IERs and the WHO IAQGs: How Clean is Clean Enough?

Symposium on the WHO Indoor Air Quality Guidelines

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Integrated Exposure-Response (IER) Functions

- Linking exposures and risks across four sources of combustion particles
  - Ambient air pollution (AAP)
  - Secondhand tobacco smoke (SHS)
  - Household air pollution (HAP)
  - Active tobacco smoking (ATS)
- 3+ orders of magnitude range of exposure

Integrated Exposure-Response Functions

- Why do it?
- What does it reveal?
- What's good about it?
- What's not so good
- What does it mean for the IAQGs?

Why do it?

- In the recent AAP Comparative Risk Assessment, it was found that much of the world's population is exposed to PM2.5 levels well above where good epi studies have been done
- Long-term cohort studies in North America and Europe not more than 35 ug/m3, but
- Parts of India and China well above this
- What is their risk?

Extrapolation?

- Much of toxicology and epidemiology has focused on extrapolating from high to low exposures
- Has distinct advantage of at least one anchor point available – zero exposure and zero risk
- Even then, often problematic to understand shape of curve at low levels

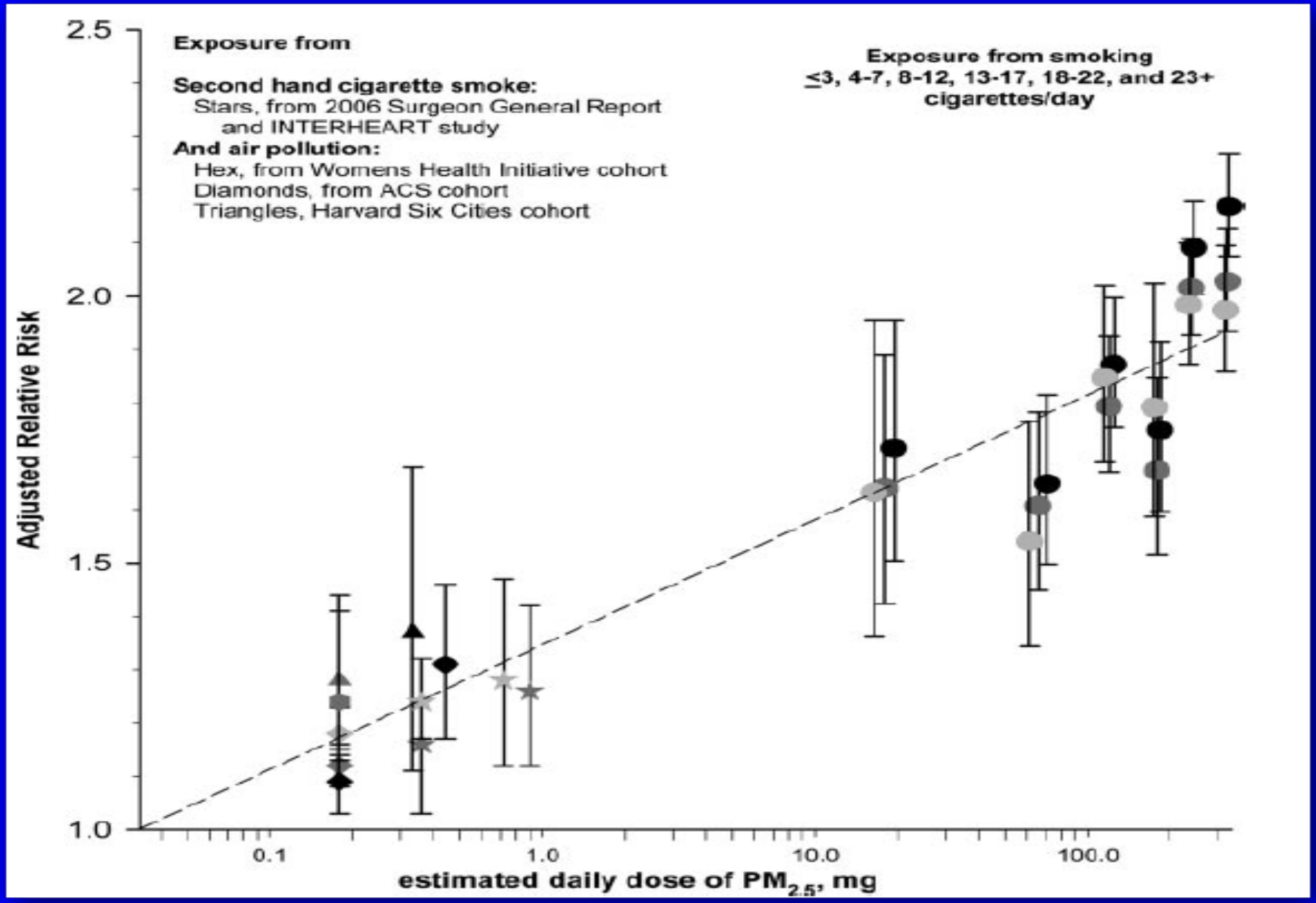
Extrapolation upwards?

- Many shapes possible, i.e., different models fit data ok at lower exposures but are wildly different at high levels.
- Many also do not pass the smoking laugh test, i.e. reach relative risks for AAP well above what smokers experience for several important diseases
- Need to anchor the upper end of the exposure range with smoking levels to derive exposure curve.

Thus the first IER curves

- Impacts from AAP, smoking, and secondhand smoke need to be put on same exposure axis
- Use inhaled dose in mg PM2.5/day (applied since 1980s to compare air pollution with smoking)
- Not actual dose – deposition not known
- Exposure concentration converted to inhaled dose by population breathing rates
- Two papers led by Arden Pope in 2009/11

