CORRESPONDENCE

RE: The Diesel Exhaust in Miners Study (DEMS): A Nested Case-Control Study of Lung Cancer and Diesel Exhaust

Because our original publication (1) generated considerable interest over the past two years, we now provide additional data from our nested case-control study that are valuable in evaluating the relation between diesel exhaust exposure and lung cancer. Here we include results based on alternative exposure metrics (Table 1) and alternative approaches for adjusting for cigarette smoking as a confounder (Table 2), for comparison with results that appeared in Table 3 of Silverman et al. (1).

In Table 1, we estimate the lung cancer risk associated with average respirable elemental carbon (REC) intensity and cumulative REC, lagging exposure by 15 years, based on three alternative exposure metrics (2–6). The ".58" REC metrics assume that changes in REC over time are not directly proportional to changes in carbon monoxide (CO) over time, whereas the original REC metrics assumed direct proportionality (1). The "5-year mean" REC metrics use 5-year averages in CO between 1976 and the last year of the exposure assessment at each mine (1998–2001) and the ratio of horsepower over ventilation before 1976 (when CO measurements were unavailable) in the time trend models to predict historical REC levels. The "median" REC metrics were based on the median of the REC measurements instead of the mean of the REC measurements to derive the 1998–2001 reference values used in the original time trend models. Results based on these alternative exposure metrics closely reflect those originally reported in Table 3 (1), each with consistent positive trends in risk with increasing exposure. Trends tended to be highly statistically significant for cumulative REC and statistically significant or borderline significant for average REC intensity.

In Table 2, we estimate the lung cancer risk associated with average REC intensity and cumulative REC, lagging 15 years, based on three approaches for smoking adjustment. We present odds ratios by increasing exposure levels adjusting for: 1) smoking status (never, former, current smoker) and duration smoked; 2) status and pack-years smoked; and 3) status and both duration and packs/day in the same model. Regardless of the approach for smoking adjustment, we observed consistent highly statistically significant trends for cumulative REC and borderline significant trends for average REC intensity. Results are strikingly consistent with the previously published odds ratios in Table 3 (1).

In conclusion, these sensitivity analyses underscore the robustness of our original findings (1) and provide further evidence that diesel exhaust causes lung cancer in humans.

DEBRA T. SILVERMAN
JAY H. LUBIN
AARON E. BLAIR
ROEL VERMEULEN
PATRICIA A. STEWART
PATRICIA L. SCHLEIFF
MICHAEL D. ATTFIELD

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Notes

Affiliations of authors: Occupational and Environmental Epidemiology Branch (DTS, AEB) and Biostatistics Branch (JHL) and formerly of Occupational and Environmental Epidemiology Branch (RV, PAS), Division of Cancer Epidemiology and Genetics, National Cancer Institute, Bethesda, MD; Institute for Risk Assessment Sciences, Utrecht University, Utrecht, the Netherlands (RV); Stewart Exposure Assessments, LLC, Arlington, VA (PAS); Surveillance Branch (PLS) and formerly of Surveillance Branch (MDA), Division of Respiratory Disease Studies, National Institute for Occupational Safety and Health, Morgantown, WV.

Correspondence to: Debra T. Silverman, ScD, Occupational and Environmental Epidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rm 6E142, 9609 Medical Center Drive, Bethesda, MD 20892 (e-mail: silvermd@mail.nih.gov).

Table 1. Odds ratios and 95% confidence intervals for average and cumulative REC lagged 15 years based on alternative exposure metrics*, †

