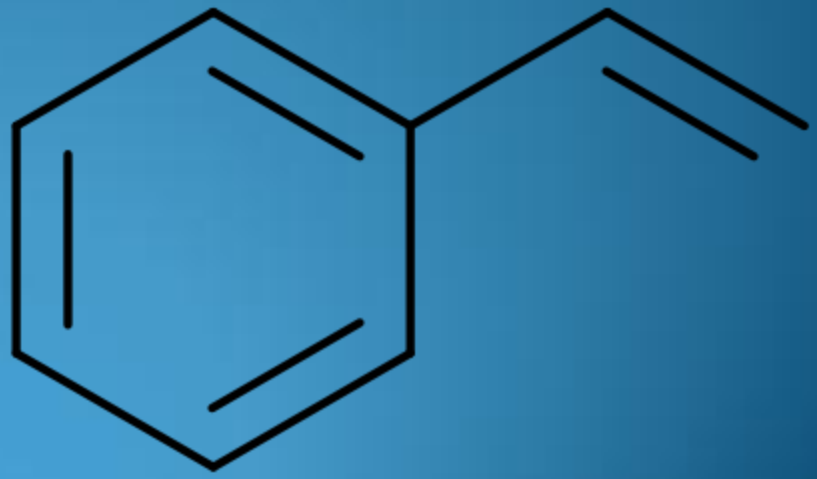
Lung Cancer Mortality: Worker Exposed to Styrene, Ethylbenzene, or Naphthalene

