A Case-Control Study of Lung Cancer and Diesel Exhaust Exposure in Railroad Workers[1–4]

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SUMMARY A case-control study of deaths among U.S. railroad workers was conducted to test the hypothesis that lung cancer is associated with exposure to diesel exhaust. Employed and retired male workers with ≥ 10 yr of service who were born on or after January 1, 1900 and who died between March 1, 1981 and February 28, 1982 were eligible. We collected 87% of the death certificates from 15,059 deaths reported to the U.S. Railroad Retirement Board (RRB). Cases of lung cancer (1,256) were matched to controls by *age* (± 2.5 yr) and date of death (± 31 days). Potential exposure to diesel exhaust was assigned based on an industrial hygiene evaluation of jobs and work areas. Each subject's work history was determined from a yearly job report filed by his employer with the RRB from 1959 until death or retirement. Asbestos exposure prior to 1959 was categorized by the job held in 1959, the end of the steam locomotive era, or by the last job held if retirement occurred before 1959. Smoking histories were obtained by questionnaire from next of kin. Using multiple conditional logistic regression analysis to adjust for smoking and asbestos exposure, workers 64 yr of age or younger at the time of death with work in a diesel exhaust exposed job for 20 yr had a significantly increased relative odds (odds ratio = 1.41, 95% CI = 1.06, 1.88) of lung cancer. No effect of diesel exhaust exposure was seen in workers 65 yr of age or older because many of these men retired shortly after the transition to diesel-powered locomotives. This study supports the hypothesis that occupational exposure to diesel exhaust increases lung cancer risk.

AM REV RESPIR DIS 1987; 135:1242–1248

Introduction

A variety of mutagenic and carcinogenic substances have been identified on particles from diesel exhaust emissions (1). Occupational groups with potential diesel exhaust exposure include underground miners (2), bus maintenance workers (3, 4), heavy construction equipment operators (5), truck drivers (6), and railroad workers (7–11). In a recent study (12), diesel exhaust inhaled at high concentrations in rats resulted in lung cancer. There is concern that diesel exhaust exposure in occupational groups and in the general population may be a risk factor for lung cancer, but this has not yet been demonstrated.

Previous studies of lung cancer and diesel exhaust exposure have been limited by several deficiencies including inadequate statistical power, inaccurate or absent classification of diesel exhaust exposure, and failure to consider when diesel exhaust exposure began (8, 13). Possible confounding factors such as asbestos exposure and cigarette smoking also have not been considered in some studies. We have completed a case-control study of lung cancer deaths in relation to diesel exhaust exposure occurring in U. S. railroad workers that considered such factors.

Methods

Population

The population base for this study was the approximately 650,000 active and retired male U. S. railroad workers with 10 yr or more of railroad service who were born in 1900 or after. The U. S. Railroad Retirement Board (RRB) operates the retirement system for these workers; it is separate from the Social Security System. To qualify for either retirement or survivor benefits, 10 yr or more of service must be acquired by the worker. For the next of kin to qualify for benefits, the railroad board must be notified of the railroad worker's death. It is estimated that less than 2% of eligible retirees and next of kin do not receive benefits.

Reports of deaths that occurred between March 1, 1981 and February 28, 1982 were collected from the RRB during the course of the year. Death certificates were received from the RRB for approximately three fourths of the deaths, and the remainder of the death certificates were requested from the appropriate state boards of health. Cause of death was coded according to the International Classification of Diseases, eighth revision, (ICD-8).

The cases were selected from deaths with primary lung cancer (ICD 162). which was the underlying cause of death in most cases. Each case was matched to 2 controls who were within 2.5 yr of the date of birth and within 31 days of the date of death noted in the lung cancer cases. The controls were selected randomly from workers who did not have cancer noted anywhere on their death certificate, and who did not die of suicide or of accidental or unknown causes.

After informing the certifying physician of our intentions, a questionnaire was sent to the deceased's next of kin that included questions about the deceased's smoking habits, place of residence, and duration and type of relationship the respondent had with the deceased. A second questionnaire was sent if there was no response, and no response to either questionnaire resulted in a phone call to the next of kin.