Exposure metric	".58"			"5-Year Mean"			"Median"		
	Case patients	Control subjects	OR (95%CI)	Case subjects	Control subjects	OR (95%CI)	Case subjects	Control subjects	OR (95%CI)
Average REC intensity									
Quartiles, µg/m³									
0 to < 1	47	187	1.0 (referent)	47	191	1.0 (referent)	47	190	1.0 (referent)
1 to < 6	49	173	1.04 (0.55 to 1.96)	48	161	1.28 (0.68 to 2.41)	52	189	1.10 (0.59 to 2.05)
6 to < 57	35	109	1.46 (0.66 to 3.23)	53	167	1.51 (0.72 to 3.17)	54	167	1.80 (0.86 to 3.76)
≥ 57	67	197	1.99 (0.96 to 4.11)	50	147	2.00 (0.93 to 4.33)	45	120	2.65 (1.22 to 5.75)
			P_{trend} = .0497			P_{trend} = .127			P_{trend} = .017
Cumulative REC									
Quartiles, µg/m³-yr									
0 to < 3	49	157	1.0 (referent)	49	155	1.0 (referent)	49	158	1.0 (referent)
3 to < 72	48	219	0.73 (0.39 to 1.37)	48	226	0.71 (0.38 to 1.31)	50	233	0.71 (0.38 to 1.32)
72 to < 536	40	131	1.48 (0.72 to 3.05)	57	169	1.73 (0.84 to 3.59)	58	172	1.67 (0.81 to 3.45)
≥ 536	61	159	2.34 (1.08 to 5.10)	44	116	2.28 (1.02 to 5.08)	41	103	3.03 (1.35 to 6.79)
			P_{trend} = .004			P_{trend} = .015			P_{trend} = .001

* Adjusted for mine location/smoking status/packs/day combination (surface work only/never smoker, surface work only/unknown/occasional smoker, surface work only/former smoker/< 1 pack/day, surface work only/former smoker/1 to < 2 packs/day, surface work only/former smoker/≥ 2 packs/day, surface work only /current smoker/< 1 pack/day, surface work only/current smoker/1 to < 2 packs/day, surface work only/current smoker/≥ 2 packs/day, ever underground [UG] work/never smoker, ever UG work/unknown/occasional smoker, ever UG work/former smoker/< 1 pack/day, ever UG work/former smoker/1 to < 2 packs/day, ever UG work/former smoker/≥ 2 packs/day, ever UG work/current smoker/< 1 pack/day, ever UG work/current smoker/1 to < 2 packs/day, ever UG work/current smoker/≥ 2 packs/day); history of respiratory disease five or more years before date of death/reference date; and history of a high-risk job for lung cancer for at least 10 years. CI = confidence interval; CO = carbon monoxide; DEMS = Diesel Exhaust in Miners Study; OR = odds ratio; REC = respirable elemental carbon; UG = underground.

† Alternative exposure metrics were defined as:

".58" REC metrics were based on $REC_x = REC_R(CO_x/CO_R)^b$, where R and X refer to estimates for the reference and for other years, respectively, and the constant, b = 0.58, was estimated from the DEMS measurements. This contrasts with b = 1, which assumes changes in REC over time were directly proportional to changes in CO over time, as in Silverman et al. (1).

"5-year mean" REC metrics used five-year averages in CO between 1976 and 1998–2001 and the ratio of horsepower over ventilation before 1976 in time trend models to predict historical REC levels.

"Median" REC metrics were based on the median of the REC measurements to derive 1998–2001 reference values used in the time trend models, instead of the mean of the REC measurements, as in Silverman et al. (1).

Table 2. Odds ratios and 95% confidence intervals for average and cumulative REC lagged 15 years with alternative approaches for smoking adjustment

Exposure metric	Case subjects	Status: duration*, †		Status: pack-years‡	Status: packs/day, duration†, §
		Control subjects	OR (95%CI)	OR (95%CI)	OR (95%CI)
Average REC intensity					
Quartiles, µg/m³					
0 to < 1	47	190	1.0 (referent)	1.0 (referent)	1.0 (referent)
1 to < 6	52	187	1.25 (0.67 to 2.31)	1.25 (0.68 to 2.31)	1.34 (0.70 to 2.57)
6 to < 57	49	141	1.89 (0.90 to 3.98)	1.88 (0.89 to 3.97)	2.23 (1.02 to 4.85)
≥ 57	50	148	2.48 (1.16 to 5.29)	2.25 (1.05 to 4.84)	2.66 (1.20 to 5.87)
			$P_{trend} = .040$	$P_{trend} = .090$	$P_{trend} = .051$
Cumulative REC					
Quartiles, µg/m³-yr					
0 to < 3	49	158	1.0 (referent)	1.0 (referent)	1.0 (referent)
3 to < 72	50	228	0.86 (0.47 to 1.59)	0.79 (0.43 to 1.45)	0.87 (0.45 to 1.67)
72 to < 536	49	157	1.58 (0.77 to 3.27)	1.47 (0.71 to 3.03)	1.73 (0.80 to 3.74)
≥ 536	50	123	3.19 (1.44 to 7.06)	2.88 (1.31 to 6.36)	3.72 (1.61 to 8.60)
			$P_{trend} = .0004$	$P_{trend} = .001$	$P_{trend} = .0002$

