Breast, Cervical and Colorectal Cancer Survival Rates for Northern Saskatchewan Residents and First Nations

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By

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ABSTRACT

This descriptive study was done 1) to explore and describe the proportional distribution of breast, cervical and colorectal cancers by stage (a proxy measure of availability, access, and utilization of secondary prevention strategies) in northern Saskatchewan First Nations and non-First Nations in comparison to southern Saskatchewan First Nations and non-First Nations; 2) to assess the impact of stage and age on the survival patterns for these cancers in northerners and First Nations whose survival patterns have been shown by previous research to be equal or poorer in comparison to southerners. Univariate and multivariate survival analyses were carried out to ascertain the impact of the different proportions of stage for each study group on survival. Stage at time of diagnosis is a proxy assessment of secondary prevention services, which include formal screening programs.

Data for this study was obtained from the Saskatchewan Cancer Registry, which has been maintaining cancer data since 1932. Cancer stage at time of diagnosis information is complete in the registry for different years for each cancer site. Hence data for breast cancer was for the years 1970 to 1995; cervical cancer data for the years 1980 to 1995; colorectal cancer data for the years 1990 to 1995.

The proportion of cancer cases for each site by TNM stage and age were compared among the four study groups. First Nation and northern populations were found to have a larger proportion of diagnoses at a later stage in comparison to the southern non-First Nation group.

Using Cox's proportional hazards model, both stage and age at time of diagnosis were found to be significant predictors of survival for all study groups. Age and stage adjusted relative risks were calculated and found to be significant in comparison to the southern non-First Nation group for cancer of the breast (RR = 1.81 p = 0.013). For cervical cancer the relative risk of dying of cervical cancer for southern First Nations in comparison to southern non-First Nations was found to be 1.38 but this was not statistically significant (p = 0.097). For colorectal cancer, the relative risk of dying of colorectal cancer was found to be better for northern First Nations in comparison to southern non-First Nations (RR = 0.59), however this was not statistically significant (p = 0.45).

This study showed that despite adjusting for stage and age at time of diagnosis, there were still some unexplained differences in the survival pattern of northern First Nations, northern non-First Nations and southern First Nations in comparison to southern non-First Nations. Hypotheses as to what these unexplained differences are have been offered. These include differences in socio-economic status as well as availability, accessibility, attitudes towards and knowledge of secondary prevention strategies. Further study into these unexplained differences should be carried out.

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DEDICATION

This thesis is dedicated to my family in recognition of their love and support.

To my parents, Zaheer and Gaiti Alvi and my wife, Renée:

Thank You - I did it!

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1. Introduction

Prevention and early detection strategies for breast, cervical and colorectal cancers are available yet mortality rates are high or rising among First Nation groups in North America. Examining survival patterns and factors that influence these patterns can perhaps give insight as to why this is happening.

1.1 Nomenclature

Most Indian bands in Saskatchewan refer to themselves and are referred to by others as "First Nations". For the purpose of this study the term "First Nations" will be used to refer to people who had identified themselves to Saskatchewan Health as being registered members of an Indian band, under provisions of the federal Indian Act. Saskatchewan Health's registry of persons eligible for health services benefits distinguishes between First Nations and other Saskatchewan residents. Non-treaty Aboriginal people and Métis are not uniquely identified in Saskatchewan Health's registry of persons and therefore can not be identified for separate comparison analyses. All Saskatchewan people who are not identified as a First Nation in the Cancer registry data, including those people without treaty status, Métis, and people of other races, will be referred to as "Non-First Nations" in this study.(1) For American studies referred to, the American term for First Nations will be used, this being "American Indian".

1.2 The Problem

North American First Nations have experience well documented health inequalities compared to non-First Nations. Studies of mortality, using vital statistics information, morbidity, using hospitalization information and disease specific studies such as cancer, using cancer registry as well as the afore mentioned sources of data, have all given evidence to this.(2-4) Within Saskatchewan, while there is some information on cancer incidence and survival, little of this information pertains to the First Nation population of the province as a whole and even less is known about the northern population (First Nation and non-First Nation). Looking at cancer in northern Saskatchewan, Gillis et al's study entitled "Cancer Incidence and Survival of Saskatchewan Northerners and Registered Indians, 1967-1986" was one of the first cancer studies conducted on the population of Northern Saskatchewan. In their analysis, an increasing age-adjusted incidence rate of lung, breast and cervical cancer over time was demonstrated in the northern population of Saskatchewan, as compared to the rest of the province.(5) In a subsequent study on lung, breast , and cervical cancer incidence and survival in northern Saskatchewan, Irvine et al. found lung, breast, and cervical cancer survival to be equal or less for the northern and First Nations groups.(6) For both of these studies the possible explanations for the differing survival rates were outlined. Cancer survival is influenced by such factors as age, extent or stage of disease, cancer histology, response to treatment, access to and utilization

of medical care, compliance with therapy, general state of health, and socioeconomic circumstances.(6) Irvine et al went on to suggest that Northerners and Registered First Nations poorer survival for cancer may be attributable to differences in stage of cancer at diagnosis and medical care access, utilization, and compliance with therapy. (6) In addition to this, survival analysis is prone to lead-time bias. Lead-time bias can be defined using the following example. When survival curves of two groups are to be compared, it is important that both have the same starting point. Consider a study to evaluate the efficacy of a new procedure for the early diagnosis of a disease. Even if detecting the disease early does not prolong life, it might appear to do so if survival is measured from the date of early diagnosis instead of from the usual diagnosis date resulting from traditional methods. (7) Survival without stage assessment is prone to lead-time bias. For this study lead-time bias may be present when comparing survival between northern First Nations, northern non-First Nations, southern First Nations, and southern non-First Nations. Although survival is calculated from time of diagnosis for all groups, the stage of disease for each study group may be different at time of diagnosis. By controlling for this and thus in essence making it so that all study groups are at effectively the same stage of disease at time of diagnosis, the stage adjusted survival time for the cancer of interest may be less biased. This thesis sets out to look at the role of differing stage at diagnosis and medical care access with respect to differing survival rates between the northern population of Saskatchewan and the

south. This is keeping in mind the issue of lead-time bias and its impact on mortality.

In the most recent study of cancer done in Saskatchewan (1999), it has been found that incidence rates among First Nations and northerners for cervical cancer are higher and more recently for colorectal cancer, are rising more quickly in comparison to the province as a whole. While breast cancer incidence has been found to be lower than the rate for the whole province, it has been increasing over the last twenty-five years. (8) Cancer survival was not studied in the most recent study.

In 1998 for all of Canada, breast and colorectal cancers were second and third respectively in number of estimated new cancer cases, number one being lung cancer.(9) Cervical cancer was much lower on the list but this information was for all ethnic groups combined (First Nations and non-First Nations together). Incidence rates for all of Canada show a similar pattern, for males the top three are; cancer of the prostate, lung cancer and colorectal cancer. For females the top three are; breast cancer, lung cancer and colorectal cancer. (9)

The burden of cancer among cancer patients can be described in many ways (mortality, incidence), but the most direct representation of the severity of disease is provided by survival rates. This is in contrast to incidence rates, which indicate how frequently cancer occurs, and mortality rates, which indicate how frequently deaths due to cancer occur.(10) Having observed through other studies in Saskatchewan that Northerners and First

Nations experience incidence rates for cervical, breast, and colorectal cancers that are interestingly different in comparison to the non-First Nation population of Saskatchewan, it is of some interest to gain knowledge of the severity of these cancers. This can be measured by comparing survival between these population groups. Factors that influence survival such as stage of disease at time of diagnosis can also be examined, and this may help offset the effects of lead-time bias that occur when looking at survival alone.

It is important to study cervical, breast and colorectal cancers in that they are:

1. Two of the top three cancer diagnoses in Canada and Saskatchewan, with lung cancer being number one.
2. There are clear secondary prevention strategies for cervical, colorectal, and breast cancers. i.e.) PAP smear, fecal occult blood, digital examination and sigmoidoscopy/colonoscopy-screening, and mammography, clinical breast examination, and breast self-examination respectively
3. The staging information in the Saskatchewan Cancer Registry database is quite good for these three sites.

Both lung and prostatic cancers are not being studied, as the staging information in the Saskatchewan Cancer Registry database is quite poor for these sites. As well, prostatic cancer has a low proportion of cases among First Nation populations and as this is one of the groups of interest in this study, it will not be studied.

By examining survival among the northern population and First Nations in more detail an assessment of their access to secondary prevention can be ascertained.

1.3 Purpose of the Study

The aim of this study is to explore and describe cancer survival patterns in Northern Saskatchewan First Nations and non-First Nations in comparison to southern Saskatchewan First Nations and non-First Nations. This study also serves the purpose to explore factors, such as staging at time of diagnosis, that could explain the disparity in survival rates for cervical, colorectal, and breast cancer experienced by northerners (First Nations and Non-First Nation) in comparison to southerners (First Nation and Non-First Nation). Staging can be used as a proxy for access and utilization of secondary prevention strategies. The study was stimulated by inquiries from northern community leaders and health workers regarding cancer trends in northern Saskatchewan.

1.4 Relevance & Significance

Population-based survival rates and survival rates adjusted for factors such as stage at diagnosis, treatment, age, etc. can be used to monitor cancer patient care, and can serve as a basis for evaluating the impact of treatment and other cancer control activities such as early detection

programs. By comparing survival rates between different population groups in the province, focusing on First Nations, the cancer burden and the effect of the provinces cancer control program as it pertains to northerners and First Nations can be better understood. This can then help guide health care planners and policy makers as they develop strategies for cancer control. For researchers, survival information, along with factors that influence survival, can be used to identify areas where new research is needed into the determinants of survival among cancer patients and where further advances are needed to control the suffering caused by cancer. (10) Survival by stage at time of diagnosis of disease can be assessed in comparison to unadjusted survival.

2. Review of the Literature:

2.1 Cancer of the Female Breast

Breast cancer is the most common malignancy among women in Western society. Over the past decade it has become apparent that breast cancer incidence rates are increasing steadily, whereas mortality rates have remained relatively constant. This increase in incidence rates may be due to increased use of breast cancer screening. At the current time it is difficult to identify risk factors that can explain a major part of the incidence. Thus, with the current knowledge, the most important strategy to reduce breast cancer mortality is early detection through secondary prevention strategies such as breast cancer screening programs.(11) Beyond formal screening programs, secondary prevention strategies also include knowledge of breast self-examination and annual examination of the breasts by a physician or health care professional.

2.1.1 Breast Cancer Incidence

Breast cancer is the leading type of cancer in Canadian women (excluding skin cancer), with 19,300 new cases expected to be diagnosed in 1998. It is the second leading cause of cancer death among women at 5,300 deaths, it is behind lung cancer with 6,500 expected deaths.(9) Breast cancer is thus a very important health problem for women in Canada. It is a disease

that often strikes women in the prime of their life, at the peak of their work and family responsibilities. From 1990-95 in Saskatchewan, cancer of the breast follows the same incidence trend as the rest of the country. This site has the highest incidence of any cancer for females. Among northern Saskatchewan residents (First Nation and non-First Nations), northern First Nations on reserve, and First Nations for the entire province, cancer of the breast has the highest incidence.(8) Studies across North America comparing First Nation populations with non-First Nations in northern and southern locations, have shown that the First Nation population experience lower rates of breast cancer when compared to non-First Nations.(12-15) In a study done in Saskatchewan from 1967-86 breast cancer incidence rates for First Nations and northerners revealed a dramatic increase over the 20 year study period, while the rate remained relatively stable for the province as a whole.(6) In a more recent study of Saskatchewan cancer incidence trends from 1970 to 1995 (8) similar results were revealed. In the early 1970's the incidence of female breast cancer among First Nations was low compared to that of the whole province. During 1970-74, First Nations incidence rate was less than one fourth of that of the whole province. In the subsequent 25 years, First Nation breast cancer incidence rose steadily so that by 1990-95 their incidence has increased nearly four times that of the rate in 1970-74. In 1990-95 the incidence rate for First Nations was still lower than that of the whole province.

2.1.2 Breast Cancer Survival

Survival rates for breast cancer are higher than those for most other cancers. Canada wide, the relative five-year survival rate for breast cancer is 74% based on cases diagnosed between 1980-84.(16) In addition, survival rates are better for younger women and for women whose cancer was detected at an early stage.(17) In Saskatchewan, breast cancer survival was studied for the entire population by Yang et al. and in a separate study by Tan and Robson. Both of these studies examined cancer for the years 1967-86. (18, 19)In both of these studies the five-year breast cancer survival rate was found to be similar to that of the Canadian rate, approximately 74%. Among First Nations populations, breast cancer survival has been found to be poorer in comparison to non-First Nations. (6, 12, 20-22) Giuliano et al write that late stage of breast cancer diagnosis is one of the major factors contributing to the poorer rate of survival among American Indian women.(12) In Irvine et al. study from 1967-86, First Nations and northerners in Saskatchewan five-year breast cancer survival rates were 74%, 70% and 77% for the First Nations, northerners and the province as a whole.(6) Here to the authors suggest further investigation into the influence of age and cancer stage at diagnosis on survival. McLaughlin et al also suggest that stage at diagnosis is linked to survival. In their Ontario study of cancer survival for the entire population (First Nation and non-First Nation) breast cancer survival showed some improvement over time. They hypothesized that along with other factors this may be due to enhanced case detection by screening in recent years, which

would lead to the identification of more women with disease at an earlier stage.(10)

2.1.3 Breast Cancer Screening

Of the three strategies for cancer control, [prevention(primary), screening(secondary), and treatment(tertiary)], early detection through screening currently offers the best chance of reducing overall mortality from breast cancer.(16, 23, 24) By detecting cancers at an earlier stage, screening mammography can reduce breast cancer mortality by 30% among women ages 50-69 years, thus survival can be improved. Since the late 1980's, Health and Welfare Canada has sponsored regular meetings with provincial and territorial representatives to facilitate development of breast screening programs.(16) In Saskatchewan a breast screening program was initiated in 1990, targeting women aged 50 to 69.(16) For northern Saskatchewan, a screening program was established in 1992 and expanded since that time.(25) Some work has been done indicating that the number of First Nations participating in screening programs in other parts of North America is low in comparison to non-First Nations populations.(12, 23, 26)

2.1.4 Summary

First Nations and northern populations experience lower incidence rates of breast cancer but these rates have been shown to be rising over time.

Within these population groups incidence rates are high on their own. Survival rates for First Nations and northerners in comparison to non-First Nations have been shown to be slightly worse. By establishing screening programs, breast cancer cases can be diagnosed at an earlier stage and this can perhaps lead to better survival outcome.

2.2 Cancer of the Cervix

Cancer of the cervix is the eleventh most frequently diagnosed cancer among Canadian women (in contrast it is the second most common form of cancer in women worldwide) and despite being almost completely preventable through regular screening, continues to be an important cause of morbidity and mortality.(27)

2.2.1 Cervical Cancer Incidence

In 1998 in Canada, it was estimated that approximately 1400 women would develop cervical cancer and 400 would die from this disease.(9) Incidence trends for cervical cancer in Canada have decreased steadily in the 1970's and early 1980's and showed a more moderate decline since the mid 1980's.(27) This decline in incidence is for all Canadian women, First Nation and non-First Nation. The likely explanation for this decline in incidence is a plateau in screening activity for cervical cancer at the national level.(27) Among First Nations however the incidence description is quite different. It is

well documented that First Nations women experience much higher incidence of cervical cancer in comparison to non-First Nations. (5, 14, 27) (28, 29) Among northern populations, cancer of the cervix incidence has also been found to be high. (27, 30-32) In Saskatchewan, from 1967-86 cervical cancer incidence has decreased for the entire Saskatchewan population, however, for First Nations the incidence has risen over this 20 year study time frame.(6) In a separate study of cancer in Saskatchewan from 1970-95 the incidence of cervical cancer among First Nations has been at least 3 times higher than that of the whole province over the twenty five year study period. The First Nations incidence peaked in the early 1980's . In the meanwhile, the incidence for the whole province has been steady during the twenty five year period.(8)

2.2.2 Cervical Cancer Survival

Survival rates provide a direct indication of disease severity and the impact of cancer treatment and secondary prevention. In Canada, for cervical cancer the 5-year survival rates are generally high, at 74% for all ages. Survival varies depending on age at diagnosis. Generally those women diagnosed at an early age and early stage have a better prognosis than those diagnosed at an older age and later stage.(10, 33) Cervical cancer survival for Saskatchewan is similar to the national rates. The five year relative survival rate for cervical cancer for the entire population of Saskatchewan for the years 1967-86 was found to be 67.3% for all ages.(18) A study by Tan et al.

found that on average the 5-year relative survival rate for all ages was 68%.(19) For First Nations populations survival for cervical cancer has been shown to be poorer in comparison to non-First Nations populations.(21) Irvine et al. study of northerners and First Nations in Saskatchewan found five-year cervical cancer survival rates to be 75%, 66% and 76% for First Nations, northerners and the province as a whole respectively.(6) As with breast cancer, the authors suggest further investigation into the influence of age and cancer stage at diagnosis on survival.