Diesel Exhaust Exposure Estimates

There are more than 150 three-digit Interstate Commerce Commission (ICC) railroad job codes (14). Job codes for each worker were available from the RRB starting in 1959 and ending with death or retirement. For workers who retired between 1955 and 1959, last railroad job worked was available Some work·

(*Received in original form August 28, 1986 and in revised form November 20. 1986*)

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[2] Supported in part by Grant No. R807515 from the Environmental Protection Agency, Individual Research Award No. ES-05157 from the National Institute of Environmental Health Sciences, and Institutional Research Award NO. HL-07427 from the National Heart, Lung and Blood Institute.

[3] Presented in part at the Annual Meeting of the American Thoracic Society, Miami, May 1984.

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ers had additional job codes reported between 1955 and 1959. Most diesel exhaust exposure in the U.S. railroad industry began when the industry changed from steam- to diesel-powered locomotives after World War II. This transition occurred primarily during the 1950s; and by 1959, 95% of the locomotives in the United States were diesel powered (15). The approximate midpoint for the transition to diesel power in the United States was 1952. We have chosen 1959 as the effective start of diesel exhaust exposure for this study, recognizing that some workers had additional earlier years of exposure to diesel exhaust. If a worker retired before 1959, he was considered unexposed.

An industrial hygiene survey of the U.S. railroad industry was conducted as part of this investigation. Selected jobs with and without regular diesel exhaust exposure were identified by a review of job title and duties, and confirmed by industrial hygiene sampling (16, 17). Personal exposure was assessed in 39 job categories representative of workers with and without diesel exhaust exposure in 4 railroads. Workers with regular diesel exhaust exposure were found in several job locations: jobs inside the roundhouse and diesel locomotive repair facilities had exposure during the repair and maintenance of diesel locomotives; locomotive engineers and firemen who operated the diesel locomotives; and conductors and brakemen who worked on or near running trains. Hostlers had exposure while driving locomotives in and out of shops. We found that the workers were exposed to other respirable particulate, including cigarette particulate, which required adjustment of the measured values of respirable particulate obtained (16, 17). Mean estimates of current exposure among the diesel exposed groups adjusted for cigarette smoke ranged from 83 to 168 $\mu g/m^3$. For the shopworkers, mean estimates in the individual railroads varied between 87 and 322 $\mu g/m^3$. In contrast, the clerks and station agents (nonexposed) had values between 9 and 76 $\mu g/m^3$. Detailed discussion of the interpretation and use of these values and other indices of diesel exhaust exposure will be presented in future work. In this study, diesel exhaust exposure is considered to be a dichotomous (yes/no) variable

Job codes for which no personal sampling was performed were considered exposed or unexposed based on similarities in job activities and work locations to sampled jobs, and by degree of contact with operating diesel equipment. For example, carmen (car main-*— workers) generally worked away from operating trains and were classified as unexposed to diesel exhaust. Maintenance-of-way workers and others with potential or occasional diesel exhaust exposure were considered not to be significantly exposed. The appropriateness of these classifications was verified by a questionnaire survey of 534 workers at one survey railroad. Workers indicated approximately how much time was spent in several railroad locations (i.e., near or away from diesel trains, trucks, or equipment). The railroad surveyed did not have a passenger service, but the job codes including train attendants and passenger car waiters and chefs were considered to be exposed to diesel exhaust based on their work on operating trains.

Years of exposure to diesel exhaust were totaled from 1959 to death or retirement for each worker, and summarized as "diesel-years." Years not working for the railroad, or without reported jobs or unknown jobs, were considered as unexposed years (2.4% of the total years from 1959 to death or retirement).

As a result of the transition from steam to diesel locomotives in the 1950s. age and the year a worker retired relative to 1959 influenced the chance of working in a diesel-exhaust-exposed job. Workers who retired prior to death in 1981 or 1982 were less likely to have worked in a diesel-exhaust-exposed job (table 2). Roughly half of the older workers were unexposed to diesel exhaust, and those exposed had a short duration of exposure For this reason, and because of the suggestion that older workers might have less accurate certification of death (18). the cases and accompanying controls were analyzed in 2 groups, workers ≤ 64 yr of age (i.e., retirement age) at death and those ≥ 65 yr of age at death.

