CANCER IN CANADA

AN EPIDEMIOLOGIC OVERVIEW

A report based on the *Cancer Incidence Atlas — Volume 2, 2000–2006*

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Également disponible en français sous le titre :
Le cancer au Canada – Aperçu épidémiologique
Rapport basé sur la publication Répartition géographique
de l'incidence du cancer au Canada – Volume 2, 2000–2006

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This publication can be made available in alternative formats upon request.

Publication date: February 2014

Cat.: HP35-43/2014E-PDF
ISBN: 978-1-100-22759-7
Pub.: 130371

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ACKNOWLEDGEMENTS

We would like to acknowledge the contribution of the following individuals:

- The Health Statistics Division of Statistics Canada, for providing data from the Canadian Cancer Registry (CCR) and the Canadian provincial/territorial cancer registries for providing data to the CCR;
- The staff members of CancerCare Manitoba who reviewed the risk factor information for each cancer. This includes Deepak Pruthi and Alain Demers along with their site-specific contributors: Dr. Piotr Czaykowski, Dr. Steven Latosinsky, Dr. Robert Lotocki, Dr. Marshall Pitz, Dr. Richard Nason, Dr. Mathew Seftel, Dr. Harminder Singh, Dr. Marni Wiseman.

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REPORT SUMMARY

This report provides an overview of the epidemiology of the 23 most common cancer sites in Canada. It includes information on the burden of illness, temporal trends, survival, types of cancer, provincial/territorial distribution and risk factors which increase the risk of developing cancer. Finally, data quality issues are also discussed where appropriate. The report is an excerpt from another publication, the *Cancer Incidence Atlas — Volume 2, 2000–2006*. While, the primary purpose of the atlas is for hypothesis generation and for suggesting health policy and program opportunities and priorities for cancer prevention, this report is envisioned to serve as a reference document for cancer epidemiology in Canada.

The report summarizes the current state of knowledge regarding significant spatial (geographic) aggregation in Canada; findings are suggestive that a significant proportion of some cancers are preventable. Potential explanations for the observed patterns are discussed.

Cancer incidence data were provided by the provincial and territorial cancer registries through the Canadian Cancer Registry database at Statistics Canada. Incidence rates were calculated per 100,000 population per year and adjusted to the 1991 Canadian standard distribution. The ratio of the provincial/territorial incidence rate to the Canadian rate was used to illustrate the relative risk of cancer in each area.

The most frequent cancer sites were prostate, lung, breast and colorectal. All provinces reported statistically significant prostate cancer rates, either low or high compared to the national rate. Low rates were reported in Newfoundland and Labrador, Quebec, Manitoba, British Columbia and Nunavut, while high rates were reported in Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Saskatchewan and Alberta. Incidence rates would be expected to be higher in places that have more screening for prostate cancer with the prostate-specific antigen (PSA) test.

Significantly lower incidence rates of lung cancer were observed for Newfoundland and Labrador, Ontario, Alberta and British Columbia, and among males in Manitoba and Saskatchewan. The significantly lower rates in Newfoundland and Labrador may be artefactual because death certificates were not available to the cancer registry for the period of data covered by this publication, so some individuals with lung cancer were not counted in the registry. Significantly elevated rates of lung cancer were observed in Nova Scotia, New Brunswick, Quebec and Nunavut, and among males in Prince Edward Island.

Breast cancer rates were relatively uniform with the highest provincial rate 5% higher than the Canadian rate. Significantly lower incidence rates for colorectal cancer were seen in Ontario, Alberta and British Columbia. Increased rates for colorectal cancer were seen in Newfoundland and Labrador, Nova Scotia, Quebec and the Northwest Territories, and among females in Prince Edward Island and Nunavut.

Where issues of data quality have been ruled out and associations with cancer risk factors have been demonstrated in epidemiologic studies, results can be used in planning cancer control programs that aim to reduce the burden of cancer. Cancer prevention includes avoiding risk factors such as smoking, obesity, lack of exercise and radiation exposure, and the promotion of protective factors such as being physically active, maintaining healthy weight, eating well and participating in screening and vaccination programs shown to reduce the risk of cancer.

1. INTRODUCTION

The purpose of this report is to provide an overview of the epidemiology of the 23 most common cancer sites in Canada. It includes information on burden of illness, temporal trends, survival, types of cancer, geographical variation and finally risk factors. The document is an excerpt of the *Cancer Incidence Atlas — Volume 2, 2000–2006* in order to make this information available to a wider audience.[1] It is directed towards epidemiologists and other health professionals. The websites of the Public Health Agency of Canada and Statistics Canada can be consulted for more detailed statistics from the latest release of the Canadian Cancer Registry.[2,3]

The data in this report identify provinces/territories in Canada that exhibit incidence rates for certain types of cancer that are either higher or lower than the rate for Canada as a whole. The nature of the data, however, does not allow for the identification of factors that may contribute to these differences in rates. Differences in rates may be a result of known or unknown risk and protective factors, differences in cancer detection and/or registration techniques. These hypotheses can only be investigated using stronger, more appropriate study designs.

2. METHODOLOGY

Details on the methodology used for analysis can be found in the *Cancer Incidence Atlas — Volume 2, 2000–2006*. In summary, information on cancer incidence was obtained from the Canadian Cancer Registry (CCR) database housed at Statistics Canada. Intercensal and post-censal population estimates were obtained from the Census and Demographics Branch of Statistics Canada. The most recent 7 year period of national cancer incidence data were used for analysis (2000 to 2006). IARC rules were used to determine multiple primary histologies.

Incidence rates were calculated per 100,000 population per year and adjusted to the 1991 Canadian standard distribution (Appendix 1). The comparative incidence figure (CIF) was used to compare the provincial/territorial incidence rate to the Canadian rate. The national and provincial/territorial age standardized incidence rates and CIFs for this report can be found at the website of the Public Health Agency of Canada.[2]

A data quality assessment was performed as part of the *Cancer Incidence Atlas — Volume 2, 2000–2006*. The assessment includes a comparison of incidence rates using first primary only versus IARC rules for multiple primaries; percent of cases with full 6-digit postal code; percent of death certificate only cases; percent of cases with microscopic confirmation; percent of women with a hysterectomy; and incidence to mortality ratios. All results are displayed by province/territory and for Canada as a whole.

For the *Cancer Incidence Atlas — Volume 2, 2000–2006* and this summary report, the World Health Organization's International Classification of Diseases for Oncology, Third Edition (ICD-O-3) coding rules were used.[4] Cancer sites and the order of presentation follow the recode tables of the United States Surveillance, Epidemiology and End Results (SEER) Program for ICDO-3 codes and include *in situ* bladder cancer cases (Appendix 2).[5]

LIMITATIONS

Readers should be aware that variation in cancer incidence rates may be a result of differences in cancer registration practices; known differences in practices are noted below in the site-specific text. In particular, the percentage of death certificate only (DCO) cases is higher than the ideal Canadian range of 1 to 3% for the categories of: other, ill-defined and unknown; other digestive system; pancreas; and liver. The percentage of microscopically confirmed cases is lower than 80% for: pancreas; liver; other ill-defined and unknown; other digestive system; leukemia; multiple myeloma; brain and nervous system; lung and bronchus; and kidney and renal pelvis.

The percentage of women with hysterectomies was removed for the population at risk for cervix and uterus excluding cervix. However, there was not sufficient data to estimate the percentage of women with both ovaries removed to adjust the population at risk for ovarian cancer.

In Quebec, because of the registry's dependence on hospital data, the numbers of microscopically confirmed prostate, melanoma and bladder cases have been estimated to be under-reported.[6] For Ontario *in situ* bladder cancer cases were not reported for the period covered by the *Incidence Atlas* and this summary report. To make comparisons more useful, rates presented for melanoma exclude Quebec and rates presented for bladder cancer exclude Ontario.

3. ALL CANCER SITES

In 2006, there were approximately 159,000 new cases of cancer in Canadians. The variation in overall cancer incidence rates is determined mostly by the variation in the incidence of leading cancer sites across the country. From 2000 to 2006, 4 sites collectively accounted for over half of all cancers (i.e., breast [28%], colon and rectum [13%], and lung [13%] among females, and prostate [26%], lung [16%], and colon and rectum [14%] among males).

The distribution of cancers is influenced in part by variation in the past prevalence of risk factors across the country, in keeping with the long latency between the beginning of the exposure and the appearance of most cancers. For lung cancer, this latent period is recognized as a considerable fraction of a lifetime and is measured in decades. Risk factors for cancer are numerous and widely present. Cancer risk factors include cigarette smoking, alcohol consumption, obesity, low fruit and vegetable consumption, food contaminants, radiation, some chronic infections, medicinal drugs, immunosuppression, and occupational and environmental contaminants. Short-term variation in cancer incidence may also be due to the availability of screening and diagnostic services for breast, colorectal, prostate and cervical cancers; places with such services can detect more cancers than those without these services. These factors are discussed in more detail by type of cancer.

