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A review of cancer risk in the trucking industry, with emphasis on exposure to diesel exhaust

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ABSTRACT. Two large cohort studies of members of US unions in the trucking industries provided some evidence of an increased risk of lung cancer. However, no increased risk was reported in comparisons with an external (unexposed) population, the evidence of an association rests on the results of analyses by duration of employment, or by estimated exposure to elemental carbon. These estimates are subjects to uncertainties and potential misclassification bias. In addition, residual confounding by tobacco smoking and by other occupational exposures cannot be excluded. The hypothesis of carcinogenicity of diesel exhaust (DE) is biologically plausible; an IARC Working Group has recently concluded that the evidence is sufficient to classify DE as human carcinogen. This review of studies of truck drivers illustrates the problems of epidemiology of DE-exposed workers, and stresses the need for careful consideration to potential sources of bias and confounding.

Key words: truck drivers, diesel engine exhaust, lung cancer, epidemiology.

RIASSUNTO. RISCHIO DI TUMORE TRA GLI AUTISTI DI CAMION: REVISIONE DELLA LETTERATURA CON ENFASI SULL'ESPOSIZIONE A EMISSIONI DI MOTORI DIESEL. Due grandi coorti di lavoratori americani nell'industria del trasporto su strada hanno contribuito all'evidenza di un aumento di rischio del tumore del polmone. Tuttavia, in questi studi non si è dimostrato un aumento di rischio nei confronti di popolazioni esterne di riferimento, e l'evidenza si basa sui risultati di analisi della durata di impiego o l'esposizione stimata a carbone. Queste stime sono soggette a incertezza e possibile bias da misclassificazione. Non si può inoltre escludere la possibilità di un confondimento residuo da fumo di tabacco o altre esposizioni occupazionali. L'ipotesi di effetto cancerogeno delle emissioni di motori diesel è biologicamente plausibile; un gruppo di lavoro della IARC ha recentemente concluso che l'evidenza è sufficiente a classificare le emissioni come cancerogene per l'uomo. Questa revisione degli studi sui guidatori di camion illustra i problemi degli studi epidemiologici di lavoratori esposti ad emissioni diesel e la necessità di considerare attentamente le sorgenti potenziali di bias e confondimento.

Parole chiave: guidatori di camion, emissioni di motori diesel, tumore del polmone, epidemiologia.

Introduction

The International Agency for Research on Cancer has recently re-evaluated the evidence of carcinogenicity of diesel engine exhaust and has concluded that this agent is carcinogenic to humans (1). Specifically, the evidence from epidemiologic studies was considered sufficient to conclude that a causal association exists. A number of recent reviews have stressed the limitations and the inconsistencies of available results and have concluded that it is premature to conclude that a carcinogenic effect has been demonstrated (2-4). Furthermore, it is important to consider that the technology of diesel engines has dramatically changed during the last decades and current physical and chemical characteristics of the exhaust no longer correspond to those experienced by workers included in the epidemiologic studies. It has been argued that "New Technology Diesel Exhaust" (NTDE) should not be combined with traditional diesel exhaust for evaluation or regulatory purposes (5, 6). Unfortunately, data on carcinogenicity of NTDE in humans are not yet available.

The strongest evidence for carcinogenicity of DE in humans comes from a study of US non-metal miners (7, 8). Supportive evidence comes from studies of railroad workers (9, 10) and workers in the trucking industries (11). Given the heterogeneity in exposure circumstances among workers exposed to DE, and the weak associations detected in the most informative studies (workers at highest exposure usually had less than 2-fold increase in risk of cancer, and most comparisons with external standards did not show an excess risk), it is important to avoid extrapolations of results across industries.

In the following sections, I will review the two most informative studies of workers in the trucking industry, and discuss some general issues in the epidemiology of DE and lung cancer.

Study of US Teamster Union members

This study consisted of several separate analyses (12-14) of the same study population of retired Teamsters members who had applied for pensions (requires 20 years tenure in the union) and had died in 1982-1983. Cases

were all deaths from lung cancer, and controls were every sixth death from the entire file that had not died from lung cancer, bladder cancer, or motor vehicle accidents. Data on potential confounders (e.g., other jobs, smoking, and asbestos) from next of kin were included in the final models for estimating risk. Additionally, an exposure assessment of trucking job categories (15) was conducted.