2.2.3 Cervical Cancer Screening

Regular screening and early detection can prevent significant morbidity and mortality due to cervical cancer.(23, 31) The Canadian Task Force on the Periodic Health Examination recommends annual screening with the Pap smear after initiation of sexual activity or at age 18. If an organized screening program is in place with appropriate quality control measures and information systems, the screening frequency may be reduced (for women with 2 previous normal smears) to every 3 years until age 69.(27) A series of national workshops on cervical cancer screening have urged the establishment of organized, provincial screening programs with centralized laboratory and information systems. As of April 1998, 3 provinces (B.C., Nova Scotia, and P.E.I.) have adopted these recommendations in whole or part.(27) In Saskatchewan in 1997, a Cervical Screening Program was approved and was said that it will "become operational in the coming months".(34) Studies in

Canada and the United States have shown that First Nations women have lower participation in cervical cancer screening in comparison to non-First Nations.(23, 29, 31) (35) There have been suggestions that this may be due to less access to screening programs(26) or other factors such as lack of knowledge of Pap smear, feelings of embarrassment, lack of community care or lack of culturally suitable health care services. (29, 36)

2.2.4 Summary

It has been well documented that cervical cancer can be prevented through thorough screening programs. Diagnosing cervical cancer at an early stage or even a pre-cancerous stage is possible through diligent screening programs. Incidence rates for First Nations women and northerners are higher than non-First Nations. Survival rates for First Nations and northerners have been shown to be equal or poorer than non-First Nations. Poorer survival may be attributable to less access to screening programs or other factors.

2.3 Colorectal Cancer

Cancer of the colon and rectum together constitute the third most important cancer in each sex in most Western countries. When both sexes are considered together colorectal cancer becomes the second most frequently diagnosed cancer behind lung cancer.

2.3.1 Colorectal Cancer Incidence

Colorectal cancer is the third most common site in terms of cancer incidence, and the second-ranked cause of cancer death among Canadians. In 1998, 16,500 new cases of colorectal cancer are expected to be diagnosed in Canadian men and women, this is compared to 20,400 new cases of lung cancer, 19,300 female breast cancers, and 16,100 prostate cancers.(9) The estimated 7,300 deaths from colorectal cancer place it ahead of the 5,300 expected deaths due to breast cancer and 4,300 prostate cancer deaths.(9) Canada wide, incidence and mortality rates for colorectal cancer continue to decrease, particularly among women, although the reasons are not completely understood. Research conducted in the United States suggests that more widespread use of methods for early detection may allow for more effective treatment for earlier staged disease, particularly among the elderly. Also, some evidence suggests that lifestyle changes such as diet may have contributed to the declines.(9) Although there has been a decline, cancers of the colon and rectum still represent an important health problem for Canadians.

Within Saskatchewan approximately 580 new cases of colorectal cancer have been estimated for 1998.(9) In a study for the years 1970-95 incidence rates for the entire provincial population, northerners, and First Nations, have risen over this time period(8). In the early 1970's, the incidence for colorectal cancer among First Nations in Saskatchewan was low compared to that of the province as a whole. During 1970-74, First Nations colorectal cancer

incidence rate was less than one half of that of the whole province. In the subsequent 25 years, First Nations colorectal cancer incidence took a dramatic increase so that by 1990-95 First Nations incidence was comparable to that of the whole province. In the meantime, the incidence of colorectal cancer for the whole province has increased only slightly. In the early 1970's the northern First Nations incidence of colorectal cancer has been lower than that of the First Nations of the entire province. By 1990-95 however, northern First Nations incidence are the same as that of all First Nations (north and south) of Saskatchewan. Many other studies have shown that colorectal cancer incidence is increasing among northerners and registered Fist Nations populations in comparison to non-First Nations populations.(37-39)

2.3.2 Colorectal Cancer Survival

Colorectal cancer has a fair prognosis with a five-year relative survival rate of 54% among females and 52% among males for all ages combined based on recent data from Ontario.(10) Within Saskatchewan Tan et al found that on the average the five-year relative survival rate for cancer of the colon is 54% for males and females combined. This is lower than the 60% five-year survival rate for all cancers combined for the entire Saskatchewan population calculated by Gillis et al.(5) Among northern populations and First Nations, survival for colorectal cancer has been shown to be poorer than non-First

Nations.(21, 40) Among Saskatchewan First Nations and northerners, the survival rates for colorectal cancer have yet to be published in any detail.

2.3.3 Colorectal Cancer Screening

It has been suggested that recent declines in mortality for colorectal cancer may be due to more widespread use of methods for early detection which may allow for more effective treatment for earlier staged disease.(41) There is no formal colorectal screening program per se in Canada at the present time. The Canadian Task Force on the Periodic Health Examination has concluded that there is insufficient evidence to support the inclusion or exclusion of fecal occult blood, sigmoidoscopic or colonoscopic screening of asymptomatic individuals over the age of 40 years as colorectal cancer screening methods.(42) Some rectal exam screening is also done. There is some screening in an unorganized way in Canada however.(25) Colorectal cancer if detected early can be effectively treated.(33) Among northerners and First Nations populations, high incidence and poorer survival suggest a need for intensified secondary prevention strategies for colorectal cancer.(43)

2.3.4 Summary

Incidence rates for colorectal cancer among First Nations and non-First Nations are ranked third highest behind cancer of the lung and breast cancer. Incidence trends for the entire population (First Nation and non-First Nations) have declined somewhat over the last decade. For northerners and First Nations populations incidence rates have increased over the last 25 years and

now are comparable to those of non-First Nations. In studies conducted outside of Saskatchewan, survival for this cancer site has been found to be poorer for First Nations and northerners in comparison to non-First Nations. Early detection can lead to better survival. It can be said therefore that colorectal cancer is a significant problem for First Nations and northerners and with early detection strategies its survival could be improved.

2.4 Cancer Stage at Diagnosis and Survival

By controlling for cancer stage at diagnosis when examining cancer survival one can asses such factors as access to and utilization of secondary prevention strategies. By diagnosing some cancers, including breast, cervical and colorectal cancers, at an early stage, there is a better chance that the cancer can be treated with better success and thus possibly improve survival.

Cancer survival for all causes comparing northerners, First Nations and the population as a whole in Saskatchewan has been shown to be different. Northerners and First Nations experience poorer survival than the Saskatchewan population as a whole (First Nation and non-First Nation). Particularly interesting is the finding that, even though the average age of diagnosis of cancer is 10 and 6 years younger in First Nations and northerners respectively their survival is poorer even when the survival analysis has not adjusted for this age difference. Generally one would expect better survival when cancer is diagnosed at younger ages.(5) Gillis et al go on to point out that stage of cancer at diagnosis may explain this poorer survival.

Furthermore they point out that American research has indicated that First Nation populations tend to have more advanced disease at the time of cancer diagnosis. Other studies have also shown this(40, 44).

There have been many studies that have explored the relationship between cancer survival and stage of cancer at time of diagnosis.(20, 21, 40, 45-48) These studies have had mixed conclusions. Sugarman et al conducted a study in 1994 on First Nations in Washington State concentrating on prostate, breast, cervical, and colorectal cancers. They found that the cancer stage at diagnosis distribution for First Nations was not significantly different from Whites. Their survival analysis showed that after adjustment for such factors as age, stage at diagnosis, lack of cancer treatment, and residence in a non-urban county, that First Nations poorer survival persisted in comparison to Whites.(21) Frost et al looked at breast cancer survival among New Mexico Hispanic, American Indians, and non-Hispanic women adjusting for first treatment and stage of disease at diagnosis. They used stage distribution, five-year relative survival curves and Cox proportional hazards model to assess the influence of stage on survival. They found that the stage distribution changed for all three groups between the time point of 1973-82 to 1983-92. The later time point distribution according to stage of cancer at diagnosis was mostly local compared to 1973-82. In their 5-year relative survival analysis the American Indians group and the non-Hispanic whites experienced statistically significant better survival when the stage at diagnosis was local. The Cox model indicated that American Indian women

experienced poorer survival in comparison to non-Hispanic whites during both time periods.(20) Gilliland et al examined cancer survival comparing American Indians, Hispanic and non-Hispanic whites in New Mexico and Arizona controlling for such factors as age, gender, stage at diagnosis, histologic grade, and treatment. They found that over time survival had improved for each ethnic group however this improvement was seen more in the non-Hispanic whites than the American Indians and Hispanics also, disparities in survival for the different ethnic groups widened over the study time period (1969-1994). They went on to remark that controlling for the distribution of age, gender, stage at diagnosis, histologic grade, and treatment did not completely explain the improved survival or ethnic disparities regarding survival. They did mention factors such as lower socioeconomic status, poverty and lower educational attainment as possible contributors to advanced stage at diagnosis and poorer survival. Zhang et al recently examined the impact of stage and treatment on short-term survival of lung, colorectal, and breast cancers. They calculated relative survival rates according to age, sex, stage, and treatment. They also calculated multivariate relative survival to examine the relative risk of dying from cancer and 95% confidence intervals. They found that those individuals diagnosed with advanced (TNM stage III or IV) stages of cancer had significantly lower relative survival rates than those diagnosed at early stages (TNM stage I or II). For colorectal cancer, their results suggest that age and sex have little impact on cancer survival but TNM stage and initial treatment strongly influence 2-

year relative survival rates. For breast cancer, their study demonstrated that TNM stage as well as age at diagnosis play an important role in breast cancer survival. They go on to conclude that TNM stage is the strongest prognostic factor for the survival of lung, colorectal and breast cancer patients. Initial treatment and age also play important roles. Certain effect modifications between age and stage need to be investigated in further studies.

Cancer stage at diagnosis may be used as a proxy measure for access to diagnostic and or preventive services especially in the context of the north of Saskatchewan. As Gillis et al point out, First Nations and northerners on social assistance experience few financial problems in accessing hospital and physician services when they are required. As with the all other residents of Saskatchewan, there are free physician and hospitalization services through the universal health plan. First Nations people and northerners on social assistance benefit from health travel coverage; however, even with this assistance, access is not always easy. Individuals living in the north must travel between 200 and 800 miles to a secondary or tertiary hospital. Thus diagnosis may be delayed and follow-up treatment is made difficult.(5) One can deduce that a diagnosis at early stage is perhaps related to readily accessible diagnostic and treatment services.

Factors such as cancer stage at time of diagnosis, age and treatment are important variables to examine when describing and comparing the survival patterns of different populations. By controlling for these factors one

can better understand the severity of cancer in a population and hence try to impact prevention and treatment strategies.

2.5 Summary

Breast, colorectal and cervical cancer incidence is high or increasing or relatively high among northerners and First Nations as compared to non-First Nations. Survival for these three sites is poorer or equal for northerners and First Nations in comparison to non-First Nations populations. Colorectal, breast and cervical cancers have secondary prevention strategies attached to them, they all have improved survival with early detection. It is useful to examine stage specific distribution and survival for these sites to see what influence stage has on survival. Stage can be used as a proxy measure for access to secondary prevention and treatment services, especially in the context of the north.

3. Objectives:

This study serves to:

1. Explore and describe the Breast, Cervical, and Colorectal cancer distribution by stage at the time of diagnosis of the northern First Nation, northern non-First Nation, southern First Nation, and southern non-First Nation population groups in Saskatchewan.

2. Explore and describe the unadjusted Breast, Cervical, and Colorectal cancer survival pattern among the northern First Nation, northern non-First Nation, southern First Nation, and southern non-First Nation population groups in Saskatchewan.

3. Ascertain what role if any, severity of cancer at time of diagnosis, measured by stage of cancer at time of diagnosis, has in survival of breast, cervical, and colorectal cancers among northern First Nation, northern non-First Nation, and southern First Nation populations in comparison to southern non-First Nations.

4. Methods:

4.1 Design

This is a descriptive epidemiological study of cancer incidence and survival for the period of 1970 to 1995 for cancer of the female breast, cancer of the cervix, and colorectal cancer. The setting for the study is Saskatchewan, with the four study groups being, northern First Nations, northern non-First Nations, southern First Nations, and southern non-First Nations. Comparisons will be made between these groups. Data from the Saskatchewan Cancer Registry will be analyzed.

4.2 Setting and Population

4.2.1 Setting

Northern Saskatchewan can be considered a unique population given its geographic and ethnic make-up. It is defined geographically by Saskatchewan Health as roughly the northern half of Saskatchewan and historically has been the Northern Administrative District and Northern Health Services Branch area. It coincides with the boundaries of Census Division #18, and now approximates the health service areas of the Mamawetan/Churchill River Health District, Keewatin Yathe' Health District, and the Athabasca Health Authority area.(see Appendix A) Health care services are provided in a somewhat different manner in the north as compared to the south. Physicians from larger centres in the

north travel regularly to smaller communities in the north to provide routine medical care. In most of the communities that do not have resident physicians, primary care nurses that live in the community, along with community health workers and other allied health workers, provide both clinical diagnostic and treatment services as well as public health services.(1) The ethnic makeup of the north compared to the south is quite different. First Nations comprise just over half of the population of Northern Saskatchewan, however just over 7% of the provincial population is First Nation in 1993/94. The northern population of Saskatchewan in 1993-94 is spread over more than 40 communities, a few of which have no road access.

4.2.2 Population

For the purpose of this study, the Saskatchewan population will be divided into four mutually exclusive groups. This is outlined in the following table and described in more detail following:

Table 4.2.2.1 - Study Groups used for this study

Location	Population Group	
North	First Nation	Non-First Nation
South	First Nation	Non-First Nation

Residents of northern and southern Saskatchewan were grouped as First Nations and Non-First Nations

As in the Irvine et al study on hospitalization for northern Saskatchewan residents and Saskatchewan First Nations, the definition of the northern residents is persons with residence codes in the area covered by the previous Northern Health Services Branch. This now approximates the new service areas of Mamawetan/Churchill River Health District, Keewatin Yathe' Health District, and the Athabasca Health Authority area. Those in the south are those persons not in the area.(2). For more detail of what communities were used to define the north see Appendix B.

4.3 Data

The data used in the study is derived from the Saskatchewan Cancer Registry, which has been maintaining cancer data since 1932.

4.3.1 The Saskatchewan Cancer Registry

The Saskatchewan Cancer Foundation is an autonomous body responsible for the provincial Cancer Control Program. It is incorporated under the Saskatchewan Cancer Foundation Act; its board of governors is appointed by Lieutenant Governor-in-Council. The Saskatchewan Cancer Program encompasses prevention, detection, diagnosis, treatment, and follow-up of patients with malignant or premalignant disease.(49) Cancer services data are maintained in the population-based registry which has a record of all people in Saskatchewan who have been diagnosed as having

cancer. The registry was established in 1932, but complete computerized data (all cancer sites) are available since 1967; pre- 1967 data are being computerized retroactively. There have been no major changes in data collection since 1985. The registry increases by about 6,000 cases per year (including non-melanoma skin cancer and in-situ cancers); the database includes approximately 137,000 individual patients and over 170,700 case records (the difference indicates the number of patients with cancer of two or more primary sites). Within Canada, patients who move out of province receive continued surveillance through the appropriate provincial cancer clinic. All cases of invasive cancer are maintained on a follow-up program for a minimum of 20 years. The rate of loss-to-follow-up is approximately 3%. The Saskatchewan Cancer Foundation Act dictates that information from medical professionals and hospital records required to complete the cancer registration must be provided upon request. All pathology reports indicating a cancer diagnosis are forwarded to the Cancer Clinics, as are death certificates with a cancer diagnosis.(49)

The cancer registry contains patient identification, case, death, and review information. Cancer site data are coded using International Classification of Diseases for Oncology (ICDO) Version 2; death information is coded using International Classification of Diseases version 9 (ICD-9).
The basic information include:

1. Patient Identification:

    - health services number (encrypted for the analysis for confidentiality)

2. Case Information:

   - including information on registration, final diagnostic information (e.g. ICDO-T, ICDO-M, grade, laterality, dates of diagnosis, method of diagnosis, TNM Stage, metastases at diagnosis).