Asbestos Exposure Estimates

Asbestos exposure in the railroads occurred primarily during the steam engine era. Exposure was related mostly to the repair of locomotive steam boilers, which were insulated with asbestos. Other potential exposures were in the repair of asbestos-insulated passenger cars, in the railroad bridge and building construction trades, in steam pipe repair, and in the repair of stationary boilers. We developed asbestos exposure categories based on the results of a survey of current employees of one railroad that asked about prior asbestos exposure (19) and on a review of railroad, medical, and industrial Literature (20–23). Asbestos exposure category was based on job held in 1959 (or before if available) or on the last job held if the subject retired before 1959. As a result of the transition to diesel-powered engines, subjects starting work in or after 1959 would not have had opportunity for significant asbestos exposure and were considered unexposed regardless of job code Workers categorized with likely regular past asbestos exposure were subjects who had worked in and around boiler and locomotive repair facilities. Exposure to uniformly high levels of asbestos would have occurred in a subset of shop workers responsible for boiler lagging removal; others in the shop area would have had less exposure Workers responsible for the maintenance of railroad structures and car repair had more intermittent asbestos exposure but were also categorized as exposed. Among active workers older than 50 yr of age in the surveyed railroad (19), past asbestos exposure was short, a median of 3 yr.[5]

[5] A detailed list of ICC job coda and diesel exhaust and asbestos exposure assignments are available from the authors upon request.

Analysis

To preserve the matching on age and date of death, analysis was done using multivariate conditional logistic regression (24). Additional regression analyses were done for various subgroups with unconditional (i.e., matching not preserved) logistic regression but adjusting for age. Logistic regression specifies that the natural logarithm of the odds of disease depends on a set of variables; in this study, diesel exhaust exposure, asbestos exposure, and cigarette smoking. The relative odds for lung cancer attributable to each exposure is derived from the exponent of the regression coefficient for each exposure parameter. Regression coefficients and their standard deviations were calculated using a Fortran program provided by Thomas (25). All p values presented are two-sided.

Results

Cause-specific death certificates were obtained for approximately 87% of the 15,059 deaths reported by the RRB, and we identified 1,374 cases of lung cancer. Twenty cases of lung cancer were excluded because of incomplete data, and 35 were excluded because 2 states would not provide permission to use information on the death certificate to contact the next of kin. Of the remaining cases, 335 (96%) of the 349 subjects ≤ 64 yr of age at death and 921 (95%) of 970 subjects ≥ 65 yr of age at death were successfully matched to at least 1 control and had work histories available for analysis. Ninety percent of the cases in both age groups had 2 controls. Of the 2,385 controls in the study, 98% were matched to cases within ± 31 days of the date of death, and the remaining 2% were matched within 100 days. Eighteen controls who died within 10 days before the end of February 1981 were included in the study. Ninety-five percent of the controls were matched within 2.5 yr of the date of birth of the case, and the remaining 5% were matched within 6 yr. Initial date of railroad service was estimated from the RRB reported years of service for most workers and was only reliable since the late 1930s because of the limitations of computerized RRB records. Some workers starting work in 1947 or later had first year of railroad service supplied by the RRB. Thus, the total number of years worked is underestimated and inaccurate for the older group, and could be slightly underestimated for the younger group. Although we lacked specific information on jobs worked outside the railroads, on the basis of the retirement year and initial years of railroad service, most workers in this study appeared to be lifelong railroad employees.

There were no significant differences between cases and controls in each of the 2 age groups for age, race, year first worked, retirement year, and total years worked, only available for the younger group (table 1). Of the controls in the younger age group, 80% had disease of the circulatory system (ICD 390–458) as the underlying cause of death, 7% died of disease of the respiratory system (ICD 460–519), and 7% died of disease of the digestive system (ICD 520–577). In the older age group, 74% of the controls had a disease of the circulatory system as the underlying cause of death, 15% died of disease of the respiratory system, and 4% died of digestive diseases. In the 2 age groups, only 5 of the controls (0.2%) were coded to illdefined causes (ICD 7%).

