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Occupational exposure to diesel engine emissions and risk of cancer in Swedish men and women

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Abstract

Objective: To investigate the risk of cancer among workers exposed to diesel emissions in a large record-linkage study from Sweden.
Methods: The Swedish Cancer Environment Register III contains nationwide data on cancer incidence during 1971–1989, by occupation and industry of employment as reported in the 1960 and 1970 censuses. After excluding farmers, we classified job and industry titles according to estimated probability and intensity of exposure to diesel emissions. Exposed men in the 1960 census contributed over 7,400,000 person-years, and exposed women contributed over 240,000. We compared them to the remainder of the employed population, using indirect standardization and multivariate Poisson regression analysis.
Results: Men exposed in the 1960 census experienced an increased risk of lung cancer: the relative risks (RRs) were 0.95 (95% confidence interval [CI] 0.9–1.0), 1.1 (1.1–1.2) and 1.3 (1.3–1.4) for low, medium, and high intensity of exposure. Corresponding results for probability of exposure were 1.1 (1.0–1.1), 0.9 (0.86–0.94) and 1.2 (1.1–1.2). The risk was higher for squamous cell carcinoma of the lung than for other histological types. Results in women were not suggestive of an effect (RR in the category of medium or high intensity of exposure 1.1, 95% CI 0.6–1.8). A small but significant increase in risk of cancers of the stomach (SIR 1.06), pancreas (SIR 1.05), larynx (SIR 1.09), and the kidney (SIR 1.06) was present among men exposed to diesel emissions, without a clear trend according to either probability or intensity of exposure. The SIR among women was non-significantly increased for stomach, pancreatic, and laryngeal cancers, but not for kidney cancer. Furthermore, a significantly increased risk of oral/pharyngeal (SIR 1.64) and cervical (SIR 1.48) cancers was present among women, with a suggestion of a dose–response relationship. There was no increased risk of bladder cancer in either gender.
Conclusions: The results of this study provide evidence of a positive exposure–response relationship between exposure to diesel emissions and lung cancer risk among men. The positive results for other neoplasms, such as stomach, pancreatic, oral/pharyngeal, and cervical cancers, cannot be attributed to diesel exposure, but they deserve attention in future investigations.

Introduction

Exposure to diesel engine emissions has been classified by the International Agency for Research on Cancer as probably carcinogenic to humans, on the basis of sufficient evidence of carcinogenicity in experimental animals and limited evidence of carcinogenicity in humans [1]. Since then, a number of additional epidemiological studies have been published that provide information on cancer risk in occupational groups exposed to diesel emissions. A recent meta-analysis resulted in an overall relative risk (RR) of lung cancer of 1.3 (95% confidence interval [CI] 1.2–1.5) [2]. The

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available studies have involved railroad workers, heavy equipment operators, garage workers, truck and bus drivers, and dock workers. In a few instances several occupational groups were classified according to probability or intensity of exposure to diesel emissions on the basis of a "job-exposure matrix" or an expert assessment of occupational histories [3–8]. Several studies have reported an excess risk of cancers other than the lung: in particular, the risk of bladder cancer was reported to be elevated among truck drivers [9–11] and other occupational groups exposed to diesel emissions [4, 12–14]. An excess of kidney cancer has also been reported among railroad workers exposed to diesel emissions [15]. In addition, other neoplasms, such as multiple myeloma, leukemia, and Hodgkin's disease, have been sporadically associated with diesel emission exposure [1, 16].

We have conducted a study of the risk of cancer among Swedish men and women with available occupational data from the 1960 and 1970 censuses according to intensity and probability of exposure to diesel emissions.

Methods

In 1960 and 1970, information was collected through questionnaires on demographic characteristics and employment status, including job and industry title, for each member of the Swedish population [17]. Study subjects were followed up for mortality during 1 January 1971–31 December 1989 through a linkage with the national Register of Causes of Death. The further linkage of this population with the Swedish Cancer Register for the same period 1971–1989 created the database used in this study (Cancer Environment Register III).

Each cohort member contributed person-years of observation from 1 January 1971 until death or 31 December 1989. For the purpose of this analysis we excluded individuals without employment and those employed as farmers at either census. We classified job and industry titles according to probability and intensity of exposure to diesel engine emissions and according to our confidence in the assessment. The matrix consisted of one category of unexposed jobs and three categories (low, medium, and high) of probability and intensity of exposure. The category of low probability included jobs in which 1–24% of workers experience exposure to diesel emissions. Corresponding ranges were 25–74% for medium probability and 75–100% for high probability. There were in total eight combinations of exposure, since no jobs were classified as having low probability and high intensity of exposure. In some instances the job title determined the final exposure assessment, while in other instances both the job and the industry titles contributed to the assessment. For most jobs and industries we assessed exposure with high confidence; for a few, however, our confidence in the assessment of exposure was lower. Job and industries classified at medium or high probability of exposure are listed in the Appendix.