The first analysis (13) was a nested case-control study of 996 cases and 1085 controls that had applied for pensions and who died in 1982-1983. Study subjects were classified into job categories of longest duration, based on union records supplemented by information from next-of-kin on both occupation and smoking. The highest risks were for mechanics (OR 1.89; 95% CI 0.92-3.09) and 'other potentially diesel exposed' jobs (OR 1.44; 95% CI 0.88-2.39). There were no statistically significant differences in risk by job category (Table I). There were a positive dose-response relation among drivers of diesel, gasoline, and both gasoline and diesel trucks, but not among mechanics (Figure 1). This study suffers from several limitations. Latency was rather short as DE exposure occurred late in the working life, since diesel engines were used only since the mid-1960s in short-haul and in the 1980s in long-haul trucks. There were no measurements of exposure to DE or other agents. There were only 120 un-

exposed cohort members, resulting in unstable risk estimates. Smoking information was derived from next-of-kin, which leaves open the possibility of residual confounding.

The second analysis of this study added a quantitative dose-response analysis, using elemental carbon (EC) as surrogate for diesel exposure (14, 15). Historical DE exposure estimates were analyzed as a function of the number of heavy-duty trucks and of particulate emissions over time. Cabs of long-haul trucks were assumed to leak. There were positive trends by both categorical and continuous exposure variables (Figure 2).

The possibility of inadequate latency remains the same as in the original study (13) as there was no update of the study population. The limitation from the small size of the unexposed control group also remained, although this group was enlarged to 150 cohort members. An additional problem is the use of a single year as onset of use of diesel engines. A revised analysis took into account turnover in the fleet and projected lower exposure estimates (12). Exposure estimates were from a survey in 1990 (15) when dieselization was more complete and engines were cleaner. This may lead to underestimate of early exposures, and overestimate of dose-response trends. In addition, exposures for all job categories were assumed to be

Table I. Risk of lung cancer by job categories in two cohort studies of truck drivers

Job category	Steenland <i>et al.</i> , 1990		Garshick <i>et al.</i> , 2008	
	EC level ($\mu\text{g}/\text{m}^3$)	RR (95% CI)	EC level ($\mu\text{g}/\text{m}^3$)	HR (95% CI)
Long-haul driver	3.8	1.27 (0.83-1.93)	1.12	1.15 (0.92-1.43)
Short-haul driver	4.0	1.31 (0.81-2.11)	1.09	1.19 (0.99-1.42)
Truck mechanic	12.1	1.89 (0.92-3.09)	2.0	0.95 (0.66-1.38)
Dockworker	13.8	0.92 (0.55-1.55)	0.76	1.30 (1.07-1.58)
Other jobs	NA	1.44 (0.88-2.39)	0.88	0.89 (0.48-1.63)

EC, elemental carbon, measured in the late 1980s (13) and in the late 1990s (20); NA, not available; RR, relative risk; HR, hazard ratio; CI, confidence interval

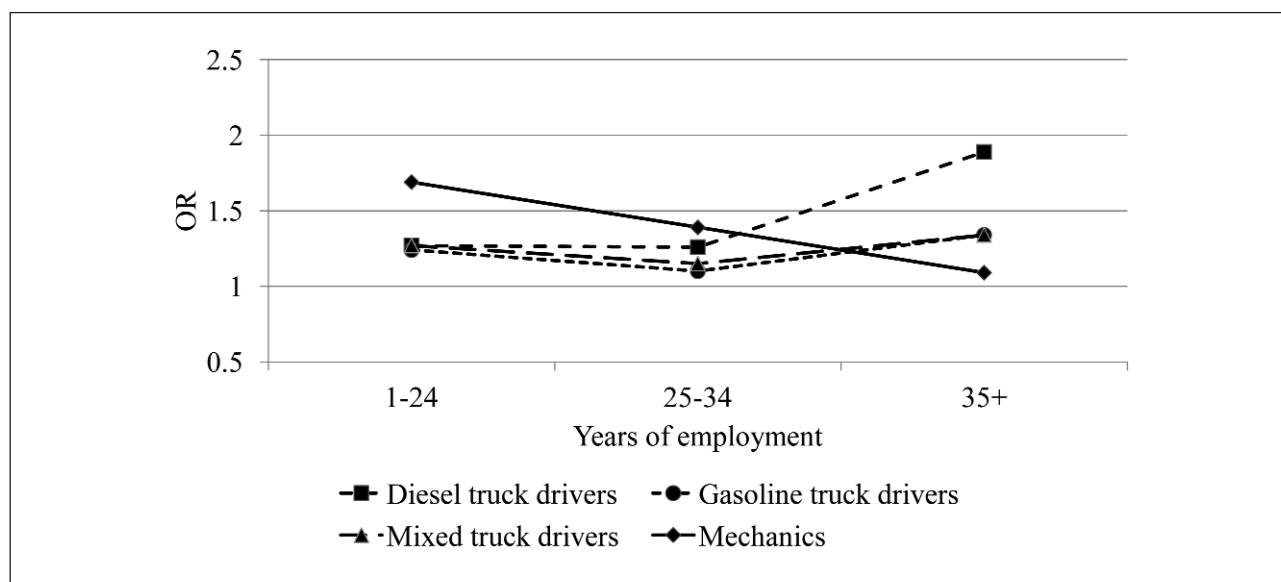


Figure 1. Odds ratio of lung cancer duration of employment - drivers and mechanics (Steenland *et al.*, 1990)

