ABSTRACT

Objectives. This is the second of 2 papers reporting on the result of the Circumpolar Inuit Cancer Review, an international collaborative effort involving researchers and health officials from Alaska, Canada and Greenland.

Methods. Inuit cancer cases by age-sex group and anatomic site were obtained from the regional cancer registries.

Results. Cancer in general is increasing among Inuit, in all regions, and among both men and women. Inuit continue to be at extreme high risk, relative to non-Inuit and to comparisons of global populations, for the historically recognized so-called traditional cancers (such as cancer of the nasopharynx and salivary glands). Among the so-called modern cancers prevalent in developed societies, lung cancer is rapidly increasing in incidence (especially in Canada), such that the rate in both Inuit men and women is the highest in the world; other cancers, such as colorectal cancer, are also on the rise (especially in Alaska), while breast and prostate cancer remain low relative to the non-Inuit population. The decline in cervical cancer is a positive development; in the 3 regions, the rate in Greenland is the highest.

Conclusions. Data such as these can form the basis of interventions directed towards known risk factors such as smoking, diet, obesity, viral and bacterial infections, and low screening prevalence. Cancer surveillance is a basic task of the public health system; in the Arctic, it is particularly important as Inuit continue to undergo further changes in their life-styles and social environments.

(Int J Circumpolar Health 2008; 67(5):408-420)

Keywords: cancer, Inuit, epidemiology, surveillance, registries
INTRODUCTION

This paper reports on the international circumpolar review of cancer among the Inuit population of Alaska, Canada and Greenland during the period 1989–2003 (2002 in the case of Greenland). Combined with data collected in the previous review for the period 1969–1988, reported in a special issue of the journal Acta Oncologica in 1996 (1), the patterns and trends over a 35-year period can be discerned. (Note that for Alaska, data from all Alaska Natives rather than Inuit/Eskimo exclusively were presented in that review. Inuit/Eskimo comprised approximately 53% of the Alaska Native population during that period.)

Increasingly, cancer has become a major health concern for many Arctic communities. Regional health care agencies and Inuit organizations require Inuit-specific data to plan programs and to deliver services. The rigorous collection of data across national and regional boundaries in a standardized and consistent manner can provide the needed quantitative evidence to support public health interventions.

MATERIAL AND METHODS

Detailed methods have been described in the companion paper in this Special Issue.

RESULTS

Table I and Table II present the number of cases and rates of cancer by site in the Inuit regions in the 1989–2003 period, among men and women respectively, using the methods detailed in the previous paper. Cancer incidence rates among Inuit men are similar to rates among women (315 vs. 323 per 100,000, respectively). The 5 leading cancer sites among Inuit men in all regions combined were, in descending order, lung (32%), colorectal (15%), stomach (9%), kidney (4%) and nasopharynx (4%). For Inuit women, leading cancers included lung (18%), breast (17%), colorectal (16%), cervix (7%) and pancreas (4%).

Time trends

The rate of cancer incidence for all sites combined has increased during the 35-year period in all regions (Fig. 1). Comparing 1969–1973 and 1999–2003, the all-site combined rate increased by 35% among Inuit men and by 44% among Inuit women. There has been a substantial increase in lung cancer rates among both men (by 136%) and women (by 344%) in all regions (Fig. 2), most notably among Canadian Inuit.

Increases in colorectal cancer incidence have also been observed in all regions, by 60% among men and 85% among women. While Alaska has maintained its leading position throughout the 35-year period, Canadian Inuit have experienced substantial increases of this cancer, especially among men for whom rates have tripled during this period (Fig. 3). Among Inuit women, the breast cancer incidence has doubled (Fig. 4). However, cervical cancer, once high during the 1970s and 1980s, has declined to less than half the former rates for all 3 Inuit groups (Fig. 5).
Table I. Average annual number of cases, crude and age-standardized cancer incidence rates (per 100,000) among Inuit men by regions and cancer site, 1989–2003.

