

# Lung cancer and occupation: results of a multicentre case-control study

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## Abstract

The objective of the current study was to estimate the risk of lung cancer attributable to occupational factors and not due to tobacco. At 24 hospitals in nine metropolitan areas in the United States, 1793 male lung cancer cases were matched for race, age, hospital, year of interview, and cigarette smoking (never smoker, ex-smoker, smoker (1-19 and  $\geq 20$  cigarettes per day)) to two types of controls (cancer and non-cancer hospital patients). Information on usual occupation, exposure to specific potential carcinogens, and cigarette smoking was obtained by interview. Risk of lung cancer was increased significantly for electricians; sheetmetal workers and tinsmiths; bookbinders and related printing trade workers; cranemen, derrickmen, and hoistmen; moulders, heat treaters, annealers and other heated metal workers; and construction labourers. All of these occupations are potentially exposed to known carcinogens. Odds ratios (ORs) were increased for exposure to coal dust (adjusted OR = 1.5; 95% confidence interval (95% CI) 1.1-2.1). After stratification, this association was statistically significant only after 10 or more years of exposure. Lung cancer was also related to exposure to asbestos (adjusted OR = 1.8; 95% CI 1.5-2.2). The ORs increased with increasing duration of exposure to asbestos for all smoking categories except for current smokers of 1-19 cigarettes per day. The statistical power to detect ORs among occupations that were previously reported to be at increased risk of lung cancer but that failed to show an OR of at least 1.5 in the current study was small. The cumulative

population attributable risk (PAR) of lung cancer due to occupation was 9.2%. It is concluded that occupational factors play an important part in the development of lung cancer independently of cigarette smoking. Because occupations at high risk of lung cancer were under-represented, the cumulative PAR of the present study is likely to be an underestimate of the true contribution of occupation to risk of lung cancer.

That specific chemical and physical agents including asbestos, arsenic, radon daughters, nickel, coke oven emissions, and chromates, and the occupations that involve exposure to these agents increase the risk of lung cancer is well documented.<sup>1-3</sup> Risk of lung cancer is also increased in other occupational groups such as butchers that do not involve exposure to known lung carcinogens.<sup>4-6</sup> Nevertheless, despite an abundance of publications, the nature and magnitude of the relation between lung cancer and occupation have not been fully delineated.

In 1982, Dubrow and Wegman published a comprehensive review and discussion of existing epidemiological studies relating occupation to various cancers.<sup>7</sup> They identified 34 occupations with consistent evidence of an excess risk of lung cancer, mostly in the manufacturing sector and construction trades, and, to a lesser extent, in the transportation and service sectors. The publications encompassed by their review, however, often contained inadequate information on cigarette smoking and, hence, could not account for cigarette smoking as a confounding factor.

In the past 10 years, at least 13 case-control studies have examined possible occupational risk factors for lung cancer<sup>8-20</sup> and have confirmed, to varying degrees, many of the associations highlighted by Dubrow and Wegman.<sup>7</sup> Unlike previous studies, the effects of occupational exposures were adjusted for cigarette smoking, but the power to detect associations between occupations and lung cancer was principally limited by sample size and by the distribution of occupations in the geographical area under study. These two related factors serve to explain, in part, discrepancies among studies.

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In the present study we examine the occupational contribution to lung cancer in a longstanding, multicentre case-control study. Advantages of the current study include a large sample of cases and controls, inclusion of multiple geographical locations, personal interview of cases and controls, histological confirmation of all cases, and detailed smoking histories.

## Materials and methods

### THE AMERICAN HEALTH FOUNDATION DATABASE

Since 1969, the American Health Foundation has conducted a longstanding hospital based case-control study.<sup>21</sup> Between 1980 and 1989, 1793 male patients with the diagnosis of lung cancer (International Classification of Diseases, 9th edition, rubric 162.0-162.9) were identified in 24 hospitals in the following cities or areas: Detroit, Chicago, Philadelphia, Pittsburgh, New York, Long Island, San Francisco, Birmingham, and Atlanta. The objective was to interview all cases with tobacco related conditions (cancers of the lung, upper respiratory, and digestive tracts, pancreas, kidney and bladder, and myocardial infarctions) that are admitted to participating hospitals. All cases were confirmed histologically by review of the pathology report. For each case, one or two patients of the same age, race, hospital, and date of admission, but admitted for a condition not related to tobacco consumption, were interviewed as controls.

