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# A case-control study of occupational risk factors for laryngeal cancer

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**Abstract**

**To determine whether specific jobs and occupational exposures are associated with laryngeal cancer lifetime occupational histories from a population-based case-control study in western Washington were examined. The study included 235 cases diagnosed between September 1983 and February 1987, and 547 controls identified by random digit dialling. After controlling for alcohol use, cigarette smoking, age and education, significantly increased risks were found for painters in construction (odds ratio (OR)) = 2·8, (95% confidence interval (95% CI) 1·1–6·9), supervisors and miscellaneous mechanics (OR = 2·3, 95% CI 1·1–4·8), construction workers (OR = 3·4, 95% CI 1·4–8·1), metalworking and plastic working machine operators (OR = 2·6, 95% CI 1·3–4·9) and handlers, and equipment cleaners and labourers (OR = 1·5, 95% CI 1·0–2·2). Allowing for a 10 year induction and latent period did not have a consistent effect on the associations. Potential exposures to asbestos, chromium, nickel, formaldehyde, diesel fumes, and cutting oils were assessed by using a job exposure matrix developed for this study. Three measures of exposure were examined—namely, peak, duration, and an intensity weighted exposure score. No significantly raised risks were seen, although increased risk was suggested among those exposed long term to formaldehyde in jobs with the highest exposures.**


Although cigarette smoking and alcohol consumption are well accepted as the dominant risk factors for laryngeal cancer, it is recognised that exposure to agents in the occupational environment may also play an aetiological part. Investigation of specific exposures in case-control studies by means of job exposure matrices or in cohort studies of specific occupational groups have suggested associations between laryngeal cancer and exposure to asbestos,[1-7] paint,[2 8 9] nickel,[3 10] and wood dust.[11 12] Increased risk has also been noted in at least two separate studies for employment as plumbers and pipefitters,[1 2] carpenters,[1 2] construction workers,[2 13] drivers,[2 3] and farmers.[10 14]

We examined lifetime occupational histories from a population based case-control study of laryngeal cancer in western Washington to determine whether specific jobs and exposures considered previously to be potential risk factors are associated with the disease in this geographical area, and to identify new hypotheses relating occupational exposures and laryngeal cancer. Advantages of the present study include availability of (1) a fairly large number of cases and controls from the general population, (2) detailed information derived from personal interviews on lifetime occupational history and the major potentially confounding factors, and (3) information on specific site of origin within the larynx.

## Methods

Incident cases of laryngeal cancer diagnosed between September 1983 and February 1987 were identified through the cancer surveillance system of the Fred Hutchinson Cancer Research Centre in Seattle, WA. This is a population based cancer registry and participates in the Surveillance, Epidemiology, and End Results (SEER) programme of the National Cancer Institute. The registry covers a 13 county area in western Washington with an estimated population of three million. All persons diagnosed with cancer of the larynx (ICD-0 codes 161·0–161·9) between the ages of 20 and 74 who were residents of the three largest counties in this area were eligible.

A total of 291 cases were found, 235 (80·8%) of which were successfully interviewed. Reasons for non-interview were refusal by the subject's physician (n = 21), refusal by subject (n = 22), inability to locate (n = 4), and other reasons such as language barrier or incompetence (n = 9). The closest next of

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kin, preferably the spouse, was interviewed if a case was deceased. Seven per cent (n = 17) of the case interviews were with surrogates.

Controls were identified by random digit dialling[15] and selected to be similar in age and sex distribution to the cases, with at least twice as many in each five year age and sex band. Phone numbers were randomly generated from a list of working exchanges for the same 13 county area from which the cases came. Each number was called up to nine times at different times of the day and week to detemine if the number was a residence and if so, whether an eligible person lived in the household. If multiple persons at one residence were eligible, only one was randomly selected. Because all the controls had a phone, only cases with telephones at the time of the diagnosis were interviewed. Ninety five per cent of the households were successfully screened and 80% of eligible subjects were interviewed, leaving 547 for analysis.

In person interviews were conducted with each study participant, and lasted roughly 60 minutes. Lifetime occupational histories as well as smoking and drinking histories were collected. Job titles, description of tasks performed, and the nature of the industry were collected for each job held for six months or longer. Job title and industry were coded according to the 1980 United States census codes.[16] The 505 individual occupation codes were compressed into 62 broader categories, based largely on the minor headings. Specific job titles were examined as well, both for categories with increased risk in this study and for occupations previously associated with laryngeal cancer. Job titles were analysed according to duration of exosure: up to nine years and 10 years or more.

