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The Health Science of Ozone

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OTC Annual Meeting June 4, 2015

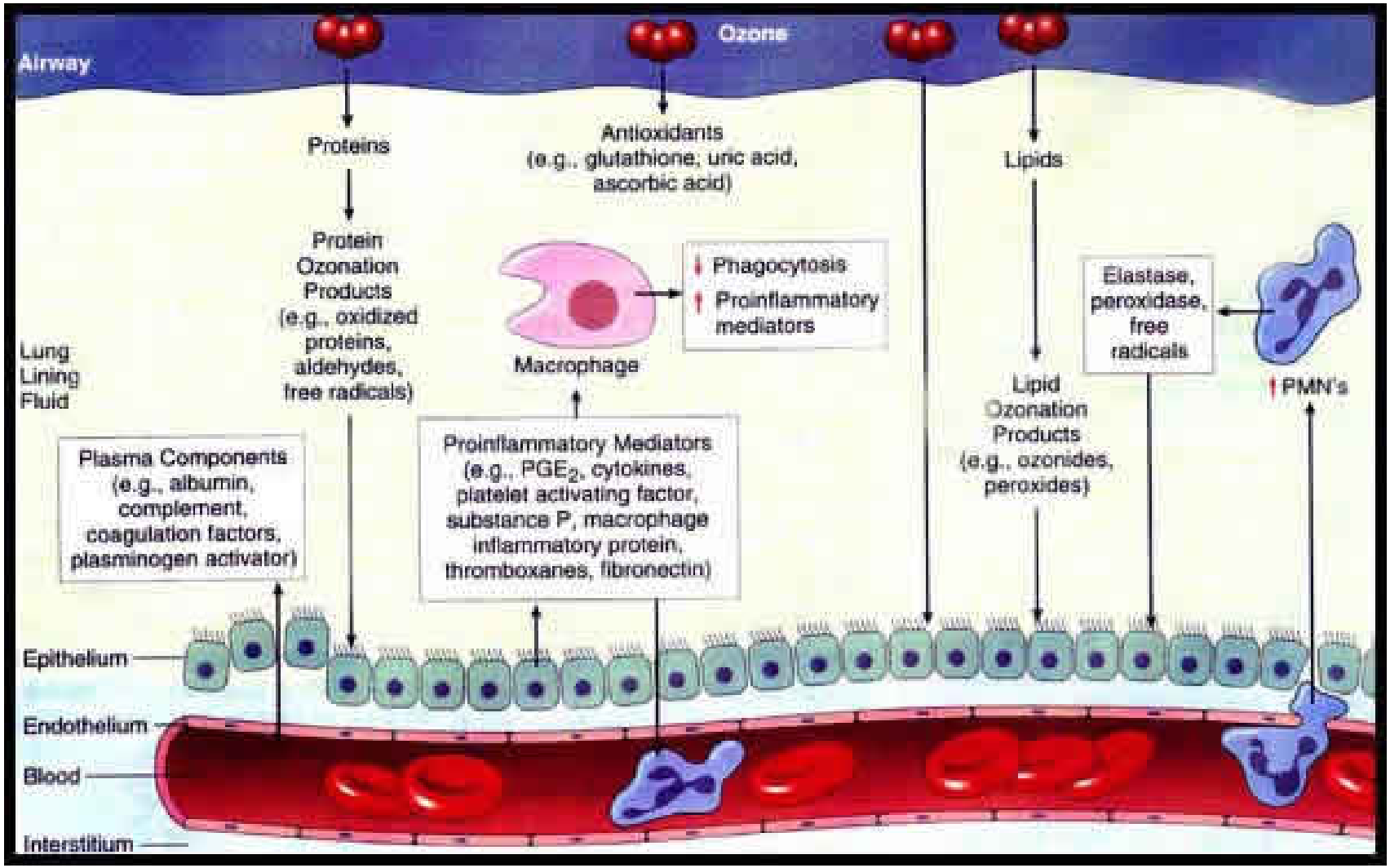
Objectives

- Review known health effects of ozone
- Identify and discuss key issues:
  - Establishing causation
  - Dose-response relationships
  - Sensitivity of individuals/groups
  - Health costs

Ozone (O_3) Toxicity

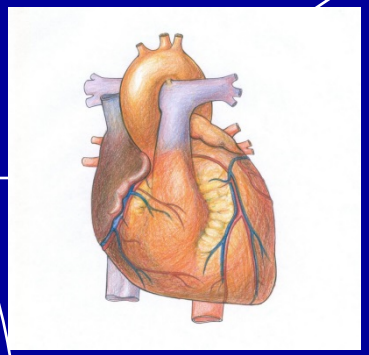
- Reactive, strong oxidant
- But poorly soluble → gets deep in lungs
- Oxidation → injury (damage to cells)
- Inflammation → release of mediators in respiratory tract and into the body
- Reversible health effects: symptoms, inflammation, loss of lung function, asthma attacks
- Irreversible health effects: loss of lung function, new-onset asthma, respiratory and cardiovascular mortality

Mechanisms of O_3 Toxicity



Source: Devlin et al. 1997

OZONE



Pulmonary Reflexes

Pulmonary Inflammation

Systemic Inflammation

Autonomic Nervous System

Endothelial Dysfunction

Oxidant Stress

Leukocyte & Platelet Activation

Automaticity Conduction Repolarization

Atherosclerosis Progression and Plaque Instability

Acute Phase Response & Coagulation Factors

Heart Rate Rhythm

Plaque Rapture

Thrombosis

Arrhythmia

Myocardial Infarction

Does O_3 cause ____ (health effect)?

Factors considered:

- **Is it biologically plausible?**
- **Is the observed epidemiological association strong?**
- **Is the association consistent across studies?**
- **Is there experimental evidence?**
- **Is there a exposure-response relationship?**

- USEPA weight-of-evidence determinations:
  - "Causal relationship"
  - "Likely to be a causal relationship"
  - "Suggestive of a causal relationship"
  - "Inadequate to infer a causal relationship"
  - "Not likely to be a causal relationship"

