

The Economic Burden of Occupational Cancers in Alberta

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Executive summary

Background

There has been an increasing focus worldwide on identifying and preventing occupational (or work-related) cancers. These prevention efforts have been driven by several factors, foremost among which is the understanding that occupational cancers are largely preventable. They can also be seen as unfair, in that they result from involuntary exposures among employees. It has been argued that preventing such exposures is more ethical, effective and enforceable when the primary responsibility rests not with workers but with the manufacturers and distributors of known and suspected carcinogenic substances and with employers that use them. Furthermore, occupational cancers are costly; a 2003 study estimated that the direct and indirect cost of the most prevalent occupational cancers in the United States was over US\$4 billion.

Occupational cancer refers to cancer cases that would be eliminated if exposure to carcinogens in the workplace were completely removed. Studies conducted worldwide have estimated that between three per cent and 11 per cent of all cancer deaths, and a higher proportion of cancer cases, may be caused by occupational exposure to carcinogens. The cancers that are most strongly associated with occupational exposure include mesothelioma, lung cancer, bladder cancer, non-melanoma skin cancer and leukemia.

Unfortunately, few studies that have been undertaken on the numbers or costs of occupational cancers are directly applicable to Alberta. With a significant proportion of the Alberta working population employed in occupations such as painting, construction and metalwork with a known risk of exposure to carcinogens, information on the cancer burden experienced by the Alberta workforce is greatly needed. Cost information is also crucial to justifying, developing and carrying out effective prevention strategies.

This study attempts to fill the information gaps identified above by providing an assessment of the burden of occupational cancers in Alberta, including both the numbers of workplace-related cancers and an estimate of their associated economic costs. The findings from this study will enable Alberta Health Services (AHS) to develop a better understanding of the economic burden of cancer in the province and to develop appropriate prevention strategies that enhance the current and future health of Alberta's workforce.

Purpose of this study

The overall aim of this study was to generate an estimate of the economic burden of occupational cancers in Alberta. A number of specific objectives were met by conducting the study. These were

- to estimate the current number of occupational cancers in Alberta
- to estimate the direct and indirect costs associated with these cancers
- to identify recommendations for the development of a comprehensive occupational cancer prevention strategy for Alberta
- to present a framework that will allow AHS to better understand the business case (costs and benefits) of implementing a future prevention strategy

Study findings

The burden of occupational cancers in the province is significant. Based on the current analysis, the research team's best estimates indicate that 761 new occupational cancers develop in Alberta every year, and that there are over 2,700 people in the province who are currently living with cancer due to occupational exposures. These estimates may be as low as 217 new cancers per year and 786 current cases, or they may be as high as 1,520 new cancers per year and over 5,400 current cases. The costs associated with these cancers are similarly high. The direct cost to the medical system is estimated to be approximately \$15,682,000 per year. These direct medical costs refer to out-of-pocket expenditures by the government for the costs of treating these cancer patients. In addition, indirect costs—resulting from loss of economic resources and reduced productivity—are estimated at approximately \$64.1 million per year.

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The direct cost to the medical system is estimated to be approximately \$15,682,000 per year.

Strategies for prevention

Strategies relevant to the reduction of occupational cancer in Alberta are provided in the report. Specific recommendations are discussed that relate to high-level approaches to preventing occupational cancer and to improving the process of estimating numbers and costs of occupational cancers. Several key considerations emerged:

- Prevention and control of exposure to occupational carcinogens is most effective if confronted as close to the source as possible: at the level of the workplace rather than the worker.
- The process by which cancer prevention strategies are translated into action needs to involve a broad array of stakeholders including regulators, interest groups and employers, and must be weighed against scientific evidence and feasibility considerations.
- A focus on occupational cancer prevention in the workplace may have a spinoff effect in reducing carcinogen exposure in other populations outside the work setting.
- There is a critical need to improve understanding of occupational exposure to carcinogens in the province. Exposure information specific to Alberta is almost completely lacking at this time, meaning that we have little understanding of what proportion of the Alberta workforce is exposed to carcinogens, which carcinogens they are exposed to, and what sort of protective equipment or measures are being used. This information is critical both for improving estimates of cancer burden in the province and, more important, for developing appropriate intervention strategies that will provide a return on investment.
- An improved method for ascertaining the occupational history of cancer patients is also a key component in understanding workplace carcinogens, developing effective prevention strategies, and demonstrating changes in the rates of occupational disease.
- A point of agreement among many occupational cancer prevention experts is that action should not wait for definitive evidence when there are known and proven interventions available.

Conclusions

This report describes the current understanding of what comprises an occupational cancer, presents results on the number and economic costs of occupational cancers in Alberta, and discusses considerations relevant to cancer prevention in the province, including target areas, costs and benefits, and overall approaches.

The research team found that occupational cancers in Alberta are numerous and costly; however, these cancers are also preventable. There exists the potential for reducing cancer incidence, reducing medical costs and lost productivity associated with these cancers, and improving the lives of Albertans.

SECTION 1. Introduction

Background

There has been an increasing focus worldwide on identifying and preventing work-related cancers (Rushton, 2009). These efforts have been driven by several factors, foremost among which is the understanding that occupational cancers are largely preventable (Cherrie, 2009; Clapp, Jacobs, & Loechler, 2007). Occupational cancers can also be seen as unfair. They result almost exclusively from involuntary exposures, and very often it is “blue-collar” workers who bear the brunt of exposure. It has been argued that preventing such exposures is more ethical, effective and enforceable when the primary responsibility rests not with workers but with the manufacturers and distributors of known and suspected carcinogenic substances, and with employers that use them (LaMontagne & Christiani, 2002). Furthermore, occupational cancers are costly: a 2003 study estimated that the combined direct and indirect costs of the most prevalent occupational cancers in the United States were over US\$4 billion (Leigh, Yasmeeen, & Miller, 2003).

Studies conducted worldwide have estimated that between 3% and 11% of all cancer deaths, and a higher proportion of cancer cases, may be caused by occupational exposure to carcinogens (Fritschi & Driscoll, 2006; Nurminen & Karjalainen, 2001; Rushton, 2009). The variation between study findings arises from several factors, including differences in study methodology, differences in the carcinogenic agents examined, and differences in exposure patterns in the population being studied. However, although the estimates differ in magnitude, the patterns of association found between workplace exposures and cancer development are generally similar (Rushton, 2009), with certain cancers—including mesothelioma, lung cancer, bladder cancer and leukemia—demonstrating the strongest links (International Agency for Research on Cancer [IARC], 2008).

Few of the studies that have been undertaken are directly applicable to Alberta, because of significant differences in the composition of the working population, the cancer profile across the general population, or differences in working conditions that would affect carcinogen exposure. With a large number of Albertans employed in occupations—such as painting, construction and metalwork—with known risk of exposure to carcinogens (Rushton, Hutchings, & Brown, 2008), information on the cancer burden experienced by the Alberta workforce is greatly needed.

In addition, it is important to be able to estimate the direct and indirect costs of this exposure to justify, develop and carry out effective prevention strategies. There are few studies worldwide that examine the financial costs of cancer on health systems and businesses, and even fewer that are directly applicable to Canada and Alberta. To the knowledge of the research team, there has been only one study published to date that attempts to estimate the costs of occupational cancers specifically, and that study is over 10 years old and was conducted in the United States (Leigh, Markowitz, Fahs, Shin, & Landrigan, 1997).

Table 1: Worldwide estimates of cancer cases and deaths attributable to occupational exposure

Author, year	Location	% of cancer deaths attributable to occupational exposures ^a		% of cancer cases attributable to occupational exposures ^a	
		Men (%)	Women (%)	Men (%)	Women (%)
Rushton et al., 2008	UK	6.0–8.0	1.0–1.5	5.4–6.7	1.0–1.2
Hamalainen et al., 2007	Global	13.8	2.2		
Fritschi & Driscoll, 2006	Australia			10.8	1.8
Deschamps et al., 2006	France			3.18 ^b	
Steenland et al., 2003	USA	3.3–7.3	0.8–1.0		
Nurminen & Karjalainen, 2001	Finland	13.8	2.2		
Dreyer et al., 1997	Nordic countries			3	<0.1
Leigh et al., 1997	USA	6–10 ^b			
Doll & Peto, 1981	USA	7.0	1.2		

^a Not all cancer types are included. For details see Table 6.

^b Men and women combined

This study attempts to fill the information gap identified above by providing an assessment of the burden of occupational cancers in Alberta, including both the numbers of workplace-related cancers and their associated economic costs. The findings from this study will enable Alberta Health Services (AHS) to develop a better understanding of the economic burden of cancer in the province and to develop appropriate prevention strategies that enhance the current and future health of Alberta's workforce.

This study comprises one component of a joint initiative between AHS and Alberta Employment and Immigration to develop a comprehensive, provincial occupational cancer prevention strategy. Other stakeholders include Alberta Health and Wellness, Alberta Environment, employer and worker representatives, and representatives from industry, labour, professional associations and educational institutions. This initiative aligns with the AHS goal of effective and efficient delivery of programs in the areas of chronic disease and injury prevention. It also supports the AHS Health Protection, Environment Unit's 2009–2011 strategic plan to reduce and eliminate exposure to environmental and occupational carcinogens.

Purpose of the study

The study was conducted by Habitat Health Impact Consulting (Calgary, Alberta) and the Lewin Group (Falls Church, Virginia) in close collaboration with Alberta Health Services. The study was initiated in February 2009, and was originally anticipated to take four months. The study approach and methods were chosen to be able to meet this schedule and to reflect the availability of data. The project ultimately lasted six months to adequately address complex technical issues.

The overall aim of this study was to generate an estimate of the economic burden of occupational cancers in Alberta. A number of specific objectives were met by conducting the study. These were

- to estimate the current number of occupational cancers in Alberta
- to estimate the direct and indirect costs associated with these cancers
- to identify recommendations for the development of a comprehensive occupational cancer prevention strategy for Alberta
- to present a framework that will allow AHS to better understand the business case (costs and benefits) of implementing a future prevention strategy

Identifying occupational cancers

The crux of this study rests on the understanding of what is meant by an “occupational cancer.” In its broadest sense, this term refers to cancer cases that would be eliminated if exposure to carcinogens in the workplace were completely removed. In reality, there are a number of factors that make it difficult to determine exactly what constitutes an occupational cancer, and what comprises the total burden of occupational cancers. Several of these difficulties are discussed below.

The term “occupational cancer” refers to cancer cases that would be eliminated if exposure to carcinogens in the workplace were completely removed.

The first difficulty pertains to defining which substances in the workplace are carcinogenic. There are several ways of identifying carcinogens, but the majority of studies concerning environmental or occupational cancers have relied on the classifications of chemical substances produced by the International Agency for Research on Cancer (IARC). Since 1971, IARC has evaluated more than 900 agents, of which approximately 400 have been identified as carcinogenic or potentially carcinogenic to humans (groups 1, 2A and 2B) (IARC, 2008). The definition of the levels of evidence supporting each grouping of carcinogen is presented below.

The majority of studies on occupational cancers have included only substances in groups 1 and 2A that are used in workplace settings, comprising approximately 55 to 60 substances (see Appendix A) (Rushton, 2009; Siemiatycki et al., 2004). Many of these substances, including benzene, asbestos, beryllium and chromium, are found in Albertan workplaces. These studies have limited the definition of

Table 2: Carcinogenicity defined by IARC

Group	Definition
1	Carcinogenic to humans; sufficient evidence in humans
2A	Probably carcinogenic to humans; limited evidence in humans and sufficient evidence in experimental animals
2B	Possibly carcinogenic to humans; limited evidence in humans and absence of sufficient evidence in experimental animals, or inadequate evidence in humans or human data non-existent and sufficient evidence in experimental animals
3	Not classifiable as to carcinogenicity to humans; inadequate or unavailable evidence in humans and inadequate or limited evidence in animals
4	Probably not carcinogenic to humans; evidence suggests a lack of carcinogenicity in humans and in experimental animals

occupational carcinogens to substances with well-established data in order to avoid potentially overestimating the true burden of occupational cancers. At the same time, however, the substances in IARC groups 1 and 2A likely represent only a small proportion of carcinogens that may be present in the workplace. In 1996 it was estimated that only 30% of the 70,000 chemical compounds listed with the Environmental Protection Agency at that time had even been tested for carcinogenicity (Landrigan, 1996). As a result, studies that define occupational cancers as those cancers caused by confirmed exposure to Group 1 and 2A substances are at risk of substantially underestimating the true burden of disease.

A second challenge is that it is almost impossible to ascertain whether or not an individual's cancer is caused by workplace exposure to a specific carcinogen. There are a very small number of exposure–cancer pairs that have been unambiguously linked, and that are almost always related to carcinogen exposure in the workplace. These include asbestos exposure and the development of mesothelioma, and vinyl chloride exposure and the subsequent development of hemangiosarcoma. However, for most cancers, it is very difficult to ascertain a specific cause at an individual level. This situation is analogous to the difficulty of attributing bladder cancer in any one individual to his or her smoking habits. The difficulties in attributing cause in an individual may be avoided when we look at occupational cancer (or tobacco-related cancer among smokers) on a population level. By grouping individuals together, we are able to compare differences between groups, and more confidently estimate risk to the entire population.

Last, it is important to remember that most cancers can have a long latency period (for example, 15 to 40 years for mesothelioma and up to 30 years for bladder cancer) (Miyakawa et al., 2001). Estimates of occupational cancer based on current disease profiles—such as those presented in this report—reflect exposures that likely occurred decades previously. In the meantime, potential exposure circumstances may have changed greatly due to different regulations, different workplace practices, and different availability of chemical substances. To properly target occupational cancer prevention efforts today, it is critical to understand workplace exposure circumstances in the present. This is particularly true as new carcinogens continue to be created, the effects of which will not be seen for decades.

A 2004 publication by Siemiatycki et al. summarizes the best available information on which cancers are associated with occupational exposure. The summary is based on a review of IARC data on carcinogenicity, and is supplemented by additional evaluation and analysis. Table 3 is reproduced from this publication. It presents, for each cancer site, the strength of the evidence tying that cancer to occupational exposure to definite (Group 1) or probable (Group 2A) carcinogens. It should be noted that although the table contains the most up-to-date information at the time of its publication, it should be considered only a “snapshot in time” of the state of the evidence of carcinogens and their link to occupational cancers. New associations in occupational cancer continue to be identified (for example, between shift work that involves circadian disruption and breast cancer), and carcinogens in IARC groupings are often reclassified based on new available evidence.

The Siemiatycki et al. (2004) publication was subsequently updated to address many important changes in the list of occupational carcinogens based on findings from IARC monographs 84–90. For example, in the IARC monograph

Table 3: Definite or probable occupational carcinogens and carcinogenic circumstances, by site

Site	Strength of evidence ^a	High-risk substance or circumstance
Pharynx and nasopharynx	Suggestive	Mustard gas; formaldehyde
Nasal cavities and paranasal sinuses	Strong Suggestive	Boot and shoe manufacture and repair; furniture and cabinet making; isopropanol manufacture, strong acid process; selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel-refining industry; wood dust Chromium compounds, hexavalent; formaldehyde; mineral oils, untreated and mildly treated
Esophagus	Suggestive	Soots; tetrachloroethylene
Stomach	Suggestive	Painters; rubber industry
Gastrointestinal tract	Suggestive	Asbestos
Liver and biliary tract	Strong Suggestive	Aflatoxin; ionizing radiation Polychlorinated biphenyls; trichloroethylene
Liver (angiosarcoma)	Strong Suggestive	Vinyl chloride Arsenic and arsenic compounds
Liver (hepatocellular)	Suggestive	Vinyl chloride
Pancreas	Suggestive	Acrylamide
Larynx	Strong Suggestive	Isopropanol manufacture, strong acid process; inorganic acid mists containing sulfuric acid; mustard gas Asbestos; rubber industry
Lung	Strong Suggestive	Aluminum production; arsenic and arsenic compounds; asbestos; beryllium; cadmium and cadmium compounds; chromium compounds, hexavalent; coal gasification; coke production; hematite mining, underground, with radon exposure; involuntary (passive) smoking; ionizing radiation; iron and steel founding; selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry; painters; silica, crystalline; soots; talc containing asbestiform fibers Benz[<i>a</i>]anthracene; benzo[<i>a</i>]pyrene; α -chlorinated toluenes; coal tars and pitches; dibenz[<i>a,h</i>]anthracene; diesel engine exhaust; epichlorohydrin; hairdressers and barbers; inorganic acid mists containing sulfuric acid; isopropanol manufacture (strong acid process); mineral oils (untreated and mildly treated); nonarsenical insecticides; mustard gas; production of art glass, glass containers, and pressed ware; rubber industry; TCDD
Lung (oat cell)	Strong	Bis(chloromethyl) ether and chloromethyl methyl ether (technical grade)
Bone	Strong	Ionizing radiation
Melanoma	Strong Suggestive	Solar radiation Ultraviolet radiation (A, B and C) from artificial sources
Skin	Strong Suggestive	Arsenic and arsenic compounds; Coal tars and pitches; coal gasification; coke production; dibenz[<i>a,h</i>]anthracene; mineral oils, untreated and mildly treated; shale oils or shale-derived lubricants; solar radiation; soots Benz[<i>a</i>]anthracene; benzo[<i>a</i>]pyrene; creosotes
Mesothelioma	Strong	Asbestos; erionite; talc containing asbestiform fibers
CNS	Suggestive	Epichlorohydrin
Sarcoma	Suggestive	TCDD
Cervix	Suggestive	Tetrachloroethylene
Ovary	Suggestive	Hairdressers and barbers
Kidney	Suggestive	Coke production
Kidney (renal cell)	Suggestive	Trichlorethylene
Bladder	Strong Suggestive	Aluminum production; 4-aminobiphenyl; auramine manufacture; benzidine; coal gasification; magenta manufacture; 2-naphthylamine; rubber industry Benz[<i>a</i>]anthracene; benzidine-based dyes; benzo[<i>a</i>]pyrene; boot and shoe manufacture and repair; 4-chloro- <i>ortho</i> -toluidine; coal tars and pitches; coke production; dibenz[<i>a,h</i>]anthracene; diesel engine exhaust; hairdressers and barbers; 4,4'-methylene bis(2-chloroaniline); mineral oils, untreated and mildly treated; <i>ortho</i> -toluidine; painters; petroleum refining
Brain	Suggestive	Nonarsenical insecticides; petroleum refining
Thyroid	Strong	Ionizing radiation
Non-Hodgkin lymphoma	Suggestive	Hairdressers and barbers; nonarsenical insecticides; TCDD; tetrachloroethylene; trichloroethylene
Lympho-hematopoietic system	Suggestive	1,3-Butadiene
Multiple myeloma	Suggestive	Nonarsenical insecticides
Leukemia	Strong Suggestive	Benzene; boot and shoe manufacture and repair; ethylene oxide; ionizing radiation Formaldehyde; nonarsenical insecticides; petroleum refining; rubber industry
Other sites	Suggestive	Ionizing radiation ^b
All sites combined	Strong	TCDD ^c

CNS, central nervous system; TCDD, 2,3,7,8-tetrachlorodibenzo-para-dioxin.

^aOur judgment of strength of evidence regarding each site. ^bThere is suggestive evidence of an effect of ionizing radiation on several sites in addition to those shown here.

^cThe evidence for an association with TCDD only becomes strong when data are combined for all cancer sites.

Note: From "Listing occupational carcinogens," by J. Siemiatycki, L. Richardson, K. Straif, B. Latreille, R. Lakhani, S. Campbell, et al., 2004, *Environmental Health Perspectives*, 112(15), p. 1458. Reprinted with permission.

Volume 88, formaldehyde was upgraded from a Group 2A (probable) to a Group 1 (known) human carcinogen. As a result, according to the 2005 update, the strength of the evidence for nasopharynx and formaldehyde was deemed “sufficient.” In addition, three substances for which there were no previous IARC evaluations have now been evaluated and re-classified: gallium arsenide as a Group 1 (known) human carcinogen, indium phosphide as a Group 2A (probable) human carcinogen, and vanadium pentoxide as a Group 2B (possible) human carcinogen (Rousseau, Straif, & Siemiatycki, 2005).

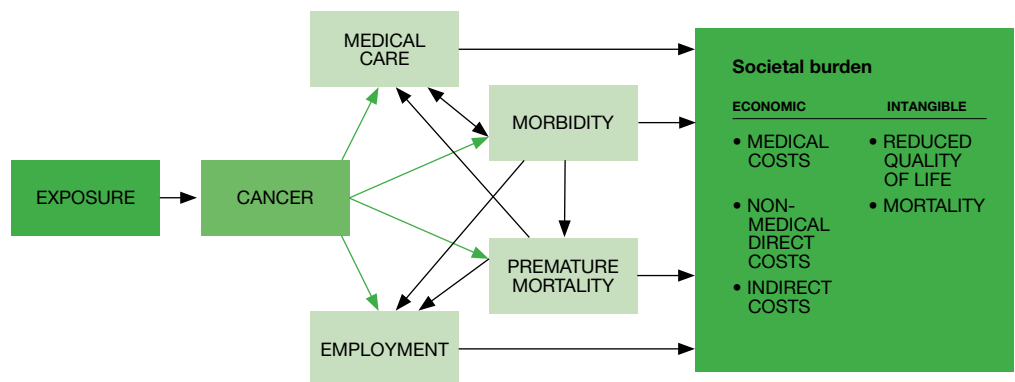
Conceptual framework for the economic burden of occupational cancer

As discussed above, to support public health policy and business case development, detailed information is needed on the development of occupational cancers in the province of Alberta and the associated economic burden. Guiding the methodology of this study is a paradigm that describes the relationship between the development and progression of cancer, and the medical and societal consequences. This can be termed a conceptual framework for assessing the burden of occupational cancer.

As shown in Figure 1 below, the increased risk of an occupational cancer starts with exposure to carcinogens. Although cancer generally develops from an interactive and multi-factorial web of causes (Clapp et al., 2007), environmental exposure, including occupational exposure, can act as a trigger for such an event. This is demonstrated in the association between exposure to workplace carcinogens and occupational cancer risk.

This exposure leads to new cancer cases, which can be diagnosed at differing levels of disease severity as defined by cancer stage. Cancer stage is associated with a higher level of medical care required, risk for premature mortality, and employment-related factors. These consequences of cancer incidence and disease progression, in turn, result in an associated burden for the patient, family and friends, and society. Cancer and its treatment result in pain and suffering, limitation in activity, reduced productivity in the workplace, premature mortality, and financial losses for the patient and family. In addition to the costs of medical care, all of these factors affect society as a whole, and it is important to identify what determines these costs, which occupations and risks generate these costs, and who pays for these costs.

Figure 1: Conceptual framework for the burden of occupational cancer



For this study, the research team adopted the societal perspective of cancer burden, which includes two cost domains: the economic category, including medical costs, non-medical direct costs, and indirect costs; and the intangible category, including reduced quality of life and premature mortality. Understanding and measuring the burden of occupational cancers is important at many levels: for medical resource allocation, reimbursement decisions, and evaluation of specific programs throughout the course of cancer care, from prevention and early detection to treatment, survivorship, and end of life.

SECTION 2. Burden of cancer in Alberta

Alberta is a province in the western part of Canada, with a population of approximately 3.4 million in 2008 (Alberta Municipal Affairs, 2009). Just over half the population is concentrated in the province's two largest cities, Calgary and Edmonton. Health care, including cancer treatment and detection, is provided to all Albertans through Alberta Health Services, a provincial government agency. All cases of cancer are required to be reported to the Alberta Cancer Registry, which has recorded information on new cancer cases and deaths since 1942.

Cancer is the leading cause of death in Alberta and across Canada, outranking all other major diseases. In 2004, cancer accounted for 29% of all deaths, ahead of heart disease (28%) and stroke (7%). One in two people are at risk of developing cancer in Alberta over their lifetime and one in four people are at risk of dying from it (Alberta Cancer Board, 2007). Cancer causes hardship and loss to people diagnosed with it, as well as to their families and communities. In addition, cancer poses a burden to society at large in the form of lost resources and the monetary costs required to treat and care for cancer patients. This section provides a snapshot of the current burden of cancer in Alberta, presenting data on new cancer cases and deaths, time trends, and implications for cancer prevention.

According to the Alberta Cancer Registry (A. Karosas, personal communication, June 12, 2009), there were approximately 19,000 new cases of cancer in Alberta in 2006 and about 5,500 cancer deaths. Table 4 below shows the current burden of cancer in Alberta for 2006.¹ The cancer rates are presented in two ways. Cancer *incidence* describes the number of people who develop new cancers in a given year. Cancer *mortality* describes the number of deaths due to cancer in a given year. Disease *prevalence* is another measure that is commonly used, and refers to the number of people in a defined population who have a particular disease at any given time. For chronic diseases such as cancer, people often live many years with the condition; therefore, the prevalence is usually much greater than the incidence. Data on cancer prevalence are not regularly reported at the provincial level for Alberta.