Six exposures were chosen for further investigation, based on hypotheses generated by the analysis of job titles and by a review of published data. The exposures were to asbestos, chromium, nickel, cutting oils, diesel fumes, and formaldehyde. A panel of four experienced industrial hygienists from the Department of Environmental Health at the University of Washington who were familiar with local industries created a job exposure matrix (JEM) for these selected exposures. This group had participated in the creation of similar JEMs for previous analyses of possible associations between occupational exposures and incidence of Wilms' tumour[17] and upper respiratory tract cancers.[18] Jobs were classified into four levels of exposure to each agent based on judgement of both likelihood and degree of exposure.

For each job listed for a subject, the number of years in that job was calculated and an exposure code (0 = no, 1 = low, 2 = medium and 3 = high exposure) for each of the six selected exposures was assigned. Three different summary variables were then calculated: (1) lifetime peak exposure (highest code for subject); (2) duration of exposure (less than 10 years or 10 years or more); and (3) an exposure score based both on duration and level of exposure (a weighted sum of the number of years spent in a job, the weight being the level of exposure). In separate analyses we excluded all exposures coded as low level to look for associations that might be obscured by the inclusion of low level exposures when an effect is less likely.

To allow for a possible induction and latency effect, the duration and exposure score variables were also calculated after excluding all exposures in the 10 years immediately before diagnosis. Based on the assumption that an induction and latency period of 10 or more years exists, this method would reduce the dilution of an effect by excluding irrelevant exposures.[19]

The measure of association was the odds ratio (OR). A multiple logistic regression model[20] was used for the analyses adjusting for smoking, drinking, age and education (coded as described in table 2). Further adjustment for sex did not substantially change any results. A test for trend to detemine whether risk increased significantly with duration of exposure was performed by adding to the model already containing the adjustment variables the exposure variable of interest in grouped linear form.

## Results

Table 1 presents the clinical characteristics of the cases. Table 2 shows selected demographic characteristics and histories of cigarette and alcohol use for cases and controls. Cases were less likely to be women, and to have had a college education than controls and more likely to smoke cigarettes and to drink alcohol.

Table 3 presents ORs for the 56 job categories with at least five subjects ever employed. Among the jobs associated with increased risks, these were significant for supervisors and miscellaneous mechanics (OR = 2·3, 95% confidence interval (95% CI) 1·1–4·8),

*Table 1 Clinical features of cases*

| *Characteristic* | *No (%)* |
|---|---|
| Site: | |
| Glottic | 141 (60·6) |
| Supraglottic | 73 (31·1) |
| Subglottic | 5 (2·1) |
| Laryngeal cartilage | 2 (0·9) |
| NOS | 5 (2·1) |
| Origin undetermined | 9 (3·8) |
| Histology: | |
| Squamous cell | 222 (94·5) |
| Adenocarcinoma | 1 (0·4) |
| Epithelial, NOS | 12 (5·1) |
| Stage: | |
| In situ | 21 (8·9) |
| Local | 144 (61·3) |
| Regional/distant | 61 (26·0) |
| Unknown | 9 (3·8) |

*Table 2 Selected characteristics of cases and controls*

| | Cases No (%) | Controls No (%) |
|---|---|---|
| Age at diagnosis (y): | | |
| 20–39 | 9 (3·8) | 27 (4·9) |
| 40–49 | 16 (6·8) | 55 (10·1) |
| 50–59 | 72 (30·6) | 149 (27·2) |
| 60–69 | 101 (43·0) | 230 (42·1) |
| 70–74 | 37 (15·7) | 86 (15·7) |
| Sex: | | |
| Men | 185 (78·7) | 356 (65·1) |
| Women | 50 (21·3) | 191 (34·9) |
| Education: | | |
| No college | 160 (68·0) | 272 (49·7) |
| College | 72 (30·6) | 269 (49·2) |
| Unknown | 3 (1·3) | 6 (1·1) |
| Cigarette smoking: | | |
| Non-smokers: | | |
| Never or stopped ≥ 15 y | 32 (13·6) | 313 (57·2) |
| Stopped < 15 y | 34 (14·5) | 106 (19·4) |
| Current smokers: | | |
| < 20 a day | 23 (9·8) | 42 (7·7) |
| 20–39 a day | 100 (42·6) | 72 (13·2) |
| ≥40 a day | 39 (16·6) | 12 (2·2) |
| Unknown | 7 (3·0) | 2 (0·4) |
| Alcohol intake (drinks per week): | | |
| None | 8 (3·4) | 68 (12·4) |
| <7 | 81 (34·5) | 343 (62·7) |
| 7–13 | 42 (17·9) | 68 (12·4) |
| 14–20 | 27 (11·5) | 25 (4·6) |
| >21 | 61 (25·9) | 35 (6·4) |
| Unknown | 16 (6·8) | 8 (1·5) |