For the younger age group, the proportion of cases with asbestos exposure (25%) was slightly, but not significantly greater than in the controls (22%). In the older group, slightly more controls had asbestos exposure than did cases. Approximately 60% of all the younger workers had some exposure to diesel exhaust. In contrast, only 47% of all the older workers had some diesel exhaust exposure in their jobs, $p < 0.001$ (table 2).

Smoking information (table 3) was obtained from next of kin. Ninety-two percent of the questionnaire or phone respondents for the younger group were female, and in most (83%) they were the spouse In the older group, 88% of the respondents were female and the spouse in 76%. Information on smoking (yes/no) was missing for 17% of the cases and 16% of controls in the younger age group, and 13% of the cases and 18% of the controls in the older group. Most smokers were long-term smokers who had continued to smoke within 5 yr of their deaths. More cases than controls were cigarette smokers and had a greater pack-year history of smoking. When age started smoking was not obtained (< 6% of both cases and controls), we assumed a starting age of 16.

Diesel exhaust exposure (table 2) was summarized as the number of years in dieselexposed jobs. Years of diesel exposure was used as a continuous exposure variable in regression models. In the younger age group, the unadjusted coefficient for diesel-years was 0.01648, with an odds ratio of disease over 20 yr of 1.39 (95% CI = 1.05, 1.83). When adjusted for any asbestos exposure (yes/no) and lifetime smoking (pack-years), the estimate of the effect of diesel exhaust exposure remained close to the crude estimate, with a relative odds of 1.41 (95% CI = 1.06, 1.88) (table 4). In the older age group, the unadjusted coefficient for diesel-years was 0.00084 ($p = 0.89$), with the adjusted value (table 4) also not significant and near the null value

To verify that risk in the younger group increased with increasing years of diesel exposure, diesel-years was categorized as ≥ 20 diesel-years, and 5 to 19 diesel-years, with 0 to 4 yr as the referent group. Adjusting for asbestos exposure and pack-year category of smoking, subjects with ≥ 20 yr of diesel exhaust exposure had the highest, significantly elevated odds ratio (OR = 1.64; 95% CI = 1.18, 2.29). Subjects with 5 to 19 diesel-years had an odds ratio of 1.02 (95% CI = 0.72, 1.45).

Only 3% of the older workers had diesel exhaust exposure for 20 yr or more. For comparison, the odds ratio for 5 to 19 yr of exposure in the older group was 0.95 (95% CI = 0.79, 1.13) and for ≥ 20 yr of exposure was 0.94 (95% CI = 0.56, 1.59), adjusting for smoking and asbestos exposure

Because workers in the diesel engine repair shop were the diesel-exposed workers with the most potential for past asbestos exposure, a regression model in the

TABLE 1

AGE, RACE, WORK HISTORY SUMMARY. AND ASBESTOS EXPOSURE CATEGORIES FOR BOTH YOUNGER (≤ 64) AND OLDER (≥ 65) CASES AND THEIR CONTROLS

	Younger Workers Case ≤ 64		Older Workers Case ≥ 65	
	Case	Control	Case	Control
Number	335	637	921	1748
Age. Median	60	60	73	73
Range	35-84	37-69	65-82	62-82
Race, white	310 (93)*	585 (92)	837 (91)	1576 (91)
Started work				
≥ 1949	109 (33)	184 (29)	68 (7)	126 (7)
< 1948	226 (68)	453 (71)	853 (93)	1622 (93)
Years worked mean ± SD	29.2 ± 7.4	29.4 ± 7.0	NA†	NA†
Retirement year median	1980	1979	1972	1971
Asbestos exposure				
Regular	47 (14)	78 (12)	129 (14)	289 (17)
Intermittent	37 (11)	63 (10)	108 (12)	193 (11)
None	251 (75)	496 (78)	684 (74)	1266 (72)

* Numbers in parentheses are percentages.
† Not available for workers starting before the late 1930s

TABLE 2

DISTRIBUTION OF YEARS OF DIESEL EXHAUST EXPOSURE IN THE THREE WWSED JOB LOCATIONS AND SUMMARY CATEGORY (DIESEL-YEAAS)

