Heart Journal
doi:10.1093/eurheartj/ehu458

CURRENT OPINION

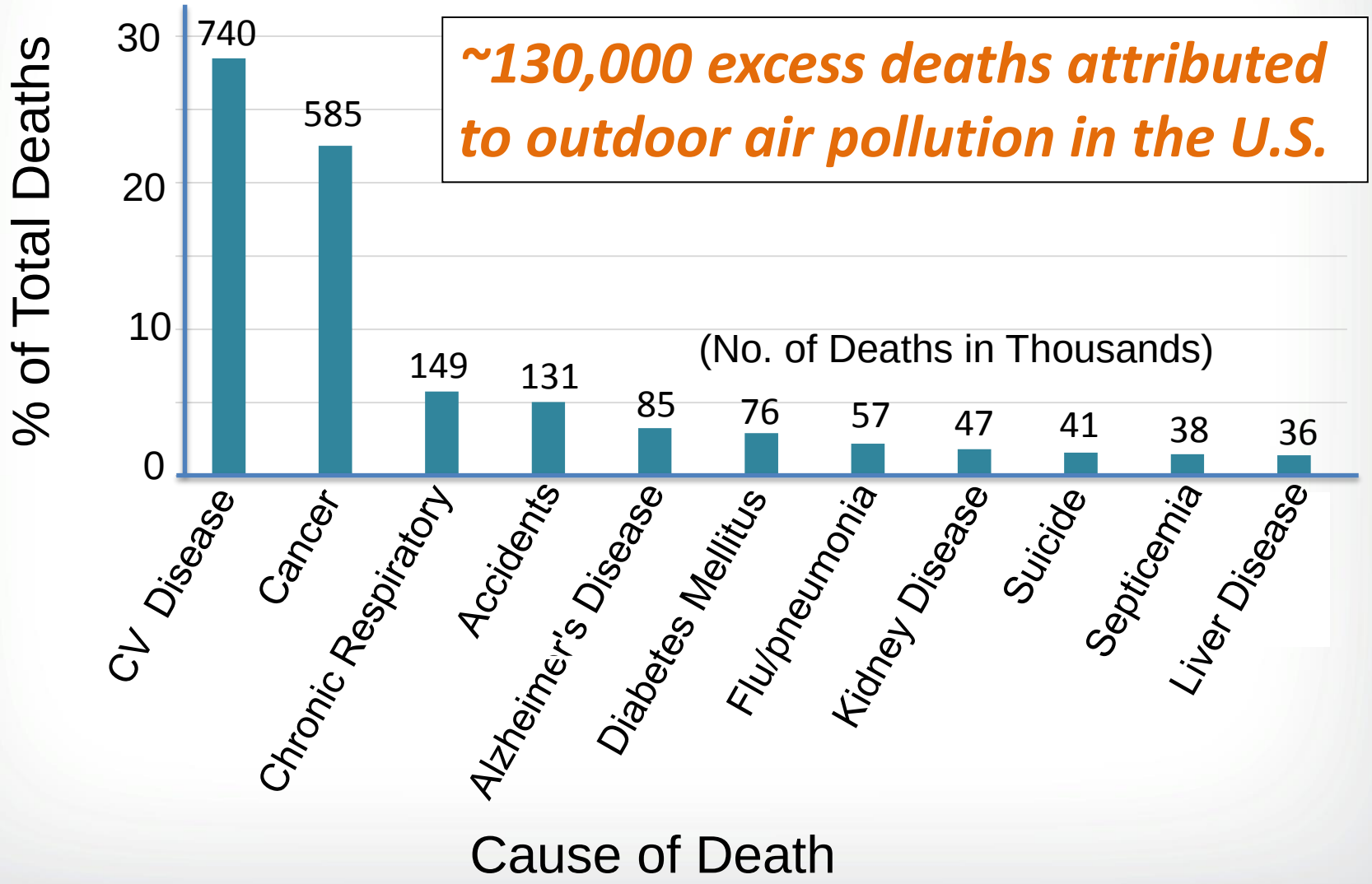
## Expert position paper on air pollution and cardiovascular disease

David E. Newby[1], Pier M. Mannucci[2], Grethe S. Tell[3], Andrea A. Baccarelli[4], Robert D. Brook[5], Ken Donaldson[6], Francesco Forastiere[7], Massimo Franchini[8], Oscar H. Franco[9], Ian Graham[10], Gerard Hoek[11], Barbara Hoffmann[12], Marc F. Hoylaerts[13], Nino Künzli[14,15], Nicholas Mills[1], Juha Pekkanen[16,17], Annette Peters[18,19], Massimo F. Piepoli[20], Sanjay Rajagopalan[21], and Robert F. Storey[22]*, on behalf of ESC Working Group on Thrombosis, European Association for Cardiovascular Prevention and Rehabilitation and ESC Heart Failure Association

- *"Health professionals, including cardiologists, have an important role to play in supporting educational and policy initiatives as well as counseling their patients."*