Review of Evidence Regarding Health Effects of O_3

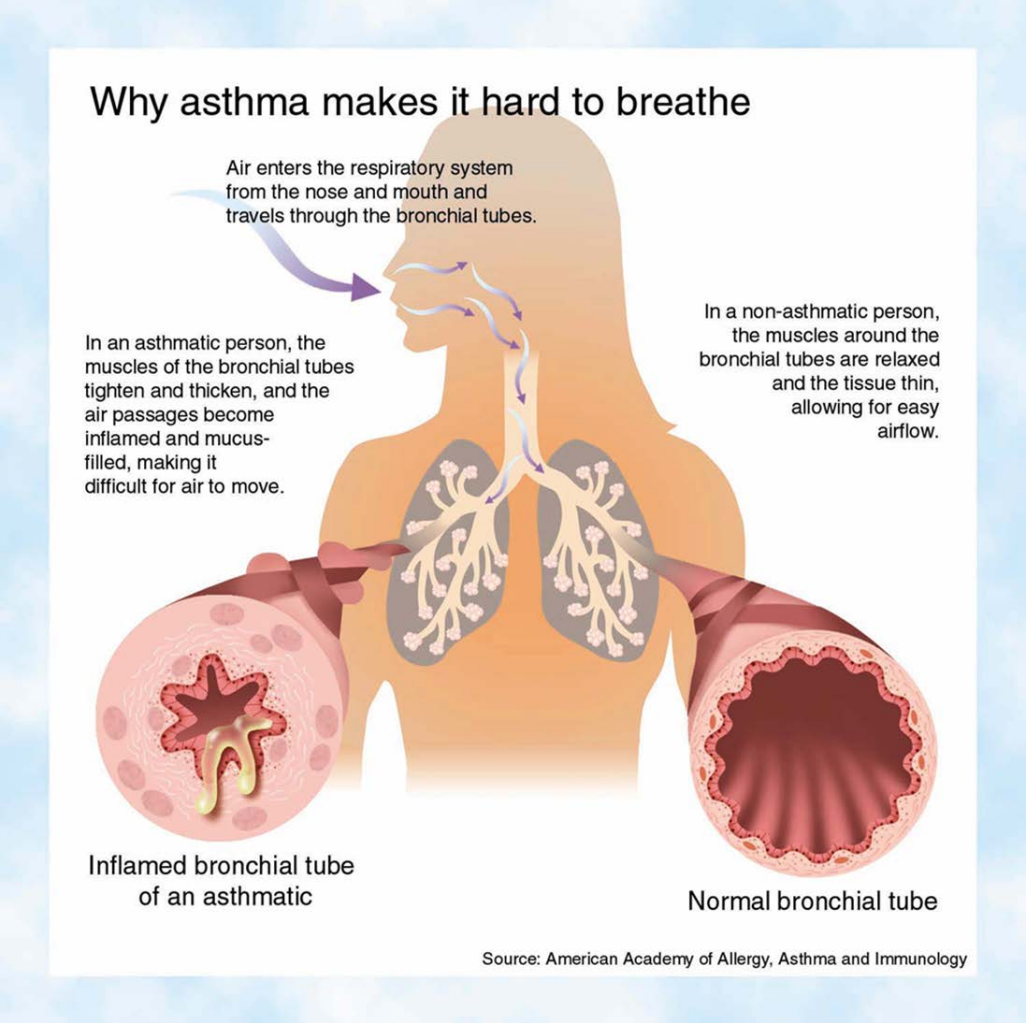
- EPA Integrated Science Assessment for Ozone and Related Photochemical Oxidants, February 2013 (1,251 pages)
- Last review was for 2008 standard update
- EPA considered more than 1,000 new studies
- Review by the independent Clean Air Science Advisory Committee (CASAC)

Other Public Health Considerations

- Sensitive groups
- Populations at risk (how large?)
  - Relatively small risk to a large exposed population may be of public health concern
- What is an “adequate margin of safety”?

Health Effects of Short-Term Exposure to O_3

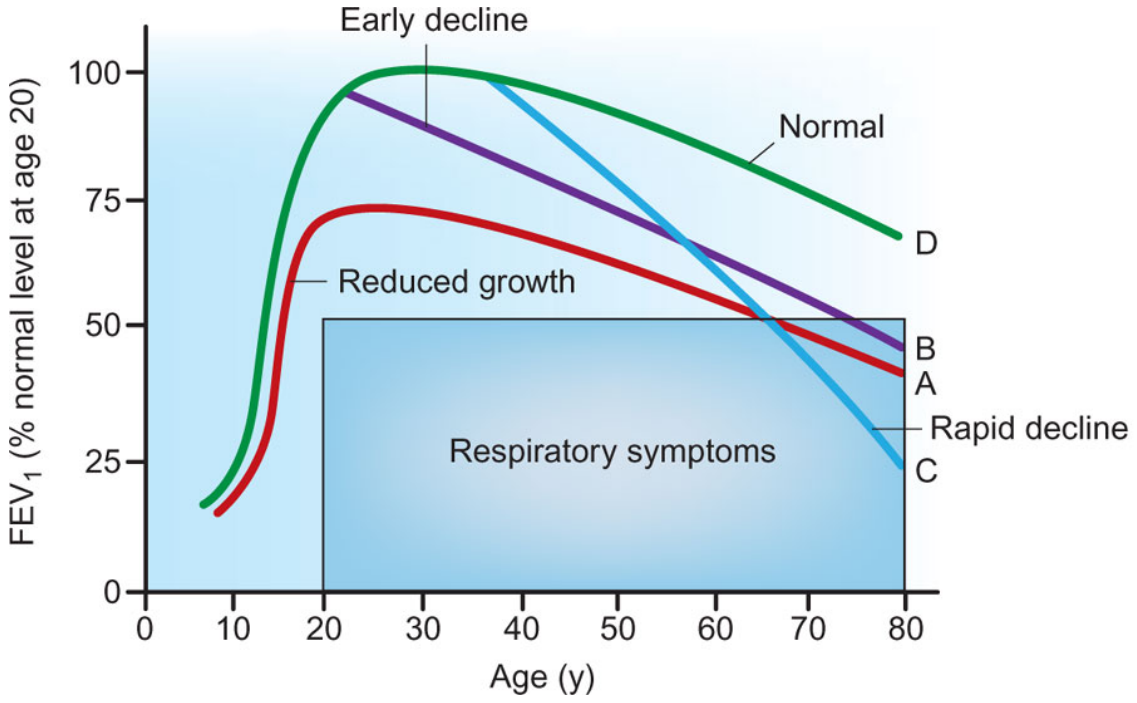
- Respiratory effects (*causal*)
  - Respiratory irritation, cough, reduced lung function
  - Airway hyperreactivity
  - Asthma attacks
  - Hospitalizations
- Cardiovascular effects (*likely to be causal*)
  - Heart attacks, sudden cardiac death, worsening of heart failure



Health Effects of Long-Term Expsoure to O_3

- Respiratory effects (*likely to be causal*)
  - Reduced lung growth
  - New-onset asthma

Model of changes in lung function over a lifetime in health and disease



(From Weiss, S. Nature Genetics 2010)

Health Effects for which Evidence is "Suggestive" of Causal Relationship with O_3

- Short-term exposure to O_3 :
  - Central nervous system effects
- Long-term exposure to O_3 :
  - Cardiovascular effects
  - Reproductive and developmental effects
  - Central nervous system effects
  - Total mortality