painters (OR = 2·8, 95% CI 1·1–6·9), construction workers (OR = 3·4, 95% CI 1·4–8·1), metalworking and plastic working machine operators and handlers (OR = 2·6, 95% CI 1·3–4·9), and equipment cleaners and labourers (OR = 1·5, 95% CI 1·0–2·2). Other jobs with a suggestion of increased risk included cleaning and building service personnel (OR = 1·4, 95% CI 0·8–2·7), plumbers and pipefitters (OR = 4·1, 95% CI 0·9–17·9), textile machine operators (OR = 2·2, 95% CI 0·9–5·4), and motor vehicle operators (OR = 1·3, 95% CI 0·8–2·1). Food preparation workers (OR = 3·1, 95% CI 1·2–8·2), vehicle mechanics (OR = 3·2, 95% CI 1·2–8·2), carpenters (OR = 4·2, 95% CI 1·1–16·9), and construction workers (OR = 5·7, 95% CI 1·3–26·3) had significantly raised risks if they had been employed 10 years or more. The trend test for increasing risk with duration of exposure was significant only for construction workers. The analysis was repeated after excluding all jobs held in the 10 years before diagnosis. No important differences were found with the assumption of 10 year induction.

Several occupation groups were associated with decreased risk. These included administration and management (OR = 0·5, 95% CI 0·3–0·8), administrative support (OR = 0·7, 95% CI 0·5–1·0), teachers (OR = 0·4, 95% CI 0·2–1·0), and personal service occupations (OR = 0·4, 95% CI 0·2–1·1).

Specific job titles were examined within the larger job categories. In the general category of vehicle mechanics, increased risks were seen across most subgroups—namely car mechanics (OR = 2·2, 95% CI 0·4–11·7), bus, lorry, and stationary engine mechanics (OR = 2·2, 95% CI 0·4–11·9), aircraft engine mechanics (OR = 7·6, 95% CI 0·6–102·0), and autobody mechanics (OR = 5·6, 95% CI 0·7–43·0). Among the motor vehicle operators, the drivers of light lorries (OR = 2·3, 95% CI 1·0–5·5) were significantly at greater risk; whereas the drivers of heavy lorries (OR = 1·1, 95% CI 0·5–2·3) were not. In the miscellaneous mechanics category, the strongest association was with specified mechanics not elsewhere classified (OR = 4·7, 95% CI 0·9–25·6). In the category of metal and plastic working machine operators, the risk was associated with the grinding, abrading, and buffing operators (OR = 1·8, 95% CI 0·5–6·2). Among the food preparation occupations bartenders were at increased risk (OR = 2·3, 95% CI 0·9–6·5). Among painters, spray paint machine operators (OR = 2·4, 95% CI 0·5–11·2) were at greater risk than painters in construction (OR = 1·6, 95% CI 0·4–6·6). Three job categories, construction workers, textile machine operators and handlers, and equipment cleaners and labourers, were each composed of numerous specific job titles, many of which included less than three subjects. No single occupation could explain the associations noted. No striking differences were found for specific occupations after taking into account a 10 year induction and latency period.

Table 4 presents the analysis from the job exposure matrix. For all six exposures examined, none of the summary variables was significantly associated with laryngeal cancer. There were suggestions of increased risk associated with exposure to chromium and nickel in the high exposure score group. Chromium and nickel cannot be considered separately in this data set as only nine of the 75 of the subjects exposed to chromium had no exposure to nickel. The 10 year induction period had no important effect for the exposures studied with the exception of nickel and chromium where the risks increased in the high exposure score groups to 3·1 (95% CI 0·6–17·1) and 3·4 (95% CI 0·7–19·2) respectively.

The repeat analyses, which excluded low level exposures, resulted in different findings only for formaldehyde. This was attributed to the comparatively large number of persons with low level exposures. The OR of laryngeal cancer in the group with medium or high exposures for 10 years or more compared with the non-exposed group was 4·2 (95% CI 0·9–19·4) and the OR for those in the high exposure score category was 4·3 (95% CI 1·0–18·7). These estimates of risk increased only slightly when an induction and latency period was accounted for.

