Lung cancer risk among firefighters when accounting for tobacco smoking - a pooled analysis of case-control studies from Europe, Canada, New Zealand and China

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STUDY APPROVAL

Ethical approvals for the original studies were obtained in accordance with legislation in each country, and for the SYNERGY project from the IARC Institutional Review Board Committee. The Regional Ethics Committee in Stockholm, Sweden gave approval for the present analyses.

ABSTRACT

Objectives: To investigate the risk of lung cancer among firefighters, while controlling for smoking.

Methods: We used data from the SYNERGY project including pooled information on lifetime work histories and smoking habits for 14,748 lung cancer cases and 17,543 controls from 14 case-control studies conducted in Europe, Canada, New Zealand and China. Odds ratios were estimated by unconditional logistic regression with adjustment for smoking and ever employment in a job with established lung cancer risk.

Results: We observed no increased risk of lung cancer overall or by specific cell type among firefighters (n=190), neither before nor after adjustment. There was no significant exposure-response relationship and no significant heterogeneity in lung cancer risk among firefighters across the studies.

Conclusions: We found no evidence of an excess lung cancer risk related to occupational exposure as a firefighter.

Key terms: epidemiology, lung neoplasms, carcinogens, occupational exposure, fire exhaust, air pollution, aerosols, polycyclic aromatic hydrocarbons (PAHs)

Clinical significance: Even though firefighters worldwide are potentially exposed to a wide variety of carcinogens during work, of which some are known lung carcinogens, we did not observe an excess risk of lung cancer overall or by specific cell type among firefighters in this pooled analysis of case-control studies.

INTRODUCTION

Firefighters are potentially exposed to a wide variety of chemical compounds by inhalation of particulate matter, gases and vapours during the course of their work. A large number of known (e.g. arsenic, asbestos, benzene, benzopyrene, 1,3-butadiene, cadmium, formaldehyde and silica) or suspected (e.g. acetaldehyde, naphthalene, polychlorinated biphenyls, styrene, tetrachlorethylene, trichlorethylene and toluene diisocyanates) human carcinogens have been detected in smoke at fires, several of which are known to cause lung cancer.[1] Many of the carcinogenic products identified at municipal structural fires are volatile organic compunds (VOCs) common to most burning materials and are dominated by benzene, toluene and naphthalene.[1,2] Firefighters may also be exposed to diesel engine exhaust which is associated with an increased risk for lung cancer.[3] Exposure of firefighters may vary considerably depending on their job activities, time spent at fires and use of respiratory equipment. Inhalation is considered to be the major source of exposure although dermal absorbation is also an important route of exposure for polycyclic aromatic hydrocarbons and polychlorinated biphenyls.[1] Occupational exposure as a firefighter is classified as possibly carcinogenic to humans (Group 2B) by the International Agency for Research on Cancer (IARC), on the basis of limited evidence in humans (strongest evidence for testicular cancer, prostate cancer and non-Hodgkin lymphoma) and inadequate evidence in experimental animals.[1]

Some previous studies among firefighters indicate an excess of lung cancer overall,[4,5] lung cancer of a specific cell type,[6,7] or positive exposure-response associations,[8] whereas most studies do not.[9-20] Pukkala et al. observed an excess incidence of lung adenocarcinoma among firefighters in the Nordic countries,[6] Tsai et al. observed an excess risk of non-specific, non-small cell lung cancer among firefighters in California,[7] Hansen et al. observed an excess risk of lung cancer mortality among Danish firefighters in the group aged 60 to 74,[21] and in a study by Heyer et al. in Seattle the lung cancer mortality was elevated among firefighters of 65 years or older.[22] Further, a large comprehensive review of 32 studies by LeMasters et al. 2006, including a meta-analysis of 26 studies, evaluated the likelihood of cancer risk among firefighters and found no excess of lung cancer.[23] Their findings indicated that firefighters had a probable cancer risk for multiple myeloma, non-Hodgkin lymphoma, prostate cancer, and testicular cancer. Eight additional cancers were listed as possibly associated with firefighting. The risk of cancer in the lung was designated as unlikely and the summary risk estimate for lung cancer was 1.03 (95 % CI 0.97-1.08). A second comprehensive review by the IARC monograph working group 2010 included 42 studies of cancer in firefighters,[1] of which two large epidemiological studies had been reported since the review by LeMasters et al. A meta-analysis including these two studies was performed by the Working Group for the four primary cancer sites listed above and showed strongest evidence for testicular cancer, prostate cancer and non-Hodgkin lymphoma.[1] Overall, it is still unclear whether there is an increased risk of lung cancer among firefighters. Only two of the above mentioned lung cancer studies had adequate information on individual smoking habits,[4,15] while no study had information on employment in occupations with established lung cancer risk. Previous studies have shown diverging results regarding the risk of lung cancer of various cell types among firefighters,[4,6,7,9] and the impact of smoking on lung cancer risk may vary between different histological subtypes of lung cancer.[24]