As shown in the table, the most common new (incident) cancers are non-melanoma skin cancer, prostate, lung and colorectal cancer in men, and non-melanoma skin cancer, breast, lung and colorectal cancer in women. Together, these comprise almost 69% of the total number of incident cancers. However, because different cancer types have different prognoses, some of the rarer cancers make a relatively large contribution to cancer deaths. Lung cancer accounts for almost 25% of cancer deaths, but only about 9% of new cases. Brain, stomach and pancreatic cancer make up 11.7% of deaths, but fewer than 4% of new cancer cases.

The absolute number of cancer cases in Alberta has been increasing over time. This has been attributed to several factors (Alberta Cancer Board, 2007). The first is the growing population: an increase in the number of people in the province leads to a higher number of cancers even if the rate of cancer were to remain the same or decrease. The second is our aging population. Cancer

¹ Non-melanoma skin cancer is not always included in cancer estimates; this is because it is not a reportable disease in some jurisdictions, and has a low mortality rate. However, NMSC is a common cancer, is reportable to the Alberta Cancer Registry, and is frequently associated with occupational exposure. For these reasons, NMSC is included throughout the analyses.

Table 4: Numbers of new cancer cases and deaths due to cancer in Alberta, 2006

Cancer site	Incidence (new cases per year)			Deaths		
	M	F	Total	M	F	Total
All Cancers	10,153	9,171	19,324	2,882	2,626	5,508
Bladder	246	72	318	108	45	153
Brain	106	76	182	95	66	161
Breast	12	1,901	1,913	5	384	389
Cervix uteri	0	157	157	0	45	45
Colorectal	926	752	1,678	325	290	615
Endometrium	0	355	355	0	57	57
Esophagus	104	31	135	83	22	105
Kidney	249	150	399	63	46	109
Leukemia	239	203	442	112	75	187
Liver and intrahepatic bile ducts	111	51	162	77	46	123
Lung/bronchus	931	812	1,743	727	638	1,365
Melanoma of skin	255	227	482	36	34	70
Multiple myeloma and plasmacytoma	82	73	155	57	50	107
Non-Hodgkin lymphoma	302	249	551	120	84	204
Non-melanoma of skin (NMSC)	3,152	2,681	5,833	17	6	23
Other hematopoietic and reticuloendothelia	109	102	211	41	24	65
Ovary	0	159	159	0	123	123
Pancreas	152	177	329	146	168	314
Prostate	2,111	0	2,111	337	0	337
Stomach	166	86	252	121	50	171
Testis	102	0	102	4	0	4
Thyroid gland	89	251	340	9	9	18
Unknown primary	121	129	250	103	123	226
Other cancers	588	477	1,065	296	241	537

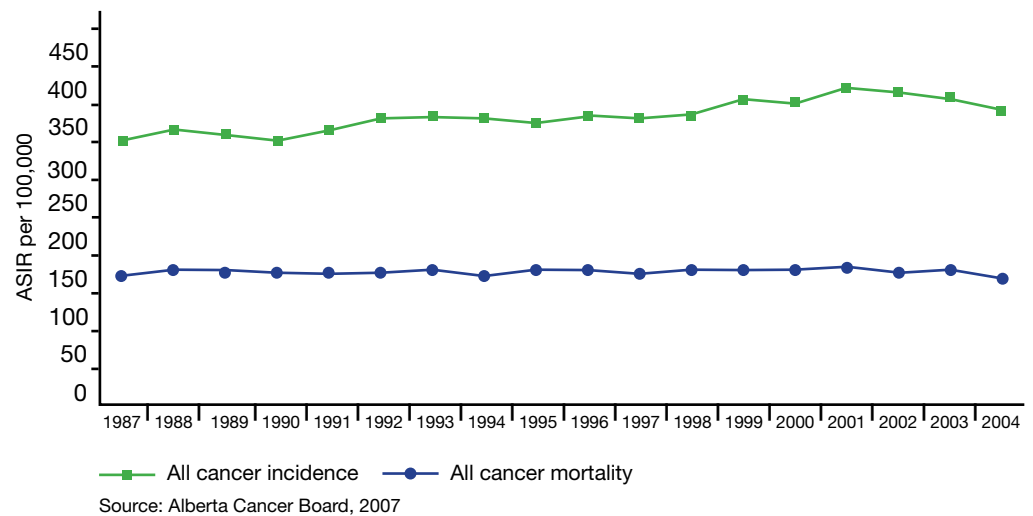
Source: Alberta Cancer Registry, 2009

occurs at higher rates in older populations, and as Alberta's population structure shifts towards an increasing proportion of older people, the number of cancers in the province increases as well.

However, the age-standardized incidence rate of cancer has also been increasing over time. The age-standardized rate adjusts for both the size of the population and relative differences in age structure. In 1987, there were approximately 350 new cases of cancer for every 100,000 population. The age-standardized rate increased to almost 400 new cases per 100,000 population in 2004, as shown in Figure 2 (Alberta Cancer Board, 2007). Cancer incidence has been increasing across all age groups, especially among children and adolescents (Canadian Cancer Society/National Cancer Institute of Canada, 2009). This across-the-board increase suggests that there may also be external factors affecting the rate at which the population is developing cancer.

Some researchers have postulated that these external factors include increasing environmental or occupational exposure to carcinogens (Irigaray et al., 2007). Despite efforts to reduce production and use of environmental carcinogens,

Figure 2: Age-standardized incidence and mortality rates, Alberta (1987–2004)



hundreds of new chemicals are being introduced into household, farming and industrial products every year (U.S. Government Accountability Office, 2009). At the same time, the potential carcinogenic effects of the majority of these products have yet to be seen or quantified. The risk assessments required for a substance to be brought to market do not always bring to light the carcinogenic potential of the substance; it may be years before the full effects on human health are understood.

Despite the large increase in the number and rate of new cancer cases, the rate of deaths due to cancer has remained relatively constant over the last 20 years, at about 150 cancer deaths per 100,000 population. Some of this trend speaks to the success of cancer screening programs (such as for breast and cervical cancers), and some to improvements in cancer treatment. A large part is due to the substantial decrease in lung cancer deaths among men, stemming from decreased smoking in the general population.

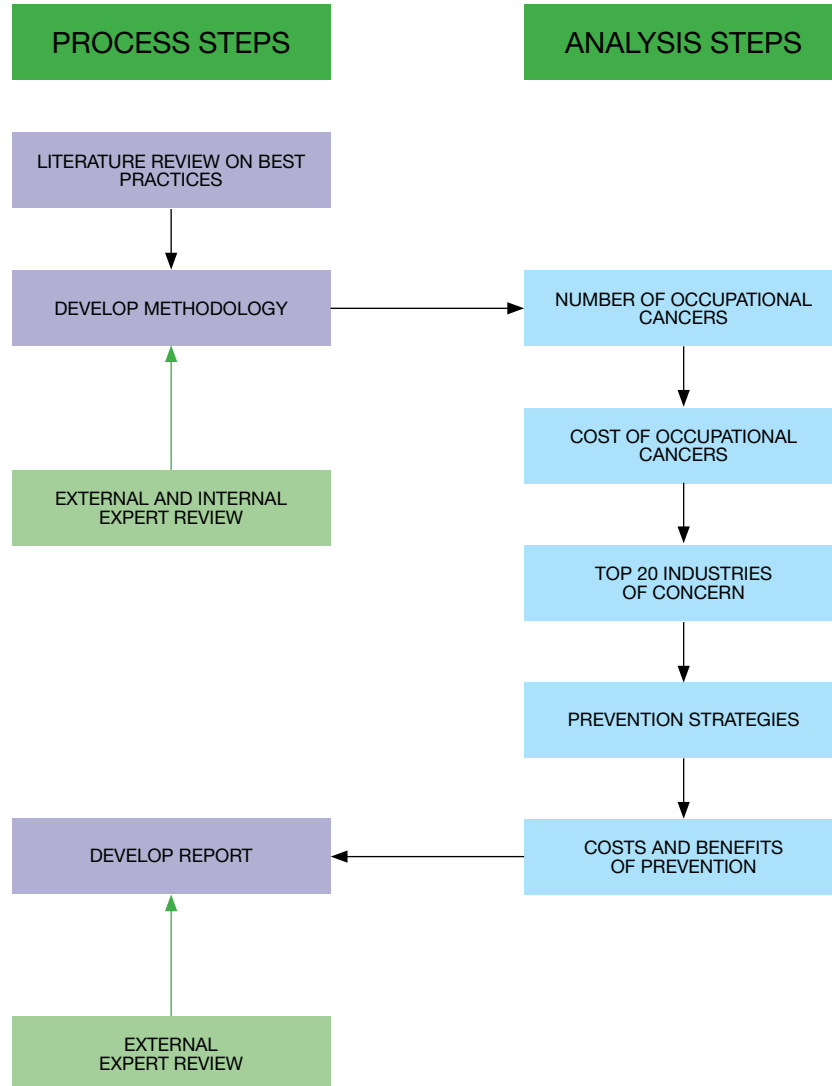
Decreasing the number of deaths due to cancer is a positive step forward. However, it also provides the province with different challenges in cancer management. With more cases of cancer occurring each year and fewer deaths resulting, the overall economic burden of cancer is increasing in Alberta. As a result, more people in the province are living with a risk of recurrence and subsequent treatments many years after their initial diagnosis (Alberta Cancer Board, 2007). For this reason, it is important to remain vigilant in cancer prevention efforts.

SECTION 3. Overview of study approach

This section reviews the overall approach that was used for this study and describes the distinct components that comprise it. The study results, along with additional detail about the methods used, are presented in subsequent sections.

Figure 3 provides a graphical overview of how the study was conducted. As shown in the figure, the study approach comprised components related to the overall process as well as to the analysis itself. These components are described below.

Figure 3: Graphical overview of study approach



Literature review on best practices/Develop methodology

The initial step involved gathering information that allowed the research team to determine the model with the strongest conceptual and empirical basis to use in assessing the direct and indirect costs of the most prevalent occupational cancers in the Alberta setting. Several approaches have been used to quantify the economic burden of cancer and other chronic diseases. Each approach has strengths and limitations, and sometimes a combination of approaches is needed.

A systematic review of the published literature identified best practices related to the estimation of occupational cancer burden, analysis of associated costs, and relevant prevention strategies that could be adapted to fit the time frame of this study. The literature review process, described in more detail in subsequent sections, identified peer-reviewed publications, government reports, related databases and other sources. To supplement this search, the research team held discussions with subject-area experts and reviewed modelling approaches previously developed for assessing the economic burden of chronic disease.

Based on the literature review, the research team developed the methodology to be used in the study. The methodology selection took into account

- best practice standards
- the time frame available
- current availability of data
- Alberta’s cancer profile and other attributes relevant to the Alberta working population

The chosen methodology is described below for each of the analysis components.

Number of occupational cancers

The estimation of the number of occupational cancers provides the foundation for all the analyses in this study, and was also the component that generated the greatest amount of discussion among the researchers. Two main methodologies, identified through the literature review, were considered for the current study.

The first approach, representing the “gold standard” for occupational cancer studies, is based on evaluating actual exposure to carcinogens in the local population. Four steps are generally used:

1. Evaluate the proportion of the population that is likely exposed to hazardous agents in the workplace.
2. Obtain estimates of absolute or relative risk for cancer associated with potential exposure levels.
3. Generate an “attributable fraction”—the proportion of cancer cases that can be linked with occupational exposure. As described by Steenland et al. (2003), the formula used to calculate the attributable fraction is as follows, where $P(E)$ is the proportion of the general population exposed to a particular agent, and RR is the relative risk (typically estimated as a rate ratio) of disease or death for those exposed versus those not exposed.

$$AF = \frac{P(E)(RR-1)}{1+P(E)(RR-1)}$$

4. Apply the attributable fraction to local cancer rates to generate the number of occupational cancers.

Examples of studies that have used this approach include Nurminen and Karjalainen (2001), Driscoll et al. (2005), Rushton et al. (2008) and Siemiatycki (1991). This type of assessment is very labour-intensive. As an example, in the Siemiatycki study, the exposure assessment was conducted by a team of industrial hygienists and coders who spent 10 years (representing 40 person-years of work) on the project (Parent, Siemiatycki, & Fritschi, 2000).

A second approach, which the research team called the “attributable fraction” approach, is similar. However, instead of generating attributable fractions through a population-specific examination of workplace conditions and associated risk estimates (steps 1 to 3 above), this approach uses attributable fractions that have been developed in previous occupational cancer studies and applies those attributable fractions to cancer rates in the local population (step 4 above). Examples of studies that have used this attributable fraction approach include Fritschi (2006), Leigh et al. (2003), and Doll and Peto (1981).

Although the first approach provides occupational cancer estimates that are more directly tailored to the local population, it relies on having an accurate characterization of the exposure circumstances in the local population. The local exposure data needed for the first approach are not currently available for Alberta, and it was not feasible to generate it within the time frame of this study.² Based on this consideration, and on feedback from internal and external experts, the decision was made to use the attributable fraction approach for the current analysis.

The main drawback to this approach is that attributable fractions (AFs) available from the literature may have only limited relevance for the Alberta working population, because exposure conditions can vary significantly over time, in different locations, and due to different regulatory circumstances. To address this limitation, a sensitivity analysis using a range of AF values (including high, low and average values) was performed to provide a range for estimated occupational cancer burden in Alberta. The methods used to identify these AF values are described in Section 4. The way in which the limitations and uncertainties of this approach may affect the occupational cancer estimates are further described in Section 6.

Costs of occupational cancers

To quantify the annual economic burden of occupational cancers in Alberta, the research team applied a traditional cost-of-illness approach that estimates the number of adverse events associated with occupational cancers and estimates the monetary value of each event. This process produces an estimate of the annual aggregate burden of illness measured by the value of goods and services diverted from other uses to provide medical care, and resources lost because of idled labour. Morbidity and mortality from cancer are translated into use and expenditures for medical care, time lost from work and housekeeping, and forgone salaries and wages.

Alberta-specific estimates of the direct cost per case to treat individual cancers were unavailable for analysis for all but lung cancer. The lack of population-based medical claims data for Alberta required that published medical claim data from other jurisdictions be used. Briefly, to estimate Alberta-specific costs per case to treat individual cancers, the research team multiplied (1) the known, published

² The CAREX (CARcinogen EXposure) database was created by the Finnish Institute of Occupational Health to help estimate the potential for carcinogen exposure in workplace and community environments. The CAREX database has been established for European populations. It is being tailored for use in Alberta and other parts of Canada and, when available, will have the potential to improve estimates for the Alberta population.

estimates for lung cancer in Alberta and (2) estimates from other literature sources for the costs per case to treat individual cancers, including the ratio of cost to treat specific cancers compared with the cost to treat lung cancer. This approach is described in more detail in Section 5 of this report.

Information from the literature was used to estimate the indirect (lost productivity) costs associated with occupational cancer—namely, days absent from work (absenteeism), reduced job performance due to health problems (presenteeism³), and inability to work due to disability. Two approaches were used to estimate the cost associated with premature mortality. The primary approach builds on human-capital theory: sex- and age-specific average earnings are combined with expected productivity trends and years of life lost to estimate forgone earnings. This approach provides estimates of lost productivity to society. A second approach, the willingness-to-pay approach, is based on estimates of the intrinsic value of life as estimated by the amount that society typically has been willing to pay to save a “statistical” life.

Cancer prevention considerations

The ultimate goal of assessing occupational cancer burden is to reduce that burden through prevention efforts. Prevention strategies and considerations relevant to the findings of the cancer burden analysis are presented in Section 7 of this report. The strategies were broken out into two specific target areas, which have differing relevance for ongoing efforts by AHS:

- **General recommendations.** The general recommendations present approaches relevant to the prevention of all types of cancers in all industry and occupational sectors. These general recommendations were developed from a review of best practices in recent occupational cancer literature.
- **Process-related recommendations.** This refers to lessons that can be learned about how a future analysis of occupational cancer costs could be improved, based on the limitations that were encountered in the present study.

Costs and benefits of prevention

In this study component, the research team reviewed the costs and benefits of cancer prevention initiatives in broad terms. While cancer prevention initiatives can have a demonstrable benefit in terms of cancer reduction, they also generate financial costs. To ensure a return on investment, there needs to be a framework for assessing the costs and benefits associated with any given prevention initiative.

A search was conducted for published literature that specifically addressed cancer prevention from the perspective of identifying a potential return on investment. The main findings that emerged from the literature were reviewed and summarized to present information relevant to the decision-making processes of AHS. These findings are presented in Section 8 of this report.

³ Presenteeism refers to “being at work but not being on the job” (i.e., not functioning to full capacity) because of illness or other medical conditions (Hemp, 2004). Presenteeism is not about being lazy; it is about genuine health issues reducing a person’s ability to function fully. Presenteeism can cut individual productivity by a third or more (both by slowing employees down and by increasing the number of mistakes they make), and it appears to be more costly than absenteeism (Hemp, 2004).

External and internal expert review

At several points during the study, the overall approach and specific methodology were reviewed by internal and external experts to ensure that the methods being used and the conclusions being drawn were sound.

After the study methodology was developed, the approach was reviewed by two experts within Alberta Health Services (Lorraine Shack and Graham Petz, Public Health Innovation and Decision Support, Population and Public Health) and by three external experts (Paul Demers, School of Environmental Health and School of Population and Public Health, University of British Columbia; Cheryl Peters, School of Environmental Health, University of British Columbia; and Hans Krueger, H. Krueger and Associates). Specific suggestions were given to refine and improve the methods to be used.

In addition, the final report was reviewed by two other external specialists with expertise in occupational cancer research (Dr. Lin Fritschi) and the economic burden of chronic disease in Canada (Dr. Jayadeep Patra). These experts were asked to review not only the methods, but also the results of the analysis and the conclusions that were drawn.

SECTION 4. Estimating the number of occupational cancers in Alberta

Overview

This section presents information on the first component of the study: the estimation of the numbers of cancers in Alberta that can be considered likely to have been caused by occupational exposure. For the results presented in this section and also in Section 5, an estimate of the burden of cancer is provided for year 2006 (most recent year available) based on historical exposure that has taken place in the past few decades. These estimates provide the amount of cancers diagnosed currently (2006), rather than predicting future cancer rates based on current exposure patterns.

Methods

As discussed in Section 3, the approach chosen to estimate the number of occupational cancers in Alberta was based on applying attributable fractions (AFs) for specific cancer sites to Alberta data on cancer rates in the province. The steps used in this analysis are described below.

Step 1: Systematically identify studies that have previously generated attributable fractions based on original estimates of occupational exposure.

To comprehensively identify original research that provided AFs for occupational cancers, the research team conducted a systematic literature search in April and May of 2009. The literature search was initially conducted using PubMed and Google Scholar to identify articles (peer-reviewed journal articles, official reports or grey literature) based on the following search strategy. The research team searched for all variants on the following three sets of terms:

1. *cancer* or *neoplasm*
2. *work*, *workplace* or *occupation*
3. *attributable fraction*, *attributable risk*, *PAR* or *etiologic fraction*

Publications were identified that included all three of these sets. In addition, the reference lists of relevant publications were hand-searched to identify additional related material. All materials with published information on methods were initially considered for review, and were not restricted by language or location. Studies were limited to those published since 1989, for reasons described in Step 2 below. The PubMed search, last repeated on July 12, 2009, turned up an initial 401 articles for consideration.

Step 2: Apply exclusion criteria to exclude studies inappropriate for use.

The exclusion criteria shown in Table 5 were applied to screen out ineligible studies.

Appendix C lists the studies that were identified through the literature search, and presents relevant information on the study population, the main findings, whether the study was included or excluded, and the justification for exclusion, if applicable.

Table 5. Exclusion criteria applied

Exclusion criterion	Justification
Duplicate study	The publication presented material previously published from the same study (i.e., multiple publications arising from a single study).
Study was published prior to 1989.	A cut-off of 20 years helps minimize the differences between historical and current exposure, particularly given the long lag time for cancer development.
The AF applied only to an exposed population, not to the general population.	Because the AFs will be applied to the entire Alberta population and not just the exposed population, the AFs generated in the original material must be comparable.
The AF was based on data from developing economies.	Exposure conditions and cancer identification can be significantly different between developing and developed countries and the AFs are much less likely to apply to conditions in Alberta.
The AF was generated in a population with a significant proportion of workers in known hazardous occupations that do not exist in Alberta.	A number of studies on occupational cancers focus on the risks associated with asbestos mining and manufacturing, activities with a very strong link to cancer but that do not take place in Alberta.
No new AFs were produced.	Studies that used existing AFs and applied them to a new population do not represent a new data source and were not used. The exception is where cancer-specific AFs were applied and summed over the entire population to create a new estimate of the AF for all cancers.
Overall study quality was poor.	Studies were defined as being of poor quality if the methods used for measuring exposure were poor, the study size was small compared with other studies, or the method used to calculate AFs was not standard.

Step 3: Extract data on AFs and identify attributable fraction(s) most appropriate for Alberta.

For each of the studies that met the eligibility criteria, the data on attributable fractions were identified. AFs were extracted separately for each cancer site, with sex-specific information used where available. Table 6 shows the values that were identified from each of the eligible studies, by cancer site. For two studies—Rushton et al. (2008) and Siemiatycki (1991)—two sets of estimates were included. This was because both these studies used two separate modelling approaches to estimate occupational cancers: a more conservative approach based on a restricted group of carcinogens, and a less conservative approach based on a broader interpretation of occupational cancers. The two sets of estimates therefore do not represent a confidence interval or a range of uncertainty, but rather two separate modelling efforts. Thus, the research team felt it was appropriate to present both sets of estimates in Table 6.

No single study stood out as having the “best” fit for Alberta. As can be seen from the study descriptions in Appendix C, each study has a combination of strengths and weaknesses with respect to its application for this analysis, based on factors such as similarity to Alberta industries, carcinogens in use in the workplace, number of cancers studied, and time period of exposure.

Therefore, the decision was made to use a range of estimates, including a low-end estimate, a high-end estimate, and an average. These are also shown in Table 6. For each cancer type, the research team identified the lowest and the highest AF figures from the eligible studies, and used these as the low and high end for Alberta. For example, for nasal cancer in men, the low end is represented by the AF of 24% found by Nurminen and Karjalainen (2001), whereas the high end is represented by the AF of 64.3% found by Rushton et al. using approach (b). The best estimate is generated by taking an average of all AFs for any given cancer site. For the Siemiatycki and Rushton et al. studies, only one set of estimates was used, to avoid the problem of distorting the estimate by including the same study twice.