In Canada, the 2006 age-standardized incidence rate (ASIR) of cancer for all sites combined (excluding non-melanoma skin cancer) was 29% higher in males than in females. Prior to age 55, females have a higher rate of cancer, mostly because of breast cancer. However, the all-site incidence rate for males increases more rapidly with age than that for females after age 55, and it is nearly double the female rate by age 85 years or over.[7]

The annual ASIRs of cancer for all sites combined were relatively stable for the period 1997–2006.[8] The 5-year relative survival is better among females (63%) than males (61%) (statistically significant), and it has increased by 4.5 percentage points for the period 2002–2004 versus 1992–1994 (absolute difference in age-standardized relative survival rates).[9]

GEOGRAPHIC VARIATION

The overall cancer incidence rate for females in Newfoundland and Labrador was lowest among the provinces/territories and statistically significantly lower than the Canadian rate with a CIF (ratio to Canadian rate) of 0.87. The cancer registry in Newfoundland and Labrador did not include death certificate only (DCO) cases for the period of analysis of this publication. This falsely lowers the number of newly diagnosed cases, mainly among those cancers with a poor prognosis, such as lung and pancreatic cancers. However, the percentage of death certificate only cases is relatively small for all cancers combined, and these cases do not entirely explain the lower incidence rates. The incidence-to-mortality ratio is also lower in Newfoundland and Labrador than the other Canadian provinces and may indicate under-ascertainment of cases. British Columbia also had lower overall cancer incidence rates for females with the second lowest CIF of 0.92. The lower rates in British Columbia partly reflect its lower rates of colorectal, breast and lung cancers. The all cancer rate was also lower among females in Saskatchewan. The lowest rates among males were observed in Yukon with a CIF of 0.83, British Columbia with a CIF of 0.91 and Newfoundland and Labrador with a CIF of 0.92. All cancer rates were also lower among males in Ontario and Manitoba.

Among females the highest overall cancer incidence rates were observed in Nunavut with a CIF of 1.77 and Nova Scotia with a CIF of 1.07. Significantly higher rates were also observed among females in Quebec, Ontario and Manitoba. Among males rates were highest in Prince Edward Island and Nova Scotia with a CIF of 1.14 in each province. Increased rates among males also occurred in New Brunswick, Quebec and Alberta.

4. SITE-SPECIFIC CANCER DISTRIBUTION

4a) BUCCAL CAVITY AND PHARYNX (C00-C14)

Cancers of the buccal cavity and pharynx, also referred to as oral cancer, were responsible for approximately 2.1% of all new Canadian cases of cancer in 2006 (1,102 in females; 2,228 in males).[7] Oral cancer includes cancers of the mouth, salivary glands and pharynx. The pharynx is the hollow tube about 13 centimetres (5 inches) long that starts behind the nose and leads to the esophagus (the tube that goes to the stomach) and the trachea (the tube that goes to the lungs). The age-at-incidence curve indicates that the incidence rates for both sexes are low before about age 35. Rates then increase and reach a plateau at ages 70–74 or greater among females and at ages 65–69 or greater among males, with the risk for males being about twice that of females.[7] In recent years, the age-standardized incidence rates for females have remained relatively static, while they have gradually declined among males. The 5-year relative survival rate for the period 2002–2004 was 66% in females and 62% in males.[9]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for mouth and pharynx cancers among females were observed in Newfoundland and Labrador, New Brunswick and Quebec. Among males, lower rates occurred in Alberta and British Columbia. Significantly higher incidence rates for mouth and pharynx cancers were observed among females in Ontario, Manitoba and Nunavut. Among males, increased rates occurred in Newfoundland and Labrador, Nova Scotia, Quebec and Manitoba.

KNOWN AND SUSPECTED RISK FACTORS

Tobacco and alcohol, both risk factors for buccal cavity and pharyngeal cancers, have been implicated as independent risk factors whose combined effects are synergistic. With the exception of salivary gland, nasopharyngeal and lip cancers, more than 80% of oral cancers in some regions can be attributed to alcohol and tobacco use.[10,11]

Two infectious agents, human papilloma virus (HPV) and Epstein-Barr virus (EBV), also are implicated in distinct pathways resulting in cancer. Studies vary with respect to the percentage of oral cancers caused by HPV. Some have estimated as high as 50% for oropharyngeal cancers,[12] the site with the highest effect. Other risk factors such as wood dust, formaldehyde, alcohol, tobacco, deep-fried foods and salted fish have been associated with nasopharyngeal carcinoma.[12,13]

4b) ESOPHAGUS (C15)

In 2006 in Canada, there were approximately 1,500 cases (401 among females; 1,101 among males) and a similar number of deaths.[7,14] The age-at-incidence curve indicates that those aged 75 and older are at the highest risk when the population in each age group is taken into account. The age-standardized incidence rates during 1997–2006 were relatively stable.[8] This cancer is rapidly fatal with a poor overall 5-year relative survival at 14% (period 2002–2004), with little variation between females and males.[9]

Esophageal cancer is divided into either squamous cell carcinoma (SCC), the most common histologic type of esophageal cancer, or adenocarcinoma (AC), which has a better prognosis than the former type.[15] Combined, these 2 epithelial carcinomas account for 95% of the esophageal cancers.[16] In contrast to the pattern of decreasing or stable rates for esophageal cancer as a whole, rates of esophageal AC have increased.

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for cancer of the esophagus were observed in Newfoundland and Labrador, Quebec and Saskatchewan. Increased rates were observed in Nova Scotia, British Columbia and Yukon.

KNOWN AND SUSPECTED RISK FACTORS

These 2 main histologic types (SCC+AC) have slightly different etiologic factors. The 2 central etiologic factors, alcohol use and tobacco use, are more pronounced in SCC; alcohol is not an important risk factor for AC, and AC is only weakly associated with tobacco use. In Western Europe and in North America, these 2 factors combined can account for up to 90% of the risk of esophageal SCCs.[17] Alcohol consumption and smoking function synergistically, increasing the risk for esophageal cancer by up to 100 times.[12,18] Dietary factors are probable causes of the disease. In particular, diets high in calories, total fat, saturated fat, cholesterol, butter and oils, and diets low in fibre have been shown to increase the risk for esophageal cancer and for esophageal AC, in particular.[12,13,19–21]

Gastroesophageal reflux disease (GERD), a precursor stage to Barrett's syndrome, is noted as a strong risk factor for the development of esophageal AC. Obesity is a risk factor for GERD and consequently increases the risk for esophageal AC by 7-fold.[16,17] Some studies have shown that the use of non-steroidal anti-inflammatory drugs, or NSAIDs (such as aspirin and other drugs that reduce fever, swelling, pain and redness), is associated with a reduced risk of developing both SC and AC of the esophagus, but potentially serious side-effects need to be considered.[22] While *Helicobacter pylori* bacteria has been associated with increased risk for SCC, it is associated with reduced risk for AC.[23]

4c) STOMACH (C16)

In Canada, stomach cancer accounted for 1,083 cases among females and 1,928 cases among males in 2006, indicating that the risk among males is about double that among females.[7] During the period 1997–2006, annual average declines in age-standardized incidence rates were 1.6% among females and 2.1% among males.[8] Incidence increases rapidly with age, although this may partly reflect lower rates among younger birth cohorts. The 5-year survival for this cancer for the period 2002–2004 was only 22–24%.[9] This cancer is divided into two main classes based on location: gastric cardia cancer (the top inch of the stomach, where it meets the esophagus) and non-cardia gastric cancer (all other areas of the stomach). About 90% of stomach tumours are adenocarcinomas, which are subdivided into 2 main histological types: (1) well-differentiated or intestinal type, and (2) undifferentiated or diffuse type.

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for stomach cancer were observed in Ontario, Saskatchewan and British Columbia, and among males in Prince Edward Island and Alberta. Increased rates were observed in Newfoundland and Labrador, Quebec and Northwest Territories among females and in Nunavut among males. The highest provincial rates were found in Newfoundland and Labrador with a comparative incidence figure (CIF) of 1.50 for females and 1.58 for males.

KNOWN AND SUSPECTED RISK FACTORS

Cancer develops through the initiation of long-term chronic inflammation.[24] One of the strongest etiological factors for gastric cancer, a group I carcinogen as defined by the International Agency for Research on Cancer (IARC),[25] is *Helicobacter pylori* (*H. pylori*). Worldwide, the countries with the highest gastric cancer rates concurrently have the highest prevalence for *H. pylori*, a trend consistent with the declines in the incidence of *H. pylori* in countries with low gastric cancer incidence.[24,25] The gram-negative bacterium is believed to cause anywhere from a 3- to 6-fold increase in the risk for noncardia carcinoma, adenocarcinoma and primary non-Hodgkin lymphoma of the stomach lining.[12,17] Although, please note that the lymphomas are not included with stomach cancer statistics.

Salted and salt-preserved foods may facilitate the risk of *H. pylori* infection and function synergistically in the development of cancer.[25,26] Low intake of fruits and vegetables also enhances the risk for gastric cancer.[21] High consumption of cured or smoked meats or fish (containing N-nitroso compounds), well-cooked meats and pickled vegetables may increase the risk

for gastric cancer. The IARC has evaluated ingested nitrate or nitrite under conditions that result in endogenous nitrosation as probably being carcinogenic to humans (Group 2A).[27,28]

4d) COLON AND RECTUM (C18-C20, C26.0)

Colorectal cancer was responsible for 12.5% of all new Canadian cases of cancer in 2006 (9,021 in females; 10,837 in males).[7] Slightly more than two-thirds of new cases of colorectal cancer are cancers of the colon. Several changes in trend have been observed over the past 25 years. For both sexes, the incidence rose between 1980 and 1985, then declined to the mid-1990s (more strongly in females than in males), and then rose again through 2000 only to decline significantly thereafter.[8]

The dominant morphology for colorectal cancer is adenocarcinoma, accounting for over 95% of the morphologically confirmed cases. The age-specific incidence rises throughout life to age 90, although this rise is attenuated after age 50, particularly among females.[7] About 93% of all colorectal cancers occur in females and males aged 50 and above. The 5-year relative survival rate has slowly improved to 62% for both sexes combined for the period 2002–2004.[9]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for colorectal cancer were seen in Ontario, Alberta and British Columbia. Increased rates were seen in Newfoundland and Labrador, Nova Scotia, Quebec and the Northwest Territories, and among females in Prince Edward Island and Nunavut. The highest provincial comparative incidence figures (CIF) of 1.2 to 1.3 were observed in Newfoundland and Labrador, Prince Edward Island (females), and Nova Scotia. Among females in Nunavut the CIF was 3.0.

