Diesel Engine Exhaust Exposure, Smoking, and Lung Cancer Subtype Risks: A Pooled Exposure-response Analysis of 14 Case–control Studies

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ABSTRACT:

Rationale and objectives: We expanded upon a previous pooled case-control analysis on diesel engine exhaust and lung cancer by including 3 additional studies and quantitative exposure assessment to evaluate lung cancer and subtype risks associated with occupational exposure to diesel exhaust, characterized by elemental carbon (EC) concentrations.

Methods: We used a quantitative EC job-exposure matrix for exposure assessment. Unconditional logistic regression models were used to calculate lung cancer odds ratios (ORs) and 95% confidence intervals (CI) associated with various metrics of EC exposure. Lung cancer excess lifetime risks (ELR) were calculated using life-tables accounting for all-cause mortality. Additional stratified analyses by smoking history and lung cancer subtypes were performed in men.

Results: Our study included 16,901 cases and 20,965 controls. In men, exposure-response between EC and lung cancer was observed: ORs ranged from 1.09 (95% CI 1.00, 1.18) to 1.41 (95% CI 1.30, 1.52) for the lowest and highest cumulative exposure groups, respectively. EC-exposed men had elevated risks in all lung cancer subtypes investigated; associations were strongest for squamous and small cell carcinomas and weaker for adenocarcinoma. EC-lung cancer exposure-response was observed in men regardless of smoking history, including among never smokers. ELR associated with 45 years of EC exposure at 50, 20, and 1 $\mu g/m^3$ were 3.0%, 0.99%, and, 0.04%, respectively, for both sexes combined.

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Conclusion: We observed a consistent exposure-response relationship between EC exposure and lung cancer in men. Reduction of workplace EC levels to background environmental levels will further reduce lung cancer ELR in exposed workers.

(Abstract word count 248)

Key words: Occupational exposure, diesel exhaust, lung neoplasms, epidemiology

INTRODUCTION

The International Agency for Research on Cancer (IARC) classifies diesel engine exhaust (hereafter: diesel exhaust) as a Group 1 human carcinogen [1]. Previous studies have provided consistent epidemiological evidence that lung cancer is associated with occupational exposure to diesel exhaust [2–5]. Positive exposure-response relationships of diesel exhaust exposure and lung cancer were also reported by studies with quantitative exposure assessment for elemental carbon (EC), which is a measure of diesel exhaust exposure [4–7].

However, few studies have explored the risk of lung cancer associated with low exposure levels and none have observed a positive association at lifetime cumulative EC exposure levels below 50 $\mu g/m^3$-years. Questions also remain regarding the role of cigarette smoking as a potential confounder or effect modifier in the relationship between EC exposure and lung cancer. For instance, although a handful of studies have shown suggestive elevated lung cancer risks in diesel exhaust-exposed workers who were never smokers [2,8,9], only one study reported a significant effect [4]. The same study also reported attenuated lung cancer risk in subjects who were heavy smokers and highly exposed to diesel exhaust (i.e. a negative interaction). Finally, results reported by studies on risks of major lung cancer subtypes associated with diesel exhaust exposure have been inconsistent. Some studies reported the strongest association in large cell carcinoma compared to other major lung cancer subtypes [2,9], whereas others observed higher risks in squamous cell carcinoma [8,10].

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Previously we published a study with pooled subjects from 11 lung cancer case-control studies from Europe and Canada [3]. In the current study we increased the study population by including three additional studies (3,663 cases; 4,805 controls). Occupational exposure assessment was also enhanced with the use of a new job-exposure matrix (JEM), where EC exposure was estimated quantitatively based on subject occupations. The purposes of our work were to evaluate: 1) the lung cancer risks associated with various indices of occupational diesel exhaust exposure by sex; 2) the associations between diesel exhaust exposure and lung cancer by smoking status and cancer subtype in men; 3) the joint effects of diesel exhaust exposure and smoking on the risk of lung cancer and its major subtypes on the additive and multiplicative scale in men; and 4) the excess lifetime lung cancer risks associated with various levels of occupational diesel exhaust exposure in both sexes combined.

METHODS

Study population

Subjects from 14 hospital- and population-based lung cancer case-control studies in 13 European countries and Canada were pooled. Detailed description of the original study population is available elsewhere [3]. The current study updated the population with 3,663 cases and 4,805 controls from the TORONTO, CAPUA, and ICARE studies in Canada, Spain, and France respectively (Table E1 in online supplement). The project received ethical approvals from all participating countries and the IARC institutional review board. More information about the SYNERGY project is available online: http://synergy.iarc.fr.

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Job-exposure matrix and exposure assessment

A quantitative diesel engine exhaust job-exposure matrix (DEE-JEM) was developed by CG and RV. The DEE-JEM consists of EC exposure (in ug/m^3) assigned to all 1,506 five-digit International Standard Classification of Occupations (version 1968, or ISCO-68)[11] and was constructed based on 4,417 occupational EC measurements (data sources available in Supplementary Methods and Table E6 in online supplement). For occupations represented in the EC exposure measurements, the mean exposure concentrations were directly assigned. For occupations without measurement data, exposure concentrations from similar occupations with measurement data were assigned using expert decisions. An exposure probability factor was also assigned by expert decision to each exposed job (details on probability factors available in Supplementary Methods in online supplement). The DEE-JEM was linked to study participant job histories by ISCO-68 occupations. Probability-weighted cumulative EC exposure (hereafter: cumulative EC, expressed in μg/m^3-years) was calculated as the sum of the product of exposure levels, probabilities, and duration (in years) across all reported job periods for each subject. The DEE-JEM is available upon request from the corresponding author.

Main Statistical analysis

Separately for men and women, unconditional logistic regression models were used to calculate the odds ratios (ORs) and 95% confidence intervals (CI) of lung cancer associated with various categorical EC exposure metrics, including ever/never exposure, duration of exposure (<10; 10–19; 20–29; >29 years), and cumulative exposure (quartiles of exposure distribution among controls: >0–22; 23–70; 71–178; >178 μg/m^3-years).

Trends were assessed using p-values from the respective indices of EC exposure as continuous variables for all subjects and for exposed subjects only. Adjustments for the main analyses were determined *a priori* within the SYNERGY consortium and identical with our previous occupational exposure publications[3,12]; these adjustments included study, age group (<45; 45–49; 50–54; 55–59; 60–64; 65–69; 70–74; >74 years), smoking (log(cigarette pack-years+1)), smoking cessation prior to interview/diagnosis (current smokers; >0-7; 8-15; 16-25; >25 years; never smokers), and having been ever employed in occupations with known lung cancer risks (List A jobs ever/never; full list in Table E7 in online supplement). First published in 1982, List A jobs include occupations with definite lung cancer risks according to the IARC Monographs; the list was updated in 1995 and 2000 to cover all IARC-reviewed agents up to volume 75 of the Monographs [13,14]. Smokers were defined as smoking more than one cigarette per day for more than one year. Smoking pack-year was calculated by summing the products of average daily smoking amount in 20-cigarettes packs and smoking duration in years. Association between lung cancer and cumulative EC exposure as a continuous metric was assessed with a logistic linear regression model for men, women, and all subjects with identical adjustments as the categorical models.

Models with various cumulative EC exposure lag times (i.e. omitting exposure in the last 5, 10, 15, or 20 years, or no omission at all) were constructed. Model fit was the best, according to minimized Akaike information criterion value, when lag time was 10 years – therefore only results from models with a 10-year lag are presented.

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Using the lung cancer risk from our linear continuous exposure model with all subjects, we calculated lung cancer excess lifetime risks (ELR) at age 80 associated with 45 years of occupational EC exposure at 50, 20, and 1 μg/m^3 using life-table methods accounting for all-cause mortality outlined by Vermeulen and colleagues [7]. The selected exposure levels at 50, 20, and 1 μg/m^3 represented recommended limit values from: 1) the German Committee for Hazardous Substances (AGS) in 2017 based on a study on lung irritation after controlled human exposure [15]; 2) the US National Institute of Occupational Safety and Health (NIOSH) in 2003 that was later withdrawn [16]; and 3) the Health Council of the Netherlands in 2019 based on exposure-response estimates from Vermeulen and colleagues [7,17], respectively. 2008 European data on mortality from all causes and lung cancer were used in our calculations [18].

Extended analysis for male subjects

To further investigate the exposure-response relationship between EC exposure and lung cancer in men, stratified analyses were performed to calculate lung cancer ORs associated with cumulative EC exposure categories with different major lung cancer subtypes and smoking histories. In addition, non-parametric thin-plate regression splines were created, as implemented in the R package *mgcv,* to visualize the shape of the exposure-response relationships between EC exposure and lung cancer subtypes in men. The number of basis functions was limited to three (k=3) and the smoothing parameter was estimated using the relative maximum likelihood method. Spline model results were truncated at the 99th percentile of EC exposure to emphasize on results with greater data support.

Additive interactions of cigarette smoking and EC exposure on lung cancer and subtype risks in men were assessed by calculating the excess risks due to interaction (RERI) using ORs from our logistic models as defined by Rothman and Greenland [19] and as implemented in the *epi.interaction* package in R. RERI values measure departure from additivity with 0 representing no interaction on the additive scale [20]. Interactions in men on the multiplicative scale were assessed using p-values obtained from the cross products of smoking and EC exposure in the adjusted logistic models.

Statistical analyses were conducted using SAS (version 9.3, SAS Institute, Cary, NC) and R (version 3.6).

RESULTS

37,866 subjects (16,901 cases; 20,965 controls) were included in our final analyses (Table 1). Among the lung cancer cases there were 4,752 adenocarcinomas, 810 large cell carcinomas, 2,730 small cell carcinomas, 6,503 squamous cell carcinomas, 2,012 other lung cancers, and 94 cases without subtype information.

