

# **Cancer Incidence in Fort Chipewyan, Alberta 1995-2006**

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Division of Population Health and Information  
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## **Executive summary**

### **Background**

Fort Chipewyan is a small community located approximately 600 kilometres north-east of Edmonton, Alberta, Canada. In 2006, Dr. John O'Connor, a physician working in Fort Chipewyan, reported a high number of cases of cholangiocarcinoma, a rare form of bile duct cancer, as well as high rates of other cancers.

Local residents echoed his concerns, attributing cancers in their community to environmental contamination from a range of industrial development including the oil sands 250 kilometres upstream, uranium mining and pulp mills.

An initial review of the Alberta Cancer Registry, the usual first step, did not confirm an increased incidence of cancer in Fort Chipewyan.

The community called for a further investigation, and after Dr. O'Connor submitted his list of cases in August 2007, a working group was formed to support the Alberta Cancer Board in doing a cluster investigation based on the guidelines of the U.S. Centre for Disease Control and Prevention.

### **Purpose**

The purpose of the investigation is to determine if there is an elevated rate of cholangiocarcinoma in Fort Chipewyan and whether there is an elevated rate of cancers overall in Fort Chipewyan.

### **Methods**

- The number of observed cancer cases in the community was compared with the number of expected cases over a 12-year study period (1995-2006)
- Observed cases were determined through the Alberta Cancer Registry and cancer case reports from the community physicians.
- Expected cases were determined by applying yearly Alberta rates to the population in Fort Chipewyan, taking into account
  - the size of the population
  - the composition of the population by age, sex, and First Nations status.
- To ensure accurate comparisons, only those cases where the individual resided in Fort Chipewyan at the time of diagnosis were included.
- Cancer rates for several communities in similar geographic locations were calculated for comparison.
- A simulation was done (one million times) to provide the specific probability of observing the same or a higher number of cases.
- The simulation results were compared from a range of perspectives: a 90%, 95% and 99% Confidence Intervals.
- For the conclusions of this investigation, an increase was considered statistically significant if there was less than a 5% chance of observing the same number or a higher number of cancers in that community.

## **Overall findings**

- The two cholangiocarcinomas in Fort Chipewyan were within the expected range.
- The cancer rate overall (51 cancers in 47 individuals) was higher than expected (39).
- Higher than expected numbers of cancers of the blood and lymphatic system, biliary tract cancers as a group, and soft tissue cancers were found.
- These findings were based on a small number of cases and could be due to chance, increased detection or increased risk in the community.

## **Specific findings**

### **Cholangiocarcinoma**

- The observed number of cases of cholangiocarcinoma was within the expected range.
- Of six suspected cases reported by Dr. O'Connor, two were confirmed.
- Three reported cases were other types of cancer, one was not cancer.
- No suspected cases of cholangiocarcinoma were excluded from the study due to residency at the time of diagnosis.
- The two cases of cholangiocarcinoma were diagnosed in individuals older than 60 and 80 respectively.
- The two cases of cholangiocarcinoma were diagnosed in 2003/2004.
- No cases of cholangiocarcinoma were found before or since 2003/2004.
- One case was diagnosed by Ultrasound and the other case was diagnosed by cytology test. Both cases were included in the analysis in order to be inclusive.
- In each case, the individuals were found to have known risk factors for cholangiocarcinoma.
- Further investigation was done to identify all Albertans of First Nations status diagnosed with cholangiocarcinoma since 1983. None had lived in Fort Chipewyan between 1983 and the present (apart from the two in the investigation).

### **Biliary tract cancers**

- Cholangiocarcinoma is one type of biliary tract cancer.
- The observed number of cases of biliary tract cancers as a whole is greater than would be expected as a result of finding one additional case of biliary tract cancer of another type, adenocarcinoma of Ampulla of Vater.

### **Colon cancers**

- The observed number of cases of colon cancer was within the expected range.
- Of the 12 suspected cases reported by Dr. O'Connor, three were confirmed as colon cancer diagnosed in Fort Chipewyan residents during the study period.
- An additional three were found through the Alberta Cancer Registry for a total of six cases, although two were cases within the same individual who had been diagnosed with prostate cancer four years before.
- Only one of the six cases was diagnosed in the most recent six years of the 12-year study period.

### **Cancers of the blood and lymphatic system**

- The observed number of cases of blood and lymphatic system cancers was higher than expected.
- Seven of the eight cases occurred within the most recent six years of the 12-year study period.
- Two of the seven cases were diagnosed in the same patient.

### **Lung cancers**

- Lung cancers as a whole were within the expected range.
- When women were looked at separately, however, the number of cases of lung cancer (7) was higher than expected (2).

### **Soft tissue cancers**

- Soft tissue cancers were observed (2) to be higher than expected (0.3).

### **All cancer combined**

- The total observed number of cancer cases in Fort Chipewyan (51 cancers in 47 individuals) was higher than the expected number (39).
- The ages of the individuals ranged from 26 to 87 with an average age of 66 at the time of diagnosis.

### **Cancer in First Nations in Alberta**

- Adjusting for the high proportion of First Nations people in Fort Chipewyan is the main reason the current findings differ from the initial 2006 analysis.
- First Nations Albertans have a significantly lower rate than non-First Nations Albertans for all cancer, leukemia and breast cancer.
- The rate for cholangiocarcinoma in First Nations Albertans, however, is significantly higher than that in non-First Nations.
- No difference was seen for lung cancer and colon cancer between First Nations and non-First Nations in Alberta.

### **Strengths of the study**

- This investigation takes a cautious approach that identifies increased incidence of cancers that are border line statistically significant and may turn out to be of no concern upon follow up. This cautious approach insures, however, that cancers that may turn out to be of concern are identified so appropriate follow-up can be done.
- The investigation is based on general guidelines from cluster investigations outlined by the Centre for Disease Control and Prevention in the U.S.
- Processes were established to ensure all relevant cancer cases in the community were counted.
- Population data and geographic boundaries were reviewed and confirmed with community representatives.

- The diagnosis and classification of cancer cases in the community were reviewed and confirmed with the current community physician. The community nurse practitioner confirmed she had asked Dr. O'Connor to inform the clinic about any more suspected cases.
- Cancer rates within First Nations populations in Alberta were calculated for the first time and incorporated into the analysis for a more accurate calculation of the expected cancer rate.

### **Limitations of the study**

- The small population size of Fort Chipewyan limits the ability to interpret results. In larger populations, one additional case does not have the same impact.
- The increased rates observed were all based on a small number of cases.
- The First Nations in Fort Chipewyan may have unique characteristics that are different from other First Nations communities in Alberta; this cannot be accounted for in the current analysis.
- This study was not able to account for the effect of migration on the cancer rate calculation.
- The study was not designed to determine whether living in Fort Chipewyan elevated cancer risk.
- The study was not designed to determine the cause of any of the cancers experienced in Fort Chipewyan.

### **Conclusions**

The observed cases of cholangiocarcinoma and colon cancer during the period of investigation (1995-2006) are within the expected range of cancer occurrence.

The number of cancer cases overall was higher than expected. In particular, increases of observed over expected were found for biliary tract cancers as a group and cancers of the blood and lymphatic system. These increases were based on a small number of cases and could be due to chance or increased detection. The possibility that the increased rate is due to increased risk in the community, however, cannot be ruled out.

The increased number of cases of biliary tract cancers, cancers in the blood and lymphatic system and cancers of unknown primary seen in the most recent six years (2001-2006) compared to the years 1995-2000 of the investigation warrant closer monitoring of cancer occurrences in Fort Chipewyan in the coming years.

Further investigation is required to evaluate if there is a risk posed by living in Fort Chipewyan. This would be done by tracking a cohort of residents who have lived in the area within the past 20 to 30 years.

As part of an overall assessment of the health status of the community, further analysis should also be done of many potential risk factors, such as lifestyle risk factors, family history and occupational and environmental exposures.

## Introduction

Fort Chipewyan is a small community located approximately 600 kilometres north-east of Edmonton, Alberta, Canada. In 2006, a physician providing services to Fort Chipewyan reported to the media that there were a high number of cases of cholangiocarcinoma, a rare form of bile duct cancer, in the community. The physician and some of the local residents expressed the belief that the main reason for their ill health was environmental contamination possibly from the oil sands developments located 250 kilometres upstream from the community on the Athabasca River. The community also raised concerns about other environmental contaminants that are possibly associated with industrial developments such as pulp mills and uranium mining. In response to these concerns, the Alberta Cancer Board launched an investigation to evaluate whether or not there is an actual increase in the number of cholangiocarcinoma and an increase in rates of overall cancers in Fort Chipewyan.

This report describes the investigation that the Alberta Cancer Board has carried out to verify the number of cholangiocarcinoma cases in Fort Chipewyan and to determine whether the observed number of cancer cases in Fort Chipewyan is higher than expected, accounting for the size as well as the composition of the community population by age, sex and First Nation status. To summarize findings and draw conclusions, an increase is considered statistically significant if there is less than a 5% chance of observing the same or a higher number of cases in Fort Chipewyan; in other words, if the chance is lower than 1 out of 20 observations. The identification and the verification of reported cancer cases are crucial components to a cluster investigation, as is the review of the definition for particular cancers of concern, such as cholangiocarcinoma and colon cancer. This report presents the methods of data collection and analyses used in the investigation, as well as the results. This document also summarizes the timeline of events and the concern expressed by the Fort Chipewyan community, outlines the process followed in the current cancer cluster investigation, and highlights recommendations for future action. This investigation follows the generally accepted Guidelines for Investigating Clusters of Health Events published by the U.S. Centers for Disease Control and Prevention (CDC)<sup>1,2</sup> A cancer cluster occurs if there are a greater than expected number of cancer cases within a group of people, geographic area or time period.<sup>3</sup>

An investigation into whether or not there is an elevated rate of cancer in the community is often the first step before pursuing a more detailed evaluation of cancer risks and related causes. This investigation was not designed to determine the risk of developing cancer posed by living in the community, nor did the study investigate any possible association between the risk of cancer for Fort Chipewyan residents and environmental exposures, although a preliminary discussion is included. This report will be submitted to Alberta Health Services, the Nunee Health Board Society, Alberta Health and Wellness, the Northern Lights Health Region and Health Canada, as agreed upon by all stakeholders in a community meeting in February 2008. The results presented protect the confidentiality of cancer patients.

## Background

### The Athabasca Oil Sands, uranium mining and Fort Chipewyan

Alberta has the second largest oil reserve in the world, after Saudi Arabia. The majority of these reserves are in the form of oil sands found in three regions: Athabasca, Peace River and Cold Lake. Of the three regions, the Athabasca Oil Sands has the biggest deposit and is the only large oil sands field that is suitable for surface mining. In 2006, oil production from the Alberta oil sands totalled about 1.26 million barrels per day (bpd), of which one million bpd were produced from the Athabasca Oil Sands.<sup>4</sup> The Athabasca River cuts through the vast Athabasca Oil Sands deposit and ends in Lake Athabasca.

Fort Chipewyan is a small rural community in northern Alberta. It has a population of about 1,200 people, and is situated at the western shore of Lake Athabasca, 250 kilometres downstream from the Athabasca Oil Sands open mining operation (Figure 1). Lake Athabasca is surrounded by areas that are naturally rich in uranium. On the northern shore of the Lake, there are several abandoned uranium mines.<sup>5</sup> On the south-eastern shore of the Lake, there are many companies exploring for uranium in the Athabasca Basin.<sup>6</sup> This area is currently the world's largest producer of uranium, accounting for approximately 30% of global primary uranium production<sup>7</sup> (Figure 1). Residents from the community have raised concerns that their health has been adversely affected by contaminants that has possibly originated from the upstream oil sands or uranium mining.

The majority of community residents are First Nations people. Trapping, fishing and lumber production are three major economic activities in the community. Many community members also work in government and the private sector, including large oil manufacturing and related companies. Some residents work in uranium mines on the opposite side of Lake Athabasca. There are no permanent roads that lead to the community; the primary method of transportation to Fort Chipewyan is by airplane, however, access is also possible by ice roads during the winter and by boat in the summer. There is a nursing station in the community with employed registered nurses and community health representatives. The community is also visited regularly by a physician. The frequency of visits varies but has increased since 2000 from approximately one visit in two months to every other week. A program exists to provide accommodation, transportation and meal costs to First Nations residents who require medical attention not available in the community.<sup>8</sup> Community residents need to travel south 270 kilometres to the hospital in Fort McMurray or even further south, 600 kilometres, to the cancer centre in Edmonton for cancer diagnosis and treatment. In 2006, Alberta Health and Wellness conducted an analysis on the health status of Fort Chipewyan residents using existing health-care data mostly collected between 1995 and 2005. Results were presented at a community meeting in July 2006. The analysis showed that Fort Chipewyan residents have elevated prevalence rates of diabetes, hypertension, renal failure and lupus. The prevalence rates of chronic obstructive pulmonary disease (COPD), however, as well as asthma and rheumatoid arthritis were not elevated; neither were the incidence rates of congenital anomalies in 1985 and 2005, nor the incidence rate of cancer from 1995-2005.<sup>9</sup>

## **Previous investigations of cancer incidence in Fort Chipewyan**

In March 2006, the Fort Chipewyan community physician, Dr. John O'Connor, reported to CBC (Canadian Broadcasting Corporation) News<sup>10</sup> that “the community with a population of 1,200 had been disproportionately affected by a high number of both rare and common cancers.” The physician stated that “five people in Fort Chipewyan had died since 2000 from cholangiocarcinoma, a rare form of bile duct cancer that normally affects one in 100,000 people.” He also reported that he had seen a high number of illnesses such as leukemia, lymphomas, lupus, thyroid problems and autoimmune diseases. The community physician speculated that oil and gas activity might be the cause.

In April 2006, in response to the health concerns expressed by the Fort Chipewyan community, Alberta Health and Wellness convened a meeting that included community leaders, Health Canada, the Alberta Cancer Board, Northern Lights Health Region and industry to discuss community concerns. At the meeting, it was agreed that Health Canada staff would travel to Fort Chipewyan to meet with clinic staff and Dr. O'Connor to clarify concerns, examine available data in the community, and to do a chart review; Alberta Health and Wellness would assess the overall health status of the community members using its existing data. As part of this overall health assessment, the Alberta Cancer Board conducted a cancer rate analysis for the community based on data routinely collected in the Alberta Cancer Registry to evaluate whether the number of the cancer cases found in Fort Chipewyan was higher than expected. The study period was set between 1995 and 2005 for the incidence rate calculation (rate at which new cancers were occurring) and between 1995 and 2004 for the mortality rate calculation (rate at which deaths from cancer were occurring). At the time of the study, registration of death information in the Alberta Cancer Registry for 2005 was not yet complete and, therefore, was not included in mortality rate analyses.

In July 2006, the results of the cancer rate analysis were presented at a community meeting held at the Fort Chipewyan Health Centre. According to this analysis, only one case of cholangiocarcinoma and two cases of other biliary tract cancers were found in Fort Chipewyan. The two other biliary tract cancers included a case of bile duct adenocarcinoma, not otherwise specified, and a case of adenocarcinoma of Ampulla of Vater. There were challenges in the classification of cholangiocarcinoma which required further review and expert consultation (Appendix 3). The analysis did not find a statistically significant increase (that is, a greater increase than might have occurred by chance) of the cancer incidence rate in Fort Chipewyan when compared to the rates in the rest of the Northern Lights Health Region and the rest of the province. While not specifically part of the cancer study, high rates of diabetes and lupus were found in the community.<sup>9</sup>

In March 2007, the Alberta Cancer Board provided updated Fort Chipewyan cancer rate information to Alberta Health and Wellness and then to both CBC News and Dr. O'Connor, the Fort Chipewyan community physician. The news reporter commented that the number of observed cases of liver, bile duct, colon cancer and cancers of the blood were disproportionately higher than normal, but were not as high as the physician had previously reported.<sup>11</sup>

Because cancer is a reportable disease mandated under the Cancer Programs Act in Alberta, in June 2007, the acting Chief Medical Officer of Health of Alberta Health and Wellness requested in writing that Dr. O'Connor report suspected cancer cases and supporting evidence to the Alberta Cancer Registry. Subsequently, in August 2007, Dr. O'Connor provided a list of 18 names to the Alberta Cancer Registry, including 12 suspected colon cancer patients and six suspected cholangiocarcinoma patients.

## **Background to the present report**

The community physician and other Fort Chipewyan representatives called for a more comprehensive study on the health of Fort Chipewyan residents.<sup>12</sup> In January 2008, representatives from Alberta Health and Wellness, Health Canada, Northern Lights Health Region and the Alberta Cancer Board met to review the cancer case ascertainment and verification of the suspected cancer cases reported by Dr. O'Connor. In response to concerns voiced by the Fort Chipewyan community, a cancer cluster investigation process was proposed (Appendix 1) and a plan for engaging the community in further investigation strategies was discussed. In February 2008, representatives from Northern Lights Health Region, Alberta Cancer Board and Health Canada visited the Fort Chipewyan community and met with the Nunee Health Board Society and Dr. Griffin, the current community physician. The proposed process for the current Fort Chipewyan cancer investigation was discussed with the community representatives. Also discussed was the ascertainment of possible unreported cancer cases in the community and the population data used in the data analysis. Several comparison communities to be included in the investigation of cancer rates in Fort Chipewyan were recommended by the community representatives. Dr. O'Connor, the community physician who originally raised the cancer concern, left the community in early 2007. Since then, primary correspondence has been with the current community physician, Dr. Griffin; however, Dr. O'Connor has also been consulted through the community nurse practitioner.

The rationale for a more detailed analysis of cancer rates in Fort Chipewyan included:

- 1) The residents of Fort Chipewyan have expressed concerns about their health, in particular about the perceived high rate of cancer for those who live in the community. It was necessary to do a detailed evaluation and report back to the community.
- 2) Fort Chipewyan's comparatively small population means that the cancer rate calculation would be easily influenced by variations in cancer diagnosis, disease classification, the definition of the study period, and the defined geographic boundary. One case, more or less, in a small population, could have a large effect on the calculation of cancer rates. It was, therefore, important to clarify these parameters according to the best current assessment in a more detailed evaluation.
- 3) Cancer rates in several other communities located in the same geographical region as Fort Chipewyan would provide comparison data to assist in the interpretation of the cancer rates in Fort Chipewyan.
- 4) Registration of the Alberta 2006 cancer incidence cases was now complete and was ready to be included in the analyses. This would also help to maintain the on-going monitoring of cancer incidence in the region.

## **Methods**

The investigation into the incidence rate of cancer in Fort Chipewyan and the comparison communities entailed the following steps:

- 1) The population (group) being studied was defined, in this case, as the residents of Fort Chipewyan and the comparison communities from 1995-2006. Reliable population count data were investigated and obtained.
- 2) An “incident case of cancer” was defined, in this case, to enable cases to be selected from the Alberta Cancer Registry. In particular, the selection criteria for cholangiocarcinoma were defined based on expert consultation and literature review.
- 3) Possible un-reported cancer cases among Fort Chipewyan residents were searched.
- 4) The methods of analysis and comparison were specified, and what constituted a significant result was discussed.

These steps are detailed below.

### **Study and comparison populations**

The study population included people living in Fort Chipewyan during the years of interest (1995-2006). A person was defined as a resident of Fort Chipewyan if their address had the postal code “T0P1B0”, which is the only postal code that has been used to direct mail to Fort Chipewyan since 1986. Postal code is the only method currently available to obtain a population estimates from the population database for Fort Chipewyan and the comparison communities according to the same standard. The population data source will be described in detail later in the report.

The comparison populations were chosen following a consultation with the Nunee Health Board Society. There were four comparison communities which included Conklin/Chard/Janvier, Fort Vermilion, Fort McMurray, and the entire Northern Lights Health Region. The postal codes used to define the geographic boundaries of these four comparison communities can be provided upon request. Their geographic relationship to Fort Chipewyan and the Athabasca Oil Sands mining area is shown in Figure 1. Conklin/Chard/Janvier is a rural community located in the eastern part of the Northern Lights Health Region and is geographically isolated from both the main oil sands fields and the Athabasca River. Fort McMurray, also in the eastern part of the Northern Lights Health Region, is located along the Athabasca River and is a major city that houses the majority of the population in the region, including a large number of migrant workers in the oil sands industry. Fort Vermilion is a rural community, like Fort Chipewyan, but located in the western side of the Northern Lights Health Region along the Peace River, removed from the Athabasca River and open-pit oil sand mining fields. The population size and the population distribution by age, sex and First Nations status of Fort Chipewyan and the comparison communities will be presented at the beginning of the Results section.

In the initial consultation, Fort Chipewyan community representative recommended including Fort McKay as one of comparison communities. Fort McKay is a First Nation community located in the Athabasca Oil Sands mining area. The Aboriginal Health Program Officer from Alberta Cancer Board contacted Fort McKay's band administrator about including Fort McKay as one of the comparison communities but Fort McKay did not want its cancer information to be included in the report as they want to pursue their own comprehensive health study.

Population information for Alberta and the study communities were obtained from the Alberta Health Care Insurance Plan database, which maintains records of all Alberta residents eligible for publicly funded health insurance. This database can be used to generate population estimates. Mid-year population estimates were derived from this database.<sup>13</sup> The population data can be broken down by sex, age group and year at the postal code level. Five-year age groups (0-4, 5-9 ...80-84, and  $\geq 85$  years) were used. First Nations residents, whose health insurance premiums are paid by the Federal government of Canada, were identified using a cumulative method. A person was classified as having First Nations status for the purpose of the data analysis if his/her health insurance premium was ever paid by the Federal government between 1983 and 2006. Other sources of population information, such as the Federal Census, the Municipal Census and the files in the nursing station in Fort Chipewyan were also investigated and compared. The universal Alberta Health Care Insurance Plan database was considered the best among the four data sources because it provides complete annual population counts for all study areas. A more detailed discussion of the Fort Chipewyan population data can be found in Appendix 2.

