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LACK OF CONCORDANCE BETWEEN REPORTED LUNG-CANCER RISK LEVELS AND OCCUPATION-SPECIFIC DIESEL-EXHAUST EXPOSURE

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Some epidemiologic studies of occupational groups show associations between surrogates of diesel-exhaust exposure and increased lung cancer, but causality has not been established. For several occupational groups, we compared information on the reported lung-cancer risk with estimated diesel-exhaust concentrations. Although none of the epidemiologic studies had concurrent measurements of diesel-exhaust concentrations, such data are available from more contemporary studies. Measurements of particle concentrations yield three, overlapping "order-of-magnitude" groups:

Truck drivers, dock workers, railroad workers (excluding shop workers, hostlers), 5–100 μg/m³.
Bus garage workers, railroad shop workers, and hostlers, 50–700 μg/m³.
Underground miners, 500–2000 μg/m³.

Bhatia et al. (1998) conducted a meta-analysis of lung-cancer risk with occupational exposure to diesel exhaust and found an overall relative risk (RR) value of 1.33, with a range of 1.11 to 1.49 in the subanalysis by occupation. If diesel exhaust were causally increasing lung-cancer risk by 50% for low-exposure occupations (for example, truck drivers, RR = 1.49), then the lung-cancer risk in a more heavily exposed population (for example, railroad shop workers) should be much higher; however, the shop workers experienced an RR of around 1.0 (Crump, 1999; HEI, 1999). Similarly, the added lung-cancer risk for bus garage workers (RR = 1.24) is half that of truck drivers, but diesel-exhaust concentrations were considerably higher for garage workers. There is an approximately two orders of magnitude difference in potential diesel-exhaust exposure, yet, the epidemiologic relative risks cluster in a narrow range. Such a lack of concordance between reported lung-cancer risk and estimated exposure argues against a causal role for diesel exhaust in the epidemiologic associations.

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The health effects from diesel-engine exhaust have been debated for nearly two decades. Initial concerns were based on the fact that diesel-exhaust particles contain organic compounds, some of which cause mutations in short-term, single-cell assays. In the 1980s and early 1990s, the tumorigenic potential of diesel exhaust was evaluated in long-term, animal assays. In these studies, animals inhaled high concentrations of diesel-engine exhaust over their lifetimes. Rats, and only rats, developed lung tumors; moreover, rats developed lung tumors when exposed to high concentrations of any number of different types of insoluble particles (reviewed by Busby & Newberne, 1995; Watson & Valberg, 1996; International Life Sciences Institute, 1999). There is a growing consensus that lung tumors observed in rats exposed to high concentrations of particles are due to impaired lung clearance of insoluble particles with subsequent lung inflammation and lung-cell hyperplasia. In contrast to high-dose exposures, there has been some concern that at low-dose exposures, diesel exhaust could be tumorigenic in rats via genotoxic mechanisms. However, meta-analysis of low-dose exposed rats (Valberg & Crouch, 1999) indicates that particle-bound organic compounds do not exert an independent tumorigenic effect.

Some epidemiologic studies of occupational groups show associations between surrogates of diesel-exhaust exposure and increased lung cancer, but causality has not been established. Whether this risk is causally associated with a worker's actual diesel exhaust exposure is not known. Causality would be supported by finding that reported lung-cancer risk increased with increasing potential for diesel-exhaust exposure. Thus, one can ask the question: Is there an exposure/response relationship across occupations between diesel-exhaust exposure and lung-cancer risk?

METHODS OF ANALYSIS

We compiled information on the reported lung-cancer risk and on the estimated diesel-exhaust concentrations for various occupations.

Lung-Cancer Risk

For meta-analysis results, we utilized Bhatia et al. (1998). For risk estimates from individual studies, we relied on the reviews by Bhatia et al. (1998), Cohen and Higgins (1995), California Environmental Protection Agency (CalEPA) (1997), Crump (1999), and the Health Effects Institute (HEI) (1999). In those studies with subanalyses by age and/or duration of employment, the risk values for the highest category were usually given by the reviewers. For our analysis, we excluded studies published before 1980 and those studies in which diesel-exhaust exposure was ambiguous (for example, mixed or obscure job categories). Otherwise, we did not screen the studies for overall quality. Risk estimates were available for bus garage workers, dock workers, heavy equipment operators, railroad workers, truck drivers, and underground miners. For miners, we only used relative risk values for underground miners, because particle concentrations are so much higher underground than at the surface.