   - residence, age and gender information

3. Death Information:

   - primary and secondary cause;

   - disease status at death.

4. Review Information:

   - including review date, recurrence, metastases, treatment, performance.(48)

4.3.2 Data for this study

The data for this study has been obtained from the Saskatchewan Cancer Registry. As this study is examining stage information for breast, colorectal and cervical cancer sites, three data files have been obtained. Each file covers different time points. This can be explained as follows. The data quality for the stage variable is different for different cancer sites. As there are data quality issues with the stage variable, different time points for stage will be used. For breast cancer the stage variable is complete from 1970-95 and therefore diagnoses occurring from the years 1970 to 1995 will be used. For colorectal cancer the stage variable is complete from 1990-95 and

therefore diagnoses occurring from the years 1990 to 1995 will be used. For cervical cancer the staging variable is complete from 1980-95 and therefore diagnoses occurring from the years 1980 to 1995 will be used. Hence, the three data files are as follows:

1. Breast cancer data for the years 1970 to 1995
2. Cervical cancer data for the years 1980 to 1995
3. Colorectal cancer data for the years 1990 to 1995

4.3.3 Data limitations

Given the high quality of medical care and universal coverage in Saskatchewan, missed diagnoses should be uncommon and therefore data quality is quite good. This is with the exception of the staging variable mentioned above.

4.4 Method of Analysis

This section describes the general methodology used in this study.

4.4.1 Stage

Cancer staging systems describe how far cancer has spread anatomically. The stage is one of the most important factors in determining both the treatment and prognosis. The concept of stage is applicable to almost all cancers except for most forms of leukemia. The cancer staging system used in this study is the "TNM" system where TNM stands for Tumor,

Nodes and Metastases. Each of these is classified with a number to give the total stage. Thus a T1 N1 M0 cancer is defined as having a T1 tumor, N1 lymph node involvement, and no metastases.

T - T Classifies the extent of the primary tumor, and is normally given as T0 through T4. T0 represents a tumor that has not even started to invade the local tissues. This is called "In Situ". T4 on the other hand represents a large primary tumor that has probably invaded other organs by direct extension and is usually inoperable.

N - N classifies the amount of regional lymph node involvement. It is important to understand that only the lymph nodes draining the area of the primary tumor are considered in this classification. Involvement of distant lymph nodes is considered to be metastatic disease. The definition of just which lymph nodes are regional depends on the type of cancer. N0 means no lymph node involvement while N4 means extensive involvement. In general more extensive involvement means some combination of more nodes involved, greater enlargement of the involved nodes, and more distant (but still regional) node involvement.

M - M is either M0 if there are no metastases or M1 if there are metastases. The exact definitions for T and N are different for each different kind of cancer. The various combinations of T, N, and M are grouped to describe the stage of the cancer numerically into four stages(50). These are: for breast cancer and cervical cancer TNM stages I, II, II, and IV. Colorectal cancer will be divided into four comparable stages using the Dukes system of staging

classification, Dukes stage A, B, C, and D. Cancer staging is done at the time of diagnosis. For the descriptive and survival analyses stage will be used as a categorical variable.

4.4.2 Age-groups

Within the cancer registry data, age at time of diagnosis is recorded. For the purpose of the descriptive analysis of the data for each cancer site, age-groupings will be constructed. For cancer of the breast the age-groups will be as follows: 14 to 39, 40 to 49, 50 to 64, and 65 & above. The youngest case in the breast data is 14 years old and therefore the age-groups start at 14 to 39. The 40 to 49 age-group is a pre-screening age-group. The 50 to 64 age-group contains the age at which breast cancer screening is targeted (50 and above). For cervical cancer the age-groups are as follows: 18 to 34, 35 to 49 , 50 to 69, 70 and above. Screening for cervical cancer starts at age 18 or after initiation of sexual activity. For colorectal cancer the age-groups are as follows: 20 to 49, 50 to 64, 65 and above. For the survival analysis age will be used as a continuous variable.

4.4.3 Survival

Cancer survival is an indicator which quantifies the effects of cancer detection and treatment on the natural history of the disease. It can be simply expressed as the percentage of patients alive at a certain point in time after the first diagnosis.

Survival analysis takes the survival times of a group of subjects and generates a survival curve, which shows how many of the members remain alive over time. Survival time is usually defined as the length of the interval between diagnosis and death. The major mathematical complication with survival analysis is that you usually do not have the luxury of waiting until the very last subject has died of old age; you normally have to analyze the data while some subjects are still alive. Also, some subjects may have moved away, and may be lost to follow-up. In both cases, the subjects were known to have survived for some amount of time (up until the time you last saw them), but you don't know how much longer they might ultimately have survived. In this case these subjects are known as "censored". Several methods have been developed for using this "at least this long" information for preparing unbiased survival curve estimates, the most common being the Life Table method and the method of Kaplan and Meier(51).

The Kaplan Meier method will be used to calculate the crude survival experience for the four study groups. With the Kaplan-Meier method, the survival rate is recalculated every time a patient dies. To calculate the fraction of subjects who survived on a particular day, the number alive at the end of the day is divided by the number alive at the beginning of the day (excluding any who were censored on that day from both the numerator and denominator). This is the fraction of subjects who were alive at the beginning of a particular day who were still alive at the beginning of the next day. To calculate the fraction of subjects who survive from day 0 until a particular

day, the fraction of subjects who survive day 1 is multiplied by the fraction of those subjects who survive day 2, multiplied by the fraction of those subjects who survive day 3 ... multiplied by the fraction who survive day k. This method automatically accounts for censored subjects, as both the numerator and denominator are reduced on the day a patient is censored. Because the product of many survival fractions is calculated, this method is also called the product-limit method. Note that day refers to day of the study, not a particular day on the calendar. Day I is the first day of the study for each subject(51).

It is sometimes necessary to know whether survival is influenced by one or more factors, called "predictors" or "covariates", which may be categorical (such as TNM stage at time of diagnosis) or continuous (such as the subjects age). For these complicated situations we need a special kind of regression that lets us assess the effect of each predictor on the shape of the survival curve. This regression is referred to as the Cox proportional hazards model.

To understand the method of proportional hazards, first consider a "baseline" survival curve. This can be thought of as the survival curve of a hypothetical "completely average" subject, someone for whom each predictor variable is equal to the average value of that variable for the entire set of subjects in the study. This baseline survival curve doesn't have to have any particular formula representation; it can have any shape whatever, as long as it starts at 1.0 at time 0 and descends steadily with increasing survival time. The baseline survival curve is then systematically "flexed" up or down by each

of the predictor variables, while still keeping its general shape. The proportional hazards method computes a coefficient for each predictor variable that indicates the direction and degree of flexing that the predictor has on the survival curve. Zero means that a variable has no effect on the curve, it is not a predictor at all; a positive variable indicates that larger values of the variable are associated with greater mortality. Knowing these coefficients, we could construct a "customized" survival curve for any particular combination of predictor values. More importantly, the method provides a measure of the sampling error associated with each predictor's coefficient. This assess which variables' coefficients are significantly different from zero; that is: which variables are significantly related to survival(52).

The Cox proportional hazards model will be used to calculate the relative risks and adjusted survival curves for each of the study groups in comparison with the southern non-Fist Nation group. The Cox proportional hazards model allows for adjustment of covariates when examining survival. In this case the covariates will be stage of disease at time of diagnosis and age at time of diagnosis.

Using the Cox proportional hazards model, comparison of the relative risk of dying from breast cancer, colorectal cancer or cervical cancer between study groups can be calculated after controlling for the effects of age and staging. Two analyses have been undertaken here. The first one uses death from all causes as the end point. The second one uses death from breast cancer as the end point. The survival analysis using death from all causes is

calculated for two reasons. One can argue that although the official cause of death on the death certificate may be something other than breast cancer, breast cancer may have influenced or had an effect on the death of the person. Second, using death from all causes allows for larger a number of cases to be used in the analysis thus increasing the precision of the relative risk estimate. This can be illustrated by noting the smaller confidence interval about the relative risk estimate. The relative risk of dying of cancer for each study group is calculated and compared to the southern non-First Nations group or the reference group.

Length of survival for this study is defined as the interval between date of diagnosis and either date of death or date of last follow-up. The statistical program SPSS 9.0 is used for all analyses including Kaplan-Meier and Cox proportional hazards model.

5. Results

In this section results for breast, cervix, and colorectal cancers will be presented. A brief discussion of these results will follow each section presentation. Some more detailed discussion will be presented in Chapter 6, Summary Discussion.

5.1 Cancer of the Female Breast

The International Classification of Diseases for Oncology (ICDO) codes for cancer of the female breast used were; C50.0 to C50.9.

5.1.1 Distribution of Breast Cancer cases

Table 5.1.1.1 - Distribution of Breast Cancer by study group and TNM stage, 1970-1995

Study Group	TNM Stage				Total
	I	II	III	IV	
Northern FN	6 (15.8%)	25 (65.8%)	4 (10.5%)	3 (7.9%)	38 (100.0%)
Northern Non-FN	25 (34.7%)	42 (58.3%)	2 (2.8%)	3 (4.2%)	72 (100.0%)
Southern FN	19 (18.6%)	66 (64.7%)	10 (9.8%)	7 (6.9%)	102 (100.0%)
Southern Non-FN	4300 (40.3%)	4880 (45.8%)	804 (7.5%)	681 (6.4%)	10665 (100.0%)
Total	4350 (40.0%)	5013 (46.1%)	820 (7.5%)	694 (6.4%)	10877 (100.0%)

FN = First Nation

679 cases with missing stage data

Table 5.1.1.1 examines the proportion of breast cancer cases over the four TNM stages by study group. The distribution of cases within the two First

Nation groups is quite similar. More striking is the differences between TNM stage I and TNM stage II between the four study groups. For the northern First Nation and southern First Nation groups approximately 65% of those women with breast cancer between the years 1970 and 1995 were diagnosed at TNM stage II where as only 18.6% and 15.8% were diagnosed at stage I for Southern First Nations and Northern First Nations respectively. This finding is in contrast to the northern non-First Nation group and more so the Southern non-First Nation group. For the Southern non-First Nation group 40.3% of women were diagnosed with breast cancer at TNM stage I and 45.8% were diagnosed at TNM stage II. The northern First Nation group had a similar distribution with 34.7% diagnosed at TNM stage I and 58.3% diagnosed at TNM stage II.

Table 5.1.1.2 - Distribution of Breast Cancer by study group and age, 1970-1995

Study Group	Age Group (years)				Total
	14 to 39	40 to 49	50 to 64	65 & above	
Northern FN	8 (19.5%)	10 (24.4%)	13 (31.7%)	10 (24.4%)	41 (100.0%)
Northern Non-FN	14 (16.7%)	23 (27.4%)	19 (22.6%)	28 (33.3%)	84 (100.0%)
Southern FN	19 (17.9%)	24 (22.6%)	32 (30.2%)	31 (29.2%)	106 (100.0%)
Southern Non-FN	628 (5.5%)	1561 (13.8%)	3803 (33.6%)	5333 (47.1%)	11325 (100.0%)
Total	669 (5.8%)	1618 (14.0%)	3867 (33.5%)	5402 (46.7%)	11556 (100.0%)

FN = First Nation

Before examining age comparisons between the four study groups it is important to mention the differing age structures between these population groups.

Both the northern and southern First Nation groups have higher proportion of their populations as infants and children than the southern non-First Nation population and lower proportions of their populations over age 65 years. The First Nation populations have over twice the proportion of persons under age 5 compared to the southern non-First Nation group. Conversely the southern non-First Nation group has almost three times the proportion of persons aged 50 and over compared to the First Nation populations and to a lesser extent the northern non-First Nation group.(2) It is therefore important to keep this differing population structure in mind when age is compared between the different study groups.

In Table 5.1.1.2 the distribution women diagnosed with breast cancer is displayed by study group. This table includes the distribution between all the different age groups as well as the distribution between the age groups 40 to 49 (pre-screening age) and 50 to 64 (targeted screening ages). Looking at all the age groups first, the Northern First Nation group had a fairly even distribution of cases over the four different age groups. The Southern non-First Nation group had a much larger proportion of cases at ages 50 to 64 and 65 and above.

Table 5.1.1.3 - Distribution of Breast Cancer by study group, TNM Stage and age, 1970-1995

		Age Group (Years)				Total
Study Group	TNM Stage	14 to 39	40 to 49	50 to 64	65 and above	
Northern FN	I	1 (16.7%)	2 (22.2%)	1 (7.7%)	2 (20.0%)	6 (15.8%)
	II	4 (66.7%)	7 (77.8%)	10 (76.9%)	4 (40.0%)	25 (65.8%)
	III	1 (16.7%)	-	2 (15.4%)	1 (10.0%)	4 (10.5%)
	IV	-	-	-	3 (30.0%)	3 (7.9%)
Total		6 (100.0%)	9 (100.0%)	13 (100.0%)	10 (100.0%)	38 (100.0%)
Northern Non-FN	I	3 (27.3%)	7 (33.3%)	4 (22.2%)	11 (50.0%)	25 (34.7%)
	II	8 (72.7%)	12 (57.1%)	13 (72.2%)	9 (40.9%)	42 (58.3%)
	III	-	1 (4.8%)	1 (5.6%)	-	2 (2.8%)
	IV	-	1 (4.8%)	-	2 (9.1%)	3 (4.2%)
Total		11 (100.0%)	21 (100.0%)	18 (100.0%)	22 (100.0%)	72 (100.0%)
Southern FN	I	3 (16.7%)	2 (8.3%)	10 (33.3%)	4 (13.3%)	19 (18.6%)
	II	11 (61.1%)	19 (79.2%)	16 (53.3%)	20 (66.7%)	66 (64.7%)
	III	3 (16.7%)	2 (8.3%)	1 (3.3%)	4 (13.3%)	10 (9.8%)
	IV	1 (5.6%)	1 (4.2%)	3 (10.0%)	2 (6.7%)	7 (6.9%)
Total		18 (100.0%)	24 (100.0%)	30 (100.0%)	30 (100.0%)	102 (100.0%)
Southern Non-FN	I	194 (33.0%)	571 (38.4%)	1480 (40.6%)	2055 (41.6%)	4300 (40.3%)
	II	320 (54.4%)	760 (51.1%)	1685 (46.2%)	2115 (42.8%)	4880 (45.8%)
	III	50 (8.5%)	97 (6.5%)	252 (6.9%)	405 (8.2%)	804 (7.5%)
	IV	24 (4.1%)	59 (4.0%)	230 (6.3%)	368 (7.4%)	681 (6.4%)
Total		588 (100.0%)	1487 (100.0%)	3647 (100.0%)	4943 (100.0%)	10665 (100.0%)

FN = First Nation

Table 5.1.1.3 examines the distribution of breast cancer by study group, TNM stage and age. For all study groups throughout all the age groups the large majority of cases were either TNM stage I or II. It is interesting to note that in the southern non-First Nations group for ages 40 to 49 (pre-screening), 38.4% of those women diagnosed with breast cancer were diagnosed at TNM stage I where 51.1% were diagnosed at TNM stage II. In the age group 50 to 64 (targeted screening) the distribution between TNM stage I and II is different, with 40.6% diagnosed at stage I and 46.2% diagnosed at stage II. In comparison to this the two First Nation groups in the age group 40 to 49, over 75% of those women diagnosed with breast cancer were diagnosed with TNM stage II. In the 50 to 64 age-group the northern First Nation group had 76.9% of the breast cancer diagnoses at TNM stage II with only 7.7% at stage I. In the southern First Nation group 53.5% were diagnosed at stage II and 33.3% at stage I. For the northern First Nation group there appears to be less effect of the screening program catching cases at an earlier stage. The mammography screening program in the north was started in 1990, therefore, for this study only diagnoses for the last five years of data (1990 to 1995) are available since the screening program inception. The larger proportion of TNM stage II breast cancer diagnoses in the 50 to 64 age-group in comparison to the proportion of TNM stage I diagnoses for the northern First Nations group, may be a reflection of a slightly later start for mammography in the north, but also perhaps a reflection of clinical breast examination and breast self-examination practices in this population group. It must be kept in mind

however that the number of cases for the northern First Nation group in these age groups is small.