### **Cancer classification and inclusion criteria**

The cancer cases included in this study were patients who were diagnosed with invasive cancer (that is, cancer advanced beyond a very early stage) between January 1995 and December 2006 and were residents of the study area at the time of diagnosis. Former residents who were diagnosed with cancer after they had moved out of the Fort Chipewyan area were not included, as the Cancer Registry only records a patient's residence at the time of diagnosis and would not have information on a patient's residence history. The same standard used to identify cancer cases in Fort Chipewyan was applied to identify cancer cases for the other comparison communities and for Alberta. All cancer cases were identified from the Alberta Cancer Registry (ACR) according to the International Classification of Diseases for Oncology (ICD-O), using a combination of anatomic site (location of the cancer, ICD-O topography code) and histology (microscopic appearance of the cancer, ICD-O histology code).<sup>14</sup> These cases were allocated to specific body systems (e.g., digestive system) and organs (e.g., bile duct) for further analysis. Cases of skin cancer were excluded, with the exception of melanoma, as non-melanoma skin cancers are usually excluded from cancer incidence statistics. In order to consider every possible cancer case in the study areas, cases diagnosed without pathological evidence (biopsy or examination of a removed tumour) were included in the analysis. If a person was diagnosed with more than one type of cancer during the study period, all their primary invasive cancers were counted. Once again, the same practice was applied for both the study populations and for Alberta as a whole. The number of patients with multiple primary cancers was also reported for clarity. Cancer can arise from any organ or tissue of the body (the primary site) and can also spread (metastasize) from the primary site to other parts of body. Only new primary cancers

were included in the study; cases of cancer metastasis were not included in the analysis. This is a standard practice in the calculation of cancer incidence rates.

Cancer cases were assigned to study areas according to the postal code of the patient's address at the time of his/her diagnosis. This is a standard practice to ensure consistency, accuracy and comparability of cancer incidence statistics among populations in different geographic locations.<sup>15;16</sup>

Cholangiocarcinoma is one of the cancers of particular concern to the Fort Chipewyan community. The identification of cholangiocarcinoma cases was complicated because this type of cancer is infrequently encountered in clinical practice, and varies in its classification in literature and among clinicians.<sup>17;18</sup> In this study, the case definition and selection criteria for cholangiocarcinoma were established following expert consultation and according to the definitions used in peer-reviewed literature. More detailed information on how cholangiocarcinoma was defined can be found in Appendix 3. It is worth noting that the same criteria were used consistently for the selection of cholangiocarcinoma cases for Fort Chipewyan, the comparison communities, and for all of Alberta.

### **Active case ascertainment and verification**

Cancer cases in Fort Chipewyan and the comparison areas were identified from the Alberta Cancer Registry (ACR). The most current Cancer Registry dataset was used (on the 5<sup>th</sup> of September 2008). The ACR is a population-based cancer registry that has a proven high level (greater than 95%) of completeness for registration of all new cases of cancer and deaths from cancer in Alberta, according to the standards of the North American Association of Central Cancer Registries (NAACCR).<sup>19</sup> ACR is the only available source of reliable information on cancer incidence in Alberta. Details about data collection and the registration process in the ACR are provided in Appendix 4.

In addition, active case ascertainment was used in order to capture previously unreported cancer cases in Fort Chipewyan. Firstly, a complete list of cancer cases obtained from the Alberta Cancer Registry for Fort Chipewyan was given to Dr. Griffin, the current community physician. The physician and community representatives were asked to report any additional cases not included in the list to the Alberta Cancer Registry via a Suspected Cancer Case Reporting form. Secondly, Dr. O'Connor, the former community physician who originally had raised concerns about a high cancer rate in Fort Chipewyan, was asked for information about the cancer cases that he had seen in the community. He provided a list of 18 names to the Alberta Cancer Registry, including the names of 12 suspected colon cancer patients and the names of six suspected cholangiocarcinoma patients. These names were checked against the Alberta Cancer Registry database and, if required, other provincial health records, and a chart review was carried out. The outcome of this case verification process was presented to the Health Director of the Nuneen Health Board Society and the current community physician, Dr. Griffin. The reasons why some of the cases were included in the analysis, but not others, were explained in a face-to-face meeting. This information is also presented in this report.

## Methods of analysis

Age-Standardized-Incidence Rates (ASIRs) and the corresponding 95% confidence intervals<sup>20</sup> for all cancers were calculated for Fort Chipewyan and the comparison communities over the entire 12-year study period. The 1991 Canadian population was used as the standard population for the rate calculation. The incidence rate is a measure of the rate at which cancers occur in a population. Age standardization adjusts for the presence of younger (generally lower risk) or older (generally higher risk) patients, and allows populations with different age mixtures to be compared to each other. The ASIRs for Fort Chipewyan were presented with the rates for each comparison communities, as well as to the whole of Alberta. In addition, the ASIRs and the corresponding confidence intervals for the most recent six years (2001-2006) were compared to the previous six years (1995-2000) in order to determine whether the incidence rates have changed over time.

The observed number of cancer cases was also compared to the expected number for Fort Chipewyan and for the individual comparison communities. Using population estimates from the Alberta Health Care Insurance Plan database and cancer incidence data from the Alberta Cancer Registry for Alberta as a whole, the expected number of cases for all cancers and for specific types of cancers were calculated for Fort Chipewyan and the comparison communities. These analyses applied age, sex, First Nations status, and calendar-year specific rates in Alberta to the appropriate subgroups in the study populations to give the expected number of cases for each subgroup. Summing across these subgroups yielded the total expected number of cases for each study population. The resulting expected number of cases was then compared to the observed number of cases for the same time period. To assist the comparison, Indirect Standardized Incidence Ratios (ISIRs) were calculated through the division of the observed number of cases by the expected number of cases. The ISIR would be 1 if the number of observed cases is equal to the number of expected. The ISIR would be larger than 1 if the observed number of cases was higher than expected and smaller than 1 if the observed number of cases was lower than expected. These ratios are measurements of how much higher or lower the incidence of cancer was in the study population compared to the general population in Alberta. "Standardized" indicates that both the observed and the expected number of cases were based on the same population distribution by age, sex, First Nation status and calendar year. Assuming a Poisson distribution for the observed number of cases, 95% CIs for the ISIRs were calculated using the Chi-Square method<sup>21</sup> which is a tool used to complete a two-sided equal tail test. Poisson distribution is a distribution function used to describe the occurrence of numbers of rare events in a continuum of time or space.<sup>22</sup> 95% CIs were used to evaluate whether the observed number of cases was significantly different from the expected number at the 5% significance level and did not discriminate whether the observed number of cases was higher or lower than the expected number. If the confidence interval of the ISIR did not include one, the observed number of cases would be significantly (with 95% likelihood) different from the expected number. If the lower limit of the confidence interval was higher than one, the observed number of cases would be significantly (with more than 97.5% likelihood) higher than expected. If the upper limit of the CI was lower than one, the observed number of cases would be significantly (more than 97.5% likelihood) lower than expected. The appropriate methods used for confidence interval calculation in this study were referenced from the Guidelines for Using Confidence Intervals for Public Health Assessments that was published by the Washington State Department of Health.<sup>23</sup> The ISIRs were calculated for all cancers and specific types of cancers in Fort Chipewyan and the

comparison communities. A more detailed analysis was completed for Fort Chipewyan residents, which included the calculation of ISIRs by men and women separately. The ISIRs for the most recent six years (2001-2006) were also compared to those for the previous six years (1995-2000). A comparison between the two consecutive time periods was used to assess whether the observed to the expected ratio has changed over time.

The number of cancer cases that occurred in the small population of Fort Chipewyan is subject to considerable random variation. In order to show the extent of the variation, a simulation method<sup>24,25</sup> was used to derive the possible cancer incidence counts in the community. For all possible cancer incidence counts, the percentage of the simulated counts that are equal or higher than the observed counts in Fort Chipewyan can be derived. This percentage can help to draw conclusions about whether the observed number of cases is higher than the expected number of cases to a statistically significant degree. The simulation assumed that the cancer rate for Fort Chipewyan residents was the same as that for any other group of Albertans with the same mix of age, sex and First Nations status in each calendar year. The simulation process started by applying the age, sex, First Nations status and calendar-year specific rate in Alberta to the appropriate subgroup of the population in Fort Chipewyan. Assuming that cancer incidence in each subgroup followed a binomial distribution, the possible number of cancer cases in each of the subgroups was derived; the application was repeated 1,000,000 times. Binomial distribution is a probability distribution that describes how many members of the population have cancer. Because the number of people in each subgroup of the Fort Chipewyan population is small, the binomial distribution assumption is appropriate. Summing across the subgroups, a distribution of the possible cancer incidence counts in the community was produced. The percentage of the simulated counts that were equal or higher than the actual observed count was calculated. The lower the percentage, the lower the chance of observing the same or a higher number of cases in the community and, therefore, the higher the probability that the increase in the observed number of cases is not due to chance. In this investigation, an increase is considered statistically significant if there is less than a 5% chance of observing the same or higher number of cases in Fort Chipewyan.

The computer program used for simulation in this study was SAS software that was developed based on the original idea using Excel.<sup>26</sup> The SAS program is more flexible than the Excel program because it can simulate data from either Poisson or Binomial distribution and can carry out further adjustments by calendar year and First Nations status in the simulation analysis. Results from the simulation were compared to the results from the 99%CI, 95%CI and the 90%CI of ISIRs in order to validate whether findings based on the simulation method are consistent with those based on the confidence intervals of ISIRs. The conclusion drawn using 5% probability level in the simulation is consistent with 90%CI of ISIRs. The probabilities of observing the same or a higher number of cases in Fort Chipewyan, however, were presented for all cancers and for specific cancer sites in order to assist interpretation.

Statistical analyses were performed using the statistical package SAS 9.1 (SAS Institute Inc, Cary, NC, USA).

## **Ethical approval**

Ethical approval for this study was obtained from the Research Ethics Board of the Alberta Cancer Board.

## **Results**

### **Study populations**

The total population of Fort Chipewyan remained relatively stable over the 12-year period examined with an average of 1,162 persons per year, ranging from 1,114 to 1,213 (Table 1). This was higher than the comparison population of Conklin/Chard/Janvier (679 persons) and lower than the population of Fort Vermilion (3,409 persons). The population of Fort McMurray averaged 41,185 persons in the 12-year study period, but the population increased considerably from about 34,000 to 50,000, presumably because of migration related to the oil sands development in the area. All of these communities are located in the Northern Lights Health Region which had an approximate total population of 64,000. In comparison, Alberta had a total population of approximately 3 million, on average, over the 12-years of the study period. The large increase in the total population of Fort McMurray over the past few years indicates that the relevant exposures for a large proportion of the population likely occurred elsewhere and, therefore, Fort McMurray may not be a suitable community for a meaningful comparison of cancer rates. The population size of Fort Chipewyan and Fort Vermilion has been relatively stable over the 12-year study period.

The population distribution by age group, namely children and youth (0-19 years), middle age (20-54 years) and old age (55+ years), is also presented in Table 1. Fort Vermilion had the highest proportion of population in the 0-19 year age group (47.7%), while Fort McMurray had the highest proportion of people in the 20-54 year age group (60.9%). All study communities had a smaller proportion of people in the 55+ year age group compared to Alberta as a whole. However, Fort Chipewyan had the highest proportion in this older age group (15.8%) amongst the comparison communities. A slightly higher proportion of males can be seen in all of the northern communities, with the opposite true for the whole of Alberta, although the difference is very small (Table 1).

On average, 82.6% of the population in Fort Chipewyan were First Nations, compared to 4.6% of the population across the province of Alberta (Table 1). Conklin/Chard/Janvier and Fort Vermilion also had a relatively large proportion of First Nations people at 65.6% and 57.1%, respectively.

Table 2 shows the changes in population distribution across three age groups over the 12-year period for Fort Chipewyan and Alberta. Population aging can be seen in Fort Chipewyan, where the proportion of younger residents (age 0-19) had continuously decreased over the study period, whereas the proportion of older residents (age 55+) had continuously increased. The pattern of population aging in Fort Chipewyan is similar to that for the whole of Alberta.

## **Results from verification of suspected cancer cases**

In August 2007, Dr. O'Connor, the former Fort Chipewyan community physician provided a list of 12 suspected colon cancer cases and six suspected cholangiocarcinoma cases to the Alberta Cancer Registry. Only the names of the patients were provided.

Of the 12 suspected colon cancer cases, six were confirmed from the Alberta Cancer Registry data to be colon cancer, one was colon cancer in situ (not invasive), and the remaining five were other types of cancer (Table 3). Of the six confirmed colon cancer patients, four were residents of Fort Chipewyan at the time of the diagnosis and the other two were not. Of the four colon cancer cases that were also Fort Chipewyan residents, three were diagnosed in the study period, 1995-2006, and one was diagnosed outside the study period in 2007 (Table 3). In addition to the three cases confirmed based on the list of names provided by Dr. O'Connor, three additional colon cancer cases in Fort Chipewyan residents were also identified directly from the Alberta Cancer Registry for the study period. Therefore, a total of six colon cancer cases were included in the analysis.

Of the six suspected cholangiocarcinoma cases, only two were confirmed to be cholangiocarcinoma (Table 4). Of the remaining cases, three were other types of cancer, and one was not cancer. The two cholangiocarcinoma cases were diagnosed in Fort Chipewyan residents in 2003 and 2004, respectively. These are the only two cases of cholangiocarcinoma found in Fort Chipewyan in all of the records at the Alberta Cancer Registry. The case in 2004 was diagnosed as bile duct adenocarcinoma and was not included as cholangiocarcinoma in the initial review in 2006. Following consultation with a medical oncologist specialising in gastrointestinal tumour diagnosis and treatment, as well as the Data Quality and Management Committee of the Canadian Cancer Registry, this case was re-classified as cholangiocarcinoma. The case definition and selection criteria for cholangiocarcinoma were also developed based on consultation with other experts and the completion of a literature review (Appendix 3).

## **Results from active case ascertainment**

A complete list of cancer cases in Fort Chipewyan, together with patient diagnosis and residence information based on the Alberta Cancer Registry database, was provided to the current community physician, Dr. Griffin. A Suspected Cancer Case Reporting Form was also provided for the timely reporting of any un-reported or new cancer cases. In total, nine cancer cases had been reported from the Fort Chipewyan Nursing Station to the Cancer Registry directly. All of these cases were diagnosed in Fort Chipewyan residents. They included two cases of breast cancer, two cases of prostate cancer, one case of kidney cancer, one case of colon cancer, one case of cervical cancer, one case of multiple myeloma, and one case of non-Hodgkin lymphoma. The kidney cancer case was diagnosed in 2006 but was not reported to the Cancer Registry. The remaining cancer cases were diagnosed in recent years, 2007-2008, and had been reported to the Alberta Cancer Registry before being submitted by the Fort Chipewyan Nursing Station.

The verification of suspected cancer cases reported by the former community physician has revealed two additional cancer cases that had not been reported to the Alberta Cancer Registry. These

included one case of colon cancer diagnosed in 2005 and one case of cancer of unknown primary diagnosed in 2006. Furthermore, through the active ascertainment of unreported cancer cases from the current community physician, an additional case of kidney cancer diagnosed in 2006 was found. These recently diagnosed cases were added once further information was received from the physicians through active case ascertainment for this investigation. The colon cancer was a very early stage tumour with pathologic confirmation. Both the kidney cancer and the cancer with unknown primary site were diagnosed clinically without pathologic confirmation. For cancer cases diagnosed without pathologic confirmation, the Cancer Registry is very dependant on reporting from physicians and hospitals (Appendix 4). These additional cases did not make significant changes to the total number of incidence cases in Fort Chipewyan, indicating that both the initial analysis in 2006 and the current repeat analysis did not overlook a considerable number of cancer cases. The impact of an active case ascertainment process in Fort Chipewyan, but not in other comparison communities, will be discussed later in the report.

### **Number of cancer cases and age-standardized incidence rates (ASIRs)**

In total, 51 cases of cancer were diagnosed in 47 Fort Chipewyan residents between 1995 and 2006. The average age of the cancer patients at the time of diagnosis was 66 years, ranging from 26 to 87 years. The youngest patient was a 26 year-old man who was diagnosed with soft tissue sarcoma in 2006. No cancer cases were found in children or youth. One patient was diagnosed with a primary prostate cancer in 1996 and two primaries of colon cancer in 2000; one patient was diagnosed with both breast cancer and lung cancer in 2003; and another patient was diagnosed with lymphoid leukemia in 2001 and Hodgkin lymphoma in 2003. The remaining 44 patients had one primary cancer diagnosed during the study period. The diagnoses for 44 (86.3%) out of 51 cancers in Fort Chipewyan were confirmed by pathology. This proportion was slightly lower than the 91.6% that were confirmed by pathology for all cancer cases registered in Alberta in the same study period. The cancer cases in Fort Chipewyan whose diagnoses were not confirmed by pathology included one cholangiocarcinoma, one liver cancer, one prostate cancer, one kidney cancer, one cancer of unknown primary origin, and two cases of lung cancer. In total, three of the 51 cancer cases in Fort Chipewyan were cancers of unknown primary for which metastatic cancer was found, but the primary site where the cancer originated could not be determined.

The Age-Standardized Incidence Rates (ASIRs) per 100,000 for all cancers in Fort Chipewyan was 475 (95%CI: 352-626) over the 12-year period (Table 5). The ASIRs and the responding 95%CIs for Fort Chipewyan, the comparison communities and Alberta are also presented in Figure 2.

When the cancer rates for the two six-year periods were compared, the rate per 100,000 in Fort Chipewyan increased from 459 (95%CI: 285-700) in 1995-2000 to 490 (95%CI: 326-709) in 2001-2006. It is worth noting that the overall cancer incidence rate in Alberta also increased; it rose from 389 (95%CI: 386-392) to 404 (95%CI: 401-407) over the two six-year periods (Table 5).

## **Cancer rates by sex, age group and First Nation status**

Table 6 shows that, in Alberta, the majority (76%) of all cancers diagnosed were in residents aged 55+. In Fort Chipewyan, most of the cancer cases (82%) were also found in residents aged 55+. Compared to Alberta, the increased rate in Fort Chipewyan was limited to residents who were aged 55+, with the age specific incidence rate of 1912.6 per 100,000 for Fort Chipewyan which was higher than 1556.1 per 100,000 for Albertans in the same age group. The rates for young adult and middle aged residents were relatively low and no childhood cancer was found in Fort Chipewyan. Men generally had higher cancer rates than women (Table 7). Fort Chipewyan men have the highest rate of cancer when compared to the other comparison communities, with an age standardized incidence rate of 583 (95%CI: 398-825) per 100,000 compared to 454 (95%CI: 451-458) for Albertan men. This is not statistically significant, however, because the observed number of cases in Fort Chipewyan was small, which resulted in a wide 95%CI. The cancer rate for Fort Chipewyan women is the same as that for Albertan women.

The majority of residents in Fort Chipewyan are First Nations. Previous evidence has shown First Nations people have different risk of cancer than non-First Nations.<sup>27;28</sup> The number of cases of cancer in Fort Chipewyan was too small to permit a meaningful comparison of rates between First Nations and non-First Nations; however, the age standardized incidence rates between these two population groups could be compared at the provincial level for all cancers and for specific types of cancers (Table 8). First Nations in Alberta have a lower incidence rate than non-First Nations for all cancers combined, as well as for leukemia and breast cancer. For all cancer combined, the ASIR per 100,000 was 334.6 (95%CI: 316.6-353.5) for First Nations people, compared to 398.9 (95%CI: 395.8-401.1) for non-First Nations people. For leukemia, the corresponding values were 9.2 (95%CI 6.6-12.5) and 13.0 (95%CI: 12.6-13.4), respectively and for breast cancer, 41.9 (95%CI: 36.5-48.0) and 55.4 (95%CI: 54.6-56.2), respectively. In contrast, the rate of cholangiocarcinoma in First Nations people across Alberta was more than double the rate for non-First Nations (ASIR 4.7, 95%CI: 2.5-8.0 versus ASIR 1.8, 95%CI: 1.7-1.9). This noticeable increase in rate was based on a total of 20 cases in Alberta's First Nations people over the 12-year period. These findings suggest that Alberta's First Nations people have a different cancer risk profile than non-First Nations people. This evidence supported the decision to make adjustments for First Nation status of the residents, in addition to age, sex and calendar year, when comparing the observed and the expected number of cancer cases in Fort Chipewyan.

## **Observed versus expected number of cases of cancer: all cancers**

Table 9 shows a comparison between the observed and expected number of cases, as well as the Indirect Standardized Incidence Ratios (ratio of observed to expected cases) for all cancers combined and for specific cancers diagnosed between 1995 and 2006 in Fort Chipewyan and the comparison populations.

An estimated 39 cases of cancer were expected in Fort Chipewyan between 1995 and 2006, given the size and structure of the population by age, sex and First Nation status (Table 9). This compared

to a total of 51 observed cases in Fort Chipewyan. The Indirect Standardized Incidence Ratio (ISIR) was 1.31 (95% confidence interval: 0.98-1.72). A 95%CI of 0.98 to 1.72 implies that the confidence interval has a 95% chance of covering the true value of the ISIR; however, the true value has a 2.5% chance of being lower than 0.98 and a 2.5% chance of being higher than 1.72. The 95%CI would have been wider if the observed number of cases was smaller. Much wider confidence intervals can be seen for the ISIRs of the rare cancer types.

The observed number of cases for all cancers combined was lower than expected for most of the comparison communities. Fort McMurray and the Northern Lights Health Region, in particular, had a significantly lower number of cancer cases than expected. For specific cancer types, many increases and decreases in the observed number of cases are seen, particularly in areas with small populations, such as Conklin/Chard/Janvier. This may be due to the large random variation of cancer incidence that occurs in small populations, where one case more or less can have a large effect on the calculation of the incidence ratio. Statistically, most of the variations were not significant.

### **Observed versus expected number of cases of cholangiocarcinoma, leukemia and lymphoma, and colon cancer**

In total, two cases of cholangiocarcinoma were found in Fort Chipewyan compared to 0.4 expected (ISIR 4.78, 95%CI: 0.58-17.27; Table 9). The other biliary tract cancer found in a resident of the community was adenocarcinoma of Ampulla of Vater, which is not considered cholangiocarcinoma (see Appendix 3). Three cases of cholangiocarcinoma were also seen in Fort McMurray (ISIR 0.93, 95%CI: 0.19-2.72) and one case in Fort Vermilion (ISIR 1.89, 95%CI: 0.05-10.52). These numbers were within the expected range for those communities. No cases of cholangiocarcinoma were found in Conklin/Chard/Janvier.