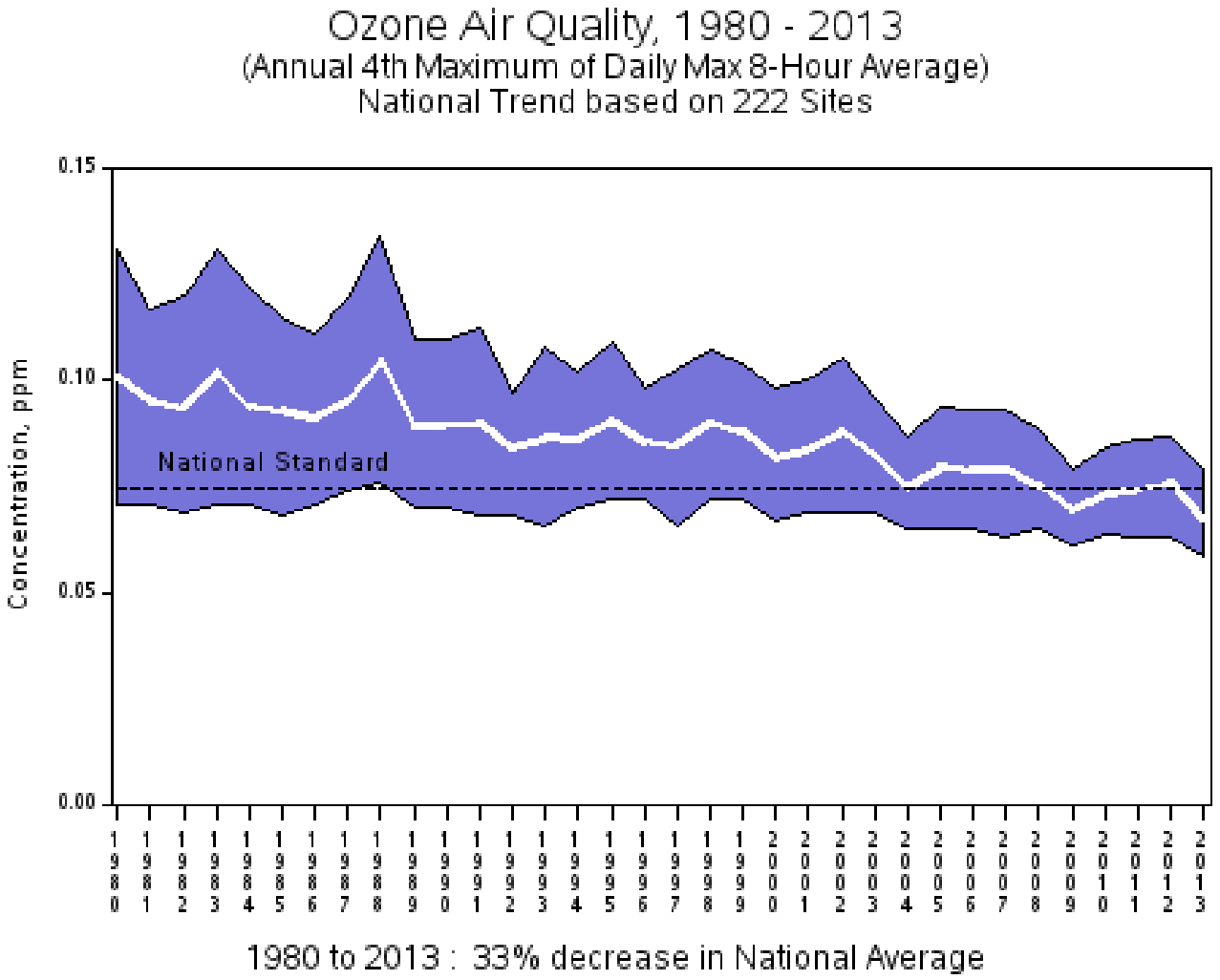
Questions Beyond Causation

- Clean Air Act:
  - EPA to set standards to protect public health, including the health of sensitive populations including asthmatics, children, and the elderly.
  - Allowing an adequate margin of safety
- How low is low enough?
  - Science can inform, but decisions rely on intrinsic value judgments
    - Range of estimates of predicted outcomes
    - Need to act in the face of uncertainty

Sensitive Groups

- People who have asthma:
  - Increased inflammation and sensitivity to allergens
- Children:
  - More vulnerable due to greater exposure, growing lungs
- Elderly:
  - More susceptible to pulmonary and cardiovascular effects

How Low Do We Have to Go?



Approaches to Investigating Health Effects of Ozone

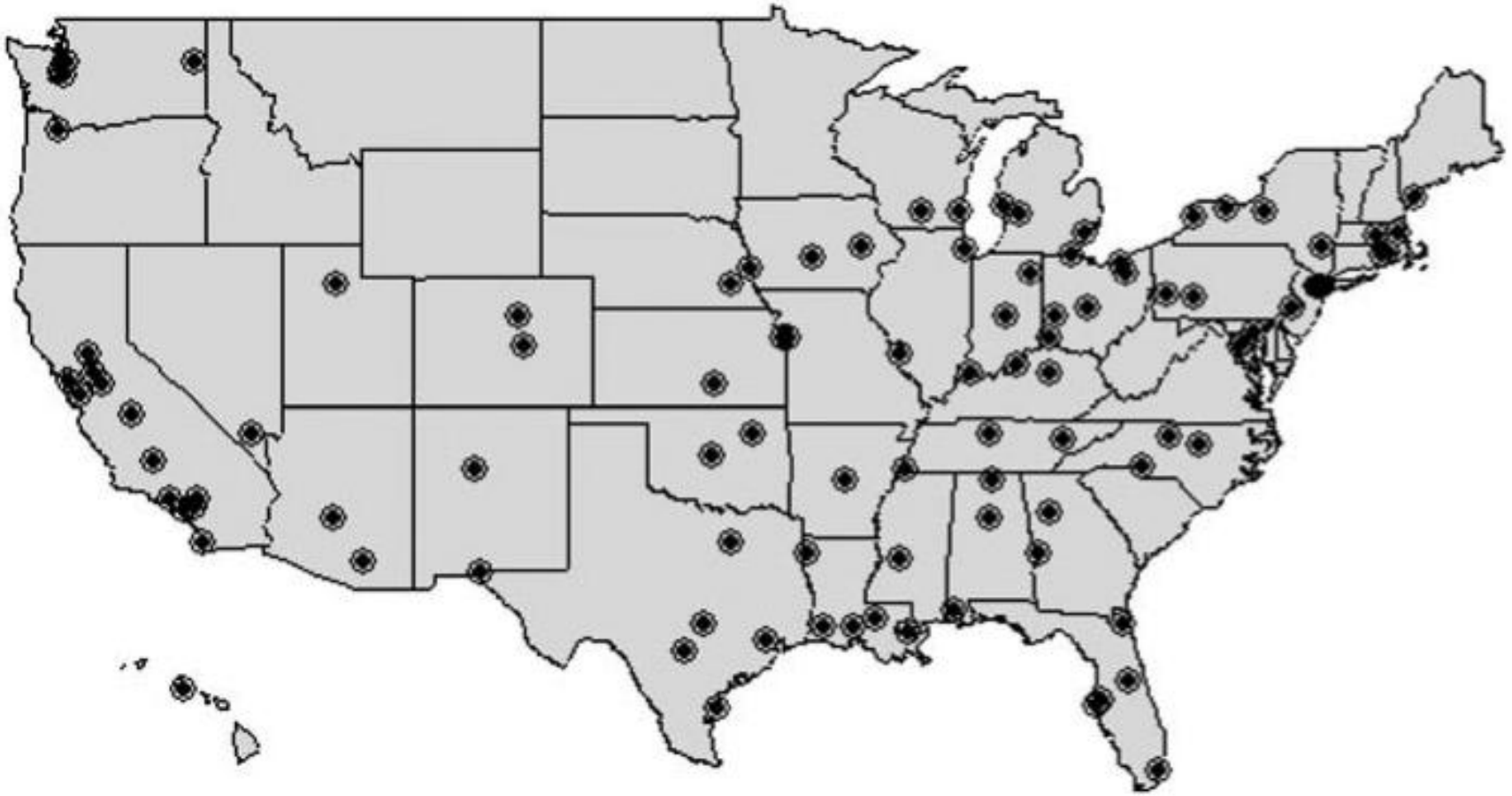
- Toxicology in cells and in-silico
- Whole-animal studies
- Human epidemiological studies
  - Analytical “observational” studies to test hypotheses
    - Time-series studies
    - Cohort studies
    - Panel studies
- Controlled human exposure studies

Epidemiological Studies of Ozone

- Time-series studies
  - Relating short-term changes in ozone to acute health effects (eg. deaths, asthma and heart attacks)
  - Daily data from EPA monitoring stations
  - Changes in ozone concentrations from day-to-day
  - Reliable all-cause mortality data
  - Associations between lagged ozone and daily mortality, adjusting for ambient temperature, humidity, day of the week, etc.