Table 5.1.1.4 - Distribution of deaths among breast cancer patients from breast cancer and all causes by study group, 1970-1995

Study Group	Death from Breast Cancer	Death from all causes	Proportion of Breast Cancer Deaths
Northern FN	19	21	90.5%
Northern Non-FN	27	47	57.4%
Southern FN	33	53	62.3%
Southern Non-FN	3452	6337	54.5%
Total	3531	6458	54.7%

FN = First Nation

Comparing the cause of death by study group (Table 5.1.1.4) a striking difference can be noticed. For the southern non-First Nation group 54.5% of those women who died with a diagnosis of breast cancer, died from breast cancer. The northern non-First Nation and southern First Nation groups had similar distributions. Conversely 90.5% of those women with breast cancer in the northern First Nation group who died from breast cancer.

Table 5.1.1.5 - Distribution of death among breast cancer patients from breast cancer and all causes by study group and TNM stage, 1970-1995

Study Group	TNM Stage	Death from Breast Cancer	Death from all causes	Proportion of Breast Cancer Deaths
Northern FN	I	3	3	100.0%
	II	9	11	81.8%
	III	4	4	100.0%
	IV	2	2	100.0%
Total		18	20	90.0%
Northern Non-FN	I	2	6	33.3%
	II	16	26	61.5%
	III	2	2	100.0%
	IV	1	3	33.3%
Total		21	37	56.8%
Southern FN	I	2	5	40.0%
	II	20	31	64.5%
	III	4	7	57.1%
	IV	5	7	71.4%
Total		31	50	62.0%
Southern Non-FN	I	613	1718	35.7%
	II	1597	2827	56.5%
	III	459	655	70.1%
	IV	530	655	80.9%
Total		3199	5855	54.6%

FN = First Nation

Table 5.1.1.5 describes the distribution of deaths of those women who were diagnosed with breast cancer by study group and stage. For the southern First Nation and southern non-First Nation groups the pattern of distribution is as expected with the worse the stage of disease at diagnosis, the more likely one dies from the underlying cancer, in this case cancer of the breast. The two northern study groups however, have a different distribution in comparison to the south. In the northern First Nation group for TNM stages I, II, and IV, 100% of those women who died with a breast cancer diagnosis, actually died from breast cancer. Of those that died with a diagnosis at TNM stage II, 81.8% died

from breast cancer. In the northern non-First Nation group 33.3% of the deaths were attributable to breast cancer among the TNM stage I and IV diagnoses. Of those diagnosed at TNM stage II, 61.5% of the deaths were attributable to breast cancer. All of the deaths of those women diagnosed at TNM stage III were attributable to breast cancer.

Table 5.1.1.6 - Distribution of deaths among breast cancer patients from breast cancer and all causes by study group and age, 1970-1995

Study Group	Age Group (Years)	Death from Breast Cancer	Death from all causes	Proportion of Breast Cancer Deaths
Northern FN	14 to 39	3	4	75.0%
	40 to 49	3	3	100.0%
	50 to 64	5	6	83.3%
	65 and above	8	8	100.0%
Total		19	21	90.5%
Northern Non-FN	14 to 39	4	5	80.0%
	40 to 49	8	12	66.7%
	50 to 64	8	11	72.7%
	65 and above	7	19	36.8%
Total		27	47	57.4%
Southern FN	14 to 39	10	10	100.0%
	40 to 49	6	10	60.0%
	50 to 64	7	13	53.8%
	65 and above	10	20	50.0%
Total		33	53	62.3%
Southern Non-FN	14 to 39	220	276	79.7%
	40 to 49	482	631	76.4%
	50 to 64	1256	1882	66.7%
	65 and above	1494	3548	42.1%
Total		3452	6337	54.5%

FN = First Nation

Table 5.1.1.6 describes the distribution of the deaths of those women diagnosed with breast cancer by study group and age. An interesting pattern is seen here amongst all the study groups. The younger age-groups have a higher proportion of deaths attributable to breast cancer in comparison to the

older age- groups. In the northern First Nation group however, the percentage of deaths attributable to breast cancer is high (75% or more) for all four age-groups.

5.1.2 Breast Cancer Survival 1970 to 1995

The crude survival for breast cancer was calculated using the Kaplan Meier method. Two end points for survival were used;

1) death from all causes and; 2) death from breast cancer.

Figure 5.1.2.1 - Survival curves of breast cancer patients by study group (death from all causes) 1970 - 1995

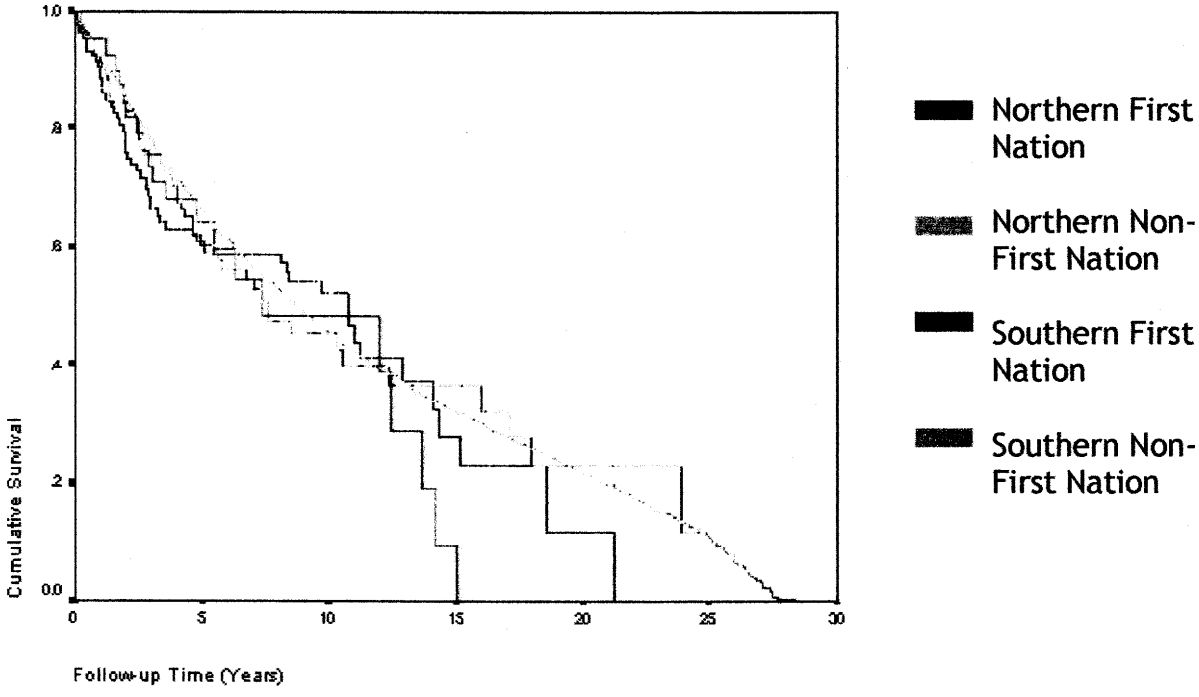


Figure 5.1.2.1 shows the probability of survival over time (Kaplan Meier Curves), where time zero is the time of diagnosis. By looking at the curves alone the four study groups have a similar survival experience over the first

five years after diagnosis. The northern First Nation group had a five-year survival rate of 61%. While the northern non-First Nation group had a survival rate of 59%. The southern First Nation group had a five-year survival of 60%. The comparison group, the southern non-First Nation group, had a five-year survival rate of 66%. Using the Log Rank test to compare the survival distribution between the four study groups, the four study groups are found to be not significantly different (p=0.61) where the end point is death from all causes.

Figure 5.1.2.2 - Survival curves of breast cancer patients by study group (death from breast cancer) 1970 - 1995

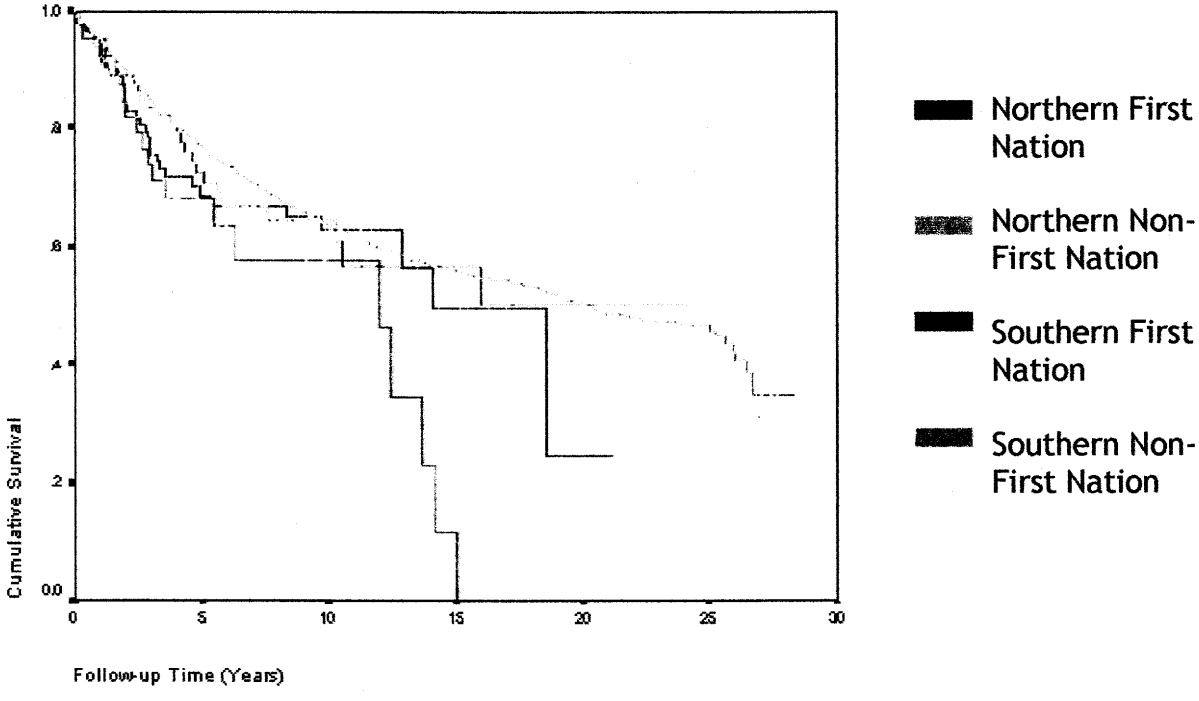


Figure 5.1.2.2 displays the Kaplan Meier survival curves for the four study groups using death from breast cancer as the end point. In this instance the

four curves have a different pattern in relation to one another compared to the survival curves calculated using death from all causes as the end point (Figure 5.1.2.1). As expected, the survival for the northern First Nation group is worse in comparison to the other study groups. This is to be expected as table 5.1.1.4 showed 90.5% of those women in the northern First Nation group who died with a diagnosis of breast cancer died of breast cancer. For the other three study groups, 62.3% or less died from breast cancer. The 5 year survival rate for each study group is as follows: northern First Nation 67%, northern non-First Nation 71%, southern First Nation 69%, southern non-First Nation 77%. When the end point is death from breast cancer, there was a significant difference in the survival distribution between the four study groups ($p = 0.02$, Log-rank test).

5.1.3 Cox Proportional Hazards Model

Univariate or crude survival analysis and multivariate or adjusted survival are presented here. Comparison of crude and adjusted survival is useful as crude survival was used to calculate cancer survival in previous Saskatchewan studies. As mentioned earlier, the authors of the previous study on this population suggest an examination of survival adjusting for factors such as stage of disease at diagnosis and age.

Table 5.1.3.1 - Univariate and Multivariate Relative Risks for Study Groups from Cox's model, breast cancer 1970-95 (death from all causes)

Model	Variable	RR	95% C.I.	p-value
Study Group alone	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.28	0.83 - 1.96	0.26
	Northern Non-FN	1.07	0.80 - 1.42	0.65
	Southern FN	1.12	0.86 - 1.48	0.38
Age + Study Group	Age	1.04	1.03 - 1.04	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.65	1.07 - 2.53	0.0011
	Northern Non-FN	1.36	1.02 - 1.82	0.02
	Southern FN	1.42	1.09 - 1.87	0.0104
Stage + Study Group	TNM Stage			
	I	1.00	-	-
	II	1.64	1.55 - 1.74	< 0.0001
	III	4.22	3.85 - 4.62	< 0.0001
	IV	9.87	8.99 - 10.84	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.25	0.81 - 1.94	0.32
	Northern Non-FN	0.97	0.70 - 1.35	0.87
	Southern FN	0.91	0.69 - 1.20	0.51
Age + Stage + Study Group	Age	1.04	1.03 - 1.04	< 0.0001
	TNM Stage			
	I	1.00	-	-
	II	1.70	1.60 - 1.81	< 0.0001
	III	4.11	3.76 - 4.50	< 0.0001
	IV	9.03	8.22 - 9.91	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.50	0.97 - 2.32	0.072
	Northern Non-FN	1.22	0.88 - 1.68	0.24
	Southern FN	1.20	0.91 - 1.58	0.20

FN = First Nation, RR = Relative Risk, C.I. = Confidence Interval

Table 5.1.3.1 displays the results of the Cox's proportional hazards model analysis. The results from the univariate (crude) and multivariate (adjusted) Cox's model is presented where the end point for survival is death from all causes. Four models are presented here. Each model is necessary in order to

asses the influence of covariates on the relative risk of dying of breast cancer for each study group in comparison to the reference group, the southern non-First Nation group. The main interest here is the comparison of survival distribution between study groups. The first model, a univariate model, has study group alone in the model. With a relative risk greater than one the northern First Nation, northern non-First Nation and southern First Nation groups have a worse prognosis for breast cancer in comparison to the southern non-First Nation group. It is very important to note however that these relative risk estimates are not statistically significant and therefore these relative risk estimates may occur by chance alone. Examining the second model (Age and Study Group in the model) age is shown to be a strong predictor of survival. This is seen by the tight 95% confidence interval about the relative risk for age (1.04) and the highly significant p-value ($p < 0.0001$). The relative risk of age can be interpreted as follows. For a ten year increase in age, breast cancer patients are 1.48 times more likely to die of all causes ($1.48 = 1.04^{10}$). In comparison to the southern non-First Nation group, all other three groups have increased risk of dying from breast cancer. This is indicated by the statistically significant relative risks greater than one. The third model examines TNM stage and study group. Here TNM stage is shown to be a strong predictor of survival with highly significant p-values for stages II, III, and IV in comparison to the reference group, TNM stage I. After controlling for staging none of the study groups are significantly different from the southern non-First Nation group. The final model contains study

group, stage, and age. The final model presents the stage and age adjusted relative risk for each study group in comparison to the southern non-First Nation group. In this model both age at time of diagnosis and stage of disease at time of diagnosis are taken into account when calculating the relative risk of dying after a diagnosis of breast cancer. None of the three study groups, northern First Nation, northern non-First Nation, and southern First Nation are statistically different in comparison to the southern non-First Nation study group.

Table 5.1.3.2 - Univariate and Multivariate Relative Risks for Study Groups from Cox's model, breast cancer 1970-95 (death from breast cancer)

Model	Variable	RR	95% C.I.	p-value
Study Group alone	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.94	1.24 - 3.05	0.004
	Northern Non-FN	1.11	0.76 - 1.62	0.59
	Southern FN	1.23	0.87 - 1.74	0.23
Age + Study Group	Age	1.01	1.00 - 1.01	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	2.06	1.31 - 3.23	0.0017
	Northern Non-FN	1.18	0.81 - 1.73	0.39
	Southern FN	1.30	0.92 - 1.83	0.13
Stage + Study Group	TNM Stage			
	I	1.00	-	-
	II	2.55	2.33 - 2.80	< 0.0001
	III	7.54	6.69 - 8.51	< 0.0001
	IV	19.48	17.28 - 21.97	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.76	1.11 - 2.81	0.016
	Northern Non-FN	1.01	0.66 - 1.55	0.96
	Southern FN	0.91	0.64 - 1.30	0.62
Age + Stage + Study Group	Age	1.00	1.00 - 1.01	0.0009
	TNM Stage			
	I	1.00	-	-
	II	2.56	2.34 - 2.81	< 0.0001
	III	7.52	6.67 - 8.49	< 0.0001
	IV	19.22	17.04 - 21.68	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.81	1.14 - 2.87	0.013
	Northern Non-FN	1.05	0.68 - 1.61	0.84
	Southern FN	0.95	0.67 - 1.36	0.79

FN = First Nation, RR = Relative Risk, C.I. = Confidence Interval

Table 5.1.3.2 displays the results of the Cox's proportional hazards model analysis, where the end point is death from breast cancer. This analysis describes the relative risks of dying from breast cancer for each study group in comparison to the southern non-First Nation group. The relative risk

described here is calculated using the end point for survival as death from breast cancer. In the first model with study group alone, the northern First Nation group is found to have a 1.94 times greater risk of dying of breast cancer in comparison to the southern non-First Nation group. The risk of dying from breast cancer for the northern non-First Nation and southern First Nation groups in comparison to the southern non-First Nation group are not significantly different. From the second and third models, age at time of diagnosis and stage at time of diagnosis are both found to be statistically significant predictors of survival ($p<0.0001$). The final model shows northern First Nation women diagnosed with breast cancer have 1.8 times greater probability of dying of breast cancer in comparison to southern non-First Nation women, where the end point is death from breast cancer ($p = 0.01$). The two other study groups (northern non-First Nation and southern First Nation) did not show a significantly different risk of breast cancer deaths in comparison to the southern non-First Nation group. It is interesting to compare the relative risk for northern First Nation in model one (study group alone) and model four (study group +age + stage) to see the effect of adjusting for age and stage at time of diagnosis. In both models the northern First Nation group have a statistically significant relative risk in comparison to the southern non-First Nation group, however the strength of relative risk does change. The relative risk for the northern First Nation group is slightly lower when taking into account stage and age. As the 95% confidence interval in the stage and age adjusted survival model is tighter than the 95%

confidence interval for the non-adjusted model, it can be said that the relative risk for the stage and age adjusted model is more precise.