*Newby DE et al. Eur Heart J 2014*

# Air Pollution Deaths
## Comparable to Alzheimer's, Diabetes, Flu

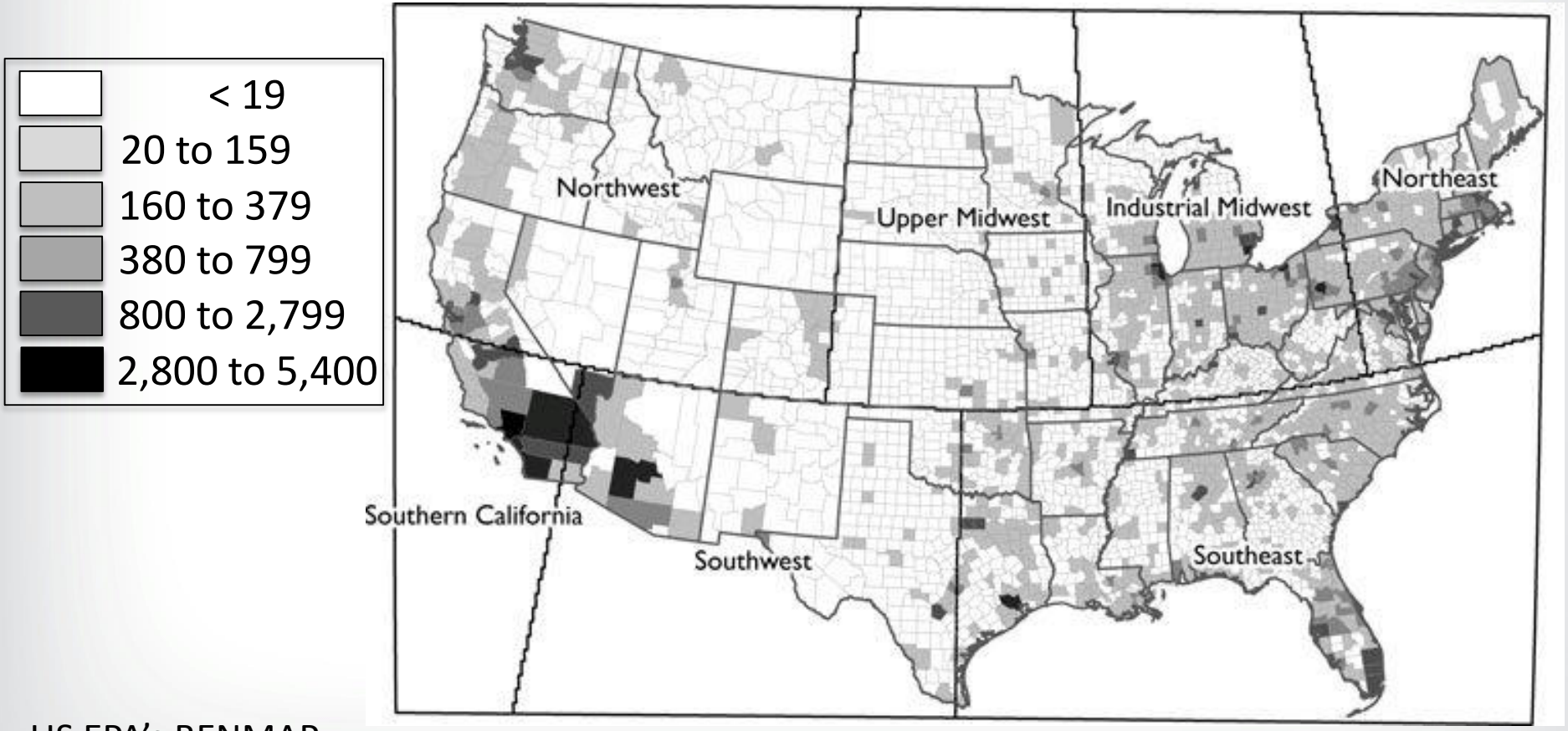



*National Vital Statistics Report 2016*

# Estimated Excess Mortality

## Burden of Air Pollution Deaths by County

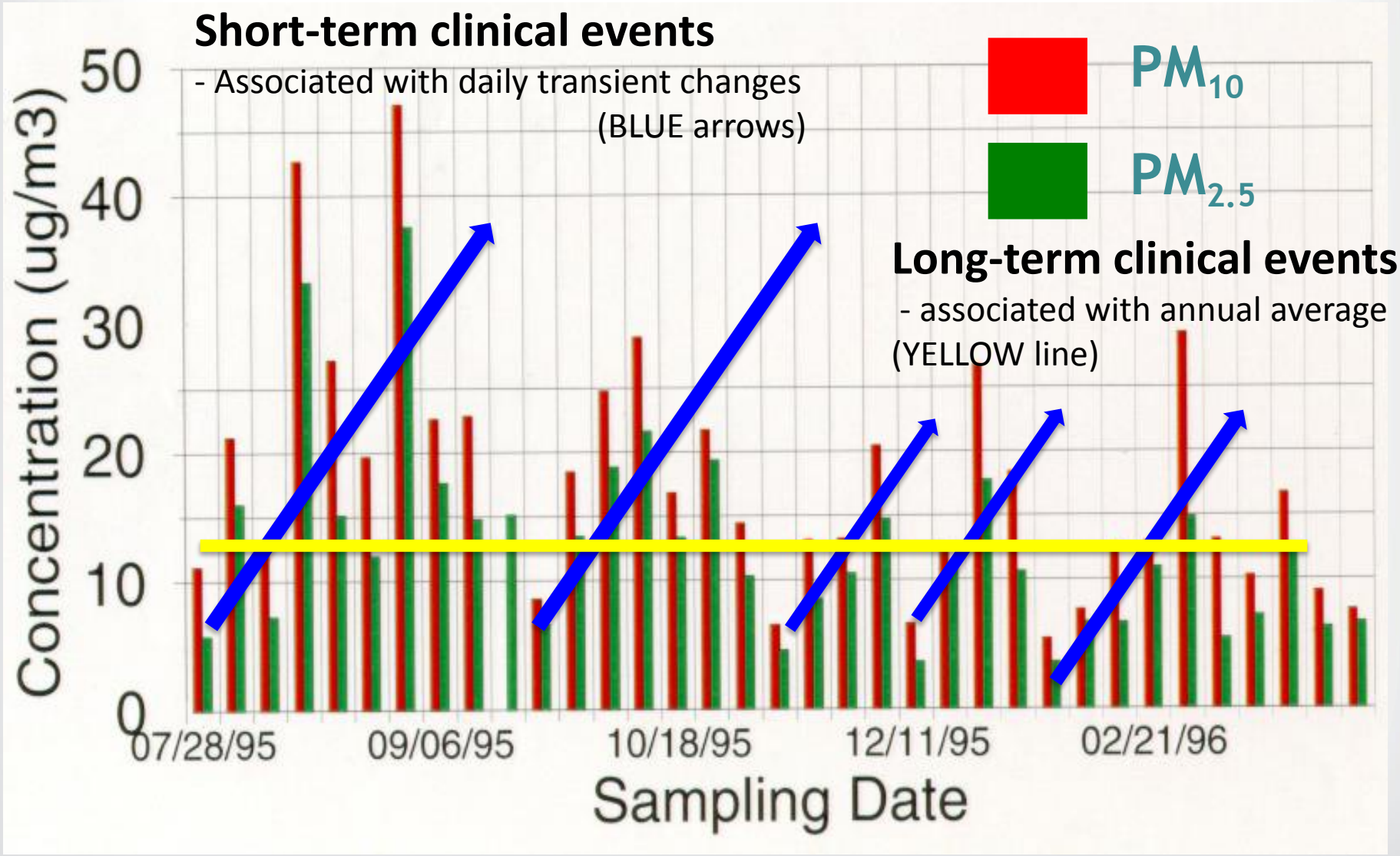
***$PM_{2.5}$ and $O_3$-related Mortality by County based on 2005 air pollution levels***