James J. Collins, PhD

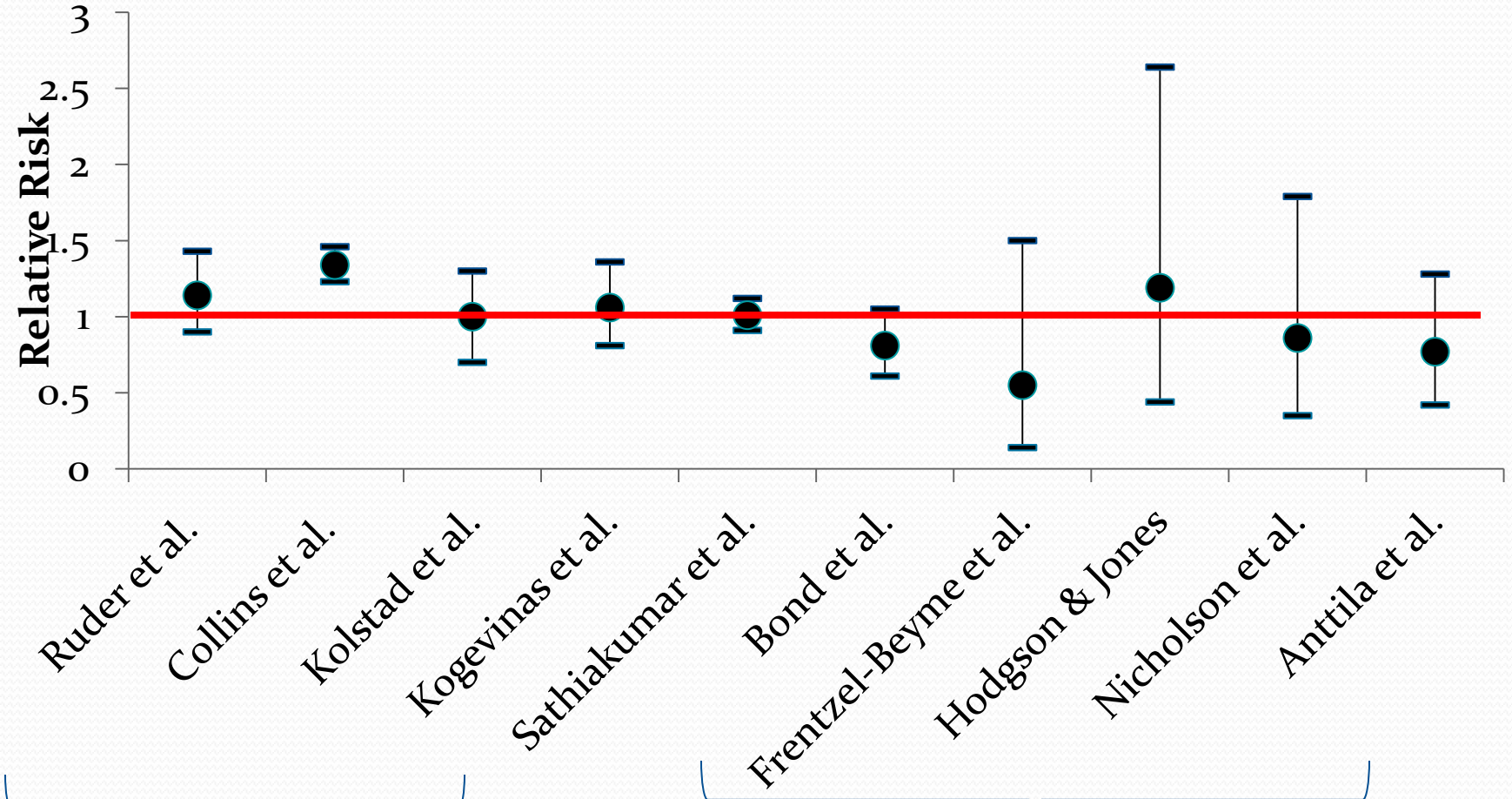
Styrene – Lung Cancer



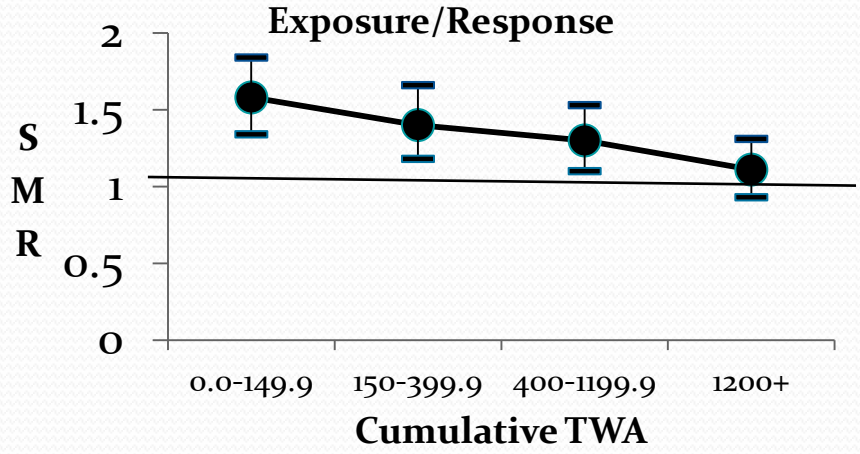
Styrene Epidemiology

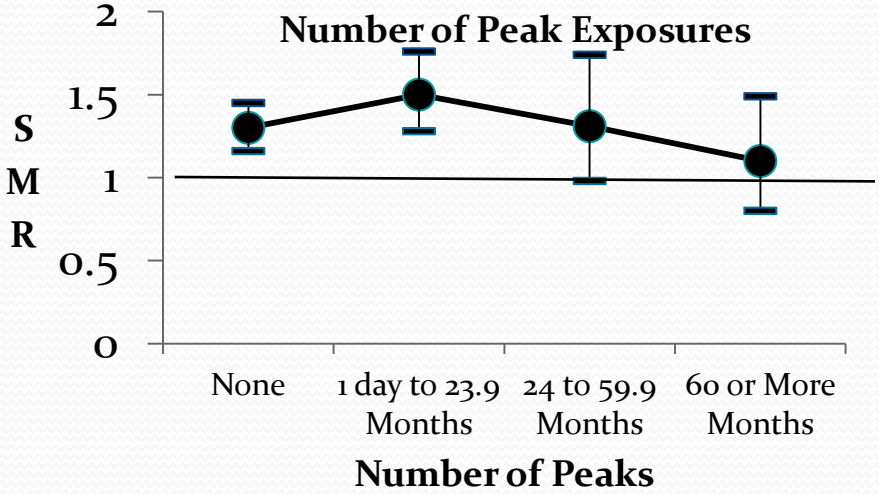
- Epidemiology studies focus on 3 industries:
  - Styrene-butadiene rubber,
  - Reinforce plastics from styrene, and
  - Styrene monomer /polymer production
- IARC 2002 - "possibly carcinogenetic to humans" – Category 2B
  - ***Concern - lymphatic and hematopoietic tissues cancers in epidemiology studies***
  - "The studies of glass fibre-reinforced plastics workers are the most informative ….because these workers had higher styrene exposures and less potential for exposure to other substances than the other cohorts studied." (519)

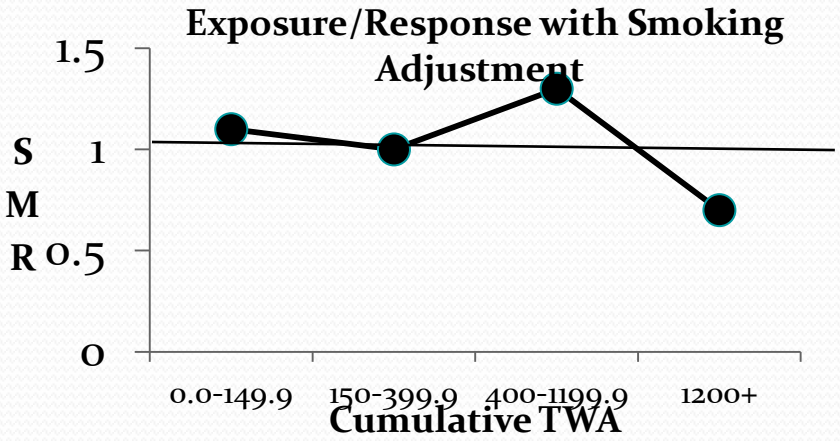
Relative Risks for Lung Cancers

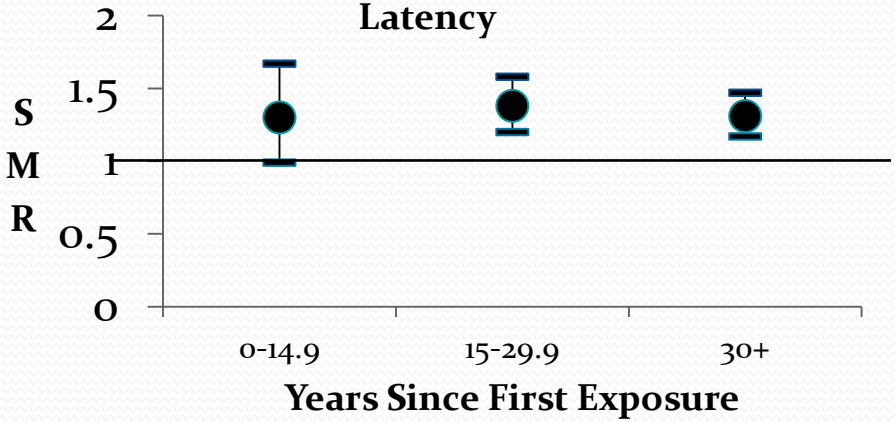


Lung Cancer (Collins et al.)