The aim of this study was to investigate if working as a firefighter is associated with an increased risk of lung cancer, while controlling for smoking using individual data on life time smoking habits, as well as for ever employment in a job with established lung cancer risk. We also aimed to analyze the results by cell types.

METHODS

SYNERGY is a large pooled analysis of case-control studies on the joint effects of occupational carcinogens and smoking in the development of lung cancer. Detailed information about the SYNERGY project and included studies has been presented elsewhere,[25] see also www.synergy.iarc.fr. We used the SYNERGY database including information on lifetime work histories and lifetime tobacco smoking habits from 14 case-control studies conducted in Europe (10 studies), Canada (2 studies), New Zealand (1 study) and China (1 study). Three of the original studies in SYNERGY (Rome, Paris and MORGEN) had no firefighters among either cases or controls, and were therefore omitted. A general description of the studies included in this analysis is presented in Table 1. The data were collected in 15 countries between 1985 and 2010. The studies included are well-designed population- or hospital-based case-control studies. In most studies controls were frequency-matched to the cases regarding sex and age. The overall response rate was 82% among cases and 67% among controls. Next-of-kin were interviewed for the majority of cases and some controls in LUCAS and some study participants in ICARE and MONTREAL (9% of all cases; 7% of all controls). The subtypes of lung cancer were classified according to WHO guidelines after histological or cytological confirmation. Reference pathology was performed for the German cases. The SYNERGY-studies included both men and women but only 2 women had ever worked as a firefighter (0 cases and 2 controls), therefore the analysis was restricted to men. The study comprised 15,110 male cases and 17,931 male controls. Subjects providing incomplete information for calculating duration of jobs or cumulative smoking were omitted (132 cases and 149 controls), as well as subjects who never held a job during at least 1 year (230 cases and 239 controls), leaving 14,748 cases of lung cancer and 17,543 controls for analysis.

Identification of Firefighters

The occupational data was originally coded according to national classifications for most studies along with the years of start and end, and was recoded to the International Standard Classification of Occupations (ISCO-68)[39] within SYNERGY. Firefighters were identified from the ISCO-68 code (“5-81”). There were 190 men who had ever worked as a firefighter, among them 86 cases of lung cancer and 104 controls. The group “Firefighters” includes “General firefighters” (66 cases, 89 controls), “Fire prevention firefighters” (9 cases, 4 controls), “Aircraft accident firefighters” (0 cases, 3 controls) and “Other firefighters” (15 cases, 12 controls). There were 4 cases and 4 controls who had worked as two types of firefighters. Therefore, the sum of the number of firefighters in the different categories differs from the number of all firefighters.

Statistical analyses

Odds ratios (OR) for lung cancer associated with work as a fire-fighter and 95% confidence intervals (CI) were estimated by unconditional logistic regression. For all associations, three levels of adjustments were made: the first (OR1) adjusting for age (ln(age)), and study; the second (OR2) additionally adjusting for cumulative cigarette smoking (log(cigarette packyears+1)) and time-since-quitting smoking cigarettes (current smokers, stopped smoking since 2-9 years, 10-19 years, 20+ years before interview/diagnosis, never smokers). The pack-year variable was log-transformed because this fitted the data better. A third level of adjustment (OR3) included adjusting for ever employment in an occupation with established lung cancer risk ("List A" job, yes/no). This list of occupations and industries was identified by Ahrens and Merletti in 1998 and updated by Mirabelli et al. in 2001.[40,41]

Persons smoking ≥ 1 cigarette per day for ≥ 1 year were coded as current smokers, including those who had stopped smoking within 2 years before diagnose/interview. Cigarette pack-years were calculated as: Σ duration x average intensity per day / 20.