Table 6: Attributable fractions used for modelling

Author	Nurminen & Karjalainen		Siemiatycki	Rushton et al.			Steenland et al.		Dreyer et al.		Driscoll et al.		Others		AFs for use with Alberta data (%)					
	2001		1991	2008			2003		1997		2005				Average		Low estimate		High estimate	
Location	Finland		Canada (Montreal)	UK			USA		Nordic countries		Americas									
	M*	W**	M	M	W	M	W	M	W	M	W	M	W	M	W	M	W	M	W	
GROUP A - Cancers with a strong link to occupational exposure																				
Bladder	14.2	0.7	a) 1.2 b) 10.8	a) 1.3 b) 11.6	a) 0.6 b) 2.0	7.0–19.0	3.0–19.0	2.0	0.4			21–27 ^a		11.0	3.5	1.2	0.4	27.0	19.0	
Bone	0.6	0.6												0.6	0.6	0.6	0.6	0.6	0.6	
Larynx	9.3	0.5				1–20		6.0	<1.0					8.6	0.5	1.0	0.5	20.0	0.5	
Leukemia	18.5	2.5		a) 0.3 b) 2.7	a) 0.5 b) 0.8	0.8–2.8 (m/w)		1.0	1.0	3.0	3.0			5.1	6.3	1.8	0.5	18.5	3.0	
Liver	3.5	5.3				0.04–0.11								2.1	5.3	0.0	5.3	3.5	5.3	
Lung	29.0	5.3	a) 8.0 b) 20.3	a) 16.5 b) 21.6	a) 4.5 b) 5.5	8.0–19.2	2.0	18.0	1.0	6.0	2.0	10–33 ^a 9.5 ^b		15.9	3.2	6.0	1.0	33.0	5.5	
Melanoma	4.3	0.4												4.3	0.4	4.3	0.4	4.3	0.4	
Mesothelioma	90.0	21.0		a) 87.0 b) 98.0	a) 25.0 b) 90.0	85–90	23–90	83.0	1.0					89.6	42.1	83.0	1.0	98.0	90.0	
Nose and nasal sinuses	24.0	6.7		a) 34.1 b) 64.3	a) 10.8 b) 18.4	31–43		30.0	2.0			60.0 ^c		43.1	9.0	24.0	2.0	64.3	18.4	
Skin (NMSC)	13.1	3.8		a) 11.8 b) 11.8	a) 3.0 b) 3.0	1.2–6.0								9.5	3.4	1.2	3.0	13.1	3.8	
All cancer deaths	13.8	2.2		a) 6.0 b) 8.0	a) 1.0 b) 1.5	3.3–7.3	0.8–1.0	11.0 ^e	0.1 ^e			10.8 ^{d,e}	1.8 ^{d,e}	9.8	1.3	3.3	0.1	13.8	2.2	
GROUP B - Cancers with a suspected link to occupational exposure																				
Brain	10.6	1.3												10.6	1.3	10.6	1.3	10.6	1.3	
Cervix		5.9												0.0	5.9	0.0	5.9	0.0	5.9	
Colon	5.6	0.0	a) 0.4 b) 3.4											3.0	0.0	0.4	0.0	5.6	0.0	
Esophagus	6.4	0.2	a) 3.5 b) 20.4											5.0	0.2	3.5	0.2	20.4	0.2	
Kidney	4.7	0.8	a) 0.0 b) 20.8			0–2.3		2.0	1.0					2.0	0.9	0.0	0.8	20.8	1.0	
Non-Hodgkin lymphoma	13.5	3.1												13.5	3.1	13.5	3.1	13.5	3.1	
Oral Cavity	1.2	0.3												1.2	0.3	1.2	0.3	1.2	0.3	
Ovary		2.1												0.0	2.1	0.0	2.1	0.0	2.1	
Pancreas	13.4	3.5	a) 0.0 b) 20.6											6.7	3.5	0.0	3.5	20.6	3.5	
Pharynx	2.0	0.5												2.0	0.5	2.0	0.5	2.0	0.5	
Rectum	3.1	0.1	a) 0.0 b) 21.8											1.6	0.1	0.0	0.1	21.8	0.1	
Stomach	10.3	5.4	a) 4.0 b) 14.2											7.2	5.4	4.0	5.4	14.2	5.4	
Cancer associated with elevated risk in some occupations																				
Breast		1.7												0.0	1.7	0.0	1.7	0.0	1.7	
Corpus uteri		1.1												0.0	1.1	0.0	1.1	0.0	1.1	
Gallbladder	0.2	0.4												0.2	0.4	0.2	0.4	0.2	0.4	
Hodgkin's disease	3.9	0.0												3.9	0.0	3.9	0.0	3.9	0.0	
Prostate	6.0		a) 0.2 b) 9.9											3.1	0.0	0.2	0.0	9.9	0.0	

^aLeigh, 1997. ^bGustavsson, 2000. ^cComba, 1992. ^dFritschi, 2006. ^eStudy used incidence rather than mortality.

* Men; ** Women

Table 7: Example of how occupational cancer numbers were generated

	Average	Low	High
Number of bladder cancers in men in Alberta per year	206.2	206.2	206.2
x AF for bladder cancer in men	11.0%	1.2%	27.0%
= Subtotal (men)	22.7	2.5	55.7
+			
Number of bladder cancers in women in Alberta per year	67.8	67.8	67.8
x AF for bladder cancer in women	3.5%	0.4%	19.0%
= Subtotal (women)	2.4	0.3	12.9
Total (men and women)	25.1	2.7	68.6

For the Siemiatycki study, the more conservative estimate (a) was included, because it conformed more closely to the set of carcinogens (IARC groups 1 and 2A) used in the other studies. For the Rushton et al. study, the less conservative approach (b) represented IARC groups 1 and 2A and was therefore chosen. This average value necessarily falls in the middle of the range represented by the low- and high-end estimates. It should be emphasized that the low and high values do not represent a confidence interval.

Step 4: Apply AFs to local cancer data. Step 4 required applying the AFs generated in Step 3 to local cancer data. Data on cancer incidence and mortality for 2002–2006 were obtained from the Alberta Cancer Registry. A five-year window was used so that there would be sufficient study power to examine cancers with small numbers of cases. Data were provided stratified by sex and five-year age categories. Because adults form the target population for occupational cancer studies, only cases among people aged 20 or over were included in the analysis. A sensitivity analysis was applied that used 40 as a minimum age for possible occupational cancers. The results of this sensitivity analysis are included in Section 5. To generate the numbers of occupational cancers in Alberta, the data on Alberta cancer rates were multiplied by the relevant attributable fraction. An example using bladder cancer is shown in Table 7.

From this example, it can be seen that the average estimate for the incidence of occupationally linked bladder cancers per year in Alberta is about 25; a low and high estimate (not a confidence interval) would be 3 and 69 cancers per year.

Prevalence estimates

The data available from the Alberta Cancer Registry included five-year (2002–2006) incidence (new cancer cases) and mortality rates for the province. Information on prevalence—the number of people with a specific cancer at any time in a defined population—is not something that is routinely calculated. However, prevalence data were needed for the estimations of cost described in Section 5. The methods for calculating prevalence are described below.

Prevalence is a useful estimate in its own right, because it provides a different view of the burden of cancer than either incidence or mortality, and may be a more appropriate measure for certain planning decisions, especially from a cross-section perspective to evaluate the epidemiologic burden of illness over a period of time.

Table 8: Steps to calculate Alberta-specific prevalence data using bladder cancer as example

Step	Description	Male	Female
1	2002–2006 new bladder cancer cases from the Alberta Cancer Registry	1,026	304
2	Divide 2002–2006 data by 5 to calculate annual new bladder cancer cases in 2004 and fill data gaps with Annual Reports	206	69
3	To estimate the five-year bladder cancer prevalent cases in 2008, use the average relative survival at five years after diagnosis for bladder cancer patients diagnosed between 2004 and 2008 and the number of incident cases for 2004 to provide a conservative estimate of the number of individuals with bladder cancer expected to be alive by the end of 2008.	890	290
4	Convert bladder cancer prevalent cases into prevalent individuals in Alberta	863	283

The data on aggregate cancer incidence for 2002–2006 were obtained from the Alberta Cancer Registry. The research team used 2004 (the middle year between 2002 and 2006) as the year to report average, annual new cases by tumour site. For certain demographic (i.e., age and sex) groups where the five-year aggregate incidence data were fewer than 10 and were not provided as part of the incidence data, incidence estimates from the Alberta Cancer Registry’s annual reports for cancer statistics in 2004 and 2005 were used to fill the gaps.

Cancer prevalence is a function of both the incidence of and survival from the disease. To estimate the five-year cancer prevalent cases by tumour site, the annual relative survival ratios using the five-year relative survival ratios were first calculated. The five-year relative survival ratio in Alberta was assumed to be the same as the estimated five-year relative survival ratio reported in *Canadian Cancer Statistics 2009* (Canadian Cancer Society/National Cancer Institute of Canada, 2009). For a handful of tumour sites (i.e., nose and nasal sinuses, pharynx, and non-melanoma skin cancer) for which Canadian Cancer Statistics did not have reported data, the five-year relative survival ratios from the U.S. Surveillance, Epidemiology and End Results (SEER) data were used as a proxy (Surveillance, Epidemiology and End Results, 2009). Then, the research team applied the annual relative survival ratio to the number of new cancer cases (i.e., incidence) in 2004, forecasted over a period of five years, to estimate the total survived number of 2004 new cases after five years (i.e., prevalence by the end of 2008). With no access to individual-level data for each year, the research team only could use average estimates of incidence and survival ratio per year to calculate prevalence. The underlying linear growth assumption may cause overestimation for the survival ratio and underestimation for the incidence rate.

In addition to cancer prevalence, the research team was also interested in Alberta-specific estimates of the number of unique prevalent individuals to facilitate later cost calculations. The research team first generated the ratio of case prevalence to individual person prevalence by tumour site using prevalence estimates for all of Canada. Then, these ratios were applied to case prevalence estimates for Alberta to calculate estimates of the number of unique individuals in Alberta with each type of cancer (Ellison & Wilkins, 2009). Table 8 uses bladder cancer as an example to illustrate the calculation steps.

Results

The results of the analysis in this section are presented both as incidence figures and as five-year prevalence figures. Table 9 shows the annual incidence of occupational cancers in Alberta. For each cancer site, the average estimate is provided (absolute numbers of cases, based on a multi-year average), along with both a low and high estimate. Cancers are grouped into three categories. Those in the first group are cancers with a strong link to occupational exposure, as identified by Siemiatycki et al. (2004) in their review of occupational cancers (which is described in Section 1). There is little doubt that occupational exposure is a substantial contributor to cancer development for these sites. The second group comprises cancers with a suspected link to occupational exposure. Although the evidence is not as strong for the cancers in this group, these cancers are also linked to occupational exposures (Clapp et al., 2007). There is more controversy regarding the association between occupational carcinogen exposure and the cancers in the third group. Though a number of studies have shown elevated risks of these cancers associated with certain occupations, the evidence is not consistent. Additionally, the number of cases attributable to occupational exposures is relatively small compared with that attributable to non-occupational risk factors.

As can be seen in Table 9, the cancer sites resulting in the largest annual incidence are skin (non-melanoma skin cancer) with 370 incident cancers per year, lung (165 cancers per year), non-Hodgkin lymphoma (46 cases) and mesothelioma (28 cases). Although prostate and breast cancer contribute approximately 64 and 31 cases per year respectively, these figures are driven primarily by the very large number of prostate and breast cancers per year in Alberta, rather than by a strong association with occupational exposures or a high attributable fraction. All cancer deaths are also important: an estimated 263 cancer deaths per year result from occupational exposure.

Table 10 provides similar results for five-year prevalence, rather than incidence. The relative ranking of different cancer sites is somewhat different than for incidence; this is because prevalence is based not only on the number of new cases per year, but also on how long people tend to live with the cancer. As with incident cancers, skin, lung, and non-Hodgkin lymphoma are among the top contributors.

Table 11 presents a summary of the numbers of occupational cancers in Alberta, drawn from the information in Table 9 and Table 10. Average, low and high estimates are presented for several groupings of cancers: Group A (cancers with a strong link to occupational exposure); groups A and B (cancers with a strong or suspected link), all cancers, and all cancer deaths. Cancers associated with elevated risk in some occupations were not included for this analysis. The research team believed the strongest argument may be made for using *strong or suspected* cancers (groups A and B) as the basis for the most reliable, but still conservative, figure for Alberta. This would give a best estimate of 761 new occupational cancers per year (with a low value of 314 and a high value of 1,283) and a five-year prevalence estimate of 2,734 occupational cancer cases in the province as of 2006 (with a low and high values range of 1,055 to 4,457). To place this in perspective, 761 cancers represent 8.6% of the total number of incident cancers in Alberta in people at or over age 20.

Table 9: Annual incidence of occupational cancers in Alberta

Cancer site	Annual incidence in Alberta (ages 20 or older)*			Occupational cancers AVERAGE estimate*			Occupational cancers LOW estimate*			Occupational cancers HIGH estimate*		
	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total
Group A - Cancers with a strong link to occupational exposure												
Bladder	206.2	67.8	274.0	22.7	2.4	25.1	2.5	0.3	2.7	55.7	12.9	68.6
Bone	49.0	45.0	94.0	0.3	0.3	0.6	0.3	0.3	0.6	0.3	0.3	0.6
Larynx	56.2	11.4	67.6	4.8	0.1	4.9	0.6	0.1	0.6	11.2	0.1	11.3
Leukemia	220.6	154.6	375.2	13.9	2.8	16.7	0.7	0.8	1.4	40.8	4.6	45.4
Liver	104.2	45.4	149.6	2.2	2.4	4.6	0.0	2.4	2.4	3.6	2.4	6.1
Lung	882.4	761.2	1,643.6	140.3	24.1	164.4	52.9	7.6	60.6	291.2	41.9	333.1
Melanoma	223.2	207.0	430.2	9.6	0.8	10.4	9.6	0.8	10.4	9.6	0.8	10.4
Mesothelioma	31.4	0.0	31.4	28.1	0.0	28.1	26.1	0.0	26.1	30.8	0.0	30.8
Nose/nasal sinuses	4.0	2.0	6.0	1.7	0.2	1.9	1.0	0.0	1.0	2.6	0.4	2.9
Skin (NMSC)	2,992.2	2,512.2	5,504.4	284.3	85.4	369.7	35.9	75.4	111.3	392.0	95.5	487.4
All cancer deaths	2,409.8	2,042.0	4,452.0	235.7	27.0	262.7	79.5	2.0	81.5	332.6	45.0	377.6
Group B - Cancers with a suspected link to occupational exposure												
Brain	102.8	73.0	175.8	10.9	0.9	11.8	10.9	0.9	11.8	10.9	0.9	11.8
Cervix	0.0	155.0	155.0	0.0	9.1	9.1	0.0	9.1	9.1	0.0	9.1	9.1
Colon	526.4	472.6	999.0	15.8	0.0	15.8	2.1	0.0	2.1	29.5	0.0	29.5
Esophagus	94.8	24.6	119.4	4.7	0.0	4.7	3.3	0.0	3.4	19.3	0.0	19.4
Kidney	216.4	125.4	341.8	4.2	1.1	5.4	0.0	1.0	1.0	45.0	1.3	46.3
Non-Hodgkin lymphoma	287.0	232.6	519.6	38.7	7.2	46.0	38.7	7.2	46.0	38.7	7.2	46.0
Oral cavity	141.6	75.8	217.4	1.7	0.2	1.9	1.7	0.2	1.9	1.7	0.2	1.9
Ovary	0.0	178.2	178.2	0.0	3.7	3.7	0.0	3.7	3.7	0.0	3.7	3.7
Pancreas	153.4	169.0	322.4	10.3	5.9	16.2	0.0	5.9	5.9	31.6	5.9	37.5
Pharynx	34.0	5.0	39.0	0.7	0.0	0.7	0.7	0.0	0.7	0.7	0.0	0.7
Rectum	251.0	144.8	395.8	3.9	0.1	4.0	0.0	0.1	0.1	54.7	0.1	54.9
Stomach	147.4	86.8	234.2	10.5	4.7	15.2	5.9	4.7	10.6	20.9	4.7	25.6
Cancer associated with elevated risk in some occupations												
Breast	15.4	1,845.8	1,861.2	0.0	31.4	31.4	0.0	31.4	31.4	0.0	31.4	31.4
Corpus uteri	0.0	15.0	15.0	0.0	0.2	0.2	0.0	0.2	0.2	0.0	0.2	0.2
Gallbladder	14.2	25.0	39.2	0.0	0.1	0.1	0.0	0.1	0.1	0.0	0.1	0.1
Hodgkin's disease	44.2	27.6	71.8	1.7	0.0	1.7	1.7	0.0	1.7	1.7	0.0	1.7
Prostate	2,057.2	0.0	2,057.2	63.8	0.0	63.8	4.1	0.0	4.1	203.7	0.0	203.7

*This number is an absolute value, not a rate. Because of multi-year averaging, values may not be whole numbers.

Table 10: Five-year prevalence of occupational cancers in Alberta

Cancer site	Annual incidence in Alberta (ages 20 or older)*			Occupational cancers AVERAGE estimate*			Occupational cancers LOW estimate*			Occupational cancers HIGH estimate*		
	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total
Group A - Cancers with a strong link to occupational exposure												
Bladder	872	281	1,153	95.9	30.7	126.6	10.5	3.5	13.9	235.4	165.6	401.0
Bone	181	183	364	1.1	1.1	2.2	1.1	1.1	2.2	1.1	1.1	2.2
Larynx	216	42	258	18.5	1.1	19.6	2.2	1.1	3.2	43.1	1.1	44.2
Leukemia	735	517	1,251	46.3	13.4	59.7	2.2	3.7	5.9	135.9	22.0	158.0
Liver	204	85	289	4.3	10.8	15.2	0.1	10.8	10.9	7.2	10.8	18.0
Lung	1,493	1,460	2,953	237.4	47.2	284.6	89.6	14.9	104.5	492.7	82.1	574.9
Melanoma	1,001	976	1,977	43.0	4.0	47.0	43.0	4.0	47.0	43.0	4.0	47.0
Mesothelioma	25	0	25	22.8	10.7	33.6	21.1	0.3	21.4	25.0	22.9	47.9
Nose/nasal sinuses	14	7	21	5.9	1.2	7.1	3.3	0.3	3.6	8.8	2.5	11.3
Skin (NMSC)	13,666	11,893	25,559	1,298.3	464.6	1,762.9	164.0	410.0	574.0	1,790.3	519.3	2,309.6
Group B- Cancers with a suspected link to occupational exposure												
Brain	223	165	388	23.6	2.9	26.5	23.6	2.9	26.5	23.6	2.9	26.5
Cervix	0	646	646	0.0	38	38	0.0	38	38	0.0	38	38
Colon	1,931	1,746	3,676	57.9	0.0	57.9	7.7	0.0	7.7	108.1	0.0	108.1
Esophagus	166	42	207	8.2	0.3	8.5	5.8	0.3	6.1	33.8	0.3	34.1
Kidney	824	488	1,312	16.2	7.4	23.6	0.0	6.6	6.6	171.4	8.2	179.7
Non-Hodgkin lymphoma	1,047	874	1,921	141.3	32.4	173.7	141.3	32.4	173.7	141.3	32.4	173.7
Oral cavity	525	292	818	6.3	1.6	7.9	6.3	1.6	7.9	6.3	1.6	7.9
Ovary	0	522	522	0.0	11	11	0.0	11	11	0.0	11	11
Pancreas	187	207	393	12.5	6.5	19.1	0.0	6.5	6.5	38.5	6.5	45.0
Pharynx	100	15	116	2.0	0.5	2.5	2.0	0.5	2.5	2.0	0.5	2.5
Rectum	928	551	1,478	14.4	0.9	15.3	0.0	0.9	0.9	202.3	0.9	203.2
Stomach	318	196	515	22.8	17.2	40.0	12.7	17.2	29.9	45.2	17.2	62.4
Cancer associated with elevated risk in some occupations												
Breast	68	8,351	8,418	0.0	1.2	1.2	0.0	1.2	1.2	0.0	1.2	1.2
Corpus uteri	0	67	67	0.0	0.7	0.7	0.0	0.7	0.7	0.0	0.7	0.7
Gallbladder	29	41	70	0.1	0.1	0.2	0.1	0.1	0.2	0.1	0.1	0.2
Hodgkin's disease	197	125	323	7.7	0.0	7.7	7.7	0.0	7.7	7.7	0.0	7.7
Prostate	9,765	0	9,765	302.7	0.0	302.7	19.5	0.0	19.5	966.8	0.0	966.8

*This number is an absolute value, not a rate. Because of multi-year averaging, values may not be whole numbers.

Table 11: Summary of incident and prevalent occupational cancers in Alberta

	Occupational cancers AVERAGE estimate*			Occupational cancers LOW estimate*			Occupational cancers HIGH estimate*		
	Men	Women	Total	Men	Women	Total	Men	Women	Total
Annual incidence									
Group A - Cancers with a strong link to occupational exposure	507.9	118.4	626.4	129.5	87.6	217.1	837.8	158.8	996.6
Groups A and B - Cancers with a strong or suspected link to occupational exposure	609.4	151.6	761.0	192.8	120.7	313.6	1,090.9	192.1	1,283.0
All cancers	675	183	858	199	152	351	1,296	224	1,520
All cancer deaths	235.7	27.0	262.7	79.5	2.0	81.5	332.6	45.0	377.6
Five-year prevalence									
Group A - Cancers with a strong link to occupational exposure	1,773.6	584.9	2,358.5	337.0	449.6	786.6	2,782.4	831.5	3,614.0
Groups A and B - Cancers with a strong or suspected link to occupational exposure	2,078.7	654.8	2,733.5	536.5	518.6	1,055.1	3,554.9	902.2	4,457.1
All cancers (including NMSC)	2,389.2	656.0	3,045.3	563.8	519.9	1,083.6	4,529.5	903.5	5,432.9
All cancers (not including NMSC)	1,090.9	191.4	1,282.3	399.8	109.9	509.7	2,739.2	384.2	3,123.4

*This number is an absolute value, not a rate. Because of multi-year averaging, values may not be whole numbers.

Discussion

As can be seen in the figures above, occupational cancers comprise a significant burden in Alberta, whether considered in terms of new cancer cases, the total number of cancers at any time in the province, or premature deaths from occupational cancer. The most conservative estimates put this figure at 217 new cases per year; however, the most likely figure appears to be 761 new cases per year.

A large number of assumptions have gone into creating this estimate, and a certain degree of uncertainty is introduced with each assumption. The main limitations and uncertainties relevant to this analysis are discussed in Section 6. However, the largest area of uncertainty is the degree of comparability between Alberta and the populations from which the attributable fractions were drawn in terms of occupational carcinogen exposure. Without Alberta-specific data on exposure, it is not possible to create a more precise estimate of the numbers of occupational cancers in the province.

In the following section, the economic burden of these occupational cancer cases will be discussed. However, the human toll of this disease is also significant. Cancer results in ill health and shortened life for the affected individuals, affects their families and communities, and imposes a burden on society as a whole.

SECTION 5. Estimating the annual cost of occupational cancers in Alberta

Overview

Improved understanding of the cost burden associated with occupational cancers can lead to a more efficient allocation of societal resources and can inform policies to reduce exposure to occupational and environmental carcinogens. The cost of cancers can be estimated from different perspectives (e.g., individual, family, employer, government, society). In addition, the overall burden consists of economic costs as well as intangible costs that reduce quality of life.

The economic burden is a monetary valuation of resources used for disease screening and treatment, in addition to the loss of economic opportunities related to disease occurrence and treatment. The major cost domains include *direct medical costs* resulting from the use of health care resources, *direct non-medical costs* for items such as transportation and help with activities of daily living limitations, *indirect costs* resulting from the loss of economic resources and reduced productivity, and *intangible costs* reflecting pain, suffering and reduced quality of life (Table 12). Intangible costs, by their nature, are difficult to quantify in monetary terms. Furthermore, there is no consensus by researchers on how to place a dollar value on reduced quality of life. For this study the research team focused on the two largest components of economic burden: medical costs and indirect costs.

Table 12: Cancer relevant cost domains

Direct costs	Medical costs	Hospitalizations
		Physician visits
		Home health care
		Hospice
		Pharmaceutical agents
		Chemotherapy
		Radiation
		Equipment and medical devices
	Non-medical costs	Transportation to hospital or physician's office
		Housekeeping services
Costs of moving		
Alterations to property		
Indirect costs	Time lost from work/lost productivity	
	Economic productivity lost due to premature death	
	Caregiver time or changes in caregivers' employment	
Intangible costs/lost quality-adjusted life years	Pain	
	Suffering	
	Grief	

Methods

This section describes the methods, data and assumptions used to quantify the direct and indirect costs associated with occupational cancers.

Direct costs

Direct costs refer to the monetary value of resources used for medical care in the prevention, diagnosis, and treatment of disease and for continuing care or surveillance, rehabilitation, and end-of-life care that are directly related to occupational cancers.

Ideally, direct costs are measured by analyzing medical claims data or through a chart review of medical records for health care provided across all delivery settings. However, detailed information on health-care utilization per cancer case and associated medical costs was not readily available for the present study, so the research team estimated cost per cancer case using the following steps:

Step 1. Obtain previously estimated Alberta-specific direct medical costs per cancer case from existing studies (i.e., for lung cancer). The direct costs related to lung cancer in Alberta are known from a study based on a medical chart review (Table 13) (Demeter et al., 2007).⁴ Cost estimates in this study were not standardized to a particular year, nor were they discounted for its short enrollment period (January 1998 to December 2000). The research team chose the midpoint of the period (i.e., 1999) as the year to adjust the cost estimates to 2008 dollars for this study. The review identified no other Alberta-specific estimates of the cost per cancer case.

Table 13: Medical cost per case by lung cancer type (in 2008 dollars)

Type	Number of cases	Medical cost per case		
		Median	Lower	Upper
Non-small cell lung cancer	448	\$10,928	\$9,234	\$11,047
Small cell lung cancer	105	\$15,350	\$13,033	\$21,436
Weighted median value of medical cost per lung cancer case (in 1999 dollars)		\$11,768		
Weighted median value of medical cost per lung cancer case (in 2008 dollars)		\$13,214		

Step 2. Obtain and apply estimates of ratios between known Alberta-specific cancer cost per case (i.e., lung cancer) and other occupational cancers. Two approaches were employed to calculate these ratios; these ratios and the estimated Alberta-specific annual medical cost associated with each cancer type are summarized in Table 14.

Approach 1 used a single data source, the Medical Expenditure Panel Survey (MEPS), to calculate the ratio:

$$\frac{\text{annual medical cost to treat cancer X}}{\text{annual cost to treat lung cancer}}$$

⁴ The study by Demeter et al. is significant in several respects: it is the only published study that provides a cost-per-case basis for cancers in Alberta, and it generated cost estimates based on chart review for individual cases rather than relying on administrative data.