### PRESENT STUDY DESIGN

To study the relation between occupational exposures and cancer we used the American Health Foundation database to design a specific case-control study. All 1793 patients with lung cancer were included as cases. For each case, we selected at least one and usually two controls from the pool of all patients without lung cancer, including tobacco related diagnoses, who were interviewed between 1980 and 1989. Each control was matched to the case on the following variables: race (black, white), age (within five years), hospital, and cigarette smoking history (never smoker, ex-smoker, current smoker of 1-19 cigarettes per day, and current smoker of 20 or more cigarettes per day). All controls were interviewed within two years of the case interview.

Diagnoses among the 3228 controls included cancers (2230, (69.0%)) of the following primary sites: bladder (11.2%), gastrointestinal (10.2%), oral cavity and pharynx (9.0%), prostate (4.5%), larynx (4.1%), lymphoma (3.1%), sarcoma (2.4%), leukaemia and myeloma (2.2%), and other (22.3%). Non-cancer controls (998 (31.0%)) had musculoskeletal (6.8%), thromboembolic (4.5%), cardiovascular (3.4%), benign neoplastic (2.2%), and other diseases (14.1%).

Information on sociodemographic and anthropometric characteristics, and cigarette smoking was collected from the study participants through a structured, standardised questionnaire administered by trained interviewers. The occupational history included job title ("What has been your usual occupation?") and specific exposure to a list of 44 different agents ("Have you been exposed to any of the following substances, either on the job or while working on a hobby, during eight hours a week or more for at least one year?"). Subjects interviewed between 1980 and 1984 (n = 2686) could report the duration of occupational exposure for up to two different agents only. The interviewer recorded the two agents that the subject perceived to be the most important. In 1985 the occupational history was expanded so that participants (n = 2335) could report the duration of exposure to a maximum of six different agents. Since 1985 the questionnaire also recorded whether the exposure to the agent had occurred at a job or while engaging in a hobby. Job titles were coded according to an abbreviated list of the United States Bureau of Census codes.<sup>22</sup>

### STATISTICAL ANALYSIS

Self reported occupational exposures were coded as ever or never exposed. When an exposure was reported as related to a hobby, its duration was divided by two to give it one half the weight of a job exposure, assuming that a job exposure may be at least twice the frequency or intensity of a hobby exposure. The analysis by duration of exposure (< 10 years, ≥ 10 years) was limited to occupational exposures that were found related to lung cancer in the ever *v* never exposed analysis.

Unconditional logistic regression<sup>23</sup> was used to compute odds ratios (ORs) adjusted for all matching factors—that is, age, cigarette smoking (never, ex-smoking, current one to 19 cigarettes per day, current 20 or more cigarettes per day), geographical area (New York; Atlanta and Birmingham combined; Detroit; Chicago; San Francisco; Philadelphia and Pittsburgh combined), race, and questionnaire version (two categories corresponding to the years of interview 1980-4 and 1985-9). As shown by Breslow *et al*,<sup>24</sup> an unmatched analysis of a matched case-control study is more efficient than the matched analysis and produces similar ORs, given that the ORs are adjusted for the matching factors.

Trends in the ORs and potential interactions between job exposure and smoking were assessed using logistic regression. When assessing the ORs of lung cancer related to exposure to asbestos, subjects having gastrointestinal, oropharyngeal, and laryngeal cancers were removed from the cancer controls, as there is evidence that these cancers are causally related to asbestos.<sup>25-27</sup> Departure from the assumption of the logistic regression model was checked by

Table 1 Distribution of occupations among controls v United States general population

Occupation (Census code)	Study controls		1980 US population	
	No	(%)	No	(%)
I Managers (201-245)	499	(15.5)	7 063 304	(12.6)
II Professionals and technicians (001-195)	647	(20.0)	7 812 583	(13.9)
III Sales workers (260-280)	293	(9.1)	5 088 664	(9.1)
IV Administrative support and clerical workers (301-395)	167	(5.2)	3 854 322	(6.9)
V Service workers (901-984)	119	(3.7)	5 177 580	(9.3)
VI Farming, forestry, and fishing workers (801-824)	19	(0.6)	2 406 989	(4.3)
VII Skilled crafts and repair workers (401-580)	897	(27.8)	11 616 225	(20.7)
VIII Operatives, assemblers, inspectors (601-695)	264	(8.2)	5 438 751	(9.7)
IX Transportation workers (701-715)	194	(6.0)	4 041 532	(7.2)
X Labourers (740-785)	125	(3.9)	3 504 760	(6.3)
No code	4	(0.1)	—	—
Total	3228	(100)	56 004 710	(100)

examination of the stratum specific differences between observed and expected numbers of cases.<sup>23</sup>

In the results section we report adjusted ORs for job titles only if (1) the OR is greater than or equal to 1.5, and (2) if at least five subjects (cases and controls) have the job title.