KNOWN AND SUSPECTED RISK FACTORS

Red meat is a recognized risk factor for colorectal cancer, and there is suggestive evidence that diets high in fat and low in fruits and non-starchy vegetables also result in increased risk.[12,17,21,29,30]

Obesity and physical inactivity, in association with poor dietary intake, have also been associated with increased risk for colorectal cancer.[29,30] Individuals with a body mass index (BMI) in the top 20% have a 2-fold elevated risk for colorectal cancer when compared with those in the lower 20% of BMIs; this relationship is stronger for colon cancer.[17,29,30]

Any disease, illness or syndrome that increases the likelihood of polyps indirectly increases the probability of developing colorectal cancer. Genetic factors are implicated in the development of adenomatous polyps and colorectal cancer.[17] Familial adenomatous polyposis, an autosomal dominant disorder, accounts for between 1% and 5% of colorectal cancer.[13,17,31]

4e) LIVER (C22.0)

Primary malignancies of the liver accounted for 1,465 new Canadian cancer cases in 2006 (394 in females; 1,071 in males).[7] These figures exclude cases of intrahepatic bile duct cancer. Survival is poor, with a 5-year relative survival rate of 18% for the period 2002–2004.[9] For 1997–2006, the annual percentage change in age-standardized rates was 2.3% among females and 3.1% among males.[8] Liver cancer is very rare below age 40, but the risk increases from age 40 to ages 70–74 and the rate remains relatively constant for older age groups.[7] About 90% of these cases are hepatocellular carcinoma (HCC).

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for liver cancer were observed in Nova Scotia, New Brunswick and Saskatchewan. Increased rates were observed in Quebec, Alberta and British Columbia.

KNOWN AND SUSPECTED RISK FACTORS

Cirrhosis of the liver is a risk factor for HCC. Approximately 80% of patients with HCC have concurrent cirrhosis.[13,32] Whether cirrhosis is itself a predisposing factor or whether the underlying causes of cirrhosis are responsible for the development of HCC still needs clarification.[17] There are multiple causes of cirrhosis, including alcohol-related liver disease, chronic hepatitis B, C and D, nonalcoholic fatty liver disease, autoimmune hepatitis, diseases that damage or destroy bile ducts such as primary biliary cirrhosis or primary sclerosing cholangitis, inherited diseases, drugs, toxins and infections.[33]

Chronic infection with the hepatitis B virus (HBV) or the hepatitis C virus (HCV) is a leading risk factor for the development of a majority of the cases of HCC. Whereas HBV is more common in the developing world, HCV is more prevalent in the Western world—especially in Canada. Although infection with HBV is declining and was 3.1 per 100,000 people in 2000, HCV infection is increasing and was 61.0 per 100,000 people in the same year.[34] An HBV vaccination in early childhood will greatly reduce the likelihood of the disease.[35] Currently, all provinces and territories have a childhood hepatitis B immunization program.

4f) PANCREAS (C25)

Cancer of the pancreas is the second most common digestive system cancer after colorectal cancer. In Canada in 2006, there were 3,651 new cases diagnosed (1,850 in females; 1,801 in males).[7] The disease is very rare before the age of 40, at which point the risk increases steadily to the age group of 85 or more. Of the leading cancers, pancreatic cancers have the poorest 5-year relative survival rate, at just 6% for the period 2000–2002,[9] and this can largely be attributed to the fact that 80% of the cancers are diagnosed at the metastatic state.[17] However, a small percentage of total cases, those diagnosed with pancreatoblastomas (a cancer with an early age at diagnosis and more common in children), have a 55% overall 5-year survival rate.[17] Incidence and mortality rates have remained relatively constant during the last decade.

GEOGRAPHIC VARIATION

Significantly lower incidence rates for cancer of the pancreas were observed in Newfoundland and Labrador and Ontario, and among males in British Columbia. Increased rates were observed in New Brunswick and Quebec, and among females in Alberta.

KNOWN AND SUSPECTED RISK FACTORS

Cigarette smoking is a risk factor for pancreatic cancer. In some studies, the relative risk was 2.5 times greater in smokers than in non-smokers,[36] while this relative risk was seen at 3.3 in heavy smokers.[37] The risk for developing pancreatic cancer is dependent on duration and amount; studies estimate that tobacco smoking contributes to between 27% and 33% of pancreatic cancers.[12,38] Certain hereditary conditions such as hereditary pancreatitis also increase the risk.[13,17,39] Body mass index and increased height have both been found to be risk factors for this cancer.[17,40] Diabetes mellitus is positively associated with malignancies of the pancreas, with insulin resistance-related hyperinsulinemia hypothesized to play a role in the etiology.[41,42]

4g) LARYNX (C32)

Cancer of the larynx is relatively rare, accounting for less than 1% (1,024 cases) of all cancer cases in 2006, with over 80% of cases found among males.[7] The annual percentage change in incidence rates has been a decrease of over 3% per year among both sexes.[8] Cancer of the larynx is rarely seen below age 50; rates peak among persons aged 70–79 and then decline.[7] The overall 5-year relative survival rate for both sexes combined for the period 2002–2004 was 65%.[9]

GEOGRAPHIC VARIATION

Due to the smaller number of cases, rates for females and males were combined for analysis. At the provincial/territorial level, significantly lower incidence rates for cancer of the larynx were observed from Ontario to British Columbia. Significantly elevated rates were observed in Newfoundland and Labrador, Prince Edward Island and Quebec. The highest comparative incidence figure (CIF) of 1.42 was observed in Quebec with slightly lower rates in Newfoundland and Labrador and Prince Edward Island.

KNOWN AND SUSPECTED RISK FACTORS

Despite the difficulties in separating the effects of alcohol consumption and smoking, the 2 risk factors are believed to act independently and jointly. Alcohol, the weaker of the 2 factors, is believed to facilitate carcinogenic effects such as those of tobacco and of other unrecognized carcinogens.[43] It has been suggested that 25% of laryngeal cancer cases are attributable to alcohol consumption and that the risk is increased by 3- to 4-fold.[44,45]

4h) LUNG AND BRONCHUS (C34)

Lung cancer, which includes tumours of the bronchus and lung (but not trachea and pleura), accounted for 22,534 new cases in 2006 (10,238 in females; 12,296 in males).[7] Among females, incidence rates increased by 1.2% per year while, among males, incidence rates declined by 2.1% per year for the period 1997–2006. As a result, the male-to-female ratio of age-standardized rates has decreased to about 1.4.[8] For females less than age 55, incidence rates are currently higher than for males. Lung cancer is rare before age 35, and incidence rates currently peak among those aged 80–84.[7] Lung cancer continues to have a poor prognosis: the 5-year relative survival rate for the period 2000–2002 was 17% among females and 13% among males.[9]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for lung cancer were observed for Newfoundland and Labrador, Ontario, Alberta and British Columbia, and among males in Manitoba and Saskatchewan. The significantly lower rates in Newfoundland and Labrador may be artefactual because death certificates were not available to the cancer registry for the period of data covered by this publication, so some individuals with lung cancer were not counted in the registry. Significantly elevated rates were observed in Nova Scotia, New Brunswick, Quebec and Nunavut, and among males in Prince Edward Island. The highest provincial comparative incidence figures (CIF) of 1.1 to 1.4 were observed in Nova Scotia, New Brunswick and Quebec. In Nunavut the CIF was 6.0 among females and 3.4 among males.

KNOWN AND SUSPECTED RISK FACTORS

In populations with a long duration and heavy intensity of cigarette usage, the proportion of lung cancer attributable to smoking is of the order of 90%. The new filters and low-tar cigarettes have not been found to diminish cancer rates appreciatively; users of such cigarettes engage in deeper inhalation and in more vigorous puffing, and often consume more cigarettes.[17,46] Increases in the proportion of adenocarcinoma cases have been reported to be associated with the introduction of filter-tip cigarettes.[47] Residential exposure to radon has been estimated to be responsible for over 1,500 cases of lung cancer a year in Canada (about 8% of lung cancer cases).[48] A number of techniques are available to homeowners to reduce radon concentrations in their homes.

4i) MELANOMA OF THE SKIN (C44 HISTOLOGIES 8720-8790)

Melanoma is the most serious histological type of skin cancer, representing tumours that arise in the melanocytes. In 2006, there were 4,580 cases in Canada (2,135 in females; 2,445 in males).[7] The annual percentage change for 1997–2006 has been a 1.2% increase among females and a 1.5% increase among males.[8] Melanoma is one of the most common cancers in young adults. Incidence rates increase with age, but for those over 50 the increase is less pronounced among females than males, and age-standardized rates are lower for females than males above this age.[7] For the period 2000–2002, the 5-year survival rate was higher for females (93%) than for males (86%).[9] The rate of survival is greatly dependent on the tumour thickness.[49]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for melanoma were observed in Newfoundland and Labrador, Manitoba and

Saskatchewan, and among males in Alberta. Significantly elevated rates were observed in Nova Scotia and among females in Prince Edward Island and among males in Ontario. Quebec is excluded since the number of cases of melanoma are known to be under-reported (see Limitations).