The MEPS is a set of large-scale surveys of families and individuals, their medical providers, and employers across the United States. The advantage of the MEPS is that it contains comprehensive data elements for all cost domains except for institutionalized care. The research team combined five years (2002–2006) of MEPS data on patients' health care and expenditure received in the settings of hospital inpatient, hospital outpatient, emergency room, and physician office. Then, the research team generated per capita annual cost for lung cancer and 15 of the 21 other types of cancers (from groups A or B, tumour sites with strong or suspected links to occupational cancer) that are of top research interest in the present study.

Approach 2 obtains estimates of the above ratio (i.e., medical costs associated with cancer X divided by medical costs associated with lung cancer) using estimates from the literature. These ratios derived from the literature are used for the other six tumour sites (i.e., mesothelioma, nose and nasal sinuses, esophagus, ovary, pharynx, and stomach), though for comparison purposes the research team obtained and reports ratios for other cancers. These ratios from the published literature reflect studies conducted in other countries (e.g., Australia, United States and Korea). In many cases, multiple ratios are available for a particular cancer type, which presents the option to use the average of ratio estimates from multiple studies or make adjustments based on the factors of jurisdiction, study design (prevalence-based or incidence-based model), population (general population or elderly population), time frame of cost estimation (annual or lifetime), or whether recorded by cancer registry (non-melanoma skin cancer or other registry-documented cancers). None of the published studies capture more than half of the tumour sites of interest, which results in the application of various types of adjustments. Simply using the average values from multiple studies will overlook the heterogeneous nature of cost results; however, the effort to adjust for different factors itself may cause biases and these adjustments cannot be consistently defined and implemented.

Using this research strategy, the research team assumed that the health service utilization pattern for cancer patients and the patient severity mix are similar in Alberta and the United States. The research team also assumed that cost ratios across different cancer types have remained relatively constant in recent years, recognizing that over time the average cost per cancer case can grow at different rates for different types of cancers. The research team then applied these ratios to the actual annual cost of lung cancer treatment in Alberta to create an estimate of direct costs associated with other occupational cancer types. The estimated medical costs per person by tumour site are presented in Table 14. Full citations of all literature can be found in the references section of this report. All cost estimates are in 2008 dollars.

Step 3. Multiply the number of attributable occupational cancer cases and estimated average cost per case to calculate the total medical cost of cancers attributable to workplace exposure. The research team applied the numbers of type- and gender-specific prevalent cases of occupational cancers in Alberta (from Section 4 of this report) to Alberta's direct cost estimates by occupational cancer type to estimate medical costs for treating occupational cancers that are attributable to workplace risks.

Table 14: Estimated per patient medical cost ratios and medical costs (in 2008 dollars)

Group	Tumour site	1st approach for cost ratio: from 2002–2006 MEPS	2nd approach for cost ratio: from literature review	Sources for 2nd approach	Cost ratio used in the model	Estimated annual medical cost per case in Alberta (\$)
Group A						
	Bladder	0.46	0.35	AIHW, 2005; Bosanquet, 2004; Hertz, 2005; Kim, 2008	0.46	6,040
	Bone	1.00	0.68	AIHW, 2005; Hertz, 2005	1.00	13,264
	Larynx	1.10	0.42	AIHW, 2005	1.10	14,471
	Leukemia	0.85	1.07	AIHW, 2005; Bosanquet, 2004; Hertz, 2005; Kim, 2008	0.85	11,219
	Liver	1.08	0.91	AIHW, 2005; Kim, 2008	1.08	14,329
	Lung	1.00	1.00	AIHW, 2005; Bosanquet, 2004; Chang, 2004; Hertz, 2005; Kim, 2008	1.00	13,214
	Melanoma	0.30	0.22	AIHW, 2005; Bosanquet, 2004; Hertz, 2005; Kim, 2008	0.30	3,954
	Mesothelioma	N/A	1.23	AIHW, 2005; Bosanquet, 2004; Chang, 2004; Kim, 2008	1.23	16,198
	Nose and nasal sinuses	N/A	0.60	Bosanquet, 2004; Hertz, 2005	0.60	7,977
	Skin (NMSC)	0.19	N/A	N/A	0.19	2,484
Group B						
	Brain	1.32	1.37	AIHW, 2005; Chang, 2004; Hertz, 2005; Kim, 2008	1.32	17,387
	Cervix	0.49	0.34	AIHW, 2005; Bosanquet, 2004; Hertz, 2005; Kim, 2008	0.49	6,454
	Colon	0.68	0.51	AIHW, 2005; Bosanquet, 2004; Chang, 2004; Hertz, 2005; Kim, 2008	0.68	9,006
	Esophagus	N/A	1.37	AIHW, 2005; Bosanquet, 2004; Kim, 2008	1.37	18,165
	Kidney	0.76	0.46	AIHW, 2005; Kim, 2008	0.76	10,014
	Non-Hodgkin lymphoma	1.27	0.63	AIHW, 2005; Bosanquet, 2004; Hertz, 2005; Kim, 2008	1.27	16,773
	Oral cavity	0.38	0.44	Kim, 2008	0.38	5,030
	Ovary	N/A	1.05	AIHW, 2005; Bosanquet, 2004; Chang, 2004; Hertz, 2005; Kim, 2008	1.05	13,813
	Pancreas	1.22	1.23	AIHW, 2005; Bosanquet, 2004; Chang, 2004; Kim, 2008	1.22	16,131
	Pharynx	N/A	0.62	AIHW, 2005; Kim, 2008	0.62	8,236
	Rectum	0.64	0.60	AIHW, 2005; Chang, 2004; Hertz, 2005; Kim, 2008	0.64	8,506
	Stomach	N/A	0.82	AIHW, 2005; Hertz, 2005; Kim, 2008	0.82	10,854

Note: Lung cancer is used as the reference disease for calculating medical costs.

Step 4. Validate and benchmark cost estimates. The research team compared the estimates of medical cost with the following available sources to validate and benchmark cost estimates:

- studies on the costs of cancer treatment across Canada (e.g., breast cancer, colon cancer, prostate cancer) (Grover et al., 2000; Maroun et al., 2003; Will et al., 2000)
- the Ontario Case Costing Project (OCCP) (<http://www.occp.com>) on cost estimates. In the OCCP, costs are presented as direct cost per event and the patient's cost is determined by costs incurred within the patient's admission and discharge dates in the functional centre. OCCP data do not directly help determine the medical costs on a per-patient basis because the system does not control for either the volume of patient use of different medical services or the severity mix of patient populations. Therefore, the research team and external reviewers felt that the data from the OCCP could only be used to validate the unit cost by type but could not be directly used in the model.

Indirect costs

Indirect costs are defined as the value of economic output lost because of occupational cancer-related work disability, lower productivity (work days absent and reduced performance while at work) or premature death. These costs are not reflected by direct monetary transactions but do reflect the use of economic resources in response to disease occurrence and treatment—resources that could be used for other purposes in the absence of occupational cancer. The indirect costs associated with occupational cancer include health-related days absent from work (absenteeism), reduced job performance due to health problems (presenteeism), reduced labour force participation, reduced earning capacity as a result of disabilities, and lost productivity from premature mortality.

Components of indirect costs are known to be morbidity and premature mortality.

Morbidity

Morbidity costs are the value of lost economic output for people who are ill or disabled and unable to work or participate in their usual activities. Like estimation of direct costs, indirect cost estimation relies heavily on data availability.

Estimated morbidity costs of occupational cancers typically include losses measured by the value of forgone earnings. These losses are measured among currently employed persons not in institutions who are unable to work or participate in usual activities, and persons in extended care facilities (e.g., nursing homes or homes for aged). Ideally, we would generate estimates on the duration or probability of lost productivity (absenteeism, presenteeism and disability) by using population-based surveys that can monitor people's health conditions. For example, we may first identify demographic-specific productivity loss (e.g., days lost per worker, level of activity limitation, and short-term or long-term disability) due to illness or disability and then attribute productivity loss to specific tumour sites.

However, the Canadian Community Health Survey—the main source for productivity loss—has significant data gaps in several major parameters (e.g., disability days are too unreliable to be published for most demographic groups), which prevented the research team from pursuing the population-based method further. The unavailability of another key data source, the Canada-specific Quebec Health and Social Survey,⁵ the best data option to pursue in attributing productivity loss to specific conditions, also limited the option of using a population-based approach.

Indirect costs were calculated using the following data segments:

1. **Annual number of prevalent cases.** Prevalent cases by sex, age, and occupational cancer site are prepared using data from the Alberta Cancer Registry, as described in Section 4.
2. **Days lost per worker per year due to absenteeism.** Due to the lack of population-based data sources, a secondary approach of literature review was adopted to synthesize lost-days information by tumour site from multiple study sources. The research team closely reviewed a series of studies that reported days absent from work. The research team considered the studies' characteristics (e.g., study design, stage of disease, population composition), to determine whether to directly use the published absenteeism statistics or to impute the number of absent days using the length of inpatient days plus half of the number of physician visits. Published sources on work days lost (by tumour site) and estimates used in modelling are listed in Table 15. As the heterogeneity of existing literature cannot be accommodated by analytical techniques such as meta-analysis to generate confidence intervals, the research team tested different values for work days lost in the sensitivity analysis.
3. **Probability of short- and long-term disability by cause.** The literature was reviewed and synthesized to estimate the extent to which patients with occupational cancers have health-related disability rates that are higher than people without occupational cancers. Statistics such as odds ratios (OR) and relative risks (RR) were translated into the probability of disability. Literature sources for probability of disability by tumour site are listed in Table 15. Confidence intervals cannot be generated, but the research team conducted a sensitivity analysis on the disability probability estimates.
4. **Labour force participation rates.** The workforce participation estimates by sex and age groups were prepared using Alberta-specific data from the General Social Survey (GSS) 2005 and the Labour Force Survey (LFS) 2008.
5. **Average daily earnings.** The estimates by sex and age groups were prepared using Alberta annual earning data from the Income Statistics Division, Statistics Canada. The annual earnings were reported in 2006 constant dollars and the study team escalated the annual earnings to 2008 estimates using the average income growth rate over the past decade. The average daily earnings were derived from the annual earnings divided by annual work days; the number of 240 work days per year was used in the cost model.

⁵ Data from this source were unavailable in the time frame of data gathering for the present study.

Table 15: Value used and literature source for work days lost and disability probability by tumour site

Cancer site	Disability probability			Work days lost	
	Male	Female	Source	Both sexes	Source
Group A - cancers with a strong link to occupational exposure					
Bladder	0.20	0.15	Syse, 2008; Taskila, 2004	13.8	Kim, 2008; Yabroff, 2007; Syse, 2008; New South Wales, 2007
Bone	0.26	0.20	Syse, 2008; Schultz, 2002; Short, 2005; de Boer, 2009	33.4	Kim, 2008
Larynx	0.32	0.48	Short, 2005; Hewitt, 2003; Syse, 2008	18.1	Kim, 2008; Yabroff, 2007
Leukemia	0.32	0.37	de Lima et al., 1997; Syse, 2008; Spelten, 2002; Hewitt, 2003; Schultz, 2002	43.3	Syse, 2008; New South Wales, 2007; Kim, 2008
Liver	0.32	0.48	Syse, 2008; Short, 2005; Yabroff, 2004; Taskila, 2004	27.4	Kim, 2008; Yabroff, 2004
Lung	0.32	0.48	Syse, 2008; Short, 2005; Yabroff, 2004; Taskila, 2004; Hewitt, 2003; Schultz, 2002	23.7	Yabroff, 2004, 2007; Kim, 2008; New South Wales, 2007; Syse, 2008
Melanoma	0.21	0.20	New South Wales, 2007; Syse, 2008; de Boer, 2009; Short, 2005; Hewitt, 2003; Schultz, 2002	11.0	Kim, 2008; Yabroff, 2007; New South Wales, 2007
Mesothelioma	0.21	0.19	Siskind, 1987; Cookson, 1985	38.9	Kim, 2008
Nose and nasal sinuses	0.21	0.16	Short, 2005; Schultz, 2002; Syse, 2008; de Boer, 2009	18.1	Kim, 2008; Yabroff, 2007
Skin (NMSC)	0.03	0.03	Syse, 2008; Taskila, 2004	0.9	Chen, 2006
Group B - Cancers with a suspected link to occupational exposure					
Brain	0.23	0.18	Short, 2002; Syse, 2008	31.6	Kim, 2008; New South Wales, 2007
Cervix	NA	0.36	Short, 2002; Syse, 2008; Hewitt, 2003; de Boer, 2009; Schultz, 2002	11.4	Kim 2008, Hewitt 2003
Colon	0.22	0.17	Syse, 2008; Yabroff, 2004; Hewitt, 2003; Schultz, 2002; Taskila, 2004	17.4	New South Wales, 2007; Yabroff, 2004, 2007; Kim, 2008
Esophagus	0.32	0.48	Syse, 2008; Short, 2005; Yabroff, 2004; Taskila, 2004	33.4	Kim, 2008; Yabroff, 2004, 2007
Kidney	0.52	0.52	Taskila, 2004	18.9	Kim, 2008; New South Wales, 2007
Non-Hodgkin lymphoma	0.37	0.37	Syse, 2008; Taskila, 2004	26.9	Kim, 2008; New South Wales, 2007
Oral cavity	0.19	0.14	Short, 2005; Syse, 2008; Schultz, 2002	21.8	Kim, 2008; Yabroff, 2007
Ovary	NA	0.38	Syse, 2008; Hewitt, 2003; de Boer, 2009; Schultz, 2002	25.4	Kim, 2008; Yabroff, 2007; Hewitt, 2003
Pancreas	0.32	0.48	Syse, 2008; Short, 2005; Yabroff, 2004; Taskila, 2004; Hewitt, 2003	39.8	Kim, 2008; Yabroff, 2004
Pharynx	0.20	0.16	Short, 2005; Syse, 2008; Hewitt, 2003	24.3	Kim, 2008; Hewitt, 2003
Rectum	0.22	0.17	Syse, 2008; Yabroff, 2004; Hewitt, 2003; Taskila, 2004	17.4	New South Wales, 2007; Yabroff, 2004, 2007; Kim, 2008
Stomach	0.27	0.21	Taskila, 2004; Lee, 2008; Yabroff, 2004	24.2	Kim, 2008; New South Wales, 2007; Yabroff, 2004, 2007; Lee, 2008

For other analyses (e.g., labour productivity growth rate, discount rate), the research team used the same assumptions used in the national Economic Burden of Illness in Canada (EBIC) study (Policy Research Division, Health Canada, 2002) while applying additional sensitivity analyses. For the labour productivity growth rate, the research team adopted the rate of 1.1% and for the discount rate applied to the value of future production, 5% was employed as recommended by the Canadian Coordinating Office for Health Technology Assessment. Sensitivity analyses were conducted for both parameters with plausible values. Analysis of the occupational cancers' impact on presenteeism was not included in this study due to the lack of published data.

Mortality

Mortality costs refer to the present value of future output lost because of premature death due to occupational cancers. Costs associated with premature deaths as mortality costs are generally investigated using one of two methods to estimate their value: the human-capital approach or the willingness-to-pay (WTP) approach.

In the human-capital approach, sex- and age-specific average earnings are combined with expected productivity trends and years of life lost to estimate unrealized lifetime earnings. This approach explicitly values the years of life lost of individuals with greater earnings (e.g., men aged 35 to 55 years) as higher than those of individuals with fewer earnings (e.g., women aged ≥ 75 years). The WTP approach, in contrast, incorporates both lost productivity due to death and the intrinsic value of life by estimating the amount an average individual would be willing to pay for an additional year of life.

Both approaches are relevant for informing health policy. The human-capital approach estimates the impact of premature deaths on the economy, whereas the WTP approach offers a more global estimate of the value of economic loss due to premature deaths. Because incidence and mortality rates for most tumour sites are highest in the elderly—a population that is less likely to be in the workforce than their younger counterparts—comparison of the results of these two approaches is particularly relevant for evaluating the burden of cancer. The research team's estimation for the cost of premature mortality adopts both human-capital and WTP approaches: human-capital is the primary method and WTP serves the secondary role.

The indirect cost estimates calculated using the human-capital approach were based on the results from the following components:

- **Annual number of deaths caused by occupational cancer.** The estimates by sex, age, and occupational cancer site are prepared using data provided by the Alberta Cancer Registry.
- **Life expectancy by age and sex groups.** The estimates by sex and age groups were prepared using data from the Complete Life Table, Alberta, 2000 to 2002 (Depository Services Program, 2006).
- **Labour force participation rates.** The workforce participation estimates by sex and age groups were prepared using Alberta-specific data from the General Social Survey (GSS) 2005 and the Labour Force Survey (LFS) 2008.
- **Average annual earnings.** The estimates by sex and age groups were prepared using Alberta annual earning data from the Income Statistics Division, Statistics Canada (2006). The annual earnings were reported in 2006 constant dollars and the study team escalated the annual earnings to 2008 estimates using the average income growth rate over the past decade.
- **Other analytical parameters.** For the labour productivity growth rate, the research team adopted the rate of 1.1%; for the discount rate applied to the value of future production, 5% was employed as recommended by the Canadian Coordinating Office for Health Technology Assessment; and for

the discount adjustment on the productivity of unemployed working-age population, 75% of the value of the employed people of the same age and sex was applied in the model. Sensitivity analyses were conducted for all these parameters.

For the WTP approach, value-of-life estimates as derived from these studies vary widely, from a few hundred thousand dollars to several million dollars (Cutler et al., 2002). It also has been shown that the value of life increases over time, which can be explained in part by the increase in national wealth per capita, which makes investments in life-extending interventions more affordable, and by an increase in life expectancy itself, which increases the value of death averted at any given age (Costa & Kahn, 2004). Estimates implicitly incorporate both economic losses due to illness and the intrinsic value of living; therefore, the WTP measure is not directly comparable with mortality cost as measured by the human-capital approach. The research team used the WTP measure to supplement the human-capital measure in estimating indirect costs of occupational cancer.

The research team reviewed a wide range of value-of-life studies that include occupational cancers and decided to use the approach recommended by the World Health Organization Commission on Macroeconomics and Health (2001). This approach suggests that, as a benchmark for evaluating the cost-effectiveness of health interventions, a cost-effectiveness ratio of less than three times per capita gross domestic product (GDP) should be considered favourable. The per capita GDP in 2008 in Canada was about \$36,400 according to the World Bank (2009), and three times the 2008 per capita GDP would be about \$109,200. Although there is no consensus on the appropriate value of a year of life, the value approach chosen is consistent with other estimates and the methods are sufficiently transparent to allow application of other dollar amounts that are based on other approaches (Hirth, Chernew, Miller, Fendrick, & Weissert, 2000; Nordhaus, 2002).

Specific steps to implement the WTP analysis are as follows:

- Estimate age- and gender-specific cancer mortality rates in 2008.
- Apply age- and gender-specific mortality rates to their corresponding populations to estimate the number of cancer deaths in 2008.
- For each death, compute person-years of life lost (PYLL) by looking up cohort life tables.
- Multiply the PYLL by the value of a life year to calculate the value of life lost.
- Apply gender- and tumour-site-specific attributable fractions to calculate the value of life lost that is attributable to workplace risk factors.

Adjusting for inflation

Because the results of many cost-of-cancer studies conducted in past years need to be expressed in current-year dollars, the research team used the health-care component of the Alberta-specific Consumer Price Index (CPI) to adjust for inflation. All the cost estimates are reported in 2008 dollars.

Results

Occupational cancers have imposed a significant burden in Alberta. Table 16 shows that in 2008 there were 2,254 prevalent cases among Group A (cancers with a *strong* link to occupational exposure) that were attributable to occupational risk factors, of which more than three-quarters were non-melanoma skin cancer (NMSC). These cancers also contributed to 217 disability cases, 137 early mortality cases, and 14,211 absent days. Group B (cancers with a *suspected* link to occupational exposure) comprised an attributable burden of 407 cancer cases, 131 disability cases, 119 early mortality cases, and 9,788 absent days.

Table 16: Prevalent cases and reduced productivity attributable to occupational risks in 2008 by tumour site

Cancer site	Total prevalent cancer cases	Total cases attributable to occupational exposure	Attributed disability cases	Attributed early mortality cases	Attributed lost work days due to absenteeism per year
Group A - Cancers with a strong link to occupational exposure					
Bladder	1,153	106	21	11	1,456
Bone	364	2	1	2	73
Larynx	258	19	6	3	339
Leukemia	1,251	56	18	12	2,410
Liver	289	9	4	8	242
Lung	2,953	284	99	91	6,713
Melanoma	1,977	47	10	5	516
Mesothelioma	25	23	5	3	888
Nose and nasal sinuses	21	7	1	0	119
Skin (NMSC)	25,559	1,703	53	2	1,455
SUBTOTAL	33,850	2,254	217	137	14,211
Group B - Cancers with a suspected link to occupational exposure					
Brain	388	26	6	11	812
Cervix	646	38	14	1	434
Colon	3,676	58	13	25	1,009
Esophagus	207	8	3	9	276
Kidney	1,312	21	11	9	389
Non-Hodgkin lymphoma	1,921	168	62	14	4,529
Oral cavity	818	7	1	6	157
Ovary	522	11	4	2	279
Pancreas	393	20	8	18	786
Pharynx	116	2	0	3	51
Rectum	1,478	15	3	11	260
Stomach	515	33	7	13	806
SUBTOTAL	11,992	407	131	119	9,788
Groups A and B combined					
TOTAL	45,841	2,661	348	256	23,999

Table 17: Per capita costs attributable to occupational risks in 2008 by tumour site

Cancer site	Per capita total annual attributable cost (\$)	Per capita annual attributed medical cost (\$)	Per capita annual attributed indirect cost (\$)
Group A - cancers with a strong link to occupational exposure			
Bladder	25,360	6,040	19,320
Bone	455,480	13,264	442,216
Larynx	54,912	14,471	40,441
Leukemia	69,000	11,219	57,781
Liver	280,256	14,329	265,927
Lung	78,499	13,214	65,285
Melanoma	45,393	3,954	41,439
Mesothelioma	40,487	16,198	24,288
Nose and nasal sinuses	15,106	7,977	7,129
Skin (NMSC)	3,233	2,484	749
Group B - Cancers with a suspected link to occupational exposure			
Brain	225,304	17,387	207,917
Cervix	17,736	6,454	11,282
Colon	95,049	9,006	86,043
Esophagus	288,739	18,165	270,574
Kidney	121,026	10,014	111,012
Non-Hodgkin lymphoma	44,979	16,773	28,206
Oral cavity	240,595	5,030	235,565
Ovary	46,603	13,813	32,790
Pancreas	206,262	16,131	190,130
Pharynx	499,302	8,236	491,066
Rectum	153,177	8,506	144,671
Stomach	114,218	10,854	103,364

Per capita costs (total, medical, and indirect) that were attributable to occupational risks by tumour site are organized in Table 17 and are presented in 2008 dollars.

Monetary values were applied to prevalence and forgone productivity to generate the cost estimates of occupational cancers. Table 18 shows the estimates of direct and indirect costs by cancer site in Alberta; indirect costs are composed of morbidity and mortality costs estimated using the human-capital approach. Group A was associated with an increased cost of \$42 million (\$10 million in medical costs and \$32 million in indirect costs) and Group B was associated with an increased cost of \$37.9 million (\$5.4 million in medical costs and \$32.5 million in indirect costs). By cancer site, lung cancer was the biggest cost driver, associated with approximately \$22.3 million dollars (\$3.7 million in medical costs and \$18.5 million in indirect costs). Non-Hodgkin lymphoma, the second most resource-consuming cancer, was associated with an increased cost of \$7.6 million (\$2.8 million in medical costs and \$4.7 million in indirect costs).

Overall, medical cost contributed 20% of the total cost with groups A and B combined, and this cost component represented 24% and 14% of the total costs in the groups A and B, respectively.