Adjusted population attributable risk per cent (PAR) was computed for specific occupations using Levin's formula and the adjusted ORs.<sup>23</sup> The prevalence of exposure in the population was obtained from census information on distribution of

job categories in the United States in 1980.<sup>22</sup> Power calculations were done using the formula for an unmatched case-control study with unequal number of cases and controls given by Schlesselman.<sup>28</sup>

## Results

Because one of the objectives of the study was to estimate the PAR of lung cancer due to occupation, we compared the distribution of occupations in the study population with that of the United States

Table 2 Odds ratios and population attributable risks of lung cancer by occupation among male United States hospital patients, 1980-9

Job title*	Cases No ‡	Controls No ‡	Adjusted OR†	(95% CI)	PAR
Electricians	27	28	1.7	(1.1- 2.9)	0.0071
Sheet metal workers, tinsmiths	14	7	3.7	(1.5- 9.2)	0.0069
Bookbinders, related printing trade workers	11	6	3.3	(1.2- 8.9)	0.0013
Cranemen, derrickmen, hoistmen	9	1	14.4	(1.8-114.2)	0.0336
Moulders, heat treaters, annealers, other heated metal workers	15	8	3.0	(1.3- 7.1)	0.0029
Construction labourers	30	26	1.9	(1.1- 3.3)	0.0101
Checkers, inspectors, examiners	17	16	1.9	(0.9- 3.7)	0.0052
Welders and flame cutters	18	22	1.5	(0.8- 2.7)	0.0059
Cement finishers, tile setters, masons, plasterers	15	17	1.6	(0.8- 3.3)	0.0029
Merchant seamen, sailors and deckhands	7	6	2.1	(0.7- 6.2)	0.0010
Gold and silversmiths, watchmakers, jewellers and other metal crafts	7	6	2.2	(0.7- 6.2)	0.0005
Roofers and slaters	7	6	2.1	(0.7- 6.2)	0.0019
Transportation equipment manufacturing operatives	10	10	2.1	(0.7- 6.2)	0.0017
Transportation, communication, utility operatives	7	5	2.4	(0.7- 7.5)	0.0012
Stationary firemen, furnacemen, smelters, and pourers	4	4	1.6	(0.7- 6.3)	0.0013
Metal industries labourers	15	18	1.5	(0.6- 2.5)	0.0008
Communications, utilities, sanitation service labourers	5	5	1.7	(0.5- 5.9)	0.0016
Mine operatives	4	3	2.3	(0.5- 10.5)	0.0029
Apparel, other fabricated textile products	5	5	1.6	(0.5- 5.4)	0.0001
Bus and taxi dispatchers	5	3	2.6	(0.6- 10.9)	§
Taxi drivers, chauffeurs and parking attendants	7	8	1.5	(0.5- 4.1)	0.0016
Fishermen	3	2	2.9	(0.5- 18.1)	0.0015
Unemployed	3	2	2.5	(0.4- 15.2)	§
Other job titles	1548	3014	—	—	0.0920

PAR = Population attributable risk.

\*Job titles having at least five subjects and a crude OR  $\geq$  1.5.

†OR adjusted simultaneously for age, race, geographical area, questionnaire version, and smoking (never, current 1-19 cigarettes per day, current  $\geq$  20 cigarettes per day, ex-smokers).

‡Total cases = 1793. Total controls = 3228.

§Not classified as such by the US Bureau of Census.

Table 3 Odds ratio of lung cancer according to duration of exposure to coal dust by types of controls among male United States hospital patients, 1980-9

Coal dust exposure (y)	Cases (n = 1793)	Controls		Adjusted OR*			
		Cancer (n = 2230)	Non-cancer (n = 998)	CC†	NC†	All	(95% CI)
Never	1721	2174	972	1.0§	1.0§	1.0§	(reference)
<10‡	37	35	14	1.2	1.6	1.3	(0.8-2.0)
≥10	35	21	12	1.5	2.0	1.7	(1.1-2.7)

\*Simultaneously adjusted for smoking, age, exposure to asbestos (ever/never), geographical area, and version of questionnaire.