We repeated the analyses on lung cancer risk among firefighters with restriction to never smokers, former smokers, and current smokers to explore potential residual confounding by smoking. We also analyzed the lung cancer risk among firefighters by duration of work in order to investigate whether those with a longer duration of employment had a higher risk. The cutoffs for categories of work duration were based on the quartiles of the distribution of employment duration among firefighters in the control group (<6 years, 6-21, 22-32, >32 years). In addition, we stratified the analyses by the major histological subtypes of lung cancer (adenocarcinoma, squamous cell carcinoma, small cell carcinoma, and others/unspecified). We also analyzed the lung cancer risk in relation to employment as a "General firefighter", i.e. excluding "Fire prevention firefighters", "Aircraft accident firefighters" and "Other firefighters". Subjects who had never worked as firefighters were the reference category in all analyses. P-values for trend were obtained by including a continuous variable for duration (years) in the logistic regression model.

Meta-analysis was used to explore extent of heterogeneity between the studies and study-specific ORs, calculated with logistic regression, adjusted for age, cigarette pack-years, and smoking status for all types of tobacco smoking (never/former/current). The heterogeneity was assessed using a chi-square test with the inverse of the variance as weights. The extent of inconsistency between OR estimates was assessed as a percentage (I^2).

We provide an update of the meta-analysis of LeMasters et al. by including new studies published since 2005. Here, we restricted the analysis to studies reporting standardized incidence (SIR) and mortality ratios (SMR). We excluded two case-controls studies using cancer controls (Bates, 2007 and Tsai et al., 2015). For the mortality meta-analysis, we added Amadeo et al. (2015),[18] Daniels et al. (2014),[5] Ma et al. (2005),[12] and Ahn et al (2015).[20] For the incidence analysis, we additionally incorporated Ma et al. (2006),[13] Pukkala et al. (2014),[6] Daniels et al. (2014),[5] Glass et al. (2014),[19] and Ahn et al. (2012).[16] Instead of Demers et al. (1992), we included Demers et al. (1994),[9] because the first study included also policemen. Random-effect models for the lung cancer incidence and mortality were calculated according to LeMasters et al.,[23] and Byar's approximation was used for calculating 95% CIs.[42]

Analyses were conducted using Stata v. 11.0 for Windows (StataCorp LP, College Station, Texas) and the command "metan" was used for the meta-analyses. SAS V9.4 software (SAS Institute, Cary, North Carolina, USA) was used for the updated meta-analysis of LeMasters et al.

RESULTS

Characteristics of the study subjects are presented in Table 2. Smoking was similarly common among the firefighters as among non-firefighters; among the controls, 74.1% of the firefighters were current or former smokers, compared with 73.8% among non-firefighters. However, the percentage of ever smokers with more than 20 pack-years was slightly higher among firefighters; 62.3% among firefighters, compared with 54.8% in non-firefighters. Having ever been employed in an occupation with established lung cancer risk was more common among firefighters than among non-firefighters; among the controls, 13.5% of the firefighters, compared with 9.1% among non-firefighters. The most common lung cancer cell type was squamous cell carcinoma, followed by adenocarcinoma and small cell carcinoma, both among firefighters and non-firefighters.

Overall, we observed no increased risk of lung cancer in firefighters. Before adjustment for smoking the OR was 1.03 (95% CI 0.77-1.38) and after adjusting for smoking 0.95 (95% CI 0.68-1.32). Additional adjustment for ever employment in an occupation with established lung cancer risk did not change the OR (Table 3). There was no evidence of a trend of increasing lung cancer risk with increasing duration of work as a firefighter (p=0.46-0.58). (Table 3). Analyses of lung cancer risk in relation to smoking status showed no increased risk in firefighters when restricted to never smokers (OR=0.60, 95% CI 0.14-2.58), former smokers (OR=0.75, 95% CI 0.45-1.26) or current smokers (OR=1.18, 95% CI 0.73-1.90), though the number of non-smoking firefighters was small. There were only two cases of lung cancer in firefighters who had never smoked (Table 4). Analyses restricted to never employed in an occupation with established lung cancer risk showed no increased lung cancer risk in firefighters (OR2= 0.98, 95% CI 0.69-1.39) and neither did analyses restricted to ever employed in such an occupation (OR2=0.79, 95% CI 0.31-1.99) (not shown in table). When we analysed the results by cell types, none of the cell types was associated with work as a firefighter (Table 5). The study specific ORs for firefighters are shown in figure 1. No study showed a statistically significantly elevated OR. We observed no significant heterogeneity in lung cancer risk among firefighters across the studies (I^2 0.0%, p-value=0.738). Additional analyses including only “General firefighters” did not show any increased lung cancer risk (OR3=0.88, 95% CI 0.61-1.26) (not shown in table).

