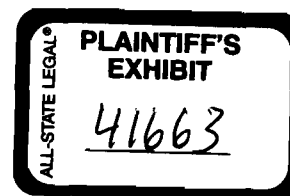


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TITLE: Cancer Mortality (1965-77) in Relation to **Diesel** Fume and Coal Exposure in a Cohort of Retired Railway Workers <1,2>

AUTHOR: Geoffrey R. Howe, <3> Drora Fraser, <3> Joan Lindsay, <4> Bryn Presnal, <3> and Shun Zhang Yu <3,5,6>

ABSTRACT: A cohort study of 43,826 male pensioners of the Canadian National Railway Company was conducted. The cause of death of 17,838 pensioners who died between 1965 and 1977 was ascertained by computerized record linkage to the Canadian national mortality data base. The main finding was an elevated risk of lung cancer for those employed in occupations involving exposure to **diesel** fumes and coal dust, with highly significant dose-response relationships observed. That such association may be due in part to smoking cannot be excluded; but in view of the widespread exposure to **diesel** fumes, the finding warrants further investigation. The present study also demonstrated the utility and feasibility of large-scale occupational cohort studies conducted with the use of computerized record linkage to national mortality records.

TEXT:

Excess cancers of the respiratory system have been reported for a number of occupations associated with exposure to **diesel** fumes, such as truck drivers [n1,n2], transportation workers [n2,n3], and automobile mechanics [n4]. In addition, certain organic extracts of **diesel** engine exhaust have been shown to be carcinogenic in small animals [n5]. Schenker [n6] has pointed out that one major group of workers with relatively high exposure to **diesel** fumes are those employed in certain railway occupations. In an earlier case-control study [n7] we reported an association between exposure to dust and fumes by railway workers and bladder cancer.

Three previous studies of railway workers have been reported. Kaplan [n8] reviewed the causes of death of 6,506 Baltimore and Ohio railway workers; these deaths occurred between 1953 and 1958. He found no association between level of exposure to **diesel** fumes and rate of bronchopulmonary carcinoma. Hueper [n9] compared the causes of death between operating and nonoperating employees of two large American railway companies between 1939 and 1950. There appeared to be an excess of lung cancer among the operating employees, though the associations were based on the comparison of crude rather than standardized rates. **Diesel** locomotives were not introduced into general service until the mid-1950's in the United States [n10]. It is unlikely therefore that these two studies include any workers with exposure to **diesel** fumes over a long period time or workers who had experienced the usual lengthy latent period [n11] associated with carcinogenesis. The third study was of disability and mortality among Finnish railway workers [n12] between 1955 and 1973. Although engineers had the highest rates for cancer and all causes of death combined, the few cancer deaths observed (47) precluded any possibility of meaningfully distinguishing the effects for individual cancer sites.

This paper reports the results of a cohort study of the mortality experience of 43,826 male pensioners of the CNR between 1965 and 1977. A total of 17,838 deaths were observed in the cohort during the study period, the specific cause of death being ascertained by computerized record linkage of the individual records with the Canadian mortality data base maintained by Statistics Canada. Analyses are reported both for specific occupations and for occupations grouped by varying levels of exposure to **diesel** fumes and coal dust.

MATERIALS AND METHODS

The cohort consisted of all male CNR pensioners who had retired before 1965 and who were known to be alive at the start of that year as well as those who retired between 1965 and 1977. A computer file containing records for all members of the cohort was supplied directly to the Health Division of Statistics Canada by the CNR. The records contained identifying

information (given name, surname, month and year of birth, province of residence); date of retirement; occupation in which the individual was employed at the time of retirement; and, where applicable, fact and the date of death. (The date of death was also used as an identifying item for record linkage.) Since this file is used by the company for payment of pensions, it is regularly updated, and in particular the status of each individual (dead or alive) is accurately known. (To receive his pension, each pensioner has to provide on a yearly basis evidence to the effect that he is alive.) However, the specific cause of death was not present on these records, and for the cause to be ascertained it was necessary to link the records to the Canadian mortality data base, which contains records of all deaths registered in Canada since 1950. (It was not necessary to confirm the status of those known to be alive at the end of 1977 in view of the accuracy of CNR's record-keeping system.) The computerized record linkage was carried out with the use of a generalized record linkage system developed specifically for use in medical follow-up studies in Canada [n13]. The linkage was done in Statistics Canada under the auspices of the Canadian Statistics Act. For the preservation of the confidentiality of the data, after the linkage, identifying items such as names were removed from the data and the nonidentifiable records were then used for statistical analyses in the Epidemiology Unit of the National Cancer Institute of Canada.