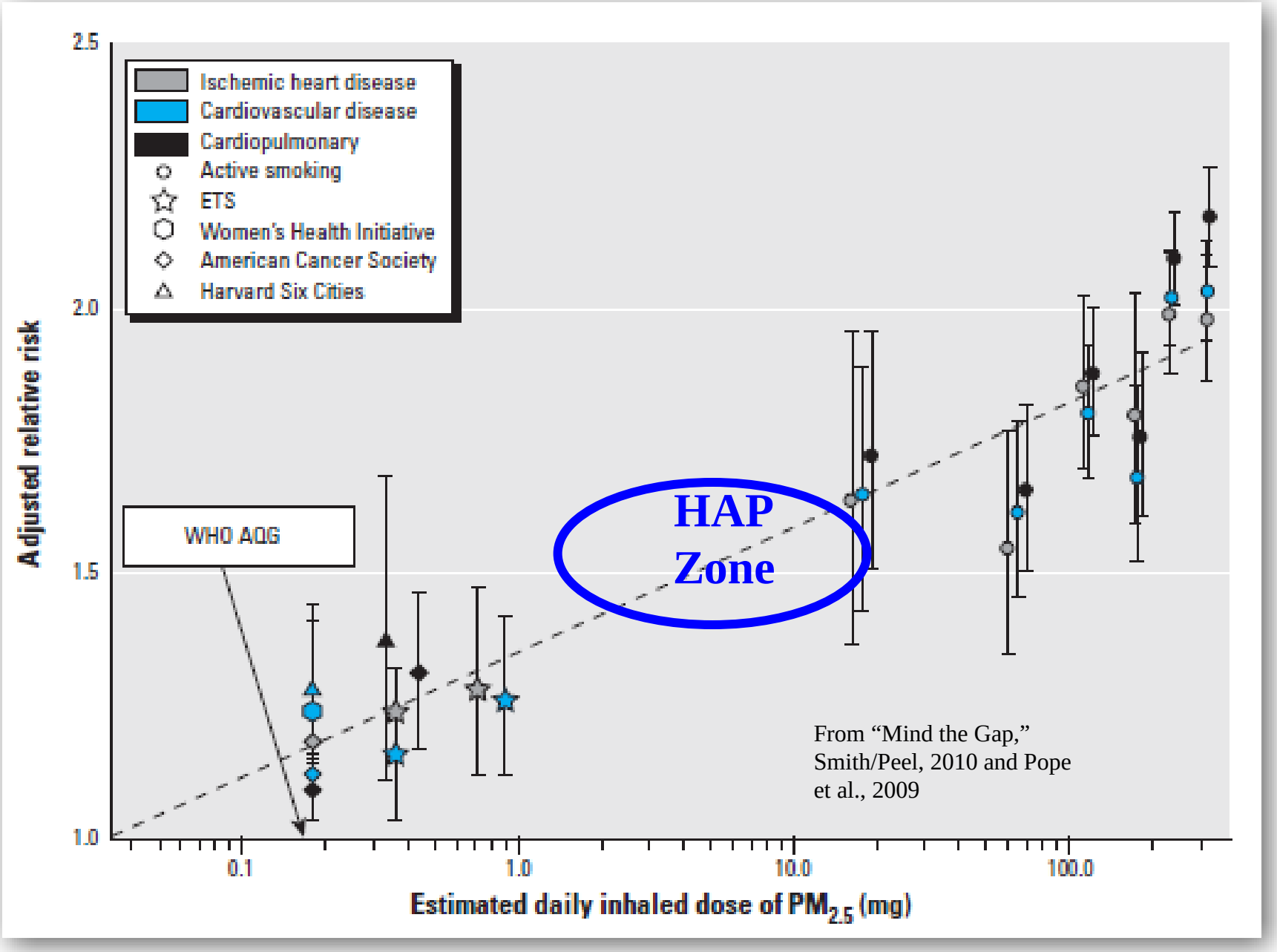
Risk of IHD (light grey), Cardiovascular Disease (incl. stroke) (dark grey) and Cardio-pulmonary disease (black). Pope et al 2009



Opportunity Presents itself for HAP

- HAP exposure tend to lie between those for AAP/SHS and active smoking
- Risks must lie between as well, even for diseases for which little HAP data are yet available, like cardiovascular disease
- Thus, IERs could be used for interpolation as well as extrapolation.

Heart Disease and Combustion Particle Doses



From "Mind the Gap," Smith/Peel, 2010 and Pope et al., 2009

GBD Comparative Risk Assessments

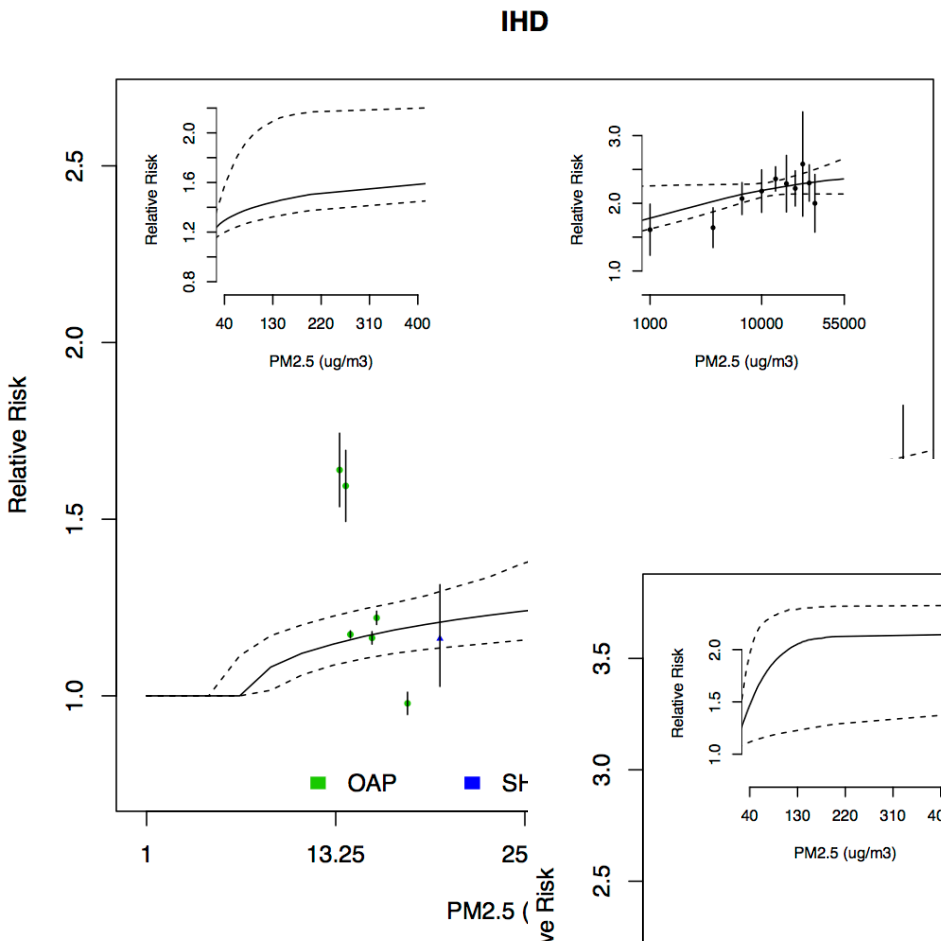
- More sophisticated modeling, systematic estimation of uncertainty bounds, and inclusion of more studies was done for IERs (Burnett, Cohen, Lim, and others)
- In addition, for some outcomes, results of household air pollution studies also included
- These IERs were adopted for use in the AAP and HAP CRAs with a common counterfactual ~7 ug/m3 annual average