KNOWN AND SUSPECTED RISK FACTORS

Exposure to ultraviolet radiation is implicated in as much as 80% or more of melanomas.[46,50,51] The risks associated with intense and intermittent exposure tend to be greater than those associated with chronic exposure, especially for younger individuals.[52] People with fair complexions are generally at higher risk. Red hair colour, the presence of multiple benign or atypical nevi and the presence of freckles are also risk factors.[12,53,54] Having a history of severe sunburn increases melanoma risk,[12,32,54] and being easily susceptible to burning has been shown to increase the risk by 2- to 3-fold.[17] A previous history of melanoma is also known to elevate the lifetime risk by at least 3%,[32] and perhaps as high as 5–10%.[17] In addition, a family history of melanoma is a strong indicator for risk, with at least 10% of patients reporting the presence of the disease in a close relative.[17] When compared with the general population, the presence of a family history of melanoma increases the risk of the disease by 3–4 times[13] and is suggestive of a possible genetic influence.

4j) FEMALE BREAST (C50)

One in every 9 Canadian women will develop breast cancer in her lifetime, based on current rates. In 2006, there were over 20,600 new cases.[7] These statistics exclude *in situ* breast cancer cases. Incidence rates have been relatively stable since the early 1990s, with evidence of a recent decline of about 1% per year from 1999 to 2006. By ages 30–34, breast cancer is the most common cancer among women. The age-specific incidence rates rise to a plateau for women aged 65–69 or greater.[7] The 5-year relative survival has improved to 87% for the period 2002–2004.[9]

Carcinomas of the breast are ordinarily divided into ductal and lobular histologies. The former account for 65–80% of cases and the latter, for 5–10% of cases; other types, including medullary, adenoid cystic, mucinous and tubular, make up the remainder. Breast cancers are also classified by estrogen receptor and progesterone receptor status, human epidermal growth factor type 2 receptor (HER2/neu) overexpression, stage and nuclear grade.

Screening mammography for breast cancer is available across the country. Early detection of breast cancer through screening programs can improve quality of life and reduce the risk of death from breast cancer.[55,56] For ages 50 to 69, screening has been shown to reduce mortality. Equivocal evidence is found with screening in younger women. It should be noted that a significant fraction (15–30%) of screen-detected cancers of the breast are indolent and quite likely would not have become clinically apparent in the absence of screening. This "over-diagnosis" could well distort spatial patterns if there is sufficient spatial variation in screening activity.[57,58]

GEOGRAPHIC VARIATION

There was a relatively uniform distribution of the incidence of breast cancer among women across the country. Significantly lower incidence rates were observed in Newfoundland and Labrador, New Brunswick, Saskatchewan and British Columbia. Significantly elevated rates were observed in Quebec, but the increase in the age-standardized rate compared with Canada was small, at 4%.

KNOWN AND SUSPECTED RISK FACTORS

There is considerable evidence that the major risk factors for breast cancer are largely related to reproductive hormones. Women with early menarche, those with late menopause and women who have never been pregnant have increased risks.[59] A woman who has a late first pregnancy has a higher risk for breast cancer than a woman who has never had a full-term pregnancy. Oral contraceptives, especially when taken in the early teenage years, may modestly increase the incidence for breast cancer.[60] Hormone replacement therapy may slightly raise the risk for breast cancer, though this depends on duration and marginally on formulation.[61] Exercising strenuously for more than 4 hours per week is associated with reduced breast cancer risk of up to 40%.[62] Family

history is also a risk factor. Mutations in the autosomal dominant BRCA1 and BRCA2 genes increase the lifetime risk to 40–85%[12] but account for less than 10% of breast cancer cases.[63,64] Premenopausal obesity is likely protective, whereas the opposite is true among postmenopausal women and obesity, in general, increases the risk of breast cancer.[12,17,65,66] There is a linear increase in risk for breast cancer with increased alcoholic beverage consumption.[21]

4k) CERVIX UTERI (C53)

Due in large part to early detection of pre-malignant lesions by screening with Papanicolaou (Pap) tests, the incidence rates of cervical cancer have declined substantially; the annual percentage change for 1997–2006 was a decline of 1.8%,[8] with 1,332 cases in 2006.[7] The age-at-incidence curve rises steeply from puberty to age 40, after which it plateaus.[7] The relative 5-year survival rate for the period 2002–2004 was 75%.[9]

There are 2 major histological subtypes of cervical cancer. Squamous cell carcinoma (SCC) accounts for 80–85% of the cases, while adenocarcinoma (AC) is less common, accounting for approximately 10–15% of the cases. The last 30 years have been marked by changing trends as the incidence of SCC has decreased and stabilized, whereas the incidence of AC has been increasing.[12,13,32,67]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower incidence rates for cancer of the cervix were observed for Quebec and British Columbia. Significantly elevated rates were observed in Newfoundland and Labrador, Nova Scotia, New Brunswick and Alberta. The highest provincial comparative incidence figure (CIF) was observed in Nova Scotia at 1.56.

KNOWN AND SUSPECTED RISK FACTORS

Infection with human papillomavirus (HPV) plays the strongest etiologic role in the development of cervical neoplasia. HPV DNA has been identified in more than 99% of cervical carcinomas.[17] HPV types 18 and 16 have been identified as human carcinogens that jointly cause greater than 70% of all cervical carcinomas.[68,69] The overall prevalence of high- and low-risk HPV types was estimated among women in the United States aged 14 to 59 as 15.2% and 17.8%, respectively.[70] HPV DNA point prevalence will most certainly underestimate cumulative incidence of infection because many infections clear up. A vaccine has been shown to prevent infection with HPV-16 and HPV-18, the types that cause most cervical cancers. Smoking, in conjunction with HPV-16, functions synergistically in the development of cervical cancer.[71] Overall, the risk of developing cervical cancer that is attributable to cigarette smoking is generally 2-fold and increases with duration and intensity.[12] Individuals with immunosuppression caused by HIV infection or organ transplantation are also at increased risk.[72]

4l) UTERUS EXCLUDING CERVIX (C54-C55)

Uterine cancer, or endometrial cancer, most of which arise in the body of the uterus, is the most common gynecological malignancy and was responsible for 4,242 cases in 2006.[7] The age-standardized incidence rate has gradually risen over the last decade, with an annual percentage change of 0.4%.[8] Incidence of uterine cancer is rare before age 30, and the rate peaks between ages 65 and 69. About 2% of the cases occur in women below age 40, and approximately 48% occur among those aged 60–79.[7] Of all gynecological cancers, it has the highest overall 5-year relative survival rate, at 85% for the period 2002–2004 (excludes uterus unspecified).[9] Most cancers in the group are adenocarcinomas of the endometrium (lining of the uterus), while a small percentage of the cases (less than 5%) are sarcomas of the myometrium (thick, middle muscular layer).

GEOGRAPHIC VARIATION

Provinces/territories with significantly lower rates for cancer of the uterus excluding cervix included Newfoundland and Labrador, Quebec, British Columbia and the Northwest Territories. Provinces with significantly higher rates included Manitoba and Alberta.

KNOWN AND SUSPECTED RISK FACTORS

Chronic estrogen exposure unopposed by progesterone, be it endogenous or exogenous, is known to increase the risk of hyperplasia, an abnormal increase in the number of normal cells. Related factors include low parity or nulliparity, early menarche, late menopause and extended periods of absence of ovulation (commonly seen in polycystic ovarian syndrome).[12,32,73,74]

Excess weight is known to be a significant risk factor and is estimated to account for close to half of all cases of endometrial cancer in Europe and the United States.[74,75] A meta-analysis has reported a relative risk for endometrial cancer of 1.59 for a 5 kg/m² increase in BMI.[75] It is believed that obesity facilitates reactions in the adipose tissue, increasing the levels of estrogen.[74]

4m) OVARY (C56)

Ovarian cancer is the leading form of gynecological cancer death and was responsible for 1,569 deaths and 2,410 new cases in 2006.[7,14] Both incidence and mortality rates have been relatively stable over the most recent decade. Incidence rates are low among adolescents and young adults below age 35, and then increase to a plateau at ages 75 or more.[7] Approximately three-quarters of the cases occur in postmenopausal women (aged 52 and above). The 5-year relative survival rate is low, at 40% for the period 2002–2004.[9]

Three types of ovarian cancer predominate: epithelial tumours, germ cell tumours and sex cord-stromal tumours. The epithelial type accounts for 85–90% of all malignant cases, which generally occur in women aged 40 and over, and arise from the surface epithelium of the ovary.[12,17]

GEOGRAPHIC VARIATION

Significantly lower incidence rates for cancer of the ovary were observed in 3 eastern provinces (Newfoundland and Labrador, Prince Edward Island and Nova Scotia) and 3 western provinces (Saskatchewan, Alberta and British Columbia). Significantly elevated rates were observed in Ontario, with the ratio of the Ontario rate to the Canada rate at 1.06, making it 6% higher than the national rate.