The observed number of cancers in the blood and lymphatic system (leukemia and lymphomas) in Fort Chipewyan was more than double the number expected (Table 9). In total, eight observed cases were compared to 3.4 expected (ISIR 2.37, 95%CI: 1.02-4.68), which is a statistically significant increase based on 95%CI of the ISIR. These eight observed cases included four cases of leukemia, three cases of non-Hodgkin lymphoma and one case of Hodgkin lymphoma. These patients had an average age at diagnosis of 58 and the ages ranged from 36 to 87. One male patient was diagnosed with leukemia first in 2001 and then with Hodgkin lymphoma two years later. The observed numbers of these types of cancer in the comparison communities were all lower than expected (Table 9).

The observed number of colon cancers in Fort Chipewyan was within the expected range (6 observed compared to 3.3 expected; ISIR 1.84, 95%CI: 0.68-4.01; Table 9). In the entire Northern Lights Health Region, the number of cancers of the rectosigmoid junction was statistically significantly higher than expected; however, the number of rectum cancer cases in the same region was significantly lower than expected. The observed number of colorectal cancers, which includes cancer of the colon, rectum and rectosigmoid junction, was the same as expected.

### **Observed versus expected number of cases of cancer by sex**

Table 10 shows a comparison between the observed and the expected number of cancer cases for men and women separately in Fort Chipewyan. For men, a statistically significant increase can be seen for cancers of the digestive system (ISIR 1.98, 95%CI: 1.02-3.46), biliary tract cancer (ISIR 7.02 (1.45-20.51) and cancers of the blood and lymphatic system (ISIR 2.91, 95%CI: 1.07-6.34). The increase for all cancers combined in men was marginally significant (ISIR 1.45, 95%CI: 1.00-2.04). Two primary colon cancer cases and a Hodgkin lymphoma were diagnosed in patients who had been previously diagnosed with another primary cancer during the study period. For women, a statistically significant increase was found for lung cancer (ISIR 3.47, 95%CI: 1.40-7.15). One female resident was diagnosed with primary lung cancer on the 7<sup>th</sup> day of a month and then with primary breast cancer on the 21<sup>st</sup> day of the same month; she died one month later. It was difficult to determine which primary cancers had occurred first for this patient, but both primary cancers were counted in the analysis.

### **Observed versus expected number of cases of cancer: trends over time**

When the 12-year study period was separated into two six-year periods for further analysis (Table 11), the observed number of colon cancer cases in the first six years, 1995-2000, was significantly higher than expected in Fort Chipewyan (5 observed compared to 1.3 expected; ISIR 3.75, 95%CI: 1.22-8.75), but the observed colon cancer cases in the most recent six years (2001-2006) were lower than expected (1 observed compared to 1.9 expected; ISIR 0.52, 95%CI: 0.01-2.90). It is worth noting that two of the colon cancer cases in the first six years were secondary primary cancers in the same patient who was diagnosed with prostate cancer four years earlier. Conversely, biliary tract cancers (ISIR 5.99; 95%CI: 1.24-17.51) and cancers of the blood and lymphatic system (ISIR 3.22; 95%CI: 1.29 - 6.63) had increases only in the most recent six years. In total, eight cases of cancers of the blood and lymphatic system were diagnosed during the 12-year period, with seven of the eight diagnosed between 2001 and 2006. Although the numbers of both non-Hodgkin lymphoma and leukemia cases were two to three times higher than expected, the increases were not statistically significant due to the small number of cases. Furthermore, all three cases of cancer of unknown primary were diagnosed in the most recent six years.

### **Observed versus expected number of cases based on simulation**

The simulated frequency of possible cancer incidence counts for all cancers and for specific types of cancers in Fort Chipewyan is illustrated in Figure 3 ((a), (b), (c) and (d)). According to the simulation in Figure 3 (a), the number of cancer cases in Fort Chipewyan over the 12-year period could be as low as 12 or as high as 76 (Figure 3, (a)). The most likely cancer case count over the 12-year period in the community was 39, which was the expected number of cancer cases for the community. Cumulatively, the 51 observed cases were lower than 3.5% of the possible case counts, but were higher than 96.5% of the possible case counts. Accordingly, the chance of observing 51 or more cancer cases in Fort Chipewyan was low at 3.5%.

The distribution of possible cancer incidence counts was also obtained for cholangiocarcinoma, leukemia and colon cancer, which were the cancers of particular concern in the Fort Chipewyan community (Figure 3, (b), (c) and (d)). The results from the simulation model suggest that there was a low chance of observing two cases of cholangiocarcinoma, four cases of leukemia or six cases of colon cancer in the small population of Fort Chipewyan. The chances of observing the same or greater numbers of cases of the three cancers in the community were low at 6.7% (cholangiocarcinoma), 3.4% (leukemia) and 11.1% (colon), respectively.

Table 12 presents the chance of observing the same or a greater number of cases for all cancers combined and for specific types of cancer in Fort Chipewyan. The chance of observing 10 or more cases of lung cancer (5.7%), or observing nine or more cases of colorectal cancer cases (8%) were relatively low. In contrast, there was a high likelihood of observing three or more cases of breast cancer (83.3%), or five or more prostate cancer cases (75%). Based on a 5% probability level, statistically significant increases were seen for blood and lymphatic system cancers (2.2%), leukemia (3.4%), biliary tract cancers (3%), soft tissue sarcoma (4.1%) and all cancers combined (3.5%).

The types of cancers found to have statistically significant increases based on simulation were consistent with statistical significance determinations based on confidence intervals of ISIRs (Table 12). Using the Chi-Square method, the 99%CI, 95%CI and 90%CI of the ISIRs were calculated<sup>21</sup>. The Chi-Square method is a two-sided equal tail test that does not discriminate whether the aim was to examine an ISIR that is greater than 1 (Observed>Expected), or an ISIR that is less than 1 (Observed<Expected). None of the cancer sites had a statistically significant increase based on 99%CI. Cancers of the blood and lymphatic system were the only group of cancers that had a statistically significant increase based on 95%CI. This means that the chance of observing eight or more cases of this type of cancer in Fort Chipewyan over the 12-year period was lower than 2.5%. Consistent findings were derived from the simulation method. Furthermore, based on 90%CI, statistically significant increases were found for several cancer sites, such as biliary tract cancers, leukemia, soft tissue sarcoma and all cancers combined. The chances of observing the same or a higher number of cases for these types of cancers in Fort Chipewyan were less than 5%. Once again, consistent findings were noted with the simulation method (Table 12).

## **Discussion**

Only two out of six suspected cholangiocarcinoma cases and three out of 12 suspected colon cancer cases reported by Dr. O'Connor, the former community physician, were confirmed. The remaining reported cases were different types of cancer, were not cancer, or were not Fort Chipewyan residents.

In total, 51 cases of cancer were found in Fort Chipewyan residents over the 12-year study period, through a combination of review of the Alberta Cancer Registry database and active case ascertainment. Most of the cases of cancer were diagnosed among residents aged 55+ and among male residents. No increase was noted in middle age persons or young adults and no childhood cancer case was found. The most frequently reported cancers in Fort Chipewyan were lung cancer and colorectal cancer, which are common cancers in the general population, and the remaining cancers comprised a wide variety of types.

The objective of this study was to determine whether the observed number of cancer cases in Fort Chipewyan is higher than expected. The observed number of cases in the blood and lymphatic system was higher than expected, in this case, with less than one in 40 chance of observing the same or a higher number cases in Fort Chipewyan. The observed number of cases of biliary tract cancers, leukemia, soft tissue sarcomas and all cancers combined in Fort Chipewyan were also higher than expected to a statistically significant degree, in these cases, with less than one in 20 chance of observing the same or a higher number cases. When considering men and women in the community separately, a statistically significant increase was seen for biliary tract cancer in men and for lung cancer in women, in these cases, with less than one in 40 chance of observing the same or a higher number of cases.

Many of the increases found in specific types of cancers, such as biliary tract cancer (three cases), leukemia (four cases) and soft tissue cancers (two cases) were based on a very small number of cases which can easily lead to borderline significant results. A single case can make the difference between a statistically significant increase and no increase in a small population like Fort Chipewyan; one cannot rule out the possibility that these increases were due to chance or that they were a result of increased detection or increased risk. For example, the increase of the soft tissue sarcoma cases were based on two different types of sarcomas and occurred six years apart, with one case diagnosed in a 26 year-old man in 2000 and the other one in a 77 year-old man in 2006. Although finding a soft tissue sarcoma in a young man in a community of just over a thousand residents was unusual, it was difficult to interpret the results based on one case. The epidemiologic characteristics of the three cancers that were of specific concern to the Fort Chipewyan community (cholangiocarcinoma, leukemia, and colon cancer) are discussed further below.

### **Cholangiocarcinoma**

In total, two cases of cholangiocarcinoma were diagnosed in Fort Chipewyan residents within a short period of time, one in 2003 and the other one in 2004. Three cases of cholangiocarcinoma were found in Fort McMurray (>40,000 persons), a number that was not higher than expected. Another

case was found in Fort Vermilion which was within the expected range. No case was found in Conklin/Chard/Janvier. The diagnosis of two cases of cholangiocarcinoma within a community of Fort Chipewyan's size (1,200 persons) in a relatively short period has caused concern. A review of the Alberta Cancer Registry data, however, confirmed that no other cases of cholangiocarcinoma have been reported in Fort Chipewyan. The fact that no case of cholangiocarcinoma was reported in 2005 and 2006, suggests that the two cases found might have been the result of a random variation of cancer occurrence. Based on the population file containing yearly residence information for First Nations people in Alberta provided by Alberta Health and Wellness, a search of First Nations people who had ever lived in Fort Chipewyan since 1983 was conducted. Apart from the two cases found in this investigation, no other cases of cholangiocarcinoma were found in First Nation residents who had moved away from the community.

The patients' medical records were reviewed for details of the diagnosis and possible risk factors. The first case of cholangiocarcinoma was diagnosed in a man aged 80+ who used to be a trapper. The diagnosis was confirmed by ultrasound, more specifically, Endoscopic Retrograde Cholangiopancreatography (ERCP), which showed "distal common bile duct obstruction mostly likely secondary to a neoplastic process like cholangiocarcinoma." The bile duct cytology specimen collected from the patient had an air-drying artifact and, therefore, was not diagnostic. In cytopathology testing, collected specimens require immediate immersion in an alcohol fixative. Air-drying occurs if there is even a short delay in the process. Air-drying artefact is one of the most common problems in specimen preparation for cytopathology testing which render specimens un-interpretable.<sup>29-31</sup> Although this was not a conclusive case of cholangiocarcinoma, it was included for the purposes of the inclusive investigation. Some information on the challenges of cholangiocarcinoma diagnosis is available in Appendix 3. The second case of cholangiocarcinoma was diagnosed in a man aged 60+ who used to be a bus driver. The diagnosis was confirmed by cytology as extrahepatic bile duct cholangiocarcinoma. If only pathologically-confirmed cases were included in the analysis, only one cholangiocarcinoma would be counted for Fort Chipewyan.

Cholangiocarcinomas are rare and fatal malignancies arising from bile duct epithelium (cells of the bile duct lining). They are slow-growing tumours that are usually diagnosed in patients over 60 years of age. Based on a recent literature review, cholangiocarcinomas occur in approximately two out of 100,000 people<sup>32-34</sup> but vary considerably with geographic region. For example, the incidence rates of intrahepatic (occurring within the liver) cholangiocarcinoma vary from as high as 96 per 100,000 in men and 38 per 100,000 in women in Northeast Thailand to as low as 0.2 and 0.1 per 100,000 among Australian men and women, respectively.<sup>35</sup> So far, there is no incidence rate information for cholangiocarcinoma in Canada.

A number of risk factors for cholangiocarcinoma have been recognized.<sup>36</sup> These include primary sclerosing cholangitis, liver fluke infection, Caroli's disease, congenital choledochal cysts, chronic cholelithiasis, chronic hepatitis C virus infection, dietary habits (i.e. nitrosamines) and Thorotrast (a no-longer used X-ray contrast medium containing radioactive thorium) deposition. The recognized risk factors only account for about 10% of cholangiocarcinoma,<sup>37</sup> however, and seem to be associated with chronic inflammation of the biliary epithelium.<sup>38</sup> Other possible risk factors include biliary cirrhosis, cholelithiasis (gallstones) and choledocholithiasis (biliary tract stone disease), cholecystitis and cholecystectomy, heavy alcohol consumption,<sup>39</sup> alcoholic liver disease, liver

cirrhosis, diabetes, thyrotoxicosis, chronic pancreatitis, and possibly duodenal ulcer disease.<sup>40;41</sup> New evidence supports previous findings that excess body weight or obesity may be associated with an increased risk of extrahepatic bile duct cancers.<sup>40;42-45</sup> In addition, smoking is associated with increased risk of intrahepatic bile duct cancers.<sup>40;46</sup> Environmental toxins such as dioxin, vinyl chloride and PCBs have been hypothesized to cause cholangiocarcinoma.<sup>47</sup> Cholangiocarcinomas have been associated with increased exposure to by-products from rubber and chemical industries, including dioxins and nitrosamines but results have been conflicting and no firm conclusions can be drawn.<sup>38;48</sup> Based on the review of the medical charts, the two patients diagnosed with cholangiocarcinoma in Fort Chipewyan had medical conditions or other known lifestyle risk factors that may have predisposed them to cholangiocarcinoma. Existing knowledge about the risk factors associated with cholangiocarcinoma in general is limited, however, and apart from the existing medical charts, we were not able to obtain more information about these two cases. Therefore, we were not able to develop a complete risk profile for these two patients.

The two cholangiocarcinoma cases in Fort Chipewyan appear against a background of changing incidence of this type of cancer in Alberta and in other parts of the world. The incidence rate of intrahepatic cholangiocarcinoma has been increasing in the UK, US, Japan and Australia, where rates were previously low.<sup>34;35;49-51</sup> Although there is not as much data for extrahepatic cholangiocarcinoma, incidence rates seem to be declining in many countries.<sup>32;34;50;51</sup> The rise in intrahepatic tumours is greater than the relative decline in extrahepatic tumours resulting in an overall increase.<sup>34;35;49</sup> In Alberta itself, the incidence rate of cholangiocarcinoma has increased progressively over the past 30 years, which may be due to changes in disease coding and changes in diagnostic methods.<sup>52</sup> In total, 906 cholangiocarcinomas were diagnosed in 1975-2004, comprising 0.28% of all cancers and a quarter of all liver and biliary-tract cancers in Alberta. The annual incidence rate has increased in Alberta from 1.0 per 100,000 in 1975 to 2.3 per 100,000 in 2004, with an approximate annual increase of 2%. The noted increase was limited to the population over 70 years of age. The proportion of cholangiocarcinoma cases confirmed by diagnostic imaging has increased from 2% to 30% over the 30-year period. One of the two cholangiocarcinoma cases in Fort Chipewyan was only confirmed by ultrasound, a type of diagnostic imaging. The observed increase in the number of cases of cholangiocarcinoma in Fort Chipewyan may be partly due to increased use of diagnostic imaging or increased awareness.

The current study found that the incidence rate of cholangiocarcinoma in all Alberta First Nations was two to three times higher than that in non-First Nations people. A previous study by McLean & Patel using data from the Surveillance Epidemiology and End Results (SEER) database, also supported our findings.<sup>53</sup> Results from their study showed that the overall age-adjusted incidence rates for intrahepatic cholangiocarcinoma were higher for American Indian/Alaska Native (1.6 in 100,000 persons) when compared to Asian Pacific groups (1.2 in 100,000), Hispanics (1.1 in 100,000), White (0.8 in 100,000) or Black (0.6 in 100,000) populations. Because most of the Fort Chipewyan residents were First Nations, we would expect to see more cases of cholangiocarcinoma in Fort Chipewyan than in other communities with the same population size and the same age and sex structure, but with a different representation of First Nations. In the simulation analysis that did not account for First Nation status, the two observed cases of cholangiocarcinoma in Fort Chipewyan were higher than expected to a statistically significant degree, with only a 1.8% chance of observing two or more cases of cholangiocarcinoma in the community. The increase became

insignificant, however, once the high proportion of First Nations residents in the Fort Chipewyan population was factored in; the adjusted probability became 6.7%, which was greater than the 5% probability level and was, therefore, considered more likely due to chance.

## **Leukemia**

The four cases of leukemia observed in Fort Chipewyan over the 12-year study period was more than three times the number expected. According to the collective evaluation that was based on 95%CI and 90%CI of ISIR, as well as the simulation analysis, the chance of having observed four or more cases in the community was small (3.4%). No unanticipated increase in leukemia was noted in any of the comparison populations of Conklin/Chard/Janvier, Fort Vermilion or Fort McMurray.

Leukemia can be classified into four major subtypes<sup>54</sup> according to the International Classification of Diseases for Oncology (ICD-O):<sup>14</sup> acute lymphoid leukemia (ALL), chronic lymphoid leukemia (CLL), acute myeloid leukemia (AML) and chronic myeloid leukemia (CML). Among them, AML has the poorest prognosis with a 10% five-year relative survival ratio. Although leukemia is the most common malignancy in children, the age-specific incidence rates are substantially higher in elderly populations, with a small peak in early childhood and a high peak in the elderly. Childhood cancers, particularly childhood leukemia, have frequently been studied for the assessment of the health impacts from environmental pollution.<sup>55</sup> All four cases of leukemia found in Fort Chipewyan were in adult residents aged between 35+ and 60+. These four cases comprised two cases of acute myeloid leukemia (AML) and two cases of chronic lymphoid leukemia (CLL). These are cancers of later adulthood<sup>54</sup> and may be more frequent in an elderly population, such as Fort Chipewyan.

The causes of leukemia remain largely unclear and the different subtypes of leukemia may have different etiologic factors.<sup>56</sup> A few established causes of AML in adults include chemotherapy,<sup>57</sup> ionizing radiation,<sup>58</sup> chemicals that include petroleum products and organic solvents (benzene),<sup>59;60</sup> as well as smoking.<sup>61;62</sup> Occupational benzene exposure in leather, printing and petrochemical industries has been linked to AML but occupational exposure may only account for a small proportion of the total exposure to benzene. Other sources of exposure may include tobacco smoking and environmental pollution.<sup>56</sup>

While several risk factors for AML have been established, the aetiology of CLL remains poorly understood. Genetic factors, such as having a family history of CLL, are so far the strongest risk factor for the development of CLL.<sup>63</sup> Studies have also reported an increased risk of CLL among workers in the petroleum, rubber, mining and agriculture industries who were exposed to solvents, styrene, butadiene, and ethylene oxide; however, there have also been studies which did not report excesses. Therefore, the association between exposure to these chemicals and CLL remains inconclusive.<sup>64</sup> Evidence from previous studies of atom bomb survivors and of patients treated with ionizing radiation for benign conditions suggests that CLL is not caused by ionizing radiation, however, recent evidence disagreed with this earlier conclusion.<sup>65</sup> A retrospective case-cohort study among 23,043 uranium miners found that radon exposure was associated with an increased risk of developing leukemia, particularly CCL, in underground uranium mining.<sup>66</sup> A study among individuals exposed to radionuclides following the accident at the Chernobyl nuclear power

plant found that clean-up workers developed a more aggressive form of CLL than is normally seen in the community.<sup>67</sup>

## **Colon cancer**

The six observed colon cancers cases found in Fort Chipewyan was within the expected range. The chance of observing the same or a higher number of cases in the community was 11.1%. Five out of the six cases were diagnosed in the first six years of the study period (1995-2000) and two out of the five were secondary primary cancers diagnosed in one patient. Only one of the six cases was diagnosed in the most recent six years of the study period (2001-2006). A search among the latest Cancer Registry data has found only one extra colon cancer case in 2007. As a result, the rate of colon cancer in Fort Chipewyan was not elevated.

## **Cancer in First Nations in Alberta**

In the current study, age standardized incidence rates of cancer in First Nation were compared to that in non-First Nations in Alberta. This analysis confirmed, for the first time that First Nations in Alberta had a significantly lower rate than non-First Nations for all cancer, leukemia and breast cancer. Conversely, the rate for cholangiocarcinoma in Alberta's First Nations population was significantly higher than that in non-First Nations people. No difference was seen for lung cancer and colon cancer between First Nations and non-First Nations people in Alberta. Considering that the prevalence rate of smoking in the First Nations population is about twice the rate in the non-First Nations population,<sup>68</sup> it is surprising to see that lung cancer incidence for First Nations was not higher than that for non-First Nations. Other studies on cancer incidence in native populations in the US and in Canada support the results found in Alberta First Nations people.

A meta-analysis of cancer incidence in the US and Canadian native populations, which included data from the provinces of Ontario and Manitoba in Canada and from the states of Alaska, New Mexico, New York and Washington in the US, was published in 1991.<sup>28</sup> The study found that native men and women have a significantly lower incidence of cancer for all cancers combined when compared to the general population. Specifically, native men have a significantly lower incidence of cancers of the colon, lung, prostate, and of leukemia and lymphoma, but a significantly higher incidence of kidney cancer. Native women have a significantly lower incidence of cancers of the colon, breast and uterus, and of lymphoma, but a significantly higher incidence of cancers of the kidney, gallbladder and cervix. A recently published study in 2003 on cancer incidence and mortality in Ontario First Nations in Canada over a 24-year (1968-1991) study period found similar results. First Nations men and women in Ontario have a significantly lower incidence of all cancers combined, as well as for colon/rectum cancer, but a significantly higher incidence of gallbladder cancer when compared to the general population.<sup>27</sup> In particular, First Nations women have a significantly lower breast cancer incidence and a significantly higher cervical cancer incidence; First Nations men have significantly lower lung cancer incidence. Although the incidence of lymphoma and leukemia among Ontario First Nations was lower than the general population, as suggested in the meta-analysis published in 1991, the decrease was not statistically significant. First Nations people in the

Fort Chipewyan community make up 83% of the population, however, a lower than expected number of cervical cancer and gallbladder cancer cases and a higher than expected number of lung cancer, leukemia and lymphoma cases were observed.

The study on cancer incidence in Ontario First Nations also examined trends of cancer incidence rates for frequently occurring cancers over three eight-year time periods. The analysis showed that the speed of the rate increase for all cancers, colon/rectum cancers and lung cancer for First Nations was faster than that observed in the general population. The study suggested that Ontario First Nations were experiencing an epidemiologic transition where infectious disease occurrence was declining and cancer and other chronic disease occurrences were increasing. The likely explanations for the changes in pattern of cancer incidence were thought to be related to lifestyle, socio-cultural factors and genes. Among the factors discussed were the high prevalence of smoking, changing diet and physical activity patterns, high level of obesity, low participation rates in cancer screening, a relative low socio-economic status and possible environmental contaminants.<sup>27</sup> Although the current study was not able to investigate the lifestyle and socio-economic status of the Fort Chipewyan community members, information from the initial assessment on the health status of the community in 2006 showed that Fort Chipewyan residents have elevated prevalence rates of diabetes, hypertension, renal failure and lupus.<sup>9</sup> A more detailed assessment of the overall health status and associated risk factors for Fort Chipewyan residents is required, for both cancer and other chronic diseases of concern.