	Years of Exposure	Younger workers Case ≤ 64		Older Workers Case ≥ 65	
		case	Control	Case	control
No Exposure	0	120 (36)*	272 (43)	480 (52)	930 (53)
Shopworkers	1–10	39 (12)	53 (8)	89 (10)	146 (8)
	11–19	15 (5)	38 (6)	62 (7)	166 (10)
	≥ 20	21 (6)	24 (4)	6 (1)	6 (0)
Engineer and firemen	1–10	7 (2)	14 (2)	27 (3)	48 (3)
	11–19	13 (4)	31 (5)	83 (9)	132 (8)
	≥ 20	35 (10)	40 (6)	5 (0)	22 (1)
Brakemen and conductors	1–10	11 (3)	36 (6)	56 (6)	119 (7)
	11–19	27 (8)	58 (9)	114 (12)	183 (11)
	≥ 20	58 (17)	96 (15)	14 (2)	25 (1)
Diesel-years	1–10	45 (13)	77 (12)	155 (17)	275 (18)
	11–19	53 (16)	122 (19)	260 (28)	489 (28)
	≥ 20	117 (35)	166 (26)	26 (3)	54 (3)

* Numbers in parentheses are percentages.

and death 5 yr later. For workers with 5 to 14 yr of cumulative exposure, the odds ratio was 1.07 (95% CI = 0.69, 1.66), with a referent category 0 to 4 diesel-years.

Discussion

We have conducted a population-based case-control study of U.S. railroad workers to test the hypothesis that diesel exhaust exposure results in an increased risk of lung cancer. Because diesel-powered locomotives were not fully introduced into the railroads until the late 1950s, only in a group who worked sufficiently long after that time could an effect of diesel exhaust exposure be expected to be seen. For cases greater than or equal to 65 yr of age at death (in 1981 and 1982) and their matched controls (i.e., retired workers), no effect of diesel exhaust exposure was seen. In the younger age group (≤ 64 yr of age at death), there was both an increased prevalence and duration of diesel exhaust exposure. Controlling for cigarette smoking and for potential past asbestos exposure, a significantly elevated odds ratio for lung cancer was observed. Workers with 20 yr of more of exposure had the highest, significant odds ratio when exposure was analyzed with categorical rather than with continuous variables. The alternative regression model using the categorical variables of 5 to 19 and ≥ 20 yr of diesel exposure suggests an apparent nonlinear relation between number of years of exposure and lung cancer risk. However, the confidence limits are wide, and it is not possible to define the precise shape of this relationship.

Asbestos exposure, a possible confounding variable, was in the final model because of its biologic importance. We were not able to individually identify the small group of workers with past heavy asbestos exposure. In addition, some of the ICC job codes used to assign potential asbestos exposure were broadly defined and contained some workers without asbestos exposure. To estimate stability in the asbestos exposure categories over time, we examined job mobility during the years between 1959 and 1979 (although exposure occurred before 1959). Of the workers less than or equal to 44 yr of age in 1959 and still working in 1979 (approximately 50% had retired), 72% who would have been categorized in the regular asbestos exposure group 20 yr later were in the regular group in 1959, and 17% were in the intermittent asbestos exposure category in 1959. Of workers categorized as unexposed to asbestos, 96% would have been in the unexposed category 20 yr earlier. Of workers in the intermittent category, 20 yr earlier 67% would have also been in the intermittent category and 21% in the regular category. Those with any exposure (regular and intermittent), 20 yr earlier 88% would have been in an exposed category. The misclassification from assigning past asbestos exposure based on the 1959 job would be expected to have an effect apparent more readily in the older age group, and would result in a reduction of the apparent asbestos effect. In the younger group, there would be less misclassification but also less real exposure.

Despite the asbestos exposure misclassification, the effect of asbestos exposure on lung cancer in the younger age group is within an expected range. These younger railroad workers, who were in their thirties during the 1950s, if exposed to asbestos would have had relatively short exposure Studies of lung cancer among former shipyard workers with mostly wartime exposure have demonstrated odds ratios for asbestos exposure of similar magnitude as found in this study (26–28). In a study in Swedish railroad shop workers with more than 30 yr service, the *standardized* mortality ratio was 192 (29). In our study, workers located in the diesel repair shop were most likely to have had past asbestos exposure. Workers in the other diesel exhaust jobs exposure did not include workers with significant potential for prior asbestos exposure. Only the hostlers had the potential for asbestos exposure, and they were a small subset (10 workers in the younger group in 1959) of the remaining diesel-exhaust-exposed workers. With the shop workers excluded from the other diesel-exposed workers, a significantly elevated odds ratio for the effect of diesel exhaust was still obtained.

