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# OCCUPATIONAL RISK FACTORS FOR LUNG CANCER: A POPULATION-BASED CASE-CONTROL STUDY IN BRITISH COLUMBIA

by

**Dr. NAGARAJKUMAR YENUGADHATI**

**Thesis Submitted to the Faculty of Graduate and Postdoctoral Studies in partial fulfillment of the requirements for the M.Sc degree in Epidemiology**

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*This thesis is dedicated to my parents*

*Sri.Y.V.Raju & Smt.Y.Sree Nirmala*

*I love you Mom and Dad.*

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# Abstract

Occupational carcinogens have been linked to lung cancer: among 74 known occupational carcinogens and carcinogenic circumstances, 37 have been associated with lung cancer. We report on a large population-based case-control study in British Columbia (2998 lung cancer cases). In the absence of a non-cancer control group, patients with cancers other than lung cancer (11,737) served as controls. Logistic regression, adjusted for smoking history, was used to examine occupationally related lung cancer risk with histological subtypes. Elevated risk was found in several occupational circumstances: metal working, mining, deck crew of ship, bakers, workers in electric power systems, construction workers (all histological types), chefs and cooks (large cell carcinoma only), and medical workers (large cell carcinoma only). Odd ratios varied from 1.6 to 4.6, with most being around 2.0. Potential exposures found in these high risk occupational groups which warrant further evaluation include: formaldehyde, radiation, electromagnetic fields, wood dust, and cooking fumes.

# Executive Summary

Lung cancer is the leading cause of cancer mortality in the world. Occupational carcinogens have been linked to lung cancer: among 74 known occupational carcinogens and carcinogenic circumstances, 37 have been associated with lung cancer. We conducted an investigation to identify high risk occupations and industries using data from a population-based case-control study in British Columbia to expand current knowledge of occupational risk factors for lung cancer. An attempt was made to identify the lung cancer risk of specific agents with in high risk occupations and industries using a job exposure matrix (JEM) developed by NIOSH.

**Methods**: Subjects were 14,755 male incident cancer cases from British Columbia aged above 20 years for the years 1983-1990, for whom lifetime occupational histories and information on, smoking and other key covariates were collected. Cases comprised 2,998 subjects with lung cancer. All other cancer cases (11,757) accrued during this same period served as controls. A separate analysis was performed using a subset of the other cancer cases excluding smoking-related cancers. The relationship between occupational risk factors and lung cancer, including histopathological subtypes of lung cancer, was assessed by logistic regression analysis.

**Results**: High risk occupations for lung cancer included those involving metal processing (odds ratio (OR)=2.54, 95% confidence interval (CI): 1.39-4.64) and machining (OR=1.88, 95% CI: 1.17-3), and employment as deck crew of ship (OR=2.42, 95% CI: 1.02-5.75), and bakers (OR=2.72, 95% CI: 1.13-6.55). An increased risk of lung cancer was observed among men employed in various industries including: mining (OR=1.57, 95% CI: 1.12-2.21), primary metal manufacturing (OR=1.76, 95% CI: 1.21-2.56), and electric power systems (OR=2.01, 95% CI: 1.26-3.19). The analysis within histological subtypes revealed a high risk of lung cancer in carpenters (squamous cell - OR=1.76, 95% CI: 1.17-2.63), insulators (adenocarcinoma - OR=4.6, 95% CI: 1.15-18.35), electricians (small cell - OR=3.43, 95% CI: 1.34-8.77), medical workers (large cell - OR=2.45, 95% CI: 1.1-5.47), and chefs and cooks (large cell - OR=2.95, 95% CI: 1.08-8.1).

**Conclusion**: Most of our findings are consistent with the existing literature on known occupational risk factors for lung cancer. However, the high risk in medical workers, electricians, carpenters, bakers, and chefs and cooks requires attention in future studies. Potential exposures to specific agents within these occupational groups which warrant further evaluation include: formaldehyde, radiation, electromagnetic fields, wood dust, and cooking fumes. Since our attempt to apply the NIOSH-JEM to estimate exposures to specific agents present in the occupational environment was unsuccessful due to several logistical difficulties and the potential for bias, we recommend the development of a Canadian JEM.

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# 1. Introduction

Lung cancer is the most common cancer and leading cause of cancer mortality in the world (1;2). In Canada, lung cancer is the leading cause of cancer mortality, with an estimated 10,700 deaths in males (29% of the total cancer deaths) and 8600 deaths in females (26% of the total cancer deaths) for the year 2006 (3). The five-year survival rate for lung cancer in Canada is 16%, based on the cases diagnosed from 1995-1997 (3). The high incidence rate and poor survival rate for lung cancer demonstrates the need for primary prevention.

Epidemiological research has contributed greatly towards identification of the determinants of lung cancer. One major contribution was identifying cigarette smoking as the major causative factor for lung cancer. It is estimated that 90% (about 5/6th) of the lung cancer cases in the United States and Canada can be attributed to smoking (4;5). However, Doll and Peto in 1981, reported that occupational factors also contribute to the etiology of lung cancer, attributing one-sixth of the lung cancers in men to occupational factors (6). Other recent studies have attributed 9% of lung cancer cases to occupational factors (7;8).

Occupational studies have contributed greatly towards the identification of many carcinogenic substances. The first occupational carcinogen was identified by Percival Pott in 1775, who noted an excess of scrotal cancer among chimney sweeps (9;10). He attributed soot deposition on the scrotum as the cause of the elevated cancer risk (10). Asbestos has been found to contribute to the high lung cancer risk among British textile workers and American ship yard workers (11-13). Most of the carcinogens that have been identified in occupational settings have been associated with excess risk of lung cancer

(14;15). Several occupational groups (including metal workers, cleaners, painters, bakers, and wood workers) and industries (highway construction, textile, and water treatment plants) at high risk of lung cancer have been consistently identified in studies across the globe (7;14;16-37). Identification of these occupational risk factors has prompted regulatory changes to improve work-place hygiene (9).

Many occupational lung carcinogens have been identified to date, including: asbestos, hexavalent chromium, arsenic, radon, beryllium, silica, cadmium, and some nickel compounds (8;14;27;38-51), as well as acrylonitrite, nickel dust, and cobalt (38;46;52-54). Epidemiological evidence for an increased risk of lung cancer in relation to exposure to wood pulp, cotton dust, non-arsenical insecticides has been inconsistent (38;46). Further discussion of occupational risk factors for lung cancer is provided in the literature review section.

The purpose of this study is to identify high-risk occupations and industries in British Columbia, thereby contributing to current scientific knowledge about occupational risk factors for lung cancer. In this section, a general overview of pathology, pathophysiology, clinical features, and descriptive epidemiology of lung cancer is provided. The known risk factors for lung cancer are described in the literature review section.

## *1.1 Histopathology*

Tumors arising from the respiratory epithelium constitute lung cancer. The major histological types of lung cancer (accounting for 88% of all primary lung tumours) are squamous cell carcinoma, small cell (oat cell) carcinoma, adenocarcinoma (including bronchioloalveolar carcinoma), and large cell carcinoma (55). Other histological types include: undifferentiated carcinomas, carcinoids, and bronchial gland tumors (including adenoid cystic carcinomas and mucoepidermoid tumors). Adenocarcinoma has recently replaced squamous cell carcinoma as most common histological type of lung cancer (55). Squamous cell and small cell cancers usually present as central masses with endobronchial growth, whereas adenocarcinoma and large cell cancers present as peripheral nodules or masses. Cavitation is observed in approximately 10-20% of squamous and large cell cancer cases (55).

Different histological types have different natural histories and responses to therapy (55). Major treatment decisions are made based on whether the lung cancer is either of the small cell or non-small cell type (squamous cell, or adenocarcinoma including bronchioloalveolar type, large cell, and mixed types). Small cell carcinomas are primarily treated with chemotherapy with or without radiotherapy, whereas non-small cell carcinomas (usually localized at the time of presentation) are treated with surgery or radiotherapy (55). The knowledge of specific risk factors for a histological type of lung cancer is essential for filling the gaps in the natural history, thereby aiding in formulation of better preventive strategies.

### *1.2 Pathophysiology*

The pathophysiology of lung cancer development is incompletely understood. Tumor development is most commonly triggered by repetitive carcinogenic stimuli, inflammation, or irritation of the mucosal lining, leading to a slow transformation of normal cells to malignant cells (56). A series of biological changes occur, starting with cellular proliferation and hyperplasia followed by cellular metaplasia and dysplasia resulting in atypical cell formation that eventually leads to carcinoma in-situ and invasive cancer (56).

Recent advances in molecular biology have identified certain genetic alterations associated with lung cancer. The abnormal genes could be somatic (mutations in somatic cell lines from exposure to chemicals or radiation) or germline (inherited from parents). A dynamic interaction exists between dominant oncogenes (proto-oncogene) that regulate cell growth and development, and tumour suppressor genes that check cell proliferation within a cell (57). Major molecular abnormalities in the pathogenesis of lung cancer include activation of proto-oncogenes (by DNA amplification, translocation and point mutations), expression of growth factors and their receptors, loss of tumour suppressor genes (p53, p16, adenomatous polyposis coli gene etc), aberrant methylation resulting in loss of gene expression, activation of tumour-stimulated angiogenesis for tumour growth, expression of telomerase activity and cellular immortality, loss of components of apoptosis pathways, and loss of DNA repair mechanisms (57).

## *1.3 Clinical features*

Most patients with lung cancer are symptomatic, although 5-15% of patients are asymptomatic, and identified from a routine chest radiograph. The signs and symptoms experienced by lung cancer cases include: local tumor growth, invasion or obstruction of adjacent structures, growth in regional nodes (via lymphatic spread), growth in distant metastatic sites (haematogenous dissemination), and the remote effects of tumor products (paraneoplastic syndrome) (55).

Primary central tumors (endobronchial) may cause cough, haemoptysis, wheeze and stridor, dyspnoea, and post-obstructive pneumonitis (fever and productive cough).

Primary peripheral tumours may lead to pain, cough, dyspnoea, and symptoms of lung abscess due to tumour cavitation. Local spread of the tumor in the thorax (contiguous growth or lymph node extension) may lead to tracheal obstruction, esophageal compression (resulting in dysphagia), recurrent laryngeal nerve paralysis (resulting in hoarseness of voice), phrenic nerve paralysis (resulting in elevation of the hemi-diaphragm and dyspnoea), and sympathetic nerve paralysis (resulting in Horner's syndrome). Local spread of the tumor growing in the apex of the lung results in Pancoast's syndrome (involving the eighth cervical and first and second thoracic nerves, leading to shoulder pain that radiates in the ulnar distribution of the arm). Local spread of the tumor can also produce other effects including: superior vena cava syndrome (from vascular obstruction); cardiac tamponade, arrhythmia, or cardiac failure (from pericardial and cardiac extension); pleural effusion (from lymphatic obstruction); or hypoxemia and dyspnoea (from lymphangitic spread). Transbronchial spread of bronchioloalveolar carcinoma leads to the tumor growing along multiple alveolar surfaces resulting in impairment of gas exchange, respiratory insufficiency, dyspnoea, hypoxemia, and sputum production.

Lung cancer metastasis can occur to any organ system. The clinical manifestations depend on the site involved (such as neurological deficits due to brain metastasis). Lung cancer may also present with paraneoplastic syndromes, and certain skeletal & connective tissue syndromes (clubbing and hypertrophic pulmonary osteoarthropathy).

## *1.4 Descriptive Epidemiology of Lung Cancer*

A full review of the lung cancer literature is beyond the scope of this thesis. Information for this section is primarily derived from three secondary sources: the text *Cancer Epidemiology* by Schottenfeld & Fraumeni (46), monographs published by the International Agency for Research on Cancer monographs (15;58), and a recent review by Alberg & Samet (4).

Lung cancer is the most common cancer in the world with 1.35 million new cases in 2002, representing 12.4% of total incident cancers (1;2). Moreover, it is the leading cause of cancer death in the world with 1.18 million deaths (17.6% of the world total) (1;2). It is estimated that, 14.8% of the total incident cancers in Canada in 2006 were lung cancers. Lung cancer is the leading cause of cancer deaths in Canada accounting for an estimated 27.4% of all cancer deaths (3).

### 1.4.1 Geographic Variation

The incidence and mortality of lung cancer varies across the globe. Table-1 provides annual age adjusted rates (relative to a standard world population) per 100,000 people derived from the GLOBOCAN 2002 database based on the data from the 1990's (2). The highest annual age standardized incidence rates for males have been reported in North America (61.2 per 100,000 person-years) and Eastern Europe (65.7 per 100,000 person-years), while the lowest incidence rates are in Western Africa (2.4 per 100,000 person-years) and Eastern Africa (3.6 per 100,000 person-years). There was a similar pattern in females: the highest incidence rates were predominantly noted in North America (35.6/100,000 person-years), while the lowest rates were reported in Eastern and North African women (2.2/100,000 person-years).

**Table 1:** Annual Age-adjusted Lung Cancer Incidence Rates Among Males in Selected Countries

| **Lung Cancer Incidence (per 100,000 person-years*)** | | | | |
|---|---|---|---|---|
| **<10** | **10-25** | **26-50** | **51-75** | **>75** |
| Fiji | Saudi Arabia | Thailand | Philippines | Belgium |
| Sudan | Peru | Caribbean | France | Croatia |
| Nigeria | Nepal | Israel | Korean Republic | Kazakhstan |
| Ethiopia | Zimbabwe | Vietnam | Spain | Poland |
| Cameroon | U.A.E | Malaysia | **Canada** | Hungary |
| Uganda | Mauritius | Portugal | Italy | |
| Kenya | Mexico | Norway | Greece | |
| Namibia | Venezuela | New Zealand | Ukraine | |
| Iran | Puerto Rico | Georgia | Netherlands | |
| Egypt | Indonesia | Japan | **U.S.A** | |
| India | Sweden | Australia | Czech republic | |
| Sri Lanka | Brazil | Cuba | Russian Federation | |
| | Iraq | China | Slovakia | |
| | South African Republic | Austria | | |
| | | Argentina | | |
| | | Switzerland | | |
| | | Denmark | | |
| | | Singapore | | |
| | | Germany | | |
| | | Turkey | | |
| | | U.K | | |
| | | Romania | | |

From *GLOBOCAN 2002* (2) and *Cancer Incidence in Five Continents, Vol. VIII* (58).
*Rates are based on the data in 1990's, relative to a standard world population; the countries are arranged in the ascending order of incidence within each group.

Country specific annual incidence rates in males were highest in Hungary (94.6/100,000 person-years) and lowest in Fiji (0.2/100,000 person-years) (2;58). The incidence rate for males in more developed nations (54.9/100,000 person-years) is almost two-fold higher than the rate in less developed nations (25.9/100,000 person-years).

A similar pattern was noted in females, with incidence rates of 17/100,000 person-years and 9.4/100,000 person-years in more developed and less developed nations, respectively.

The highest mortality rates were reported in Eastern Europe (59.7/100,000) for men and in North America for women (26.7/100,000) (2). In general, the mortality rates followed the pattern of the incidence rates. This is mainly due to the high case fatality rate of lung cancer (4).

Geographic variation in lung cancer incidence has also been noted within a country. In Canada, the age standardized incidence rates in males for the year 2001 were highest in Nunavut (241.3/100,000 person-years) and Quebec (102.6/100,000 person-years), while the rates were lowest in the provinces of Alberta (60.0/100,000 person-years) and British Columbia (60.5/100,000 person-years) (59). Similarly, age standardized mortality rates in males (for the year 2002) were highest in Nunavut (127.7/100,000) and Quebec (84.6/100,000), with the lowest rates in the provinces of Alberta (50.0/100,000) and British Columbia (51.0/100,000) (60).

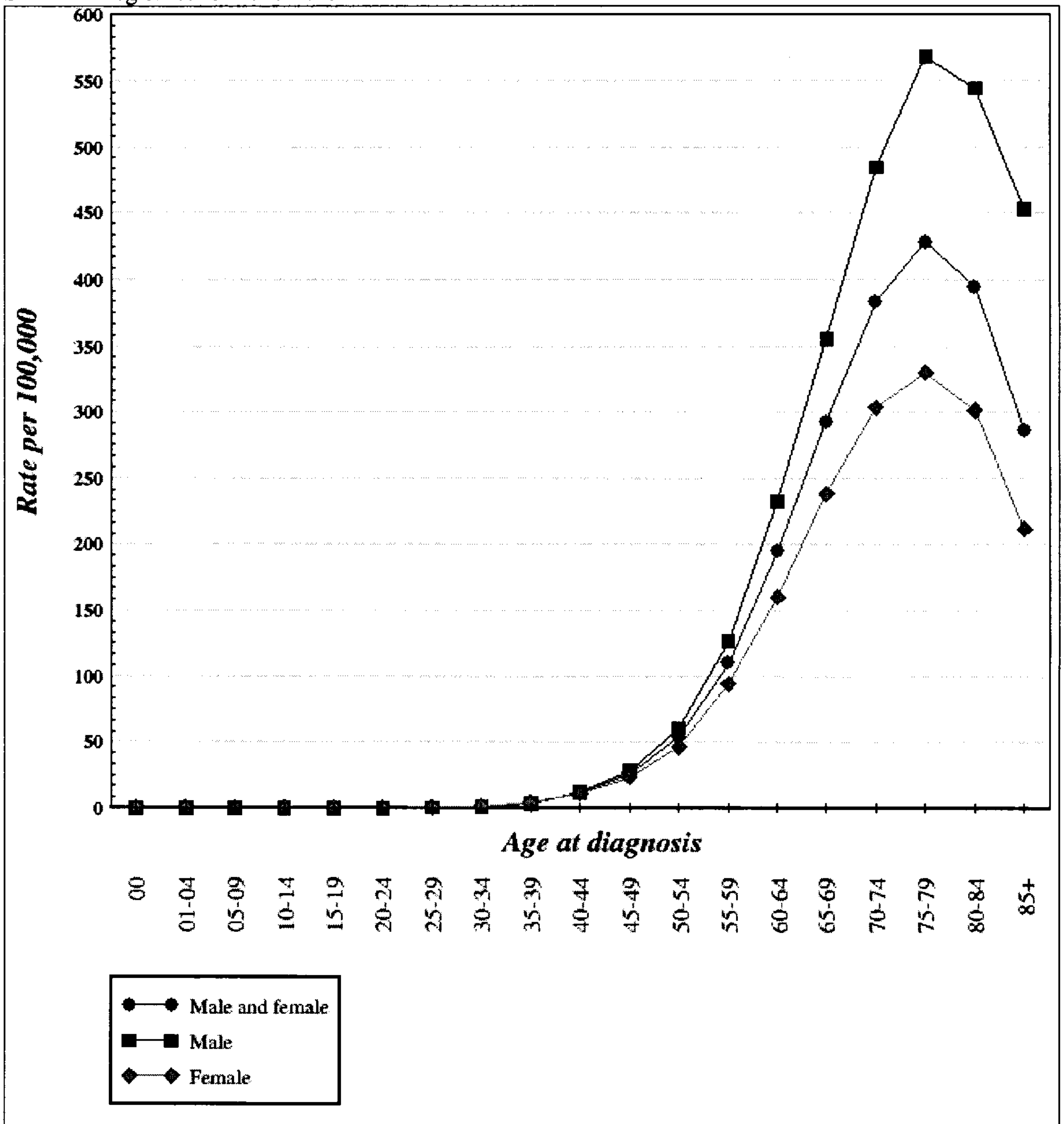
Higher rates of lung cancer were noted in urban areas than rural areas across the globe. This pattern of lung cancer is related to the patterns of smoking in urban and rural areas (6). A recent study in Scotland noted higher standardized incidence ratios for lung cancer in urban (SIR=124.5) as compared to rural (SIR=63.8) areas (61). The authors hypothesized that these results may be due to variations in air pollution, occupational differences and selective migration between urban and rural areas, in addition to the differences in the smoking behavior between urban and rural areas (62). Regional variation in lung cancer rates can provide clues as to the etiology of this disease. For example, the high rates of lung cancer observed in the U.S Atlantic and Gulf coasts during 1960s and 1970s lead to series of studies resulting in the identification of excess risk of lung cancer in shipyard workers exposed to asbestos (4;12;13;46).

### 1.4.2 Gender and Age

Overall, the world age standardized annual incidence rates of lung cancer in men and women were 35.5 and 12.1 per 100,000 person-years, respectively in the 1990s (2). The 3 fold excess risk of lung cancer in men has been attributed to higher smoking rates in males as compared to females. With an increase in smoking among women, these gender differences have been narrowing (46). In Canada, lung cancer incidence and mortality rates have been rising in women while the rates, in men are now decreasing (3). In the year 2001, 15.9 % of all new cancer cases in men were lung cancers, as were 12.9%of all lung cancer cases in women. Moreover, lung cancer is the leading cause of cancer deaths with an estimated 10,185 deaths in males (29.6% of the total cancer deaths in males) and 6998 deaths in females (22.8% of the total cancer deaths in females) for the year 2002 in Canada (3). The five-year relative survival rates for lung cancer cases in Canada is 14% and 18% in men and women, respectively (for the years 1995-1997) (3).

The incidence rates of lung cancer increases with age (Figure 1) (46;62). The drop in lung cancer incidence rates in men over 80 years and in women over 70 years of age could be due to a birth cohort effect.

**Figure 1:** Age-Specific (Crude) SEER Incidence Rates by Sex for Lung and Bronchus Cancer, All Races SEER 17 Registries for 2000-2003

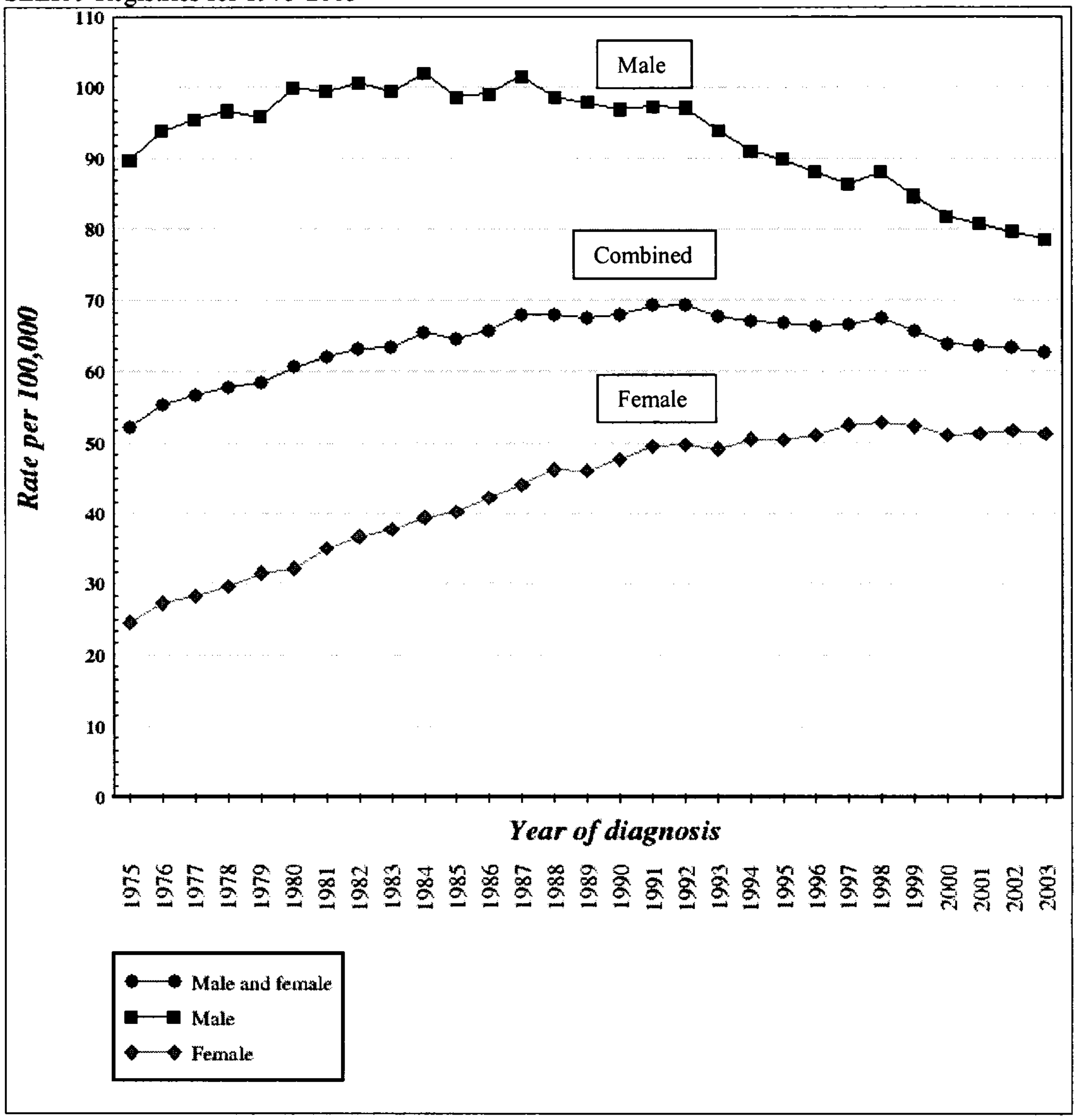



From: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 17 Regs Public-Use, Nov 2005 Sub (2000-2003), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2006, based on the November 2005 submission (62).

### 1.4.3 Temporal Trends

The epidemic of lung cancer in males began around 1930, when a dramatic increase in lung cancer rates became apparent. The epidemic in women started later (around the 1960s), with a sharp rise in lung cancer mortality (4;63). The age adjusted incidence rates for the period 1975-2003 based on the SEER 9 registries in the U.S are illustrated in Figure 2 (64). Lung cancer incidence rates began declining in men after 1985 while the rates in women continued to increase until at least 1998 (64). In Canada, the peak rates of lung cancer in males were attained in the mid-1980s, with a constant decline reported since then. This has been attributed to the decline in tobacco consumption in the 1960s. A 1.6% average annual decrease in age standardized incidence rates from 1992-2001 has been observed among men in Canada (3). In contrast, lung cancer rates continued to increase in Canadian women. An annual increase in the lung cancer incidence rate of 1.4% has been reported in females in Canada over the period 1993-2002 (3). Similar patterns have been noted in age-standardized lung cancer mortality rates in Canada (3). The annual percentage change in the incidence and mortality rates in the U.S are similar to those in Canada (65). Lung cancer rates are still rising in some countries, while age-adjusted mortality rates have been declining since the 1980s in England and Wales, Scotland, and Finland (46).

**Figure 2**: SEER Age-adjusted Incidence Rates by Sex for Lung and Bronchus Cancer, All Ages, All Races SEER 9 Registries for 1975-2003




Note: Age-adjusted to the 2000 U.S standard population.

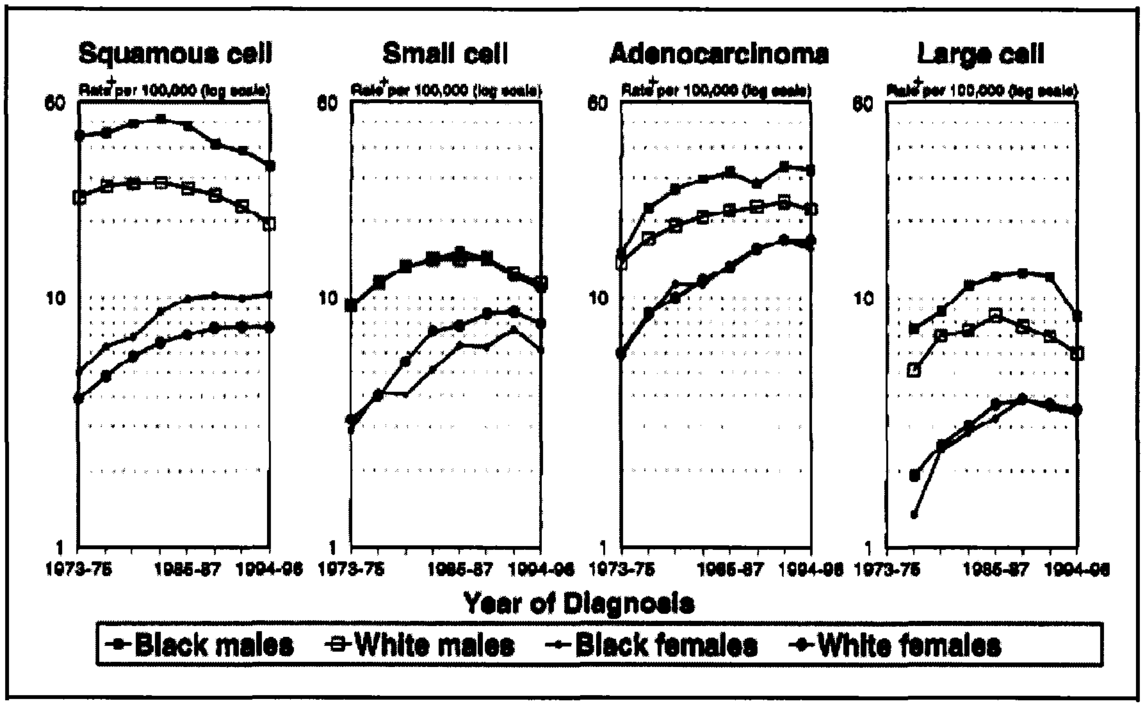
From: Surveillance, Epidemiology, and End Results (SEER) Program (www.seer.cancer.gov) SEER*Stat Database: Incidence - SEER 9 Regs Public-Use, Nov 2005 Sub (1973-2003), National Cancer Institute, DCCPS, Surveillance Research Program, Cancer Statistics Branch, released April 2006, based on the November 2005 submission (64).

### 1.4.4 Trends in the Histopathological Subtypes of Lung Cancer

Squamous cell carcinoma, small cell (oat cell) carcinoma, adenocarcinoma (including bronchioloalveolar carcinoma), and large cell carcinoma are the major histological types of lung cancer, accounting for 88% of all primary lung tumours (55). Squamous and small cell carcinomas are strongly related to smoking (46;66).

The SEER incidence rates of lung and bronchus cancer by histopathology subtypes, sex, race and ethnicity for all ages during 1973-1996 are illustrated in Figure 3 (67). Squamous cell cancer has been replaced by adenocarcinoma as most common cell type (46;67). Since the mid-1980s the incidence rates have been declining for squamous, small cell and large cell carcinomas in U.S men, although the incidence of adenocarcinoma did not peak until the early 1990s in males (67). In U.S women, the rates of squamous cell carcinoma stabilized in the late-1980s. A decrease in the incidence of large cell carcinoma was noted in the late 1980s, followed by a decrease in the incidence of small cell carcinoma in the early 1990s (67). This shift towards a preponderance of adenocarcinoma has been attributed to the change in the type of cigarettes smoked (specifically, low tar filtered cigarettes) rather than changes in the diagnostic practices (68).

**Figure 3**: SEER Incidence Rates of Lung and Bronchus Cancer by Histology Type, Sex, Race, and Ethnicity for All Ages (1973-1996)




From: Wingo PA, Ries LA, Giovino GA, Miller DS, Rosenberg HM, Shopland DR, Thun MJ, Edwards BK. Annual report to the nation on the status of cancer, 1973-1996, with a special section on lung cancer and tobacco smoking. *J Natl Cancer Inst* 1999; 91(8):675-90 (67).
(Reproduced with permission from JNCI)

### 1.4.5 Race, Ethnicity & Socioeconomic Patterns

The incidence of lung cancer is higher among African-American men than in white men (Figure 3) (4;46). In the U.S, incidence rates of 81.7 and 112.2 per 100,000 men per year has been reported in whites and blacks respectively, during the period 2000-2003 (65). In contrast, no such variation is seen in U.S women. Lung cancer incidence rates in white and black females were 54.7 and 53.1 per 100,000 person-years, respectively, during the period 2000-2003 (65). Similar patterns in lung cancer mortality rates are also seen in U.S men and women (65). Low rates of lung cancer were seen in Hispanic males, American Indians, and Japanese (46). Moreover, lower risk was also observed in Mormons and Seventh-Day Adventists among whom tobacco use is prohibited by their religion (46). An inverse relationship is observed between lung cancer mortality and socioeconomic status (46;69). Higher smoking rates and low education have been hypothesized to explain the higher rates of lung cancer among blue collar as compared to white collar workers (46).

# 2. Literature Review

## *2.1 Non-occupational Risk Factors*

In this section, a brief description of smoking and other non-occupational risk factors is provided. Due to the extensive literature on this topic, we have relied primarily on secondary sources for this review, mainly the text *Cancer Epidemiology* by Schottenfeld & Fraumeni (46).

### 2.1.1 Smoking

The U.S. Surgeon General declared smoking to be a cause of lung cancer in 1964 (70). In a recent IARC monograph, tobacco smoking and tobacco smoke were identified as being carcinogenic to humans (71). Cigarette smoking is the leading causative factor for lung cancer, contributing to approximately 90% of all lung cancer cases in the U.S. and other countries where smoking is common (4;5;71). Trends in lung cancer rates reflect trends in the smoking patterns with a lag period of about 20 years. As a consequence, the reduced consumption of tobacco in the mid-1960s among Canadian men is reflected in the declining incidence rates of lung cancer in the mid-1980s (3).

Numerous toxic compounds have been identified in tobacco smoke. Out of 4,800 compounds present in tobacco smoke, 69 carcinogens (e.g., PAH, aromatic amines, and formaldehyde) and several tumor promoters or co-carcinogens have been identified (72). Major toxic agents in tobacco smoke include nicotine, carbon monoxide, hydrogen cyanide, nitrogen oxides, some volatile aldehydes, alkenes, and aromatic hydrocarbons (72).

Three large cohort studies conducted in the U.S (73;74) and Britain (75) have found a consistent increase in lung cancer mortality with the number of cigarettes smoked; the relative risks (RR) of death in males from these studies are summarized in Table 2 (adapted from (46)). A 20-fold increase in the risk of lung cancer has been observed in heavy smokers (2 or more packs per day), as compared to non-smokers (46). Similarly, a 20-fold excess risk of lung cancer was observed among women in the American Cancer Society (ACS) cohort who smoked more than 30 cigarettes per day (46). The duration of smoking has also been shown to influence the risk of lung cancer, to a greater extent than the intensity of smoking (number of cigarettes smoked per day) (46;71;76). A large case-control study in China (1,400 cases and 1,500 controls) showed a 3 to 4-fold increase in lung cancer risk associated with a doubling in the intensity of smoking, whereas doubling in the duration of smoking increased the lung cancer risk by 4 to 5-fold (46;77); the relative risks from this study are summarized in Table 3 (adapted from (46)).

The composition of cigarettes has been changing since the 1950s. There has been a shift from non-filtered to filtered cigarettes and to low tar yielding varieties (4). Considerable changes in the design of cigarettes have also taken place. Ventilation holes for filtered cigarettes were introduced in the mid-1960s, with an intention to dilute the cigarette smoke (4).

The use of filtered and low tar yielding cigarettes has been associated with lower risk of lung cancer, as compared to non-filtered, high tar yielding varieties (46). A 1984 Western European study found a 40% lower risk in men and 20% lower risk in women for filtered cigarettes, as compared to non-filtered cigarettes (78). Although initial studies also reported a lower risk of lung cancer in low tar yielding cigarettes than high tar varieties, no such effect was reported in a later study in the U.S.A (46;78;79).

**Table 2:** Relative Risks of Death From Lung Cancer Among Male Smokers According to Number of Cigarettes Smoked

| Number of Cigarettes Smoked Per Day | American Cancer Society (ACS) Volunteers | United States Veterans | British Physicians |
|---|---|---|---|
| Nonsmokers[a] | 1.0 | 1.0 | 1.0 |
| Current cigarette smokers[b] | 9.2 | 11.6 | 14.9 |
| 1-9 | 4.6 | 3.7 | 7.5 |
| 10-19 | 8.6 | 9.9 | 14.9 |
| 20-39 | 14.7 | 16.9 | 25.4 |
| 40+ | 18.8 | 22.9 | |

[a]Did not smoke any form of tobacco.

[b]Classification refers to ACS study. The categories for U.S veterans were 1-9, 10-20, 21-39, and 40+, and for British Physicians were 1-14, 15-24, and 25+ per day. Only current smokers included.

From: Schottenfeld D, Fraumeni JF J. Cancer epidemiology and prevention. New York: Oxford University Press; 1996 (46). (Reproduced with permission from OUP)

**Table 3:** Relative Risks of Lung Cancer Among Chinese Men Associated with Intensity and Duration of Cigarette Smoking*

| | Duration of Smoking (Years) | | |
|---|---|---|---|
| Number of Cigarettes Smoked Per Day | 1-29 | 30-39 | 40+ |
| 1-19 | 0.9 | 3.2 | 3.8 |
| 20-29 | 2.1 | 7.1 | 7.2 |
| 30+ | 3.0 | 10.8 | 15.4 |

*Reference group-Lifelong nonsmokers.

From: Schottenfeld D, Fraumeni JF J. Cancer epidemiology and prevention. New York: Oxford University Press; 1996 (46). (Reproduced with permission from OUP)

The Institute of Medicine concluded that low tar yielding varieties have not resulted in decreased tobacco related harm (80). In addition, a recent National Cancer Institute monograph on smoking low tar yielding cigarettes concluded that no public health benefit had been achieved by cigarette design changes (81). Compensatory maneuvers adopted by the habitual smokers, such as increase in the intensity and depth of inhalation, and the increased nitrate concentration in U.S. blended cigarettes have been hypothesized to explain this effect (72). While a reduction in the health risk of newer cigarettes is debatable, cessation of smoking has proved to benefit smokers (46;71;82;83). However, lung cancer risk does not completely decline to the levels in non-smokers with the cessation of smoking (82;83).

An increased risk of lung cancer has also been observed among pipe and cigar smokers (46). However, the risk of lung cancer associated with cigar or pipe smoking is less than the risk associated with cigarette smoking; relative risks were approximately 2 in the ACS and U.S veterans' studies (46;73;74).

Changes in smoking mechanics related to the introduction of filter cigarettes have been implicated in the increased incidence of adenocarcinoma of lung (4;68;84). The use of filter cigarettes leads to smaller smoke particles and to increased puff volumes and a more peripheral deposition of tobacco smoke in the airways (4). The increased nitrate content in U.S. blend low tar cigarettes have reduced the concentrations of polycyclic aromatic hydrocarbons in cigarette smoke, although an increase in nitrosamine formation has been observed. A tobacco specific nitrosamine, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), has been implicated in the observed increase in adenocarcinoma rates

(84). The evidence has been inconclusive for the alternative explanations (such as hormonal factors) offered in the literature (4).

### 2.1.2 Passive Smoking

Passive smoking was first suggested as possible risk factor for lung cancer in 1981 (4;46). The smoke inhaled by the passive smokers is referred as 'environmental tobacco smoke' or ETS. ETS contains toxic substances including mutagens and carcinogens (e.g., 4-aminobiphenyl, nitrosamines). Nitrosamines were found in greater quantity in ETS than in the smoke inhaled directly by smokers (46). About 30% of the workplaces in the United States still allowed smoking and hence exposure to ETS (85). Considering the large number of workers exposed, ETS is an important occupational exposure (86;87). Initial evidence of lung cancer risk due to ETS exposure came from studies on spouses of smokers (88-90). A study in Japan reported a relative risk of 1.9 for lung cancer among non-smoking spouses of heavy smoking husbands (88). Similar results were also observed in a study in Athens (89). A review conducted by the U.S National Cancer Institute concluded that non-smoking spouses of smoking husbands were about 30% more likely to develop lung cancer than non-smoking spouses of non-smoking husbands (90). In 1986, a US Surgeon General's Report concluded that involuntary smoking (passive smoking) caused lung cancer (91). In a meta-analysis published in the year 2002, an RR of 1.25 (95% confidence interval (CI): 1.15-1.37) was estimated for spousal ETS exposure, and an RR of 1.17 (95% CI: 1.04-1.32) for work place ETS exposure (92). A recent meta-analysis of 22 studies on non-smokers at workplace (published in the year 2007) yielded an estimated RR of 1.24 (95% CI: 1.18-1.29) for the workers exposed to ETS (87). The combined relative risk of lung cancer was doubled for highly exposed workers (RR=2.01, 95% CI: 1.33-2.6) (87). In addition, a strong dose-response relationship between ETS exposure and lung cancer was observed (87). These meta-analyses found a significant increase in lung cancer risk due to ETS in the workplace (87;92). In a 2004 review, the International Agency for Research on Cancer (IARC) concluded that exposure to ETS causes lung cancer, with an excess lung cancer risk of 20% in women and 30% in men (71).

### 2.1.3 Outdoor Air Pollution

Outdoor air pollution has been attributed to 1-2% of lung cancer cases (93). Air pollution is mainly caused by motor vehicle emissions containing various particulate and gaseous substances including substances with carcinogenic potential (9). Other sources of air pollution include: industrial emissions, residential and commercial space heating, and oil & coal fired power plants. Recently, a reduction in the concentration of traditional air pollutants ($SO_2$ and smoke particles) from industrial emissions has been observed (9;46). Difficulties in estimating the exposure to air pollutants have limited epidemiologic investigations. However, the descriptive evidence has been consistent in linking air pollution to an increased risk of lung cancer (4). A relative risk of 1.5 (approx.) has been noted in studies comparing urban and rural residence (or high and low exposure to air pollution) (9). The Harvard Six Cities Study found an increased risk of lung cancer mortality in the most polluted city as compared to the least polluted city with respect to exposure to fine particulate matter (RR=1.37, 95% CI: 0.81-2.31) (94). In the ACS study, Pope and colleagues observed an increased risk of lung cancer mortality among people living in areas with high sulfate concentrations when compared to people living in the least polluted areas (RR=1.4, 95% CI: 1.1-1.7) (95). A reanalysis of the Harvard Six Cities Study and the ACS study has confirmed the original findings (96-98). Despite certain methodological problems, the evidence is strongly indicative of a relationship between outdoor air pollution and an excess risk of lung cancer (9;99).

### 2.1.4 Other Non-occupational Risk Factors

Heritable factors have been hypothesized in the familial aggregation of lung cancer (46). The epidemiological evidence showing family history as a predictive factor for lung cancer is supportive of this hypothesis (4). While a segregation analysis indicated a co-dominant inheritance pattern determining the early onset of tumors, a study on twins was not supportive of genetic susceptibility for lung tumors (46;100). The observed familial aggregation could also be due to aggregation of behavior (smoking) or other shared environmental exposures (such as ETS) (46).

Subjects with preexisting pulmonary diseases, including obstructive pulmonary diseases (chronic bronchitis, emphysema and pneumonia) and disorders leading to fibrosis (such as tuberculosis, asbestosis, and silicosis), have shown greater susceptibility to lung cancer (46). The evidence for the risk of lung cancer was fairly strong for tuberculosis (46). A 50% increase in lung cancer risk has been observed among tuberculosis patients in a case-control study in Shanghai (101).

The role of alcohol in the causation of lung cancer is controversial. In general, alcohol hasn't been considered as a risk factor for lung cancer (46). An IARC evaluation in 1988 concluded that alcohol consumption was not a causative factor for lung cancer (102). However, a recent meta-analysis has suggested an elevated risk of lung cancer with alcohol consumption. It estimated that the RR for the men consuming ≥30 g of alcohol per day was 1.2 (95% CI: 0.9-1.6) and that the RR for nonsmoking men consuming ≥15g of alcohol per day was 6.4 (95% CI: 2.7-14.9) when compared with never drinkers (103).

## *2.2 Occupations, Industries and Lung Cancer*

Several occupations and industries have been linked to an excess risk of lung cancer. In view of the voluminous literature on occupational risk factors for lung cancer, a detailed review of all the occupational circumstances is outside the scope of this thesis. For purposes of this review, we will draw heavily on a major review of occupational risk factors for lung cancer conducted by the IARC (14). In addition, we have summarized the evidence from selected studies to give a flavor of the epidemiological literature on occupational lung cancer, concentrating on relatively new studies (published after 1985), and studies with large sample size that have evaluated the risk of lung cancer for multiple occupations and industries.

The IARC monographs program was established in 1969, with an objective to publish critical reviews on the carcinogenicity of individual agents, mixtures, and specific circumstances to which humans are known to be exposed. For each identified agent, an international working group of experts is appointed to synthesize the available evidence from the epidemiological studies and experimental studies on humans and animals to determine the carcinogenicity of the exposure and to indicate where additional research efforts are needed. Based on the evidence, the agents, mixtures, or exposure circumstances are classified into one of five groups: definitely carcinogenic (Group 1), probably carcinogenic (Group 2A), possibly carcinogenic (Group 2B), not classifiable (Group 3), or probably not carcinogenic (Group 4). Several reviews have been published based on the IARC list of carcinogens (14;48;104). In a recent review of the IARC monographs, Siemiatycki and colleagues (14) identified 28 definite, 27 probable, and 113 possible occupational carcinogens which had been reviewed by IARC. In addition to 150 specific agents, this list also included 18 occupations or industries. In their review, Siemiatycki and colleagues specifically examined the lung cancer risk for the definite and probable carcinogens, including the carcinogenic occupational circumstances (14). This report was updated in 2005 by Rousseau et al (104). The results relevant to this thesis are summarized in Table 4.

### 2.2.1 Occupations as Risk Factors for Lung Cancer

In addition to the key secondary sources (14;104), our review identified 23 additional studies for review (including studies published after 1985 and those with large sample size) that have evaluated the risk of lung cancer for a range of occupations (7;16-21;24;26-37;105-107). Among the cohort studies that have observed an increased risk of lung cancer risk in various occupational groups (29;31-33;35;37), the confounding effect of smoking was adjusted for only a few studies (32). Many case-control studies have been conducted to evaluate the risk of lung cancer for specific occupations (7;16-21;24;26-28;30;34;36;105-107). The ability to adjust for confounding by potential risk factors and, to evaluate a wide range of occupations represent important advantages of case-control studies over cohort studies (26).

IARC examined 18 occupational circumstances/processes as risk factors for cancer. From this list, Siemiatycki and colleagues identified 10 occupational circumstances/processes which were risk factors for lung cancer, of which 2 were occupations ('painters', and 'hairdressers & barbers') while 8 were industries (see Table 4) (14). With respect to the two occupations identified by Siemiatycki et al, IARC classified one occupation as a definite carcinogen (painters) (108). Siemiatycki et al judged the evidence was strong for lung carcinogenicity in painters (14).

**Table 4:** Definite or Probable Occupational Carcinogens and Carcinogenic Circumstances for Lung Cancer.

| Strength of Evidence[a] | High-risk Substance or Circumstance[b] |
|---|---|
| **Strong** | ***Definite (Group-1):***<br>Occupational circumstances:<br>Aluminum production; coal gasification; coke production; hematite mining, underground, with radon exposure; iron and steel founding; painters;<br><br>Agents:<br>Arsenic and arsenic compounds; asbestos; beryllium; cadmium and cadmium compounds; chromium compounds, hexavalent; involuntary (passive) smoking; ionizing radiation; silica, crystalline; soots; talc containing asbestiform fibers; selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry;<br>Bis (chloromethyl) ether and chloromethyl ether (technical grade) [for Oat cell carcinoma only] |
| **Suggestive** | ***Definite (Group-1):***<br>Occupational circumstances:<br>Isopropanol manufacture (strong acid process); rubber industry;<br><br>Agents:<br>Coal tars and pitches; inorganic acid mists containing sulfuric acid; mineral oils (untreated and mildly treated); mustard gas; 2,3,7,8-tetrachlorodibenzo- para-dioxin (TCDD).<br><br>***Probable (Group-2A):***<br>Occupational circumstances:<br>Hairdressers and barbers; production of art glass, glass containers, and pressed ware.<br><br>Agents:<br>Benz[ a]anthracene; benzo[*a*]pyrene; α-chlorinated toluenes; dibenz[*a,h*]anthracene; diesel engine exhaust; epichlorohydrin; nonarsenical insecticides; cobalt metal with tungsten carbide; inorganic lead compounds. |

[a]Siemiatycki et al judgment of strength of evidence with lung cancer.
[b]IARC classification of carcinogenicity.

Extracted from Siemiatycki J, Richardson L, Straif K, Latreille B, Lakhani R, Campbell S, Rousseau MC, Boffetta P. Listing occupational carcinogens. *Environmental Health Perspectives.* Nov 2004; 112(15):1447-59 (14) and Rousseau MC, Straif K, Siemiatycki J. IARC carcinogen update. *Environmental Health Perspectives.* 2005; 113(9):A580-A581 (104) (with permission from Environmental Health Perspectives).

Painters are exposed to a wide range of potential carcinogens, including: petroleum solvents, toluene, xylene, ketones, alcohols, esters, and glycol ethers, titanium dioxide, chromium, asbestos, and silica (108). IARC classified the other occupation (hairdressers & barbers) as a probable carcinogen (Group 2A) (109). Siemiatycki et al judged that the evidence was suggestive of lung carcinogenicity for this occupation (14). Suspected key carcinogenic substances found in this occupation include: solvents, propellants, and aerosols.

Our review of recent articles identified a number of specific occupations which were not studied in the IARC monographs but which were potentially linked to lung cancer risk. Occupations involving processing of metals (including machining & fabricating tasks) have been identified as high risk occupations for lung cancer in several studies (7;17;18;24;26-36;107). Other occupations linked to lung cancer risk include: miners, drillers of oil wells, motor vehicle drivers, 'freight/material handlers & equipment operators', and various occupations in construction trades (7;17;20;21;24;26-35;37;52;54;105).

#### 2.2.1.1 At-risk Occupations Identified from the Recent Literature

Tables 5a (pg 27), 5b (pg 34) and 5c (pg 40) present detailed information abstracted from the identified studies. Occupations have been classified into 22 broad categories (alphabetically represented) and 53 specific categories (numerically represented) based on the 1980 Canadian Standard Occupational Classification (SOC) and the 1980 U.S Bureau of Census occupation codes (USCENOCC) (110;111). Related occupations are listed in the tables according to these groupings in order to take into account the use of different job titles among the various studies. The results from these studies are summarized in Table 6 (pg 46). [Continued on pg-47]

**Table 5a: Lung Cancer Risk by the Occupations (Studies 1-8)**

*Foot notes are provided in page-45 at the end of table-5c*

| | Study author ► | Aronson (33)‡ | NIOSH (31) | Lee (32) | Siemiatycki (26)§ | Spinelli (28) | Morabia (7) | Burns (34) | Zahm (21) |
|---|---|---|---|---|---|---|---|---|---|
| I | **Study features:** | | | | | | | | |
| | **Country/ Area, Published year** | Canada, 2000 | USA, 2003 | USA, 2006 | Montreal, 1991 | BC, Canada, 1990 | USA, 1992 | Detroit, 1991 | Missouri, 1989 |
| | **Study design** | Cohort mortality (1965-1991) | Cohort mortality (1999) | Cohort mortality (1986-1994) | Case-Control | Case-Control | Case-Control | Case-Control | Case-Control |
| | **Sample size** | 457,224 | NCHS data | 143,863 NHIS | 2217 | 6389 | 5221 | 9891 | 15,757 |
| | **Cases/Controls** | 116,000 total deaths | | 1812 cases | 857/1360 | 1687/4702 | 1793/3228 | 5935/3956 | 4431/11,326 |
| | **Gender (M/F/B)*** | B; only M reported | Both | M/F/B | M | M | M | Both | M |
| | **Total jobs studied** | 670 | COC all | 41 major; 27 specific groups | 98 | Not available | 102 | 43 | 51 |
| | **Type of controls** | | | | Cancer | Cancer | Cancer & non-cancer hospital controls | Cancer | Cancer |
| | **Job exposure/ reference jobs** | Ever (for 1 yr)/ other occupations in same class and sex | Usual | Ever | Ever (E) and substantial (S)/ Never | Usual/Never | Usual/Never | Usual/Selected list of jobs | Ever/Never |
| | **Analysis strategy** | Poisson regression | | Cox regression | Mantel-Haenszel | Logistic regression, Unconditional | Logistic regression, Unconditional | Logistic regression, Unconditional | Maximum likelihood by Gart's method |
| | **Risk measure†** | RR | PMR | Mortality Hazard ratio | Incidence OR (90% CI) | OR | OR | OR | OR |
| | **Confounders adjusted** | Age, calendar periods in 5 year groups | Age, sex, race | Age, smoking, sample weights & design effects | Age, smoking, family income, ethnicity, alcohol, respondent to the questionnaire | Age, year of diagnosis | Matched on age, smoking, geographic area, race, & questionnaire version | Age, race, smoking & gender | Age, smoking |
| II | **Occupational groups:** | | | | | | | | |
| A. | **Managerial administrative & related occupations** | NS | + | -ve | **na** | **-Ve** | **na** | **na** | **NS** |
| | *1. Managers & Administrators* | NS | Managers & administrators n.e.c 1.1 (1.0-1.1) | Managers & administrators 0.7 (0.5-0.9) | na | Administration 0.6 (0.4-0.8) | na | na | NS |
| B. | **Mining and quarrying including oil & gas field occupations** | + | + | **na** | **na** | + | **na** | + | **NS** |

| | Study author ► | Aronson (33)‡ | NIOSH (31) | Lee (32) | Siemiatycki (26)§ | Spinelli (28) | Morabia (7) | Burns (34) | Zahm (21) |
|---|---|---|---|---|---|---|---|---|---|
| | *2. Miners, general* | Miners n.e.c 1.4 (1.1-1.6) | na | na | na | Mining 2.8 (1.6-4.8) | na | Excavating and mining workers 4.0 (1.3-12.1) | NS |
| | *3. Foremen* | Foremen-mine, quarry & petroleum well 2.1 (1.5-3.0) | Related to below | na | na | na | na | na | NS |
| | *4. Drillers* | NS | Drillers, oil wells 1.7 ( 1.0-2.7) | na | na | na | na | na | NS |
| | *5. Machine operator* | NS | Mining machine operators 1.3 (1.1-1.4) | na | na | na | na | Machine operators 1.5 (1.1-2.18) | NS |
| **C.** | **Metal & related occupations (processing, machining, & fabricating)** | + | + | + | + | + | + | + | **NS** |
| | *6. Metal Processor* | NS | na | na | Metal processors 3.1 (1.4-7.0) (E) | Metal processing 2.8, 1.6-4.8 | Moulders, heat treaters, annealers & other heated metal workers 3.0 (1.3-7.1) | Furnace workers 3.1 (1.7-5.8) | NS |
| | *7. Moulders* | Moulders 2.0 (1.4-2.8) | na | na | na | na | Related to above | NS | na |
| | *8. Fabricators & Assemblers* | NS | Lay-out workers 2.5 (1.3-4.3) Precision metal assemblers 2.4 (1.3-4.0) | Precision production, includes metal 1.4 (1.0-1.9) | Metal product fabricators 2.7 (1.0-7.3) (S) | na | NS | Metal finishers 1.7 (1.2-2.3) | NS |
| | *9. Metal Machining (shaping, forming etc)* | NS | Sheet metal workers 1.3 (1.0-1.6) | Same as above | na | Machining 1.4 (1.0-2.0) | Sheet metal workers, tinsmiths 3.7 (1.5-9.2) | Related to the above job | NS |
| **D.** | **Processing, machining, fabricating, assembling occupations, General** | **NS** | + | + | **NS** | **na** | **na** | + | **NS** |
| | *10. Processing, general (granite, stone, paper etc)* | NS | Inspectors, testers, & graders 1.4 (1.0-1.8) Supervisors, production occupations 1.2 (1.1-1.3) | Precision production, includes metal 1.4 (1.0-1.9) | NS | na | na | Production inspectors 1.7 (1.2-2.5) | Na |

| | **Study author ▶** | **Aronson** (33)‡ | **NIOSH** (31) | **Lee** (32) | **Siemiatycki** (26)§ | **Spinelli** (28) | **Morabia** (7) | **Burns** (34) | **Zahm** (21) |
|---|---|---|---|---|---|---|---|---|---|
| | *11. Bakers* | NS | General bakers<br>4.6 (1.1-19) | na | na | May be related to Food preparation<br>1.4 (1.0-1.9) | na | na | na |
| | *12. Machine operator* | NS | Mixing and blending , machine operators<br>1.4 (1.0-1.9) | na | na | na | na | Machine operators<br>1.5 (1.1-2.18) | NS |
| | *13. Assemblers* | NS | Assemblers<br>1.1 (1.0-1.2)<br>Electrical & electronic equipment<br>1.4 (1.1-1.8) | NS | na | na | na | Assemblers<br>1.5 (1.2-1.9) | NS |
| **E.** | **Textile & related occupations** | **NS** | **na** | **na** | **na** | **na** | **NS** | **NS** | **NS** |
| | *14. Tailors & Textile workers* | NS | na | na | na | na | NS | NS | NS |
| **F.** | **Sales occupations** | **NS** | **+** | **-Ve** | **na** | **na** | **na** | **+** | **NS** |
| | *15. Buyers* | NS | Buyers, Whole sale & retail except farm products<br>1.5 (1.0-2.0) | na | na | na | na | na | na |
| | *16. Sales workers* | NS | na | Sales representatives, commodities, and finance<br>0.7 (0.4-1.0) | na | na | na | NS | NS |
| | *17. Other workers* | na | na | na | na | na | na | Driver sales<br>2.2 (1.1-4.3) | na |
| **G.** | **Clerical & related occupations** | **NS** | **+** | **+ & -ve** | **na** | **na** | **na** | **NS** | **NS** |
| | *18. Clerks & auditors* | NS | Bookkeeper, accounting, & auditing clerks<br>1.2 (1.1-1.4) | Financial records processing<br>1.8 (1.3-2.5) | na | na | na | NS | NS |
| | *19. Mail* | NS | na | Mail and message distributing<br>0.4 (0.2-1.0) | na | na | na | NS | NS |
| | *20. Others (Health records etc.)* | NS | Health record technologists & technicians<br>3.1 (1.0-7.3) | na | na | na | na | na | NS |
| **H.** | **Service occupations** | + | **+** | **NS** | **NS** | **+** | **NS** | **NS** | **+** |

| | Study author ▶ | Aronson (33)‡ | NIOSH (31) | Lee (32) | Siemiatycki (26)§ | Spinelli (28) | Morabia (7) | Burns (34) | Zahm (21) |
|---|---|---|---|---|---|---|---|---|---|
| | *21. Protection* | Guards and watchmen n.e.c 1.3 (1.2-1.5) | na | NS | NS | na | na | NS | Police, firemen, & protective services 1.6 (1.1-2.3) |
| | *22. Military* | NS | Military occupations 1.1 (1.1-1.2) | na | na | na | na | Armed services personnel 3.1 (1.4-7.1) | NS |
| | *23. Waiters* | Bartenders 1.6 (1.2-2.0) | Waiters & waitresses 1.4 (1.3-1.6) | NS | na | na | na | NS | Food services 1.8 (1.0-3.5) |
| | *24. Cooks* | Chefs & cooks 2.6 (1.3-5.2) | na | NS | na | Food preparation 1.4 (1.0-1.9) | na | NS | Related to above |
| | *25.Hair dressers & personal service* | NS | Hairdressers and cosmetologists 1.3 (1.1-1.4) Personal service occupations, n.e.c. 1.4 (1.1-1.8) | NS | na | na | na | NS | NS |
| | *26. Cleaners* | NS | Janitors & cleaners 1.1 (1.0-1.2) | NS | na | na | NS in a related occupation | NS | NS |
| **I.** | **Mechanics and Repairers** | + | + | + | + | **na** | **na** | + | + |
| | *27. Mechanics, General* | Foreman: mechanics & repairmen except electrical 1.9 (1.1-3.5) | Supervisors, mechanics & repairers 1.3 (1.0-1.5) Industrial machinery repairers 1.3 (1.1-1.5) Millwrights 1.3, 1.0-1.7 | Not specified mechanics & repairers 2.8 (1.3-6.0) | Mechanics (Broadly grouped) 1.6 (1.1-2.4 (S)) | na | na | Machine repairers 1.6 (1.0-2.5) | Mechanics & repairers 1.3 (1.0-1.7) |
| | *28.Electrical & Electronic equipment* | NS | Heating, air conditioning, and refrigeration mechanics 1.4 (1.1-1.8) | Heating, air conditioning, and refrigeration mechanics 3.0 (1.2-7.2) | Same as above | na | na | na | May be related to above |
| | *29. Automobile mechanics* | NS | Automobile mechanics 1.2 (1.0-1.3) | na | Same as above | na | na | Mechanics, motor vehicles 1.7 (1.2-2.6) | May be related to above |
| **J.** | **Construction trades occupations** | + | + | **na** | **NS** | **na** | + | **NS** | + |

| | Study author ▶ | Aronson (33)‡ | NIOSH (31) | Lee (32) | Siemiatycki (26)§ | Spinelli (28) | Morabia (7) | Burns (34) | Zahm (21) |
|---|---|---|---|---|---|---|---|---|---|
| | *30. Plumbers* | Plumbers and pipe fitters 1.2 (1.0-1.5) | Plumbers, pipe fitters, & steamfitters 1.2 (1.1-1.4) | na | na | na | na | NS | NS |
| | *31. Foremen, Supervisors, machine operators, & others* | General foreman, Construction 1.3 (1.0-1.6) | Supervisors: painters, paperhangers, & plasterers 1.5 (1.0-2.2) | na | NS | na | na | na | Painters, paperhangers, & plasterers 2.0 (1.2-3.3) |
| | *32. Insulators* | Insulation appliers 2.4 (1.5-4.0) | na | na | na | na | na | na | NS |
| | *33. Electricians* | NS | Electricians 1.2 (1.1-1.4) | NS | na | na | Electricians 1.7 (1.1-2.9) | NS | NS |
| | *34. Laborers* | NS | Construction laborers 1.2 (1.1-1.3) | na | NS | na | 0 | NS | NS |
| **K.** | **Painters** | **NS** | + | na | **na** | na | na | + | + |
| | *35. Painters, general* | NS | na | na | na | na | na | Painters 2.0 (1.2-3.1) | Painters, paperhangers, & plasterers 2.0 (1.2-3.3) |
| | *36. Painters, Construction* | NS | Painters, construction & maintenance 1.3 (1.1-1.4) | na | na | na | na | na | Related to above |
| **L.** | **Carpenters & wood workers** | **NS** | + | **na** | **na** | **na** | **na** | **na** | **NS** |
| | *37. Carpenters & Wood workers* | NS | Carpenters 1.2 (1.1-1.2) | na | na | na | na | na | NS |
| **M.** | **Welders and cutters** | **NS** | + | **na** | + | **na** | **NS** | **NS** | **NS** |
| | *38. Welders & cutter* | NS | Welders and cutters 1.2 (1.1-1.4) | na | Welders & flame cutters 1.6 (1.1-2.4) (E) | na | NS | NS | NS |
| **N.** | **Transportation & related occupations** | + | + | **NS** | **na** | **+ & -ve** | **NS** | + | + |
| | *39. Inspectors/ Foremen& others* | Inspectors & foremen 1.4 (1.1-1.7) Boiler firemen (except ship) 1.5 (1.1-2.1) | na | NS | na | na | na | NS in a related occupation | na |
| | *40. Rail transport* | NS | Railroad conductors & yard masters 1.4 (1.0-1.9) | na | na | Rail transport 0.5 (0.2-1.0) | na | na | NS |

| | Study author ▶ | Aronson (33)‡ | NIOSH (31) | Lee (32) | Siemiatycki (26)§ | Spinelli (28) | Morabia (7) | Burns (34) | Zahm (21) |
|---|---|---|---|---|---|---|---|---|---|
| | *41. Water transport* | NS | na | na | na | na | na | na | na |
| | *42. Motor transport* | Truck drivers 1.4 (1.2-1.5) | Truck drivers 1.2 (1.1-1.2) | NS | na | Motor transport 1.5 (1.1-2.1) | NS | Drivers 1.9 (1.4-2.6) | Motor vehicle drivers 1.5 (1.2-1.8) |
| **O.** | **Material moving & related occupations** | + | + | + | + | **Na** | + | **NS** | **NS** |
| | *43.Dockers & freight handlers* | Longshoremen, stevedores and freight handlers 2.1 (1.3-3.3) | See operating engineers | Freight, Stock, and Material Handlers 1.5, 1.1-2.1 | Dock workers 3.1, 1.2-8.0 (E) 9.6, 1.9-48.5 (S) | Na | NS | NS | 0 |
| | *44. Equipment operators& other handlers* | NS | na | Material moving equipment Operators 6.2, 1.4-27.3 (F) | Material handlers 2.5, 1.2-5.1 (S) | Na | Cranemen, derrickmen, & hoistmen 14.4 (1.8-114.2) | NS | 0 |
| **P.** | **Doctors, other medical & health related professions** | **NS** | **na** | **NS** | **na** | **-ve** | **na** | **NS** | **NS** |
| | *45. Medicine* | NS | na | NS | na | Medicine 0.5 (0.2-1.0) | na | NS | NS |
| **Q.** | **Engineers & related professions** | **NS** | + | **-ve** | **na** | **na** | **na** | **NS** | **NS** |
| | *46. Engineers* | NS | Operating engineers 1.2 (1.0-1.3) | Engineers 0.4 (0.2-0.9) | na | na | na | na | NS |
| **R.** | **Recreation, amusement & other service related occupations** | **NS** | + | **-ve** | **NS** | **na** | **na** | **na** | **NS** |
| | *47.Artists, Writers etc* | NS | Attendants, amusement and recreational facilities 1.7 (1.3-2.3) | Writers, artists, entertainers, & athletes 0.3 (0.1-0.8) | NS | na | na | na | NS |
| **S.** | **Agriculture, forestry & related occupation** | **NS** | **na** | **NS** | **na** | **-ve** | **na** | + | **NS** |
| | *48. Farmers* | NS | na | NS | na | Farmers 0.6 (0.5-0.8) | na | Agricultural workers 2.1 (1.2-3.4) | NS |
| | *49. Forestry workers* | NS | na | NS | na | Forestry 0.7 (0.5-1.0) | na | na | NS |
| **T.** | **Printing & related occupations** | **NS** | **na** | **NS** | + | **na** | + | **NS** | **NS** |

| | Study author ▶ | Aronson (33)‡ | NIOSH (31) | Lee (32) | Siemiatycki (26)§ | Spinelli (28) | Morabia (7) | Burns (34) | Zahm (21) |
|---|---|---|---|---|---|---|---|---|---|
| | *50. Printers* | NS | na | NS | Printers 2.1 (1.2-3.7) (E) | na | Bookbinders & related printing trade workers 3.3 (1.2-8.9) | NS | NS |
| | *51.Press & other workers* | NS | na | NS | Printing press workers 3.1 (1.3-7.3) (E) | na | Same as above | NS | NS |
| **U.** | **Teaching & related occupations** | **NS** | **na** | **NS** | **NS** | **na** | **na** | **na** | **-ve** |
| | *52. Teachers* | NS | na | NS | NS | na | na | na | Teachers 0.5 (0.3-0.8) |
| **V.** | **Other occupations** | + | **na** | **na** | **na** | **na** | **na** | **na** | **na** |
| | *53. Others* | Supervisors and Foremen, n.e.c. 3.2 (1.4-7.0) | na | na | na | na | na | na | na |