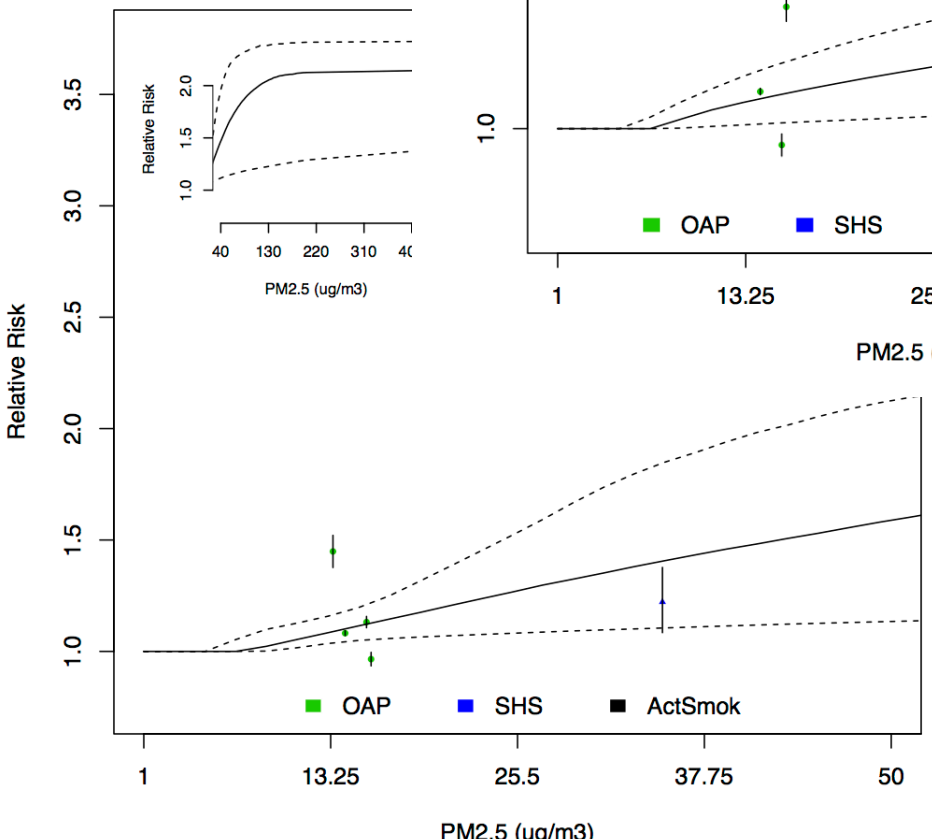
In the GBD Project

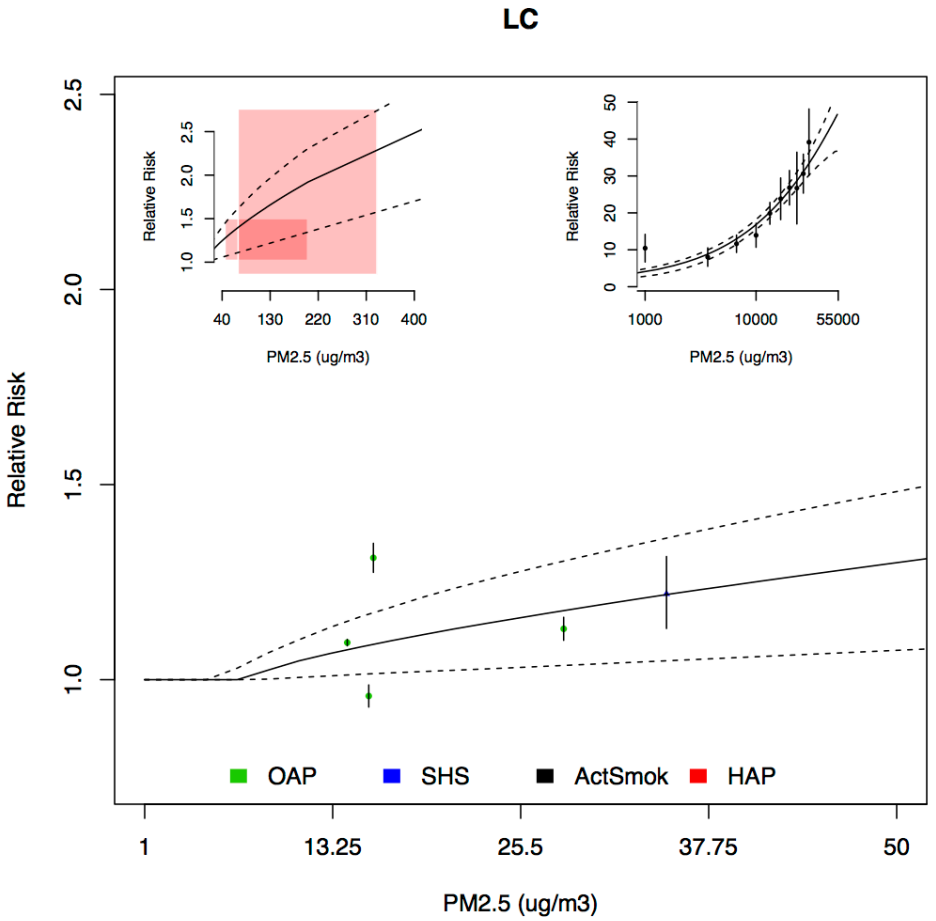
- IERs used in the HAP CRAs for 4 major outcomes
  - Ischemic Heart Disease (IHD)
  - Stroke
  - Lung cancer
  - ALRI in children – no ATS evidence
- For COPD and cataracts – relied on systematic reviews and meta analyses

Argument from consistency across combustion particle exposure settings

- Assumes fine combustion particles are best measure of risk in each setting and have similar effects per unit mass across the four source types
  - Three are mainly biomass
  - AAP contains significant biomass particles
  - Probably difference by outcome, however – e.g., LBW and lung cancer may be related to other components as well
- Remarkable consistency across 3 orders of magnitude of dose measured in mg/day of $PM_{2.5}$
- Where HAP has no direct epi data, seems reasonable to interpolate for outcomes where there are well established effects at both lower and higher doses.