Next of kin were used to obtain information on cigarette smoking, and the estimates for the smoking effect on lung cancer are within the expected range (30). Rogot and Reid (31) found that surrogates identified 91% of ex-smokers or nonsmokers compared to previously obtained personal questionnaire response. There was a tendency for the surrogate to overestimate the amount smoked. Kolonel and coworkers (32) compared the response of subjects (mostly husbands) with wives interviewed separately. Ninety-six percent of those identified as ever smoking were in agreement. Age started smoking was in agreement 84% of the time to within ± 4 yr. These surrogates also tended to overestimate daily cigarette consumption. Thus, surrogate response data appear to overestimate cigarette consumption. This could exaggerate the contribution of cigarette smoking to lung cancer risk if the next of kin of subjects dying of lung cancer were more likely to report smoking histories than were those of controls.

Several models relating cigarette smoking to lung cancer have been described. Doll and Peto (33) in their study of British doctors expressed the dose-response relationship as the product of a power of duration of smoking and a power of dose for lifelong smokers smoking less than 2 packs per day. Others have used estimated pack-years (34) and cigarettes per day (26). We used pack-years expressed as a categorical variable to control for the effect of cigarette smoking, The category of pack-years "missing" served as an additional level of cigarette smoking. Further regression analyses in the subgroup of workers with pack-year data available showed no advantage over any other modeling of cigarette smoking in this population.

Another potential source of error in our study is the misclassification of diesel exhaust exposure using the ICC job classification as a surrogate for exposure Jobs with potential diesel exhaust exposure included railroad express drivers, railroad police, bus drivers, and operators of diesel powered equipment. Such exposure was likely to be low intensity and intermittent, and as a result these persons were considered unexposed. Misclassification by assigning exposure to an ICC code job group that contained nondiesel exposed workers (as in some of the diesel shop codes) would reduce the likelihood of seeing a significant effect of diesel exhaust exposure.

Two types of misclassification may result from the use of death certificates to identify cases and controls in this study. Controls not suspected of having lung cancer may actually have had undiagnosed pulmonary malignancies, and identified lung cancer cases might be other lesions misdiagnosed as primary lung cancer. It is unlikely that many cases or controls were misclassified for several reasons. First, we excluded as eligible controls subjects with death caused by accidents, by other cancers, or by uncertain causes. Second, lung cancer, particularly in younger men, is usually a clinically obvious disease that is rapidly fatal. It was in this group of younger workers that a significant effect of diesel

TABLE 3

SMOKING HISTORY FOR CASES AND CONTROLS IN THE YOUNGER AND OLDER AGE GROUPS

	Younger Workers Case ≤ 64		Older Workers Case ≥ 65	
	Case	Control	Case	Control
Smoker				
Yes	269 (80)*	466 (73)	771 (84)	1130 (65)
No	9 (3)	69 (11)	32 (4)	294 (17)
Missing	57 (17)	102 (16)	118 (13)	324 (18)
Pack-years				
≤ 50	106 (32)	241 (38)	234 (25)	514 (29)
> 50	144 (43)	189 (30)	464 (50)	471 (27)
Missing	76 (23)	138 (22)	191 (21)	469 (27)
Nonsmoker	9 (3)	69 (11)	32 (4)	294 (17)
Years smoked. ≥ 20	239 (96)	397 (92)	683 (98)	917 (93)
Cigarettes per day				
1-15	19 (8)	60 (14)	86 (12)	222 (23)
16-25	80 (32)	159 (37)	307 (44)	442 (50)
26-35	42 (17)	69 (16)	111 (16)	113 (12)
≥ 36	109 (44)	142 (33)	114 (28)	208 (21)
Years stopped smoking before death				
0–4	202 (81)	298 (69)	455 (65)	484 (49)
5–14	31 (12)	68 (16)	135 (19)	222 (23)
≥ 15	17 (7)	64 (15)	108 (16)	279 (28)

* Numbers in parentheses are percentages.

younger group was constructed, entering the diesel exposure of the shop workers separately from the other diesel exposed job categories. When adjusted for past asbestos exposure and smoking as in earlier models, the odds ratio for ≥ 20 yr of exposure (exclusive of the shop workers) was 1.55 (95% CI = 1.09, 2.21, with 0 to 4 yr used as the referent category).