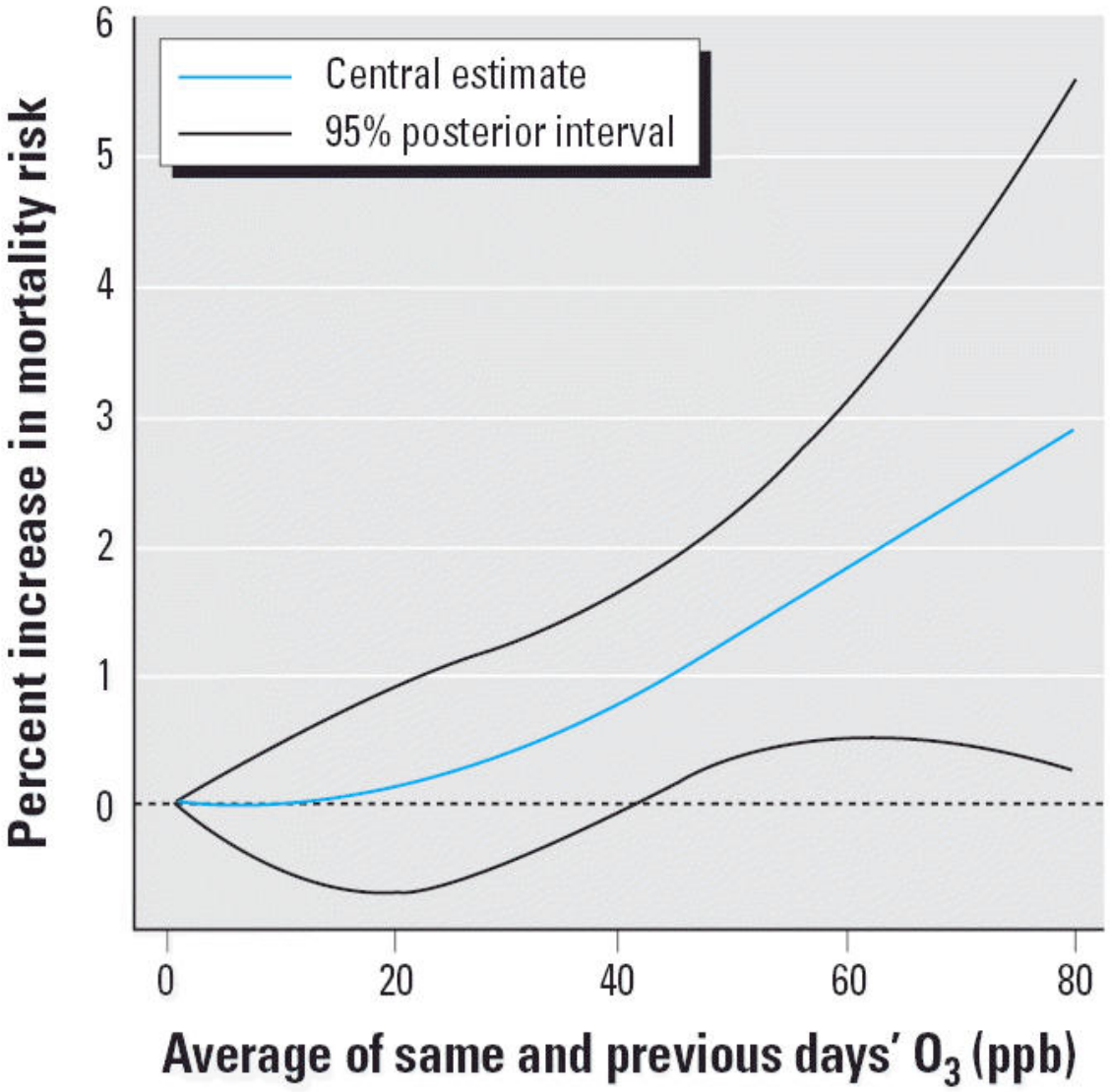
The Exposure–Response Curve for Ozone and Risk of Mortality and the Adequacy of Current Ozone Regulations (Bell et al. EHP 2006)

98 counties across the US, 1987-2000 (NMMAPS) study



Ambient O3 and Total Mortality

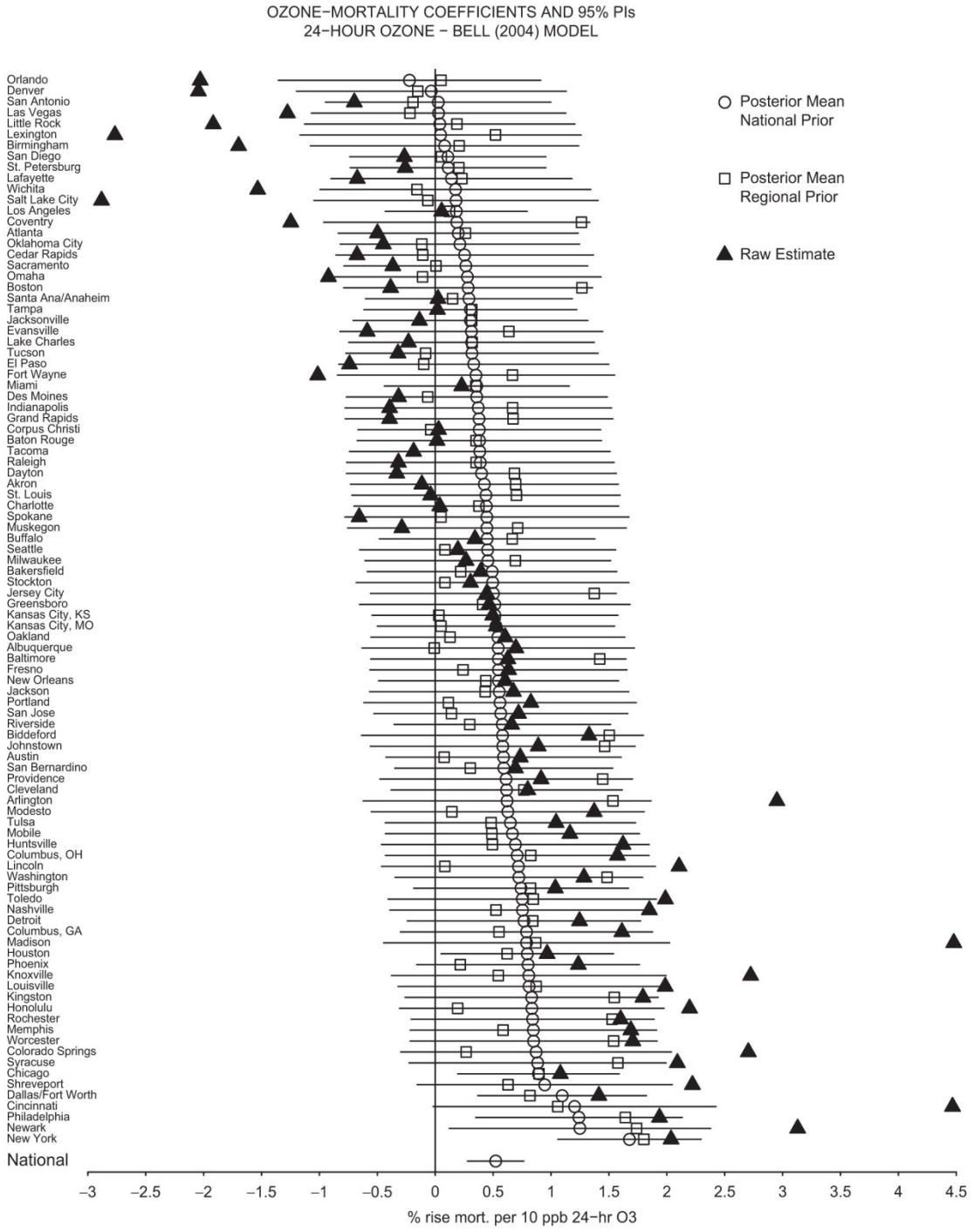
Time-series study of daily mortality experience of 98 US cities from 1987 to 2000
(Bell et al EHP 2006)