**Table 5b: Lung Cancer Risk by the Occupations (continued) (Studies 9-16)**

| | Study author ▶ | Schoenberg (106) | Richiardi (18) | Elci (20) | Bruske-Hohlfeld (27) | Jockel (30)†† | Matos (16) | Pezzotto (17)‡‡ | Sankila (29) |
|---|---|---|---|---|---|---|---|---|---|
| I | **Study features:** | | | | | | | | |
| | **Country/ Area, Published year** | New Jersey, 1987 | Italy, 2004 | Turkey, 2003 | Germany, 2000 | West Germany, 1998 | Buenos Aires, Argentina, 2000 | Rosario, Argentina, 1999 | Finland, 1989 |
| | **Study design** | Case-control | Case-Control | Case-Control | Case-Control, pooled | Case-Control | Case-Control | Case-Control | Cohort incidence (1971-1980) |
| | **Sample size** | 1663 | 2209 | 2873 | 7039 | 2008 | 592 | 943 | 6878 total cases |
| | **Cases/Controls** | 763/900 | 956/1253 | 1354/1519 | 3498/3541 | 1004/1004 | 199/393 | 367/576 | 3178 cases in 38 high risk occupations |
| | **Gender (M/F/B)*** | M | Reported M not B | M | M | Reported M not B | M | M | M |
| | **Total jobs studied** | 42 | About 109 jobs studied; 47 reported; | 27 | 33 | 32 grouped; 111 specific (Sp) | 30 titles reported | 13 broad groups | 39 |
| | **Type of controls** | Population | Population | Cancer | Population | Population | Hospital controls | Hospital controls | |
| | **Job exposure/ reference jobs** | Ever/ Never | Ever/ Selected list of jobs | Ever/Never | Ever/Never | Ever/Never | Ever/Never | Ever/ Selected list of occupations with out cancer risk | Ever/ Never |
| | **Analysis strategy** | Mantel-Haenszel | Logistic regression, Unconditional | Logistic regression, Unconditional | Logistic regression, Conditional | Logistic regression, Conditional | Logistic regression, Unconditional | Logistic regression | Poisson |
| | **Risk measure†** | OR | OR | OR | OR | OR | OR | OR | SIR |
| | **Confounders adjusted** | Smoking | Age, study area, smoking, number of job periods, and education. | Age, smoking | Matched on age, region; Adjusted for smoking, asbestos exposure | Matched on age, sex, region; adjusted for smoking & asbestos | Matched on age & hospital; adjusted for age group, hospital, smoking, & other occupations with $P<0.05$ | Age, smoking habit, & lifelong cigarette consumption | Standardized by age |
| II | **Occupational groups:** | | | | | | | | |
| A. | **Managerial administrative & related occupations** | **na** | **na** | **NS** | **-ve** | **-ve** | **na** | **na** | **na** |
| | *1. Managers & Administrators* | na | na | NS | Administrative & clerical worker 0.7 (0.6-0.7) | Administrative & clerical worker 0.6 ( 0.4-0.7) | na | na | na |

| | Study author ▶ | Schoenberg (106) | Richiardi (18) | Elci (20) | Bruske-Hohlfeld (27) | Jockel (30)†† | Matos (16) | Pezzotto (17)‡‡ | Sankila (29) |
|---|---|---|---|---|---|---|---|---|---|
| **B.** | **Mining and quarrying including oil & gas field occupations** | **na** | **NS** | **na** | + | **NS** | **na** | **na** | + |
| | *2. Miners, general* | na | NS | na | Miners & quarrymen 1.7 (1.3-2.0) | NS | na | na | Miners & quarriers 238 (191-293) |
| | *3. Foremen* | na | na | na | Related to above | NS | na | na | Related to above |
| | *4. Drillers* | na | na | na | Related to above | NS | na | na | Related to above |
| | *5. Machine operator* | na | na | na | Related to above | NS | na | na | Related to above |
| **C.** | **Metal & related occupations (processing, machining, & fabricating)** | **NS** | + | **NS** | + | + | **NS** | + | + |
| | *6. Metal Processor* | NS | Processing, Various nonferrous metals 1.8 (1.1-3.0) | NS | Metal producers & processors 1.4 (1.2-1.7) | Metal production & processing workers 1.6 (1.2-2.2) | NS | Agric-MTFW ‡‡ (Broad group) 4.1 (2.0-8.1) | Other occupations in metal industry 138 (106-176) |
| | *7. Moulders* | NS | na | NS | Related to above | Related to above | na | Related to above | NS for Foundry workers |
| | *8. Fabricators & Assemblers* | NS | Na | NS | NS in a related job | NS in a related job | NS | Related to above | Service & repairmen in metal industry 123 (103-146) NS - blacksmiths |
| | *9. Metal Machining (shaping, forming etc)* | NS | NS | NS | NS in a related job | Sheet metal workers (Sp) 2.0 (1.1-3.6) | NS | Related to above | Thin sheet metal workers 170 (133-214) Machinists 119 (100-142) |
| **D.** | **Processing, machining, fabricating, assembling occupations, General** | **NS** | + | **NS** | + | + | **NS** | **NS** | + & **NS** |
| | *10. Processing, general (granite, stone, paper etc)* | NS | NS | NS | Chemical processors 1.6 (1.1-2.1) | NS (G) Plastic processing worker (Sp) 3.5 (1.1-11.4) | NS | NS for butchers; NS for leather workers | Pulp workers 174 (124-238) NS for stone cutters |
| | *11. Bakers* | NS | General bakers 4.6 (1.1-19) | NS | NS in a related job | NS in a related job | na | na | NS |
| | *12. Machine operator* | NS | NS | NS | NS in a related job | NS in a related job | na | na | na |

| | Study author ▶ | Schoenberg (106) | Richiardi (18) | Elci (20) | Bruske-Hohlfeld (27) | Jockel (30)†† | Matos (16) | Pezzotto (17)‡‡ | Sankila (29) |
|---|---|---|---|---|---|---|---|---|---|
| | *13. Assemblers* | na | NS | NS | NS in a related job | NS in a related job | NS | na | na |
| **E.** | **Textile & related occupations** | **na** | + | + | **NS** | **NS** | **NS** | **na** | **na** |
| | *14.Tailors & Textile workers* | na | Tailors 5.3 (1.0-30) | Textile workers 1.7 (1.1-2.0) | NS | NS | NS | na | na |
| **F.** | **Sales occupations** | **na** | **na** | **na** | **-ve** | **-Ve** | + | **na** | **NS** |
| | *15. Buyers* | na | na | na | na | na | na | na | na |
| | *16. Sales workers* | na | na | na | Sales workers 0.7 (0.6-0.9) | Sales workers 0.6 (0.5-0.9) | Sales workers (not street) 1.8 (1.1-3.5) | na | NS |
| | *17. Other workers* | na | na | na | na | na | na | na | na |
| **G.** | **Clerical & related occupations** | **na** | **NS** | **NS** | **NS & -Ve** | **NS & -ve** | **na** | **na** | **na** |
| | *18.Clerks & auditors* | na | NS | NS | NS | NS | na | na | na |
| | *19. Mail* | na | na | na | na | na | na | na | na |
| | *20.Others (Health records etc.)* | na | na | NS | Administrative and clerical workers 0.7 (0.6-0.7) | Administrative & clerical workers 0.6 (0.4-0.7) | na | na | na |
| **H.** | **Service occupations** | **+ & NS** | **NS** | **+ , -ve & NS** | **+** | **NS** | **NS** | **na** | **NS** |
| | *21. Protection* | NS | na | Firefighters only 6.8 (1.3-37.4) | Protective service worker 0.9 (0.7-1.0) | NS | Na | Na | na |
| | *22. Military* | na | na | na | na | na | na | na | NS |
| | *23. Waiters* | NS | na | NS | Service worker (Broad group) 0.4 (0.3-0.5) | NS | NS | na | na |
| | *24. Cooks* | NS | na | na | Same as above | NS | NS | na | na |
| | *25.Hair dressers & personal service* | NS | na | na | Same as above | NS | na | na | na |
| | *26. Cleaners* | Janitors & cleaners 1.5 (1.1-2.1) | NS | Cleaners 0.6 (0.4-0.9) | Same as above | NS | NS | na | na |
| **I.** | **Mechanics and Repairers** | **NS** | **NS** | **NS** | **NS** | **NS** | + | + & NS | **NS** |
| | *27. Mechanics, General* | na | na | NS | NS | NS | na | NS for mechanics; Agric-MTFW ‡‡ (Broad group) 4.1 (2.0-8.1) | NS |

| | Study author ► | Schoenberg (106) | Richiardi (18) | Elci (20) | Bruske-Hohlfeld (27) | Jockel (30)†† | Matos (16) | Pezzotto (17)‡‡ | Sankila (29) |
|---|---|---|---|---|---|---|---|---|---|
| | *28. Electrical & Electronic equipment* | na | na | na | na | na | na | na | na |
| | *29. Automobile mechanics* | NS | NS | na | na | na | Motor vehicle mechanics 2.1 (1.0-4.5) | na | na |
| **J.** | **Construction trades occupations** | **NS** | **NS** | **NS** | + | **NS** | **NS** | + | + |
| | *30. Plumbers* | NS | NS | na | Pipe layers, road construction 1.2 (1.0-1.5) | NS (G) Pipe fitters (Sp) 2.8 (1.2-6.4) | NS | Construction workers (Broad group) 2.5 (1.0-5.9) Agric-Const 3.6 (1.1-12.4) | Plumbers 171 (138-209) |
| | *31. Foremen, Supervisors, machine operators, & others* | NS | NS | na | Stationary engine & heavy equipment operators 1.8 (1.4-2.3) Plasterers, insulators, and upholsterers 1.3 (1.0-1.8) | NS (G) Structural metal workers (Sp) 2.0 (1.1-3.6) | NS | Related to above jobs | Masons 166 (133-204) Construction machine drivers 172 (132-214) |
| | *32. Insulators* | NS | na | na | Related to above job | NS | na | Related to above jobs | Insulators 384 (261-544) Asphalt workers 396 (198-708) |
| | *33. Electricians* | NS | NS | NS | NS | NS | NS | Related to above jobs | NS |
| | *34. Laborers* | NS | na | NS | NS | NS | NS | Related to above jobs | Concrete workers 168 (126-220) Concrete reinforcers 174 (104-271) Helpers-construction 156 (138-177) Helpers-road constr 148 (127-171) |
| **K.** | **Painters** | **NS** | + | **na** | + | **NS** | **NS** | **NS** | + |
| | *35. Painters, general* | NS | Painters 1.7 (1.1-2.8) | na | Painters & lacquerer 1.4 (1.1-1.9) | NS | NS | na | Painters 127 (105-153) |
| | *36. Painters, Construction* | na | Painters in construction 1.7 (1.0-3.0) | na | Same as above | NS | NS | NS | na |

| | Study author ► | Schoenberg (106) | Richiardi (18) | Elci (20) | Bruske-Hohlfeld (27) | Jockel (30)†† | Matos (16) | Pezzotto (17)‡‡ | Sankila (29) |
|---|---|---|---|---|---|---|---|---|---|
| **L.** | **Carpenters & wood workers** | **NS** | **NS** | **NS** | + | **NS** | **NS** | **NS** | + |
| | *37. Carpenters & Wood workers* | NS | NS | NS | Brick layers & carpenters 1.3 (1.1-1.6) Cabinet maker & wood processing 1.4 (1.1-1.7) | NS | NS | NS | Carpenters 132 (120-144) NS for plywood workers |
| **M.** | **Welders and cutters** | **NS** | + | **NS** | + | + | **NS** | + & **NS** | + |
| | *38. Welders & cutter* | NS | Welders & flame cutters 5.0 (1.9-13) | NS | Related to Metal producers & processors 1.4 (1.2-1.7) | Welders (Sp) 1.9 (1.0-3.6 ) | NS | NS - Welders; Agric-MTFW ‡‡ (Broad group) 4.1 (2.0-8.1) | Welders 150 (114-195) |
| **N.** | **Transportation & related occupations** | **NS** | **-ve** | + | + | + | **NS** | + | + |
| | *39. Inspectors/ Foremen& others* | NS | na | na | Transport worker and freight handler 1.3 (1.1-1.5) | Transport worker and freight handler 1.5 (1.2-1.9) | na | na | na |
| | *40. Rail transport* | NS | NS | na | Related to the above job | Related to the above job | na | na | na |
| | *41. Water transport* | NS | na | NS | Related to the above job | Related to the above job | na | na | na |
| | *42. Motor transport* | NS | Motor vehicle drivers 0.4 (0.2-0.9) | Drivers 1.4 (1.1-2.0) | Related to the above job | Related to the above job | NS | Drivers 1.9 (1.1-4.0) | Vehicle drivers 116 (105-128) |
| **O.** | **Material moving & related occupations** | **NS** | **NS** | **NS** | + | + | **na** | **na** | + |
| | *43.Dockers & freight handlers* | na | NS | NS in a related job | Transport worker and freight handler 1.3 (1.1-1.5) | Transport worker and freight handler 1.5 (1.2-1.9) | na | na | Stevedores 153 (116-199) |
| | *44. Equipment operators& other handlers* | NS | NS | NS in a related job | Related to above | Related to above | na | na | na |
| **P.** | **Doctors, other medical & health related professions** | **na** | **na** | **na** | **-Ve** | **-Ve** | **na** | **na** | **na** |
| | *45. Medicine* | na | na | na | Medical, dental & veterinary workers 0.6 (0.4-0.9) | Medical, dental & veterinary workers 0.5 (0.2-1.0) | na | na | na |
| **Q.** | **Engineers & related professions** | **na** | **-ve** | **na** | **-Ve** | **NS** | **na** | **na** | **na** |

| | Study author ▶ | Schoenberg (106) | Richiardi (18) | Elci (20) | Bruske-Hohlfeld (27) | Jockel (30)†† | Matos (16) | Pezzotto (17)‡‡ | Sankila (29) |
|---|---|---|---|---|---|---|---|---|---|
| | *46. Engineers* | na | Draughtsmen 0.3 (0.1-0.9) | na | Architects, technicians, & engineers 0.6 (0.5-0.7) | NS (G) Engineer (Sp) 0.5 (0.2-1.0) | na | na | na |
| **R.** | **Recreation, amusement & other service related occupations** | **na** | **na** | **na** | **-Ve** | **NS** | **na** | **na** | **na** |
| | *47.Artists, Writers etc* | na | na | na | Journalist, jurist, artist 0.5 (0.3-0.6) | NS | na | na | na |
| **S.** | **Agriculture, forestry & related occupation** | **na** | **NS** | **NS** | + | **NS** | + | + | **-Ve & NS** |
| | *48. Farmers* | na | NS | NS | Farmers & agricultural workers 1.3 (1.1-1.5) | NS | Field crop workers 3.5 (1.1-10.5) | Agricultural workers 1.8 (1.1-3.1) | Farmers 73 (70-77) NS - Fur farmers |
| | *49. Forestry workers* | na | na | na | Fisherman, forestry&livestock 1.6 (1.2-2.1) | NS | na | na | Forestry workers 159 (143-178) |
| **T.** | **Printing & related occupations** | + | **NS** | **na** | **NS** | **NS** | **NS** | **NS** | **na** |
| | *50. Printers* | Printing workers 2.5 (1.0-6.1) | NS | na | NS | NS | NS | NS | na |
| | *51.Press & other workers* | Same as above | NS | na | NS | NS | na | na | na |
| **U.** | **Teaching & related occupations** | **na** | **NS** | **na** | **-Ve** | **-Ve** | **Na** | **Na** | **Na** |
| | *52. Teachers* | na | NS | na | Teachers, social workers &scientist 0.4 (0.3-0.5) | Teachers, social workers, & scientists 0.4 (0.2-0.7) | Na | Na | Na |
| **V.** | **Other occupations** | **na** | **na** | **na** | **na** | **na** | **na** | **na** | + |
| | *53. Others* | na | na | na | na | na | na | na | Unskilled workers 146 (124-172) Warehousemen,other 147 (101-208) |

**Table 5c: Lung Cancer Risk by the Occupations (continued) (Studies 17-23)**

| | **Study author ►** | **Notani** (19) | **Firth** (35) | **Levin** (36) | **Blair** (37) U.S Veterans | **Lerchen**(105) | **Menvielle** (24) | **Swanson** (107) ¥ White males | **Swanson** (107) ¥ Black males |
|---|---|---|---|---|---|---|---|---|---|
| **I** | **Study features:** | | | | | | | | |
| | **Country/ Area, Published year** | Bombay, India, 1993 | New Zealand, 1996 | Shanghai, 1988 | USA, 1985 | New Mexico, 1987 | New Caledonia, 2003 | Detroit, 1993 | Detroit, 1993 |
| | **Study design** | Case-Control | Cohort incidence (1972-1984) | Case-Control | Cohort mortality, veterans (1954-1970) | Case-control | Case-control | Case-control | Case-control |
| | **Sample size** | 458 | 26,207 cancer registrations | 1493 | 293,958 total cohort | 832 | 411 | 4462 | 1296 |
| | **Cases/Controls** | 246/212 | | 733/760 | 107,563 deaths | 333/499 | 175/236 | 2866/1596 | 926/370 |
| | **Gender (M/F/B)*** | M | M | M | | M | B; only M reported | White M | Black M |
| | **Total jobs studied** | 17 | 19 groups for all cancers; | 29 reported | 71 | 14 reported | 7 reported | 24 reported | 24 reported |
| | **Type of controls** | Hospital; cancer & oral diseases | | Population | | Population | Population | Cancer | Cancer |
| | **Job exposure/ reference jobs** | Ever (for I yr)/ Never | | Ever/Never | Usual | Ever (1 year)/ never | Ever/ Never | Usual/Selected list of industries | Usual/Selected list of industries |
| | **Analysis strategy** | Mantel-Haenszel (Multivariate analysis by loglinear models that are transformed to logistic regression models by Fienberg's method) | Poisson | Maximum likelihood & CI by Gart's method | Observed/expected x100 | Logistic regression | Logistic regression, Unconditional | Logistic regression, Unconditional | Logistic regression, Unconditional |
| | **Risk measure†** | OR | SIR | OR | SMR | OR | OR | OR | OR |
| | **Confounders adjusted** | Matched on sex; Stratified analysis adjusted for age, & smoking | Standardized by age & socioeconomic level | Age, smoking | Authors reported that SMR were similar for smoking adjusted and unadjusted; crude SMR reported | Age, smoking status, ethnicity | Age, ethnicity, & smoking | Age & smoking | Age & smoking |
| **II** | **Occupational groups:** | | | | | | | | |
| **A.** | **Managerial administrative & related occupations** | **na** | **na** | **NS** | **NS** | **na** | **na** | **na** | **na** |
| | *1. Managers & Administrators* | na | na | NS | NS | na | na | na | na |
| **B.** | **Mining and quarrying including oil & gas field occupations** | **na** | + | **na** | **NS** | + | **na** | **na** | **na** |

| | Study author ▶ | Notani (19) | Firth (35) | Levin (36) | Blair (37) U.S Veterans | Lerchen(105) | Menvielle (24) | Swanson (107) ¥ White males | Swanson (107) ¥ Black males |
|---|---|---|---|---|---|---|---|---|---|
| | *2. Miners, general* | na | Miners, quarrymen & well drillers 178 (123-249) | na | NS | Under ground miners 2.1 (1.1-3.7) | na | na | na |
| | *3. Foremen* | na | Related to above job | na | na | na | na | na | na |
| | *4. Drillers* | na | Related to above job | na | na | na | na | na | na |
| | *5. Machine operator* | na | Related to above job | na | na | na | na | na | na |
| **C.** | **Metal & related occupations (processing, machining, & fabricating)** | **NS** | + | + & NS | **NS** | **na** | + | + | + |
| | *6. Metal Processor* | na | na | NS | NS | na | na | Furnace operators 4.2 (1.1-15.7) | Furnace operators 5.9 (1.1-39.4) |
| | *7. Moulders* | na | na | na | NS | na | na | na | na |
| | *8. Fabricators & Assemblers* | NS for goldsmiths | Jewelers, & precious metal workers 241 (120-433) | Na | NS | na | Machinery fitters & assemblers (broad group) 7.1 (1.1-48) | na | na |
| | *9. Metal Machining (shaping, forming etc)* | na | Related to above job | Metal forgers, tool makers, machine tool installers 1.4 (1.0-1.9) | NS | na | Related to above job | na | na |
| **D.** | **Processing, machining, fabricating, assembling occupations, General** | **NS** | **na** | **NS** | **NS** | **na** | **Na** | + | + |
| | *10. Processing, general (granite, stone, paper etc)* | NS for workers in chemical/ pharmaceutical/ rubber etc. plants | na | NS | NS | na | na | Production supervisors 1.9 (1.0-3.7) Inspectors 2.1 (1.0-4.2) | Production supervisors 15.2 (1.5-159.6) Inspectors 5.6 (1.0-32.3) |
| | *11. Bakers* | na | na | NS | na | na | na | na | na |

| | **Study author ▶** | **Notani** (19) | **Firth** (35) | **Levin** (36) | **Blair** (37) U.S Veterans | **Lerchen**(105) | **Menvielle** (24) | **Swanson** (107) ¥ White males | **Swanson** (107) ¥ Black males |
|---|---|---|---|---|---|---|---|---|---|
| | *12. Machine operator* | NS for flour mill operators | na | na | NS in related occupation | na | na | Grinding 2.3 (1.2-4.4) Heat treating 9.2 (1.1-76.4) Slicing, cutting 2.0 (0.8-5.2) Miscellaneous 1.9 (1.0-3.9) | Slicing & cutting 9.8 (0.6-152.6) Industrial equipment 6.1 (1.4-27.7) |
| | *13. Assemblers* | na | na | NS | na | na | na | Assemblers 2.3 (1.2-4.2) | Assemblers 5.3 (1.5-18.5) |
| **E.** | **Textile & related occupations** | + & NS | + | **NS** | **na** | **na** | **na** | **na** | **na** |
| | *14.Tailors & Textile workers* | Textile workers 2.0 (1.1-3.6) NS for Tailors | Spinners, weavers, knitters, & dyers (Broad group) 189 (142-245) Weavers 273 (187-386) | NS | na | na | na | na | na |
| **F.** | **Sales occupations** | **NS** | **na** | **na** | **+ & NS** | **na** | **na** | + | **NS** |
| | *15. Buyers* | NS for small business men, salesmen etc. | Na | Na | NS | na | na | | |
| | *16. Sales workers* | Related to above job | na | na | Salesmen & sales clerks-127 | na | na | Sales drivers 2.5 (1.3-5.0) | NS |
| | *17. Other workers* | Related to above job | na | na | Na | na | na | | |
| **G.** | **Clerical & related occupations** | **NS** | **na** | **NS** | + | **na** | **na** | **na** | **na** |
| | *18.Clerks & auditors* | NS in a related occupation | na | NS | Salesmen & sales clerks-127 | na | na | na | na |
| | *19. Mail* | na | na | na | NS | na | na | na | na |
| | *20.Others (Health records etc.)* | na | na | na | NS | na | na | na | na |
| **H.** | **Service occupations** | + | + | **NS** | **NS** | **na** | **NS** | **NS** | + |
| | *21. Protection* | NS | na | na | NS | na | NS in a related occupation | na | na |
| | *22. Military* | na | na | na | NS | na | na | NS | Armed service 14.5 (1.1-186.2) |
| | *23. Waiters* | na | Cooks, waiters & bartenders (Broad group) 203 (160-253) Waiters, bartenders 303 (230-392) | NS - service workers | na | na | na | na | na |

| | Study author ▶ | Notani (19) | Firth (35) | Levin (36) | Blair (37) U.S Veterans | Lerchen(105) | Menvielle (24) | Swanson (107) ¥ White males | Swanson (107) ¥ Black males |
|---|---|---|---|---|---|---|---|---|---|
| | *24. Cooks* | Cooks/ helpers in kitchen 4.5 (1.2-16.9) | Cooks 272 (166-421) | Related to above job | na | na | na | na | na |
| | *25.Hair dressers & personal service* | na | na | Related to above job | NS | na | na | na | na |
| | *26. Cleaners* | na | na | Related to above job | na | na | NS in a related occupation | NS | Garbage collectors 12.5 (1.0-156.1) |
| **I.** | **Mechanics and Repairers** | **NS** | **NS** | **na** | **NS** | **NS** | **na** | + | + |
| | *27. Mechanics, General* | NS for mechanical, electrical, & electronic workers | na | na | NS | NS | na | Industrial maintenance 4.1 (1.3-13.4) | na |
| | *28.Electrical & Electronic equipment* | Related to above job | na | NS | NS | na | na | na | na |
| | *29. Automobile mechanics* | Related to above job | na | na | NS | NS | na | Garage & service station 2.2 (1.1-4.4) | Automobile mechanics 6.9 (1.4-39.0) |
| **J.** | **Construction trades occupations** | **NS** | + | **NS** | **+ & NS** | **NS** | **na** | + | + |
| | *30. Plumbers* | 0 for construction workers (broad group) | Na | NS | Plumbers & pipe fitters-184 | NS | na | na | na |
| | *31. Foremen, Supervisors, machine operators, & others* | Related to above job | Plasterers 228 (143-345) | NS | NS | NS | na | Concrete & terrazzo finishers 8.5 (1.0-72.8) | na |
| | *32. Insulators* | Related to above job | na | na | na | NS | na | na | na |
| | *33. Electricians* | na | na | na | NS | na | na | na | na |
| | *34. Laborers* | NS | Reinforced concreters 305 (138-581) | NS | NS | NS | na | NS | Construction laborers 4.4 (1.2-16.0) |
| **K.** | **Painters** | **NS** | **na** | **NS** | **NS** | **NS** | **na** | + | + |
| | *35. Painters, general* | NS | na | NS | NS | na | na | Painting machine operators 3.9 (1.2-13.0) | Painting machine operators 8.7 (0.9-89.3) |
| | *36. Painters, Construction* | na | na | na | NS | NS | na | na | na |
| **L.** | **Carpenters & wood workers** | **NS** | + | **na** | **NS** | **NS** | **na** | **na** | **na** |

| | Study author ► | Notani (19) | Firth (35) | Levin (36) | Blair (37) U.S Veterans | Lerchen(105) | Menvielle (24) | Swanson (107) ¥ White males | Swanson (107) ¥ Black males |
|---|---|---|---|---|---|---|---|---|---|
| | *37. Carpenters & Wood workers* | NS | Brick layers & carpenters 138 (115-164) Carpenters 165 (141-193) Wood workers 151 (133-169) | na | NS | NS | na | na | na |
| **M.** | **Welders and cutters** | **na** | **na** | **na** | **NS** | + | **na** | **NS** | + |
| | *38. Welders & cutter* | na | na | na | NS | Welders 3.2 (1.4-7.4) | na | NS | Welders 4.9 (1.2-20.0) |
| **N.** | **Transportation & related occupations** | **NS** | + | **NS** | + | **NS** | **NS** | + | **NS** |
| | *39. Inspectors/ Foremen& others* | na | na | NS | Pilots & navigators-204 | na | na | na | na |
| | *40. Rail transport* | na | Transport equipment operators (Broad group) 123 (109-137) | na | na | na | NS for transportation equipment operators (Broad group) | na | na |
| | *41. Water transport* | NS - ship and dock yard workers | Same as above | na | na | NS | Same as above | | |
| | *42. Motor transport* | NS | Same as above | NS | NS | na | Bus, Lorry, & Van drivers 2.7 91.1-7.0) | Heavy truck drivers 2.5 (1.4-4.4) | NS |
| **O.** | **Material moving & related occupations** | **NS** | **na** | **NS** | **na** | **na** | NS | **na** | **na** |
| | *43.Dockers & freight handlers* | NS - ship and dock yard workers | na | na | na | na | NS | na | na |
| | *44. Equipment operators& other handlers* | na | na | NS | na | na | na | na | na |
| **P.** | **Doctors, other medical & health related professions** | **na** | **na** | **NS** | **-Ve & NS** | **na** | **na** | **na** | **na** |
| | *45. Medicine* | na | na | NS - professionals & technicians | Physicians & surgeons-79 NS - other medical professions | na | na | na | na |
| **Q.** | **Engineers & related professions** | **na** | **na** | **NS** | **-Ve & NS** | **NS** | **na** | **na** | **na** |
| | *46. Engineers* | na | na | NS in professionals & technicians | Electrical engineers-68 Chemists-46 NS - certain engineers | NS | na | na | na |

| | Study author ▶ | Notani (19) | Firth (35) | Levin (36) | Blair (37) U.S Veterans | Lerchen(105) | Menvielle (24) | Swanson (107) ¥ White males | Swanson (107) ¥ Black males |
|---|---|---|---|---|---|---|---|---|---|
| **R.** | **Recreation, amusement & other service related occupations** | **na** | **na** | **na** | **NS** | **na** | **na** | **na** | **na** |
| | *47.Artists, Writers etc* | na | na | na | NS | na | na | na | na |
| **S.** | **Agriculture, forestry & related occupation** | **0** | **na** | + | **NS** | **na** | + | + | + |
| | *48. Farmers* | 0 | na | Agricultural workers 1.6 (1.0-2.5) | NS | na | NS | Farmers 2.1 (0.9-5.1) Farm workers 2.0 (1.0-3.7) | Farmers 10.4 (1.4-77.1) Farm workers 4.2 (1.1-16.8) |
| | *49. Forestry workers* | na | na | na | na | na | Forestry workers 15.8 (1.5-172) | na | na |
| **T.** | **Printing & related occupations** | **na** | **na** | **na** | **NS** | **NS** | **na** | **na** | **na** |
| | *50. Printers* | na | na | na | NS | NS | na | na | na |
| | *51.Press & other workers* | na | na | na | NS | na | na | na | na |
| **U.** | **Teaching & related occupations** | **NS** | **na** | **na** | **-Ve** | **na** | **Na** | **na** | **na** |
| | *52. Teachers* | NS – in a related occupation | na | na | Teachers n.e.c -53 College professors-40 | na | Na | na | na |
| **V.** | **Other occupations** | **na** | **na** | **na** | **na** | **na** | **na** | + | + |
| | *53. Others* | na | na | na | na | na | na | Laborers 2.0 (0.8-4.8) | Laborers 4.0 (1.2-13.4) |

**Note**: The mortality or incidence measures that were significantly elevated for lung cancer risk are reported with 95% Confidence intervals (CI) (eg. Mortality/incidence, lower CI-Upper CI); "NS" indicates no risk for that occupation; "na" indicates that either the occupation is not studied or unknown.
NHIS=National Health Interview Survey; NCHS: National Center for Health Statistics; n.e.c=not elsewhere classified.
*Gender: M=male; F=female; B=both combined.
†PMR=Proportionate mortality ratio; SIR=Standardized incidence ratio; SMR=Standardized mortality ratio; HR=Hazard ratio; OR= Odds ratio; RR=Relative risk;
‡Only results for males of all ages are reproduced in this table; exposure was the occupation worked for at least 1year, reference group included all other occupations within the same class (blue/white collar) in the same sex; occupations with RR > 1, observed deaths ≥5 & P-value < 0.05 are reported.
§Substantial exposure (S)=10 years of work in an occupation until 5 years before diagnosis of cancer; Ever exposure (E)=working in an occupation until 5 years before diagnosis of cancer.
††The reported results are for grouped (G) occupations; but, specific occupations with significantly elevated/decreased risk are reported with suffix "(Sp)" for contradictory results.
‡‡Authors defined: "Agric-MTFW" as "Mechanics, turners, foundries, & welders that began their working life in agriculture"; and "Agric-Const" as "Construction workers that began their working life in agriculture".
¥The odds ratios for lung cancer risk in an industry was estimated according to the categories of duration of employment (0, 1-9, 10+ and, for some, 20+ years); the ORs that were showing positive trend test or significant in any of these categories were reported. In this table OR in either the longest duration category or an OR significant in any of these categories of duration are listed

**Table 6**: Summary of the Literature Review of Occupations (23 studies) and Lung Cancer*

| Code in Tables-5a, b, c | Occupation | Positive | Negative | Null | Unknown |
|---|---|---|---|---|---|
| A. | Managerial administrative & related occupations | 1 | 4 | 5 | 13 |
| B. | Mining and quarrying including oil & gas field occupations | 8 | 0 | 4 | 11 |
| C. | Metal & related occupations (processing, machining, & fabricating) | 16 | 0 | 6 | 1 |
| D. | Processing, machining, fabricating, assembling occupations, General | 8 | 0 | 11 | 4 |
| E. | Textile & related occupations | 4 | 0 | 8 | 11 |
| F. | Sales occupations | 5 | 3 | 4 | 11 |
| G. | Clerical & related occupations | 3 | 1 | 8 | 11 |
| H. | Service occupations | 10 | 0 | 11 | 2 |
| I. | Mechanics and Repairers | 9 | 0 | 10 | 4 |
| J. | Construction trades occupations | 10 | 0 | 10 | 3 |
| K. | Painters | 7 | 0 | 9 | 7 |
| L. | Carpenters & wood workers | 4 | 0 | 11 | 8 |
| M. | Welders and cutters | 9 | 0 | 8 | 6 |
| N. | Transportation & related occupations | 13 | 1 | 8 | 1 |
| O. | Material moving & related occupations | 8 | 0 | 8 | 7 |
| P. | Doctors, other medical & health related professions | 0 | 3 | 6 | 14 |
| Q. | Engineers & related professions | 1 | 3 | 7 | 12 |
| R. | Recreation, amusement & other service related occupations | 1 | 2 | 5 | 15 |
| S. | Agriculture, forestry & related occupations | 7 | 1 | 11 | 4 |
| T. | Printing & related occupations | 3 | 0 | 11 | 9 |
| U. | Teaching & related occupations | 0 | 4 | 5 | 14 |
| V. | Other occupations | 3 | 0 | 0 | 20 |

*The studies that found more than one association (i.e., +/-/null) for the occupations within a broad group are counted only once in the following order of preference: '+ve', 'null' and '-ve'.
†Unknown=Not studied or not reported.

which provides the number of studies which found positive, negative, and null associations were found according to the broad occupational groups; those studies that have not reported or assessed the lung cancer risk for an occupational category are labeled as "Unknown".

Overall, the evidence has been fairly consistent for the elevated risk of lung cancer in the metal related occupations (7;17;18;24;26-36;107). The risk estimates of lung cancer ranged between 1.3 and 7.1 for all the 'metal & related occupations'; in particular, the range for metal processors was 1.5-3.1. However, 6 studies found no excess risk of lung cancer in this group (16;19-21;37;106). This could be due to various reasons, including: differences in the study design and exposure definition, and small sample size. Exposure to various metallic carcinogens has been documented in these occupations in these occupations: arsenic and its compounds, beryllium, cadmium and its compounds, hexavalent chromium compounds, and nickel compounds (14;39;51;112). Other carcinogenic substances such as asbestos and silica that are strongly related to lung cancer were also found in these occupational environments (14;112-114).

Among studies that showed an excess risk of lung cancer for the workers in 'mining & quarrying, including oil & gas field occupations', the risk estimates ranged from 1.3 to 4.0 (27-29;31;33-35;105). However, four studies did not find any excess risk of lung cancer in miners. This could be due to different exposure profiles among the subjects in these studies attributable to differences in the occupational classification systems (18;21;30;37). Miners are exposed to various carcinogens, including: metallic substances (such as arsenic, and hexavalent chromium) and non-metals (silica) during the extraction and processing of the ore. In addition, underground hematite miners and uranium miners are mainly exposed to radon, a known lung carcinogen (8;14;41).

An increased risk of lung cancer has been observed among motor vehicle drivers in many studies (17;20;21;24;27-31;33-35;52;107), although some studies found no increased risk (7;16;19;26;32;36;37;106) and one reported a reduced risk (18). Statistically significant estimates of risk ranged from 1.2 to 2.7 in the studies showing an excess risk of lung cancer. Exposure to diesel exhaust has been hypothesized to be responsible for the observed risk, since this substance has been identified as a probable carcinogen to humans by IARC (46;115). PAHs are found adsorbed to diesel exhaust; benz[a]anthracene, benzo[*a*]pyrene, dibenz[*a,h*]anthracene have been identified as probable human carcinogens by IARC (116;117). Siemiatycki and colleagues judged the evidence was suggestive of lung carcinogenicity for these substances (14).

Workers in the ‘construction trades & related occupations’ showed an excess risk of lung cancer in many studies (7;17;21;27;29;31;33;35;37;54;107). However, other studies suggested no association (16;18-20;26;30;34;36;105;106). This broad group of ‘construction trades’ is comprised of wide range of occupations, with different exposure profiles, including: construction labourers, masons, supervisors, electricians, insulators, metal erectors, concrete workers, and equipment operators. The overall risk estimate is determined by the composition of these subgroups within a study; the variability in composition could be a possible explanation for the observed variation in results across the different studies. The statistically significant risk estimates of lung cancer ranged from 1.2 to 3.6 in the eleven studies that found an increased risk of lung cancer. Certain known human carcinogens (such as asbestos, silica, metallic exposures, and PAHs) are found in these occupations (14).

The occupation 'painter' was classified as a Group 1 carcinogen by IARC in 1989 (108). Siemiatycki et al judged that the evidence was strong for an increased risk of lung cancer in painters (14). However, the evidence is equivocal within the studies selected for this review, particularly in those studies that were published after IARC report. An increased risk of lung cancer was observed in 7 studies, with risk estimates ranging between 1.3 and 8.7 (18;21;27;29;31;34;107), however no increased risk was found in 9 studies (16;17;19;30;33;36;37;105;106). All of these studies are based on large sample sizes, rendering it difficult to favor one over other. The tendency of the recent studies towards no increased risk in painters could be due to the increased use of safety devices (such as face masks, goggles, and protective clothing) that may have resulted from the awareness of cancer risk following the IARC review. Painters are mainly exposed to solvents, including: petroleum solvents, toluene, xylene, ketones, alcohols, esters, and glycol ethers (14;108).

Among the other occupations that were associated with lung cancer the evidence was equivocal for workers employed as welders and mechanics. An increased risk of lung cancer was observed for welders in 9 studies (17;18;26;27;29-31;105;107), while no increased risk was found in 8 studies (7;16;20;21;33;34;37;106). Welding fumes were identified as possible human carcinogens (Group 2B) by IARC (51). In addition, known human lung carcinogens such as chromium and nickel were found in the fumes released during stainless steel welding that could be responsible for the elevated risk of lung cancer (14;51). While many studies found an increased risk of lung cancer for 'mechanics

& repairers' (16;21;26;31-34;107), other studies found no increased risk in this group (17-20;27;29;30;35;37;105;106).

A number of other occupations have been associated with higher lung cancer risk in one or more studies. However, the evidence of a higher risk is less consistent for these occupations. An excess risk of lung cancer has been suggested in few studies of specific occupational groups, including: bakers (18;31), tailors (18), textile workers (19;20;35), sales workers (16;31;34;37;107), bartenders (33;35), cooks & chefs (19;21;27;28;33;35), waiters (21;27;31;35), hairdressers (27;31), cleaners & janitors (27;31;106;107), protection services (20;21;27;33), plumbers & pipe fitters (17;27;29-31;33;37), insulators (17;27;33), electricians (7;31), carpenters & wood workers (27;29;31;35), and agricultural workers (16;17;27;34;36;107). Risk estimates and corresponding confidence limits based on these studies are summarized in Tables 5a (pg 27), 5b (pg 34) and 5c (pg 40).

A reduced risk of lung cancer has been observed in teachers (21;27;30;37), 'doctors & other medical personnel' (27;28;30;37), and engineers (18;27;32;37). The evidence of a risk for clerks was conflicting, with both elevated (27;32;37) and reduced (30;31) risk estimates being reported. The respective risk measures and confidence intervals are summarized in Tables 5a (pg 27), 5b (pg 34) and 5c (pg 40).

**2.2.1.2 Detailed Discussion of Selected Studies**

A detailed description of the studies that are particularly relevant to Canadian occupational settings is provided in this section (26;31;33). In addition, results from two studies on specific populations (notably U.S. Veterans, and African-Americans in a Detroit study) are discussed (37;107).

Aronson and colleagues assessed the relationship between occupations and various causes of death, including death from lung cancer, in a cohort of 457,224 men and 242,196 women in Canada (33). The cohort represented 10% of the labour force for whom employment surveys were conducted each year from 1965-1969 and 1971 (data for 1970 was destroyed). A surveillance system was created based on this data using a computerized record linkage system with the Canadian mortality database from 1965-1991; a total of 116,000 and 26,800 deaths were observed among males and females, respectively, during this period. The cause of death was obtained from death certificates. An exposure was defined as an occupation held for at least one year. The relative risks of lung cancer for 670 occupations were assessed. The occupations were classified as white collar or blue collar based on the Pineo socio-economic classification (118). The sex-specific mortality rate for lung cancer in an occupation was compared with the lung cancer mortality rate in other occupations within the same class (white/ blue collar) to estimate the relative risk. All the analyses were adjusted for age and calendar period (5-year groups). A significant excess risk of lung cancer was found among foremen in mines, quarry & petroleum wells (RR=2.1), other miners (RR=1.4), mechanics & repairmen (except electrical) (RR=2.6), metal moulders (RR=1.4), boiler fireman (except ship) (RR=1.5), guards & watchmen n.e.c (RR=1.3), bartenders (RR=1.6), chefs & cooks (RR=2.6), plumbers & pipefitters (RR=1.2), construction foreman (RR=1.3), insulation appliers (RR=1.3), inspectors & foreman in transportation (RR=1.4), truck drivers (RR=1.4), longshoremen, stevedores & freight handlers (RR=2.1), and supervisors and foremen, n.e.c. (RR=3.2). Overall, these results indicated an excess risk among supervisors and foremen in various occupations including mining, transportation, construction, and material handling. In addition, occupations in food service (bartenders, chefs & cooks), protection service, mechanics, and metal moulders contributed to the excess lung cancer mortality. A major drawback of this study was the lack of adjustment for smoking.

Siemiatycki and colleagues have conducted a large case-control study in Montreal to assess occupational risk factors for cancer (26). A total of 4,576 male incident cancer patients 35-70 years of age in the Montreal metropolitan area were ascertained through hospital pathology departments between September 1979 and June 1985. Patients with cancers of brain, buccal cavity, and larynx or with leukemia were not included in the study. Lung cancer risk has been estimated for 98 occupational groups and 77 industry categories using 857 lung cancer cases. The control series is restricted to the cancer patients that were ascertained in the same years as cases (no single cancer site was allowed to represent more than 20% of the control group). These criteria resulted in 1,360 cancer controls for this study. Detailed job histories and information on confounders (such as age, smoking, and alcohol consumption) was collected by personal interview. All the exposure definitions were based on exposure (occupation/industry/agent) occurring at least five years prior to the diagnosis of the cancer to take in to account the latency period for lung cancer. Odds ratios (ORs) and 90% confidence intervals for lung cancer risk were estimated by the Mantel-Haenszel method using two exposure definitions: 1) substantial exposure, 'S' (10 years of work in an occupation/industry); 2) any exposure (ever worked in an occupation). A significant excess risk of lung cancer was observed in dock workers for both definitions of exposure (OR=3.1, $OR^S$=9.6). Metal product fabricators ($OR^S$=2.7), mechanics ($OR^S$=1.6), material handlers ($OR^S$=2.5) showed an excess risk of lung cancer with substantial exposure, while metal processors (OR=3.1), welders & flame cutters (OR=1.6), printers (OR=2.1), and printing press workers (OR=3.1) showed an excess lung cancer risk with any exposure level. Overall, these results were suggestive of an excess risk of lung cancer in metal related occupations and dock workers.

In the Work-Related Lung Disease Surveillance Report (2002), the National Institute for Occupational Safety and Health (NIOSH) reported proportionate mortality ratios (PMR) for lung cancer (adjusted for age, sex, and race) by usual occupation and industry categories for U.S residents 15 years of age and older for the year 1999 (31). These PMRs were calculated using a subset of the 'multiple cause of death data' from the National Center for Health Statistics (NCHS) that contained information on usual occupation (and usual industry). A total of 19 states had met the quality criteria of NCHS in 1999. The highest PMR for lung cancer was seen in health record technologists & technicians (PMR=3.1), although this estimate was based on only 5 deaths. PMRs of 2.5 and 2.4 were reported for lay-out workers and precision metal assemblers, respectively. Most of the PMRs raged between 1.1 and 1.4 in the high risk occupations. A PMR of 1.1 and 1.2 was reported for 'managers & administrators not elsewhere classified (n.e.c)' and truck drivers, respectively. Overall, excess mortality (as reflected in the PMR) due to lung cancer was observed among workers in metal related occupations, construction trades, truck drivers, and certain service workers. Further details are summarized in Table 5a under the heading-'NIOSH'.

In a cohort mortality study, standardized mortality ratios (SMRs) were estimated for the risk of lung cancer among the cohort members of the U.S veterans (37). An excess risk of lung cancer was observed in plumbers & pipe fitters (SMR=184), and workers in shipbuilding & repair (SMR=180); asbestos exposure has been hypothesized to explain the observed risk (37). An excess risk of lung cancer was also observed among the veterans employed as 'salesmen & sales clerks', and 'pilots & navigators' (37). Overall, the findings among veterans were in agreement with the literature (17;27;29-31;33;37).

Ethnic variations were observed for the associations between lung cancer and occupations after adjusting for age and smoking in a Detroit case-control study focusing on male cancer cases (107). An excess risk of lung cancer was observed in heavy truck drivers (OR=2.5) among white males, but not in black males; an excess risk of lung cancer was observed in black armed service workers (OR=14.5), garbage collectors (OR=12.5), and welders (OR=4.9) (107). In general, the magnitude of the point estimates was higher among blacks for the high-risk occupations that were common to both the groups; the odds ratios and corresponding 95% confidence intervals are summarized in Table 5c. The nature of the job task (reflecting job 'dirtiness') assigned to men from different racial groups was hypothesized as an explanation for the observed differences between black and white workers (107).

#### 2.2.1.3 Variation Among Studies

Studies from various geographic areas yielded different results for some occupational categories. For example, an excess risk of lung cancer was observed among sales workers and clerks in a recent report by the NIOSH in the U.S (31), but not in the Canadian mortality study by Aronson (33). An excess risk of lung cancer was observed in the Montreal study (26) for dock workers and material handlers but not in the Detroit case-control study (34). Differences in the characteristics of the study population, environmental conditions, research methodology, industrial processes & practices, and safety regulations might have contributed to the observed variations in study results. Differences in the study design (cohort vs. case-control, data collection strategies, confounders selected for adjustment, definition of an exposure- usual occupation vs ever having worked in an occupation) could contribute to the observed variations. For example, the NIOSH mortality estimates (which were unadjusted for smoking) (31) indicated an excess risk of lung cancer in the service related occupations, but, no such effect was observed after adjusting for smoking in another cohort mortality study in the U.S (32).

Differences in the industrial practices and processes in various geographic regions could modify the exposure to industrial carcinogens. Stringent safety regulations on ventilation and utilization of safety devices (such as masks, gloves, and electronic warning systems) could reduce the actual exposure to an industrial carcinogen even if the workers in an occupation are potentially exposed to high concentrations of that particular agent. In contrast, in some countries, especially developing countries, where safety regulations are not as stringent as in the US, lower concentrations of the industrial carcinogens in the workplace might be associated with higher actual exposure levels (15).

#### 2.2.1.4 Histological Subtypes of Lung Cancer

The evaluation of lung cancer risk by histological subtypes has been limited in the occupational studies, primarily due to lack of information on histopathology and sample size restrictions in the available databases. Among 23 studies selected for this review, only six studies evaluated the occupational risk of lung cancer within histopathological subtypes. Three histopathological subtypes have been examined: adenocarcinoma, squamous cell, and small cell (17;20;21;26). The odds ratios and confidence intervals are summarized in Table 7.

**Table 7:** High-risk occupations for Histological Subtypes of Lung Cancer in the Literature

| Source of Evidence | **Squamous Cell Carcinoma** | | **Adenocarcinoma** | | **Small Cell Carcinoma** | |
|---|---|---|---|---|---|---|
| | OCCUPATIONAL GROUP | OR (CI*) | OCCUPATIONAL GROUP | OR (CI) | OCCUPATIONAL GROUP | OR (CI) |
| **Siemiatycki**(26)† | Metal processors | 3.3 (1.4-8.0) | Metal machinists | 2.3 (1.0-5.1) | Metal product fabricators | 10.3 (3.2-33.0) |
| | Metal moulders & casters | 10.5 (1.3-85.1) | Mechanics | 2.0 (1.0-3.8) | Other fabricators | 2.7 (1.0-7.5) |
| | Grinders & polishers | 12.9 (1.0-99.9) | Material handlers | 3.2 (1.6-6.2) | Construction workers | 1.5 (1.0-2.4) |
| | Construction workers | 1.3 (1.0-1.8) | Dockworkers | 3.6 (1.4-9.2) | Plumbers & pipe fitters | 2.6 (1.1-6.5) |
| | Excavators & pavers | 3.4 (1.0-12.3) | Medical occupations | 2.5 (1.1-6.1) | Heat, water, light operators | 4.0 (1.4-11.4) |
| | Painters, construction | 2.2 (1.0-4.8) | | | Stationary engineers | 3.7 (1.3-11.0) |
| | Carpenters | 2.1 (1.1-4.1) | | | | |
| | Welders & flame cutters | 1.9 (1.0-3.9) | | | | |
| | Dockworkers | 8.8 (1.3-58.5) | | | | |
| | Farmers & horticulturists | 1.8 (1.0-3.1) | | | | |
| | Nursery workers | 3.5 (1.0-12.4) | | | | |
| | School teachers, vocational | 7.8 (1.3-45.9) | | | | |
| **Zahm** (21) | Police, fireman & protective services | 1.8 (1.1-3.0) | Mechanics & repairers | 1.5 (1.0-2.4) | Precision work (misc. hand & tool & dye workers) | 1.5 (1.0-2.1) |
| | Motor vehicle drivers | 1.5 (1.1-1.9) | Painters, paperhangers, & plasterers | 2.7 (1.2-5.6) | Police, fireman & protective services | 2.3 (1.3-4.2) |
| | | | Plumbers & pipe fitters | 2.0 (1.0-3.8) | Motor vehicle drivers | 1.5 (1.0-2.2) |
| | | | Freight, stock & garbage handlers | 4.0 (1.6-9.7) | | |
| | | | Carpenters | 1.6 (1.0-2.5) | | |
| **Elci** (20) | Textile workers | 2.0 (1.1-3.5 ) | Construction workers | 4.5 (1.9-10.7) | Textile workers | 2.2 (1.0-4.8) |
| **Pezzotto** (17)‡ | Agric-MTFW | 8.3 (2.9-19.3) | Agric-Const | 4.0 (1.1-25.7) | - | - |
| | Construction workers | 3.2 (1.2-10.9) | Carpenters | 4.7 (1.5-14.6) | | |
| | Agric-Const | 6.1 (1.1-29.0) | | | | |
| | Welders | 2.9 (1.0-10.1) | | | | |
| | Drivers | 3.1 (1.2-7.1) | | | | |
| | Agricultural workers | 3.1 (1.5-6.9) | | | | |
| **Sankila** (29) | Service and repairman, metal | 1.6 (1.2-2.1) | Miners & quarriers | 2.4 (1.3-4.6) | Miners & quarries | 3.9 (2.6-5.8) |
| | Welders | 2.0 (1.3-3.0) | Farmers | 0.6 (0.5-0.8) | Farmers | 0.8 (0.7-0.9) |
| | Farmers | 0.8 (0.7-0.9) | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Levin** (36)§ | Foundry workers | 2.4 | Foundry workers | 1.0 | Foundry workers | 1.6 |
| | Metal forgers, tool makers, machine tools installers, & operators | 1.0 | Metal forgers, tool makers, machine tools installers, & operators | 1.8 | Metal forgers, tool makers, machine tools installers, & operators | 1.5 |
| | Pipefitters, welders, cold workers, & metal component installers | 0.8 | Pipefitters, welders, cold workers, & metal component installers | 0.7 | Pipefitters, welders, cold workers, & metal component installers | 2.0 |
| | Construction workers | 1.8 | Construction workers | 1.3 | Construction workers | 1.8 |

*OR= Odds ratio; CI= 95% Confidence intervals for all, except for Siemiatycki-90% confidence intervals (CI) are provided;

† Odds ratios for the substantial exposure (10 years of work in an occupation until 5 years before diagnosis of cancer) are reported here;

‡Authors defined: "Agric-MTFW" as "Mechanics, turners, foundries, & welders that began their working life in agriculture"; and "Agric-Const" as "Construction workers that began their working life in agriculture".

§Only odds ratios were mentioned in this study

Occupations involving metal work have been associated with an increased risk for all types of lung cancer (17;20;21;26). However, some occupational categories within this group (such as processors and fabricators) were predominantly associated with certain histological types of lung cancer. An excess risk of squamous and small cell carcinoma was observed in metal processors (26), while metal fabricators & metal machinists were at increased risk of small cell and adenocarcinoma, respectively (26). Excess risk of lung cancer risk was limited to squamous cell carcinoma and adenocarcinoma among welders (17;26;29) and mechanics, respectively (21;26).