Table 18: Costs attributable to occupational risks in 2008 by tumour site

Cancer site	Total annual attributable cost (\$ in thousands)	Attributed medical cost (\$ in thousands) and its proportion (%) of the total		Attributed indirect cost (\$ in thousands) and its proportion (%) of the total	
Group A - Cancers with a strong link to occupational exposure					
Bladder	2,683	639	24%	2,044	76%
Bone	995	29	3%	966	97%
Larynx	1,030	271	26%	758	74%
Leukemia	3,845	625	16%	3,219	84%
Liver	2,473	126	5%	2,347	95%
Lung	22,257	3,747	17%	18,511	83%
Melanoma	2,131	186	9%	1,945	91%
Mesothelioma	924	370	40%	554	60%
Nose and nasal sinuses	99	52	53%	47	47%
Skin (NMSC)	5,504	4,229	77%	1,276	23%
SUBTOTAL	41,941	10,274	24%	31,667	76%
Group B - Cancers with a suspected link to occupational exposure					
Brain	5,798	447	8%	5,351	92%
Cervix	676	246	36%	430	64%
Colon	5,505	522	9%	4,984	91%
Esophagus	2,390	150	6%	2,239	94%
Kidney	2,489	206	8%	2,283	92%
Non-Hodgkin lymphoma	7,574	2,824	37%	4,749	63%
Oral cavity	1,728	36	2%	1,692	98%
Ovary	511	151	30%	360	70%
Pancreas	4,074	319	8%	3,755	92%
Pharynx	1,041	17	2%	1,024	98%
Rectum	2,287	127	6%	2,160	94%
Stomach	3,811	362	10%	3,449	90%
SUBTOTAL	37,883	5,408	14%	32,475	86%
Groups A & B combined					
TOTAL	79,824	15,682	20%	64,142	80%

Indirect costs (as measured by morbidity and mortality costs) were the majority of the total economic burden. Most of the indirect costs were attributable to mortality costs, as shown in Table 19. These are the same costs shown as indirect costs in Table 18, but are here broken out by indirect cost component.

Indirect costs weighed heavily in the burden of occupational cancers in Alberta. Premature deaths from occupational cancers attributable to workplace risks were associated with a burden of approximately \$27 million for Group A cancers and about \$56 million for cancers in groups A and B combined. Morbidity (i.e., absenteeism and disability) was responsible for 13% of total costs in Group A cancers, 9% for Group B cancers, and 11% for both groups combined.

Table 19: Indirect costs attributable to occupational risks in 2008 by tumour site

Cancer site	Attributed absenteeism cost (\$ in thousands) and its proportion (%) of the total		Attributed disability cost (\$ in thousands) and its proportion (%) of the total		Attributed early mortality cost (\$ in thousands) and its proportion (%) of the total	
Group A - cancers with a strong link to occupational exposure						
Bladder	179	7%	300	12%	1,564	61%
Bone	11	1%	7	0.7%	948	96%
Larynx	60	6%	88	9%	611	63%
Leukemia	364	10%	264	7%	2,592	70%
Liver	31	1%	51	2%	2,265	93%
Lung	817	4%	1,425	7%	16,268	76%
Melanoma	97	5%	142	7%	1,706	82%
Mesothelioma	90	11%	70	8%	395	47%
Nose and nasal sinuses	17	19%	19	22%	11	12%
Skin (NMSC)	209	5%	767	17%	300	6%
SUBTOTAL	1,875	5%	3,134	8%	26,659	67%
Group B - Cancers with a suspected link to occupational exposure						
Brain	162	3%	84	1%	5,104	89%
Cervix	56	9%	199	32%	176	28%
Colon	140	3%	184	3%	4,660	86%
Esophagus	47	2%	39	2%	2,154	91%
Kidney	64	3%	155	6%	2,064	84%
Non-Hodgkin lymphoma	726	10%	891	13%	3,132	45%
Oral Cavity	30	2%	19	1%	1,644	96%
Ovary	28	6%	60	12%	272	57%
Pancreas	91	2%	108	3%	3,556	89%
Pharynx	10	1%	6	1%	1,008	97%
Rectum	40	2%	46	2%	2,074	92%
Stomach	103	3%	94	3%	3,252	87%
SUBTOTAL	1,497	4%	1,884	5%	29,094	79%
Groups A & B combined						
TOTAL	3,372	4%	5,018	7%	55,753	73%

As a supplement to the mortality costs measured by the human-capital approach, the research team applied the secondary approach (WTP) to quantify the economic burden of premature mortality. Person-years of life lost (PYLL) due to attributable cancer deaths varied by sex, age, and tumour site, reflecting sex- and age-specific mortality rates, population size, and the years of life lost compared with life expectancy in the relevant birth cohort (Table 20). PYLL estimates from all occupational cancers (in groups A and B separately or together) combined were higher in men and women younger than 65 than in those aged 65 and older. Among all gender and age groups, lung cancer was the single largest contributor to PYLL due to early death from cancer and higher attributable fractions related to occupational risk factors.

Table 20: Person-years of life lost (PYLL) due to attributable cancer deaths in 2008 by tumour site

Cancer site	Men		Women	
	<65 years	65+ years	<65 years	65+ years
Group A - cancers with a strong link to occupational exposure				
Bladder	54	76	1	5
Bone	36	9	2	1
Larynx	26	16	0	1
Leukemia	92.5	80.2	7.4	9.1
Liver	89.2	50.7	4.6	3.7
Lung	587.8	602.8	83.2	74.7
Melanoma	65.4	21.8	6.1	2.6
Mesothelioma	14.9	24.4	0.0	0.0
Nose and nasal sinuses	0.0	2.3	0.0	0.3
Skin (NMSC)	9.6	9.8	0.4	0.9
SUBTOTAL	976	893	104	98
Group B - Cancers with a suspected link to occupational exposure				
Brain	197	41.5	14.0	5.7
Cervix	NA		14.7	2.1
Colon	162	154.0	20.7	22.7
Esophagus	89	51.1	1.3	3.1
Kidney	78	51.4	5.3	5.4
Non-Hodgkin lymphoma	115	83.4	9.3	11.0
Oral cavity	65	30.0	3.5	3.0
Ovary	NA		22.1	11.9
Pancreas	127	110.8	15.6	18.7
Pharynx	38	13.6	0.5	0.4
Rectum	79	66.6	6.1	6.4
Stomach	126	70.4	7.3	5.1
SUBTOTAL	1,077	673	120	96
Groups A & B combined				
TOTAL	2,053	1,566	225	194

The value of life lost that was associated with occupational cancer deaths in 2008 for men younger than 65 and men aged 65 and older were \$107 million and \$98 million in Group A, and \$118 million and \$74 million in Group B, respectively. Estimates for women younger than 65 and women aged 65 and older were \$11.4 million and \$10.8 million for Group A cancers, and \$13.2 million and \$10.5 million for Group B cancers, respectively (Table 21). For specific cancer sites, lung cancer is again the biggest contributor to value of life lost in all categories, followed by brain cancer in men younger than 65, and colon cancer in men of both age groups.

Table 21: Value of life lost due to attributable cancer deaths in 2008 by tumour site

Cancer site	Men		Women	
	<65 years (\$ in thousands)	65+ years (\$ in thousands)	<65 years (\$ in thousands)	65+ years (\$ in thousands)
Group A - cancers with a strong link to occupational exposure				
Bladder	5,899	8,326	57	540
Bone	3,984	1,012	205	122
Larynx	2,885	1,695	0	131
Leukemia	10,108	8,773	814	995
Liver	9,752	5,543	498	401
Lung	64,270	65,905	9,099	8,162
Melanoma	7,151	2,383	665	288
Mesothelioma	1,624	2,663	0	0
Nose and nasal sinuses	0	251	0	31
Skin (NMSC)	1,050	1,074	47	95
SUBTOTAL	106,724	97,625	11,384	10,766
Group B - Cancers with a suspected link to occupational exposure				
Brain	21,567	4,542	1,535	625
Cervix	NA		1,605	234
Colon	17,732	16,841	2,259	2,478
Esophagus	9,752	5,582	142	337
Kidney	8,546	5,622	576	592
Non-Hodgkin lymphoma	12,566	9,119	1,015	1,206
Oral cavity	7,087	3,279	385	332
Ovary	NA		2,421	1,300
Pancreas	13,920	12,118	1,708	2,047
Pharynx	4,195	1,486	57	41
Rectum	8,683	7,277	671	702
Stomach	13,735	7,702	797	558
SUBTOTAL	117,782	73,569	13,171	10,451
Groups A & B combined				
TOTAL	224,506	171,193	24,555	21,217

Sensitivity analysis

For sensitivity analyses, the research team employed a series of “what if” scenarios to test the robustness of the evaluation, and thus the degree of confidence that can be placed in the cost results. In addition to further testing synthesized estimates from the literature review (i.e., attributable fractions by cancer site plus low and high bounds), the research team conducted sensitivity analyses by altering values in discounting to the value of future production, future productivity growth, and adjustment in the productivity of the unemployed working-age population. The one-way analysis method was used with one parameter varied at a time.

Discounting

As mentioned above, mortality costs are usually expressed in terms of present value: the sum of discounted annual costs. Discounting is applied to adjust the value of costs incurred in the future because the same resources, if available and invested today, would yield a return if placed in a productive activity. The most commonly used value in the health economics literature is 5% in real terms (adjusted for inflation). A range of recommended rates from 2% to 10% were applied in sensitivity analyses.

Productivity growth

To be consistent with the 2002 national study, baseline estimates assume that future labour productivity will grow by 1.1% per year, a value chosen by Health Canada to reflect Canadian historical rates over the preceding decade. Sensitivity analyses were conducted with growth rates of -0.3% and 2.8%, reflecting average annual labour productivity growth rates observed in recent years (Statistics Canada, 2005).

Adjustment in the productivity of the unemployed, working-age population

The value of 75% of the average earnings for people in the labour force was used as a proxy for the value of productivity for people of working age but not in the work force. The research team tested values between 50% and 90% in the sensitivity analyses.

Changes in the values of disability probability

Disability probability for each tumour site was collected through a literature review. For the sensitivity analyses the research team used the base case values for model parameters $\pm 40\%$.

Changes in the values of work days lost (i.e., absenteeism)

Work days lost by tumour site were collected through a literature review. For the sensitivity analyses the research team used the base case values for model parameters $\pm 40\%$.

Limit modelling estimates to populations aged 40+

To test the results' sensitivity to age groups, the research team changed the cut-off age limit for the analytical population from ages 20 and up to ages 40 and up.

This series of sensitivity analyses, shown in Table 22, demonstrates that the economic burden estimates of occupational cancer are most sensitive to changes in assumptions for attributable fractions. The indirect cost component, the main driver of the total economic burden, is sensitive to the discount rate applied to the value of future production, and to adjustment in productivity of the unemployed, working-age population.

Table 22: Sensitivity of estimates of the economic burden of occupational cancers in Alberta in 2008 to changing assumptions

	Group A cancers only			Group A and B cancers		
	Total direct costs (\$)	Total indirect costs (\$)	Total costs (\$)	Total direct costs (\$)	Total indirect costs (\$)	Total costs (\$)
(\$ in thousands)						
Base case	10,274	31,667	41,941	15,682	64,142	79,824
Attributable fractions						
Average estimate	(base case)					
Low estimate	3,478	10,302	13,780	7,790	22,315	30,105
High estimate	18,077	47,765	65,841	28,222	96,427	124,649
Discount rate applied to the value of future production						
5%	(base case)					
2%	10,274	38,321	48,595	15,682	78,813	94,495
7%	10,274	28,504	38,777	15,682	57,239	72,921
10%	10,274	24,931	35,205	15,682	49,515	65,197
Labour productivity growth						
1.1%	(base case)					
-0.3%	10,274	28,788	39,062	15,682	57,959	73,640
0.4%	10,274	30,173	40,446	15,682	60,927	76,608
1.8%	10,274	33,285	43,559	15,682	67,637	83,319
2.8%	10,274	35,842	46,116	15,682	73,185	88,867
Adjustment in the productivity of unemployed, working-age population						
75%	(base case)					
50%	10,274	28,254	38,528	15,682	57,476	73,157
65%	10,274	30,302	40,575	15,682	61,476	77,157
80%	10,274	32,350	42,623	15,682	65,476	81,157
90%	10,274	33,715	43,988	15,682	68,142	83,824
Changes in the values of disability probability						
-40% of base case value	10,274	30,413	40,687	15,682	62,135	77,817
-20% of base case value	10,274	31,040	41,314	15,682	63,139	78,821
+20% of base case value	10,274	32,294	42,567	15,682	65,146	80,828
+40% of base case value	10,274	32,921	43,194	15,682	66,150	81,831
Changes in the values of work days lost (absenteeism)						
-40% of base case value	10,274	30,917	41,191	15,682	62,794	78,475
-20% of base case value	10,274	31,292	41,566	15,682	63,468	79,150
+20% of base case value	10,274	32,042	42,316	15,682	64,817	80,498
+40% of base case value	10,274	32,417	42,690	15,682	65,491	81,173
Limit to age 40+ population						
Aged 40+ only	9,997	29,963	39,960	15,007	59,007	74,014

Discussion

The estimates of the economic burden of occupational cancers in Alberta were constrained by the limited availability of data sources. There are no large national or regional health surveys available, so the analysis must rely on either a literature review when data synthesis is challenging or a small local study (e.g., the study by Demeter et al. on lung cancer) that addresses only one cancer site in a highly selected population.

It is important to note that the medical costs in this study are based on current cancer-related expenditures. The costs associated with cancer treatment, especially cancer drugs, have been rising far faster than the costs of inflation, driven mainly by new technologies, and new and more expensive cancer drugs. Therefore, future costs associated with occupational cancers will likely continue to rise, even if the number of occupational cancers remains constant or decreases.

SECTION 6. Discussion of limitations and uncertainties

Although this analysis was conducted with as much precision as possible given the available data, there were uncertainties and limitations that may have added imprecision to the estimates of cancer numbers and costs. A number of these uncertainties and limitations are described below and in Table 23, along with a description of how the estimates of cancer numbers and costs may have been affected. This format for presenting limitations was adapted from Rushton et al. (2008).

- There is a great deal of uncertainty as to whether exposure to workplace carcinogens is different in Alberta from exposure in the populations in which the attributable fractions were developed. The AFs used in the analysis were drawn from a number of countries, and from both recent and not-as-recent time periods. It is likely that the proportion of workers exposed to carcinogens is different in these populations; there may also be differences in the types of carcinogens used in the workplace, and the degree of exposure. The extent of these differences, however, is not known. This adds imprecision to the estimate, but it is not possible to determine the direction of the effect.
- Similarly, there may be other, unknown differences between the original populations and Alberta's population that are relevant to cancer development, including lifestyle and behavioural risk factors, and environmental exposures to carcinogens.
- The attributable fraction estimates that form the basis of the analysis are themselves imprecise and hindered by a number of limitations. These limitations are usually catalogued in each original study (for example, see Rushton, 2009). The estimates for Alberta will reflect these uncertainties.
- Many cancer sites are not included in the analysis because not enough is known about the relationship between occupational exposure and the development of cancer at that site. This would tend to result in underestimates of the true number of occupational cancers (Straif, 2008). However, the known carcinogen exposures do represent the most appropriate targets for prevention efforts.
- Many potential carcinogens were not included in the original AF estimates. As discussed in Section 1, a relatively low number of substances have been assessed for carcinogenicity, and new substances are being added to the work environment every year. However, the original studies from which the AFs were derived tend to use a conservative approach that is based solely on exposure to IARC Group 1 and 2A carcinogens. This would tend to result in an underestimation of the true burden of occupational cancer (Clapp et al., 2007).
- Environmental tobacco smoke (ETS, also known as second-hand smoke) was a nearly ubiquitous workplace exposure 20+ years ago and was included as a carcinogen in most of the cancer estimates. Very few workers are exposed to ETS on the job currently in Alberta; this could inflate the

estimates of occupational lung cancer and other cancers for which tobacco smoke increases risk. Similarly, many workers were themselves smokers, which would have increased their risk of lung and other cancers. However, smoking outside the workplace was also extremely common in the past; therefore, the estimates of relative risk on which the attributable fractions were based may not have been affected.

- The exposure control conditions in Alberta workplaces are likely better than they were 20+ years ago. Although this would not affect the estimate of the numbers of current cases that can be linked to occupation, it means that the future burden of cancer is likely to be lower.
- The cost to treat various cancers in Alberta (relative to one another) could be different from the cost to treat cancers (relative to one another) in other geographic areas. For example, differences in access to diagnostic equipment and differences in financing medical care in different locations could lead to differences in treatment patterns and associated medical costs.
- Lung cancer is relatively expensive compared with many other cancer types. Because excellent lung cancer cost data were available for Alberta, these data were used as the basis for costing all types of cancer. This may lead to an overestimation of the actual cost for other cancers. However, not all components of direct medical costs associated with lung cancer were included in the original study (e.g., clinician visits were omitted, and only those drugs used for chemotherapy were included). This may have caused an underestimation of true costs.
- The research team’s approach to measuring the cost components has been driven by the availability of existing data rather than by explicit consideration of design strength and limits. The limited data availability by tumour site and demographic group prevented the research team from conducting a more consistently defined analysis for absenteeism and disability.

Table 23: Uncertainties and limitations of the methodology and their potential impact on the estimates of burden of disease and cost due to occupation

Source of uncertainty	Potential impact on numbers and/or cost estimate
Dissimilarity of occupational exposures between Alberta and other populations	↓↑
Dissimilarity of non-occupational cancer risk factors between Alberta and other populations	↓↑
Imprecision of source data for attributable fractions	↓↑
Not all cancer sites included	↓
Exclusion of unknown or unproven carcinogens	↓
Environmental tobacco smoke no longer a common workplace exposure	↑
Current exposure control conditions likely better than in the past	↑
Cost of cancers may be different between Alberta and regions from which cost information was drawn	↓↑
Lung cancer costs used for economic analysis may not be comparable with other cancer costs	↓↑

↑ means the estimate of potential burden may have been elevated.
 ↓ means the estimate of potential burden may have been decreased.

SECTION 7. Occupational cancer prevention

This section discusses prevention strategies relevant to the reduction of occupational cancer in Alberta. The strategies are broken out into two specific target areas:

- **General recommendations.** The general recommendations present approaches relevant to the prevention of all types of cancers in all industry and occupational sectors. These general recommendations have been developed from a review of best practices in the occupational cancer literature.
- **Process-related recommendations.** This refers to lessons that can be learned about how a future analysis of occupational cancer costs could be improved, based on the limitations that were encountered in the present study.

The focus of this report up to this point has been on estimating the current cancer burden in Alberta based on historical exposure levels. From this point on, the focus shifts to a discussion of current occupational carcinogen exposures to identify target areas to reduce the future burden of cancer in the province.

General recommendations

Occupational and environmental cancer prevention has received a great deal of attention within Alberta, across Canada and internationally. Recent examples of large-scale activities addressing this issue within Canada include the development of a 2005 report entitled *Prevention of Occupational and Environmental Cancers in Canada: A Best Practices Review and Recommendations* by the Canadian Strategy for Cancer Control; work at the national and provincial level on identifying priority occupational carcinogens for surveillance (see Appendix B); and a 2008 workshop sponsored by the Canadian Cancer Society, entitled “Exploring the Connection: A State of the Science Conference on Pesticides and Cancer.”

A number of experts have pointed out that occupational cancers are among the most preventable. There are a number of reasons for this, including well-developed methods for identifying carcinogens and exposure circumstances, restriction or concentration of exposure to relatively small groups, easy identification of a point source of exposure (i.e., the workplace), and well-developed methodologies for exposure prevention and control (Doll & Peto, 1981; LaMontagne & Christiani, 2002; Landrigan, 1996; Straif, 2008).

Prevention and control of exposure to occupational carcinogens is ideally confronted as close to the source as possible. This means targeting, wherever possible, the manufacturers and distributors of carcinogenic substances and the companies who use these substances, rather than the workers who are affected by the exposure. This is done for both ethical and practical reasons. As an ethical issue, it is more appropriate to impose limitations on the voluntary risk takers (i.e., the industries that benefit from carcinogen use) rather than the involuntary risk receivers. In practical terms, controlling close to the source is more likely to result in compliance. Regulations are also more easily enforceable at an industrial rather than a personal scale. And regulating further upstream can also help prevent occupational carcinogens from turning into environmental concerns.

Figure 4: Hierarchy of occupational cancer prevention levels

Effectiveness	Prevention level	Prevention target	Hierarchy of controls
	Primary	Control at the source of hazard	Elimination Substitution Use reduction
	Primary	Controlling dispersion	Engineering controls (e.g., local exhaust ventilation, process enclosure) Exposure assessment administrative controls (e.g., workplace policies and procedures)
	Primary	Control at the worker	Safe work practices Personal protective equipment Biological monitoring for absorption of a toxicant
	Secondary	Control at the worker	Pre-clinical medical exams/screening Biological monitoring for effects of absorbed toxicants
	Least effective	Tertiary	Control at the worker

Note: From “Prevention of Work-Related Cancers,” by A. D. LaMontagne and D. C. Christiani, 2002, *New Solutions*, 12(2), p. 144. Copyright 2002 by Baywood Publishing. Reprinted with permission.

LaMontagne and Christiani (2002) have identified a hierarchy of workplace cancer prevention and control strategies. This hierarchy clearly specifies, from most effective to least effective, appropriate targets for prevention and specific control mechanisms associated with each target. This hierarchy is presented in Figure 4 and is further described below.

At the top of the list is control at the source of the hazard. Through elimination or substitution of materials, exposure to specific known carcinogens can be essentially eliminated. An important consideration is ensuring that the materials substituted do not create new hazards. An example of controlling at the source of the hazard can be found in the dry cleaning industry, with efforts to replace perchloroethylene with safer substitutes.

Controlling dispersion refers to using engineering or process technologies to reduce worker exposure to the lowest practicable levels. Examples include using dust bags on power tools used for sanding or cutting, or improving exhaust ventilation systems for indoor machinery. A reduction in allowable occupational exposure limits is also an example of a control target that falls into this category. As with control of the source of the hazard, the onus is on the industrial user—the company or manufacturer—rather than on the individual worker, improving the likelihood of success. Local regulations or industry-wide norms may play a part in the adoption of and adherence to these technologies.

There are several methods for controlling carcinogen exposure at the level of the individual worker. The most important and effective of these are education and training in hazard recognition and in the use of personal protective equipment such as masks and respirators. These activities require engagement at all levels of the workplace hierarchy, including workers, unions, supervisors and managers.

Secondary prevention at the worker level comprises screening and surveillance activities to regularly monitor individuals who may be exposed to carcinogens but who show no signs of disease. Early detection may allow the identification of industrial processes that contribute to high levels of exposure; however, it is unlikely to play a direct role in preventing work-related cancer among individuals who have been found to have abnormally high concentrations of toxins.

Finally, the diagnosis and treatment of workers with cancers play important roles in assisting those individuals, but are quite ineffective as a population control approach.

In a 2009 publication, Cherrie described a series of eight generic principles for good control practices that were set out in 2004 in the United Kingdom through the Control of Substances Hazardous to Health (COSHH) regulations. These good control practices are reproduced in Table 24.⁶ The eight guidelines reinforce the principles described above in Figure 4: prevention or reduction of carcinogen exposure can take place at the level of the workplace or of the worker, but the former is more effective than the latter. Additionally, the COSHH guidelines present several concrete measures that should be taken by responsible agencies and organizations.

The process by which cancer prevention strategies are developed and translated into action almost invariably involves a broad array of stakeholders (Canadian Strategy for Cancer Control, 2005). Trade-offs and compromises need to be made to meet the needs and perspectives of a variety of groups including regulators, interest groups and employers, and must be weighed against scientific evidence and feasibility considerations (Verma, Purdham, & Roels, 2002). Though regulation and legislation are effective approaches, their impact can be strengthened if coupled with employer and public education or awareness campaigns (Cherrie, 2009; Verma et al., 2002).

Table 24: Guidelines for “good control practice” in the COSHH regulations

- | |
|---|
| 1. Design and operate processes and activities to minimize emission, release and spread of substances hazardous to health. |
| 2. Take into account all relevant routes of exposure—inhalation, skin absorption and ingestion—when developing control measures. |
| 3. Control exposure by measures that are proportionate to the health risk. |
| 4. Choose the most effective and reliable control options that minimize the escape and spread of substances hazardous to health. |
| 5. Where adequate control of exposure cannot be achieved by other means, provide, in combination with other control measures, suitable personal protective equipment. |
| 6. Check and review regularly all elements of control measures for their continuing effectiveness. |
| 7. Inform and train all employees about the hazards and risks from the substances with which they work and the use of control measures developed to minimize the risks. |
| 8. Ensure that the introduction of control measures does not increase the overall risk to health and safety. |

Source: Cherrie, 2009

⁶ Cherrie also reports that the “good control practice” approach is supplemented by an online tool to assist with implementing these control approaches in specific situations where hazardous substances are used. This tool is available at <http://www.coshh-essentials.org.uk>

In Canada, the National Committee on Environmental and Occupational Exposures (NCEOE) has developed seven recommendations for priority areas to address current gaps in the prevention of occupational and environmental cancers. For each priority area, best practices are identified from among those in use worldwide. The seven priority areas are surveillance, information disclosure and labelling, community education and action, worker education and action, non-governmental organizations' work in cancer prevention, employer and industry reduction of carcinogens, and government intervention via legislation, regulation and policy (Canadian Strategy for Cancer Control, 2005).