We applied the matrix to the job and industry titles of the cohort members, as recorded at both the 1960 and the 1970 censuses. Given the high concordance of categories at the two censuses in men (82% concordant person-years for any exposure; 77% for probability and 82% for intensity level among those classified as exposed at both censuses), we report mainly results based on the data collected at the 1960 census.

Subjects in the cohort were classified according to residence in one of four main regions of the country, and according to residence in large urban areas (Stockholm, Gothenburg, Malmo) or the rest of the country.

We calculated the expected number of cancers in each category of exposure by applying the 5-year gender-, age- and calendar year-specific cancer incidence rates from the whole national population. For all neoplasms combined, and for specific neoplasms, we derived the standardized incidence ratios (SIRs), defined as the ratio of the observed to the expected cases. Second primary cancers were included in the calculation of both observed and expected cases. We calculated the 95% CIs assuming a Poisson distribution of the observed number of cases.

In addition, we conducted multivariate Poisson regression analyses [18] on the occurrence of cancers of the larynx, lung (including specific histological types in order to obtain further insight into the possible mechanism of diesel-related lung cancer), bladder, kidney, oral cavity and pharynx, stomach, pancreas, and cervix among workers exposed to diesel emissions as compared to unexposed workers. These cancer sites either represented neoplasms of *a-priori* interest [1, 16], or were found at increased risk in the SIR analysis. In the multivariate regression analysis, we adjusted for 5-year age groups and 4-year calendar periods, as well as for region of residence and urban or rural residence. In this analysis, we excluded second primary neoplasms, and truncated the follow-up of subjects at the date of diagnosis of the first cancer. The number of cases of cancer is therefore slightly lower than that of the analysis based on the comparison to the external reference population.

We repeated most analyses after exclusion of subjects employed in jobs with low confidence of assessment of diesel emission exposure. Given the small number of women employed in jobs classified at high intensity of exposure, we combined them with women at medium intensity of exposure.

Results

Table 1 presents the distribution of person-years of observation according to categories of exposure to diesel emissions based on employment information from the 1960 census. There were about 28 million person-years contributed by men in this population and about 15 million person-years contributed by women. More than 7,400,000 person-years (26.5% of the total) among men were classified as exposed to diesel emissions: this number was over 240,000 (1.6%) among women. Most individuals classified at low or medium probability of exposure were also classified at low intensity; conversely, individuals at high probability were mainly classified at medium or high intensity.

Table 2 reports the incidence of cancer among subjects exposed to any level of probability or intensity of diesel emissions according to the 1960 census data. Among exposed men, a total of 54,404 cases of cancer occurred, versus 54,109 expected cases (SIR 1.005, 95% CI 0.997–1.014). The figures for observed and expected cases among women were 1479 and 1502.5 (SIR 0.98, 95% CI 0.93–1.04). Among men a significant increase was present for cancers of the oral cavity and pharynx, stomach, pancreas, larynx, lung, and kidney, and among women there were significant excesses of oral and pharyngeal and of cervical cancers and non-significant excesses of stomach, laryngeal, and lung cancers. When the analysis was restricted to subjects with high probability of exposure the increase in risk of cancers of the stomach (SIR 1.10, 95% CI 1.04–1.17), larynx (SIR 1.15, 95% CI 1.00–1.31), lung (SIR 1.21, 95% CI 1.16–1.27), and kidney (SIR 1.10, 95% CI 1.02–1.19) was confirmed among men and there was also an increased risk of lymphocytic leukemia (SIR 1.16, 95% CI 1.01–1.31). Women in the corresponding category had increased SIRs for cervical cancer (1.86, 95% CI 1.10–2.94) and for laryngeal cancer (7.15, 95% CI 1.44–20.9).

When we used the 1970 census information to classify subjects according to exposure to diesel emissions, the results were remarkably similar to those reported in Table 2, reflecting the high proportion of individuals with the same (or a similar) job and industry title at the two censuses.