As a group, construction workers were at excess risk of all types of lung cancer (36). The predominant histopathological associations were different for different occupations within this broad group. For example, painters and carpenters were predominantly associated with squamous cell cancer (26) and adenocarcinoma (17;21), while plumbers were predominantly associated with small cell cancer (26) and adenocarcinoma (21).

Among the service related occupations, an elevated risk of squamous cell and small cell carcinoma was observed in 'policeman, firefighters & other protective service workers' (21).

The elevated risk of adenocarcinoma observed in medical workers is noteworthy, as no increase risk of lung cancer as a whole has been observed. This might be due to a diluting effect of combining the higher risk of adenocarcinoma with a null risk for other histological subtypes (26).

Other noteworthy associations include: an excess risk of squamous cell carcinoma among agricultural workers and vocational school teachers (26), and an excess risk of small cell & adenocarcinoma of the lung among printers, including press workers (26). Motor vehicle drivers have demonstrated an excess risk of squamous cell and small cell lung cancer (21). An elevated risk of squamous cell cancer and adenocarcinoma was observed among dock workers and other material handlers (21;26). A non-significant excess risk of large cell carcinoma was reported among laborers (OR=2.0, 95% CI: 0.5-8.8) in one study (20).

### 2.2.2 Industries as Risk Factors for Lung Cancer

In addition to the key secondary sources on industries as risk factors for lung cancer (14;104), our review identified 14 additional studies for review (including relatively new studies published after 1985 and those with large sample size that have evaluated the risk of lung cancer for a range of industries) (16;18;20;26;27;30;31;34;36;105-107;119;120). Among the selected studies, there are two cohort studies (31;120) and 12 case-control studies (16;18;20;26;27;30;34;36;105-107;119).

Among 18 occupational circumstances/processes examined by IARC, 15 industries (including industrial processes) were identified as definite or probable human carcinogens (14;39;109;112;121). From this list Siemiatycki and colleagues identified 8 industries (including industrial processes) as risk factors for lung cancer (14). The results with respect to lung cancer carcinogenicity are summarized in Table-4. The industries and industrial processes identified as definite carcinogenic circumstances by IARC are: aluminum production, coal gasification, coke production, 'iron & steel founding', underground hematite mining, isopropanol manufacturing (strong acid processes), and the rubber industry (112). Siemiatycki et al judged that the evidence for lung carcinogenicity in these industries to be strong, with the exception of isopropanol manufacturing and rubber industries, for which the evidence was judged to be only suggestive (14). Various carcinogenic substances were identified in these industries (including metallic fumes, radon, pitch volatiles, coal-tar fumes, PAH, silica, and asbestos) (14;112;122;123). The glass manufacturing industries that were involved in the production of art glass, glass containers, and pressed ware were classified as a probable carcinogenic circumstance by IARC, and the evidence was judged to be suggestive of lung carcinogenicity by Siemiatycki and colleagues (14;39).

Our review of recent articles identified a number of specific industries which were not studied in the IARC monographs but which were potentially linked to lung cancer risk. The majority of the studies identified an increased risk of lung cancer among workers in the metal manufacturing industries, particularly those involving primary metals (18;26;27;30;31;34;107;119;120). Other industries linked to lung cancer included: transport equipment manufacturing industries, construction industry, 'transportation & storage industries', and 'agriculture, forestry, fishing & trapping industries' (16;18;20;26;27;30;31;34;36;106;107;119;120).

#### 2.2.2.1 At-risk Industries Identified from the Recent Literature

Tables 8a (pg 61) and 8b (pg 66) present detailed information abstracted from studies identified in the recent literature. Industries have been classified into 23 broad categories (alphabetically represented) and 39 specific categories (numerically represented) based on 1980 Canadian Standard Industry Codes (SIC) and the industrial grouping developed by Siemiatycki et al (26;124). Related occupations have been listed according to these groups to control for the use of different industry titles among the various studies. The results of these studies are summarized in Table 9 (pg 72),

[Continued on pg 73]

**Table 8a: Lung Cancer Risk by the Industries (Studies 1-7)**
*Foot notes are provided in page-71 at the end of table-8b*

| | Study author ► | Siemiatycki (26)‡ | NIOSH (31) | Burns (34) | Droste (119) | Hall (120)†† | Lerchen (105) | Schoenberg (106)‡‡ |
|---|---|---|---|---|---|---|---|---|
| I | **Study features:** | | | | | | | |
| | **Country/ Area, Published year** | Montreal, 1991 | USA, 2003 | Detroit, 1991 | Western Europe, 1999 | New Jersey, 1991 | New Mexico, 1987 | New Jersey, 1987 |
| | **Study design** | Case-Control | Cohort mortality (1999) | Case-Control | Case-Control | Cohort incidence | Case-control | Case-control |
| | **Sample size** | 2217 | Sub-sample of NCHS data | 9891 | 1014 | 17,621 incident cancer cases | 832 | 1663 |
| | **Cases/Controls** | 857/1360 | | 5935/3956 | 478/536 | 10,824 WM; 4248 WF; 1,957 BM; 592 BF. | 333/499 | 763/900 |
| | **Gender (M/F/B)*** | M | Both | Both | M | B | M | M |
| | **Total jobs studied** | 77 | CIC | 48 | 25 reported | 10 reported | 9 reported | 34 |
| | **Type of controls** | Cancer | | Cancer, colon & rectum | Hospital | | Population | Population |
| | **Industry as exposure/ reference industries** | Ever (E) and substantial (S)/ Never | Usual | Usual/Selected list of industries | Ever/Never | Industry | Ever (1 year)/ never | Ever/ Never |
| | **Analysis strategy** | Mantel-Haenszel | | Logistic regression, Unconditional | Logistic regression | Observed / expected; Mantel-Haenszel Chi-square, Monson | Logistic regression | Mantel-Haenszel |
| | **Risk measure†** | Incidence OR (90% CI) | PMR | OR | OR | PCIR | OR | OR |
| | **Confounders adjusted** | Age, smoking, family income, ethnicity, alcohol, respondent to the questionnaire | Age, sex, race | Age, race, smoking & gender | Age, smoking history, cigarette consumption, civil & socioeconomic status | Race & sex specific standardized PCIR | Age, smoking status, ethnicity | Smoking |
| II | **Industry groups:** | | | | | | | |
| A. | **Agriculture, forestry, fishing, & trapping industries** | **na** | **na** | + | **NS** | **na** | **na** | **na** |
| | *1. Agriculture* | na | na | Farming 2.2 (1.2-4.1) | NS | na | na | na |
| | *2. Forestry & fishing* | na | na | na | na | na | na | na |
| B. | **Mining, milling, quarrying & oil well industries** | **NS** | + | + | **NS** | **na** | **NS** | **NS** |
| | *3. Metal mining* | na | na | Mining 3.0 (1.1-8.4) | NS | na | NS | na |
| | *4. Non-metal mining & others* | NS | Coal mining 1.3 (1.1-1.4) | Related to above | Related to above | na | na | NS |

| Study author ► | Siemiatycki (26)‡ | NIOSH (31) | Burns (34) | Droste (119) | Hall (120)†† | Lerchen (105) | Schoenberg (106)‡‡ |
|---|---|---|---|---|---|---|---|
| **C. Metal manufacturing** | **+ & NS** | **+** | **+ & NS** | **+ & NS** | **+** | **NS** | **NS** |
| *5. Primary metal* | Non-ferrous casting, rolling<br>3.2 (1.1-9.4) (E) | Iron & steel foundries<br>1.3 (1.1-1.6) | Ferrous primary metal manufacturing<br>2.4 (1.6-3.8)<br>Blast furnaces, steel workers, rolling & finishing mills<br>2.1 (1.3-3.4)<br>NS for non-ferrous | NS | Primary metal manufacturing (WM)<br>136<br>Non-ferrous industry (WM)<br>137 | NS | NS |
| *6. Metal fabricating & machining* | NS | Fabricated structural metal products<br>1.2 (1.0-1.4) | NS | Manufacturing of metal goods<br>1.6 (1.0-2.5) | Fabricated metal manufacturing (WM)<br>116 | na | NS |
| **D. Printing, publishing, & allied industries** | **+** | **+** | **NS** | **na** | **na** | **NS** | **NS** |
| *7. Printing & others* | Printing & publishing (E,S)<br>2.0 (1.0-4.0) (S) | Printing, publishing, & allied industries except newspapers<br>1.2 (1.1-1.4) | NS | na | na | NS | NS |
| **E. Chemical products** | **NS** | **na** | **NS** | **NS** | **na** | **na** | **-Ve** |
| *8. Chemical & drug* | NS | na | NS | NS | na | na | Other chemical workers<br>OR: <0.8 (significant) |
| **F. Food & beverage production** | **+** | **na** | **NS** | **NS** | **na** | **na** | **na** |
| *9. Food related* | Meat, poultry & fish products (E,S)<br>6.8 (1.1-42.8) (S)<br>Flour, feed & bakery prod.(E)<br>1.7 (1.0-2.9) | na | NS | NS | na | na | na |
| **G. Wood & furniture manufacturing** | **NS** | **na** | **NS** | **NS** | **+** | **na** | **NS** |
| *10. Wood industries* | na | na | NS | na | Lumber & wood prod. (BF) – 253 | na | NS |
| *11. Furniture & fixtures* | NS | na | na | na | na | na | NS |
| **H. Textile, clothing & leather industries** | **na** | **na** | **NS** | **NS** | **na** | **na** | **NS** |
| *12. Textile & leather* | na | na | NS | NS | na | na | NS |
| **I. Paper & allied products** | **+** | **na** | **na** | **NS** | **+** | **na** | **NS** |
| *13. Paper* | Pulp & paper mills (E)<br>1.6 (1.0-2.5)<br>Misc paper prod. (E)<br>5.8 (1.5-22.4) | na | na | NS | Paper & allied prod<br>156 (WF) | na | NS |

| | Study author ▶ | Siemiatycki (26)‡ | NIOSH (31) | Burns (34) | Droste (119) | Hall (120)†† | Lerchen (105) | Schoenberg (106)‡‡ |
|---|---|---|---|---|---|---|---|---|
| **J.** | **Rubber & plastic industries** | **na** | **na** | **NS** | **NS** | **na** | **na** | **NS** |
| | *14. Rubber & plastic* | na | na | NS | NS | na | na | NS |
| **K.** | **Other manufacturing industries** | **na** | **na** | **NS** | **na** | + | **na** | **NS** |
| | *15. Clay, stone & glass* | na | na | NS | na | Stone, clay & glass 125 (WM); 148 (WF) | na | NS |
| | *16. Others* | Non-metallic mineral products (E) 1.9 (1.1-3.2) | Scientific & controlling instruments 1.4 (1.1-1.9) Tobacco manuf. 1.3 (1.1-1.6) Not specified manuf. 1.1 (1.0-1.2) | NS machinery manuf.; computer | NS | na | NS for petroleum refining | NS for petroleum, tobacco, paint, cement, & misc. nonmetallic mineral product manuf |
| **L.** | **Transport equipment manufacturing** | + | + | **NS** | **na** | + | **NS** | + |
| | *17. Ship & boat* | na | Ship & boat building, & repairing 1.3 (1.1-1.7) | na | na | Shipbuilding 240 (BM); 183 (WM). | NS | Shipbuilding workers 1.6 (1.2-2.2) |
| | *18. Motor vehicle* | na | Motor vehicles & equipment 1.2 (1.1-1.3) | NS | NS | Transport manufacturing 143 (BM); 137 (WM). | na | na |
| | *19. Aircraft, rail & others* | Aircraft manufacture (E,S) 2.1 (1.2-3.7) (S) | na | NS | Other transport equipment 2.3 (1.3-4.0) | Related to above | na | na |
| **M.** | **Construction** | + | + | **NS** | **-Ve** | + | **NS** | **NS** |
| | *20. Construction* | Construction (E, S) 1.3 (1.0-1.6) (S) | Construction 1.2 (1.2-1.2) | NS | Building or road construction 0.6 (0.4-0.9) | General construction 124 (WM) Plumbing, carpentry, masonry & demolition 124 (WM) | NS | NS |
| **N.** | **Transportation & storage industries** | + | + | **NS** | + & **NS** | **na** | **na** | + |
| | *21. Land transportation* | na | Trucking service 1.2 (1.1-1.3) | NS | NS | na | na | Trucking service, warehousing & storage workers 1.8 (1.1-3.0) |
| | *22. Rail transport* | na | Railroads 1.1 (1.0-1.2) | NS | NS | na | na | NS |

| | Study author ► | Siemiatycki (26)‡ | NIOSH (31) | Burns (34) | Droste (119) | Hall (120)†† | Lerchen (105) | Schoenberg (106)‡‡ |
|---|---|---|---|---|---|---|---|---|
| | *23. Water transport* | Water transport (E, S) 14.0 (2.7-71.6) (S) | na | NS | NS | na | na | NS |
| | *24.Storage & others* | NS | na | NS | Transport support service: 1.6 (1.1-2.4) | na | na | NS for air transport |
| **O.** | **Utility industries** | + | + | **-Ve** | **na** | **na** | **na** | **na** |
| | *25. Electric, gas, & water utilities* | Power, gas & water utilities (E,S) 3.7 (1.6-8.5) (S) | na | Gas & electric utilities 0.5 (0.3-0.9) NS for water utility | na | na | na | na |
| | *26.Communication & others* | na | Not specified utilities 1.3 (1.0-1.7) | na | na | na | na | na |
| **P.** | **Whole sale & retail trade** | + | + | **-Ve** | **na** | **na** | **na** | **na** |
| | *27. Whole sale* | Coal & coke wholesale (E) 3.7 (1.5-9.1) | na | na | na | na | na | na |
| | *28. Retail (food, beverage, drugs etc.)* | Jewelery retail & repair (S) 14.0 (1.7-99.9) | Miscellaneous retail stores 1.2 (1.0-1.4) | Drug sales 0.3 (0.1-1.0) | na | na | na | na |
| **Q.** | **Motor vehicle sales & service** | **na** | + | **NS** | **NS** | **na** | **na** | **NS** |
| | *29. Motor vehicle sales & service* | na | Automotive repair & related services 1.1 (1.0-1.3) | NS | NS | na | na | NS |
| **R.** | **Finance, insurance, and real estate** | **na** | **na** | **na** | **NS** | **na** | **na** | **na** |
| | | na | na | na | NS | na | na | na |
| **S.** | **Education service** | **na** | **na** | **na** | **NS** | **na** | **na** | **na** |
| | *30. Education & research* | na | na | na | NS | na | na | na |
| **T.** | **Health, & social service** | + | **na** | **NS** | **NS** | **na** | **na** | **na** |
| | *31. Health* | na | na | NS | NS | na | na | na |
| | *32. Others* | Welfare & religious services 3.4 (1.1-10.5) (S) | na | NS | na | na | na | na |
| **U.** | **Food & personal services** | **na** | + | **-Ve** | **-Ve** | **na** | **NS** | **NS** |
| | *33. Food service* | na | Eating & drinking places 1.2 (1.1-1.2) | NS | NS | na | NS | na |

| | Study author ► | Siemiatycki (26)‡ | NIOSH (31) | Burns (34) | Droste (119) | Hall (120)†† | Lerchen (105) | Schoenberg (106)‡‡ |
|---|---|---|---|---|---|---|---|---|
| | *34. Personal service* | na | Beauty shops<br>1.3 (1.1-1.5) | NS | Cultural, domestic & personal services<br>0.5 (0.2-0.9) | na | na | NS for shoe-repair etc., barber, laundry etc. |
| | *35. Household service* | na | na | Private households<br>0.6 (0.4-1.0) | Related to above | na | na | na |
| **V.** | **Other service industries** | + | + | **NS** | **NS** | **na** | + | **na** |
| | *36. Amusement & recreational service* | Amusement & recreation (S)<br>2.5 (1.1-5.8) | Bowling alleys, billiard & pool parlors<br>1.8 (1.1-2.8)<br>Miscellaneous entertainment & recreational services<br>1.2 (1.1-1.4) | na | na | na | Motion pictures<br>5.0 (1.2-21.4) | na |
| | *37. Engineering & others* | na | na | NS for engineering & postal service | NS | na | na | na |
| **W.** | **Government & other administrative services** | + | + | + | **NS** | **na** | **na** | **na** |
| | *38. Defence* | Defence services (E,S)<br>2.8 (1.0-8.0) (S) | Military<br>1.1 (1.1-1.2) | Armed services<br>2.3 (1.0-5.3) | na | na | na | na |
| | *39. Administration & others* | na | na | na | NS | na | na | na |

**Table 8b: Lung Cancer Risk by the Industries (continued) (Studies 8-14)**

| | Study author ► | Richiardi (18) | Bruske-Hohlfeld (27) | Jockel (30) § | Matos (16) | Levin (36) | Elci (20) | Swanson (107) ¥ White | Swanson (107) ¥ Black |
|---|---|---|---|---|---|---|---|---|---|
| I | **Study features:** | | | | | | | | |
| | **Country/ Area, Published year** | Italy, 2004 | Germany, 2000 | West Germany, 1998 | Buenos Aires, Argentina, 2000 | Shanghai, 1988 | Turkey, 2003 | Detroit, 1993 | Detroit, 1993 |
| | **Study design** | Case-Control | Case-Control, pooled | Case-Control | Case-Control | Case-Control | Case-Control | Case-control | Case-control |
| | **Sample size** | 2209 | 7039 | 2008 | 592 | 1493 | 2873 | 4462 | 1296 |
| | **Cases/Controls** | 956/1253 | 3498/3541 | 1004/1004 | 199/393 | 733/760 | 1354/1519 | 2866/1596 | 926/370 |
| | **Gender (M/F/B)*** | Reported M not B | M | Reported M not B | M | M | M | White M | Black M |
| | **Total jobs studied** | About 92 industries studied; 38 reported | 21 | 21 grouped; Specific (Sp)-na | 34 titles reported | 25 | 30 | 20 reported | 20 reported |
| | **Type of controls** | Population | Population | Population | Hospital controls | Population | Cancer | Cancer | Cancer |
| | **Industry as exposure/ reference industries** | Ever/ Selected list of jobs | Ever/Never | Ever/Never | Ever/Never | Ever/Never | Ever/Never | Usual/Selected list of industries | Usual/Selected list of industries |
| | **Analysis strategy** | Logistic regression, Unconditional | Logistic regression, Conditional | Logistic regression, Conditional | Logistic regression, Unconditional | Maximum likelihood & CI by Gart's method | Logistic regression, Unconditional | Logistic regression, Unconditional | Logistic regression, Unconditional |
| | **Risk measure†** | OR | OR | OR | OR | OR | OR | OR | OR |
| | **Confounders adjusted** | Age, study area, smoking, number of job periods, and education. | Matched on age, region; Adjusted for smoking, asbestos exposure | Matched on age, sex, region; adjusted for smoking & asbestos | Matched on age and hospital; adjusted for age group, hospital, smoking, & other occupations with $P<0.05$ | Age, smoking | Age, smoking | Age & smoking | Age & smoking |
| II | **Occupational group:** | | | | | | | | |
| A. | **Agriculture, forestry, fishing, & trapping industries** | **NS** | + | **NS** | + | + | **na** | **NS** | + |
| | *1. Agriculture* | NS | General farming 1.3 (1.2-1.5) Horticulture 1.6 (1.0-2.4) Agriculture, forestry & fishing (Broad group) 1.3 (1.1-1.5) | NS | Agriculture 1.7 (1.0-2.8) | Agriculture production 1.6 (1.0-2.6) | na | NS | Farming 17.3 (2.6-115.7) |
| | *2. Forestry & fishing* | na | Deep sea fishing 4.4 (1.4-14.4) | NS | na | na | na | na | na |
| B. | **Mining, milling, quarrying & oil well industries** | **NS** | + | **NS** | **na** | **na** | **NS** | + | **NS** |

| | Study author ▶ | Richiardi (18) | Bruske-Hohlfeld (27) | Jockel (30) § | Matos (16) | Levin (36) | Elci (20) | Swanson (107) ¥ White | Swanson (107) ¥ Black |
|---|---|---|---|---|---|---|---|---|---|
| | *3. Metal mining* | NS | Energy & mining (Broad group) 1.4 (1.2-1.7) | NS | na | na | NS | na | na |
| | *4. Non-metal mining & others* | NS | Coal mining, briquette prod, & coke plants 1.4 (1.1-1.8) | na | na | na | NS for coal | Coal mining 1.9 (0.9-4.2) | NS |
| **C.** | **Metal manufacturing** | + | + | + | **NS** | **NS** | na | + | + |
| | *5. Primary metal* | Non-ferrous metals 1.8 (1.1-3.0) NS for iron & steel | Metal production 1.3 (1.1-1.5) | Metal production 1.8 (1.3-2.6) | NS | NS | na | Blast furnaces & steel mills 2.3 (1.2-4.3) Iron & steel foundries 3.9 (0.7-20.1) Aluminum manuf. 4.7 (1.2-18.1) | Blast furnaces & steel mills 8.5 (1.8-39.8) Iron & steel foundries 7.4 (1.4-37.9) Aluminum manuf. 5.3 (1.1-26.4) |
| | *6. Metal fabricating & machining* | Fabricated metal products 1.5 (1.0-2.2) Metal furniture & fixtures 11 (1.2-102) Fabricated n.e.c 2.2 (1.3-3.7) | NS | NS | NS | NS | na | na | na |
| **D.** | **Printing, publishing, & allied industries** | **NS** | + | **na** | **NS** | **NS** | **na** | **na** | **na** |
| | *7. Printing & others* | NS | Paper, wood, & printing 1.3 (1.1-1.6) | na | NS | NS | na | na | na |
| **E.** | **Chemical products** | **na** | **NS** | **NS** | + | **NS** | **NS** | **na** | **na** |
| | *8. Chemical & drug* | na | NS | NS | Chemicals/plastics 1.9 (1.1-3.3) | NS | NS for pharma | na | na |
| **F.** | **Food & beverage production** | **NS** | **NS** | **NS** | **+ & NS** | **NS** | **NS** | **NS** | + |
| | *9. Food related* | NS | NS | NS | Alcoholic beverages 5.2 (1.1-23.1) NS for food | NS | NS | NS | Meat production 8.1 (1.0-63.5) |
| **G.** | **Wood & furniture manufacturing** | **NS** | + | **na** | + | **NS** | **NS** | **na** | **na** |
| | *10. Wood industries* | NS | Wood processing 1.4 (1.1-1.7) | na | Saw & wood mills 4.8 (1.2-19.0) | na | NS | na | na |

| | Study author ► | Richiardi (18) | Bruske-Hohlfeld (27) | Jockel (30) § | Matos (16) | Levin (36) | Elci (20) | Swanson (107) ¥ White | Swanson (107) ¥ Black |
|---|---|---|---|---|---|---|---|---|---|
| | *11. Furniture & fixtures* | na | na | na | NS | NS | na | na | na |
| **H.** | **Textile, clothing & leather industries** | **NS** | **NS** | **NS** | **NS** | **-Ve** | **NS** | **na** | **na** |
| | *12. Textile & leather* | NS for leather | NS | NS | NS | Textile industry 0.7 (0.5-1.0) | NS | na | na |
| **I.** | **Paper & allied products** | **na** | + | **NS** | **NS** | **na** | **NS** | **na** | **na** |
| | *13. Paper* | na | Paper, wood, & printing 1.3 (1.1-1.6) | NS | NS | na | NS | na | na |
| **J.** | **Rubber & plastic industries** | **NS** | + | + | + | **NS** | **NS** | **na** | **na** |
| | *14. Rubber & plastic* | NS for rubber | Rubber & plastics 1.9 (1.2-2.9) | Rubber & plastics 2.6 (1.0-5.0) NS for plastic (Sp) | Chemicals/plastics 1.9 (1.1-3.3) | NS | NS | na | na |
| **K.** | **Other manufacturing industries** | **-Ve & NS** | + | + | + | **NS** | **NS** | + | **na** |
| | *15. Clay, stone & glass* | na | Stone, glass, & pottery 1.5 (1.2-1.9) | na | Pottery, glass, & minerals 3.3 (1.0-11.1) | na | NS | na | na |
| | *16. Others* | Other manuf. 0.3 (0.1-0.7) NS for asbestos, granite production, glass, & ceramic & refractory brick | na | Grain mill (Sp) 5.8 (1.1-31.2) NS for stone & glass | na | NS | NS for grain mills, cement, tea, clay & glass production. | Not specified manuf. 2.7 (0.6-12.1) | na |
| **L.** | **Transport equipment manufacturing** | **NS** | + | + | **NS** | **NS** | **NS** | + | + |
| | *17. Ship & boat* | NS | Engine & vehicle building 1.2 (1.1-1.4) | Engine & vehicle building 1.3 (1.0-1.7) | na | NS | NS | Other transportation 3.7 (1.0-14.3) | Other transportation manuf. 10.5 (1.1-102.6) |
| | *18. Motor vehicle* | NS | Related to above | na | NS | NS | na | NS | Automobile manuf. 3.8 (1.4-10.1) |
| | *19. Aircraft, rail & others* | NS for railroad | Related to above | na | NS | NS | na | Other transportation manuf. 3.7 (1.0-14.3) | Other transportation manuf. 10.5 (1.1-102.6) |
| **M.** | **Construction** | **+ & NS** | + | **+ & NS** | **NS** | **NS** | **+ & NS** | **NS** | + |

| | **Study author ▶** | **Richiardi** (18) | **Bruske-Hohlfeld** (27) | **Jockel** (30) § | **Matos** (16) | **Levin** (36) | **Elci** (20) | **Swanson** (107) ¥ White | **Swanson** (107) ¥ Black |
|---|---|---|---|---|---|---|---|---|---|
| | *20. Construction* | NS for Painters, Construction<br>1.7 (1.0-3.0) | Construction<br>1.3 (1.2-1.5) | Installation<br>1.5 (1.0-2.1)<br>NS for construction | NS | NS | Highway construction<br>1.5 (1.1-2.5)<br>NS-Construction | NS | Construction<br>3.1 (1.0-9.1) |
| **N.** | **Transportation & storage industries** | **-Ve & NS** | + | **NS** | **+ & NS** | **NS** | **NS** | + | **NS** |
| | *21. Land transportation* | Land transport<br>0.5 (0.3-0.9) | Transportation<br>1.2 (1.1-1.4) | NS | NS | NS | NS | Taxi service<br>4.1 (0.8-20.4)<br>Trucking service<br>1.6 (0.9-3.0) | NS |
| | *22. Rail transport* | Railway transport<br>0.1 (0.1-0.7) | Related to above | NS | NS | NS | NS | Railroads<br>2.4 (1.1-5.1) | NS |
| | *23. Water transport* | na | Related to above | NS (G)<br>Seaport (Sp)<br>1.6 (1.0-2.6) | Water<br>3.3 (1.1-12.1) | NS | NS | na | na |
| | *24.Storage & others* | NS | NS | NS | na | na | na | na | na |
| **O.** | **Utility industries** | **NS** | **na** | **na** | **NS** | **NS** | + | **na** | **na** |
| | *25. Electric, gas, & water utilities* | NS for gas | na | na | na | na | Water treatment plants<br>2.2 (1.1-4.3) | na | na |
| | *26.Communication & others* | na | na | na | NS for communication | NS for communication | NS for gasoline serv. | na | na |
| **P.** | **Whole sale & retail trade** | **na** | **-Ve** | **-Ve & NS** | **NS** | **NS** | **na** | + | + |
| | *27. Whole sale* | na | Wholesale & retail trade<br>0.7 (0.6-0.9) | NS (G)<br>Paper, wholesale (Sp)<br>0.2 (0.0-1.0) | NS | na | na | na | na |
| | *28. Retail (food, beverage, drugs etc.)* | na | na | na | na | NS | na | Grocery stores<br>2.8 (1.0-7.7) | Grocery stores<br>11.6 (1.1-120.5) |
| **Q.** | **Motor vehicle sales & service** | + & NS | **na** | **na** | **NS** | **na** | **na** | **NS** | + |
| | *29. Motor vehicle sales & service* | Painters (construction, automotive, other)<br>1.7 (1.1-2.8)<br>NS for motor vehicle repair | na | na | NS | na | na | NS | Automotive services<br>8.8 (1.5-50.8)<br>Automotive repair<br>11.9 (2.0-71.1) |
| **R.** | **Finance, insurance, and real estate** | **-Ve & NS** | **NS** | **+ & NS** | **NS** | **NS** | **na** | **na** | **na** |

| | Study author ▶ | **Richiardi** (18) | **Bruske-Hohlfeld** (27) | **Jockel** (30) § | **Matos** (16) | **Levin** (36) | **Elci** (20) | **Swanson** (107) ¥ White | **Swanson** (107) ¥ Black |
|---|---|---|---|---|---|---|---|---|---|
| | | Financial institution<br>0.5 (0.2-1.0)<br>NS for insurance | NS | NS (G)<br>Life insurance (Sp)<br>5.3 (1.1-25.7) | NS | NS | na | na | na |
| **S.** | **Education service** | **na** | **-Ve** | **-Ve** | **na** | **NS** | **na** | **na** | **na** |
| | *30. Education & research* | na | Education, health, research & sports<br>0.6 (0.5-0.7) | Education, health, cultural, & sports<br>0.5 (0.4-0.8) | na | NS | na | na | na |
| **T.** | **Health, & social service** | **na** | **-Ve** | **-Ve** | **NS** | **NS** | **na** | + | + |
| | *31. Health* | na | Education, health, research & sports<br>0.6 (0.5-0.7) | Education, health, cultural, & sports<br>0.5 (0.4-0.8) | na | NS | na | Hospitals<br>2.7 (1.1-6.4) | Hospitals<br>7.3 (1.7-30.4) |
| | *32. Others* | na | Administration & welfare<br>0.6 (0.5-0.7) | | NS for social services | na | na | na | na |
| **U.** | **Food & personal services** | **NS** | **NS** | **NS** | **NS** | **NS** | **NS** | **na** | **na** |
| | *33. Food service* | na | NS | NS | NS | na | NS | na | na |
| | *34. Personal service* | NS for laundry & dry cleaning | NS | NS | NS | NS | na | na | na |
| | *35. Household service* | na | NS | NS | na | NS | na | na | na |
| **V.** | **Other service industries** | **NS** | **na** | **na** | **na** | **na** | **na** | **na** | **na** |
| | *36. Amusement & recreational service* | NS | na | na | na | na | na | na | na |
| | *37. Engineering & others* | na | na | na | na | na | na | na | na |
| **W.** | **Government & other administrative services** | **na** | **-Ve** | **-Ve** | **na** | **NS** | **na** | **NS** | + |
| | *38. Defence* | na | na | Public administration, defence, community service & membership organizations<br>0.8 (0.6-1.0) | na | na | na | NS | Armed services<br>8.9 (1.3-63.4) |
| | *39. Administration & others* | na | Administration & welfare<br>0.6 (0.5-0.7) | na | na | NS | na | na | Protective services<br>7.4 (1.4-40) |

**Note**: The mortality or incidence measures that were significantly elevated for lung cancer risk are reported with 95% Confidence intervals (CI) (eg. Mortality/incidence, lower CI-Upper CI); "NS" indicates no risk for that occupation; "na" indicates that either the occupation is not studied or unknown.

NHIS=National Health Interview Survey; NCHS: National Center for Health Statistics; n.e.c=not elsewhere classified.

*Gender: M=male; F=female; B=both combined.

†PMR=Proportionate mortality ratio; SIR=Standardized incidence ratio; SMR=Standardized mortality ratio; HR=Hazard ratio; OR= Odds ratio; RR=Relative risk; PCIR: Proportionate cancer incidence ratio.

‡Substantial exposure (S)=10 years of work in an occupation until 5 years before diagnosis of cancer; Ever exposure (E)=working in an occupation until 5 years before diagnosis of cancer.

††WM=white males; WF=White females; BM=Blacks males; BF=Black females.

‡‡For non-high risk occupations smoking adjusted OR range (ORR) is provided in the table.

§The reported results are for grouped (G) occupations; but, specific occupations with significantly elevated/decreased risk are reported with suffix "(Sp)" for contradictory results; "na"=not available.

¥The odds ratios for lung cancer risk in an industry was estimated according to the categories of duration of employment (0, 1-9, 10+ and, for some, 20+ years); the ORs that were showing positive trend test or significant in any of these categories were reported. In this table OR in either the longest duration category or an OR significant in any of these categories of duration are listed.

**Table 9:** Summary of the Literature Review of Industries (14 studies) Associated with Lung Cancer *

| Code in Tables (8a, b) | Industry | Positive | Negative | Null | Unknown |
|---|---|---|---|---|---|
| A. | Agriculture, forestry, fishing, & trapping industries | 5 | 0 | 3 | 6 |
| B. | Mining, milling, quarrying & oil well industries | 4 | 0 | 7 | 3 |
| C. | Metal manufacturing | 9 | 0 | 4 | 1 |
| D. | Printing, publishing, & allied industries | 3 | 0 | 6 | 5 |
| E. | Chemical products | 1 | 1 | 7 | 5 |
| F. | Food & beverage production | 3 | 0 | 7 | 4 |
| G. | Wood & furniture manufacturing | 3 | 0 | 7 | 4 |
| H. | Textile, clothing & leather industries | 0 | 1 | 8 | 5 |
| I. | Paper & allied products | 3 | 0 | 5 | 6 |
| J. | Rubber & plastic industries | 3 | 0 | 6 | 5 |
| K. | Other manufacturing industries | 5 | 0 | 5 | 4 |
| L. | Transport equipment manufacturing | 7 | 0 | 6 | 1 |
| M. | Construction | 8 | 1 | 5 | 0 |
| N. | Transportation & storage industries | 7 | 0 | 5 | 2 |
| O. | Utility industries | 3 | 1 | 3 | 7 |
| P. | Whole sale & retail trade | 3 | 2 | 3 | 6 |
| Q. | Motor vehicle sales & service | 3 | 0 | 4 | 7 |
| R. | Finance, insurance, and real estate | 1 | 0 | 5 | 8 |
| S. | Education service | 0 | 2 | 2 | 10 |
| T. | Health, & social service | 2 | 2 | 4 | 6 |
| U. | Food & personal services | 1 | 2 | 8 | 3 |
| V. | Other service industries | 3 | 0 | 3 | 8 |
| W. | Government & other administrative services | 4 | 2 | 2 | 6 |

*The studies that found more than one association (i.e., +/-/null) for the industries within a broad group are counted only once in the following order of preference: '+ve', 'null' and '-ve'.

†Unknown=Not studied or not reported.

which provides the number of studies which found positive, negative, and null associations according to the broad occupational groups; those studies that have not reported or assessed the lung cancer risk for an occupational category are counted as "unknown".

Overall, the evidence from our selected studies and IARC has been fairly consistent for an elevated risk of lung cancer with metal working (14;18;26;27;30;31;34;107;112;119;120). Many studies found an increased risk of lung cancer among the workers in the primary metal manufacturing (18;26;27;30;31;34;107;120), and 'metal fabricating & machining industries' (18;31;119;120). It should be acknowledged that four studies found no increased risk in metal manufacturing and related industries (16;36;105;106), but these studies have relatively small sample sizes. The statistically significant risk estimates ranged between 1.3 and 8.5 among the workers in the primary metal manufacturing; the range for the workers in 'metal fabricating and machining' was 1.2-11.0. Workers in the metal industry are exposed to a number of carcinogenic substances including: metals, asbestos, PAHs, and silica (14;112). The majority of these substances are strongly associated with lung cancer (14).

In the studies that showed an excess risk of lung cancer among the workers in the transport equipment manufacturing industries, the odds ratios ranged between 1.2 and 10.5, with the majority of the odds ratios being about 1.5 (26;27;30;31;106;107;120). However, six studies found no increased risk of lung cancer in this industry; this could be due to relatively low sample size or a different exposure profile within the study population (16;18;20;34;36;105). Among the workers in the transport equipment manufacturing industries, an excess risk of lung cancer was suggested for those working in the ship building industry (31;106;120), motor vehicle manufacturing (31;107;120) and aircraft manufacturing (26). Workers in the ship building industry are mainly exposed to asbestos, which is a known lung carcinogen (14;120). Workers in the automobile industries are mainly exposed to metallic substances, asbestos and mineral oils during manufacturing and assembly (125;126).

An excess risk of lung cancer has been noted among workers in the construction industry in many studies (18;20;26;27;30;31;107;120), although some found no increased risk (16;34;36;105;106) and one reported a reduced risk (119). The risk estimates (ORs, and RRs) were typically about 1.4 in many of these studies, with a range of 0.6 to 3.1. Some studies that were specific to the workers in construction industry confirmed the excess lung cancer risk observed in the above mentioned studies (45;54;127-129). A proportionate cancer mortality ratio of 1.1 (CI: 1.0-1.1) was noted among construction laborers in a cohort of 11,685 members of the Labourer's International Union of North America (LIUNA) during 1985-1988 in comparison with the U.S population (128). Similarly, a significantly elevated proportionate mortality ratio (PMR=113) of lung cancer was noted in North Carolina construction workers during 1988-1994 (129). Similar results were observed in other cohort mortality studies involving construction workers (45;54;127). Workers in the construction industry are exposed to various known lung carcinogens (including asbestos, silica, metallic substances, PAH, and wood dust) (14;125;126).

The evidence for an increased risk of lung cancer in transportation & storage industry workers is inconclusive. An increased risk of lung cancer was found in seven studies (16;26;27;31;106;107;119), while 5 studies found no increased risk (perhaps due the variations in study design, or industrial classification/definition) (18;20;30;34;36). Within this industry, an excess risk of lung cancer was observed among the workers involved in: land transportation (18;27;107), including trucking service (31;106); railroad work (31;107); water transportation (16;26); and transport support services (119). However, one study reported a reduced risk of lung cancer for the workers in the rail (OR=0.1) and land transportation (OR=0.5) industries (18). Among the studies that suggested an elevated risk of lung cancer the risk estimates (RRS and ORs) ranged between 1.1 and 14.0. Workers in the transportation industry are mainly exposed to diesel exhaust, which has been classified as a probable human carcinogen by IARC (115).

Five studies have found an elevated risk of lung cancer among workers in agriculture and related industries (16;27;34;36;107), including farming (27;34;107), forestry (27), and fishing (27); while three studies found no increased risk (perhaps due to variations in the study design and exposure definition) (18;30;119). The risk estimates (RRs and ORs) ranged between 1.3 and 17.3 for agricultural workers among the studies showing an excess risk of lung cancer. Workers involved in farming are mainly exposed to pesticides. The evidence for the lung cancer association was judged to be strong for certain constituents of pesticides, such as TCDD, and ethylene oxide (14).

A number of other industries have been associated with higher lung cancer risk in one or more studies, however with less consistent evidence. Some noteworthy high risk industries that have been suggested in the literature include: mining (31;34;107); printing & publishing (26;27;31); chemical products (16); food & beverage production (16;26;107); wood & furniture (16;27;120); paper & allied products (26;27;120); rubber

& plastic industry (16;27;30); stone, clay & glass products (16;27;120); utility industries including, power, gas & water (20;26); automobile sales & services (18;31;107); and defense services (26;31;34;107). The risk estimates for these occupations are summarized in Tables 8a (pg 61) and 8b (pgs 66) .

The literature was suggestive of a reduced risk of lung cancer among workers in certain industries including: education services (27;30) and household services (34;119). The respective risk measures and confidence intervals are provided in Tables 8a (pg 61) and 8b (pgs 66).

**2.2.2.2 Detailed Discussion of Selected Studies**

In the large case-control study that was conducted in the Montreal, Siemiatycki and colleagues assessed the lung cancer risk in 77 industry groups for two exposure definitions [any or substantial(S) exposure] (26). The details of this study have been described previously (see section 2.2.1.2). A significant excess risk of lung cancer was observed in the following industries for both the definitions of exposure: meat, poultry & fish product industries (OR=3.7, $OR^S$=6.8); printing & publishing industries (OR=2.0, $OR^S$=2.0); aircraft manufacturing (OR=1.4, $OR^S$=2.1); construction industry (OR=1.2, $OR^S$=1.3); water transport (OR=3.4, $OR^S$=14.0); power, gas & water utility industries (OR=1.8, $OR^S$=3.7); and defense services (OR=1.3, $OR^S$=2.8). Workers in the 'jewelry retail & repair industry' ($OR^S$=14.0), 'welfare & religious services' ($OR^S$=3.4), and 'amusement & recreation' ($OR^S$=2.5) showed an excess risk of lung cancer with 'substantial' exposure. Workers in 'pulp & paper mills' (OR=1.6), 'flour, feed & bakery product industries' (OR=1.7), 'non-ferrous casting & rolling industries' (OR=3.2), 'non-metallic mineral product industries' (OR=1.9), and 'coal & coke wholesale industries' (OR=3.7) showed an excess risk of lung cancer at 'any' exposure. Overall these results were suggestive on an excess risk of lung cancer among the workers in manufacturing and construction industries. Other noteworthy findings include the excess risk of lung cancer among the workers in the printing & publishing industries, defense services, and certain utility industries. The occupational exposures in the printing processes industry were classified as possibly carcinogenic to humans by IARC (130).

In the Work-Related Lung Disease Surveillance Report (2002), the NIOSH reported PMRs for lung cancer by usual industry categories (31). The PMRs among the high-risk occupations ranged between 1.1 and 1.8. The highest PMR for lung cancer was reported for the workers in 'bowling alleys, billiard & pool parlors' (PMR=3.1). A PMR of 1.2 has been reported for workers in the construction and trucking service industries. Overall, the workers in the manufacturing and construction industries showed an excess risk of lung cancer in this report (31). Further details are summarized in the Table 8a (pg 61) under the heading-'NIOSH'.

Ethnic variation was observed in the associations between lung cancer and industries after adjusting for age and smoking in a Detroit case-control study focussin on male cancer cases (107). An excess risk of lung cancer was observed among white males working in coal mines (OR=1.9), but not in black males. An excess risk of lung cancer was observed only for black workers in various industries, including: meat production (OR=8.1), automobile manufacturing (OR=3.8), automotive service industry (OR=8.8), automotive repair industry (OR=11.9), and armed services (OR=8.9). Among the workers in the high risk industries, the magnitude of the odds ratios was higher in black males; the odds ratios and the corresponding 95% confidence intervals are summarized in Table 8b (pg 66). It was hypothesized that this elevated risk might reflect either the nature of the job task (dirtier jobs) or an unknown factor (107).

### 2.2.2.3 Histological Subtypes of Lung Cancer

Only 3 of the 14 studies selected for this review evaluated the association between industry and histopathological subtypes of lung cancer (20;26;36). The odds ratios and confidence intervals are summarized in Table 10.

Workers in the metal manufacturing industries were associated with an excess risk of squamous cell and small cell carcinoma (26;36). However, squamous cell carcinoma was the predominant type of lung cancer for metal workers involved in casting & rolling of nonferrous metals (26).

In the Montreal study, an excess risk of all the types of lung cancer was observed among workers in the aircraft manufacturing industry (26). However, a study in a cohort of 77,965 aircraft manufacturing workers in California did not find an excess risk of lung cancer among these workers (SMR=0.9) (131). Although this large cohort study was specific to aircraft manufacturing workers, an assessment of histopathological subtypes of lung cancer was lacking. Therefore, the findings in the Montreal study have yet to be confirmed. Workers in this industry are exposed to various carcinogenic substances, including: metallic substances (beryllium, chromium etc), cutting fluids, and lubricants (14;132); the majority of the exposures found in the metal manufacturing industries were also found in aircraft manufacturers (132).

**Table 10:** High-risk Industries for Histological Subtypes of Lung Cancer in the Literature

| | **Squamous Cell Carcinoma** | | **Adenocarcinoma** | | **Small Cell Carcinoma** | |
|---|---|---|---|---|---|---|
| | OCCUPATIONAL GROUP | OR (CI*) | OCCUPATIONAL GROUP | OR (CI) | OCCUPATIONAL GROUP | OR (CI) |
| **Siemiatycki** (26)† | Leather goods | 3.0 (1.0-8.9) | Flour, feed & bakery products | 3.2 (1.0-9.8) | Beverages | 3.0 (1.0-8.9) |
| | Non-ferrous casting & rolling | 3.7 (1.4-10.2) | Clothing | 2.1 (1.0-4.8) | Aircraft manufacture | 2.6 (1.0-6.4) |
| | Aircraft manufacture | 2.2 (1.1-4.6) | Printing & publishing | 4.5 (1.3-15.3) | Other transport equipment | 2.6 (1.0-6.4) |
| | Chemical products | 3.3 (1.1-9.9) | Aircraft manufacture | 3.2 (1.4-7.4) | Construction | 1.6 (1.0-2.4) |
| | Construction | 1.6 (1.1-2.3) | Water transport | 2.8 (1.2-6.6) | Amusement & recreation | 5.3 (1.3-21.8) |
| | Water transport | 4.5 (1.3-16.2) | Petroleum products, wholesale | 17.6 (1.9-99.9) | | |
| | Power, gas & water utilities | 3.4 (1.2-10.2) | | | | |
| **Elci** (20) | Grain mills | 3.4 (1.2-9.4) | - | - | Water treatment plants | 4.3 (1.8-10.3) |
| **Levin** (36)‡ | Agricultural production | 1.8 | Agricultural production | 1.5 | Agricultural production | 1.1 |
| | Textile industry | 0.5 | Textile industry | 0.7 | Textile industry | 0.8 |
| | Chemical industry | 2.2 | Chemical industry | 1.4 | Chemical industry | 3.4 |
| | Metallurgical industries | 1.2 | Metallurgical industries | 0.8 | Metallurgical industries | 2.4 |
| | Shipbuilding & repair | 1.5 | Shipbuilding & repair | 1.2 | Shipbuilding & repair | 1.2 |

*OR= Odds ratio; CI= 95% Confidence intervals; for Siemiatycki-90% confidence intervals (CI) were reported;

† Odds ratios for the substantial exposure (10 years of work in an occupation until 5 years before diagnosis of cancer) are reported here;

‡Only odds ratios were mentioned in this study.

The histopathological associations were different in the different subgroups of workers within the food industry. For example, workers involved in the beverage manufacturing had an increased risk of small cell cancer (26), while those in the 'flour, feed & bakery product industries' had an increased risk of adenocarcinoma (26).

Some noteworthy associations were observed in other groups of industries in relation to histological subtypes of lung cancer. An increased risk of squamous cell and small cell carcinoma was observed among construction workers, while an excess risk of squamous cell and adenocarcinoma was observed among workers in the water transportation industry (26). Workers in the printing & publishing industry were exclusively associated with an excess risk of adenocarcinoma of lung (26). A reduced risk of all types of lung cancer was reported in one study for workers in textile industry (36).

## *2.3 Occupational Exposures and Lung Cancer*

A large number of work place carcinogens have been linked to lung cancer (14;15). Work place exposure to known carcinogens has been reduced in recent years due to more stringent occupational health regulations in developed countries. However, the burden of past exposures and new carcinogenic substances in the work place warrant continued research in identifying work place carcinogens (9;14;15). Moreover, exposure to occupational carcinogens is mainly involuntary and mostly avoidable with the work place regulations (9).

Owing to the vast literature on occupational lung carcinogens, a detailed review of all lung carcinogens is out of the scope of this thesis. However, a brief overview of selected carcinogens that were identified by the IARC is provided in this section (Table 4). This review will discuss risk associated with asbestos, silica, radon, arsenic, chromium, beryllium, and nickel. The primary sources of information for this section are the book by Schottenfeld & Fraumeni (46), and review articles by Alberg & Samet, Siemiatycki, and Steenland (4;8;14).

### 2.3.1 Asbestos

Asbestos is a well known cause of mesothelioma but is also an established occupational lung carcinogen (46). Amosite, anthophyllite, chrysotile, and crocidolite constitute different types of asbestos fibers. Chrysotile is the most common form of asbestos and less hazardous than the other types (4;46). The current Occupational Safety and Health Administration (OSHA) standard for asbestos is 0.1 fibres/ml for fibers greater than 5 microns in length (133)

An increased risk of lung cancer has been observed in various asbestos related industries, including: miners, millers, textile, gas mask, friction product, insulation, shipyard, and cement workers (14;46). A latency period of 15-20 years was observed for the occurrence of lung cancer following exposure to asbestos (46). Asbestos exposure affects the risk of all histological types of lung cancer although the tumors tend to occur more in the periphery and in the lower lobes (46). In a meta-analysis of the six cohort studies on the subjects with asbestosis, a combined relative risk of lung cancer of 5.9 (95% CI: 5.0-7.0) has been estimated (8). However, limiting the meta-analysis to the cohort studies of workers exposed to asbestos resulted in a lower risk of lung cancer, with a combined RR of 2.0 (95% CI: 1.9-2.1) (8). It is unclear whether the induction of lung cancer is direct or via an indirect mechanism mediated by chronic inflammation and fibrosis (134;135). Some studies have suggested that asbestos related fibrosis is in the causal pathway of lung cancer (136;137). Current occupational exposure limits for asbestos preclude the high levels of exposure associated with asbestosis, thereby reducing asbestos related lung cancer risk (8;46). An important characteristic of asbestos is its synergistic effect with cigarette smoking: a 'more than an additive interaction' (probably a multiplicative interaction) has been observed between asbestos exposure and smoking for the risk of lung cancer (138;139). A decrease in lung cancer risk has been observed in insulation and shipyard workers following the cessation of asbestos exposure (140;141). No excess risk of lung cancer has been observed 7 - 15 years after cessation of (chrysotile) asbestos exposure in shipyard workers; which is indicative of a role for asbestos as tumor promoter for lung cancer (141). No such effect was observed for mesothelioma (141). Asbestos is classified as a human carcinogen by the IARC; Siemiatycki et al. judged the evidence of asbestos to lung carcinogenicity to be strong (14;112).

### 2.3.2 Arsenic

Exposure to arsenic and its compounds occurs in various occupational settings including: nonferrous metal smelting; production, packaging, and use of arsenic-containing pesticides; sheep dip manufacture; wool fibre production; and mining of ores containing arsenic (14;46). The OSHA standard for airborne inorganic arsenic is $10 \mu g/m^3$.

Experimental evidence is lacking for the carcinogenicity of arsenic; however, strong epidemiologic evidence confirmed the carcinogenic potential of arsenic (14;46-49). In Taiwan, consumption of high-arsenic contaminated well water was associated with an increased risk of lung cancer (OR=3.4) (142). In a meta-analysis of studies involving arsenic exposure, a combined RR of 3.7 (95% CI: 3.1-4.5) was estimated for lung cancer risk (8). Moreover, a clear dose-response relationship has been observed (8;46). Arsenic and its compounds have been classified as human carcinogens by IARC (112). Recently, IARC has concluded that drinking water containing high levels of arsenic (above the WHO standard-10μg/l) causes lung cancer and classified it as a Group 1 carcinogen (143).

### 2.3.3 Silica

Exposure to silica occurs among workers in various industries including: granite and stone industries; ceramics, glass, and related industries; foundries and metallurgical industries; abrasives; construction and farming (14;46). The OSHA standard for quartz exposure is $100\mu g/m^3$. Other occupational exposures (including PAHs, radon, and asbestos) co-exist with silica in most occupational circumstances (46).

There exists a body of evidence indicating silica exposure is associated with an increased risk of lung cancer (8;14;46;113). A meta-analysis of 15 studies involving silica exposure in patients with silicosis and of 13 studies on silica exposed workers estimated RRs of 2.8 (95% CI: 2.5-3.2) and 1.3 (95% CI: 1.2-1.5), respectively. In these meta-analyses, autopsy studies, PMR studies, and the studies in miners involving potential confounders were excluded to control for bias (8). In a recent meta-analysis, studies involving exposure to asbestos and radioactive materials including radon have been excluded; the summary estimate of the relative risk for lung cancer risk for the exposure to silica was 1.3 (95% CI: 1.2-1.4). However, a separate meta-analysis of 16 studies on the silicotics and 8 studies on non-silicotics resulted in summary estimates of 2.4 (95% CI: 2.0-2.8) and (1.0, 95% CI: 0.8-1.2), respectively, thereby suggesting a less prominent role of silica as a lung carcinogen than silicosis (144). In 1997, IARC classified crystalline silica as carcinogenic to humans (Group 1) (113). In addition, the evidence for lung carcinogenicity of crystalline silica was judged to be strong by Siemiatycki and colleagues (14).

### 2.3.4 Chromium

Chromium (Cr) exists mostly in the trivalent and hexavalent states (50). Chromium is used in the production of alloys such as stainless steel to confer hardness, and rust and acid resistance to the alloy (8). Other industrial processes which are major sources of occupational chromium exposure include: chrome pigment production, chrome plating, stainless steel production & welding, and tanning of leather (50;145). Several occupational groups (including painters, battery makers, candle makers, printers, and rubber makers) are also exposed to chromium (50). The OSHA standard for chromic acid and Cr(VI) containing chromates is 0.1mg/m$^3$ (8).

A meta-analysis of the ten largest and best–designed studies of chromium production workers, chrome platers, and chromate paint producers yielded an estimated summary relative risk of 2.8 (2.5-3.5) for lung cancer in relation to chromium exposure, after ruling out a confounding effect of smoking, asbestos, and nickel exposure (8). A recent study has documented an elevated risk of lung cancer (SMR=365) at exposures to hexavalent Cr over 1.05 mg/m$^3$-years (44). Hexavalent chromium compounds have been classified by the IARC as human carcinogens (14;51). The U.S Environment Protection Agency (EPA) had classified hexavalent chromium as a known carcinogen by the inhalation route, especially for lung cancer (146).

### 2.3.5 Beryllium

Exposure to beryllium occurs in various occupational settings including: beryllium mining and processing; aircraft and aerospace industries; electronics and nuclear industries; and ceramic manufacturing industries and jewelers (8;14). A cohort mortality study involving 689 patients with beryllium disease noted an elevated risk of lung cancer (SMR=2, 95% CI: 1.3-2.9) (147). In a 1992 cohort mortality study of 9,225 male workers at seven beryllium processing plants, an elevated risk of lung cancer (SMR= 1.3, 95% CI: 1.1-1.4) was observed (148). A recent reanalysis of this NIOSH cohort mortality study did not support the findings of the original study; an overall SMR for lung cancer that was estimated using a more appropriate reference population cancer rates was not statistically significant (149). In 1993, IARC classified beryllium as being carcinogenic to humans (39).

### 2.3.6 Nickel

Exposure to nickel and its compounds occurs in the nickel refining industry, in the production of nickel alloys & nickel salts, in grinding & cutting of stainless-steel, and in other industries, including, welding, electroplating and manufacturing of batteries (14;46;51). The OSHA standard for soluble nickel compounds is $0.1 mg/m^3$, and $1 mg/m^3$ for nickel metal and insoluble nickel compounds, respectively (8).

An increased risk of lung cancer has been observed among nickel refinery workers in South Wales, Norway and Canada (46). Exposure to the substances released during the processing of ore (roasting, sintering and calcining) has been associated with an excess risk of lung cancer in nickel workers in Canada and Norway (46;51). A meta-analysis of 13 studies indicated an increased risk of lung cancer in exposed workers at nickel refineries; a summary relative risk of lung cancer of 1.6 (95% CI: 1.4-1.7) was estimated (8). IARC had classified nickel compounds as human carcinogens (Group 1) to humans, although metallic nickel was classified as a possible human carcinogen (Group 2B) (51). Some selected nickel compounds (including nickel oxides and sulfides) in the nickel refining industry have been identified as Group 1 lung carcinogens (14).

### 2.3.7 Ionizing radiation

Radiation has been classified into two types based on the rate of energy transfer to tissues: low linear energy transfer (LET) radiation (such as X-rays and gamma rays), and high-LET radiation (such as neutrons and radon) (4). Exposures to both types of radiation occur in different occupational environments.

Radon is a radioactive gas formed during the decay of radioactive uranium-238. In the past, underground miners, notably uranium miners, have been exposed to high levels of radon. Other exposure circumstances include underground hematite mining. The current standard is 4 Working Level Months (WLM) per year for radon exposure in mines (8). However, the median level of exposure observed for U.S uranium miners is 430 WLM (8). The evidence from the literature has been strong for an association between radon exposure and lung cancer (8;14;150-153). Although, radon exposure induced mainly small cell cancers, occurrence of other cancer types was also noted (46). Lubin and colleagues have estimated a linear increase of relative risk (of lung cancer) in the order of 0.0049 per WLM from 11 cohort studies of underground miners; they attributed 40% of the lung cancer deaths to radon progeny exposure (154). Lubin and colleagues observed a 3-fold greater exposure-response trend in non-smokers than in smokers (154). Radon has been determined to be second leading cause of lung cancer by the U.S Environmental Protection Agency (123). Radon and its decay products are classified as human carcinogens by the IARC (122).

Occupational exposure to low-LET radiation (X-rays and gamma rays) occurs in nuclear workers, clean-up workers after nuclear accidents, radiologists, and technologists (14;155). Epidemiological evidence for carcinogenic risk derives largely from survivors of the atomic bomb explosions in Japan and medically exposed patients (diagnostic &

therapeutic X-ray irradiation) (155). Ionizing radiation and their sources (including X-rays and $\gamma$-rays) have been identified as human carcinogens by IARC (155;156). It has been suggested that the lung cancer risk associated with low-LET radiation occurs mainly at higher doses (as experienced by the atomic bomb survivors) and that the risk is minimal in clinically exposed patients: a relative risk of 1.0 (95% CI: 0.9-1.1) & 1.6 (1.3-2.0) has been reported for irradiated tuberculosis patients and atom bomb survivors at a dose of 1 Sievert (Sv) (157).

### 2.3.8 Other Occupational Exposures

Polycyclic aromatic hydrocarbons (PAH) are a complex mixture of benzene compounds generated mainly from combustion of organic matter; they are also found adsorbed to diesel exhausts (46). Exposure to PAHs occurs in various occupational circumstances including: steel mills, work involving combustion of organic matter (including coke oven emissions and gas works), foundries, firefighters, and vehicle mechanics. A recent review and meta-analysis concluded that occupational exposure to PAHs by inhalation was associated with an elevated lung cancer risk; a relative risk of 1.20 (95% CI: 1.11-1.29) was estimated for the exposure to PAHs at 100 $\mu g/m^3$ years benzo(*a)*pyrene (158). Benz[a]anthracene, benzo[*a*]pyrene, dibenz[*a,h*]anthracene have been identified as probable human carcinogens in the IARC monograph evaluation (116;117). Siemiatycki et al judged the evidence of lung carcinogenicity to be suggestive (14).

Diesel exhaust exposure occurs mainly in railroad workers, professional drivers, mechanics, and dock workers. In a recent meta-analysis of six studies involving subjects with diesel exposure, an excess risk of lung cancer was found (RR=1.31, 95% CI: 1.13-1.44) (8). The particulate phase of the exhaust has been implicated in the induction of cancer (8). Diesel engine exhaust have been identified as a probable human carcinogen by the IARC (115).

Occupational exposure to chloromethyl ethers occurs during production of these chemicals, ion-exchange resins & polymers, and other occupational circumstances including, plastic manufacturing, and the use of chloromethyl ether as a laboratory reagent (14). An elevated risk of lung cancer (predominantly small cell carcinoma) was observed among workers involved in the manufacture of ion exchange resins (159-162). The IARC identified bis(chloromethyl)ether (BCME) and chloromethyl methyl ether (CMME) as known causes of cancer in humans (112). Siemiatycki and colleagues judged the evidence was strong for small cell lung cancer (14). Other substances such as mustard gas, coal tars and pitches, and certain mineral oils were also suggested to be lung carcinogens (14).

## *2.4 Summary of Literature Review*

In summary, our literature review identified various high-risk occupations and industries. An elevated risk of lung cancer was observed mainly in occupations involving metal work and other occupational circumstances, including: mining, transportation, and construction work. Various carcinogenic exposures have been identified in these occupations, including: metallic substances, asbestos, and chromium. With this background we conducted an investigation to identify occupational risk factors for lung cancer using the data from a large population-based study of occupational cancer in British Columbia (BC) (163).