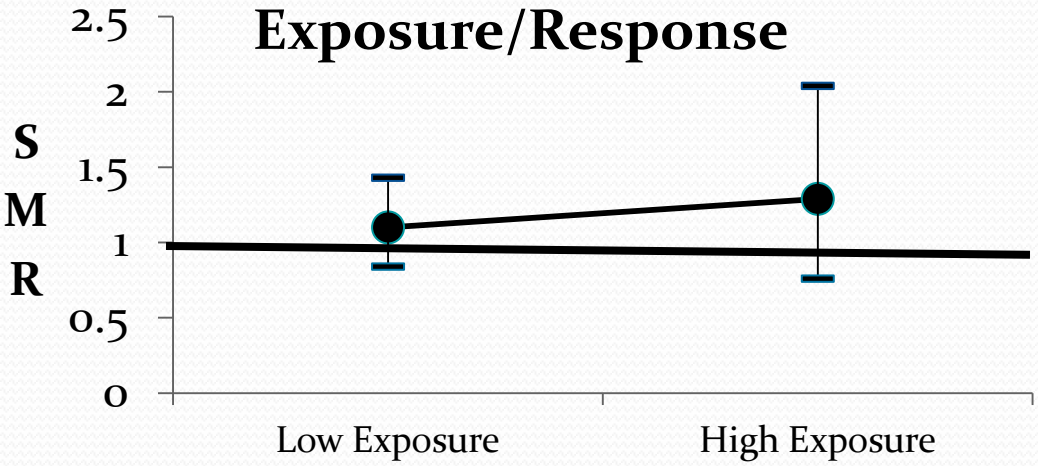


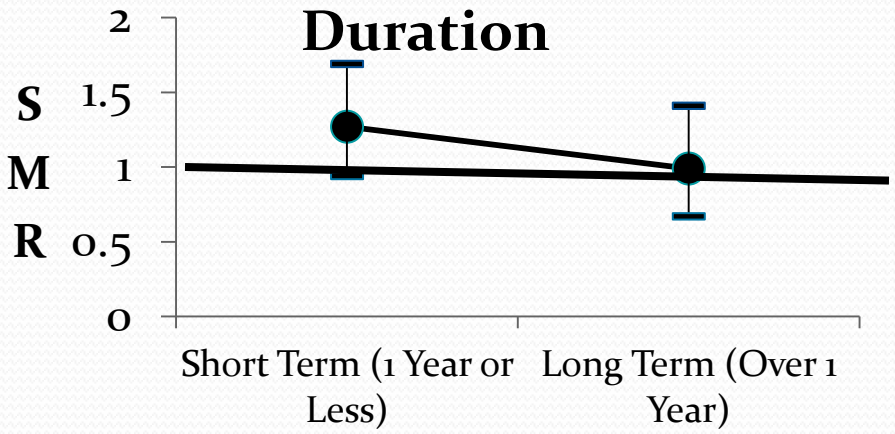


Lung Cancer Etiology – Collins et al.

- Earlier nested c-c study of lung cancer cases indicated smoking cause of lung cancer excess.
- Updated study supported this conclusion:
  - No increased risk with increasing styrene exposure, increasing peak exposures, or latency
  - Increase in cancers (bladder, kidney) & other causes (non-malignant respiratory , heart disease) associated with smoking
  - Adjustment for smoking (bronchitis, emphysema, and asthma) produced flat exposure/response
- Limitation – No formal assessment of smoking in recent update

Lung Cancer (Ruder et al. Study)





Lung Cancer Etiology – Ruder et al.

- Workers **ever exposed** to high levels of styrene had higher lung cancer rates than worker **never exposed** to high levels
- Lung cancer excess limited to short term workers
- Limitations
  - Relatively small study
  - Qualitative exposure assessment
  - Workers classified by longest job held

Lung Cancer (Kogevinas et al.)

