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# Lung Cancer Among Firefighters: Smoking-Adjusted Risk Estimates in a Pooled Analysis of Case-Control Studies

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## Abstract

**Objectives:** The aim of this study was to explore lung cancer risk among firefighters, with adjustment for smoking.

**Methods:** We used pooled information from the SYNERGY project including 14 case-control studies conducted in Europe, Canada, New Zealand, and China, with lifetime work histories and smoking habits for 14,748 cases of lung cancer and 17,543 controls. We estimated odds ratios by unconditional logistic regression with adjustment for smoking and having ever been employed in a job known to present an excess risk of lung cancer.

**Results:** There was no increased lung cancer risk overall or by specific cell type among firefighters (n = 190), neither before nor after smoking adjustment. We observed no significant exposure-response relationship in terms of work duration.

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

Firefighters have a potential for exposure to different types of chemical compounds by inhalation of particulate matter, gases, and vapors during the course of their work. A large number of known (eg, arsenic, asbestos, benzene, benzopyrene, 1,3-butadiene, cadmium, formaldehyde and silica) or suspected (eg, 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.<sup>1</sup> Many of the carcinogens identified are volatile organic compounds (VOCs) common to most burning materials and are dominated by benzene, toluene, and naphthalene.<sup>1,2</sup> Firefighters may also be exposed to exhaust from diesel engines, which is known to increase the risk of lung cancer.<sup>3</sup> The exposure may vary widely among firefighters depending on the type of work activities, time spent at fires, and use of respiratory equipment. They are exposed mainly by inhalation, but for some chemicals, such as polycyclic aromatic hydrocarbons and polychlorinated biphenyls, exposure through dermal absorption may also be important.<sup>1</sup> “Occupational exposure as a firefighter” has been evaluated by the International Agency for Research on Cancer (IARC) and classified as “possibly carcinogenic to humans,” with strongest evidence for testicular cancer, prostate cancer, and non-Hodgkin lymphoma.<sup>1</sup>

Some previous studies among firefighters indicate an excess of lung cancer overall,<sup>4–6</sup> lung cancer of a specific cell type,<sup>7,8</sup> or positive exposure-response associations,<sup>9</sup> whereas most studies do not.<sup>10–20</sup> Pukkala et al<sup>7</sup> observed an increased incidence of lung adenocarcinoma among firefighters in the Nordic countries, Tsai et al<sup>8</sup> observed an excess risk of nonspecific, nonsmall cell lung cancer among California firefighters, Hansen<sup>21</sup> observed an increase in lung cancer mortality in the oldest age group of Danish firefighters, and in a study by Heyer et al,<sup>22</sup> the lung cancer mortality among Seattle firefighters was elevated in the oldest age group. Further, a large

comprehensive review and meta-analysis by LeMasters et al<sup>23</sup> evaluated cancer risk among firefighters. The lung cancer risk was classified as unlikely with a summary risk estimate of 1.03 [95% confidence interval (95% CI) 0.97 to 1.08].<sup>23</sup> Overall, findings from previous studies of cancer in firefighters have been inconsistent. In particular, few studies have provided evidence of increased lung cancer risk among firefighters, although inhalation is a primary route of exposure. Negative confounding by smoking is one among the possible explanations of the absence of excess of lung cancer risk in previous studies, which nearly all lack information on tobacco use. Only two of the above-mentioned lung cancer studies had adequate information on individual smoking habits.<sup>4,15</sup> Previous studies have shown diverging results regarding lung cancer of various cell types among firefighters,<sup>4,7,8,10</sup> and the impact of smoking on lung cancer risk may vary between different histological subtypes of lung cancer.<sup>24</sup>

The aim of this study was to explore lung cancer risk among firefighters taking into account individual lifetime history of smoking and having ever been employed in a job with established lung cancer risk. We also aimed to analyze the results by cell types.

## METHODS

We used pooled information from the SYNERGY project including case-control studies conducted in Europe, Canada, New Zealand, and China, with data on lifetime work histories and individual smoking habits. The SYNERGY project has already been described in detail elsewhere.<sup>25,26</sup> In a previous paper in this journal, we reported lung cancer risk among cooks using the same database and methods,<sup>26</sup> with only minor differences, mainly regarding included studies. Therefore, only part of the study setting and methods is repeated in the present article. Table 1 provides information about the studies included in the present analysis.<sup>27–39</sup> The SYNERGY studies included both men and women, but only two women had ever worked as a firefighter (zero cases and two controls); therefore, the analysis was restricted to men. Three of the original studies (Rome, Paris, and MORGEN) had no firefighters among either cases or controls, and were therefore omitted. The present analysis included 14,748 male lung cancer cases and 17,543 male controls, after excluding 132 cases and 149 controls with incomplete information on smoking or work history and 230 cases and 239 controls who never worked for at least 1 year.

### Identification of Firefighters

We identified 190 male firefighters (86 lung cancer cases, 104 controls) from the ISCO-68 code (“5–81”).<sup>40</sup> The group “Firefighters” includes “General firefighters” (66 cases, 89 controls), “Fire prevention firefighters” (nine cases, four controls), “Aircraft accident firefighters” (zero cases, three controls), and “Other firefighters” (15 cases, 12 controls). Some of them had worked as two types of firefighters (four cases, four controls). Therefore, the sum of the number of firefighters in the different categories differs from that of all firefighters.