# 3. Methods

## *3.1 Introduction*

This research is based on a secondary analysis of data from a population based occupational cancer study in British Columbia. The electronic version of this data was provided by Dr. Pierre Band from Health Canada. The risk of lung cancer in various occupations and industries was estimated by comparing men with lung cancer to men with other types of cancer. Analyses were done for all lung cancer types combined as well as within histopathological sub-types of lung cancer. The primary methods of data analysis was unconditional logistic regression. A separate analysis of never smokers was considered, but not done because 97% of cases and 81% of controls smoked. We initially planned to conduct exposure-specific analyses after converting occupational histories to substances of exposure using the National Institute for Occupational Safety and Health (NIOSH) job exposure matrix (JEM) (164). However, technical issues precluded this aspect of the analysis. The issues associated with the JEM are discussed in Chapter 5.

### 3.1.1 Study Objectives

The primary objective of the thesis was to determine if work activities are associated with an excess risk of lung cancer. More specifically, the thesis will determine if lung cancer is elevated for men working in certain occupations or industries. It will also examine whether lung cancer risks associated with specific occupations and industries differ according to the histopathology subtypes of lung cancer.

### 3.1.2 The British Columbia Occupational Cancer Study

The present analysis is based on a British Columbia occupational cancer study in which information on cancer histopathology and occupational history was collected for cancer cases reported to the population-based British Columbia Cancer Registry (BCCR). (163). A brief description of this study is given here.

The study was restricted to male cancer patients 20 years of age and older who were ascertained by the BCCR during the period 1983-1990. Information on surname, first name, age, residential address, telephone number, anatomic site and histology of the primary cancer of all the cancer cases was obtained from BCCR records. A self-administered questionnaire (a copy of questionnaire is available from Dr. Pierre Band on request) was sent to all identified cancer patients to collect information on occupational history (lifetime job descriptions, occupation and industry titles, duration and period of work). This questionnaire also provided information on ethnic origin, lifetime smoking habits, education status and alcohol consumption (questions on alcohol consumption was included after the first year of study). This study recruited subjects with cancers at various sites; recruitment for each cancer site continued until 1,000 completed questionnaires were returned for the cancer site, at which time recruitment for that cancer site was discontinued. However, for all cancer sites, all cases diagnosed in the first two years were admitted into the study, even if that led to more than 1000 subjects being recruited for that cancer site. The questionnaires that were returned with incomplete information were completed by contacting the patient or next of kin (when patient was too ill or deceased) by telephone. For patients who did not return the questionnaire within two weeks, reminders were sent: a post card and two telephone reminders at two week intervals. Non-response after this period was considered as refusal to participate in the study. Of the 25,726 questionnaires that were mailed out initially, a total of 15,463 questionnaires were returned, for a response rate of 60%. Non-response bias was determined by the principal investigators to be minimal (163).

The topography and pathology of the primary tumour were coded using the 9th revision of the International Classification of Diseases (ICD-9) and the International Classification of Diseases for Oncology (ICD-O), respectively (165;166). Work histories of the subjects recorded in the self-administered questionnaire were coded using the occupations and the industries given in the Canadian Standard Occupational Classification (SOC) and the Canadian Standard Industrial Classification (SIC), respectively (110;124). The SOC and SIC are hierarchical coding systems in which 2, 3 and 4 digit codes are utilized. The SOC classifies occupations by 2, 3 and 4-digit (SOC) codes representing major groups, minor groups, and unit groups of occupations, respectively. The 2, 3 and 4-digit industry (SIC) codes represent major groups, groups, and classes of industries, respectively. In addition, industries are classified into divisions, represented by an alphabetical code. In addition two new SOC codes and one SIC code were developed in BC: 'teacher not elsewhere classified (SOC-2738)' and 'mixed farmer not elsewhere classified (SOC-7118)'. Workers involved in the 'general construction' were coded as SIC-4099.

## *3.2 Study Design*

A case-control study design was used to assess the relationship between occupations and industries and lung cancer, including histological sub-types of lung cancer. Cases were men with biopsy proven lung cancer. Controls were selected from among men with other types of cancer. Two analytic strategies were used: a matched analysis using conditional logistic regression (with cases and controls stratified by age and year of diagnosis), and an unmatched analysis using unconditional logistic regression with age and year of diagnosis included as covariates.

## *3.3 Study Population*

The dataset available for analysis was comprised of 14,755 subjects, including 2,998 cases of lung cancer. The overall response rate was 60%, with a slightly lower response rate in men with lung cancer (2,988 responses from 5,528 eligible men for a response rate of 54.2%). Histopathology for all lung cancer cases was obtained from the BCCR.

### 3.3.1 Selection of Cases

All patients with lung cancer who returned questionnaires in the BC occupational cancer study during the period 1983-1990 inclusive were defined as cases. The pathological grouping of lung cancer cases was based on the ICD-O classification shown in Table 11 (166); the histopathological sub-types of lung cancer were classified according to the World Health Organization (WHO) guidelines (167).

**Table 11:** Histopathology subtypes of lung cancer

| Cancer sub-type | ICD-O codes |
|---|---|
| Squamous cell carcinoma | 8050-8052, 8070-8076s |
| Adenocarcinoma | 8140, 8211, 8230, 8231, 8250, 8251, 8260, 8323, 8480, 8481, 8490, 8550, 8560, 8570, 8571, 8572 |
| Small cell carcinoma | 8041-8043 |
| Large cell carcinoma | 8012, 8020-8022, 8030, 8031, 8310 |

A detailed description of the histopathological sub-types of lung cancer and the ICD-O codes for each sub-type is provided in Appendix 1.

### 3.3.2 Selection of Controls

Controls were selected from patients with cancers other than lung cancer (no cancer free control group was available for use in this study). All patients with cancers other than lung cancer and cancers of unknown primary site were included in the basic control group (Control 1). In addition, we report analyses using a second control group (Control 2), derived from the basic control group after excluding subjects with cancers that are strongly related to smoking. Cancers strongly related to smoking were identified from the literature (71;168) and included: cancers of the lip, oral cavity & pharynx, nasal cavity & nasal sinuses, larynx, oesophagus, stomach, liver, pancreas, bladder, kidney, and myeloid leukemia. Therefore, patients with these cancers were excluded from the second control group. The implications of this control selection methodology are examined in the sections 6.3.2.1 and 6.3.3.

### 3.3.3 Occupational Risk Factors

The primary risk factors of interest consisted of the occupation or industry in which the subject worked. These variables were based on the Canadian SOC and SIC codes assigned for each job reported by the subject. Information for multiple jobs held by the same subject was combined using two strategies. The 'usual occupation' of a subject was defined as the occupation held for the maximum length of time. Subjects were also classified as having 'ever' worked in an occupation; each subject was permitted more than one occupation in which they had 'ever worked'. Separate analyses were performed based on the 'usual occupation', and on which occupations the subject had 'ever' held. A subject was classified as exposed if their usual occupation was the occupation of interest. Separate analyses were conducted according to the 2, 3, 4-digit hierarchical codes of Canadian SOC. A similar strategy was used for industries in which the subjects had reported working.

### 3.3.4 Other Covariates

Information was available for the following potential confounding factors: age at cancer diagnosis, year of diagnosis, smoking, ethnic status, educational status, marital status, alcohol consumption, and respondent to the questionnaire.

The exact age at cancer diagnosis (in years) was available for all the subjects in our data. Based on the exact age of the subjects, we defined nine age groups for the purpose of our analysis (20-39, 40-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, and ≥80 years). The subjects in the youngest age group (20-39 years) are used as the reference group.

The subjects in the BC study were incident cancer cases. Therefore, the year of diagnosis of all the subjects in our study falls within the study period 1983 to 1990. We defined 8 groups based on the exact year of diagnosis corresponding to each year of the 8 year duration of the study: 1983, 1984, 1985, 1986, 1987, 1988, 1989, and 1990. The cancer subjects diagnosed in the year 1983 served as reference group in our analysis.

The following information was available on smoking in the dataset: age when started smoking, age at smoking cessation, average number of cigarettes smoked per day, pipes/cigars smoked per day, total years smoked, and pack-years of smoking. Pack-years of smoking were derived by multiplying the number of packs of cigarettes smoked per day (assuming 20 cigarettes per pack) by the total duration of smoking (in years). Based on these pack-years, the smokers were classified into four groups (0, 1-24, 25-49, and ≥50 pack-years) for the purpose of our analysis. Non-smokers (with zero pack-years of smoking) served as reference group.

The subjects in the BC data represented 4 ethnic groups: Caucasians, Asians, native Indians, and others. We re-grouped the subjects into 'Caucasians' and 'non-

Caucasians'. The 'non-Caucasians', comprised of Asians, native Indians, and other ethnic groups, served as reference group in our analysis.

Information on the number of years of education and post-secondary education status was available in the BC data. Using this information, subjects were grouped into following categories of educational attainment: '<8 years of education', '8-11 years of education', 'high school education', and 'post secondary education'. We used the same categories to define the educational status of the subjects in our analysis. The subjects with less than 8 years of education served as the reference group.

The subjects in the BC data were classified into four groups based on marital status: 'single', 'married/common law', 'widowed', and 'separated/divorced'. We used the same categories to define the marital status of the subjects in our analysis. The unmarried ('single') subjects served as reference group.

In our analysis, we defined two groups to represent the respondents to the questionnaire (patient/ proxy). Proxy respondents are relatives and other individuals who completed the questionnaire on behalf of the patients. The proxy respondents served as reference group in our analysis.

Information on the consumption of various alcoholic beverages, including beer, wine, and spirits (age when started consuming alcohol; average number of bottles of beer, glasses of wine, and ounces of spirits per day; and total years of consuming alcohol) was used to derive the cumulative alcohol consumption score included in the BC data. The cumulative alcohol consumption score is estimated by multiplying the number of alcoholic beverages consumed per week by the duration of alcohol use (in years). For the purpose of our initial analysis, we defined two groups based on the alcohol consumption status (ever/never drinkers). The subjects who indicated a positive response to alcohol consumption during their lifetime were defined as 'ever drinkers'. The subjects who never consumed alcohol during lifetime were defined as 'never drinkers', and were used as the reference group.

The choice of the covariates to be included in the analysis was not only data driven, but also based on the existing evidence on established risk factors for lung cancer (see section 3.5.2).

## *3.4 Power*

A total of 14,755 cancer cases, including 2,998 lung cancer cases, were available in the analytic dataset. If the power is fixed at 80% and the level of significance at 5%, then the detectable odds ratios were 1.7, 1.4, and 1.2, assuming an exposure of 1, 3 and 10%, respectively in the study population. The sample size was reduced for some of the analyses owing to the choice of control group and exclusion of subjects with missing information on covariates (see Section 4.3). The sample size is smallest for the analysis of large cell carcinoma (using second control group) constituted by 7,333 subjects (including 311 cases, and 7,022 controls). For this sample size, the detectable odds ratios were 3.3, 2.2 and 1.6 for exposure prevalences of 1, 3 and 10%, respectively. All power calculations were done using the online power calculator provided by UCLA Department of statistics available at the following web address: http://calculators.stat.ucla.edu/powercalc/.

## *3.5 Statistical Analysis*

Statistical analysis involved a combination of descriptive and analytic data analytical techniques. Descriptive analyses included the calculation of means, variances, and frequency distributions of key covariates, as appropriate. All missing values were examined to identify data entry or management issues. For example, if the information on 'pack-years of smoking' variable was missing for a subject, then the information on smoking status (smoker/non-smoker) was used to determine whether the subject was a non-smoker, or the information was totally unknown/missing.

Subjects were classified as 'exposed' or 'unexposed' based on SOC and SIC codes: the unexposed group consisted of all subjects who did not meet the criterion for exposure. Separate analyses were conducted for 'usual' occupation/industry and for exposure based on whether the subject had 'ever' worked in the target occupation/industry. Occupations and industries with fewer than three cases of lung cancer were not included in the analysis (163). Odds ratios for lung cancer in relation to occupation and industry were calculated using logistic regression models, along with their associated confidence limits. Initial logistic regression modelling was conducted to identify relevant covariates for inclusion in the final logistic regression models (see section 3.5.2) and to determine if there were a need to use conditional logistic regression models. All analyses conducted for lung cancer as an endpoint were repeated for each of the histopathological sub-groups of lung cancer. All the analyses were performed using SAS version-9 running under Windows-XP (169).

### 3.5.1 Unconditional vs Conditional Logistic Regression

Conditional logistic regression is normally used when the number of matching variables is large. However, conditional logistic regression has somewhat lower power than unconditional logistic regression (170) if the bias introduced by the latter model as a consequence of ignoring the matching is small.

Preliminary comparisons were performed to determine whether conditional logistic regression models were required in this study. The 23 'usual' major occupational categories (2-digit SOC codes) and the 18 'usual' industrial divisions (alphabetical SIC codes) were selected as exposures for this comparison. The unconditional regression model included age and year of diagnosis as categorical predictors converted to dummy variables based on nine age groups (20-39, 40-49, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, and ≥80 years) and eight single year categories (1983, 1984, 1985, 1986, 1987, 1988, 1989, and 1990). Two conditional logistic regression models were examined. The first model used age (in single year categories) and year of diagnosis (in single year categories) as stratification variables. The second conditional logistic regression model was similar to the first model, except that age was re-coded into 9 categories (similar to the unconditional model) and used as stratification variable. All the three models were adjusted for smoking (0, 1-24, 25-49, and ≥50 pack-years), educational status (<8 years, 8-11 years, high school, and post secondary), respondent to questionnaire (patient, or proxy), and ethnic status (caucasian, or non-caucasian). For each of the exposures, the estimated OR and 95% confidence intervals were compared across the three (one unconditional and two conditional) fitted logistic regression models.

### 3.5.2 Selection of Confounders

Potential confounders were selected from the available non-occupational variables: smoking, age, year of diagnosis, respondent to questionnaire, ethnic status, alcohol consumption status, education status, and marital status. Based on existing literature, age, smoking (pack-years), and year of diagnosis were selected as *a priori* covariates for inclusion in the model (4;46;55;163;171;172). The model containing these factors (age, smoking and year of diagnosis) constituted the base model; the corresponding odds ratio for this model was denoted as $OR_1$ for the respective occupation/industry.

The importance of the remaining covariates (marital status, education status, ethnic status, and respondent to questionnaire) as confounders was assessed by comparing the odds ratios for selected exposures after adjusting for each covariate ($OR_2$) to the model without the covariate ($OR_1$). The large number of occupational and industrial exposures rendered it infeasible to evaluate the possibility of confounding in all possible situations. Instead, we selected a representative group of occupations and industries to act as a guideline. For each selected exposure group, two unconditional logistic regression models were used: the base model (the selected exposure group, age, year of diagnosis and smoking variable) and the adjusted model (the base model along with a candidate confounder). The difference in the odds ratio estimates for selected (occupations) was noted. This analysis was performed with both control groups. The variables which resulted in a 10% or greater change in the odds ratio estimates were selected as candidate covariates for inclusion in the final model. The number of times a covariate was selected across the selected exposures was determined. The most frequently occurring covariates were retained in the final model.

The information on alcohol consumption status (ever/never-drinkers) was not available for 2,064 subjects in the BC data set (approximately 14% of total number of subjects). Including this variable in the analysis therefore resulted in substantial drop in sample size. Since alcohol consumption is generally not considered to be related to lung cancer (102), we considered excluding alcohol from the confounder list. An empirical comparison within the current data sets by using the 'usual' major occupational categories (23 groups) supported this decision (see section 4.3). This analysis was limited to control group 1.

### 3.5.3 Final Analysis

The occupations and the industries that were associated with an increased risk of lung cancer were identified by performing unconditional logistic regression analyses on 2, 3, 4 digit hierarchical SOC and SIC codes whenever there were at least 3 lung cancer cases within the selected SOC/SIC code. All analyses were adjusted for the selected confounders. Separate analyses were conducted for 'usual' and 'ever' occupation/industry. These analyses were performed using both control groups. Because of the two exposure definitions ('usual' and 'ever') and two control groups, we obtained four odds ratio estimates and 95% confidence intervals for each occupation/industry considered. All the analyses were repeated by re-defining the outcome based on histopathological subtypes of lung cancer.

The occupations and industries (SOC/SIC codes) associated with a significant OR ($p<0.05$) are summarized in tabular form in the next chapter; separate tables are provided for each of the histopathological subtypes of lung cancer considered. For the purpose of clarity, the tables also report the OR estimates for the major hierarchical categories for each significant occupation/industry. For example, if a SOC code 3111 was found to be significantly associated with lung cancer, the odds ratios and 95% confidence intervals in the SOC categories 31 and 311 are also reported. Results of the non-significant analyses are not included in the thesis owing to their length but available on request from the author.

# 4. Results

## *4.1 Characteristics of the Study Subjects*

The basic characteristics of the cases and both control groups, including the histopathology sub-types of lung cancer, are summarized in Table 12. The mean age at diagnosis (±standard deviation) of cancer for cases and controls was 66.4 (±9.5) and 63.8 (±13.7) years, respectively. The majority of cases and controls were caucasians with 8-11 years of education, and were mostly smokers; about 25% of responses were from proxies.

The subjects in our dataset represented a total of 605 occupational categories (23 major, 83 minor, and 499 unit groups) and 1,223 industrial categories (18 divisions, 76 major, 314 minor groups, and 815 classes), based on Canadian SOC and SIC codes, respectively. Our analysis was restricted to occupations and industries having more than 3 cases and controls. As a consequence, our assessment of lung cancer risk (all types) for 'usual' employment was limited to subjects in 279 occupational categories and 443 industrial categories. Similarly, lung cancer risk assessment for the occupational exposures based on the 'ever' held jobs was limited to 427 occupational and 745 industrial categories. The mean duration of employment (±standard deviation) for cases was 39.1 (±12.3) years; the means for control group 1 and control group 2 were 37.9 (±14.2) and 37.7 (±14.6) years, respectively.

**Table 12**: Characteristics of Cases and Controls (Groups 1 & 2) for Lung Cancer and Histopathological Subtypes

| Characteristics | No. of Cases (%) | | | | | No. of Controls (%) | |
|---|---|---|---|---|---|---|---|
| | All types (n=2998) | Squamous cell (n=1055) | Adenocarcinoma (n=912) | Small cell (n=545) | Large cell (n=356) | Group-1* (n=11,757) | Group-2† (n=8013) |
| Age at cancer diagnosis (years) Mean ±SD | 66.4±9.5 | 67.6±9.2 | 65.3±9.8 | 65.9±8.3 | 66.1±9.9 | 63.8±13.7 | 63.3±14.5 |
| Age group (years) | | | | | | | |
| 20-39 | 21(0.7) | 4 (0.4) | 8 (0.9) | 0 | 4 (1.1) | 839 (7.1) | 728 (9.1) |
| 40-49 | 126 (4.2) | 29 (2.8) | 55 (6.0) | 16 (2.9) | 18 (5.1) | 845 (7.2) | 587 (7.3) |
| 50-54 | 178 (5.9) | 50 (4.7) | 67 (7.4) | 33 (6.1) | 24 (6.7) | 778 (6.6) | 494 (6.2) |
| 55-59 | 336 (11.2) | 102 (9.7) | 99 (10.9) | 78 (14.3) | 40 (11.2) | 1163 (9.9) | 712 (8.9) |
| 60-64 | 497 (16.6) | 173 (16.4) | 169 (18.5) | 93 (17.1) | 48 (13.5) | 1651 (14.0) | 1065 (13.3) |
| 65-69 | 647 (21.6) | 229 (21.7) | 180 (19.7) | 139 (25.5) | 72 (20.2) | 1962 (16.7) | 1320 (16.5) |
| 70-74 | 601 (20.1) | 226 (21.4) | 182 (20.0) | 100 (18.4) | 75 (21.1) | 1993 (17.0) | 1359 (17.0) |
| 75-79 | 401 (13.4) | 156 (14.8) | 101 (11.1) | 64 (11.7) | 59 (16.6) | 1494 (12.7) | 1034 (12.9) |
| ≥80 | 191 (6.4) | 86 (8.2) | 51 (5.6) | 22 (4.0) | 16 (4.5) | 1032 (8.8) | 714 (8.9) |
| Year of diagnosis | | | | | | | |
| 1983 | 396 (13.2) | 181 (17.2) | 122 (13.4) | 55 (10.1) | 33 (9.3) | 3283 (27.9) | 2636 (32.9) |
| 1984 | 447 (14.9) | 207 (19.6) | 122 (13.4) | 69 (12.7) | 42 (11.8) | 2306 (19.6) | 1606 (20.0) |
| 1985 | 472 (15.7) | 177 (16.8) | 143 (15.7) | 83 (15.2) | 47 (13.2) | 1948 (16.6) | 1288 (16.1) |
| 1986 | 432 (14.4) | 155 (14.7) | 140 (15.4) | 74 (13.6) | 35 (9.8) | 1619 (13.8) | 993 (12.4) |
| 1987 | 418 (13.9) | 173 (16.4) | 105 (11.5) | 70 (12.8) | 48 (13.5) | 1504 (12.8) | 902 (11.3) |
| 1988 | 415 (13.8) | 162 (15.4) | 113 (12.4) | 76 (13.9) | 47 (13.2) | 553 (4.7) | 340 (4.2) |
| 1989 | 186 (6.0) | 0 | 74 (8.1) | 61 (11.2) | 43 (12.1) | 249 (2.1) | 115 (1.4) |
| 1990 | 232 (7.7) | 0 | 93 (10.2) | 57 (10.5) | 61 (17.1) | 295 (2.5) | 133 (1.7) |
| Marital Status | | | | | | | |
| Single | 149 (5.0) | 63 (6.0) | 31 (3.4) | 21 (3.9) | 23 (6.5) | 744 (6.3) | 525 (6.6) |
| Married/common law | 2398 (80.0) | 824 (78.1) | 745 (81.7) | 448 (82.2) | 281 (78.9) | 9592 (81.6) | 6557 (81.8) |
| Widowed | 211 (7.0) | 80 (7.6) | 62 (6.8) | 33 (6.1) | 24 (6.7) | 695 (5.9) | 468 (5.8) |
| Separated/ divorced | 213 (7.1) | 79 (7.5) | 67 (7.4) | 37 (6.7) | 24 (6.7) | 622 (5.3) | 389 (4.9) |
| Unknown | 27 (0.9) | 9 (0.9) | 7 (0.8) | 6 (1.1) | 4 (1.1) | 104 (0.9) | 74 (0.9) |
| Educational status | | | | | | | |
| < 8 yrs | 394 (13.1) | 151 (14.3) | 103 (11.3) | 74 (13.6) | 49 (13.8) | 1261 (10.7) | 813 (10.2) |
| 8-11 yrs | 1463 (48.8) | 521 (49.4) | 419 (45.9) | 273 (50.1) | 187 (52.5) | 5031 (42.8) | 3344 (41.7) |
| High school | 321 (10.7) | 105 (10.0) | 105 (11.5) | 54 (9.9) | 38 (10.7) | 1352 (11.5) | 935 (11.7) |
| Post secondary | 652 (21.8) | 215 (20.4) | 239 (26.2) | 114 (20.9) | 63 (17.7) | 3535 (30.1) | 2548 (31.8) |
| Unknown | 168 (5.6) | 63 (6.0) | 46 (5.0) | 30 (5.5) | 19 (5.3) | 578 (4.9) | 373 (4.7) |
| Ethnic status | | | | | | | |
| Caucasian | 2803 (93.5) | 998 (94.6) | 841 (92.2) | 517 (94.9) | 330 (92.7) | 11121 (94.6) | 7669 (95.7) |
| Non-Caucasian | 153 (5.1) | 42 (4.0) | 61 (6.7) | 19 (3.5) | 21 (5.9) | 571 (4.9) | 308 (3.8) |
| Unknown | 42 (1.4) | 15 (1.4) | 10 (1.1) | 9 (1.7) | 5 (1.4) | 65 (0.6) | 36 (0.5) |
| Respondent to questionnaire | | | | | | | |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Patient | 2123 (70.8) | 745 (70.6) | 691 (75.8) | 364 (66.8) | 240 (67.4) | 9349 (79.5) | 6461 (80.6) |
| Proxy | 839 (28.0) | 292 (27.7) | 214 (23.5) | 175 (32.1) | 112 (31.5) | 2142 (18.2) | 1354 (17.0) |
| Unknown | 36 (1.2) | 18 (1.7) | 7 (0.8) | 6 (1.1) | 4 (1.1) | 266 (2.3) | 198 (2.5) |
| Smoking status | | | | | | | |
| Non-smoker | 72 (2.4) | 8 (0.8) | 47 (5.2) | 3 (0.6) | 10 (2.8) | 2176 (18.5) | 1710 (21.3) |
| Smoker | 2921 (97.4) | 1042 (98.8) | 865 (94.9) | 542 (99.5) | 346 (97.2) | 9540 (81.1) | 6272 (78.3) |
| Unknown | 5 (0.2) | 5 (0.5) | 0 | 0 | 0 | 41 (0.4) | 31 (0.4) |
| Smoking duration (years) | | | | | | | |
| 0 | 130 (4.3) | 34 (3.2) | 68 (7.5) | 10 (1.8) | 13 (3.7) | 2618 (22.3) | 2040 (25.5) |
| 1-29 | 366 (12.2) | 104 (9.9) | 145 (15.9) | 54 (9.9) | 39 (11.0) | 3551 (30.2) | 2607 (32.5) |
| 30-44 | 1119 (37.3) | 387 (36.7) | 326 (35.8) | 222 (40.7) | 136 (38.2) | 3153 (26.8) | 1951 (24.4) |
| 45-98 | 1354 (45.2) | 519 (49.2) | 362 (39.7) | 256 (47.0) | 164 (46.1) | 2244 (19.1) | 1280 (16.0) |
| Unknown | 29 (1.0) | 11 (1.0) | 11 (1.2) | 3 (0.6) | 4 (1.1) | 191 (1.6) | 135 (1.7) |
| Cigarette pack-years | | | | | | | |
| 0 | 131 (4.4) | 35 (3.3) | 68 (7.5) | 10 (1.8) | 13 (3.7) | 2618 (22.3) | 2040 (25.5) |
| 1-24 | 375 (12.5) | 108 (10.2) | 145 (15.9) | 58 (10.6) | 42 (11.8) | 3443 (29.3) | 2497 (31.2) |
| 25-49 | 972 (32.4) | 324 (30.7) | 318 (34.9) | 174 (31.9) | 115 (32.3) | 2927 (24.9) | 1852 (23.1) |
| ≥ 50 | 1412 (47.1) | 543 (51.5) | 353 (38.7) | 287 (52.7) | 171 (48.0) | 2178 (18.5) | 1199 (15.0) |
| Unknown | 108 (3.6) | 45 (4.3) | 28 (3.1) | 16 (2.9) | 15 (4.2) | 591 (5.0) | 425 (5.3) |
| Alcohol consumption status | | | | | | | |
| Never drinker | 267 (8.9) | 98 (9.3) | 84 (9.2) | 38 (7.0) | 35 (9.8) | 1246 (10.6) | 838 (10.5) |
| Ever drinker | 2411 (80.4) | 815 (77.3) | 727 (79.7) | 464 (85.1) | 291 (81.7) | 8767 (74.6) | 5861 (73.1) |
| Unknown | 320 (10.7) | 142 (13.5) | 101 (11.1) | 43 (7.9) | 30 (8.4) | 1744 (14.8) | 1314 (16.4) |
| Cumulative alcohol consumption score | | | | | | | |
| 0-49 | 384 (12.8) | 140 (13.3) | 122 (13.4) | 54 (9.9) | 48 (13.5) | 1875 (16.0) | 1293 (16.1) |
| 50-199 | 473 (15.8) | 153 (14.5) | 152 (16.7) | 94 (17.3) | 53 (14.9) | 2050 (17.4) | 1469 (18.3) |
| 200-499 | 478 (15.9) | 159 (15.1) | 165 (18.1) | 79 (14.5) | 55 (15.5) | 1734 (14.8) | 1154 (14.4) |
| 500+ | 686 (22.9) | 223 (21.1) | 205 (22.5) | 139 (25.5) | 88 (24.7) | 1885 (16.0) | 1139 (14.2) |
| Unknown | 977 (33.9) | 380 (36.0) | 268 (29.4) | 179 (32.8) | 112 (31.5) | 4213 (35.8) | 2958 (36.9) |

*Group-1=base control group with all cancer patients other than lung and unknown primary cancers;
†Group-2=a subset of the base control group constituted by the subjects with cancers that are not strongly related to smoking;
Legend: SD=Standard deviation; n=total number of subjects; No.=number of subjects; %=percentage compared to total subjects (i.e., n).
Note: Only, age at diagnosis, age groups, year of diagnosis, cigarette pack years, education status, ethnic status, and respondent to questionnaire variables were used in the analyses.

More than 50% of the subjects belonged to 5 major 'usual' occupational categories: managerial, administrative & related occupations (12.8%); sales occupations (8.7%); service occupations (7.8%); product fabricating, assembling & repairing occupations (9.7%); and construction trades occupations (11.5%). Similarly, the 'usual' industries of employment were manufacturing industries (20.4%), construction industries (10.9%), transportation & storage industries (9.8%); and government service industries (9.7%).

### *4.2 Unconditional vs Conditional Logistic Regression models*

As indicated in Tables 13 and 14, conditional and unconditional regression analyses yielded similar results for the selected list of occupations considered. These tables provide odds ratios for lung cancer risk (all types) computed using conditional (CLR) and unconditional (ULR) logistic regression. The conditional models based on the year of diagnosis, and actual age (CLR-1) or the nine age groups (CLR-2) did not make a material difference over the unconditional model (ULR, adjusting for these same covariates) with respect to the conclusions or inferences drawn in this study. After considering issues such as lower power in the conditional models (170) and easy interpretability of the results from the unconditional model, we preferred to present the results from the unconditional logistic regression analysis in this study. These issues are described in more detail in section 6.3.3.

**Table 13:** Risk of Lung Cancer among Subjects in Broad Categories of Usual Occupation, based on Conditional and Unconditional Logistic Regression

| CSOC Code - Occupation title | Analysis using Control Group 1 | | | Analysis using Control Group 2 | | |
|---|---|---|---|---|---|---|
| | CLR OR (95% CI) | ACLR OR (95% CI) | ULR OR (95% CI) | CLR OR (95% CI) | ACLR OR (95% CI) | ULR OR (95% CI) |
| 11 Managerial administrative & related occupations | 0.94 (0.80 - 1.09) | 0.95 (0.81 - 1.10) | 0.95 (0.81 - 1.10) | 0.88 (0.74 - 1.05) | 0.90 (0.76 - 1.06) | 0.90 (0.76 - 1.06) |
| 21 Occupations in Natural sciences, Engineering and Mathematics | 0.83 (0.60 - 1.14) | 0.80 (0.58 - 1.09) | 0.79 (0.58 - 1.08) | 0.81 (0.57 - 1.14) | 0.79 (0.56 - 1.11) | 0.78 (0.55 - 1.09) |
| 23 Occupations in Social sciences and related fields | 0.62 (0.31 - 1.24) | 0.62 (0.32 - 1.23) | 0.64 (0.33 - 1.25) | 0.51 (0.24 - 1.09) | 0.54 (0.26 - 1.13) | 0.56 (0.28 - 1.15) |
| 27 Teaching and related occupations | 0.55 (0.33 – 0.90) | 0.58 (0.36 - 0.95) | 0.58 (0.36 - 0.95) | 0.55 (0.32 - 0.94) | 0.60 (0.35 - 1.00) | 0.59 (0.35 - 0.99) |
| 31 Occupations in Medicine and health | 1.19 (0.83 - 1.70) | 1.18 (0.83 - 1.68) | 1.17 (0.82 – 1.66) | 1.12 (0.75 - 1.68) | 1.18 (0.80 - 1.74) | 1.18 (0.80 - 1.75) |
| 33 Artistic, Literary, Recreational and related occupations | 0.97 (0.59 – 1.59) | 0.98 (0.61 - 1.57) | 1.01 (0.63 - 1.61) | 0.97 (0.55 - 1.70) | 0.91 (0.53 – 1.56) | 0.95 (0.56 - 1.61) |
| 41 Clerical and related occupations | 1.10 (0.87 - 1.38) | 1.11 (0.88 - 1.38) | 1.10 (0.88 - 1.37) | 1.15 (0.90 - 1.48) | 1.13 (0.88 - 1.45) | 1.11 (0.87 - 1.42) |
| 51 Sales occupations | 0.84 (0.71 – 1.00) | 0.84 (0.71 - 1.00) | 0.85 (0.72 – 1.01) | 0.83 (0.69 – 1.00) | 0.82 (0.68 – 0.98) | 0.83 (0.69 - 0.99) |
| 61 Service occupations | 1.17 (0.99 - 1.38) | 1.15 (0.98 - 1.36) | 1.16 (0.98 - 1.37) | 1.17 (0.97 - 1.42) | 1.14 (0.95 - 1.38) | 1.15 (0.95 - 1.39) |
| 71 Farming, Horticultural and Animal husbandry occupations | 0.90 (0.72 - 1.11) | 0.89 (0.72 – 1.10) | 0.89 (0.72 – 1.09) | 0.84 (0.67 - 1.06) | 0.83 (0.66 - 1.04) | 0.82 (0.65 - 1.02) |
| 73 Fishing, Trapping and related occupations | 0.60 (0.35 - 1.00) | 0.58 (0.35 - 0.96) | 0.57 (0.34 - 0.95) | 0.79 (0.43 – 1.44) | 0.79 (0.44 – 1.42) | 0.75 (0.42 – 1.34) |
| 75 Forestry and Logging | 0.89 (0.66 – 1.20) | 0.88 (0.66 – 1.18) | 0.90 (0.67 - 1.20) | 0.84 (0.60 - 1.17) | 0.82 (0.59 - 1.14) | 0.82 (0.59 - 1.14) |
| 77 Mining and Quarrying including Oil and Gas field | 1.41 (0.97 - 2.05) | 1.43 (0.99 - 2.07) | 1.42 (0.98 - 2.06) | 1.30 (0.85 - 2.00) | 1.36 (0.90 - 2.07) | 1.36 (0.89 - 2.06) |
| 81/82 Processing Occupations | 1.08 (0.89 - 1.30) | 1.09 (0.90 - 1.31) | 1.08 (0.90 - 1.30) | 1.12 (0.90 - 1.39) | 1.13 (0.91 – 1.40) | 1.13 (0.91 – 1.39) |
| 83 Machining and related Occupations | 1.37 (1.07 - 1.75) | 1.43 (1.12 - 1.82) | 1.42 (1.12 - 1.80) | 1.35 (1.02 – 1.78) | 1.42 (1.08 – 1.87) | 1.42 (1.08 – 1.85) |
| 85 Product fabricating, Assembling and Repairing | 1.05 (0.90 - 1.23) | 1.05 (0.90 - 1.23) | 1.05 (0.90 – 1.23) | 1.09 (0.91 - 1.31) | 1.11 (0.93 - 1.32) | 1.11 (0.93 - 1.32) |
| 87 Construction trades | 1.07 (0.92 - 1.23) | 1.05 (0.91 - 1.21) | 1.05 (0.91 - 1.21) | 1.16 (0.98 – 1.37) | 1.12 (0.96 - 1.32) | 1.14 (0.97 - 1.34) |
| 91 Transport equipment operating occupations | 0.93 (0.78 - 1.10) | 0.93 (0.79 - 1.11) | 0.93 (0.78 - 1.10) | 0.88 (0.72 - 1.07) | 0.89 (0.73 - 1.08) | 0.88 (0.73 - 1.07) |
| 93 Material handling and related occupations, N.E.C. | 1.05 (0.78 - 1.40) | 1.04 (0.78 - 1.38) | 1.06 (0.80 - 1.41) | 1.16 (0.84 - 1.62) | 1.15 (0.84 - 1.59) | 1.18 (0.86 – 1.62) |
| 95 Other crafts and equipment operating occupations | 1.12 (0.82 - 1.52) | 1.11 (0.82 - 1.51) | 1.11 (0.82 - 1.50) | 1.18 (0.83 - 1.67) | 1.17 (0.83 – 1.65) | 1.16 (0.83 - 1.64) |
| 99 Occupations not elsewhere classified | 1.10 (0.55 - 2.21) | 1.02 (0.52 - 2.01) | 1.06 (0.54 - 2.07) | 1.27 (0.54 - 3.00) | 1.26 (0.55 - 2.88) | 1.28 (0.56 - 2.95) |

CSOC= Canadian Standard Occupational Classification;
CLR: Conditional logistic regression, stratified on age and year of diagnosis, and adjusted for smoking, ethnicity, and respondent to the questionnaire;
ACLR: Adjusted conditional logistic regression, stratified on age groups (9-groups) and year of diagnosis;
ULR: Unconditional logistic regression, adjusted for age groups (9 groups) and year of diagnosis in addition to the covariates in CLR; OR= Odds ratio; CI=Confidence interval.

**Table 14**: Risk of Lung Cancer among Subjects in Broad Categories of Usual Industry, based on Conditional and Unconditional Logistic Regression

| **CSIC Code - Industry title** | **Analysis using Control Group 1** | | | **Analysis using Control Group 2** | | |
|---|---|---|---|---|---|---|
| | CLR OR (95% CI) | ACLR OR (95% CI) | ULR OR (95% CI) | CLR OR (95% CI) | ACLR OR (95% CI) | ULR OR (95% CI) |
| A. Agriculture and Related Service Industries | 0.93 (0.75 - 1.15) | 0.91 (0.73 - 1.12) | 0.91 (0.74 - 1.12) | 0.85 (0.67 - 1.08) | 0.84 (0.67 - 1.06) | 0.83 (0.66 - 1.05) |
| B. Fishing and Trapping Industries | 0.59 (0.36 - 0.95) | 0.56 (0.35 - 0.91) | 0.55 (0.34 - 0.90) | 0.75 (0.43 - 1.31) | 0.75 (0.43 - 1.30) | 0.71 (0.41 - 1.23) |
| C. Logging and Forestry Industries | 0.94 (0.72 - 1.22) | 0.95 (0.74 - 1.23) | 0.96 (0.75 - 1.24) | 0.91 (0.68 - 1.23) | 0.93 (0.70 - 1.24) | 0.93 (0.70 - 1.23) |
| D. Mining (Including Milling), Quarrying and Oil Well Industries | 1.45 (1.10 - 1.92) | 1.46 (1.11 - 1.92) | 1.45 (1.11 - 1.91) | 1.42 (1.04 - 1.96) | 1.46 (1.07 - 2.00) | 1.47 (1.08 - 2.01) |
| E. Manufacturing Industries | 1.02 (0.90 - 1.14) | 1.03 (0.91 - 1.15) | 1.02 (0.91 - 1.15) | 1.05 (0.91 - 1.20) | 1.06 (0.93 - 1.21) | 1.05 (0.92 - 1.20) |
| F. Construction Industries | 1.09 (0.94 - 1.26) | 1.08 (0.93 - 1.25) | 1.08 (0.94 - 1.25) | 1.20 (1.01 - 1.42) | 1.16 (0.98 - 1.36) | 1.17 (0.99 - 1.37) |
| G. Transportation and Storage Industries | 0.96 (0.81 - 1.12) | 0.95 (0.81 - 1.11) | 0.94 (0.81 - 1.10) | 0.92 (0.77 - 1.10) | 0.91 (0.77 - 1.08) | 0.91 (0.76 - 1.08) |
| H. Communication and Other Utility Industries | 1.16 (0.92 - 1.48) | 1.20 (0.95 - 1.52) | 1.19 (0.94 - 1.51) | 1.17 (0.99 - 1.54) | 1.18 (0.90 - 1.54) | 1.17 (0.99 - 1.52) |
| I. Wholesale Trade Industries | 0.93 (0.75 - 1.16) | 0.93 (0.75 - 1.15) | 0.94 (0.76 - 1.16) | 0.94 (0.74 - 1.20) | 0.92 (0.72 - 1.17) | 0.94 (0.74 - 1.19) |
| J. Retail Trade Industries | 0.93 (0.78 - 1.11) | 0.94 (0.79 - 1.12) | 0.95 (0.80 - 1.12) | 0.94 (0.77 - 1.14) | 0.96 (0.79 - 1.16) | 0.97 (0.80 - 1.17) |
| K. Finance and Insurance Industries | 0.66 (0.44 - 1.00) | 0.64 (0.43 - 0.96) | 0.64 (0.43 - 0.96) | 0.66 (0.42 - 1.03) | 0.62 (0.40 - 0.95) | 0.61 (0.40 - 0.94) |
| L. Real Estate Operator and Insurance Agent Industries | 0.97 (0.65 - 1.44) | 0.92 (0.63 - 1.37) | 0.92 (0.62 – 1.35) | 0.90 (0.58 - 1.40) | 0.87 (0.57 - 1.33) | 0.89 (0.59 - 1.36) |
| M. Business Service Industries | 0.96 (0.67 - 1.37) | 0.91 (0.64 - 1.29) | 0.92 (0.65 - 1.30) | 1.00 (0.68 - 1.48) | 0.96 (0.66 – 1.41) | 0.98 (0.67 - 1.43) |
| N. Government Service Industries | 1.03 (0.88 - 1.21) | 1.03 (0.88 - 1.21) | 1.04 (0.89 - 1.21) | 0.93 (0.78 - 1.11) | 0.94 (0.79 - 1.11) | 0.94 (0.79 - 1.12) |
| O. Educational Service Industries | 0.85 (0.62 - 1.15) | 0.87 (0.64 - 1.19) | 0.88 (0.65 - 1.20) | 0.82 (0.59 - 1.16) | 0.86 (0.62 - 1.20) | 0.85 (0.61 - 1.18) |
| P. Health and Social Service | 1.14 (0.82 - 1.59) | 1.14 (0.82 - 1.58) | 1.11 (0.80 - 1.54) | 1.13 (0.78 - 1.65) | 1.18 (0.82 - 1.70) | 1.14 (0.79 - 1.64) |
| Q. Accommodation, Food and Beverage Service Industries | 0.96 (0.70 - 1.33) | 0.96 (0.70 - 1.32) | 0.97 (0.70 - 1.33) | 1.07 (0.73 - 1.57) | 1.07 (0.73 - 1.55) | 1.09 (0.75 - 1.58) |
| R. Other Service Industries | 1.17 (0.88 - 1.56) | 1.20 (0.91 - 1.59) | 1.21 (0.91 - 1.60) | 1.19 (0.85 - 1.66) | 1.24 (0.90 - 1.71) | 1.24 (0.90 - 1.70) |

CSIC= Canadian Standard industrial Classification;
CLR: Conditional logistic regression, stratified on age and year of diagnosis, and adjusted for smoking, ethnicity, and respondent to the questionnaire;
ACLR: Adjusted conditional logistic regression, stratified on age groups (9-groups) and year of diagnosis;
ULR: Unconditional logistic regression, adjusted for age groups (9 groups) and year of diagnosis in addition to the covariates in CLR; OR= Odds ratio; CI=Confidence interval.

### *4.3 Selection of Covariates*

We excluded alcohol from the confounder list. An empirical comparison within the current datasets supported this decision (Table 15). The percent difference in the odds ratios (OR1 to OR2) for the main exposure variable (occupation) after adjusting for alcohol intake did not exceed 10% in any of the cases considered, indicating that alcohol was not confounding the relationship between occupation and lung cancer.

A similar analysis on the 279 usual occupations and 427 occupations ever held by the subjects (data not reported) indicated that the marital status of the subjects had no confounding effect on the relationship between occupational exposures and lung cancer (percent difference between the odds ratios, OR1 to OR2, was < 10%).

The most commonly identified confounders during our empirical search were educational status and the type of respondent to the questionnaire. Ethnicity was identified as a predominant confounder in the analysis of adenocarcinoma of lung. The literature suggests a possible role of ethnicity in lung cancer incidence (173).

In the final model, educational status, ethnic status, and proxy response were included as covariates along with other non-occupational variables in the base model (age, year of diagnosis, and smoking). However, two exceptions should be noted in the definitions of the covariates: (i) since no cases of squamous cell lung cancer were diagnosed in 1989 and 1990, the subjects diagnosed in the period 1988 - 1990 were analyzed as one group; and (ii) since there were no cases of small cell carcinoma, among subjects 20-39 years of age, the two youngest age groups were analyzed as one group (20-49 years of age).

**Table 15**: Odds Ratios for Lung Cancer in Relation to Usual Occupation, with and without Adjustment for Alcohol Consumption (results based on control group 1)

| CSOC code | Occupation title | Odds ratios* | | OR1 to OR2 (% difference) | Alcohol Confounder? |
|---|---|---|---|---|---|
| | | OR1 | OR2 | | |
| 11 | Managerial administrative & related occupations | 0.846 (0.732-0.977) | 0.853 (0.738-0.986) | 0.8 | No |
| 21 | Occupations in Natural sciences, Engineering and Mathematics | 0.750 (0.554-1.017) | 0.757 (0.558-1.026) | 0.9 | No |
| 23 | Occupations in Social sciences and related fields | 0.511 (0.264-0.990) | 0.519 (0.268-1.005) | 1.6 | No |
| 27 | Teaching and related occupations | 0.509 (0.313-0.827) | 0.507 (0.312-0.824) | 0.4 | No |
| 31 | Occupations in Medicine and health | 1.160 (0.824-1.633) | 1.154 (0.820-1.626) | 0.5 | No |
| 33 | Artistic, Literary, Recreational and related occupations | 0.817 (0.507-1.317) | 0.807 (0.501-1.301) | 1.2 | No |
| 41 | Clerical and related occupations | 1.106 (0.874-1.400) | 1.105 (0.873-1.398) | 0.1 | No |
| 51 | Sales occupations | 0.942 (0.794-1.118) | 0.943 (0.795-1.120) | 0.1 | No |
| 61 | Service occupations | 1.229 (1.039-1.455) | 1.225 (1.035-1.450) | 0.3 | No |
| 71 | Farming, Horticultural and Animal husbandry occupations | 0.952 (0.772-1.175) | 0.936 (0.759-1.156) | 1.7 | No |
| 73 | Fishing, Trapping and related occupations | 0.492 (0.283-0.854) | 0.492 (0.284-0.855) | 0 | No |
| 75 | Forestry and Logging occupations | 0.805 (0.589-1.101) | 0.808 (0.591-1.105) | 0.4 | No |
| 77 | Mining and Quarrying including Oil and Gas field occupations | 1.694 (1.164-2.467) | 1.700 (1.167-2.475) | 0.4 | No |
| 81/82 | Processing Occupations | 1.239 (1.024-1.499) | 1.233 (1.019-1.492) | 0.5 | No |
| 83 | Machining and related occupations | 1.304 (1.019-1.669) | 1.301 (1.017-1.666) | 0.2 | No |
| 85 | Product fabricating, Assembling and Repairing occupations | 1.115 (0.952-1.306) | 1.115 (0.952-1.306) | 0 | No |
| 87 | Construction trades occupations | 1.032 (0.893-1.193) | 1.033 (0.894-1.194) | 0.1 | No |
| 91 | Transport equipment operating occupations | 0.950 (0.799-1.130) | 0.954 (0.802-1.134) | 0.4 | No |
| 93 | Material handling and related occupations, n.e.c. | 1.025 (0.767-1.370) | 1.017 (0.761-1.360) | 0.8 | No |
| 95 | Other crafts and equipment operating occupations | 0.861 (0.617-1.201) | 0.870 (0.623-1.214) | 1 | No |
| 99 | Occupations not elsewhere classified | 1.425 (0.743-2.733) | 1.430 (0.745-2.745) | 0.4 | No |

CSOC=Canadian Standard Occupational Classification;
*Sample size= 12,139 subjects; OR1= Base odds ratio adjusted for age (nine groups), year of diagnosis, and smoking (pack-years) in an unconditional logistic regression;
OR2= Odds ratio adjusted for age, year of diagnosis, smoking (pack-years), and alcohol consumption (ever/ never drinkers) using unconditional logistic regression;

There are 14,755 subjects in the dataset, including 2,998 lung cancer cases. The exclusion of subjects having no information on the covariates in the final model, and a subject with erroneously coded occupation resulted in an effective sample of 13,061 (2,671 cases and 10,390 controls) for the analysis on occupational groups and 12,958 subjects (2,646 cases & 10,312 controls) for the analysis based on industrial categories. However, a much smaller sample was available for the sub-analysis based on histological subtypes of lung cancer. The number of cases and controls available for the final data analysis of lung cancer risk assessment (including histological subtypes) is summarized in Table 16.

## *4.4 Occupations Associated with Lung Cancer*

The subjects in our dataset represented a total of 605 occupational categories listed in the Canadian SOC, including: 23 major groups, 83 minor groups, and 499 unit groups. Our analysis is limited to the occupations containing at least 3 cases and 3 controls. We have estimated two odds ratios using control groups 1 and 2 in each of the 'usually' employed occupational categories and the occupations 'ever' held, resulting in 4 odds ratios for each occupation analyzed. The results for 'usual' occupation and for occupations 'ever' held are presented in separate sections. Although the analyses based on 'usual' and 'ever' employment categories yielded generally similar results, the concordance was poor for some specific occupations. The occupations with a significantly elevated OR ($P<0.05$) in any of the four OR estimates are selected for reporting. However, the OR estimates and the 95% confidence intervals (CI) in the broad hierarchical categories of a significant occupational group are also reported for the purpose of clarity.

**Table 16:** Effective Sample Size for the Analysis of the Association between Occupations/Industries and Lung Cancer

| Type of Lung Cancer | Cases | Controls* | | Total† | |
|---|---|---|---|---|---|
| | | Group 1 | Group 2 | Total 1 | Total 2 |
| | | Occupations | | | |
| All types | 2,671 | 10,390 | 7,074 | 13,061 | 9,745 |
| Squamous cell carcinoma | 928 | 10,390 | 7,074 | 11,318 | 8,002 |
| Adenocarcinoma | 824 | 10,390 | 7,074 | 11,214 | 7,898 |
| Small cell carcinoma | 490 | 10,390 | 7,074 | 10,880 | 7,564 |
| Large cell carcinoma | 315 | 10,390 | 7,074 | 10,705 | 7,389 |
| | | Industries | | | |
| All types | 2,646 | 10,312 | 7,022 | 12,958 | 9,668 |
| Squamous cell carcinoma | 922 | 10,312 | 7,022 | 11,234 | 7,944 |
| Adenocarcinoma | 815 | 10,312 | 7,022 | 11,127 | 7,837 |
| Small cell carcinoma | 485 | 10,312 | 7,022 | 10,797 | 7,507 |
| Large cell carcinoma | 311 | 10,312 | 7,022 | 10,623 | 7,333 |

*Group 1=Control group 1; Group-2= Control group 2.

† Total 1=Total sample for the analysis with control group 1;
Total 2=Total sample for the analysis with control group 2.

Although our main objective is identifying occupations with an elevated risk of lung cancer, we have reported some noteworthy protective associations in the analyses based on the 'usual' occupation analyses.

### 4.4.1 All Types of Lung Cancer

#### 4.4.1.1 'Usual' Occupations

The odds ratios and associated 95% confidence intervals in relation to 'usual' occupations showing an excess risk of lung cancer are reported in Table 17. There were a total of 551 occupation categories, including: 23 major groups, 83 minor groups, and 445 unit groups. We evaluated the risk of lung cancer for the occupational groups having at least 3 cases and 3 controls, which included 279 occupations represented in 21 major groups, 69 minor groups and 189 unit groups. In addition, a unit group (SOC-8549) with less than 3 controls was not evaluated in the analysis with the second control group. Overall, concordance of the results between both the control groups was good (95% agreement). Overall, 5% of the analyses (out of 10% total significant results) were significant in both two control groups with an elevated risk of lung cancer being observed in 10 occupations and a reduced risk of lung cancer in 4 occupations.

Among occupations showing an excess risk of lung cancer, the majority of the subjects with lung cancer were employed in the major occupational groups involved in machining and processing. Most of the observed odds ratios ranged between 1.4 and 3, indicating a moderate to weak association with lung cancer; the larger odds ratios observed in some of the occupations should be interpreted with caution due to small number of lung cancer cases in those occupations.

**Table 17:** Occupations at Significantly Increased Risk of Lung Cancer - All cases

| | Occupation (Usual) | | | Occupation (Ever) | | |
|---|---|---|---|---|---|---|
| **CSOC Code Occupation Title** | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| 31 Occupations in Medicine & Health | 48 | 1.17 (0.82 - 1.66) | 1.18 (0.80 - 1.75) | 87 | 1.19 (0.91 - 1.56) | 1.19 (0.89 - 1.60) |
| 313 Nursing, Therapy & Related Assisting | 14 | 1.08 (0.56 - 2.09) | 1.13 (0.54 - 2.40) | 47 | 1.18 (0.82 - 1.70) | 1.14 (0.76 - 1.72) |
| 3135 Nursing Attendants | 5 | 1.72 (0.54 - 5.48) | 1.51 (0.43 - 5.37) | 27 | *2.03 (1.19 - 3.46)* | *1.95 (1.07 - 3.58)* |
| 41 Clerical & Related Occupations | 123 | 1.10 (0.88 - 1.37) | 1.11 (0.87 - 1.42) | 390 | 0.90 (0.79 - 1.02) | 0.86 (0.74 - 0.99) |
| 415 Material Recording, Scheduling & Distributing | 45 | 1.29 (0.89 - 1.87) | 1.40 (0.92 - 2.12) | 159 | 0.97 (0.80 - 1.18) | 1.05 (0.85 - 1.31) |
| 4150 Supervisors | 11 | *2.48 (1.12 - 5.48)* | *3.20 (1.31 - 7.88)* | 24 | 1.09 (0.67 - 1.76) | 1.03 (0.62 - 1.73) |
| 77 Mining and Quarrying including Oil and Gas Field | 50 | 1.42 (0.98 - 2.06) | 1.36 (0.90 - 2.06) | 230 | *1.20 (1.01 - 1.43)* | *1.26 (1.03 - 1.53)* |
| 771 Mining & Quarrying Including Oil & Gas | 50 | 1.42 (0.98 - 2.06) | 1.36 (0.90 - 2.06) | 230 | *1.20 (1.01 - 1.43)* | *1.26 (1.03 - 1.53)* |
| 7710 Foremen/women | 8 | 2.49 (0.90 - 6.88) | *4.59 (1.27 - 16.56)* | 20 | 0.95 (0.56 - 1.62) | 0.84 (0.47 - 1.49) |
| 7717 Mining & Quarrying: Cutting, Handling and Loading | 25 | 1.59 (0.95 - 2.65) | 1.67 (0.93 - 2.98) | 138 | *1.46 (1.17 - 1.83)* | *1.61 (1.25 - 2.09)* |
| 81/ 82 Processing Occupations | 184 | 1.08 (0.89 - 1.30) | 1.13 (0.91 - 1.39) | 614 | 0.98 (0.87 - 1.10) | 0.99 (0.87 - 1.12) |
| 811 Mineral Ore Treating | 15 | *2.29 (1.14 - 4.61)* | *2.71 (1.22 – 6.03)* | 66 | *1.47 (1.07 - 2.04)* | *1.49 (1.03 - 2.16)* |
| 8110 Foremen/women: Mineral Ore Treating | 5 | *4.53 (1.07 - 19.09)* | 4.19 (0.85 - 20.78) | 7 | 1.69 (0.62 - 4.63) | 1.75 (0.55 - 5.51) |
| 813/814 Metal Processing and Related | 32 | *1.71 (1.05 - 2.77)* | *2.54 (1.39 - 4.64)* | 97 | 1.22 (0.94 - 1.59) | *1.49 (1.10 - 2.03)* |
| 8130 Foremen/ women | 9 | 1.54 (0.60 - 4.00) | *4.30 (1.02 - 18.14)* | 12 | 0.89 (0.43 - 1.84) | 0.95 (0.40 - 2.22) |
| 8149 Metal Processing and Related, n.e.c. | 6 | *3.45 (1.05 - 11.40)* | *5.92 (1.25 - 28.12)* | 23 | 1.65 (0.92 - 2.95) | 1.80 (0.90 - 3.60) |
| 816/ 817 Chemicals, Petroleum, Rubber, Plastic & Related Materials Processing | 10 | 1.79 (0.81 - 3.97) | 1.65 (0.71 - 3.84) | 28 | 0.89 (0.57 - 1.38) | 0.83 (0.52 - 1.34) |
| 8165 Distilling, Subliming and Carbonizing: Chemicals and Related Materials | 4 | *14.54 (3.32 - 63.78)* | *14.79 (2.82 - 77.53)* | 6 | 1.95 (0.75 - 5.12) | 1.62 (0.59 - 4.41) |
| 821/ 822 Food, Beverage & Related Processing | 43 | 1.30 (0.88 - 1.92) | 1.26 (0.82 - 1.94) | 145 | 1.03 (0.84 - 1.27) | 1.04 (0.82 - 1.31) |
| 8213 Baking, Confectionery Making and Related | 12 | *3.01 (1.33 - 6.81)* | *2.72 (1.13 - 6.55)* | 32 | 1.22 (0.79 - 1.90) | 1.52 (0.92 - 2.51) |
| 83 Machining and related occupations | 115 | *1.42 (1.11 - 1.80)* | *1.42 (1.08 - 1.85)* | 295 | *1.18 (1.02 - 1.38)* | 1.17 (0.99 - 1.38) |
| 831 Metal Machining | 37 | *1.76 (1.16 - 2.68)* | *1.88 (1.17 - 3.00)* | 95 | 1.12 (0.87 - 1.45) | 1.11 (0.84 - 1.47) |
| 8315 Machine Tool Operating | 3 | 4.02 (0.87 - 18.58) | 3.88 (0.79 - 18.96) | 16 | *1.90 (1.00 - 3.61)* | *2.15 (1.06 - 4.32)* |
| 833 Metal Shaping & Forming, Except Machining | 68 | *1.39 (1.02 - 1.89)* | 1.22 (0.86 - 1.74) | 176 | *1.30 (1.07 - 1.59)* | 1.24 (1.00 - 1.55) |
| 8331 Forging Occupation | 3 | 3.62 (0.79 - 16.65) | *7.68 (1.13 - 52.14)* | 15 | 1.73 (0.90 - 3.30) | 1.78 (0.85 - 3.75) |
| 8336 Inspecting, Testing, Grading and Sampling | 1 | - | - | 4 | *5.44 (1.22 - 24.19)* | *8.51 (1.45 - 49.93)* |
| 85 Product Fabricating, Assembling & Repairing | 277 | 1.05 (0.90 - 1.23) | 1.11 (0.93 - 1.32) | 685 | 1.09 (0.97 - 1.21) | 1.12 (0.99 - 1.27) |
| 853 Fabricating, Assembling, Installing & Repairing Occupations: Electrical, Electronic and Related Equipment | 43 | 1.07 (0.74 - 1.54) | 1.06 (0.71 - 1.59) | 104 | 1.09 (0.86 - 1.39) | 1.01 (0.77 - 1.32) |
| 8531 Electrical and Related Equipment Fabricating and Assembling | 2 | - | - | 11 | *2.30 (1.06 - 4.97)* | 1.86 (0.81 - 4.26) |
| 857 Fabricating, Assembling & Repairing: Textile, Fur & Leather Products | 4 | 2.12 (0.50 - 8.97) | 1.18 (0.27 - 5.21) | 18 | 1.76 (0.92 - 3.39) | 1.63 (0.78 - 3.40) |
| 8571 Bonding & Cementing Occupations: Rubber, Plastic & Related Products | 2 | - | - | 10 | *2.65 (1.04 -6.72)* | *3.06 (1.07 -8.78)* |

| | | | | | | |
|---|---|---|---|---|---|---|
| 87 Construction Trades | 357 | 1.05 (0.91 - 1.21) | 1.14 (0.97 - 1.34) | 762 | 1.01 (0.91 - 1.12) | 1.11 (0.98 - 1.25) |
| 871 Excavating, Grading, Paving & Related | 69 | 1.12 (0.82 - 1.53) | 1.16 (0.81 - 1.65) | 178 | 1.03 (0.85 - 1.25) | 1.18 (0.94 - 1.47) |
| 8713 Paving, Surfacing & Related | 3 | 1.83 (0.40 - 8.31) | 3.63 (0.50 - 26.30) | 12 | 2.19 (1.00 - 4.85) | *3.14 (1.17 - 8.41)* |
| 873 Electrical Power, Lighting & Wire Communications Equipment Erecting, Installing & Repairing | 53 | 1.28 (0.90 - 1.81) | 1.39 (0.94 - 2.07) | 93 | 1.10 (0.85 - 1.41) | 1.18 (0.89 - 1.57) |
| 8731 Electrical Power Line Workers & Related | 15 | 1.61 (0.76 - 3.42) | 1.78 (0.71 - 4.46) | 26 | *2.07 (1.17 - 3.64)* | 1.85 (0.98 - 3.50) |
| 91 Transport Equipment Operating | 227 | 0.93 (0.78 - 1.10) | 0.88 (0.73 - 1.07) | 676 | 1.05 (0.94 - 1.18) | 1.02 (0.90 - 1.16) |
| 915 Water Transport Operating | 42 | 1.05 (0.71 - 1.54) | 1.08 (0.70 - 1.66) | 152 | *1.25 (1.01 - 1.54)* | *1.27 (1.00 - 1.62)* |
| 9155 Deck Crew, Ship | 14 | *3.38 (1.51 - 7.59)* | *2.42 (1.02 - 5.75)* | 71 | 1.28 (0.95 - 1.74) | 1.40 (0.99 - 2.00) |
| 9157 Engine and Boiler-room Crew, Ship | 7 | 1.57 (0.59 - 4.18) | 1.50 (0.49 - 4.57) | 44 | *1.58 (1.07 - 2.33)* | *1.68 (1.07 - 2.65)* |
| 919 Other Transport Equipment Operating | 6 | 2.17 (0.59 - 7.95) | 1.46 (0.33 - 6.39) | 47 | 1.36 (0.93 - 1.98) | 1.14 (0.75 - 1.74) |
| 9191 Subway and Street Railway Operating | 3 | *6.13 (1.09 -34.58)* | *7.97 (1.21 - 52.34)* | 16 | 1.05 (0.57 - 1.92) | 0.96 (0.48 - 1.91) |
| 9193 Rail Vehicle Operators, Except Rail Transport | - | - | - | 13 | *2.58 (1.15 - 5.79)* | 2.03 (0.83 - 5.00) |

Note: *Significant estimates* (in any one of the analyses conducted) *are in italics (p<0.05).*
CSOC: Canadian Standard Occupational Classification, 1980; CI: Confidence interval;
N1=Number of exposed cases in the corresponding usual occupation; N2=Number of cases exposed in the corresponding ever occupation.
*Control group-1= Basic control group after excluding unknown primary cancer subjects.
† Control group-2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.
‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

An elevated risk of lung cancer was seen among workers in machining & related occupations (SOC-83; OR=1.42); an excess risk was seen, predominantly in the metal machining occupations (OR=1.8 and 1.9 with control groups 1 and 2, respectively). Among the workers in the processing occupations, an elevated risk of lung cancer was observed in the mineral ore treating occupations (SOC-811), and the metal processing occupations (SOC-813/814), including the subgroup 'metal processing and related occupations not elsewhere classified' (SOC-8149). An elevated risk of lung cancer (OR > 10) was noted in the occupations dealing with distilling, subliming & carbonizing of chemicals & related materials (SOC-8165); the few cases working in this occupation warrant caution in the interpretation of this result. Workers in baking, confectionery making & related occupations (SOC-8213) showed a moderate to strong association ($OR \approx 3$) with lung cancer. Among the transport equipment operating occupations, an elevated risk of lung cancer was noted in the ship deck crew (SOC-9155), and subway & street railway operating occupations (SOC-9191). In addition, supervisors in material recording, scheduling & distributing occupations (SOC-4150) showed an excess risk of lung cancer.