In men, we observed elevated ORs for subjects with ever occupational exposure to EC (OR 1.22; 95% CI 1.15, 1.29; Table 2). Increasing trends in lung cancer risks in men were associated with increases in both exposure duration and cumulative exposure (p-trends<0.01). Elevated male lung cancer ORs were also observed in the lowest categories of exposure duration (1-9 years; OR 1.07; 95% CI 1.00, 1.16) and cumulative exposure (>0–22 μg/m^3-years; OR 1.09; 95% CI 1.00, 1.19). In our female population, we observed no associations between lung cancer and different EC exposure metrics.

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Our continuous EC exposure models show that one μg/m^3-year increase in cumulative exposure was associated with an increase in lung cancer OR by a factor of 1.00001 (95% CI 0.9987, 1.00131) for women. The corresponding results for men and for all subjects were identical: lung cancer OR increased by a factor of 1.00034 (95% CI 1.00021, 1.00048) per μg/m^3-year increase in cumulative EC exposure. Lung cancer ELR associated with lifetime occupational EC exposure at 50, 20, and 1 μg/m^3 were 3.0%, 0.99%, and, 0.04%, respectively, for both sexes combined.

By lung cancer subtype, increasing cumulative EC exposure was associated with increasing ORs of squamous cell (p-trend<0.01) and small cell carcinomas (p-trend 0.02) in men (Table 3). For squamous cell carcinoma, all categories of cumulative EC exposure were associated with elevated ORs in males, including the lowest (OR 1.13; 95% CI 1.01, 1.26). The highest risks for both adenocarcinoma (OR 1.23; 95% CI 1.09, 1.39) and large cell carcinoma (OR 1.31; 95% CI 1.02, 1.67) were also observed in men in the highest exposed group.

Results from the non-parametric spline analyses for male subjects show monotonic increases in cancer risks for overall lung cancer and all four included subtypes (Figure 1). Among the lung cancer subtypes, squamous cell and small cell carcinomas show the strongest association with cumulative EC exposure, followed by large cell carcinoma and adenocarcinoma.

In our analyses stratified by smoking status, exposure-response associations between cumulative EC exposure and lung cancer were observed in men regardless of smoking history (Table 4). Lung cancer risks were similar for men in the highest EC exposure group who were never smokers (OR 1.41; 95% CI 1.04, 1.88), former smokers (OR 1.47; 95% CI 1.31, 1.65), and current smokers (OR 1.40; 95% CI 1.24, 1.57).

Super-additive joint effects of smoking and EC exposure were observed in men for overall lung cancer and all four cancer subtypes (Table 5). Suggestive super-multiplicative joint effects of smoking and EC exposure were observed for large cell carcinoma in men ($p=0.05$).

DISCUSSION

In a large pooled case-control population, we observed in men positive associations between lung cancer and different occupational EC exposure metrics, including ever EC exposure, exposure duration, and cumulative exposure. Increasing exposure duration and cumulative exposure were associated with increases in lung cancer risks in men, exhibiting monotonic exposure-response relationships. Our results are in accordance, and further expand upon, results from our earlier analysis within the SYNERGY study with 11 studies and semi-quantitative exposure assessment, where we reported a consistent exposure-response relationship between lung cancer and EC exposure [3]. Additional evidence of the exposure-response relationship between diesel exhaust exposure and lung cancer is provided by studies on workers in highly exposed industries such as mining [4,21–23] and trucking [5,6].

In a meta-regression analysis of the exposure-response relationship of lung cancer and diesel exhaust exposure based on data from three occupational cohort studies, Vermeulen and colleagues estimated that each $\mu g/m^3$-year increase in cumulative EC exposure results in a lung cancer relative risk (RR) of 1.00098 [7]. A subsequent sensitivity analysis reported a range of lung cancer RR of 1.0006 to 1.0012 per μg/m^3-year increase in cumulative EC exposure from several alternative models [24]. These exposure-response slope estimates are approximately 2-3 times higher than our present linear model estimate of 1.00034 for all subjects. This difference may be due to factors such as occupational cohorts having higher cumulative EC exposures and more accurate exposure assessment in specific industries. Despite the differences on the exact risk magnitude, a consistent exposure-response trend between occupational diesel exhaust exposure and lung cancer was reported by studies with different designs among different populations.

We did not observe an exposure threshold for diesel exhaust-related lung cancer in males within the cumulative EC exposure ranges we investigated; increased lung cancer risk in men was observed in the lowest cumulative EC exposure group with a median exposure of 11 μg/m^3-years. An additional sensitivity analysis with 10 cumulative exposure groups suggested (naturally, with less precision) an increased risk among the lowest exposure group with a median EC exposure of 3.3 μg/m^3-years (Table E2 in online supplement). Few other studies investigated lung cancer risks in similar cumulative EC exposure ranges quantitatively. In occupational cohorts with higher EC exposures, one study reported a lung cancer OR of 1.31 (95% CI 1.01, 1.71) in US trucking workers with a cumulative exposure of approximately 51 μg/m^3-years [6], while another reported a lung cancer OR of 0.74 (95% CI 0.40, 1.38) for US miners with a cumulative EC exposure around 37 μg/m^3-years [4].

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We found that diesel exhaust exposure was associated with all four major lung cancer subtypes in men, although differential risks were observed by subtype. Both our logistic regression and spline models showed that the associations were the strongest for squamous cell and small cell carcinomas, moderate for large cell carcinoma, and weakest for adenocarcinoma. Similar findings supportive of a stronger link between diesel exhaust exposure and lung squamous cell carcinoma were reported in populations in Canada [8–10], Finland [25] and Sweden [2,26]. This is the first report of a positive exposure-response relationship for diesel exhaust exposure and lung small cell carcinoma in men. Guo and colleagues observed a small cell carcinoma OR of 2.31 (95% CI 1.02, 5.25) for female Finnish workers in the low diesel exhaust exposure category, based on six exposed cases [25]. Elevated point estimates of small cell carcinoma risks were also observed in population-based studies from different countries [2,10,25]. For adenocarcinoma, in accordance with our current observations, previous studies were consistent in reporting ORs that were lower than overall lung cancer risks [2,8–10,25,26]. Information on risk of large cell carcinoma related to diesel exhaust exposure is limited; only two previous studies included large cell carcinoma in subtype analyses [2,9]. These studies reported exposure-response relationships for duration, intensity, and lifetime cumulative exposure to diesel exhaust and large cell carcinoma. In our male population we observed a clear increased large cell carcinoma risk only in the group with the highest cumulative EC exposure (>178 $\mu g/m^3$-years), with a suggestive elevated OR estimate for the second highest exposed group.

We observed a lung cancer exposure-response risk trend in never smoking males who were exposed to EC. Similarly, Silverman and colleagues reported a significant lung cancer OR of 7.30 (95% CI 1.46, 36.57) among highly exposed US miners who never smoked [4]. The very high risk observed in the US miners may be attributable to higher cumulative EC exposure in mining occupations or the fact that the estimate was based on only seven exposed cases.

The observed super-additive joint effects between EC exposure and smoking for overall lung cancer and its subtypes in men indicated that the absolute risk of cancer for men exposed to both EC and smoking was higher than the sum of the absolute risks of cancer from EC exposure and smoking alone [27]. Only one other study in Swedish dock workers investigated EC and smoking interaction on the additive scale and similarly reported a super-additive effect [28]. Interaction in other studies were assessed on the multiplicative scale, where super-multiplicative interaction represents a scenario where the risk ratios (e.g. OR) of cancer for those exposed to both EC and smoking was higher than the product of cancer risk ratios from EC exposure and smoking alone [27]. In two non-overlapping Canadian population-based case-control studies, no significant multiplicative interaction was observed [9,10]. Lastly, in the US Miners Study Silverman and colleagues reported a suggestive sub-multiplicative interaction, where high exposure to both EC and cigarette smoke resulted in an attenuation of lung cancer risk increase [4]. In additional analyses where we explored cancer risks in four groups of male smokers (<10, 10-19, 20-39 and >39 pack-years, respectively) with cumulative EC exposures similar to those in Silverman and colleagues, we did not observe sub-multiplicative interactive effects and found consistent risk increases across all EC exposure categories for subjects with increasing pack-years of smoking (Table E3 in online supplement).

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Strengths of our study include a large pooled population with detailed smoking and occupational histories. Our sample size allowed for stratified analyses to explore the exposure-response relationship in different subgroups, while high-quality smoking and occupational histories allowed for the control of important potential confounders such as smoking and exposure to other occupational carcinogens. Exposure assessment was performed with a quantitative JEM developed using a combination of exposure measurements and expert assessment. The current DEE-JEM was developed independently from the DOM-JEM (Domtoren-JEM), an expert judgment JEM we used in an earlier analysis [3]. Despite this difference, results of both analyses showed consistent exposure-response between occupational exposure to diesel exhaust and lung cancer. Reliability studies on occupational exposure assessment also suggested that incorporating measurements in the exposure assessment process may improve expert judgment [29,30]. Finally, the exposure-response between EC exposure and lung cancer in our male population was robust and present in various sensitivity analyses, including when we limited analyses to a more homogenous group of studies, when we limited our analyses to blue-collar workers only, and when we assessed EC exposure with alternative JEM configurations (Tables E4.1-4.9 in online supplement).

There are also limitations in our work. Our DEE-JEM did not account for changes in exposure in different time periods and therefore may underestimate exposure for earlier periods when exposure was likely higher [31]. The EC measurements used in our JEM were collected from 1985 to 2016 (median: 2002) whereas our subjects were assessed as exposed from 1923 to 2020 (median: 1968). However, the association between EC exposure and lung cancer was still present when we restricted our analyses to subjects exposed after 1960 (Table E4.2 in online supplement). Because List A jobs included some jobs with potential diesel exhaust exposure, adjustment for ever-employment in any List A jobs in our main model may represent over-adjustment for co-exposures to other lung carcinogens. Removing all jobs with EC exposure from List A, however, may lead to under-adjustment as many EC-exposed jobs have concurrent exposures to other lung carcinogens. We explored the co-exposure adjustments using two additional sensitivity models: one with no adjustment and another adjusting for ever exposure to crystalline silica, asbestos, polycyclic aromatic hydrocarbons (PAHs), and hexavalent chromium as assessed by the DOM-JEM (Table E4.4 in online supplement). All three categorical EC models (i.e. main model plus the two sensitivity models) showed the EC-lung cancer exposure response among men, suggesting that the association is unlikely to be fully explained by confounding due to exposures to other occupational lung carcinogens. Further, because our JEM assigned EC exposures based on job titles, individual exposures may be misclassified in occupations with large exposure variability. This misclassification, however, was not likely to be differential by case status and introduced Berkson-like error that likely affected the precision, but not magnitude, of our risk estimates [32,33]. Exposure misclassification of jobs within the DEE-JEM may also have occurred due to the fact that our EC exposure data was limited and did not represent all jobs in all study regions. If present, this would introduce classical error in our work and bias the observed effect towards the null, meaning that the true effect of diesel exhaust exposure on lung cancer may be stronger than our observed results. However, the aforementioned shortcomings related to retrospective exposure assessment are almost inevitable due to our study design and size. We have provided

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details on all data sources, assessment procedures, and various sensitivity analyses in an effort to maximize transparency.