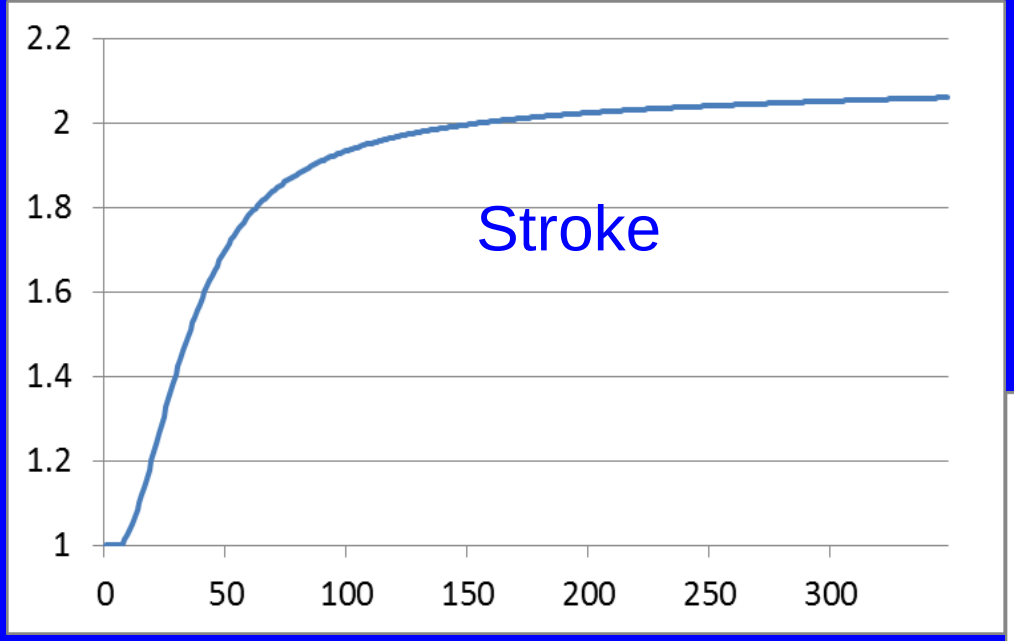


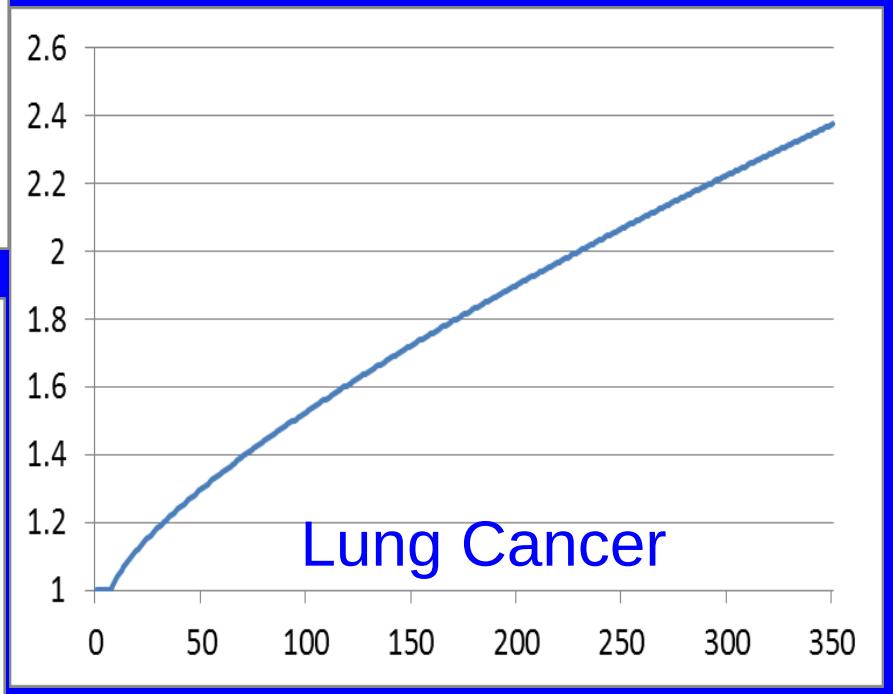


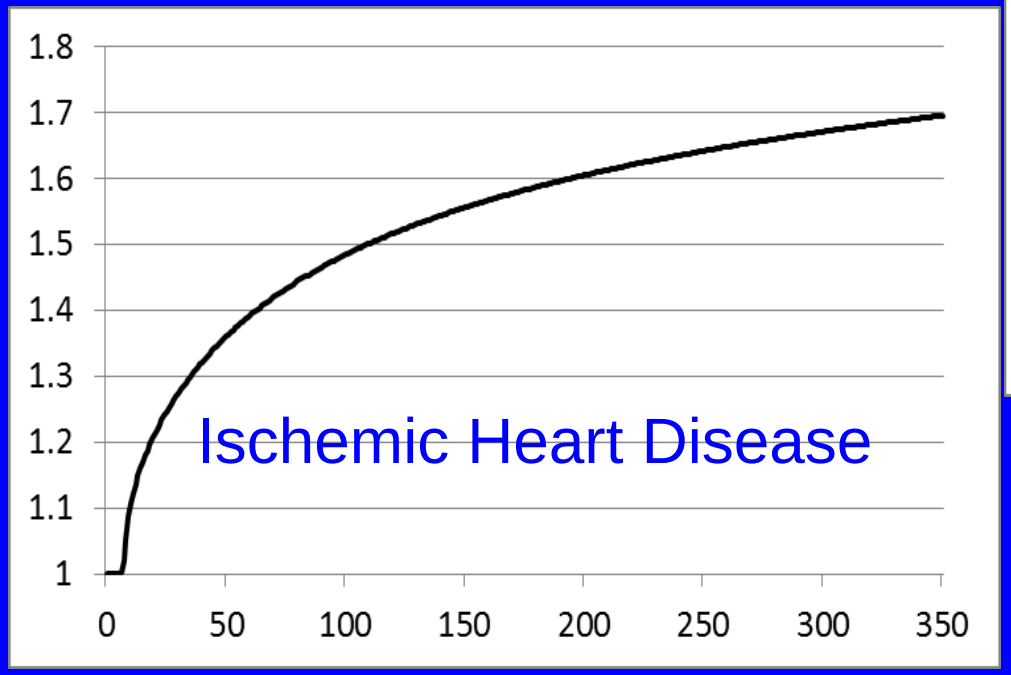
Burnett et al. submitted