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



*Population studies and cardiovascular health effects of particle air pollution*

# Epidemiological Evidence

## $PM_{2.5}$-Related Air Pollution Effects

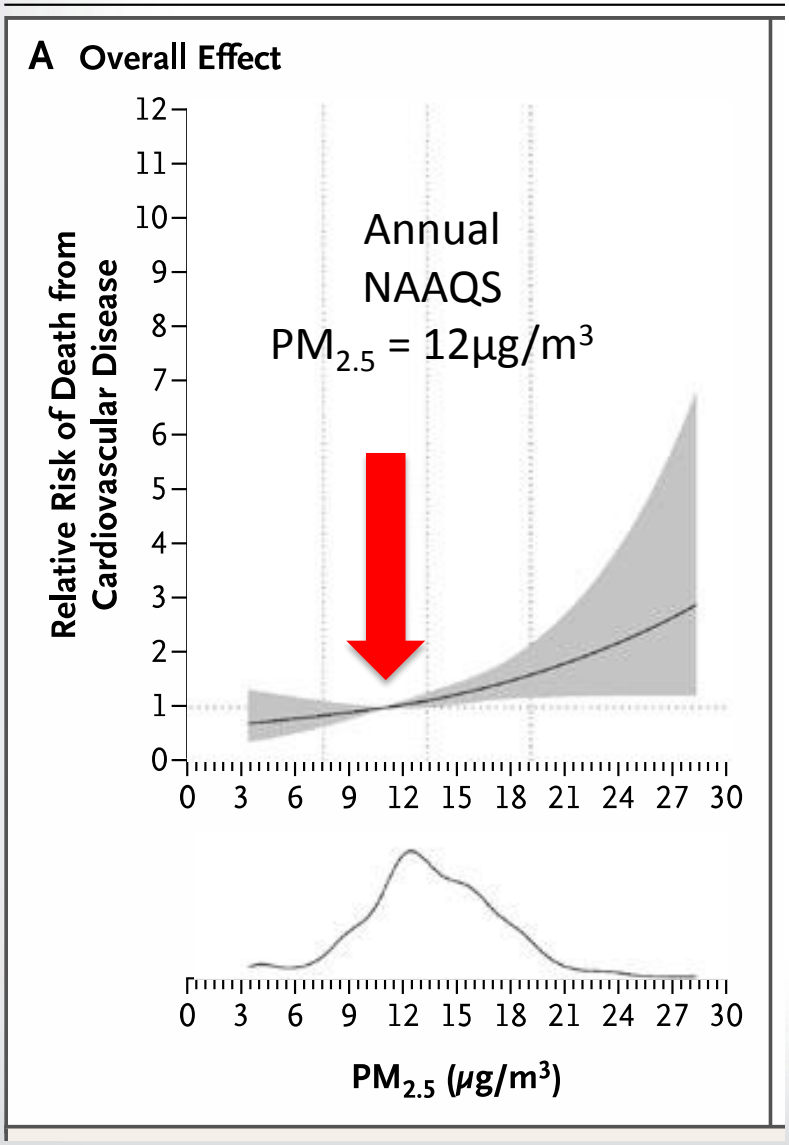
***Clinical cardiovascular endpoints from epidemiological studies at ambient concentrations***

| Health Outcomes | Short-Term Exposure (Days) | Longer-Term Exposure (Months to Years) |
|---|---|---|
| Cardiovascular mortality | ↑ ↑ ↑ | ↑ ↑ ↑ |
| Cardiovascular hospitalizations | ↑ ↑ ↑ | ↑ |
| Ischemic heart disease* | ↑ ↑ ↑ | ↑ ↑ ↑ |
| Heart failure* | ↑ ↑ | ↑ |
| Ischemic stroke* | ↑ ↑ | ↑ |
| Vascular diseases | ↑ | ↑ † |
| Cardiac arrhythmia/cardiac arrest | ↑ | ↑ |

*Brook et al. Circulation 2010*

# $PM_{2.5}$ Increases Risk in Women

## First Cardiovascular Event or Death




| Outcome | Hazard Ratio Overall |
|---|---|
| **First cardiovascular event** | |
| Any cardiovascular event† | 1.24 (1.09–1.41) |
| Coronary heart disease‡ | 1.21 (1.04–1.42) |
| Cerebrovascular disease§ | 1.35 (1.08–1.68) |
| Myocardial infarction | 1.06 (0.85–1.34) |
| Coronary revascularization | 1.20 (1.00–1.43) |
| Stroke | 1.28 (1.02–1.61) |
| **Death from cardiovascular cause** | |
| Any death from cardiovascular cause | 1.76 (1.25–2.47) |
| Coronary heart disease | |
| Definite diagnosis | 2.21 (1.17–4.16) |
| Possible diagnosis | 1.26 (0.62–2.56) |
| Cerebrovascular disease | 1.83 (1.11–3.00) |