Diesel-Exhaust Concentrations

None of the epidemiologic studies had available concurrent measurements of diesel-exhaust concentrations. Rather, investigators used union records, interviews, questionnaires, and death-certificate information to assess indirectly the potential for diesel-exhaust exposure. However, data on diesel-exhaust concentrations in occupational settings are available for a later time period than when the actual exposures occurred for the worker populations in the epidemiologic studies. Thus, available information on diesel-exhaust concentrations for these occupations derives from more contemporary studies, but the relative ranking of the diesel-particle concentrations is likely to have remained constant. For data on diesel-particle concentrations we used Woskie et al. (1988), National Institute for Occupational Safety and Health (NIOSH) (1990a, 1990b), Bagley et al. (1990), Rubow et al. (1990), Zaebst et al. (1991), Watts et al. (1992), Watts (1995), and the World Health Organization (WHO) (1996). In some studies, particle data were given as elemental carbon, which represents approximately 50% of the diesel-particulate mass. Thus, for our exposure/response analysis, we doubled those particle-concentration values given as elemental carbon.

RESULTS

Table 1 summarizes the lung-cancer risk reported by various authors. The Bhatia et al. (1998) summary meta-analysis RR value is 1.33 for all occupations. In the subanalysis by occupation, the investigators reported a range of 1.11 to 1.49. Table 2 summarizes diesel-exhaust concentrations for various occupations. Particle-concentration measurements yield three overlapping "order-of-magnitude" groups:

Truck drivers, dock workers, railroad workers (excluding shop workers, hostlers), 5–100 μg/m^3.
Bus garage workers, railroad shop workers, and hostlers, 50–700 μg/m^3.
Underground miners, 500–2000 μg/m^3.

Figures 1 and 2 plot relative risk (± 95% CI) and diesel-exhaust concentrations (± range) for various occupational groups. Because of the large overall range of diesel-exhaust concentrations, we plotted these values on a logarithmic axis. A trend of increasing risk with increasing exposure to diesel exhaust is not apparent. For example, for a low-exposure occupation (for example, truck drivers), the lung-cancer risk is increased 50% (RR = 1.49). The lung-cancer risk in a more heavily exposed population (for example, railroad shop workers) should be much higher; however, the shop workers experienced a

TABLE 1. Reported Lung-Cancer Risk for Various Occupations

Occupation	Meta-analysis relative risk (from Bhatia et al., 1998) (95% CI)	Reported relative risk for lung cancer (RR, SMR, OR) (95% CI)	Dates of study period	Reference
Bus garage workers	1.24 (0.93–1.64)	0.90 (0.77–1.04)	1950–1974	Waller, 1981
		1.01 (0.82–1.22)	1967–1975	Rushton et al., 1983
		1.22 (0.71–1.96)	1945–1970	Gustavsson et al., 1990
		2.43 (1.32–4.47)	1945–1970	Gustavsson et al., 1990
Dock workers/stevedores	Not given	1.32 (1.05–1.66)	1961–1980	Gustafsson et al., 1986
Heavy equipment operators	1.11 (0.89–1.38)	1.07 (0.92–1.25)	—[a]	Wong et al., 1985
		2.60 (1.12–6.06)	1982–1984	Boffetta et al., 1988
		2.10 (0.60–3.10)	1982–1987	Hayes et al., 1989
Railroad workers (all)	1.44 (1.30–1.60)	1.35 (1.20–1.52)	1965–1977	Howe et al., 1983
		1.41 (1.06–1.88)	1981–1982	Garshick et al., 1987
		1.72 (1.27–2.33)	1959–1980	Garshick et al., 1988
		1.59 (0.94–2.69)	1982–1984	Boffetta et al., 1988
		2.40 (1.10–5.10)	1984–1987	Swanson et al., 1993
Railroad workers (excluding shop workers, hostlers)	Not given	1.82 (1.30–2.55)	1959–1980	Garshick et al., 1988, as used by CalEPA, 1997
Railroad workers (excluding shop workers)	Not given	0.7 (0.6–0.9)[b]	1959–1980	Garshick et al., 1988, as calculated in HEI, 1999
Railroad shop workers	Not given	1.08	1959–1980	Garshick et al., 1988, as calculated by Crump, 1999
		0.8 (0.6–1.1)[b]	1959–1980	Garshick et al., 1988, as calculated in HEI, 1999
Truck drivers	1.49 (1.36–1.65)	1.30 (1.10–1.60)	—[a]	Ahlberg et al., 1981
		1.24 (0.93–1.66)	1982–1984	Boffetta et al., 1988
		1.50 (1.10–2.00)	1982–1987	Hayes et al., 1989
		1.27 (0.83–1.93)	1982–1983	Steenland et al., 1990
		1.60 (1.26–2.00)	1970–1980	Hansen, 1993
		2.50 (1.40–4.40)	1984–1987	Swanson et al., 1993
Underground miners	Not given	2.10 (1.10–3.70)	1980–1982	Lerchen et al., 1987
		1.45 (0.74–2.58)	1965–1985	Ahlman et al., 1991