Relative Risks by Exposure-

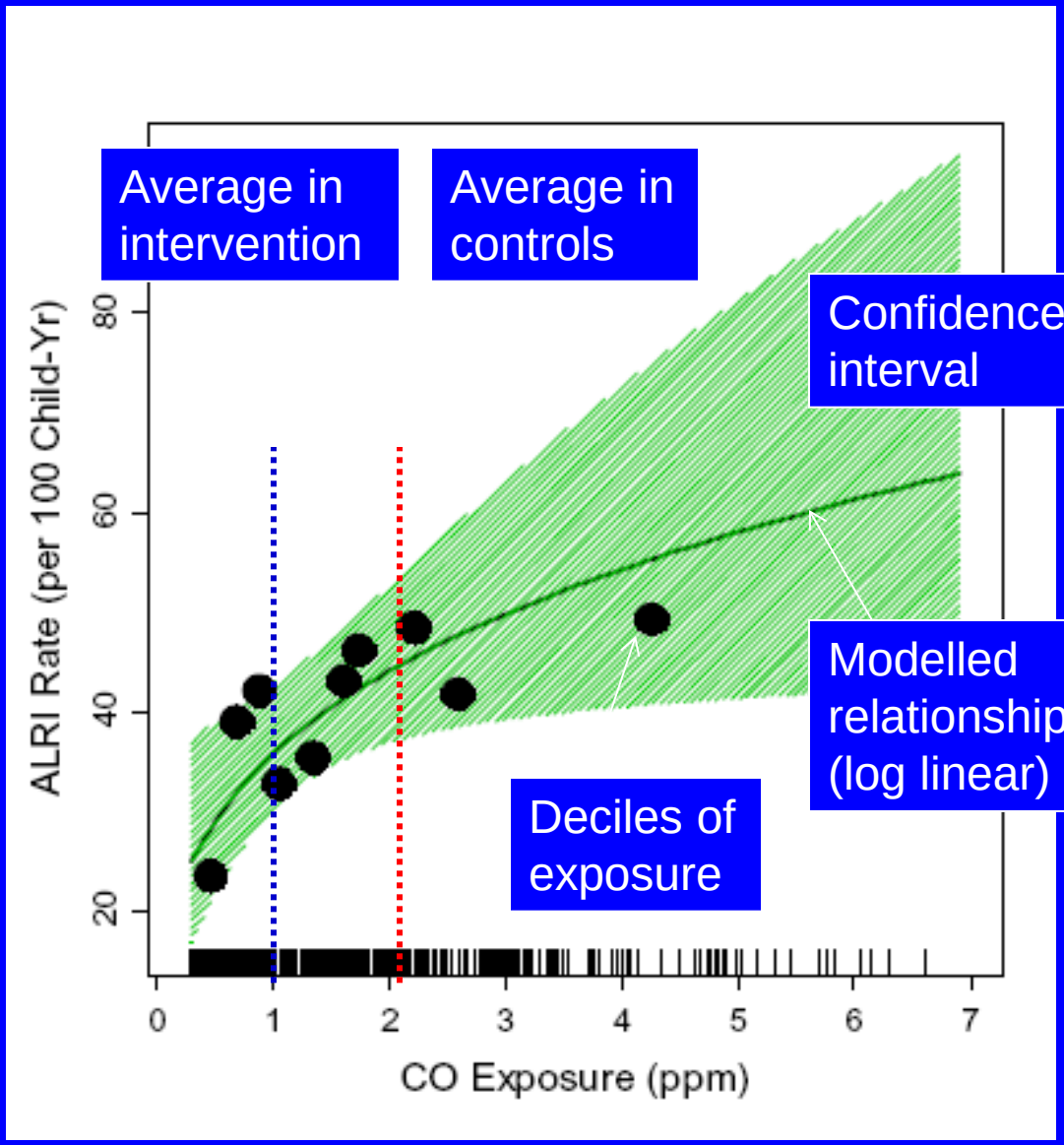
Annual ug/m3 PM2.5







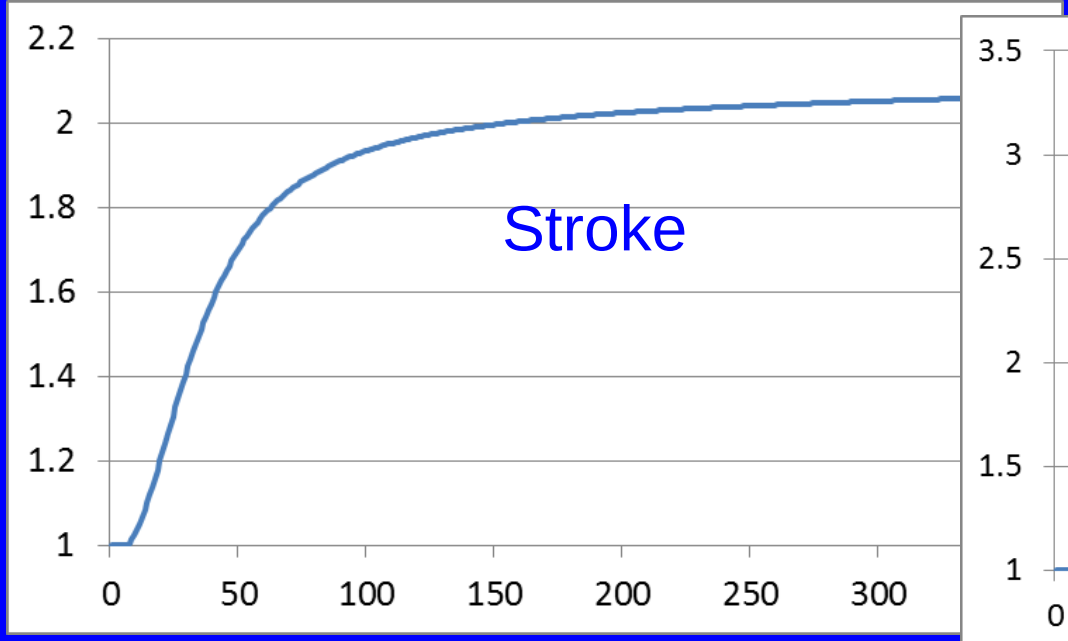
Exposure – response relationship