KNOWN AND SUSPECTED RISK FACTORS

Established risk factors for epithelial ovarian cancer are reproductive and genetic in nature.[76] Uninterrupted and prolonged ovulary cycles can significantly increase the risk of ovarian cancers, as demonstrated in the increased incidence of ovarian cancer among nuns, single women and women who have never been pregnant. Protective effects have been observed for oral contraceptive use and increased number of births.[12,77] Oral contraceptive use for just 1 year decreased the risk of ovarian cancer by 15%—a value that increases to 38% with 6 years or more of use.[77] A single pregnancy significantly reduces the risk for ovarian cancer, with a risk ratio of 0.4 to 0.7, and there is a further reduction in the odds of ovarian cancer of about 12% for each additional birth.[32,78] As body mass index increases, the risk of ovarian cancer increases; however, this effect is modest.[79]

A family history of ovarian or breast cancer is also a risk factor. Studies indicate a hereditary basis for about 5–10% of cases; however, the risk changes and is 4-fold in women who have a first-degree relative with the disease.[17,46,80] Different authors associate between 60% and 90% of these hereditary cases with the breast-ovarian cancer syndrome involving mutations in the BRCA1 and BRCA2 genes.[17,32,80] Those women with mutations in BRCA1-associated cancers are believed to have a 16–63% lifetime risk and an average age of diagnosis of 48.[17,32] The lifetime risk for those with BRCA2-associated cancers is 10–35%, and an average age at diagnosis is 61.[17,32] Hereditary nonpolyposis colorectal cancer syndrome, or Lynch Type II syndrome, is also a known risk factor, accounting for approximately 5% of all hereditary ovarian cancer cases.[32]

4n) PROSTATE (C61)

The clinical presentation and progression of prostate cancer can vary greatly. Patients with prostate cancer may receive prognoses of short life expectancies, or

the disease may have no effect on either their longevity or their quality of life. Prostate cancer is the most frequently diagnosed cancer in Canadian men. In 2006, 22,610 new cases were reported.[7] Incidence is rare below age 40, but rates then increase so that about 36% of cases occur by the age of 65.[7] The risk for developing prostate cancer increases with age more than any other major cancer. Currently, 1 in 7 Canadian men will develop the disease in their lifetime, and 1 in 26 will die of it.[9]

Peaks in incidence rates of prostate cancer occurred in 1993 and 2001, probably due to increased screening. Since 2001, incidence rates have been stable. In contrast, mortality rates have decreased significantly in the last decade. Since 1992–1994, the 5-year relative survival rate increased by about 7 percentage points to reach 95% for the period 2002–2004.[9]

GEOGRAPHIC VARIATION

All provinces reported statistically significant rates, either low or high compared to the national rate. Low rates were reported in Newfoundland and Labrador, Quebec, Manitoba, British Columbia and Nunavut, while high rates were reported in Prince Edward Island, Nova Scotia, New Brunswick, Ontario, Saskatchewan and Alberta. Incidence rates would be expected to be higher in places that have more screening for prostate cancer with the prostate-specific antigen (PSA) test. Nevertheless, published rates of provincial/territorial PSA screening rates from the Canadian Community Health Survey for 2000 and 2003 do not indicate an obvious relationship with cancer incidence rates for 2000–2006.[81,82] Low rates in Quebec are probably a result of the cancer registry relying on hospitalization data and the resulting incomplete inclusion of individuals with prostate cancer.

KNOWN AND SUSPECTED RISK FACTORS

The causes of prostate cancer are largely unknown. The risk for prostate cancer increases among men as they age, but many of these cancers are slow-growing and don't cause any clinical symptoms. As early as their 20s, 10% of men show evidence of non-clinical prostate carcinoma.[83] However, the change from virtual non-existence to pathogenesis decades later remains a mystery. By the age of 80, as many as 60–70% of men show histologic evidence of carcinoma of the prostate.[12]

Other well-established risk factors for prostate cancer include race and family history. It is known that African American men have an age-adjusted incidence rate 1.6-fold higher than Caucasian Americans, who in turn have an incidence rate of about 1.6-fold that of Asian Americans. A genetic component that functions in a Mendelian fashion is also implicated, and 6 potential susceptibility loci have been identified.[84] In addition, an increased risk for prostate cancer is seen in males who have a relative with the disease, and the risk increases if the relative is first-degree. Studies generally indicate that family history may account for 5–10% of all prostate cancers.[85]

Dietary factors have also been suggested as a risk factor for prostate cancer, but evidence to date is limited.[21] This conjecture is given more credence by the fact that Americans of Japanese origin, whose native country has a lower incidence of prostate cancer and a pattern of low-fat diets, reported incidence rates higher than men in Japan.[86] This result is largely attributed to the Western lifestyle and diet, since Western diets are generally higher in caloric intake and substantially greater in fat content. Certain studies have rejected the influence of caloric intake alone; however, fats, particularly saturated fats, were highly correlated with increased risk. Intake of total meat, red meat and animal fat were also implicated as risk factors, as was the possibility of alpha-linolenic acid.[12,84]

4o) TESTIS (C62)

With 845 cases in 2006, testicular cancer represented 1.0% of the cancers in males.[7] It occurs predominantly among young and middle-aged men. Typically manifesting as early as age 15, it is the leading cause of cancer in males aged between 15–39. The age-standardized incidence rate (ASIR) increases relatively rapidly beginning between ages 15 and 19 and peaks between ages 25 and 34; thereafter, the rate gradually declines. By age 55–59, the cancer becomes rare.[7] A high 5-year relative survival rate of 96% was reported for the period 2002–2004.[9] The all-age incidence

rate of testicular cancer in Canada has increased by about 80% in the last quarter of the 20th century, and the ASIR continues to rise, albeit marginally so in recent years.[9,87]

The vast majority (95%) of all testicular neoplasms arise in the germ cells of the testes, referred to as germ cell tumours (GCTs); the remaining cases arise in the sex cord-stromal tissue.[12,13] Two main cell types of testicular cancer are seminomas, which are more sensitive to radiation, and nonseminomas.

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for cancer of the testis were observed in Newfoundland and Labrador, New Brunswick and Quebec, while higher rates were observed in Alberta.

KNOWN AND SUSPECTED RISK FACTORS

The causes of testicular cancer are largely unknown. Syndromes noted for abnormal testicular and urogenital development are known to elevate risk. A history of cryptorchidism, a condition in which 1 or both testes fail to descend normally, can account for approximately 10% of all cases of GCTs and increases the relative risk by between 2.5 times and 15 times.[12,13] Furthermore, in approximately 5–20% of cryptorchid patients, tumours develop in the contralateral normally descended testis.[12,13,17] Klinefelter's syndrome is another hereditary disorder that has also been suggested for predisposition to the neoplasm; approximately 10% of all mediastinal nonseminomatous GCTs are attributable to Klinefelter's syndrome.[12,17,46,88]

4p) BLADDER (C67 INCLUDING *IN SITU*)

Bladder cancer was responsible for 6,607 new cancer cases in 2006 (1,695 cases among females; 4,912 cases among males).[7] The age-standardized incidence rates (ASIRs) for the period 1997–2006 decreased on average by 0.3% per year among females and by 0.7% among males.[8] The incidence increases greatly with age; the age-at-incidence curve is exponential for males and is linear for females. The incidence for men aged 75–79 is approximately 11 times greater than it is for men aged 50–54; in women, the incidence is 8 times greater for the same age cohorts. Moreover, approximately 70% of cases occur in seniors (aged 65 and above).[7] The all-age 5-year relative survival rate was 75% among females and 78% among males for the period 2002–2004.[9]

The large majority of bladder cancers in Canada are transitional cell carcinomas (over 90%); an additional 2% are squamous cell carcinomas and 2% are adenocarcinomas.

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for cancer of the bladder were observed in Saskatchewan, Alberta and British Columbia and for males in Newfoundland and Labrador, Manitoba and the Northwest Territories, while significantly higher rates were observed in Nova Scotia, and for males in Quebec. Ontario is excluded since *in situ* bladder cancer cases have not been reported for the period covered by this atlas.

The provincial and territorial cancer registries now report the combined total of *in situ* and invasive bladder cancers. This is due to the difficulty in distinguishing the presence or absence of superficial or early invasion in pathology reports and the high recurrence and progression rates of the tumours classified to the *in situ* group with their associated significant morbidity and mortality. The large inter-provincial/territorial variation seen for bladder cancer rates is likely due to differences in the reporting of bladder cancer *in situ*.

KNOWN AND SUSPECTED RISK FACTORS

Cigarette smoking is the most important risk factor associated with bladder cancer. Individuals who smoke are thought to have a 2- to 4-fold increase in risk for bladder cancer compared with those who do not smoke.[89,90] Moreover, in industrialized countries, approximately 66% of male bladder cancer cases and 23–33% of all female cases of bladder cancer can be attributed to cigarette smoking.[12,13,89–91]

A case-control study in the Montreal area during 1979–1986 estimated that 6.5% (95% confidence interval 2.0–9.9) of bladder cancer cases were attributable to occupational exposures.[92] A study in Canada reported that elevated risks were also observed among miners, mechanics, lumber processors and primary metal workers, all of whom were linked in their exposure to combustion products and/or oils.[93] A history of schistosomiasis, a parasitic infectious disease, also increases the risk of bladder cancer, with endemic areas including most of Africa and several West Asian countries.[46,89,94]

4q) KIDNEY AND RENAL PELVIS (C64-C65)

Kidney cancer is a broad term encompassing many histological types of cancer, each with its unique clinical course. Taken in its broad meaning, kidney cancer was responsible for 4,436 new cases of cancer in 2006 and accounted for approximately 2.8% of all new cases in Canada (1,697 female cases; 2,739 male cases).[7] The annual age-standardized incidence rates are rising gradually, and this cannot be attributed merely to increases in detection. The annual percentage change for 1997–2006 was 1.4% among females and 1.0% among males.[9]

Age-specific incidence shows a peak in early childhood and then follows the more usual pattern of a steep rise through adulthood. While the 5-year relative survival rate was 66% for the period 2002–2004,[9] the rate drops to between 5% and 10% once metastatic disease develops.[13] Moreover, the rate is highly dependent on the type of kidney neoplasm and the histologic subtype.