Another notable limitation of our study is the lower statistical power to assess risk in female workers (390 exposed cases) compared to males (7,843 exposed cases). Our results on female cancer risks may also have been affected by more exposure misclassification of women compared to men, since the supporting EC exposure data were collected almost exclusively among male workers. Adenocarcinoma, for which we observed the weakest association with diesel exhaust exposure among the lung cancer subtypes, were also more common in women than in men. However, our results should not be interpreted as diesel exhaust having no effect on lung cancer risks in women. A sensitivity analysis among women with lung cancer subtypes other than adenocarcinoma showed increased OR point estimates for cancer for all cumulative EC exposure groups, albeit with larger uncertainties (Table E4.9 in online supplement).

In risk assessment for occupational carcinogen exposure, definitions for "tolerable" ELR range from 4 in 1,000 (0.4%) in the Netherlands and Germany to 1 in 1,000 (0.1%) in the US [17,34,35]. Of our three ELR estimates derived from different exposure limits, only the scenario with 1 $\mu g/m^3$ EC exposure and 0.04% ELR is below these levels. Another study using data from the US trucking industry estimated that male workers exposed to 5 $\mu g/m^3$ EC would have a lung cancer ELR of 1-2% [5]. A separate study calculated a lung cancer ELR of 0.17% for workers exposed to 1 $\mu g/m^3$ EC using data from three US mining and trucking industry cohorts [7]. Despite variations in the exact risk magnitude, estimates from different studies suggest that workplace EC levels should be at or near environmental background

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levels in order to reduce the lung cancer ELR for workers with lifetime exposure to diesel exhaust to “tolerable levels” as defined by various national risk assessment agencies. Although multiple diesel engine emission control standards have been introduced in Europe since 2006 [17], these standards alone cannot be expected to reduce workplace EC exposure to environmental levels in the near future because they do not apply to the large number of existing diesel equipment that still is and will probably remain in use for many more years.

In summary, we observed a consistent exposure-response relationship between occupational diesel exhaust exposure and lung cancer in men in a large pooled analysis of case-control studies. Increased lung cancer risks were found in EC-exposed men who were never smokers and smokers. Increased risks in males were also observed for all lung cancer subtypes included, with associations strongest for squamous cell and small cell carcinomas and weaker for adenocarcinoma. The joint effects of EC exposure and smoking were super-additive on risks of overall lung cancer and all included subtypes. Our findings support efforts to further reduce workplace diesel exhaust exposure to protect workers against risks of lung cancer.

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FIGURE LEGEND:

Figure 1 Title: Spline analyses showing exposure-response relationships in men between cumulative elemental carbon (EC) exposure and risks of overall lung cancer plus subtypes.

Figure 1 Abbreviation: μg/m^3-years = microgram per cubic metre years

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TABLES

Table 1. Selected study population characteristics by lung cancer status and elemental carbon (EC) exposure

		Ever exposed to EC				Never exposed to EC			
Characteristic	**Category**	**Cases**	**%**	**Controls**	**%**	**Cases**	**%**	**Controls**	**%**
Sex	Male	8045	95.4	8181	94.1	5560	65.6	8270	67.4
	Female	386	4.6	512	5.9	2910	34.4	4002	32.6
Age group	<45 years	267	3.2	359	4.1	448	5.3	1012	8.2
	45-64 years	4195	49.8	4120	47.4	4568	53.9	6234	50.8
	>64 years	3969	47.1	4214	48.5	3454	40.8	5026	41.0
Smoking status	Never smoker	379	4.5	2287	26.3	990	11.7	4866	39.7
	Former smoker	2966	35.2	3880	44.6	2466	29.1	4340	35.4
	Current smoker	5086	60.3	2526	29.1	5014	59.2	3066	25.0
Smoking pack years	Never smoker	379	4.5	2287	26.3	990	11.7	4866	39.7
	<10	381	4.5	1287	14.8	428	5.1	1782	14.5
	10-19	765	9.1	1206	13.9	837	9.9	1656	13.5
	>19	6906	81.9	3913	45.0	6215	73.4	3968	32.3
Years-since-quitting-smoking	Never smoker	379	4.5	2287	26.3	990	11.7	4866	39.7
	>0-7 years	1085	12.9	644	7.4	941	11.1	778	6.3
	8-15 years	836	9.9	883	10.2	695	8.2	1015	8.3
	16-25 years	637	7.6	1088	12.5	534	6.3	1258	10.3
	>25 years	408	4.8	1265	14.6	296	3.5	1289	10.5
	Current smoker	5086	60.3	2526	29.1	5014	59.2	3066	25.0
'List A' job	Ever employment	1143	13.6	866	10.0	644	7.6	498	4.1
	Never employment	7288	86.4	7827	90.0	7712	92.4	11629	95.9
Lung cancer subtype	Adenocarcinoma	1953	23.2	-		2799	33.0	-	
	Large cell carcinoma	390	4.6	-		420	5.0	-	
	Small cell carcinoma	1427	16.9	-		1303	15.4	-	
	Squamous cell carcinoma	3704	43.9	-		2799	33.0	-	
	Other/unspecified	914	10.8	-		1098	13.0	-	
	Not available	43	0.5	-		51	0.6	-	

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Table 2. Lung cancer odds ratios (OR) associated with categorical indices of occupational elemental carbon (EC) exposure

Subject	Occupational EC exposure	Exposure category	Cases (%)	Controls (%)	OR*	95% CI
Men	**Reference**	Never	5560 (40.9)	8270 (50.3)	1.0	Referent
	Ever exposure	Ever	8045 (59.1)	8181 (49.7)	1.22	1.15–1.29
	Duration	1–9	2346 (17.2)	2750 (16.7)	1.07	1.00–1.16
	(years)	10–19	1774 (13.0)	1774 (10.8)	1.23	1.13–1.34
		20–29	1578 (11.6)	1471 (8.9)	1.23	1.12–1.35
		>29	2347 (17.3)	2186 (13.3)	1.39	1.28–1.51
	Test for trend, p-value				*<0.01*	
	Excl. never exposed				*<0.01*	
	Cumulative exposure	>0–22	1684 (12.4)	2002 (12.2)	1.09	1.00–1.19
	(μg/m^3-years)	23–70	1858 (13.7)	2005 (12.2)	1.10	1.02–1.20
		71–178	2113 (15.5)	2074 (12.6)	1.24	1.15–1.35
		>178	2390 (17.6)	2100 (12.8)	1.43	1.32–1.54
	Test for trend, p-value				*<0.01*	
	Excl. never exposed				*<0.01*	
Women	**Reference**	Never	2910 (88.3)	4002 (88.7)	1.0	Referent
	Ever exposure	Ever	386 (11.7)	512 (11.3)	1.00	0.85–1.18
	Duration	1–9	235 (7.1)	273 (6.0)	1.02	0.83–1.26
	(years)	10–19	86 (2.6)	112 (2.5)	1.07	0.77–1.47
		20–29	25 (0.8)	49 (1.1)	0.69	0.39–1.17
		>29	40 (1.2)	78 (1.7)	1.05	0.69–1.58
	Test for trend, p-value				*0.85*	
	Excl. never exposed				*0.74*	
	Cumulative exposure	>0–22	165 (5.0)	179 (4.0)	1.03	0.80–1.33
	(μg/m^3-years)	23–70	118 (3.6)	162 (3.6)	1.03	0.78–1.36
		71–178	64 (1.9)	99 (2.2)	0.92	0.64–1.31
		>178	39 (1.2)	72 (1.6)	0.97	0.62–1.48
	Test for trend, p-value				*0.99*	
	Excl. never exposed				*0.82*	

*OR adjusted for study, age group, smoking pack-years (log(cigarette pack-years+1)), time-since-quitting smoking, and List A jobs.

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Table 3. Lung cancer major subtype risks (OR) associated with cumulative occupational elemental carbon (EC) exposure in men

Lung cancer subtype	Cumulative EC exposure (μg/m³-years)	Cases	OR*	95% CI
Adenocarcinoma	Never	1513	1.0	Referent
	>0–22	414	1.09	0.95–1.24
	23–70	415	1.00	0.88–1.14
	71–178	452	1.07	0.94–1.21
	>178	531	1.23	1.09–1.39
	Test for trend, p-value		*0.14*	
	Excl. never exposed		*0.49*	
Large cell carcinoma	Never	257	1.0	Referent
	>0–22	84	1.04	0.79–1.36
	23–70	76	0.90	0.68–1.18
	71–178	93	1.14	0.88–1.47
	>178	109	1.31	1.02–1.67
	Test for trend, p-value		*0.11*	
	Excl. never exposed		*0.14*	
Squamous cell carcinoma	Never	2216	1.0	Referent
	>0–22	742	1.13	1.01–1.26
	23–70	819	1.14	1.03–1.27
	71–178	982	1.37	1.24–1.52
	>178	1069	1.54	1.39–1.70
	Test for trend, p-value		*<0.01*	
	Excl. never exposed		*0.01*	
Small cell carcinoma	Never	850	1.0	Referent
	>0–22	249	0.99	0.84–1.16
	23–70	334	1.20	1.03–1.39
	71–178	360	1.31	1.14–1.53
	>178	407	1.53	1.32–1.76
	Test for trend, p-value		*0.02*	
	Excl. never exposed		*0.39*	

*OR adjusted for study, age group, smoking pack-years (log(cigarette pack-years+1)), time-since-quitting smoking, and List A jobs.