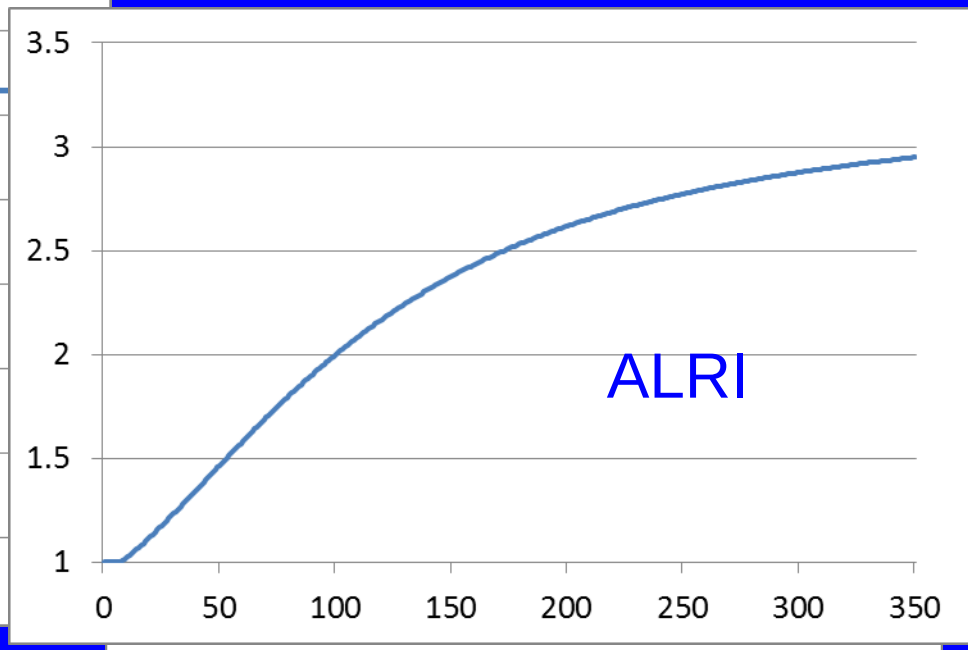


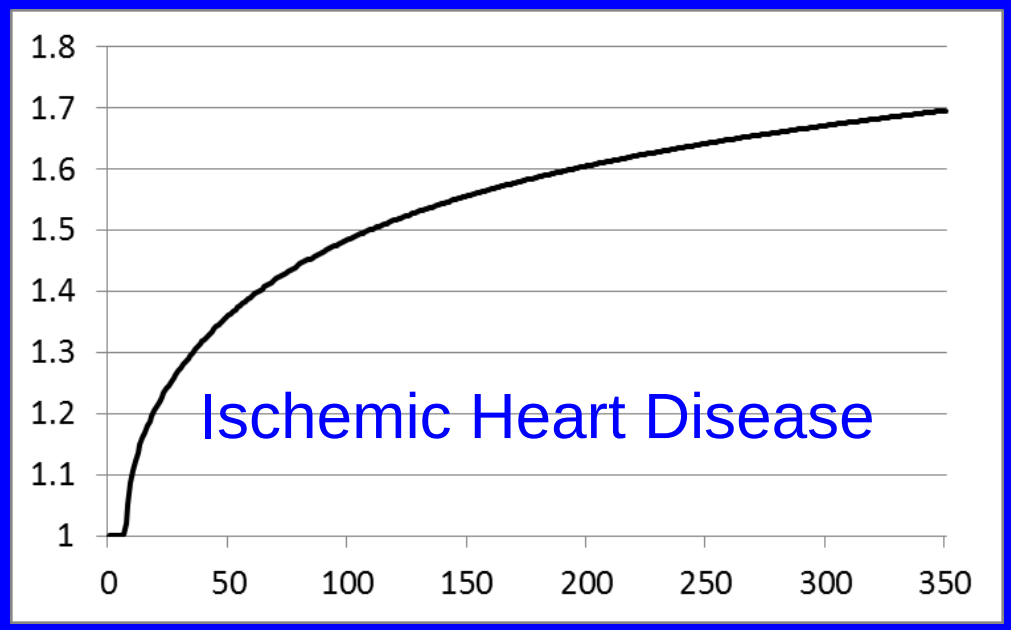
Upper end of ALRI-IER from RESPIRE studies
In Guatemala