Why so much variability between cities?

"Reassessing the relationship between ozone and short-term mortality in U.S. urban communities."
Smith, Xu, and Schwitzer. Inhal. Tox. (2009)

Random variability or systematic error?



Between-city variability in ozone infiltration to indoors may explain some of the variability between cities

- Cities have different average rates of air exchange rates in homes
- Modeled by Persily et al (2010), including 18 NMMAPS cities
- Modeled air exhange used by Weschler to examine relationship between ozone dose-response and A.E.R. and total ozone exposure in 18 cities with detailed infiltration rates

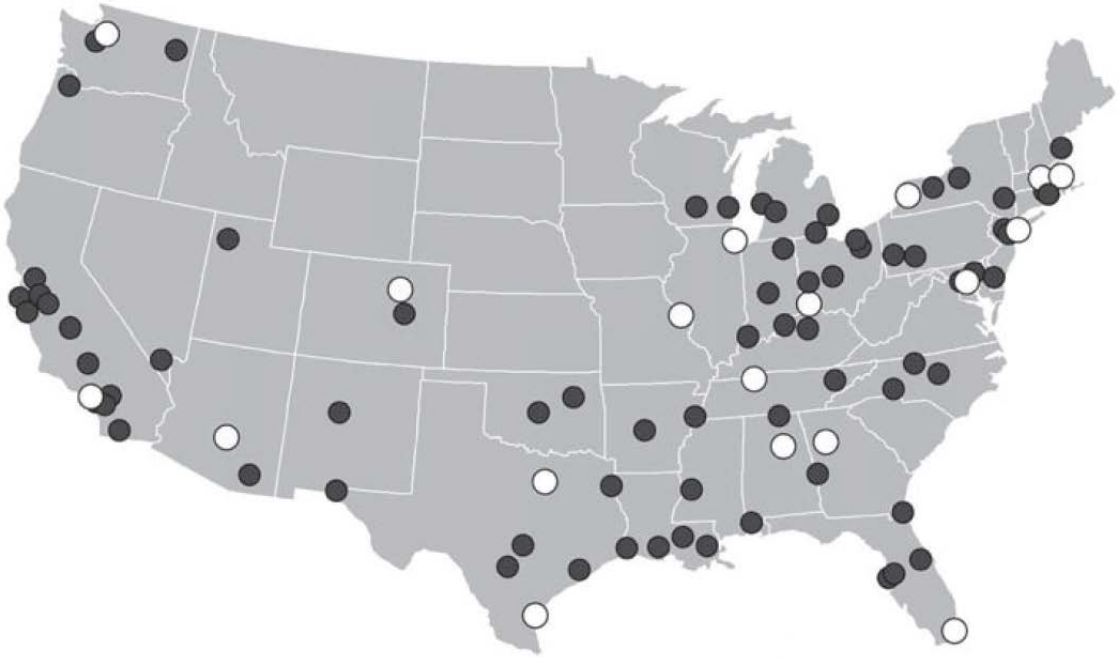


Figure 1. Location of the 18 NMMAPS cities for which detailed modeled infiltration rates were available (open circles) and the 72 additional NMMAPS cities included in the extended analysis (filled circles).

Between-city variability in ozone infiltration to indoors may explain some of the variability between cities