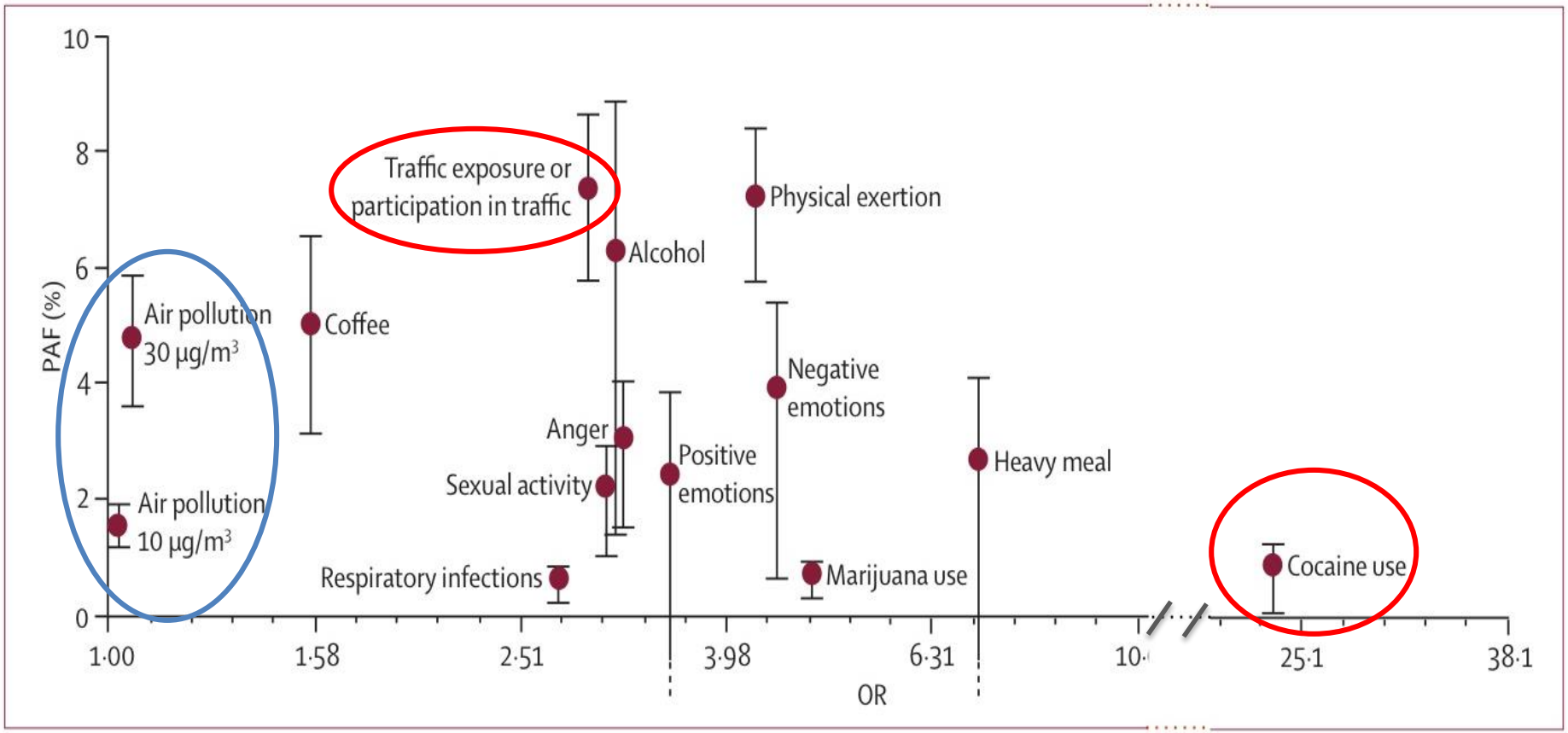
*Miller et al. NEJM 2007*

# 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

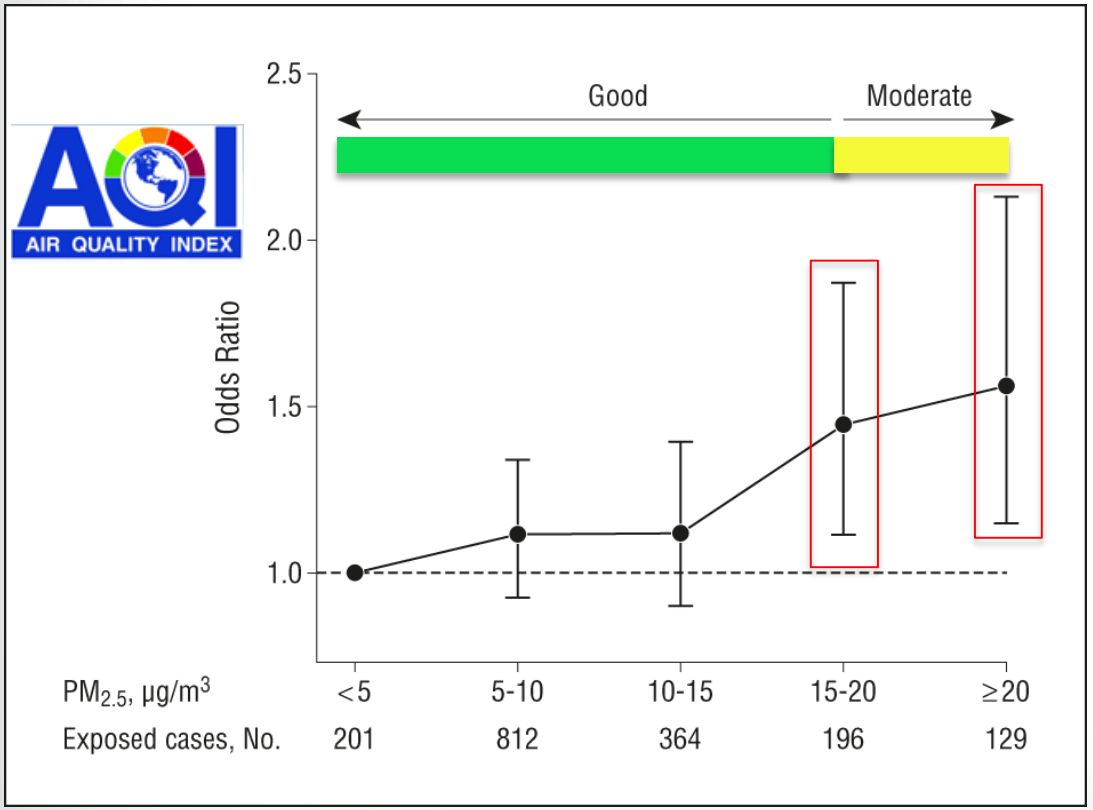


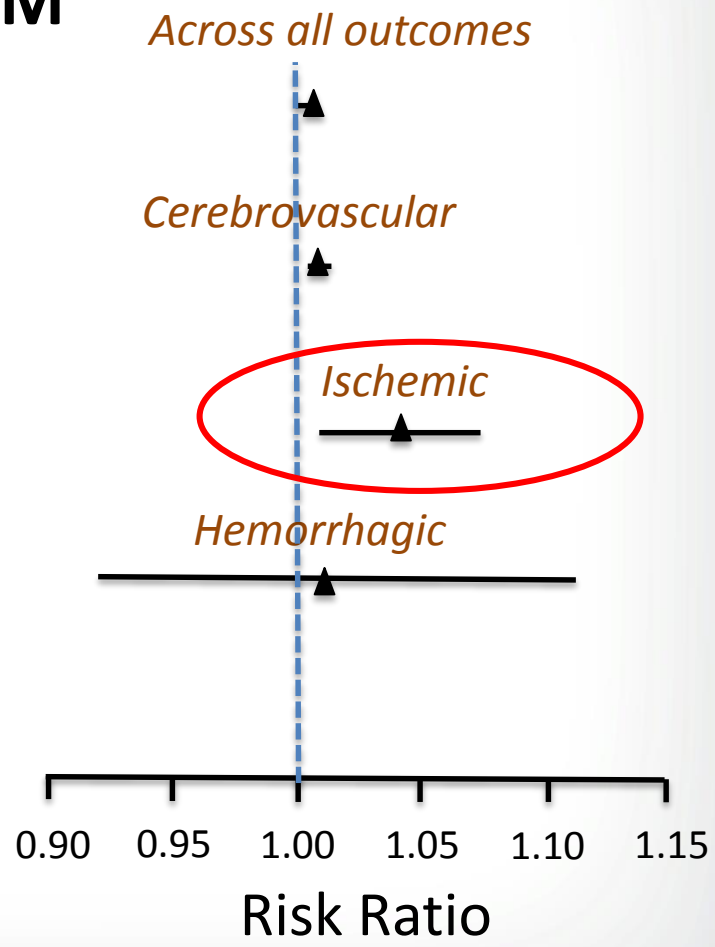

*Modified from Nawrot et al. Lancet 2011*

# Air Particle Pollution and Stroke

## Short-term Exposure & Ischemic Stroke

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



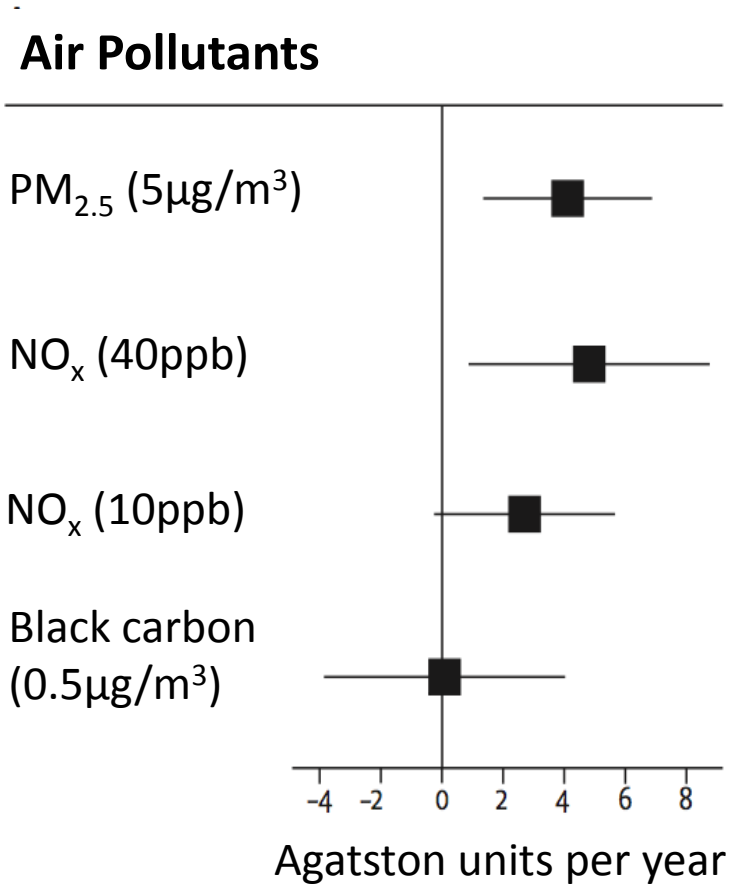



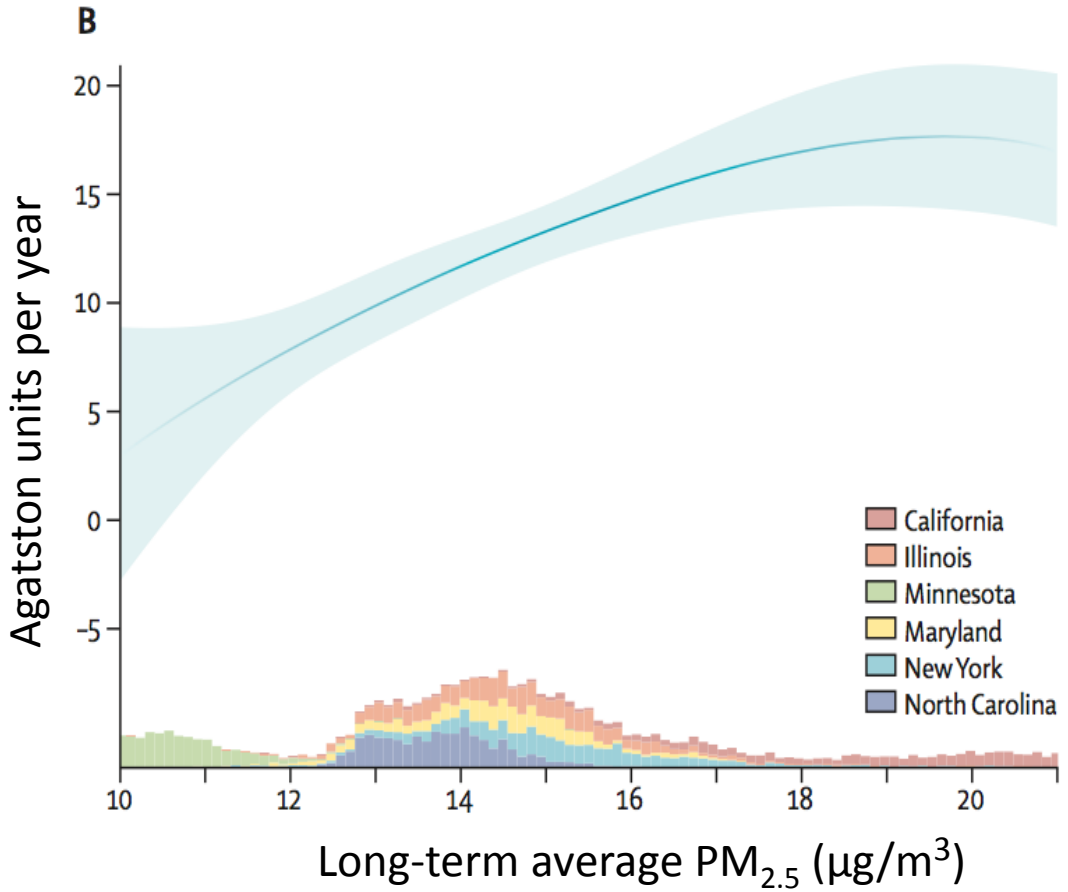

*Wellenius G, et al. Arch Intern Med 2012*

*Shin HH, et al. Epidemiology 2014*