Of the 17,838 known deaths among the members of the cohort between 1965 and 1977, 16,812 (94.4%) successfully linked to a record on the mortality file. A random sample of 332 unlinked records was matched manually, and from this sample it was estimated that the main reason for linkage failure was missing identifying data on 3.2% of the records. Out-of-Canada residence accounted for 0.9% of records remaining unlinked, miscoding accounted for 0.2%, and surname misspelling accounted for a further 0.2%. In the remaining 1.1% of the records, no apparent reason for the failure to link was found.

Data analyses. -- Occupation at time of retirement (the only occupational information available) was coded to a five-digit code with the use of the Uniform Canadian Classification of Railway Employees [n14]. A total of 76 different occupations were represented in the cohort. Experts in the Department of Industrial Relations, CNR, classified each occupation in terms of exposure to **diesel** fumes (nonexposed, possibly exposed, probably exposed), to coal dust (nonexposed, possibly exposed, probably exposed), and to any other fumes or substances. The other substances involved were welding and paint fumes; propane, acetylene, and oxyacetylene gasses; and dust and grain dust. Statistical analyses were then conducted separately for all individual occupations with at least 50 individuals and for occupations grouped by **diesel** fume exposure, coal exposure, and exposure to other substances.

Person-years of observation were calculated and classified by age at observation (35-39, 40-44, . . . 80-84, ≥ 85 yr old). Members of the cohort either entered the study on January 1, 1965, if they had retired before that date, or entered the study on the date of their retirement; they either left the study on December 31, 1977, if still alive, or left on their date of death. The numbers of observed deaths were classified by age at death (table 2) with the use of the 19 different cancers, for all cancers combined, and for all causes of death combined. SMR were then computed in the usual way as the ratio of the observed death rate in the group under consideration to the expected rate, i.e., the rate in the comparison group, standardized by age at observation (observed number of deaths/expected number of deaths). Since lung cancer mortality rates have changed considerably between 1965 and 1977, SMR for lung cancer were standardized by calendar year of observation (1965-69, 1970-74, 1975-77) as well as by age. For comparisons between subgroups of the cohort, relative risks were estimated as the ratio of their SMR. Comparison rates were those of the Canadian population for the period 1965-77. We computed significance tests and confidence intervals by treating the observed number of deaths as a Poisson variable, and we used the Mantel extension [n15] of the Mantel-Haenszel procedures [n16] to test for trends in relative risk. All *P*-values quoted are one-sided unless otherwise indicated.

RESULTS

Table 1 shows the distribution of year of retirement and age at observation during the study for members of the cohort. Table 2 shows the observed numbers of deaths and SMR for the entire cohort compared to those for the Canadian population for those deaths ascribed to cancer and for all causes combined. The total mortality was less than that expected from population rates, and the difference was highly significant ($P < 0.001$). However, the magnitude of the deficit (5%) was much less than that typically seen in a working population due to the healthy-worker effect [n19]; although this deficit can probably be ascribed to such an effect, it was presumably mitigated by the fact that this was a retired population rather than an actively working population. There was no such deficit in the total number of deaths from malignant neoplasms, and again this finding was consistent with other observations of the healthy-worker effect in which cancer is usually less affected than other chronic conditions. In addition, some 5.6% of deaths could not be ascribed to a specific cause; therefore, if the deaths show the same distribution as the remaining 94.4%, the SMR in table 2 should be increased by about 5.9% (with the exception of all causes combined). In general this correction factor was ignored in subsequent analyses since it would make only a very small difference to the estimated SMR, and its effect would of course be conservative. The only statistically significant difference from a specific cause seen in the cohort was for leukemia and aleukemia, where a 20% decrease in deaths was observed compared to the expected number, on the basis of population rates.