[a] Study period dates were not provided in the review article.

[b] For each job category, HEI (1999) estimated the relative risk as a function of diesel-exhaust exposure, and expressed the result of fitting the data as a relative risk per 10 yr of exposure in that job category. For all job categories, the relation of lung-cancer risk to duration of employment was found to be inverse (lung-cancer risk decreased with duration of diesel exhaust exposure).

TABLE 2. Diesel-Exhaust Concentrations for Various Occupations

Occupation	Particle concentration ($\mu g/m^3$)	Dates of particle measurements	Reference
Bus garage workers	14–326[a]	~1989	NIOSH, 1990a, as given in WHO (1996)
	220–370[b]	~1989	Blome et al., 1990, as given in WHO (1996)
	10–730[c]		Gamble et al., 1987, as given in WHO (1996)
Dock workers/stevedores	13.8[d]	1989	Zaebst et al., 1991
	24[d]	1989	NIOSH, 1990b
Heavy equipment operators	No occupation-specific exposure data are available		
Railroad workers	Engineer/firer, 39–73[e]	~1983	Woskie et al., 1988
	Braker/conductor, 52–92[e]		
	Shop worker, hostler, 114–191[e]		
Truck drivers	3.8[d]	1989	Zaebst et al., 1991
Underground miners	900–1900[f]	Late 1980s	Bagley et al., 1990
	670–1430[g]	Late 1980s	Watts et al., 1992
	650–1020[h]	Late 1980s	Rubow et al., 1990
	560–840[i]	Late 1980s	Ambs et al., 1991, as given in Watts (1995)
	830–1740[j]	Early 1990s	Ambs et al., 1994, as given in Watts (1995)

[a] Elemental carbon (diesel-particle concentration estimated as two times this value).
[b] Incinerable fine dust.
[c] Respirable dust.
[d] Geometric mean elemental carbon (diesel-particle concentration estimated as two times this value).
[e] Geometric mean of respirable particulate corrected for cigarette smoke but not for nondiesel particles. Range represents values for job subcategories.
[f] Mean "diesel particulate matter" in haulageway. Range represents values from three different mines.
[g] Mean "diesel particulate matter" from five mines. Range represents values from three locations (haulage, shuttle car, return).
[h] Mean "<0.8 μm particle mass." Range represents values from three locations (haulageway, shuttle car, return) in two different mines.
[i] Mean "diesel particulate matter." Range represents values from two locations (haulageway and return).
[j] Mean "diesel particulate matter" in haulageway. Range represents values from two mines.