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Table 4. Lung cancer risks (OR) associated with cumulative occupational elemental carbon (EC) exposure by smoking status in men

Cumulative EC exposure	**Never smokers**			**Former smokers**			**Current smokers**		
(µg/m³-years)	Cases	OR*	95% CI	Cases	OR†	95% CI	Cases	OR‡	95% CI
Never	256	1.0	Referent	1868	1.0	Referent	3436	1.0	Referent
>0–22	66	1.40	1.03–1.88	624	1.11	0.98–1.26	994	1.04	0.92–1.18
23–70	41	0.94	0.65–1.33	656	1.23	1.09–1.40	1161	1.01	0.90–1.14
71–178	55	1.17	0.85–1.60	764	1.33	1.18–1.50	1294	1.15	1.03–1.29
>178	72	1.41	1.04–1.88	875	1.47	1.31–1.65	1443	1.40	1.24–1.57
Test for trend, p-value		*0.03*			*<0.01*			*<0.01*	
Excl. never exposed		*0.11*			*0.08*			*0.05*	

*OR adjusted for study, age group and "List A" jobs.

†OR adjusted for study, age group, "List A" jobs, smoking pack-years (log(cigarette pack-years+1)) and time-since-quitting smoking.

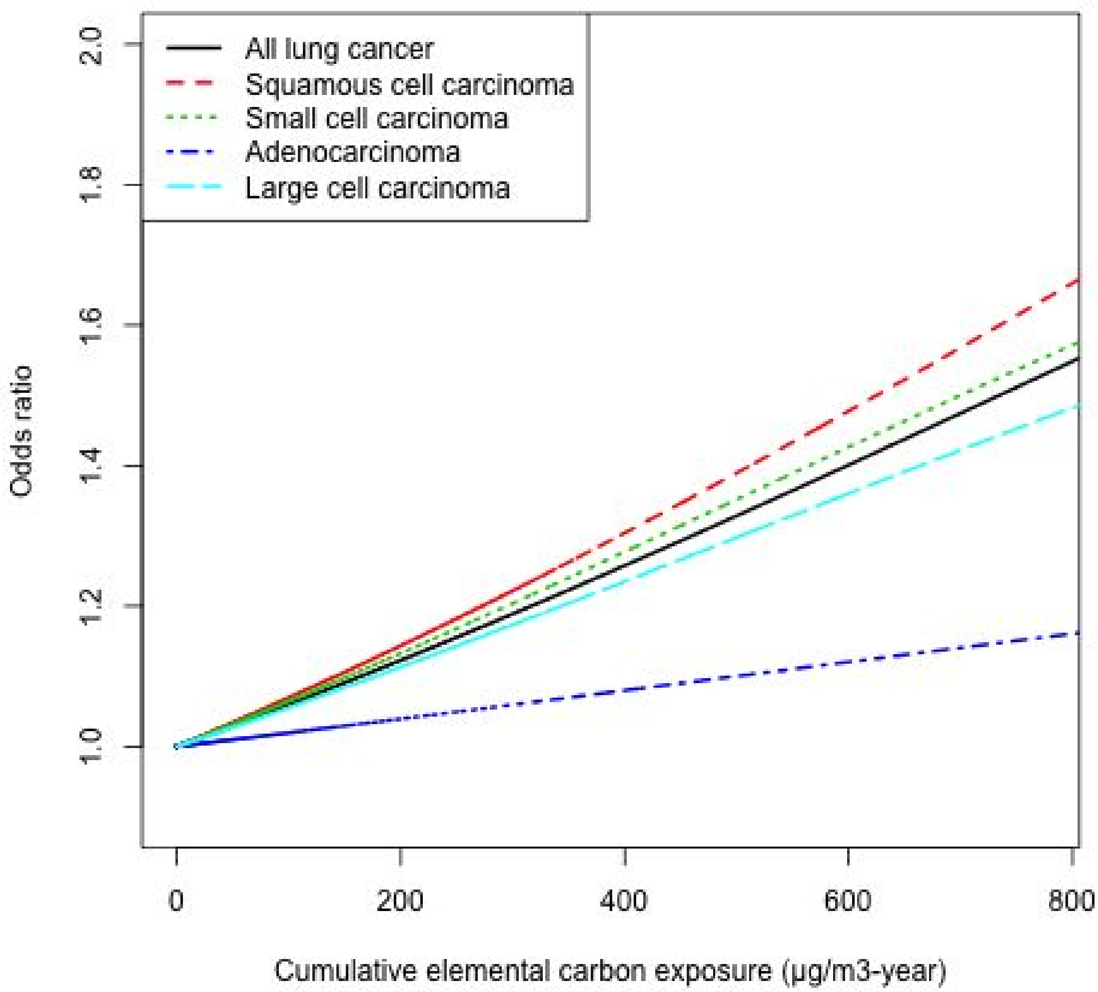
‡OR adjusted for study, age group, "List A" jobs, and smoking pack-years (log(cigarette pack-years+1)).

Table 5: Interactions between occupational elemental carbon (EC) exposure and smoking for overall lung cancer and major subtypes in men

Lung cancer subtype	Exposure status	Controls	Cases	OR*	95%CI
All lung cancers	Never Smoker & Never EC	2525	256	1.0	Referent
	Never Smoker & Ever EC	1912	234	1.14	0.95–1.38
	Ever Smoker & Never EC	5745	5304	8.71	7.62–10.0
	Ever Smoker & Ever EC	6269	7811	11.4	9.93–13.0
	p-value multiplicative†			*0.18*	
	RERI‡			*2.49*	*1.92–3.07*
Adenocarcinom	Never Smoker & Never EC	2525	100	1.0	Referent
	Never Smoker & Ever EC	1912	79	1.05	0.77–1.42
	Ever Smoker & Never EC	5745	1413	6.14	4.99–7.63
	Ever Smoker & Ever EC	6269	1733	7.22	5.87–8.98
	p-value multiplicative†			*0.47*	
	RERI‡			*1.03*	*0.43–1.63*
Large cell carcinoma	Never Smoker & Never EC	2525	14	1.0	Referent
	Never Smoker & Ever EC	1912	5	0.43	0.14–1.14
	Ever Smoker & Never EC	5745	243	7.57	4.57–13.7
	Ever Smoker & Ever EC	6269	357	9.35	5.66–16.8
	p-value multiplicative†			*0.05*	
	RERI‡			*2.34*	*0.67–4.02*
Squamous cell carcinoma	Never Smoker & Never EC	2525	64	1.0	Referent
	Never Smoker & Ever EC	1912	77	1.38	0.98–1.94
	Ever Smoker & Never EC	5745	2152	13.4	10.5–17.1
	Ever Smoker & Ever EC	6269	3535	18.1	14.4–24.0
	p-value multiplicative†			*0.99*	
	RERI‡			*4.66*	*3.23–6.09*
Small cell carcinoma	Never Smoker & Never EC	2525	26	1.0	Referent
	Never Smoker & Ever EC	1912	30	1.38	0.81–2.36
	Ever Smoker & Never EC	5745	824	13.5	9.32–20.6
	Ever Smoker & Ever EC	6269	1320	18.5	12.8–28.1
	p-value multiplicative†			*0.96*	
	RERI‡			*4.56*	*2.42–6.69*

* OR adjusted for study, age group and "List A" jobs.
†RERI: Excess risks due to interaction. Interaction on the additive scale is present when RERI deviates from 0.
‡ p-value for the EC and smoking interaction cross product term coefficient in fully adjusted logistic models. Interaction on the multiplicative scale is present when p<0.05.

FIGURE


All lung cancer
Squamous cell carcinoma
Small cell carcinoma
Adenocarcinoma
Large cell carcinoma
Odds ratio
1.0
1.2
1.4
1.6
1.8
2.0
0
200
400
600
800
Cumulative elemental carbon exposure (µg/m3-year)

Diesel Engine Exhaust Exposure, Smoking, and Lung Cancer Subtype Risks: A Pooled Exposure-response Analysis of 14 Case–control Studies

Online Data Supplement

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SUPPLEMENTARY METHODS

Elemental carbon (EC) data sources and additional description for the DEE-JEM

We chose EC as an exposure proxy for diesel engine exhaust because of its high specificity to diesel engine emissions and general acceptance as the best marker for diesel engine exhaust [E1]. The occupational EC exposure measurements for the JEM were obtained from three sources. Studies published from 1957 to 2007 that were included in an earlier review of EC occupational exposure by Pronk and colleagues [E2]. An additional literature review was performed in the MEDLINE database for studies with EC measurements published between January 1st 2008 and May 31st 2017. Specifically, Medical Subject Headings (MeSH) terms “vehicle emissions” and “occupational exposures” were used in conjunction with all fields keywords “elemental carbon” and “diesel” to search for studies containing EC measurements. The search resulted in 34 matches and 9 publications contained relevant EC measurements for extraction [E3–11]. Two additional reports on EC exposures in firefighters were also added [E11, E12]. Finally, occupational EC measurements from the UK Health and Safety Executive (HSE) National Exposure Database (NEDB) were also screened for extraction [E14]. For inclusion in our JEM, EC measurements had to be: 1) personal measurements or area measurements representative of personal exposure (e.g. inside a vehicle cabin); 2) sampled with duration longer than 1 hour; 3) representative of typical exposures experienced by workers (i.e. not worst-case or complaint-driven sampling); and 4) taken in actual workplaces rather than other simulated controlled settings. In total, 3,528 EC measurements were extracted from studies covered by the review by Pronk and colleagues, 700 were extracted from the additional literature review, and 189 were extracted from the NEDB. The EC measurements included 2,066 in the respirable fraction, 1,333 in the submicron fraction, 665 in the inhalable fraction, and 353 with no size fraction information. Measurements of all size fractions were treated equally as studies suggest the submicron size fraction captures approximately 75% of EC particulates whereas respirable and larger size fractions captures nearly all EC [E15,E16]. Sampling year for EC measurements used to construct the JEM ranged from 1985 to 2016 (median: 2002). Additional information on all EC measurements used for the DEE-JEM, including occupation, country, and sampling year, is available in Supplementary Table E6.