Kidney cancers primarily consist of 3 major types: renal cell carcinoma (RCC), cancer of the renal pelvis or ureter, and Wilms tumour. RCCs are found in the renal parenchyma (body of the kidney), are largely adenocarcinomas, and account for approximately 80–85% of all renal tumours.[12,32] Cancer of the renal pelvis is primarily a transitional cell neoplasm, and accounts for approximately 7–8% of the cases.[12] Wilms tumour, the third major type, accounts for approximately 5–6% of the cases, principally occurring within the first 5 years of life.[12]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for cancers of the kidney and renal pelvis were observed in Ontario and British Columbia, while higher rates were observed in Nova Scotia, New Brunswick, Quebec and Manitoba, and for females in Nunavut and males in Prince Edward Island, Saskatchewan and Alberta.

KNOWN AND SUSPECTED RISK FACTORS

This risk factor section will largely focus on RCCs. Cigarette smoking, obesity and hypertension are the 3 major risk factors and, for example, account for up to half of all US cases.[95] Cigarette smoking is a significant risk factor for both RCC and renal pelvic cancer.[13,17] Functioning in a dose-dependent manner, the risk attributable to smoking has been assessed at approximately 20–30% in men and 10–24% in women.[17,95–97] Obesity, accounting for approximately 20% of RCC cases, is a significant risk factor for both sexes.[95,98] Hypertension influences the development of renal cell cancer and may be associated with an excess risk ranging from 20% to 300%.[95,96] Developing cystic disease of the kidneys is known to increase the risk for developing kidney cancer by 30 times, as compared with the risk for the general population.[17,95] Hereditary forms, responsible for a small percentage of cases, are characterized as occurring earlier in life. Four such forms are von Hippel-Lindau disease, hereditary papillary renal carcinoma, hereditary leiomyomatosis renal cell carcinoma and Birt-Hogg-Dubé syndrome (BHD).[17]

4r) BRAIN AND OTHER NERVOUS SYSTEM (C70-C72)

There were over 2,400 new cases of cancers of the brain and of the nervous system in Canada in 2006 (1,068 in females; 1,383 in males).[7] Cancers of the brain and of the nervous system can be referred to collectively as "CNS" (central nervous

system) cancers. The age-standardized incidence rate (ASIR) of CNS cancers has declined during the period 1997–2006 by approximately 1.1% and 0.7% per year among females and males, respectively.[8] The age-at-incidence curve is bimodal, with a small peak occurring in childhood, a slight decline in incidence during young adulthood and a gradual increase peaking between ages 60 and 79, when the rate plateaus; thereafter, the rate diminishes.[7] The peak observed during childhood is important; CNS cancer represents 20% of all cancers in children under age 15 and is the second most frequently diagnosed childhood malignancy.[9] The 5-year relative survival rate for the brain cancer cases aged 15 and above diagnosed during 1998–2000 was 21%, which is in contrast to that of the other nervous system cancer cases, which was 67%.[99] Survival is substantially better for younger adults and children.[9] The statistics presented do not include tumours classified as benign since reporting completeness for these cases varies by registry.

There are many types of brain and other nervous system tumours. Approximately 94% of CNS cancers occur in the brain, about 3% are malignancies of the cerebral meninges, and the remainder occur in the spinal cord or cranial nerves. Of cases with known morphology, the majority (about 95%) are gliomas, of which the most common types include glioblastomas and astrocytomas. Of the remainder, the most common morphologies are malignant meningiomas and medulloblastomas.

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for cancers of the brain and nervous system were observed in Manitoba and British Columbia, and among females in Alberta and males in Saskatchewan. Significantly elevated rates were observed in Quebec.

KNOWN AND SUSPECTED RISK FACTORS

This section will primarily focus on malignant tumours of the brain, cranial nerves and cranial meninges, which, when pooled, account for 95% of all CNS tumours.[100] Little is known about the risk factors for CNS cancers, particularly for levels of exposure experienced by the general population. Children who are exposed to CNS irradiation as treatment for acute lymphoblastic leukemia seem to have an increased risk of developing brain tumours.[101] A study of atomic bomb survivors has shown a dose-related excess of brain tumours.[102] Genetic and hereditary disorders and syndromes can also increase risk. In childhood, CNS cancers of genetic predisposition can account for up to 5% of the cases.[103]

4s) THYROID (C73)

Cancers of the thyroid are unusual in that the overall female-to-male ratio is greater than 3:1 (in 2006, 2,999 cases in females; 883 in males).[7] For the period 1997–2006, the annual percentage change in the age-standardized incidence rates was 9.5% in females and 6.8% in males.[8] Developments in and more frequent use of medical imaging (ultrasound, needle biopsy, and potentially computed tomography [CT scan] and magnetic resonance imaging) may have resulted in detection of earlier stage, asymptomatic cancers more frequently than was possible in the past.[104] The survival after diagnosis with this cancer is favourable, with a 5-year survival rate of 99% among females and 94% among males for the period 2002–2004.[9] Cases are generally diagnosed at younger ages relative to other cancers. For females, approximately 55% of all thyroid cancers occur before the age of 50; for males, the corresponding percentage is approximately 40%.[7]

The histologies are chiefly composed of 2 types arising from the two cell types present in the thyroid gland: follicular and parafollicular. Well-differentiated cancers and anaplastic thyroid cancers arise from the former, whereas medullary thyroid carcinomas (MTCs) arise from the latter. Well-differentiated cancers of follicular cell origin (papillary and follicular) account for about 80–90% of all thyroid cancers.[13,17,105]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for thyroid cancer were observed for males and females combined in Newfoundland and Labrador, Prince Edward Island, Nova Scotia, Quebec, Manitoba, Saskatchewan, British Columbia and

Yukon. Significantly elevated rates for thyroid cancer were observed only in Ontario with a comparative incidence ratio of 1.32.

KNOWN AND SUSPECTED RISK FACTORS

Radiation exposure is an established risk factor; however, both MTCs and follicular thyroid carcinomas are unaffected by such exposure and appear in a more sporadic manner. Radiation can occur by either ingestion of radioactive substances or by external exposure. Irradiation for benign conditions was common decades ago, and even today radiation is therapeutically administered to the neck for treatment of Hodgkin lymphoma. However, since more than 90% of thyroid cancer cases occur independently of radiation exposure,[17,32] other factors such as diet and environmental exposures have been suggested.[17,32,106] To date, however, none has shown any clear association. No effect of hormones, parity, menarche or menopause has been consistently shown to affect incidence.[107] The risk of thyroid cancer as a function of iodine intake is complex. Iodine-deficient diets are associated with elevated rates of follicular and anaplastic cancer, whereas diets rich in iodine are associated with papillary cancers.[17,32,46,108] Furthermore, goitres and benign nodules are also risk factors associated with elevated relative risks of 3 and 30, respectively.[46]

Genetics also influences the risk of both well-differentiated cancers and MTCs.[17,108] MTC is associated with multiple endocrine neoplasia (MEN) type 2 syndromes and familial, non-MEN medullary thyroid carcinoma. Familial adenomatous polyposis is known to increase the risk for developing papillary or follicular tumours. Follicular carcinomas are associated with Gardner's syndrome as well as Cowden's syndrome. A familial history of benign and malignant thyroid tumours also elevates risk.[109] People with first-degree relatives with well-differentiated thyroid cancers have an increased risk of between 4- and 10-fold.[17]

4t) HODGKIN LYMPHOMA (HISTOLOGY BASED)

Hodgkin lymphoma, a malignancy of the lymph nodes, spleen and other lymphoid tissue, is a relatively rare cancer that, in 2006, accounted for 884 cases (397 in females; 487 in males).[7] Hodgkin lymphoma has a bimodal age-at-incidence curve with peaks at ages 20–24 years and 65 or more.[7] Age-standardized incidence rates have been stable over the last decade.[8] The 5-year relative survival rate for the period 2000–2004 was 86%.[9]

The 2 major types of Hodgkin lymphoma are classical Hodgkin lymphoma, the most frequent type, and nodular lymphocyte-predominant Hodgkin lymphoma, which accounts for approximately 4–5% of cases.[17,110]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for Hodgkin lymphoma were observed for males and females combined in Newfoundland and Labrador and British Columbia. A significantly elevated rate was observed in Quebec.