| Site                              | Alaska Cases/yr | Alaska Crude R ASIR 95% CI | Canada Cases/yr | Canada Crude R ASIR 95% CI | Greenland Cases/yr | Greenland Crude R ASIR 95% CI | Circumpolar Inuit Cases/yr | Circumpolar Inuit Crude R ASIR 95% CI |
|-----------------------------------|----------------|-----------------------------|----------------|-----------------------------|-------------------|-----------------------------|-----------------------------|----------------------------------|
| **Oral cavity and pharynx**       |                |                             |                |                             |                   |                             |                             |                                  |
| Salivary glands                   | 0.27           | 1.1                         | 1.4            | 0.0                         | 2.8               | 0.8                        | 4.5                         | 7.7                              |
| Mouth                             | 0.20           | 0.8                         | 1.4            | 0.0                         | 3.0               | 0.3                        | 3.0                         | 5.6                              |
| Nasopharynx                       | 2.20           | 9.3                         | 13.2           | 8.7                         | 17.8              | 1.5                        | 12.7                        | 18.1                             |
| **Digestive organs**              |                |                             |                |                             |                   |                             |                             |                                  |
| Esophagus                         | 1.00           | 4.2                         | 6.5            | 3.2                         | 9.8               | 0.6                        | 3.7                         | 7.6                              |
| Stomach                           | 5.40           | 22.9                        | 32.1           | 24.9                        | 39.2              | 1.8                        | 10.4                        | 19.7                             |
| Colon/rectum                      | 11.20          | 47.5                        | 69.8           | 55.5                        | 84.2              | 4.2                        | 23.4                        | 46.7                             |
| Liver                             | 1.47           | 6.2                         | 8.0            | 4.5                         | 11.5              | 0.6                        | 3.3                         | 6.1                              |
| Gallbladder/bile ducts            | 0.73           | 3.1                         | 4.8            | 2.0                         | 7.7               | 0.2                        | 1.5                         | 2.7                              |
| Pancreas                          | 1.60           | 6.8                         | 9.8            | 5.8                         | 13.7              | 0.6                        | 3.7                         | 7.9                              |
| **Respiratory/intrathoracic organs** |              |                             |                |                             |                   |                             |                             |                                  |
| Nasal cavities/sinuses            | 0.00           | 0.0                         | 0.0            | 0.0                         | 0.0               | 0.0                        | 0.0                         | 0.0                              |
| Larynx                           | 0.40           | 1.7                         | 2.8            | 0.5                         | 5.0               | 0.2                        | 1.1                         | 1.9                              |
| Lung                              | 14.27          | 60.5                        | 92.0           | 79.6                        | 104.4             | 13.0                       | 72.9                        | 148.6                            |
| **Bone and soft tissues**         |                |                             |                |                             |                   |                             |                             |                                  |
| Bone                              | 0.33           | 1.4                         | 1.8            | 0.2                         | 3.3               | 0.1                        | 0.7                         | 1.3                              |
| Connective tissue                 | 0.20           | 0.8                         | 0.8            | 0.0                         | 1.8               | 0.0                        | 0.4                         | 0.6                              |
| **Skin**                          |                |                             |                |                             |                   |                             |                             |                                  |
| Malignant melanoma skin           | 0.07           | 0.3                         | 0.3            | 0.0                         | 1.0               | 0.0                        | 0.0                         | 0.0                              |
| Breast                            | 0.07           | 0.3                         | 0.3            | 0.0                         | 1.5               | 0.0                        | 0.0                         | 0.0                              |
| **Male genital organs**           |                |                             |                |                             |                   |                             |                             |                                  |
| Prostate                          | 3.53           | 15.0                        | 22.9           | 16.7                        | 29.1              | 0.8                        | 4.8                         | 10.5                             |
| Testis                            | 0.80           | 3.4                         | 3.5            | 1.5                         | 5.5               | 0.2                        | 1.1                         | 1.6                              |
| **Urinary tract**                 |                |                             |                |                             |                   |                             |                             |                                  |
| Kidney                            | 2.67           | 11.3                        | 16.8           | 11.5                        | 22.0              | 1.2                        | 7.1                         | 12.8                             |
| Bladder                           | 0.53           | 2.3                         | 3.4            | 1.0                         | 5.8               | 0.3                        | 1.9                         | 4.2                              |
| **Eye, brain and other CNS**      |                |                             |                |                             |                   |                             |                             |                                  |
| Eye                               | 0.00           | 0.0                         | 0.0            | 0.0                         | 0.0               | 0.0                        | 0.0                         | 0.0                              |
| Brain/CNS                         | 0.33           | 1.4                         | 1.5            | 0.2                         | 2.9               | 0.6                        | 3.7                         | 3.8                              |
| **Endocrine glands**              |                |                             |                |                             |                   |                             |                             |                                  |
| Thyroid                           | 0.20           | 0.8                         | 0.9            | 0.0                         | 1.9               | 0.0                        | 0.0                         | 0.0                              |
| **Lymphoid/haematopoietic tissues** |            |                             |                |                             |                   |                             |                             |                                  |
| Non-Hodgkin lymphoma              | 1.13           | 4.8                         | 5.3            | 2.7                         | 7.9               | 0.5                        | 3.0                         | 5.6                              |
| Hodgkin’s disease                 | 0.07           | 0.3                         | 0.2            | 0.0                         | 0.7               | 0.0                        | 0.4                         | 0.3                              |
| Leukemia                          | 1.07           | 4.5                         | 4.2            | 2.1                         | 6.3               | 0.5                        | 3.0                         | 3.5                              |
| Multiple myeloma                  | 0.40           | 1.7                         | 2.0            | 0.4                         | 3.6               | 0.2                        | 1.5                         | 3.2                              |
| **All sites**                     | 53.53          | 227.2                       | 326.3          | 303.4                       | 349.2             | 31.0                       | 172.9                       | 332.0                            |