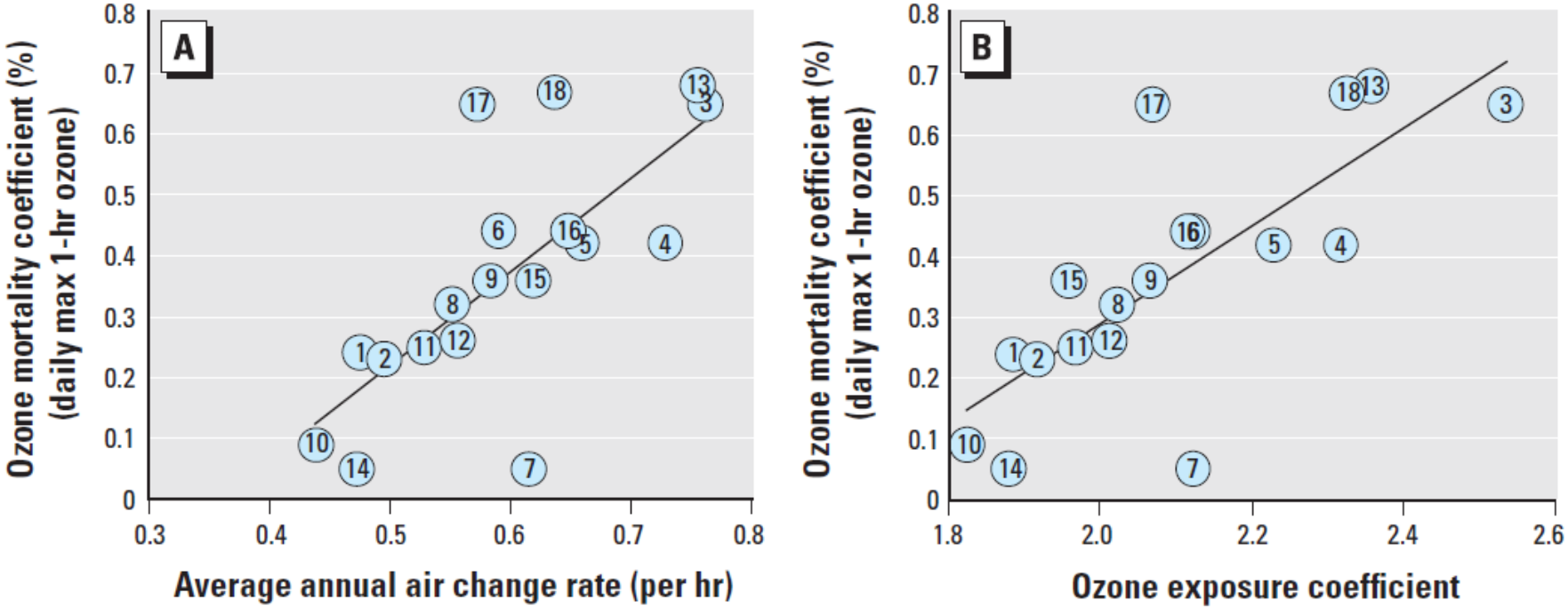
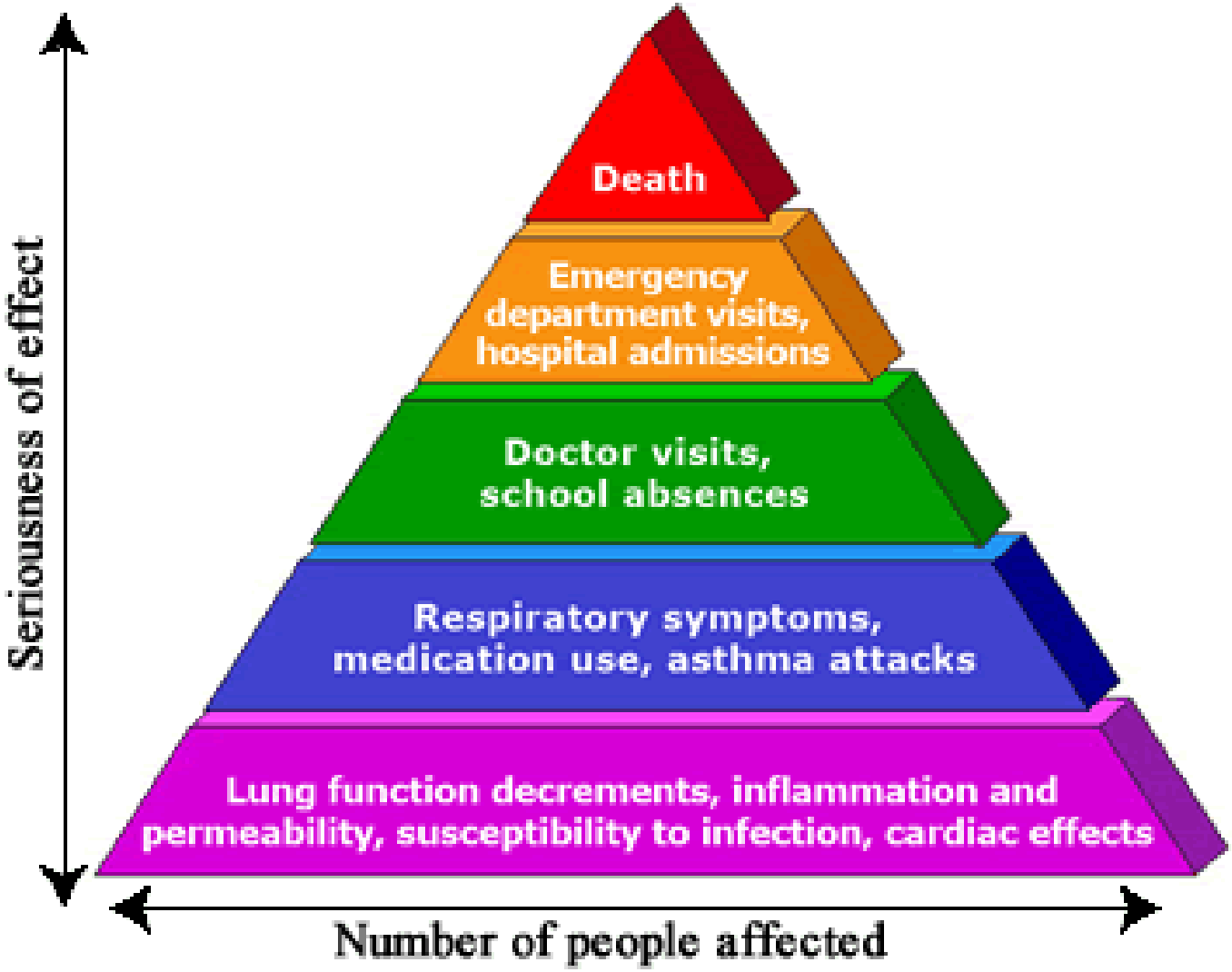


Figure 2. For the 18 NMMAPS cities for which detailed modeled infiltration rates were available, ozone mortality coefficients versus (*A*) average annual air change rates ($y = 1.54x - 0.55$, $R^2 = 0.51$), and (*B*) ozone exposure coefficients ($y = 0.81x - 1.32$, $R^2 = 0.58$). Ozone mortality coefficients based on daily maximum (max) 1-hr ozone. Numbers within circles refer to numbers listed in the first column of Table 1.

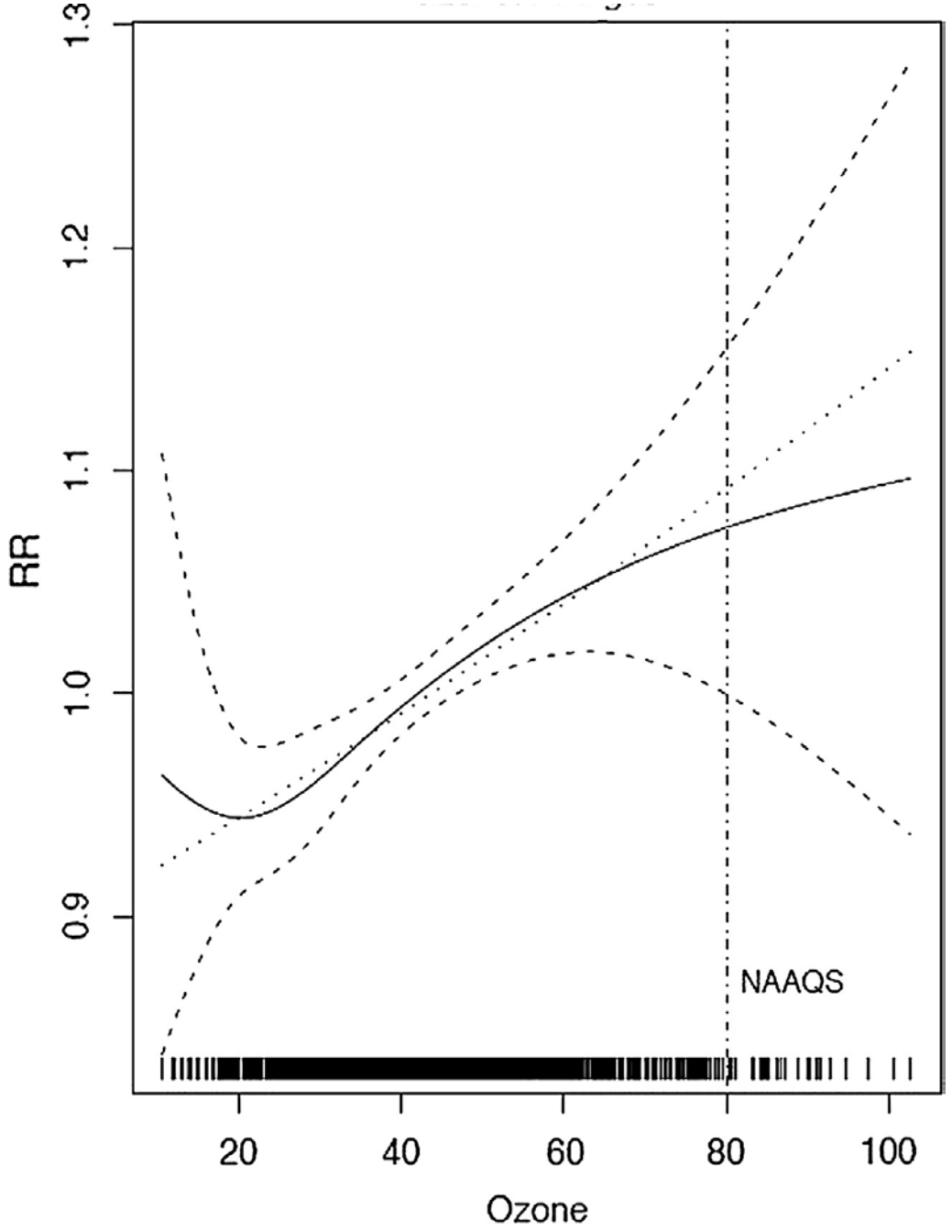
Pyramid of Effects (the Iceberg)