5.1.4 Cox Proportional Hazards Model - Survival Curves

In addition to calculating the adjusted relative risks, adjusted survival curves can also be obtained from Cox's proportional hazards model. The survival curves for the final model (age, stage, and study group) is presented below. Figures 5.1.4.1 to 5.1.4.4 are the age and stage adjusted survival curves, where the end point is death from all causes. The pattern for survival for each study group is consistent after adjusting for stage and age. The northern First Nations group has the worst survival pattern followed by the southern First Nation and northern non-First Nation groups. The best survival pattern is seen consistently in the southern non-First Nations group. The pattern of distribution between the four study groups remains similar for each TNM stage of disease. Figures 5.1.4.5 to 5.1.4.8 examine and compare the cumulative survival pattern for each study group controlling for stage and age, where the end point is death for breast cancer. Here there is a change in the pattern of survival in comparison to the previous analysis where the end point was death from all causes. The northern First Nation group experiences noticeably worse survival in comparison to the three other study groups, however, the three other study groups (northern non-First Nations, southern First Nations, and southern non-First Nations) all have a very comparable survival pattern. The southern First Nation group experience the best survival followed by the southern non-First Nation group and the

northern non-First Nation group. The difference between these three groups is very small however.

Figure 5.1.4.1 - Age adjusted survival from cancer of the Breast, TNM Stage I (death from all causes) 1970 - 1995

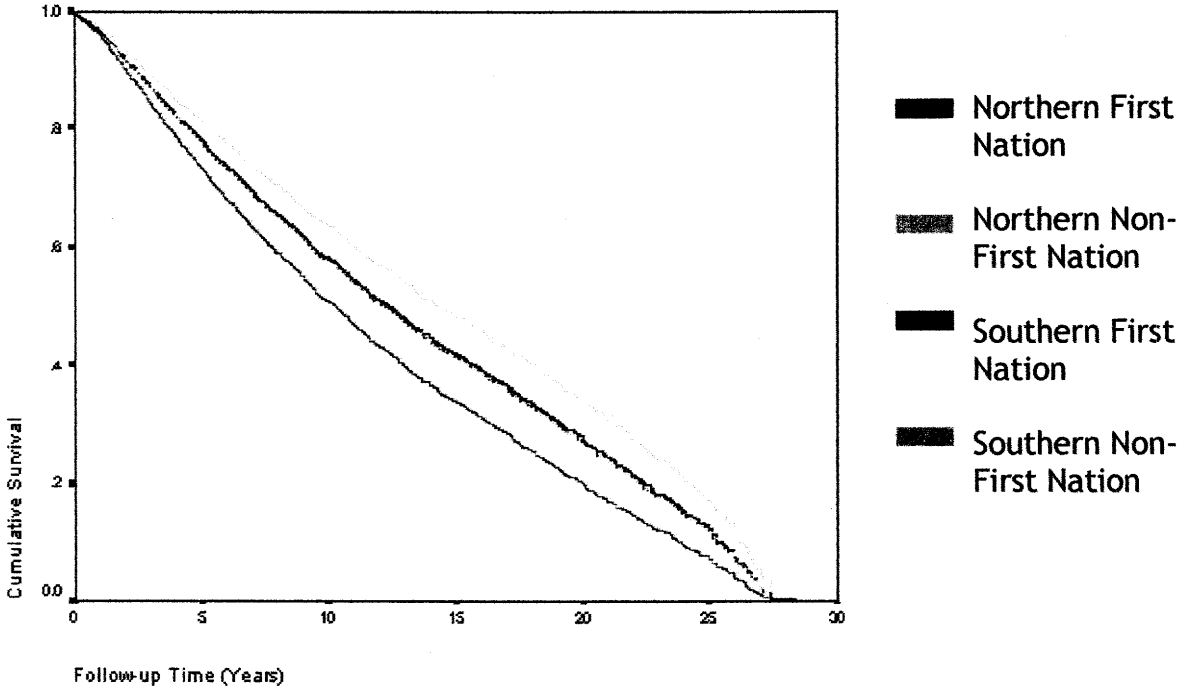


Figure 5.1.4.2 - Age adjusted survival from cancer of the Breast, TNM Stage II (death from all causes) 1970 - 1995

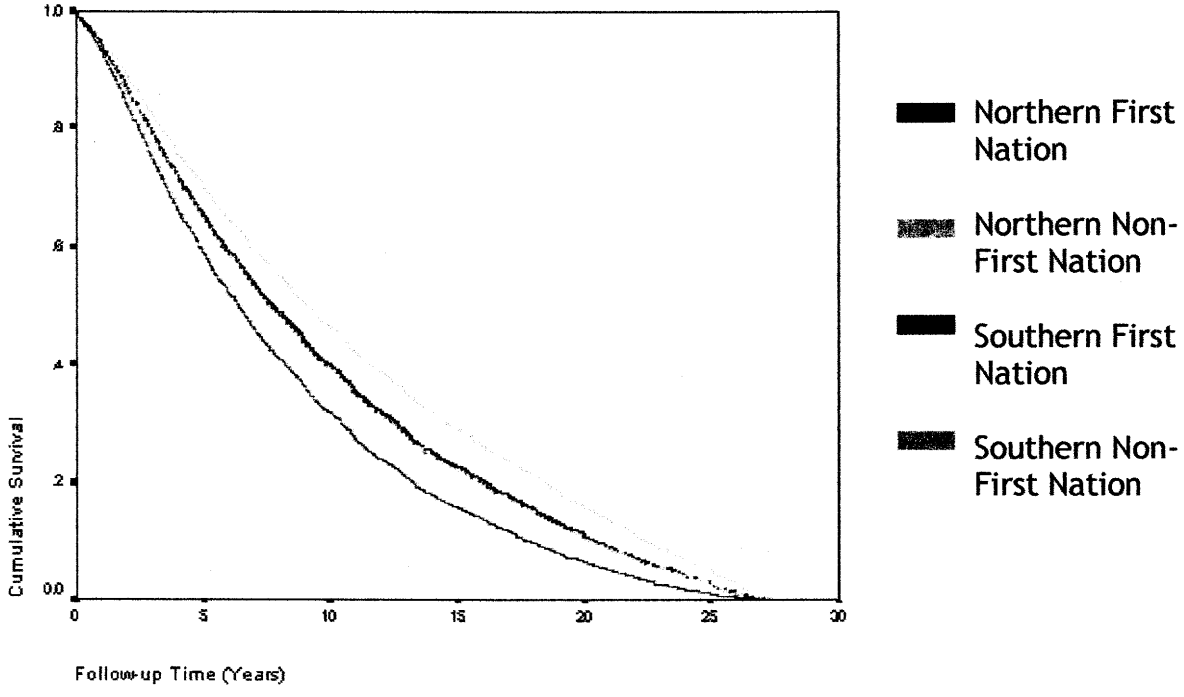


Figure 5.1.4.3 - Age adjusted survival from cancer of the Breast, TNM Stage III (death from all causes) 1970 - 1995

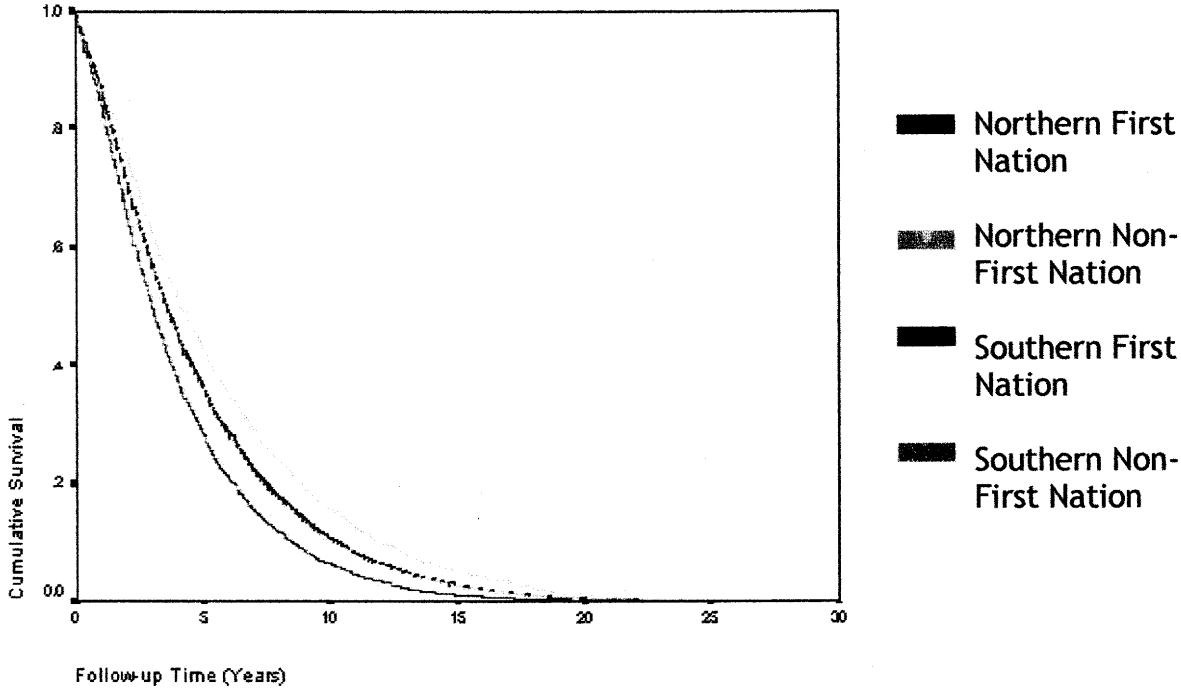


Figure 5.1.4.4 - Age adjusted survival from cancer of the Breast, TNM Stage IV (death from all causes) 1970 - 1995

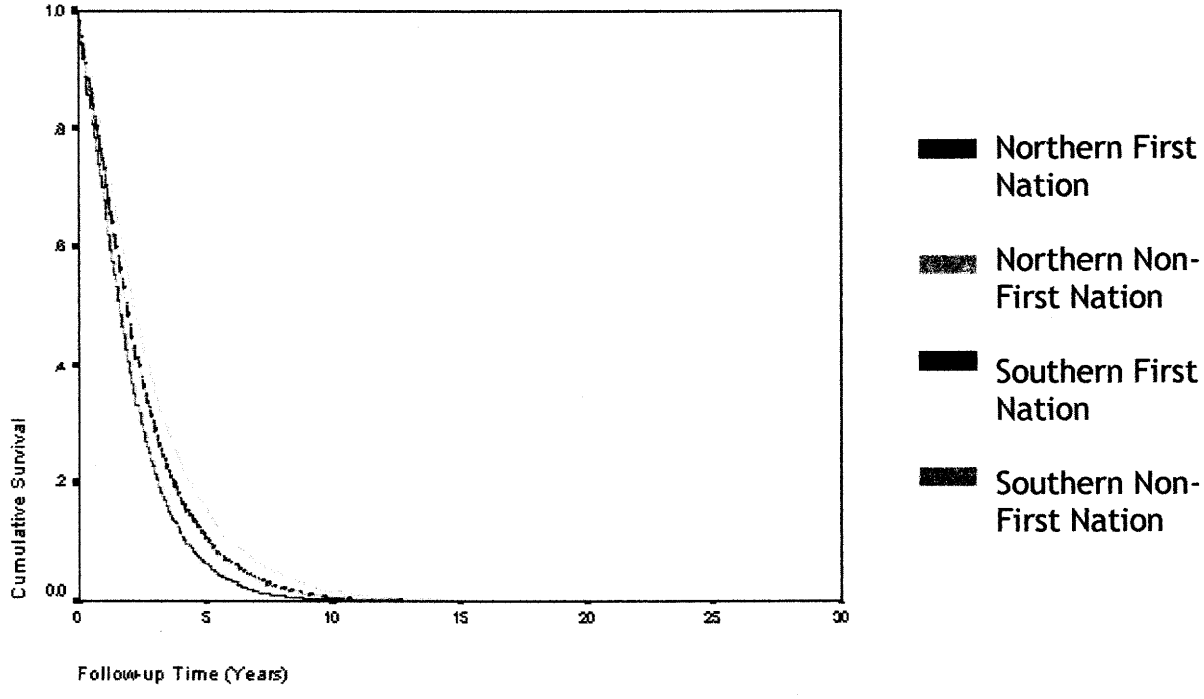


Figure 5.1.4.5 - Age adjusted survival from cancer of the Breast, TNM Stage I (death from breast cancer) 1970 - 1995

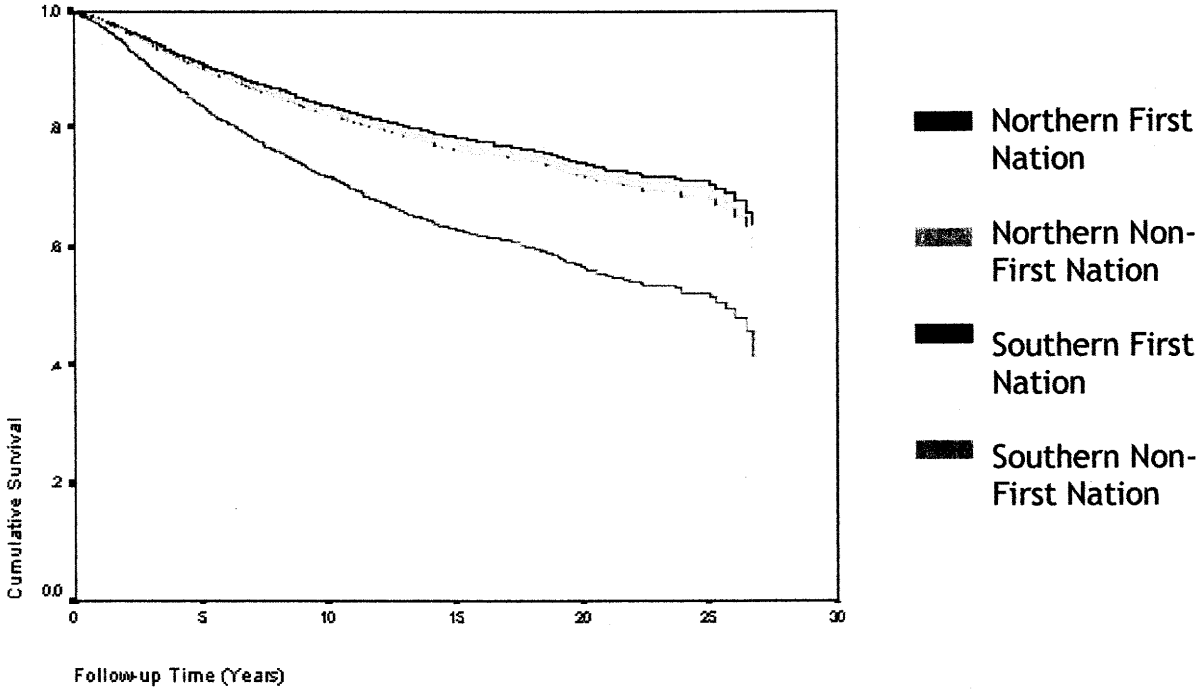


Figure 5.1.4.6 - Age adjusted survival from cancer of the Breast, TNM Stage II (death from breast cancer) 1970 - 1995