Cancer among Inuit (II)
Table II. Average annual number of cases, crude and age-standardized cancer incidence rates (per 100,000) among Inuit women by regions and cancer site, 1989–2003.

| Site                          | 1989–2003 Alaska Cases/yr | 1989–2003 Canada Cases/yr | 1989–2003 Greenland Cases/yr | Circumpolar Inuit Cases/yr |
|-------------------------------|---------------------------|---------------------------|-------------------------------|---------------------------|
|                               | Crude R | ASIR | 95% CI | Crude R | ASIR | 95% CI | Crude R | ASIR | 95% CI | Crude R | ASIR | 95% CI |
| **FEMALE**                    |         |      |        |         |      |        |         |      |        |         |      |        |
| Oral cavity and pharynx       |         |      |        |         |      |        |         |      |        |         |      |        |
| Salivary glands               | 0.33    | 1.5  | 1.7    | 3.2    | 0.2  | 0.60   | 3.5    | 4.5  | 7.7    | 1.2    | 0.50  | 2.1  |
| Mouth                         | 0.07    | 0.3  | 0.3    | 0.8    | 0.0  | 0.00   | 0.0    | 0.0  | 0.0    | 0.0    | 0.86  | 3.6  |
| Nasopharynx                   | 0.53    | 2.3  | 3.1    | 5.4    | 0.9  | 1.40   | 8.2    | 13.9 | 20.3   | 7.5    | 1.86  | 7.9  |
| **Digestive organs**          |         |      |        |         |      |        |         |      |        |         |      |        |
| Esophagus                     | 0.60    | 2.6  | 3.7    | 6.2    | 1.3  | 0.2    | 1.2    | 1.9  | 4.1    | 0.0    | 1.71  | 7.2  |
| Stomach                       | 2.27    | 9.9  | 12.4   | 16.6   | 8.1  | 0.8    | 4.7    | 6.8  | 10.8   | 2.7    | 1.71  | 7.2  |
| Colon/rectum                  | 14.27   | 62.2 | 77.8   | 92.2   | 63.4 | 4.4    | 26.3   | 47.1 | 62.9   | 31.3   | 6.36  | 26.9 |
| Liver                         | 0.87    | 3.8  | 4.5    | 7.0    | 2.0  | 0.13   | 0.8    | 1.4  | 3.6    | 0.0    | 0.79  | 3.3  |
| Gallbladder/bile ducts        | 1.33    | 5.8  | 7.2    | 10.4   | 4.0  | 0.47   | 2.7    | 5.2  | 9.2    | 1.1    | 0.93  | 3.9  |
| Pancreas                      | 1.93    | 8.4  | 10.7   | 14.7   | 6.8  | 0.53   | 3.2    | 7.3  | 12.4   | 2.1    | 1.40  | 7.8  |
| Respiratory/intrathoracic organs |         |      |        |         |      |        |         |      |        |         |      |        |
| Nasal cavities/sinuses        | 0.00    | 0.0  | 0.0    | 0.0    | 0.0  | 0.07   | 0.4    | 0.6  | 1.8    | 0.0    | 0.00  | 0.0  |
| Larynx                        | 0.00    | 0.0  | 0.0    | 0.0    | 0.0  | 0.07   | 0.4    | 1.1  | 3.2    | 0.0    | 0.00  | 0.0  |
| Lung                          | 7.07    | 30.8 | 40.7   | 48.5   | 32.8 | 10.4   | 61.1   | 132.4 | 153.8  | 111.0  | 11.57 | 48.9 |
| Bone and soft tissues         |         |      |        |         |      |        |         |      |        |         |      |        |
| Bone                          | 0.20    | 0.9  | 1.1    | 2.4    | 0.0  | 0.20   | 1.2    | 1.7  | 3.8    | 0.0    | 0.07  | 0.3  |
| Connective tissue             | 0.07    | 0.3  | 0.8    | 1.8    | 0.0  | 0.07   | 0.4    | 0.3  | 1.0    | 0.0    | 0.29  | 1.2  |
| Skin                          | 0.27    | 1.2  | 1.4    | 2.8    | 0.0  | 0.13   | 0.8    | 1.5  | 3.7    | 0.0    | 0.14  | 0.6  |
| Cancer among Inuit (II)       | 59.20   | 257.9| 323.4  | 345.0  | 30.17 | 38.73  | 227.7  | 379.6 | 413.0  | 346.1  | 62.43 | 263.9|
Figure 1. Trend in cancer incidence among Inuit, all sites combined, 1969–1973 to 1999–2003.