Ambient O_3 and Hospital Admissions for Asthma

Daily time-series of asthma admissions to 74 NYC hospitals 1999-2006. Estimated relative risks (RR) of asthma hospital admissions for 8-hr max O_3 concentrations at lag 0-1 days.

(Silverman JACI 2010)



Controlled Exposure Studies

EPA Facilities

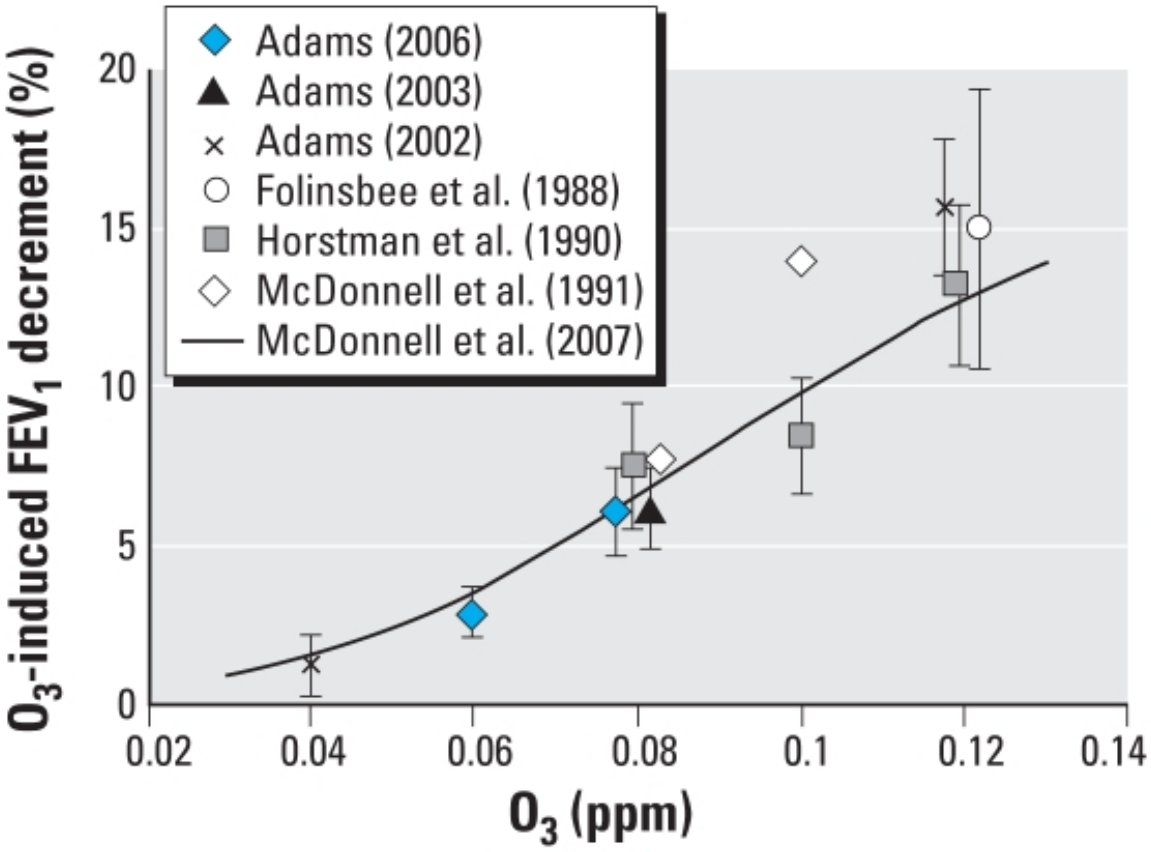
Controlled Exposure Studies

- Mild, temporary, and reversible effects
- Strengths
  - Quantitative control of exposure and dose
  - Few confounders
  - Species of interest
- Limitations:
  - Short-term exposures
  - Exposure to a single compound or specific mixture
  - Limited spectrum of participants
- Especially valuable for biomarker studies to learn about biological mechanisms
- Many studies done over decades to evaluate respiratory effects of ozone

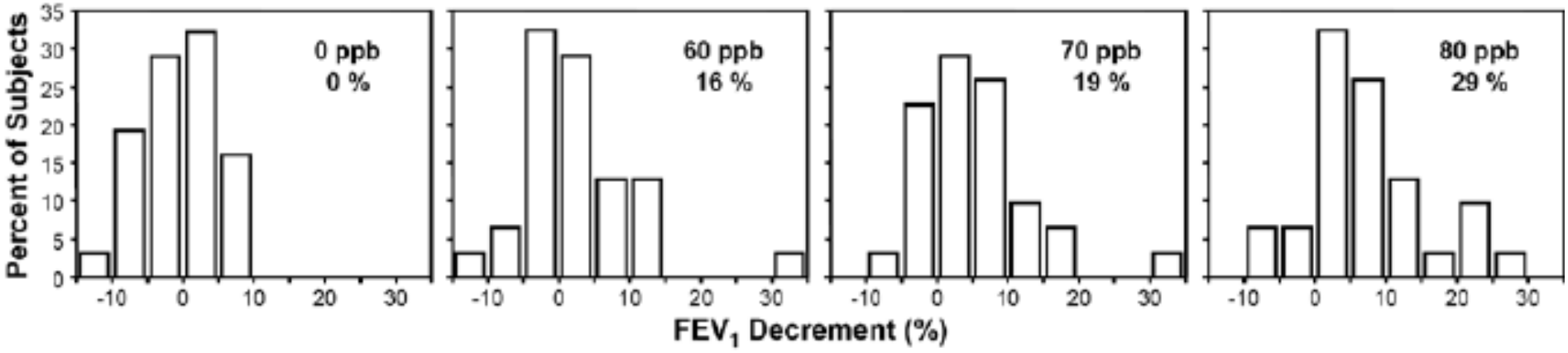
Controlled Exposure Studies of Short-term O_3: Is there a threshold for lung function response?

