Diesel Exhaust Epidemiology

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Relevant sources in Oregon

- Trucks
- Buses
- School buses
- Locomotives
- Power generators
- Specialty equipment
  - Construction
  - Material handling

Life-cycle/ equipment turnover is variable and reliable data is not available for Oregon

Defining issues in risk assessment

- Rodent data on diesel are not considered suitable models for humans at low exposures
- Roles of particles and other exhaust constituents not known
- Possible confounding by smoking, radon, metals, and asbestos exposure in occupational epi studies
- Occupational exposure is not representative of general population and vulnerable subgroups
  - Low dose extrapolation necessary

US EPA Approach

- Preamble to IRIS Toxicological Reviews:
  - Quantitative measures of dose and response are required
  - Then all other factors being equal
    - Epidemiologic studies are preferred over animal studies
    - Among animal models, use those that respond most like humans
    - Use studies by relevant route of human environmental exposure
    - Use studies with longer exposure duration and follow-up
    - Use studies with multiple exposure levels
    - Use studies with adequate power to detect effects at lower levels

Adapted from Vincent Cogliano remarks (2014) HEI Diesel Workshop

Defining Issues in Epi Studies

- Exposures are difficult to precisely quantify because of its complex composition
- Many components are also emitted from other sources or formed through atmospheric photochemical processes
- No single constituent serves as a unique marker of exposure
- Fine particles and elemental carbon have been used a surrogate measures
- EC used in most health studies

Exposure Ranges

- Average trucking exposures: 5 $\mu g/m^3$
- Average railroad exposures: 50 $\mu g/m^3$
- Average underground mine : 100 $\mu g/m^3$
- Average dockworkers: 10 $\mu g/m^3$
- Average US urban ambient air exposure:

  1.0 $\mu g/m^3$ (old diesel, US EPA 1994)
- New diesel estimate for workers: 0.1 $\mu g/m^3$

Available Epidemiological Studies

Old diesel technology (pre-2008) and lung cancer

1. Trucking workers
   - Multiple studies available with convergent estimates
   - Garshick et al. 2012 corrected healthy worker survivor bias present in the earlier studies
2. Railroad workers
   - Evidence of strong negative confounding by duration
   - Probably related to healthy worker survivor bias
   - Data being reanalyzed by NIOSH
3. Miners
   - Multiple studies in various sectors
   - NIOSH/NCI DEMS study (*analysis in progress*)

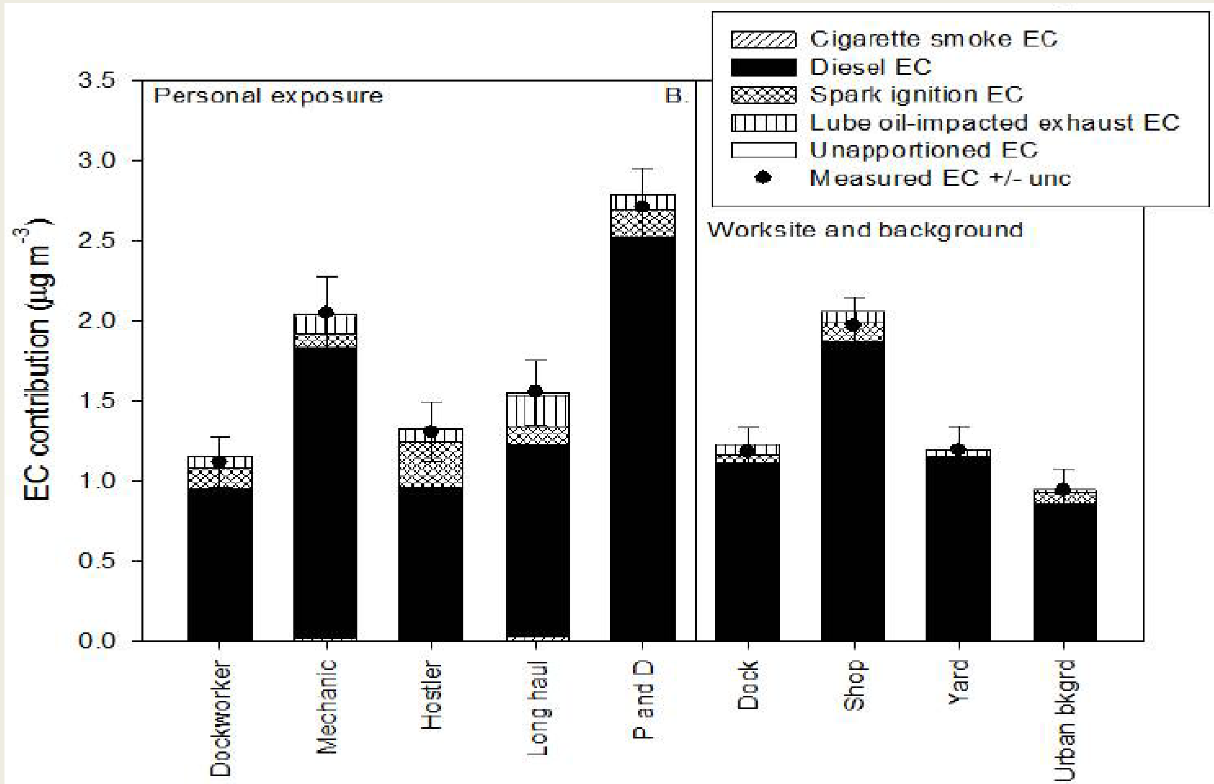
Garshick Trucking Study
Mortality Ratios and Cumulative EC