Alternative models were explored to better explain past asbestos exposure They included separate dichotomous Variables for the regular and intermittent exposure groups and an estimate of years of exposure based on estimated years worked prior to 1959. None of these alternatives gave a stronger association with risk than the dichotomous variable used.

Because of the incompleteness of the next of kin responses, we were not able to calculate pack-years smoked for all those in the study. To preserve the matched nature of the study and minimize exclusions, we treated "pack-years missing" as a category of smoking. This gave an odds ratio between the value for subjects with greater than 50 and less than or equal to 50 pack-years of smoking in the younger group. Analysis using unconditional logistic regression on the subset of younger workers (n = 758) with known pack-years was done to explore the impact of other smoking models in the magnitude of diesel exhaust lung cancer risk. Adjusting for age and asbestos exposure, there was no significant difference in lung cancer risk among the different models that included pack-years expressed as a single continuous variable, 2 independent variables, cigarettes per day and years of smoking, or pack-year category categorized by the number of years the subject had stopped smoking prior to death. Adjusting for age and asbestos exposure, with diesel years used as a continuous variable in these models, the odds ratio for 20 yr of diesel exposure ranged from 1.50 to 1.53 ($p < 0.02$). Expressed as a continuous variable, the coefficient for pack-years was 0.01278 ($p < 0.001$), and used together the coefficient for cigarettes smoked per day was 0.01604 ($p = 0.006$) and for years of smoking was 0.02484 ($p = 0.001$). Smoking ≤ 50 pack-years 4 yr or less before death had a risk of lung cancer of 4.08 ($p < 0.001$), smoking > 50 pack-years 4 yr or less before death had a lung cancer risk of 6.08 ($p < 0.001$), smoking ≤ 50 pack-years 5 yr or more before death had a risk of 2.47 ($p = 0.027$), and smoking > 50 pack-years 5 yr or more before death had an odds ratio of 3.93 ($p = 0.004$). In the entire younger data set (n = 972), retaining the category of pack-years missing but categorizing the remaining subjects with known smoking information as ex-smokers (quitting 5 yr or more before death) and as current smokers in daily cigarette consumption categories, adjusting for asbestos exposure, gave an odds ratio for 20 yr of diesel exposure of 1.46 ($p = 0.01$).

The interaction between diesel exposure and the 3 pack-year categories was assessed by constructing 3 cross-product terms between the categories ≤ 50, >50, and missing pack-year indicator variables and the indicator variable for ≥ 20 diesel yr. The cross-product terms were not significant (chi-square = 2.05, df = 3, $p = 0.56$).

To exclude the effect of recent diesel exhaust exposure, a model was tested that excluded exposure occurring with the 5 yr before death. The regression coefficient, adjusted for cigarette smoking and asbestos exposure, yielded an odds ratio of 1.43 (95% CI = 1.06, 1.94) for workers with 15 yr of cumulative exposure,

TABLE 4

REGRESSION RESULTS USING DIESEL EXHAUST EXPOSURE AS A SINGLE CONTINUOUS VARIABLE (DIESEL-YEARS) ADJUSTED FOR CIGARETTE SMOKING AND ASBESTOS EXPOSURE

Exposure Category	Coefficient	Odds Ratio	95% CI	p values
Case age ≤ 64				
Diesel-years	0.01719	1.41*	1.06,1.88	0.02
Asbestos, Y/N	0.18111	1.20	0.87,1.65	0.27
≤ 50 pack-years†	1.19196	3.29	1.57,6.93	< 0.01
> 50 pack-years†	1.73606	5.68	2.73,11.80	< 0.01
Pack-years missing†	1.37975	3.97	1.86,8.51	< 0.01
Case age ≥ 65				
Diesel-years	−0.00461	0.91*	0.71,1.17	0.47
Asbestos, Y/N	−0.01807	0.98	0.81,1.20	0.86
≤ 50 pack-years†	1.47641	4.38	2.90,6.60	< 0.01
> 50 pack-years†	2.21321	9.14	8.11,13.70	< 0.01
Pack-years missing†	1.35379	3.87	2.56,5.84	< 0.01

* Calculated on the basis of 20 yr of exposure.