Figure 2. Trend in incidence of lung cancer among Inuit, 1969–1973 to 1999–2003.
Figure 3. Trend in incidence of colorectal cancer among Inuit, 1969–1973 to 1999–2003.

Figure 4. Trend in incidence of breast cancer among Inuit, 1969–1973 to 1999–2003.
Comparison with non-Inuit populations

The incidence rate of cancer among Inuit during the 1989–2003 period can be compared to non-Inuit populations to determine which cancer sites pose a greater (or reduced) risk for Inuit populations. While one could compare Inuit with non-Inuit within each country, in this paper the circumpolar Inuit were compared to U.S. Whites whose numbers were taken from the U.S. National Cancer Institute’s Surveillance, Epidemiology and End Results (SEER) Program of cancer registries. Data pertaining to the 1993–1997 period as reported in Cancer Incidence in Five Continents (2) were used (Fig. 6 and Fig. 7). The populations of Canada and Denmark (to which Greenland is usually compared) are also predominantly of European origin, although they do not have cancer rates identical to those of U.S. Whites.

Nasopharyngeal cancer (NPC) among Inuit is exceedingly high relative to U.S. Whites: 24 times higher in men and 37 times higher in women. Other high risk sites among Inuit include stomach (4 times higher in both men and women), salivary glands (3 times higher in men and 4 times higher in women), esophagus (3 times higher in men and 5 times in women), gallbladder/bile ducts (2 times higher in men and 4 times in women), liver (2 times higher in men and 3 times in women) and lung (2 times higher in both men and women). Among Inuit women, high risk sites also include cervix (3 times higher) and pancreas, colorectal, kidney and thyroid (2 times higher).
Figure 6. Ratio of age-standardized incidence rates among men: Circumpolar Inuit (1989–2003) to U.S. Whites (1993–1997).