Native groups living in different areas may have unique genetic characteristics and different cancer risk factors, and/or be exposed to different socio-cultural or environmental conditions affecting the cancer risks of the individual groups.<sup>28</sup> This is the reason why it is important to assess cancer occurrence as well as cancer risk factor prevalence among First Nations communities in Alberta. A study is underway to investigate cancer incidence rates and incidence trends in Alberta First Nations. The findings of that study will be published next year. In the current report on cancer in Fort Chipewyan, the assessment of cancer incidence in Alberta First Nations was necessary in order to verify that First Nations people have a different risk of cancer than non-First Nations. As a result, the calculation of the expected number of cancer cases in Fort Chipewyan was able to account for the high proportion of First Nations residents in the community.

### **Possible explanation of the results**

There are several potential reasons for an observed increase in the number of cancer cases diagnosed in a community, including 1) chance, 2) increased detection or 3) increased risk due to changes in lifestyle, occupational and environmental exposures.

#### **1) Chance**

It was unusual to find the increased number of cases for all cancers and for several specific types of cancers in Fort Chipewyan, given the number expected. Any search for a cancer cluster is likely to find some aggregation of cases in a geographic location or over a period of time, even if there is no causal explanation.

The selection of the study area and the calendar time period was strongly influenced by the community physician's report of an increase in cancer cases since 2000. As a result, our analysis would have an increased probability of finding a higher than expected number of cancer cases in the community as a result of a phenomenon termed the "Texas-sharp shooter fallacy".<sup>69</sup> This is named for the anecdotal Texan who fired his gun randomly at the side of a barn, then drew a target around the spot where most of the bullet holes clustered and claimed to be a sharpshooter. This has two implications for cancer cluster studies in a population.<sup>70:71</sup> The first implication is that an unusually high number of cancer cases found in a community can be a random aggregation of cases that depends on how the geographic boundaries and study time periods are defined. In the previous analogy, the bullet holes occurred randomly and the Texan drew a circle around a cluster of holes. The second implication is that a cancer cluster found in a community may not be the result of a specific cause. Following the same analogy, the appearance of a cluster of bullet holes was not the result of sharp shooting by the Texan. One of the approaches used to rule out random aggregation of cases is to establish close monitoring to see whether new cases of the same type of cancer continue to occur in the area. The detection of an increased occurrence of cholangiocarcinoma or leukemia, for example, in Fort Chipewyan in the next 5-10 years would substantiate the suggestion that there are elevated cancer rates in the area and would justify more extensive investigations into possible causes. Conversely, the absence of an increase of cholangiocarcinoma or leukemia in the next five to 10 years would suggest that the increase in the number of observed cases in the community was likely due to random aggregation of cancer cases or increased detection.

## 2) Increased Detection

Increased incidence may also be a result of increased detection and diagnosis of cancer by physicians working in the community. Dr. O'Connor, the community physician who initially raised concern about the possible excess in cancer risk began working in Fort Chipewyan in 2000. Since then, there have been more visits by the community physician, increasing from approximately one visit in two months to every other week. According to a community representative, this physician had built and maintained a much closer relationship with the residents than had previous physicians. As a result, he was able to follow-up patients and to refer community residents to the Fort McMurray hospital for diagnostic testing or treatment. For example, seven cases of cancer were reported in 2006, compared to an average of four cases per year from 1995-2005. It is possible that previous cases of cancer might not have been detected before the patient moved from the area or died from other causes, or that deaths from cancer might have been attributed to other causes. Although these cases were unable to be recovered, the implementation of a monitoring process would help to ensure that future cases will be diagnosed and reported.

## 3) Increased Risk

The study confirmed that there was a higher than expected number of cases for all cancers and for several specific types of cancers in Fort Chipewyan. Data from Canadian Cancer Registries up to 2004 showed that one in two Canadians will develop cancer in their lifetime.<sup>72</sup> Because the risk of an individual developing cancer increases with age, age is a major risk factor for cancer. As people live longer, they are more likely to be diagnosed with cancer. This age effect has also been demonstrated in the current study, based on age specific incidence rate calculations. However, compared to the Alberta population as a whole, Fort Chipewyan had a lower proportion of residents in the over 55

age group. The patterns of population aging in Fort Chipewyan were similar to that for all Albertans. In addition, when comparing the observed number of cases to the expected number of cases in Fort Chipewyan, the age, sex and First Nations status of the Fort Chipewyan residents has been accounted for. Therefore, population aging can not explain why there was a higher than expected number of cancer cases in Fort Chipewyan.

Childhood cancers have often been studied in relation to environmental exposures to carcinogens because children have a greater risk of cancer than adults from environmental toxins, which may be due to the physiological immaturity and rapid growth of children.<sup>73</sup> Because childhood cancer is extremely rare, less than one case of childhood cancer (more specifically, 0.45) would be expected in Fort Chipewyan for the 12-year study period. The fact that no cancer cases were found in children and youth in Fort Chipewyan does not support an environmental cause for the cancers in the community.

The objective of the current study was to determine whether there is an elevated rate of cancer in Fort Chipewyan by comparing the number of observed cancer cases in the community with the number of expected cases. In the calculation of the expected numbers in Fort Chipewyan, the cancer rate in Alberta was applied to the community of Fort Chipewyan. Adjustments were made according to the population size and population structure by age, sex, and First Nations status in the community. There are many other factors, however, that can also contribute to variations in risk, such as socio-economic factors, lifestyle, nutrition, as well as factors related to occupational and environmental exposure. These factors may contribute to the differences in cancer incidence found between Fort Chipewyan and the rest of Alberta, but we were not able to measure them in the current study.

### **Review of the literature on health effects of living near an oil field**

Residents of Fort Chipewyan believe that the increased rate of cancer in their community is caused by the oil sands development located upstream of the Athabasca River, or by other industrial development activities such as uranium mining and pulp mills. Previous investigations of environmental contamination, both naturally occurring and related to industrial developments, in Fort Chipewyan and the surrounding areas are summarized in Appendix 5. According to these investigations, there are environmental contaminants that have occurred naturally from oil deposits and uranium in the area and have been released from historical industrial developments (e.g. coal mines, pulp mills, oil sands and uranium mining activities) along the Athabasca River,<sup>74-78</sup> all of which may have an impact on the health of the people living downstream of the river.<sup>79</sup> The relationship, particularly to the cancer risk among residents living in the lower Athabasca River area, has not been studied. The following discussion reviews the literature on cancer occurrence in oil exploration industries and in communities living near an oil field.

Crude oil is a major product from oil sands developments. According to the International Agency for Research on Cancer, there is inadequate evidence to classify crude oil as a human carcinogen, however, there is limited evidence for the carcinogenicity of crude oil in experimental animals.<sup>80</sup> Crude oil is a complex mixture of many chemical compounds, mostly hydrocarbons; the

composition varies with source and type of crude oil. The petroleum hydrocarbons of most toxicological interest are volatile organic compounds (i.e. benzene) and polycyclic aromatic hydrocarbons (PAHs).<sup>80</sup>

PAHs are a group of more than 100 chemicals that generally occur as complex mixtures. The International Agency for Research on Cancer (IARC) has determined that two types of PAHs, namely benz[a]anthracene and benzo[a]pyrene, are probably carcinogenic to humans; and several other types of PAH compounds are possibly carcinogenic to humans.<sup>81</sup> The evidence of the carcinogenicity of PAHs in humans is primarily based on occupational studies of workers exposed to mixtures containing PAHs.<sup>82</sup> The primary pathway of PAH exposure is by inhalation, ingestion, and skin contact. Non-occupational respiratory exposure is mainly from tobacco smoke and urban air, while the major sources of ingested PAHs are drinking water and cooked food. Some people are exposed to PAHs at their workplace through inhalation and skin contact.<sup>83</sup> PAHs tend to be stored mostly in kidneys, liver, and fat. PAHs or their metabolites can be measured in urine, blood, or body tissues. Although these tests can show that exposure to PAHs have occurred, they cannot be used to determine the extent or source of the exposure, nor can they to be used to predict whether any health effect will occur.<sup>81</sup>

In the areas near oil sands developments, PAHs can come from the oil production process and can also occur naturally in waters within the oil sand deposit areas<sup>77</sup> (Appendix 5). Review of evidence from epidemiological studies has shown associations between PAHs and the development of skin, scrotum, bladder and lung cancer among workers occupationally exposed to PAHs.<sup>83;84</sup> There was no case of skin melanoma or bladder cancer in Fort Chipewyan. The observed number of lung cancers was almost double the number expected, with the same scale of increase not shown in the other study communities. Furthermore, the increase was only seen in women where the number of observed cases was more than three times higher than the number expected.

Tobacco smoking is a major risk factor for lung cancer. According to the First Nations Regional Longitudinal Health Survey (RHS) 2002/03, the smoking rate in First Nations is 59%,<sup>85</sup> compared to about 23% among Albertans according to the Canadian Community Health Survey (CCHS) 2002/2003.<sup>86</sup> The average daily number of cigarettes consumed by First Nations smokers is 10 which is lower than the Canadian average of about 15 cigarettes a day. According to RHS, the smoking rate is as high as 70% for First Nations people in the 18-29 age group and young men consume more cigarettes a day than young women. The smoking rate among female teenagers is, however, much higher than among teenage boys. Furthermore, nearly half of First Nations people (44.2%) are exposed to cigarette smoke at home.<sup>68</sup> The smoking rate in Fort Chipewyan residents has not been determined, but given the proportion of First Nations residents, it could be much higher than that in the general Alberta population.

A few epidemiological studies have investigated the risk of cancer among workers in petrochemical industries and residents living in the areas close to the oil refineries. Studies of cancer among workers in petroleum exploration and production are very limited, however, and studies of cancer among residents living near the oil fields are hard to find. No study was found that assessed the cancer risk of residents living in or close to an oil sands area, probably because mining of oil sands

is a relatively recent development in response to increases in oil prices and the availability of new oil exploration technology.

One of the initial steps often used to investigate cancer risk in relation to industrial development is to study cancer occurrence among the workers who have been employed in the industry, as they would have higher levels of exposure than people living close to the industrial areas but not working in the industry. A cohort study, conducted in 2000, evaluated 49 years of mortality experienced by over 24,000 crude oil production workers.<sup>87</sup> The study found that the production workers had a higher risk of dying from all cancers and lung cancer than the general population. Workers who were first employed before 1940 and had been employed in production and pipeline jobs for more than 30 years had a statistically significant increased risk of dying from acute myeloid leukemia (AML). A recent retrospective cohort study of 27,919 offshore petroleum workers showed that upstream operators, whose job involved the extraction of crude oil and natural gas, have more than three times higher risk of developing hematologic neoplasms, especially AML and multiple myeloma, than the general working population.<sup>88</sup> The author attributed these increases to benzene exposure because of the established association between benzene exposure and hematologic neoplasms. The workers' smoking history was not available, however, to allow assessment of the important effect of benzene exposure through smoking.

Based on our communications with the community, many Fort Chipewyan residents have worked, or are currently working, in the oil sands industry. Some Fort Chipewyan residents worked in uranium mines on the other side of Lake Athabasca many years ago. Previous studies of cancer risk and occupational exposure have suggested increased risk of leukemia<sup>88</sup> and lung cancer<sup>83</sup> in oil field workers, and increased risk of leukemia,<sup>66,89</sup> lung cancer,<sup>90</sup> and cancers in gallbladder and extrahepatic bile ducts<sup>91</sup> in uranium miners. A study of 4320 uranium miners in West Bohemia found significantly increased risk of death from cancer of the gallbladder and extrahepatic bile ducts; mortality increased with cumulative exposure to radon. Although no similar findings were found from other studies of uranium miners, the known association between injected Thorotrast and bile duct cancer supports the biological plausibility of the finding.<sup>92</sup> The relevant types of cancers in these occupational studies, such as leukemia, lung cancer, and bile duct cancers, have been found to be elevated in Fort Chipewyan. Recording patients' occupational information is not required in cancer registration and, therefore, patients' occupational information is not recorded in the Cancer Registry database. Despite this, the limited patient occupational information recorded in the paper files of the Cancer Registry was searched for the Fort Chipewyan cancer cases. The recorded occupations of the two cholangiocarcinoma patients were trapper and bus driver, respectively. The occupations of the four leukemia patients were custodian, crisis intervention worker, police officer and trapper, respectively. The search for lung cancer patients found several homemakers, trapper and retiree. Information about the occupational history of Fort Chipewyan residents and their possible exposures at work could be very important; however, this could not be collected at this stage of the investigation. Future studies should evaluate the occupational history and the employment-related migration pattern of the cancer patients in the community.

There is a lack of epidemiological studies of cancer risk in communities near oil fields. A study was conducted in a village of 1000 residents located near oil fields in the Amazon basin of Ecuador where more than two billion barrels of crude oil have been extracted since 1972.<sup>93</sup> The timeframe of

oil production was similar to the Athabasca oil sands development. The population size of the village was also similar to that in Fort Chipewyan. In total, only 10 cancer cases were found over the 10-year study period, 1989-1998, compared to eight expected cases. The excess of cancers was limited to male residents in the village. Unusual cancers, such as liver cancer, cancer of Ampulla of Vater, an acute lymphoblastic leukemia in a child, non-Hodgkin lymphoma and larynx cancer were found; however, common cancers, such as lung cancer or colorectal cancer were not. The study also found an elevated concentration of total petroleum hydrocarbons in the local rivers. Although the authors concluded that there was a possible association between the observed excess cases of cancer and pollution from the oil fields, they cautioned against making a causal association because of the small numbers of cancer cases in the study and the incompleteness in counting of the population and the cancer cases. In addition, the migration patterns and other cancer risk factors that are associated with lifestyle, socio-economic and health services of the community had not been measured and accounted for.<sup>93</sup> Subsequently, a larger study was conducted in three provinces in the eastern part of Ecuador with a total population of 280,000. This later study found that the rates of all cancers were higher among residents living close to the oil fields than those who lived in areas free from oil production.<sup>94</sup> The cancers with elevated rates included cancer of the stomach, rectum, melanoma, soft tissue and kidney in men, and cancer of the cervix in women. Although the ecologic study provided some evidence to suggest the relationship between elevated cancer incidence and living close to oil fields, the authors acknowledged the limitations in making causal inference in this study. In addition to the limitations mentioned in the previous study in a village, the authors also considered the relative long latency of cancer development. Because the cancer cases were counted based on county of residence at time of diagnosis, the study was not able to consider the length of time of a resident living in the study area. Furthermore, the relevant exposure information for cancers 10-20 years before was not available. Apart from having complete counts for population and cancer cases, the current study in Fort Chipewyan has similar limitations, as described for the two cancer studies in communities near oil fields. These limitations prevent any conclusions from being reached about whether the cancer rates are related to living near the oil sands.

The extraction of bitumen and refining it into crude oil during oil sands industrial activity may have different impacts on the environment and human health from those of conventional crude oil production using oil wells. Findings of cancer risk from communities near the conventional oil extraction fields cannot be applied directly to communities near the oil sands area. The health impact of the oil sands development could be a unique situation that requires detailed evaluation.

Oil shale is one kind of unconventional petroleum resource that is similar to oil sands. Oil sands are a combination of clay, sand, water and bitumen whereas oil shale is sedimentary rock that contains solid bituminous materials that can be released as petroleum-like liquids when the rock is heated. Shale-oils are the product of thermal processing of raw oil shale. The cost of shale-oils extraction and upgrading has been much higher than conventional oil extraction through well-bores. The International Agency for Research on Cancer classified shale-oil as a human carcinogen in 1985.<sup>82</sup> Most of the evidence for carcinogenic risks of shale-oils to humans was based on data from occupational studies. Skin cancer is the type of cancer that was linked to the dermal exposure to shale-oil.<sup>95-98</sup>

## Strengths of the current study

The current study has investigated whether there was an increased rate of cancer in Fort Chipewyan by comparing the observed number of cases with the number expected, taking the population mixture of the study areas into account. The investigation was conducted according to the generally accepted guidelines for cancer cluster investigations.<sup>1;2;99</sup> In the initial response to the Fort Chipewyan community in 2006, cancer rates among community members were calculated based on existing cancer information that covered the time period 1995-2005. The results of the initial analysis showed that the community's cancer rates were comparable to the provincial average. The current study on cancer incidence in Fort Chipewyan covers the time period of 1995-2006 and the results show that the number of cancer cases observed in the community is higher than expected for all cancers combined and for specific types of cancer. Compared to the preliminary evaluation in 2006, the current study provides a more detailed investigation. The strengths of the current study are outlined in the following and might explain the differences in findings between the two analyses.

- 1) Active case ascertainment and verification were performed in order to include every cancer case diagnosed in Fort Chipewyan. Suspected cancer cases reported from the former community physician were verified and possible un-reported cases were identified through communications with the current community physician. As a result, three extra cases were found that had been diagnosed recently in 2005 and 2006. It is worth noting that active case ascertainment was conducted for Fort Chipewyan and not for the other study areas; therefore, a more complete case count for Fort Chipewyan compared to the other communities might have been used. Comparisons between the number of observed cases and the number of expected cases within Fort Chipewyan, however, were conducted using the whole Alberta population as the reference population to calculate the expected number of cases. Cancer registration was over 95% complete for all of Alberta (Appendix 4). Having a more complete case count in Fort Chipewyan would prevent the likelihood of underestimating the cancer rate in Fort Chipewyan.<sup>100</sup>
- 2) The case definition and criteria used for the collection of cholangiocarcinoma cases from the Alberta Cancer Registry were reviewed and revised according to scientific literature and expert advice. Please refer to Appendix 1 for a list of the experts used as external support for this study. For the initial analysis in 2006, only one case of cholangiocarcinoma diagnosed by ultrasound was found in Fort Chipewyan. Using the revised selection criteria in the current study, an additional case was found in the community which was diagnosed by cytology (a type of pathological testing). The same criteria were applied for cases diagnosed in Fort Chipewyan, the other comparison communities, as well as across Alberta. As a result, the total number of cholangiocarcinoma cases increased from one to two for Fort Chipewyan and from 367 to 625 for Alberta as a whole. Detailed information about the revised selection criteria for cholangiocarcinoma is available in Appendix 3.
- 3) The calculations of the expected number of cancer cases were adjusted to account for the high proportion of First Nation residents in Fort Chipewyan and the comparison communities, relative to the total number of First Nations people in the province. Less than 5% of the Alberta population are First Nations people. This has been shown in a previous study<sup>101</sup> and confirmed in the current study. The Fort Chipewyan community, however, has mostly First Nations people who have a different risk of cancer than the general population in Alberta.<sup>27;28</sup>

Making adjustments for the high proportion of First Nations people in Fort Chipewyan was one of the main reasons that the current study findings differ from the initial analysis in 2006. For example, the expected number of cancer cases in Fort Chipewyan was 45 over the 12-year study period without adjustment for First Nations status and was 39 following the adjustment. The 51 cancer cases found in Fort Chipewyan was higher when compared to the 39 expected cases than it was compared to the 45 cases expected prior to adjustment. Similarly, the adjustment has also affected the findings for cholangiocarcinoma and leukemia. Making adjustment for the high proportion of First Nations in Fort Chipewyan can partially account for the lifestyle and socio-economic characteristics of Alberta's First Nations that might be associated with cancer occurrence. The First Nations people in Fort Chipewyan, however, may have unique characteristics that are different from other First Nations communities in Alberta; this cannot be accounted for in the current analysis.

4) Several communities that are located in the northern part of Alberta and close to the Fort Chipewyan community were included for comparison. These communities were selected by Fort Chipewyan community representatives in a meeting with the Nunee Health Board Society in February, 2008. Patterns of cancer occurrence in residents of Fort Chipewyan were compared to those within the populations of the comparison communities. The increased number of cases of biliary tract cancer, leukemia and lymphoma in Fort Chipewyan were not seen in the comparison communities.

5) The study investigated patterns of cancer occurrence by region, as well as by time and by specific cancer type. Cancer rates over two consecutive six-year time periods were compared. An increase in the number of cancer cases found in the most recent six years, such as biliary tract cancers and cancers in the blood and lymphatic system warrant closer monitoring of cancer occurrence in upcoming years. In addition, all three cancers of unknown primary were found in the most recent six years. Further occurrence of these cases requires more rigorous diagnostic investigation. The study population was small and only a few cancer cases were found in each of the specific cancer types. Therefore, the study includes a comparison of the observed and expected rates for all cancers, for major groups of cancer (for example, cancers in the digestive system) and for specific cancer types (for example, cholangiocarcinoma and colon cancer).

### **Evaluation of the degree of an increase**

When comparing the observed number of cancer cases to the expected in the small population of Fort Chipewyan, the degree of an increase was assessed using simulation, as well as confidence intervals of ISIRs at the 99%, 95% and 90% confidence levels. Findings from the simulation were consistent with the findings that were based on the confidence intervals of ISIRs. The calculation of ISIR and its confidence interval is a well established method for comparing the observed and the expected number of cases in a cancer cluster investigation. It is a two-sided statistical test to assess whether the observed is significantly different from the expected, rather than a one-sided statistical test to assess whether the observed is significantly higher than the expected. Although the two-sided test is suitable for general assessment of cancer rates for both the study and comparison populations and for all types of cancers, it may not directly address whether there was an increased rate of cancer

in Fort Chipewyan where the concern of an increase already existed. Therefore, in order to determine whether there is an elevated cancer rate in Fort Chipewyan, the investigation has evaluated the chance of observing the same or a greater number of cancer cases in Fort Chipewyan using the simulation method, supported by the findings based on the confidence intervals of ISIRs.