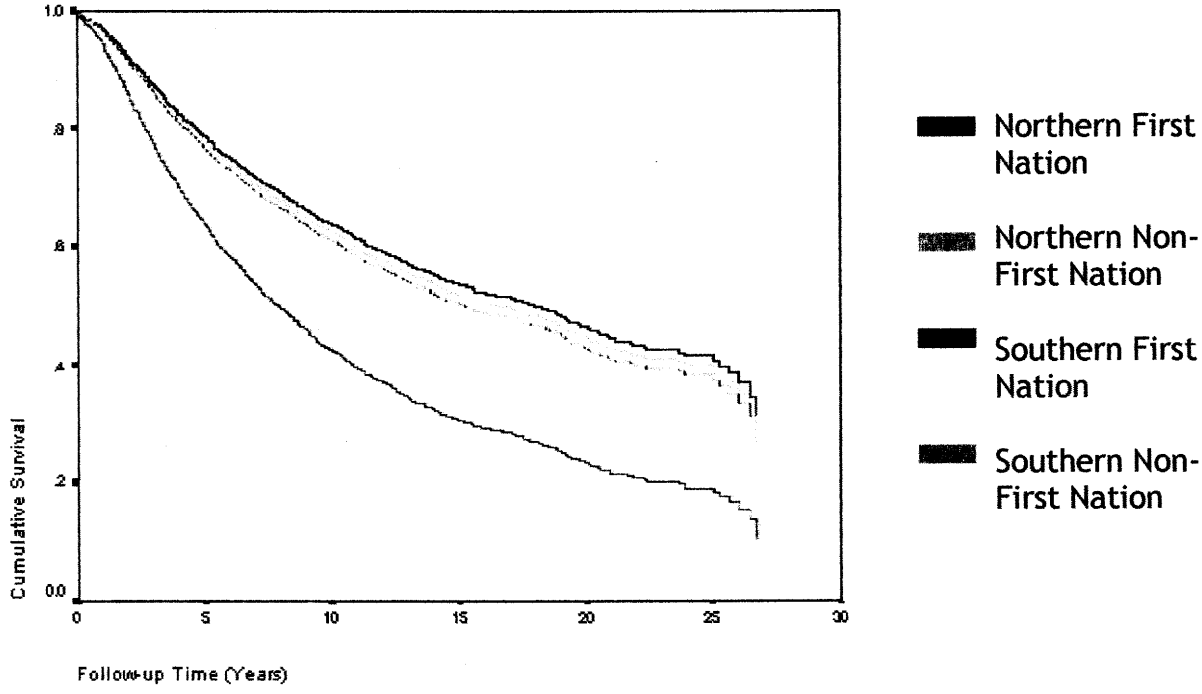


Figure 5.1.4.7 - Age adjusted survival from cancer of the Breast, TNM Stage III (death from breast cancer) 1970 - 1995

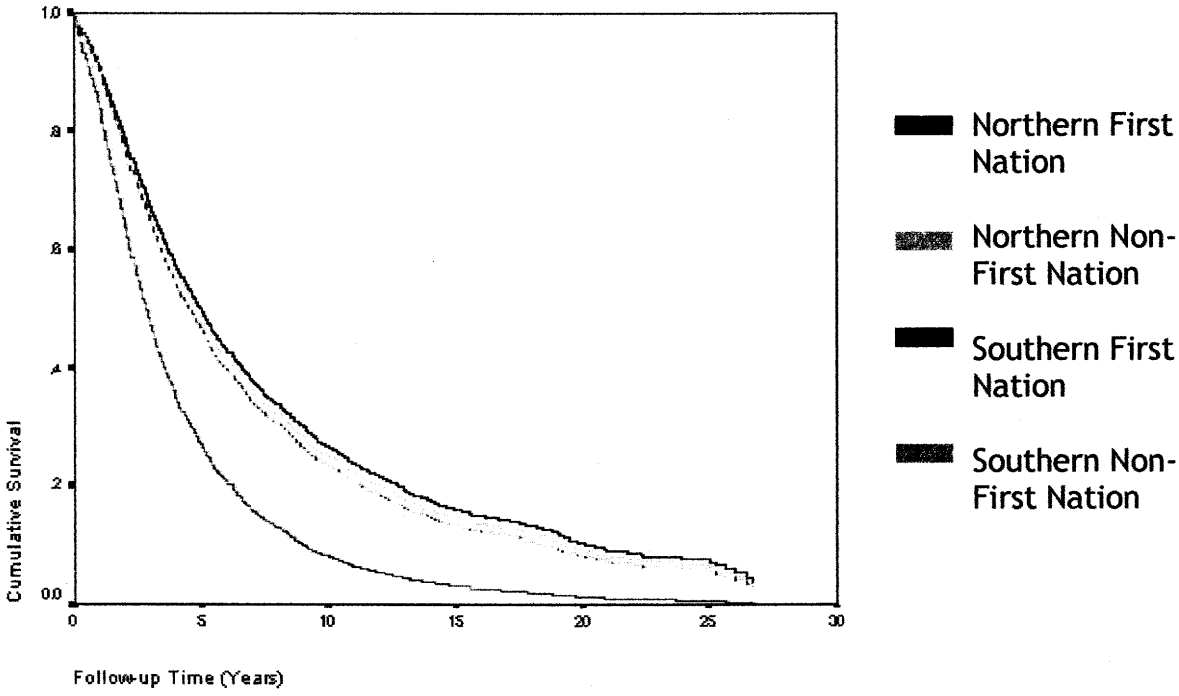
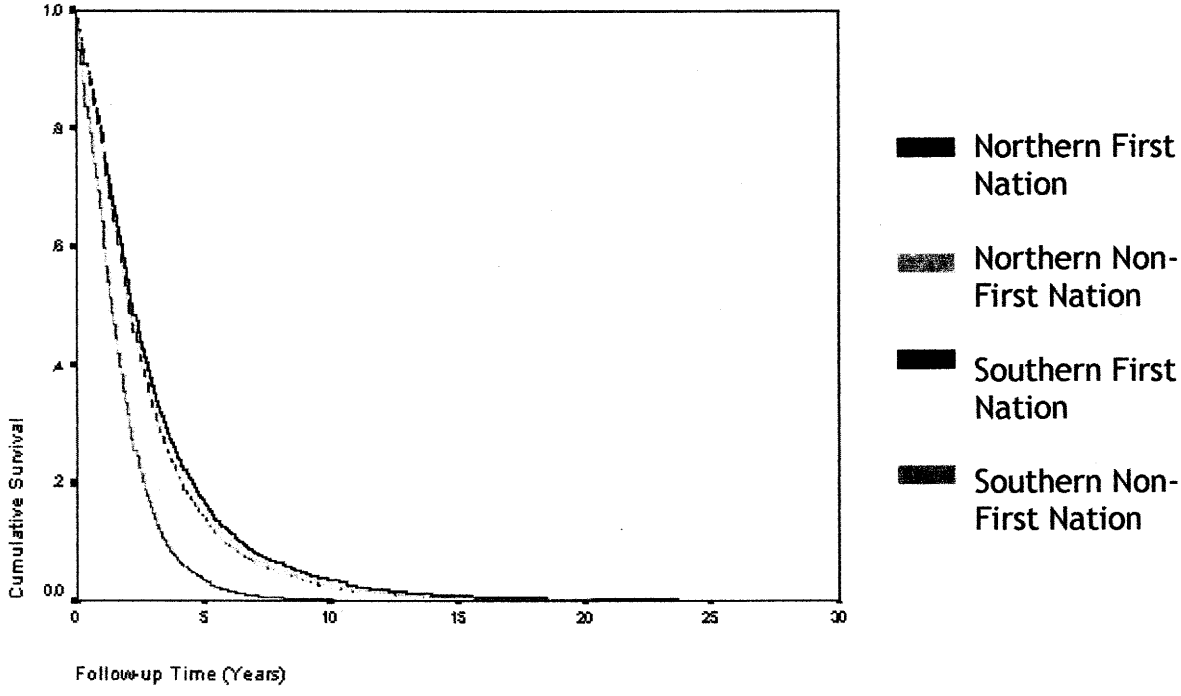


Figure 5.1.4.8 - Age adjusted survival from cancer of the Breast, TNM Stage IV (death from breast cancer) 1970 - 1995



5.2 Cancer of the Cervix

The International Classification of Diseases for Oncology (ICDO) codes for cancer of the cervix used were; C180 toC180.9.

5.2.1 Distribution of Cervical Cancer Cases

Table 5.2.1.1 - Distribution of Cervical Cancer by study group and TNM stage, 1980-1995

Study Group	Stage				Total
	I	II	III	IV	
Northern FN	6 (33.3%)	6 (33.3%)	6 (33.3%)	-	18 (100.0%)
Northern Non-FN	4 (36.4%)	4 (36.4%)	2 (18.2%)	1 (9.1%)	11 (100.0%)
Southern FN	53 (50.0%)	22 (20.8%)	24 (22.6%)	7 (6.6%)	106 (100.0%)
Southern Non-FN	298 (56.0%)	105 (19.7%)	98 (18.4%)	31 (5.8%)	532 (100.0%)
Total	361 (54.1%)	137 (20.5%)	130 (19.5%)	39 (5.8%)	667 (100.0%)

FN = First Nation

96 cases with missing stage data

As seen in Table 5.2.1.1, the total number of cervical cancer cases was small in the northern study groups. The northern First Nation group had a total of 18 cases and the northern non-First Nation group with a total of 11 cases. When comparing the proportions of cases over the four TNM stages by study group it is important to keep in mind that the number of cases are small in the north and results from this analysis should be interpreted with caution as a small number of cases may not reflect true differences or trends. Examining the proportional distribution, it is noteworthy that of those women

diagnosed with cervical cancer in the southern non-First Nation group and the southern First Nation group, 50% or more were diagnosed at TNM stage I. In contrast, for the northern First Nation group 33.3% were diagnosed at TNM stage I. In the northern non-First Nation group 36.4% were diagnosed at TNM stage I. Again it is important to remember that the number of cases in the north are quite small and therefore interpretation of these proportions should not necessarily carry much weight. It is interesting to note however that the age-standardized incidence rates of cervical cancer among all Saskatchewan First Nations and First Nations on reserve in northern Saskatchewan since 1980 are higher than the rate for the province as a whole(53). The total number of diagnoses from 1980 to 1995 for cervical cancer was 715 yet 667 had staging information. All of these 96 cases with missing stage data were in the south.

Table 5.2.1.2 - Distribution of Cervical Cancer by study group and age, 1980-1995

Study Group	Age Group (years)				Total
	18 to 34	35 to 49	50 to 69	70 & above	
Northern FN	3 (16.7%)	8 (44.4%)	6 (33.3%)	1 (5.6%)	18 (100.0%)
Northern Non-FN	4 (36.4%)	4 (36.4%)	2 (18.2%)	1 (9.1%)	11 (100.0%)
Southern FN	30 (27.0%)	45 (40.5%)	23 (20.7%)	13 (11.7%)	111 (100.0%)
Southern Non-FN	122 (21.2%)	177 (30.8%)	162 (28.2%)	114 (19.8%)	575 (100.0%)
Total	159 (22.2%)	234 (32.7%)	193 (27.0 %)	129 (18.0%)	715 (100.0%)

FN = First Nation

Table 5.2.1.2 explores the distribution of age by study group. As age is being examined it is important to remember the demography of the study

population. The northern First Nation population is much younger than the other populations. Recall the information on the age compositions of these populations presented in section 5.1. Looking at the highlights of this table it can be observed that for all the study groups over 50% of those women diagnosed with cervical cancer are diagnosed at the age of 49 or younger. The southern non-First Nation groups proportional distribution of cervical cancer is more evenly distributed across the 4 age-groupings in comparison to the three other study groups.

Table 5.2.1.3 - Distribution of Cervical Cancer by study group, TNM stage, and age, 1980-1995

Study Group		Age Group (years)				Total
	Stage	18 to 34	35 to 49	50 to 69	70 & above	
Northern FN	I	2 (66.7%)	2 (25.0%)	2 (33.3%)	0 (0.0%)	6 (33.3%)
	II	1 (33.3%)	1 (12.5%)	3 (50.0%)	1 (100.0%)	6 (33.3%)
	III	0 (0.0%)	5 (62.5%)	1 (16.7%)	0 (0.0%)	6 (33.3%)
	IV	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total		3 (100.0%)	8 (100.0%)	6 (100.0%)	1 (100.0%)	18 (100.0%)
Northern Non-FN	I	2 (50.0%)	2 (50.0%)	0 (0.0%)	0 (0.0%)	4 (36.4%)
	II	1 (25.0%)	1 (25.0%)	1 50.0%)	1 (100.0%)	4 (36.4%)
	III	1 (25.0%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	2 (18.2%)
	IV	0 (0.0%)	0 (0.0%)	1 (50.0%)	0 (0.0%)	1 (9.1%)
Total		4 (100.0%)	4 (100.0%)	2 (100.0%)	1 (100.0%)	11 (100.0%)
Southern FN	I	22 (73.3%)	22 (50.0%)	9 (39.1%)	0 (0.0%)	53 (50.0%)
	II	3 (10.0%)	11 (25.0%)	4 (17.4%)	4 (33.3%)	22 (20.8%)
	III	5 (16.7%)	6 (13.6%)	7 (30.4%)	6 (50.0%)	24 (22.6%)
	IV	0 (0.0%)	2 (4.5%)	3 (13.0%)	2 (16.7%)	7 (6.6%)
Total		30 41 (100.0%)	23 (100.0%)	12 (100.0%)	106 (100.0%)	(100.0%)
Southern Non-FN	I	87 (75.0%)	111 (66.5%)	66 (43.4%)	34 (35.1%)	298 (56.0%)
	II	11 (9.5%)	27 (16.2%)	37 (24.3%)	30 (30.9%)	105 (19.7%)
	III	18 (15.5%)	24 (14.4%)	31 (20.4%)	25 (25.8%)	98 (18.4%)
	IV	0 (0.0%)	5 (3.0%)	18 (11.8%)	8 (8.2%)	31 (5.8%)
Total		116 (100.0%)	167 (100.0%)	152 (100.0%)	97 (100.0%)	532 (100.0%)

FN = First Nation

In Table 5.2.1.3 the distribution of cervical cancer is presented by age and TNM stage for each study group. Some highlights from this table are as follows. For all study groups the largest proportion of cases for each age-group occurred at TNM stage II or less. That is to say that the most diagnoses of cervical cancer occur at an early stage for all age-groups. For the southern non-First Nation group the largest proportion of cases were diagnosed at TNM stage I for each age-group.

Table 5.2.1.4 - Distribution of deaths among cervical cancer patients from cervical cancer and all causes by study group, 1980-1995

Study Group	Death from Cervical Cancer	Death from all causes	Proportion of Cervical Cancer Deaths
Northern FN	4	11	36.4%
Northern Non-FN	3	4	75.0%
Southern FN	36	54	66.7%
Southern Non-FN	138	254	54.3%
Total	181	323	56.0%

FN = First Nation

Table 5.2.1.4 presents the distribution of cervical cancer deaths from 1980 to 1995 by study group. For the southern non-First Nation group 54.3% of cervical cancer patients, died of cervical cancer. In the northern First Nation group 36.4% of cervical cancer patients, died of cervical cancer. In the northern non-First Nation group, 75% of the cervical cancer patients deaths were due to cervical cancer, this group however had very few cases during this time frame. In the southern First Nation group 66.7% of cervical cancer patients died of cervical cancer.

Table 5.2.1.5 - Distribution of deaths from Cervical cancer and all causes by study group and Stage, 1980-1995

Study Group	Stage	Death from Cervical Cancer	Death from all causes	Proportion of Cervical Cancer Deaths
Northern FN	I	1	2	50.0%
	II	2	6	33.3%
	III	1	3	33.3%
	IV	-	-	-
Total		4	11	36.4%
Northern Non-FN	I	-	-	-
	II	1	2	50.0%
	III	1	1	100.0%
	IV	1	1	100.0%
Total		3	4	75.0%
Southern FN	I	7	12	58.3%
	II	11	16	68.8%
	III	12	17	70.6%
	IV	5	7	71.4%
Total		35	52	69.2%
Southern Non-FN	I	18	68	26.5%
	II	35	65	53.8%
	III	48	70	68.6%
	IV	26	29	89.7%
Total		127	232	54.7%

FN = First Nation, "-" = no cases observed

Table 5.2.1.5 describes the proportion of deaths from cervical cancer in comparison to all causes by TNM stage and study group. As one would expect the worse the TNM stage at the time of diagnosis the higher the proportion of deaths attributable to cervical cancer. In the southern non-First Nation group 89.7% of those women who died with a cervical cancer diagnosis, died from

cervical cancer. This is in contrast to 36.5% of those diagnosed at TNM stage I actually died of cervical cancer compared to all deaths. This points to the conclusion that early diagnosis can perhaps lead to a better chance of survival. In other words, if one is diagnosed early they may die of other causes before they die of cervical cancer.