The updated meta-analysis of LeMasters et al. is based on 1,363 incident and 3,156 deceased cases of professional firefighters. The incidence (SIR=0.97, 95% CI 0.91-1.02) and mortality (SMR=0.99, 95% CI 0.95-1.03) of firefighters was not increased.

DISCUSSION

We observed no increased risk of lung cancer in firefighters overall, neither before nor after adjustment for smoking and ever employment in an occupation with established lung cancer risk, and there was no positive association between employment duration and risk. When analyzing stratified by cell type, none of the major histological subtypes of lung cancer was associated with work as a firefighter. There was no excess risk of lung cancer among firefighters when restricting the analyses to never smokers, former smokers, or current smokers.

Several factors should be taken into account in the interpretation of current findings. An advantage of the study is that it covers occupational information and detailed smoking information for the whole lifetime, for almost 15,000 cases and 17,000 controls. However, there were only 86 cases who had ever worked as a firefighter. Even so, the power of this study is high relative to most other case-control studies and we also have the ability to stratify by histology, and to examine heterogeneity between studies. A limitation is that we only have duration of employment as a surrogate for exposure.

Firefighters were identified by occupational codes, which could be a further limitation of our study, as information on their exact tasks and length of employment in such tasks was not available. The vast majority (77%) were “General firefighters” but some were “Fire prevention firefighters” or “Aircraft accident firefighters”, with possibly lower exposure to fire smoke. However, additional analyses including only “General firefighters” did not change the results. In this study, employment in jobs known to entail increased lung cancer risk was more common among firefighters compared with those who were never employed as a firefighter. However, analyses restricted to subjects who were never employed in an occupation with established lung cancer risk, or restricted to subjects ever employed in such an occupation, did not change the results. Analysis of study specific ORs showed that none of the included studies showed a statistically significantly elevated OR2 for ever working as a firefighter (Figure 1).

Many of the previously performed studies on lung cancer risk among firefighters also have not found an excess risk of lung cancer.[9-20] Among them one study of firefighters in the US also examined different cell types of lung cancer and found no increased risk for adenocarcinoma, squamous cell, small cell, or large cell carcinoma.[9] Three of the studies observed a significantly decreased risk of lung cancer among firefighters.[13,17,18] However, some previous studies indicate an excess risk of lung cancer among firefighters overall or by specific cell type.[4-7] Among them, a hospital-based case-control study from Turkey,[4] a case-control study using California cancer registry data,[7] a study on mortality and cancer incidence in a cohort of US firefighters from San Francisco, Chicago and Philadelphia,[5] and a study of cancer incidence in a cohort of Nordic firefighters.[6] Only the studies from Turkey and California were controlled for smoking habits. The case-control study from Turkey showed an increased risk of lung cancer among firefighters overall (OR 6.8, 95% CI 1.3-37.4) after smoking adjustment, but not for squamous cell carcinoma, and faced low statistical power with only 10 exposed (firefighters) cases overall and 4 exposed cases with squamous cell carcinoma.[4] In the Californian study the power was better with 533 exposed cases overall, and firefighters were found to have an increased risk of non-small cell lung cancer (OR 2.01, 95% CI 1.38-2.93) after smoking adjustment, but not for other cell types or overall lung cancer.[7] In the study of firefighters in San Francisco, Chicago and Philadelphia there was an increased overall mortality of lung cancer (SMR 1.10, 95% CI 1.04-1.17), and overall incidence of lung cancer (SIR 1.12, 95% CI 1.04-1.21), based on 1,046 and 716 exposed cases respectively.[5] Pukkala et al. observed an excess incidence of lung adenocarcinoma among firefighters in the Nordic countries combined (SIR 1.90, 95% CI 1.34-2.32), but not for squamous cell carcinoma or small cell carcinoma, and no overall excess of lung cancer (SIR 0.97, 95% CI 0.87-1.09), although an excess was observed in the Danish data.[6] Hansen et al. observed an excess risk of lung cancer mortality among Danish firefighters in the group aged 60 to 74 (SMR 317, 95% CI 117-691), but no increased risk of lung cancer overall (based on 9 exposed cases),[21] and Heyer et al. found an elevated lung cancer mortality among firefighters 65 year or older (SMR 177, 95% CI 105-278) but no overall lung cancer mortality (based on 29 exposed cases).[22]

