Dioxin and Cancer: A Critical Review by Cole et al., 2003

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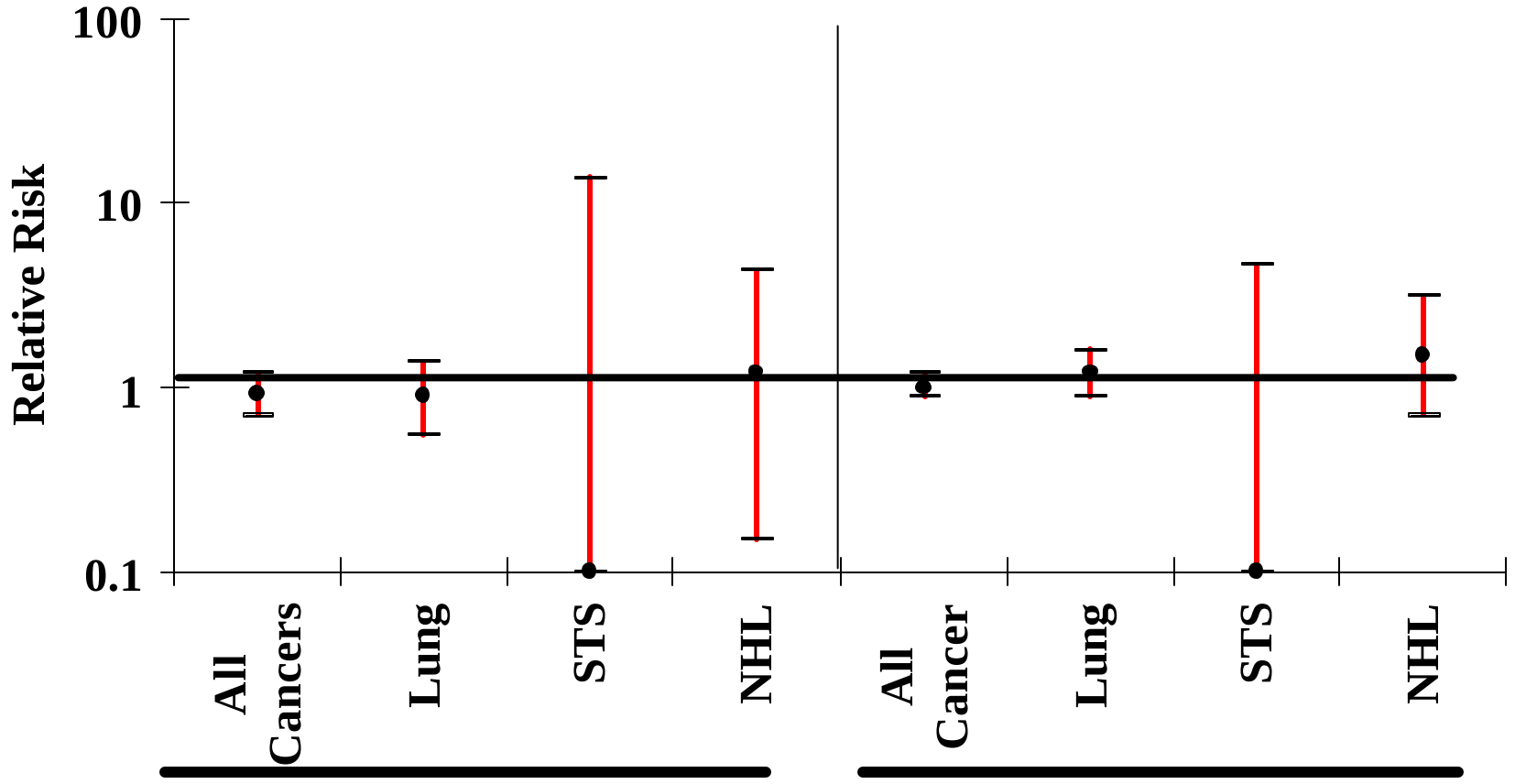
Overview of Finding in Cancer Epidemiology of Dioxin Exposure

- Exposure-response observed for all cancers combined in some studies
- However, little consistency in specific cancer sites across studies regardless of exposure

- Pluripotential Carcinogen
  - "This lack of precedent for a multi-site carcinogen without particular sites predominating means that the epidemiology data must be treated with caution…" – IARC, 1997
  - "There is …no single chemical that is known to cause cancer at many organ sites" Cole et al., 2003
  - Confounding with other occupational exposures (e.g., aromatic amines, asbestos), smoking or socio-economic status could account for these findings
  - Some sub-groups have increased cancer rates, but studies overall do not show increased cancer rates.