Table 5.2.1.6 - Distribution of deaths from cervical cancer and all causes by study group and age, 1980-1995

Study Group	Age Group (years)	Death from Cervical Cancer	Death from all causes	Proportion of Cervical Cancer Deaths
Northern FN	18 to 34	1	1	100.0%
	35 to 49	2	4	50.0%
	50 to 69	-	5	-
	70 and above	1	1	100.0%
Total		4	11	36.4%
Northern Non-FN	18 to 34	1	1	100.0%
	35 to 49	-	-	-
	50 to 69	2	2	100.0%
	70 and above	-	1	-
Total		3	4	75.0%
Southern FN	18 to 34	5	5	100.0%
	35 to 49	20	24	83.3%
	50 to 69	4	13	30.8%
	70 and above	7	12	58.3%
Total		36	54	66.7%
Southern Non-FN	18 to 34	15	16	93.8%
	35 to 49	27	44	61.4%
	50 to 69	54	97	55.7%
	70 and above	42	97	43.3%
Total		138	254	54.3%

FN = First Nation, "-" = no cases observed

Table 5.2.1.6 describes the distribution deaths from cervical cancer among all those women that died with a diagnosis of cervical cancer by age-group and study group. An interesting distribution of deaths is in the age-group 18 to 34 in the southern non-First Nation group. In this group 93.8% of those

women who died with a cervical cancer diagnosis died from cervical cancer. In the southern First Nation group for the 18 to 34 age-group, 100% of those women diagnosed with cervical cancer who died, died of cervical cancer. For the 35 to 49 year age-group 83.3% of those southern First Nation women that died, died from cervical cancer. The number of deaths in the two northern study groups is quite small and it would be inappropriate to comment on the distribution of deaths for these study groups.

5.2.2 Cervical Cancer Survival 1980 to 1995

The crude survival for cervical cancer was calculated using the Kaplan Meier method. Two end points for survival were used;

1) death from all causes and; 2) death from cervical cancer.

Figure 5.2.2.1 - Survival from cancer of the Cervix (death from all causes) 1980 - 1995

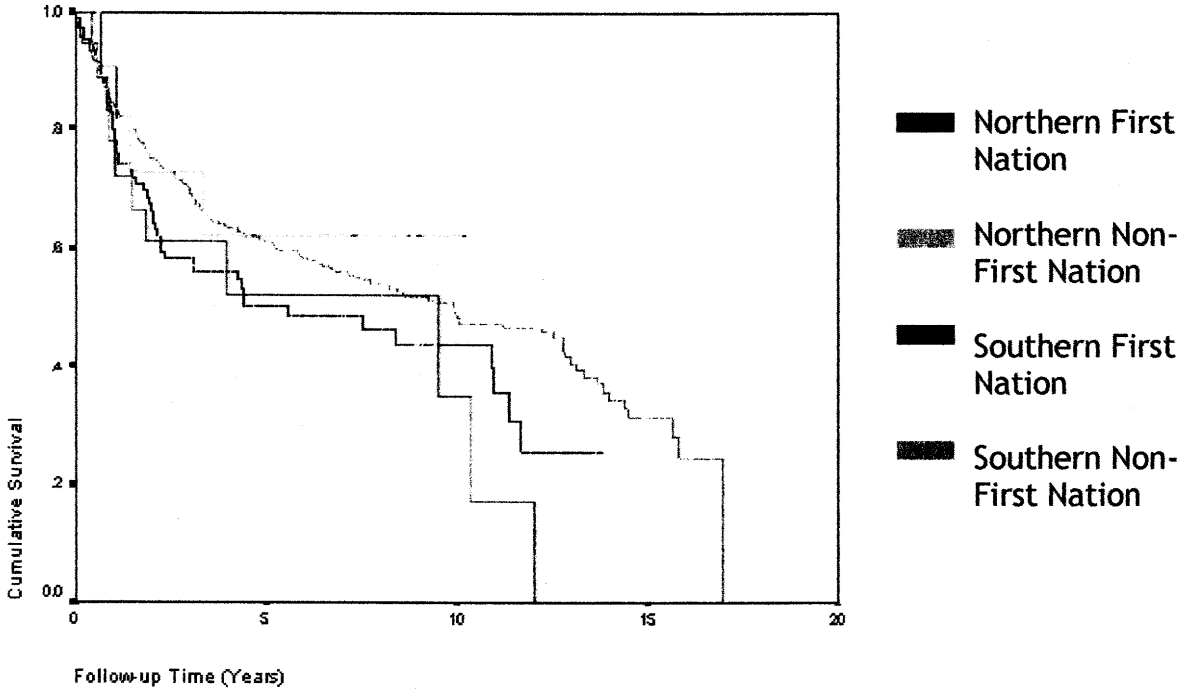


Figure 5.2.2.1 shows the proportion of women who remain alive over time, where time zero is the time of diagnosis. By looking at the curves alone the northern First Nation and southern First Nation study groups have a similar survival experience over the first five years after diagnosis. The survival curves for the northern First Nation, northern non-First Nation, and the southern First Nation groups are jagged in appearance as the number of cases for these groups is small. The northern First Nation group had a five-year survival rate of 52%. The northern non-First Nation group had a five-year survival rate of 62%. The southern First Nation group had a five year-survival rate of 50%. The comparison group, the southern non-First Nation group, had a five-year survival rate of 61%. Using the Log Rank test to compare the survival between the four study groups, the four study groups are found to be

not significantly different (p = 0.08) where the end point is death from all causes.

Figure 5.2.2.2 - Survival from cancer of the Cervix (death from cervical cancer) 1980 - 1995

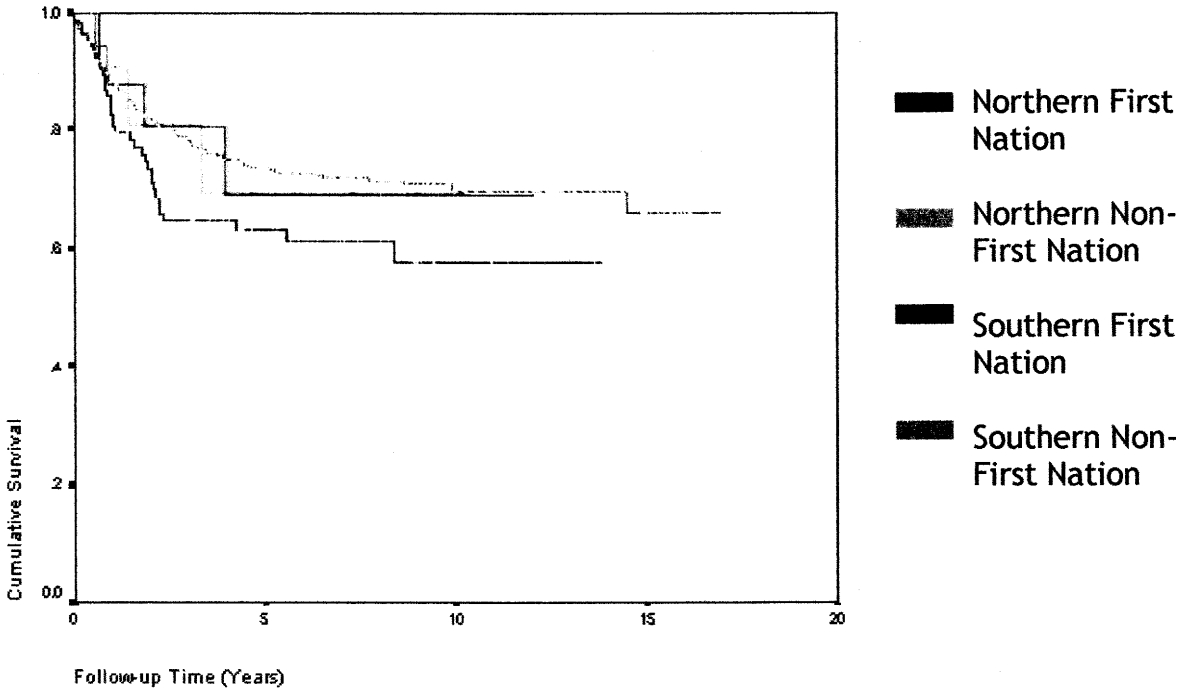


Figure 5.2.2.2 displays the Kaplan Meier survival curves for the four study groups using death from cervical cancer as the end point. In this instance the four curves have a similar pattern in relation to one another. The long term survival for all four study groups is better in comparison to the analysis using death from all causes as the end point. The southern First Nation group shows a noticeably worse survival pattern compared to the other study groups. The five-year survival rate for each study group is as follows: northern First Nation 69%, northern non-First Nation 69%, southern First Nation 63%,

southern non-First Nation 73%. The Log Rank test comparing the four study groups survival yields a p value of 0.13 and thus when the end point is death from cervical cancer the four study groups survival are not significantly different.

5.2.3 Cox Proportional Hazards Model

Similar to the analysis for breast cancer, a Cox's proportional hazards model has been used to compare the relative risk of dying for those diagnosed with cervical cancer. Two analyses have been undertaken here. The first one uses death from all causes as the end point. The second one uses death from cervical cancer as the end point.

Table 5.2.3.1 - Univariate and Multivariate Relative Risks for Study Groups from Cox's model, cervical cancer 1980-95 (death from all causes)

Model	Variable	R.R.	95% C.I.	p-value
Study Group alone	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.67	0.91 - 3.07	0.095
	Northern Non-FN	0.84	0.31 - 2.25	0.723
	Southern FN	1.38	1.02 - 1.86	0.034
Age + Study Group	Age	1.05	1.04 - 1.05	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.97	1.07 - 3.61	0.028
	Northern Non-FN	1.34	0.50 - 3.61	0.564
	Southern FN	1.85	1.37 - 2.50	0.0001
Stage + Study Group	TNM Stage			
	I	1.00	-	-
	II	3.82	2.81 - 5.18	< 0.0001
	III	6.51	4.78 - 8.88	< 0.0001
	IV	16.13	10.67 - 24.39	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.40	0.76 - 2.57	0.283
	Northern Non-FN	0.61	0.23 - 1.65	0.334
	Southern FN	1.18	0.87 - 1.60	0.294
Age + Stage + Study Group	Age	1.03	1.02 - 1.04	< 0.0001
	TNM Stage			
	I	1.00	-	-
	II	2.70	1.96 - 3.71	< 0.0001
	III	5.05	3.68 - 6.92	< 0.0001
	IV	9.49	6.18 - 14.56	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.71	0.93 - 3.15	0.087
	Northern Non-FN	0.95	0.35 - 2.56	0.913
	Southern FN	1.41	1.04 - 1.92	0.029

FN = First Nation, RR = Relative Risk, C.I. = Confidence Interval

Table 5.2.3.1 displays the results of the Cox proportional hazard model analysis for those women diagnosed with cervical cancer where the end point for survival is death from all causes. The first model (univariate or unadjusted) shows southern First Nation women diagnosed with cervical

cancer have 1.38 times greater risk of dying of cervical cancer in comparison to southern non-First Nation women, where the end point is death from all causes. This difference is statistically significant, $p = 0.034$. The second model (study group and age) shows the southern First Nation group to have a statistically significant relative risk in comparison to the southern non-First Nation group when adjusting for age at time of diagnosis. Age is shown to be highly significant ($p < 0.0001$) as a predictor of survival. The third model (stage and study group) shows all stage to be highly statistically significantly different from stage I and the relative risk for each TNM stage (II, III, IV) is progressively worse. This would mean that the worse the stage at time of diagnosis, the greater the relative risk of dying. The final model shows both stage and age at time of diagnosis are statistically significant predictors of survival ($p<0.0001$). For the southern First Nation group the relative risk of dying from any cause is significant in comparison to the southern non-First Nation group ($p = 0.03$). Southern First Nation women diagnosed with cervical cancer have 1.41 times greater risk of dying of cervical cancer in comparison to southern non-First Nation women, where the end point is death from cervical cancer. Compared to the non-adjusted or univariate model, the relative risk for the southern First Nation group is slightly greater when adjusting for both stage and age at time of diagnosis.

Table 5.2.3.2 - Univariate and Multivariate Relative Risks for Study Groups from Cox's model, cervical cancer 1980-95 (death from cervical cancer)

Model	Variable	R.R.	95% C.I.	p-value
Study Group alone	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.01	0.37 - 2.72	0.990
	Northern Non-FN	1.06	0.34 - 3.33	0.921
	Southern FN	1.53	1.06 - 2.22	0.025
Age + Study Group	Age	1.03	1.02 - 1.04	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	1.14	0.42 - 3.09	0.793
	Northern Non-FN	1.41	0.45 - 4.43	0.559
	Southern FN	1.84	1.26 - 2.68	0.002
Stage + Study Group	TNM Stage			
	I	1.00	-	-
	II	5.96	3.70 - 9.61	< 0.0001
	III	11.32	7.11 - 18.04	< 0.0001
	IV	33.32	19.53 - 56.84	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.82	0.30 - 2.23	0.695
	Northern Non-FN	0.72	0.23 - 2.27	0.576
	Southern FN	1.32	0.91 - 1.93	0.148
Age + Stage + Study Group	Age	1.01	1.00 - 1.02	0.0310
	TNM Stage			
	I	1.00	-	-
	II	5.27	3.23 - 8.61	< 0.0001
	III	10.39	6.48 - 16.67	< 0.0001
	IV	27.38	15.62 - 48.00	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.88	0.32 - 2.40	0.805
	Northern Non-FN	0.82	0.26 - 2.60	0.737
	Southern FN	1.38	0.94 - 2.01	0.0970

FN = First Nation, RR = Relative Risk, C.I. = Confidence Interval

Table 5.2.3.2 displays the results of the Cox's model where the end point for survival is death from cervical cancer. The first model shows that southern First Nation women diagnosed with cervical cancer have 1.53 times greater risk of dying of cervical cancer in comparison to southern non-First Nation

women, where the end point is death cervical cancer (p = 0.025). In the second model, the southern First Nation group again is found to have a statistically significant relative risk in comparison to the southern non-First Nation group (relative risk = 1.84 p = 0.002). Age is found to be a significant predictor of survival when controlling for study group. Model three shows that when controlling for study group the relative risk from dying from cervical cancer at stage II, III, and IV are greater than dying from cervical cancer when diagnosed at TNM stage I. The final model (stage, age and study group) shows that the northern First Nation and the northern non-First Nation groups have a relative risk of less than one, meaning that their e risk of dying from cervical cancer is better in comparison to the southern non-First Nation group. It is important to note here that both of these relative risks are not statistically significant. Southern First Nation women diagnosed with cervical cancer have 1.38 times greater risk of dying of cervical cancer in comparison to southern non-First Nation women, where the end point is death from cervical cancer. Here again however, this relationship is shown to be not statistically significant. Comparing the non-adjusted model to the adjusted model, the southern First Nation group goes from having a significant relative risk to a non-significant relative risk. One must be aware here that the adjusted model allows for a better analysis of survival for each study group as both age and stage (strong predictors of survival on their own) are included in the calculation of the relative risk estimate.

5.2.4 Cox Proportional Hazards Model - Survival Curves

In addition to calculating the adjusted relative risks, the Cox's model also produces survival curves adjusting for covariates. The survival curves for the final model (age, stage, and study group) is presented below. Figures 5.2.4.1 to 5.2.4.4 present the age and stage adjusted survival curves for cervical cancer, where the end point is death from all causes. The consistent pattern seen here shows the two non-First Nation groups to have very similar survival patterns. Both of these study groups show consistently better survival in comparison to the two Fist Nation groups. The northern First Nation group consistently has the worst survival for each TNM stage. The southern First Nation group has a similar survival pattern to the northern First Nation group and is slightly better off in survival.