Since the meta-analysis of LeMasters et al. in 2006 several studies were published, including the two large cohort studies by Daniels et al. and Pukkala et al.,[5,6,12,13,18,20] and the report of the Australian firefighters' health study was available.[19] Our update of the former meta-analysis, including these newly published studies found no increased risk of the lung cancer incidence and mortality using random-effect models. This analysis supports the former results of LeMasters et al. and our analysis of no excess lung cancer risk in firefighters.

Most previous studies exploring exposure-response trends found no trend in increasing lung cancer risk among firefighters with employment duration,[5,9,11,16,19,20,43] as in our analysis, whereas modest positive exposure-response associations between fire-hours and lung cancer mortality and incidence was reported by Daniels et al.[8] This is an important result, stemming from a very large cohort study with the power to detect relatively small overall increases in lung cancer risk, and with the potential for conducting an exposure-response analysis. One study observed no consistent association between lung cancer mortality and duration of employment or exposure opportunity (weighted index term reflecting estimates of relative time spent in close proximity to fires) even if the highest risk was observed among firefighters with over 35 weighted years.[43] Only one study reported the prevalence of smoking among firefighters, with a slightly lower proportion of current smokers among male Massachusetts firefighters (25.7%) than in the control group of police men (28.4%) or men in all other occupations (28.8%), but with the highest proportion of past smokers (46.5% compared to 45.1% and 41.1% respectively).[15] In this study, current smoking was less common among the firefighters than among non-firefighters (26.0% compared to 29.2%, among the controls), with a slightly higher percentage of ever smokers with more than 20 pack-years among firefighters.

A difficulty in interpreting our results, and the overall pattern of findings from previous studies and meta-analyses, is that different exposure patterns have probably been experienced by firefighters in different countries, regions and periods of time. This point has been extensively addressed by Fritschi and Glass in a recent commentary.[44] For instance, focusing on one of the most important carcinogens, friable asbestoscontaining materials have been widely used in construction in certain urban areas, but less or not at all in others, and opportunities for exposure have varied, as shown by the extreme case of the Twin Tower rescue teams.

In summary, even though firefighters worldwide are potentially exposed to a wide variety of known or suspected carcinogens during work, of which some are known lung carcinogens, we did not observe an excess risk of lung cancer overall or by specific cell type among firefighters in this pooled analysis of case-control studies. There are certainly major differences in work practices for firefighters between countries and the exposure to carcinogens by inhalation and dermal absorption may vary considerably depending on job activities and use of protective equipment. In the present pooled study, no study showed a significantly increased lung cancer risk among firefighters.

However, since firefighters are potentially exposed to a wide variety of chemical compounds during the course of their work, including carcinogenic products such as benzene, arsenic, asbestos, benzo[*a*]pyrene, cadmium and silica, it is still important to reduce exposure as much as possible, by safe working practices and the use of adequate protective clothing and respiratory equipment.

Concluding remarks

In conclusion, we did not detect an increased risk of lung cancer overall or for a specific cell type among male firefighters in Europe, Canada, New Zealand and China, when lifetime history of tobacco smoking and exposure to other occupational lung carcinogens was taken into account.