When confidence intervals are used to describe health data, such as the indirect standardized incidence ratio (ISIR) in this report, a confidence level of 95% is generally used, although 90% or 99% confidence intervals are not uncommon.<sup>23</sup> Testing statistical significance using the 99%CI of the ISIR is less likely to find a significant increase, given that the chance of observing the same or a greater number of cases in Fort Chipewyan needs to be less than 0.5% for statistical significance to be reached. On the other hand, using 90%CI of the ISIR is more likely to find a significant increase, with the tolerable threshold increased to 5% for significance. Using a 99%CI will reduce the chance of false positive and using a 90%CI will reduce the chance of a false negative result. It is important to note that the levels of significance evaluated by using 99%CI, 95%CI or 90%CI are arbitrary distinctions.<sup>23</sup> Whether or not the observed increase in cancer rate in the community was significant is subjective.

To assist interpretation and communication, a simulation approach was used to generate a distribution of possible cancer case counts in Fort Chipewyan. Comparing the observed number to the distribution of all possible case counts, the chance of observing the same or a higher number of cancer cases in Fort Chipewyan were presented for all cancers and for specific cancer sites. Subjective conclusions can be drawn based on the detailed information provided. This approach has avoided using the arbitrary cut off points of 0.5% (based on 99%CI), 2.5% (based on a 95%CI) or 5% (based on a 90%CI) to evaluate the significance of an increase. Some may consider a 2.2% chance of observing eight or more cases (as in the case of cancers of the blood and lymphatic system) as statistically significant, while others may consider a 5.7% chance of observing 10 or more cases (as in the case of lung cancer in Fort Chipewyan) as statistically significant. In order to summarize findings and draw conclusions for this study, an increase was considered statistically significant if there was less than a 5% chance (less than one in 20) of observing the same or higher number of cases in the community. This 5% probability level in the simulation was consistent with a 90%CI of ISIRs. Using this relatively low confidence level ensures that cancer sites with a borderline statistical significant increase can be identified for further assessment and closer monitoring.

The number of cancer cases that occur in a small population like Fort Chipewyan is subject to considerable random variation. The simulation approach used in this study was able to quantitatively demonstrate the variability of possible cancer incidence in the small community and was able to estimate the likelihood that the observed number of cancer cases was higher than the expected number in Fort Chipewyan for all cancers combined and for specific cancer types. Although previous examples of the applications of simulation to evaluate the possible cancer case counts in small study population are limited, some examples have been found in literature.<sup>25;102;103</sup> These applications have shown that simulation can be used as a simple and easily interpretable tool to facilitate explanations of the large random variation of cancer occurrence in a small community to members of the public, as has been previously proposed.<sup>25;26</sup>

## Potential limitations of the study

1) Only cancer patients who were living in Fort Chipewyan at the time of their diagnoses were counted in the analyses. This is standard practice to ensure consistency in the calculation and subsequent comparison of cancer incidence rates among different geographic areas.<sup>15;16</sup> This approach, however, was not able to account for the effect of migration on the cancer rate calculation and, therefore, the cancer incidence rate for Fort Chipewyan may not represent the risk of living in the area.

Cancer usually takes a long time to develop, particularly for cancers like cholangiocarcinoma which are slow-growing tumours that are usually diagnosed in patients over 60 years of age. The cancer incidence cases seen in the present year may be associated with exposures that took place 10, 20 or 30 years ago. Because cancer cases in Fort Chipewyan residents who moved away before the diagnosis were not included, the cancer risk in the study area may have been underestimated. On the other hand, including cancer cases in people who had moved to Fort Chipewyan from other places soon before diagnosis might have overestimated the cancer risk, as the relevant time of exposure for these cancer cases might have occurred before the patients moved to Fort Chipewyan.

The Fort Chipewyan population size was relatively stable over the 12-year study period. Alberta Health and Wellness was able to provide postal code information since 1983 for each cancer patient's residence history in Alberta. The residence history of the 18 suspected cancer cases were reviewed. Of the six suspected cases of cholangiocarcinoma reported by Dr. O'Connor, none were excluded because they were not a resident of Fort Chipewyan at the time diagnosis. Four of the cases were not included because they were not cholangiocarcinoma. Of the 12 suspected cases of colon cancer reported by Dr. O'Connor, two were excluded because they were not Fort Chipewyan residents at the time of diagnosis.

Alberta Health and Wellness also provided residence history information based on postal code for all First Nations people in Alberta since 1983. First Nations people who lived in Fort Chipewyan between 1983 and 2006 were identified. In total, 40 First Nations people were diagnosed with cancer between 1995 and 2006 and were living in Fort Chipewyan at the time of their diagnosis. There were 14 First Nations people diagnosed with cancer during the same study period who lived outside of the community at the time of diagnosis; these 14 cases could not be added directly to the total cancer case count in Fort Chipewyan. This was to ensure that a consistent method was used to count both the cancer incidence cases and the study population, so that the resulting cancer incidence rates are comparable. If the standard used to count cancer cases changes, the standard for counting population must also change. Although a more detailed investigation has not been completed to track residence history at this stage of the investigation, several observations are worth noting. The location of residence at the time of diagnosis for the 14 patients who had moved out of Fort Chipewyan was mostly in Fort McMurray, a major city where the majority of the Northern Lights Health Region population live, including a large number of mobile workers employed in the oil sands industry. The average age at the time of diagnosis was 42 for the 14 patients living outside of Fort Chipewyan, compared to 68 for the 40 cases living in Fort Chipewyan. Cases of blood and lymphatic system cancers or biliary tract cancer that were found in Fort Chipewyan were not found in the 14 patients living outside the community. For the 14 patients living outside the community at the time of

diagnosis, three cases of testis cancer and three cases of brain and other central nervous system cancers were found.

The risk of developing cancer greatly increases with age. If the migration patterns in Fort Chipewyan were more likely to involve young residents moving out to seek employment opportunities elsewhere and then moving back to the community after their retirement, the current rate calculation may have overestimated the cancer risk associated with living in the study area by counting the cancer patients for whom the relevant exposure occurred outside of the area. In addition, according to community members, some community members reside in Fort Chipewyan but travel regularly to work for nearby oil production companies. This evidence suggests the need to investigate further the migration pattern and occupational history of the current and former Fort Chipewyan residents in order to build a better understanding of the risk posed by living in the community.

2) First Nations individuals in the population were identified using a cumulative method, in which a person was classified as First Nation if a portion of his/her Health Insurance Premium was paid by Health Canada in any of the years since 1983. This may have led to an over-counting of people who obtained their First Nations status through marriage. Alternatively, if a non-cumulative method had been used, there would have been problems in under-counting First Nations persons whose health insurance were paid in some years by sources other than Health Canada, such as by their employer. For example, if a First Nations person was diagnosed with cancer in 2005, but was only categorised as First Nations in 2001, 2002, 2003 and 2007 according to health insurance data, this case would have been counted as cancer in First Nations according to the cumulative method used in this study, but not according to a non-cumulative method.

Because cancer concern from the community focused more on the potential environmental exposures or lifestyle factor compared to genetic composition, it was preferable to slightly over-count First Nations people by including those who obtained First Nation status through marriage, rather than to exclude First Nations people whose insurance had been paid by their employer. Although the majority of Fort Chipewyan residents are First Nations, the current study was not limited to the First Nations population. Because concerns about community exposure to environmental contaminants were the impetus for the study, all individuals, regardless of ethnicity, were included in the analyses.

### **Next steps**

The current study has found an increased number of cancer cases compared to the total number expected in Fort Chipewyan. This observed increase could be due to chance, increased detection or increased risk. Regardless of whether or not there is truly an increased risk of cancer in Fort Chipewyan, one immediate step should be to investigate whether or not cancer patients in Fort Chipewyan were exposed to potential causative agents that can be identified and removed, and if the investigation should progress to a more systematic review of exposure and incidence.

Rigorous and on-going monitoring of any new cancer cases in Fort Chipewyan is important; a continuous increase in the cancer rate in the next few years would substantiate the suggestion that there is elevated cancer rate in the community. On the other hand, absence of an increase in the

cancer rate would suggest that the previously observed increase in the community was likely due to random aggregation of cancer cases or increased detection.

The cancer rate calculation in the current study did not account for potential migration patterns of Fort Chipewyan residents and, therefore, the cancer incidence rate in Fort Chipewyan may not represent the risk of living in the area. The next step to study cancer risk in Fort Chipewyan should include identifying geographically-based cohorts of residents who had ever lived in the area and retrospectively follow-up these residents for any cancer incidence. Cancer rates would be compared among sub-population cohorts that are grouped based on the length of time that they have lived in the study area. For example, the cancer rate for residents who had lived in the area for 10 years would be compared to the rate for those who had lived in the area for 20 years. Furthermore, the cancer rate for residents who had lived in the area before the start of follow-up would be compared to the rate for those who moved to the study area in the most recent 10 years.

The lack of understanding about risk factors for most cases of cholangiocarcinoma, the higher incidence rate of this cancer among First Nations people than non-First Nations people, and the recent trend of increasing incidence of cholangiocarcinoma in Alberta, support the need for further investigation into the causes of this cancer. Existing evidence about the variations of cholangiocarcinoma incidence by geography and race offers opportunities for further epidemiologic studies to investigate the risk factors for this cancer. Most published epidemiologic studies on the risk factors of cholangiocarcinoma have focused on patients' pre-existing medical conditions, using record linkage between cancer registry and clinical databases. For future studies, special focus should be given to lifestyle risk factors and environmental exposures.<sup>35</sup> Because cholangiocarcinoma is a rare cancer, further study using national cancer information, rather than provincial cancer registry data would be more likely to provide a representative study population for the generation of etiological hypotheses of this rare cancer.

A cancer cluster investigation, such as the cancer study in Fort Chipewyan, is a form of public health surveillance initiated in response to community concerns about a possible increased cancer risk. A cancer surveillance system is required to closely monitor cancer occurrence and outline potential reasons for changes in cancer risk over time and among different geographic areas. The current study can contribute to the development of an appropriate process for conducting a rapid investigation in response to a community's concerns about cancer risk in Alberta. A high-quality population-based cancer registry is a valuable source of reliable information on cancer incidence in Alberta. Cancer reporting and case verification are the most important steps in the initial stage of a cancer cluster investigation.

## **Conclusions**

The investigation has confirmed a total of two cholangiocarcinoma cases and six colon cancer cases in Fort Chipewyan over the 12-year study period (1995-2006). The observed number of cases of these two types of cancers was within the expected range of cancer occurrence of the community.

The number of cancer cases observed in Fort Chipewyan was higher than expected for all cancers combined and for specific types of cancer, such as biliary tract cancer and cancers in the blood and lymphatic system. In particular, increases were found for biliary tract cancer in men and for lung cancer in women. This increase was based on a small number of cases and could be due to chance or increased detection. The possibility that the increased rate of cancer is due to increased risk in the community, however, cannot be ruled out. An increased number of cases of biliary tract cancers, cancers in the blood and lymphatic system and cancers of unknown primary seen in the most recent six years (2001-2006) compared to the first six years (1995-2000) of the study period warrant closer monitoring of cancer occurrence in upcoming years.

Before epidemiologic studies are used to investigate the causes of the increase, further studies are required in order to evaluate the possible cancer risk posed by living in Fort Chipewyan, by tracking a cohort of residents who have lived in the area within the past 20-30 years.

Whether people living in Fort Chipewyan have an increased risk of developing cancer is still not clear. This study did not investigate the association between the risk of cancer for Fort Chipewyan residents and the effects of possible environmental exposures. Health concerns voiced by the Fort Chipewyan community, the existing evidence about the potential environmental contaminants in the area, along with an absence of a general increase in cancer rates in the comparison communities, justify further investigations that would include the analysis of many potential risk factors, such as lifestyle risk factors, family history, as well as occupational and environmental exposures. Future work on cancer investigation and control needs to be part of the overall assessment of health status in the community.

## **Conflict of Interest**

No extra funding was received for this study. The investigation of a possible cancer cluster in Fort Chipewyan was part of cancer surveillance activities with the purpose of answering the community's concern about cancer rates.

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## Abbreviations

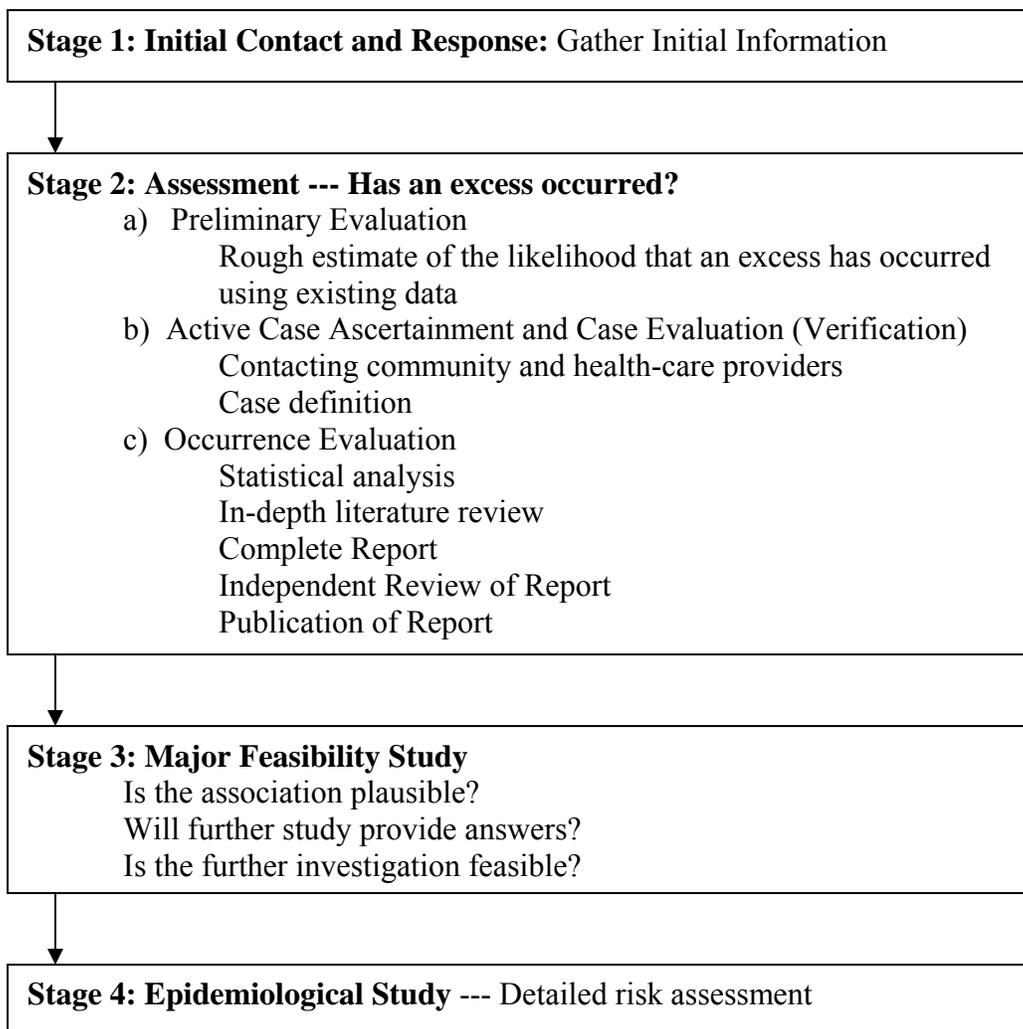
ACR:	Alberta Cancer Registry
ASIR:	Age-Standardized Incidence Rate
ALL:	Acute Lymphoid Leukemia
AML:	Acute Myeloid Leukemia
CBC:	Canadian Broadcasting Corporation
CCR:	Canadian Cancer Registry
CDC:	Centers for Disease Control and Prevention
CLL:	Chronic Lymphoid Leukemia
CML:	Chronic Myeloid Leukemia
CI:	Confidence interval
E:	Expected number of cases
O:	Observed number of cases
IARC:	International Agency for Research on Cancer
ICD:	International Classification of Disease
ICD-O:	International Classification of Disease for Oncology
ISIR:	Indirect Standardized Incidence Ratio
NAACCR:	North American Association of Central Cancer Registries
PAHs:	Polycyclic Aromatic Hydrocarbons
RAMP:	Regional Aquatics Monitoring Program
SEER:	Surveillance Epidemiology and End Results

# Appendices

## Appendix 1: Overview of the study process

The cancer cluster investigation process used in the current study is outlined in the following chart. We have followed the Guidelines for Investigating Clusters of Health Events published by Centers for Disease Control and Prevention (CDC)<sup>1,2</sup> with some variation to suit the current situation in Alberta. The current study corresponds to Stage 2 of the CDC guidelines.

**App-Table 1: Fort Chipewyan Cancer Cluster Investigation Process: modelled after the Guidelines for Investigating Clusters of Health Events published by Centers for Disease Control and Prevention (CDC) in 1990**



A stepwise process and timeline for the current study is also outlined as follows:

1. Preliminary communication and planning (Alberta Health and Wellness, First Nations and Inuit Health Branch of Health Canada and the Alberta Cancer Board) (April 2006)
2. Initial analysis using existing data on cancer incidence, cancer mortality and population estimates (Alberta Cancer Board and Alberta Health and Wellness) (May-June 2006)
3. Presentation of the results to the Fort Chipewyan community (Alberta Cancer Board and Alberta Health and Wellness) (July 2006)
4. Receipt of the names of 18 suspected cancer patients from Dr. O'Connor by the Alberta Cancer Registry (August 2007)
5. Re-establishment of a Working Group and clarify the roles and responsibilities of the Working Group members (December 2007 - January 2008)
6. Meeting with Nunee Health Board Society and community physician to seek clarification on the following issues: (February 2008)
  - propose the cancer cluster study process with the community representatives
  - discuss the study time period
  - discuss the types of cancer to be investigated
  - discuss the validation of reported cases and ascertainment of any unreported cases
  - reach an agreement about the geographical boundaries and population used in the study
  - determine which comparator communities would be used in the study
7. Ascertainment of any unreported cases from the community and community physician and nurses (March-May 2008)
8. Review of case definition and data extraction criteria (November 2007 – May 2008)
9. Validation of the suspected cases reported from Fort Chipewyan (February-May 2008)
10. Literature review (February – July 2008)
  - What is already known about the alleged cancer source?
  - What are the risk factors for cancers of concern?
  - What are the rates of cancers in different population groups?
11. Review of the privacy issues related to cancer patient information, as well as the study finding disclosure process (December 2007 – July 2008)
12. Analyses (February 2007 – September 2008)

13. Prepare a report based on the study findings (July – September 2008)
14. Contact the Nunee Health Board Society about the progress of the report and the selection of peer-reviewers (August 2008)
15. Independent peer-review of the report (October 2008)
16. Contact the community representatives about the communication plan for release of the study to the community (*proposed for October-November 2008*).
17. Present the study findings and recommendations to the community (*proposed for November 2008*)
18. Publish the investigation process and peer-reviewed study results (*proposed for December 2008*)
19. Develop a plan for further study and on-going monitoring (*proposed for January 2009*)

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## Appendix 2: Counting the Fort Chipewyan population

In order to obtain an accurate cancer rate, a consistent method must be used to obtain complete counts for cancer cases and populations, both for the study area (i.e. Fort Chipewyan) and for the reference areas (i.e. Alberta). For population estimates, the Alberta Health Care Insurance Plan database was considered to be the most appropriate data source because it can provide complete annual population estimates based on postal codes for all of the study areas. It can also enable a consistent approach for the collection of both the population data and cancer incidence data using postal codes. Other data sources for population estimates were also explored.

**App-Table 2: Fort Chipewyan Population Count, by Data Source, 1995-2006**

Data Source	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006
<b>Health Care Insurance</b>												
First Nations	940	960	959	950	963	973	1006	980	967	941	954	927
non-First Nations	225	203	198	183	205	195	207	202	187	221	209	187
<b>Total</b>	<b>1165</b>	<b>1163</b>	<b>1157</b>	<b>1133</b>	<b>1168</b>	<b>1168</b>	<b>1213</b>	<b>1182</b>	<b>1154</b>	<b>1162</b>	<b>1163</b>	<b>1114</b>
<b>Municipal Census</b>					1020	1036		1012		1146	744	915
<b>Federal Census</b>		797					902					756

Three main data sources provide population data for the Fort Chipewyan area. These include Alberta Health Care Insurance Plan data,<sup>13</sup> Federal Census data,<sup>104</sup> and Wood Buffalo Municipal Census data.<sup>105</sup> As can be seen in App-Table 2, the reported population varies among the sources. Population figures from these data sources are not directly comparable. Some of the reasons for the discrepancies are:

- 1) The three data sources do not count people in the same way. The Health Care Insurance Plan is an administrative database and is updated on an ongoing basis, while the census is a population survey that provides population counts at a single point in time on the Census Day. Census counts individuals at the place they considered to be their usual residence, where they have spent the majority of the past year.
- 2) The geographic boundaries of Fort Chipewyan may vary amongst the three data sources.
- 3) Discrepancies in counts can also be attributed to factors such as incomplete enumeration and under-coverage in the census survey. The Health Care Insurance Plan covers more than 95% of the Alberta population and is completed annually. According to this Health Care Insurance data, the total population in Fort Chipewyan over the past 12-years has been stable at around 1,200. Municipal Census population data, conversely, are collected fairly irregularly and the response rate is estimated to be between 85% and 90%.<sup>105</sup> The Municipal Census Report represents only the houses that were canvassed which are approximately 85% to 90% of the households in the area. When this is taken into consideration, the population estimates from the Municipal Census and the Health Insurance Plan become much closer. A sudden drop in population can be seen in

the 2005 Municipal Census. When the Planning and Development Department of the Regional Municipality of Wood Buffalo was contacted for an explanation, they stated it was likely due to a lower response rate during 2005. Federal Census data are only updated every five years. These data are collected through in-person interviews or through the completion of on-line or mail-in self-declaration forms. Because Canadian citizens are required by law to fill out the form, there is typically a very high response rate, estimated to be approximately 95% by Stats Canada.<sup>104</sup> Although the coverage and the response rate of the Federal Census are very high at the national-level and most provincial-levels, the coverage in some small rural areas or First Nations Reserves may be low.<sup>106</sup> The coverage could vary substantially from community to community and could be 20%-30% lower than survey estimates.<sup>107</sup>

The client records in the Fort Chipewyan Nursing Station were considered as a potential data source for population estimates of the area. The Nursing Station stores paper charts of residents who have had at least one interaction with the station. These charts could not provide accurate estimates of population counts for the following reasons:

- 1) Only residents who have interacted with the Nursing Station are recorded.
- 2) The clients' charts will remain active unless the person is deceased or has permanently left the community and has filed a notification confirming of their permanent departure. Often the charts remain in the station even though the person has moved to another community. Some clients return after having moved away for a period of time; however, the total length of time away is not recorded. There are usually more charts than the number of clients in Fort Chipewyan at any given time.
- 3) Fort Chipewyan is a community with a diverse and transient population. Transient people like teachers, nurses, police and government workers who reside in the community because of employment may have their charts transferred at their request when they are posted elsewhere. Files for these residents may not be found in the station. Community members often move between Fort McMurray and Fort Chipewyan depending on employment opportunities and place of residence.
- 4) Residents of other communities that have visited the Nursing Station in Fort Chipewyan may also be registered.