KNOWN AND SUSPECTED RISK FACTORS

Little is known regarding causes for Hodgkin lymphoma. Although there are no established risk factors, several suspected causes and associations have been identified. Epstein-Barr virus (EBV), a ubiquitous virus infecting over 90% of the world population, has a causative role in the development of Hodgkin lymphoma for some cases. The difference between the developed and less developed nations is rooted in the time of infection. In developing countries, infection with EBV occurs within the first several years of life and has high prevalence by the age of 4. In the developed countries, however, infection with the disease occurs during one's 20s or 30s. Furthermore, it has been observed that EBV is more commonly associated with cases of Hodgkin lymphoma in older adults or younger children, possibly suggesting an alternate age-dependent pathway.[111] When the infection is delayed, as is the case for the

more developed countries, EBV causes infectious mononucleosis in up to 50% of patients.[112] This virus is associated with a 2- to 3-fold increase in the risk of developing Hodgkin lymphoma.[12,111]

Socio-economic gradient is also associated with the risk of developing Hodgkin lymphoma for patients up to middle age. Higher socio-economic standing, lower numbers of siblings, single family housing and high level of maternal education are associated with an increased risk of developing the neoplasm. The suggested mechanism alleges that such factors mitigate exposure to common infectious agents. Early exposure, however, to infections such as chicken pox, measles, mumps, pertussis and rubella plays a protective role, apparently because it stimulates immunity.[112]

Familial history of disease or immune deficiency may also have a role. Increased incidence of Hodgkin lymphoma is observed for first-degree relatives. Siblings, for instance, have a 2- to 7-fold increased risk; same-sex siblings have a 9-fold increase—double the risk of siblings of the opposite sex.[12,17,112]

4u) NON-HODGKIN LYMPHOMA (HISTOLOGY BASED)

Non-Hodgkin lymphoma (NHL) encompasses a wide variety of malignancies arising in lymphoid tissue. Depending on the subtype according to cell origin (described below), it may grow slowly or rapidly, and it often involves the bone marrow. It may arise in or spread to other organs, including the central nervous system. Although both children and adults develop non-Hodgkin lymphoma, in contrast to adult lymphomas, childhood NHL occurs predominantly in the chest and abdomen and less commonly at peripheral nodal sites.

NHL was diagnosed in 6,540 new patients in 2006 (3,048 females and 3,492 males).[7] NHL also occurs among children, with 191 cases diagnosed per year in Canada in children aged 0–14 years during 2001–2005.[9] It has an age-standardized incidence rate that increases to a maximum at ages 80–84, and approximately 99% of the cases occur in patients aged 20 and above.[7] The 5-year relative survival for the period 2002–2004 was 63% for females and 60% among males.[9] Among females, a change point in the annual incidence rates was detected starting from 2001, followed by an annual increase of 1.4%.[8] Among males, there has been a statistically significant annual percentage increase of 0.5% during the period 1997–2006.[8] Incidence rates among children aged 0–14 during this period have been stable. The lifetime risk for developing NHL is 1.9% among women and 2.2% among men.[9]

The current classification scheme for NHL is an updated World Health Organization (WHO) version of the Revised European American Lymphoma (REAL) classification, which refers to morphology and cell lineage, and divides NHL according to B-cell or T-cell/natural killer (NK)-cell origin and whether they are composed of precursor (thymic or lymphoblastic) or peripheral (mature or post-thymic) lymphocytes.[4] Mature B-cell lymphomas account for the majority of lymphomas, with the largest 2 subsets accounting for approximately 50% of NHLs: diffuse large B-cell lymphoma making up about 30% and follicular lymphoma, about 20%.[113] The four major types of childhood non-Hodgkin lymphoma are Burkitt lymphoma (a type of B-cell lymphoma), lymphoblastic lymphoma, diffuse large B-cell lymphoma and anaplastic large cell lymphoma.

GEOGRAPHIC VARIATION

At the provincial/territorial level, NHL rates among males and females did not correspond closely. Significantly lower rates for NHL were observed for both males and females in Newfoundland and Labrador and Alberta, and among females in British Columbia. Significantly elevated rates were observed among females in Ontario and among males in New Brunswick.

KNOWN AND SUSPECTED RISK FACTORS

The various subtypes of NHL may each have different risk factors.[114] Major risk factors have been identified for only some specific lymphomas. Risk for NHL is

positively associated with family history, and a stronger aggregation is observed among siblings.[115,116] Research has been centred on immunologic genes such as regulatory cytokines or inflammatory genes. Furthermore, both human T-cell lymphotropic virus type 1 (HTLV-1) and Epstein-Barr virus (EBV) are infectious pathogenic agents for NHL, wherein the former is responsible for adult T-cell leukemia/lymphoma.[12,13,17] EBV on the other hand, is responsible for several subtypes, including 45–70% of the cases of human immunodeficiency virus 1 (HIV-1)-related lymphoma, almost all of the cases of primary central nervous system lymphomas, approximately half of all diffuse large cell and immunoblastic NHLs, approximately 20% of the cases of Burkitt's lymphoma, and several other subtypes.[12,117]

Other infectious agents associated with increased risk of NHL include bacterial agents such as *Helicobacter pylori, Chlamydia psittaci, Campylobacter jejuni, Mycobacterium tuberculosis, Borrelia burgdorferi,* hepatitis C and human herpesvirus 8 (HHV-8).[12,13] Imunocompromised individuals have greater risk of NHL.[12,13,115] Acquired immunodeficiency syndrome (AIDS) elevates the risk for NHL by greater than 30-fold.[117] Inherited immunodeficiency diseases are rare but nevertheless increase the risk for NHL. These include diseases such as ataxia telangiectasia, Wiskott-Aldrich syndrome, Chédiak-Higashi syndrome, X-linked lymphoproliferative syndrome, severe combined immunodeficiency syndrome and common variable immunodeficiency syndrome.[12,17] Moreover, the risk for NHL increases in patients who have undergone organ transplantation (renal or cardiac) and are subsequently placed on immunosuppressive drugs;[12,115] typically the elevated risk is in the order of 10- to 50-fold with a latency as short as a year or less.[117]

4v) MULTIPLE MYELOMA (HISTOLOGY BASED)

Multiple myeloma is the third most common hematologic cancer behind non-Hodgkin lymphoma and leukemias, accounting for 2,044 cases in 2006 (917 in females; 1,127 in males).[7] The age-standardized incidence rates have remained stable for the past decade. Among males, the age-at-incidence curve increases to age 85 or more, while the rate among females peaks among ages 80–84.[7] Multiple myeloma is rare in younger people, with only about 6% of the cases occurring before the age of 50. Relative to other hematopoietic cancers, multiple myeloma has a poor survival with a 5-year survival rate of 34% for the period 2002–2004.[9]

Multiple myeloma, or plasma cell myeloma, is a plasma cell tumour that begins when plasma cells, the final product of B-cell differentiation, excessively proliferate. Included in the multiple myeloma category is plasmacytoma, which occurs when the abnormal cells collect to form a tumour. Other types of plasma cell neoplasms not included in the multiple myeloma category include macroglobulinemia, in which abnormal plasma cells build up in the bone marrow, and monoclonal gammapathy of undetermined significance (MGUS), in which there are abnormal plasma cells in the bone marrow but which is not classified as a malignant neoplasm.

GEOGRAPHIC VARIATION

Significantly lower rates for multiple myeloma were observed for both males and females in Newfoundland and Labrador and British Columbia, and among females in Alberta. Significantly elevated rates were observed in Quebec and Ontario, and among males in Prince Edward Island.

KNOWN AND SUSPECTED RISK FACTORS

Modifiable risk factors for multiple myeloma remain largely unknown. Previously high exposure to ionizing radiation has been established as a risk factor for developing multiple myeloma, with a latent period lasting anywhere from 10 to 30 years.[13,17] This risk has been observed in occupations such as radiology, nuclear weapons industries and radium dial painters.[13,17]

Genetic and hereditary factors are believed to play a role, which increases the risk between 2- and 4-fold.[13,118,119] Moreover, multiple myeloma shows strong familial clustering, and HLA-Cw2 may be an implicated gene.[17,118] In one study,[119] the relative risk for a personal history of cancer prior to the

diagnosis was 3.84, while a family history of cancer in a first-degree relative resulted in a relative risk of approximately 2-fold.

MGUS is a condition in which abnormal plasma cells produce high levels of monoclonal protein. Individuals with MGUS are at increased risk for developing multiple myeloma.[120]

A history of illness may also increase the risk for developing multiple myeloma. Illnesses include rheumatoid arthritis, shingles, tuberculosis, kidney or bladder infection, scarlet fever, pernicious anemia, musculoskeletal disorders and eczema.[119]

4w) LEUKEMIA (HISTOLOGY BASED)

Leukemia is a heterogeneous group of neoplasms of the white blood cells, arising mostly in the bone marrow. The group is presented as a whole due to the limited numbers of cases in the subgroups. Leukemia is subdivided according to the cell origin, either lymphoid or myeloid, and also based on progression, either acute or chronic. Whereas chronic leukemia tends to be slow developing, acute leukemia grows quickly. Four distinct common leukemia categories exist: acute lymphocytic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML).

In 2006, there were 4,523 new cases of leukemia (1,951 in females; 2,572 in males).[7] It is the most common malignancy in early childhood (ages 0–14), accounting for 73% of hematological malignancies in this age group for 2001–2005 and 32% of all Canadian childhood malignancies.[9] The age-standardized incidence curve has a peak during early childhood (ages 0–4), then decreases and is not exceeded until the age group 50–54. Thereafter, the incidence escalates with increasing age, and the vast majority of leukemia cases (approximately 80%) occur from age 50 onward.[7] The annual percentage change for 1997–2006 was 0.8% among females and 0.5% among males.[8] The 5-year relative survival rate is moderate, at 51%, but has increased by about 5 percentage points from the period 1992–1994 to 2002–2004.[9] Among children aged 0–14, the 5-year observed survival is 86% overall, 91% for lymphoid leukemia and 67% for acute myeloid leukemia.[9]

GEOGRAPHIC VARIATION

At the provincial/territorial level, significantly lower rates for leukemia were observed for both males and females in Newfoundland and Labrador and British Columbia, and among males in Nova Scotia and New Brunswick. Significantly elevated rates were observed for both males and females in Manitoba, Saskatchewan and Alberta, and among males in Ontario.

KNOWN AND SUSPECTED RISK FACTORS

The causes of leukemia are largely unknown. Known risk factors can broadly be grouped into hereditary, viral and environmental categories and may vary according to subtype.