While the above mentioned occupations were significantly associated with lung cancer in the analyses with both the control groups, a total of 5 occupations were associated with an elevated risk in only one of the control group analyses. Most of these occupations were subgroups of machining or metal processing occupations with few cases (Table 17). However, the elevated risk of lung cancer among foremen/women in mining and quarrying (including oil & gas field) occupations (OR=4.59, 95% CI: 1.27-16.56) is noteworthy. This observation could be due to the small number of cases in this occupation, or due to the diluting effect of smoking related cancers in the analysis with control group 1.

Overall, an excess risk of lung cancer was observed among workers employed in occupations involving processing & machining of metals, and certain transport operating occupations.

We observed a significantly reduced risk ($p<0.05$) of lung cancer among the men in 4 occupational categories, in the analyses with both the control groups. Specifically, employment in the teaching & related occupations (SOC 27), especially secondary school teachers (SOC-2773), occupations in law & jurisprudence (SOC-234), and sales occupations in the service sector (SOC-517) was associated with a significantly reduced risk of lung cancer; odds ratios (95% CIs) with control group 1 were 0.58 (0.36-0.95), 0.22 (0.07-0.77), 0.32 (0.11-0.94), and 0.66 (0.43-0.99), respectively; odds ratios with control group 2 were 0.59 (0.35-0.99), 0.24 (0.07-0.91), 0.25 (0.08-0.81), and 0.55 (0.35-0.85), respectively.

#### 4.4.1.2 Occupations 'Ever' Held

The significantly elevated odds ratios for lung cancer and the associated 95% confidence intervals in relation to the occupations 'ever' held are reported in Table 17. Our analysis on the occupations 'ever' held was restricted to the occupations having at least 3 cases and 3 controls (approximately 70% of the total number of occupations); this analysis included 427 occupations represented in 23 major groups, 76 minor groups, and 328 unit groups. Moreover, one unit group with less than 3 controls was not evaluated in the analysis based on the second control group. In general, the concordance of the results between the control groups 1 and 2 was good (96% agreement). Overall, 6% of the analyses (out of 10% total significant results) were significant in both two control groups with an elevated risk of lung cancer being observed in 9 occupations and a reduced risk of lung cancer in 17 occupations.

A moderate to weak association with lung cancer was seen in most of the occupational groups, with the odds ratios ranging from 1.2 to 3. An elevated risk of lung cancer was observed among workers in mining and quarrying occupations (including oil & gas field occupations) (SOC-77), including a sub-group of workers involved in cutting, handling & loading tasks (SOC-7717). Occupations involving water transportation (SOC-915) are also associated with an elevated risk of lung cancer; an excess risk is seen predominantly in the engine & boiler-room crew in a ship (SOC-9157), but not in the deck crew, as was indicated in the analysis of usual occupations. Workers in the 'bonding & cementing occupations' involving rubber, plastic & related products (SOC-8571) demonstrated a significant excess risk of lung cancer; however, this assessment was restricted due to few cases in the analysis based on 'usual' occupation.

### 4.4.2 Squamous Cell Carcinoma of the Lung

#### 4.4.2.1 'Usual' Occupation

The odds ratios and associated 95% confidence intervals in relation to 'usual' occupation showing an excess risk of squamous cell lung cancer are reported in Table 18. When we limited our analysis to squamous cell carcinoma of the lung, there are a total of 549 'usual' occupations, including: 23 major groups, 83 minor groups, and 443 unit groups. We evaluated the risk of lung cancer for the occupational groups having at least 3 cases and controls, which included 179 occupations represented in 20 major groups, 56 minor groups, and 103 unit groups. Overall concordance of the results between both the control groups was good (93% agreement).

**Table 18:** Occupations with Significantly Elevated risk of Squamous Cell Carcinoma of the Lung

| CSOC Code Occupation Title | Occupation (Usual) | | | Occupation (Ever) | | |
|---|---|---|---|---|---|---|
| | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| 61 Service Occupations | 89 | 1.22 (0.96 - 1.56) | 1.20 (0.92 - 1.55) | 358 | 1.08 (0.94 - 1.26) | 1.06 (0.91 - 1.24) |
| 611 Protective Service | 41 | 1.21 (0.86 - 1.71) | 1.16 (0.81 - 1.68) | 258 | 1.12 (0.95 - 1.32) | 1.09 (0.92 - 1.30) |
| 6117 Other Ranks, Armed Forces | 15 | *1.88 (1.04 - 3.38)* | *1.96 (1.04 - 3.72)* | 196 | 1.17 (0.98 - 1.40) | 1.16 (0.96 - 1.41) |
| 612 Food & Beverage Preparation & Related Service | 21 | 1.34 (0.82 - 2.19) | 1.35 (0.79 - 2.31) | 63 | 1.07 (0.80 - 1.42) | 1.23 (0.90 - 1.67) |
| 6129 Food & Beverage Preparation & Related, n.e.c | 4 | 3.23 (0.99 - 10.58) | *4.97 (1.31 - 18.81)* | 11 | 0.95 (0.49 - 1.82) | 1.11 (0.55 - 2.25) |
| 77 Mining & Quarrying including Oil & Gas field | 20 | 1.56 (0.94 - 2.60) | 1.45 (0.84 - 2.52) | 92 | *1.35 (1.06 - 1.72)* | *1.38 (1.06 - 1.79)* |
| 771 Mining & Quarrying including Oil & Gas field | 20 | 1.56 (0.94 - 2.60) | 1.45 (0.84 - 2.52) | 92 | *1.35 (1.06 - 1.72)* | *1.38 (1.06 - 1.79)* |
| 7710 Foremen/women | 3 | 3.05 (0.76 - 12.23) | *7.59 (1.53 - 37.72)* | 6 | 0.80 (0.34 - 1.90) | 0.73 (0.30 - 1.79) |
| 7717 Mining & Quarrying: Cutting, Handling & Loading | 12 | *1.97 (1.01 - 3.83)* | 2.06 (0.99 - 4.30) | 59 | *1.71 (1.27 - 2.32)* | *1.86 (1.33 - 2.59)* |
| 81/ 82 Processing Occupations | 67 | 1.09 (0.83 - 1.44) | 1.11 (0.82 - 1.49) | 230 | 1.06 (0.90 - 1.25) | 1.07 (0.89 - 1.27) |
| 811 Mineral Ore Treating | 9 | *3.14 (1.38 - 7.17)* | *3.62 (1.42 - 9.20)* | 30 | *1.80 (1.18 - 2.75)* | *1.84 (1.16 - 2.93)* |
| 8110 Foremen/women: Mineral Ore Treating | 3 | *5.49 (1.01 -29.80)* | 5.25 (0.78 - 35.45) | 4 | 2.20 (0.65 - 7.47) | 2.45 (0.61 - 9.79) |
| 8118 Occupations in Labouring & Other Elemental Work | 4 | 2.49 (0.76 - 8.20) | 3.18 (0.85 - 11.99) | 21 | *2.12 (1.27 - 3.54)* | *2.26 (1.28 - 4.01)* |
| 813/ 814 Metal Processing & Related | 9 | 1.35 (0.64 - 2.84) | 2.04 (0.86 - 4.79) | 32 | 1.16 (0.79 - 1.72) | 1.49 (0.97 - 2.29) |
| 8143 Plating, Metal Spraying & Related | 2 | - | - | 3 | *5.18 (1.26 - 21.22)* | *6.22 (1.38 - 28.08)* |
| 815 Clay, Glass and Stone Processing, Forming & Related | 2 | - | - | 10 | *2.05 (1.01 - 4.17)* | *2.49 (1.15 - 5.38)* |
| 8155 Forming Occupations, Clay, Glass and Stone | 0 | - | - | 4 | *3.85 (1.20 - 12.41)* | 2.90 (0.85 - 9.92) |
| 816/ 817 Chemicals, Petroleum, Rubber, Plastic & Related Materials Processing | 4 | 1.73 (0.57 - 5.21) | 1.50 (0.47 - 4.76) | 12 | 1.02 (0.55 - 1.90) | 0.94 (0.49 - 1.79) |
| 8165 Distilling, Subliming & Carbonizing: Chemicals & Related Materials | 0 | - | - | 4 | 3.11 (0.99 - 9.81) | 2.50 (0.76 - 8.23) |
| 821/ 822 Food, Beverage & Related Processing | 15 | 1.22 (0.69 - 2.16) | 1.17 (0.64 - 2.16) | 56 | 1.07 (0.79 - 1.44) | 1.10 (0.80 - 1.52) |
| 8213 Baking, Confectionery Making & Related | 6 | *3.51 (1.24 - 9.90)* | *3.41 (1.15 - 10.10)* | 16 | 1.48 (0.84 - 2.61) | 1.87 (1.00 - 3.50) |
| 83 Machining & Related Occupations | 43 | *1.54 (1.09 - 2.17)* | *1.57 (1.08 - 2.27)* | 99 | 1.12 (0.89 - 1.41) | 1.11 (0.87 - 1.41) |
| 831 Metal Machining | 18 | *2.61 (1.51 - 4.49)* | *3.08 (1.70 - 5.57)* | 40 | 1.42 (1.00 - 2.02) | 1.46 (1.00 - 2.12) |
| 8310 Foremen/women: Other Processing | 2 | - | - | 7 | *2.84 (1.20 - 6.75)* | *2.58 (1.04 - 6.37)* |
| 8311 Tool and Die Making | 3 | 3.85 (0.95 - 15.58) | *7.29 (1.54 - 34.57)* | 7 | 2.10 (0.88 - 4.99) | 2.41 (0.93 - 6.24) |
| 833 Metal Shaping & Forming, Except Machining | 22 | 1.31 (0.82 - 2.10) | 1.12 (0.68 - 1.85) | 56 | 1.16 (0.86 - 1.56) | 1.09 (0.79 - 1.50) |
| 8333 Sheet Metal Workers | 5 | 2.15 (0.79 - 5.87) | 1.79 (0.62 - 5.17) | 17 | *2.01 (1.15 - 3.49)* | *1.99 (1.10 - 3.60)* |
| 85 Product fabricating, Assembling and Repairing occupations | 108 | 1.21 (0.97 - 1.52) | *1.30 (1.02 - 1.65)* | 264 | *1.27 (1.08 - 1.49)* | *1.31 (1.11 - 1.56)* |
| 851/ 852 Fabricating & Assembling: Metals Products, n.e.c | 5 | 1.81 (0.67 - 4.87) | 1.83 (0.64 - 5.24) | 31 | 1.37 (0.92 - 2.04) | 1.31 (0.85 - 2.01) |
| 8510 Foremen/women | 0 | - | - | 7 | *3.23 (1.30 - 8.07)* | 2.12 (0.80 - 5.58) |
| 853 Fabricating, Assembling, Installing & Repairing: Electrical, Electronic & Related Equipment | 15 | 1.10 (0.63 - 1.92) | 1.12 (0.63 - 2.02) | 38 | 1.17 (0.82 - 1.68) | 1.08 (0.74 - 1.57) |
| 8531 Electrical & Rela Equip Fabricat & Assembling | 1 | - | - | 6 | *3.31 (1.27 -8.59)* | 2.58 (0.94 - 7.05) |
| 8533 Electrical & Rela Equip Installing & Repairing | 13 | *1.87 (1.00 - 3.48)* | *2.00 (1.03 - 3.89)* | 28 | 1.48 (0.97 - 2.25) | 1.52 (0.97 - 2.38) |
| 855/856 Fabricating, Assembling & Repairing: Textile, Fur & Leather Products | 10 | 1.80 (0.86 - 3.77) | *2.40 (1.07 - 5.40)* | 13 | 1.18 (0.64 - 2.18) | 1.48 (0.77 - 2.88) |
| 8562 Upholsterers | 4 | 2.77 (0.82 - 9.40) | *5.11 (1.27 - 20.63)* | 6 | 2.51 (0.97 - 6.51) | *2.84 (1.04 - 7.74)* |
| 859 Other product Fabricating, Assembling & Repairing | 13 | 1.59 (0.86 - 2.96) | 1.62 (0.83 - 3.15) | 69 | *1.62 (1.23 - 2.14)* | *1.69 (1.25 - 2.29)* |
| 8592 Marine Craft Fabricating, Assembling & Repairing | 6 | 1.18 (0.49 - 2.85) | 1.33 (0.53 - 3.37) | 41 | 1.42 (1.00 - 2.01) | *1.47 (1.01 - 2.15)* |
| 8595 Painting and Decorating, n.e.c. | 3 | 1.42 (0.39 - 5.10) | 1.90 (0.46 - 7.87) | 17 | *1.82 (1.05 - 3.17)* | *1.96 (1.06 - 3.62)* |

| | | | | | | |
|---|---|---|---|---|---|---|
| 87 Construction trades occupations | 140 | *1.25 (1.02 - 1.53)* | *1.39 (1.11 - 1.73)* | 287 | 1.14 (0.97 - 1.33) | *1.26 (1.06 - 1.49)* |
| 871 Excavating, Grading, Paving & Related | 30 | 1.46 (0.97 - 2.22) | *1.64 (1.04 - 2.59)* | 73 | 1.20 (0.91 - 1.57) | *1.39 (1.04 - 1.87)* |
| 8718 Occupations in Labouring & Other Elemental Work | 6 | 2.54 (0.96 - 6.71) | *3.94 (1.27 - 12.25)* | 19 | 1.63 (0.97 - 2.76) | *2.05 (1.14 - 3.68)* |
| 873 Electrical Power, Lighting & Wire Communications Equipment Erecting, Installing & Repairing | 17 | 1.23 (0.72 - 2.10) | 1.33 (0.74 - 2.36) | 32 | 1.09 (0.74 - 1.60) | 1.18 (0.78 - 1.78) |
| 8731 Electrical Power Line Workers & Related | 5 | 1.71 (0.59 - 4.92) | 1.91 (0.57 - 6.40) | 11 | *2.73 (1.31 - 5.71)* | *2.45 (1.09 - 5.50)* |
| 878/879 Other Construction Trades | 93 | 1.16 (0.91 - 1.47) | 1.28 (0.99 - 1.66) | 209 | 1.14 (0.96 - 1.35) | *1.22 (1.01 - 1.47)* |
| 8781 Carpenters and Related | 38 | *1.60 (1.10 - 2.32)* | *1.76 (1.17 - 2.63)* | 82 | *1.34 (1.04 - 1.73)* | *1.47 (1.12 - 1.93)* |
| 91 Transport Equipment Operating | 65 | 0.78 (0.60 - 1.03) | 0.75 (0.56 - 1.00) | 230 | 1.03 (0.87 - 1.21) | 1.00 (0.84 - 1.19) |
| 915 Water Transport Operating | 17 | 1.29 (0.76 - 2.19) | 1.36 (0.77 - 2.41) | 55 | 1.31 (0.97 - 1.78) | 1.32 (0.95 - 1.83) |
| 9155 Deck Crew, Ship | 7 | *5.14 (1.94 -13.62)* | *3.63 (1.30 - 10.17)* | 27 | 1.39 (0.91 - 2.14) | 1.46 (0.92 - 2.34) |
| 919 Other Transport Equipment Operating | 0 | - | - | 17 | 1.32 (0.77 - 2.26) | 1.14 (0.64 - 2.01) |
| 9193 Rail Vehicle Operators, Except Rail Transport | 0 | - | - | 7 | *3.85 (1.48 - 10.04)* | *3.12 (1.10 - 8.79)* |
| 95 Other Crafts & Equipment Operating | 25 | 1.12 (0.72 - 1.74) | 1.14 (0.71 - 1.82) | 57 | 1.20 (0.89 - 1.61) | 1.19 (0.87 - 1.63) |
| 955 Electronic & Related Communications Equip Oper, n.e.c | 5 | 1.13 (0.43 - 2.96) | 1.09 (0.39 - 3.06) | 15 | 1.44 (0.81 - 2.54) | 1.47 (0.80 - 2.71) |
| 9557 Motion Picture Projectionists | 1 | - | - | 4 | *6.71 (1.70 - 26.53)* | *9.58 (1.75 - 52.43)* |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics ($p<0.05$).*

CSOC: Canadian Standard Occupational Classification, 1980; CI: Confidence interval;

N1=Number of exposed cases in the corresponding usual occupation; N2=Number of cases exposed in the corresponding ever occupation.

*Control group 1= Basic control group after excluding unknown primary cancer subjects.

† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.

‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

Overall, 6% of the analyses (out of 13% total significant results) were significant in both two control groups with an elevated risk of squamous cell lung cancer being observed in 9 occupations and a reduced risk of squamous cell lung cancer in 4 occupations.

Among the occupations showing an excess risk of lung cancer, the majority of the squamous cell carcinoma cases were employed in the major occupational groups, including: construction trades; fabricating, assembling & repairing occupation; and machining occupations. Most of the observed odds ratios ranged between 1.5 and 4, indicating a moderate to strong association with squamous cell lung cancer. The elevated risk of squamous cell lung cancer among workers in the construction trades (SOC-87; OR = 1.3) is noteworthy in that this association was not seen in the combined analysis of all types of lung cancer; the excess risk of squamous cell lung cancer in the subgroup of carpenters (SOC-8781; OR = 1.7) is also noteworthy. Workers involved in the installation and repairing of electrical equipment (SOC-8533) and army men (excluding commissioned officers; SOC-6117) also demonstrated an excess risk of squamous cell lung cancer.

As in the combined analysis of all the types of lung cancer, an elevated risk of squamous cell lung cancer was observed among the workers employed in the machining and related occupations (SOC-83), including metal machining occupations (SOC-831); mineral ore treating occupations (SOC-811); baking, confectionery making & related occupations (SOC-8213); and ship deck crew (SOC-9155).

While the above mentioned usual occupations were significantly associated with squamous cell lung cancer using both control groups, a total of 10 occupations were associated with an elevated risk of lung cancer using either one or the other control group. Most of these occupations were subgroups of machining or construction trade occupations (Table 18). The elevated risk of squamous cell lung cancer among workers in the 'fabricating, assembling & repairing' occupations (SOC-85; OR=1.3), involving textile, fur & leather products (SOC-855), including upholsterers (SOC-8562), is noteworthy; smoking related cancers in the control group 1 might have diluted the effect towards the null in the analysis based on control group 1. An excess risk of squamous cell lung cancer was also observed in certain mining related occupations (SOC-7710, 7717).

Overall, the squamous cell specific analysis was suggestive of an excess risk of lung cancer among workers in the construction trades, metal machining, some mining related occupations, ship deck crew, and the occupations involving fabricating, assembling or repairing of electrical equipment, textiles, fur and leather products.

We observed a reduced risk of lung cancer among men in 4 occupational categories in the analysis with both the control groups. Specifically, employment in 'managerial administrative & related occupations' (SOC 11), including the subgroup-'sales & advertising management occupations' (SOC 1137), and sales occupations (SOC 51) was associated with a significantly reduced risk of squamous cell carcinoma of lung; odds ratios (95% confidence intervals) with control group 1 were 0.76 (0.60-0.97), 0.48 (0.25-0.92), and 0.76 (0.59-0.99) respectively, while odds ratios with control group 2 were 0.75 (0.58-0.97), 0.44 (0.22-0.86), and 0.73 (0.55-0.96), respectively.

#### 4.4.2.2 Occupations 'Ever' Held

The significantly elevated odds ratios for squamous cell lung cancer and the associated 95% confidence intervals in relation to the occupations 'ever' held are reported in Table 18. Our analysis of the squamous cell lung cancer was restricted to occupations 'ever' held having at least 3 cases and 3 controls (approximately 51% of the total number of occupations); this analysis included 306 occupations represented in 21 major groups, 66 minor groups, and 219 unit groups. In general, the concordance of the results between the control groups 1 and 2 was good (96% agreement). Overall, 9% of the analyses (out of 13% total significant results) were significant in both two control groups with an elevated risk of squamous cell lung cancer being observed in 15 occupations and a reduced risk of squamous cell lung cancer in 12 occupations.

The odds ratios among the high risk occupations ranged between 1.5 and 3.3, indicating a moderate to strong association with squamous cell lung cancer. An elevated risk of squamous cell lung cancer was seen among workers in mining and quarrying occupations (including oil & gas field occupations) (SOC-77), including the subgroup of workers involved in cutting, handling & loading tasks (SOC-7717); similar associations were seen in the analysis of all histological types of lung cancer combined. An elevated risk of squamous cell lung cancer among the workers in certain processing occupations involving clay, glass & stone (SOC-815) and metals (SOC-8143) is noteworthy. Electrical power line workers in the construction trades (SOC-8731), rail vehicle operators (except rail transport; SOC-9193), and motion picture projectionists (SOC-9557) also demonstrated an excess risk of squamous cell lung cancer.

### 4.4.3 Adenocarcinoma of the Lung

#### 4.4.3.1 'Usual' Occupation

The odds ratios and associated 95% confidence intervals in relation to 'usual' occupation showing an excess risk of adenocarcinoma of the lung are reported in Table 19. When we limited our analysis to adenocarcinoma of the lung, there were a total of 541 'usual' occupations, including 23 major groups, 83 minor groups and 435 unit groups.

**Table 19:** Occupations with Significantly Elevated Risk of Adenocarcinoma of the Lung

| CSOC Code Occupation Title | Occupation (Usual) N1 | Occupation (Usual) Control Group 1* OR‡ (95% CI) | Occupation (Usual) Control Group 2 † OR (95% CI) | Occupation (Ever) N2 | Occupation (Ever) Control Group 1 OR (95% CI) | Occupation (Ever) Control Group 2 OR (95% CI) |
|---|---|---|---|---|---|---|
| 21 Natural Sciences, Engineering & Mathematics | 23 | 0.94 (0.60 - 1.48) | 0.97 (0.61 - 1.56) | 47 | 0.84 (0.60 - 1.16) | 0.82 (0.58 - 1.15) |
| 214 Architects, Engineers & Community Planners | 16 | 1.46 (0.84 - 2.54) | 1.66 (0.93 - 2.95) | 23 | 1.09 (0.69 - 1.72) | 1.22 (0.76 - 1.97) |
| 2147 Mechanical Engineers | 3 | 3.76 (0.96 - 14.75) | *7.79 (1.80 - 33.78)* | 3 | 1.37 (0.40 - 4.67) | 1.63 (0.46 - 5.83) |
| 31 Medicine & Health | 19 | 1.36 (0.83 – 2.25) | 1.46 (0.86 - 2.47) | 30 | 1.25 (0.83 - 1.86) | 1.29 (0.85 - 1.97) |
| 313 Nursing, Therapy & Related Assisting | 4 | 1.02 (0.35 - 2.96) | 1.14 (0.37 - 3.57) | 12 | 0.97 (0.52 - 1.80) | 0.98 (0.51 - 1.88) |
| 3135 Nursing Attendants | 2 | - | - | 9 | *2.47 (1.15 - 5.29)* | *2.66 (1.18 - 6.00)* |
| 315 Others | 5 | 1.21 (0.46 - 3.16) | 1.25 (0.47 - 3.34) | 8 | 1.27 (0.59 - 2.70) | 1.33 (0.61 - 2.90) |
| 3155 Radiological Technologists& Technicians | 1 | - | - | 3 | *4.20 (1.05 - 16.72)* | 3.78 (0.80 - 17.79) |
| 41 Clerical & Related | 41 | 1.15 (0.82 - 1.62) | 1.14 (0.80 - 1.64) | 138 | 1.00 (0.82 - 1.22) | 0.96 (0.78 - 1.19) |
| 419 Others | 14 | 1.65 (0.92 - 2.97) | 1.71 (0.91 - 3.23) | 45 | 1.17 (0.84 - 1.62) | 1.06 (0.75 - 1.49) |
| 4197 General Office Clerks | 6 | *2.49 (1.02 - 6.04)* | *2.84 (1.10 - 7.36)* | 23 | 1.25 (0.80 - 1.94) | 1.12 (0.71 - 1.77) |
| 51 Sales Occupations | 78 | 0.97 (0.75 - 1.26) | 0.96 (0.73 - 1.25) | 194 | 0.99 (0.83 - 1.18) | 0.94 (0.78 - 1.13) |
| 517 Services | 9 | 0.62 (0.31 - 1.24) | 0.51 (0.25 - 1.05) | 39 | 0.89 (0.63 - 1.26) | 0.79 (0.55 - 1.14) |
| 5174 Advertising Sales | 2 | - | - | 3 | *4.90 (1.16 - 20.71)* | 3.46 (0.72 - 16.71) |
| 61 Service Occupations | 77 | 1.20 (0.93 - 1.56) | 1.20 (0.91 - 1.58) | 285 | 1.00 (0.85 - 1.17) | 0.99 (0.84 - 1.18) |
| 619 Others | 15 | 1.44 (0.81 - 2.54) | 1.51 (0.82 - 2.77) | 43 | 1.03 (0.74 - 1.44) | 1.05 (0.73 - 1.50) |
| 6199 Other services, n.e.c. | 1 | - | - | 4 | *4.16 (1.33 - 12.95)* | *4.89 (1.42 -16.79)* |
| 73 Fishing, Trapping & Related | 5 | 0.55 (0.22 - 1.37) | 0.77 (0.30 - 2.00) | 29 | 0.99 (0.66 - 1.48) | 1.04 (0.68 - 1.60) |
| 731 Fishing, Trapping & Related | 5 | 0.55 (0.22 - 1.37) | 0.77 (0.30 - 2.00) | 29 | 0.99 (0.66 - 1.48) | 1.04 (0.68 - 1.60) |
| 7311 Captains & Other officer, Fishing Vessels | 1 | - | - | 4 | 2.87 (0.91 - 8.98) | *4.58 (1.39 - 15.14)* |
| 81/ 82 Processing Occupations | 54 | 1.03 (0.76 - 1.40) | 1.07 (0.77 - 1.48) | 153 | *0.78 (0.65 - 0.95)* | *0.78 (0.64 - 0.95)* |
| 813/ 814 Metal Processing & Related | 10 | 1.69 (0.82 - 3.48) | 2.25 (0.96 - 5.28) | 24 | 1.01 (0.65 - 1.58) | 1.23 (0.76 - 2.00) |
| 8149 Metal Processing & Related, n.e.c | 4 | *6.38 (1.63 - 25.04)* | *9.48 (1.61 - 55.91)* | 6 | 1.40 (0.55 - 3.56) | 1.47 (0.50 - 4.31) |
| 83 Machining and related occupations | 36 | *1.45 (1.00 - 2.09)* | 1.44 (0.97 - 2.13) | 97 | *1.29 (1.02 - 1.63)* | 1.28 (1.00 - 1.63) |
| 831 Metal Machining | 11 | 1.64 (0.85 - 3.14) | 1.74 (0.87 - 3.48) | 33 | 1.22 (0.84 - 1.79) | 1.22 (0.81 - 1.82) |
| 8315 Machine Tool Operating Occupations | 2 | - | - | 10 | *3.29 (1.55 - 6.99)* | *3.73 (1.65 - 8.40)* |
| 833 Metal Shaping & Forming, Except Machining | 21 | 1.41 (0.87 - 2.28) | 1.22 (0.73 - 2.04) | 56 | *1.42 (1.05 - 1.91)* | 1.35 (0.98 - 1.86) |
| 8333 Sheet Metal Workers | 6 | *2.56 (1.02 - 6.44)* | 2.34 (0.88 - 6.20) | 13 | 1.61 (0.87 - 2.96) | 1.58 (0.82 - 3.03) |
| 85 Product fabricating, Assembling and Repairing | 87 | 1.05 (0.82 - 1.34) | 1.08 (0.83 - 1.41) | 203 | 1.02 (0.85 - 1.21) | 1.04 (0.86 - 1.25) |
| 853 Fabricating, Assembling, Installing & Repairing: Electrical, Electronic & Related Equipment | 14 | 1.02 (0.57 - 1.81) | 0.96 (0.52 - 1.77) | 34 | 1.05 (0.72 - 1.53) | 0.93 (0.62 - 1.38) |
| 8534 Electronic & Related Equipment Fabricating & Assembling n.e.c. | 2 | - | - | 6 | *8.97 (3.09 - 26.04)* | *7.71 (2.34 - 25.48)* |
| 87 Construction trades occupations | 94 | 0.92 (0.73 - 1.17) | 1.01 (0.78 - 1.29) | 202 | 0.86 (0.72 - 1.02) | 0.93 (0.77 - 1.12) |
| 873 Electrical Power, Lighting & Wire Communications Equipment Erecting, Installing & Repairing | 15 | 1.16 (0.67 - 2.03) | 1.30 (0.71 - 2.36) | 26 | 1.00 (0.66 - 1.52) | 1.10 (0.70 - 1.71) |
| 8731 Electrical Power Line Workers & Related | 5 | 1.70 (0.60 - 4.84) | 1.81 (0.55 - 5.95) | 8 | 1.94 (0.85 - 4.43) | 1.72 (0.70 - 4.20) |
| 878/879 Other Construction Trades | 64 | 0.90 (0.68 - 1.19) | 1.00 (0.75 - 1.35) | 148 | 0.88 (0.73 - 1.07) | 0.94 (0.76 - 1.15) |
| 8786 Insulating, Construction | 4 | *4.43 (1.28 -15.32)* | *4.60 (1.15 - 18.35)* | 7 | *3.43 (1.39 - 8.45)* | *3.16 (1.16 - 8.55)* |
| 91 Transport Equipment Operating | 66 | 0.89 (0.68 - 1.18) | 0.84 (0.62 - 1.12) | 207 | 1.06 (0.89 - 1.27) | 1.01 (0.84 - 1.22) |
| 915 Water Transport Operating | 12 | 0.99 (0.53 - 1.85) | 1.03 (0.53 - 2.00) | 52 | 1.35 (0.99 - 1.85) | 1.33 (0.94 - 1.87) |
| 9157 Engine & Boiler-room Crew, Ship | 3 | 2.66 (0.74 - 9.59) | 2.56 (0.64 - 10.17) | 16 | *2.06 (1.18 - 3.57)* | *2.14 (1.17 - 3.92)* |
| 919 Other Transport Equipment Operating | 4 | *6.44 (1.58 - 26.21)* | 4.49 (0.94 - 21.41) | 18 | 1.87 (1.10 - 3.19) | 1.52 (0.86 - 2.71) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 95 Other Crafts & Equipment Operating | 21 | 1.15 (0.72 - 1.83) | 1.18 (0.71 - 1.93) | 43 | 1.07 (0.77 - 1.49) | 1.04 (0.73 - 1.47) |
| 955 Electronic & Related Communic Equip Oper, n.e.c | 9 | *2.99 (1.40 - 6.37)* | *3.21 (1.40 - 7.35)* | 17 | *1.99 (1.16 - 3.42)* | *2.06 (1.16 - 3.65)* |
| 9551 Radio & TV Broadcasting Equip Operators | 4 | *9.32 ( 2.62 - 33.12)* | *8.18 ( 2.19 - 30.61)* | 6 | 2.05 (0.84 - 5.04) | 2.04 (0.80 - 5.22) |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics (p<0.05).*
CSOC: Canadian Standard Occupational Classification, 1980; CI: Confidence interval;
N1=Number of exposed cases in the corresponding usual occupation; N2=Number of cases exposed in the corresponding ever occupation.
*Control group 1= Basic control group after excluding unknown primary cancer subjects.
† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.
‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

We evaluated the risk of lung cancer for the occupational groups having at least 3 cases and 3 controls, which included 165 occupations represented in 20 major groups, 53 minor groups, and 92 unit groups. Overall, concordance of the results between both the control groups was good (95% agreement). Overall, 4% of the analyses (out of 7% total significant results) were significant in both two control groups with an elevated risk of adenocarcinoma of the lung being observed in 5 occupations and a reduced risk of adenocarcinoma of the lung in 2 occupations.

Among the occupations showing an excess risk of adenocarcinoma of the lung, the majority of the cases are employed in the major occupation: machining & related occupations. The odds ratios ranged between 1.5 and 9.5, indicating a moderate to strong association with adenocarcinoma of the lung; however, since there were few cases in most of the occupational groups, caution is warranted in interpreting the results. An excess risk of lung cancer was observed among the workers in the major occupational group, including: 'machining & related occupations' (SOC-83). An elevated risk of adenocarcinoma of the lung was exclusively seen among workers employed in the 'electronics & related communications equipment operating occupations n.e.c' (SOC-955), including the subgroup of the workers involved in the radio & television broadcasting (SOC-9551). Other noteworthy occupational groups that were exclusively associated with adenocarcinoma of the lung include: general office clerks (SOC-4197) and insulators in the construction trades (SOC-8786).

While the above mentioned occupations were significantly associated with adenocarcinoma of the lung in the analyses with both the control groups, a total of 4 occupations were associated with an increased risk of adenocarcinoma of the lung in only one of the control group analyses. These results were suggestive of an excess risk of lung cancer among workers in the machining and related occupations (SOC-83), including the subgroup, sheet metal workers (SOC-8333)In addition, workers in the other transport equipment operating occupations (SOC-919) consisting of the rail vehicle operators (except rail transport), subway & street railway operators, and mechanical engineers (SOC-2147) were at excess risk of adenocarcinoma (Table 19).

Overall, the adenocarcinoma specific analysis was suggestive of an excess risk of lung cancer among workers in certain occupations involving electronics & related communications equipment operation, machining, transport equipment operation, office clerks, and insulators in the construction trade occupations.

Among the 7 total significant results in the analysis with both the control groups, 2 occupational groups demonstrated a reduced risk of adenocarcinoma of lung. Specifically, employment in 'farming, horticultural & animal husbandry' occupations (SOC 71), including the subgroup, constituted by farmers (SOC 711), was associated with a significantly reduced risk of adenocarcinoma of the lung; odds ratios (95% confidence intervals) with control group 1 were 0.64 (0.43-0.94) and 0.60 (0.38-0.94), respectively, while odds ratios with control group 2 were 0.6 (0.4-0.9) and 0.57 (0.36-0.91), respectively.

#### 4.4.3.2 Occupations 'Ever' Held

The significantly elevated odds ratio estimates for adenocarcinoma of lung and the associated 95% confidence intervals in relation to the occupations 'ever' held are reported in Table 19. Our analysis of adenocarcinoma of the lung was restricted to the occupations 'ever' held having at least 3 cases and 3 controls (approximately 50% of the total number of occupations), which included 303 occupations represented in 23 major groups, 69 minor groups, and 211 unit groups. In general, the concordance of the results between the control groups 1 and 2 was good (98% agreement). Overall, 4% of the analyses (out of 6% total significant results) were significant in both two control groups with an elevated risk of adenocarcinoma of lung being observed in 7 occupations and a reduced risk of adenocarcinoma of the lung in 4 occupations.

The odds ratios among the significant positive associations ranged between 1.4 and 9.0, indicating a moderate to strong association between occupation and adenocarcinoma of the lung. An increased risk of adenocarcinoma of the lung was observed among men employed as nursing attendants (SOC-3135; OR ≈2.5), engine & boiler room crew in a ship (SOC-9157), and workers in certain metal machining occupations involving machine tool operation (SOC-8315).

### 4.4.4 Small Cell Carcinoma of the Lung

#### 4.4.4.1 'Usual' Occupation

The odds ratios and associated 95% confidence intervals in relation to 'usual' occupation showing an excess risk of small cell lung cancer are reported in Table 20. When we limited the analysis to small cell lung cancer, there are a total of 542 'usual' occupational categories, including 23 major groups, 83 minor groups, and 436 unit groups. We evaluated the risk of lung cancer for about 21% of these occupational groups having at least 3 cases and 3 controls; this subset included 116 occupations represented in 20 major groups, 37 minor groups, and 59 unit groups. Overall concordance of the results between both the control groups was good (99% agreement). Overall, 3% of the analyses (out of 4% total significant results) were significant in both two control groups with an elevated risk of small cell lung cancer being observed in 5 occupations.

**Table 20:** Occupations with Significantly Elevated Risk of Small Cell Carcinoma of the Lung

| | Occupation (Usual) | | | Occupation (Ever) | | |
|---|---|---|---|---|---|---|
| **CSOC Code Occupation Title** | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| 21 Natural Sciences, Engineering & Mathematics | 9 | 0.77 (0.38 - 1.56) | 0.72 (0.35 - 1.52) | 18 | 0.64 (0.39 - 1.06) | *0.58 (0.34 - 0.98)* |
| 214 Architects, Engineers & Community Planners | 1 | - | - | 6 | 0.63 (0.27 - 1.46) | 0.71 (0.30 - 1.68) |
| 2142 Chemical Engineers | 1 | - | - | 3 | *4.68 (1.24 - 17.65)* | 2.96 (0.75 - 11.75) |
| 23 Occupations in Social Sciences & Related Fields | 2 | - | - | 7 | 1.29 (0.56 - 2.94) | 1.21 (0.51 - 2.90) |
| 233 Social Work & related Fields | 2 | - | - | 5 | 3.03 (1.09 - 8.43) | 2.31 (0.76 - 7.04) |
| 2333 Welfare and Community Services | 1 | - | - | 4 | *5.94 (1.58 - 22.36)* | 4.09 (0.92 - 18.17) |
| 41 Clerical & Related | 28 | 1.40 (0.92 - 2.13) | 1.40 (0.89 - 2.21) | 71 | 0.90 (0.68 - 1.18) | 0.84 (0.63 - 1.12) |
| 415 Material Recording, Scheduling & Distributing | 8 | 1.18 (0.55 - 2.52) | 1.24 (0.55 - 2.81) | 25 | 0.77 (0.50 - 1.19) | 0.87 (0.55 - 1.37) |
| 4150 Supervisors | 3 | *3.83 (1.01 - 14.53)* | *6.07 (1.55 - 23.78)* | 7 | 1.83 (0.80 - 4.19) | 1.93 (0.84 - 4.46) |
| 419 Others | 9 | 1.90 (0.90 - 4.05) | 1.88 (0.80 - 4.38) | 22 | 1.06 (0.66 - 1.68) | 0.91 (0.55 - 1.49) |
| 4190 Supervisors, n.e.c | 2 | - | - | 9 | *2.31 (1.07 - 5.02)* | 2.04 (0.85 - 4.90) |
| 71 Farming, Horticultural & Animal husbandry | 30 | 1.19 (0.79 - 1.80) | 1.20 (0.78 - 1.86) | 126 | 1.00 (0.80 - 1.26) | 1.02 (0.80 - 1.30) |
| 711 Farmers | 25 | 1.29 (0.82 - 2.01) | 1.30 (0.81 - 2.08) | 92 | *1.45 (1.12 - 1.88)* | *1.49 (1.13 - 1.96)* |
| 7118 Mixed Farmers, n.e.c. | 18 | 1.56 (0.92 - 2.64) | *1.84 (1.05 - 3.21)* | 56 | *1.41 (1.03 - 1.93)* | *1.56 (1.12 - 2.17)* |
| 77 Mining & Quarrying including Oil & Gas field | 10 | 1.60 (0.80 - 3.20) | 1.52 (0.73 - 3.17) | 41 | 1.19 (0.84 - 1.69) | 1.23 (0.84 - 1.79) |
| 771 Mining & Quarrying including Oil & Gas field | 10 | 1.60 (0.80 - 3.20) | 1.52 (0.73 - 3.17) | 41 | 1.19 (0.84 - 1.69) | 1.23 (0.84 - 1.79) |
| 7717 Mining & Quarrying: Cutting,Handling &Loading | 5 | 1.81 (0.68 - 4.83) | 2.13 (0.75 - 6.03) | 26 | 1.49 (0.97 - 2.31) | *1.65 (1.03 - 2.66)* |
| 83 Machining and related occupations | 19 | 1.26 (0.76 - 2.09) | 1.20 (0.69 - 2.07) | 56 | 1.19 (0.88 - 1.62) | 1.13 (0.81 - 1.56) |
| 833 Metal Shaping & Forming, Except Machining | 16 | *1.84 (1.04 - 3.25)* | 1.49 (0.81 - 2.74) | 38 | *1.56 (1.08 - 2.25)* | 1.41 (0.95 - 2.09) |
| 8331 Forging Occupation | 2 | - | - | 6 | *5.28 ( 2.08 - 13.43)* | *5.47 (1.92 - 15.57)* |
| 8337 Boilermakers, Platers & Structural Metal Workers | 2 | - | - | 7 | *2.56 (1.02 - 6.43)* | 2.05 (0.74 - 5.68) |
| 8339 Metal Shap & Forming, Except Machining, n.e.c. | 0 | - | - | 3 | 3.99 (0.91 - 17.52) | 2.87 (0.56 - 14.60) |
| 839 Others, n.e.c | 2 | - | - | 9 | 2.10 (0.97 - 4.57) | 2.31 (0.97 - 5.47) |
| 8393 Filing,Grinding,Buffing, Cleaning&Polishing n.e.c | 1 | - | - | 8 | *2.46 (1.07 - 5.65)* | *2.88 (1.15 -7.22)* |
| 87 Construction trades occupations | 65 | 0.96 (0.72 - 1.28) | 1.07 (0.78 - 1.46) | 147 | 1.00 (0.80 - 1.24) | 1.10 (0.87 - 1.38) |
| 873 Electrical Power, Lighting & Wire Communications Equipment Erecting, Installing & Repairing | 11 | 1.52 (0.78 - 2.96) | 1.65 (0.79 - 3.48) | 19 | 1.23 (0.74 - 2.03) | 1.32 (0.76 - 2.28) |
| 8733 Construction Electricians and Repairers | 7 | *2.83 (1.19 - 6.69)* | *3.43 (1.34 - 8.77)* | 12 | 1.62 (0.85 - 3.09) | *2.12 (1.04 - 4.29)* |
| 91 Transport Equipment Operating | 48 | 1.08 (0.78 - 1.50) | 1.07 (0.75 - 1.51) | 129 | 1.09 (0.87 - 1.36) | 1.06 (0.84 - 1.34) |
| 913 Railway Transport Operating | 7 | 1.63 (0.71 - 3.75) | 1.31 (0.53 - 3.24) | 13 | 1.34 (0.73 - 2.45) | 1.20 (0.62 - 2.32) |
| 9131 Locomotive Operating Occupations | 3 | *4.36 (1.18 - 16.13)* | *7.06 (1.59 - 31.44)* | 6 | 2.08 (0.85 - 5.11) | *2.80 (1.06 - 7.40)* |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics (p<0.05).*
CSOC: Canadian Standard Occupational Classification, 1980; CI: Confidence interval;
N1=Number of exposed cases in the corresponding usual occupation; N2=Number of cases exposed in the corresponding ever occupation.
*Control group 1= Basic control group after excluding unknown primary cancer subjects.
† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.
‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

None of the occupations showed a reduced risk of small cell lung cancer. In these occupations the majority of cases are farmers.

Overall, this analysis provided little evidence of an excess risk of small cell lung cancer in relation to occupation. However, the excess risk of small cell lung cancer among construction electricians & repairers (SOC-8733) is noteworthy. None of the occupations were associated with a significantly reduced risk of small cell lung cancer.

#### 4.4.4.2 Occupations 'Ever' Held

The significantly elevated odds ratio estimates for small cell lung cancer and the associated 95% confidence intervals in relation to the occupations 'ever' held are reported in Table 20. Our analysis of small cell lung cancer was restricted to the occupations 'ever' held having at least 3 cases and 3 controls (approximately 38% of the total number of occupations), which included 231 occupations represented in 21 major groups, 60 minor groups, and 150 unit groups. In general, the concordance of the results between the control groups 1 and 2 was good (94% agreement). Overall, 4% of the analyses were significant in both two control groups with an elevated risk of small cell lung cancer being observed in 4 occupations and a reduced risk of small cell lung cancer in 5 occupations. Although there was little evidence of an excess risk of small cell carcinoma of the lung in relation to occupations, the excess risk among farmers is noteworthy (SOC-711; OR = 1.5).

### 4.4.5 Large Cell Carcinoma of the Lung

#### 4.4.5.1 'Usual' Occupation

The odds ratios and associated 95% confidence intervals in relation to 'usual' occupation showing an excess risk of large cell carcinoma are reported in Table 21. When we limited our analysis to large cell carcinoma of lung, there were a total of 526 'usual' occupational categories, including 23 major groups, 83 minor groups, and 435 unit groups. We evaluated the risk of lung cancer for about 17% of these occupational groups having at least 3 cases and 3 controls; this subset of the data included 87 occupations represented in 18 major groups, 32 minor groups, and 37 unit groups. Overall, concordance of the results between both the control groups was good (96% agreement). Overall, 9% of the analyses (out of 13% total significant results) were significant in both two control groups with an elevated risk of large cell lung cancer being observed in 8 occupations. None of the occupational groups had a significantly reduced risk of large cell lung cancer.

We observed a moderate to strong positive association between large cell lung cancer and workers involved in medicine & health related occupations (SOC-31; OR = 2.2), including the subgroups, health diagnosing & treating occupations (SOC-311) consisting of physicians & surgeons (SOC-3111). These results should be interpreted with caution as most of these odds ratios are based on a small number of exposed cases. Another important finding was the increased risk of large cell lung cancer among workers in 'food & beverage preparation & related service' occupations (SOC-612; OR = 2.2), including: chefs & cooks (SOC-6121), and bartenders (SOC-6123).

**Table 21:** Occupations with Significantly Elevated Risk of Large Cell Carcinoma of the Lung

| CSOC Code Occupation Title | Occupation (Usual) | | | Occupation (Ever) | | |
|---|---|---|---|---|---|---|
| | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| 31 Occupations in Medicine and health | 8 | *2.16 (1.00 - 4.67)* | *2.45 (1.10 - 5.47)* | 11 | 1.46 (0.77 - 2.79) | 1.64 (0.84 - 3.22) |
| 311 Health Diagnosing and Treating Occupations | 6 | *5.19 (2.11 - 12.76)* | *5.35 (2.09 - 13.69)* | 6 | *5.00 (2.04 - 12.25)* | *5.05 (1.98 - 12.87)* |
| 3111 Physicians and Surgeons | 5 | *6.03 (2.25 - 16.17)* | *6.47 (2.30 - 18.25)* | 5 | *6.03 (2.25 -16.17)* | *6.47 (2.30 - 18.25)* |
| 41 Clerical & Related | 12 | 0.91 (0.49 - 1.68) | 0.90 (0.47 - 1.71) | 44 | 0.87 (0.62 - 1.23) | 0.86 (0.60 - 1.24) |
| 417 Reception, Information, Mail & Message Distribution | 1 | - | - | 7 | 0.75 (0.34 - 1.67) | 0.78 (0.34 - 1.78) |
| 4177 Messengers | 0 | - | - | 5 | *2.83 (1.08 - 7.41)* | 2.55 (0.94 - 6.94) |
| 61 Service Occupations | 28 | 1.10 (0.72 - 1.67) | 1.07 (0.69 - 1.68) | 105 | 0.91 (0.71 - 1.18) | 0.88 (0.68 - 1.16) |
| 611 Protective Services | 9 | 0.81 (0.40 - 1.62) | 0.79 (0.38 - 1.64) | 71 | 0.95 (0.71 - 1.27) | 0.96 (0.70 - 1.30) |
| 6119 Protective Service Occupations, n.e.c. | 1 | - | - | 3 | *4.57 (1.17 - 17.86)* | 4.21 (0.80 - 22.14) |
| 612 Food & Beverage Preparation & Related Service | 13 | *2.26 (1.18 - 4.31)* | *2.23 (1.08 - 4.59)* | 26 | 1.28 (0.82 - 1.98) | 1.51 (0.94 - 2.43) |
| 6121 Chefs and Cooks | 8 | *2.83 (1.21 - 6.63)* | *2.95 (1.08 - 8.10)* | 18 | *2.41 (1.40 - 4.16)* | *2.76 (1.50 - 5.11)* |
| 6123 Bartenders | 3 | *4.96 (1.37 - 17.91)* | *4.81 (1.21 - 19.11)* | 4 | 0.91 (0.32 - 2.59) | 0.87 (0.29 - 2.63) |
| 77 Mining and Quarrying including Oil and Gas field | 7 | 1.66 (0.73 - 3.76) | 1.55 (0.65 - 3.68) | 32 | *1.49 (1.00 - 2.21)* | *1.56 (1.02 - 2.38)* |
| 771 Mining & Quarrying including Oil & Gas field | 7 | 1.66 (0.73 - 3.76) | 1.55 (0.65 - 3.68) | 32 | *1.49 (1.00 - 2.21)* | *1.56 (1.02 - 2.38)* |
| 7710 Foremen/women | 3 | *6.61 (1.43 - 30.66)* | *16.73 (2.77 - 101.20)* | 4 | 1.70 (0.58 - 4.98) | 1.45 (0.47 - 4.48) |
| 7717 Mining & Quarrying: Cutting,Handling &Loading | 3 | 1.57 (0.46 - 5.36) | 1.78 (0.51 - 6.29) | 19 | 1.66 (1.00 - 2.75) | *1.75 (1.01 - 3.00)* |
| 81/ 82 Processing Occupations | 23 | 1.08 (0.68 - 1.70) | 1.15 (0.71 – 1.87) | 82 | 1.14 (0.87 - 1.49) | 1.13 (0.85 - 1.50) |
| 813/814 Metal Processing & Related | 5 | 2.50 (0.94 - 6.65) | *4.45 (1.52 - 13.04)* | 16 | *1.92 (1.10 - 3.34)* | *2.65 (1.46 - 4.82)* |
| 8149 Metal Processing and Related, n.e.c | 1 | - | - | 6 | *3.92 (1.48 - 10.38)* | *4.16 (1.36 - 12.69)* |
| 823 Wood Processing, except Pulp & Papermaking | 10 | 0.97 (0.49 - 1.91) | 1.00 (0.49 - 2.06) | 36 | 0.96 (0.66 - 1.39) | 0.87 (0.58 - 1.29) |
| 8238 Occupations in Labouring & Other Elemental Work | 4 | 2.16 (0.72 - 6.47) | 2.58 (0.78 - 8.52) | 22 | *1.68 (1.04 - 2.72)* | 1.54 (0.92 - 2.59) |
| 83 Machining and related occupations | 14 | 1.58 (0.89 - 2.81) | 1.63 (0.89 - 2.97) | 31 | 1.03 (0.69 - 1.53) | 1.04 (0.68 - 1.57) |
| 831 Metal Machining | 5 | 2.30 (0.88 - 5.97) | 2.61 (0.95 - 7.15) | 8 | 0.79 (0.38 - 1.66) | 0.87 (0.41 - 1.87) |
| 8313 Machinist and Machine Tool Setting-up Occupations | 5 | *2.86 (1.08 - 7.59)* | 2.83 (1.00 - 8.00) | 8 | 1.12 (0.53 - 2.37) | 1.14 (0.52 - 2.49) |
| 87 Construction Trades | 46 | 1.05 (0.75 - 1.48) | 1.17 (0.81 - 1.70) | 92 | 0.96 (0.73 - 1.25) | 1.03 (0.77 - 1.36) |
| 871 Excavating, Grading, Paving & Related | 11 | 1.52 (0.79 - 2.94) | 1.51 (0.74 - 3.06) | 28 | 1.33 (0.87 - 2.03) | *1.60 (1.02 - 2.52)* |
| 8715 Railway Section and Track Workers | 2 | - | - | 9 | 1.74 (0.84 - 3.62) | *2.33 (1.06 - 5.09)* |
| 8718 Occupations in Labouring & Other Elemental Work | 3 | 3.02 (0.83 - 11.05) | *4.75 (1.09 - 20.69)* | 4 | 0.80 (0.28 - 2.32) | 1.09 (0.36 - 3.35) |
| 873 Electrical Power, Lighting & Wire Communications Equipment Erecting, Installing & Repairing | 8 | 1.78 (0.82 - 3.85) | 1.98 (0.86 - 4.57) | 12 | 1.35 (0.73 - 2.50) | 1.50 (0.78 - 2.88) |
| 8733 Construction Electricians and Repairers | 4 | 2.51 (0.85 - 7.38) | 2.85 (0.88 - 9.21) | 7 | 1.70 (0.76 - 3.80) | *2.36 (1.01 - 5.50)* |
| 91 Transport Equipment Operating | 32 | 1.03 (0.69 - 1.53) | 0.91 (0.59 - 1.39) | 79 | 0.95 (0.72 - 1.26) | 0.86 (0.64 - 1.15) |
| 913 Railway Transport Operating | 6 | 1.73 (0.70 - 4.30) | 1.25 (0.46 - 3.37) | 8 | 1.18 (0.55 - 2.53) | 0.92 (0.40 - 2.10) |
| 9131 Locomotive Operating Occupations | 3 | *5.10 (1.33 - 19.48)* | *6.14 (1.35 - 27.90)* | 6 | *2.95 (1.18 - 7.38)* | *3.37 (1.23 - 9.21)* |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics ($p<0.05$).*

CSOC: Canadian Standard Occupational Classification, 1980; CI: Confidence interval;

N1=Number of exposed cases in the corresponding usual occupation; N2=Number of cases exposed in the corresponding ever occupation.

*Control group 1= Basic control group after excluding unknown primary cancer subjects.

† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.

‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

#### 4.4.5.2 Occupations 'Ever' Held

The significantly elevated odds ratios for large cell carcinoma of lung and the associated 95% confidence intervals in relation to the occupations 'ever' held are reported in Table 21. Our analysis was restricted to occupations 'ever' held having at least 3 cases and 3 controls (approximately 30% of the total number of occupations); which included 182 occupations represented in 21 major groups, 53 minor groups, and 108 unit groups. In general, the concordance of the results between the control groups 1 and 2 was good (95% agreement). Overall, 4% of the analyses were significant in both two control groups with an elevated risk of large cell lung cancer being observed in 7 occupational groups and a reduced risk of large cell lung cancer in 1 occupation.

In general, the associations observed among 'usual' occupations were reproduced in this analysis, either at the major group level or other hierarchical levels of the occupational coding system. An excess risk of large cell lung cancer among the workers in the locomotive operating occupations (SOC-9131) is noteworthy; this relationship was apparent for both 'usual' and 'ever' occupation.

## *4.5 Industries Associated with Lung Cancer*

The subjects in our dataset represented a total of 1,223 industry categories listed in the Canadian SIC, including 18 divisions, 76 major groups, 314 minor groups, and 815 classes. Our analysis is limited to the industries containing at least 3 cases and 3 controls. We estimated two odds ratios using control groups 1 and 2 separately in each of the 'usually' employed industry categories and the 'ever' employed industry categories, resulting in 4 odds ratios for each industry analyzed. The results for the industries in which subjects were 'usually', or 'ever' employed are presented in separate sections.

Although the analysis based on 'usual' and 'ever' employment categories yielded generally similar results, the concordance was poor for some industry categories. The industries with a significantly elevated OR ($P<0.05$) among any of the 4 OR estimates are selected for reporting. However, the OR estimates and the 95% confidence intervals (CI) in the broad hierarchical categories of a significant industrial category are also reported for clarity. Although our main objective is identifying industries with an elevated risk of lung cancer, we have reported some noteworthy protective associations in the analyses based on the 'usual' industry of employment.

## 4.5.1 All Types of Lung Cancer

### 4.5.1.1 'Usual' Industry of Employment

The odds ratios and associated 95% confidence intervals in relation to the 'usual' industry of employment, which showed an excess risk of lung cancer, are reported in Table 22. There were a total of 1,073 industry categories (1,043 for control group-2 analyses), including: 18 divisions, 76 major groups, 299 minor groups, and 680 classes. We evaluated the risk of lung cancer for about 41% of these industry groups having at least 3 cases and 3 controls; which included 443 industries represented in 18 divisions, 65 major groups, 161 minor groups, and 199 classes. In addition, 12 industrial categories with less than 3 controls were not evaluated in analyses based on the second control group. Overall concordance between the results from both the control groups was good (96% agreement). Overall, 3% of the analyses (out of 7% total significant results) were significant in both two control groups with an elevated risk of lung cancer being observed among the workers in 13 industries and a reduced risk of lung cancer among the workers in 1 industry.