Assigned probabilities in the DEE-JEM consisted of one of three values in 0.1, 0.25, 0.5 and were given based on expert decision by two experts (CG, RV) consecutively. Probabilities were only assigned to occupations where the experts were confident that EC exposure does not occur for all workers with the same job title. A few ISCO-68 occupations at the 2- or 3-digit level received probabilities of 0.4 (n=3) and 0.6 (n=4) as median values of probabilities assigned to their respective 5-digit daughter occupations. In total, the DEE-JEM assigned EC exposure to 248 of 1,506 ISCO-68 jobs. Probability factors for these jobs were: 0.1 for 12 jobs, 0.25 for 84 jobs, 0.4 for 3 jobs, 0.5 for 46 jobs, 0.6 for 4 jobs and 1.0 for 100 jobs.

Sensitivity analyses

Stratified models were used to assess if cancer risks associated with cumulative EC exposure categories differed between population- versus hospital-based case control studies in men. Restricted models were created for male blue-collar workers and workers employed after 1960 to investigate whether cancer risks differed for workers with lower socioeconomic status and for workers whose exposures were more recent when diesel equipment became more common in the workplace, respectively. Because miners and farmers may account for large proportions of the exposed population and may have different exposure patterns than other occupations, restricted analyses were performed on the male study population without those ever-employed in mining and agriculture industries to see if risks differed compared to our main analyses. As an alternative to List-A job adjustment for exposures to other lung carcinogens, we controlled for ever exposure to asbestos, crystalline silica, hexavalent chromium, and polycyclic aromatic hydrocarbons (PAHs) as assessed by the DOM-JEM [E17] in our main categorical exposure model for men. Heterogeneity in lung cancer ORs in men associated with ever EC exposure between 14 studies was measured using the p-value of the Cochran's Q statistic and as a percentage in I^2 [E18].

To assess the impact of various decisions during the development of the DEE-JEM, we also carried out multiple sensitivity analyses with different JEM configurations. In our male categorical cumulative EC exposure model, we tested the impact of including expert-assigned probabilities by using a JEM with no probabilities (i.e. all probabilities=1 for exposed job titles) and a JEM with no expert-assigned probabilities <1. We also tested the same model with a JEM with EC measurement data restricted in the respirable size fraction to see if this changes the findings obtained from the JEM with EC data in various size fractions.

To further explore lung cancer risks in women related to EC exposure, we limited our cumulative EC exposure model to women with lung cancer subtypes other than adenocarcinoma. Additional analysis to calculate lung cancer OR and 95% CIs associated with time-since-last-exposure (<10; 10–19; 20–29; 30–39; >39 years) for men and women separately, with similar adjustments as our main analyses. Trends

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were assessed using p-values from the respective indices of EC exposure as continuous variables for exposed subjects only.

SUPPLEMENTARY RESULTS

Sensitivity analyses

We observed associations between cumulative EC exposure and lung cancer in all stratified and restricted sensitivity analyses in men (Tables E4.1-4.5). Associations were similar or stronger compared to our main models in models restricted to studies with population controls and models restricted to subjects who never worked in agriculture. Risk estimates were more attenuated and less precise in models restricted to studies with hospital controls, subjects who were blue-collar workers, workers employed after 1960, workers who were never-miners, as well as in the model with alternative control for exposure to other occupational lung carcinogens.

Heterogeneity was observed in the lung cancer ORs related to ever EC exposure in the 14 included studies (I^2=50%; Q=40; p<0.01). Significant reduction in heterogeneity was observed (I^2=18%; Q=24; p=0.13) in the remaining subgroup after excluding two studies: AUT and PARIS. Exposure-response patterns between lung cancer and cumulative EC exposure in this more homogeneous subgroup were attenuated, but the risk pattern was generally similar to those observed in the main analyses (Table E4.5).

All analyses involving alternative JEM configurations produced results that were more attenuated than results from the main analyses; however elevated lung cancer ORs and exposure-response between EC exposure and lung cancer were observed in all three alternative models (Tables E4.6-4.8).

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For women with lung cancer subtypes other than adenocarcinoma, we observed elevated OR point estimates for all EC exposure categories compared with unexposed subjects (Table E4.9). However the uncertainties around these estimates were large due to limited statistical power. Among women we observed an indication of increasing risk trend (p=0.04) with longer time since last exposure (Table E5). No trends were observed in men.

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Table E1: Description of the studies included in these analyses in the SYNERGY project

Study	Country	Data collection	Cases N	Cases Response rate (%)	Controls N	Controls Response rate (%)	EC exposure	Control source[b]	Interview[c]
AUT-Munich	Germany	90–95	3180	77	3249	41	31-95	P	S
CAPUA	Spain	00–10	559	91	512	96	26-10	H	S
EAGLE	Italy	02–05	1908	87	2065	72	32-05	P	S
HdA	Germany	88–93	1004	69	1002	68	26-93	P	S
ICARE	France	01–07	2739	63	3449	77	37-07	P	S & NOK
INCO	Czech Republic	99–02	304	94	452	80	37-02	H	S
INCO	Hungary	98–01	391	90	305	100	31-99	H	S
INCO	Poland	98–02	793	88	835	88	33-01	P & H	S
INCO	Romania	98–02	179	90	225	99	43-01	H	S
INCO	Russia	98–01	599	96	580	90	38-00	H	S
INCO	Slovakia	98–02	345	90	285	84	37-02	H	S
INCO/LLP	United Kingdom	98–05	441	78	916	84	34-04	P	S
LUCA	France	89–92	280	98	282	98	27-92	H	S
LUCAS	Sweden	85–90	1014	87	2307	85	23-90	P	S & NOK
MONTREAL	Canada	96–02	1176	85	1505	69	36-99	P	S & NOK
MORGEN[a]	Netherlands	93–97	43	N/A	115	N/A	45-94	P	S
PARIS	France	88–92	169	95	227	95	29-92	H	S
ROME	Italy	93–96	326	74	321	63	26-95	H	S
TORONTO	Canada	97–02	365	62	844	71	29-02	P & H	S
TURIN/ VENETO	Italy	90–94	1086	79	1489	80	25-94	P	S
Overall	14 countries	85–10	16 901	78%	20 965	69%	23-10	P=79%	S=92.7 %

a Nested case-control study: 45% of invited participants to the original cohort completed the baseline questionnaire.

b P = population controls; H = hospital controls

c S = subject; NOK = Next-of-kin

Table E2 Sensitivity analyses in men for the association between cumulative exposure to elemental carbon (EC) in decile groups and lung cancer

Cumulative EC exposure	All studies		
µg/m^3-years	Cases/controls	OR	95%CI
Unexposed	5560/8270	1.0	Referent
>0–6.5	663/819	1.04	0.92–1.18
6.6–16	685/788	1.10	0.97–1.24
17–29	638/786	1.04	0.92–1.18
30–47	759/786	1.18	1.04–1.33
48–71	797/828	1.12	1.00–1.26
72–104	907/847	1.30	1.16–1.46
105–148	800/813	1.20	1.07–1.36
149–218	875/822	1.33	1.18–1.49
219–322	925/834	1.41	1.25–1.58
>322	996/858	1.42	1.27–1.59
Test for trend, p-value§		<0.01	
Excl. never exposed		<0.01	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

Table E3: Odds ratios (OR) and 95% confidence intervals (CIs) of lung cancer for cumulative elemental carbon (EC) for male subjects with different smoking habits (packyears).

Smoking and EC exposure	Controls	Cases	OR	95% CI	
Never smokers					
Unexposed	2525	256	1.0	ref	
>0–22 μg/m³-years	453	66	1.33	0.99	1.7
23–70 μg/m³-years	445	41	0.88	0.61	1.2
71–178 μg/m³-years	485	55	1.10	0.80	1.4
179–218 μg/m³-years	95	17	1.60	0.91	2.6
219–261 μg/m³-years	112	11	0.89	0.45	1.6
262–322 μg/m³-years	115	10	0.79	0.39	1.4
>322 μg/m³-years	207	34	1.50	1.00	2.1
<10 pack-years					
Unexposed	1226	244	1.91	1.58	2.3
>0–22 μg/m³-years	336	81	2.12	1.60	2.7
22–70.6 μg/m³-years	302	76	2.28	1.70	3.0
70.6–178 μg/m³-years	305	89	2.59	1.97	3.3
178–218 μg/m³-years	69	18	2.28	1.29	3.8
218–261 μg/m³-years	54	30	5.07	3.14	8.0
261–322 μg/m³-years	61	18	2.60	1.47	4.4
>322 μg/m³-years	113	52	4.21	2.93	5.9
10-19 pack-years					
Unexposed	1245	494	3.78	3.20	4.4
>0–22 μg/m³-years	322	153	4.30	3.39	5.4
22–70.6 μg/m³-years	287	168	5.25	4.16	6.6
70.6–178 μg/m³-years	278	197	6.51	5.19	8.1
178–218 μg/m³-years	59	45	6.76	4.46	10.
218–261 μg/m³-years	53	44	7.32	4.77	11.
261–322 μg/m³-years	65	38	5.14	3.34	7.8
>322 μg/m³-years	114	76	6.21	4.49	8.5
20-39 pack-years					
Unexposed	1934	1904	13.7	12.0	15.
>0–22 μg/m³-years	509	603	14.6	12.5	17.
22–70.6 μg/m³-years	543	654	15.2	13.1	17.
70.6–178 μg/m³-years	572	749	16.6	14.3	19.
178–218 μg/m³-years	107	170	19.9	16.0	24.
218–261 μg/m³-years	103	159	18.8	15.1	23.
261–322 μg/m³-years	95	151	19.8	15.9	24.
>322 μg/m³-years	236	316	18.5	15.5	22.
>39 pack-years					
Unexposed	1340	2662	21.1	18.2	24.5
>0–22 μg/m³-years	382	781	20.5	17.1	24.6
22–70.6 μg/m³-years	428	919	21.8	18.3	26.1
70.6–178 μg/m³-years	434	1023	24.0	20.2	28.6
178–218 μg/m³-years	78	219	30.0	22.5	40.4
218–261 μg/m³-years	92	231	25.4	19.3	33.7
261–322 μg/m³-years	84	233	28.0	21.1	37.3
>322 μg/m³-years	188	518	28.1	22.7	34.9