TABLE 1. -- *Distribution of year of retirement and age at observation*

Yr of retirement	No. of CNR employees	Percentage
<1950	2,527	5.8
1950-54	3,875	8.8
1955-59	5,511	12.6
1960-64	6,783	15.5
1965-69	9,242	21.1
1970-74	8,738	19.9
1975-77	7,150	16.3
Total	43,826	100.0

Age at observation, yr	Person-years	Percentage
<65	37,581	13.0
65-69	84,340	29.1
70-74	70,661	24.4
75-79	50,008	17.2
80-84	30,630	10.6
>=85	16,965	5.8
Total	290,185	100.0

TABLE 2. -- SMR for entire cohort n1 for deaths due to cancer (1965-77)

Cancer site or type	International Classifica- tion of Diseases n2		Observed No. of deaths	Expected No. of deaths	SMR (P-value) n3
	Seventh Re- vision n17	Eighth Re- vision n18			
Buccal cavity & pharynx, except lip	141-148	141-149	71	87.7	0.81
Lip	140	140	5	11.3	0.44
Esophagus	150	150	74	82.4	0.90
Stomach	151	151	362	389.1	0.91
Intestine, except rectum	152-153	152-153	382	382.4	1.00
Rectum and rectosigmoid junction	154	154	175	178.2	0.98
Larynx	161	161	49	44.7	1.10
Trachea, bronchus & lung	162-163	162	933	881.0	1.06
Bone	196	170	21	15.7	1.34
Skin	190-191	172-173	25	36.9	0.68
Prostate gland	177	185	492	499.1	0.99
Bladder	181.0	188	175	169.6	1.03
Other & unspecified					

urinary organs	181.7-181.8	189	58	45.9	1.26
Brain	193.0	191, 192.0	38	33.1	1.15
Liver	155	155-156	68	69.0	0.99
Pancreas	157	157	197	211.1	0.93
Leukemia & aleukemia	204	204-207	97	121.8	0.80 (0.024)
Other neoplasms of lymphatic & hematopoietic tissues	200-205	200-203	150	133.1	1.13
Other & unspecified cancers			201	228.9	0.88
All cancers	140-205	140-209	3,573	2,625.9	0.99
All causes of death	001-999	001-999	17,838	18,833.0	0.95 (<0.001)

n1 Total person-years of observation, 290,186.

n2 The Seventh Revision of the International Classification of Diseases applies to deaths occurring from 1965 to 1968 and the Eighth Revision, from 1969 to 1977.

n3 Two-sided *P*-value.

Diesel exposure. -- When individuals were grouped according to their exposure to diesel fumes at three levels (nonexposed, possibly exposed, and probably exposed), the only cancer cause of death in which the corresponding trend test was statistically significant and in which the relative risk consistently increased with increasing exposure was lung cancer. The data for lung cancer are shown in table 3, the trend being highly significant ($P < 0.001$). (Few individuals could not be classified for their diesel fume exposure, so the total observed deaths and person-years in table 3 were slightly smaller than the corresponding values in table 2.) Although the mortality rate for all causes of death combined also showed a significant trend, the increases in relative risks were much smaller than those for lung cancer, being respectively 1.00, 1.04, and 1.09 for nonexposed, possibly exposed, and probably exposed groups.

TABLE 3. -- *Cancers of the trachea, bronchus, and lung in workers exposed to varying levels of diesel fumes*

Parameter	Level of exposure (<i>P</i> -value)		
	Non-exposed	Possibly exposed	Probably exposed
Observed No. of deaths	239	407	279
Person-years of observation	85,200	121,850	74,571
Relative risk n1	1.00	1.20 (0.013)	1.35 (<0.001)

n1 Risk relative to nonexposed group. *P*-trend, <0.001.

Coal exposure. -- When trend analyses were conducted for coal exposure in a similar way to the trend analyses for diesel exposure, only lung cancer showed consistent elevations in risk with increasing exposure, with a corresponding statistically significant trend. The data are shown in table 4. The corresponding relative risks for all causes of death combined were 1.00, 1.04, and 1.08, for nonexposed, possibly exposed, and probably exposed groups, respectively, again the increase being considerably less than the corresponding increase for lung cancer.

TABLE 4. -- *Cancers of the trachea, bronchus, and lung in workers exposed to varying levels of coal*

*dust*Level of exposure (*P*-value)

Parameter	Non-exposed	Possibly exposed	Probably exposed
Observed No. of deaths	245	374	306
Person-years of observation	87,723	111,950	81,948
Relative risk n1	1.00	1.21 (0.012)	1.35 (<0.001)

n1 Risk relative to nonexposed group. *P*-trend, <0.001.