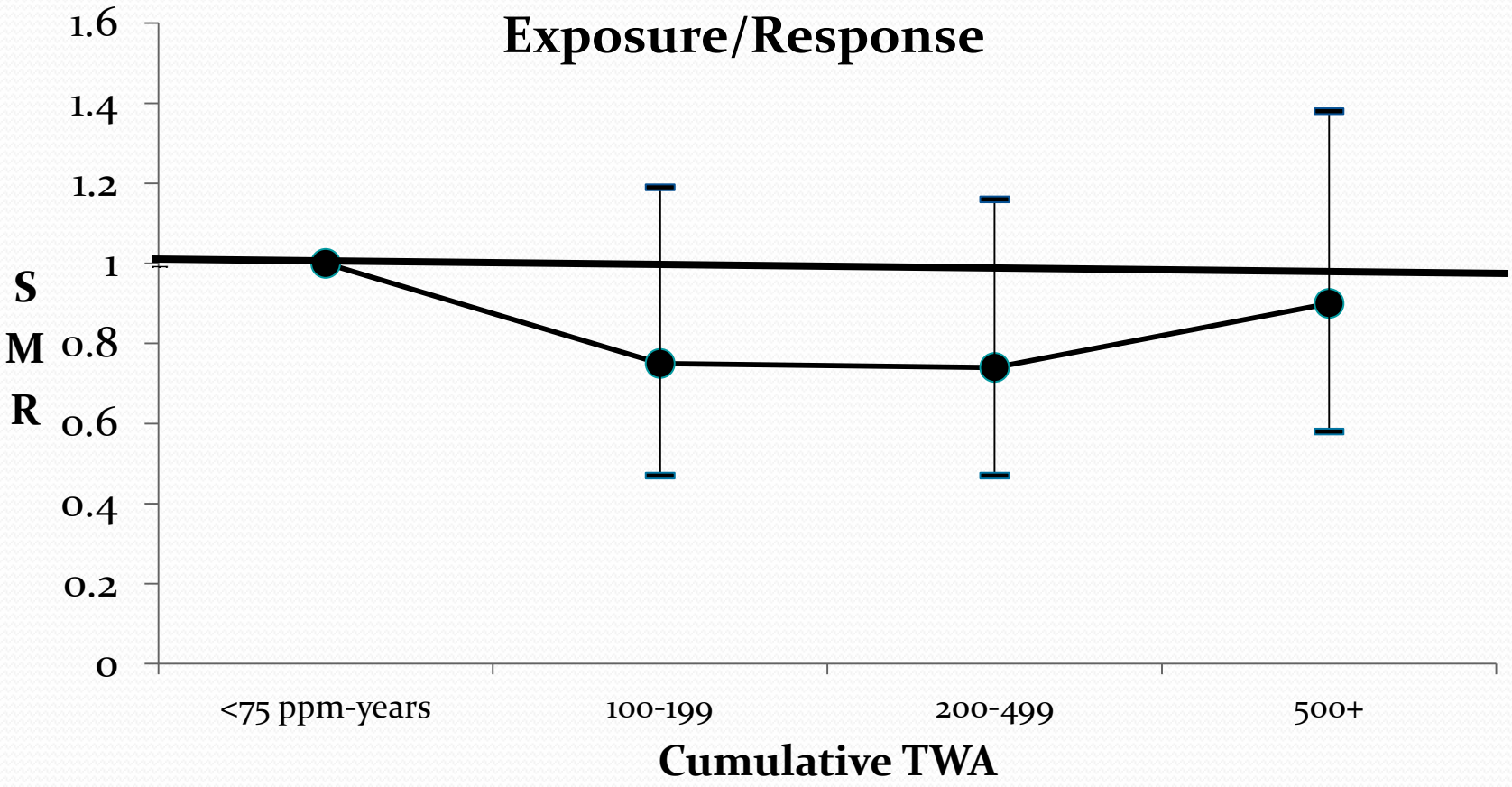


Table 5 (page 258) Poisson regression

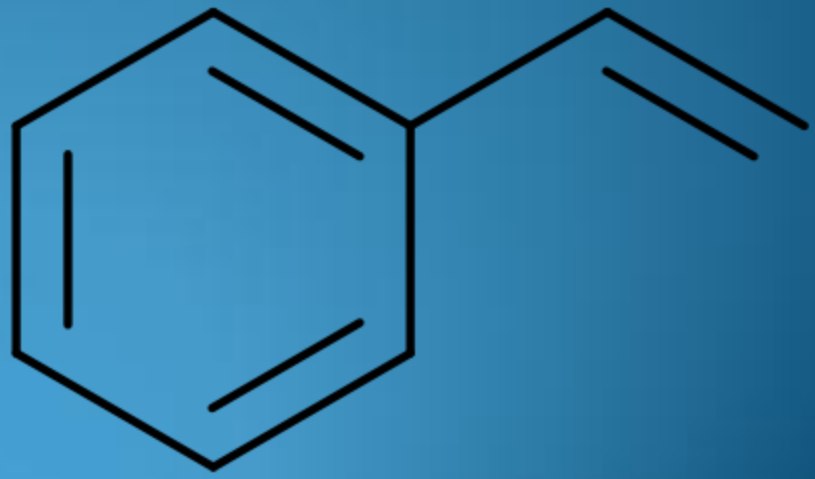
Lung Cancer Etiology – Kogevinas et al.

- No excess of lung cancer observed and no relation with exposure to styrene
- Limitations
  - Exposure assessment
    - may not be comparable across all countries in study
    - workers classified by longest held job

Summary of Previous Studies

- No consistent findings across studies for lung cancer
- Little indication of increasing risk with increasing exposure to styrene
- Evidence of confounding by smoking
- In 2002, IARC review of these studies
  - Did not mention lung cancer as an issue
  - "The increased risks for lymphatic and hematopoietic neoplasms observed in some of the studies are generally small, statistically unstable and often based on subgroup analyses."

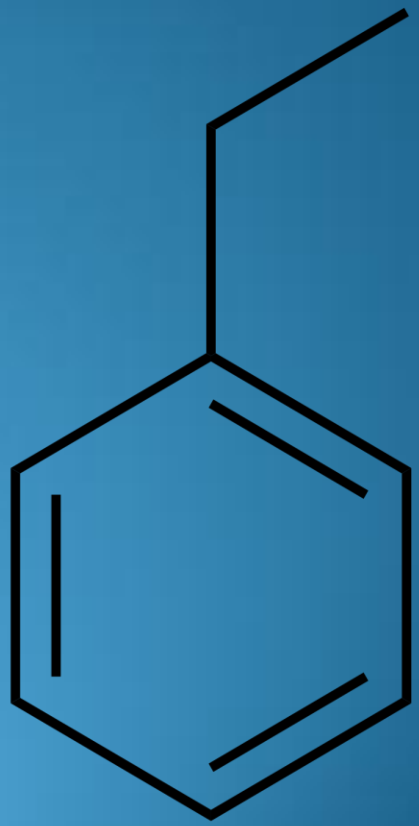
Styrene – Immunological Effects



Epidemiology Styrene Immunological Effects

- Several studies examining leukocytes and lymphocyte subpopulations
  - Limitations – control for smoking, small study size, multiple exposures, limited exposure characterization
- IARC 2002 – "Studies of effects on … immune systems … in exposed workers did not reveal consistent changes." (pages 520-521)