**Table 22:** Industries with Significantly Elevated Risk of lung cancer – All cases

| CSIC Code Industry Title | Industry (Usual) | | | Industry (Ever) | | |
|---|---|---|---|---|---|---|
| | N1 | CONTROL GROUP 1 * OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| A. Agricultural & Related Service Industries | 139 | 0.91 (0.74 - 1.12) | 0.83 (0.66 - 1.05) | 634 | *0.89 (0.80 - 1.00)* | *0.86 (0.76 - 0.98)* |
| 02 Service Industries Incidental to Agriculture | 4 | 0.87 (0.28 - 2.75) | 1.21 (0.33 – 4.39) | 16 | 1.21 (0.33 - 4.39) | 1.52 (0.76 - 3.00) |
| 023 Other Services Incidental to Agriculture | 2 | - | - | 6 | 1.24 (0.47 - 3.26) | 2.41 (0.82 - 7.04) |
| 0239 Other Services Incidental to Agriculture n.e.c | 2 | - | - | 5 | 1.20 (0.41 - 3.49) | *3.39 (1.01 -11.42)* |
| D. Mining (Including Milling), Quarrying and Oil Well industries | 89 | *1.45 (1.11 - 1.91)* | *1.47 (1.08 - 2.01)* | 357 | *1.26 (1.20 - 1.46)* | *1.29 (1.10 - 1.52)* |
| 06 Mining Industries | 75 | *1.54 (1.14 - 2.08)* | *1.57 (1.12 - 2.21)* | 319 | *1.32 (1.14 -1.54)* | *1.37 (1.15 - 1.62)* |
| 061 Metal Mines | 63 | *1.79 (1.29 - 2.49)* | *1.90 (1.30 - 2.77)* | 236 | *1.27 (1.07 - 1.51)* | *1.28 (1.06 - 1.56)* |
| 0611 Gold Mines | 10 | 1.65 (0.74 - 3.65) | 2.10 (0.85 - 5.20) | 99 | *1.36 (1.05 - 1.76)* | 1.31 (0.98 - 1.75) |
| 0612 Copper and Copper-Zinc Mines | 18 | *2.71 (1.41 - 5.22)* | *2.82 (1.32 - 6.01)* | 90 | *1.34 (1.02 - 1.76)* | *1.40 (1.03 - 1.91)* |
| 0616 Uranium Mines | 2 | - | - | 27 | *2.63 (1.52 - 4.55)* | *3.52 (1.76 - 7.05)* |
| 0619 Other Metal Mine | 8 | 1.54 (0.64 - 3.74) | 2.62 (0.88 - 7.76) | 34 | *1.56 (1.01 - 2.40)* | *2.02 (1.22 - 3.34)* |
| 062 Non-Metal Mines (except Coal) | 4 | 2.60 (0.50 - 13.49) | 2.28 (0.32 - 16.18) | 22 | 1.73 (0.97 - 3.11) | *2.21 (1.07 - 4.56)* |
| 0621 Asbestos Mines | 1 | - | - | 9 | 1.44 (0.60 - 3.46) | *4.40 (1.17 - 16.55)* |
| E. Manufacturing Industries | 560 | 1.02 (0.91 - 1.15) | 1.05 (0.92 - 1.20) | 1291 | 1.02 (0.92 - 1.12) | 1.02 (0.92 - 1.14) |
| 10 Food Industries | 51 | 0.93 (0.66 - 1.30) | 0.92 (0.63 - 1.34) | 186 | 0.93 (0.78 - 1.12) | 0.94 (0.76 - 1.15) |
| 103 Fruits & Vegetables | 4 | 0.88 (0.27 - 2.86) | 0.85 (0.24 - 2.99) | 25 | 1.38 (0.83 - 2.32) | 1.25 (0.71 - 2.20) |
| 1031 Canned & Preserved Fruit & Vegetable | 2 | - | - | 5 | *3.36 (1.01 - 11.21)* | 2.91 (0.82 - 10.39) |
| 11 Beverage Industry | 14 | 1.36 (0.67 - 2.78) | 1.13 (0.49 - 2.59) | 37 | 1.24 (0.82 - 1.89) | 1.14 (0.71 - 1.85) |
| 112 Distillery Products Industry | 2 | - | - | 9 | 1.92 (0.82 - 4.50) | *2.94 (1.07 - 8.08)* |
| 24 Wood Industries | 5 | 1.39 (0.44 - 4.42) | 1.66 (0.46 - 6.06) | 14 | 1.18 (0.60 - 2.28) | 1.65 (0.77 - 3.50) |
| 244 Women's Clothing Industries | 1 | - | - | 4 | 4.43 (0.92 - 21.45) | *7.64 (1.18 - 49.56)* |
| 26 Furniture & Fixture Industries | 12 | 1.11 (0.54 - 2.31) | 1.09 (0.49 - 2.43) | 38 | 1.16 (0.77 - 1.74) | 1.38 (0.88 - 2.18) |
| 261 Household Furniture | 9 | 0.84 (0.37 - 1.91) | 0.81 (0.33 - 2.02) | 29 | 0.99 (0.62 - 1.56) | 1.19 (0.72 - 1.99) |
| 2619 Other Household Furniture | - | - | - | 4 | 2.32 (0.63 - 8.51) | *7.14 (1.22 - 41.62)* |
| 269 Other Furniture & Fixture Industries | 2 | - | - | 9 | *2.62 (1.04 - 6.62)* | 2.17 (0.80 - 5.89) |
| 2691 Bed Spring & Mattress Industry | 1 | - | - | 6 | *5.52 (1.37 - 22.33)* | 4.51 (0.90 - 22.70) |
| 29 Primary Metal Industries | 66 | *1.42 (1.03 - 1.96)* | *1.76 (1.21 - 2.56)* | 159 | 1.14 (0.93 - 1.40) | *1.29 (1.02 - 1.62)* |
| 291 Primary Steel Industries | 13 | *2.51 (1.12 - 5.64)* | *3.27 (1.29 - 8.25)* | 41 | *1.75 (1.15 - 2.66)* | *2.18 (1.35 - 3.51)* |
| 2912 Steel Foundries | 5 | 3.02 (0.93 - 9.80) | *3.41 (1.01 - 11.57)* | 13 | 1.51 (0.77 - 2.96) | 1.84 (0.88 - 3.84) |
| 2919 Other Primary Steel Industries | 8 | 2.59 (0.84 - 7.99) | 3.07 (0.75 - 12.59) | 26 | *1.97 (1.13 - 3.43)* | *2.55 (1.33 - 4.92)* |
| 295 Non-Ferrous Metal Smelting and Refining Industries | 16 | 1.23 (0.65 - 2.34) | *2.56 (1.11 - 5.88)* | 37 | 1.02 (0.68 - 1.53) | 1.33 (0.82 - 2.15) |
| 2951 Primary Production of Aluminum Industry | 10 | 0.97 (0.44 - 2.14) | *3.16 (1.00 - 9.92)* | 24 | 1.13 (0.67 - 1.90) | 1.85 (0.96 - 3.55) |
| 30 Fabricated Metal Products (Except Machinery & Transport) | 52 | 1.36 (0.96 - 1.94) | 1.24 (0.84 - 1.84) | 158 | 1.22 (0.99 - 1.49) | 1.19 (0.95 - 1.50) |
| 305 Wire and Wire Products Industries | 4 | 0.85 (0.25 - 2.90) | 0.52 (0.14 - 1.91) | 18 | *2.08 (1.10 - 3.96)* | 1.40 (0.70 - 2.81) |
| 3053 Industrial Fastener Industry | 2 | - | - | 4 | *5.76 (1.07 – 30.91)* | 3.89 (0.61 - 25.02) |
| 3059 Other Wire Products Industries | 0 | - | - | 6 | *3.98 (1.15 - 13.83)* | *5.94 (1.16 - 30.50)* |
| 309 Other Metal Fabricating Industries | 6 | 2.57 (0.82 - 8.10) | 1.93 (0.55 - 6.74) | 23 | *1.90 (1.12 - 3.24)* | *2.19 (1.20 - 4.00)* |
| 3099 Other Metal Fabricating Industries n.e.c. | 6 | 2.73 (0.85 - 8.78) | 2.08 (0.58 - 7.50) | 22 | *2.17 (1.24 - 3.78)* | *2.33 (1.24 - 4.38)* |
| 32 Transportation Equipment | 57 | 1.23 (0.88 - 1.71) | 1.24 (0.85 - 1.79) | 282 | 1.05 (0.90 - 1.22) | 1.06 (0.90 - 1.26) |
| 321 Aircraft and Aircraft Parts | 10 | *2.59 (1.12 - 6.00)* | 2.38 (0.95 - 5.95) | 63 | 1.24 (0.90 - 1.70) | 1.31 (0.92 - 1.86) |
| 33 Electrical & Electronic Products | 10 | 0.79 (0.39 - 1.63) | 0.73 (0.34 - 1.58) | 38 | 0.99 (0.67 - 1.47) | 0.93 (0.60 - 1.44) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 335 Communications & Other electronic Equipment | 4 | 0.95 (0.31 - 2.92) | 1.18 (0.18 - 7.75) | 14 | 1.41 (0.72 - 2.73) | 1.14 (0.55 - 2.38) |
| 3351 Telecommunication Equipment Industry | 4 | 3.02 (0.79 - 11.53) | 2.08 (0.50 - 8.64) | 9 | *3.76 (1.42 - 9.97)* | *3.11 (1.08 - 9.00)* |
| 39 Other Manufacturing | 13 | 1.24 (0.61 - 2.53) | 1.45 (0.65 - 3.23) | 33 | 1.16 (0.75 - 1.79) | 1.11 (0.69 - 1.79) |
| 399 Other Manufactured Product Industries | 9 | *3.39 (1.27 - 9.09)* | 2.65 (0.91 - 7.73) | 20 | 1.48 (0.83 - 2.63) | 1.09 (0.59 - 2.03) |
| F. Construction Industries | 348 | 1.08 (0.94 - 1.25) | 1.17 (0.99 - 1.37) | 772 | 1.04 (0.94 - 1.16) | 1.11 (0.99 - 1.25) |
| 41 Industrial & Heavy (Engineering) Construction | 62 | 1.13 (0.82 - 1.56) | 1.19 (0.82 - 1.73) | 195 | 1.05 (0.87 - 1.26) | 1.13 (0.91 - 1.39) |
| 412 Highway & Heavy Construction | 55 | 1.13 (0.80 - 1.60) | 1.15 (0.77 - 1.72) | 167 | 1.06 (0.87 - 1.30) | 1.17 (0.93 - 1.47) |
| 4129 Other Heavy Construction | 14 | 1.19 (0.58 - 2.41) | 1.08 (0.49 - 2.37) | 52 | 1.29 (0.90 - 1.86) | *1.61 (1.05 - 2.48)* |
| 42 Trade Contracting | 142 | 0.97 (0.78 - 1.20) | 1.09 (0.85 - 1.39) | 324 | 1.02 (0.88 - 1.18) | 1.14 (0.97 - 1.35) |
| 421 Site Work | 13 | 0.92 (0.46 - 1.81) | 1.10 (0.48 - 2.50) | 48 | 0.94 (0.66 - 1.34) | 1.13 (0.75 - 1.70) |
| 4211 Wrecking and Demolition | 1 | - | - | 4 | 2.30 (0.59 - 9.05) | *6.36 (1.09 - 37.11)* |
| 426 Electrical Work | 18 | 1.66 (0.93 - 2.97) | 1.63 (0.87 - 3.06) | 42 | 1.29 (0.88 - 1.88) | *1.59 (1.04 - 2.44)* |
| 429 Other Trade Work | 2 | - | - | 12 | 1.59 (0.73 - 3.47) | 1.68 (0.70 - 4.07) |
| 4299 Other Trade Work n.e.c. | 2 | - | - | 8 | *7.53 (1.73 - 32.81)* | *8.16 (1.29 - 51.62)* |
| H. Communication & Other Utility | 119 | 1.19 (0.94 - 1.51) | 1.17 (0.90 - 1.52) | 210 | 1.04 (0.87 - 1.25) | 0.99 (0.81 - 1.20) |
| 49 Other Utility Industries | 74 | *1.65 (1.20 - 2.26)* | *1.74 (1.21 - 2.51)* | 124 | *1.42 (1.12 - 1.80)* | *1.44 (1.10 - 1.89)* |
| 491 Electric Power Systems Industry | 49 | *1.97 (1.32 - 2.94)* | *2.01 (1.26 - 3.19)* | 73 | *1.45 (1.06 - 1.97)* | *1.42 (1.00 - 2.01)* |
| 499 Other Utility Industries, n.e.c. | 12 | *2.91 (1.21 - 6.96)* | 2.68 (0.99 - 7.26) | 21 | 1.57 (0.88 - 2.82) | 1.88 (0.95 - 3.73) |
| I. Wholesale Trade | 134 | 0.94 (0.76 - 1.16) | 0.94 (0.74 - 1.19) | 374 | 1.04 (0.90 - 1.19) | 1.04 (0.89 - 1.21) |
| 52 Food, Beverage, Drug & Tobacco | 24 | 1.13 (0.68 - 1.88) | 0.91 (0.52 - 1.59) | 72 | 1.00 (0.75 - 1.34) | 1.00 (0.72 - 1.38) |
| 521 Food | 18 | 1.07 (0.59 - 1.93) | 0.87 (0.45 - 1.69) | 53 | 0.90 (0.64 - 1.26) | 0.89 (0.61 - 1.30) |
| 5217 Meat and Meat Products | 1 | - | - | 4 | *5.93 (1.27 - 27.74)* | *6.17 (1.09 - 35.04)* |
| 53 Apparel and Dry Goods Industries, Wholesale | 5 | 2.29 (0.68 - 7.73) | *5.58 (1.13 - 27.48)* | 11 | 1.02 (0.49 - 2.12) | 1.79 (0.77 - 4.16) |
| 56 Metal, Hardware, Plumbing, Heating &Building Material | 27 | 0.83 (0.52 - 1.35) | 0.96 (0.56 - 1.63) | 83 | 1.04 (0.79 - 1.37) | 1.05 (0.77 - 1.42) |
| 562 Hardware & Plumbing, Heating & AC Equip & Supplies | 11 | 1.22 (0.53 - 2.82) | 2.72 (0.90 - 8.22) | 28 | 1.28 (0.78 - 2.09) | 1.50 (0.86 - 2.63) |
| 5621 Hardware | 7 | 1.40 (0.49 - 3.99) | *7.45 (1.44 - 38.52)* | 20 | 1.30 (0.73 - 2.31) | 1.57 (0.82 - 3.04) |
| 57 Machinery, Equipment & Supplies | 30 | 1.00 (0.65 - 1.54) | 0.95 (0.59 - 1.52) | 88 | 1.00 (0.77 - 1.30) | 0.91 (0.68 - 1.22) |
| 573 Industrial Machinery, Equipment and Supplies, Wholesale | 12 | *2.35 (1.11 - 4.99)* | *2.79 (1.21 - 6.45)* | 19 | 1.45 (0.83 - 2.53) | 1.44 (0.78 - 2.68) |
| J. Retail Trade Industries | 215 | 0.95 (0.80 - 1.12) | 0.97 (0.80 - 1.17) | 548 | 0.98 (0.87 - 1.10) | 0.99 (0.87 - 1.12) |
| 60 Food, Beverage & Drug | 59 | 1.12 (0.81 - 1.55) | 1.33 (0.93 - 1.92) | 147 | 0.99 (0.80 - 1.21) | 1.05 (0.84 - 1.32) |
| 601 Food Stores | 48 | 1.23 (0.85 - 1.77) | 1.50 (0.99 - 2.28) | 118 | 1.50 (0.99 - 2.28) | 1.07 (0.83 - 1.38) |
| 6011 Food (Groceries) Store | 33 | 1.17 (0.75 - 1.81) | *1.81 (1.08 - 3.04)* | 86 | 0.96 (0.74 - 1.25) | 1.08 (0.80 - 1.45) |
| 63 Automotive Vehicles, Parts & Accessories, Sales & Service | 79 | 1.02 (0.78 - 1.35) | 1.03 (0.76 - 1.41) | 236 | 1.07 (0.90 - 1.26) | 1.09 (0.90 - 1.31) |
| 635 Motor Vehicle Repair Shops | 46 | 1.17 (0.81 - 1.69) | 1.17 (0.78 - 1.78) | 122 | 1.09 (0.87 - 1.37) | 1.15 (0.90 - 1.49) |
| 6352 Paint and Body Repair Shops | 11 | *3.59 (1.39 - 9.24)* | *3.54 (1.20 - 10.50)* | 20 | 1.54 (0.87 - 2.73) | 1.66 (0.87 - 3.18) |
| 65 Other Retail Store | 18 | 0.64 (0.37 - 1.09) | 0.63 (0.35 - 1.13) | 79 | 0.84 (0.64 - 1.10) | 0.76 (0.56 - 1.03) |
| 652 Florists, Lawn & Garden Centres | 1 | - | - | 7 | 1.64 (0.63 - 4.28) | 1.56 (0.54 - 4.50) |
| 6522 Lawn and Garden Centres | 1 | - | - | 5 | 3.54 (0.89 - 14.10) | *8.40 (1.41 - 50.16)* |
| M. Business Service Industries | 48 | 0.92 (0.65 - 1.30) | 0.98 (0.67 - 1.43) | 144 | 1.03 (0.84 - 1.27) | 1.06 (0.84 - 1.34) |
| 77 Business Service | 48 | 0.92 (0.65 - 1.30) | 0.98 (0.67 - 1.43) | 144 | 1.03 (0.84 - 1.27) | 1.06 (0.84 - 1.34) |
| 772 Computer and Related Services | 3 | *8.05 (1.80 - 36.01)* | *7.47 (1.49 - 37.38)* | 3 | 1.44 (0.38 - 5.49) | 1.79 (0.41 - 7.70) |
| 774 Advertising Services | 6 | 2.15 (0.73 - 6.34) | 2.47 (0.71 - 8.58) | 15 | *2.44 (1.24 - 4.79)* | *2.55 (1.18 - 5.52)* |
| N. Government Service Industries | 271 | 1.04 (0.89 - 1.21) | 0.94 (0.79 - 1.12) | 908 | 1.04 (0.94 - 1.16) | 1.03 (0.92 - 1.16) |
| 81 Federal Government Service | 191 | 1.04 (0.87 - 1.26) | 0.99 (0.81 - 1.21) | 817 | 1.05 (0.95 - 1.17) | 1.05 (0.93 - 1.18) |
| 811 Defence Services | 150 | 1.13 (0.92 - 1.39) | 1.06 (0.84 - 1.34) | 781 | *1.12 (1.00 - 1.24)* | 1.12 (0.99 - 1.26) |
| 83 Local Government Service | 40 | 1.00 (0.68 - 1.46) | 0.86 (0.57 - 1.30) | 77 | 0.84 (0.64 - 1.10) | 0.77 (0.57 - 1.04) |
| 836 Human Resource Administration | 7 | *3.13 (1.18 - 8.28)* | 2.62 (0.91 - 7.53) | 12 | 1.10 (0.55 - 2.19) | 1.23 (0.58 - 2.61) |
| R. Other Service Industries | 80 | 1.21 (0.91 - 1.60) | 1.24 (0.90 - 1.70) | 252 | 1.09 (0.93 - 1.28) | 1.09 (0.91 - 1.31) |
| 96 Amusement & Recreational Service | 18 | 1.31 (0.74 - 2.35) | 1.40 (0.72 - 2.71) | 78 | 1.16 (0.87 - 1.54) | 1.28 (0.92 - 1.77) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 962 Motion Picture Exhibition | 3 | 2.00 (0.48 - 8.33) | 1.50 (0.31 - 7.20) | 13 | *2.92 (1.41 - 6.02)* | *2.85 (1.25 - 6.49)* |
| 9621 Regular Motion Picture Theatres | 3 | 2.00 (0.48 - 8.33) | 1.50 (0.31 - 7.20) | 10 | *2.44 (1.11 - 5.36)* | 2.44 (1.00 - 5.94) |
| 97 Personal & Household Service | 24 | 1.11 (0.67 - 1.85) | 1.33 (0.75 - 2.37) | 70 | 1.26 (0.92 - 1.71) | 1.24 (0.87 - 1.75) |
| 971 Barber & Beauty Shops | 6 | 0.91 (0.36 - 2.31) | 1.02 (0.37 - 2.78) | 13 | 1.28 (0.65 - 2.53) | 1.39 (0.65 - 2.97) |
| 9713 Combination Barber and Beauty Shops | 2 | - | - | 3 | *6.72 (1.34 - 33.79)* | 5.85 (0.98 - 34.88) |
| 99 Other Service Industries | 27 | 1.48 (0.89 - 2.44) | 1.52 (0.84 - 2.76) | 81 | 0.99 (0.75 - 1.31) | 0.98 (0.72 - 1.34) |
| 994 Other Repair Services | 11 | *2.98 (1.30 - 6.82)* | *2.83 (1.10 - 7.30)* | 28 | 1.38 (0.86 - 2.23) | 1.30 (0.77 - 2.19) |
| 9942 Welding | 10 | *4.83 (1.82 - 12.81)* | *4.61 (1.46 - 14.58)* | 19 | 1.79 (1.00 - 3.22) | 1.69 (0.87 - 3.26) |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics ($p<0.05$).*

CSIC: Canadian Standard Industrial Classification, 1980; CI: Confidence interval;

N1=Number of exposed cases in the corresponding usual industry; N2=Number of cases exposed in the corresponding ever industry category.

*Control group 1= Basic control group after excluding unknown primary cancer subjects.

† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.

‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

Among the industries showing an elevated risk of lung cancer, the majority of the lung cancer cases were employed in the mining industry and in defense services. Most of the observed odds ratios ranged between 1.5 and 3.5, indicating a moderate to strong association with lung cancer; however, the larger odds ratios observed in some of the industries should be interpreted with caution due to few cases in those industry categories. An elevated risk of lung cancer was observed among workers in mining (including milling), quarrying & oil well industries (SIC Division-D; OR = 1.5) and its subgroups; an excess risk of lung cancer was seen predominantly among the workers in the mining industry (SIC-06; OR = 1.5) who were involved in the metal mining (SIC-061) of copper & copper-zinc metals (SIC-0612). Employment in the primary metal manufacturing industries (SIC-29; OR=1.4 and 1.8), including the subgroup, steel manufacturing industry (SIC-291) was associated with an increased risk of lung cancer. Workers in the other utility industries (SIC-49; OR≈1.7), including workers in the electric power systems industry (SIC-491), also showed an excess risk of lung cancer. The excess risk of lung cancer observed in other repair service workers (SIC-994; OR≈3) was predominantly seen in welders (SIC-9942; OR≈5). In the wholesale & retail trade industries, an elevated risk of lung cancer was observed among workers in the 'wholesale industrial machinery, equipment & supplies' industry (SIC-573; OR≈2.5), and 'motor vehicle paint & body repair shops' (SIC-6352; OR≈3.5).

While the above mentioned 'usual' industry of employment categories were significantly associated with lung cancer in the analyses based on both control groups, a total of 10 industry categories were associated with an elevated risk in only one of the control group analyses. Most of these industry categories were either subgroups of primary metal industries or certain wholesale industries (Table 22). The elevated risk of lung cancer observed in the 'apparel & dry goods wholesale' industry workers (SIC-53), and the workers in certain manufacturing industries including: aircraft (and parts) manufacturing (SIC-321), and aluminum production (SIC-2951) were noteworthy.

Overall, an excess risk of lung cancer was seen among workers in the mining industry, primary metal manufacturing industry, electric power systems industry, welding, and certain wholesale & retail trade industries.

We observed a reduced risk of lung cancer among workers usually employed in 'finance & insurance' industries (SIC-K), in the analyses with both control groups; the odds ratios (95% confidence intervals) with the control group 1 and control group 2 were 0.64 (0.43-0.96) and 0.61 (0.40-0.94), respectively. In the analysis based on control group 1, a decreased risk of lung cancer was observed among workers in 'fishing & trapping' industries (SIC B), including their subcategories: fishing industries (SIC 031), and salt water fishing industry (SIC 0311); the odds ratios were 0.55 (0.34-0.90), 0.54 (0.33-0.90), and 0.53 (0.32-0.90) for these three industries, respectively.

#### 4.5.1.2 Industries 'Ever' Worked

The significantly elevated odds ratio estimates for lung cancer and the associated 95% confidence intervals in relation to the industries 'ever' worked in are reported in Table 22. Our analysis on the 'ever' employed industrial groups was restricted to industries having at least 3 cases and 3 controls (61% of the total), which included 745 industries represented in 18 divisions, 73 major groups, 254 minor groups, and 400 classes. Moreover, one industry class with less than 3 controls was not evaluated in the analysis based on the second control group. In general, the concordance of results between the control groups 1 and 2 was good (96% agreement). Overall, 3% of the analyses (out of 7% total significant results) were significant in both two control groups with an elevated risk of lung cancer being observed among the workers in 18 industrial categories and a reduced risk of lung cancer among the workers in 4 industrial categories.

In general, the associations observed among the 'usual' industries of employment were reproduced in the analyses based on the industries 'ever' worked, either at the major group level, or at the other hierarchical levels of the industrial categories. Most of the significantly positive odds ratios ranged between 1.3 and 3.5, indicating a moderate to strong association with lung cancer. An increased risk of lung cancer among workers in the telecommunication equipment manufacturing (SIC-3351) and wholesale meat & meat product industries (SIC-5217) is noteworthy. This assessment was restricted to the analysis based on the industries 'ever' worked in, due to small number of lung cancer cases in 'usual' industry of employment. An excess risk of lung cancer was also seen among workers in certain fabricated metal product manufacturing industries, including other wire product industries (SIC-3059) and other metal fabricating industries not elsewhere classified (SIC-3099).

### 4.5.2 Squamous Cell Carcinoma of the Lung

#### 4.5.2.1 'Usual' Industry of Employment

The odds ratios and associated 95% confidence intervals in relation to the 'usual' industry of employment showing an excess risk of squamous cell lung cancer are reported in Table 23. There were a total of 1,052 usually employed industry categories (1,010 for control group 2 analyses), including: 18 divisions, 76 major groups, 296 minor groups, and 662 classes. We evaluated the risk of lung cancer for the industrial categories having at least 3 cases and 3 controls; which included 240 industries represented in 18 divisions, 51 major groups, 87 minor groups, and 84 classes.

**Table 23:** Industries with Significantly Elevated Risk of Squamous Cell Carcinoma of the Lung

| CSIC Code Industry Title | Industry (Usual) | | | Industry (Ever) | | |
|---|---|---|---|---|---|---|
| | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| D. Mining (Including Milling), Quarrying and Oil Well Industries | 29 | 1.27 (0.84 - 1.92) | 1.28 (0.82 - 2.00) | 130 | *1.30 (1.06 - 1.60)* | *1.32 (1.05 - 1.65)* |
| 06 Mining Industries | 27 | 1.49 (0.97 - 2.31) | 1.51 (0.94 - 2.43) | 118 | *1.37 (1.10 - 1.70)* | *1.40 (1.11 - 1.78)* |
| 061 Metal Mines | 25 | *1.91 (1.21 - 3.03)* | *2.00 (1.20 - 3.32)* | 88 | *1.32 (1.04 - 1.69)* | *1.32 (1.01 - 1.71)* |
| 0612 Copper and Copper-Zinc Mines | 7 | *3.24 (1.31 - 8.02)* | *3.52 (1.29 - 9.61)* | 35 | 1.46 (0.99 - 2.13) | *1.52 (1.01 - 2.31)* |
| 0619 Other Metal Mines | 5 | 2.65 (0.92 - 7.64) | *5.06 (1.43 - 17.84)* | 13 | 1.67 (0.91 - 3.09) | *2.23 (1.13 - 4.41)* |
| 062 Non-Metal Mines (Except Coal) | 1 | - | - | 6 | 1.51 (0.61 - 3.75) | 1.94 (0.68 - 5.51) |
| 0621 Asbestos Mines | 0 | - | - | 3 | 1.65 (0.46 - 5.90) | *5.91 (1.12 - 31.11)* |
| E. Manufacturing Industries | 195 | 1.03 (0.87 - 1.23) | 1.05 (0.87 - 1.26) | 464 | 1.07 (0.93 - 1.23) | 1.06 (0.92 - 1.24) |
| 10 Food Industries | 14 | 0.68 (0.39 - 1.20) | 0.65 (0.36 - 1.19) | 66 | 0.92 (0.70 - 1.21) | 0.90 (0.67 - 1.20) |
| 103 Fruit and Vegetable Industries | 2 | - | - | 13 | *2.03 (1.07 - 3.86)* | 1.77 (0.89 - 3.52) |
| 1032 Frozen Fruit and Vegetable Industry | 1 | - | - | 4 | *8.72 (2.41 - 31.53)* | *7.70 (2.00 - 9.64)* |
| 11 Beverage Industries | 4 | 1.12 (0.37 - 3.39) | 0.89 (0.27 - 2.99) | 14 | 1.40 (0.77 - 2.53) | 1.33 (0.70 - 2.52) |
| 112 Distillery Products Industry | 0 | - | - | 6 | *3.33 (1.24 - 8.94)* | *5.29 (1.69 - 16.55)* |
| 26 Furniture & Fixture Industries | 4 | 1.06 (0.36 - 3.13) | 0.94 (0.30 - 3.00) | 16 | 1.51 (0.86 - 2.62) | *1.83 (1.00 - 3.32)* |
| 261 Household Furniture | 3 | 0.87 (0.25 - 2.99) | 0.80 (0.22 - 2.95) | 13 | 1.41 (0.77 - 2.59) | 1.75 (0.91 - 3.37) |
| 2619 Other Household Furniture Industries | - | - | - | 3 | 4.22 (0.97 - 18.34) | *13.00 (1.98 - 85.47)* |
| 291 Primary Steel Industries | 3 | 1.99 (0.53 - 7.46) | 2.62 (0.59 - 11.69) | 16 | *2.10 (1.18 - 3.72)* | *2.80 (1.48 - 5.30)* |
| 2919 Other Primary Steel Industries | 2 | - | - | 12 | *3.08 (1.53 - 6.21)* | *4.28 (1.91 - 9.62)* |
| 32 Transportation Equipment | 23 | 1.50 (0.94 - 2.38) | 1.62 (0.98 - 2.67) | 111 | 1.15 (0.92 - 1.43) | 1.18 (0.93 - 1.49) |
| 321 Aircraft and Aircraft Parts Industry | 5 | *3.40 (1.17 - 9.90)* | *3.27 (1.04 - 10.30)* | 22 | 1.22 (0.76 - 1.94) | 1.25 (0.76 - 2.07) |
| 328 Boatbuilding and Repair Industries | 3 | 3.96 (1.00 - 15.72) | 4.24 (0.96 -18.74) | 9 | *2.37 (1.09 - 5.14)* | 2.33 (0.99 - 5.44) |
| 33 Electrical & Electronic Products | 3 | 0.70 (0.21 - 2.30) | 0.66 (0.20 - 2.25) | 11 | 0.86 (0.46 - 1.63) | 0.83 (0.43 - 1.62) |
| 335 Communications & Other electronic Equipment | 1 | - | - | 6 | 1.73 (0.70 - 4.25) | 1.45 (0.56 - 3.74) |
| 3351 Telecommunication Equipment Industry | 1 | - | - | 5 | *5.95 (1.87 - 18.98)* | *5.24 (1.50 - 18.28)* |
| 36 Refined Petroleum and Coal Products Industries | 9 | *3.03 (1.37 - 6.68)* | *2.57 (1.13 - 5.87)* | 14 | 1.35 (0.75 - 2.45) | 1.34 (0.72 - 2.51) |
| 361 Refined Petroleum Products Industries | 9 | *3.03 (1.37 - 6.68)* | *2.57 (1.13 - 5.87)* | 14 | 1.35 (0.75 - 2.45) | 1.34 (0.72 - 2.51) |
| 3611 Refined Petroleum Prod (Except Lubricating Oil & Grease) | 9 | *3.03 (1.37 - 6.68)* | *2.57 (1.13 - 5.87)* | 14 | 1.35 (0.75 - 2.45) | 1.34 (0.72 - 2.51) |
| F. Construction Industries | 124 | 1.14 (0.92 - 1.41) | *1.26 (1.01 - 1.59)* | 289 | *1.18 (1.01 - 1.38)* | *1.26 (1.07 - 1.49)* |
| 40 Building, Developing & General Contracting | 46 | 1.10 (0.79 - 1.53) | 1.13 (0.80 - 1.61) | 131 | 1.06 (0.86 - 1.30) | 1.05 (0.84 - 1.31) |
| 401 Residential Building & Development | 6 | 0.97 (0.41 - 2.32) | 1.04 (0.41 - 2.61) | 30 | 1.26 (0.84 - 1.89) | 1.37 (0.89 - 2.10) |
| 4013 Residential Renovation | 3 | 4.40 (0.99 - 19.66) | *5.98 (1.01 - 35.63)* | 7 | 2.19 (0.92 - 5.22) | 2.22 (0.86 - 5.74) |
| 402 Non-Residential Building & Development | 1 | - | - | 7 | 0.90 (0.40 - 2.02) | 0.89 (0.38 - 2.09) |
| 4023 Institutional Building | 0 | - | - | 4 | *3.54 (1.04 -12.07)* | *4.24 (1.05 - 17.03)* |
| 42 Trade Contracting Industries | 56 | 1.15 (0.85 - 1.56) | 1.34 (0.96 - 1.85) | 126 | 1.20 (0.98 - 1.49) | *1.36 (1.08 - 1.71)* |
| 422 Structural & Related Work | 7 | 1.14 (0.50 - 2.60) | 1.44 (0.59 - 3.54) | 23 | 1.35 (0.85 - 2.15) | 1.51 (0.91 - 2.51) |
| 4222 Form Work | 0 | - | - | 3 | *7.57 (1.69 - 33.96)* | *8.08 (1.48 - 44.25)* |
| 427 Interior and Finishing Work | 15 | 0.98 (0.56 - 1.72) | 1.27 (0.68 - 2.37) | 34 | 1.13 (0.77 - 1.66) | *1.54 (1.01 - 2.34)* |
| 4274 Finish Carpentry | 4 | 2.71 (0.84 - 8.79) | *5.50 (1.64 - 18.43)* | 8 | 1.28 (0.59 - 2.79) | *2.53 (1.10 - 5.85)* |
| 429 Other Trade Work | 2 | - | - | 5 | 2.22 (0.79 - 6.25) | 2.35 (0.75 - 7.36) |
| 4299 Other Interior and Finishing Work | 2 | - | - | 3 | *9.85 (1.63 - 59.67)* | *11.68 (1.26 - 108.07)* |
| G. Transportation & Storage | 98 | 0.98 (0.78 - 1.23) | 0.94 (0.74 - 1.20) | 257 | 1.11 (0.94 - 1.30) | 1.06 (0.90 - 1.26) |
| 45 Transportation | 92 | 0.96 (0.76 - 1.21) | 0.92 (0.72 - 1.19) | 247 | 1.10 (0.94 - 1.29) | 1.06 (0.90 - 1.26) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 454 Water Transport Industries | 18 | 1.67 (0.98 - 2.83) | *1.84 (1.03 - 3.29)* | 54 | *1.41 (1.04 - 1.92)* | *1.50 (1.07 - 2.10)* |
| 4541 Freight and Passenger Water Transport Industry | 12 | *2.19 (1.12 - 4.27)* | *2.43 (1.16 - 5.10)* | 43 | *1.52 (1.08 - 2.15)* | *1.60 (1.10 - 2.33)* |
| H. Communication & Other Utility | 36 | 1.05 (0.73 - 1.51) | 1.03 (0.70 - 1.52) | 73 | 1.08 (0.83 - 1.41) | 1.05 (0.80 - 1.39) |
| 49 Other Utility Industries | 24 | 1.52 (0.96 - 2.42) | 1.60 (0.96 - 2.65) | 43 | *1.42 (1.00 - 2.00)* | 1.44 (0.99 - 2.09) |
| 491 Electric Power Systems Industry | 17 | *2.03 (1.15 - 3.57)* | *2.09 (1.12 - 3.89)* | 26 | 1.50 (0.96 - 2.33) | 1.49 (0.93 - 2.40) |
| I. Wholesale Trade | 42 | 0.83 (0.60 - 1.17) | 0.83 (0.58 - 1.19) | 126 | 1.01 (0.82 - 1.24) | 1.01 (0.82 - 1.26) |
| 57 Machinery, Equipment & Supplies | 12 | 1.17 (0.63 - 2.18) | 1.06 (0.55 - 2.03) | 28 | 0.96 (0.64 - 1.44) | 0.88 (0.57 - 1.34) |
| 572 Construction, Forestry & Mining Machinery, Equip & Supplies | 4 | 2.53 (0.80 - 8.06) | 2.67 (0.71 - 10.07) | 7 | 1.44 (0.62 - 3.34) | 1.55 (0.62 - 3.83) |
| 5721 Construction and Forestry Machinery, Equip & Supplies | 5 | *4.52 (1.48 - 13.81)* | *5.05 (1.41 - 18.16)* | 6 | 1.57 (0.63 - 3.92) | 2.01 (0.75 - 5.38) |
| 59 Other Products | 7 | 1.00 (0.44 - 2.26) | 0.84 (0.36 - 1.99) | 26 | 1.14 (0.74 - 1.75) | 1.12 (0.71 - 1.77) |
| 594 Toys, Amusement and Sporting Goods, Wholesale | 0 | - | - | 3 | *4.71 (1.02 - 21.84)* | 4.72 (0.74 - 30.20) |
| J. Retail Trade Industries | 78 | 0.99 (0.77 - 1.27) | 1.02 (0.78 - 1.33) | 185 | 0.94 (0.79 - 1.12) | 0.96 (0.80 - 1.16) |
| 61 Shoe, Apparel, Fabric & Yarn | 6 | 1.78 (0.71 - 4.48) | 1.70 (0.64 - 4.53) | 12 | 1.11 (0.60 - 2.07) | 1.11 (0.58 - 2.12) |
| 614 Clothing Stores n.e.c. | 1 | - | - | 3 | 3.49 (0.91 - 13.35) | *5.84 (1.26 - 27.03)* |
| M. Business Service Industries | 10 | 0.56 (0.29 - 1.09) | 0.59 (0.30 - 1.16) | 46 | 0.96 (0.69 - 1.33) | 0.98 (0.70 - 1.39) |
| 77 Business Service Industries | 10 | 0.56 (0.29 - 1.09) | 0.59 (0.30 - 1.16) | 46 | 0.96 (0.69 - 1.33) | 0.98 (0.70 - 1.39) |
| 774 Advertising Services | 2 | - | - | 7 | *2.97 (1.23 - 7.15)* | *3.05 (1.18 - 7.91)* |
| N. Government Service Industries | 95 | 1.05 (0.83 - 1.33) | 0.96 (0.75 - 1.23) | 332 | 1.09 (0.93 - 1.27) | 1.05 (0.90 - 1.24) |
| 82 Provincial & Territorial Government Service | 15 | 1.16 (0.66 - 2.02) | 1.01 (0.56 - 1.82) | 37 | 1.13 (0.78 - 1.62) | 1.03 (0.70 - 1.50) |
| 826 Human Resource Administration | 5 | *2.76 (1.01 - 7.54)* | 1.96 (0.70 - 5.50) | 11 | *2.48 (1.23 - 4.99)* | *2.38 (1.12 - 5.06)* |
| 83 Local Government Service | 14 | 1.09 (0.61 - 1.92) | 0.93 (0.52 - 1.69) | 28 | 0.89 (0.59 - 1.34) | 0.83 (0.54 - 1.27) |
| 836 Human Resource Administration | 5 | *7.08 (2.30 - 21.74)* | *5.82 (1.75 -19.30)* | 8 | 2.10 (0.94 - 4.70) | *2.52 (1.06 - 5.98)* |
| 8364 Recreation and Culture Administration | 3 | *7.53 (1.73 - 32.69)* | *7.18 (1.37 - 37.78)* | 5 | 1.40 (0.52 - 3.78) | 1.80 (0.62 - 5.28) |
| Q. Accommodation, Food & Beverage Service Industries | 24 | 1.15 (0.73 - 1.80) | 1.30 (0.79 - 2.13) | 77 | 0.96 (0.74 - 1.24) | 1.04 (0.79 - 1.36) |
| 92 Food and Beverage Service Industries | 15 | 1.65 (0.91 - 2.98) | *2.00 (1.03 - 3.88)* | 37 | 1.03 (0.72 - 1.49) | 1.22 (0.82 - 1.82) |
| R. Other Services Industries | 22 | 0.94 (0.60 - 1.49) | 0.95 (0.58 - 1.56) | 91 | 1.15 (0.90 - 1.46) | 1.14 (0.88 - 1.47) |
| 96 Amusement & Recreational Service | 5 | 0.85 (0.33 - 2.23) | 0.78 (0.28 - 2.19) | 31 | 1.27 (0.85 - 1.90) | 1.35 (0.87 - 2.10) |
| 962 Motion Picture Exhibition | 1 | - | - | 7 | *4.43 (1.79 - 10.94)* | *4.25 (1.57 - 11.50)* |
| 9621 Regular Motion Picture Theatres | 1 | - | - | 6 | *4.21 (1.63 - 10.90)* | *4.17 (1.47 - 11.86)* |
| 969 Other Amusement & Recreational Services | 2 | - | - | 11 | 1.55 (0.79 - 3.05) | 1.43 (0.69 - 2.99) |
| 9699 Other Amusement and Recreational Services n.e.c. | 1 | - | - | 6 | *3.01 (1.12 - 8.08)* | 3.12 (0.99 - 9.81) |
| 97 Personal & Household Service | 9 | 1.16 (0.56 - 2.40) | 1.46 (0.65 - 3.24) | 27 | 1.45 (0.94 - 2.23) | 1.44 (0.90 - 2.30) |
| 971 Barber & Beauty Shops | 3 | 1.16 (0.33 - 4.03) | 1.34 (0.36 - 5.02) | 6 | 1.72 (0.69 - 4.25) | 1.96 (0.74 - 5.21) |
| 9713 Combination Barber and Beauty Shops | 2 | - | - | 3 | *20.17 (3.83 -106.26)* | *17.12 (2.75 - 106.61)* |
| 973 Funeral Services | 2 | - | - | 6 | *2.79 (1.08 - 7.17)* | *3.28 (1.14 - 9.40)* |
| 9732 Cemeteries and Crematoria | 0 | - | - | 3 | 3.54 (0.88 - 14.28) | *6.26 (1.08 - 36.31)* |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics (p<0.05).*
CSIC: Canadian Standard Industrial Classification, 1980; CI: Confidence interval;
N1=Number of exposed cases in the corresponding usual industry; N2=Number of cases exposed in the corresponding ever industry category.
*Control group 1= Basic control group after excluding unknown primary cancer subjects.
† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.
‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

In addition, 2 industrial categories with less than 3 controls were not evaluated in the analysis with the second control group. Overall concordance of the results obtained from both the control groups is good (97% agreement). Overall, 5% of the analyses (out of 8% total significant results) were significant in both two control groups with an elevated risk of squamous cell lung cancer being observed among the workers in 11 industries and a reduced risk of squamous cell lung cancer among the workers in 2 industries.

Among industries showing an increased risk of squamous cell lung cancer, the majority of the lung cancer cases were employed in the construction and mining industries. Most of the observed odds ratios ranged between 2.0 and 3.5, indicating a moderate to strong association with squamous cell lung cancer; however, the larger odds ratios observed in some of the industries should be interpreted with caution due to the small number of cases in those industry categories. The elevated risk of squamous cell lung cancer among workers in the 'refined petroleum & coal products' industries (SIC-36; OR≈3), and its subgroup, refined petroleum products industries (SIC-361), especially in the industries not involved in the refining of lubricating oil & grease (SIC-3611), was unique to squamous cell carcinoma – this relationship was not observed in the analysis of all types of lung cancer combined. The excess risk of lung cancer among workers in freight & passenger water transport industries (SIC-4541; OR≈2) was also noteworthy. In agreement with the results from all the types of lung cancer, an elevated risk of squamous cell lung cancer was seen among workers in certain metal mines (SIC-061; 0612), aircraft (and parts) manufacturing (SIC-321), and electric power systems industries (SIC-491).

While the above mentioned usually employed industrial categories were significantly associated with lung cancer in the analyses with both the control groups, a total of 6 industry categories were associated with an elevated risk in only one of the control group analyses. The elevated risk of lung cancer observed among workers in the construction industries (SIC Division-F), including the workers involved in residential renovation (SIC-4013) and finish carpentry (SIC-4274), were noteworthy. Employment in the major industry group involving food and beverage services (SIC-92; OR=2) was also associated with an increased risk of squamous cell lung cancer.

Overall, an excess risk of squamous cell lung cancer was seen among workers employed in petroleum refining, construction, government services (i.e., human resource administration), mining, aircraft manufacturing, electric power systems, and food service industries.

The significantly reduced risk ($p<0.05$) of squamous cell lung cancer among workers in 'other retail store' industries (SIC-65) was noteworthy; odds ratios (95% confidence intervals) with control group 1 and control group 2 were 0.29 (0.09-0.92) and 0.28 (0.09-0.94), respectively.

#### 4.5.2.2 Industries 'Ever' Worked

The significantly elevated odds ratio estimates for squamous cell lung cancer and the associated 95% confidence intervals in relation to the industries 'ever' worked in are reported in Table 23. Our analysis of the squamous cell lung cancer was restricted to the industries (ever worked) having at least 3 cases and 3 controls (39% of the total), which included: 474 industries represented in 18 divisions, 65 major groups, 165 minor groups, and 226 classes. In general, the concordance of the results between the control groups 1 and 2 was good (96% agreement). Overall, 4% of the analyses (out of 8% total significant results) were significant in both two control groups with an elevated risk of squamous cell lung cancer being observed among the workers in 20 industries and a reduced risk of squamous cell lung cancer among the workers in 2 industries.

Among the industrial categories showing a significant excess risk of squamous cell lung cancer, most of the odds ratios ranged between 1.5 and 5.0, indicating a moderate to strong association with squamous cell lung cancer. In general, the associations observed in the analysis of 'usual' industrial categories of employment were reproduced in this analysis, either at the major group level or at the other hierarchical levels of the industrial categories. The excess risk of lung cancer among workers in the fruit & vegetable industries (SIC-103, 1032), distillery products manufacturing (SIC-112), primary steel manufacturing (SIC-291, 2919), and certain service industries including, motion picture exhibition (SIC-962), especially workers in the movie theatres (SIC-9621) was noteworthy. Elevated risk of squamous cell lung cancer was also suggested for workers in the advertising (SIC-774), and funeral services (SIC-973). The majority of these assessments were restricted in the analyses of 'usual' industry of employment due to few cases.

### 4.5.3 Adenocarcinoma of the Lung

#### 4.5.3.1 'Usual' Industry of employment

The odds ratios and associated 95% confidence intervals in relation to the 'usual' industry of employment showing an excess risk of adenocarcinoma of the lung are reported in Table 24. There were a total of 1,052 usually employed industrial categories (1,014 for control group 2 analyses), including: 18 divisions, 76 major groups, 295 minor groups, and 663 classes.

**Table 24:** Industries with Significantly Elevated Risk of Adenocarcinoma of the Lung

| | Industry (Usual) | | | Industry (Ever) | | |
|---|---|---|---|---|---|---|
| **CSIC Code Industry Title** | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| D. Mining (Including Milling), Quarrying and Oil Well | 27 | 1.46 (0.96 - 2.23) | 1.43 (0.91 - 2.26) | 90 | 1.08 (0.85 - 1.36) | 1.09 (0.85 - 1.40) |
| 06 Mining Industries | 24 | *1.62 (1.03 - 2.55)* | 1.56 (0.96 - 2.56) | 78 | 1.10 (0.85 - 1.42) | 1.13 (0.86 - 1.48) |
| 061 Metal Mines | 20 | *1.78 (1.08 - 2.92)* | *1.79 (1.05 - 3.08)* | 62 | 1.15 (0.87 - 1.52) | 1.15 (0.86 - 1.56) |
| 0612 Copper and Copper-Zinc Mines | 6 | *2.79 (1.09 - 7.16)* | 2.59 (0.91 - 7.40) | 23 | 1.17 (0.74 - 1.83) | 1.22 (0.75 - 1.98) |
| 0616 Uranium Mines | 1 | - | - | 7 | 2.13 (0.91 - 4.98) | *2.88 (1.10 - 7.56)* |
| 062 Non-Metal Mines (Except Coal) | 3 | *6.07 (1.01 -36.32)* | 4.73 (0.56 - 39.72) | 6 | 1.31 (0.53 - 3.25) | 1.32 (0.47 - 3.73) |
| 0622 Peat Industry | 2 | - | - | 3 | *4.74 (1.01 - 22.26)* | 3.64 (0.68 - 19.56) |
| E. Manufacturing Industries | 168 | 0.98 (0.82 - 1.18) | 1.01 (0.83 - 1.22) | 382 | 0.96 (0.83 - 1.11) | 0.96 (0.82 - 1.12) |
| 10 Food Industries | 14 | 0.82 (0.47 - 1.45) | 0.79 (0.43 - 1.44) | 54 | 0.86 (0.63 - 1.15) | 0.84 (0.61 - 1.15) |
| 102 Fish Products Industry | 4 | 2.95 (0.89 - 9.84) | 3.44 (0.90 - 13.09) | 11 | 1.50 (0.76 - 2.93) | 1.52 (0.72 - 3.19) |
| 29 Primary Metal Industries | 16 | 1.16 (0.68 - 1.99) | 1.47 (0.82 - 2.64) | 41 | 0.94 (0.67 - 1.32) | 1.03 (0.71 - 1.49) |
| 291 Primary Steel Industries | 3 | 1.60 (0.43 - 6.01) | 2.70 (0.62 - 11.67) | 13 | 1.68 (0.90 - 3.12) | *2.07 (1.05 - 4.10)* |
| 30 Fabricated Metal Prod (Except Machinery & Transport) | 15 | 1.25 (0.71 - 2.20) | 1.09 (0.59 - 2.00) | 52 | 1.27 (0.94 - 1.73) | 1.23 (0.89 - 1.71) |
| 305 Wire and Wire Products Industries | 2 | - | - | 5 | 1.84 (0.68 - 5.01) | 1.20 (0.42 - 3.45) |
| 3059 Other Wire Products Industries | 0 | - | - | 3 | *7.09 (1.64 - 30.70)* | *11.23 (1.92 - 65.58)* |
| 306 Hardware, Tool and Cutlery Industries | 2 | - | - | 7 | 1.69 (0.73 - 3.90) | *2.55 (1.02 - 6.35)* |
| 309 Other Metal fabricating Industries | 4 | *4.80 (1.32 - 17.42)* | 3.64 (0.89 - 14.89) | 11 | *2.46 (1.22 - 4.96)* | *2.65 (1.22 - 5.78)* |
| 3099 Other Metal Fabricating Industries n.e.c. | 4 | *5.07 (1.37 - 18.74)* | 3.91 (0.93 - 16.48) | 10 | *2.57 (1.22 - 5.42)* | *2.59 (1.13 - 5.92)* |
| 31 Machinery Industries (Except Electrical Machinery) | 8 | 1.90 (0.87 - 4.18) | *2.37 (1.02 - 5.48)* | 19 | 1.35 (0.82 - 2.22) | 1.66 (0.99 - 2.81) |
| 319 Other Machinery and Equipment Industries | 8 | 2.05 (0.92 - 4.54) | *2.55 (1.09 - 5.96)* | 19 | 1.60 (0.97 - 2.66) | *2.05 (1.20 - 3.51)* |
| 3199 Other Machinery and Equipment Industries n.e.c. | 3 | 3.11 (0.84 - 11.47) | 2.34 (0.60 - 9.22) | 10 | 1.72 (0.85 - 3.46) | 2.08 (0.99 - 4.38) |
| 32 Transportation Equipment | 17 | 1.20 (0.71 - 2.03) | 1.17 (0.67 - 2.04) | 78 | 0.95 (0.74 - 1.22) | 0.98 (0.75 - 1.27) |
| 326 Railroad Rolling Stock Industry | 1 | - | - | 4 | *5.86 (1.65 -20.75)* | *4.71 (1.21 - 18.33)* |
| 33 Electrical & Electronic Products | 5 | 1.08 (0.42 - 2.83) | 0.95 (0.34 - 2.60) | 18 | 1.50 (0.89 - 2.53) | 1.36 (0.77 - 2.37) |
| 334 Record Player, Radio and Television Receiver | 0 | - | - | 3 | *5.56 (1.42 - 21.68)* | *4.79 (1.11 - 20.64)* |
| 335 Communications & Other electronic Equipment | 3 | 2.16 (0.62 - 7.53) | 1.56 (0.43 - 5.73) | 6 | 1.81 (0.73 - 4.51) | 1.37 (0.51 - 3.64) |
| 3351 Telecommunication Equipment Industry | 3 | *6.82 (1.64 - 28.38)* | *4.53 (1.02 - 20.15)* | 3 | *4.42 (1.18 - 16.58)* | 3.41 (0.85 - 13.65) |
| 37 Chemical & Chemical Products | 9 | 1.75 (0.84 - 3.67) | 1.62 (0.74 - 3.56) | 19 | 1.24 (0.75 - 2.03) | 1.18 (0.70 - 1.99) |
| 375 Paint and Varnish Industry | 4 | *6.48 (1.78 - 23.50)* | *4.86 (1.24 - 19.06)* | 5 | *3.46 (1.23 - 9.70)* | 2.68 (0.92 - 7.83) |
| F. Construction Industries | 106 | 1.12 (0.89 - 1.40) | 1.22 (0.96 - 1.56) | 213 | 0.93 (0.78 - 1.10) | 0.98 (0.82 - 1.18) |
| 42 Trade Contracting | 41 | 0.94 (0.67 - 1.33) | 1.08 (0.75 - 1.56) | 90 | 0.92 (0.73 - 1.17) | 1.05 (0.81 - 1.35) |
| 423 Exterior Close-In Work | 10 | 1.80 (0.87 - 3.70) | 1.88 (0.85 - 4.16) | 14 | 1.06 (0.59 - 1.90) | 1.05 (0.56 - 1.97) |
| 4234 Insulation Work | 3 | *5.05 (1.18 - 21.70)* | *5.25 (1.06 - 26.00)* | 4 | *3.77 (1.15 - 12.32)* | *4.01 (1.09 - 14.85)* |
| I. Wholesale Trade | 43 | 0.96 (0.69 - 1.34) | 0.95 (0.67 - 1.36) | 131 | 1.18 (0.96 - 1.44) | 1.19 (0.96 - 1.49) |
| 52 Food, Beverage, Drug & Tobacco | 9 | 1.32 (0.63 - 2.77) | 1.03 (0.45 - 2.32) | 24 | 1.08 (0.69 - 1.68) | 1.08 (0.67 - 1.75) |
| 521 Food | 7 | 1.25 (0.54 - 2.94) | 0.97 (0.37 - 2.52) | 18 | 0.97 (0.58 - 1.61) | 0.96 (0.55 - 1.67) |
| 5211 Confectionery Wholesale | 2 | - | - | 4 | 2.91 (0.90 - 9.37) | *4.57 (1.24 - 16.80)* |
| 53 Apparel and Dry Goods Industries, Wholesale | 3 | 3.24 (0.79 - 13.27) | *7.08 (1.19 - 42.17)* | 6 | 1.68 (0.67 - 4.17) | *3.03 (1.13 - 8.13)* |
| 56 Metal, Hardware, Plumbing, Heating &Building Material | 10 | 0.94 (0.47 - 1.89) | 1.14 (0.55 - 2.37) | 31 | 1.23 (0.83 - 1.83) | 1.28 (0.84 - 1.95) |
| 562 Hardware & Plumbing,Heating & AC Equip Supplies | 5 | 1.83 (0.64 - 5.23) | *4.40 (1.32 - 14.69)* | 14 | *2.07 (1.12 - 3.83)* | *2.67 (1.38 - 5.18)* |
| 5621 Hardware, Wholesale | 3 | 1.73 (0.45 - 6.61) | *8.23 (1.33 - 51.06)* | 9 | 1.80 (0.85 - 3.82) | *2.35 (1.04 - 5.34)* |
| 5622 Plumbing Heating & AC Equipment & Supplies | 2 | - | - | 5 | 2.81 (0.97 - 8.14) | *3.38 (1.11 - 10.32)* |

| | | | | | | |
|---|---|---|---|---|---|---|
| 563 Lumber & Building Materials | 5 | 0.76 (0.29 - 1.98) | 0.67 (0.24 - 1.84) | 15 | 0.88 (0.51 - 1.54) | 0.78 (0.44 - 1.40) |
| 5632 Paint Glass and Wallpaper Wholesale | 1 | - | - | 5 | *3.56 (1.17 - 10.85)* | 3.03 (0.87 - 10.52) |
| 59 Other Products, Wholesale | 10 | 1.68 (0.83 - 3.41) | 1.33 (0.62 - 2.83) | 26 | 1.36 (0.89 - 2.09) | 1.37 (0.87 - 2.17) |
| 598 General Merchandise, Wholesale | 2 | - | - | 4 | *5.89 (1.77 - 19.64)* | *4.09 (1.14 - 14.67)* |
| J. Retail Trade Industries | 79 | 1.14 (0.88 - 1.46) | 1.17 (0.89 - 1.53) | 179 | 1.05 (0.88 - 1.26) | 1.07 (0.88 - 1.29) |
| 60 Food, Beverage & Drug | 22 | 1.33 (0.83 - 2.13) | 1.63 (0.99 - 2.70) | 47 | 1.02 (0.74 - 1.40) | 1.10 (0.78 - 1.55) |
| 601 Food Stores | 18 | 1.44 (0.85 - 2.43) | *1.79 (1.01 - 3.16)* | 36 | 0.95 (0.66 - 1.37) | 1.06 (0.72 - 1.56) |
| 6011 Food (Groceries) Store | 14 | 1.52 (0.83 - 2.78) | *2.36 (1.20 - 4.61)* | 30 | 1.07 (0.72 - 1.60) | 1.21 (0.79 - 1.86) |
| 61 Shoe, Apparel, Fabric & Yarn Industries | 5 | 1.60 (0.60 - 4.28) | 1.46 (0.53 - 4.01) | 9 | 0.92 (0.45 - 1.85) | 0.94 (0.45 - 1.94) |
| 612 Men's Clothing Stores | 5 | *4.67 (1.61 - 13.52)* | *3.44 (1.12 - 10.59)* | 8 | 2.05 (0.95 - 4.45) | 1.68 (0.74 - 3.79) |
| 63 Automotive Vehicles, Parts & Accessor, Sales &Service | 31 | 1.31 (0.88 - 1.95) | 1.29 (0.84 - 1.98) | 77 | 1.17 (0.90 - 1.51) | 1.20 (0.92 - 1.59) |
| 635 Motor Vehicle Repair Shops | 16 | 1.25 (0.72 - 2.17) | 1.18 (0.65 - 2.14) | 39 | 1.12 (0.79 - 1.59) | 1.16 (0.80 - 1.69) |
| 6352 Paint and Body Repair Shops | 5 | *4.45 (1.36 - 14.61)* | *4.13 (1.08 - 15.79)* | 6 | 1.38 (0.56 - 3.37) | 1.53 (0.58 - 4.01) |
| 65 Other Retail Store | 8 | 0.96 (0.46 - 2.01) | 0.97 (0.45 - 2.08) | 27 | 0.90 (0.59 - 1.36) | 0.78 (0.50 - 1.22) |
| 652 Florists, Lawn & Garden Centres | 1 | - | - | 3 | 2.02 (0.55 - 7.44) | 2.05 (0.53 - 7.90) |
| 6522 Lawn and Garden Centres | 1 | - | - | 3 | *5.31 (1.13 - 25.00)* | *10.43 (1.56 - 69.68)* |
| M. Business Service Industries | 21 | 1.12 (0.69 - 1.80) | 1.21 (0.73 - 2.01) | 58 | 1.19 (0.88 - 1.60) | 1.22 (0.89 - 1.68) |
| 77 Business Service | 21 | 1.12 (0.69 - 1.80) | 1.21 (0.73 - 2.01) | 58 | 1.19 (0.88 - 1.60) | 1.22 (0.89 - 1.68) |
| 773 Accounting & Bookkeeping Services | 5 | 1.30 (0.49 - 3.46) | 1.32 (0.48 - 3.66) | 10 | 1.03 (0.52 - 2.06) | 1.26 (0.61 - 2.57) |
| 7739 Other Accounting & Bookkeeping Services | 4 | *5.07 (1.40 - 18.46)* | *4.80 (1.12 - 20.53)* | 6 | 2.20 (0.83 - 5.83) | 2.65 (0.91 - 7.67) |
| 774 Advertising Services | 3 | 3.59 (0.96 -13.44) | *4.41 (1.03 - 18.85)* | 7 | *3.37 (1.41 - 8.03)* | *3.56 (1.37 - 9.25)* |
| N. Government Service Industries | 94 | 1.13 (0.89 - 1.43) | 1.03 (0.81 - 1.33) | 290 | 1.10 (0.94 - 1.30) | 1.10 (0.93 - 1.31) |
| 82 Provincial & Territorial Government Service | 14 | 1.08 (0.61 - 1.93) | 0.94 (0.52 - 1.72) | 42 | 1.32 (0.94 - 1.87) | 1.22 (0.85 - 1.75) |
| 826 Human Resource Administration | 2 | - | - | 6 | 1.15 (0.47 - 2.84) | 1.20 (0.46 - 3.12) |
| 8262 Social Service Administration | 2 | - | - | 3 | *4.73 (1.10 - 20.39)* | 3.80 (0.76 - 18.99) |
| R. Other Service Industries | 26 | 1.31 (0.85 - 2.00) | 1.33 (0.84 - 2.09) | 69 | 0.98 (0.75 - 1.28) | 1.00 (0.76 - 1.33) |
| 99 Other Service Industries | 7 | 1.37 (0.61 - 3.09) | 1.33 (0.55 - 3.20) | 21 | 0.84 (0.52 - 1.33) | 0.84 (0.52 - 1.38) |
| 994 Other Repair Services | 3 | 2.45 (0.67 - 8.89) | 2.20 (0.54 - 9.02) | 7 | 0.97 (0.43 - 2.19) | 0.91 (0.39 - 2.13) |
| 9942 Welding | 3 | *4.83 (1.19 - 19.60)* | 4.22 (0.86 - 20.74) | 4 | 1.23 (0.43 - 3.52) | 1.12 (0.37 - 3.37) |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics ($p<0.05$).*

CSIC: Canadian Standard Industrial Classification, 1980; CI: Confidence interval;

N1=Number of exposed cases in the corresponding usual industry; N2=Number of cases exposed in the corresponding ever industry category.