Table 3 presents the results of the Poisson regression analysis among men for selected cancers. Subjects with high probability of exposure had an increased risk of lung cancer, and the trend according to probability of exposure was statistically significant ($p = 0.004$), despite a decrease in risk in the middle category. The analysis of lung cancer risk according to intensity of exposure resulted in an increasing trend ($p < 0.001$), with RR in the category at high intensity of 1.3 (95% CI 1.26–1.42). Within each category of probability of exposure there was an increase in risk according to estimated intensity of exposure (not shown in detail). The RR in the category at high probability and intensity of exposure was 1.3 (95% CI 1.25–1.44).

The regression analysis based on information collected at the 1970 census produced results very similar to those reported in Table 3 (not shown in detail). When we restricted the analysis to subjects classified in the same category of probability or intensity of exposure at both the 1960 and the 1970 censuses, RRs were 1.1 (95% CI 0.93–1.13), 0.86 (0.80–0.94) and 1.2 (1.08–1.27) in the three categories of probability of exposure and 0.95 (0.90–1.00), 1.1 (1.00–1.22), and 1.3 (1.21–1.47) in the categories of intensity of exposure.

When we analyzed the risk of different histological types of lung cancer (Figure 1), an increased risk with increasing estimated intensity of exposure was present for all three major histological types (squamous cell carcinoma, small cell carcinoma, adenocarcinoma), but it was strongest for squamous cell carcinoma (RR in the category at high exposure 1.4, 95% CI 1.28–1.56). Similarly, the risk of squamous cell carcinoma was higher than that of other histological types of lung cancer among men classified at high intensity and probability of exposure in 1960 (RR 1.5, 95% CI 1.36–1.69).

No clear trend was apparent among men in laryngeal or bladder cancer risk according to either probability or intensity of diesel emission exposure (Table 3). No trend

Table 1. Person-years of observation by intensity and probability of exposure to diesel exhaust in 1960

Probability	Intensity		
	Low	Medium	High
Men[a]			
Low	2,577,940	77,676	0
Medium	2,076,112	270,842	291,492
High	207,394	1,002,027	921,448
Women[a]			
Low	144,065	584	0
Medium	51,628	3098	437
High	2534	37,953	287

[a] Person-years among unexposed subjects: 20,700,000 among men; 14,800,000 among women.

Table 2. Standardized incidence ratio of selected neoplasms among subjects exposed in 1960 to diesel emissions

Neoplasm	ICD-7	Men			Women		
		N	SIR	95% CI	N	SIR	95% CI
All cancers	140–209	54,404	1.01	1.00–1.01	1479	0.98	0.93–1.04
Oral and pharyngeal cancer	140–148	1733	1.05	1.00–1.10	31	1.64	1.11–2.33
Esophageal cancer	150	701	0.98	0.91–1.05	8	1.14	0.49–2.25
Stomach cancer	151	3651	1.06	1.03–1.10	65	1.16	0.90–1.48
Colon cancer	153	3829	0.97	0.94–1.00	106	0.90	0.74–1.09
Rectal cancer	154	2804	1.00	0.96–1.04	58	0.96	0.73–1.24
Liver and biliary tract cancer	155	1196	1.03	0.97–1.09	42	0.95	0.69–1.29
Pancreatic cancer	157	1859	1.05	1.00–1.10	47	1.09	0.80–1.45
Sinonasal cancer	160	151	1.16	0.98–1.36	3	1.50	0.31–4.38
Laryngeal cancer	161	730	1.09	1.01–1.17	5	2.39	0.78–5.57
Lung cancer	162	6266	1.09	1.06–1.12	57	1.09	0.83–1.42
Breast cancer	170	95	1.01	0.81–1.23	360	0.89	0.80–0.99
Cervical cancer	171	–	–	–	79	1.48	1.17–1.84
Endometrial cancer	172	–	–	–	77	0.85	0.67–1.07
Ovarian cancer	175	–	–	–	106	1.12	0.92–1.36
Testicular cancer	178	197	0.80	0.70–0.92	–	–	–
Prostate cancer	177	11,875	0.99	0.97–1.01	–	–	–
Kidney cancer	180	2243	1.06	1.02–1.11	33	0.82	0.57–1.16
Bladder cancer	181	4018	1.00	0.97–1.03	38	1.02	0.72–1.41
Skin melanoma	190	1272	0.88	0.83–0.93	37	0.87	0.61–1.19
Brain cancer	193	1318	0.94	0.89–0.99	40	0.90	0.65–1.23
Thyroid cancer	194	263	1.00	0.88–1.13	18	0.94	0.56–1.48
Connective tissue sarcoma	197	364	1.00	0.89–1.10	9	0.95	0.43–1.80
Hodgkin's disease	201	306	1.00	0.89–1.11	8	1.33	0.57–2.63
Non-Hodgkin's lymphoma	200–202	1531	0.96	0.91–1.01	33	0.93	0.64–1.31
Multiple myeloma	203	865	0.98	0.92–1.05	14	0.68	0.37–1.15
Leukemia	204–207	1504	1.00	0.95–1.05	28	0.93	0.62–1.35