Separate analyses of supraglottic and glottic tumours failed to show any difference in relative risks according to tumour site for the six exposures examined.

*Table 3 Odds ratios for laryngeal cancer and occupation*

| Occupation | No cases | No controls | All years OR* Ever employed | All years OR* <10 y | All years OR* ≥10 y | All years OR* Trend p Value | Induction period OR*† Ever employed | Induction period OR*† <10 y | Induction period OR*† ≥10 y | Induction period OR*† Trend p Value |
|---|---|---|---|---|---|---|---|---|---|---|
| Administration, management | 47 | 178 | 0·5 (0·3–0·8) | 0·5 | 0·7 | 0·06 | 0·6 (0·4–0·9) | 0·5 | 0·7 | 0·03 |
| Engineers, architects, surveyors | 13 | 42 | 0·8 (0·4–1·8) | 1·0 | 1·1 | 0·90 | 1·0 (0·5–2·3) | 1·1 | 0·9 | 0·51 |
| Maths, computer scientists | 11 | 38 | 0·6 (0·3–1·4) | 0·6 | 1·5 | 0·60 | 0·7 (0·3–1·6) | 0·7 | 1·1 | 0·42 |
| Natural scientists | 1 | 4 | 1·8 (0·2–16·5) | 2·3 | 0·0 | 0·60 | 2·5 (0·3–23·6) | 3·2 | 0·0 | 0·60 |
| Nurses | 1 | 15 | 0·2 (0·0–1·4) | 0·0 | 0·5 | 0·15 | 0·2 (0·2–1·6) | 0·0 | 0·7 | 0·18 |
| Teachers | 9 | 55 | 0·4 (0·2–1·0) | 0·3 | 0·5 | 0·20 | 0·5 (0·2–1·2) | 0·3 | 0·8 | 0·27 |
| Social scientists | 3 | 17 | 0·4 (0·1–1·7) | 0·3 | 0·5 | 0·49 | 0·6 (0·1–2·3) | 0·3 | 1·0 | 0·50 |
| Writers, artists, athletes | 10 | 27 | 0·7 (0·3–1·6) | 0·7 | 0·6 | 0·53 | 0·7 (0·3–1·9) | 0·6 | 1·2 | 0·96 |
| Painters, sculptors | 3 | 5 | 1·0 (0·2–6·3) | 1·2 | 0·9 | 0·93 | 1·2 (0·2–7·7) | 1·5 | 0·0 | 0·86 |
| Technicians (except health) | 12 | 32 | 0·8 (0·3–1·8) | 1·0 | 0·7 | 0·65 | 0·9 (0·4–2·0) | 0·0 | 0·8 | 0·36 |
| Other technicians | 1 | 8 | 0·5 (0·0–5·2) | 0·0 | 1·0 | 0·70 | 0·5 (0·0–6·0) | 0·0 | 1·3 | 0·75 |
| Sales | 77 | 173 | 1·0 (0·7–1·4) | 1·1 | 1·1 | 0·64 | 1·1 (0·7–1·6) | 1·1 | 1·2 | 0·93 |
| Administrative support | 81 | 246 | 0·7 (0·5–1·0) | 0·9 | 0·7 | 0·20 | 0·8 (0·5–1·2) | 0·9 | 0·7 | 0·14 |
| Cook, housekeeper | 5 | 17 | 1·3 (0·4–4·1) | 1·2 | 1·3 | 0·70 | 1·1 (0·4–3·6) | 1·4 | 0·8 | 0·75 |
| Protective services, firefighters | 2 | 6 | 0·5 (0·0–2·9) | 0·0 | 1·2 | 0·10 | 0·4 (0·6–2·2) | 0·0 | 1·2 | 0·10 |
| Police | 8 | 24 | 0·7 (0·3–1·8) | 0·6 | 1·1 | 0·70 | 0·8 (0·3–1·9) | 0·6 | 1·1 | 0·63 |