In summary, the charts in the Fort Chipewyan Nursing Station may identify a person who has ever been seen in the community clinic, however, there is no reliable method to identify when and how long this person lived in the area. Records of some residents may not be in the station. In contrast, records of some residents from other communities may also be stored in the station. The charts cannot be used to estimate the number of residents in Fort Chipewyan for a specific calendar year.

### **Appendix 3: Case definition and selection criteria for cholangiocarcinoma for epidemiologic studies**

#### Challenges in the classification of cholangiocarcinoma

In Cancer Registries, the International Classification of Diseases for Oncology (ICD-O) is used to code the site (location of the cancer, indicated by ICD-O typography code) and the histology (appearance of the cancer under a microscope, indicated by ICD-O histology code) of cancers.<sup>14</sup> For the initial analysis of cancer rate in Fort Chipewyan, in June 2006, cases of cholangiocarcinoma were extracted from the Alberta Cancer Registry using a combination of anatomic codes (liver C22.0, intrahepatic C22.1 and extrahepatic C24.0) and histology codes (M8160/3, M8180/3, M8162/3, M8260/3, M8481/3, M8500/3, and M8560/3). The histology codes were referenced from a U.S. study on cholangiocarcinoma.<sup>35;108</sup>

The selection criteria of cholangiocarcinoma that was used in the original cancer rate analysis did not include cases of bile duct adenocarcinoma, not otherwise specified (NOS, M8140/3). Following the initial analysis, the classification of bile duct adenocarcinoma was reviewed by a medical oncologist specializing in gastrointestinal tumour diagnosis and treatment. The Data Quality and Management Committee of the Canadian Cancer Registry were consulted. Both the physician and the National Data Quality Committee recommended that bile duct adenocarcinoma be included as cholangiocarcinoma. Furthermore, the definition and case selection criteria for cholangiocarcinoma that was used in recently published epidemiologic studies were reviewed. In light of the new information, it was decided to further clarify the case definition and selection criteria for cholangiocarcinoma and use the revised criteria to select cases of cholangiocarcinoma from the Alberta Cancer Registry for the current study. Using the revised criteria, the total number of cholangiocarcinoma cases extracted from the Alberta Cancer Registry increased from one to two for Fort Chipewyan and from 367 to 625 for Alberta as a whole.

Cholangiocarcinomas are rare and therefore infrequently encountered in clinical practice. There are wide variations in the definition of cholangiocarcinoma in the literature and among clinicians.<sup>17;18</sup> The term “cholangiocarcinoma” originally referred only to primary tumours of the intrahepatic bile ducts (those within the liver) and was not used for extrahepatic bile duct tumours (those outside the liver). More recently, however, the term cholangiocarcinoma has been used to include tumours of the entire biliary tree.<sup>36;109-111</sup> However, in the routine reporting of cancer statistics, (Alberta, Canadian or the International Association of Cancer Registries (IARC)) intrahepatic cholangiocarcinoma is grouped together with liver cancer, whereas extrahepatic cholangiocarcinoma is grouped into other biliary tract cancers. Normally, cancers of the gallbladder and Ampulla of Vater are not considered cholangiocarcinoma.

Histologically, most cholangiocarcinomas are tubular adenocarcinomas but other variants have been described. These include papillary adenocarcinoma, signet-ring carcinoma, squamous cell or mucoepidermoid carcinoma, a spindle cell variant, and a lymphoepithelioma-like form.<sup>36</sup> Restricting the case selection criteria to a limited number of histology types would exclude a substantial number of cases that should be classified as cholangiocarcinoma.

## Development of case definition and selection criteria

Welzel et al applied the classification system published by the World Health Organization (WHO)<sup>112</sup> to develop criteria for selecting cases of cholangiocarcinoma from the U.S. SEER database using a combination of anatomic site (based on ICD-O topography codes) and histology (based on ICD-O morphology codes).<sup>17</sup> Subsequently, similar criteria were used to extract cases of cholangiocarcinoma in three large population-based studies in Denmark and in the U.S.<sup>32;41;113</sup> Extra morphology codes and topography codes were included in these case selection criteria, probably to reflect the type of cases recorded in the cancer databases and the coding practice used in the cancer registries. Using an approach similar to the above three studies, cases of cholangiocarcinoma for the current study were selected from the Alberta Cancer Registry. The criteria include all cases of primary malignant carcinoma of the bile ducts, but exclude cases of sarcoma and lymphoma. However, the anatomic site and the histology of the selected cholangiocarcinoma cases needed to be reviewed in order to correct any possible coding errors. The numbers of cholangiocarcinoma cases diagnosed between 1995 and 2006 in Alberta are listed by their anatomic site and histology in the following App-Table 3 for review.

In total, 625 cases of cholangiocarcinoma were selected from the Alberta Cancer Registry using the revised criteria for the period of 1995-2006. Only 63% of the intrahepatic and 37% of the extrahepatic cholangiocarcinoma cases were coded specifically as cholangiocarcinoma (M8160/3). A considerable number of cases (28%) were coded as adenocarcinoma NOS (M8140/3) of the bile duct. Using the same criteria, 17,208 cases of cholangiocarcinoma could be selected from the Surveillance, Epidemiology, and End Results (SEER) for the period of 1995-2005 (2006 data were not available at the time of this analysis).<sup>114</sup> The SEER database housed data from 17 cancer registries in the US. For 17,208 cases of cholangiocarcinoma selected from SEER, 5346 (31%) were coded as adenocarcinoma, NOS (M8140/3) of the bile duct. This evidence suggests that a substantial number of cholangiocarcinoma cases, such as cases of adenocarcinoma of the bile duct or other histology variants of bile duct carcinoma would be excluded from the analysis if only the limited number of histology types (e.g. M8160) were included in the case selection criteria of cholangiocarcinoma from the cancer registry.

It is worth noting that three quarters of Klatskin tumours (M8162/3) in the Alberta Cancer Registry, 1995-2006, were coded as intrahepatic and the remaining quarter was coded as extrahepatic. A previous study has shown inconsistency in coding Klatskin tumors, not only with different versions of the International Disease Classification (ICD-O) used in cancer registries, but also between medical experts.<sup>18</sup> Analysis of SEER data between 1995 and 2005 also showed that more than two-third of Klatskin tumours were coded as intrahepatic and about a third was coded as extrahepatic. Due to the inconsistencies found in the classification of intrahepatic and extrahepatic cholangiocarcinoma and the small number of cases in this study, intrahepatic and extrahepatic cholangiocarcinoma were analyzed together rather than were analyzed separately.

## Challenges in the diagnosis of cholangiocarcinoma

One case of cholangiocarcinoma diagnosed in a Fort Chipewyan resident was confirmed only by ultrasound, and the accuracy of the diagnosis was questioned. If possible, the diagnosis of cholangiocarcinoma should be confirmed by histologic or cytologic findings. Unlike most human cancers, however, a microscopic diagnosis (based on cytology or histology) of cholangiocarcinoma is often extremely difficult because of tumour location, size, and desmoplastic characteristics.<sup>115</sup> There is a risk in performing biopsies in patients with potentially resectable disease (removable by surgery) because of tumour seeding (spreading tumour cells) along the biopsy track. Furthermore, the sensitivity of detecting cholangiocarcinoma may not be high, even if is based on cytology or histology. Bile cytology obtained by endoscopic retrograde cholangiopancreatography has a sensitivity of only 30-50%, endobiliary brush cytology has a sensitivity of 40-80%, and the endoscopic transpapillary biopsy has a sensitivity of 53-86%.<sup>116</sup> For these reasons, the absence of a tissue diagnosis is common and the diagnosis of cholangiocarcinoma is often based on a combination of clinical symptoms, laboratory findings and imaging studies. On average, 62% of the cholangiocarcinoma cases diagnosed in Alberta during the study period were microscopically verified (confirmed by histology or cytology), compared to 67% for liver (hepatocellular) cancer cases and 96% for colorectal cancers. Including only the microscopically confirmed cases for epidemiologic study of cholangiocarcinoma would have greatly reduced the total number of cases evaluated in all of Alberta. Therefore, in the current study, clinically diagnosed cholangiocarcinomas, without confirmation by a cytological or histological examination, were also included. However, if only the microscopically confirmed cancer cases were included in the analysis, only one case of cholangiocarcinoma could be found in Fort Chipewyan.

### App-Table 3: The Distribution of 625 Cholangiocarcinoma Cases by Anatomic Site and Histology in Alberta, 1995-2006

**Note:** Anatomic Site is the location of the cancer and is classified using ICD-O topography code. Histology is the appearance of the cancer under a microscope and is classified using ICD-O morphology codes

Site	Anatomic Site	Histology (number of cases)
<b>Intrahepatic cholangiocarcinoma</b>	C22.0-Liver	M8160/3 Cholangiocarcinoma (10) M8161/3 Bile duct cystadenocarcinoma (0) M8180/3 Combined hepatocellular carcinoma and cholangiocarcinoma (10)
	C22.1-Intrahepatic Bile duct	M8000/3 Neoplasm, malignant (10) M8001/3 Tumor cells, malignant (2) M8010/3 Carcinoma, NOS (6) M8020/3 Carcinoma, undifferentiated type, NOS (1) M8140/3 Adenocarcinoma, NOS (39) M8160/3 Cholangiocarcinoma (190) M8161/3 Bile duct cystadenocarcinoma (0) M8162/3 Klatskin tumor (30) M8260/3 Papillary adenocarcinoma, NOS (1) M8481/3 Mucin-producing adenocarcinoma (1) M8560/3 Adenosquamous carcinoma (0)
<b>Extrahepatic Cholangiocarcinoma</b>	C24.0-Extrahepatic Bile duct	M8000/3 Neoplasm, malignant (12) M8001/3 Tumor cells, malignant (6) M8010/3 Carcinoma, NOS (23) M8020/3 Carcinoma, undifferentiated type, NOS (1) M8050/3 Papillary carcinoma, NOS (1) M8140/3 Adenocarcinoma, NOS (132) M8141/3 Scirrhus adenocarcinoma (2) M8160/3 Cholangiocarcinoma (116) M8161/3 Bile duct cystadenocarcinoma (0) M8162/3 Klatskin tumor (11) M8240/3 Carcinoid tumor, malignant (1) M8260/3 Papillary adenocarcinoma, NOS (4) M8480/3 Mucinous adenocarcinoma (3) M8481/3 Mucin-producing adenocarcinoma (2) M8500/3 Infiltrating duct carcinoma, NOS (1) M8560/3 Adenosquamous carcinoma (0)
<b>Other cholangiocarcinoma</b>	C24.8-Overlapping intrahepatic and extrahepatic bile ducts	M8140/3 Adenocarcinoma, NOS (5) M8160/3 Cholangiocarcinoma (1)
	C23.9-Gallbladder C24.1-Ampulla of Vater C24.9-biliary tract, NOS, C26.9-Gastrointestinal tract, NOS	M8160/3 Cholangiocarcinoma (4)

## **Appendix 4: Data collection by the Alberta Cancer Registry**

Cancer cases used for this study were selected from the Alberta Cancer Registry (ACR) which is a population-based registry that has a proven high level (over 95%) of completeness for registration of all new primary cancers and cancer deaths occurring in Alberta. The quality of data collected by the registry can be evaluated in four ways: completeness, timeliness, validity and comparability.

### Completeness

Completeness refers to the extent to which all cancers in Alberta are captured by the registry. Cancer is a reportable disease mandated under the Cancer Programs Act in Alberta. Physicians and laboratories throughout the province are required by law to report all new cancer cases to the ACR. A physician who knows or has reason to believe that a patient under his/her care has cancer must report the cancer to the Registry. However, a majority of the new cancer cases are discovered through pathological testing. These cases are registered through laboratories sending the pathology reports to the ACR. When the Cancer Registry receives a pathology report confirming a newly diagnosed cancer, a cancer registration form and a referral form may be sent to the patient's physician to enhance the information for cancer reporting and to confirm if the patient requires a referral to the Alberta Cancer Board (ACB) treatment facility. Often, cancer cases are registered based on pathology reports before the patient is treated in the cancer centre. Occasionally, through human error, pathology reports may not be sent to the Registry, even if the patient is attending a cancer treatment centre. In this situation, the Cancer Registry will be notified by the treatment centre and will subsequently contact the laboratory to obtain the pathology report if the report is not available on the medical chart. Some cancers may be diagnosed clinically without pathology testing. These cancer cases are sporadically reported through medical documents such as scans, x-rays, discharge summaries, operative reports, etc. For cancer cases that are confirmed clinically, the Cancer Registry is very dependant on the reporting from physicians and hospitals. Based on the experiences of the Cancer Registry staff, a majority of the un-registered cancer cases are confirmed by clinical diagnosis and without pathology testing.

In addition, The ACR also obtains electronic files each month from Alberta Vital Statistics for all individuals who have die in the province. Individuals who have die from cancer but their information had not been forwarded to the Registry are identified. When these types of cases are identified, the Cancer Registry is obligated to write to the responsible physician or hospital to confirm the cancer diagnosis.

Furthermore, by reciprocal arrangement with other provincial registries, if an individual had lived in Alberta at the time of diagnosis, but is treated in another province, the information is forwarded to the ACR to ensure that all cases of cancer in Alberta are registered.

The ACR takes every opportunity to ensure that all incident cancers are recorded. In order to quantitatively assess the level of completeness, a case ascertainment project was conducted by the ACR. Any patients who had cancer documented in their hospital discharge summaries in 1994-1996 were identified from the Alberta Health and Wellness health service database. This information was linked with the ACR to determine the number of patients who were diagnosed with cancer but were

not registered. The Registry wrote to the relevant hospital and pathology laboratories to verify these possibly un-registered cases and subsequently complete the registration once the diagnosis was verified. As a result, 348 extra cancer cases were found, which comprised only 1.25% of the total 27,752 cancer cases diagnosed in 1994-1996. Some cancers were more likely to be under-reported than others. For example, the under-ascertainment rate was 5.39% (based on 48 cases) for leukemia and 1.04% (based on 34 cases) for colorectal cancer. These compared to 0.95% (based on 36 cases) for lung cancer and 0.31% (based on 12 cases) for breast cancer. The variations in completeness of case ascertainment between different geographic areas were not assessed.

In brief, the Alberta Cancer Registry (ACR) collects information about new cancers from a variety of information sources, primarily via a passive case-finding method used in combination with active case-finding to ensure the complete registration of all cancer cases in Alberta. The ACR has received a Gold Certification for their completeness of registration from the North American Association of Central Cancer Registries, indicating that the ACR captures greater than 95% of all new cancer cases in the province.

### Timeliness

The second data quality indicator is timeliness. The ACR usually reports incident cases within eighteen months following the end of the calendar year (e.g. 2006 data is complete before June 2008), which is in conformity with the Surveillance Epidemiology and End Results (SEER) standard.<sup>117</sup>

### Validity

The third data quality indicator is validity of the data collected and coded. Validity depends on the documentation available from physician reports, pathology reports and discharge summaries. It also depends on the level of expertise in coding, abstracting, and staging of the data within the Registry. The ACR has numerous data edits within its program to ensure that all information is entered into the database correctly. There are additional data quality reviews performed on data recorded in the Registry by the Canadian Cancer Registry (CCR) and the North American Association of Central Cancer Registries (NAACCR). The Canadian Institute for Health Information and Statistics Canada has produced a Provincial/Territorial Data Quality Report. The report states that the ACR is close to optimal for accuracy and the data provided by the ACR are of high quality.

### Comparability

The final data quality indicator is comparability. The operation of the ACR follows the SEER coding rules and the management guidelines also set up by NAACCR<sup>16;19</sup> to ensure comparability across North America.

## Information Used in This Study

The ACR records detailed information for each cancer patient. The following data types are used in the current study:

### Patient demographics:

- Patient's Name (surname, first, and middle name)

- Sex

- Date of Birth

- Alberta Health Care Insurance Number (Personal Health Number)

### Details collected for the cancer diagnosis

- Diagnosis

- The method of confirming the diagnosis

- The anatomic site and histology type of the cancer

### Time period

- The date of diagnosis

- The date of death

- The date when the case was first reported to the registry

### The geographic location

- The birth place

- The place of residence at the time of diagnosis

- The place of residence at the time of death

- The location of death

## **Appendix 5: Previous investigation of environmental contamination in Fort Chipewyan and the surrounding areas**

Evidence from several previous reports on environmental assessments and from peer-reviewed publications suggests that water contamination in the Athabasca River is due to both natural occurrence and industrial activities. The Athabasca River originates from the melting snow and glaciers of the Rocky Mountains. It travels 1,231 km north east, through several open-pit coal mines, pulp mills, oil and gas deposits, oil refineries and Athabasca open-pit Oil Sands mining, draining into Lake Athabasca at the border between Alberta and the neighbouring province Saskatchewan. Lake Athabasca is itself surrounded by areas that are naturally rich in uranium (Figure 1). Previous environmental assessments have shown that the natural erosion of the exposed oil sands deposits has distributed hydrocarbons throughout the region's river system.<sup>77</sup> Heavy metals and major ions co-occur with elevated levels of naturally occurring petroleum hydrocarbons and complex mixtures of naphthenic acids.<sup>74-76</sup> As part of the mining process, the extraction of bitumen from the oil sands generates large volumes of process-affected waters containing elevated levels of naphthenic acids, salinity and polycyclic aromatic hydrocarbons. The wastewater is stored in tailing ponds; release into the environment is prohibited. The Regional Aquatics Monitoring Program (RAMP) was established in 2000 to assess the health of rivers and lakes in the oil sands region. The 2005 RAMP report did not show negative impact of the Oil Sands development on the regional water system.<sup>118</sup>

In November 2007, a report, funded by the Nunee Health Board Society and written by Kevin P. Timoney,<sup>119</sup> evaluated environmental contaminants in the area surrounding Fort Chipewyan. From 2001 to 2005, concentrations of polycyclic aromatic hydrocarbons (PAHs) rose within the sediment around Lake Athabasca. The report indicated that the treated drinking water in Fort Chipewyan was safe, but described high levels of arsenic, mercury and PAHs in fish, which is the main diet of many people in Fort Chipewyan, especially members of its Aboriginal communities. Dr. Timoney also quoted evidence from previous documents that there has been water contamination in the region since the 1960s, including evidence of oil spills and leaking. No evidence was available to determine how much of the measured chemicals were due to naturally occurring sources or how much resulted from human activity. The study did not make any connection between oil sands developments and the high chemical levels found in sediment, nor did it connect the community's perceptions of elevated cancer and disease rates to chemicals within the sediment.

Cancer usually takes more than 10-20 years to develop. Cancer cases diagnosed after 2000 might be associated with patients' exposure in 1990s, 1980s or even in earlier years. Information on environmental pollutions in the lower Athabasca River region before 2000 was searched. The Northern River Basins Study, conducted in 1991-1996, identified contaminants from the pulp mills, oil sands, atmosphere and uranium mines in the lower Athabasca River region.<sup>78</sup> The study stated that the environmental concentrations of chlorinated organic compounds (mainly from pulp mills), such as dioxins, furans, chlorinate resin acids and chlorophenols, had declined overall since the late 1980s but were still found in detectable levels in sediments and fish. Traces of pulp mill related chemical compounds in sediments from Great Slave Lake, confirmed that these compounds had been transported in great distances downstream. Mercury in walleye fish in the lower Athabasca exceeded Health Canada mercury guidelines. Anecdotal evidence also suggested that fish were tainted

downstream from pulp mills and in the oil sands regions near Fort McMurray. Natural hydrocarbon seeps were evident along the Athabasca River when it passed through massive oil sand open-pit mines and reached the Peace-Athabasca Delta. The report also stated that industrial contaminants in drinking water did not appear to be a public health issue at that time.<sup>78</sup> Soon after the Northern River Basins Study, another study called Northern River Basins Human Health Monitoring Program was conducted. The results were published in 1999.<sup>79</sup> This study examined the prevalence of certain disease and disorders within the Peace and Athabasca river basins, focusing on reproductive health congenital anomalies, respiratory ailments, circulatory diseases, gastrointestinal disorders, endocrine and metabolic disorders, and neurocognitive disorders. This study did not provide specific information about the lower Athabasca region. Furthermore, cancer was not part of the outcome assessment.