N, number of cases; ICD-7, *International Classification of Diseases*, 7th version; SIR, standardized incidence ratio; CI, confidence interval.

in either cancer was observed for either probability or intensity of exposure when we combined the two dimensions of exposure: the RR in the category at high probability and intensity of exposure was 0.92 (95% CI 0.83–1.02) for bladder cancer and 1.1 (0.84–1.34) for laryngeal cancer (other results not shown in detail). No clear trend in kidney cancer risk was present according to probability of diesel emission exposure. Risk of kidney cancer tended to increase slightly with increasing intensity of exposure, although the trend was not significant (*p*-value 0.11).

The detailed analysis of cancer of the oral cavity among men (Table 3) did not suggest an association with diesel emission exposure: RRs were higher in the categories of low intensity or low probability of exposure as compared to categories at higher exposure. The risk of stomach cancer was slightly higher among men at high probability of diesel emission exposure than among other men (Table 3); no clear trend was present, however, according to intensity of exposure or according to the combined indicator of probability and intensity of exposure. The RR for the category of high probability and intensity of exposure was 1.1 (95% CI 0.99–1.22).

A weak, non-significant trend in risk of pancreatic cancer was suggested among men according to both probability and intensity of exposure to diesel emissions (*p*-values 0.19 for intensity and 0.33 for probability of exposure, Table 3). The RR in the category at high probability and intensity of exposure was 1.2 (95% CI 1.01–1.33).

The results of risk of cancers of the larynx, bladder, kidney, oral cavity, stomach, and pancreas were not substantially modified when we assessed diesel emission exposure based either on the 1970 data, or on the data from both censuses taken together.

When we excluded men employed in jobs for which our confidence in the exposure assessment was low (4.1% of person-years among exposed), the results were virtually unchanged, although the precision of the risk estimates was slightly reduced. For example, the RR of lung cancer in the three categories of probability of exposure shown in Table 3 were 1.1 (95% CI 1.04–1.14), 0.90 (95% CI 0.86–0.94) and 1.2 (95% CI 1.10–1.21).

Table 3. Relative risk of selected cancers among men according to intensity and probability of exposure to diesel exhaust in 1960

	Lung cancer			Laryngeal cancer			Bladder cancer			Kidney cancer			Oral and pharynx cancer			Stomach cancer			Pancreatic cancer		
	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI
Unexposed	17,979	1.0	Ref	2081	1.0	Ref	12,287	1.0	Ref	6047	1.0	Ref	4484	1.0	Ref	9847	1.0	Ref	5311	1.0	Ref
Probability																					
Low	2222	1.1	1.04–1.13	272	1.1	0.99–1.27	1380	0.99	0.94–1.05	762	1.1	0.99–1.15	633	1.2	1.11–1.26	1178	1.1	1.01–1.14	608	1.0	0.93–1.10
Medium	1881	0.90	0.86–0.94	218	0.92	0.80–1.05	1220	0.84	0.79–0.89	714	0.96	0.89–1.04	559	1.1	0.99–1.18	1296	1.1	0.99–1.11	628	0.97	0.89–1.05
High	1841	1.2	1.10–1.21	204	1.1	0.96–1.28	1069	0.98	0.92–1.04	594	1.0	0.96–1.14	439	1.1	0.99–1.21	1004	1.1	1.05–1.20	522	1.1	0.99–1.19
Intensity																					
Low	3705	0.95	0.92–0.98	473	1.1	0.95–1.17	2453	0.91	0.87–0.95	1366	0.99	0.94–1.06	1150	1.2	1.11–1.26	2371	1.1	1.01–1.11	1183	0.99	0.93–1.06
Medium	1181	1.1	1.08–1.21	127	1.1	0.88–1.26	725	1.0	0.95–1.11	382	1.0	0.94–1.16	280	1.2	0.95–1.21	648	1.1	1.05–1.23	315	1.0	0.91–1.14
High	1058	1.3	1.26–1.42	94	0.99	0.81–1.22	491	0.91	0.83–1.00	322	1.1	0.99–1.24	201	0.98	0.85–1.13	459	1.1	1.01–1.22	260	1.1	0.99–1.27

N, number of cases of cancer; RR, relative risk, adjusted for age, calendar period, geographical region, and urban/rural residence; CI, confidence interval; Ref, reference category.