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Table 1. Description of SYNERGY- studies 1985-2010 included in analysis, men and women

First Author, Year (Reference No.)	Study (Short Names)	Country	Data Collection	Cases		Controls		Source of Controls	Data Source	Interviewee
				No.	Response Rate (%)	No.	Response Rate (%)			
Bruske-Hohlfeld, 2000 (26)	AUT-MUNICH	Germany	1990–1995	3,180	77	3,249	41	P	I	S
Jöckel, 1998 (27)	HdA	Germany	1988–1993	1,004	69	1,004	68	P	I	S
Consonni, 2010 (28)	EAGLE	Italy	2002–2005	1,943	87	2,116	72	P	I	S
Richiardi, 2004 (29)	TURIN/VENETO	Italy	1990–1994	1,132	79	1,553	80	P	I	S
Stücker, 2002 (30)	LUCA	France	1989–1992	309	98	302	98	H	I	S
Guida, 2011 (31)	ICARE	France	2001–2007	2,926	87	3,555	81	P	I	S & NOK
Lopez-Cima, 2007 (32)	CAPUA	Spain	2000–2010	875	91	838	96	H	I	S
Scelo, 2004 (33)	INCO	Czech Republic	1999–2002	304	94	453	80	H	I	S
Scelo, 2004 (33)	INCO	Hungary	1998–2001	402	90	315	100	H	I	S
Scelo, 2004 (33)	INCO	Poland	1998–2002	800	88	841	88	P & H	I	S
Scelo, 2004 (33)	INCO	Slovakia	1998–2002	346	90	285	84	H	I	S
Scelo, 2004 (33)	INCO	Romania	1998–2002	181	90	228	99	H	I	S
Scelo, 2004 (33)	INCO	Russia	1998–2001	600	96	580	90	H	I	S
Scelo, 2004 (33)	INCO-LLP	United Kingdom	1998–2005	442	78	918	84	P	I	S
Gustavsson, 2000 (34)	LUCAS	Sweden	1985–1990	1,042	87	2,356	85	P	Q	S & NOK
Corbin, 2011 (35)	OCANZ	New Zealand	2003–2009	457	53	792	48	P	I & T	S & NOK
Ramanakumar, 2007 (36)	MONTREAL	Canada	1996–2002	1,203	85	1,509	69	P	I & T	S & NOK
Brenner, 2012 (37)	TORONTO	Canada	1997–2002	425	62	910	71	P & H	I & T	S
TSE, 2012 (38)	HONG KONG	China	2003–2007	1,208	96	1,069	48	P	I & T	S & NOK
Overall			1985–2010	18,779	84	22,873	78			

Abbreviations: N/A, not applicable; H, control subjects enrolled from hospitals; P, control subjects enrolled from the general population; I, interview face to face; T, interview over the phone; Q, self-administered questionnaire; S, study participant; NOK, next-of-kin e.g. husband or wife of the study participant; AUT-Munich, Arbeit und Technik; HdA, Humanisierung des Arbeitslebens; EAGLE, Environment and Genetics in Lung cancer Etiology; TURIN/VENETO, Population based case-control study of lung cancer in the the city of Turin and in the Eastern part of Veneto Region; LUCA, Lung cancer in France; ICARE, Investigations Cancers Respiratoires et Environnement; CAPUA, Cancer de Pulmon en Asturias; INCO, INCO Copernicus IARC multicenter case-control study of occupational, environment and lung cancer in Central and Eastern Europe; LLP, Liverpool Lung Project; LUCAS, Lung cancer in Stockholm; OCANZ, Occupational Cancer in New Zealand; MONTREAL, Montreal case-control study of environmental causes of lung cancer; TORONTO; Toronto lung cancer (case-control) study; HONG KONG, Male lung cancer, occupational exposures and smoking – A case-control study in Hong Kong;

Table 2. Descriptive Characteristics of the Male Study Participants by Employment Status as Firefighter