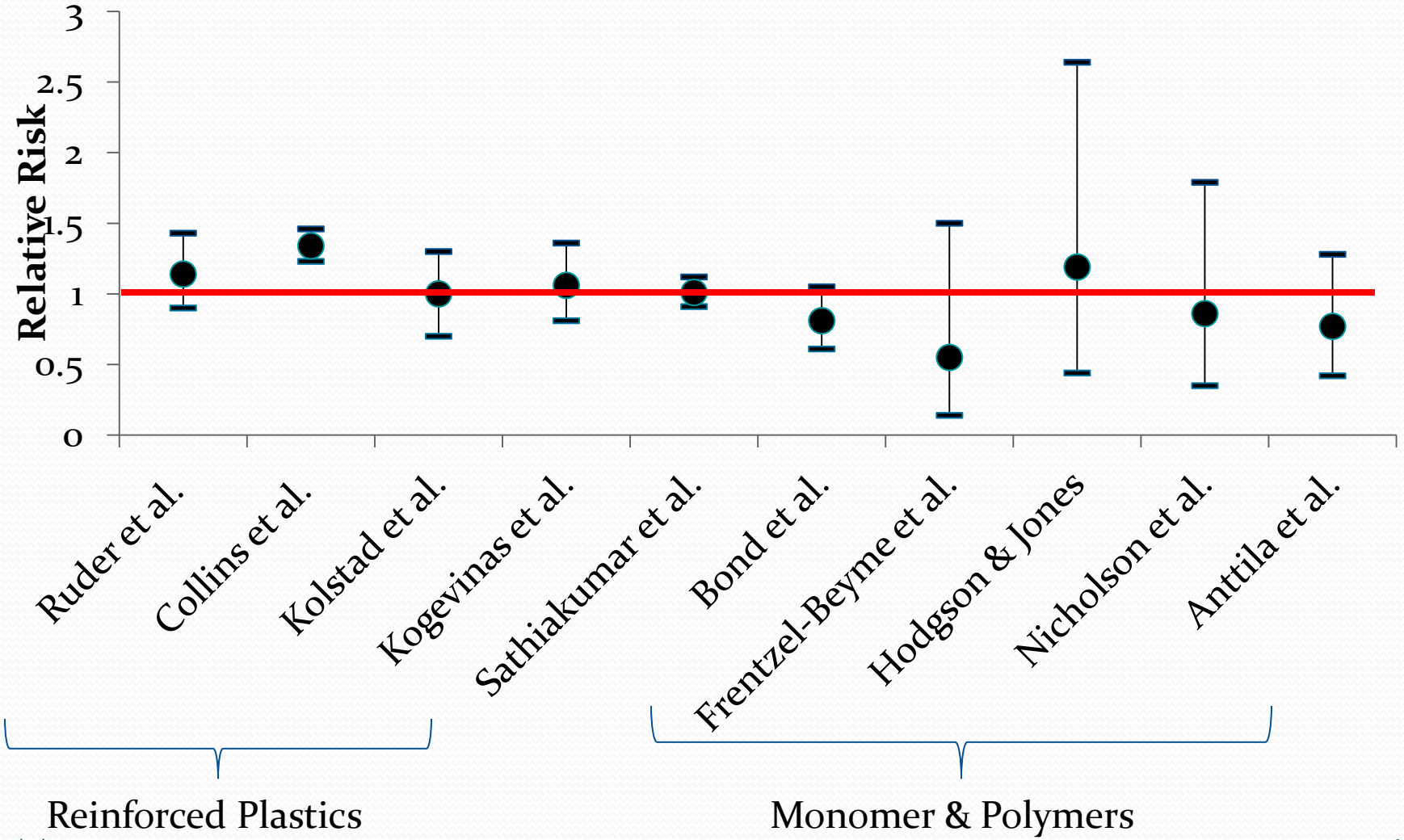
Ethylbenzene



Ethylbenzene Studies

- Two studies on ethylbenzene workers cited by IARC in 2000.
  - However, ethylbenzene is used in the production of polystyrene
    - 5 studies of polystyrene workers

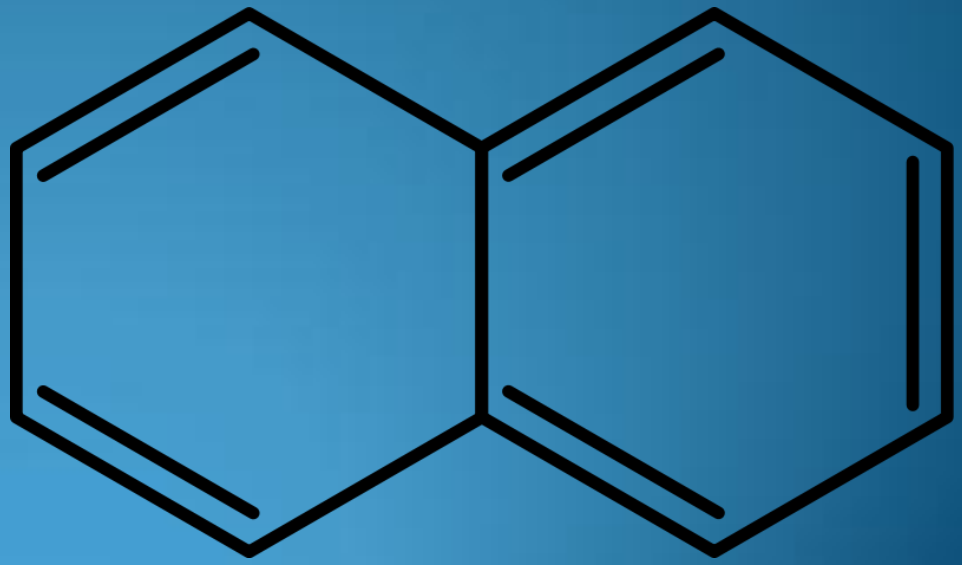
Relative Risks for Lung Cancers



Summary Ethylbenzene

- Few studies of workers with exposure to ethylbenzene
- Studies are relatively small with no quantitative estimates of ethylbenzene
  - no evidence of increased lung cancer

Naphthalene



Naphthalene

- EPA: “Adequately scaled epidemiological studies designed to examine a possible association between naphthalene exposure and cancer were not located. Overall, no data are available to evaluate the carcinogenic potential in exposed human populations
- IARC mentions two case reports
  - Concludes not useful for causal assessment

Additional Slides

Collins et al. Study

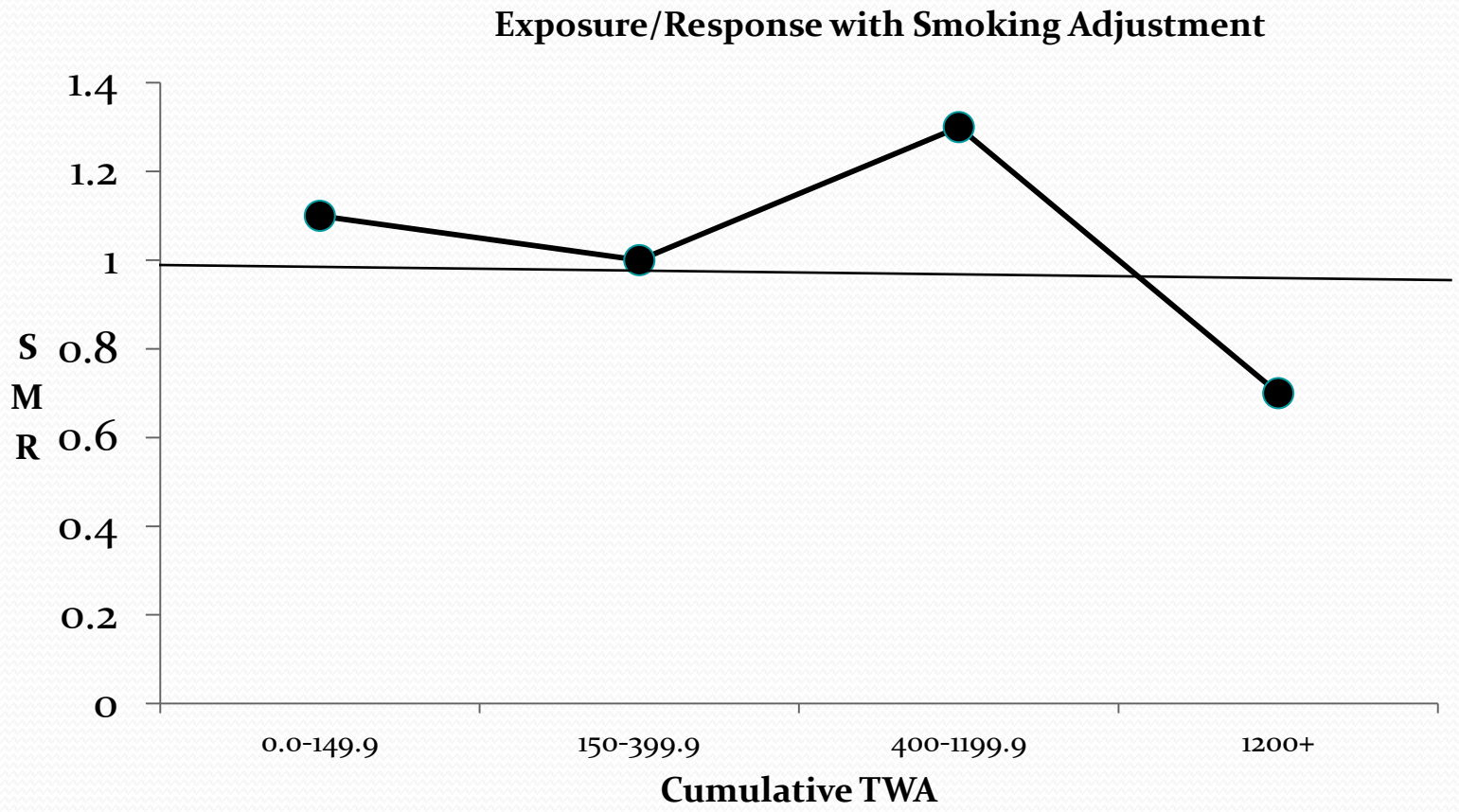
Proportional Hazards Model (Models with Sufficient Fit)