†CC = cancer controls, NC = non-cancer controls.

‡Median duration of exposure to coal dust among ever exposed.

§Reference group.

census in 1980. Table 1 shows that the control group of the present study contained more managers, professionals and technicians, and skilled crafts and repair workers, and fewer service workers, labourers, and farming, forestry, and fishing workers compared with the general population of the United States in 1980. Whereas the overall proportions of white collar (groups I to V) and blue collar (groups VI to X) workers are nearly identical in the study control group and the general United States population, study participants tended to be concentrated in the more highly paid occupations (managers, professionals and technicians, skilled crafts and repair workers) within both the white and blue collar categories. Also, only 7% of the study control group had job titles in the construction trades (selected titles from the categories of skilled crafts and repair workers and labourers) compared with 14% of the United States population with the same occupations.

Table 2 presents the adjusted ORs of lung cancer for all occupations with ORs  $\geq 1.5$  and a minimum of five or more cases and controls out of a total of 102 occupations comprising at least five or more cases and controls. Adjusted ORs with a 95% confidence interval (95% CI) not including unity were found for six occupational categories: electricians; sheet metal workers and tinsmiths; bookbinders and related printing trade workers; cranemen, derrickmen, and

hoistmen; moulders, heat treaters, annealers and other heated metal workers; and construction labourers. Table 2 also lists three other occupations showing associations of borderline statistical significance (lower limit of 95% CI  $\geq 0.8$ ).

Of the 44 specific exposures to occupational agents reported in the questionnaire, a statistically significant increase in OR was found for only two: coal dust (adjusted OR = 1.5; 95% CI 1.1-2.1) and asbestos (adjusted OR = 1.8; 95% CI 1.5-2.2) (not shown in table). Self reported occupational exposure to coal was sufficiently common to evaluate by duration of exposure (table 3). The association between coal dust and lung cancer increased with increasing duration of exposure but was only significant among men who reported 10 or more years of exposure (adjusted OR = 1.7; 95% CI 1.1-2.7). The association was present whether using cancer controls or non-cancer controls (table 3).

The relation between exposure to asbestos and lung cancer was evaluated after stratification by smoking (table 4). Subjects who smoked only pipes and cigars were excluded. Patients with oral, pharyngeal, laryngeal, and gastrointestinal cancers were excluded from the control group due to the known relation between these cancers and exposure to asbestos. The ORs increased with increasing duration of exposure to asbestos for all strata except

Table 4 Odds ratios\* of lung cancer according to asbestos exposure and smoking state among male United States hospital patients, 1980-9

Asbestos exposure (y)	Cases (No)	Cigarette smoking†				All subjects	
		Never (OR)*	Ex-smoker (OR)*	1-19 (OR)*	≥20 (OR)*	(OR)‡	(95% CI)
Never	1573	1.0†	1.2	1.1	1.2	1.0§	(Reference)
<10	78	3.8	2.9	0.7	2.2	2.0	(1.4-2.8)
≥10	112	4.9	2.2	1.2	2.8	2.1	(1.6-2.9)

\*Odds ratios are simultaneously adjusted for age, race, geographical area, and version of questionnaire. Controls (n = 2226) do not include patients with cancer of the oropharynx, larynx, or of the gastrointestinal tract.

†Subjects smoking only pipe and/or cigar were excluded.

‡Also adjusted for smoking.

§Reference group.

Table 5 Statistical power to detect ORs of 1.5 for lung cancer in current study among occupations previously reported to be at high risk of lung cancer

Occupation	No of controls in given occupation	Proportion of controls in given occupation	Adjusted OR*	Statistical power†
Painters	29	0.0090	0.8	0.33
Bus drivers	18	0.0056	1.1	0.22
Lorry and tractor drivers	132	0.0409	1.0	0.88
Mechanics and repairmen—automobile	39	0.0121	0.7	0.41
Plumbers and pipe fitters	34	0.0105	1.2	0.37
Carpenters and cabinet makers	52	0.0161	1.4	0.52
Custodial, maintenance, and cleaning workers	40	0.0124	†	†
Cooks and chefs	18	0.0056	†	†
Mechanics and repairmen (not elsewhere classified)	66	0.0205	0.7	0.61
Machinists	57	0.0177	1.0	0.56

\*Reference group is all other occupations; adjusted for age and smoking.