Table 4 presents selected results of the Poisson regression analysis among women (we did not perform this analysis on laryngeal cancer risk given the small number of cases). No clear suggestion of a trend according to either probability or intensity of exposure to diesel emissions was apparent for cancers of the lung, bladder, or kidney. However, in a separate analysis of combined level of probability and intensity of exposure, the RR of lung cancer among women employed in jobs at high probability and medium-high intensity of exposure was 1.5 (95% CI 1.22–1.91). No trend in risk of stomach or pancreatic cancer with increasing diesel emission exposure was suggested among women. In contrast, the risk of cancer of the oral cavity and pharynx, and of cancer of the cervix, increased with increasing estimated intensity and probability of exposure, although not monotonically. For both cancers the highest risk was found among women classified at high probability and medium or high intensity of exposure (oral and pharyngeal cancer: RR 1.8, 95% CI 0.82–4.08; cervical cancer: RR 1.7, 95% CI 1.10–2.78).

Discussion

The main results of this study are: (a) an increased risk of lung cancer among men with increasing estimated probability and intensity of exposure to diesel emissions; (b) an increased risk of cancers of the stomach, pancreas, larynx, and kidney among men exposed to diesel emissions, without a clear trend according to either probability or intensity of exposure; (c) an increased risk of oral, pharyngeal, and cervical cancers among women, with a suggestion of a dose–response relationship, but without a similar risk for oral cancer in men; and (d) the lack of an increased risk of bladder cancer in either gender.

An advantage of our study is its large size. The number of person-years of observation contributed by subjects classified as exposed to diesel emissions in 1960 was over 7,400,000 in men and over 240,000 in women. The nationwide coverage of the study and its almost complete follow-up are important strengths. The use of cancer incidence data is an additional important aspect of our investigation, especially for neoplasms with relatively low fatality, such as laryngeal and cervical cancers.

The main limitation of the present study is the quality of information on exposure. Exposure assessment was based on self-reported occupation and industry of employment at the time of the 1960 and 1970 censuses. These data might suffer from misclassification from errors in reporting and coding. Information on the

Table 4. Relative risk of selected cancers among women according to probability and intensity of exposure to diesel exhaust in 1960

	Lung cancer			Bladder cancer			Kidney cancer			Oral and pharynx cancer			Stomach cancer			Pancreatic cancer			Cervical cancer		
	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI	N	RR	95% CI
Unexposed	3527	1.0	Ref	2347	1.0	Ref	2208	1.0	Ref	1160	1.0	Ref	3128	1.0	Ref	2632	1.0	Ref	3561	1.0	Ref
Probability																					
Low	32	0.85	0.60–1.20	25	0.94	0.63–1.39	18	0.76	0.48–1.21	18	1.4	0.91–2.30	42	1.3	0.94–1.73	32	1.1	0.79–1.58	47	1.3	1.01–1.81
Medium	6	0.62	0.28–1.39	3	0.50	0.16–1.55	5	0.84	0.35–2.02	4	1.2	0.46–3.31	10	1.2	0.65–2.24	7	1.0	0.48–2.12	13	1.1	0.63–1.87
High	13	1.1	0.61–1.82	5	0.68	0.28–1.63	4	0.56	0.21–1.50	6	1.7	0.75–3.74	6	0.66	0.30–1.48	5	0.61	0.26–1.48	18	1.6	1.03–2.60
Intensity																					
Low	38	0.80	0.58–1.10	27	0.82	0.56–1.20	23	0.77	0.51–1.16	22	1.4	0.77–3.84	50	1.2	0.91–1.59	39	1.1	0.79–1.49	60	1.3	1.00–1.67
Medium–high	13	1.1	0.62–1.84	6	0.84	0.38–1.87	4	0.58	0.22–1.54	6	1.7	0.77–3.84	8	0.92	0.46–1.85	5	0.64	0.27–1.54	18	1.6	1.01–2.56

N, number of cases of cancer; RR, relative risk, adjusted for age, calendar period, geographical region, and urban/rural residence; CI, confidence interval; Ref, reference category.

quality of data on occupational titles at the 1960 Swedish census was provided by Warnryd and colleagues [19]. These authors used for comparison an interview-based survey of 9000 men and women conducted in 1960 and 1961. The proportion of concordant occupational titles was 72%, suggesting a reasonable quality of the census data. Given the prospective nature of our study, however, any such misclassification is likely to have operated non-differentially with respect to cancer. Another problem originating from the use of census data is the lack of information on duration of employment in jobs and industries entailing exposure to diesel emissions. We partly addressed this drawback by separately analyzing workers classified as exposed at one or both censuses.