A last point of agreement among many occupational cancer prevention experts is that action should not wait for definitive evidence. Cherrie states that "further research is needed to enable practical interventions to be identified, but this should not stop us taking action where there are clear interventions available, i.e. for hazardous substances" (2008). "Specific knowledge of cause, though always desirable, is not always necessary to effect prevention" (LaMontagne & Christiani, 2002). "The answer to whether or not a substance causes harm is rarely characterized by scientific certainty" (Verma et al., 2002). These views are in concordance with the precautionary principle endorsed by NCEOE:

Whenever reliable scientific evidence is available that a substance may have an adverse impact on human health and the environment but there is still scientific uncertainty about the precise nature or the magnitude of the potential damage, decision-making must be based on precaution in order to prevent damage to human health and the environment.

(Canadian Strategy for Cancer Control, 2005, p. 6)

Process-related recommendations

This section describes recommendations that are relevant to the improvement of future analyses of the economic burden of occupational cancer in Alberta. These recommendations stem directly from the limitations and difficulties that were encountered in the current study. Several relevant process-related recommendations from the occupational cancer literature are also included.

- **Information on carcinogen exposure conditions in Alberta.** The biggest drawback faced in this study was the lack of data specific to exposure conditions in Alberta workplaces. Fortunately, this is currently being addressed. The CAREX (CARcinogen EXposure) database was originally developed by the Finnish Institute for Occupational Health to support the carcinogen exposure estimation process. CAREX is being modified for the Canadian environment, and a Canadian Workplace Exposure Database (CWED) is being developed. When complete, this project will provide information that will improve estimation of the occupational cancer burden in Alberta. The development of this database represents a significant step forward for an evidence-based cancer prevention strategy. The research team recommends that Alberta Health Services actively support and promote the development and use of this database.

Additionally, once the CAREX/CWED database is complete, it may be worthwhile for AHS to re-run the Excel-based occupational cancer burden model created for this current study using the new CAREX/CWED data. This will enable AHS to further refine estimates of the cancer burden associated with specific industries.

- **Occupational carcinogen exposure registry.** Finland maintains a register of employees exposed to carcinogens (the ASA Register) that has been operating since 1979. A recent study of the impact of the registry showed that the registry notification process (whereby both employees and the national government are notified of an employee's carcinogen exposure) had directly prompted measures to reduce workplace carcinogen exposure in approximately 32% of workplaces. Additionally, the registry was useful in tracking changes in exposure to carcinogens across the country (Kauppinen et al., 2007). A similar registry may be useful in reducing carcinogen exposure in Alberta workplaces, and a separate assessment of the potential costs and benefits of such a registry may be needed.
- **Occupational cancer registry.** Some jurisdictions, such as Italy and Denmark, have either developed separate occupational cancer registries or collect detailed occupational carcinogen surveillance information from patients who have been diagnosed with cancer. Although the collection of this information would not aid an individual patient with his or her prognosis, it is one of the only ways to enable research on the workplace antecedents of specific cancers, and to identify carcinogenic substances and relevant exposure conditions that lead to occupational cancer development in Alberta. Such a registry would also enable development of appropriately targeted prevention programs, and demonstration of changes in the number of cancers within an occupation or task group.
- **Data sharing.** Currently, the Alberta Cancer Registry does not have a data sharing/access agreement in effect with the arm of Alberta Health Services that manages data on disease burden or resource use (Dean, S., personal communication, April 9, 2009). The lack of a data sharing agreement makes it difficult to use or triangulate information about specific cancer types with other information held by Alberta Health Services, such as service provision or cost information. A major advantage of linking administrative data with tumour registry information is that the date of cancer diagnosis and stage of disease at the time of diagnosis can be reliably ascertained. In addition, these data resources provide a longitudinal record of payments, procedures and services so long as the beneficiaries remained enrolled in the plan.

In addition, the research team experienced difficulty in receiving aggregated data from the Alberta Cancer Registry about recent cancers in Alberta. Policies that would allow easier, more timely data sharing (particularly anonymized information through the former entities that now comprise Alberta Health Services) would greatly facilitate future versions of this study or similar studies.

- **Alberta direct cost data.** For this project, little information on direct costs associated with specific cancer types was available. However, Alberta Health Services is working on a project that will allow the estimation of direct costs associated with particular disease diagnoses and other health states (Dean, April 9, 2009). Although this project is not yet complete, it may be finished by the time any updates to this study are made. The research team recommends that Alberta Health Services establish a way of obtaining cancer-specific costing based on actual expenditures.
- **Evolving knowledge.** Understanding of carcinogens continues to evolve as new chemicals are tested and declared to be carcinogenic or are removed from the list of carcinogens of concern. Future estimates of the occupational cancer burden should be updated based on evolving knowledge about carcinogens, exposed populations, current costs, specific cancers associated with occupational carcinogen exposure, and other factors relevant to this analysis.
- **Implementing cancer prevention recommendations.** In moving forward with implementing a strategy to reduce occupational cancers, it will be important to start considering both the “who” and the “how.” Under whose jurisdiction does this fall? How can it be accomplished? Who needs to be brought into the partnership? How can the likely success of this approach be maximized? It is likely that a broad group of stakeholders will need to be mobilized to accomplish these goals.

SECTION 8. Costs and benefits of prevention efforts

Decision-makers require information on the costs and benefits of prevention interventions to efficiently allocate scarce public health resources and other resources to areas where they will have the largest return on investment. Economics provides a framework to guide the efficient allocation of prevention resources.

First, resources should be allocated to prevention activities that generate the largest return on investment. When resources are allocated to one prevention intervention, the “opportunity cost” is that those same resources become unavailable to allocate to the “next best” opportunity, defined as the opportunity with the second highest return on investment.

Second, economics tells us that prevention resources should continue to be allocated until the marginal benefit of additional resources equals the marginal cost. Ideally, spending on prevention would continue until the last \$1.00 spent on prevention returns \$1.00 in benefits. Unfortunately, there is seldom sufficient information to know at what point the net benefit of additional prevention spending equals zero (i.e., marginal benefit = marginal cost).

Information on the total economic burden of occupational cancers helps us understand the magnitude of the problem, but a great deal more information is needed to understand the business case for intervention. When a prevention intervention is proposed, the cost to the payer (e.g., the government) is generally known and equals the size of the budget allocated for that intervention. This budget might underestimate the total cost to society if the intervention imposes a cost on employers or on workers (e.g., the discomfort of wearing a filter mask).

The benefits of an intervention, however, are more difficult to calculate. The actual benefits realized are a function of three factors:

1. By how much does the intervention reduce exposure?
2. By how much does reduced exposure translate into reduced cancer incidence?
3. What are the economic costs avoided (medical and indirect) for each cancer case prevented?

Estimates of annual cost per cancer case only partially inform estimates for this third factor. For example, the annual cost per case of leukemia (medical and indirect costs combined) is estimated to be \$66,300. This does not tell us the total expected costs over one’s lifetime associated with this cancer. Suppose, for example, that on average a person who developed leukemia as a result of occupational exposure lives for five years with the disease. Using a 3% discount rate, the present value of costs over the five-year period is \$304,000 per case. This suggests that interventions that can prevent a case of leukemia for \$304,000 or less would be considered cost-effective (although society would likely pay a much greater amount because the economic evaluation does not include intangible costs such as reduced quality of life).

An interesting example of the application of cost-benefit approaches to occupational cancer prevention is the **REACH** system (**R**egistration, **E**valuation, **A**uthorization and **R**estrictions of **C**hemicals), an initiative of the UK Department for Environment, Food and Rural Affairs. The REACH system aims to manage industrial chemicals to enhance protection of human health and the environment. The annual cost of the REACH program was projected at £45 million per year. The researchers used a “break-even” approach to identify how many cancers would need to be avoided to recoup the costs of the program. Based on their own assumptions about the economic valuation of cancer (which they assessed as equal to £2.46 million per year), they concluded that 18 deaths would have to be reduced per year to cover the costs of the program (Department for Environment, Food and Rural Affairs, 2006). Although the assumptions they used in generating this estimate may be quite different from those that are applicable to Alberta, it is significant to note the very small and potentially achievable cancer reduction that is required to reach a break-even return on investment, even for a very extensive and expensive cancer prevention program.

SECTION 9. Conclusions and recommendations for next steps

This report has described the current understanding of what comprises an occupational cancer, presented results on the number and economic costs of occupational cancers in Alberta, and discussed considerations relevant to cancer prevention in the province, including target areas, costs and benefits, and overall approaches.

The burden of occupational cancers in the province is significant. Based on the current analysis, the research team's best estimates indicate that 761 new occupational cancers develop in Alberta every year, and that over 2,700 people in the province are currently living with cancer due to occupational exposures. These estimates may be as low as 217 new cancers per year and 786 current cases, or they may be as high as 1,520 new cancers per year and over 5,400 current cases. The number of cancer deaths in the province due to occupational cancers is estimated at 263 deaths per year. Non-melanoma skin cancers represent a large part of the numbers of new cancers—almost half—but only a very small proportion (less than one per cent) of cancer deaths.

The costs associated with these cancers are similarly high. The direct cost to the medical system is estimated to be approximately \$15,682,000 per year. These direct medical costs refer to out-of-pocket expenditures by the government for the costs of treating these cancer patients. In addition, indirect costs resulting from the loss of economic resources and reduced productivity are estimated at approximately \$64.1 million per year.

Occupational cancers cannot be ignored. As shown in this study, they place a burden on individuals, families, communities, the health-care infrastructure, taxpayers, and the Alberta government. Unlike lifestyle or behavioural risk factors for cancer, the antecedents of occupational cancer lie outside the control of the individuals at risk. In addition, expert opinion indicates that occupational cancers are preventable. Best practices approaches for cancer prevention have been developed or implemented in a number of jurisdictions, and the benefits appear to outweigh the costs. This provides a moral imperative to move forward with cancer prevention efforts in this province.

At the same time, there is a need to improve understanding of the circumstances surrounding occupational exposure to carcinogens in the province. Exposure information specific to Alberta is almost completely lacking at this time, meaning that we have little understanding of what proportion of the Alberta workforce in each industry is exposed to carcinogens, which carcinogens they are exposed to (as well as the duration, frequency or volume of exposure), and what sorts of protective equipment or measures are being used. This information is critical for improving estimates of cancer burden in the province and, more important, for developing appropriate intervention strategies that will provide a return on investment. The efforts of CAREX Canada to develop the Canadian Workplace Exposure Database (CWED) should continue to be supported.

It is also important to note that the medical costs in this study are based on current cancer-related expenditures. The costs associated with cancer treatment,

especially cancer drugs, have been rising far faster than the costs of inflation, driven mainly by new technologies and new, more expensive cancer drugs. Therefore, future costs associated with occupational cancers will likely continue to rise, even if the number of occupational cancers remains constant or decreases.

In summary, the research team has found that occupational cancers in Alberta are numerous and costly; however, there also exists the possibility of reducing these occupational cancers, thereby saving costs related to disease and treatment, and improving the lives of Albertans.

References

- Alberta Cancer Board. (2007). *Cancer in Alberta: A regional picture 2007*. Calgary, AB: Author.
- Alberta Employment, Immigration and Industry, & Work Safe Alberta (2007). *Occupational injuries and diseases in Alberta: Lost-time claims, disabling injury claims and claim rates, 2006 summary*. Edmonton, AB: Government of Alberta.
- Alberta Municipal Affairs. (2009). *2008 official population list*. Edmonton, AB: Government of Alberta.
- Australian Institute of Health and Welfare. (2005). *Health system expenditures on cancer and other neoplasms in Australia, 2000–01* (Health and Welfare Expenditure Series No. 22). Canberra, Australia: Author.
- Bosanquet, N., & Sikora, K. (2004). The economics of cancer care in the UK. *Lancet Oncology*, 5(9), 568–574.
- Canadian Cancer Society/National Cancer Institute of Canada. (2009). *Canadian cancer statistics 2009*. Toronto, ON: Canadian Cancer Society.
- Canadian Strategy for Cancer Control. (2005). *Prevention of occupational and environmental cancers in Canada: A best practices review and recommendations*.
- Chang, S., Long, S. R., Kutikova, L., Bowman, L., Finley, D., Crown, W. H., et al. (2004). Estimating the cost of cancer: results on the basis of claims data analyses for cancer patients diagnosed with seven types of cancer during 1999 to 2000. *Journal of Clinical Oncology*, 22(17), 3524–3530.
- Chen, G. J., Yelverton, C. B., Polisetty, S. S., Housman, T. S., Williford, P. M., Teuschler, H. V., et al. (2006). Treatment patterns and cost of nonmelanoma skin cancer management. *Dermatologic Surgery*, 32(10), 1266–1271.
- Cherrie, J. W. (2008). We can eliminate occupational cancer from chemicals. *Occupational Medicine*, 58(5), 314–315.
- Cherrie, J. W. (2009). Reducing occupational exposure to chemical carcinogens. *Occupational Medicine*, 59(2), 96–100.
- Clapp, R. W., Jacobs, M. M., & Loechler, E. L. (2007). *Environmental and occupational causes of cancer: New evidence, 2005–2007*. Lowell, MA: The Lowell Center for Sustainable Production, University of Massachusetts Lowell.
- Comba, P., Battista, G., Belli, S., de Capua, B., Merler, E., Orsi, D., et al. (1992). A case-control study of cancer of the nose and paranasal sinuses and occupational exposures. *American Journal of Industrial Medicine*, 22(4), 511–520.
- Cookson, W. O., Musk, A. W., Glancy, J. J., de Klerk, N. H., Yin, R., Mele, R., et al. (1985, July). Compensation, radiographic changes, and survival in applicants for asbestosis compensation. *British Journal of Industrial Medicine*, 42(7), 461–468.
- Costa, D. L., & Kahn, M. E. (2004). Changes in the value of life, 1940–1980. *Journal of Risk and Uncertainty*, 29(2), 159–180.
- Cutler, D. M., Gruber, J., Hartman, R. S., Landrum, M. B., Newhouse, J. P., & Rosenthal, M. B. (2002). The economic impacts of the tobacco settlement. *Journal of Policy Analysis and Management*, 21(1), 1–19.
- de Boer, A. G., Taskila, T., Ojajarvi, A., van Dijk, F. J., & Verbeek, J. H. (2009, February 18). Cancer survivors and unemployment: A meta-analysis and meta-regression. *Journal of the American Medical Association*, 301(7), 753–762.
- de Lima, M., Strom, S. S., Keating, M., Kantarjian, H., Pierce, S., O'Brien, S., et al. (1997, December 15). Implications of potential cure in acute myelogenous leukemia: Development of subsequent cancer and return to work. *Blood*, 90(12), 4719–4724.
- Demers, P., Peters, C., & Nicol, A. (2008). *Priority occupational carcinogens for surveillance in Canada: Preliminary priority list*. Vancouver, BC: CAREX Canada.

- Demeter, S. J., Jacobs, P., Chmielowiec, C., Logus, W., Hailey, D., Fassbender, K., et al. (2007). The cost of lung cancer in Alberta. *Canadian Respiratory Journal*, 14(2), 81–86.
- Department for Environment, Food and Rural Affairs. (2006). *REACH partial regulatory impact assessment after common position*. London, England: Department for Environment, Food and Rural Affairs.
- Depository Services Program, Government of Canada. (2006). *Life tables, Canada, provinces and territories*. Retrieved July 8, 2006, from <http://dsp-psd.tpsgc.gc.ca/Collection/Statcan/84-537-X/84-537-XIE.htm>
- Deschamps, F., Barouh, M., Deslee, G., Prevost, A., & Munck, J. N. (2006). Estimates of work-related cancers in workers exposed to carcinogens. *Occupational Medicine*, 56(3), 204–209.
- Doll, R., & Peto, R. (1981). The causes of cancer: Quantitative estimates of avoidable risks of cancer in the United States today. *Journal of the National Cancer Institute*, 66(6), 1191–1308.
- Dreyer, L., Andersen, A., & Pukkala, E. (1997). Avoidable cancers in the Nordic countries. *Occupation. APMIS Supplementum*, 76, 68–79.
- Driscoll, T., Nelson, D. I., Steenland, K., Leigh, J., Concha-Barrientos, M., Fingerhut, M., et al. (2005). The global burden of disease due to occupational carcinogens. *American Journal of Industrial Medicine*, 48(6), 419–431.
- Ellison, L. F., & Wilkins, K. (2009). Cancer prevalence in the Canadian population. *Health Reports*, 20(1), 7–19.
- Fritschi, L. (2006). *Occupational cancer in Australia*. Canberra, Australia: Australian Safety and Compensation Council.
- Fritschi, L., & Driscoll, T. (2006). Cancer due to occupation in Australia. *Australian and New Zealand Journal of Public Health*, 30(3), 213–219.
- Grover, S. A., Coupal, L., Zowall, H., Rajan, R., Trachtenberg, J., Elhilali, M., et al. (2000). The economic burden of prostate cancer in Canada: Forecasts from the Montreal Prostate Cancer Model. *Canadian Medical Association Journal*, 162(7), 987–992.
- Gustavsson, P., Jakobsson, R., Nyberg, F., Pershagen, G., Jarup, L., & Scheele, P. (2000). Occupational exposure and lung cancer risk: A population-based case-referent study in Sweden. *American Journal of Epidemiology*, 152(1), 32–40.
- Hamalainen, P., Takala, J., & Saarela, K. L. (2007). Global estimates of fatal work-related diseases. *American Journal of Industrial Medicine*, 50(1), 28–41.
- Hemp, P. (2004, October). Presenteeism: At work—But out of it. *Harvard Business Review*, 82(10), 49–58.
- Hertz, R., McDonald, M., & Kulig, K. (2005). *The burden of cancer in American adults*. New York: Pfizer U.S. Pharmaceuticals.
- Hewitt, M., Rowland, J. H., & Yancik, R. (2003, January). Cancer survivors in the United States: Age, health, and disability. *Journals of Gerontology Series A: Biological Sciences and Medical Sciences*, 58(1), 82–91.
- Hirth, R. A., Chernew, M. E., Miller, E., Fendrick, A. M., & Weissert, W. G. (2000). Willingness to pay for a quality-adjusted life year: In search of a standard. *Medical Decision Making*, 20(3), 332–342.
- International Agency for Research on Cancer. (2008). *Overall evaluations of carcinogenicity to humans*. Retrieved November 24, 2008, from <http://monographs.iarc.fr/ENG/Classification/crthgr01.php>
- Irigaray, P., Newby, J. A., Clapp, R., Hardell, L., Howard, V., Montagnier, L., et al. (2007). Lifestyle-related factors and environmental agents causing cancer: An overview. *Biomedicine & Pharmacotherapy*, 61(10), 640–658.

- Kauppinen, T., Saalo, A., Pukkala, E., Virtanen, S., Karjalainen, A., & Vuorela, R. (2007). Evaluation of a national register on occupational exposure to carcinogens: Effectiveness in the prevention of occupational cancer, and cancer risks among the exposed workers. *Annals of Occupational Hygiene*, 51(5), 463–470.
- Kim, S. G., Hahm, M. I., Choi, K. S., Seung, N. Y., Shin, H. R., & Park, E. C. (2008, March). The economic burden of cancer in Korea in 2002. *European Journal of Cancer Care*, 17(2), 136–144.
- LaMontagne, A. D., & Christiani, D. C. (2002). Prevention of work-related cancers. *New Solutions*, 12(2), 137–156.
- Landrigan, P. J. (1996). The prevention of occupational cancer. *CA: A Cancer Journal for Clinicians*, 46(2), 67–69.
- Lee, M. K., Lee, K. M., Bae, J. M., Kim, S., Kim, Y.-W., Ryu, K. W., et al. (2008, February 26). Employment status and work-related difficulties in stomach cancer survivors compared with the general population. *British Journal of Cancer*, 98(4), 708–715.
- Leigh, J. P., Markowitz, S. B., Fahs, M., Shin, C., & Landrigan, P. J. (1997). Occupational injury and illness in the United States: Estimates of costs, morbidity, and mortality. *Archives of Internal Medicine*, 157(14), 1557–1568.
- Leigh, J. P., Yasmeeen, S., & Miller, T. R. (2003). Medical costs of fourteen occupational illnesses in the United States in 1999. *Scandinavian Journal of Work, Environment and Health*, 29(4), 304–313.
- Maroun, J., Ng, E., Berthelot, J. M., Le Petit, C., Dahrouge, S., Flanagan, W. M., et al. (2003). Lifetime costs of colon and rectal cancer management in Canada. *Chronic Diseases in Canada*, 24(4), 91–101.
- Miyakawa, M., Tachibana, M., Miyakawa, A., Yoshida, K., Shimada, N., Murai, M., et al. (2001). Re-evaluation of the latent period of bladder cancer in dyestuff-plant workers in Japan. *International Journal of Urology*, 8(8), 423–430.
- Nordhaus, W. D. (2002). *The health of nations: The contribution of improved health to living standards* (NBER Working Paper No. W8818). Cambridge, MA: National Bureau of Economic Research.
- Nurminen, M., & Karjalainen, A. (2001). Epidemiologic estimate of the proportion of fatalities related to occupational factors in Finland. *Scandinavian Journal of Work, Environment and Health*, 27(3), 161–213.
- Parent, M. E., Siemiatycki, J., & Fritschi, L. (2000). Workplace exposures and oesophageal cancer. *Occupational and Environmental Medicine*, 57(5), 325–334.
- Policy Research Division, Strategic Policy Directorate, Population and Public Health Branch, Health Canada. (2002). *Economic burden of illness in Canada, 1998*. Ottawa, ON: Health Canada.
- Rousseau, M. C., Straif, K., & Siemiatycki, J. (2005). IARC carcinogen update. *Environmental Health Perspectives*, 113(9), 580–581.
- Rushton, L. (2009). Workplace and cancer: Interactions and updates. *Occupational Medicine*, 59(2), 78–81.
- Rushton, L., Hutchings, S., & Brown, T. (2008). The burden of cancer at work: Estimation as the first step to prevention. *Occupational and Environmental Medicine*, 65(12), 789–800.
- Schultz, P., Beck, M., Stava, C., & Sellin, R. (2002). Cancer survivors: Work related issues. *American Association of Occupational Health Nurses Journal*, 50(5), 220–226.
- Short, P. F., Vasey, J. J., & Tunceli, K. (2005, March 15). Employment pathways in a large cohort of adult cancer survivors. *Cancer*, 103(6), 1292–1301.
- Siemiatycki, J. (1991). *Risk factors for cancer in the workplace*. Boca Raton, FL: CRC Press.

- Siemiatycki, J., Richardson, L., Straif, K., Latreille, B., Lakhani, R., Campbell, S., et al. (2004). Listing occupational carcinogens. *Environmental Health Perspectives*, 112(15), 1447–1459.
- Siskind, F. B. (1987, March). The cost of compensating asbestos victims under the Occupational Disease Compensation Act of 1983. *Risk Analysis*, 7(1), 59–69.
- Spelten, E. R., Sprangers, M. A., & Verbeek, J. H. (2002, March). Factors reported to influence the return to work of cancer survivors: A literature review. *Psychooncology*, 11(2), 124–131.
- Statistics Canada. (2005). *Productivity and related measures, business sector*. Ottawa, ON: Author.
- Steenland, K., Burnett, C., Lalich, N., Ward, E., & Hurrell, J. (2003). Dying for work: The magnitude of US mortality from selected causes of death associated with occupation. *American Journal of Industrial Medicine*, 43(5), 461–482.
- Straif, K. (2008). The burden of occupational cancer. *Occupational and Environmental Medicine*, 65(12), 787–788.
- Surveillance Epidemiology and End Results. (2009). *5-year survival rates*. Retrieved from http://seer.cancer.gov/csr/1975_2006/results_merged/topic_survival.pdf
- Syse, A., Tretli, S., & Kravdal, O. (2008, September). Cancer's impact on employment and earnings—A population-based study from Norway. *Journal of Cancer Survivorship*, 2(3), 149–158.
- Taskila-Brandt, T., Martikainen, R., Virtanen, S. V., Pukkala, E., Hietanen, P., & Lindbohm, M. L. (2004, November). The impact of education and occupation on the employment status of cancer survivors. *European Journal of Cancer*, 40(16), 2488–2493.
- The Cancer Council of New South Wales. (2007, April). *Cost of cancer in NSW*. Woolloomooloo, New South Wales, Australia: Author.
- U.S. Government Accountability Office. (2009, February 26). *Chemical regulation: Options for enhancing the effectiveness of the Toxic Substances Control Act* (Publication No. GAO-09-428T). Washington, DC: Author.
- Verma, D. K., Purdham, J. T., & Roels, H. A. (2002). Translating evidence about occupational conditions into strategies for prevention. *Occupational and Environmental Medicine*, 59(3), 205–213.
- Will, B. P., Berthelot, J. M., Le Petit, C., Tomiak, E. M., Verma, S., & Evans, W. K. (2000). Estimates of the lifetime costs of breast cancer treatment in Canada. *European Journal of Cancer*, 36(6), 724–735.
- World Bank. (2009). *Gross domestic product and population*. Retrieved July 24, 2009, from <http://siteresources.worldbank.org/DATASTATISTICS/Resources/POP.pdf>
- World Health Organization Commission on Macroeconomics and Health. (2001). *Macroeconomics and health: Investing in health for economic development*. Geneva, Switzerland: World Health Organization.
- Yabroff, K. R., Davis, W. W., Lamont, E. B., Fahey, A., Topor, M., Brown, M. L., et al. (2007, January 3). Patient time costs associated with cancer care. *Journal of the National Cancer Institute*, 99(1), 14–23.
- Yabroff, K. R., Lawrence, W. F., Clauser, S., Davis, W. W., & Brown, M. L. (2004, September 1). Burden of illness in cancer survivors: Findings from a population-based national sample. *Journal of the National Cancer Institute*, 96(17), 1322–1330.