Characteristic		Firefighters (ISCO 5-81)				Non-Firefighters			
		Cases		Controls		Cases		Controls	
Category		No.	% or Mean(SD)	No.	% or Mean(SD)	No.	% or Mean(SD)	No.	% or Mean(SD)
Age	Mean (SD)	86	62.9 (8.4)	104	61.6 (10.7)	14,662	62.7 (9.0)	17,439	62.3 (9.5)
Study	AUT-Munich	19	22.1	13	12.5	2,639	18.0	2,682	15.4
	CAPUA	1	1.2	2	1.9	646	4.4	588	3.4
	EAGLE	3	3.5	3	2.9	1,516	10.3	1,599	9.2
	HdA	6	7.0	11	10.6	832	5.7	825	4.7
	HONG KONG	6	7.0	10	9.6	1,188	8.1	1,033	5.9
	ICARE	14	16.3	13	12.5	2,200	15.0	2,728	15.6
	INCO CEE	9	10.5	5	4.8	2,023	13.8	1,987	11.4
	INCO/LLP-UK	5	5.8	12	11.5	276	1.9	561	3.2
	LUCA	3	3.5	4	3.8	294	2.0	290	1.7
	LUCAS	4	4.6	12	11.5	997	6.8	2,265	13.0
	MONTREAL	9	10.5	4	3.8	702	4.8	890	5.1
	OCANZ	3	3.5	5	4.8	207	1.4	410	2.4
	TORONTO	2	2.3	4	3.8	193	1.3	355	2.0
	TURIN	2	2.3	6	5.8	949	6.5	1,226	7.0
Age categorized	<45 years	2	2.3	7	6.7	516	3.5	896	5.1
	45-64 years	45	52.3	49	47.1	7,314	49.9	8,383	48.1
	65+ years	39	45.4	48	46.2	6,832	46.6	8,160	46.8
Smoking status	Never smoker	2	2.3	27	26.0	457	3.1	4,571	26.2
(any type of tobacco)	Former smoker	25	29.1	50	48.1	4,927	33.6	7,777	44.6
	Current smoker	59	68.6	27	26.0	9,278	63.3	5,091	29.2
Cigarette pack years	<10	4	4.8	12	15.6	722	5.1	2,852	22.2
(current and former	10-19	15	17.9	14	18.2	1,287	9.1	2,407	18.7
smokers)	20+	65	77.4	48	62.3	12,009	84.5	7,058	54.8
	Other tobacco	0	0	3	3.9	187	1.3	551	4.3
Years-since-quitting	2-9 years	11	44.0	9	18.0	2,160	43.8	1,649	21.2
smoking cigarettes	10-20 years	10	40.0	19	38.0	1,699	34.5	2,504	32.2
(former smokers)	21+ years	4	16.0	22	44.0	1,068	21.7	3,624	46.6
Employed in 'List A' job	Ever	12	14.0	14	13.5	2,083	14.2	1,588	9.1
Lung cancer cell type				-				-	
Adenocarcinoma		24	27.9	-		3,832	26.1	-	
Squamous cell carcinoma		34	39.5	-		5,938	40.5	-	
Small cell carcinoma		15	17.4	-		2,263	15.4	-	
Other/unspecified		13	15.1	-		2,629	17.9	-	

Table 3. Lung Cancer Relative Risks (OR) and 95% CI in Relation to Ever and Duration of Employment as Firefighter

Variable	Exposure category	Cases	Controls	OR1	95% CI	OR2	95% CI	OR3	95% CI
Firefighter	Never	14,662	17,439	1.0	Reference	1.0	Reference	1.0	Reference
	Ever	86	104	1.03	0.77-1.38	0.95	0.68-1.32	0.95	0.68-1.32
Duration	<6	32	24	1.56	0.91-2.67	1.19	0.65-2.15	1.21	0.67-2.19
firefighter	6-21	22	26	1.13	0.64-2.00	0.99	0.52-1.86	0.97	0.51-1.84
(years)	22-32	14	26	0.69	0.36-1.33	0.70	0.32-1.50	0.69	0.32-1.49
	33+	18	28	0.84	0.46-1.53	0.91	0.47-1.77	0.92	0.48-1.78
	p-value trend			*0.46*		*0.58*		*0.58*	

OR1 is adjusted for study and age
OR2 is in addition adjusted for cumulative cigarette smoking (pack-years) and time since quitting smoking
OR3 is in addition adjusted for ever employment in a List A job (ever/never)

Table 4. Lung Cancer Relative Risks (OR) and 95% CI in Relation to Ever Employment as Firefighter by Smoking Status

Smoking status	Firefighter	Cases	Controls	OR	95% CI
Never smoker*	Never	457	4,571	1.0	Reference
	Ever	2	27	0.60	0.14-2.58
Former smoker**	Never	4,922	7,746	1.0	Reference
	Ever	25	50	0.75	0.45-1.26
Current smoker***	Never	9,278	5,091	1.0	reference
	Ever	59	27	1.18	0.73-1.90

* OR in never smokers is adjusted for study and age
**OR in former smokers is adjusted for study, age, cumulative cigarette smoking (pack-years) and time since quitting smoking
***OR in current smokers is adjusted for study, age, and cumulative cigarette smoking (pack-years)