Our results were similar no matter whether we used the data from the 1960 or the 1970 census, and no trend was present according to period of employment in jobs and industries entailing diesel emission exposure. For example, men classified at high intensity of exposure in 1960 and among the unexposed in 1970 had a RR for lung cancer of 1.3 (95% CI 1.16–1.47), and those classified as unexposed in 1960 and at high intensity of exposure in 1970 had a RR of 1.3 (95% CI 1.11–1.45). The use of diesel-powered heavy-duty trucks started in Sweden in the early 1950s, that of light-duty trucks and buses started in the late 1950s. Since the beginning of the 1960s, diesel has been by far the dominating fuel for trucks and buses.

A further limitation of our exposure data concerns the use of a job-exposure matrix: the ecological nature of exposure assessment, with all individuals in the same job and industry title being assigned to the same category of probability and intensity of exposure, results in non-differential misclassification [20]. We attempted to reduce this problem by assessing different levels of probability of exposure to diesel emissions, since it is likely that misclassification was reduced in categories at increased probability of exposure.

Finally, we lacked information on potential confounders, chiefly tobacco smoking, exposure to other occupational carcinogens, and dietary factors. The presence of an increase in risk of several tobacco-related neoplasms, in particular lung and laryngeal cancers, adds to the hypothesis of a confounding effect of tobacco smoking. The lack of an increase in bladder cancer risk, on the other hand, speaks against this interpretation. Smoking habits were collected in a random survey of over 50,000 Swedish men conducted in 1963, and were linked with census information on occupation [21]. Male workers in transport and communication industries reported a higher proportion of regular smokers (59.8% in the 18–49 age group) than

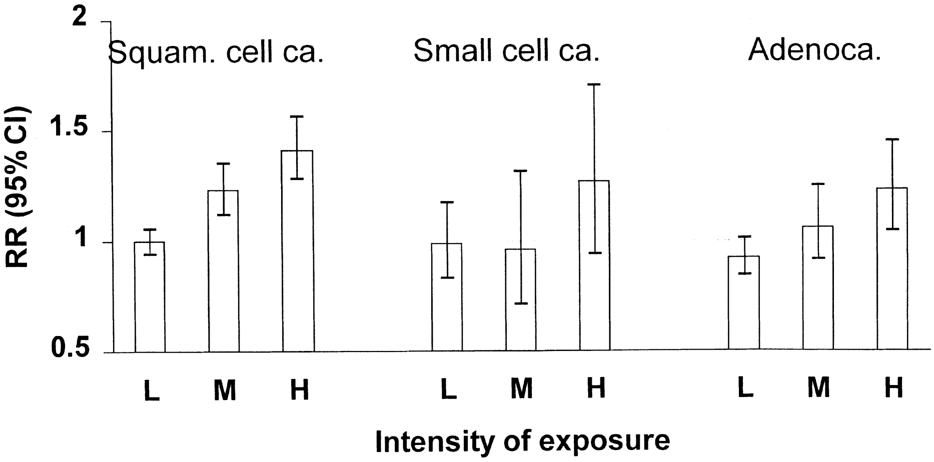

Fig. 1. Risk of lung cancer by histological type among men by intensity of exposure to diesel exhaust in 1960. L, low; M, medium; H, high; RR, relative risk; CI, confidence interval; reference category: unexposed.

other workers (52.3%). The proportion of occasional smokers was similar (8.7% and 10.3%). The difference in the proportion of smokers would result in a RR of lung cancer of 1.1, with the assumption of RRs of 3 for occasional smokers and 10 for regular smokers.

Lung cancer is the malignant neoplasm that has been most frequently associated with occupational exposure to diesel emissions [1, 16]. A recent meta-analysis resulted in a pooled RR of 1.3 (95% CI 1.22–1.49) [2]. In five previous studies [3–8] the group of exposed individuals consisted of workers employed in different occupations having in common exposure to diesel exhausts, an approach similar to the one used in our study. The meta-analysis of the five studies [2] resulted in a RR of 0.97 (95% CI 0.95–1.00).