Figure 7. Ratio of age-standardized incidence rates among women: Circumpolar Inuit (1989–2003) to U.S. Whites (1993–1997).
Inuit men are at low risk for prostate cancer, with rates only 14% that of the non-Inuit comparison group. While breast cancer ranks second among cancers in Inuit women, the risk is about 60% of that for non-Inuit.

Overall, with all sites combined, the risk of cancer among Inuit men and women is not significantly different from U.S. Whites.

The circumpolar Inuit can also be compared with populations in all the countries in the world with cancer registries listed in the Cancer Incidence in Five Continents (hereafter CI5C). Both Inuit men and women experience exceedingly high risk for nasopharyngeal cancer. Only a few registries reporting on certain Chinese populations, such as those in Hong Kong and Singapore, showed higher rates than the Inuit. Inuit men and women also have the highest incidence rate of cancer of the salivary glands in the world, with double or more the rates of other regions or countries.

Lung cancer incidence in both Inuit men and women is also the highest in the world, exceeding all other registries.

**Regional variation**

Striking differences in cancer incidence rates are apparent across various Inuit regions (Fig. 8 and Fig. 9). Lung cancer incidence is about one-and-a-half times higher among Canadian Inuit men, and 2 to 3 times higher among women, than in the other 2 regions. Inuit men and women in Alaska have the highest rates for colorectal cancer, whereas those in Greenland have the lowest rates. Greenlanders experience the highest rates of esophageal cancer, more so among men. Breast cancer in women is highest in Alaska, whereas cervical cancer is highest in Greenland. Among men, prostate cancer is highest in Alaska.

**DISCUSSION**

Several major findings are evident from the present review:

- Cancer in general is increasing among Inuit, in all regions, and among both men and women.
- The Inuit continue to be at extreme high risk, relative to non-Inuit and relative to comparisons of global populations for cancers such as nasopharynx and salivary glands, which have been recognized as historically “traditional” cancers by some authors.
- Among the “modern” cancers (i.e., cancers prevalent in the developed countries), lung cancer is rapidly increasing in incidence (especially in Canada), such that the rate in both Inuit men and women is the highest in the world; other cancers such as colorectal cancer are also on the rise (especially in Alaska), while breast and prostate cancers remain low relative to non-Inuit populations.
- The decline in cervical cancer is a positive development; in the 3 regions, the rate in Greenland is the highest.

The high risk of NPC among Inuit has long been recognized (3). Although the etiology is not completely understood, the occurrence of NPC is associated with environmental exposure to the Epstein-Barr virus (EBV) as well as with dietary factors such as the consumption of preserved foods like salted fish (4). NPC also has a strong familial marker, but major susceptibility genes have not been identified (5). The prevalence of EBV Ig-A antibodies, a tumour marker for NPC among the Chinese, has been found to be more prevalent in the general Inuit population compared to another...
Figure 8. Regional variation in cancer incidence among Inuit men, 1989–2003.

Figure 9. Regional variation in cancer incidence among Inuit women, 1989–2003.
NPC high-risk population in Taiwan, but the significance of this is unclear (6).

Cancer of the salivary glands was at one time nicknamed “eskimoma” because of its high frequency among Inuit (7). Its etiology is unclear (8), although it shares some common features with NPC. The undifferentiated carcinoma resembles NPC histopathologically and is associated with EBV infection. First-degree relatives of Inuit NPC patients are also at increased risk for salivary gland carcinoma (5). In a study of Greenlandic migrants to Denmark, it was found that the high risk of NPC and salivary gland cancer was maintained despite decades of living in a different environment (9).

Lung cancer must clearly be the focus of any cancer control strategy for Inuit – it accounts for the highest proportion of cancer cases among Inuit who are also the highest-risk population globally. One needs look no further than the extensive prevalence of smoking among Inuit populations. During the 1980s and 1990s, the rate of smoking was high across the Arctic, ranging from 43% among adults in northwest Alaska to 80% in Greenland (10: p.199). Within homes, it is likely that there is a high rate of passive smoking.