### Statistical Methods

Detailed information on the statistical analyses has been presented elsewhere.<sup>26</sup> In summary, we estimated odds ratios (ORs) by unconditional logistic regression with adjustment for study and age (OR1), additional adjustment for cumulative cigarette smoking and time since quitting smoking (OR2), and having ever been employed in a job known to present an excess risk of lung cancer (“List A” job) (OR3), such as occupations in the mining and quarrying industry, asbestos production, metals industry, construction industry (insulators and pipe coverers, roofers, asphalt

workers, and painters), and shipbuilding.<sup>41,42</sup>

The analyses were repeated in relation to smoking status (never, former, current), work duration (<6, 6 to 21, 22 to 32, >32 years), major cell types of lung cancer (adenocarcinoma, squamous cell carcinoma, small cell carcinoma, others/unspecified), and for employment as a “General firefighter” (ie, excluding “Fire prevention firefighters,” “Aircraft accident firefighters,” and “Other firefighters”). As the reference category, we always used all those who had never worked as firefighters.

We used meta-analysis to explore study-specific ORs for firefighters and the extent of heterogeneity across the studies. The “metan” command in Stata was used specifying a fixed effect model using the method of Mantel and Haenszel. We used the I-squared measure (describes the percentage of total variation between studies due to heterogeneity) to quantify heterogeneity. The  $I^2$  was estimated to be zero, which implies that there was no more variation between study estimates than would be expected by chance.<sup>43</sup> We used Stata v. 11.0 for Windows (StataCorp LP, College Station, Texas) for all analyses.

## RESULTS

Table 2 summarizes descriptive characteristics of the study participants. Among the controls, smoking was similarly common in firefighters as in nonfirefighters; 74.1% of the firefighters were current or former smokers, and 73.8% of nonfirefighters. However, the percentage of those with more than 20 pack-years among current and former smokers was slightly higher among firefighters; 62.3% among firefighters, compared with 54.8% in nonfirefighters. It was more common in firefighters than in nonfirefighters to have held a job where the lung cancer risk is known to be increased; among the controls, 13.5% of the firefighters, and 9.1% of nonfirefighters. In both firefighters and nonfirefighters, squamous cell carcinoma was the most common lung cancer type, followed by adenocarcinoma and small cell carcinoma.

Overall, we observed no increased risk of lung cancer in firefighters. Before adjustment for smoking, the OR was 1.03 (95% CI 0.77 to 1.38) and after adjusting for smoking 0.95 (95% CI 0.68 to 1.32). Additional adjustment for having ever been employed in a job with established lung cancer risk did not change the OR (Table 3). We found no trend of increasing risk of lung cancer with increasing work duration as a firefighter ( $P = 0.46$  to  $0.58$ ) (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 to 2.58), former smokers (OR = 0.75, 95% CI 0.45 to 1.26), or current smokers (OR = 1.18, 95% CI 0.73 to 1.90), though the number of nonsmoking firefighters was small. There were only two lung cancer cases in firefighters who had never smoked (Table 4). Analyses restricted to those who had never had a job where the risk of lung cancer is known to be increased showed no excess risk of lung cancer in firefighters (OR<sub>2</sub> = 0.98, 95% CI 0.69 to 1.39) and neither did analyses restricted to ever employed in such an occupation (OR<sub>2</sub> = 0.79, 95% CI 0.31 to 1.99) (not shown in table). Analyzing the results by major subtypes of lung cancer showed no association between any of the cell types and work as a firefighter (Table 5). The study-specific ORs for firefighters are shown in Fig. 1. No study showed an increased OR of statistical significance. The risk of lung cancer in firefighters across the studies showed no significant heterogeneity ( $I^2$  0.0%,  $P = 0.738$ ). Additional analyses including only “General firefighters” showed no increased lung cancer risk (OR<sub>3</sub> = 0.88, 95% CI 0.61 to 1.26) (not shown in table).

## DISCUSSION

We observed no excess risk of lung cancer in firefighters overall, neither before nor after adjustment for smoking and having ever been employed in a job known to present an excess risk of lung cancer, and there was no significant exposure-response relationship in terms of work duration. Analyses stratified by cell type showed no association between work as a firefighter and any of the major histological cell types of lung cancer. Analyses restricted to never smokers, former smokers, or current smokers showed no increased lung cancer risk in firefighters.

The study covers lifetime occupational information and detailed history of tobacco smoking for almost 15,000 cases and more than 17,000 controls. We have stratified by histology, and examined heterogeneity between studies. However, there were only 86 cases who had ever worked as a firefighter. The statistical power to detect excess risks in the subanalyses was therefore limited, which is evident from the wide CIs.

With regard to possible information bias, there is always some risk of recall bias in case-control studies. However, as only occupations were registered in this study and not more specific information of occupational exposure, the risk of recall bias would probably be low. In all, it is not likely that the absence of association between firefighting and lung cancer found in this study could be attributed to negative recall bias.