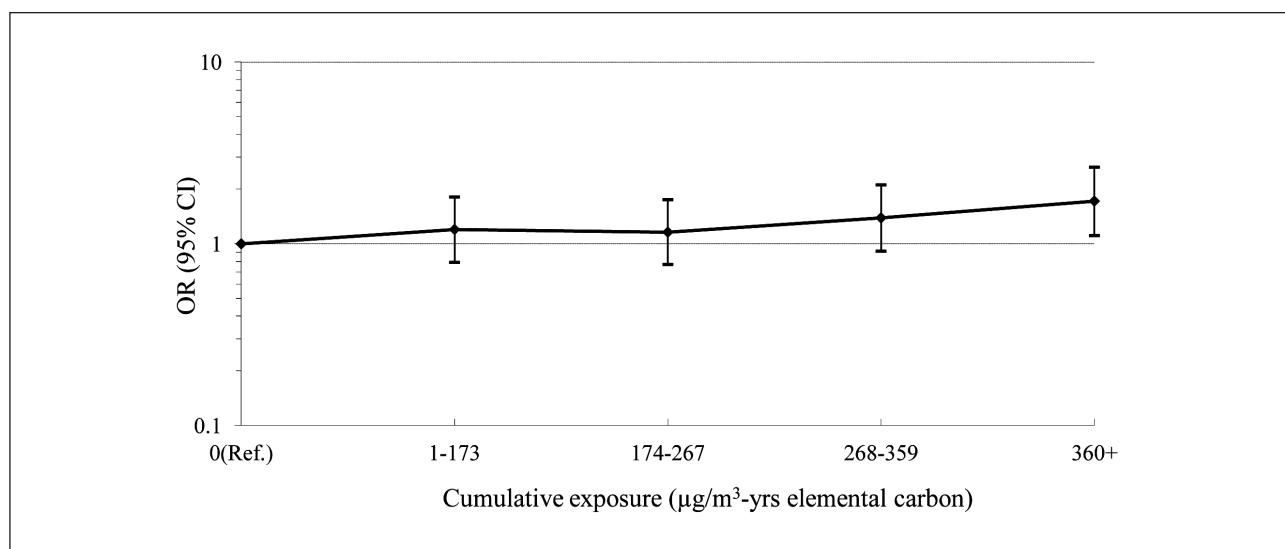


Figure 2. Cumulative exposure ($\mu\text{g}/\text{m}^3\text{-yrs}$ elemental carbon)

proportional to the vehicle miles traveled by heavy duty trucks and to the level of emissions of particulates from heavy duty engines. However, this approach might not be valid, especially for short-haul and local diesel truck drivers and for non-drivers, including mechanics, and dock-workers (16). Background sources of elemental carbon, coming in particular from gasoline engines, were not taken into account. The assumption of leakage of DE in the cabin might not be correct, as data show no differences in EC level between truck cab and highway background in warm weather or cold weather (15). Because of these limitations, the study does not provide clear evidence in favor or against the hypothesis of an association between DE and lung cancer in truck drivers. It is of interest to note that revised exposure estimates have been generated following the criticisms of the original study (12), but these have not yet been applied to the epidemiologic data to produce new risk estimates.

In general, limitations of the study of US Teamster Union members include lack of exposure data for different job categories, which were excluded from the analysis, misclassification of smoking by next-of-kin, which could produce inaccurate adjustments for confounding from smoking, misclassification of exposure by next-of-kin, which could produce biased results, although the likely direction of the bias would be toward the null hypothesis of no association, and the short latency time. Quantitative dose-response analyses in this study (14) have important limitations: the authors assumed exposures for all job categories were proportional to the vehicle-miles traveled by heavy duty trucks and to the level of emissions of particulates from heavy duty engines. However, this approach may not be appropriate for short-haul and local diesel truck drivers and for non-drivers, for whom the proportion of heavy-duty trucks is a more reasonable exposure metric. DE exposure of truck drivers is not large and related more to the roads they drive on than the type of truck. This is counter to the assumption of the authors of this study that significant DE exposure is from

engine exhaust leaking into the truck cabin: limited evidence suggests little exposure from the drivers' own trucks (15-18).