| Food preparation and service | 47 | 89 | 0·9 (0·6–1·5) | 0·6 | 3·1 | 0·53 | 0·9 (0·6–1·4) | 0·7 | 3·8 | 0·74 |
| Health service occupations | 6 | 27 | 0·5 (0·2–1·4) | 0·7 | 0·5 | 0·42 | 0·5 (0·2–1·4) | 0·6 | 1·6 | 0·56 |
| Cleaning and building service | 25 | 40 | 1·4 (0·8–2·7) | 1·6 | 0·2 | 0·80 | 1·4 (0·7–2·5) | 1·4 | 0·4 | 0·65 |
| Personal service occupations | 8 | 33 | 0·4 (0·2–1·1) | 0·4 | 0·5 | 0·09 | 0·4 (0·2–1·0) | 0·4 | 0·4 | 0·07 |
| Farmers, managers | 32 | 84 | 0·7 (0·4–1·1) | 0·7 | 0·3 | 0·03 | 0·7 (0·4–1·1) | 0·7 | 0·3 | 0·02 |
| Farm workers, nursery workers | 29 | 75 | 1·0 (0·6–1·7) | 0·7 | 1·5 | 0·90 | 0·9 (0·5–1·6) | 0·7 | 1·5 | 0·98 |
| Related farm work | 4 | 7 | 1·3 (0·3–5·7) | 1·3 | 0·0 | 0·72 | 1·4 (0·3–5·9) | 1·3 | 0·0 | 0·72 |
| Forestry | 8 | 18 | 0·8 (0·3–2·1) | 1·3 | 0·0 | 0·73 | 0·7 (0·9–2·1) | 1·3 | 0·0 | 0·41 |
| Fishers, hunters | 6 | 8 | 0·8 (0·2–2·8) | 1·1 | 0·3 | 0·40 | 0·7 (0·2–2·6) | 0·7 | 0·8 | 0·41 |
| Vehicle mechanics | 32 | 49 | 1·2 (0·6–2·1) | 0·6 | 3·2 | 0·19 | 1·1 (0·6–2·0) | 0·7 | 3·4 | 0·23 |
| Industrial machine repairer | 3 | 6 | 0·2 (0·0–1·7) | 0·0 | 0·8 | 0·31 | 0·2 (0·0–1·5) | 0·0 | 0·7 | 0·92 |
| Electrical equipment repairer | 8 | 17 | 0·5 (0·2–1·3) | 0·8 | 0·1 | 0·09 | 0·2 (0·2–1·4) | 0·8 | 0·1 | 0·21 |
| Supervisors and misc mechanics | 24 | 23 | 2·3 (1·1–4·8) | 2·6 | 1·7 | 0·06 | 2·3 (1·1–4·7) | 2·4 | 1·8 | 0·02 |
| Carpenters | 15 | 30 | 1·3 (0·6–2·7) | 0·7 | 4·2 | 0·20 | 1·2 (0·6–2·5) | 0·7 | 4·2 | 0·23 |
| Electricians | 6 | 20 | 0·6 (0·2–1·8) | 1·4 | 0·2 | 0·14 | 0·6 (0·2–1·7) | 1·0 | 0·2 | 0·17 |
| Painters | 14 | 13 | 2·8 (1·1–6·9) | 2·9 | 0·7 | 0·40 | 2·3 (0·9–5·7) | 2·9 | 0·7 | 0·35 |
| Plumber, pipefitter | 5 | 5 | 4·1 (0·9–17·9) | 3·3 | — | 0·06 | 3·7 (0·9–16·5) | 3·1 | — | 0·06 |
| Construction | 17 | 13 | 3·4 (1·4–8·1) | 2·5 | 5·7 | 0·01 | 3·3 (1·4–7·7) | 3·3 | 3·2 | 0·02 |
| Extractive | 5 | 6 | 1·6 (0·4–6·6) | 1·4 | 0·5 | 0·72 | 1·2 (0·3–5·0) | 1·4 | 0·5 | 0·53 |
| Production supervisor | 4 | 16 | 0·6 (0·2–2·3) | 0·9 | 0·5 | 0·29 | 0·5 (0·1–1·9) | 0·6 | 0·4 | 0·25 |
| Precision metal working | 19 | 37 | 1·0 (0·5–1·9) | 0·9 | 1·1 | 0·90 | 0·9 (0·4–1·9) | 1·0 | 0·7 | 0·42 |
| Precision wood working | 1 | 4 | 1·4 (0·1–15·0) | 1·7 | — | — | 1·7 (0·1–18·9) | 1·6 | — | — |