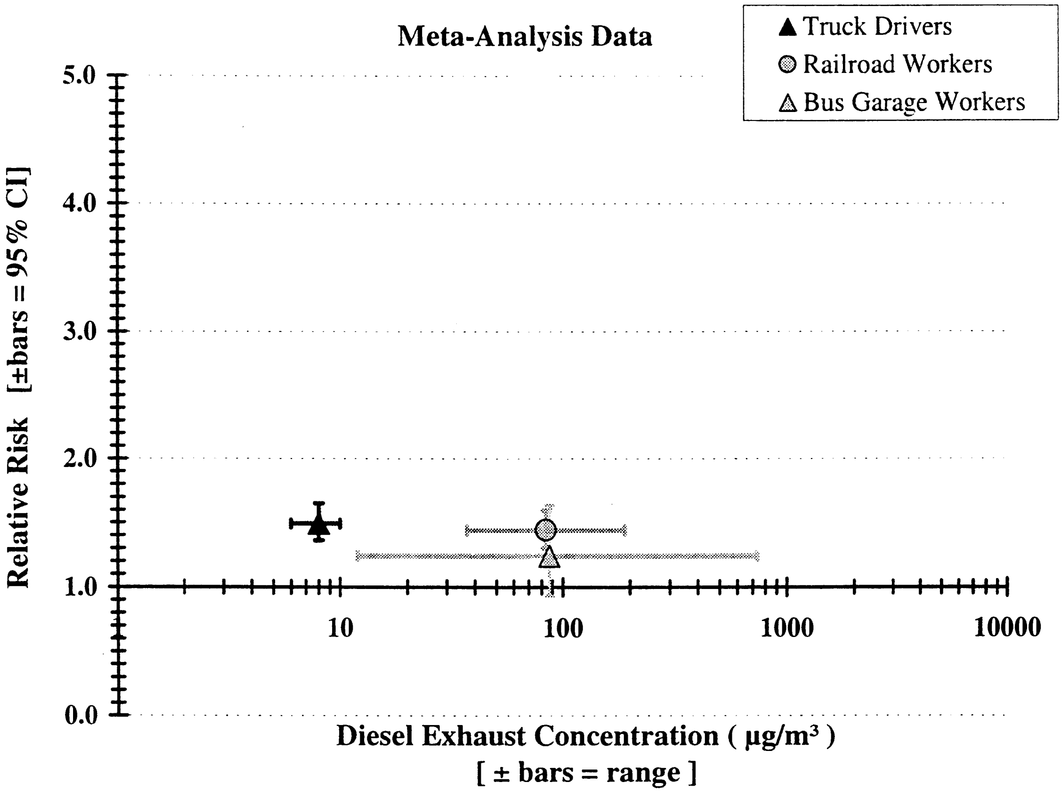

FIGURE 1. A plot of meta-analysis (Bhatia et al., 1998) relative risk for lung cancer (RR from Table 1, ± 95% CI) versus diesel-exhaust concentration (from Table 2, ± range) for three occupational groups. Estimated diesel-exhaust concentrations is plotted on a logarithmic axis. Reported risk does not increase with increasing diesel exhaust exposure concentration.

RR of around 1.0 [RR = 1.08 from Crump (1999) and 0.8 from HEI (1999)]. Similarly, the added lung-cancer risk for bus garage workers (RR = 1.24) is half that of truck drivers, but diesel-exhaust concentrations are considerably higher for the garage workers.

DISCUSSION

Our analysis was not intended to provide a quantitative risk estimate for diesel exhaust, because of uncertainties in both exposure and outcome. The currently available measurements of diesel-exhaust concentrations are valuable sources of data, but are problematic when applied retrospectively to estimate exposure. The HEI report (1999) discusses problems associated with the various measures of diesel-exhaust exposure. For railroad workers, the industrial hygiene study by Woskie and co-workers (1988) was used to estimate exposure. Woskie measured respirable-sized particles (RSP) and corrected for environmental tobacco smoke particulate. Although RSP will include diesel-exhaust particles, it is not diesel-particle specific; that is, any particle of respirable size, regardless of its source, will be included in the measure. The in-