Study of US trucking industry Union members

The first paper of this study reported a retrospective mortality analysis of 54,319 male union members employed in four national trucking companies in 1985 (19). Smoking histories were obtained by questionnaires of current workers. Mortality follow-up was to 2000. All-cause mortality was significantly reduced, with an SMR of 0.72 (95% CI 0.70-0.72); there were a total of 769 lung cancer deaths, with an SMR of 1.04 (95% CI 0.97-1.12). For different categories of drivers SMRs for lung cancer ranged from 1.08 (combination drivers) to 1.16 (pickup/delivery [P&D] drivers) with long-haul drivers and dockworkers at 1.10. Smoking rates were generally similar to the comparison general population, so smoking was thought to not be an important confounder.

A more detailed analysis of a subset of this cohort focused on lung cancer and association with years worked among jobs with different current and past exposures to DE (20). This subcohort consisted of 31,135 workers >40 years of age working in 1985 and with >1 year of employment. Hazard ratios (HRs) were adjusted for healthy worker effect, years working, years off work, race, and census region, as well as smoking. HR was statistically elevated for dockworkers (1.30; 95% CI 1.07-1.73; Table I). All jobs with enough cases showed positive and significant dose-response trends by duration of employment (Table II).

A subsequent analysis of the same group of 31,135 workers, with follow-up to 2000, focused on estimated exposure to elemental carbon (EC) (11). Industrial hygiene surveys (2001-2006) provided current levels of EC by job type in large terminals (21-23). Separate exposure models were derived for drivers and terminal workers, the latter

Table II. Risk of lung cancer for 20 years of employment in different job categories (20)

Job category	HR	95% CI
Long-haul drivers	1.40	0.88-2.24
Pick-up/delivery drivers	2.21	1.38-3.52
Dock workers	2.02	1.23-3.33
Combination workers	2.34	1.42-3.83

HR, hazard ratio; CI, confidence interval

group including dockworkers and mechanics, based on ob, terminal characteristics (size, ventilation) and background, which in turn depended on weather, distance from highway, land use and region. Historical models were based on trends in coefficient of haze, a measurement of particulate matter based on optical density (24). EC measurements from 1988-1989 were used to validate the models (15). No direct measurements were available for small terminals (50% of total exposure time); exposures were assigned based on larger terminals in the same region. Results were reported with and without adjustment for duration of work, to account for a possible healthy worker survival effect. Cumulative EC exposure was not associated with lung cancer mortality (Table III). After excluding 1,811 mechanics, risk estimates became slightly stronger: the HRs for an increased in 1000 µg/m³ cumulative EC were (excluding mechanics) 1.04 (95% CI 0.97-1.11) without lag, 1.07 (95% CI 0.99-1.15) with 5-year lag, and 1.09 (95% CI 0.99, 1.20) with 10-year lag. The limitations in this study include lack of information on tobacco smoking and lack of exposure information on a

large proportion of cohort members. The dependence of results on choices made after the data were collected (adjustment for duration of employment, exclusion of mechanisms) reduces the weight of the results.

Additional limitations of this study include the lack of individual information on smoking, and the other was the lack of pre-diesel work history. With an average age of 36 years for beginning work at these companies, some workers may have had 10 or more years of exposure to DE or vehicle emissions from other sources. A majority of workers appear to have had adequate latency, but there was considerable opportunity for non-diesel work exposures.

Other epidemiologic studies of truck drivers

A few additional cohort studies of truck drivers have been reported (Table IV) (25-28). In these studies, the exposure information is limited to job title (from census or union membership); no results are available by any index of DE exposure. These additional studies suggest a possible increase in lung cancer mortality among truck drivers, but the limitations in exposure assessment do not allow to link it with DE exposure. Overall, these studies add little to the evidence provided by the two better conducted US studies (reviewed above).

Discussion

The two main epidemiologic studies of truck drivers and other workers in the trucking industry, illustrate

Table III. Risk of lung cancer for cumulative exposure to elemental carbon (11)