*Control group 1= Basic control group after excluding unknown primary cancer subjects.

† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.

‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

We evaluated the risk of lung cancer for about 22% of these industrial groups having at least 3 cases and 3 controls, which included: 231 industries represented in 18 divisions, 49 major groups, 82 minor groups, and 82 classes. In addition, one industry category with less than 3 controls was not evaluated in the analysis with control group-2. In general, concordance of the results between the control groups 1 and 2 was good (92% agreement). Overall, 4% of the analyses (out of 12% total significant results) were significant in both two control groups with an elevated risk of adenocarcinoma of the lung being observed among the workers in 7 industries and a reduced risk of adenocarcinoma of the lung among the workers in 2 industries.

Among the industries showing a significantly elevated risk of adenocarcinoma of the lung, the majority of lung cancer cases were employed in the mining industries, and food stores; only a few cases are employed in other industries. The odds ratios ranged between 1.6 and 8.2, indicating a moderate to strong association with adenocarcinoma of lung. None of the industries were associated with lung cancer at the division level (SIC-alphabetical code). An elevated risk of lung cancer was observed among workers in metal mines (SIC-061; OR $\approx$1.8) and certain manufacturing industries, including: paint & varnish manufacturing (SIC-375) and telecommunication equipment manufacturing (SIC-3351). Among the workers in the retail trade industries, an excess risk of adenocarcinoma was observed in the men's clothing store workers (SIC-612) and motor vehicle paint & body repair shop workers (SIC-6352). For majority of these industries, a positive association was seen in the of all types of lung cancer combined.

While the above mentioned 'usual' industries of employment were significantly associated with adenocarcinoma in the analyses with both control groups, a total of 14 industrial categories were associated with an elevated risk in only one of the control group analyses. An excess risk of adenocarcinoma of the lung was observed for workers employed in the major industry categories involved in the manufacturing of 'machinery other than electrical products' (SIC-31; OR=2.4), and wholesale trade of 'apparel & dry goods' (SIC-53; OR=7.1). The elevated risk of lung cancer observed among the workers employed in the food stores (SIC-601) including, grocery stores (SIC-6011) was noteworthy.

Overall, an excess risk of adenocarcinoma of the lung was observed among workers in the metal mines, grocery stores, automobile body shops, insulators in construction, and certain industries involved in the manufacture of chemical products, machinery and telecommunication equipment.

A reduced risk of adenocarcinoma of the lung was observed in 2 'usual' industries of employment in the analysis with both two control groups. Specifically, the reduced risk of adenocarcinoma of the lung, observed in the agricultural & related service industries (SIC Division-A) was noteworthy; the odds ratios (95% confidence intervals) with control group 1 and control group 2 were 0.6 (0.4-0.9) and 0.56 (0.37-0.86), respectively.

**4.5.3.2 Industries 'Ever' Worked**

The significantly elevated odds ratio estimates for adenocarcinoma of the lung and the associated 95% confidence intervals in relation to the industries 'ever' worked in are reported in Table-24. Our analysis of adenocarcinoma of the lung was restricted to the industries ('ever' worked) having at least 3 cases and 3 controls (38% of the total industries), which included: 463 industries represented in 18 divisions, 68 major groups, 164 minor groups, and 213 classes. In general, the concordance of the results between the control groups 1 and 2 was good (96% agreement). Overall, 5% of the analyses (out of 9% total significant results) were significant in both two control groups with an elevated risk of adenocarcinoma of the lung being observed among the workers in 10 industrial categories and a reduced risk of adenocarcinoma of the lung among the workers in 9 industrial categories.

Among the industries showing an excess risk of adenocarcinoma of the lung, a moderate to strong association was observed in most of the industrial categories; the odds ratios ranged between 2 and 5. In general, the associations observed among the 'usual' industries of employment were reproduced in the analyses based on the industries 'ever' worked, either at the major group level, or at the other hierarchical levels of the industrial categories. The excess risk of adenocarcinoma of the lung among workers in certain transport equipment manufacturing industries, including railroad rolling stock industry (SIC-326), was noteworthy. Other noteworthy positive associations were observed for the workers employed in advertising services (SIC-774) and insulators in the construction industry (SIC-4234).

### 4.5.4 Small Cell Carcinoma of the Lung

#### 4.5.4.1 'Usual' industry of Employment

The odds ratios and associated 95% confidence intervals in relation to the 'usual' industry of employment showing an excess risk of small cell lung cancer are reported in Table 25. There were a total of 1,054 usually employed industrial categories (1,008 for control group 2 analyses), including: 18 divisions, 76 major groups, 295 minor groups, and 665 classes. We evaluated the risk of small cell lung cancer for about 15% of these industrial groups having at least 3 cases and 3 controls, which included: 154 industries represented in 18 divisions, 40 major groups, 51 minor groups, and 45 classes.

**Table 25**: Industries with Significantly Elevated Risk of Small Cell Carcinoma of the Lung

| | Industry (Usual) | | | Industry (Ever) | | |
|---|---|---|---|---|---|---|
| **CSIC Code Industry Title** | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| A. Agricultural & Related Service Industries | 30 | 1.27 (0.85 - 1.91) | 1.26 (0.82 - 1.93) | 127 | 1.07 (0.85 - 1.34) | 1.06 (0.84 - 1.35) |
| 01 Agricultural Industries | 29 | 1.27 (0.84 - 1.92) | 1.23 (0.80 - 1.90) | 124 | 1.04 (0.83 - 1.30) | 1.03 (0.81 - 1.32) |
| 013 Field Crop Farms | 1 | - | - | 24 | 1.05 (0.66 - 1.66) | 0.96 (0.59 - 1.57) |
| 0132 Small-Grain Farms (Except Wheat) | 0 | - | - | 5 | *2.85 (1.02 - 7.94)* | 2.67 (0.84 - 8.50) |
| 02 Service Industries Incidental to Agriculture | 1 | - | - | 7 | *3.38 (1.41 - 8.12)* | *4.68 (1.80 - 12.15)* |
| 022 Services Incidental to Agricultural Crops | 0 | - | - | 4 | *6.50 (2.03 - 20.86)* | *7.01 (1.90 - 25.89)* |
| D. Mining(Including Milling),Quarrying and Oil Well industries | 20 | *1.92 (1.16 - 3.16)* | *1.95 (1.13 - 3.36)* | 73 | *1.48 (1.12 - 1.95)* | *1.49 (1.10 - 2.01)* |
| 06 Mining Industries | 18 | *2.22 (1.31 - 3.79)* | *2.30 (1.28 - 4.15)* | 67 | *1.60 (1.20 - 2.13)* | *1.66 (1.21 - 2.26)* |
| 061 Metal Mines | 15 | *2.44 (1.35 - 4.38)* | *2.72 (1.41 - 5.27)* | 48 | *1.53 (1.10 - 2.13)* | *1.55 (1.08 - 2.22)* |
| 0612 Copper and Copper-Zinc Mines | 4 | *4.10 (1.30 - 12.93)* | *4.57 (1.29 -16.25)* | 18 | 1.57 (0.93 - 2.64) | 1.72 (0.98 - 3.04) |
| 0619 Other Metal Mines | 1 | - | - | 7 | 1.97 (0.87 - 4.46) | *3.43 (1.40 - 8.45)* |
| E. Manufacturing Industries | 93 | 0.87 (0.68 - 1.11) | 0.85 (0.66 - 1.11) | 236 | 0.98 (0.81 - 1.19) | 0.95 (0.77 - 1.17) |
| 19 Textile Products Industries | 0 | - | - | 5 | *3.33 (1.20 - 9.23)* | 2.07 (0.69 - 6.17) |
| 26 Furniture and Fixture Industries | 2 | - | - | 7 | 1.00 (0.44 - 2.31) | 1.38 (0.57 - 3.35) |
| 269 Other Furniture and Fixture Industries | 1 | - | - | 4 | *5.55 (1.65 - 18.63)* | *4.10 (1.13 - 14.84)* |
| 2691 Bed Spring and Mattress Industry | 1 | - | - | 3 | *12.61 (2.42 - 65.65)* | *8.83 (1.36 - 57.34)* |
| 291 Primary Steel Industries | 6 | *5.73 (1.92 - 17.09)* | *10.40 (3.07 - 35.26)* | 9 | 1.74 (0.80 - 3.76) | 2.37 (1.00 - 5.63) |
| 2919 Other Primary Steel Industries | 5 | *10.89 (2.92 - 40.72)* | *16.43 (3.21 -84.05)* | 8 | *3.09 (1.28 - 7.45)* | *4.33 (1.53 - 12.24)* |
| F. Construction Industries | 71 | 1.16 (0.88 - 1.54) | 1.34 (0.99 - 1.82) | 152 | 1.06 (0.86 - 1.31) | 1.11 (0.88 - 1.40) |
| 42 Trade Contracting Industries | 27 | 0.92 (0.60 - 1.41) | 1.13 (0.71 - 1.79) | 65 | 1.02 (0.77 - 1.37) | 1.15 (0.84 - 1.57) |
| 422 Structural & Related Work | 5 | 1.78 (0.67 - 4.71) | 2.38 (0.83 - 6.79) | 11 | 1.10 (0.57 - 2.13) | 1.19 (0.58 - 2.42) |
| 4224 Concrete Pouring and Finishing | 4 | *5.30 (1.56 - 17.97)* | *5.09 (1.37 - 18.90)* | 7 | *2.52 (1.03 - 6.18)* | 2.02 (0.74 - 5.49) |
| 426 Electrical Work | 6 | *3.66 (1.44 - 9.32)* | *4.03 (1.51 - 10.74)* | 12 | *2.09 (1.09 - 4.01)* | *2.73 (1.33 - 5.59)* |
| H. Communication & Other Utility | 22 | 1.11 (0.69 - 1.79) | 1.02 (0.61 - 1.70) | 39 | 1.02 (0.71 - 1.46) | 0.94 (0.64 - 1.38) |
| 49 Other Utility Industries | 15 | 1.66 (0.92 - 3.01) | 1.67 (0.87 - 3.21) | 27 | *1.60 (1.03 - 2.48)* | 1.51 (0.94 - 2.44) |
| 491 Electric Power Systems Industry | 10 | *2.16 (1.04 - 4.51)* | 2.04 (0.88 - 4.72) | 15 | 1.67 (0.94 - 2.99) | 1.54 (0.82 - 2.93) |
| I. Wholesale Trade | 31 | 1.19 (0.79 - 1.77) | 1.14 (0.74 - 1.76) | 65 | 0.96 (0.72 - 1.28) | 0.98 (0.72 - 1.32) |
| 52 Food, Beverage, Drug & Tobacco | 4 | 1.00 (0.33 - 2.98) | 0.70 (0.21 - 2.30) | 13 | 0.97 (0.53 - 1.77) | 0.93 (0.49 - 1.78) |
| 524 Tobacco Products, Wholesale | 1 | - | - | 3 | 3.55 (0.95 - 13.25) | *5.12 (1.20 - 21.86)* |
| 57 Machinery, Equipment & Supplies | 10 | 1.91 (0.95 - 3.85) | 1.71 (0.81 - 3.63) | 17 | 1.07 (0.63 - 1.82) | 0.98 (0.56 - 1.71) |
| 573 Industrial Machinery, Equipment and Supplies, Wholesale | 4 | *4.48 (1.40 - 14.32)* | *5.40 (1.51 -19.29)* | 4 | 1.65 (0.57 - 4.82) | 1.45 (0.47 - 4.49) |
| J. Retail Trade Industries | 29 | 0.69 (0.46 - 1.03) | 0.71 (0.46 - 1.09) | 90 | 0.87 (0.68 - 1.12) | 0.87 (0.67 - 1.13) |
| 63 Automotive Vehicles, Parts & Accessories, Sales & Service | 8 | 0.55 (0.26 - 1.16) | 0.53 (0.24 - 1.18) | 41 | 0.98 (0.69 - 1.39) | 1.00 (0.68 - 1.45) |
| 639 Other Motor Vehicle Services | 1 | - | - | 4 | *5.34 (1.48 -19.28)* | *8.86 (1.99 - 39.47)* |
| M. Business Service Industries | 7 | 0.81 (0.37 - 1.79) | 0.95 (0.42 - 2.15) | 24 | 0.95 ( 0.61 - 1.49) | 0.97 (0.60 - 1.55) |
| 77 Business Service | 7 | 0.81 (0.37 - 1.79) | 0.95 (0.42 - 2.15) | 24 | 0.95 ( 0.61 - 1.49) | 0.97 (0.60 - 1.55) |
| 773 Accounting & Bookkeeping Service | 4 | 2.51 (0.82 - 7.72) | 2.92 (0.90 - 9.40) | 6 | 1.14 (0.46 – 2.82) | 1.61 (0.62 - 4.22) |
| 7731 Offices of Chartered and Certified Accountants | 3 | 2.25 (0.62 - 8.25) | 2.86 (0.75 - 10.96) | 4 | 1.26 (0.43 - 3.72) | 1.81 (0.59 - 5.50) |
| R. Other Service Industries | 17 | 1.49 (0.87 - 2.55) | 1.46 (0.81 - 2.62) | 44 | 1.08 (0.77 - 1.52) | 1.06 (0.73 - 1.52) |
| 98 Membership Organization | 4 | 2.41 (0.80 - 7.27) | 2.14 (0.67 - 6.84) | 8 | 1.15 (0.54 - 2.45) | 0.98 (0.44 - 2.21) |
| 986 Civic and Fraternal Organizations | 3 | *12.81 (3.02 - 54.29)* | *11.62 (2.44 - 55.38)* | 4 | 1.62 (0.55 - 4.77) | 2.41 (0.73 - 7.93) |

| | | | | | | |
|---|---|---|---|---|---|---|
| 99 Other Service Industries | 8 | *2.73 (1.21 -6.17)* | 2.49 (0.99 - 6.29) | 17 | 1.14 (0.67 - 1.95) | 1.15 (0.65 - 2.04) |
| 994 Other Repair Services | 3 | *5.58 (1.43 - 21.70)* | *5.08 (1.10 - 23.41)* | 7 | 1.74 (0.73 - 4.13) | 1.81 (0.73 - 4.46) |
| 9942 Welding | 3 | *11.21 (2.43 - 51.80)* | *9.99 (1.70 - 58.88)* | 5 | 2.93 (1.10 - 7.84) | 2.76 (0.97 - 7.92) |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics (p<0.05).*
CSIC: Canadian Standard Industrial Classification, 1980; CI: Confidence interval;
N1=Number of exposed cases in the corresponding usual industry; N2=Number of cases exposed in the corresponding ever industry category.
*Control group 1= Basic control group after excluding unknown primary cancer subjects.
† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.
‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

In general, concordance of the results between both the control groups was good (98% agreement). Overall, 10% of the analyses (out of 12% total significant results) were significant in both two control groups with an elevated risk of small cell lung cancer being observed among the workers in 12 industrial categories. None of the industries were associated with a reduced risk of small cell lung cancer.

Among the industries showing a significantly elevated risk of small cell lung cancer, the majority of lung cancer cases were employed in the mining and certain utility industries. Most of the odds ratios for these industries ranged between 1.5 and 6.0, indicating a moderate to strong association with small cell lung cancer. An increased risk of small cell lung cancer was observed among workers in the mining (including milling), quarrying & oil well industries (SIC Division-D; OR = 2) and the subgroups; an excess risk of lung cancer was seen predominantly among workers in the mining industry (SIC-06; OR = 2.2) involved in metal mining (SIC-061) of copper and copper-zinc metals (SIC-0612). Although a similar relationship was observed in the analysis of all types of lung cancer combined, the point estimates were higher for small cell carcinoma. The excess risk of small cell lung cancer observed in the electrical workers (SIC-426) and the concrete pouring & finishing workers (SIC-4224) in the construction industry was noteworthy.

Overall, an increased risk of small cell lung cancer was observed among metal miners, primary steel manufacturing workers, and certain groups of construction workers (i.e., electrical workers, and concrete pouring & finishing workers).

#### 4.5.4.2 Industries 'Ever' Worked

The significantly elevated odds ratio estimates for small cell lung cancer and the associated 95% confidence intervals in relation to the industries 'ever' worked in are reported in Table 25. Our analysis of the small cell lung cancer was restricted to the industries ('ever' worked) having at least 3 cases and 3 controls (27% of the total), which included: 328 industries represented in 18 divisions, 61 major groups, 117 minor groups, and 132 classes. In general, the concordance of the results between the control groups 1 and 2 was good (96% agreement). Overall, 4% of the analyses (out of 8% total significant results) were significant in both two control groups with an elevated risk of small cell lung cancer being observed among the workers in 10 industrial categories and a reduced risk of small cell lung cancer among the workers in 2 industrial categories.

Among the industrial categories showing a significantly elevated odds ratio estimates, an excess risk of small cell lung cancer observed in the agricultural service industries (SIC-02, 022) and certain furniture industries (SIC-269, 2691) was noteworthy. These assessments were restricted to the analysis of industries 'ever' worked due to few cases of lung cancer in 'usual' industry of employment.

### 4.5.5 Large Cell Carcinoma of the Lung

#### 4.5.5.1 'Usual' industry of Employment

The odds ratios and associated 95% confidence intervals in relation to 'usual' industry of employment showing an excess risk of large cell lung cancer are reported in Table 26. There were a total of 1,048 usually employed industrial categories (1,000 for control group 2 analyses), including: 18 divisions, 76 major groups, 294 minor groups, and 660 classes.

**Table 26:** Industries with Significantly Elevated Risk of Large Cell Carcinoma of the Lung

| | | Industry (Usual) | | | Industry (Ever) | |
|---|---|---|---|---|---|---|
| **CSIC Code Industry Title** | N1 | CONTROL GROUP 1* OR‡ (95% CI) | CONTROL GROUP 2 † OR (95% CI) | N2 | CONTROL GROUP 1 OR (95% CI) | CONTROL GROUP 2 OR (95% CI) |
| A. Agricultural & Related Service Industries | 14 | 0.84 (0.47 - 1.50) | 0.78 (0.43 - 1.43) | 76 | 0.96 (0.72 - 1.27) | 0.96 (0.72 - 1.29) |
| 01 Agricultural Industries | 13 | 0.82 (0.45 - 1.48) | 0.75 (0.40 - 1.40) | 75 | 0.95 (0.71 - 1.26) | 0.95 (0.70 - 1.28) |
| 012 Other Animal Specialty Farms | 1 | - | - | 3 | *4.94 (1.40 - 17.36)* | *4.64 (1.23 - 17.51)* |
| D. Mining (Including Milling), Quarrying & Oil Well | 9 | 1.34 (0.66 - 2.71) | 1.31 (0.62 - 2.73) | 49 | *1.61 (1.16 - 2.24)* | *1.61 (1.13 - 2.30)* |
| 06 Mining Industries | 4 | 0.71 (0.25 - 1.97) | 0.69 (0.24 - 2.00) | 44 | *1.65 (1.17 - 2.34)* | *1.70 (1.17 - 2.47)* |
| 061 Metal Mines | 3 | 0.70 (0.22 - 2.30) | 0.71 (0.21 - 2.48) | 30 | 1.43 (0.95 - 2.15) | 1.40 (0.91 - 2.18) |
| 0619 Other Metal Mines | 1 | - | - | 6 | *2.43 (1.00 - 5.88)* | *3.26 (1.23 - 8.64)* |
| 063 Coal Mines | 1 | - | - | 14 | 1.79 (0.99 - 3.24) | *2.03 (1.08 - 3.80)* |
| 0631 Bituminous Coal Mines | 1 | - | - | 14 | 1.80 (1.00 - 3.25) | *2.04 (1.09 - 3.84)* |
| E. Manufacturing Industries | 77 | 1.25 (0.94 - 1.64) | 1.32 (0.98 - 1.77) | 152 | 1.01 (0.80 - 1.29) | 1.02 (0.79 - 1.31) |
| 25 Wood Industries | 17 | 0.73 (0.43 – 1.24) | 0.81 (0.46 - 1.41) | 52 | 0.88 (0.64 - 1.22) | 0.86 (0.61 - 1.21) |
| 256 Wooden Box and Pallet Industry | 0 | - | - | 4 | *3.91 (1.24 -12.32)* | *4.77 (1.28 - 17.75)* |
| 27 Paper & allied Products | 5 | 0.83 (0.33 - 2.06) | 0.99 (0.38 - 2.53) | 18 | 1.22 (0.74 - 2.03) | 1.35 (0.79 - 2.31) |
| 271 Pulp & Paper Industries | 4 | 0.70 (0.25 - 1.92) | 0.80 (0.28 - 2.26) | 17 | 1.26 (0.75 - 2.12) | 1.38 (0.79 - 2.39) |
| 2719 Other Paper Industries | 0 | - | - | 4 | *3.44 (1.09 - 10.88)* | 3.04 (0.84 - 11.04) |
| 29 Primary Metal Industries | 11 | *2.26 (1.16 - 4.40)* | *3.19 (1.54 - 6.61)* | 20 | 1.28 (0.78 - 2.10) | 1.65 (0.98 - 2.79) |
| 295 Non-Ferrous Metal Smelting & Refining | 4 | *3.28 (1.04 - 10.29)* | *10.05 (2.63 - 38.46)* | 5 | 1.12 (0.43 - 2.96) | 1.53 (0.50 - 4.63) |
| 2959 Other Pri. Smelting & Refining of Non-Ferrous | 3 | *13.31 (2.91 - 60.88)* | *14.65 (2.76 -77.80)* | 4 | 2.50 (0.81 - 7.78) | 3.19 (0.97 - 10.47) |
| 30 Fabricated Metal Prods (Except Machinery & Transportation Equipment Industries) | 8 | *2.16 (1.02 - 4.61)* | 2.01 (0.91 - 4.44) | 14 | 1.00 (0.57 - 1.76) | 1.02 (0.57 - 1.84) |
| 304 Stamped, Pressed and Coated Metal Products | 3 | *7.00 (1.95 - 25.14)* | *4.68 (1.24 - 17.67)* | 3 | 1.30 (0.39 - 4.25) | 1.48 (0.44 - 4.97) |
| 308 Machine Shop Industry | 3 | *3.45 (1.00 - 11.82)* | 3.23 (0.87 - 11.96) | 7 | 1.42 (0.64 - 3.15) | 1.27 (0.54 - 2.96) |
| 35 Non-Metallic Mineral Products | 2 | - | - | 5 | 0.80 (0.31 - 2.08) | 0.95 (0.34 - 2.71) |
| 352 Hydraulic Cement Industry | 1 | - | - | 3 | *7.60 (1.76 - 32.73)* | *8.93 (1.67 - 47.79)* |
| 39 Other Manufacturing | 3 | 2.33 (0.66 - 8.32) | 3.18 (0.81 - 12.49) | 5 | 1.72 (0.67 - 4.42) | 1.83 (0.69 - 4.82) |
| 399 Other Manufactured Product Industries | 3 | *13.21 (3.03 - 57.64)* | *12.26 (2.63 - 57.11)* | 3 | 2.29 (0.67 - 7.80) | 1.88 (0.54 - 6.53) |
| F. Construction Industries | 40 | 0.96 (0.67 - 1.38) | 1.08 (0.73 - 1.59) | 89 | 0.95 (0.73 - 1.24) | 0.98 (0.74 - 1.30) |
| 41 Industrial & Heavy (Engineering) Construction | 9 | 1.49 (0.72 - 3.07) | 1.62 (0.75 - 3.51) | 29 | 1.32 (0.87 - 2.00) | 1.40 (0.89 - 2.18) |
| 412 Highway & Heavy Construction | 8 | 1.49 (0.69 - 3.21) | 1.54 (0.68 - 3.50) | 26 | 1.41 (0.91 - 2.18) | 1.52 (0.95 - 2.45) |
| 4123 Hydroelectric Power Plants & Related Structures (Except Transmission Lines) | 2 | - | - | 3 | 3.46 (0.99 - 12.03) | *6.52 (1.64 - 25.90)* |
| 4129 Other Heavy Construction | 5 | *4.07 (1.43 - 11.58)* | *3.77 (1.20 - 11.86)* | 13 | *2.66 (1.41 - 5.03)* | *3.44 (1.69 - 7.00)* |
| H. Communication & Other Utility | 13 | 1.01 (0.55 - 1.87) | 1.02 (0.53 - 1.97) | 29 | 1.22 (0.81 - 1.86) | 1.19 (0.76 - 1.87) |
| 49 Other Utility Industries | 8 | 1.01 (0.55 - 1.86) | 1.02 (0.53 - 1.97) | 17 | 1.22 (0.81 - 1.86) | 1.19 (0.76 - 1.87) |
| 499 Other Utility Industries n.e.c. | 2 | - | - | 5 | *2.80 (1.01 - 7.77)* | *3.84 (1.34 - 11.04)* |
| J. Retail Trade Industries | 18 | 0.65 (0.39 - 1.07) | 0.67 (0.40 - 1.14) | 62 | 0.97 (0.72 - 1.30) | 1.01 (0.74 - 1.38) |
| 64 General Retail Merchandising | 2 | - | - | 7 | 0.58 (0.27 - 1.27) | 0.62 (0.27 - 1.39) |
| 641 General Merchandise Stores | 2 | - | - | 7 | 0.58 (0.27 - 1.27) | 0.62 (0.27 - 1.39) |
| 6411 Department Stores | 1 | - | - | 3 | *0.30 (0.09 - 0.97)* | 0.32 (0.10 - 1.06) |
| N. Government Service Industries | 27 | 0.92 (0.60 - 1.40) | 0.84 (0.54 - 1.31) | 94 | 0.91 (0.70 - 1.19) | 0.92 (0.69 - 1.22) |
| 82 Provincial & Territorial Government Service | 2 | - | - | 4 | 0.36 (0.13 - 1.00) | *0.34 (0.12 - 0.96)* |

| | | | | | | |
|---|---|---|---|---|---|---|
| P. Health and Social Service Industries | 9 | 1.96 (0.96 - 4.00) | *2.16 (1.03 - 4.57)* | 14 | 1.31 (0.74 - 2.31) | 1.36 (0.74 - 2.49) |
| 86 Health & Social Service | 9 | 1.96 (0.96 - 4.00) | *2.16 (1.03 - 4.57)* | 14 | 1.31 (0.74 - 2.31) | 1.36 (0.74 - 2.49) |
| 865 Offices of Physicians, Surgeons & Dentists, Private Practice | 3 | 3.30 (0.98 - 11.14) | *3.97 (1.13 - 13.96)* | 4 | *3.74 (1.29 - 10.86)* | *4.03 (1.34 - 12.11)* |
| 8651 Offices of Physicians General Practice | 2 | - | - | 3 | *4.35 (1.26 - 15.05)* | *4.87 (1.33 - 17.82)* |
| Q. Accommodation, Food & Beverage Service Industries | 11 | 1.37 (0.71 - 2.68) | 1.40 (0.66 - 2.96) | 28 | 0.97 (0.64 - 1.48) | 1.05 (0.67 - 1.65) |
| 92 Food and Beverage Service Industries | 8 | 1.97 (0.86 - 4.52) | 2.16 (0.83 - 5.68) | 15 | 1.07 (0.60 - 1.89) | 1.15 (0.61 - 2.18) |
| 921 Food Services | 8 | 2.07 (0.89 - 4.80) | 2.29 (0.86 - 6.10) | 15 | 1.37 (0.77 - 2.46) | 1.42 (0.74 - 2.72) |
| 9211 Restaurants, Licensed | 7 | *3.40 (1.25 - 9.22)* | *4.57 (1.31 - 15.93)* | 8 | 1.24 (0.56 - 2.76) | 1.24 (0.50 - 3.06) |
| R. Other Service Industries | 13 | 1.61 (0.87 - 2.98) | 1.50 (0.77 - 2.92) | 36 | 1.32 (0.91 - 1.93) | 1.27 (0.85 - 1.90) |
| 96 Amusement & Recreational Service | 3 | 2.06 (0.58 - 7.30) | 2.12 (0.53 - 8.51) | 11 | 1.51 (0.79 - 2.90) | 1.66 (0.82 - 3.38) |
| 962 Motion Picture Exhibition | 1 | - | - | 3 | *8.13 (2.26 - 29.22)* | *8.30 (2.12 - 32.46)* |
| 99 Other Service Industries | 6 | *2.90 (1.15 - 7.30)* | 2.55 (0.92 - 7.08) | 15 | 1.48 (0.84 - 2.61) | 1.45 (0.78 - 2.67) |
| 994 Other Repair Services | 3 | *8.57 (2.17 - 33.88)* | *7.21 (1.60 - 32.57)* | 6 | 2.08 (0.82 - 5.29) | 2.11 (0.79 - 5.64) |
| 9942 Welding | 2 | - | - | 5 | *4.47 (1.64 - 12.19)* | *4.16 (1.40 - 12.37)* |

Note: *Significant estimates* (in any one of the analyses reported) *are in italics (p<0.05).*
CSIC: Canadian Standard Industrial Classification, 1980; CI: Confidence interval;
N1=Number of exposed cases in the corresponding usual industry; N2=Number of cases exposed in the corresponding ever industry category.
*Control group 1= Basic control group after excluding unknown primary cancer subjects.
† Control group 2= Control group after excluding subjects with cancers related to smoking and unknown primary cancers.
‡ OR: Odds ratio adjusted for smoking (pack years grouped), education status, ethnic group, respondent to the questionnaire in addition to age at diagnosis (grouped) and year of diagnosis.

We evaluated the risk of large cell lung cancer for about 11% of these industrial groups having at least 3 cases and 3 controls, which included: 111 industries represented in 17 divisions, 32 major groups, 37 minor groups, and 25 classes. In general, concordance of the results between both the control groups was good (94% agreement). Overall, 7% of the analyses (out of 13% total significant results) were significant in both two control groups with an elevated risk of large cell lung cancer being observed among workers in 8 industrial categories. None of the industries were associated with a reduced risk of large cell lung cancer.

Among industries showing a significantly elevated risk of large cell lung cancer, the majority of large cell carcinoma cases were employed in the primary metal industries (SIC-29), and health & social service industries (SIC Division-P); the odds ratios were suggestive of a moderate to strong association in most of these industrial categories.

While the above mentioned 'usual' industry of employment categories were significantly associated with lung cancer in the analyses based on both control groups, a total of 6 industry categories were associated with an elevated risk in only one of the control group analyses (Table 26). We observed an excess risk of large cell carcinoma of the lung among workers in the health & social service industries (SIC Division-P; OR=2.2) and its subgroups (SIC-865, 8651). The elevated risk of large cell lung cancer among primary metal industry workers (SIC-29) involved in the smelting & refining of non-ferrous metals (SIC-295, 2959), certain metal fabricating workers (SIC-304) and other heavy construction workers (SIC-4129) was also noteworthy.

Overall, an increased risk of large cell lung cancer was observed among metal manufacturing workers, and workers in health related industries.

#### 4.5.5.2 Industries 'Ever' Worked

The significantly elevated odds ratio estimates for large cell lung cancer and the associated 95% confidence intervals in relation to the industries 'ever' worked in are reported in Table 26. Our analysis of large cell lung cancer was restricted to the industries ('ever' worked) having at least 3 cases and 3 controls (21% of the total), which included: 254 industries represented in 18 divisions, 52 major groups, 93 minor groups, and 91 classes. In general, the concordance of the results between control groups 1 and 2 was good (96% agreement). Overall, 5% of the analyses (out of 9% total significant results) were significant in both two control groups with an elevated risk of large cell lung cancer being observed among workers in 12 and none of the industries were associated with reduced risk of large cell lung cancer.

Among the industries showing a significant excess risk of large cell lung cancer, the odds ratios were suggestive of a moderate to strong association in most of the industry categories (Table 26). The industries involved in the manufacturing of wood box & pallets (SIC-256), and hydraulic cement (SIC-352) were associated with an increased risk of large cell lung cancer. Workers involved in the motion picture exhibition (SIC-962) were not only associated with an increased risk of large cell lung cancer, but also squamous cell and all types of lung cancer.

The excess risk of lung cancer observed in the above mentioned high risk occupations and industries is due to certain carcinogenic exposures found in these occupational settings. We have attempted to identify the risk of certain occupational agents using the NIOSH job-exposure matrix. However, our attempt to apply the U.S based NIOSH-JEM in a Canadian setting has been restricted. In the following section, we describe our experience with the JEM. We expect this critical discussion on the methodological difficulties in applying the JEM in the present context will contribute towards future research to make the JEM more applicable in occupational cancer epidemiology.

# 5. Job-Exposure Matrix

## *5.1 Introduction*

An excess risk of lung cancer was observed in many occupations and industries in our study. Assessing the carcinogenic risk of the key exposure(s) found in these occupations would be the next step. Certain key exposures were identified from the literature, including: metallic substances, non-metallic dusts, chemicals and solvents. Once an occupational agent has been chosen for further assessment, the next task would be the estimation of the level of exposure to this agent among the study subjects.

Exposure assessment can be based on direct hygiene measurements, self-reports, a job-exposure matrix, or an expert assessment. The ideal approach would be measuring the exposure concentrations in the work place of each subject. This is usually impossible in epidemiological research, owing to both the historical nature of the exposure assessment and the costs involved in such extensive exposure monitoring. Exposure assessment could be based on self-reports from the workers or proxies. However, logistical problems and low validity of this approach have limited its use (174;175). A third approach is an expert based exposure assessment. With this approach, experts assign a level of exposure to the agent of interest to all subjects in the study on an individual basis, based on their job history and other inputs, including the opinions of industrial consultants. The feasibility and the costs for such a process have limited its application (176;177). However, this type of expert based exposure assessment was used in an occupational cancer study in Montreal (26).

The most commonly used tool for exposure assessment is a job-exposure matrix (JEM). A JEM is an algorithm that links the job titles to a group of occupational exposures, thereby allowing exposure estimation. Various types of job-exposure matrices are found in the literature. Some JEMs are specific to an occupational setting or an agent (178-182), while others are for general use, covering a wide range of job classifications (164;183-185).

We initially proposed to use a job-exposure matrix for our study. Since the development of a new job exposure matrix was beyond the scope of this thesis, we decided to use a JEM that had been developed previously. Although a general JEM is not available in Canada, the U.S. National Institute for Occupational Safety and Health (NIOSH) had developed a job-exposure matrix based on the National Occupational Exposure Survey (NOES) (164;186-189). Considering the North American context and the availability of this JEM, we decided to use the U.S based NIOSH-JEM for the exposure assessment in our study (164).

In the following sections, we provide a brief review of the literature on job-exposure matrices, along with details on attempted application of the NIOSH-JEM in our study. Since our attempt to use the NIOSH-JEM was limited by various factors, we provide a critical discussion on the applicability of the NIOSH-JEM in the Canadian context. For this purpose we have chosen beryllium, a known lung carcinogen (14;39), to illustrate the difficulties in exposure assessment using the NIOSH-JEM.

## *5.2 JEM-Literature Review*

A JEM is a tool that allows translation of job titles or occupations or industries to a list of occupational exposures (agents). In large population-based occupational studies such as the present study, expert based exposure assessment is usually impractical given the large number of subjects, occupations and industries for which exposure levels would need to be inferred. In this situation, use of a JEM is, theoretically, a feasible alternative. Although the initial development of a JEM is a time and resource consuming process, once developed, it can be used for exposure assessment in other studies within the constraints of the JEM.

During the development of a JEM, various methods of identifying the exposures in an occupation/industry have been used, including: direct field visits (as in the NIOSH–JEM) (164;187-189), the general literature (185), and an expert assessment of exposure (as in Finnish JEM) (184). The total number of exposure agents included in a JEM varies from a single exposure (e.g., an exposure specific-JEM) to multiple exposures (e.g., the NIOSH-JEM and the Finnish-JEM) (164;178-185).

Several job-exposure matrices were found in the literature (164;178-185). While some were specific to one exposure or occupational group (178-182), others were more general (164;183-185). A specific job-exposure matrix for agriculture related occupations and industries, was developed in British Columbia (178). Similarly, job-exposure matrices for specific industries have been developed for welding (179), paint manufacturing (180), and the pulp and paper industry (181). A job-exposure matrix specific to the assessment of chemical compounds was also found in the literature (182). Although, the applicability of specific job-exposure matrices is limited to a given occupation or industry, it has been suggested that they might be more valid than general job-exposure matrices with respect to exposure assessment of the target agent (190).

General job-exposure matrices offer the potential for broader application than industry specific job-exposure matrices. A general job-exposure matrix was first developed by Hoar et al. in 1980 for U.S occupational settings (185). Her job-exposure matrix consisted of about 500 occupation-industry categories and 376 exposures that were selected from the literature (known or suspected carcinogens and other toxins). The use of this JEM in identifying new carcinogens is limited, as the exposure estimation was confined to known carcinogens (185). A JEM with a comprehensive list of exposures in the work place could serve the purpose of identifying new carcinogenic substances. One such matrix was developed by the NIOSH based on the National Occupational Hazard Survey (NOHS; 1972-1974) (164). At a later date, NIOSH developed a similar JEM, based on the National Occupational Exposure Survey (NOES; 1981-1983) (164;187-189). General job-exposure matrices have been developed in other countries, including England (183) and Finland (184).

A JEM could present exposure in various ways, including: the level of exposure, the probability of exposure (prevalence of exposed subjects in an occupation/ industry), the intensity of exposure (low, medium, or high), and whether or not exposure occurred (using a dichotomous exposed/unexposed exposure indicator) (164;184;185). While a dichotomous definition of an exposure (exposed/ unexposed) represents a crude way to measure exposure, exposure measurements based on the probability or the levels of exposure provide more informative indicators of exposure. In both NIOSH job-exposure matrices, exposure characterization in terms of probabilities was possible (164;187-189). In a Finnish-JEM, the prevalence and the level of exposure measures were provided for the exposures found in an occupation at specific time period; which could be used for exposure estimation (184).

The validity of JEM based exposure estimation has been evaluated in several studies (190-195). This was done in different ways, including: comparing two JEMs

(192), comparing a JEM to a self-report (193;196), comparing a JEM with an expert opinion (190;191;193), or examining the results from JEM-analyses for a known association (190;191). Exposure assessment based on the NIOSH-JEM has been compared to exposure assessment by experts and direct self-report for copper, lead, and iron in the metal manufacturing industries (193). This assessment was based on 115 jobs out of the available 188 study subjects. The results showed greater misclassification of exposure for the assessment based on the NIOSH-JEM. The percentage agreement between the JEM and the expert assessment was 81.5%, 86%, and 69.2% for copper, lead, and iron, respectively. For the assessment by direct self-report, the percentage agreement with the expert assessment was 94.6, 91.9 and 72.5% for exposure to copper, lead, and iron, respectively (193). The authors suggested using an expert based assessment of metal exposures to avoid misclassification whenever possible (193). Discrepancies were noted between the NIOSH-JEM predicted occupational exposures and expert assessment in relation to birth defects (190). However, in the same study, a known association between maternal benzene exposure and kidney malformations was reproduced by the JEM based evaluation of exposure to benzene (190).

Exposure assessment based on a JEM is prone to non-differential misclassification, whereas an assessment by experts depends on their ability to evaluate occupational exposures, raising concern regarding subjectivity in exposure estimation (194). In general, expert assessment was considered as a standard method in exposure estimation. However, it should be acknowledged that the validity of an expert assessment of exposure depends on the sources of exposure information; exposure estimation based on the job titles is weaker than the exposure assessment based on the industry records, or industrial hygiene measurements of the subjects. Therefore, exposure assessment based on the levels of exposures in a JEM could be more valid than the expert assessment based on the job titles.

The major advantage of a comprehensive JEM, like the NIOSH-JEM, is its utility for exposure assessment in large population based occupational studies with multiple exposures. It has been suggested that a comprehensive JEM (such as the NIOSH-JEM) will have greater ability to identify less well understood occupational exposures (191). A JEM, with a record of the level of exposures at different time periods (like the Finnish-JEM) could be a useful tool for hazard surveillance (184).

However, JEM-based exposure estimation is subject to several potential limitations. Non-differential misclassification of exposure is a major limitation of JEM based exposure estimation (164;190;194). The occupational exposures are assigned to a job title, inherently assuming similar exposure profile for workers sharing common jobs; this could result in an ecological bias. Limitations of a JEM could be inherent to the particular study, such as incorrect job classification (164). Failure to take into account the exposure trends in time and the country specific nature of a JEM are also the limitations of a JEM (184).

It has been suggested that improvements in the structure of a JEM, and in the measurement of exposure could minimize the limitations pertaining to a JEM (184). In the recently developed Finnish-JEM, a time component was incorporated. This JEM had occupations on one axis, exposures on the second axis, and time period on the third axis. For a specific occupation, an exposure could thus be gauged over a period of time. Using the level of exposure or the probability of exposure (prevalence of exposure for the subjects in an occupation/industry) in exposure estimation could minimize bias (164;184). A variant of JEM (known as the Task Exposure Matrix) was developed by taking into account the variability of exposure among different tasks in a single job (197).

## *5.3 The National Institute for Occupational Safety and Health – Job-Exposure Matrix (NIOSH-JEM)*

The NIOSH-JEM is a comprehensive computer database that allows the linkage of occupations and/or industries to the occupational exposures. The JEM data and the documentation was provided by Dr. Karl Sieber, NIOSH, Cicinati, OH, on a CD-ROM. The NIOSH-JEM was based on the National Occupational Exposure Survey (NOES) that was conducted during 1980-1983 in the U.S. A detailed description of the NOES survey, including the field guidelines, the sampling strategy, and the analysis of management interview responses can be found in NIOSH publications (187-189). A brief description of the NOES is provided below.

### 5.3.1 NOES

The NOES was conducted by the NIOSH during 1980-1983 (186-189). The objective of this survey was to develop a database that would allow the estimation of exposure for workers experiencing a range of occupational exposures, including exposures to chemical, physical, and biological agents, based on a sample of industrial facilities that represent the American work force. Information on in-plant health and safety was also collected. A secondary objective was to make this survey data comparable to the previously conducted National Occupational Hazard Suvey (NOHS; 1972-1974) to allow analysis of trends of potential occupational exposures.

The sampling of facilities for this survey was a two stage process that was designed to be respresentative of most sectors of the American work force covered under the Occupational Safety and Health Act of 1970. The target population consisted of establishments containing eight or more employees, after excluding facilities dealing with agricultural production, mining (except oil and gas extraction), railroad transportation, private house holds, finance institutions, and all federal, state and municipal government facilities. First stage sampling consisted of random selection of geographical areas (primary sampling units) from the strata defined by geography, number of employees, and the concentration of establishments included in the target population. Second stage sampling was achieved by systematic sampling of establishments obtained from the first stage, ordered by the number of employees and the U.S 1972 Standard Industrial Classification (SIC) codes (198). Finally, a total of 4,490 industrial facilities with a minimum of eight employees covering a total of 1,800,000 workers was obtained (188).

A field survey was conducted by trained surveyors on the 4,490 industrial facilities covering 523 industry categories and workers in 410 occupational categories (187). The surveyors visited each of the sites and administered a standardized questionnaire to the plant management, directly observed the processess and operations, and recorded potential exposures to all employees. No direct industrial hygeine measurements were made. Rather, the exposure estimates refer to the NOES observation of exposure in a given setting. The potential exposures were classified into full-time and part-time exposures based on the time of exposure. When the exposure time was greater than 4 hours per day on a daily basis for 90% of the company's work year or standard work year, then the exposure was classified as full-time exposure. For part-time exposures, the exposure time to an agent had to exceed 30 minutes per week on an annual average, or once each week for 90% of year's work weeks. Over 10,000 potential exposure agents and 100,000 trade name products were observed during the on-site visits. The survey also included observations on the availability and use of exposure controls (e.g., ventilation and safety equipment), job title, worker gender, and process decription. The survey data was stratified according to 1972 U.S SIC codes and 1980 U.S census occupation codes (111;198).

### 5.3.2 JEM Structure

The NOES based JEM contained 507,123 records in total, representing approximately 13,000 different agents across 522 industries and 377 occupations. Occupations were classified according to the 3-digit 1980 U.S. Bureau of the Census codes (USCENOCC) (111). Industries were coded according to the 4-digit 1972 U.S. Standard Industrial Classification (USSIC) (198). The industries and the occupations were entered as couplets in the JEM. Potential exposures were listed for each of the industry/ occupation (I/O) couplets. The name of the agent, NIOSH hazard code, Chemical Abstracts Service (CAS) number, and the Registry of Toxic Effects of Chemical Substances (RTECS) number were provided for the potential exposures listed in the JEM. No information on the actual intensity of exposure to the listed agents was available in the JEM. Other details included: the number of facilities where an I/O group was observed, the total number of employees in an I/O group, the number of employees in an I/O group that were potentially exposed to an agent, the number of employees in an I/O group that were potentially exposed working with no form of engineering control over exposure, the number of employees exposed full time, and similar details for female employees. For data retrieval, the JEM should be viewed as a three dimentional array with axes representing: the SIC code, the occupation code, and potential exposure to specific agents. For a fixed set of industry and occupation codes, the JEM lists a set of potential exposures (agents). A total of 12,398 unique I/O couplets were found in the JEM. The average number of employees per couplet was approximately 70.

In the NISOH-JEM the exposures were classified individually, but not by a group. To achieve grouping by similar agents, a hazard list was provided in the documentation, which allows grouping the individual agents listed in the JEM. For example, the agents beryllium oxide and beryllium trifluoride were listed as potential exposures in the JEM; however, both these agents are beryllium compounds and can be combined for the analysis of beryllium as an aggregate exposure. The hazard lists provide the list of such agents in the JEM that could be grouped together for beryllium exposure.

The U.S based NIOSH-JEM has been used in various occupational studies (190;191;199-201). Exposure to asbestos was assessed using the NIOSH-JEM (based on the NOHS) in a study that evaluated the risk of mesothelioma in Los Angeles County (191). In that study, the probability of exposure to asbestos in an industry/ occupation group was used to assign exposure status (191). In another study, the NIOSH-JEM was used to obtain the prevalence estimates for occupational asthmogens (199). The NIOSH-JEM was also used for the exposure assessment in a birth defects study (190). In another study, the prevalence of occupational exposure to noise and ototoxic solvents was obtained from the NIOSH-JEM (200). In yet another study, breast cancer risk was assessed for 31 occupational exposures using the NIOSH-JEM (201).

## *5.4 The Translation Monograph*

As the occupations and the industries in the NIOSH-JEM were coded using U.S. CENOCC/SIC classifications, the Canadian codes in our data need to be translated to their U.S equivalents before it would be possible to apply the JEM for exposure estimation. To achieve this task, a translation monograph prepared by the British Columbia Cancer Agency (BCCA) is available (202). The hard copy of translation monograph and an electronic document for the translation of occupations were provided by Dr. Pierre Band from Health Canada.

The monograph allows translation of the United States 1980 Census of Population Occupational Classification codes (USCENOCC) to 1980 Canadian Standard Occupational Classification codes (SOC). Although, most of the occupations in the two classifications were treated similarly, a difference was noted in the classification of fabrication, processing, assembly, and machine operating occupations. The example given in the monograph is repeated in this discussion (202). In the Canadian SOC, fabrication, processing, assembly, and machine operating occupations are classified according to the product produced, whereas in the USCENOCC, they are classified according to the equipment used. For example, crushing and grinding machine operators were coded as USCENOCC-768. However, the crushing and grinding machine operators were classified in various Canadian SOC occupation codes involving crushing and grinding: 8153 (separating, grinding & mixing operations: clay, glass, and stone), 8211 (flour and grain milling occupations), or 8251 (cellulose pulp preparing occupations) (202).

As a first step in the preparation of translation monograph, occupational titles in the Canadian SOC were matched with the USCENOCC job titles. In the next step, the USCENOCC category was compared to the definitions and job descriptions of the Canadian SOC, taking into account the number of matches in the first step. At the end, the list was reviewed to confirm the inclusion of all job classifications, and accuracy of the translation (202). It should be noted that a single SOC code can be translated in to more than one USCENOCC codes, and vice versa.

The translation of 1972 U.S. Standard Industrial Classification (USSIC) codes to 1980 Canadian Standard Industrial classification (SIC) codes is not a straight-forward task. The translation provided in this monograph was based on the Statistics Canada Convertibility Table (203). The 1980 Canadian SIC and 1972 USSIC codes (Amended in 1977) were compared (4-digit code) in this table. An imperfect match was represented by an asterisk (*) in the Statistics Canada Convertibility Table (203). Eighty two percent (2019/2452 matches) of the matches were marked as imperfect in this table. The coders at the BCCA reviewed the comparison table and provided a weight to describe the closeness of match between USSIC and Canadian SIC codes. The level of concordance was determined as shown below:

| Level of Concordance | Code |
|---|---|
| Close | 1 |
| Moderate | 2 |
| Poor | 3 |

An USSIC code was given a concordance level of "1" only once in the table by the coders, which means that an USISC can be found as a close match only once in the table. In our study, we translated the USSIC to the Canadian SIC based on the concordance level. Whenever, a close match of USSIC (level-1) was available for the Canadian SIC, we have used only that industry for the translation. When a match with level-1 concordance was not available, we used a level-2 match for the translation. We did not use any level-3 matches, even when no other match was available. For example, the ferro-alloys industry (SIC-2911) is related to the USSIC 3313 (Electrometallurgical products) with a level of concordance "1" and to the USSIC 3312 (blast furnaces and steel mills) with a level of concordance "3". In our study, we used only USSIC 3313 as a translation for the Canadian SIC 2911 and vice versa. All the translations are done manually in our study.

## *5.5 Application of the NIOSH-JEM*

In our study, we have concentrated on the applicability of NIOSH-JEM in the Canadian setting. Exposure assessment is the primary step in evaluating the risk of lung cancer for that exposure. In this section, we describe the use of the JEM for exposure assessment in the U.S setting, including exposures related to lung cancer. Unfortunately, we are unable to use the JEM for exposure estimation in our study owing to logistical difficulties and potential for bias. These issues are illustrated with an example.

### 5.5.1 Application of the NIOSH-JEM in the U.S setting

To illustrate the methodology of using the NIOSH JEM in the U.S setting, we have selected a known lung carcinogen (beryllium) for exposure estimation (14;39). The choice of beryllium, a rare exposure, could minimize the complexity in illustrating the problems of JEM application. Based on the hazard lists provided by the NIOSH, a set of agents were combined to represent the beryllium (Be) exposure. Details on the nature of exposure (full-time/part-time), and the probability of exposure in an I/O couplet could be obtained from the JEM. In this section, the methodology of beryllium exposure estimation was described using the hypothetical case-control data in Table 27 as an example. For all ten subjects in the hypothetical data, the usual industries and the usual occupations were coded according to the 1972 USSIC and 1980 USCENOCC. The duration of employment in the respective industry-occupation combinations was also provided (see Table 27).

#### 5.5.1.1 Strategy of Exposure Assessment

In the NIOSH-JEM, the occupations and the industries were recorded as industry-occupation (I/O) couplets and the potential exposures in each couplet were listed. We have defined the I/O couplets based on the usual industries and the usual occupations of the subjects in the hypothetical data. Details on the nature of beryllium exposure (full-time/part-time), and the probability of beryllium exposure in these I/O couplets could be obtained from the JEM linkage. These probabilities were used as a surrogate indicator for the intensity of exposure as no other measure of intensity was available in the JEM. The probability is calculated by the formula:

$P = (N/T)$;

Where

P = probability of exposure in an I/O group;

N = number of employees exposed to beryllium; and

T = total number of employees in the I/O group.

**Table 27:** Hypothetical U.S Data to Explain the Exposure Assessment Using the NIOSH-JEM

| ID | USSIC | U.S Industry Title | USCENOCC | U.S. Occupation Title | Case/ Control | Duration of employment (years) | Probability | CEI |
|---|---|---|---|---|---|---|---|---|
| 1 | 3069 | Fabricated Rubber Products, n.e.c. | 725 | Miscellaneous Metal & Plastic Processing Operators | Case | 20 | 1.0 | 20 |
| 2 | 3724 | Aircraft Engines & Engine Parts | 779 | Machine Operators, not Specified | Case | 20 | 0.3 | 6 |
| 3 | 3679 | Electronic Components, n.e.c. | 637 | Machinists | Case | 10 | 0.1 | 1 |
| 4 | 8062 | General medical & surgical hospitals | 073 | Chemists, except biochemists | Control | 15 | 0 | 0 |
| 5 | 3069 | Fabricated Rubber Products, n.e.c. | 725 | Miscellaneous Metal & Plastic Processing Operators | Control | 10 | 1.0 | 10 |
| 6 | 3841 | Surgical & Medical Instruments | 709 | Grinding, Abrading, Buffing, & Polishing Operators | Case | 20 | 0.7 | 14 |
| 7 | 3069 | Fabricated Rubber Products, n.e.c. | 725 | Miscellaneous Metal & Plastic Processing Operators | Control | 30 | 1.0 | 30 |
| 8 | 3671 | Electronic tubes, receiving type | 055 | Electrical and electronic engineers | Case | 20 | 0 | 0 |
| 9 | 8062 | General medical & surgical hospitals | 073 | Chemists, except biochemists | Control | 30 | 0 | 0 |
| 10 | 3671 | Electronic tubes, receiving type | 055 | Electrical and electronic engineers | Control | 40 | 0 | 0 |

USSIC= The U.S Standard Industrial Classification Code (1972);
USCENOCC= the U.S 1980 Census of Population Occupational Classification codes;
CEI= Cumulative exposure index (Duration of employment x Probability of exposure)
Probability= Prevalence /probability of beryllium exposure retrieved from the NIOSH-JEM for the corresponding industry-occupation group.

The corresponding probabilities in an I/O couplet were applied to the subjects in the hypothetical data to obtain a cumulative exposure index (CEI). A cumulative exposure index for an exposed subject is calculated as a product of duration of employment and the probability of exposure to the agent (beryllium), summed across an individual life-time occupational history. Specifically, the index is calculated as

Cumulative exposure index = (Y x P)

Where

Y=total number of years worked in an I/O group;

P=probability of beryllium exposure in this I/O group.

For example, subject 1 in our hypothetical data worked for 20 years in the fabricated rubber products industry (not elsewhere classified) as a miscellaneous metal & plastic processing operator (I/O couplet: 3069-725). For this couplet the JEM indicated a probability of one (100%) for beryllium exposure. Therefore, the cumulative exposure index for the subject-1 is 20 x 1= 20.

Once these estimates (CEI) of beryllium exposure are calculated for all the subjects in the data, the next task is defining the exposure to assess the lung cancer risk.

#### 5.5.1.2 Evaluation of Lung Cancer Risk

Exposure can be defined as a dichotomous variable (exposed/unexposed) or ordinal variable (e.g., unexposed, low exposure, high exposure) or a continuous variable. Although, defining the exposure as a dichotomous variable is the simplest method, it is a crude measure of exposure intensity. The cumulative exposure index could be used to order the exposure intensity qualitatively (e.g., low, medium, high exposure) based on given exposure cut points. For example, the subjects with CEI measure of '0', '1-7', '8-15', and 'above 15' could be defined as unexposed, low, medium, highly exposed, respectively. The cut point could be selected from the literature, or it could be based on a sensitivity analysis or even expert opinion. The CEI could also be used as a continuous variable. The choice of exposure definition is dependent on the number of exposed subjects and the overall sample size of the study. For example, if there are few exposed subjects (<3) in the study, then it is impossible to assess the lung cancer risk by defining the exposure as an ordinal variable; dichotomous definition is the only option in this case.

After defining the exposure for all the subjects, lung cancer risk can be evaluated using logistic regression. We could adjust for potential confounders (such as smoking) depending on the availability of relevant and informative data. Finally, the measure of lung cancer risk could be estimated. In addition, exposure-response relationships could also be evaluated, if the sample size permits the evaluation of lung cancer risk at various levels of exposure (ordinal/ continuous).

One should acknowledge that the cumulative exposure index measures (based on probability) are only surrogate measures of the intensity of exposure, as there is no information on the actual levels of exposure in the NIOSH-JEM.

### 5.5.2 Potential Application of the NIOSH-JEM in the Present Study

In our dataset, we have defined the I/O couplets based on the usual industries and the usual occupations of the subjects. The subjects in our dataset had 4352 unique Canadian I/O couplets. To use the NIOSH-JEM for exposure assignment to these I/O couplets in our data, the Canadian couplets need to be translated to their equivalent U.S couplets. Once this task is completed, exposure estimation could be undertaken according to the procedure described in the previous section. In this section, we describe the general methodology of translation of the Canadian couplets to their U.S equivalents. To illustrate the issues involved in this translation, we have chosen a known carcinogen (beryllium) for exposure estimation using the NIOSH-JEM (14;39).

### 5.5.2.1 General Methodology of Translation

There are no tools available to achieve the couplet level translation of the Canadian codes in to their U.S equivalents. As an alternative, we have decided to use the translation monograph prepared by the British Columbia Cancer Agency that allows us to translate the Canadian occupation and Industry codes, separately, into their U.S equivalents. This led to a three step process for the translation of Canadian I/O couplets to their U.S equivalents. In the first step, the industry code in the couplet was translated to its equivalent U.S industry codes. Next, the occupation (CSOC) in the Canadian couplet was translated to its equivalent U.S codes. Finally, the translated occupation and industry codes were combined to obtain a list of equivalent U.S I/O couplets. The exposure information for these translated U.S couplets could then be retrieved from the NIOSH-JEM and combined to provide an estimate of the probability of beryllium exposure in each Canadian I/O couplet. A schematic diagram of the translation procedure is given in Figure 4. A detailed description of this translation related issues is provided in the next section, along with an illustrative example.

The above process is very time consuming since we have to manually translate each of the Canadian couplets into their U.S equivalents. Only 9 unique I/O couplets in the JEM had full-time exposure to beryllium. Therefore, most of the Canadian couplets in our data will have no exposure to beryllium. This provides an opportunity to increase the efficiency of assigning exposure estimates to the Canadian I/O couplets (Figure 5).