Cross-study comparison of average FEV1 decrements due to 6.6 hr exposure to O3 with moderate exercise

(Brown et al EHP 2008)



Individual variability in FEV_1 decrement in controlled exposure studies of short-term O_3:



Distributions of % change in FEV1 among 31 healthy male and female participants aged 18-25 exposed to 0, 60, 70, and 80 ppb O_3 for 6.6 hours with exercise. Inset shows % of participants with ≥ 10% drop in FEV_1.

(Schelegle, AJRCCM 2009)

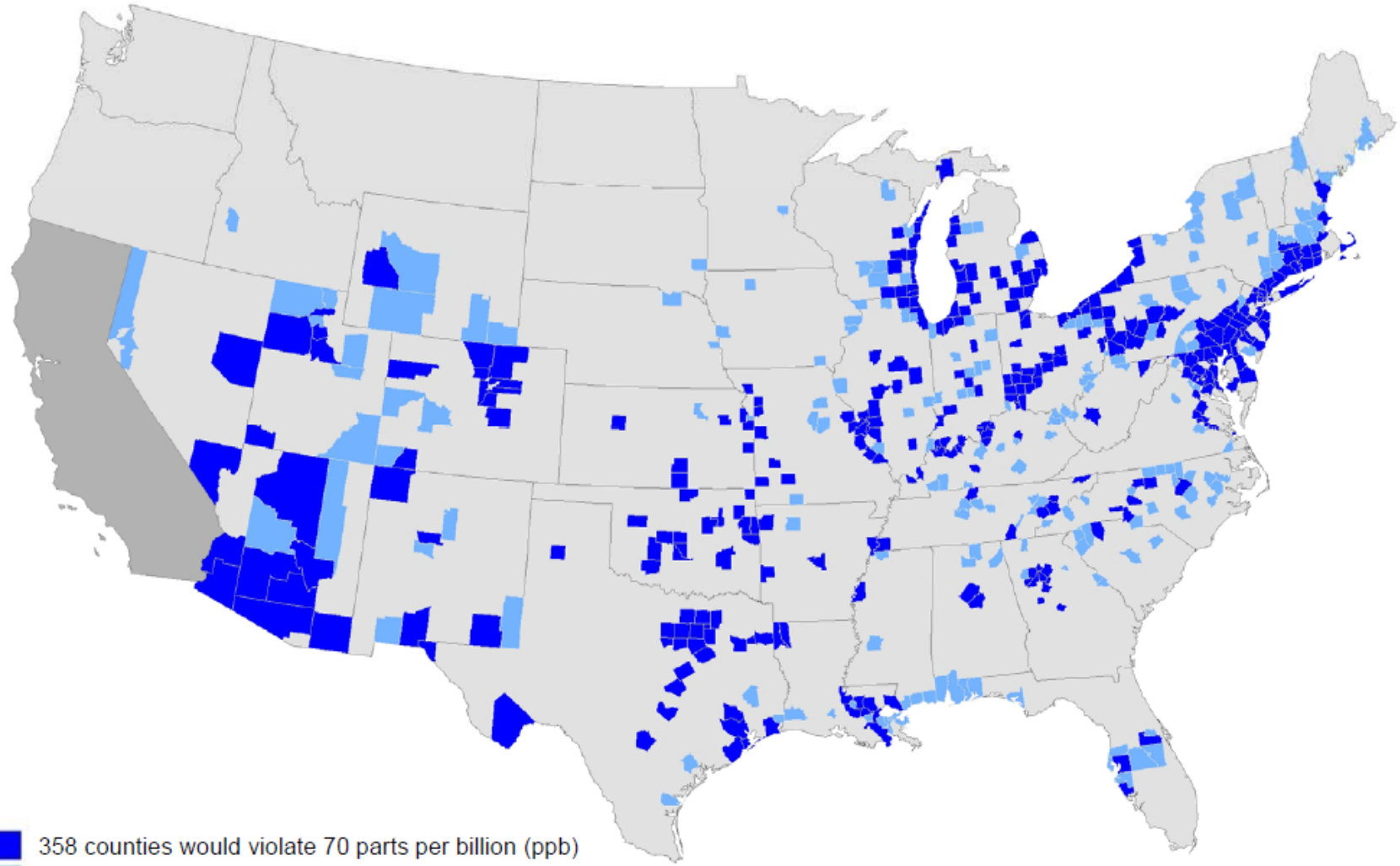
"What Constitutes a Health Effect of Air Pollution?"

- ATS 2000 Statement
- Currently undergoing revision
  - More on cardiovascular effects
  - Other extra-pulmonary effects: developmental, pregnancy, cognitive
  - Interpreting biomarkers

Direct and Indirect Costs of O_3 Pollution

- Economic:
  - Medical care: hospitalization, emergency care, routine care, more medication use
  - Absenteeism: missed work and school days
  - "Presenteeism": reduced productivity
  - Premature death: years of productive life lost
- What value do we put on health, and how do we measure it?

Counties Where Measured Ozone is Above Proposed Range of Standards (65 – 70 parts per billion)



358 counties would violate 70 parts per billion (ppb)

200 additional counties would violate 65 ppb for a total of 558

Based on 2011 – 2013 monitoring data

Clean Air Science Advisory Committee (CASAC): Review of EPA 2nd Draft Policy Assessment

- "Based on scientific evidence, a level of 70 ppb provides little margin of safety for the protection of public health."
- "At 70 ppb there is substantial scientific evidence of adverse effects…"
- "…60 ppb would certainly offer more public health protection than levels of 70 ppb or 65 ppb and would provide an adequate margin of safety."

A Few of the Health Organizations Supporting a 60 ppb limit

- American Medical Association
- American Thoracic Society
- American Academy of Pediatrics
- American Heart Association
- American Lung Association
- American Public Health Association
- Asthma and Allergy Foundation of America
- Children's Environmental Health Network

Benefits and Costs of Lowering the O_3 Standard (USEPA)

- An ozone standard in the proposed range of 65-70 parts per billion has public health benefits worth an estimated:
  - $6.4 to $13 billion for a standard of 70 ppb
  - or $19 to $38 billion for a standard of 65 ppb.
- These benefits outweigh the costs, estimated at:
  - $3.9 billion for a standard of 70 ppb
  - or $15 billion for a standard of 65 ppb.
- Reducing ozone and particle pollution nationwide (excluding California) in 2025 will avoid:
  - 710 to 4,300 premature deaths
  - 320,000 to 960,000 asthma attacks among children
  - 330,000 to 1 million days when kids miss school
  - 65,000 to 180,000 missed work days
  - 1,400 to 4,300 asthma-related emergency room visits
  - 790 to 2,300 cases of acute bronchitis among children

Conclusions

- Ozone causes a range of health effects at levels of exposure experienced by large populations in the US today
- The evidence for these health effects comes from a variety of studies that show consistent results
- Uncertainty remains about precise dose-response relationships, possible thresholds, and emerging health effects for which there is suggestive evidence of causal associations
- Ozone pollution at current levels appears to have high human and economic costs

Questions?