5-yr lag Cumulative EC	Cohort age 40+ N=31,135		Mechanics Excluded* N=29,324	
μg/m³-months	Lung cancer deaths	Hazard Ratio 95%CI	Lung cancer deaths	Hazard Ratio 95%CI
<371	122	reference	122	reference
371 to < 860	193	1.30 1.01, 1.68	191	1.31 1.01, 1.71
860 to <1803	208	1.35 1.01, 1.81	202	1.38 1.02, 1.87
≥1803	256	1.36 0.98, 1.89	226	1.48 1.05, 2.10
Trend		P=0.39		P=0.16

*Less confidence in historical estimation in mechanics due to change in job duties.
All models adjusted for calendar year of follow-up, race, census region

EC as a Marker of Diesel Exhaust:

Diesel freight terminal in St Louis, August 2003



N	14	7	4	21	18	14	6	6	9
%	85	89	73	78	93	94	94	96	91

Chemical mass balance approach using organic tracers (OCEC and TD-GCMS)

Sheesley et al. *J Expo Sci Environ Epidemiol* 2009; 19(2):172-86.

Vermeulen et al. (2014) Meta-analysis

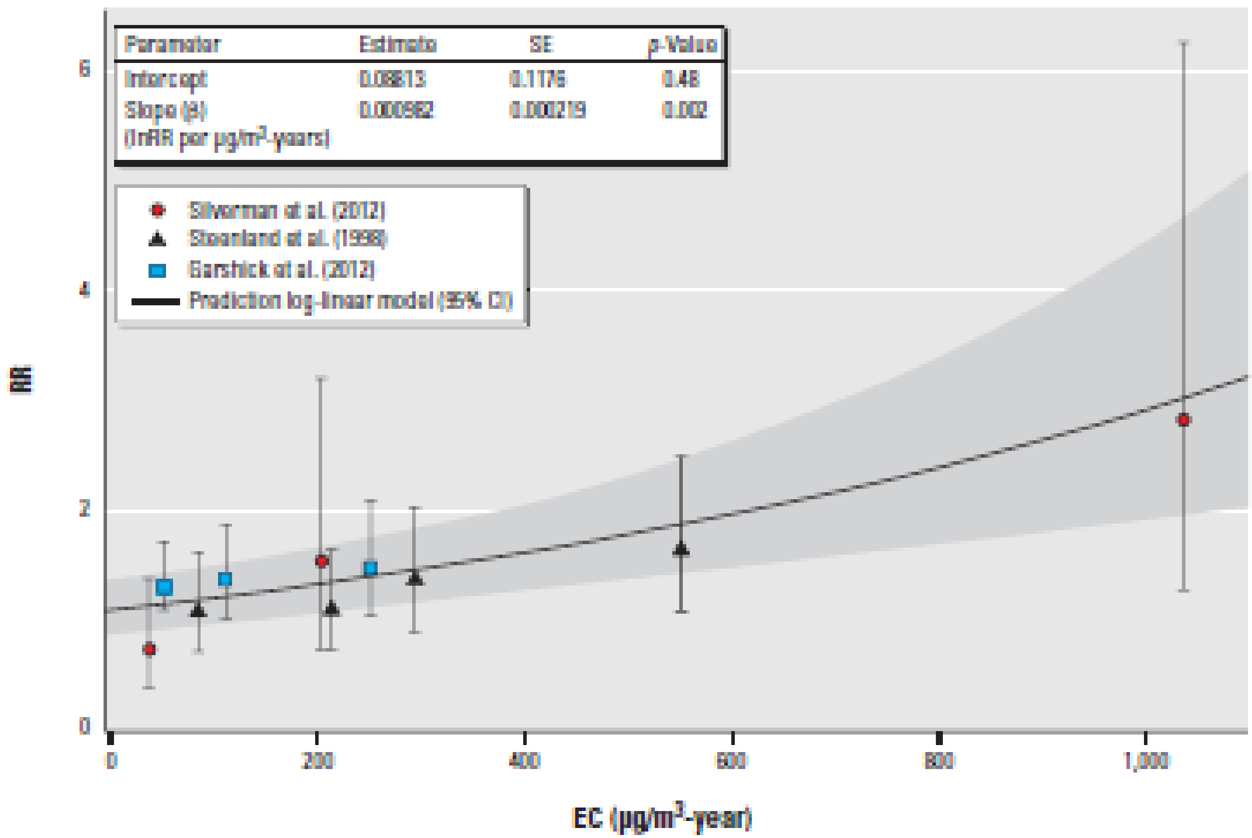


Figure 1. Predicted exposure–response curve based on a log-linear regression model using RR estimates from three cohort studies of DEE and lung cancer mortality. Individual RR estimates [based on HRs reported by Garshick et al. (2012) or ORs reported by Silverman et al. (2012) and Steenland et al. (1998)] are plotted with their 95% CI bounds indicated by the whiskers. The shaded area indicates the 95% CI estimated based on the log-linear model. The insert presents the estimates of the intercept and beta slope factor, the SE of these estimates, and the associated *p*-values.