# *Does Air Pollution Increase Atherosclerosis?*

# 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***

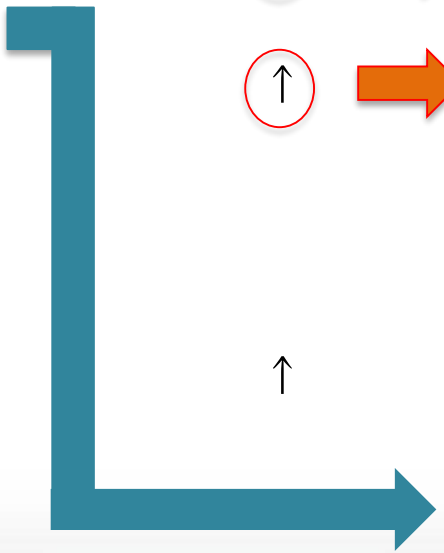
*Kaufman JD et al. Lancet 2016*

# *Possible Mechanisms*

# Human Studies Show Increases in Subclinical CV Endpoints

## Exposure to $PM_{2.5}$, Traffic- and Combustion Related Air Pollution

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



**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%)

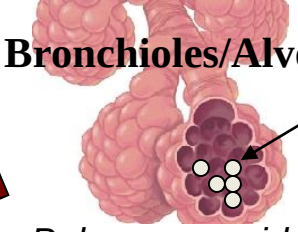
***Short-term exposure:***

Daily $PM_{2.5}$ level associated with:

- CRP
- Fibrinogen
- E-selectin

*Brook et al. Circulation 2010*

*Hajat et al. Epidemiology 2015*



Bronchioles/Alveoli

PM

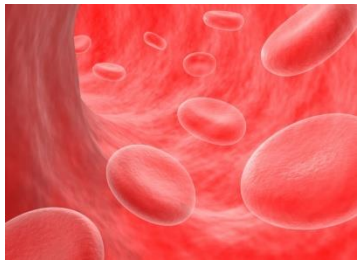
Pulmonary oxidative stress & inflammation

**Circulating Constituents**

3

Blood

PM and/or constituents transmitted into blood



**PM or constituents in the circulation**

*UFP, soluble metals*
*Organic compounds*

2 **Neural Response**

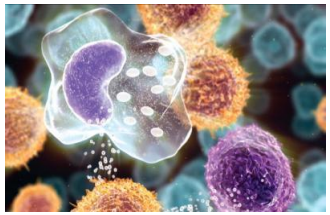
ANS

Activation of lung ANS reflex arcs

**ANS imbalance**

*↑SNS / ↓PSNS*

1 **SYSTEMIC "SPILL-OVER"**



## 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*

↑ Adipokines
(PAI-1, Resistin)