Colorectal cancer accounts for 15% of Inuit cancer cases and its incidence is increasing, especially among Inuit women in Alaska (11). Its etiology is complex, involving genetic, nutritional and inflammatory factors (12). Increasingly, its association with the metabolic syndrome or its components (such as obesity and dysglycemia) is being studied (13). As Inuit undergo further dietary transition and other life-style changes such as decreased physical activity levels, the rate of colorectal cancer can be expected to increase.

This trend can be averted through increased preventive efforts that include early screening and the identification of high-risk groups.

The low risk of prostate cancer among Inuit men does not appear to be due to a lack of screening. Despite little emphasis on screening for prostate cancer in Alaska, the proportion of cases diagnosed with local disease is similar to that in the general population of the U.S. (14). The low prevalence of latent prostate cancer was confirmed in an autopsy study in Greenland (15). The traditional Inuit diet is rich in n-6 and n-3 polyunsaturated fatty acids and selenium, which have been identified as possible protective factors (16,17).

Several other cancers have well-defined risk factors for which effective interventions are available. The causal role of human papilloma virus in cancer of the cervix is well established (18). From its peak in the 1980s (19), the incidence of cervical cancer has declined in all regions. Pap smear screening is an effective preventive strategy, and surveys in Canada’s Northwest Territories and in Nunavut indicate that coverage has now surpassed the Canadian average (20). In Alaska, 90% of Native adult women had a Pap smear within the last 2 years, which slightly exceeds the non-Native rate, based on 2005 data of the Behavioral Risk Factor Surveillance System (21). Notwithstanding the temporal decline, the risk is still 3 times that of non-Inuit (Fig. 6). The availability of an HPV vaccine presents an opportunity to lower the risk of this cancer even further.

Inuit experience 4 times the risk of stomach cancer than non-Inuit. Among the known risk factors is being infected with the bacteria *Helicobacter pylori*, which is potentially treatable
and preventable. Where it is measured, for example in Greenland and Alaska, seroprevalence of *H. pylori* is high in the Arctic (22,23). A study in Alaska, however, reported a 14.5% reinfection rate of *H. pylori* 2 years following successful treatment (24). Ultimately, prevention may need to be focused on improvement of environmental sanitation to reduce the endemicity of the bacteria.

The elevated risk of liver cancer (hepatocellular cancer, HCC), which is 2 times higher among men and 2.6 times among women (Fig. 5 and Fig. 6), is consistent with a high prevalence of the hepatitis B virus (25). The distribution of virus genotypes varies across the Arctic. HBV genotype F has been found to be associated with HCC in Alaska (26), but is rare in Greenland (27). An approach to the prevention of HCC is through vaccination against HBV, which is routinely administered to newborns in Alaska and in the Northwest Territories. Progress made in reducing HCC through hepatitis B vaccination may be masked with the emergence of hepatitis C for which there is no vaccine to date.

This paper presents a broad overview of the major trends and patterns of cancer among the circumpolar Inuit. A comparative study of this nature does have its limitations. It is highly dependent on the completeness and quality of data drawn from existing cancer registries in multiple jurisdictions. The identification of Inuit ethnicity, both in the numerator and denominator, is also fraught with problems. Nevertheless, data such as these, imperfect though they may be, can still contribute to the design and implementation of interventions directed towards known risk factors (such as smoking, diet, obesity, viral and bacterial infections) and early detection programs. Cancer surveillance is an essential part of the public health system; in the Arctic, it is particularly important as Inuit continue to undergo further changes in their life-styles and social environments. Finally, circumpolar comparisons serve not only to highlight disparities between populations but also to identify common or unique risk factors across populations, which may contribute to our understanding of cancer etiology in all human beings.

**Acknowledgements**

Funding for this international collaboration was provided by the Canadian Institute of Health Research (CIHR) through the award of a team grant on circumpolar chronic disease prevention to Kue Young (CTP-79853) and a special workshop grant from the CIHR Institute of Aboriginal People’s Health. We also want to thank Michèle Beaupré of Fichier des tumeurs du Québec for providing data from Nunavik. Funding for the Alaska Native Tumor Registry is provided by the Surveillance, Epidemiology and End Results (SEER) Program of the National Cancer Institute.

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