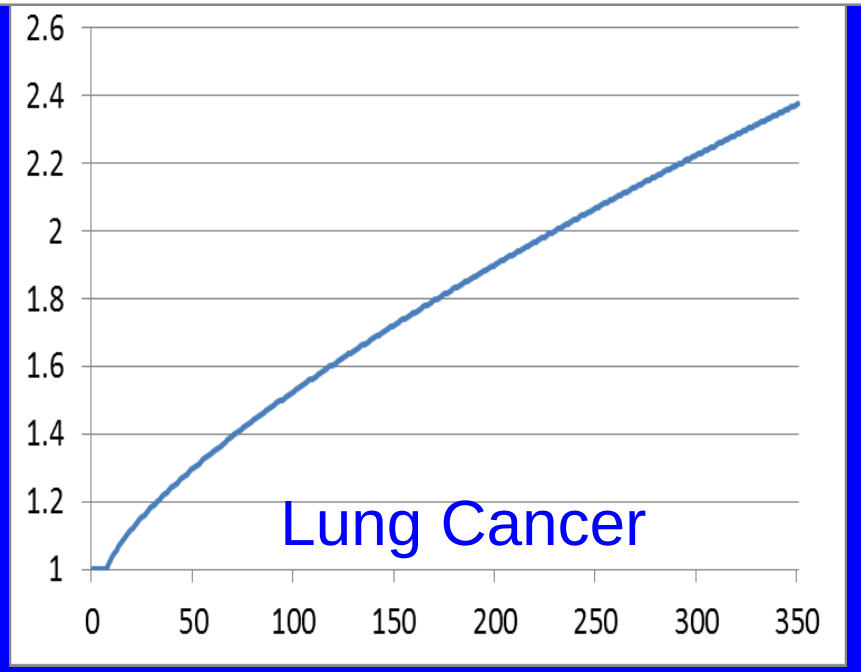
Actual personal exposure

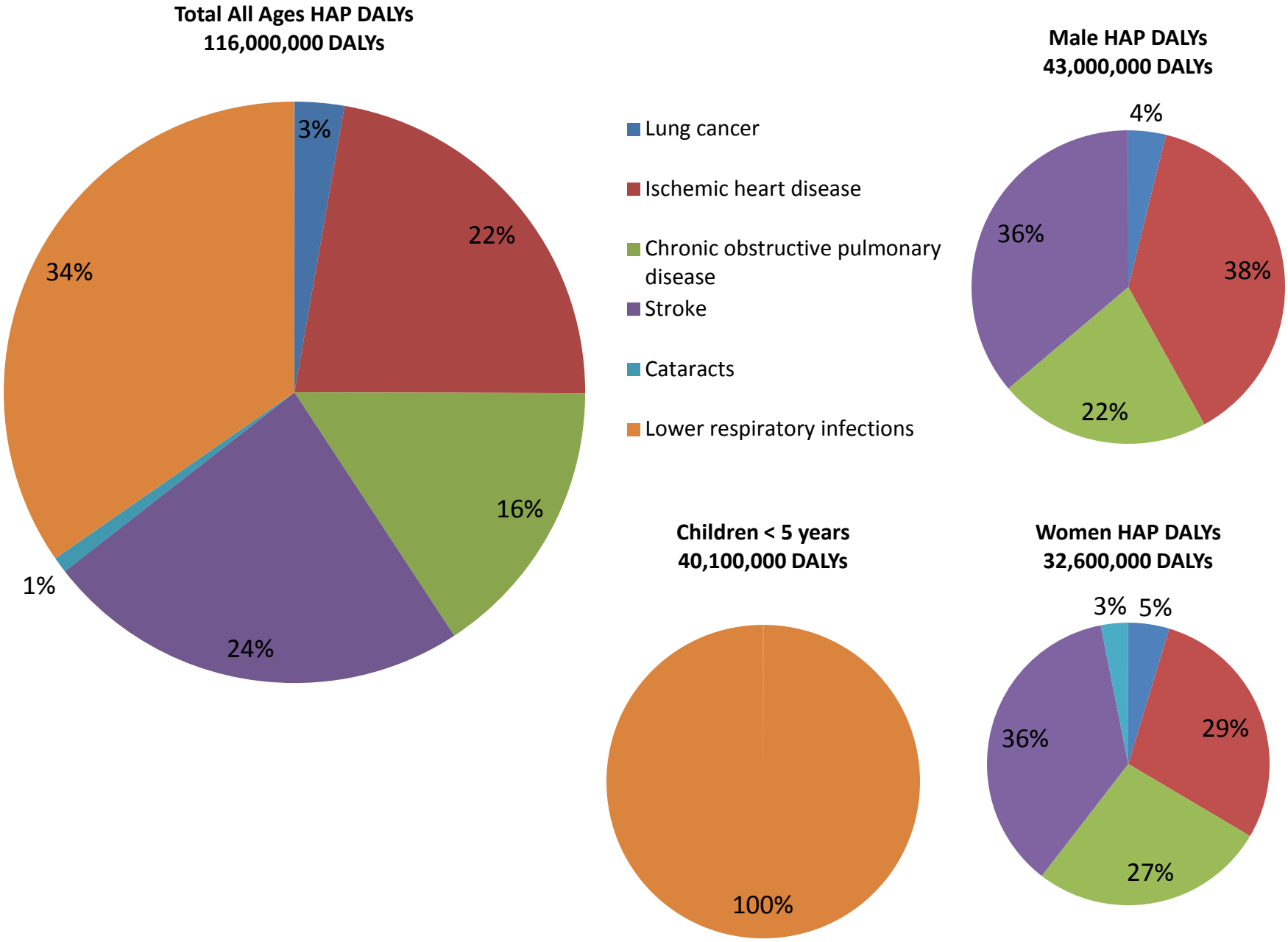
Smith et al, 2011


Stroke
2.2
2
1.8
1.6
1.4
1.2
1
0
50
100
150
200
250
300


ALRI
3.5
3
2.5
2
1.5
1
0
50
100
150
200
250
300
350


Ischemic Heart Disease
1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1
0
50
100
150
200
250
300
350


Lung Cancer
2.6
2.4
2.2
2
1.8
1.6
1.4
1.2
1
0
50
100
150
200
250
300
350


Total All Ages HAP DALYs
116,000,000 DALYs
3%
22%
34%
16%
1%
24%
Lung cancer
Ischemic heart disease
Chronic obstructive pulmonary disease
Stroke
Cataracts
Lower respiratory infections
Male HAP DALYs
43,000,000 DALYs
4%
36%
38%
22%
Children < 5 years
40,100,000 DALYs
100%
Women HAP DALYs
32,600,000 DALYs
3%
5%
36%
29%
27%

Good things about the IERs

- Allow extrapolation for AAP impacts with smoking used to anchor the upper end
- Allow interpolation for HAP with diseases for which there are few direct data
- Allows use of common low counterfactual, which is not possible with standard meta-analytic results.
- Link combustion particle exposures from many sources – adds plausibility