*Table 3 Odds ratios for laryngeal cancer and occupation—continued*

| | | | All years OR* | | | | Induction period OR*† | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Occupation | No cases | No controls | Ever employed | < 10 y | ≥ 10 y | Trend p Value | Ever employed | < 10 y | ≥ 10 y | Trend p Value |
| Precision textile clothing | 3 | 8 | 1·1 (0·2–6·2) | 0·0 | 1·4 | 0·50 | 1·0 (0·2–5·5) | 0·1 | 0·6 | 0·50 |
| Precision workers, assorted materials | 1 | 5 | 0·5 (0·0–5·9) | 0·5 | 0·0 | 0·45 | 0·4 (0·0–5·1) | 0·4 | 0·0 | 0·43 |
| Precision food production | 3 | 6 | 1·3 (0·3–6·2) | 1·1 | 1·6 | 0·71 | 1·3 (0·3–6·0) | 1·2 | 1·3 | 0·83 |
| Inspectors | 11 | 14 | 0·8 (0·3–2·1) | 0·7 | 1·7 | 0·88 | 0·9 (0·3–2·2) | 0·7 | 1·5 | 0·76 |
| Plant and systems operator | 4 | 4 | 2·0 (0·4–10·1) | 1·0 | 5·1 | 0·30 | 1·7 (0·3–8·6) | 1·0 | 4·3 | 0·41 |
| Metal and plastic working machine operator | 24 | 31 | 2·6 (1·3–4·9) | 3·0 | 0·8 | 0·04 | 2·4 (1·2–4·5) | 3·1 | 0·4 | 0·07 |
| Metal and plastic process machine operator | 4 | 4 | 1·5 (0·3–7·3) | 0·9 | — | 0·5 | 1·4 (0·3–7·2) | 1·2 | — | 0·57 |
| Woodworking machine operator | 5 | 18 | 0·5 (0·2–1·5) | 0·3 | 4·6 | 0·70 | 0·4 (0·1–1·3) | 0·4 | 2·3 | 0·36 |
| Printing machine operator | 4 | 8 | 0·9 (0·2–3·7) | 0·3 | 1·6 | 0·20 | 0·9 (0·2–3·7) | 0·7 | 1·1 | 0·76 |
| Textile, clothing machine operator | 13 | 16 | 2·2 (0·9–5·4) | 2·0 | 0·6 | 0·23 | 1·8 (0·7–4·5) | 2·0 | 0·6 | 0·26 |
| Machine operator assorted materials | 25 | 45 | 1·3 (0·7–2·4) | 1·2 | 1·4 | 0·42 | 1·1 (0·6–2·1) | 1·1 | 1·3 | 0·32 |
| Welders, cutters | 6 | 15 | 0·7 (0·2–2·4) | 0·4 | 2·0 | 0·70 | 0·6 (0·2–2·0) | 0·4 | 2·0 | 0·64 |
| Handmoulding, casting, engraving, grinding | 6 | 27 | 0·5 (0·2–1·4) | 0·5 | 0·0 | 0·20 | 0·5 (0·1–1·4) | 0·5 | 0·0 | 0·19 |
| Motor vehicle operators | 54 | 80 | 1·3 (0·8–2·1) | 1·6 | 0·8 | 0·40 | 1·3 (0·8–2·0) | 1·4 | 0·9 | 0·24 |
| Transportation, motor vehicles | 19 | 21 | 1·3 (0·6–2·8) | 1·1 | 0·8 | 0·62 | 1·1 (0·5–2·3) | 1·1 | 0·8 | 0·81 |
| Material moving equipment operator | 12 | 28 | 0·6 (0·3–1·4) | 0·9 | 0·2 | 0·05 | 0·6 (0·2–1·3) | 0·8 | 0·2 | 0·12 |
| Handlers, equipment cleaners, labourers | 80 | 150 | 1·5 (1·0–2·2) | 1·2 | 1·0 | 0·45 | 1·3 (0·9–1·9) | 1·2 | 0·9 | 0·66 |
| Garage and service station related | 12 | 38 | 0·8 (0·4–1·8) | 0·8 | 1·1 | 0·87 | 0·9 (0·4–1·9) | 0·8 | 1·1 | 0·59 |

*Adjusted for smoking, alcohol, age and education. 95% confidence intervals in parentheses.
†Duration calculated after excluding most recent 10 years before reference date.

## Discussion

Several limitations exist in studies of this kind. Firstly, although case-control studies are well suited to the investigation of rare outcomes, the population based nature of this study renders the likelihood of common occupational exposures small, thus reducing the statistical power of the analyses. For example, in the case of asbestos our power to detect a twofold increase in risk for those exposed 10 years or more was 50%.

Secondly, more specific limitations of the job title analysis include inability to account for changing safety standards over time resulting in different levels and types of exposure, different tasks performed within one job category and even within a specific job title, changes in job titles over the years as a result of changes in technology, and the existence of multiple exposures in any one job. These limitations will work together to bias the results towards the null hypothesis through a tendency to misclassify exposure, as jobs are not homogeneous in their exposures.