Table 5. Lung Cancer Relative Risks (OR) and 95% CI in Relation to Ever Employment as Firefighter by Major Subtype of Lung Cancer

Fire-fighter		Adenocarcinoma			Squamous cell carcinoma			Small cell carcinoma			Other/unspecified		
	Controls	Cases	OR2	95% CI	Cases	OR2	95% CI	Cases	OR2	95% CI	Cases	OR2	95% CI
Never	17,439	3,832	1.00	Reference	5,938	1.00	Reference	2,263	1.00	Reference	2,629	1.00	Reference
Ever	104	24	1.03	0.64-1.67	34	1.03	0.66-1.60	15	1.03	0.57-1.87	13	0.84	0.46-1.55

OR2 is adjusted for study, age, cumulative cigarette smoking (pack-years) and time since quitting smoking cigarettes

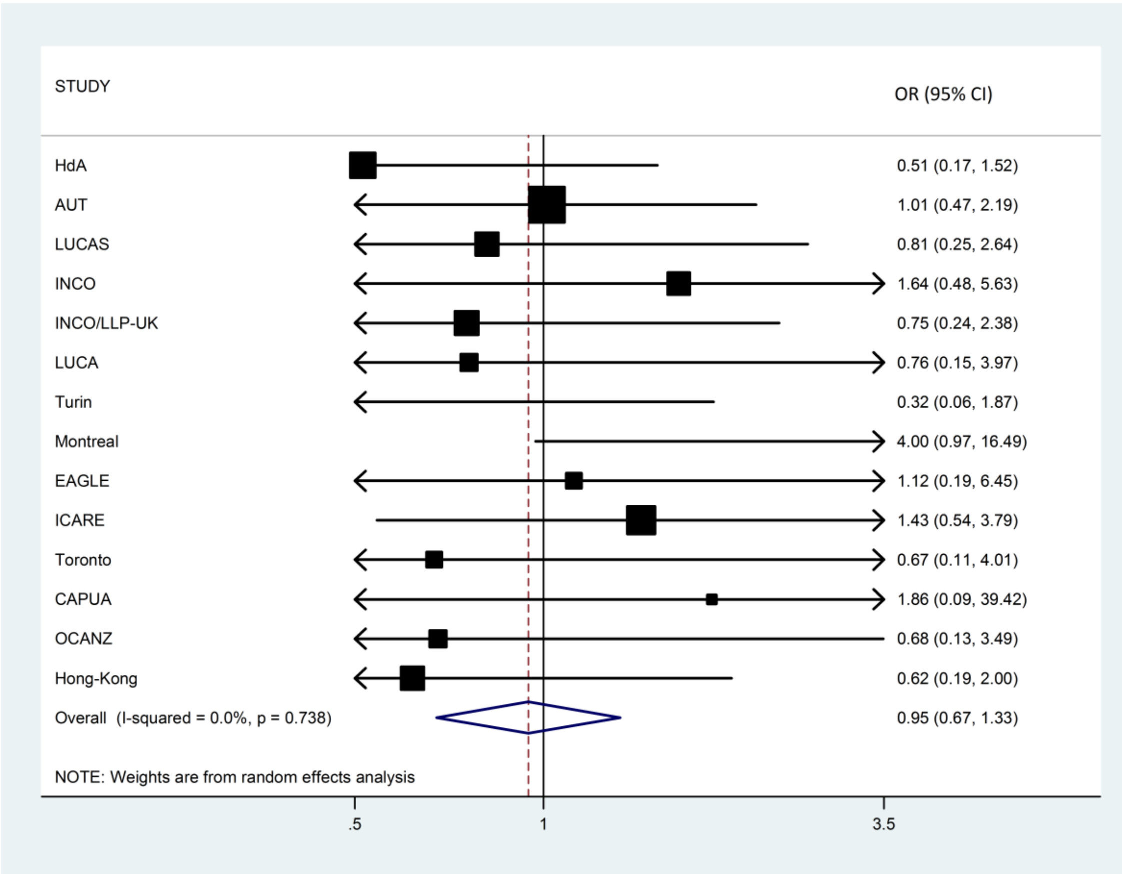

Figure 1. Study-specific odds ratios for ever employment as firefighter compared to never-employed as firefighter in men adjusted for age, smoking status (any type of tobacco) and cigarette pack-years. OR = odds ratio; CI = confidence interval.