Vermeulen et al. *Environ Health Perspect* 2014; 122(2):172-7

Vermeulen et al. (2014) Meta-analysis

Alternative low-dose extrapolations have been considered

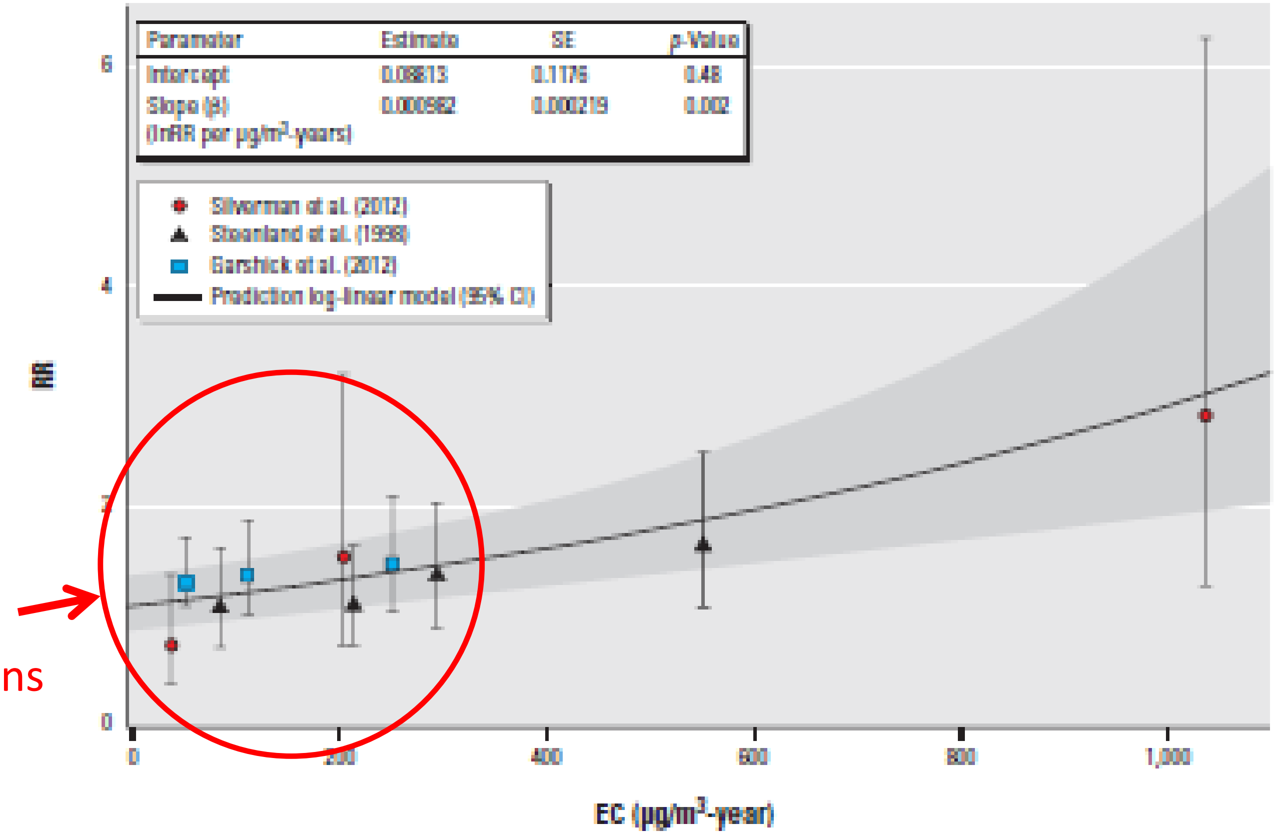


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Table 1. Exposure–response estimates (lnRR for a 1-μg/m³ increase in EC) from individual studies and the primary combined estimate based on a log-linear model.

Model[a]	Intercept	β (95%CI)
All studies combined	0.088	0.00098 (0.00055, 0.00141)
Silverman et al. (2012) only	–0.18	0.0012 (0.00053, 0.00187)
Steenland et al. (1998) only	–0.032	0.00096 (0.00033, 0.00159)
Garshick et al. (2012) only	0.24	0.00061 (–0.00088, 0.00210)

[a]Log-linear risk model (lnRR = intercept + β × exposure). Exposure defined as EC in μg/m³-years.

Table 2. Excess lifetime risk per 10,000 for several exposure levels and settings, United States in 2009.