* *P* values based on two-sided Wald test for linear trend; Adjusted for mine location/smoking status/duration smoked combination (surface work only/never smoker, surface work only/unknown/occasional smoker, surface work only/former smoker/< 20 yrs, surface work only/former smoker/20 to < 30 yrs, surface work only/former smoker/30 to < 40 yrs, surface work only/former smoker/40 to < 50 yrs, surface work only/former smoker/≥ 50 yrs, surface work only/current smoker/< 20 yrs, surface work only/current smoker/20 to < 30 yrs, surface work only/current smoker/30 to < 40 yrs, surface work only/current smoker/40 to < 50 yrs, surface work only/current smoker/≥ 50 yrs, ever underground [UG] work/never smoker, ever UG work/unknown/occasional smoker, ever UG work/former smoker/< 20 yrs, ever UG work/former smoker/20 to < 30 yrs, ever UG work/former smoker/30 to < 40 yrs, ever UG work/former smoker/40 to < 50 yrs, ever UG work/former smoker/≥ 50 yrs, ever UG work/current smoker/< 20 yrs, ever UG work/current smoker/20 to < 30 yrs, ever UG work/current smoker/30 to < 40 yrs, ever UG work/current smoker/40 to < 50 yrs, ever UG work/current smoker/≥ 50 yrs); history of respiratory disease five or more years before date of death/reference date; and history of a high-risk job for lung cancer for at least 10 years. CI = confidence interval; OR = odds ratio; pkyr = pack-year; REC = respirable elemental carbon.

† Duration smoked was computed by subtracting age started smoking from current age (current smokers) or age quit smoking (former smokers) minus any intermittent years stopped smoking. For the 72 case subjects and 107 control subjects with missing age started smoking, age started was assumed to be 17 years old, which was the average age started in the controls.

‡ *P* values based on two-sided Wald test for linear trend; Adjusted for mine location/smoking status/pkyr combination (surface work only/never smoker, surface work only/unknown/occasional smoker, surface work only/former smoker/< 33 pkyrs, surface work only/former smoker/33 to < 49 pkyrs, surface work only/former smoker/49 to < 70 pkyrs, surface work only/former smoker/≥ 70 pkyrs, surface work only/current smoker/< 33 pkyrs, surface work only/current smoker/33 to < 49 pkyrs, surface work only/current smoker/49 to < 70 pkyrs, surface work only/current smoker/≥ 70 pkyrs, ever UG work/never smoker, ever UG work/unknown/occasional smoker, ever UG work/former smoker/< 33 pkyrs, ever UG work/ former smoker/33 to < 49 pkyrs, ever UG/former smoker/49 to < 70 pkyrs, ever UG work/former smoker/≥ 70 pkyrs, ever UG work/current smoker/< 33 pkyrs, ever UG work/current smoker/33 to < 49 pkyrs, ever UG /current smoker/49 to < 70 pkyrs, ever UG work/former smoker/≥ 70 pkyrs); history of respiratory disease five or more years before date of death/reference date; and history of a high-risk job for lung cancer for at least 10 years.