Cumulative exposure (µg/m ³ · mo)	Entire cohort (N=31,135)		Excluding mechanics (N=29,324)	
	N	HR (95% CI)	N	HR (95% CI)
No lag				
<530	153	1.0 (Ref.)	153	1.0 (Ref.)
530-1060	194	1.24 (0.98-1.57)	193	1.25 (0.99-1.60)
161-2075	209	1.30 (0.99-1.70)	202	1.30 (0.99-1.72)
2076+	223	1316 (0.86-1.57) 0.92	193	1.24 (0.89-1.71) 0.71
p trend				
5-year lag				
<371	122	1.0 (Ref.)	122	1.0 (Ref.)
371-859	193	1.30 (1.01-1.68)	191	1.31 (1.01-1.71)
860-1802	208	1.35 (1.01-1.81)	202	1.38 (1.02-1.87)
1803+	256	1.36 (0.98-1.89) 0.39	226	1.48 (1.05-2.10) 0.16
p trend				
10-year lag				
<167	114	1.0 (Ref.)	112	1.0 (Ref.)
167-595	183	1.14 (0.86, 1.52)	179	1.17 (0.88-1.57)
596-1435	205	1.18 (0.85-1.64)	202	1.26 (0.90-1.78)
1435+	277	1.25 (0.86-1.82) 0.39	248	1.41 (0.95-2.11) 0.15
p trend				

HR, hazard ratio; CI, confidence interval; Ref., reference category; p trend, p-value of test for linear trend

Table IV. Results of cohort studies* of truck drivers (other than the two major US studies)

Reference	N; country; period of employment; period of follow-up	Results O/E	SMR	95% CI	Comments
Rafnsson & Gunnarsdottir, 1991	868; Iceland; 1951; 1951-1988	24/11.2	2.14	1.37-3.18	
Guberman <i>et al.</i> , 1992	1,726; Switzerland; 1949-1961; 1949-1986	77/51.4	1.50	1.23-1.81	Similar results for cancer incidence; higher prevalence of smoking than local survey; taxi and bus drivers are included (25%)
Hansen, 1993	14,225; Denmark; 1970; 1970-1980	76/NA	1.60	1.26-2.00	Comparison with unskilled workers; employment based on census
Birdsey <i>et al.</i> , 2010	156,241; USA; 1989-2004; 1989-2004	557/NA	1.00	0.92-1.09	Higher smoking prevalence than national population

N, number in the cohort; O/E, number of observed and expected lung cancer deaths; SMR, standardized mortality ratio for lung cancer; CI, confidence interval; NA, not available

* All studies were conducted in men and analyzed lung cancer mortality

several of the methodological issues to take into consideration when assessing the risk of cancer from DE exposure.

One of these cohorts did not report an estimate of the risk of lung cancer compared to an external population, and in the other cohort the comparison resulted in a small, non-statistically significant excess. This is at odds with the results of studies of other groups of workers exposed to established carcinogens, such as asbestos and heavy metals, among whom an increased mortality compared to national or regional standards has been clearly identified (29). The evidence of a carcinogenic of DE rests on the results of analysis by duration of employment, or by estimated exposure to a surrogate of DE, typically EC. Quantitative exposure estimates are based on a limited number of measurements, and on extrapolations across work places, jobs and time periods. The extrapolation from recent to past exposure circumstances is particularly problematic. The fact that truck drivers are exposed to DE through leakage of the exhaust into the cabin is an example of an important assumption that was not supported by evidence. Although it is commonly assumed that errors in exposure assessment in prospective studies tend to be non-differential and therefore to bias risk estimates towards the null, this might not be always the case. If exposure misclassification is correlated with exposure to a confounder (e.g., a carcinogen was present in the working environment in the past but not in recent times), the resulting bias can go in both directions.

Residual confounding by tobacco smoking and by other occupational exposures remains a major concern in the interpretation of the lung cancer results of studies of truck drivers. No data are available on potential exposure to carcinogens in other jobs truck drivers had in their occupational life. However, there is some evidence

that drivers included in the cohorts under consideration spent only part of their occupational life in that industry: among diesel truck drivers included as controls in the analysis of US Teamsters Union members, 23% held this occupation for 35 or more years (13). Information on smoking status and pack-years of smoking has been reported for 3362 members of the cohort of union members (30). The response rate to the smoking survey was 40.5%. Smoking prevalence was higher among long-haul drivers than among other workers included in the cohort.

A final problem in the epidemiology of truck drivers and in general of studies of workers exposed to DE is that of subgroup analyses and selective reporting of results. The exclusion of mechanics in the recent analysis of the cohort of union member (11) is an example of choice in the analytical strategy that was not present in earlier analyses of the same population (20) and might have been result-driven.

Conclusions

The hypothesis of carcinogenicity of DE is biologically plausible and supported by some epidemiologic results. An IARC Working Group has recently concluded that the evidence is sufficient to conclude that DE is carcinogenic to humans (1). Other authors have reached more conservative conclusion and argued that the available results suffer from important limitations (2-4). This review of studies of truck drivers illustrates the problems of epidemiology of DE, and stresses the need for careful consideration to potential sources of bias and confounding.

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