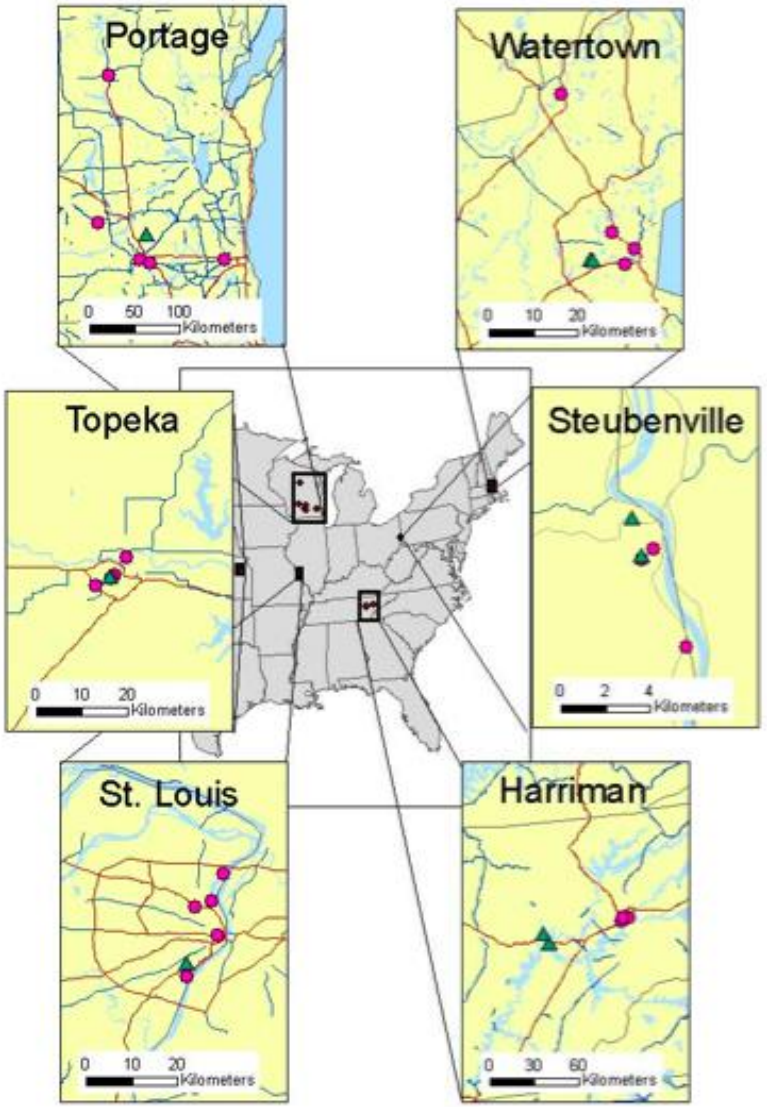
Acute phase response
↑ Clotting factors
Fibrinogen, CRP

**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

| Cox Proportional Hazards Model | Period 1 1974-89 | Period 2 1990-98 |
|---|---|---|
| Person Years | 104,243 | 54,735 |
| On follow-up | | |
| Deaths | 626 | 570 |
| **City-specific model** | | |
| Portage | 1.00 | |
| Topeka | 1.03 | 1.00 |
| Watertown | 1.19 | 0.82 |
| Harriman | 1.33 | 1.23 |
| St. Louis | 1.21 | 0.96 |
| Steubenville | 1.48 | 1.21 |
| Period | 1.00 | 0.96 |