Although we were not able to quantitatively assess the individual exposure to diesel emissions, the increase in risk we detected with increasing estimated probability and intensity of exposure is consistent with a causal dose–response relationship.

The observation of a somewhat stronger effect for squamous cell carcinoma than for small-cell carcinoma or adenocarcinoma is consistent with the only previous study which provided information on risk for specific histological types of lung cancer [7], and suggests that the carcinogenic effect of diesel emissions, if real, might operate through mechanisms similar to those of tobacco smoke. The lack of consistency of the results between men and women, however, detracts from a causal interpretation of the association detected in our data.

Our results on lung cancer might suffer from confounding by tobacco smoking, other lifestyle factors, and exposure to other occupational carcinogens. As discussed above, we have no information on tobacco smoking and we cannot estimate the magnitude of the possible bias. However, results of previous studies of workers exposed to diesel emissions, in which potential confounding by tobacco smoking was adjusted for, did not suggest that confounding by tobacco smoke explains the pattern of results [2, 22]. Furthermore, the lack of a correspondence between the results observed for lung cancer and those for other tobacco-related neoplasms detracts from the hypothesis of a strong confounding effect of tobacco. The potential effect of confounding by other lifestyle factors, such as diet poor in fresh fruits and vegetables, has not been adequately controlled for in previous epidemiological studies of diesel-exposed workers, nor in the present study. The third potential group of confounding factors, occupational exposures other than diesel emissions, is unlikely to have played a major role in our study, because exposure to diesel emissions was assessed across all job and industry codes. Even if exposure to other carcinogens (*e.g.*, asbestos or crystalline silica) does occur in some of the jobs classified at diesel exposure, such confounding is not likely to explain the complete pattern of our results.

In conclusion, our results show an increased risk of lung cancer after exposure to diesel emissions, which is very unlikely to be due to chance. Potential sources of bias are not likely to have operated toward a false-positive association. Although confounding by other carcinogens cannot be ruled out, it is unlikely that it explains the trend we observed according to intensity of exposure.

We observed an increased risk of laryngeal cancer in both men and women. However, no suggestion of a trend was present among men according to intensity or probability of exposure, and the small number of cases among women prevented a full analysis. The available results on this rare neoplasm do not suggest the presence of a strong association [15, 23–26]. Our study offers only very limited support for the hypothesis of a carcinogenic effect of diesel emission on the larynx.

An increased risk of bladder cancer has been reported in studies of truck drivers [9, 10] and other workers exposed to diesel emissions [4, 12–14, 23]. Other studies of diesel-exposed workers, however, failed to confirm this association [8, 24, 27, 28] (see ref. 29 for review). Our findings did not support the hypothesis of an association between exposure to diesel emissions and risk of bladder cancer. The impact of exposure misclassification on our results, however, is not known.

A small increase in risk of kidney cancer has been reported in two cohort studies of railroad workers [15, 27], but not in other studies of diesel-exposed workers [8, 23, 24, 28]. Our results are equivocal since the small overall increase in risk among men is counterbalanced by the lack of a trend according to probability of exposure and the negative results among women.

Among the cancer sites that were not among those of interest *a priori*, we found a small but significant excess in the risk of stomach and pancreatic cancers in men, and the risk of both cancers tended to increase, although not fully monotonically, according to estimated probability and intensity of exposure. Results among women, in contrast, do not suggest an association. Results of previous studies of diesel-exposed workers did not consistently report an excess of stomach or pancreas cancer [8, 15, 23, 24, 27, 28, 30]. Uncontrolled confounding by tobacco smoking, alcohol drinking, diet, or other lifestyle factors might explain the results among men. We therefore believe that our observations warrant attention in future studies.

The risk of cancers of the oral cavity/pharynx and of the uterine cervix was increased among exposed women. Despite the small number of cases among exposed women, a trend was suggested for both neoplasms according to probability and intensity of exposure. Among men, a small overall increase in oral and pharyngeal cancer risk was not supported by the results of the analysis by probability and intensity of exposure. Previous studies of diesel-exposed workers did not report results on cancers of the oral cavity and the cervix. Confounding by other risk factors for the disease, such as infection with human papilloma virus in the case of cervical cancer, might account for our results. The lack of consistency between genders in the results on oral and pharyngeal cancer also detracts from a causal interpretation.