† $\alpha = 0.05$ , two sided; ratio between controls and cases = 2; number of controls = 3228.

‡Not assessed because no cases in the study.

current smokers of 1–19 cigarettes per day. The highest ORs were found among never smokers.

For no single occupation or group of occupations, as categorised in table 1, did the increase in OR of lung cancer among non-smokers reach statistical significance. Of the 62 cases of lung cancer among non-smokers, four were lawyers and judges, three business executives, and two were in each of nine other occupations.

We examined the ability of the current study to detect risk of lung cancer from occupations in which we found an adjusted OR of lung cancer less than 1.5. Table 5 presents the statistical power of the current study to detect an OR of 1.5 setting  $\alpha$  at 0.05 for occupations that have been shown repeatedly in earlier studies to be at increased risk of lung cancer. With the exception of a single occupational category, truck and tractor drivers, the (remaining nine) occupations are associated with statistical power considerably less than 0.80. Power was between 0.50 and 0.80 for carpenters and cabinet makers, mechanics and repairmen, and machinists.

The total population attributable risk (PAR) of lung cancer for all occupations with ORs greater than or equal to 1.5 based on the distribution of occupations in the general United States population is 9.2%.<sup>22</sup> The PARs for specific occupations are presented in the last column of table 2.

## Discussion

We found six occupations with a statistically significant increase in risk of lung cancer independent of cigarette smoking. Four of them (sheet metal workers; cranemen, derrickmen, and hoistmen; heated metal workers; and construction labourers) have been shown in previous cohort studies to have an excess risk of lung cancer, but none of the previous reports controlled for cigarette smoking.<sup>7</sup> In more recent case-control studies, Schoenberg *et al*<sup>16</sup> and

Benhammou *et al*<sup>18</sup> found an increase in ORs of lung cancer for sheet metal workers, though of less magnitude (about 1.5) and without statistical significance. Milne *et al*<sup>11</sup> found a statistically significant OR of 1.9 for lung cancer among construction labourers. These and other recent case control studies had little power, however, to detect a possible association of lung cancer with employment as heated metal workers, cranemen, derrickmen, and hoistmen, due to small representation of these occupations in the study samples. All of these occupations are potentially exposed to confirmed or suspected lung carcinogens, including asbestos, nickel, chromium, polycyclic aromatic hydrocarbons, and diesel exhaust.

The statistically significant OR of lung cancer among electricians found in the present study agrees with three recent case-control studies.<sup>11 17 20</sup> This higher risk for lung cancer may well be explained by the exposure to asbestos experienced by electricians.<sup>29</sup> The increase in lung cancer among bookbinders and related printing trade workers represents a new finding and may be due to exposure to solvents in adhesives and cleaning products as well as other printing chemicals.

Most of the remaining occupations showing a non-statistically significant adjusted OR of 1.5 or greater have been previously found to carry an excess risk of lung cancer. These include cement finishers, masons, and tile setters,<sup>30–32</sup> roofers,<sup>33 34</sup> stationery firemen and furnace men,<sup>6 16 30 35</sup> taxi drivers,<sup>5 16 18 34</sup> fishermen,<sup>5 6</sup> and workers in sheet metal and other metal industries.<sup>36</sup> Some of these occupations are well known to be associated with recognised or suspected lung carcinogens, including asbestos, polycyclic aromatic hydrocarbons, and motor vehicle exhaust.<sup>1 37</sup>

The positive association between exposure to coal and lung cancer in our study is noteworthy, although difficult to interpret. The association increased with a longer duration of exposure and was found to be

similar using cancer and non-cancer controls. Cohort studies of coal miners do not show an excess risk of lung cancer, many showing a reduced SMR for lung cancer among coal miners.<sup>38-40</sup> On the other hand, earlier case-control studies of lung cancer show a magnitude of relative risk (RR) for lung cancer among people exposed to coal similar to that of the present study. In a study of 138 male lung cancer cases and an equal number of controls in Louisiana, Correa *et al*<sup>12</sup> reported a smoking adjusted OR of 1.5 for lung cancer and exposure to coal. In Shanghai, Levin *et al*<sup>19</sup> found a smoking adjusted OR of 1.3 (95% CI 1.0-1.9) for lung cancer and self-reported exposure to coal.