Joint exposure of diesel fumes, coal, and asbestos. -- There is considerable overlap between occupations involving probable exposure to **diesel** fumes and probable exposure to coal dust as indicated by the similarity of the results presented in tables 3 and 4. This was a consequence of the transition from steam power to **diesel** power over the years. Most members of the cohort would have had been in employment during the years when that transition occurred, which would make it difficult for one to distinguish between the **diesel** fume and coal associations with lung cancer. Analyses restricted to individuals who retired before 1950, i.e., who would probably have had essentially coal dust rather than **diesel** fume exposure, yielded relative risks of 1.0 (based on 8 deaths), 0.70 (based on 13 deaths), and 0.44 (based on 7 deaths) respectively for individuals nonexposed, possibly exposed, and probably exposed to coal dust, with similar results being obtained for "**diesel** fume exposure." Analysis restricted to individuals who retired from 1950 onward yielded relative risks of 1.0 (based on 231 deaths), 1.23 (based on 393 deaths), and 1.40 (based on 273 deaths) respectively for individuals nonexposed, possibly exposed, and probably exposed to **diesel** fumes. These figures suggested that the association was with **diesel** fumes rather than with coal, but this conclusion must, of course, remain tentative.

A further complication arose because individuals involved in the maintenance of steam locomotives may have been exposed to high levels of asbestos (Terracini B: Personal communication), and asbestos-related deaths have been reported in such individuals [n20]; thus part of the observed associations with lung cancer could be due to asbestos exposure. However, when those occupational groups that included individuals involved in locomotive maintenance were excluded from analysis, the relative risks for individuals nonexposed, possibly exposed, and probably exposed to **diesel** fumes were respectively 1.0 (based on 239 deaths), 1.21 (based on 333 deaths), and 1.33 (based on 256 deaths), again with a highly significant trend ($P<0.001$). Those individuals involved in locomotive maintenance could not be specifically identified, but the relative risk for lung cancer for the occupational groups that included such individuals was 1.25 (97 deaths), relative to individuals in the non-**diesel** fume-exposed group. Since the occupational groups involving locomotive maintenance were in the possibly or probably **diesel** fume-exposed group, no conclusion could be reached about any possible asbestos effect, which could easily be masked by dilution by other members of the group without asbestos exposure, but the **diesel** fume effect does seem to be independent of any asbestos effect.

Individual occupations. -- Table 5 shows the results of the analysis of the 70 individual occupations in which there were at least 50 individuals. Because of the problem with multiple comparisons (70 occupations combined with 21 causes of death suggest that, on the average, 73 of the comparisons will result in statistically significant results by chance), results were represented only for comparisons in which the lower 95% limit for the SMR was greater than or equal to 1.10.

TABLE 5. -- SMR for individual occupations for specific cancer causes of death n1

Job title	Cancer	Person-years of observation	No. of served deaths	SMR	Lower 95 % confidence limit
Brakeman	Buccal cavity and pharynx, except lip	3,306	4	4.08	1.39
Bridge & building master	Other neoplasms of lymphatic	2,611	4	3.67	1.25

	and hematopoietic tissue				
Carman	Brain	22,838	7	2.78	1.30
Coach cleaner	Prostate gland	1,424	6	2.93	1.27
Conductor	Trachea, bronchus, and lung	12,104	50	1.52	1.18
Cook	Trachea, bronchus, and lung	2,626	15	2.09	1.20
Cook	Other neoplasms of lymphatic and hematopoietic tissue	2,626	5	3.54	1.21
Electrical worker	Prostate gland	2,147	8	2.53	1.26
Freight loader	Bladder	5,865	8	3.40	1.69
Fuel man	Prostate gland	487	4	5.71	1.95
Locomotive engineer	Rectum	19,372	22	1.70	1.15
Motorman	Colon	1,958	8	3.08	1.53
Motorman	Rectum	1,958	4	3.31	1.13
Porter	Trachea, bronchus, and lung	1,826	11	2.13	1.19
Technical supervisor	Other neoplasms of lymphatic and hematopoietic tissue	7,822	10	3.04	1.65
Unspecified foreman	Trachea, bronchus, and lung	7,082	31	1.62	1.17
Yard helper	Trachea, bronchus, and lung	2,731	14	1.93	1.17
Yard master	Pancreas	3,507	7	2.95	1.39

n1 SMR, lower 95% confidence limit, ≥ 1.10 .