**Figure 4:** Schematic Diagram of the Application of the JEM in the Case of Beryllium

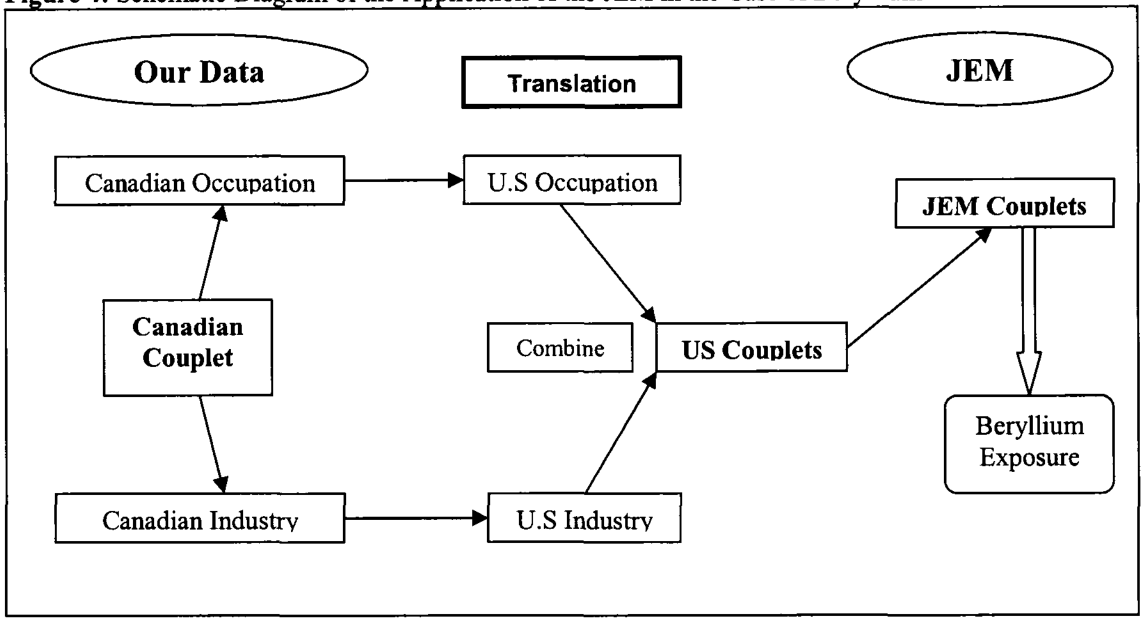
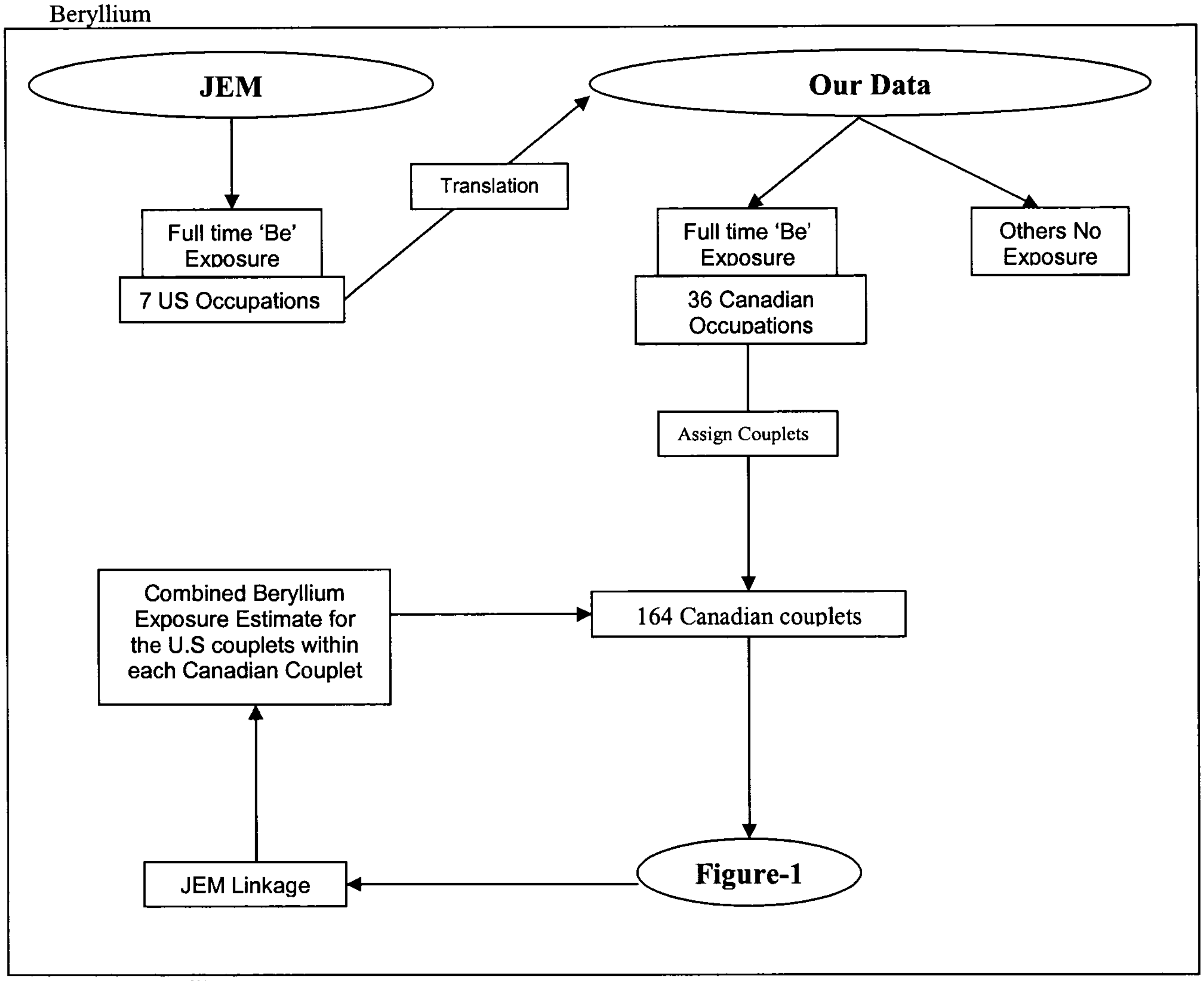


**Figure 5:** Strategy of Translating the Canadian Couplets to U.S Couplets in the Present Study in the Case of Beryllium




Note: Be=Beryllium

An electronic version of the occupational code translation was used to translate the 7 U.S occupations in the U.S couplets with full-time beryllium exposure to their Canadian equivalents; any Canadian I/O couplet which did not have an occupation of this translated list, was assigned an exposure of '0'. Next, we needed to translate the Canadian I/O couplets with non-zero exposure back to their U.S equivalents according to the procedure mentioned in the previous paragraph to obtain a list of translated U.S couplets. Finally, these U.S I/O couplets were linked to the JEM and the probability of full-time beryllium exposure in each linked U.S I/O couplet was estimated. These estimates within each Canadian I/O couplets are combined to provide an estimate of exposure. Further details are provided in the next section.

Further analysis to determine the lung cancer risk, according to the procedure described in the previous section (U.S setting), depends on how successful the exposure estimation algorithm is.

**5.5.2.2 Issues Related to the Translation of Canadian Couplets to U.S Couplets with Beryllium as an Example**

We are unable to use the NIOSH-JEM for exposure estimation in our study owing to logistical difficulties and potential for bias. The details are described in the following discussion.

For full-time beryllium exposure, the JEM identified 9 U.S I/O couplets listed across 7 occupations and 8 industries which had non-zero probability of exposure. The details of these 9 U.S couplets are summarized in Table 28. When we translated the 7 occupations in these U.S couplets, a total of 36 equivalent Canadian occupations were obtained. The Canadian I/O couplets which did not have an occupation in this translated list were assigned an exposure of '0'.

**Table 28: The NIOSH-JEM Retrieved Industry/Occupation Couplets for Full-Time Beryllium Exposure**

| USSIC | U.S Industry Title | USCENOCC | U.S. Occupation Title | Total | Exposed | Probability |
|---|---|---|---|---|---|---|
| 3662 | Radio & TV Communication Equipment | 637 | Machinists | 419 | 2 | 0.00 |
| 3679 | Electronic Components, n.e.c. | 637 | Machinists | 540 | 45 | 0.08 |
| 3573 | Electronic Computing Equipment | 683 | Electrical and Electronic Equipment Assemblers | 598 | 33 | 0.06 |
| 3724 | Aircraft Engines & Engine Parts | 709 | Grinding, Abrading, Buffing, & Polishing Operators | 659 | 42 | 0.06 |
| 3841 | Surgical & Medical Instruments | 709 | Grinding, Abrading, Buffing, & Polishing Operators | 9 | 6 | 0.67 |
| 3069 | Fabricated Rubber Products, n.e.c. | 725 | Miscellaneous Metal & Plastic Processing Operators | 2 | 2 | 1.00 |
| 3691 | Storage Batteries | 755 | Extruding & Forming Machine Operators | 19 | 15 | 0.79 |
| 3829 | Measuring & Controlling Devices, n.e.c. | 777 | Miscellaneous Machine Operators, n.e.c. | 43 | 42 | 0.98 |
| 3724 | Aircraft Engines & Engine Parts | 779 | Machine Operators, not Specified | 3 | 1 | 0.33 |

USSIC= The U.S Standard Industrial Classification Code (1972);
USCENOCC= the U.S 1980 Census of Population Occupational Classification codes.
Total= Total number of employees in the industry/occupation couplet.
Exposed= Total number of employees exposed full-time to beryllium in the industry/occupation couplet.
Probability= Prevalence /probability of exposure in the industry/occupation couplet (Exposed/Total).

All the 36 Canadian occupations with a possible full-time exposure to beryllium were paired with the corresponding industry code of the subjects in our dataset, which resulted in 164 Canadian I/O couplets. Next, the 164 Canadian I/O couplets with non-zero exposure need to be manually translated back to their U.S equivalents. We noticed multiple U.S equivalents for each Canadian couplet. The exposure estimation using the NIOSH-JEM, indicated no full-time exposure to beryllium in these translated U.S couplets. Collectively, these issues raise concerns about the use of the JEM for exposure assessment in the context of this study.

To describe the logistical problems and other issues (such as bias and exposure misclassification) in more detail, we have examined one Canadian I/O couplet; the couplet represents the electrical & related equipment fabricating & assembling occupations (CSOC-8531) in the electronic parts & components industry (CSIC-3352) [represented as 3352-8531 (CSIC-CSOC)]. Similarly, the U.S I/O couplets are represented according to the USSIC-USCENOCC pairing.

***5.5.2.2.1 Logistical Problems***

When a single Canadian I/O couplet has a single U.S couplet as a translation, the exposure estimation is straightforward, as described in the previous section (pertaining to the U.S setting). However, in most situations, one Canadian couplet links to multiple U.S couplets, complicating the task of exposure estimation. The Canadian classification system has more categories of specific occupations and industries than the U.S classification system. In this section, the logistical difficulties in translating the Canadian couplets and exposure estimation using the JEM are described by means of an example.

As a first step in translating the Canadian I/O couplet, 3352-8531, to the equivalent U.S I/O couplets, we have translated the Canadian industry code (CSIC-3352) to the equivalent U.S industry codes using the translation monograph prepared by BCCR (202). This process linked to 8 U.S industry codes (3671 to 3678). Next, the translation of the Canadian occupation code (CSOC-8531) resulted in 4 equivalent U.S occupations (533, 683, 777, 785). By combining these 8 U.S industries and 4 U.S occupations, a list of 32 potential U.S couplets is obtained as a translation to our single Canadian couplet (3352-8531). These couplets are summarized in Table 29. The first observation is that the U.S industry/occupation couplets related to occupations which, in many cases, are quite distant from the underlying Canadian occupation, electrical & related equipment fabricating & assembling (CSOC-3352).

Translating the hundreds of Canadian I/O couplets in our data, manually, to their U.S equivalents according to the procedure mentioned above is a laborious task (see Figure 4). In addition, these U.S translations are not specific to a single Canadian couplet, with some of these U.S couplets were found as translations for more than one Canadian couplet. For example, the translated U.S I/O couplet (3674-785) representing the assemblers (USCENOCC-785) in semiconductors & related devices industry (USSIC-3674) is not a specific match for the Canadian couplet (3352-8531) representing electrical & related equipment fabricating & assembling occupations (CSOC-8531) in the electronic parts & components industry (CSIC-3352) (see Table 29). This U.S couplet (3674-785) appeared as a translation for 16 other Canadian I/O couplets.

**Table 29:** Translated U.S Couplets for the Canadian Couplet, 3352-8531*

| Translated U.S couplets | | | | JEM Data | | |
|---|---|---|---|---|---|---|
| **US SIC** | **Industry title** | **USCENOCC** | **Occupation title** | **Total** | **Exposed** | **Probability (%)†** |
| Total translated U.S couplets - 32 | | | | | | |
| **JEM matches - 21** | | | | **5559** | **23** | **0.4** |
| **2 couplets with part-time exposure to beryllium:** | | | | **705** | **23** | **3.3** |
| 3673 | Electronic tubes, transmitting | 777 | Miscellaneous machine operators, n.e.c. | 73 | 6 | 8.2 |
| 3674 | Semiconductors & related devices | 785 | Assemblers | 632 | 17 | 2.7 |
| **19 couplets with no exposure to beryllium:** | | | | **4854** | **0** | **0** |
| 3671 | Electron tubes, receiving type | 683 | Electrical and electronic equipment assemblers | | | |
| 3671 | Electron tubes, receiving type | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3671 | Electron tubes, receiving type | 785 | Assemblers | | | |
| 3672 | Cathode ray television picture tubes | 683 | Electrical and electronic equipment assemblers | | | |
| 3672 | Cathode ray television picture tubes | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3672 | Cathode ray television picture tubes | 785 | Assemblers | | | |
| 3673 | Electron tubes, transmitting | 683 | Electrical and electronic equipment assemblers | | | |
| 3673 | Electron tubes, transmitting | 785 | Assemblers | | | |
| 3674 | Semiconductors & related devices | 683 | Electrical and electronic equipment assemblers | | | |
| 3674 | Semiconductors & related devices | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3675 | Electronic capacitors | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3675 | Electronic capacitors | 785 | Assemblers | | | |
| 3676 | Electronic resistors | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3677 | Electronic coils & transformers | 683 | Electrical and electronic equipment assemblers | | | |
| 3677 | Electronic coils & transformers | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3677 | Electronic coils & transformers | 785 | Assemblers | | | |
| 3678 | Electronic connectors | 683 | Electrical and electronic equipment assemblers | | | |
| 3678 | Electronic connectors | 777 | Miscellaneous machine operators, n.e.c. | | | |
| 3678 | Electronic connectors | 785 | Assemblers | | | |
| **11 couplets with no JEM entry:** | | | | **NA** | **NA** | **NA** |
| 3671 | Electron tubes, receiving type | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3672 | Cathode ray television picture tubes | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3673 | Electron tubes, transmitting | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3674 | Semiconductors & related devices | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3675 | Electronic capacitors | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3675 | Electronic capacitors | 683 | Electrical and electronic equipment assemblers | | | |
| 3676 | Electronic resistors | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3676 | Electronic resistors | 683 | Electrical and electronic equipment assemblers | | | |
| 3676 | Electronic resistors | 785 | Assemblers | | | |
| 3677 | Electronic coils & transformers | 533 | Miscellaneous electrical & electronic equipment repairers | | | |
| 3678 | Electronic connectors | 533 | Miscellaneous electrical & electronic equipment repairers | | | |

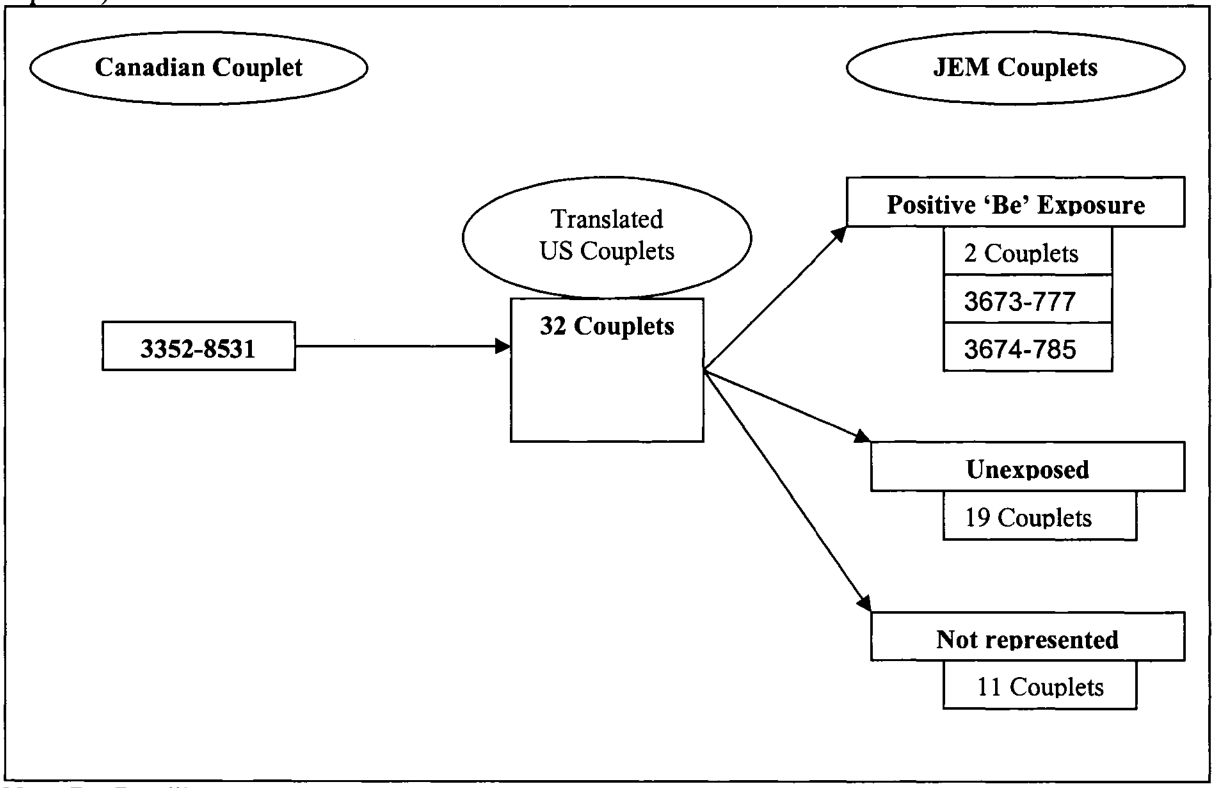
*Canadian couplet, 3352-8531represents electrical & related equipment fabricating & assembling occupations (CSOC-8531) in the electronic parts & components industry (CSIC-3352).
†Probability of part-time exposure to beryllium in the JEM data.
Note: CSIC=Canadian Standard Industrial Classification, 1980; CSOC=Canadian Standard Occupational Classification, 1980; USSIC=U.S 1972 Standard Industrial Classification; USCENOCC= United States 1980 Census of Population Occupational Classification codes; NA= Information not available in the JEM.

It would be very difficult to scan through hundreds of such translations to find a close match for our Canadian couplet; we may not able to find a suitable match due to differences in the Canadian and U.S classification schemes.

One should acknowledge that the translation of the Canadian industry codes (CSIC) to the U.S codes (USSIC) contained 82% imperfect matches (202;203). Our strategy of translating the Canadian couplets to their U.S equivalents is not an actual couplet level translation; we instead translated the occupation and the industry codes in a Canadian couplet to their U.S equivalents and combined them to obtain a list of translated U.S couplets. This procedure of cross linking the occupation and industry codes might have introduced more imperfection during translation process. Exposure estimation based on such translated U.S couplets could result in ecological bias. This issue is discussed in the next section.

The methodological complexity is further increased during the estimation of probability of exposure (e.g., to beryllium) for the subjects in a Canadian couplet. To explain the logistical problems during the estimation of probability of exposure, we have chosen one Canadian couplet (3352-8531), as an example. Part-time exposure to beryllium was indicated in two of the 32 translated U.S couplets in the JEM (3673-777, 3674-785). The schematics are illustrated in Figure 6 and the details are provided in Table 29. According to the JEM, the probabilities of part-time beryllium exposure for the subjects in the two U.S couplets, 3673-777 & 3674-785 are 8.2% and 2.7%, respectively. However, there is no beryllium exposure in the remaining of the linked U.S couplets with JEM entries (19 couplets). The probability of beryllium exposure in the Canadian couplet: 3352-8531 should be derived from all the 32 translated U.S couplets.

**Figure 6:** Schematic Illustration of Misclassification due to Translation in the Case of Beryllium (part-time exposure)




Note: Be=Beryllium;

None of the translated U.S couplets in the JEM had full-time exposure to beryllium.

Based on the NIOSH-JEM data, we can estimate a probability of 0.4% exposure to beryllium (for the Canadian couplet) based on the 21 translated couplets represented in the JEM. The validity of this estimate is questionable since it assumes that the distribution of Canadian workers in couplet 3352-8531 matches the distribution found by NIOSH for the linked US couplets. If instead, Canadian workers were clustered in only a sub-set of the US couplets, then the probability of exposure could vary anywhere between 0% and 8.2%. The potential for bias resulting from such exposure estimation further restricts our application of the NIOSH-JEM to our data. The issue of bias is described in the next section.

The major logistical difficulties that we have encountered during the use of the JEM for exposure estimation include: the need to manually translate the Canadian couplets to their U.S equivalents, and the need to estimate the exposure probabilities manually for hundreds of Canadian couplets according to the thousands of translated U.S couplets in the JEM.

##### *5.5.2.2.2 Bias and Other Issues*

In an ideal situation, a single Canadian I/O couplet would have a single U.S couplet as a translation. This would allow us to retrieve the exposure information from the JEM and assign the exposure status to the subjects in our data directly. In addition, we could assume a reasonable degree of homogeneity between the two couplets, which would gives us confidence in the exposure estimates. This is not the situation in our study.

In our case, a single Canadian I/O couplet has multiple U.S I/O couplets as translations. The validity of exposure estimates for the Canadian couplets, based on the combined probability of exposure among the translated U.S I/O couplets, is questionable due to the imperfect nature of the translation (owing to the differences in the nature of classification schemes in Canada and the U.S). Therefore, assigning such estimates to the subjects in our data could result in bias, including misclassification of exposure. Let us consider the beryllium exposure estimation for the Canadian couplet, 3352-8531, as an example. For this Canadian couplet, the probability of part-time beryllium exposure was estimated to be 0.4% based on the 21 translated U.S I/O couplets found in the JEM as there was no information on the remaining 11 translated couplets (Table 29). Some of these U.S couplets were found as translations for other Canadian couplets (e.g. 16 other Canadian couplets had the U.S couplet 3674-785 as a translation). Therefore, multiple Canadian couplets have contributed to the estimated probability of 0.4%. If we assign this group level probability to our Canadian couplet (3352-8531), an ecological bias will occur due to attribution of exposures at a group level to an individual level (204-206). The magnitude of this bias could be large since there can be hundreds of such imperfect U.S translations. As the probability estimate for part-time beryllium exposure (0.4%) in the Canadian couplet (3352-8531) was based on only 66% of the originally translated U.S couplets (21 out of 32), the validity of this estimate is questionable, unless the existence of these missing occupations is rare. Owing to the hundreds of multiple translations for the Canadian couplets, the probability of an exposure for some of the couplets could even reach zero. The validity of this exposure estimation is questionable due to lack of information about the distribution of U.S couplets within the Canadian couplet. In addition using the probability (actually prevalence) as a surrogate indicator of exposure intensity has an inherent bias as described in the later part of the discussion.

This multiple translation issue can be viewed in a more general manner in the above mentioned example. A positive beryllium exposure was indicated for two of the translated U.S I/O couplets and a null exposure in 19 U.S I/O couplets (see Figure 6). This complicates the task of assigning an exposure status to our Canadian couplet (3352-8531): should we assign a positive exposure or null exposure or an average probability of exposure? Either way, it results in a bias due to ecological assignment of the exposures and misclassification, the direction of which is unknown.

The distribution of the subjects in our data across the translated U.S couplets could also influence the misclassification of exposure. The distribution of the subjects in our data within the translated U.S couplets could be totally different from the distribution of the subjects in the JEM. To understand the misclassification due to differential distribution, let us consider three hypothetical scenarios to estimate the beryllium exposure in the Canadian couplet: 3352-8531 (see Table 30). For all the scenarios considered, let us assume that there are 100 subjects in our Canadian couplet. To simplify this explanation we have considered the exposure as a dichotomous variable (exposed/unexposed). In scenario 1, all the 100 subjects in our Canadian couplet were represented in the two U.S couplets with positive beryllium exposure. If we assign a positive exposure to the subjects in our Canadian couplet, then we are correct in our assignment of exposure. If we define the subjects in our Canadian couplet as unexposed to beryllium, then we are misclassifying the exposure by 100%. In the scenario 2, all 100 subjects in our Canadian couplet are represented in the 19 unexposed U.S couplets.

**Table 30:** Different Scenarios for Exposure Assessment and Misclassification

| | | **Scenario-1** | | **Scenario-2** | | **Scenario-3** | |
|---|---|---|---|---|---|---|---|
| **Canadian couplet** | **US couplets** | Subjects | Misclassification* | Subjects | Misclassification | Subjects | Misclassification |
| 3352-8531<br>(100 subjects) | Positive exposure<br>3673-777<br>3674-785 | 100 | No | 0 | Yes | - | Yes |
| | No exposure<br>19 Couplets | 0 | Yes | 100 | No | - | Yes |
| | No information<br>11 Couplets | - | | - | - | 100 | No |

*Misclassification due to assigning a positive beryllium exposure in the respective group.

In this case, assigning a positive exposure to the subjects in our couplet resulted in 100% misclassification. In the third scenario, all the subjects in our Canadian couplet are represented in the 11 translated couplets that are not found in the JEM. In this case, assigning either a positive or a null exposure to our couplet is nothing more than a guess work. These scenarios are indicate that the bias due to misclassification depends on the distribution of the subjects across the translated U.S couplets. In the similar fashion, misclassification also occurs when we assign the combined exposure probability that was derived from all the translated U.S couplets within a Canadian couplet to the subjects in our data. As we have no information on the distribution of the study subjects within the JEM couplets, we could neither weigh the probability nor comment on the magnitude and the direction bias in our exposure estimates. Moreover, the potential for bias is amplified with the increasing number of translations.

Less prevalent exposures (like beryllium) have fewer exposed subjects, therefore it is commonly used as a dichotomous variable (exposed/unexposed) during exposure estimation and lung cancer risk assessment. The bias resulting from the dichotomous definition of an exposure variable (exposed/unexposed) is paramount. For example, in scenario 1 (see Table 30), by defining the subjects in the Canadian couplet: 3352-8531 as an exposed group, based on the positive exposure in the two U.S couplets found in the JEM (0.4% probability of exposure), we are actually misclassifying 99.6% of the unexposed subjects even if the scenario 1 is true. Alternatively, the probability of exposure could be used as a continuous variable in exposure estimation and lung cancer risk assessment to overcome this difficulty.

Considering the hundreds of multiple U.S translations for a single Canadian couplet, the potential for bias either due to ecological assignment of the exposure estimates or misclassification is expected to be very large for exposure estimation based on the NIOSH-JEM.

**5.5.2.3 Exploration of Alternative Methods of Exposure Estimation**

We have explored an alternative method to use the NIOSH-JEM for exposure estimation in our study. The objectives of this exercise are twofold: 1) to simplify the process of exposure estimation using the JEM; and 2) to explore the potential for bias, including misclassification. To allow the comparison of this approach with the previous method, we have chosen beryllium for exposure estimation.

In this method, we assigned the beryllium exposure in our data based on only the occupations held and the industries worked in, rather than on the combination of industry/occupation. In our example, we started with 9 U.S couplets with full-time beryllium exposure (see Table 28). These couplets represent 7 U.S occupations and 8 industries. Each of these were translated to their Canadian equivalents to identify the only Canadian occupations or industries which could have non-zero beryllium exposure (36 Canadian occupations and 11 Canadian industries).

Based on occupation alone, the subjects in the 36 linked Canadian occupations would be assigned a positive exposure to full-time beryllium; the rest of the subjects would be classified as the unexposed group. This method of exposure estimation would result in 343 exposed subjects (91 cases & 252 controls) out of 12,957 subjects in our data.

Based on industry alone, the subjects in the 11 linked Canadian industries would be assigned a positive exposure to full-time beryllium; the rest of the subjects would be defined as the unexposed group. This method of exposure estimation would result in 61 exposed subjects (12 cases and 49 controls) in our data.

Attributing the beryllium exposure based on the occupations and the industries would result in 3% and 0.5% exposure among the subjects in our data, respectively. These differences in the beryllium exposure estimates indicate a problem with this alternate approach to exposure estimation. Assessing the lung cancer risk based on these estimates will result in unreliable risk estimates, indicating a potential for bias. A significant positive association between beryllium exposure and lung cancer was suggested in the analysis based on the occupations (OR=1.5, 95% CI: 1.1-1.9), whereas the analysis based on the industries indicated no association (OR=1.1, 0.5-2.1).

This exercise also illustrated the bias (ecological effect) resulting from ignoring the couplets during exposure estimation. Our previous approach with couplets indicated no full-time beryllium exposure among the subjects in our study, whereas exposure assignment based on the occupations and the industries indicated a positive beryllium exposure for some subjects. Therefore, exposure estimation based on occupations or industries alone overestimated the exposure prevalence. For example, in our previous analysis, a positive part-time beryllium exposure is suggested for the Canadian couplet, 3352-8531. Assigning the beryllium exposure based on the Canadian occupation-8531 defines all the 7 I/O couplets with this occupation as positively exposed to beryllium, thereby raising the potential for ecological bias to a greater degree than in the couplet level analysis.

Although these alternative methods of exposure estimation are simpler than couplet level analysis, the potential for bias resulting from the ecological assignment of exposure could be larger than the couplet level analysis, thereby rendering these methods unattractive for exposure estimation.

### 5.5.3 Inherent Limitations of the NIOSH-JEM

Certain inherent limitations of the NIOSH-JEM have been observed. All the occupations and industries in our dataset are not represented in the JEM. Therefore, the exposure predictions from the JEM could not be translated in entirety raising the possibility of bias.

Using the probability of exposure as a surrogate indicator for the intensity of exposure has inherent limitations. In the NIOSH-JEM, the probability estimates are actually prevalence measures in an I/O group that are subject to sampling of the study population. In addition, all the members in an I/O group need to be assigned a fixed probability of exposure, again raising the potential for bias. The actual exposure profile could vary among the workers in the same I/O group. The probability of exposure is not very informative when it was based on few subjects. Usually, we have more confidence in the probability estimates (of exposure) when they are based on large number of subjects rather than few subjects. For example, the probability estimate for beryllium exposure in the U.S couplet 3069-725 (100% probability) was based on only two subjects, while the probability estimate in the U.S couplet 3829-777 (98%) was based on 43 subjects (see Table 28). We can place a greater confidence on the later estimate. In general, the I/O couplets with a high probability of beryllium exposure contained few subjects, rendering the probability measure less informative. Similar limitations were noted in other studies that used the NIOSH-JEM for exposure estimation (190;191). One study that looked at the occupational exposures in relation to birth defects using the NIOSH-JEM noted less number of subjects in the high probability I/O categories (190).

The time frame of the NOES survey (1980-1983) should be considered while applying the NIOSH-JEM. There is a possibility of confounding due to temporal changes in the occupational settings. For example, improvements in industrial hygiene measures in recent times have reduced the carcinogenic exposures present in the workplace; as a consequence, application of the older NIOSH-JEM that was based on the NOHS (1972-1974), could result in erroneous exposure estimates (191). Confounding due to temporal effects may not be a major issue in our study, considering the relatively compact study period (1983-1990).

The extrapolation of the U.S based NIOSH-JEM to our BC data could result in a bias due to variations in the distribution of various occupations and industries.

Validity of the NIOSH-JEM has been evaluated on many occasions (190;191;207). In metal manufacturing industries the exposure assessment based on the NIOSH-JEM and self-reports was compared to expert based exposure assessment for three metals- copper, lead, and iron (193). The agreement between the NIOSH-JEM and the experts for the assessment of copper, lead, and iron was 81.5%, 86%, and 69.2%, respectively. Moreover, the JEM did not fare better than the assessment based on self-reports (193). When the NIOSH-JEM was applied to the Slone Epidemiology Unit Birth Defects Study (BDS) for exposure assessment, the authors did not find it useful (190). In addition, the authors evaluated the performance of the JEM by comparing its predictions with expert based exposure assessment. They noticed a low level of concordances for exposure estimates for benzene (69%) and xylene (59%). In the same study a known association between benzene and kidney malformations was evaluated by using the exposure predictions from the NIOSH-JEM. Out of the 38 cases and 3748 controls, the

JEM assigned benzene exposure to 13 cases and 612 controls. An odds ratio of 3.2 (95% CI: 1.5-6.8) was detected, thereby confirming the known association between maternal benzene exposure and kidney malformations. Furthermore, the authors noted certain non-sense exposure predictions by the JEM (190).

### *5.6 Conclusions and Future Directions*

After considering the logistical difficulties in manually translating hundreds of couplets, and the potential for bias during exposure estimation, we decided that a JEM analysis of exposure to individual agents in the present was infeasible at this time. Our experience with the JEM suggests that a common coding system for occupations and industries is a necessity for linking a JEM to another dataset. The lack of a common coding system for the occupations and the industries in our data and the JEM has restricted our exposure assessment. As a couplet level translation is not available to translate the Canadian couplets to the U.S couplets, we instead translated the occupation and industry in a Canadian couplet, and combined them to obtain a list of translated U.S couplets; this strategy did not prove useful. To achieve a reliable method of assessing exposure to individual agents in our study, we need to develop a new JEM or undertake expert based exposure assessment. Alternatively, development of a couplet level translation would allow us to use the NIOSH-JEM for exposure estimation. All these options are out of the scope of this thesis.

Although, we have encountered several limitations during the application of a JEM, some changes in the JEM structure and exposure measurement strategy will render it a more useful tool for exposure assessment.

Using a common coding system could make a foreign JEM transportable across nations, thereby facilitating exposure estimation. Our observations do not support the use of translation as an alternative, owing to the potential for bias and logistical difficulties.

The major limitation of a job-exposure matrix is its potential for misclassification of exposure. Certain improvements in the JEM could minimize the potential for such misclassification. During the development of a JEM, expert assessment could be used to identify workplace exposures. Alternatively, recording the actual exposure levels in an occupation/industry could further minimize the extent of exposure misclassification. In the recently developed Finnish-JEM, both prevalence and the level of exposure measures were available for exposure estimation in an occupation (184).

Temporal changes need to be considered during exposure assessment. Adding a time component in the JEM structure will allow us to monitor exposures over time, thereby aiding in hazard surveillance. In the Finnish-JEM, a temporal component was included in the JEM structure, in addition to the level of exposure (184).

A JEM could be the only alternative for the exposure assessment in large population based occupational studies, where expert assessment is usually impractical. Therefore, efforts to improve the JEM should be continued. In Canada, the development of a job-exposure matrix taking into account afore mentioned improvements could serve as a useful tool not only for exposure assessment, but also for the hazard surveillance. We expect that our practical discussion will contribute to the improvements in the JEM in future research, especially, in the Canadian occupational setting.

# 6. Discussion

In this study, we have examined the risk of developing lung cancer in regard to work experience in a wide range of occupations and industries. We observed an elevated risk of lung cancer for many occupations and industries, mainly those involving exposure to various metallic substances. These occupational circumstances included: metal processing occupations, metal machining occupations, and mineral ore treating occupations, primary metal manufacturing industries (such as iron, steel), and certain metal mining industries (notably copper). Certain occupations in the transport sector (ship deck crew, and subway & street railway operating occupations) were also associated with an increased risk of lung cancer. We also observed a higher risk of lung cancer for certain occupations in food sector, mainly those involving food processing and service (including cooks, bakers). We identified certain high risk occupations and industries that are specifically associated with some histological types of lung cancer (adenocarcinoma, squamous cell, small cell, and large cell carcinomas) but not to the overall risk for all the types of lung cancer combined. These occupational circumstances included: various occupations within construction industry (e.g., insulators, carpenters), and occupations in medicine & health (e.g., doctors).

## *6.1 Occupational Lung Cancer*

Our analyses identified several high risk occupational circumstances for lung cancer. The majority of our study findings are consistent with the available occupational literature. Some of these occupations and industries have features and risk factors in common. For the purpose of this discussion, closely related occupations and industries are described as a group.

### 6.1.1 Metallurgical work

Our study found evidence for an elevated risk of lung cancer in a number of occupations and industries related to mining and metal working – a finding corroborated by the majority of the occupational literature (7;16-18;20;21;24;26-36;41;105;107;119;120;208-211). Workers in these industries are primarily involved in the extraction and processing of the metals. While these occupational circumstances share some risk agents (e.g., airborne exposure to silica, some metals, asbestos), an examination of the risk agents and the literature suggests that the etiologically relevant agents are likely different in different occupational circumstances. For example, workers in the steel manufacturing industry are exposed to high levels of PAHs (predominantly released from coke ovens), silica, and airborne metallic fumes & acid mists (14;112;114) while uranium miners are exposed predominantly to radon (14;41;122;123). Similarly, exposure to coal tars and pitches are etiologically important agents for workers in aluminum production industry (14). The majority of these risk agents were known lung carcinogens (14;112;114;116;122;123;212). These examples suggest that the actual metal processed need not be the etiologically important agent for the observed lung cancer risk in some jobs. However, metals remain as important target etiological agents for lung cancer (14). Exposure to high levels of metallic substances, in the form of fumes or dusts, occurs during the smelting of metals (e.g., exposure to arsenic & its compounds in non-ferrous metal smelting, hexavalent chromium compounds during chromate production etc.) (14;51). These metallic exposures were associated with an excess risk of lung cancer (14). These examples also show that exposure to metallic substances depends on the metal processed. These findings further support our hypothesis of diversity in etiological factors within the occupations in metallurgical industries, rather than a single common exposure.

We observed a significant excess of lung cancer risk in the occupations involved in mineral ore processing, but not in the occupations involving mining and quarrying. Therefore, the observed risk of lung cancer in the mining industries (copper, copper-zinc mining) was influenced mostly by ore processing (dressing and beneficiating) in the BC population. Exposure to dust (containing silica, inorganic acid mists etc.) during ore processing had been suggested to be responsible for the excess risk of lung cancer in the mining industry (213;214). This warrants directing the public health efforts to reduce dust exposure in mineral ore processing occupations.

### 6.1.2 Transportation

We observed an elevated risk of lung cancer in workers employed as deck crew of ships and subway rail operators. In addition, we observed a higher risk of squamous cell carcinoma among workers in water transport industry. Engine exhausts (e.g., diesel emissions) are a common exposure in these occupations, which might explain the increased risk. Previous studies that have attributed the excess risk of lung cancer among transport workers to diesel emissions supporting our hypothesis (27;30;53;54;215). In fact, diesel emissions have been identified as probable human carcinogens, with evidence being suggestive for lung carcinogenicity (14;115).

The literature provides evidence to support higher lung cancer risk in some transport workers (e.g., drivers, and rail transport workers), but not among workers in water transportation (16;17;20;21;24;26-35;52;107). Therefore, there was no direct evidence to support our findings. The reasons for this contrasting observation could be due to the variations in the definition of exposure (i.e., broad occupational groupings in other studies), or variations in distribution of etiological agents in different populations (i.e., the exposure profile may vary depending on the regulations and practices within a country/province). However, the observed high risk among workers in the water transport industry in our study and another Canadian study (26) suggests that there may be a risk specific to Canadian setting, which needs to be addressed in further studies.

### 6.1.3 Food Sector

We found an elevated risk of lung cancer for men employed in certain food processing occupations (e.g., baking, confectionary making) and food service occupations (e.g. cooks, chefs & bartenders, but only for large cell carcinoma). This is consistent with epidemiological evidence showing an excess risk in these occupations (18;19;21;27;28;31;33;35). Cooking fumes are an important common exposure in these occupations; however, environmental tobacco smoke may also be an important exposure in bartenders. Cooking fumes are generated either from the cooking oil or cooking fuel. These fumes were found to be responsible for the excess risk of lung cancer observed among women who were primarily responsible for household cooking in India and China (216-218). The applicability of these results to the Canadian setting is unclear since there are major differences in cooking practices in North America, including: better ventilation and greater use of electricity or gas. These would tend to reduce exposure to cooking fuel by-products (219). Nonetheless, our observation warrants further investigation in future studies to confirm our findings and identify the specific risk agents.

### 6.1.4 Utility Industries

Our study found evidence for an elevated risk of lung cancer among men employed in utility industries; the risk is predominantly seen among workers in the electric power systems industry. Exposure to electromagnetic fields is common in these occupations (220-222). There is a body of evidence supporting the observed high risk in electric utility workers (20;26;223). However, previous studies were unable to link the excess risk of lung cancer to electromagnetic field exposure (220-222). The Canadian SIC does not differentiate utility workers by the source of power generation (hydro, thermal, or nuclear). Instead, all the workers are treated as a single group. Further research should examine the risk associated with specific power sources.

### 6.1.5 Painters

Our study observed no increased risk of lung cancer among painters. Although we observed an isolated increased risk among workers in paint and body repair shops, we could not attribute the risk of lung cancer to painters alone in this job. These null observations are in contrast to the published literature, which suggests an excess risk of lung cancer among painters (18;21;27;29;31;34;107;224;225). The IARC has concluded that "occupational exposure as a painter is carcinogenic (Group-1)" (108). The risk might relate to exposure to solvents and metal based antirust paints (108). However, exposure to other potentially carcinogenic substances have also been noted (e.g., asbestos, PAH, and metallic substances) (226). The observed null association could be explained in general by the high safety standards in Canada. In our study, the unexposed group contained all the occupations other than painters; therefore, the unexposed group contained certain high risk occupations. These high risk occupations in the unexposed group might have diluted the odds ratio estimates in painters towards null. Therefore, the negative findings in our study should be interpreted with caution.

### 6.1.6 Protective Effects

While most of the emphasis in occupational studies of cancer is directed at finding factors which increase risk, we did observe some occupations which appeared to be associated with a lowered risk of lung cancer. Teachers (especially in secondary schools) and sales workers showed a significant reduction in the risk of lung cancer. We speculate that the healthy lifestyle habits (e.g., non-smoking, healthy diet) are possible reasons for such an effect. While a body of scientific literature indicated either protective effect (21;27;30;37) or no risk (18;19;26;31-33) for teachers, the evidence is inconsistent for sales workers with some studies showing positive (16;31;34;37;107), protective (27;30;32), and null associations (21;26;29;33;34). These results should be interpreted with caution, for the same reasons mentioned in the previous section.

## *6.2 Results Specific to Histological Subtypes*

The large sample size and availability of histological information on the lung cancer cases allowed us to undertake analyses within histopathological subtypes. There is limited information on histopathological risk factors in the literature, since most occupational studies lack appropriate information on histopathology. We have examined the risk of developing the four major histopathological types of lung cancer (i.e., squamous cell, small cell, and large cell carcinoma as well as adenocarcinoma) in regard to work experience in a wide range of occupations and industries. While the reduced sample size for the histopathological-specific analyses would reduce power to detect elevated cancer risks, the greater homogeneity of the outcome group will increase the potential to detect associations that were diluted in the combined analysis of all types of lung cancer, thereby increasing the sensitivity of the study (227). In our study, the excess risk of lung cancer among men employed in medical occupations and construction industry was revealed only in the analysis on histopathological subtypes.

### 6.2.1 Construction Work

Our histological analysis revealed an increased risk of lung cancer among men employed as carpenters, insulators, electricians, excavators, pavers and graders in the construction industry. The histopathological relationships differed among various occupations within the construction industry; however, the majority of occupations were linked only to squamous cell cancer of lung. For example, we observed an elevated risk of squamous cell carcinoma in carpenters, excavators and pavers, while men employed as insulators had an increased risk of adenocarcinoma of lung. Although exposure to the dust containing asbestos and silica seems common in the construction industry, the predominant and the etiologically relevant exposures in the individual occupations are likely different (e.g., wood dust in carpenters, PAH in pavers) (14;21;46;127;228;229).

Among carpenters, the risk of squamous cell lung cancer was elevated in our study, while the literature suggested an excess risk of both squamous cell cancer (26) and adenocarcinoma (17;21) in this group. Exposure to wood dust is common in this group (21;228;230). Wood dust has been identified as a definite human carcinogen by the IARC, based on strong evidence for an excess risk of sinonasal cancer (228). The epidemiological evidence suggests an excess risk of lung cancer with wood dust exposure; however, definitive evidence is lacking to prove causality (228;230).

We observed an elevated risk of adenocarcinoma among insulators – a finding corroborated by a body of scientific literature (17;27;33;231). Exposure to asbestos has been observed for this group (14;112). Asbestos has been linked to the occurrence of adenocarcinoma and other types of lung cancer (46;232). In addition, asbestos is a known lung carcinogen (14;112), thereby explaining the excess risk among insulators.

Certain occupations involving exposure to PAH, silica & asbestos (i.e., excavating, grading & paving activities) were associated with an excess risk of lung cancer (squamous cell & large cell types) in our study, in agreement with the literature (26;229). We also observed an excess risk of small cell cancer among electricians, consistent with the body of literature that observed an elevated risk of lung cancer in this group (7;31). Electricians may be exposed to electromagnetic fields, asbestos, and metallic substances (112;121;233). Small cell carcinoma has the worst prognosis of all lung cancer types, warranting extensive means to identify & reduce exposure to risk agents among electricians (55).

### 6.2.2 Workers in the Medical and Health Fields

Our study found evidence for an elevated risk of lung cancer (large cell type) among men employed in medicine, health and related occupations. This risk was predominantly seen among doctors (physicians & surgeons), who share some common exposures (i.e., formaldehyde and radiation) that are associated with an increased risk of lung cancer (14;155;234). Although some published studies have found an excess risk of lung cancer among workers employed in medicine & health related occupations (26;107), the majority of published studies have found either a protective effect or no risk (21;27;30-34;37). Lack of histopathological evaluation of medical occupations could be possible explanation for the observed null associations in the majority of studies. Siemiatycki et al (26) found an excess risk of adenocarcinoma of the lung among medical workers in Montreal; however, they did not study large cell carcinoma as a separate entity. Nonetheless, the histological analysis in our study and the Montreal study found evidence for excess risk of lung cancer among Canadian medical workers, thereby emphasizing the need for further evaluation of this occupational group to confirm these findings and to identify potential risk agents.

In our study, we noticed that some occupations were associated with all the histological types of lung cancer, while some occupations were associated only with specific histological types. For example, working in the metallurgical industries was associated with all the types of lung cancer, while working in occupations involving product fabrication, water transportation, and electric power generation was predominantly associated with squamous cell carcinoma. Therefore, future studies should focus on identifying the risk agents that are specific to histological types based on these occupational risk factors. Such an investigation will not only increase the sensitivity of occupational study (for identifying risk agents), but also contribute useful information to better understand the natural history of lung cancer.

## *6.3 Methodological Considerations*

### 6.3.1 Strengths

The large sample size was one of the major advantages of this study. Furthermore, all cancer cases were pathologically confirmed incident cancer cases. This study collected information on lifetime occupational history for all the subjects. In addition, individual level information was available on key potential confounders: smoking, age, year of diagnosis, marital status, education status, ethnicity, and alcohol consumption. Hence, we were able to control for key confounding variables, unlike many other studies. The large sample size in this study enabled the evaluation of occupational lung cancer risk for specific occupations and industries according to SOC/SIC codes rather than within only broad occupational groups. The availability of histopathological information for all cases enabled the evaluation of occupational lung cancer risk for the histological subtypes, which was lacking in the majority of occupational studies.

### 6.3.2 Limitations

Despite these strengths, there were a number of serious methodological weaknesses which limit the interpretability of this study. The most important of these concerns the use of cancer patients without lung cancer as control subjects and multiple comparisons.

#### 6.3.2.1 Cancer controls

The standard approach for control selection in a case-control study involves selecting a representative sample of individuals from the general population. In this study, no cancer-free control group was available; therefore, we had to construct the control group from cancer cases other than lung cancer. The use of other cancer cases as controls might introduce biases into the study. At a general level, the selected control group might not be representative of the general population. For example, some of the cancers in the control group and the case group (lung cancer) could have certain occupational risk factors (occupations and industries) in common. In that case, we would underestimate the true effect for a positively associated risk factor. However, this bias is unlikely as it was noted that the majority of known carcinogens were not associated with multiple cancers (49;173). In addition, inclusion of different cancers in the control group could minimize or dilute this bias when an occasional association occurs between exposure of interest and certain cancers in control group (235). Therefore, our approach could be considered as a conservative approach.

Using other cancer cases as controls can have some advantages over general population controls, especially with respect to information bias (recall bias and interviewer bias) (235-239). Cancer patients often ruminate on the past life events to find possible explanation for their illness and are motivated to give more details than general population controls. In contrast, healthy population controls are generally less motivated to recall past life events, leading to recall bias. A similar bias can arise when interviewers assigned to cases delve deeper in to the details to find a possible cause for the illness. Blinding the interviewers to case or control status could theoretically minimize this bias; however, it might be difficult to achieve this blinding in actual research as patients could easily hint their illness during interview (236). No such bias should occur with cancer controls since all subjects have been diagnosed with cancer and thus should be equally diligent in reported past events (236). Owing to these advantages of cancer controls, Siemiatycki et al (26) preferred the cancer controls over general population controls in the Montreal occupational study (26). The majority of hypothesis generating occupational studies, like our study, used cancer controls as a reference group (7;19-21;26;28;34;107).

#### 6.3.2.2 Multiple Comparisons

Many individual comparisons were considered in this study, opening the door for the problem of multiple inferences. When a single hypothesis is considered with a null hypothesis (and the determinant not related to the outcome), the p value of 0.05 (two-sided) indicates the probability of false positive finding. The interpretation is straight-forward in this situation. However, when multiple comparisons are conducted in a study the false positive rate is no longer 5%. When many comparisons are addressed in a study, there is a possibility of falsely rejecting the null hypothesis with each additional hypothesis. A Bonferroni correction could be introduced to address this issue: when a study considers 'N' tests then the alpha for global null hypothesis (none of the determinants were associated with the outcome) for the entire study should be alpha/N. This will compromise the statistical power, rendering the detection of any true association less likely. However, it should be noted that the above considerations were testing a global hypothesis. In this study, we have evaluated each individual occupation or industry as if it was a separate study. Therefore, the evaluated associations should not be affected by multiple comparisons, as indicated by Siemiatycki et al. (26). In our study, about 8% of the total analyses performed were significant; therefore, chance alone could not explain these findings. However, this study should be considered as a hypothesis generating research rather than a hypothesis testing project.

**6.3.2.3 Exposure Assessment**

In our study, the subjects were classified as 'exposed' and 'unexposed' based on SOC and SIC codes: the subjects other than those employed in the occupation/industry under evaluation constituted the unexposed group. Therefore, the unexposed group included subjects who worked in other high risk occupations/industries. This could result in an underestimation of the odds ratios, rendering our positive findings more conservative. However, caution should be exercised while interpreting the negative results in our study.

The majority of subjects in our study worked in more than one job during their lifetime. Therefore, it was necessary to combine this information on multiple jobs held by the same subject in a meaningful manner. The literature had indicated various modalities of exposure classification based on job histories. Some of the studies used 'longest' job held as an exposure measure (26;31;34;107) while, others used either 'any' employment in an occupation/industry (16;18;20;27;30), or the last held job as an exposure measure (240). One study used computer simulation and empirical data to compare different exposure definitions ('only', 'ever', 'longest', and 'last' employed in a work area) to evaluate lung cancer mortality among rubber industry workers (241). It concluded that the results were valid but imprecise for 'only' employment as a surrogate indicator, while no major differences were observed in the risk estimates based on other surrogate indicators of exposure (241). In some studies the 'longest' held job was used as a standard reference to validate the use of other exposure definitions (e.g. recently held job) as a surrogate measure (242).

It is a known fact that the development of lung cancer requires long term exposure to carcinogens (due to the long latency period). Therefore, an exposure definition based on the 'longest' job held should be etiologically more relevant than the other exposure definitions based on 'any' or 'last' job held. However, the use of 'a job ever held' as a surrogate indicator of an exposure could be particularly useful in a situation where there was an exposure to a massive dose of carcinogenic substance at a single point of time. Such an exposure occurs mainly due to industrial disasters; for example, exposure to massive doses of methyl isocyanate during the Bhopal gas tragedy in India (1984) (243), and exposure to high doses of ionizing radiation during the Chernobyl nuclear disaster in Ukraine (1986) (244). Such incidents are rare in the occupational settings and we are not aware of any such occupational disasters in British Columbia.

After considering the above evidence, we preferred combining the information on multiple jobs by using the 'longest/usual' job held by the subjects. In addition, as a supplementary analysis, we also used 'any' job held ('ever' category) by the subjects for combining the information on multiple jobs with an intention to make our results comparable to previous studies. Moreover, the exposure definition based on a job 'ever' held could be useful in providing clues on occupational lung cancer risk, especially when the sample size restricts the analysis based on the 'usual' occupation/industry (e.g. uranium miners). However, it should be acknowledged that the use of a job 'ever' held as an exposure indicator could result in confounding due to the heterogeneity of the job related exposures in multiple jobs; the risk estimates could either be overestimated or underestimated. For example, if a long-term miner for 15 years is included in the analysis of teaching related occupations because he also had a short term employment as a teacher, it could result in overestimation of risk among teachers. In general, our analysis based on the 'usually' employed occupations/industries, and their corresponding 'ever' employed categories yielded similar results. However, we noted discrepant results for some of the specific occupational/industrial categories. These discrepancies could be due to the confounding effect of multiple jobs (in the 'ever' category) as mentioned above, or due to differences in the sample size. Our preferred analysis for this study has always been the analysis based on the 'usually' employed occupations/industries for the reasons mentioned above.

### 6.3.3 Other Methodological Considerations

Since smoking is a very strong predictor of several cancers and might be related to occupation, we were concerned that including smoking-related cancers in the control group could bias the results. We addressed this through the creation of a second control group, which excluded smoking related cancers. The concordance for the estimates for the two control groups was generally good. Excluding smoking-related cancers from the control group (control group 2) led, in general, to somewhat larger point estimates and broader confidence intervals for the estimates. This could be due to variation in the sample size or due to diluting effect of smoking related cancers in the control group-1.

However, the choice of control group did not affect the main conclusions of this study. We preferred using the results from second control group for the following reasons: an ideal situation demands that a control group should include only those cancers that are not associated with the exposure of interest; our second control group comes close to this assumption (213;245). In addition, we expected that the second control group might achieve better adjustment for residual confounding by smoking.

Conditional logistic regression is used when the number of matching variables is large (170). Some of the previous occupational studies used conditional logistic regression after matching on age and/or year of diagnosis in the evaluation the cancer risk (27;30;171;172;246), while others used unconditional regression (7;18;20;24;28;34;107). To evaluate whether conditional models were required for this study, we performed both conditional (stratified on age and year of diagnosis) and unconditional models (adjusted for age and year of diagnosis) for a selected list of occupational exposures (occupations and industries). We also adjusted for key confounders identified from the literature. We noted similar results in both conditional and unconditional analyses. The odds ratio estimates were very similar in both the models. The conditional model has somewhat lower power than the unconditional due to the large number of uninformative strata for age. Actually, the BC study was an unmatched study so the study design per se doesn't mandate the use of conditional models. For the above mentioned reasons and to assist in the interpretation of the results, we preferred using unconditional logistic regression analysis. Based on our analysis, we could further conclude that using age as a covariate in an unconditional model provides an adequate adjustment for the effects of age.

Information on smoking history can be used to model smoking in many ways, ranging from a simple qualitative model (current, ex- and never smoke) to a complex quantitative model that takes in to account either duration or intensity or both (e.g. pack-years), or a combination of all these variables. A simple qualitative modelling of smoking history (current, ex-, and never) has been shown to control the confounding effect of smoking in occupational studies on lung cancer (247). Pack-years, a combined measure of duration and intensity of smoking was also adequate to control for smoking related confounding. Although adding other smoking parameters (e.g. duration, qualitative smoking status) to a pack-years model might achieve a better fit, the advantage would be minimal owing to the robustness of the pack-years model in controlling smoking related confounding. The residual confounding of smoking, if any, would be minimal to affect the results of our study.

Proxy respondents (spouse or closest relative) provided the information on 28% of cases and 18% of controls in our study. Proxy response tends to underestimate exposure. Therefore, it is likely that the proxy responses would dilute the true effect rendering our odds ratio estimates conservative.

# 7. Conclusion

Overall, our study findings are in agreement with the literature. We observed an elevated risk of lung cancer, particularly with metallurgical work involving exposure to various carcinogenic metallic substances, asbestos, silica and PAH. Our study confirmed the importance of histopathological evaluation by identifying the high risk occupational circumstances that were missed in the combined analysis. These occupations included: medical doctors, and various occupations in the construction industry. Future studies should focus on confirming the lung cancer risk and identifying key exposures in medical workers, electricians, carpenters, chefs & cooks, bakers and water transport workers. Furthermore, the lung cancer risk associated with wood dust, electromagnetic fields, and formaldehyde exposures should be confirmed in future studies by taking into account the intensity of exposure

We attempted to evaluate the occupational exposures (risk agents) using the NIOSH-JEM. But, we were limited in applying the JEM to our dataset due to different occupational coding system in the NIOSH-JEM and the BC data. The use of a translation rubric to convert the Canadian occupation and industry codes to their US equivalents did not prove useful because of logistical difficulties and the potential for bias during exposure estimation. We strongly recommend the development of a Canadian job-exposure matrix.

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# APPENDICES

# Appendix-1: Histological Classification of Malignant Primary Lung Cancer

## WHO Classification (Codes applicable to ICD-O 1st edition):

**Squamous cell carcinoma:**
8050/3 Papillary carcinoma, NOS
8051/3 Verrucous carcinoma, NOS
8052/3 Papillary squamous cell carcinoma
8070/3 Squamous cell carcinoma, NOS
8071/3 Squamous cell carcinoma, keratinizing, NOS
8072/3 Squamous cell carcinoma, large cell, nonkeratinizing
8073/3 Squamous cell carcinoma, small cell, nonkeratinizing
8074/3 Squamous cell carcinoma, spindle cell
8075/3 Adenoid squamous cell carcinoma
8076/3 Squamous cell carcinoma, microinvasive

**Adenocarcinoma:**
8140/3 Adenocarcinoma, NOS
8211/3 Tubular adenocarcinoma
8230/3 Solid carcinoma, NOS
8231/3 Carcinoma simplex
8250/3 Bronchiolo-alveolar adenocarcinoma
8251/3 Alveolar adenocarcinoma
8260/3 Papillary adenocarcinoma, NOS
8323/3 Mixed cell adenocarcinoma
8480/3 Mucinous adenocarcinoma
8481/3 Mucin-producing adenocarcinoma
8490/3 Signet ring cell carcinoma
8550/3 Acinar cell carcinoma
8560/3 Adenosquamous carcinoma
8570/3 Adenocarcinoma with squamous metaplasia
8571/3 Adenocarcinoma with cartilaginous and osseous metaplasia
8572/3 Adenocarcinoma with spindle cell metaplasia

**Small cell Carcinoma (SCC):**
8041/3 Small cell carcinoma, NOS
8042/3 Oat cell carcinoma
8043/3 Small cell carcinoma, fusiform cell

**Large cell carcinoma:**
8012/3 Large cell carcinoma, NOS
8020/3 Carcinoma, undifferentiated, NOS
8021/3 Carcinoma, anaplastic, NOS
8022/3 Pleomorphic carcinoma
8030/3 Giant cell and spindle cell carcinoma
8031/3 Giant cell carcinoma
8310/3 Clear cell adenocarcinoma, NOS

**Note:** Codes 8044 & 8045 are exclusive to ICD-O 2nd edition, therefore these codes are not included in SCC.

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