The finding of an association between exposure to asbestos and lung cancer was expected.<sup>25</sup> Unlike other studies, however,<sup>41-43</sup> we did not find the highest OR among subjects exposed to both asbestos and smoking. The strength of association between asbestos and lung cancer was highest among the non-smokers. Data were insufficient to tell whether this finding was due to chance or whether the joint effect of asbestos and cigarette smoking was less than multiplicative. Because of the matched design of the study we could not assess whether there was additive interaction.

Evaluation of the occupational distribution among non-smoking cases of lung cancer was of limited value due to the small number of such cases (62). Even in a study of substantial size, 1793 cases of lung cancer, an assessment of factors causing lung cancer in the absence of cigarette smoking is difficult because cigarette smoking is such an important factor in the development of lung cancer, acting alone or in concert with other causes.

Our current study has numerous strengths, including the size of the sample, personal interview of cases and controls, and its broad geographical representation. Furthermore we used four categories of smoking as a matching factor (never smoker; ex-smoker; current 1-19 cigarettes per day; current  $\geq 20$  cigarettes per day). By matching controls to cases according to their current smoking state, we were able to control more efficiently the potential confounding effect of smoking. We are aware that using four categories of cigarette smoking may leave some residual confounding, but occupational lung cancer studies have uncommonly included this level of detail on cigarette smoking.

The PAR for lung cancer due to occupation has been estimated at 10% to 35%.<sup>44,45</sup> The 9.2% in this study is therefore low, well below Doll and Peto's estimate of 15%<sup>44</sup> and is likely an underestimate.

In considering the extent to which our findings may be generalised, there are several reasons to expect them to fall below the true PAR. The PAR is a theoretical concept where the usual computation depends only upon  $p_e$  (proportion of population exposed) and RR through the formula  $PAR = p_e (RR-1) / (p_e(RR-1) + 1)$ .<sup>47</sup> Hence, it is subject to biases in both  $p_e$  and RR.

If smoking is an important confounding factor, failure to adjust for it is likely to overestimate the RR, leading to over-rating the occupational contribution to total incidence of cancer. This possibility has been minimised through matching of controls to cases based on smoking history. Furthermore, the PAR concept is also one dimensional—it neglects the influence of interactions with the exposure of interest (occupation). These other exposures are frequently ignored altogether in occupational studies.<sup>44-46,48</sup> On the other hand, there are two potentially important sources of underestimation of the true PAR: the low power due to under-representation of occupations in the geographic area under study, and the inclusion of occupations at high risk of lung cancer in the reference category of the ORs.

The distribution of occupations in our study is determined by the catchment areas of the participating hospitals. Although this was not a population-based study, subjects were recruited in nine areas of the United States, representing a large variety of industries and services. None the less, some occupational titles were over-represented compared with the United States general population, and we thus had more power to detect statistically significant associations for these occupational groups than for others that were less numerous (table 5). This is true for most case-control studies.

Another source of underestimation of the true PAR is that the usual approach for computing ORs related to job titles is to compare subjects ever or usually employed in one occupation with subjects never or not usually employed in that occupation. In a case-control study, this approach has the advantage of treating the odds of exposure for cases and controls as random variables. On the other hand, it is likely to underestimate the true OR because the reference category ("never exposed to the studied occupation") includes jobs that are at high risk of lung cancer.

It should be noted that the PARs (table 2) are point estimates, like the RRs, with their own 95% CIs, and as such should not be taken too literally. As an illustration, the 95% CI of the PAR for electricians, obtained by substituting the corresponding RR in the formula for PAR is 0.001-0.019, whereas for cranemen it is 0.002-0.227. Obviously, 23% of lung cancers do not arise in cranemen. Rather, the wide limits are the result of low power due to few cranemen being included in the study. What is most important is the cumulative PAR, which is the sum of the point estimates for the PARs for all the individual occupations, and for which the random errors will tend to cancel, giving a fairly stable estimate of 9.2%.

In conclusion, the cumulative PAR of the present study (9.2%) is likely to be a lower limit of the true contribution of occupation to lung cancer risk as it is plagued by the inherent tendency of individual epidemiological studies to underestimate the magnitude of the relation between lung cancer and occupation. Because lung cancer comprises 19% of

total cancer incidence in men,<sup>49</sup> this would lead to an estimate that occupation is responsible for  $9.2\% \times 19\% = 1.75\%$  of all cancers in men, which is also most likely an underestimate.

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