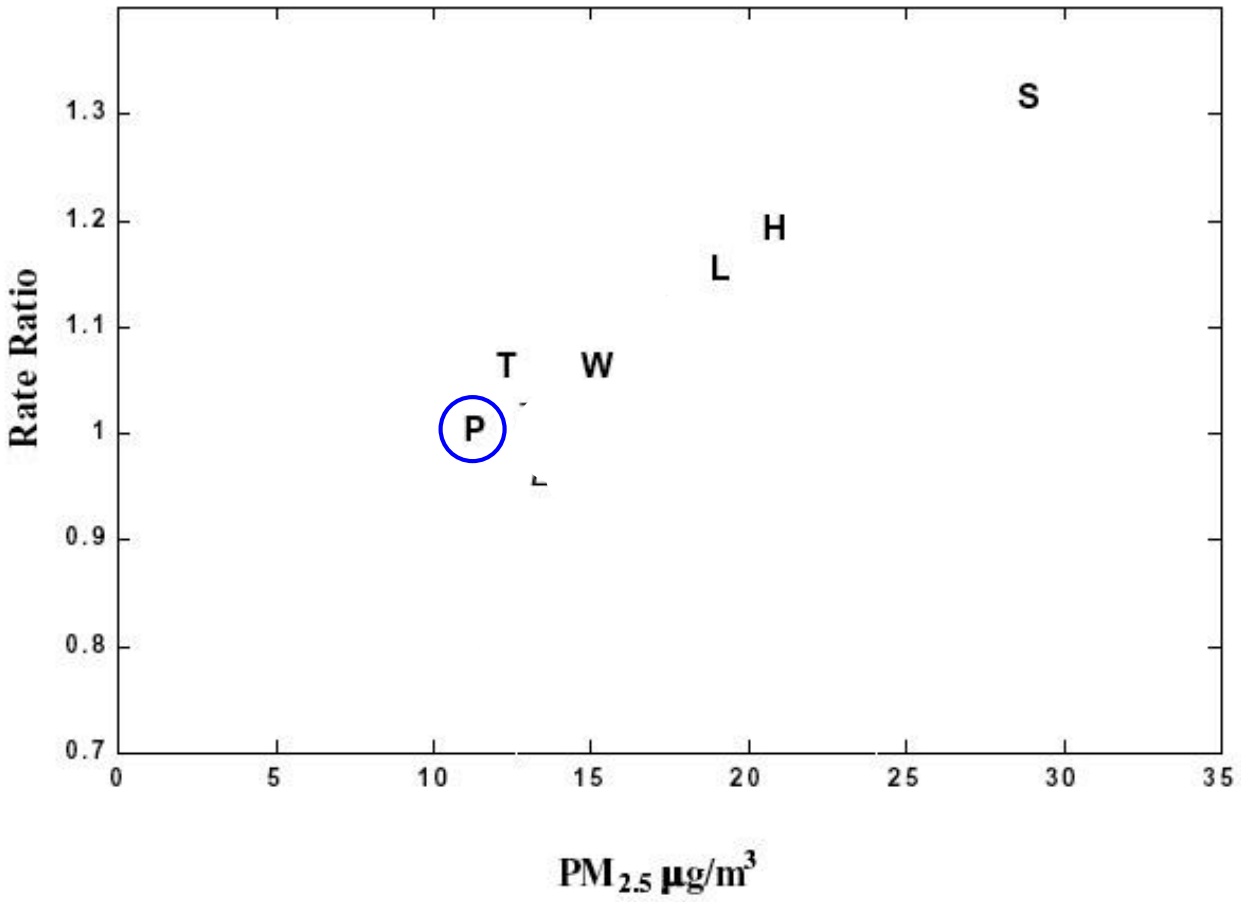
*Laden et al. AJRCCM 2006*

# Harvard Six-Cities Study

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




*Laden et al. AJRCCM 2006*

# Harvard Six-Cities Study

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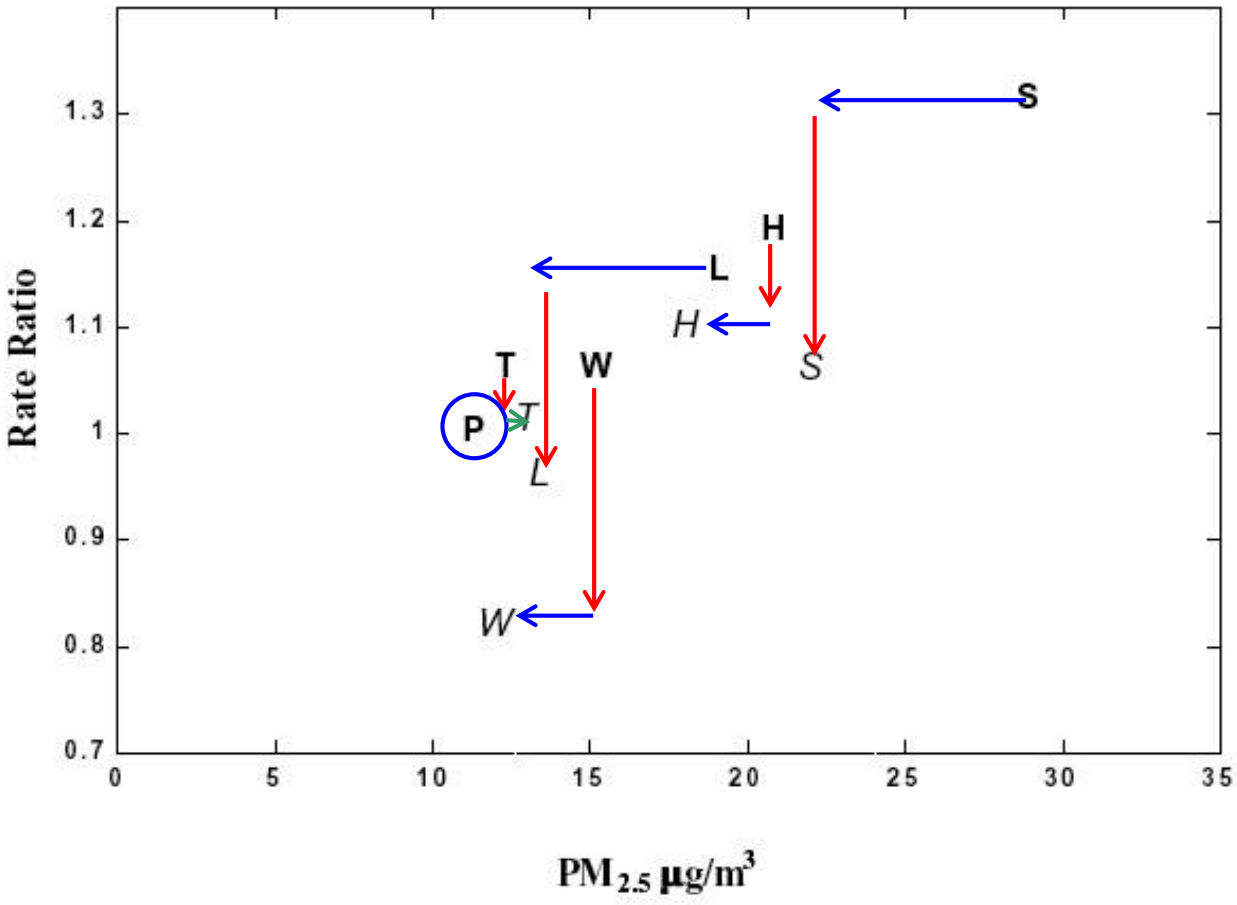
**W** - Watertown, MA
**L** - St. Louis, MO
**H** - Harriman, TN
**S** - Steubenville, OH

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




*Laden et al. AJRCCM 2006*

# Summary

- ***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?