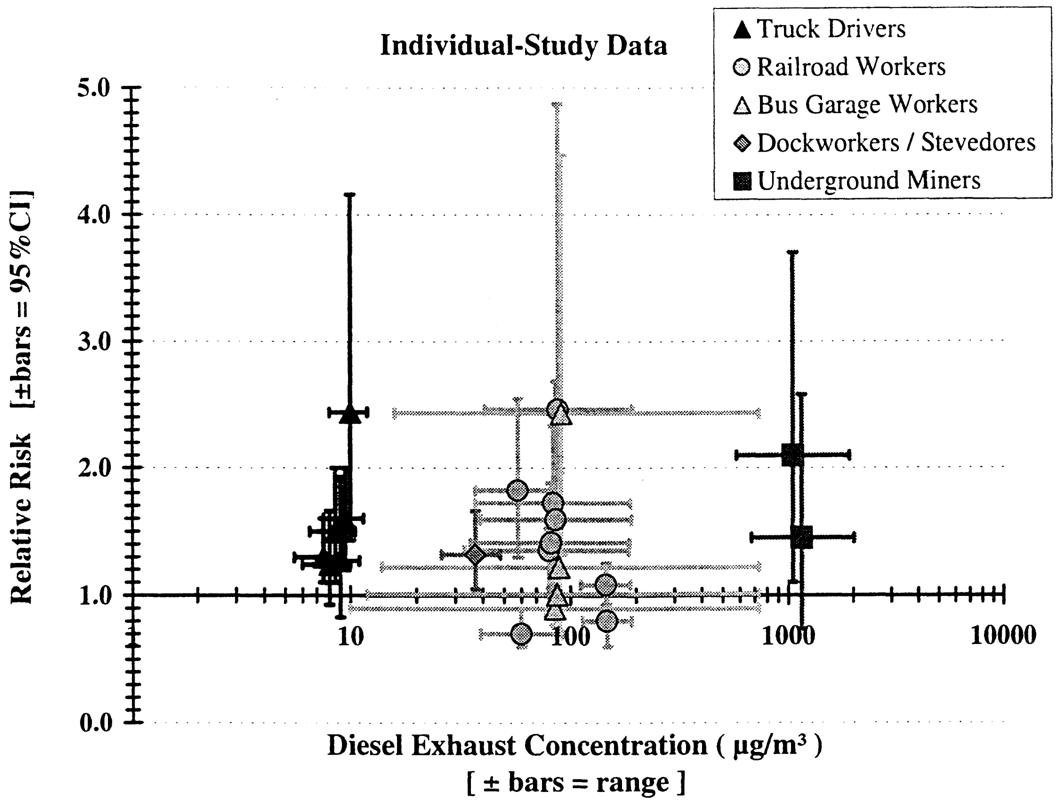

FIGURE 2. A plot of individual-study relative risk for lung cancer (RR from Table 1, ± 95% CI) versus diesel-exhaust concentration (from Table 2, ± range) for five occupational groups. Estimated diesel-exhaust concentrations is plotted on a logarithmic axis. Reported risk does not increase with increasing diesel exhaust exposure concentration.

dustrial hygiene study by Zaebst et al. (1991) was used for estimating diesel exposure for the truckers and the dock workers. Zaebst measured elemental carbon (EC), which is a more specific measure of diesel particulate than RSP but cannot distinguish particles derived from diesel engines, gasoline engines, stationary combustion sources, and industrial processes. For underground mine measurements, however, elemental carbon is a suitable measure of diesel-exhaust particulate (Watts, 1995) and was used in several of the studies cited in Table 2 (NIOSH, 1990a, 1990b; Zaebst et al., 1991). The fraction of the diesel particle composed of EC is variable, however, and for our analysis we used 50%. That is, when plotting diesel-exhaust concentrations in Figures 1 and 2, we multiplied the EC values given in Table 2 by a factor of 2. The major uncertainty, however, arises when applying diesel-exhaust concentrations to estimate exposure at an earlier time period for the worker populations in the epidemiologic studies. Historical differences in diesel fuel, engine design, and fleet composition are difficult to model accurately.

Our selection of epidemiologic studies should not be interpreted as an endorsement that these results reflect the effects of diesel-exhaust exposure.

Several critical reviews (Muscat & Wynder, 1995; Stober & Abel, 1996; Cox, 1997; Morgan et al., 1997; Stober et al., 1998; HEI, 1999) have noted problems of bias, misclassification, residual confounding, and reliance on multiple comparisons. For example, confounding by inadequate control of life-style factors could plausibly give similar risk estimates in populations exposed to different levels of diesel exhaust. It is also clear that depending upon the assumptions made, the risk estimate can vary considerably for the same data source. For example, using Garshick and co-workers' cohort study (1988) of railroad workers, various authors calculate different lung-cancer risk estimates (see Table 1). Furthermore, CalEPA (1997) calculated an increasing exposure-response relationship, but neither Crump (1999) nor HEI (1999) could validate such an association. Finally, the confidence interval (CI) in epidemiology studies reflects only the size of study populations and does not quantitatively capture the sum of all the sources of error, such as variability in cancer risk for control populations, inaccuracies in the exposure metric, and uncontrolled bias/confounding. Hence the actual "error bars" on risk estimates can be considerably larger than those reported.

CONCLUSIONS

Among different occupations, there is an approximately two orders of magnitude difference in potential diesel-exhaust particle exposure, yet the epidemiologic relative risks cluster in a narrow range. That is, there is a lack of concordance between the level of reported lung-cancer risk and diesel-exhaust particle concentrations. Such a lack of concordance is not supportive of a cause-and-effect relationship. Although the data indicate that diesel-exhaust exposure by occupation span a far greater spectrum of values than do occupation-specific risk estimates, the interpretation of this lack of concordance remains uncertain because of the lack of concurrent exposure information.

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