Cause of Death	Hazard Ratio (CI)*	p-value cumulative exposure	p-value model**
All Causes	0.999(0.998-1.001)	0.3183	<0.0001
All Cancer	0.999(0.996-1.001)	0.3737	<0.0001
Respiratory Cancer	0.997(0.993-1.001)	0.1804	<0.0001
Acute Myeloid Leukemia	0.981(0.936-1.027)	0.4017	0.0021
Multiple Myeloma	0.994(0.972-1.017)	0.6194	0.0110
Non-malignant respiratory	1.000(0.995-1.004)	0.9063	0.0191
Diabetes	1.001(0.994-1.008)	0.7187	0.0251

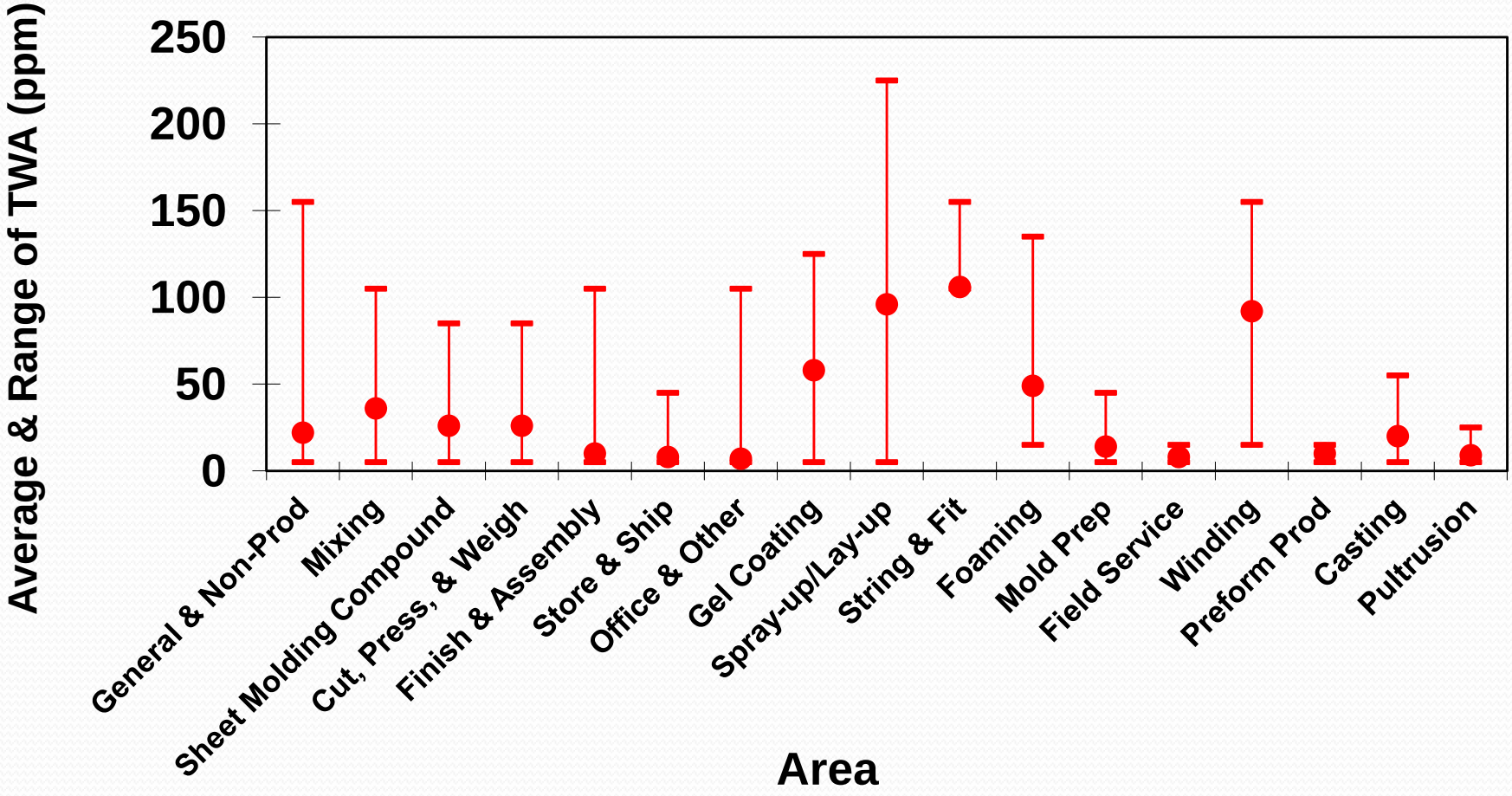
*Hazard ratio for 100 part per million-months

** Time variable is age and models include sex, year of hire, year of birth and cumulative styrene exposure

Collins et al. 2013



Styrene Average and Range of TWA Exposures



Ruder at al. Study

Lung Cancer (Ruder et al.)