The long-term impacts of oil sands in its early stages of the development since 1968 are not clear. A previous publication in the 1980s indicated that Suncor permitted effluent discharge of oil and grease to the Athabasca River at 420 kg per day.<sup>120</sup> Sometimes, operation problems resulted in excessive effluent discharge into the river.<sup>120;121</sup> In addition to water-borne effluents, the two oil sands extraction plants (Suncor and Syncrude) emitted massive amounts of particulates in the atmosphere. Particulates mass emissions from the Suncor powerhouse stack ranged from 547 to 780 kg per hour; the Syncrude Canada main stacks mass emissions ranged from 713 to 1067 kg per hour.<sup>120</sup>

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## Tables

**Table 1: Population distribution by sex, age group, First Nation status for Fort Chipewyan, the comparison communities and Alberta, 1995-2006**

Geographic area	Average population (range) <sup>a</sup> in 1995 - 2006	Age group %			Gender %		First Nations %	
		(0 - 19)	(20 - 54)	(55+)	Male	Female	Yes	No
Fort Chipewyan	1162 (1,114 - 1,213)	36.7	47.5	15.8	51.4	48.6	82.6	17.4
Conklin/Chard/Janvier	679 (622 - 726)	42.9	46.9	10.3	52.6	47.4	65.6	34.4
Fort McMurray	41185 (34,061 - 50,217)	31.8	60.9	7.3	52.0	48.0	6.3	93.7
Fort Vermilion	3409 (3,279 - 3,550)	47.7	41.8	10.4	51.4	48.6	57.1	42.9
Northern Lights Region	64005 (53,556 - 75,547)	36.4	55.6	7.9	51.8	48.2	17.3	82.7
<b>Alberta</b>	<b>2993732 (2713211 - 3297735)</b>	<b>28.5</b>	<b>52.9</b>	<b>18.6</b>	<b>49.9</b>	<b>50.1</b>	<b>4.6</b>	<b>95.4</b>

<sup>a</sup>Average population count over the 12 years period based the data provided from Alberta Health Care Insurance Plan

**Table 2: Population distribution by age group and year for Fort Chipewyan and Alberta, 1995-2006**

Year	Fort Chipewyan				Alberta			
	Population (100%)	Age group(%)			Population (100%)	Age group(%)		
		(0-19)	(20-54)	(55+)		(0-19)	(20-54)	(55+)
<b>1995</b>	1165	37.7	48.1	14.2	2713211	30.3	52.4	17.3
<b>1996</b>	1163	38.3	46.9	14.8	2741029	30.1	52.4	17.5
<b>1997</b>	1157	38.3	46.8	14.9	2791136	29.8	52.5	17.6
<b>1998</b>	1133	38.0	46.5	15.4	2854225	29.6	52.8	17.6
<b>1999</b>	1168	37.5	47.5	15.0	2923236	29.2	53.0	17.8
<b>2000</b>	1168	37.1	47.3	15.7	2967575	28.9	53.1	18.1
<b>2001</b>	1213	38.0	46.7	15.3	3022502	28.5	53.2	18.3
<b>2002</b>	1182	37.1	47.4	15.6	3086432	28.1	53.1	18.8
<b>2003</b>	1154	36.0	47.9	16.1	3134119	27.7	53.1	19.2
<b>2004</b>	1162	35.0	48.2	16.8	3178784	27.3	53.0	19.7
<b>2005</b>	1163	34.8	48.2	16.9	3221989	27.0	52.9	20.1
<b>2006</b>	1114	32.8	48.8	18.4	3297735	26.7	52.8	20.5

**Table 3: Review of the 12 suspected colon cancer cases reported by the former community physician in Fort Chipewyan**

Patient	Suspected cancer	Year of the cancer diagnosis	Confirmed diagnosis	Method of confirmation	Lived in FC at the time of diagnosis <sup>a</sup>	Included in the analysis
1	Colon Cancer	Before 1995	Cervical cancer	Pathology	No	No -- Not FC residents at the time of diagnosis
2	Colon Cancer	1995 - 2006	Colon cancer	Pathology	Yes	Yes -- As colon cancer
3	Colon Cancer	1995 - 2006	Colon cancer	Pathology	Yes	Yes -- As colon cancer
4	Colon Cancer	1995 - 2006	Rectum cancer	Pathology	No	No -- Not FC residents at the time of diagnosis
5	Colon Cancer	1995 - 2006	Cancer with unknown primary site	Pathology	Yes	Yes -- As cancer of unknown primary
6	Colon Cancer	1995 - 2006	Colon cancer	Pathology	No	No -- Not FC residents at the time of diagnosis
7	Colon Cancer	1995 - 2006	Colon cancer	Pathology	Yes	Yes -- As colon cancer
8	Colon Cancer	1995 - 2006	non-Hodgkin lymphoma	Pathology	Yes	Yes -- As non-Hodgkin lymphoma
9	Colon Cancer	1995 - 2006	Colon or Rectosigmoid Junction cancer	Death Certificate	No	No -- Not FC residents at the time of diagnosis
10	Colon Cancer	1995 - 2006	Rectum cancer	Pathology	Yes	Yes -- As rectum cancer
11	Colon Cancer	After 2006	Colon cancer	Pathology	Yes	No -- Not diagnosed between 1995 and 2006
12	Colon Cancer	After 2006	Colon tumour, not invasive cancer	Pathology	Yes	No -- Not diagnosed with invasive cancer

<sup>a</sup> Information on history of residency was available from Alberta Health Care Insurance Plan after 1983

**Table 4: Review of the six suspected cholangiocarcinoma cases reported by the former community physician in Fort Chipewyan**

Patient	Suspected cancer	Year of the cancer diagnosis	Confirmed diagnosis	Method of confirmation	Lived in FC at the time of diagnosis <sup>a</sup>	Included in the analysis
1	Cholangiocarcinoma	Before 1995	Pancreas cancer	Pathology	Yes	No -- Not diagnosed between 1995 and 2006
2	Cholangiocarcinoma	1995 - 2006	Cholangiocarcinoma	Radiology	Yes	Yes – As cholangiocarcinoma
3	Cholangiocarcinoma	1995 - 2006	Cholangiocarcinoma	Pathology	Yes	Yes – As cholangiocarcinoma
4	Cholangiocarcinoma	1995 - 2006	Liver cancer	Radiology	Yes	Yes -- As liver cancer
5	Cholangiocarcinoma	1995 - 2006	Cancer with metastasis to liver, primary site unknown	Radiology	Yes However, mailing address in Ontario	Yes -- As cancer of unknown primary to be inclusive
6	Cholangiocarcinoma	NA	Heart disease	NA	NA	No -- Not diagnosed with cancer

<sup>a</sup> Information on history of residency was available from Alberta Health Care Insurance Plan after 1983

**Table 5: Number of cancer cases <sup>a</sup> and Age-Standardized Incidence Rates (ASIRs) per 100,000<sup>b</sup> for Fort Chipewyan, the comparison communities and Alberta, 1995-2006**

Geographic area	1995-2000		2001-2006		1995-2006	
	Case	Rate(95% CI)	Case	Rate(95% CI)	Case	Rate(95% CI)
<b>Fort Chipewyan</b>	22	459 (285-700)	29	490 (326-709)	51	475 (352-626)
<b>Conklin/Chard/Janvier</b>	3	79 (14-244)	8	316 (132-637)	11	234 (109-439)
<b>Fort McMurray</b>	363	346 (297-400)	484	312 (271-357)	847	325 (293-359)
<b>Fort Vermilion</b>	31	275 (183-396)	37	322 (221-452)	68	301 (230-387)
<b>Northern Lights Region</b>	564	343 (309-379)	754	339 (309-371)	1318	340 (317-364)
<b>Alberta</b>	<b>61,149</b>	<b>389 (386-392)</b>	<b>76,330</b>	<b>404 (401-407)</b>	<b>137,479</b>	<b>397 (395-399)</b>

<sup>a</sup> Excludes cases of Non-Melanoma Skin Cancer.

<sup>b</sup> 1991 Canada population was used as the standard population

**Table 6: Number of cancer cases and Age Specific Incidence Rates per 100,000 by age group for Fort Chipewyan, the comparison communities and Alberta, 1995-2006**

Geographic area	Age 0-19		Age 20-54		Age 55+	
	Case	Crude rate <sup>a</sup>	Case	Crude rate <sup>a</sup>	Case	Crude rate <sup>a</sup>
<b>Fort Chipewyan</b>			9	135.8	42	1912.6
<b>Conklin/Chard/Janvier</b>	1	28.6	3	78.5	7	835.3
<b>Fort McMurray</b>	16	10.2	482	160.1	349	967.4
<b>Fort Vermilion</b>	4	20.5	18	105.1	46	1077.0
<b>Northern Lights Region</b>	38	13.6	620	145.1	660	1081.2
<b>Alberta</b>	<b>1589</b>	<b>15.5</b>	<b>31841</b>	<b>167.6</b>	<b>104049</b>	<b>1556.1</b>

a Crude rate/100,000 =( total cases in 1995-2006)\*100,000 / (total person years in 1995-2006)

**Table 7: Number of cancer cases<sup>a</sup> and Age Standardized Incidence Rates (ASIRs) per 100,000<sup>b</sup> by sex for Fort Chipewyan, the comparison communities and Alberta, 1995-2006**

Geographic area	Men		Women		Total	
	Case	ASIR(95% CI)	Case	ASIR(95% CI)	Case	ASIR(95% CI)
<b>Fort Chipewyan</b>	33	583 (398-825)	18	354 (207-566)	51	475 (352-626)
<b>Conklin/Chard/Janvier</b>	9	349 (148-696)	2	66 (8-238)	11	234 (109-439)
<b>Fort McMurray</b>	413	345 (294-402)	434	312 (272-356)	847	325 (293-359)
<b>Fort Vermilion</b>	41	351 (246-486)	27	235 (150-349)	68	301 (230-387)
<b>Northern Lights Region</b>	677	378 (342-417)	641	305 (277-336)	1,318	340 (317-364)
<b>Alberta</b>	<b>71,408</b>	<b>454 (451-458)</b>	<b>66,071</b>	<b>354 (352-357)</b>	<b>137,479</b>	<b>397 (395-399)</b>

<sup>a</sup> Excludes non-melanoma skin cancer cases.

<sup>b</sup> 1991 Canadian population was used as the standard population

**Table 8: Age Standardized Incidence Rates per 100,000<sup>a</sup> for all cancers and for specific type of cancers, comparing First Nations with non-First Nations in Alberta, 1995-2006**

Type of cancers	First Nations		Non-First Nations	
	Case	ASIR (95% CI)	Case	ASIR (95% CI)
<b>Cholangiocarcinoma</b>	20	4.7 (2.5-8.0)↑	605	1.8 (1.7-1.9)
<b>Leukemia</b>	79	9.2 (6.6-12.5)↓	4,400	13.0 (12.6-13.4)
<b>Colon</b>	147	29.0 (23.6-35.2)	10,485	31.0 (30.5-31.7)
<b>Lung</b>	246	52.0 (44.7-60.2)	17,246	51.9 (51.1-52.7)
<b>Breast</b>	336	41.9 (36.5-48.0)↓	19,610	55.4 (54.6-56.2)
<b>All cancers<sup>b</sup></b>	2,024	334.6 (316.6-353.5)↓	135,374	398.9 (395.8-401.1)

<sup>a</sup>1991 Canada population was used as the standard population

<sup>b</sup>Excluding cases of Non-Melanoma Skin Cancer and excluding 81(0.06%) cancer cases for which insufficient information was available to determine their First Nation status

↑:significant higher, FNs versus Non-FNs; ↓:significant lower, FNs versus Non-FNs

**Table 9: Observed (O) versus Expected (E) number of cancer cases and the Indirect Standardized Incidence Ratios (ISIRs) for Fort Chipewyan and the comparison communities, 1995-2006**

Using Alberta population as the reference population, adjusted by age, sex and First Nations status and calendar year

Cance site and sub-site	Fort Chipewyan		Conklin/Chard/Janvier		Fort McMurray		Fort Vermilion		Northern Lights Region	
	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)
<b>Digestive system</b>	14/9.3	1.51 ( 0.83 - 2.53 )	4/3.1	1.29 ( 0.35 - 3.30 )	142/150.3	0.94 ( 0.80 - 1.11 )	17/16.6	1.03 ( 0.60 - 1.64 )	250/251.5	0.99 ( 0.87 - 1.13 )
<b>Esophagus</b>	1/0.5	1.96 ( 0.05 - 10.89 )	0/0.1		5/7.0	0.72 ( 0.23 - 1.68 )	1/0.8	1.24 ( 0.03 - 6.94 )	9/11.8	0.76 ( 0.35 - 1.45 )
<b>Biliary tract cancer</b>	3/0.7	4.48 ( 0.92 - 13.08 )	0/0.2		4/6.1	0.66 ( 0.18 - 1.68 )	1/0.9	1.11 ( 0.03 - 6.21 )	10/11.6	0.86 ( 0.41 - 1.58 )
<b>Cholangiocarcinoma</b>	2/0.4	4.78 ( 0.58 - 17.27 )	0/0.1		3/3.2	0.93 ( 0.19 - 2.72 )	1/0.5	1.89 ( 0.05 - 10.52 )	7/6.5	1.07 ( 0.43 - 2.21 )
<b>Gallbladder</b>	0/0.2		0/0.0		0/1.8		0/0.2		1/3.2	0.31 ( 0.01 - 1.73 )
<b>Other biliary tract</b>	1/0.1	10.97 ( 0.28 - 61.11 )	0/0.0		1/1.1	0.93 ( 0.02 - 5.17 )	0/0.1		2/1.9	1.06 ( 0.13 - 3.81 )
<b>Liver</b>	1/0.4	2.25 ( 0.06 - 12.53 )	0/0.2		4/8.5	0.47 ( 0.13 - 1.20 )	0/0.8		11/13.7	0.81 ( 0.40 - 1.44 )
<b>Pancreas</b>	0/1.0		0/0.3		17/16.8	1.01 ( 0.59 - 1.62 )	4/1.9	2.10 ( 0.57 - 5.38 )	27/28.4	0.95 ( 0.63 - 1.38 )
<b>Colorectal</b>	9/5.2	1.74 ( 0.79 - 3.29 )	4/1.8	2.25 ( 0.61 - 5.76 )	82/88.7	0.92 ( 0.74 - 1.15 )	10/9.6	1.04 ( 0.50 - 1.91 )	149/147.2	1.01 ( 0.86 - 1.19 )
<b>Colon</b>	6/3.3	1.84 ( 0.68 - 4.01 )	2/1.1	1.86 ( 0.23 - 6.74 )	54/54.0	1.00 ( 0.75 - 1.30 )	8/6.1	1.32 ( 0.57 - 2.60 )	98/90.7	1.08 ( 0.88 - 1.32 )
<b>Rectum</b>	1/1.2	0.82 ( 0.02 - 4.58 )	1/0.4	2.25 ( 0.06 - 12.55 )	14/25.1	0.56 ( 0.31 - 0.94 )	0/2.4		24/40.0	0.60 ( 0.38 - 0.89 )
<b>Rectosigmoid junction</b>	2/0.7	2.79 ( 0.34 - 10.09 )	1/0.3	3.84 ( 0.10 - 21.39 )	14/9.6	1.46 ( 0.80 - 2.45 )	2/1.1	1.74 ( 0.21 - 6.30 )	27/16.5	1.64 ( 1.08 - 2.38 )**
<b>Lung</b>	10/5.6	1.80 ( 0.86 - 3.31 )	1/2.0	0.50 ( 0.01 - 2.77 )	102/89.0	1.15 ( 0.93 - 1.39 )	11/10.6	1.04 ( 0.52 - 1.86 )	166/151.5	1.10 ( 0.94 - 1.28 )
<b>Breast</b>	3/4.6	0.66 ( 0.14 - 1.92 )	1/2.1	0.47 ( 0.01 - 2.64 )	134/158.8	0.84 ( 0.71 - 1.00 )	3/10.9	0.28 ( 0.06 - 0.80 )	188/229.7	0.82 ( 0.71 - 0.94 )
<b>Prostate</b>	5/6.3	0.80 ( 0.26 - 1.86 )	1/2.3	0.43 ( 0.01 - 2.39 )	94/116.7	0.81 ( 0.65 - 0.99 )	11/13.2	0.84 ( 0.42 - 1.49 )	159/193.8	0.82 ( 0.70 - 0.96 )
<b>Cervix Uteri</b>	1/1.1	0.94 ( 0.02 - 5.22 )	0/0.4		24/21.9	1.10 ( 0.70 - 1.63 )	0/1.8		30/33.9	0.88 ( 0.60 - 1.26 )
<b>Kidney</b>	3/1.7	1.81 ( 0.37 - 5.29 )	0/0.6		28/28.7	0.98 ( 0.65 - 1.41 )	3/2.8	1.06 ( 0.22 - 3.10 )	43/46.2	0.93 ( 0.67 - 1.25 )
<b>Blood and lymphatic system</b>	8/3.4	2.37 ( 1.02 - 4.68 )**	1/1.5	0.66 ( 0.02 - 3.68 )	97/104.0	0.93 ( 0.76 - 1.14 )	8/8.0	1.00 ( 0.43 - 1.97 )	153/158.1	0.97 ( 0.82 - 1.13 )
<b>Non-Hodgkin Lymphoma</b>	3/1.3	2.39 ( 0.49 - 6.98 )	0/0.5		43/40.9	1.05 ( 0.76 - 1.41 )	1/2.9	0.34 ( 0.01 - 1.90 )	61/60.7	1.01 ( 0.77 - 1.29 )
<b>Leukemia</b>	4/1.2	3.32 ( 0.91 - 8.51 )	0/0.6		30/33.5	0.90 ( 0.60 - 1.28 )	5/3.0	1.67 ( 0.54 - 3.89 )	55/53.1	1.04 ( 0.78 - 1.35 )
<b>Soft tissues</b>	2/0.3	6.28 ( 0.76 - 22.68 )	0/0.1		5/6.8	0.74 ( 0.24 - 1.72 )	0/0.5		10/10.4	0.96 ( 0.46 - 1.77 )
<b>Endometrium</b>	1/0.7	1.50 ( 0.04 - 8.35 )	0/0.3		22/25.5	0.86 ( 0.54 - 1.31 )	1/1.8	0.56 ( 0.01 - 3.13 )	32/37.0	0.86 ( 0.59 - 1.22 )
<b>Brain</b>	1/0.4	2.59 ( 0.07 - 14.45 )	1/0.3	3.99 ( 0.10 - 22.24 )	20/21.9	0.91 ( 0.56 - 1.41 )	2/1.4	1.47 ( 0.18 - 5.30 )	29/31.6	0.92 ( 0.61 - 1.32 )
<b>Unknown Primary</b>	3/1.2	2.56 ( 0.53 - 7.47 )	0/0.4		13/16.6	0.78 ( 0.42 - 1.34 )	1/2.0	0.49 ( 0.01 - 2.74 )	29/29.2	0.99 ( 0.67 - 1.43 )
<b>Others</b>	0/4.6		2/2.3	0.88 ( 0.11 - 3.19 )	162/190.3	0.85 ( 0.73 - 0.99 )	11/12.2	0.90 ( 0.45 - 1.61 )	225/274.5	0.82 ( 0.72 - 0.93 )
<b>All cancers<sup>a</sup></b>	51/38.9	1.31 ( 0.98 - 1.72 )	11/15.4	0.72 ( 0.36 - 1.28 )	847/931.3	0.91 ( 0.85 - 0.97 )	68/81.8	0.83 ( 0.65 - 1.05 )	1318/1448.9	0.91 ( 0.86 - 0.96 )

<sup>a</sup> Excluding cases of Non-Melanoma Skin Cancer

\*\* Statistically significantly increase based on 95%CI of ISIR

**Table 10: Observed (O) versus Expected (E) number of cancer cases and Indirect Standardized Incidence Ratios (ISIRs) for men and women in Fort Chipewyan, 1995-2006**

Using Alberta population as the reference population, adjusted by age and First Nation status and calendar year

Cancer site and sub-site	Men		Women		Total		
	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)	(O)	(E)	ISIR (95% CI)
<b>Digestive system</b>	12/6.1	1.98 ( 1.02 - 3.46)**	2/3.2	0.62 ( 0.08 - 2.25 )	14/9.3	9.3	1.51 ( 0.83 - 2.53 )
<b>Esophagus</b>	1/0.5	2.20 ( 0.06 - 12.26 )	0/0.1		1/0.5	0.5	1.96 ( 0.05 - 10.89 )
<b>Biliary tract cancer</b>	3/0.4	7.02 ( 1.45 - 20.51)**	0/0.2		3/0.7	0.7	4.48 ( 0.92 - 13.08 )
<b>Cholangiocarcinoma</b>	2/0.3	6.60 ( 0.80 - 23.84 )	0/0.1		2/0.4	0.4	4.78 ( 0.58 - 17.27 )
<b>Other biliary tract</b>	1/0.1	18.89 ( 0.48 - 105.23 )	0/0		1/0.1	0.1	10.97 ( 0.28 - 61.11 )
<b>Liver</b>	1/0.3	2.93 ( 0.07 - 16.32 )	0/0.1		1/0.4	0.4	2.25 ( 0.06 - 12.53 )
<b>Colorectal</b>	7/3.3	2.11 ( 0.85 - 4.34 )	2/1.9	1.07 ( 0.13 - 3.88 )	9/5.2	5.2	1.74 ( 0.79 - 3.29 )
<b>Colon</b>	5/2	2.52 ( 0.82 - 5.89 )	1/1.3	0.79 ( 0.02 - 4.37 )	6/3.3	3.3	1.84 ( 0.68 - 4.01 )
<b>Rectum</b>	0/0.8		1/0.4	2.30 ( 0.06 - 12.83 )	1/1.2	1.2	0.82 ( 0.02 - 4.58 )
<b>Rectosigmoid junction</b>	2/0.6	3.56 ( 0.43 - 12.87 )	0/0.2		2/0.7	0.7	2.79 ( 0.34 - 10.09 )
<b>Lung</b>	3/3.5	0.85 ( 0.17 - 2.47 )	7/2	3.47 ( 1.40 - 7.15 )**	10/5.6	5.6	1.80 ( 0.86 - 3.31 )
<b>Breast</b>	0/0		3/4.6	0.66 ( 0.14 - 1.92 )	3/4.6	4.6	0.66 ( 0.14 - 1.92 )
<b>Prostate</b>	5/6.3	0.80 ( 0.26 - 1.86 )	0/0		5/6.3	6.3	0.80 ( 0.26 - 1.86 )
<b>Cervix Uteri</b>	0/0		1/1.1	0.94 ( 0.02 - 5.22 )	1/1.1	1.1	0.94 ( 0.02 - 5.22 )
<b>Kidney</b>	3/1.1	2.69 ( 0.56 - 7.87 )	0/0.5		3/1.7	1.7	1.81 ( 0.37 - 5.29 )
<b>Blood and lymphatic system</b>	6/2.1	2.91 ( 1.07 - 6.34)**	2/1.3	1.53 ( 0.18 - 5.52 )	8/3.4	3.4	2.37 ( 1.02 - 4.68)**
<b>Non-hodgkin Lymphoma</b>	2/0.7	2.70 ( 0.33 - 9.75 )	1/0.5	1.94 ( 0.05 - 10.82 )	3/1.3	1.3	2.39 ( 0.49 - 6.98 )
<b>Leukemia</b>	3/0.7	4.29 ( 0.88 - 12.53 )	1/0.5	1.98 ( 0.05 - 11.05 )	4/1.2	1.2	3.32 ( 0.91 - 8.51 )
<b>Soft tissues</b>	2/0.3	7.42 ( 0.90 - 26.81 )	0/0		2/0.3	0.3	6.28 ( 0.76 - 22.68 )
<b>Endometrium</b>	0/0		1/0.7	1.50 ( 0.04 - 8.35 )	1/0.7	0.7	1.50 ( 0.04 - 8.35 )
<b>Brain</b>	0/0.2		1/0.1	7.08 ( 0.18 - 39.47 )	1/0.4	0.4	2.59 ( 0.07 - 14.45 )
<b>Unknown Primary</b>	2/0.5	3.89 ( 0.47 - 14.06 )	1/0.7	1.52 ( 0.04 - 8.45 )	3/1.2	1.2	2.56 ( 0.53 - 7.47 )
<b>All cancers<sup>a</sup></b>	33/22.8	1.45 ( 1.00 - 2.04)**	18/16.2	1.11 ( 0.66 - 1.76 )	51/38.9	38.9	1.31 ( 0.98 - 1.72 )