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OR is adjusted for study, age group, and List A job

Supplementary Table E4: Sensitivity analyses for the association between cumulative exposure to elemental carbon (EC) and lung cancer

E4.1 Analyses in men by type of controls

Cumulative EC exposure	Studies with population controls*			Studies with hospital controls*		
μg/m³-years	Cases/controls	OR	95%CI	Cases/controls	OR	95%CI
Unexposed	4001/6440	1.0	Referent	1571/1901	1.0	Referent
>0–22	1302/1615	1.10	1.00–1.21	317/286	1.22	1.01–1.48
23–70	1368/1512	1.14	1.03–1.25	427/397	1.06	0.89–1.25
71–178	1535/1516	1.30	1.18–1.43	513/432	1.17	1.00–1.38
>178	1723/1495	1.56	1.42–1.71	643/544	1.20	1.03–1.40
Test for trend, p-value§		*<0.01*			*0.89*	
Excl. never exposed		*<0.01*			*0.37*	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs
*Subjects from the INCO Poland and Toronto studies were included in both analyses, since both types of controls were used

E4.2 Analyses restricted to male blue-collar workers and workers employed after 1960

Cumulative EC exposure	Restricted to blue-collar workers			Restricted to workers employed after 1960		
μg/m³-years	Cases/controls	OR	95%CI	Cases/controls	OR	95%CI
Unexposed	3559/4828	1.0	Referent	1682/2825	1.0	Referent
>0–22	1424/1567	1.01	0.92–1.11	342/460	0.98	0.82–1.17
23–70	1724/1762	1.00	0.92–1.10	443/466	1.25	1.05–1.48
71–178	1948/1830	1.10	1.01–1.21	403/429	1.17	0.98–1.39
>178	2242/1906	1.27	1.16–1.38	329/351	1.24	1.02–1.50
Test for trend, p-value§		*<0.01*			*0.18*	
Excl. never exposed		*0.05*			*0.60*	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

E4.3 Analyses restricted to male non-agricultural and non-mining workers

Cumulative EC exposure	Subjects never employed in the mining industry			Subjects never employed in the agriculture industry		
μg/m³-years	Cases/controls	OR	95%CI	Cases/controls	OR	95%CI
Unexposed	5534/8220	1.0	Referent	5414/8044	1.0	Referent
>0–22	1620/1943	1.08	0.99–1.18	1406/1666	1.09	1.00–1.20
23–70	1729/1919	1.09	1.00–1.18	1434/1496	1.13	1.03–1.24
71–178	1928/1957	1.22	1.12–1.32	1467/1387	1.28	1.17–1.41
>178	2029/1881	1.38	1.27–1.50	1655/1405	1.43	1.31–1.57
Test for trend, p-value§		*<0.01*			*<0.01*	
Excl. never exposed		*<0.01*			*<0.01*	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

E4.4 Analyses in men with alternative model adjustments for exposure to other occupational lung carcinogens

Cumulative EC exposure	No co-exposure adjustment*			Alternative adjustment†		
μg/m^3-years	Cases/controls	OR	95%CI	Cases/controls	OR	95%CI
Unexposed	5560/8270	1.0	Referent	5560/8270	1.0	Referent
>0–22	1684/2002	1.11	1.02–1.21	1684/2002	1.00	0.91–1.09
23–70	1858/2005	1.13	1.04–1.22	1858/2005	0.99	0.90–1.08
71–178	2113/2074	1.25	1.16–1.36	2113/2074	1.09	0.99–1.19
>178	2390/2100	1.43	1.32–1.55	2390/2100	1.23	1.13–1.35
Test for trend, p-value§		<0.01			0.03	
Excl. never exposed		<0.01			0.06	

* OR is adjusted for study, age group, and smoking (pack-years, time-since-quitting smoking).

† (OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and ever exposure to silica, asbestos, polycyclic aromatic hydrocarbons, and chromium.

E4.5 Analyses in men by homogenous group of studies (excluding AUT and PARIS)

Cumulative EC exposure	All studies except AUT and PARIS		
μg/m^3-years	Cases/controls	OR	95%CI
Unexposed	4745/7056	1.0	Referent
>0–22	1235/1481	1.10	0.99–1.21
23–70	1406/1563	1.09	1.00–1.20
71–178	1606/1687	1.19	1.09–1.30
>178	1793/1746	1.29	1.18–1.40
Test for trend, p-value§		<0.01	
Excl. never exposed		0.20	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

E4.6 Analyses in men with alternative JEM restricted to respirable EC data

Cumulative EC exposure	All studies		
μg/m^3-years	Cases/controls	OR	95%CI
Unexposed	5560/8270	1.0	Referent
>0–24	1621/1971	1.07	0.98–1.17
25–73	1841/2024	1.09	1.01–1.19
74–193	2207/2071	1.30	1.20–1.41
>193	2376/2115	1.39	1.29–1.51
Test for trend, p-value§		<0.01	
Excl. never exposed		<0.01	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

E4.7 Analyses in men with alternative JEM without any expert-assigned exposure probabilities

Cumulative EC exposure	All studies		
μg/m³-years	Cases/controls	OR	95%CI
Unexposed	5560/8270	1.0	Referent
	1735/2002	1.08	1.00–1.18
49–143	1982/2035	1.17	1.08–1.27
144–338	2093/2070	1.21	1.11–1.31
>338	2235/2074	1.42	1.31–1.53
Test for trend, p-value§		<0.01	
Excl. never exposed		<0.01	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

E4.8 Analyses in men with alternative JEM restricted to jobs where expert-assigned exposure probabilities=1

Cumulative EC exposure	All studies		
μg/m³-years	Cases/controls	OR	95%CI
Unexposed	9020/12051	1.0	Referent
>0–25	900/1068	0.96	0.86–1.06
26–72	1186/1096	1.12	1.02–1.24
73–209	1223/1115	1.20	1.08–1.32
>209	1276/1121	1.27	1.16–1.40
Test for trend, p-value§		<0.01	
Excl. never exposed		0.02	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

E4.9 Analyses in women with subtypes other than adenocarcinoma

Cumulative EC exposure	Female subjects with cancer subtypes other than adenocarcinoma		
μg/m³-years	Cases/controls	OR	95%CI
Unexposed	1624/4002	1.0	Referent
>0–22	110/179	1.18	0.87–1.59
23–70	74/162	1.18	0.84–1.65
71–178	38/99	1.06	0.67–1.63
>178	23/72	1.18	0.67–2.02
Test for trend, p-value§		0.33	
Excl. never exposed		0.74	

OR is adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs

Table E5: Lung cancer odds ratios (OR) in both sexes associated with time since last occupational elemental carbon (EC) exposure

Occupational EC exposure	**Exposure category**	**Cases (%)**	**Controls (%)**	**OR***	**95% CI**
Men					
Time since last exposure (years) †	Never	5560 (40.9)	8270 (50.3)	1.0	Referent
	10–19	5007 (37.3)	4992 (30.3)	1.04	0.93–1.15
	20–29	1280 (9.4)	1367 (8.3)	1.04	0.94–1.16
	30–39	979 (7.2)	1005 (6.1)	1.17	1.04–1.31
	>39	709 (5.2)	817 (5.0)	1.00	0.88–1.13
Test for trend, p-value (excl. never exposed)				*0.71*	
Women					
Time since last exposure (years) †	Never	2910 (88.3)	4002 (88.7)	1.0	Referent
	10–19	144 (4.4)	210 (4.7)	0.81	0.56–1.17
	20–29	66 (2.0)	91 (2.0)	0.82	0.54–2.22
	30–39	81 (2.5)	78 (1.7)	1.44	0.99–1.08
	>39	95 (2.9)	133 (2.9)	0.92	0.49–1.27
Test for trend, p-value (excl. never exposed)				*0.04*	

*OR adjusted for study, age group, smoking (pack-years, time-since-quitting smoking), and List A jobs
†OR in “time since last exposure” is additionally adjusted for duration (continuous) of silica exposure.
Trend test limited to exposed subjects.

Table E6* – Occupational elemental carbon (EC) exposure measurements used in the diesel engine exhaust job-exposure matrix (DEE-JEM)

Description	Agent†	Duration	N	AM (SD)	Location	Year	Source
Drivers							
Drivers - bus	ECI	>4	4	2>LOD:11-20	US	1998	Pronk et al (2009)
Drivers - bus	ECR	>4	5	10	Estonia	2002	Pronk et al (2009)
Drivers - bus	ECR	>4	39	2 (1.3)	US	2002	Pronk et al (2009)
Drivers - bus and truck	ECI	>4	20	11	Sweden	2002-2004	Pronk et al (2009)
Drivers - local truck	ECNI	>4	4	5 (0.1)	US	1985	Pronk et al (2009)
Drivers - local truck	ECR	>4	5	7	US	1999	Pronk et al (2009)
Drivers - local truck	ECS	>4	56	5 (0.9)	US	1980s	Pronk et al (2009)
Drivers - local truck	ECS	>4	576	2 (2.3)	US	2001-2005	Pronk et al (2009)
Drivers - locomotive	ECNI	>4	76	5 (1.1-15.8)	Canada	1999-2000	Pronk et al (2009)
Driver - locomotive	ECR	>4	156	2.8	US	1996-2007	Hewett and Bullock (2014)
Drivers - locomotive	ECNI	>1	8	11.4 (5.5)	UK	1996	NEDB
Drivers - locomotive in tunnel construction	ECR	>4	2	24 (12)	UK	2014	Galea et al. (2015)
Drivers - locomotive in tunnel construction	ECR	>4	2	21 (4)	UK	2014	Galea et al. (2015)
Drivers - locomotive shunter	ECR	>4	19	20 (18.7)	Russia	2002	Pronk et al (2009)
Drivers - long haul truck	ECS	>4	21	1.55 (0.42)	US	2006?	Sheesley et al (2008)
Drivers - long haul truck	ECNI	>4	4	22 (13.2)	US	1985	Pronk et al (2009)
Drivers - long haul truck	ECR	>4	5	5	US	1999	Pronk et al (2009)
Drivers - long haul truck	ECS	>4	72	5 (0.4)	US	1980s	Pronk et al (2009)
Drivers - long haul truck	ECS	>4	349	1 (0.8)	US	2001-2005	Pronk et al (2009)
Drivers - taxi	ECI	>4	8	8	Sweden	2002-2004	Pronk et al (2009)
Drivers - truck	ECS	>4	18	2.71 (1.37)	US	2006?	Sheesley et al (2008)
Drivers - truck	ECI	1->4	3	10 (6)	US	1992	Pronk et al (2009)
Mechanics							