Thirdly, the job exposure matrix approach is a qualitative method that attempts to approximate categories of exposure but cannot replace studies with actual exposure measurements. This can be seen from industry based studies of various chemicals such as chlorophenates or solvents in which exposure estimates by panels of industrial hygienists were compared with actual measurements of urinary metabolites or air sampling.[21 22] Thus the JEM approach is most strongly affected by misclassification of a non-differential nature, again biasing the results toward the null hypothesis.

Finally, the issue of multiple statistical comparisons must be borne in mind as significant associations are expected to occur by chance alone.

Despite these limitations, most of the job categories associated with increased risk in this study have been previously reported, such as vehicle mechanics,[3 23] carpenters,[3] painters[2 8 10] and construction workers,[2 13] miscellaneous mechanics,[13] textile machine operators,[14] and bartenders.[2 10 23]

The general category of drivers has been associated

*Table 4 Odds ratios for laryngeal cancer and potential occupation exposures**

| | *Asbestos* | | | | *Diesel fumes* | | | | *Cutting oils* | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Case* | *Controls* | *OR* | *(95% CI)* | *Case* | *Controls* | *OR* | *(95% CI)* | *Case* | *Controls* | *OR* | *(95% CI)* |
| Peak:† | | | | | | | | | | | | |
| None | 145 | 393 | 1·0 | — | 112 | 316 | 1·0 | — | 215 | 500 | 1·0 | — |
| Low | 3 | 6 | 1·2 | (0·6–7·1) | 58 | 113 | 1·2 | (0·7–1·9) | 8 | 17 | 0·7 | (0·2–2·3) |
| Medium | 57 | 94 | 1·3 | (0·8–2·0) | 65 | 118 | 1·1 | (0·7–1·8) | 2 | 7 | 0·4 | (0·6–2·5) |
| High | 30 | 54 | 1·1 | (0·6–1·9) | 0 | 0 | — | — | 10 | 23 | 1·0 | (0·3–2·4) |
| Duration (y): | | | | | | | | | | | | |
| <1 | 151 | 400 | 1·0 | — | 118 | 318 | 1·0 | — | 215 | 500 | 1·0 | — |
| 1–9 | 50 | 106 | 1·0 | (0·5–2·1) | 70 | 144 | 1·0 | (0·7–1·6) | 9 | 33 | 0·5 | (0·2–1·4) |
| ⩾10 | 34 | 41 | 1·2 | (0·6–2·3) | 47 | 85 | 1·0 | (0·6–1·8) | 11 | 14 | 1·0 | (0·3–3·0) |
| Exposure scores‡ | | | | | | | | | | | | |
| <5 | 173 | 455 | 1·0 | — | 158 | 408 | 1·0 | — | 219 | 519 | 1·0 | — |
| 5–19 | 25 | 50 | 1·1 | (0·6–2·1) | 39 | 71 | 1·3 | (0·7–2·2) | 3 | 13 | 0·4 | (0·1–2·2) |
| ⩾20 | 37 | 42 | 1·4 | (0·7–2·5) | 38 | 68 | 1·0 | (0·6–1·7) | 13 | 15 | 1·3 | (0·5–2·6) |

*Adjusted for age, smoking, drinking and education.
†Peak: highest lifetime exposure code.
‡Exposure score: weighted sum of number of years with exposure, the weight being the level of exposure coded 0–3.

with increased risk in at least three studies[2 3 23]; in this study drivers of light lorries specifically were found to be at significantly increased risk. The nature of most of these occupations is such that multiple potential exposures exist in the same occupation. Thus it is impossible to identify the specific causal agent with certainty. Inaccurate reporting of drinking and smoking habits or exposure to environmental tobacco smoke may explain the increased risk for bartenders and other restaurant personnel. The lack of consistent risk gradients in these occupations with increasing duration of exposure may indicate that the associations are not causal, that there is inaccurate recall, or that those employed in the jobs with the most noxious exposures stayed for shorter periods.

Several occupations previously associated with laryngeal cancer, such as farming,[10 14] boilermaking[2] and sheetmetal work[13] showed no increase in risk here, although the power of the study to detect associations with the last two groups was limited. Metal processing and metal fabricating occupations have also been implicated in previous studies.[9 10 24] In this study, whereas precision metal working occupations were not at increased risk, the category of metal and plastic working machine operators, specifically grinding, abrading and buffing operators, was associated with laryngeal cancer.