Combined Cancer Rates for Most of the Dioxin Studies

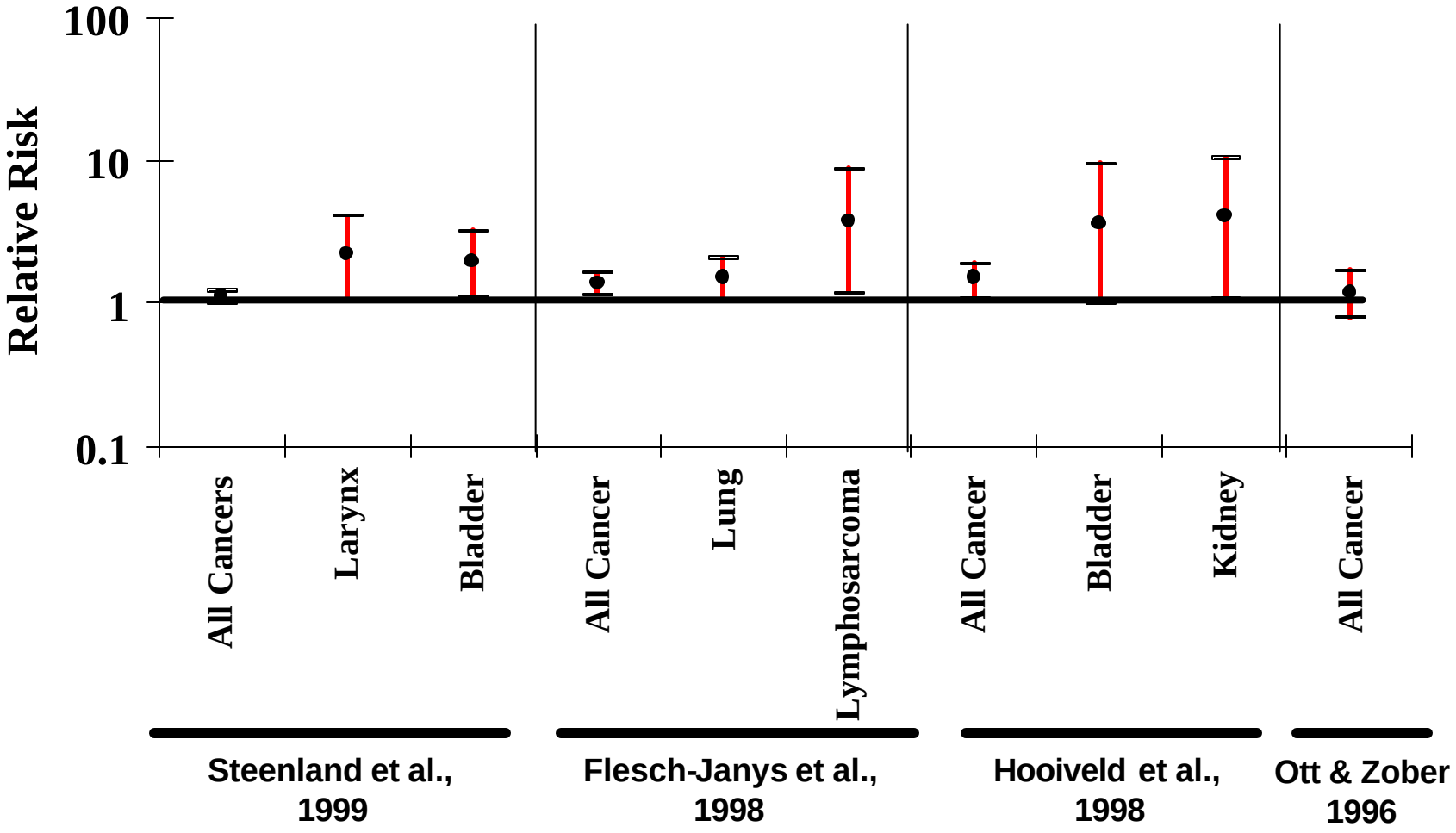


Kogevinas et al., AJE, 1997
(20 or more exposure years)

Bertazzi et al., Epi. 2001
(Zones A and B)

- Lack of consistency of cancers across studies
  - Reason why IARC judged epidemiology data to be limited
  - While total cancer rates elevated in some studies and related to dioxin exposure, no cancer site was consistently elevated across all or most studies

Cancer Rates for Selected Dioxin Studies



Conclusions

- A pluripotential carcinogen lacks biological plausibility from both a toxicological and epidemiological persppective.
- Lack of consistent findings at specific cancer sites across studies
  - wide ranging confounding exposures could account for the inconsistent tumor specific excess from study to study
- “The long-term accumulation of negative, weak, and inconsistent findings suggests that TCDD eventually will be recognized as not carcinogenic for humans.” Cole et al., 2003.