§ *P* values based on two-sided Wald test for linear trend; Adjusted for mine location/smoking status/packs/day/duration smoked combination (surface work only/never smoker, surface work only/unknown/occasional smoker, surface work only/former smoker/< 1 pack/day/< 20 yrs, surface work only/former smoker/< 1 pack/day/20 to < 30 yrs, surface work only/former smoker/< 1 pack/day/30 to < 40 yrs, surface work only/former smoker/< 1 pack/day/40 to < 50 yrs, surface work only/former smoker/< 1 pack/day/≥ 50 yrs, surface work only/former smoker/1 to < 2 packs/day/< 20 yrs, surface work only/former smoker/1 to < 2 packs/day/20 to < 30 yrs, surface work only/former smoker/1 to < 2 packs/day/30 to < 40 yrs, surface work only/former smoker/1 to < 2 packs/day/40 to < 50 yrs, surface work only/former smoker/1 to < 2 packs/day/≥ 50 yrs, surface work only/former smoker/≥ 2 packs/day/< 20 yrs, surface work only/former smoker/≥ 2 packs/day/20 to < 30 yrs, surface work only/former smoker/≥ 2 packs/day/30 to < 40 yrs, surface work only/former smoker/≥ 2 packs/day/40 to < 50 yrs, surface work only/former smoker/≥ 2 packs/day/≥ 50 yrs, surface work only/current smoker/< 1 pack/day/< 20 yrs, surface work only/current smoker/< 1 pack/day/20 to < 30 yrs, surface work only/current smoker/< 1 pack/day/30 to < 40 yrs, surface work only/current smoker/< 1 pack/day/40 to < 50 yrs, surface work only/current smoker/< 1 pack/day/≥ 50 yrs, surface work only/current smoker/1 to < 2 packs/day/< 20 yrs, surface work only/current smoker/1 to < 2 pack/day/20 to < 30 yrs, surface work only/current smoker/1 to < 2 packs/day/30 to < 40 yrs, surface work only/current smoker/1 to < 2 packs/day/40 to < 50 yrs, surface work only/current smoker/1 to < 2 packs/day/≥ 50yrs, surface work only/current smoker/≥ 2 packs/day/< 20 yrs, surface work only/current smoker/≥ 2 packs/day/20 to < 30 yrs, surface work only/current smoker/≥ 2 packs/day/30 to < 40 yrs, surface work only/current smoker/≥ 2 packs/day/40 to < 50 yrs, surface work only/current smoker/≥ 2 packs/day/≥ 50 yrs, ever UG work/never smoker, UG only/unknown/occasional smoker, ever UG work/former smoker/< 1 pack/day/< 20 yrs, ever UG work/former smoker/< 1 pack/day/20 to < 30 yrs, ever UG work/former smoker/< 1 pack/day/30 to < 40 yrs, ever UG work/former smoker/< 1 pack/day/40 to < 50 yrs, ever UG work/former smoker/< 1 pack/day/≥ 50 yrs, ever UG work/former smoker/1 to < 2 packs/day/< 20 yrs, ever UG work/former smoker/1 to < 2 packs/day/20 to < 30 yrs, ever UG work/former smoker/1 to < 2 packs/day/30 to < 40 yrs, ever UG work/former smoker/1 to < 2 packs/day/40 to < 50 yrs, ever UG work/former smoker/1 to < 2 packs/day/≥ 50 yrs, ever UG work/former smoker/≥ 2 packs/day/< 20 yrs, ever UG work/former smoker/≥ 2 packs/day/20 to < 30 yrs, ever UG work/former smoker/≥ 2 packs/day/30 to < 40 yrs, ever UG work/former smoker/≥ 2 packs/day/40 to < 50 yrs, ever UG work/former smoker/≥ 2 packs/day/≥ 50 yrs, ever UG work/current smoker/< 1 pack/day/< 20 yrs, ever UG work/current smoker/< 1 pack/day/20 to < 30 yrs, ever UG work/current smoker/< 1 pack/day/30 to < 40 yrs, ever UG work/current smoker/< 1 pack/day/40 to < 50 yrs, ever UG work/current smoker/< 1 pack/day/≥ 50 yrs, ever UG work/current smoker/1 to < 2 packs/day/< 20 yrs, ever UG work/current smoker/1 to < 2 packs/day/20 to < 30 yrs, ever UG work/current smoker/1 to < 2 packs/day/30 to < 40 yrs, ever UG work/current smoker/1 to < 2 packs/day/40 to < 50 yrs, ever UG work/ current smoker/1 to < 2 packs/day/≥ 50 yrs, ever UG work/current smoker/≥ 2 packs/day/< 20 yrs, ever UG work/current smoker/≥ 2 packs/day/20 to < 30 yrs, ever UG work/current smoker/≥ 2 packs/day/30 to < 40 yrs, ever UG work/current smoker/≥ 2 packs/day/40 to < 50 yrs, ever UG work/current smoker/≥ 2 packs/day/≥ 50 yrs.