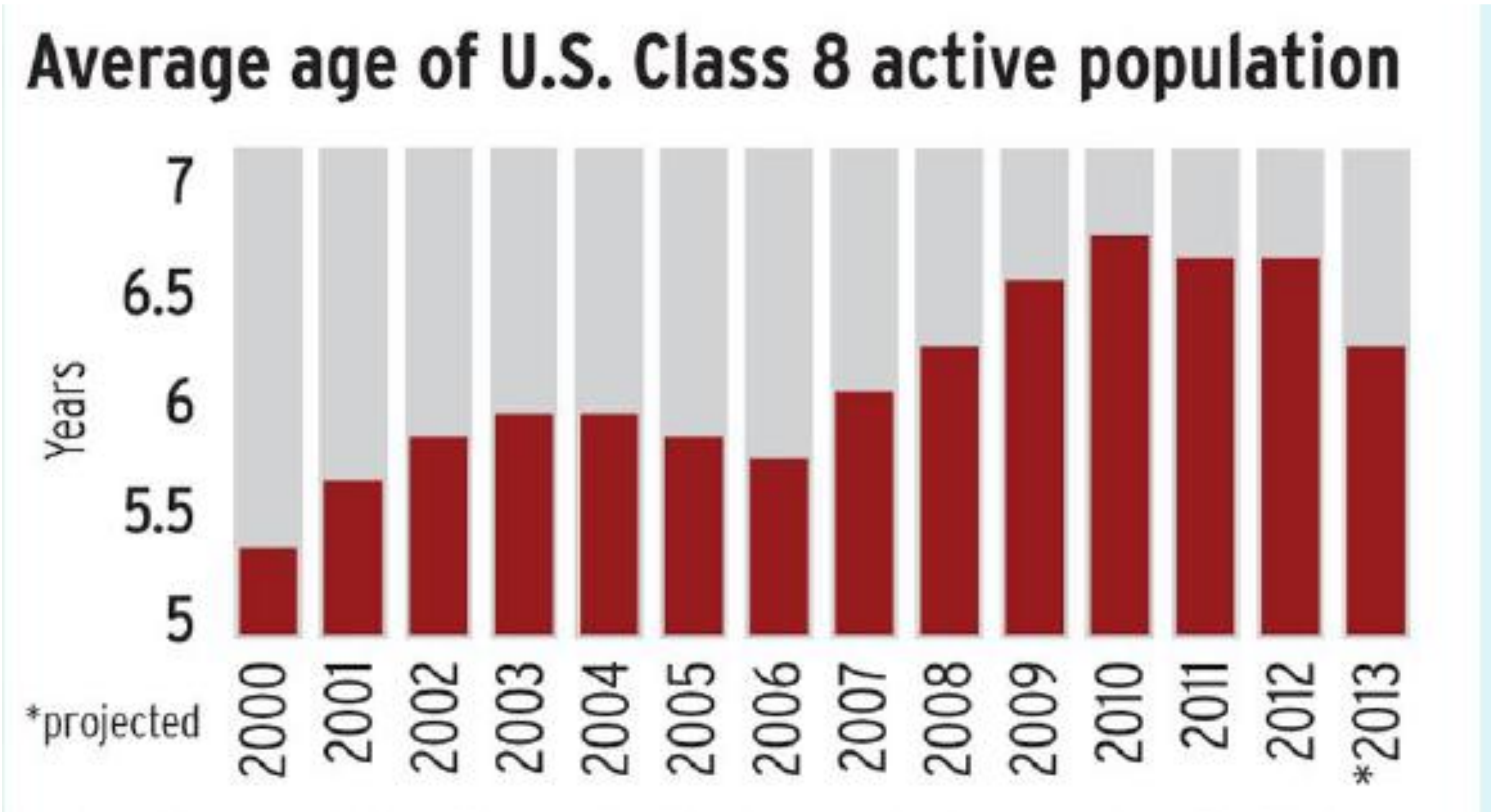
Exposure setting	Average EC exposure (μg/m³)	Excess lifetime risk through age 80 years (per 10,000)
Worker exposed, age 20–65 years	25	689
Worker exposed, age 20–65 years	10	200
Worker exposed, age 20–65 years	1	17
General public, age 5–80 years	0.8	21

Based on linear risk function, lnRR = 0.00098 × exposure, assuming a 5-year lag, using age-specific (5-year categories) all cause and lung cancer mortality rates from the United States in 2009 as referent.

New Diesel Technology studies

- No epidemiological studies available
- Latency: relatively few years of follow-up in currently exposed groups
- Challenges to measure ultrafine fraction
  - 1.0 um to 0.01 um diameter
- What if low-dose linearity is a function of particle number rather than mass?
- If less risk, more difficult to quantify

Old and New Diesel



Source: Calpin and Plaza-Jennings, American Truck Dealers, Feb 2014, "A Look Back at EPA's Cost and Other Impact Projections for 2004-2010 Heavy-Duty Truck Emissions Standards"