Some hereditary syndromes are associated with increased incidence of acute leukemias; Down syndrome, characteristically seen in younger patients with ALL, for example, is associated with an increased risk ranging from 10- to 30-fold for acute leukemia.[12,13,17,121,122] Other genetic syndromes and diseases include Klinefelter's syndrome, Bloom syndrome, ataxia telangiectasia, Li-Fraumeni syndrome, Shwachman syndrome, neurofibromatosis, Patau syndrome, Kostman syndrome, Fanconi's anaemia and Wiskott-Aldrich syndrome.[13,17,121,122] Furthermore, translocations, deletions and alterations are common for chromosomes 8 and 11 in those with acute leukemias. Despite this, only about 5% of ALL and AML have been associated with inherited genetic syndromes.[123]

CLL differs from acute leukemia in that familial patterns of inheritance are consistently observed, although they account for only a small percent of cases. First-degree relatives of CLL cases have been found to have a 7-fold increased risk for CLL.[124] Furthermore, at the molecular level, 40–50% of CLL cases are characterized by cytogenic abnormalities.[17] CML is caused by an acquired genetic defect. The chromosomal abnormality, Philadelphia chromosome,

occurs in 95% of CML cases, and the BCR-ABL gene has a principal role in CML pathogenesis. Despite this, these 2 anomalies are not exclusive to CML and are common in approximately 25–50% of adult ALL cases.[12,17]

Viruses, particularly retroviruses, may also be causative agents in the development of certain types of leukemia. Although viruses do not appear to induce CLL, adult T-cell leukemia/lymphoma is caused by the human T-cell lymphotropic virus type 1 (HTLV-1).[12,13,122,125] Infection occurs in clusters in Japan, Africa, the Caribbean, Colombia and Melanesia.[126] At times, infection with the disease is not sufficient to induce cancer; malignancy is often the product of infection concomitant with other cumulative alterations.[125] Infection with measles at an early age, psoriasis and JC polyomavirus are all associated with increased incidence of adult ALL.[13] Burkitt's lymphoma is associated with Epstein-Barr virus (EBV) and therefore may also be linked to Burkitt's leukemia (B-cell ALL). Furthermore, adult ALL and aggressive NK-cell leukemia have reported associations with EBV.[13,126,127]

Ionizing radiation is a risk factor for AML and is strongly related to increased incidence of ALL and CML. Exposures are varied and include atomic bomb exposure (Japan and Nagasaki), other nuclear exposures (Chernobyl), therapeutic radiation exposure and in utero exposure.[12,13,121,125] Furthermore, the use of chemotherapeutic agents such as alkylating agents, topoisomerase II inhibitors and taxanes, and the use of other chemotherapeutic agents such as epipodophyllotoxins and anthracyclines for other malignancies (e.g., secondary ALL) are also risk factors. The International Agency for Research on Cancer (IARC) has evaluated occupational exposure to benzene as carcinogenic to humans, with excess incidence reported for AML.[128] Benzene is also found in cigarette smoke and gasoline. IARC has also evaluated formaldehyde as carcinogenic, with risk particularly for myeloid leukemia.[128]

Exposure to tobacco smoke can elevate the risk of developing AML 2-fold and may account for up to 20% of AML cases.[12,17,125] Smoking is related to both types of acute leukemia and may function in a dose-dependent manner, particularly in patients older than 60.[13,17,129]

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APPENDICES

1. 1991 CANADIAN STANDARD POPULATION

AGE (YEARS)	<1	1–4	5–9	10–14	15–19	20–24	25–29	30–34	35–39	40–44
Percent	1.4	5.5	6.9	6.8	6.8	7.5	9.0	9.2	8.3	7.6

AGE (YEARS)	45–49	50–54	55–59	60–64	65–69	70–74	75–79	80–84	85+
Percent	6.0	4.8	4.4	4.2	3.9	3.0	2.2	1.4	1.0

2. CANCER DEFINITIONS

CANCER	ICDO-3 SITE/HISTOLOGY TYPE*
Buccal cavity and pharynx	C00–C14
Esophagus	C15
Stomach	C16
Colon and rectum	C18–C20, C26.0
Liver	C22.0
Pancreas	C25
Other digestive system	C24.0–C24.9, C22.1, C48.0–C48.2, C26.8–C26.9, C48.8
Larynx	C32
Lung and bronchus	C34
Melanoma of the skin	C44 (Type 8720–8790)
Female breast	C50
Cervix uteri	C53
Uterus excluding cervix	C54–C55
Ovary	C56
Other female genital system	C52.9, C51.0–C51.9, C57.0–C58.9
Prostate	C61
Testis	C62
Bladder (including in situ)	C67
Kidney and renal pelvis	C64–C65
Brain and other nervous system	C70–C72
Thyroid	C73
Hodgkin lymphoma*	Type 9650–9667
Non-Hodgkin lymphoma*	Type 9590–9596, 9670–9719, 9727–9729
	Type 9823, all sites except C42.0, C42.1, C42.4
	Type 9827, all sites except C42.0, C42.1, C42.4
Multiple myeloma*	Type 9731–9732, 9734
Leukemia*	Type 9733, 9742, 9800–9801, 9805, 9820, 9826, 9831–9837, 9840, 9860–9861, 9863, 9866–9867, 9870–9876, 9891, 9895–9897, 9910, 9920, 9930–9931, 9940, 9945–9946, 9948, 9963–9964
	Type 9823 and 9827, sites C42.0, C42.1, C42.4
Other, ill-defined and unknown	Type 9740–9741, 9750–9758, 9760–9769, 9950–9962, 9970–9989
	Type 8000–9049, 9060–9139, 9141–9589, sites C42.0–C42.4, C76.0–C76.8, C77.0–C77.9, C80.9
All sites	All invasive sites

* Histology types 9590–9989 (leukemia, lymphoma and multiple myeloma) and 9050–9055 (mesothelioma) are excluded from other specific organ sites.

NOTE: ICDO-3 refers to the third edition of the International Classification of Diseases for Oncology (2000).
Figures are for invasive sites, including *in situ* bladder cancer and excluding non-melanoma skin cancer.

3. ABBREVIATIONS AND GLOSSARY

ABBREVIATIONS

AC	adenocarcinoma
AIDS	acquired immunodeficiency syndrome
ALL	acute lymphocytic leukemia
AML	acute myeloid leukemia
ASIR	age-standardized incidence rate
BMI	body mass index
CCR	Canadian Cancer Registry
CIF	comparative incidence figure
CLL	chronic lymphocytic leukemia
CML	chronic myeloid leukemia
CNS	central nervous system
DCO	death certificate only
DNA	deoxyribonucleic acid
EBV	Epstein-Barr virus
GCT	germ cell tumour
GERD	gastroesophageal reflux disease
HBV	hepatitis B virus
HCC	hepatocellular carcinoma
HCV	hepatitis C virus
HIV-1	human immunodeficiency virus 1
HPV	human papilloma virus
HTLV-I	human T-cell lymphotropic virus 1
IARC	International Agency for Research on Cancer
ICD-O-3	International Classification of Diseases for Oncology, Third Edition
MALT	mucosa-associated lymphoid tissue
MEN	multiple endocrine neoplasia
MGUS	monoclonal gammopathy of undetermined significance
MTC	medullary thyroid carcinoma
NHL	non-Hodgkin lymphoma
NSAIDS	non-steroidal anti-inflammatory drugs
PSA	prostate-specific antigen (assay)
RCC	renal cell carcinoma
SCC	squamous cell carcinoma
SEER	(United States) Surveillance, Epidemiology and End Results Program
SIR	standardized incidence ratio
WHO	World Health Organization

DEFINITIONS

Age-standardization:
a procedure where weighted averages are used to adjust rates, such as incidence rates; a procedure designed to minimize the effects of differences in the age composition of given populations (such as those of census divisions) when comparing rates for these populations. In the *Canadian Cancer Incidence Atlas*, the direct method of age-standardization was used.

Age-standardized incidence rate:
a rate derived from the procedure described immediately above, expressed as cases per 100,000 person-years.

Body mass index:
defined most commonly as weight in kilograms divided by height in metres squared.

Cancer registration practices:
the methods by which cancer patients are registered in a provincial/territorial cancer registry database.

Coefficient of variation:
the standard error divided by the mean. (See "standard error" below.)

Comparative incidence figure:
the ratio of the health region age-standardized cancer incidence rate to the Canadian rate.

Covariance:
The covariance of a pair of random variables X and Y is the expected value of the product of their deviations from their means.

$$\mathrm{Cov}(X,Y) = E[(X - \xi)(Y - \eta)]$$

Decile:
the value at the 10th (or multiple of 10th) percentile. Note that the median is the 50th percentile, which is also a decile value.

Etiology:
the cause of a disease.

Incidence rate:
the number of newly diagnosed cases per 100,000 population.

Significance (in statistics):
the probability of observing an event that is as extreme or more extreme than that which occurred under a specified null hypothesis and assumed probability distribution. The null hypothesis is that the census division rate is the same as the national rate.

Standard deviation (s.d.):
a measure of dispersion within a frequency distribution of values. The mean determines the centre of the distribution. The standard deviation is a summary of how widely dispersed the values are around this centre.

$$\text{s.d.} = \sqrt{\sum_{t=1} (y_t - \bar{y})^2/(N-1)}$$

Spatial variation:
the differences in disease rates between locations or areas.

Standard error:
a measure of the variability of the sample mean as an estimate of the population mean.

Standardized incidence ratio:
the ratio of observed cases to expected cases. The expected number of cases is based on age-specific rates.