Other substances. -- Analysis of occupations involving exposure to substances other than diesel fumes and coal dust yielded only one statistically significant result in which there were at least 4 deaths. To attempt to interpret results based on any smaller number of observed deaths is probably meaningless. The 4,629 individuals who had been exposed to welding fumes showed an excess of deaths from brain tumors with 10 deaths observed compared to 3.14 expected, giving an SMR of 3.18 (95% confidence interval: 1.53-5.86).

DISCUSSION

The major finding of this study, which is the largest study to date of railway workers, is the excess risk of lung cancer associated with exposure to diesel fumes and coal dust. These elevations are highly significant and show increasing risk with increasing level of exposure. They are therefore almost certainly not due to chance. Two factors in the present study will in fact have led to a probable underestimation of risk. The first is the 5.6% of deaths that could not be ascribed to a particular cause as described above. The second factor, probably the more important, is that some misclassification of exposure almost certainly will have occurred. Since only the occupation at the time of retirement was available for analysis, some individuals undoubtedly will have had a number of years of experience in jobs other than the jobs from which they retired. In addition, although it is possible that generally an individual specified with a job title will have had a certain level of exposure, individuals with the same job title will not necessarily be completely homogeneous; again, therefore, exposure based on job title may lead to some misclassification. Since these effects will have led to an underestimate of the true underlying relative risk, this argument adds support to the reality of the observed association. One further limitation of the present study with respect to exposure classification is the unavailability of duration of employment for cohort members.

The major potential confounder of any association with lung cancer is, of course, smoking. Since data are not available on the smoking habits of individuals in the present study, it is necessary to rely on indirect evidence. Mortality from smoking-related cancers (i.e., cancers of the bladder, larynx, esophagus, and buccal cavity combined) other than lung cancer is slightly elevated in individuals with **diesel** fume exposure, with relative risks of 1.00, 1.08, and 1.16 respectively for nonexposed, possibly exposed, and probably exposed to **diesel** fumes. There is no excess for chronic bronchitis (1.00, 0.81, 1.04), but there is an excess for emphysema (1.00, 1.35, 1.44). These data suggest the possibility of some confounding of the lung cancer associations by smoking. It seems unlikely, however, particularly in view of the underestimate of relative risk, which has probably occurred due to misclassification, that the excess lung cancer is entirely due to smoking. It has been reported [n10] that railway workers do not in general have smoking habits very different from those of the general population.

As discussed above, in the present data we do not find possible to definitively distinguish between the effects of exposure to **diesel** fumes and coal dust because of the considerable overlap between these exposures. However, evidence exists both from epidemiologic studies [n1-n4] and animal studies [n21] of an increase in risk of lung cancer associated with exposure to **diesel** fumes. No such comparable evidence has been presented for exposure to coal dust. It would therefore appear that of the two substances, if one association was due to confounding by the other, **diesel** fumes are the more likely candidate for the true association. Certainly, in terms of the proportion of the population exposed, **diesel** fumes represent a greater potential hazard than does coal dust, both for individuals exposed occupationally and for the general population. The possibility of a causal association between **diesel** fume exposure and lung cancer certainly warrants further investigation.

The lack of an excess risk of death for bladder cancer suggests that the association seen in a previous case-control study [n7] was due to chance. Similarly, the leukemia and aleukemia findings in the present study may have been a chance effect, since there is no obvious rationale for such a negative association.

This study further demonstrates the utility of cohort studies of large samples of individuals employed in a specific industry. Computerized record linkage in conjunction with national mortality data provides a most useful and relatively cheap tool for the follow-up of larger numbers of individuals. For common diseases such as lung cancer, such methods can reduce sampling errors to the point where one may discount chance as an explanation of any major observed association.

ABBREVIATIONS USED: CNR=Canadian National Railway Company;

SMR=standardized mortality ratio(s).

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<3> National Cancer Institute of Canada Epidemiology Unit, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada M5S 1A8.

<4> Health Division, Statistics Canada, Ottawa, Ontario, Canada K1A 0Z5

<5> On leave from Shanghai First Medical College, Shanghai, The People's Republic of China.

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