APPENDIX A: Occupational carcinogens by IARC classification and occupational use

From “Listing occupational carcinogens,” by J. Siemiatycki, L. Richardson, K. Straif, B. Latreille, R. Lakhani, S. Campbell, et al., 2004, *Environmental Health Perspectives*, 112(15), pp. 1450–1456. Reprinted with permission.

Table 25: Substances and mixtures that have been evaluated by IARC as definite (Group 1) human carcinogens and that are occupational exposures

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c	Site(s)
Physical agents					
Ionizing radiation and sources	Radiologists; technologists; nuclear workers; radium-dial thereof, including, notably, painters; underground miners; plutonium workers; cleanup X rays, gamma rays, neutrons, and workers following nuclear accidents; aircraft crew radon gas	Vol. 75 (2000a); Vol. 78 (2001a)	Sufficient	Sufficient	Bone ^d Leukemia ^d Lung ^d Liver ^d Thyroid ^d Others ^d
Solar radiation	Outdoor workers	Vol. 55 (1992b)	Sufficient	Sufficient	Melanoma ^d Skin ^d
Respirable dusts and fibers					
Asbestos	Mining and milling; by-product manufacture; insulating; shipyard workers; sheet-metal workers; asbestos cement industry	Suppl. 7 (1987)	Sufficient	Sufficient	Lung ^d Mesothelioma ^d Larynx ^e GI tract ^e
Erionite	Waste treatment; sewage; agricultural waste; air pollution control systems; cement aggregates; building materials	Suppl. 7 (1987)	Sufficient	Sufficient	Mesothelioma ^d
Silica, crystalline	Granite and stone industries; ceramics, glass, and related industries; foundries and metallurgical industries; abrasives; construction; farming	Vol. 68 (1997b)	Sufficient	Sufficient	Lung ^d
Talc containing asbestiform fibers	Manufacture of pottery, paper, paint, and cosmetics	Suppl. 7 (1987)	Sufficient	Inadequate	Lung ^d Mesothelioma ^d
Wood dust	Logging and sawmill workers; pulp and paper and paperboard industry; woodworking trades (e.g., furniture industries, cabinetmaking, carpentry and construction); used as filler in plastic and linoleum production	Vol. 62 (1995b)	Sufficient	Inadequate	Nasal cavities and paranasal sinuses ^d
Metals and metal compounds					
Arsenic and arsenic compounds	Nonferrous metal smelting; production, packaging, and use of arsenic-containing pesticides; sheep dip manufacture; wool fiber production; mining of ores containing arsenic	Suppl. 7 (1987)	Sufficient	Limited	Skin ^d Lung ^d Liver, (angiosarcoma) ^e
Beryllium	Beryllium extraction and processing; aircraft and aerospace industries; electronics and nuclear industries; jewelers	Vol. 58 (1993a)	Sufficient	Sufficient	Lung ^d
Cadmium and cadmium compounds	Cadmium-smelter workers; battery production workers; cadmium-copper alloy workers; dyes and pigments production; electroplating processes	Vol. 58 (1993a)	Sufficient	Sufficient	Lung ^d
Chromium compounds, hexavalent	Chromate production plants; dyes and pigments; plating and engraving; chromium ferro-alloy production; stainless-steel welding; in wood preservatives; leather tanning; water treatment; inks; photography; lithography; drilling muds; synthetic perfumes; pyrotechnics; corrosion resistance	Vol. 49 (1990a)	Sufficient	Sufficient	Lung ^d Nasal sinuses ^e
Selected nickel compounds, including combinations of nickel oxides and sulfides in the nickel refining industry	Nickel refining and smelting; welding	Vol. 49 (1990a)	Sufficient	Sufficient	Lung ^d Nasal cavity and sinuses ^d

Table 25 cont. —>

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c	Site(s)
Wood and fossil fuels and their by-products					
Benzene	Production; solvents in the shoe production industry; chemical, pharmaceutical, and rubber industries; printing industry (rotogravure plants, bindery departments); gasoline additive	Suppl. 7 (1987)	Sufficient	Limited	Leukemia ^d
Coal tars and pitches	Production of refined chemicals and coal tar products (patent-fuel); coke production; coal gasification; aluminum production; foundries; road paving and construction (roofers and slaters)	Suppl. 7 (1987)	Sufficient	Sufficient	Skin ^d Lung ^e Bladder ^e
Mineral oils, untreated and mildly treated	Production; used as lubricant by metal workers, machinists, engineers; printing industry (ink formulation); used in cosmetics, medicinal and pharmaceutical preparations	Suppl. 7 (1987)	Sufficient	Inadequate	Skin ^d Bladder ^e Lung ^e Nasal sinuses ^e
Shale oils or shale-derived lubricants	Mining and processing; used as fuels or chemical-plant feedstocks; lubricant in cotton textile industry	Suppl. 7 (1987)	Sufficient	Sufficient	Skin ^d
Soots	Chimney sweeps; heating-unit service personnel; brick masons and helpers; building demolition workers; insulators; firefighters; metallurgical workers; work involving burning of organic materials	Vol. 35 (1985)	Sufficient	Inadequate	Skin ^d Lung ^d Esophagus ^e
Monomers					
Vinyl chloride	Production; production of polyvinyl chloride and co-polymers; refrigerant before 1974; extraction solvent; in aerosol propellants	Suppl. 7 (1987)	Sufficient	Sufficient	Liver (angiosarcoma) ^d Liver (hepato-cellular) ^e
Intermediates in plastics and rubber manufacturing					
Bis(chloromethyl) ether and chloromethyl methyl ether	Production; chemical intermediate; alkylating agent; laboratory reagent; plastic manufacturing; ion-exchange (technical grade) resins and polymers	Suppl. 7 (1987)	Sufficient	Sufficient	Lung (oat cell) ^d
Aromatic amine dyes					
4-Aminobiphenyl	Production; dyestuffs and pigment manufacture	Suppl. 7 (1987)	Sufficient	Sufficient	Bladder ^d
Benzidine	Production; dyestuffs and pigment manufacture	Suppl. 7 (1987)	Sufficient	Sufficient	Bladder ^d
2-Naphthylamine	Production; dyestuffs and pigment manufacture	Suppl. 7 (1987)	Sufficient	Sufficient	Bladder ^d
Pesticides					
Ethylene oxide Production;	chemical industry; sterilizing agent (hospitals, spice fumigation)	Vol. 60 (1994)	Limited	Sufficient	Leukemia ^d
2,3,7,8-Tetrachlorodibenzopara-dioxin (TCDD)	Production; use of chlorophenols and chlorophenoxy herbicides; waste incineration; PCB production; pulp and paper bleaching	Vol. 69 (1997a)	Limited	Sufficient	All sites combined ^d Lung ^e Non-Hodgkin lymphoma ^e Sarcoma ^e
Others					
Aflatoxin	Feed production industry; workers loading and unloading cargo; rice and maize processing	Vol. 82 (2002b)	Sufficient	Sufficient	Liver ^d
Involuntary (passive) smoking	Workers in bars and restaurants; office workers	Vol. 83 (2004)	Sufficient	Sufficient	Lung ^d
Mustard gas	Production; used in research laboratories; military personnel	Suppl. 7 (1987)	Sufficient	Limited	Larynx ^d Lung ^e Pharynx ^e
Strong inorganic-acid mists containing sulfuric acid	Pickling operations; steel industry; petrochemical industry; phosphate acid fertilizer manufacturing	Vol. 54 (1992a)	Sufficient	Not available	Larynx ^d Lung ^e

Note: includes corrections to errors in initial publication

^a Not necessarily an exhaustive list of occupations or industries in which this agent is found; not all workers in these occupations or industries are exposed. The term "production" is used to indicate that this substance is man-made and that workers may be exposed in the production process.

^b Most recent IARC evaluation; for those referenced to Supplement 7 (IARC, 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

^c As judged by the IARC working group; the authors added the notation "not available" to signify those substances for which there was no evidence at all.

^d The authors judged that evidence for an association with this site was strong.

^e The authors judged the evidence to be suggestive.

Table 26: Substances and mixtures that have been evaluated by IARC as probable (Group 2A) human carcinogens and that are occupational exposures

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c	Site(s)
Physical agents					
Ultraviolet radiation (A, B, and C) from artificial sources	Arc welding; industrial photoprocesses; sterilization and disinfection; phototherapy; operating theaters; research laboratories; ultraviolet fluorescence in food industry; insect traps	Vol. 55 (1992b)	Inadequate	Sufficient	Melanoma ^d
Polyaromatic hydrocarbons					
Benz[a]anthracene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Vol. 32 (1983b)	Not available	Sufficient	Lung ^d Bladder ^d Skin ^d
Benzo[a]pyrene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Vol. 32 (1983b)	Not available	Sufficient	Lung ^d Bladder ^d Skin ^d
Dibenz[a,h]anthracene	Work involving combustion of organic matter; foundries; steel mills; firefighters; vehicle mechanics	Vol. 32 (1983b)	Not available	Sufficient	Lung ^d Bladder ^d Skin ^d
Wood and fossil fuels and their by-products					
Creosotes	Brickmaking; wood preserving	Vol. 35 (1985)	Limited	Sufficient	Skin ^d
Diesel engine exhaust	Railroad workers; professional drivers; dock workers; mechanics	Vol. 46 (1989a)	Limited	Sufficient	Lung ^d Bladder ^d
Intermediates in plastics and rubber manufacturing					
4,4'-Methylene bis(2-chloroaniline)	Production; curing agent for roofing and wood sealing	Vol. 57 (1993b)	Inadequate	Sufficient	Bladder ^d
Styrene-7,8-oxide	Production; styrene glycol production; perfume preparation; reactive diluent in epoxy resin formulations; as chemical intermediate for cosmetics, surface coating, and agricultural and biological chemicals; used for treatment of fibers and textiles; in fabricated rubber products	Vol. 60 (1994)	Inadequate	Sufficient	
Chlorinated hydrocarbons					
α-Chlorinated toluenes	Production; dye and pesticide manufacture	Vol. 71 (1999a)	Limited	Sufficient	Lung ^d
Polychlorinated biphenyls	Production; electrical capacitor manufacturing	Suppl. 7 (1987)	Limited	Sufficient	Liver and biliary tract ^d
Tetrachloroethylene	Production; dry cleaning; metal degreasing	Vol. 63 (1995a)	Limited	Sufficient	Cervix ^d Esophagus ^d Non-Hodgkin lymphoma ^d
Trichloroethylene	Production; dry cleaning; metal degreasing	Vol. 63 (1995a)	Limited	Sufficient	Liver and biliary tract ^d Non-Hodgkin lymphoma ^d Renal cell ^d
Monomers					
Acrylamide	Chemical industry; water and wastewater treatment; textile, steel, and lumber industries; petroleum refining; mineral processing; sugar production; hospitals	Vol. 60 (1994)	Inadequate	Sufficient	Pancreas ^d
1,3-Butadiene	Chemical and rubber industries	Vol. 71 (1999a)	Limited	Sufficient	Lympho-hematopoietic ^d
Epichlorohydrin	Production and use of resins, glycerine, and propylene-based rubbers; used as a solvent	Vol. 71 (1999a)	Inadequate	Sufficient	Lung ^d CNS ^d
Vinyl bromide	Production; production of vinyl bromide polymers and monoacrylic fibers for carpet backing material; rubber and plastic production	Vol. 71 (1999a)	Not available	Sufficient	
Vinyl fluoride	Production; polyvinyl fluoride and fluoropolymer production	Vol. 63 (1995a)	Not available	Sufficient	

Table 26 cont. —>

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c	Site(s)
Aromatic amine dyes					
Benzidine-based dyes	Production; used in textile, paper, leather, rubber, plastics, printing, paint, and lacquer industries	Suppl. 7 (1987)	Inadequate	Sufficient	Bladder ^d
4-Chloro- <i>ortho</i> -toluidine	Dye and pigment manufacture; textile industry	Vol. 77 (2000b)	Limited	Sufficient	Bladder ^d
<i>ortho</i> -Toluidine	Production; manufacture of dyestuffs, pigments, optical brightener, pharmaceuticals, and pesticides; rubber vulcanizing; clinical laboratory reagent; cleaners and janitors	Vol. 77 (2000b)	Limited	Sufficient	Bladder ^d
Intermediates in the production of dyes					
Dimethylcarbamoyl chloride	Production; manufacture of pharmaceuticals, pesticides, and dyes	Vol. 71 (1999a)	Inadequate	Sufficient	
Pesticides					
Captafol	Production; fungicide	Vol. 53 (1991b)	Not available	Sufficient	
Ethylene dibromide	Production; pest control; petroleum refining and waterproofing; leaded gasoline additive; chemical intermediate and solvent in gums, waxes, resins, dyes, and pharmaceutical preparations	Vol. 71 (1999a)	Inadequate	Sufficient	
Nonarsenical insecticides	Production; pest control and agricultural workers; flour and grain mill workers	Vol. 53 (1991b)	Limited	Not available	Brain ^d Leukemia ^d Lung ^d Multiple myeloma ^d Non-Hodgkin lymphoma ^d
Others					
Diethyl sulfate	Ethanol production	Vol. 71 (1999a)	Not available	Sufficient	
Formaldehyde	Production; pathologists; medical laboratory technicians; plastics; textile industry	Vol. 62 (1995b)	Limited	Sufficient	Leukemia ^d Nasal sinuses ^d Nasopharynx ^d
Tris(2,3-dibromopropyl)	Production; used in the textile phosphate industry; in phenolic resins (for electronics industry), paints, paper coatings, and rubber	Vol. 71 (1999a)	Inadequate	Sufficient	

Note: includes corrections to errors in initial publication

^a Not necessarily an exhaustive list of occupations and industries in which this agent is found; not all workers in these occupations and industries are exposed. The term "production" is used to indicate that this substance is man-made and that workers may be exposed in the production process.

^b Most recent IARC evaluation; for those referenced to Supplement 7 (IARC, 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

^c As judged by the IARC working group; the authors added the notation "not available" to signify those substances for which there was no evidence at all.

^d The authors judged that evidence for an association with this site was strong.

^e The authors judged the evidence to be suggestive.

Table 27: Substances and mixtures that have been evaluated by IARC as possible (Group 2B) human carcinogens and that are occupational exposures

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c
Respirable dusts and fibers				
Palygorskite (long fibers > 5 µm)	Miners and millers; production of waste absorbents, fertilizers, and pesticides	Vol. 68 (1997b)	Inadequate	Sufficient
Refractory ceramic fibers	Production; furnace insulators; ship builders; heat-resistant fabric manufacture	Vol. 81 (2002a)	Inadequate	Sufficient
Special-purpose glass fibers such as E-glass and "475" glass fibers	High-efficiency air filtration media and battery separator media	Vol. 81 (2002a)	Not available	Sufficient
Metals and metal compounds				
Antimony trioxide	Ore processing; glass and ceramic production	Vol. 47 (1989c)	Inadequate	Sufficient
Cobalt and cobalt compounds	Miners; processing of copper and nickel ore; glass and ceramic production	Vol. 52 (1991a)	Inadequate	Sufficient
Lead and inorganic lead compounds	Lead smelters; plumbers; solderers; occupations in battery recycling smelters	Suppl. 7 (1987)	Inadequate	Sufficient
Methyl mercury compounds	Pesticide and fungicide production; paint industry	Vol. 58 (1993a)	Inadequate	Sufficient
Nickel: metallic and alloys	Nickel miners; metal fabrication, grinding, electroplating, and welding	Vol. 49 (1990a)	Inadequate	Sufficient
Wood and fossil fuels and their by-products				
Benzofuran	Production; intermediate in coumarone-indene resin polymerization; coke production; coal gasification and combustion	Vol. 63 (1995a)	Not available	Sufficient
Bitumens, extracts of steam-refined and air-refined	Production/refining; road construction; roofing and flooring	Suppl. 7 (1987)	Inadequate	Sufficient
Carbon black	Production; paint, ink, plastic and rubber industries	Vol. 65 (1996)	Inadequate	Sufficient
Diesel fuel, marine	Petroleum refineries; marine fuel; distribution	Vol. 45 (1989b)	Inadequate	Limited
Fuel oils, residual (heavy)	Petroleum refineries; distribution; marine fleets; most large diesel engines operated on land; industrial heating systems	Vol. 45 (1989b)	Inadequate	Sufficient
Gasoline	Petroleum refineries; transportation; mechanics and service station attendants	Vol. 45 (1989b)	Inadequate	Limited
Gasoline engine exhaust	Transportation and vehicle maintenance workers; drivers; toll attendants; traffic controllers	Vol. 46 (1989a)	Inadequate	Limited
Naphthalene	Production; insecticide, resin, and pharmaceutical production	Vol. 82 (2002b)	Inadequate	Sufficient
Polyaromatic hydrocarbons				
Benzo[b]fluoranthene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Benzo[j]fluoranthene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Benzo[k]fluoranthene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo[a,h]acridine	Production; used in dye synthesis; biochemical laboratory workers; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo[a,j]acridine	Production; dye synthesis; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo[a,e]pyrene	Production; biochemical laboratory workers; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo[a,h]pyrene	Production; biochemical laboratory workers; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo[a,i]pyrene	Work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Dibenzo[a,l]pyrene	Production; biochemical laboratory workers; work involving combustion of organic matter	Vol. 32 (1983b)	Not available	Sufficient
Monomers				
Acrylonitrile	Production; acrylic textile fiber and plastic production	Vol. 71 (1999a)	Inadequate	Sufficient
Chloroprene	Production; manufacture of polychloroprene (synthetic rubber)	Vol. 71 (1999a)	Inadequate	Sufficient
Ethyl acrylate	Production; plastic molding occupations using acrylate resins	Vol. 39 (1986a)	Not available	Sufficient

Table 27 cont. —>

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c
Isoprene	Production; synthetic rubber and plastics industries	Vol. 71 (1999a)	Not available	Sufficient
Styrene	Polyester resin manufacture; production of packaging materials and fiberglass-reinforced polyester	Vol. 82 (2002b)	Limited	Limited
Toluene diisocyanates	Production; production of polyurethane foams and wire coating; insulation workers; ship builders	Vol. 71 (1999a)	Inadequate	Sufficient
Urethane	Production; amino-resin production	Vol. 7 (1974a)	Not available	Sufficient
Vinyl acetate	Production; plastics, paint, and adhesive industries	Vol. 63 (1995a)	Not available	Limited
Intermediates in plastics and rubber manufacturing				
Acetaldehyde	Acetic acid production workers; dyestuff, plastic and synthetic rubber industries	Vol. 71 (1999a)	Inadequate	Sufficient
Acetamide	Production; plastics and chemical industries	Vol. 71 (1999a)	Not available	Sufficient
2,4-Diaminotoluene	Production; chemical intermediate in TDI production; dyes for textiles; leather; furs; wood; biologic stain; photo developer	Vol. 16 (1978)	Not available	Sufficient
1,2-Epoxybutane	Production; metal degreasing; plastics industry	Vol. 71 (1999a)	Not available	Limited
Ethylbenzene	Production; ink, paint, and plastic production	Vol. 77 (2000b)	Inadequate	Sufficient
Ethylene thiourea	Production; vulcanization in the rubber industry; manufacture of ethylenebisdithiocarbamate pesticides; electroplating baths; dyes; pharmaceuticals; synthetic resins	Vol. 79 (2001b)	Inadequate	Sufficient
Phenyl glycidyl ether	Production; epoxy resins; casting and molding	Vol. 71 (1999a)	Not available	Sufficient
Propylene oxide	Production; polyurethane foam and glycol production, fumigant	Vol. 60 (1994)	Inadequate	Sufficient
Chlorinated hydrocarbons				
Carbon tetrachloride	Production; industrial degreasing occupations; dry cleaners; refrigerant production	Vol. 71 (1999a)	Inadequate	Sufficient
Chlorinated paraffin of average carbon-chain length C12	Production; polyvinyl chloride processing industry	Vol. 48 (1990b)	Not available	Sufficient
Chloroform	Refrigerant production; dyes, solvents, and pesticides	Vol. 73 (1999b)	Inadequate	Sufficient
1,2-Dichloroethane	Vinyl chloride production workers	Vol. 71 (1999a)	Inadequate	Sufficient
Dichloromethane	Production; painters and furniture restorers; pharmaceutical and electronic production	Vol. 71 (1999a)	Inadequate	Sufficient
Hexachloroethane	Production; aluminum refinery; industrial firefighters	Vol. 73 (1999b)	Inadequate	Sufficient
Aromatic amine dyes				
Auramine (technical grade)	Production; textiles, plastic, and printing	Suppl. 7 (1987)	Inadequate	Sufficient
Benzyl violet 4B	Production; food; drugs; cosmetics; textiles	Vol. 16 (1978)	Not available	Sufficient
CI Basic Red 9	Production; textiles; printing; biologic stains (basic fuchsin dye in laboratories)	Vol. 57 (1993b)	Inadequate	Sufficient
2,4-Diaminoanisole	Dyestuff industry; barbers and cosmetologists; furriers	Vol. 79 (2001b)	Not available	Sufficient
3,3'-Dimethylbenzidine (o-tolidine)	Production; dye or intermediate in dye and pigment production; polyurethane elastomers; coating; plastics; clinical laboratories	Vol. 1 (1972)	Not available	Sufficient
2,6-Dimethylaniline (2,6-xylylidine)	Production; dyestuffs and pharmaceutical manufacturing	Vol. 57 (1993b)	Not available	Sufficient
3,3'-Dichlorobenzidine	Production; dyestuff manufacturing	Vol. 29 (1982b)	Inadequate	Sufficient
4,4'-Diaminodiphenyl ether	Production; polyamide-type resin manufacturing	Vol. 29 (1982b)	Not available	Sufficient
Disperse Blue 1	Production; hair coloring; textiles and plastics	Vol. 48 (1990b)	Not available	Sufficient
HC Blue No. 1	Production; hair dye	Vol. 57 (1993b)	Not available	Sufficient
4,4'-Methylenedianiline	Production; production of diisocyanates, polyisocyanates, and epoxy resins	Vol. 39 (1986a)	Not available	Sufficient
Magenta containing CI Basic Red 9	Production; textiles and printing; biologic stains in laboratories; photography	Vol. 57 (1993b)	Not available	Sufficient