It is a limitation that hospital controls were used in some of the studies in SYNERGY, as hospital controls may not adequately reflect the true exposure frequency (ie, occupation as a firefighter) in the population, due to a selection of healthy individuals in firefighting occupation. However, it is not likely that the low risk for lung cancer associated with firefighting found in this study could be explained by an inadequate control group (hospital controls), as the main part of the centers using hospital controls (the INCO study) actually showed an OR above 1.0.

The study showed no evidence of an increased risk of lung cancer, neither in the unadjusted nor adjusted analyses. As the risk estimate changed very little after adjustment for individual lifetime smoking history, it seems unlikely that there could be more than marginal residual confounding from smoking present in the adjusted risk estimates. Important confounding from socioeconomic factors (other than smoking) cannot be entirely ruled out. Firefighters represent an intermediate socioeconomic stratum in the general population, and it does not seem likely that the negative findings in this study could be explained by confounding from socioeconomic status.

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. A limitation is also that we only have duration of employment as a surrogate for exposure. 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. It was more common in firefighters than in nonfirefighters to have held a job where the lung cancer risk is known to be increased. However, analyses restricted to subjects who were never employed in a job with increased lung cancer risk, or restricted to subjects ever employed in such an occupation, did not change the results. When we analyzed the study-specific ORs for firefighters, no study showed an increased OR2 of statistical significance (Fig. 1). However, the power to detect increased study-specific ORs was very limited due to small numbers of firefighters; therefore, these results should be interpreted with caution.

Most previous studies among firefighters also found no excess risk of lung cancer.<sup>10–20</sup> 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 carcinoma, small cell carcinoma, or large cell carcinoma.<sup>10</sup> Three of the studies observed a significantly decreased lung cancer risk in firefighters.<sup>13,17,18</sup> Findings of a risk deficit are common in working populations and may reflect a selection in relation to work. A healthy worker effect is expected in the case of firefighters, as they need to be healthy to be recruited and to be capable of remaining in the profession.<sup>18</sup>

However, some studies have indicated an increased lung cancer risk in firefighters overall or by specific cell type,<sup>4–8</sup> among them, a case-control study from Turkey,<sup>4</sup> a case-control study in California,<sup>8</sup> a cohort study in San Francisco, Chicago and Philadelphia,<sup>5</sup> a Nordic cohort study,<sup>7</sup> and a cohort study in Philadelphia.<sup>6</sup> Only the studies from Turkey and California were controlled for smoking habits. The study from Turkey showed an excess risk of lung cancer in firefighters overall after smoking adjustment, but not for squamous cell carcinoma, and faced low statistical power (10 exposed cases overall and four exposed cases with squamous cell carcinoma).<sup>4</sup> In the Californian study, firefighters showed an excess risk of nonsmall cell lung cancer after smoking adjustment, but not for other cell types or overall lung cancer (533 exposed cases overall).<sup>8</sup> In the study of firefighters in San Francisco, Chicago, and Philadelphia, the overall mortality and incidence of lung cancer was increased, based on 1046 and 716 exposed cases, respectively.<sup>5</sup> Pukkala et al <sup>7</sup> observed an increased incidence of adenocarcinoma in the lung among Nordic firefighters, but not for squamous cell or small cell carcinoma, and no increased lung cancer risk overall, although an excess was observed in the Danish data. In Philadelphia firefighters, there was an elevated lung cancer mortality overall, although not statistically significant.<sup>6</sup> Hansen <sup>21</sup> observed an increased lung cancer mortality in Danish firefighters in the oldest age group, but no increased lung cancer risk overall (based on nine exposed cases), and Heyer et al <sup>22</sup> showed an increased lung cancer mortality in the highest age group of Seattle firefighters but no increased overall lung cancer mortality (based on 29 exposed cases).

Most previous studies exploring exposure-response trends found no significant relationship between work duration and lung cancer risk in firefighters,<sup>5,6,10,16,19,20,44</sup> as in our analysis, whereas a modest positive exposure-response relationship was shown by Daniels et al <sup>9</sup> regarding fire-hours and mortality and incidence of lung cancer. 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 an index reflecting exposure, even if the risk was highest in firefighters with the highest exposure.<sup>44</sup> Only the study of male Massachusetts firefighters described the percentage of smokers, with a slightly lower proportion of current smokers in 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 with 45.1% and 41.1%, respectively).<sup>15</sup> In SYNERGY, current smoking was less common among the firefighters than among nonfirefighters (26.0% compared with 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.<sup>45</sup> For instance, focusing on one of the most important carcinogens, friable asbestos-containing 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 have a potential for exposure to many different kinds of carcinogens during work, of which some are known lung carcinogens, we observed no excess risk of lung cancer overall or by specific cell type among firefighters. The exposure to carcinogens by inhalation and dermal absorption may certainly vary widely for firefighters between countries depending on work activities and use of protective equipment. In the present pooled study, no study showed an increased lung cancer risk of statistical significance among firefighters.

However, as firefighters may be 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.

## CONCLUSION

We found no excess 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 smoking and exposure to other occupational lung carcinogens was taken into account.

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