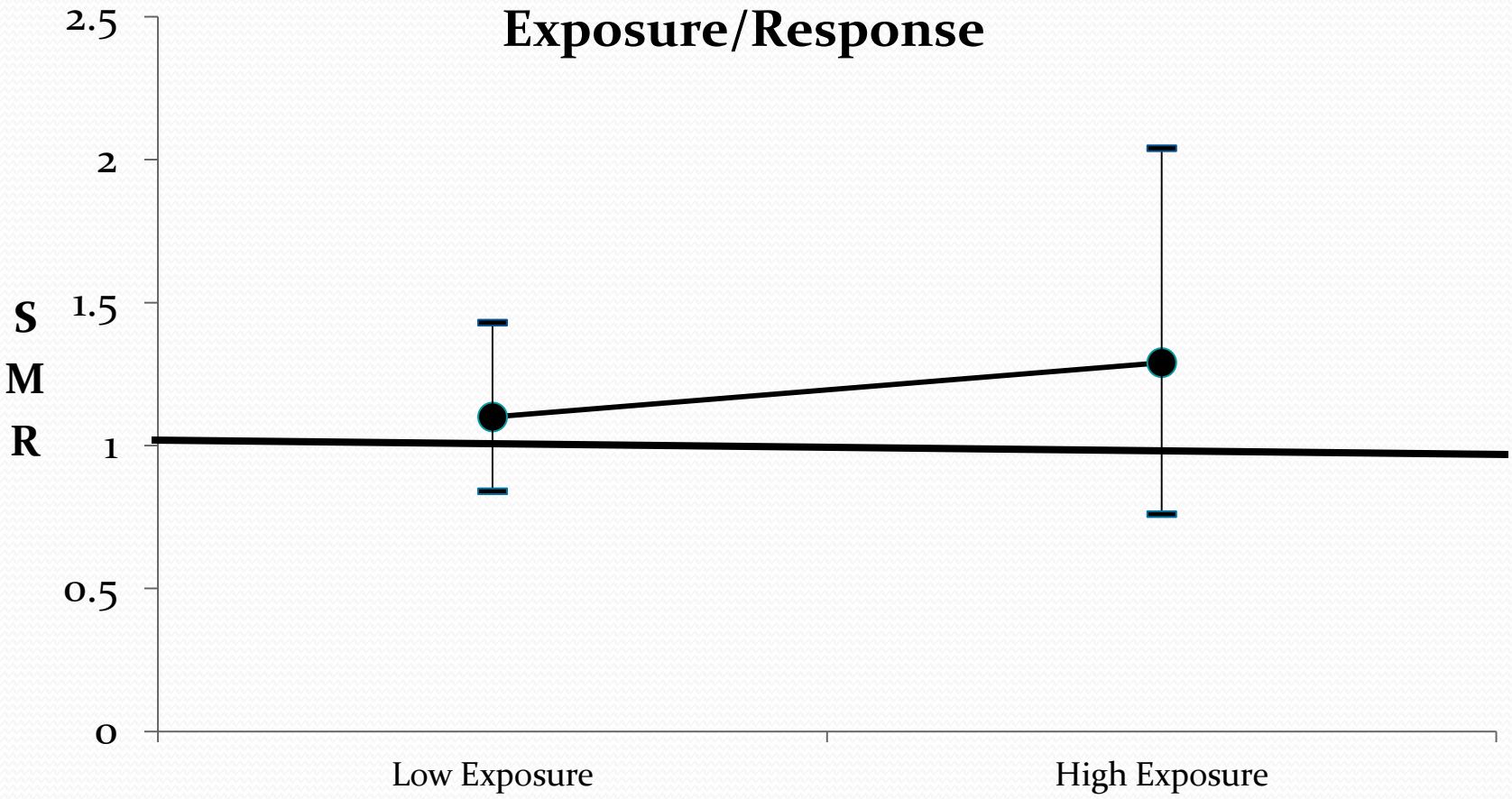


Table III (page 169)

Lung Cancer (Ruder et al.)