<sup>a</sup> Excluding cases of Non-Melanoma Skin Cancer

\*\* Statistically significantly increase based on 95% CI of ISIR

**Table 11: Observed (O) versus Expected (E) number of cancer cases and Indirect Standardized Incidence Ratios (ISIRs) for Fort Chipewyan in the two consecutive six-year time periods, 1995-2000 and 2001-2006**

Using Alberta population as the reference population, adjusted by age, sex and First Nation status and calendar year

Cance site and sub-site	1995 - 2000		2001 - 2006		1995 - 2006	
	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)	(O)/(E)	ISIR (95% CI)
<b>Digestive system</b>	7/4.1	1.73 ( 0.69 - 3.56 )	7/5.2	1.34 ( 0.54 - 2.77 )	14/9.3	1.51 ( 0.83 - 2.53 )
<b>Esophagus</b>	1/0.3	3.75 ( 0.10 - 20.91 )	0/0.2		1/0.5	1.96 ( 0.05 - 10.89 )
<b>Biliary tract cancer</b>	0/0.2		3/0.5	5.99 ( 1.24 - 17.51 )**	3/0.7	4.48 ( 0.92 - 13.08 )
<b>Cholangiocarcinoma</b>	0/0.1		2/0.3	7.00 ( 0.85 - 25.28 )	2/0.4	4.78 ( 0.58 - 17.27 )
<b>Other biliary tract</b>	0/0.0		1/0.1	11.98 ( 0.30 - 66.73 )	1/0.1	10.97 ( 0.28 - 61.11 )
<b>Liver</b>	0/0.2		1/0.3	3.50 ( 0.09 - 19.48 )	1/0.4	2.25 ( 0.06 - 12.53 )
<b>Colorectal</b>	6/2.1	2.84 ( 1.04 - 6.18 )**	3/3.1	0.98 ( 0.20 - 2.85 )	9/5.2	1.74 ( 0.79 - 3.29 )
<b>Colon</b>	5/1.3	3.75 ( 1.22 - 8.75 )**	1/1.9	0.52 ( 0.01 - 2.90 )	6/3.3	1.84 ( 0.68 - 4.01 )
<b>Rectum</b>	0/0.5		1/0.7	1.38 ( 0.03 - 7.67 )	1/1.2	0.82 ( 0.02 - 4.58 )
<b>Rectosigmoid junction</b>	1/0.3	3.45 ( 0.09 - 19.20 )	1/0.4	2.35 ( 0.06 - 13.08 )	2/0.7	2.79 ( 0.34 - 10.09 )
<b>Lung</b>	5/2.6	1.89 ( 0.61 - 4.41 )	5/2.9	1.71 ( 0.56 - 4.00 )	10/5.6	1.80 ( 0.86 - 3.31 )
<b>Breast</b>	1/2.1	0.49 ( 0.01 - 2.72 )	2/2.5	0.80 ( 0.10 - 2.88 )	3/4.6	0.66 ( 0.14 - 1.92 )
<b>Prostate</b>	3/2.4	1.24 ( 0.26 - 3.63 )	2/3.8	0.52 ( 0.06 - 1.88 )	5/6.3	0.80 ( 0.26 - 1.86 )
<b>Cervix Uteri</b>	1/0.5	1.94 ( 0.05 - 10.82 )	0/0.6		1/1.1	0.94 ( 0.02 - 5.22 )
<b>Kidney</b>	2/0.6	3.60 ( 0.44 - 13.01 )	1/1.1	0.91 ( 0.02 - 5.06 )	3/1.7	1.81 ( 0.37 - 5.29 )
<b>Blood and lymphatic system</b>	1/1.2	0.84 ( 0.02 - 4.66 )	7/2.2	3.22 ( 1.29 - 6.63 )**	8/3.4	2.37 ( 1.02 - 4.68 )**
<b>Non-hodgkin Lymphoma</b>	0/0.4		3/0.8	3.58 ( 0.74 - 10.47 )	3/1.3	2.39 ( 0.49 - 6.98 )
<b>Leukemia</b>	1/0.5	1.88 ( 0.05 - 10.45 )	3/0.7	4.47 ( 0.92 - 13.07 )	4/1.2	3.32 ( 0.91 - 8.51 )
<b>Soft tissues</b>	1/0.2	5.89 ( 0.15 - 32.84 )	1/0.1	6.72 ( 0.17 - 37.42 )	2/0.3	6.28 ( 0.76 - 22.68 )
<b>Endometrium</b>	0/0.3		1/0.4	2.71 ( 0.07 - 15.10 )	1/0.7	1.50 ( 0.04 - 8.35 )
<b>Brain</b>	1/0.2	5.18 ( 0.13 - 28.85 )	0/0.2		1/0.4	2.59 ( 0.07 - 14.45 )
<b>Unknown Primary</b>	0/0.5		3/0.6	4.74 ( 0.98 - 13.84 )	3/1.2	2.56 ( 0.53 - 7.47 )
<b>All cancers<sup>a</sup></b>	22/17.0	1.29 ( 0.81 - 1.96 )	29/21.9	1.32 ( 0.89 - 1.90 )	51/38.9	1.31 ( 0.98 - 1.72 )

<sup>a</sup> Excluding cases of Non-Melanoma Skin Cancer

\*\* Statistically significantly increase based on 95%CI of ISIR

**Table 12: Cancer sites with a statistically significant increase in the number of observed incidence cases in Fort Chipewyan, 1995-2006, comparing findings from the 99% CIs, 95% CIs and 90% CIs of ISIRs and the simulation**

Cancer site and sub-site	(O)/(E)	ISIR	(99% CI)	(95% CI)	(90% CI)	Chance of observing the same or higher number of cases, (O)<=(E)
Digestive system	14 / 9.3	1.51	( 0.67-2.90 )	( 0.83 - 2.53 )	( 0.91 - 2.36 )	8.8%
Esophagus	1 / 0.5	1.96	( 0.01-14.53 )	( 0.05 - 10.89 )	( 0.10 - 9.28 )	40.1%
Biliary tract cancer	3 / 0.7	4.48	( 0.50-16.38 )	( 0.92 - 13.08 )	( 1.22 - 11.57 )*	3.0%*
Cholangiocarcinoma	2 / 0.4	4.78	( 0.25-22.17 )	( 0.58 - 17.27 )	( 0.85 - 15.05 )	6.7%
Other biliary tract	1 / 0.1	10.97	( 0.05-81.49 )	( 0.28 - 61.11 )	( 0.56 - 52.03 )	8.7%
Liver	1 / 0.4	2.25	( 0.01-16.71 )	( 0.06 - 12.53 )	( 0.12 - 10.67 )	36.0%
Colorectal	9 / 5.2	1.74	( 0.60-3.86 )	( 0.79 - 3.29 )	( 0.91 - 3.03 )	8.0%
Colon	6 / 3.3	1.84	( 0.47-4.81 )	( 0.68 - 4.01 )	( 0.80 - 3.64 )	11.1%
Rectum	1 / 1.2	0.82	( 0.00-6.11 )	( 0.02 - 4.58 )	( 0.04 - 3.90 )	70.4%
Rectosigmoid junction	2 / 0.7	2.79	( 0.14-12.95 )	( 0.34 - 10.09 )	( 0.50 - 8.79 )	16.1%
Lung	10 / 5.6	1.80	( 0.67-3.85 )	( 0.86 - 3.31 )	( 0.98 - 3.05 )	5.7%
Breast	3 / 4.6	0.66	( 0.07-2.41 )	( 0.14 - 1.92 )	( 0.18 - 1.70 )	83.3%
Prostate	5 / 6.3	0.80	( 0.17-2.26 )	( 0.26 - 1.86 )	( 0.31 - 1.68 )	75.0%
Cervix Uteri	1 / 1.1	0.94	( 0.00-6.97 )	( 0.02 - 5.22 )	( 0.05 - 4.45 )	65.6%
Kidney	3 / 1.7	1.81	( 0.20-6.62 )	( 0.37 - 5.29 )	( 0.49 - 4.68 )	23.1%
Blood and lymphatic system	8 / 3.4	2.37	( 0.76-5.51 )	( 1.02 - 4.68 )**	( 1.18 - 4.28 )*	2.2%**
Non-hodgkin Lymphoma	3 / 1.3	2.39	( 0.27-8.74 )	( 0.49 - 6.98 )	( 0.65 - 6.17 )	13.3%
Leukemia	4 / 1.2	3.32	( 0.56-10.46 )	( 0.91 - 8.51 )	( 1.13 - 7.60 )*	3.4%*
Soft tissues	2 / 0.3	6.28	( 0.32-29.11 )	( 0.76 - 22.68 )	( 1.12 - 19.76 )*	4.1%*
Endometrium	1 / 0.7	1.50	( 0.01-11.13 )	( 0.04 - 8.35 )	( 0.08 - 7.11 )	48.8%
Brain	1 / 0.4	2.59	( 0.01-19.28 )	( 0.07 - 14.45 )	( 0.13 - 12.31 )	32.0%
Unknown Primary	3 / 1.2	2.56	( 0.29-9.35 )	( 0.53 - 7.47 )	( 0.70 - 6.61 )	11.5%
<b>All cancers<sup>a</sup></b>	<b>51 / 38.9</b>	<b>1.31</b>	<b>( 0.89-1.86 )</b>	<b>( 0.98 - 1.72 )</b>	<b>( 1.02 - 1.65 )*</b>	<b>3.5%*</b>

<sup>a</sup> Excluding cases of Non-Melanoma Skin Cancer

\* Statistically significantly increase based on 90%CI of ISIR or less than 5% chance of (O)<=(E)

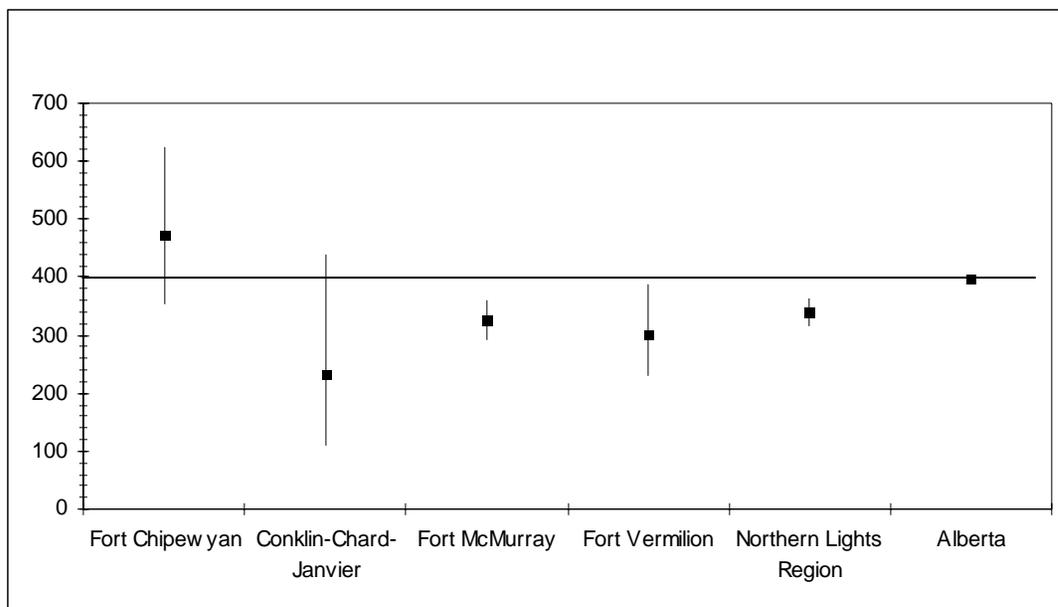
\*\* Statistically significantly increase based on 95%CI of ISIR or less than 2.5% chance of (O)<=(E)

## Figures

**Figure 1: Geographical location of Fort Chipewyan and the comparison communities in Alberta**

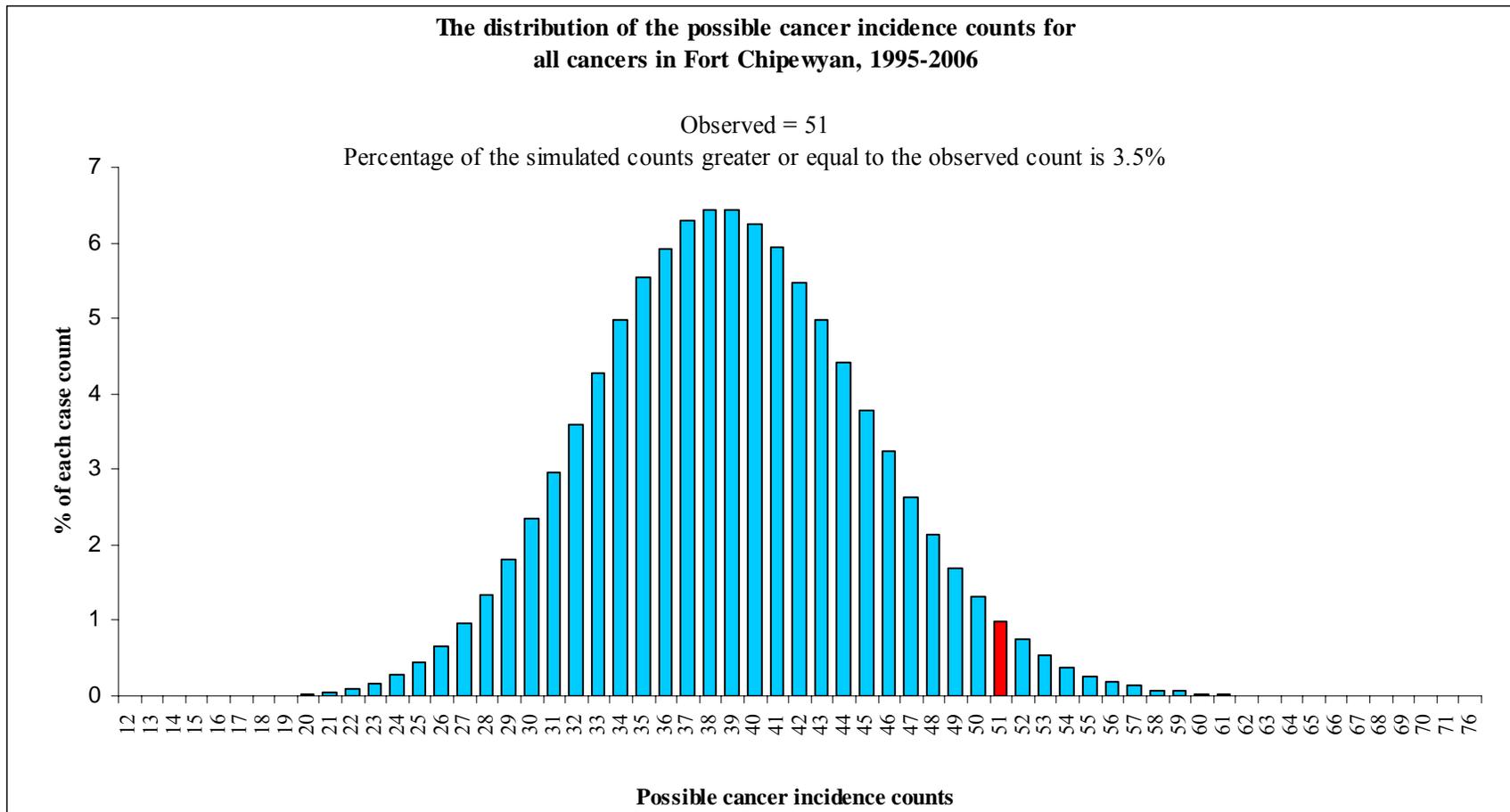


**Figure 2: Age Standardized Incidence Rates (ASIRs) and 95% Confidence Intervals (CIs) of all cancer cases for Fort Chipewyan, the comparison communities and Alberta, 1995-2006**

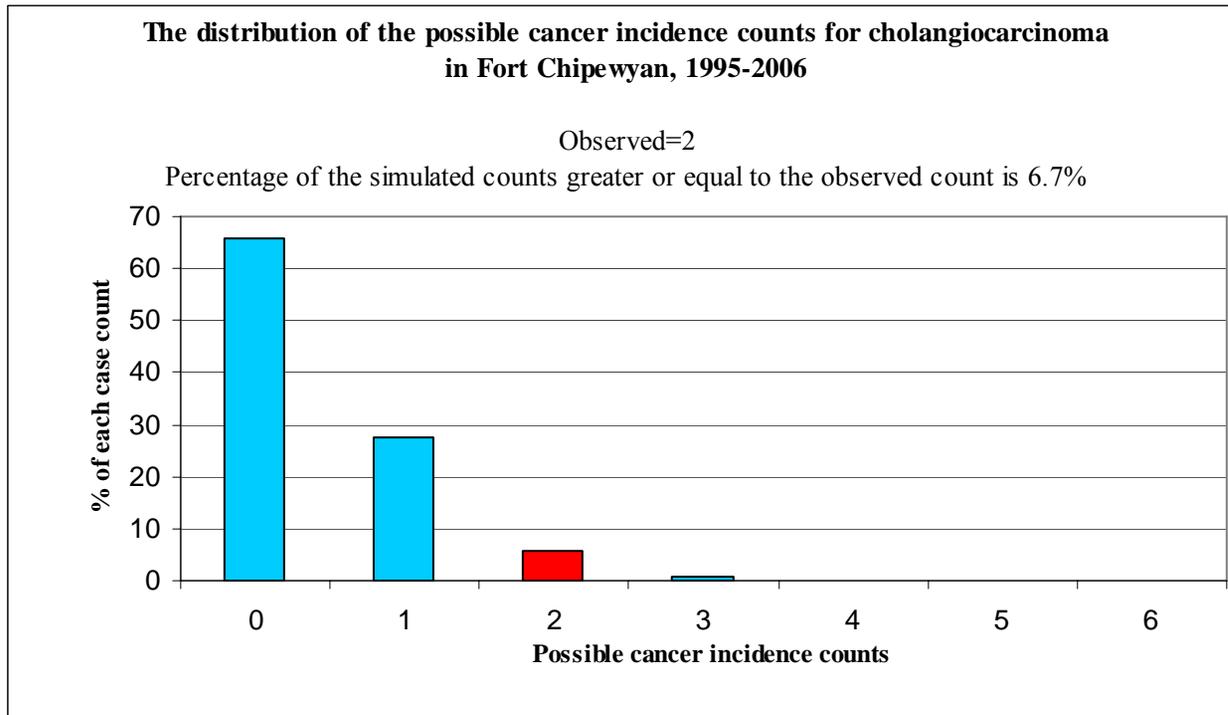


**Figure 3: Comparing the actual Observed (O) number of cancer cases to a simulated distribution of possible cancer incidence counts in Fort Chipewyan, 1995-2006**

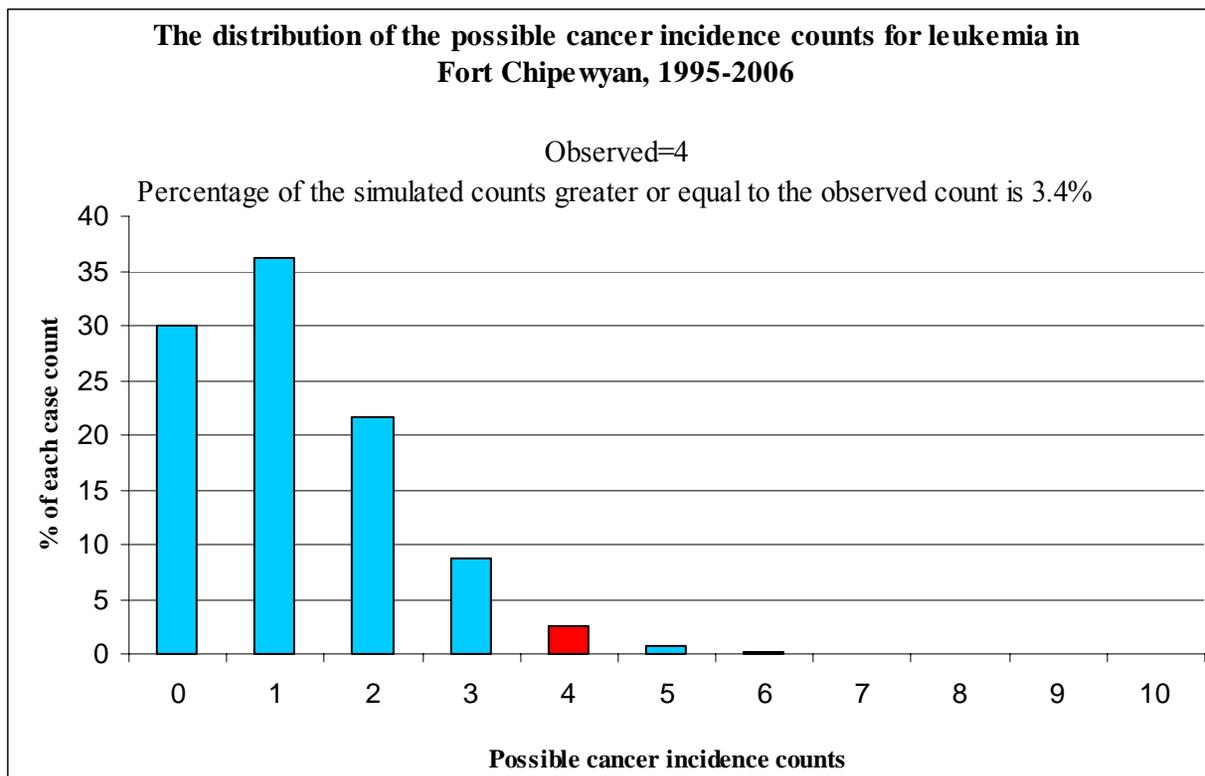
**(a) All cancers**



**Figure 3 (b) Cholangiocarcinoma**



**Figure 3 (c) Leukemia**



**Figure 3 (d) Colon Cancer**