Worrisome things about the IERs

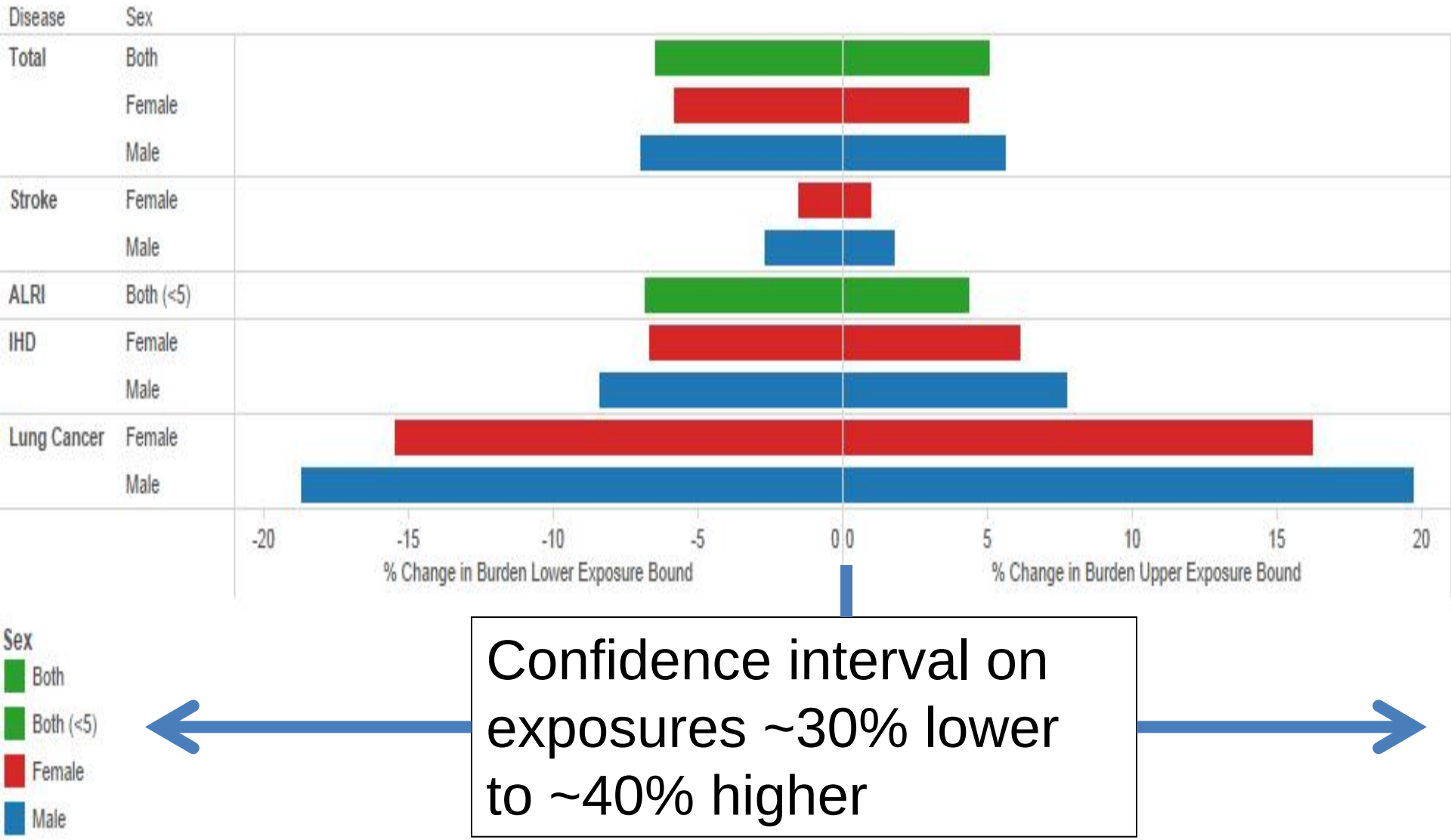
- Ignore differences in particle composition
- Ignore differences in associated pollutants
- Ignore difference in exposure patterns
- Ignore differences in populations studied
- Ignore differences in exposure misclassification among exposure types
- And more

Two striking aspects of IERs - #1

- Varying degree of flatness within the exposure ranges typical in HAP
  - Most flat: Stroke and IHD
  - Intermediate: ALRI
  - Least flat (most linear): Lung cancer
- Need to bring exposure to low levels to achieve anything like full health benefits
  - Achievable with gas or electricity, but only if used 100%
  - Not yet achievable with available biomass and coal stoves

Two striking aspects of IERs - #2

- Although better exposure assessment is needed for every study, if we believe the flatness of the curves,
  - Imprecise exposure assessment at high levels need not worry us as much
  - As imprecision/bias at levels below 100 ug/m3, where the curves are steepest



Confidence interval on exposures ~30% lower to ~40% higher

Methodological issues

- AAP studies, upon which the low end of the IERs are based, do not measure personal exposure.
- This is ok for the epi, which is comparison of changes in exposure vs changes in health
- But perhaps not for interpretations, such as risk assessments, that derive absolute risks from absolute exposures
- Reasonable concern that differential exposure misclassification may occur in the implied relation between ambient monitors and actual personal exposure, particularly at low levels.

Methodological issues, cont.

- The standard practice of transferring RR from epi studies as the vertical axis may not be appropriate for risk assessments
- Actual populations have a wide range of exposures from all four sources plus others (occupational, streetside, etc), often partly correlated
- Background disease rates also vary by exposure
- May need to switch to total exposure estimates for the x-axis and absolute risk for the y-axis.
- Certainly needs to be tried before applying IERs to outdoor air pollution policy

Implications for IAQGs - ALRI

- The IER for ALRI is based primarily on personal monitoring in children.
- Thus, it does not rely on anchoring by smoking
- Or suffer the problems of exposure misclassification in AAP studies
- It is, however, based on only one study and thus needs to be bolstered by others, which
- Fortunately are in progress in Africa and Asia.

Implications for IAQGs - adult

- Although there remain uncertainties about the shape of the IERs at the low end,
- Because of the upper end anchoring by smoking for adult outcomes, there must be considerable flattening in the intermediate levels.
- More work is needed to pin down exactly where this flattening ends, but
- We are confident presently to say that PM2.5 levels must reach down at least to WHO IT-AQGs (<35 ug/m3) to be acceptable for health, ie
- Very clean cooking is needed.

Thank you