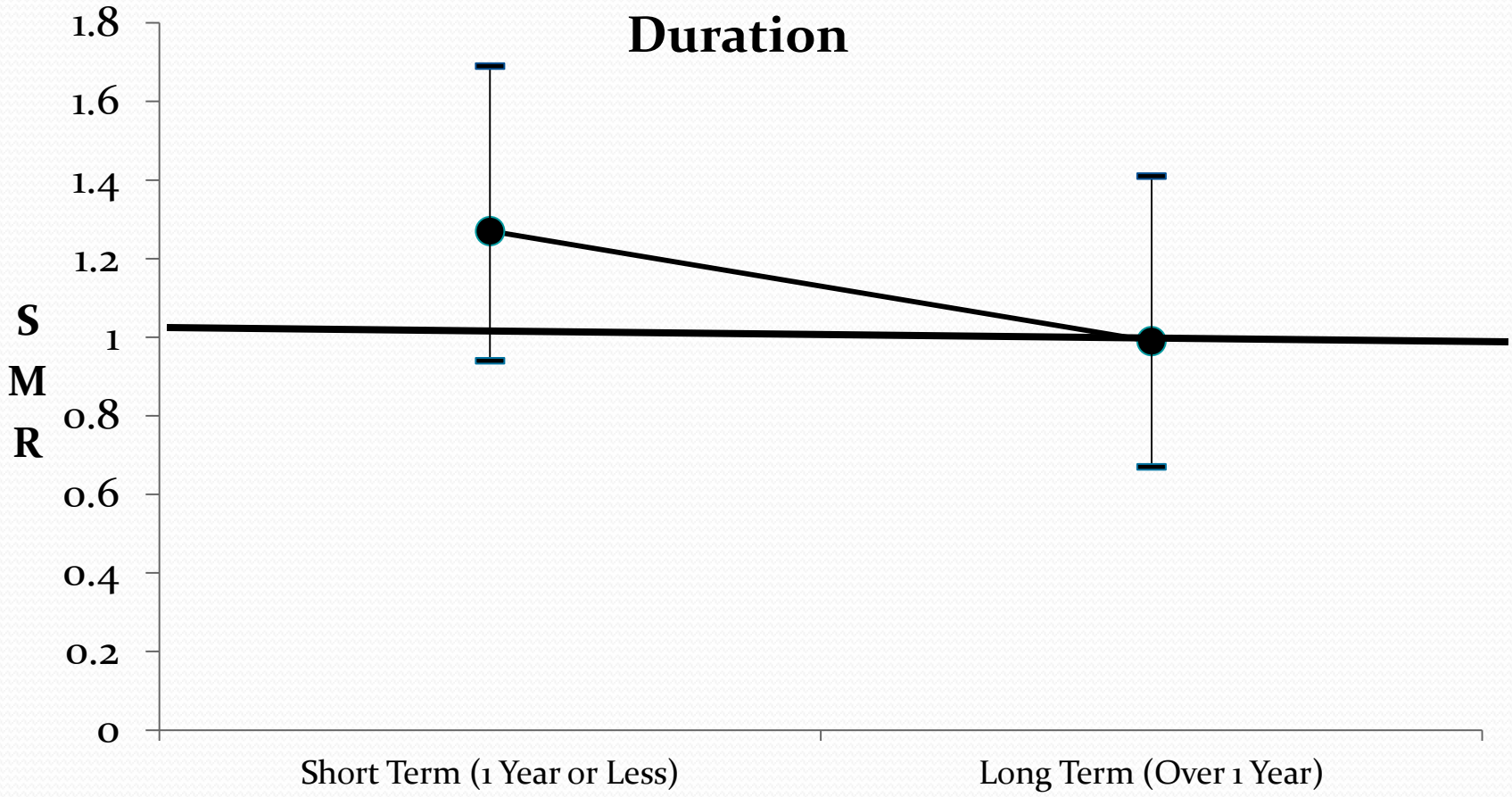


Table III (page 169) and Table IV (page 172)

Kogevinas et al. Study

Lung Cancer

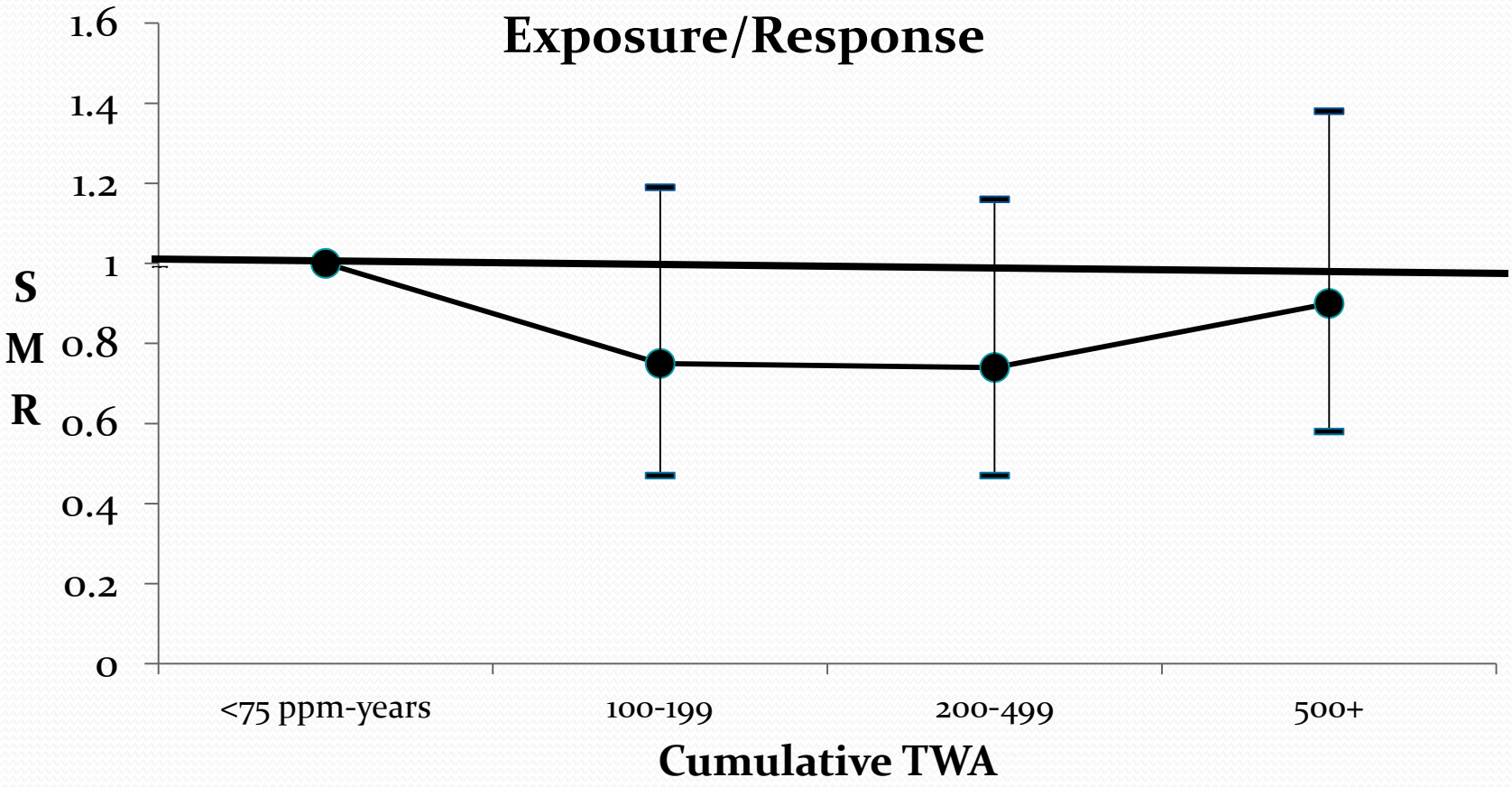


Table 5 (page 258) Poisson regression

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