Table 27 cont. —>

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c
Azo dyes				
ortho-Aminoazotoluene	Production; textiles and leather	Vol. 8 (1975)	Not available	Sufficient
para-Aminoazobenzene	Production; textiles and leather	Suppl. 7 (1987)	Not available	Sufficient
CI Acid Red 114	Production; textiles and leather	Vol. 57 (1993b)	Not available	Sufficient
CI Direct Blue 15	Production; textiles and paper	Vol. 57 (1993b)	Not available	Sufficient
Citrus Red No. 2	Production; used for food coloring	Vol. 8 (1975)	Not available	Sufficient
para-Dimethylaminoazobenzene	Production; textiles; laboratories	Vol. 8 (1975)	Not available	Sufficient
Oil orange SS	Production; dyes/pigments for varnishes, oils, fats, and waxes	Vol. 8 (1975)	Not available	Sufficient
Ponceau 3R	Production; textiles	Vol. 8 (1975)	Not available	Sufficient
Ponceau MX	Production; textiles; leather; inks; paper; wood stains; food; biology laboratories	Vol. 8 (1975)	Not available	Sufficient
Trypan blue	Production; textiles and printing; biologic stains in life science laboratories; used by ophthalmologists	Vol. 8 (1975)	Not available	Sufficient
Intermediates for the manufacture of dyes				
para-Cresidine	Production; manufacture of dyes, pigments, and perfumes	Vol. 27 (1982a)	Not available	Sufficient
3,3'-Dimethoxybenzidine (ortho-dianisidine)	Production; manufacture of dyes and pigments; dye for leather, paper, plastics, rubber, textiles, and laboratories	Suppl. 7 (1987)	Inadequate	Sufficient
2-Methyl-1-nitro anthraquinone (of uncertain purity/impurity)	Production; synthesis of anthraquinone dyes	Vol. 27 (1982a)	Not available	Sufficient
4,4'-Methylene bis (2-methylaniline)	Production; manufacture of dyes and pigments	Suppl. 7 (1987)	Inadequate	Sufficient
2-Nitroanisole	Production; manufacture of the dye intermediates ortho-anisidine and ortho-dianisidine	Vol. 65 (1996)	Not available	Sufficient
4,4'-Thiodianiline	Production; manufacture of dyes	Vol. 27 (1982a)	Not available	Sufficient
Nitro compounds				
2,4-Dinitrotoluene	Production; manufacture of diisocyanates and munitions	Vol. 65 (1996)	Inadequate	Sufficient
2,6-Dinitrotoluene	Production; manufacture of diisocyanates and munitions	Vol. 65 (1996)	Inadequate	Sufficient
Nitrobenzene	Production; manufacture of dyestuffs, detergents, and cosmetics	Vol. 65 (1996)	Not available	Sufficient
2-Nitrofluorene	Underground miners using diesel-powered machinery	Vol. 46 (1989a)	Not available	Sufficient
2-Nitropropane	Production; ink, paint, explosives industries	Vol. 71 (1999a)	Not available	Sufficient
1-Nitropyrene	Production; manufacture of azidopyrene; particulate emissions	Vol. 46 (1989a)	Not available	Sufficient
4-Nitropyrene	Production; used only as a laboratory chemical; probably present before 1980 in carbon black used in photocopy machines	Vol. 46 (1989a)	Not available	Sufficient
Tetranitromethane	Production; diesel fuel additive; TNT manufacturing	Vol. 65 (1996)	Not available	Sufficient
Pesticides				
Aramite	Production; in miticides in greenhouses, nurseries, and orchards	Vol. 5 (1974b)	Not available	Sufficient
Chlordane	Production; termite control	Vol. 79 (2001b)	Inadequate	Sufficient
Chlordecone	Production; insecticide	Vol. 20 (1979a)	Not available	Sufficient
Chlorophenoxy herbicides	Production; defoliant	Suppl. 7 (1987)	Limited	Inadequate
Chlorothalonil	Production; fungicide, bactericide, and nematocide	Vol. 73 (1999b)	Not available	Sufficient
DDT (p,p'-DDT)	Production; nonsystemic insecticide	Vol. 53 (1991b)	Inadequate	Sufficient
1,2-Dibromo-3-chloropropane	Production; pesticide, nematocide, and soil fumigant	Vol. 71 (1999a)	Inadequate	Sufficient
para-Dichlorobenzene	Production; pesticide	Vol. 73 (1999b)	Inadequate	Sufficient
Dichlorvos	Production; insecticide and miticide	Vol. 53 (1991b)	Inadequate	Sufficient
Heptachlor	Production; termite control	Vol. 79 (2001b)	Inadequate	Sufficient

Table 27 cont. —>

Substance or mixture	Occupation or industry in which the substance is found ^a	IARC Monograph volume (year) ^b	Human evidence ^c	Animal evidence ^c
Hexachlorobenzene	Production; in chlorinated pesticides and fungicides; dye manufacture and synthesis of organic chemicals and rubber; plasticizer for polyvinyl chloride; wood preservative; by-product of the production of a number of chlorinated solvents	Vol. 79 (2001b)	Inadequate	Sufficient
Hexachlorocyclohexanes (most common form is Lindane)	Production; woodworkers; farm workers	Suppl. 7 (1987)	Inadequate	Sufficient
Mirex	Production; fire-retardant additive; insecticide; workers at hazardous waste sites	Vol. 20 (1979a)	Not available	Sufficient
Nitrofen	Production; herbicide	Vol. 30 (1983a)	Not available	Sufficient
Sodium ortho-phenylphenate	Production; fungicide; chemical intermediate	Vol. 73 (1999b)	Not available	Sufficient
Toxaphene (polychlorinated camphenes)	Production; insecticide	Vol. 79 (2001b)	Inadequate	Sufficient
Others				
Butylated hydroxyanisole (BHA)	Production; food and pharmaceutical industries	Vol. 40 (1986b)	Not available	Sufficient
Catechol	Production; insecticide and pharmaceutical production; tanneries	Vol. 71 (1999a)	Not available	Sufficient
Diglycidyl resorcinol ether	Production; liquid spray epoxy resin in electrical, tooling, adhesive, and laminating applications; production of epoxy resins and rubber; aerospace industry	Vol. 71 (1999a)	Not available	Sufficient
1,4-Dioxane	Production; chlorinated solvents; textile processing; mixed with pesticides	Vol. 71 (1999a)	Inadequate	Sufficient
Hydrazine	Production; manufacture of agricultural chemicals and chemical blowing agents; water treatment; spandex fibers; rocket fuel; oxygen scavenger in water boilers and heating systems; scavenger for gases; plating metals on glass and plastics; solder fluxes; photographic developers; reactant in fuel cells in the military; reducing agent in electrode-less nickel plating; chain extender in urethane; textile dyes; explosives	Vol. 71 (1999a)	Inadequate	Sufficient
Nitritriacetic acid and its salts	Production; textiles; electroplaters; tanners	Vol. 73 (1999b)	Not available	Sufficient
Polychlorophenols and their sodium salts (mixed exposure)	Herbicide production; wood, textile and leather manufacturing	Vol. 71 (1999a)	Limited	Inadequate
Potassium bromate	Production; bakeries	Vol. 73 (1999b)	Not available	Sufficient
Thiourea	Production; photoprocessing; dyes; rubber industry	Vol. 79 (2001b)	Not available	Sufficient
Welding fumes	Metal fabricating industry	Vol. 49 (1990a)	Limited	Inadequate

Note: includes corrections to errors in initial publication

^a Not necessarily an exhaustive list of occupations/industries in which this agent is found; not all workers in these occupations/industries are exposed. The term "production" is used to indicate that this substance is man-made and that workers may be exposed in the production process.

^b Most recent IARC evaluation; for those referenced to Supplement 7 (IARC, 1987), it is possible that the 1987 review was quite perfunctory and that the essential evidence was cumulated at an earlier date.

^c As judged by the IARC working group; the authors added the notation "not available" to signify those substances for which there was no evidence at all.

APPENDIX B: Priority occupational carcinogens for surveillance in Canada

From *Priority Occupational Carcinogens for Surveillance in Canada: Preliminary Priority List* (p. 12), by P. Demers, C. Peters, and A. Nicol, 2008, Vancouver, BC: CAREX Canada. Copyright 2008 by CAREX Canada. Reprinted with permission.

Table 28 presents the findings of a study by Demers, Peters and Nicol (2008) to identify known or suspected carcinogens that were of high priority for surveillance in the Canadian occupational context. Three priority groups are established: Group A represents substances that are of immediate high priority, Group B represent a possible high priority, and Group C a moderate priority (for which further substantial investigation is warranted). The prioritization was based on three criteria: carcinogenicity and other toxic properties, prevalence of exposure in Canada and feasibility of assessing exposure. Two known occupational carcinogens, environmental tobacco smoke and sun exposure, were not included in this initial study because they were deemed to have sufficiently well-established prevention programs in Canada.

Table 28: Surveillance priority groups for occupational carcinogens

Group A (n=53)	Group B (n=61)	Group C (further investigation needed) (n=37)
Industrial chemicals	Industrial chemicals	Industrial chemicals
1,2-Dichloroethane	1,2-Epoxybutane	1,1-Dimethylhydrazine
1,3-Butadiene	1,2,3-Trichloropropane	2,2-bis(Bromomethyl)-propane-1,3-diol
1,4-Dioxane	2-Nitropropane	2,6-Dimethylaniline
Acetaldehyde	2,4-Diaminotoluene	2-Nitroanisole
Acrylamide	2,4-Dinitrotoluene	4,4'-Diaminodiphenyl ether
Acrylonitrile	2,6-Dinitrotoluene	4-Vinylcyclohexene
Benzene	3,3'-Dichlorobenzidine	4-Vinylcyclohexene diepoxide
Bitumens	3,3'-Dimethoxybenzidine	Acetamide
Chloroform	3,3'-Dimethylbenzidine	Benzoyl chloride
Coal-tar & coal-tar pitches	4,4'-Methylene bis(2-chloroaniline) (MOCA)	Chlorendic acid
Creosotes	4,4'-Methylenedianiline	Citrus Red 2
Dichloromethane	Benzyl chloride	Diethyl sulfate
Epichlorohydrin	Carbon black	Diglycidyl Resorcinol Ether
Ethylbenzene	Carbon tetrachloride	Diisopropyl sulfate
Ethylene oxide	Catechol	Dimethyl sulfate
Formaldehyde	Chlorinated paraffins	Ethyl carbamate
Naphthalene	Chloroprene	Glycidaldehyde
Nitrobenzene	Diesel fuel, marine	Glycidol
Polychlorinated biphenyls	Disperse Blue 1	N-Methyl-N-nitrosourethane
Styrene	Ethyl acrylate	o-Toluidine
Tetrachloroethylene	Fuel oils, residual	p-Dimethylaminoazobenzene
Toluene diisocyanates	Furan	Phenyl glycidyl ether
Trichloroethylene	Gasoline	Tris(2,3-dibromopropyl) phosphate
	Hexachloroethane	Vinyl bromide
	Hydrazine	
Metals	Isoprene	Pesticides
Antimony trioxide	Mineral oils, untreated & mildly treated	Ethylene dibromide
Arsenic & its compounds	Nitrilotriacetic acid	Polychlorophenols (except penta)
Beryllium & its compounds	Nitromethane	
Cadmium & its compounds	N-Nitrosodiethanolamine	Fibres and dusts
Chromium, hexavalent	N-Nitrosodiethylamine	Erionite
Cobalt and its compounds	N-Nitrosodi-n-butylamine	Palygorskite
Lead & its compounds	N-Nitrosodi-n-propylamine	Talc containing asbestiform fibres
Nickel & its compounds	N-Nitrosomorpholine	
Vanadium pentoxide	N-Nitrosopiperidine	

Table 28 cont. —>

Group A (n=53)	Group B (n=61)	Group C (further investigation needed) (n=37)
Pesticides 2,4-D Chlorothalonil MCPA MCPP Pentachlorophenol	N-Nitrosopyrrolidine o-Anisidine p-Chloroaniline Potassium bromate Propylene oxide Styrene-7,8-oxide Tetrafluoroethylene Vinyl acetate Vinyl chloride	Pharmacologic Ciclosporin Thiotepa
Fibres and dusts Asbestos Crystalline silica Refractory ceramic fibres Wood dust	Metals Gallium arsenide Indium phosphide Methylmercury compounds Titanium dioxide	Microbiological Hepatitis B virus (chronic infection) Hepatitis C virus (chronic infection)
Pharmacologic Adriamycin Chlorambucil Cisplatin Cyclophosphamide Melphalan	Pesticides 1,3-Dichloropropene 2,4-DP Dichlorvos Hexachlorobenzene Lindane p-Dichlorobenzene Sodium o-phenylphenate	Hormones Androgenic steroids Diethylstilbestrol Estrogens (steroidal & non-steroidal) Oral contraceptives (combined or sequential)
Radiation Ionizing radiation & radioactive elements Magnetic fields (extremely low frequency) Radon & its decay products UV radiation, artificial	Fibres and dusts Special purpose glass fibres	
Others PAHs (as a group) Strong inorganic mists containing sulfuric acid Shift work	Pharmacologic 1,4-Butanediol-dimethanesulfonate 1-(2-Chloroethyl)-3-cyclohexyl-1-nitrosourea Bischloroethyl nitrosourea Procarbazine hydrochloride	
	Microbiological <i>Helicobacter pylori</i> infection	

APPENDIX C: Selected literature identified on attributable fractions

Table 29: Selected literature identified and reviewed on attributable fractions for occupational cancers

Cancers studied	Exposed population	Study size	AFs found	Included/excluded	Rationale for exclusion
Author, year, location: Siemiatycki, 1991, Montreal, Canada					
Esophagus Stomach Small intestine* Colon Rectum Liver* Gallbladder* Pancreas Mesothelioma* Lung Prostate Testis* Penis* Bladder Kidney Skin melanoma Eye melanoma* Non-Hodgkin lymphoma *no AFs calculated for these cancers	Cancer cases were identified between 1979 and 1985; lifetime exposure assessed via survey during same time period; cancer cases were male, aged 35–70 years who resided in Montreal metropolitan area. Control group consisted of cancer patients with cancer at different sites than the cases as well as population-based controls. Response rate was 81.5%.	3,730 incident cancer cases 375 population controls	Esophagus: 3.5, 20.4, 0 Stomach: 4.0, 14.1, 5.6 Colon: 0.4, 3.4, 0 Rectum: 0, 21.8, 0 Pancreas: 0, 20.6, 26.1 Lung: 8.0, 20.3, 17.2 Prostate: 0.2, 9.9, 11.6 Bladder: 1.2, 10.8, 0 Kidney: 0.20.8, 16.7 Skin melanoma: 0, 11.1, 0 NHL: 0.9, 3.2, 0 Note: 3 different methods used	Included	
Nurminen and Karjalainen, 2001, Finland					
All Oral cavity Pharynx Esophagus Stomach Colon Rectum Liver Gallbladder Pancreas Nose and nasal sinuses Larynx Bronchus and lung Bone Skin melanoma Skin non-melanoma Mesothelioma Breast Cervix uteri Corpus uteri Ovary Prostate Kidney Bladder Brain Hodgkin's NHL Leukemia	Men and women, aged 25–64 years; exposure measured between 1960–1984 and 1985–1994; labour profile from 1970 and 1990 census	Entire workforce population (approx. 2.1 million)	All: 8.4%(m/w), 13.8%(m), 2.2%(w) Oral cavity: 0.8%(m/w), 1.2%(m/w), 0.3%(m/w) Pharynx: 1.9% (m/w), 2.0% (m), 0.5%(w) Esophagus: 3.6%(m/w), 6.4%(m), 0.2%(w) Stomach: 8.0% (m/w), 10.3%(m), 5.4% (w) Colon: 2.5% (m/w), 5.6% (m), 0.0%(w) Rectum: 1.7%(m/w), 3.1%(m), 0.1%(w) Liver: 4.3%(m/w), 3.5%(m), 5.3%(w) Gallbladder: 0.1%(m/w), 0.2%(m), 0.4%(w) Pancreas: 8.0%(m/w), 13.4%(m), 3.5%(w) Nose and nasal sinuses: 12.5%(m/w), 24.0%(m), 6.7% (w) Larynx: 9.1%(m/w), 9.3%(m), 0.5% (w) Bronchus and lung: 24.0%(m/w), 29.0%(m), 5.3%(w) Bone: 0.6%(m/w), 0.6%(m), 0.6%(w) Skin melanoma: 2.7%(m/w), 4.3%(m), 0.4%(w) Skin non-melanoma: 8.3%(m/w), 13.1%(m), 3.8%(w) Mesothelioma: 71.3%(m/w), 90.0%(m), 21.0%(w) - asbestos Breast: 1.7% (w) Cervix uteri: 5.9%(w) Corpus uteri: 1.1%(w) Ovary: 2.1%(w) Prostate: 6.0%(m) Kidney: 3.1%(m/w), 4.7%(m), 0.8%(w) Bladder: 10.3%(m/w), 14.2%(m), 0.7%(w) Brain: 6.4%(m/w), 10.6%(m), 1.3%(w) Hodgkin's: 2.2%(m/w), 3.9%(m), 0.0%(w) NHL: 4.7%(m/w), 13.5%(m), 3.1%(w) Leukemia: 10.9%(m/w), 18.5%(m), 2.5%(w)	Included	

Table 29 cont. —>

Cancers studied	Exposed population	Study size	AFs found	Included/ excluded	Rationale for exclusion
Rushton et al., 2008, UK					
Bladder Leukemia Lung Mesothelioma NMSC Sinonasal Total	Exposure mainly via CAREX database assessing occupational exposure in the UK 1990–1993. Labour profile examined for relevant exposure period that would result in cancer development in 2004. Men, women and combined sexes.	UK workforce	Bladder: a) 1.0%(m/w), 1.3%(m), 0.6%(w); b) 8.3% (m/w), 11.6% (m), 2.0% (w) Leukemia: a) 0.2%(m/w), 0.3%(m), 0.5%(w); b) 1.7%(m/w), 2.7%(m), 0.8%(w) Lung: a) 11.6%(m/w), 16.5%(m), 4.5%(w), b) 15.0%(m/w), 21.6%(m), 5.5%(w) Mesothelioma: a) 74–80%(m/w), 85–90%(m), 20–30%(w), b) 97%(m/w), 98%(m), 90%(w) NMSC: a) 8.4%(m/w), 11.8%(m), 3.0%(w); b) 8.4%(m/w), 11.8%(m), 3.0%(w) Sinonasal: a) 23.4%(m/w), 34.1%(m), 10.8%(w); b) 43.3%(m/w), 64.3%(m), 18.4% (w) All-deaths: a) 3.6%(m/w), 6.0%(m); 1.0%(w); b) 4.9%(m/w), 8.0%(m), 1.5%(w) All-incident: 3.2%(m/w), 5.4%(m), 1.0%(w), b) 4.0%(m/w), 6.7%(m), 1.2%(w) a) IARC Group 1 b) IARC Group 1 and 2A	Included	
Steenland et al., 2003, USA					
Lung Bladder Mesothelioma Leukemia Larynx Skin Sinonasal and nasopharyngeal Kidney Liver	Exposure assessed using early 1970 and 1980 national survey data (NOHS and NOES respectively), population estimates from 1980 census	US workforce	Lung: 8.0–19.2%(m), 2.0%(w) Bladder: 5.6–19.0%(m/w), 7.0–19.0%(m), 3.0–19.0%(w) Mesothelioma: 85–90%(m), 23–90%(w) Leukemia: 0.8–2.8%(m/w) Larynx: 1–20%(m) Skin: 1.2–6.0%(m) Sinonasal and nasopharyngeal: 31–43%(m) Kidney: 0–2.3%(m/w) Liver: 0.04–0.11%(m)	Included	
Dreyer et al., 1997, Nordic countries (Denmark, Finland, Iceland, Norway, Sweden)					
Lung Urinary bladder Larynx Mesothelioma Nasal cavity Kidney Leukemia	Exposure assessed between 1970 and 1984 for cancers in 2000, population estimates from 1970–1971 census	Nordic countries workforce	Lung: a) 12% (9–14%) (m/w), 18%(m), <1%(w); b) 4–8% (m); c) 11–14%(m), <1.0%(w) Bladder: a) 2.0% (1–2%) (m/w), 2.0%(m), <1.0%(w) Larynx: a) 5.0% (3–7%) (m/w), 6.0%(m), <1.0%(w); b) 4–9%(m) Mesothelioma: a) 71% (62–79%) (m/w), 83%(m), <1%(w); b) 78–84% (m) Nasal cavity: a) 20% (18–23%) (m/w), 30% (27–32%) (m), <2%(w) Kidney: a) 1.0% (1–2%) (m/w), 2.0% (2–3%) (m), <1%(w) Leukemia: a) 1.0% (m/w), 1.0%(m), <1.0%(w) All sites: a) includes all exposures b) asbestos only c) all except for asbestos	Included*	*Lung, larynx and mesothelioma cancer AF estimates that were due to asbestos exposure only were removed. Asbestos exposure in the Nordic countries at this time included shipbuilding and construction, production of asbestos cement and manufacture of friction materials for brakes in cars and machinery, all high-risk industries that are not relevant for Alberta.
Leigh et al., 1997, USA					
All cancer mortality	All civilian workforce mortality in the US in 1992.	US civilian workforce	All cancer death: 6–10%	Included	

Table 29 cont. —>

Cancers studied	Exposed population	Study size	AFs found	Included/ excluded	Rationale for exclusion
Comba et al., 1992, Italy					
Nose and nasal sinuses	Males and females diagnosed 1987–1987 in regional hospitals. Exposure assessed via questionnaire to determine work history in mining and quarrying, chemical industry, metal industry, textile and garment industry, wood and furniture industry, leather industry, agriculture.	78 cases and 254 controls—patients admitted to the same hospitals as the cases, with any diagnosis except chronic rhino-sinusal disease and nasal bleeding.	60.0% (m) – for occupations related to mining and quarrying, chemical industry, metal industry, textile and garment industry, wood and furniture industry, leather, agriculture.	Included	
Gustavsson et al., 2000, Stockholm County, Sweden					
Lung cancer	Males, aged 40–75 years who were stable residents of Stockholm County, Sweden, between 1950 and 1990 (did not live outside the country for more than five years); recruited between 1985 and 1990; lifetime exposure assessed via postal questionnaire	1,042 lung cancer cases 2,364 population controls frequency matched by 5-year age and year of inclusion. Both population referents and mortality referents were used.	Lung: 9.5% (95%CI = 5.5% to 13.9%) (m) – all exposures 2.5%(m) – diesel exhaust 4.0%(m) – asbestos 2.2%(m) – combustion products	Included*	*Lung cancer AF estimates that had been calculated separately for single exposures only (diesel exhaust, other combustion products, and asbestos) were removed. The estimate that considered the combination of all three exposures remained in the table because it better represented the overall AF for lung cancer.
Fritschi and Driscoll, 2006, Australia					
Same as Nurminen and Karjalainen	All cancer cases in 2000	Australian workforce	All cancers: 10.8%(m), 1.8%(w)	Included*	*The site-specific AFs were taken directly from Nurminen & Karjalainen and therefore added no new information; however, the AF for overall cancers is calculated based on the Australian cancer profile and therefore represents a “new” estimate that is appropriate to include.
Deschamps et al., 2006, Champagne-Ardenne, France					
Lung Mesothelioma Ethmoid and nasal cavity Urinary bladder Leukemia All cancer	Male and female incident cancer cases between 1995 and 1998, aged 16 and over	2,009 patients (1,092 men and 917 females)	Lung: 16.2%(m/w) Mesothelioma: 75%(m/w) Ethmoid and nasal Cavity: 1.06%(m/w) Urinary bladder: 2.1%(m/w) Leukemia: 1.2%(m/w) All cancer: 3.18%(m/w)	Excluded	Overall poor quality due to small population and an unconventional method of calculating AFs.
Doll and Peto, 1981, US					
				Excluded	Although this is an often-cited study, it fell outside of our 20-year cutoff. As a note, this study has been highly criticized in the literature for the method of calculating AFs.

Table 29 cont. —>

Cancers studied	Exposed population	Study size	AFs found	Included/ excluded	Rationale for exclusion
Kerr, 1996; Winder and Lewis, 1991; Mathers, 1999, Australia					
All cancers		N/A	All cancers: 2–4%	Excluded	These studies used Doll and Peto AF estimates while making adjustments for certain cancers that they believed were underestimated. These studies were excluded since they do not calculate original attributable fractions based on local exposure.
Barone-Adesi, 2005, Italy					
Lung – mainly All sites GI tract Bladder Nasal cavity and paranasal sinuses Larynx Skin	Italian populations, exposures assessed between 1957 and 1992	Review of 20 case-control, cohort and geographic studies	Not applicable	Excluded	This study was a review article and did not produce any original AFs.
Hamalainen et al., 2007, Global					
Malignant neoplasms (as a group)	All people over age 25 in established market economies	All people over age 25 in established market economies.	8.4%	Excluded	This study looked at global estimates. For established market economies, the category most appropriate for Alberta, the study used the AFs previously generated by Nurminen and Karjalainen with some revisions (e.g., downward adjustment for cancer in some regions).
Driscoll, 2005; Concha-Barrientos, 2004, 14 WHO subregions (Africa, Americas, Eastern Mediterranean, Europe, South-East Asia, Western Pacific)					
Bronchus and lung Leukemia	Men and women, aged 15 and over, 1990–1993, exposure assessed using CAREX database	Workforce populations of the various countries	Bronchus and lung: 10.0%(m/w), 12.0%(m), 6.0%(w) Leukemia: 2.0%(m/w), 3.0%(m), 2.0%(w) C-B: Bronchus and lung: 9.0%(m/w) Leukemia: 2.0%(m/w)	Excluded	These two publications result from the same study. Estimates included develop- ing economies. AFs used for developed countries were taken directly from Nurminen and therefore add no new information.
De Matteis, 2008, Italy and international (USA, Sweden, China, Germany, Europe, Greece, Norway)					
Lung	Italy and international populations, exposures assessed between 1957 and 2005	Review of 32 case-control and cohort studies	Not applicable	Excluded	This study was a review article and did not produce any original AFs.

Abbreviations: CI = confidence interval; N/A = not available; AF = attributable fraction