Appendix: Occupations and industries at medium or high probability of exposure

Code	Occupation/industry title	Probability	Intensity	Confidence	Type
Occupations					
002	Electrical power and communication engineers and technicians	2	1	2	2
003	Mechanical engineers and technicians	2	1	3	2
022	Biologists	2	1	3	1
023	Agricultural and horticultural researchers	2	1	3	2
334	Door-to-door sales persons	3	2	3	1
338	Gasoline sellers, demonstrators, *etc.*	3	2	3	1
402	Agricultural law enforcement	2	1	2	1
403	Forest law enforcement	2	1	2	1
404	Park law enforcement	2	1	2	1
406	Breeders of fur-bearing animals	2	1	2	1
415	Reindeer herders	2	1	1	1
431	Fishermen	2	1	2	1
441	Forestry and logging work	2	1	2	1
501	Quarry workers, rock blasters, *etc.*	3	3	3	1
502	Well drillers, diamond drillers	3	3	3	1
503	Ore beneficiation workers–sorters	3	1	3	1
504	Other mine and quarry workers	3	3	2	1
509	Unspecifiable jobs	2	2	2	1
601	Nautical law enforcement	3	1	2	1
631	Locomotive conductors, locomotive assistants	2	2	2	1
632	Railroad conductors, traffic controllers	2	1	2	1
634	Coachmen	2	1	3	1
636	Bus and streetcar conductors, ticket takers	3	2	3	1
644	Highway traffic administrators	2	1	3	1
661	Postal delivery people	3	2	2	1
662	Office caretakers, office messengers, *etc.*	2	1	2	1

Appendix (continued)

Code	Occupation/industry title	Probability	Intensity	Confidence	Type
750	Workshop mechanics (bench and machine workers)	2	3	2	2
751	Installers and machine assemblers	2	3	2	2
752	Machine, engine, and motor repairers	3	3	3	2
755	Welders, metal cutters	2	3	2	2
761	Installation, power, and machine-electrical workers	2	3	2	2
771	Construction carpenters	2	1	2	2
858	Other fabrication work	2	1	2	2
861	Heavy and miscellaneous laborers	2	1	2	2
871	Agricultural machine operators	3	2	3	1
874	Construction machine operators	3	3	3	1
875	Truck drivers, transport maintenance personnel, *etc.*	3	2	3	1
876	Oilers	2	2	3	2
882	Dock workers and other loading/unloading workers	3	2	3	1
883	Warehouse and supply room workers	2	1	3	2
901	Fire fighters	3	2	3	1
917	Pursers, parking attendants, *etc.*	2	1	2	1
Industry					
020	Forest management	2	1	2	
021	Logging	2	1	2	
022	Log driving and measurement	2	1	2	
023	Hunting and game keeping	2	1	2	
029	Unspecifiable forestry	2	1	2	
030	Deep sea fishing	2	1	3	
031	Aquatic fishing	2	1	3	
100	Coal mining	3	3	3	
101	Iron ore mines	3	3	3	
102	Other ore mines	3	3	3	
103	Crude oil plants	3	2	3	
104	Quarries	3	2	3	
105	Sand and clay pits	3	2	3	
106	Peat digging	3	2	3	
107	Other mining and quarrying	3	3	2	
109	Unspecifiable mining and quarrying	2	2	2	
320	Petroleum refineries and shale oil plant	2	2	3	
321	Other pertinent industries	2	2	2	
329	Unspecifiable coal and petroleum industries	2	2	2	
333	Cement plants	2	1	2	
334	Cement and light concrete plants	2	1	2	
335	Paving stone cutting and stone finishing	2	1	2	
336	Lime and chalk plants	2	1	2	
337	Peat and peat litter production	2	1	2	
360	Ship building	2	2	3	
361	Boat building	2	2	3	
362	Railroad and trolley works	2	2	3	
363	Automotive plants	2	2	3	
364	Automotive repair	2	3	3	
613	Wholesale fuels	2	2	3	
657	Gasoline stations	3	2	3	
700	Railroad traffic	3	2	3	
701	Trolley and bus traffic	3	2	3	
702	Automobile traffic	2	1	3	
703	Other land transport	2	1	2	
704	Long-distance travel by water	3	2	3	
705	Short-distance travel by water	3	2	3	
720	Post office	2	1	3	
806	Fire fighting	2	1	2	

Probability: 2: medium; 3: high.
Intensity and confidence: 1: low, 2: medium, 3: high.
Type: 1: occupation determines exposure; 2: occupation and industry determine exposure.

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