Potential exposure to chromium or nickel was not associated with significantly increased risk, although it was suggested for those with exposure scores of 20 and above. As mentioned these exposures show considerable overlap. The group exposed to chromium alone was made up entirely of spray painters (four cases and four controls), who were themselves at significantly higher risk. These results suggest that either the route of exposure to chromium experienced by the spray painter is particularly hazardous or that other potential concurrent exposures, such as solvents, are responsible for the increased risk.

Diesel fumes have been associated with increased risks in other studies,[12] but not in ours. This may be explained by the lack of a highly exposed group among our subjects. It is doubtful if exposure to diesel fumes would explain the elevated risk among drivers of light lorries given the lack of association with other groups exposed to diesel fumes.

The role of asbestos in laryngeal cancer has been the subject of considerable controversy, with several recent review articles reaching opposite conclusions.[25–28] The major area of disagreement is the impact of not adjusting for smoking and drinking. Exclusion of all studies that failed to adjust for these known determinants of laryngeal cancer weakens the case for asbestos.[25] In our data, the point estimate of the relative risk in persons with exposure to asbestos was increased after adjusting for cigarettes and alcohol, although this possible association could easily be explained by chance.

These data suggest that formaldehyde is associated with laryngeal cancer among people who experienced at least a medium or high level of exposure for 10 or more years. Formaldehyde has received much attention as a potential human carcinogen. It has been shown to be carcinogenic in rats and mice, causing nasal cancer.[29 30] Formaldehyde has been shown to be almost entirely absorbed in the nasal mucosa of rats,[31] although this is not the case in humans. Several cohort studies of workers exposed to formaldehyde have been carried out.[32–37] Of these studies, only that of Blair *et al*[35] suggested an increased risk for laryngeal cancer. The others either found no excess or made no mention of laryngeal cancer as a separate site. These studies typically have little power to detect increased rates of rare cancers. Also, the comparatively high survival rate for laryngeal cancer

| Chromium | | | | Nickel | | | | Formaldehyde | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Case | Controls | OR | (95% CI) | Case | Controls | OR | (95% CI) | Case | Controls | OR | (95% CI) |
| 207 | 500 | 1·0 | — | 211 | 504 | 1·0 | — | 177 | 423 | 1·0 | — |
| 13 | 24 | 0·8 | (0·3–1·9) | 14 | 23 | 0·8 | (0·3–1·9) | 42 | 88 | 1·0 | (0·6–1·7) |
| 15 | 23 | 1·1 | (0·5–2·6) | 10 | 20 | 0·6 | (0·2–1·8) | 14 | 33 | 1·0 | (0·4–2·1) |
| 0 | 0 | — | — | 0 | 0 | — | — | 2 | 3 | 2·0 | (0·2–19·5) |
| 208 | 501 | 1·0 | — | 211 | 505 | 1·0 | — | 182 | 426 | 1·0 | — |
| 20 | 36 | 0·7 | (0·4–1·5) | 16 | 33 | 0·5 | (0·3–1·3) | 27 | 94 | 0·8 | (0·4–1·3) |
| 7 | 10 | 1·1 | (0·3–4·4) | 8 | 9 | 1·4 | (0·3–4·8) | 26 | 27 | 1·3 | (0·6–3·1) |
| 219 | 528 | 1·0 | — | 221 | 529 | 1·0 | — | 201 | 493 | 1·0 | — |
| 10 | 12 | 1·1 | (0·4–3·4) | 7 | 11 | 0·6 | (0·2–2·4) | 18 | 40 | 1·0 | (0·5–2·0) |
| 6 | 7 | 1·5 | (0·3–6·5) | 7 | 7 | 1·6 | (0·4–6·7) | 16 | 16 | 1·3 | (0·5–3·3) |

creates the possibility of ascertainment bias in mortality studies.

In conclusion, we found associations with several classes of workers, most of which have been previously reported to be at increased risk of laryngeal cancer—namely, carpenters, construction workers, mechanics, painters, metalworking machine operators, textile machine operators, plumbers and pipefitters, motor vehicle operators, and bartenders. Future studies of laryngeal cancer should focus on more accurate assessment of specific exposures, which might explain the excesses found in these occupational groups. We also found a suggestion of increased risk for persons exposed to formaldehyde that needs replication in further studies. The data do not strongly support an association with either asbestos or nickel and chromium, but the limitations of the study should be kept in mind because they work together to produce conservative estimates of relative risk.

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