Mechanics - ambulance	ECR	>4	3	31	UK	2000	Pronk et al (2009)
Mechanics - bus	ECI	>4	4	ND	US	1998	Pronk et al (2009)
Mechanics - bus	ECR	>4	53	39	UK	2000	Pronk et al (2009)
Mechanics - bus	ECR	>4	15	39	Estonia	2002	Pronk et al (2009)
Mechanics - diesel engine testing	ECR	>4	54	48.5 (22.1)	US	2012-2013	Lan et al. (2015)
Mechanics - locomotive	ECNI	>1	22	31.4 (40.7)	UK	1994-2006	NEDB
Mechanics - motor vehicle	ECNI	>1	20	39.1 (45.1)	UK	1994-2006	NEDB
Mechanics - truck	ECS	>4	7	2.04 (1.02)	US	2006?	Sheesley et al (2008)
Mechanics - truck	ECR	>4	10	4	US	1999	Pronk et al (2009)
Mechanics - truck	ECS	>4	80	27 (4.1)	US	1980s	Pronk et al (2009)
Mechanics - truck and bus	ECI	>4	40	21	Sweden	2002-2004	Pronk et al (2009)
Mechanics - tunnel construction	ECR	>4	29	48.39	Norway	2010-2011	Bakke et al. (2014)
<u>Firefighters</u>							
Firefighters	ECI	>4	18	40 (20.3)	US	1995	Pronk et al (2009)
Firefighters	ECI	>4	12	10 (max)	US	1997	Pronk et al (2009)
Firefighters	ECI	<1	8	ND	US	1998	Pronk et al (2009)
Firefighters	ECI	>4	27	24 (max)	US	2002	Pronk et al (2009)
Firefighters	ECR	10	21	2	AUS	2010	Bott et al (2010)
Firefighters	ECR	>7	28	1.34 (0.56)	US	2016	Couch et al (2016)
<u>Dockworkers</u>							
Dockworker	ECS	>4	≥5		US	1990	Pronk et al (2009)
Dockworker	ECS	>4	54	24 (0.4-2.5)	US	1991	Pronk et al (2009)
Dockworker	ECI	>4	5	4 (1.8)	US	1992	Pronk et al (2009)
Dockworker	ECR	>4	12	9	US	1999	Pronk et al (2009)
Dockworker	ECR	>4	27	122	UK	2000	Pronk et al (2009)
Dockworker	ECS	>4	14	1.12 (0.41)	US	2006?	Sheesley et al (2008)
Dockworkers - ship loading	ECR	>4	20	49	UK	2000	Pronk et al (2009)
Dockworkers - ship loading	ECI	>4	168	6 (0.9-9.0)	US	2003-2005	Pronk et al (2009)

Miners							
Surface production	ECS	>4	23	23 (15-54)	US	1997	Pronk et al (2009)
Surface production	ECR	>4	164	13 (2-89)	US	2002	Pronk et al (2009)
Underground maintenance	ECS	>4	8	53 (46)	US	1997	Pronk et al (2009)
Underground maintenance	ECR	>4	269	144 (17-462)	US	2002	Pronk et al (2009)
Underground not specified	ECR	NI	7	66 (28)	UK	2004	Pronk et al (2009)
Underground not specified	ECNI	NI	27	27	Sweden	2006	Pronk et al (2009)
Underground production	ECR	>4	4	241	Estonia	2002	Pronk et al (2009)
Underground production	ECR	>4	15	637 (75-508)	US	1999	Pronk et al (2009)
Underground production	ECI	<1-4	12	538 (512)	US	2007	Pronk et al (2009)
Underground production	ECS	>4	38	219 (65-193)	US	1997	Pronk et al (2009)
Underground production	ECR	>4	343	202 (32-144)	US	2002	Pronk et al (2009)
Underground production	ECR	NI	6	148 (136)	UK	2004	Pronk et al (2009)
Underground production	ECS	1->4	13	163 (141)	US	2001-2002	Pronk et al (2009)
Others							
Asphalt road pavers	ECR	>4	3	3 (0.2)	Sweden	2005-2006	Elihn et al (2008)
Baggage handling	ECI	>4	72	11 (5.4)	US	2004	Pronk et al (2009)
Bus service workers	ECI	>4	4	2>LOD:15-30	US	1998	Pronk et al (2009)
Cleaners - general	ECNI	>1	4	22.4 (9.4)	UK	1994-2001	NEDB
Cleaners - locomotive	ECNI	>1	5	39.0 (9.4)	UK	1996-2006	NEDB
Concrete ring builders	ECR	>4	3	20 (8)	UK	2014	Galea et al. (2015)
Concrete ring segment lifters	ECR	>4	8	17 (8)	UK	2014	Galea et al. (2015)
Concrete sprayers	ECR	>4	7	57.41	Norway	2010-2011	Bakke et al. (2014)
Conductors - locomotive	ECNI	>1	14	21.9 (36.8)	UK	1994-2001	NEDB
Construction engineers	ECR	>4	6	20 (7)	UK	2014	Galea et al. (2015)
Construction workers	ECI	>4	22	13	Sweden	2002-2004	Pronk et al (2009)
Conveyor extension workers	ECR	>4	2	30 (3)	UK	2014	Galea et al. (2015)

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Curbside waste collectors	ECR	>4	72	5.53	S. Korea	2014	Lee et al. (2015)
Customer service workers - bus station	ECNI	>1	1	28.4	UK	2006	NEDB
Customer service workers - locomotive platform	ECNI	>1	14	13.2 (6.9)	UK	1996-2001	NEDB
Drill and blast workers	ECR	>4	51	47.2	Norway	2010-2011	Bakke et al. (2014)
Electric utility installers	ECI	>4	120	4	US	1996-1997	Pronk et al (2009)
Electricians - railway station	ECNI	>1	7	39.5 (25.4)	UK	1994-2006	NEDB
Engineers - locomotive	ECI	1->4	49	6	US	1996-1998	Pronk et al (2009)
Forklift operators	ECR	>4	39	36	UK	2004	Pronk et al (2009)
Forklift operators - warehouse	ECNI	>1	25	82.2 (130.8)	UK	1994-2006	NEDB
Gate controllers in booth	ECR	>4	29	1.8	Canada	2013	Debia et al. (2016)
Grout pump operators	ECR	>4	1	110	UK	2014	Galea et al. (2015)
Grout pump operators	ECR	>4	5	19 (6)	UK	2014	Galea et al. (2015)
Heavy/highway construction workers	ECR	>4	261	13	US	1994-1999	Pronk et al (2009)
Highway toll booth workers	ECR	>4	63	6.1 (4)	China	2002	Shih et al (2008)
Hostlers - locomotive	ECNI	>4	5	4 (1.3)	Canada	1999-2000	Pronk et al (2009)
Hostlers - tractor	ECS	>4	4	1.3 (1)	US	2006?	Sheesley et al (2008)
Labourers - various industries	ECNI	>1	20	60.9 (63.7)	UK	1994-2006	NEDB
Lead miners	ECR	>4	1	12	UK	2014	Galea et al. (2015)
Loading and unloading workers - passenger ferries	ECNI	>1	10	46.2 (28.2)	UK	1994-2006	NEDB
Locomotive rail extension workers	ECR	>4	2	26 (6)	UK	2014	Galea et al. (2015)
Maintenance workers - locomotive	ECR	>4	64	39	UK	2000	Pronk et al (2009)
Maintenance workers - locomotive	ECNI	>4	48	5 (4.9-8.8)	Canada	1999-2000	Pronk et al (2009)
Material loaders	ECR	>4	18	38.43	Norway	2010-2011	Bakke et al. (2014)
Non-operating crew in trailing locomotive	ECI	>4	47	10 (12)	Canada	2003	Pronk et al (2009)

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Parking booth attendants	ECR	>4	34	1.1 (0.6)	US	2002	Pronk et al (2009)
Pipe/walkway extension workers	ECR	>4	2	18 (2)	UK	2014	Galea et al. (2015)
Porters - warehouse	ECNI	>1	3	30.4 (35.1)	UK	1994-2006	NEDB
Security guards	ECNI	>1	2	60.9 (2.1)	UK	1994	NEDB
Support workers	ECR	>4	31	76.14	Norway	2010-2011	Bakke et al. (2014)
Toll attendants/cashiers	ECNI	>1	22	30.5 (22.3)	UK	1994-2006	NEDB
Tunnel boring machine operators	ECR	>4	5	17 (5)	UK	2014	Galea et al. (2015)
Tunnel construction workers	ECI	>4	10	314	Norway	1996-1999	Pronk et al (2009)
Tunnel construction workers	ECI	>4	12	132	Sweden	2002-2004	Pronk et al (2009)
Unloading equipment operator - shipyard	ECNI	>1	10	37.6 (24.9)	UK	2006	NEDB
Vehicle inspectors	ECNI	>1	2	21.8 (5.1)	UK	1999	NEDB
Vehicle testing workers	ECR	>4	11	11	UK	2000	Pronk et al (2009)
Waterproofing workers	ECR	>4	13	64.82	Norway	2010-2011	Bakke et al. (2014)
Workers in trailing locomotive	ECR	>4	22	11.1	US	1996-2007	Hewett and Bullock (2014)

*Table partially adapted from Tables 1-4 in review by Pronk and colleagues [2].