† Reference category of zero pack-years (nonsmokers).

exhaust was demonstrated. In a study based on the Third National Cancer Survey where greater than 90% of the cancers were histologically proved, the death certificate for lung cancer was coded appropriately in 95% of cases (35). Because there would be no reason for physicians to link job category with death-certificate-diagnosed lung cancer, resulting misclassification would be random and would reduce the magnitude of the diesel effect observed.

Other sources of confounding that could influence these results are the effect of other, unknown occupational or environmental exposures and passive smoking. It is unlikely that either of these are systematically related to diesel exhaust exposure.

Recently, completed epidemiologic studies have found contradictory results for the association of diesel exhaust exposure and lung cancer. A mortality study of maintenance men employed for at least 1 yr between 1967 and 1975 in the London Transport bus garages and repair facilities was done, with follow-up to 1975 (4). No excess of lung cancer deaths was seen. However, exposure to diesel exhaust was poorly characterized, with both a short duration of exposure and of follow-up. Waller (3) published a study of London Transport workers, men 45 to 64 yr of age, from 1950 through 1974, examining lung cancer deaths among different categories of workers and comparing the rates to expected rates based on London lung cancer death rates. The highest mortality ratio was among those with the highest potential diesel exhaust exposure, but the ratio was not afferent from a group with little diesel exhaust exposure. However, causes of death occurring after a worker left transit authority employment were not recorded. There was also no consideration of cigarette habits or of the ethnic composition of the workers, and, as a result, the national rates used to calculate the Standardized Mortality Ratios (SMR) may not have been appropriate.

Howe and coworkers (10) studied a cohort of retired Canadian railroad workers who were alive in 1965 as well as those who retired between 1965 and 1977. Deaths among active workers were not studied, and only last job worked was available. Analysis was done comparing SMR among population subgroups (nonexposed, possibly exposed, and probably exposed to diesel exhaust). In this study, the composition of the diesel exposure groupings were not discussed. By excluding active workers, subjects with the highest likelihood of past asbestos exposure were studied, and workers likely to have the longest duration of diesel exhaust exposure were excluded. Although these investigators acknowledged some of these limitations, they found a significant trend for lung cancer for workers who were probably exposed to diesel exhaust. Another recent study in a cohort of heavy equipment operators (5) utilizing SMR analysis found increased lung cancer by duration of union membership, but not by the limited exposure data provided. Cigarette smoking was not considered in the analysis.

The relative risk obtained in this current study is low. Some believe that at relative risks of this magnitude, epidemiologic methods cannot be used to establish risk. Critics would indicate that one could never eliminate the effects of confounding factors (36). The pilot study (9) conducted by our group also indicated that the relative risk of lung cancer would likely be of this magnitude. Risk assessment using past studies (i.e., London Transport workers study) have suggested an increased risk of similar magnitude (below 2) (37). Known confounders have been considered, and we have identified no source of systematic bias in the study that would increase the chance of seeing an effect of diesel exhaust exposure.

In the present analysis, we have assumed that each year of diesel exhaust exposure among all exposed job locations was equivalent. We plan to expand these results to consider the different levels of exposure among diesel-exposed railroad workers. Final confirmation of our results await the completion of other studies in diesel-exposed populations or studies in similar groups using different methods, Our findings suggest that other groups with occupational exposures (underground workers exposed to diesel exhaust) may be at excess risk of lung cancer in contrast to those with "background" levels.

Acknowledgment

The writers thank Harry Taplin, Cecelia Bennett, Betty Faucette, and Maureen Ireland for coordinating the collection of death certificates and questionnaires, the secretarial staff of the Channing Laboratory for help with manuscript preparation, and Charles Ford and Michael Cagan for programming assistance. They also thank staff members of the Railroad Retirement Board for their invaluable help with this study.

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