†ECR: respirable elemental carbon; ECS: submicron elemental carbon; ECI: inhalable elemental carbon; ECNI: elemental carbon size fraction not indicated.

Table E7: Job codes and descriptions for List A jobs included in study population

ISCO-68*	Job description
03810	mining technicians (general)
55130	janitor
55220	charworker
55290	other charworkers, cleaners and related workers
58110	fire fighter (general)
58190	other fire-fighters
62330	vineyard worker
70000	production supervisors and general foremen
70010	production supervisors and general foremen (general)
70020	supervisors and general foreman, mining, quarrying and well drilling
70030	supervisors and general foreman, metal processing
70050	supervisor and general foreman, manufacturing of machinery and metal products
70055	supervisor and general foreman, manufacturing and installation of electrical and electronic equipment
70075	supervisor and general foreman, construction work
70080	supervisor and general foreman, production and distribution of electricity, gas and water
70090	other production supervisors and general foremen
71100	miners and quarrymen
71105	miner (general)
71110	quarryman (general)
71120	cutting-machine operator (mine)
71130	drilling-machine operator (mine and quarry)
71150	shot-firer (mine and quarry)

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71160	underground timberman
71170	sampler (mine)
71190	other miners and quarrymen
71250	jig tender
71290	other mineral and stone treaters
72000	metal processers
72100	metal smelting, converting and refining furnacemen
72120	blast furnaceman (ore smelting)
72130	open-hearth furnacemen (steel)
72170	furnaceman (non-ferrous metal converting and refining)
72190	other metal smelting, converting and refining furnacemen
72220	hot-roller (steel)
72230	continuous-mill-roller (steel)
72250	roller (non-ferrous metals)
72260	seamless pipe and tube roller
72290	other metal rolling-mill workers
72320	furnaceman (metal melting, except cupola)
72330	cupola furnaceman
72340	furnaceman (metal reheating)
72390	other metal melters and reheaters
72400	metal casters
72420	metal pourer
72440	die-casting-machine operator
72450	continuous rod-casting-machine operator (non-ferrous metal)
72490	other metal casters

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72500	metal moulders and coremakers
72520	bench moulder (metal)
72530	floor and pit moulder
72540	moulder (machine)
72550	coremaker (hand)
72560	coremaker (machine)
72590	other metal moulders and coremakers
72620	annealer
72630	hardener
72700	metal drawers and extruders
72730	wire drawer (machine)
72740	seamless pipe and tube drawer
72750	extruder operator (metal)
72800	metal platers and coaters
72820	electroplater
72830	hot-dip plater
72840	wire-coating-machine operator
72890	other metal platers and coaters
72900	metal processers not elsewhere classified
72920	metal bluer
72930	casting finisher
72940	metal cleaner
72990	other metal processors
73210	sawmill sawyer (general)
74140	mixing-and blending-machine operator (chemical and related processes)

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74230	roaster (chemical and related processes)
74290	other cookers, roasters and related heat-treaters
74390	other filter and separator operators
74920	coke burner
74925	coal-glass maker
74990	other chemical processors and related workers
75290	other spinners and winders
79630	vehicle upholsterer
79690	other upholsterers and related workers
81120	cabinetmaker
81230	wood turner
81920	coach-body builder
81925	cartwright
81935	wooden pattern maker
81955	wooden furniture finisher
81960	smoking-pipe maker
83000	blacksmiths, toolmakers and machine-tool operators
83100	blacksmiths, hammersmiths and forging-press operators
83110	blacksmith (general)
83120	hammersmith
83130	drop-hammer operator
83140	forging-press operator
83190	other blacksmiths, hammersmiths and forging-press operators
83220	tool and die maker
83240	metal pattern maker (foundry)

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83250	metal marker
83290	other toolmakers, metal pattern makers and metal markers
83305	metalworking-machine setter (general)
83310	metalworking-machine setter-operator (general)
83320	lathe setter-operator
83330	milling-machine setter-operator
83350	boring-machine setter-operator
83370	precision-grinding-machine setter-operator
83390	other machine-tool setter-operators
83410	machine-tool operator (general)
83420	lathe operator
83430	milling-machine-operator
83440	planing-machine-operator
83450	boring-machine-operator
83460	drilling-machine-operator
83465	precision-grinding-machine-operator
83490	other machine-tool operators
83520	buffing- and polishing machine operator
83530	tool grinder, machine tools
83590	other metal grinders, polishers and tool sharpeners
83930	locksmith
83940	metal spinner
83950	metal former (hand)
83960	metal-press operator
83980	power-shear operator

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83990	other blacksmiths, toolmakers and machine-tool operators
84100	machinery fitters and machine assemblers
84105	machinery fitter (general)
84110	machinery fitter-assembler (general)
84115	internal combustion engine fitter-assembler (except aircraft and marine engines)
84125	marine engine machinery fitter-assembler
84130	turbine fitter-assembler (except aircraft and marine engines)
84135	metalworking machine-tool fitter-assembler
84175	machinery erector and installer
84180	refrigeration and air-conditioning plan installer and mechanic
84190	other machinery fitters and machine assemblers
84230	precision -instrument maker and repairer
84320	automobile mechanic
84330	motor-truck mechanic
84390	other motor-vehicle mechanics
84410	aircraft engine mechanic (general)
84490	other aircraft engine mechanics
84900	machinery fitters, machine assemblers and precision instrument makers (except electrical) not elsewhere classified
84910	machinery mechanic (general)
84915	reciprocating steam-engine mechanic
84920	diesel engine mechanic (except motor vehicle)
84930	metalworking machine-tool mechanic
84970	plant maintenance mechanic
84980	oiler and greaser (except ships' engines)

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84985	mechanical products inspector and tester
84990	other machinery fitters, machine assemblers and precision instrument makers (except electrical)
85110	electrical fitter (general)
85120	electrical motor and generator fitter
85130	electrical transformer fitter
85140	electrical switchgear and control apparatus fitter
85150	electrical instrument fitter
85190	other electrical fitters
85210	electronics fitter (general)
85250	electronics fitter (industrial equipment)
85260	electronic signalling systems fitter
85320	electrical equipment assembler
85340	coil winder (machine)
85420	radio and television mechanic
85510	electrician (general)
85520	building electrician
85530	aircraft electrician
85535	ship's electrician
85540	vehicle electrician
85560	maintenance electrician
85570	electrical repairman
85630	telephone and telegraph mechanic
85740	telephone and telegraph lineman
85920	electrical and electronic products inspector and tester
87000	plumbers, welders, sheet metal and structural metal preparers and erectors

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87105	plumber (general)
87110	pipe fitter (general)
87130	marine pipe fitter
87190	other plumbers and pipe fitters
87200	welders and flame-cutters
87210	gas and electric welder (general)
87215	gas welder
87220	electric arc welder (hand)
87225	electric arc welder (machine)
87235	resistance welder
87245	brazer
87250	flame-cutter (hand)
87255	flame-cutter (machine)
87290	other welders and flame-cutters
87300	sheet-metal workers
87310	sheet-metal worker (general)
87320	sheet-metal marker
87330	coppersmith
87340	tinsmith
87350	boilersmith
87370	vehicle sheet-metal worker
87390	other sheet-metal workers
87420	structural metal maker
87430	structural steel worker (workshop)
87440	constructional steel erector

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87450	metal shipwright
87455	ship plater
87460	hand riveter
87470	pneumatic riveter
87490	other structural metal preparers and erectors
90180	plastics products fabricator
90190	other rubber and plastic product makers (except tire makers and tire vulcanisers)
92200	printing pressmen
92700	photographic darkroom workers
93100	painters, construction
93120	building painter
93130	structural steel and ship painter
93190	other painters, construction
93900	painters not elsewhere classified
93920	brush painter (except construction)
93930	spray painter (except construction)
93940	hand dipper
93950	sign painter
93960	automobile painter
93990	other painters
94980	quality inspector
94990	other production and related workers nec
95120	bricklayer (construction)
95130	firebrick layer
95320	slate and tile roofer

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95330	composition roofer
95340	asphalt roofer
95390	other roofers
95400	carpenters, joiners and parquetry workers
95410	carpenter (general)
95415	construction carpenter
95420	construction joiner
95440	wood shipwright
95445	ship joiner
95450	wooden boatbuilder
95455	ship's carpenter
95470	bench carpenter
95475	parquetry worker
95490	other carpenters, joiners and parquetry workers
95620	building insulator (hand)
95650	boiler and pipe insulator
95790	other glaziers
95900	construction workers not elsewhere classified
95910	housebuilder (general)
95940	scaffolder
95975	building exterior cleaner
95990	other construction workers
96190	other power-generating machinery operators
96910	stationary engine operator
96930	boiler fireman

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96940	pumping-station operator
96980	heating and ventilation equipment operator
97100	dockers and freight handlers
97130	railway and road vehicle loader
97145	warehouse porter
97155	machine packer
97205	hoisting equipment rigger (general)
97230	ship rigger
97300	crane and hoist operators
97320	bridge- or gantry-crane operator
97327	tower-crane operator
97330	mobile-crane operator
97335	hoist operator (construction)
97345	mine cageman
97350	winch operator
97390	other crane and hoist operators
97445	road-grader and scraper operator
97450	road-roller operator
97460	tar-spreading machine operator
97920	lifting-truck operator
97990	other material handling equipment operators
98140	ordinary seaman
98190	other ships' deck ratings, barge crews and boatman
98290	other ships' engine-room ratings
98320	railway engine driver

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98330	railway steam-engine fireman
98420	railway brakeman (freight train)
98550	lorry and van driver (local transport)
98560	lorry and van driver (long-distance transport)
98590	other motor-vehicle drivers
99910	labourer

*ISCO-68: five-digit International Standard Classification of Occupations (version 1968); dashes and dots omitted.

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