Figure 5.2.4.1 - Age adjusted survival from cancer of the Cervix, TNM Stage I (death from all causes) 1980 - 1995

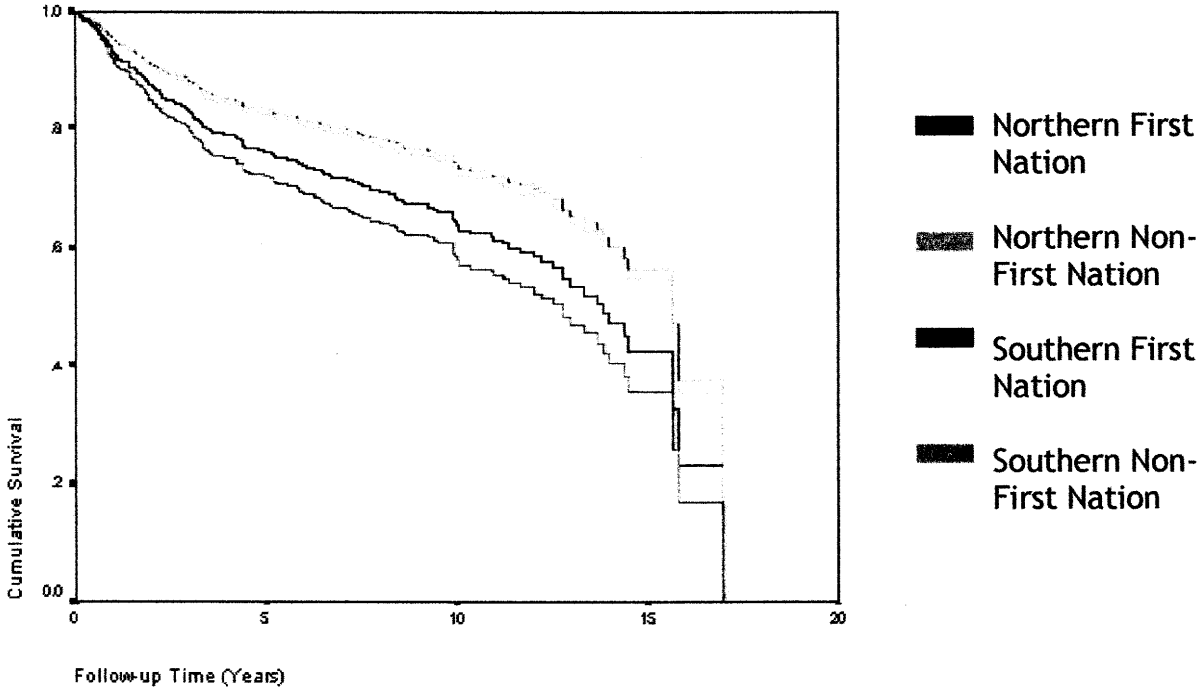


Figure 5.2.4.2 - Age adjusted survival from cancer of the Cervix, TNM Stage II (death from all causes) 1980 - 1995

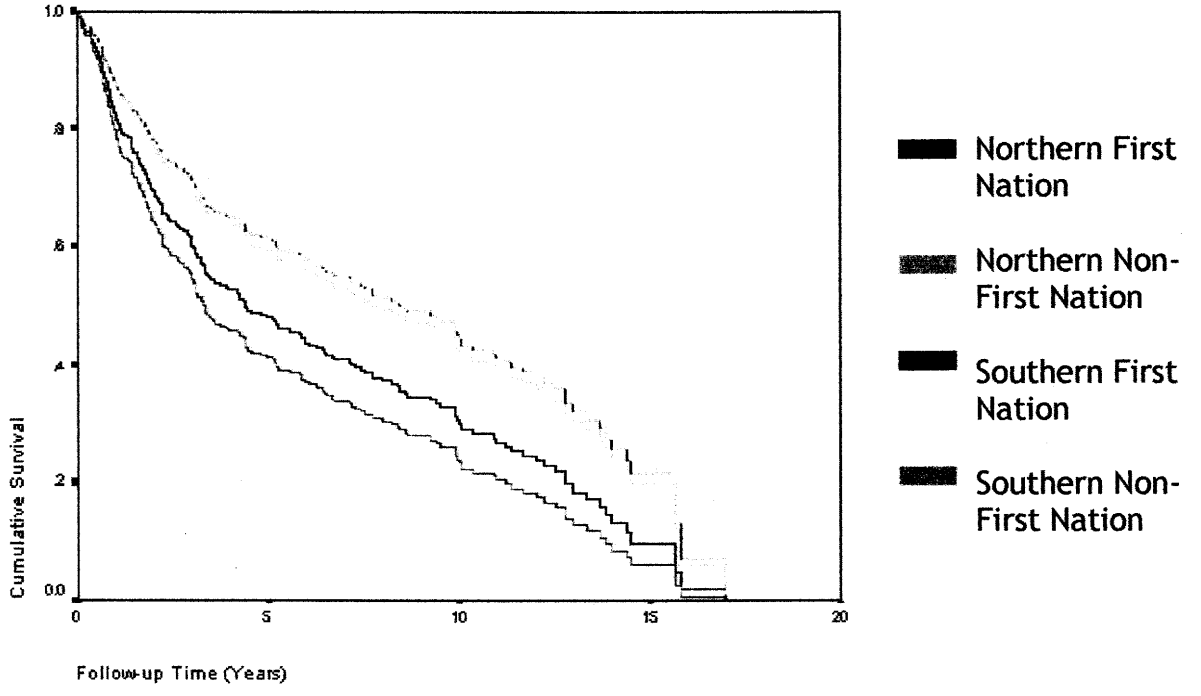


Figure 5.2.4.3 - Age adjusted survival from cancer of the Cervix, TNM Stage III (death from all causes) 1980 - 1995

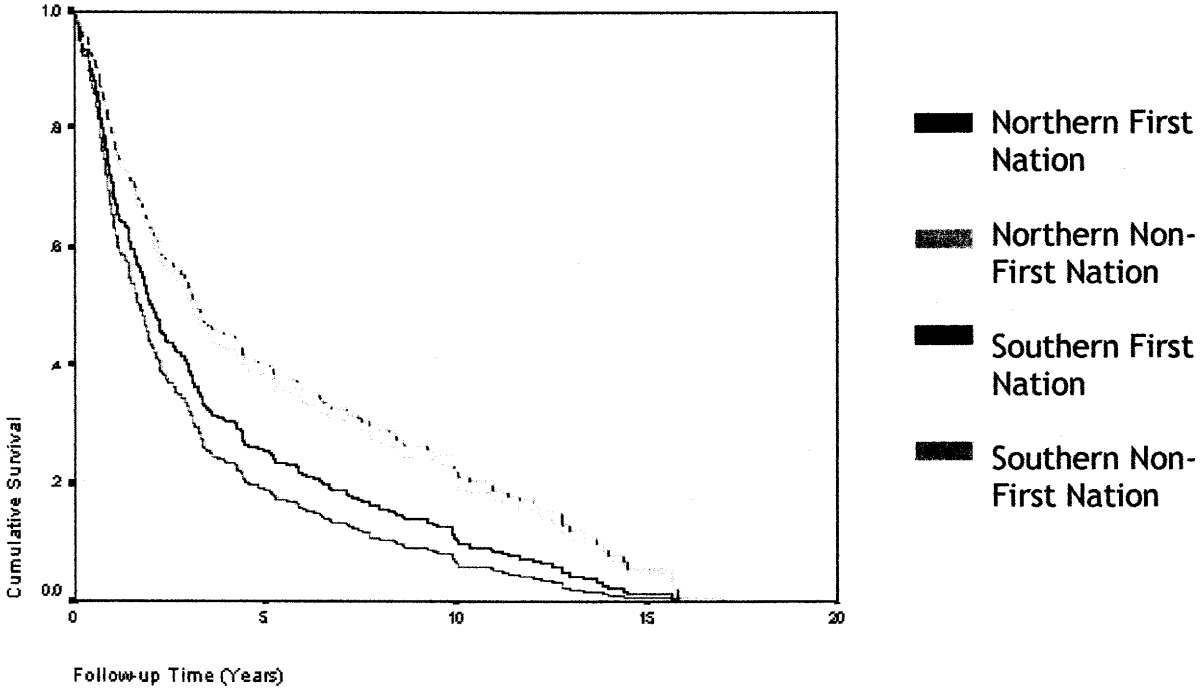
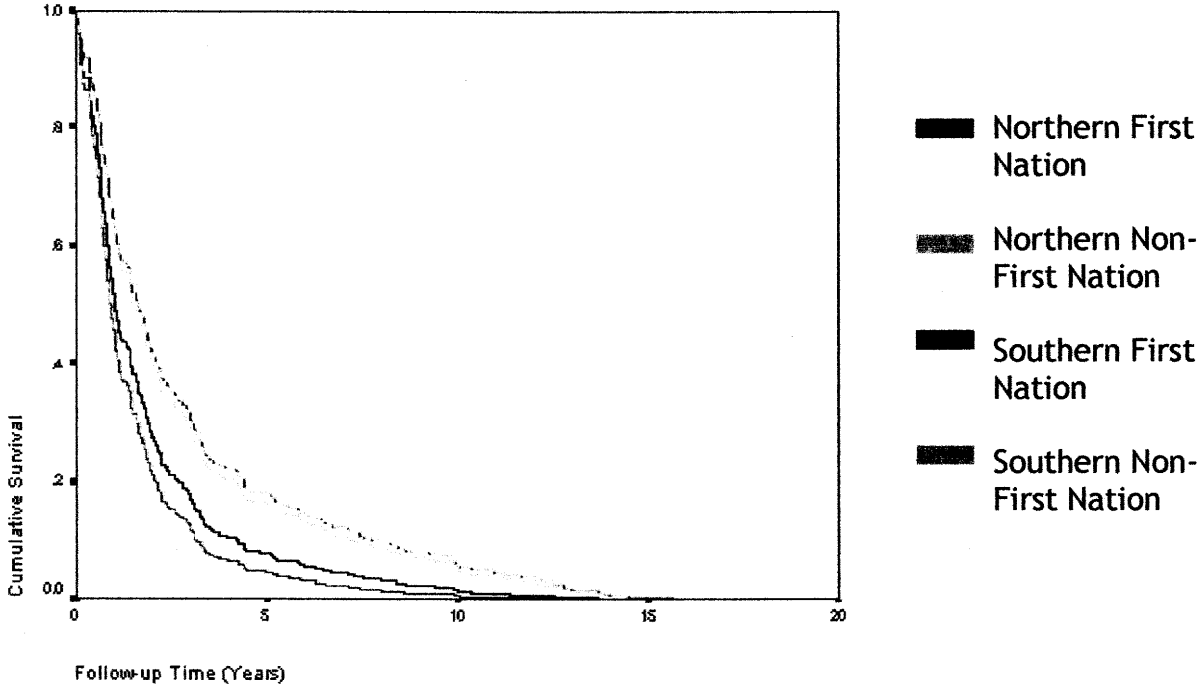


Figure 5.2.4.4 - Age adjusted survival from cancer of the Cervix, TNM Stage IV (death from all causes) 1980 - 1995



Figures 5.2.4.5 to 5.2.4.8 are the age and stage adjusted survival curves, where the end point is death from cervical cancer. Here each figure consistently shows the southern First Nation group with the worst survival. This is followed by the southern non-First Nation group, the northern First Nation group, and the northern non-First Nation group.

Figure 5.2.4.5 - Age adjusted survival from cancer of the Cervix, TNM Stage I (death from cervical cancer) 1980 - 1995

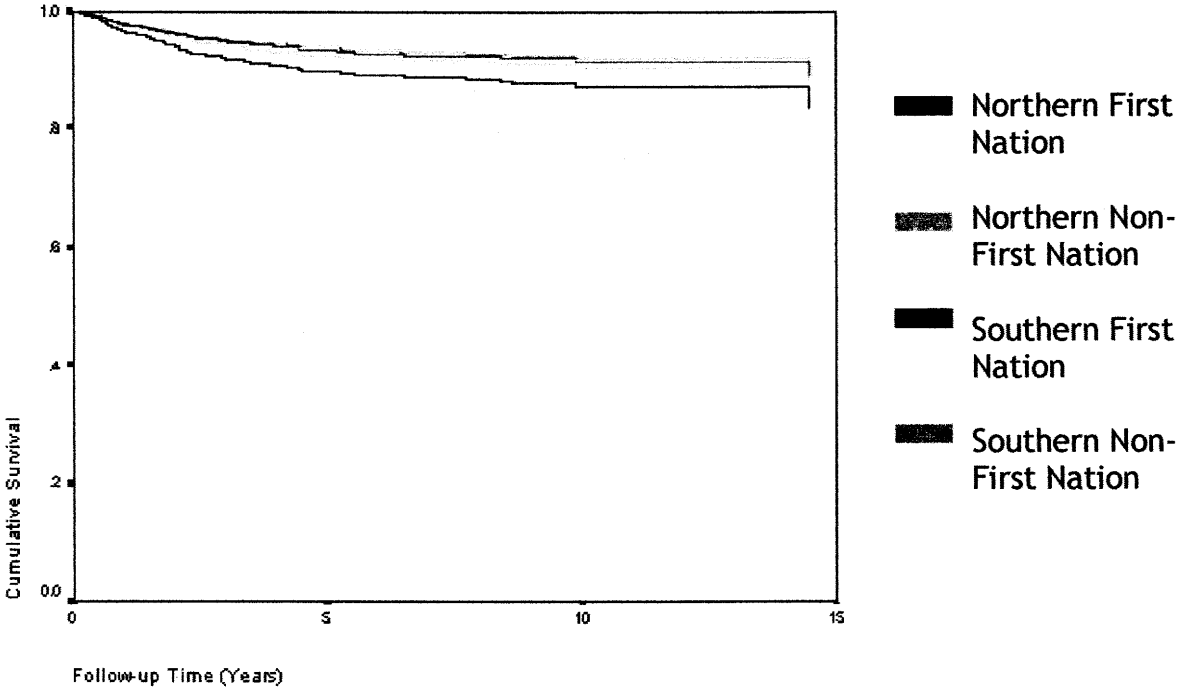


Figure 5.2.4.6 - Age adjusted survival from cancer of the Cervix, TNM Stage II (death from cervical cancer) 1980 - 1995

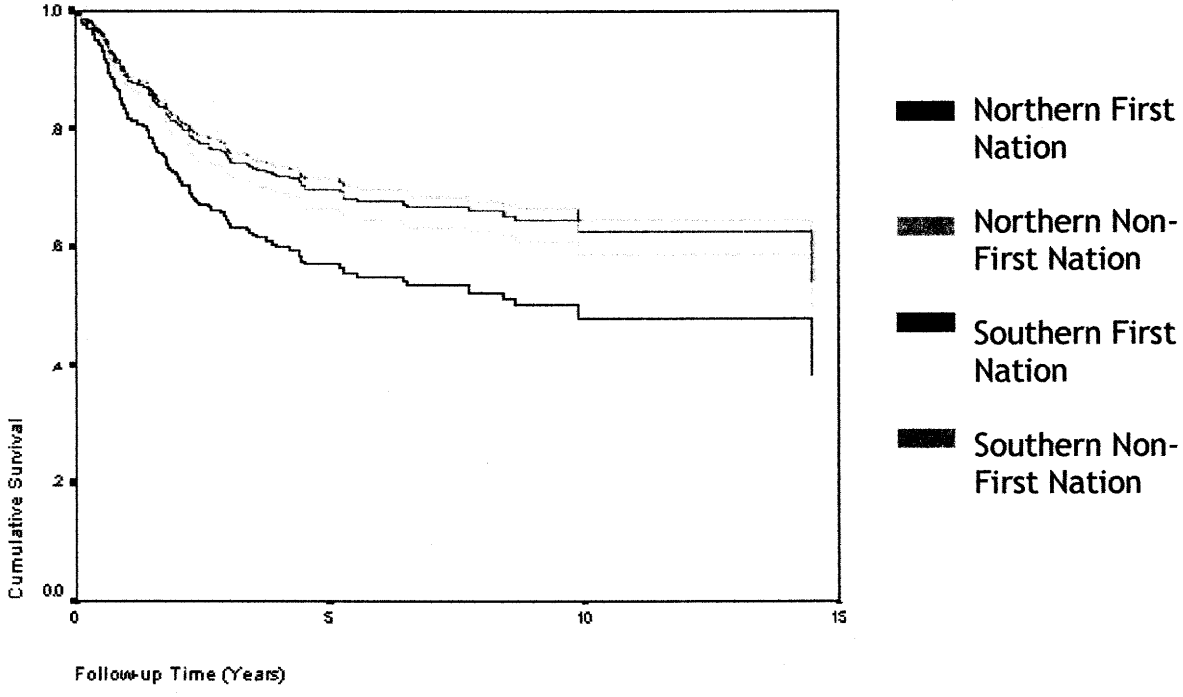


Figure 5.2.4.7 - Age adjusted survival from cancer of the Cervix, TNM Stage III (death from cervical cancer) 1980 - 1995

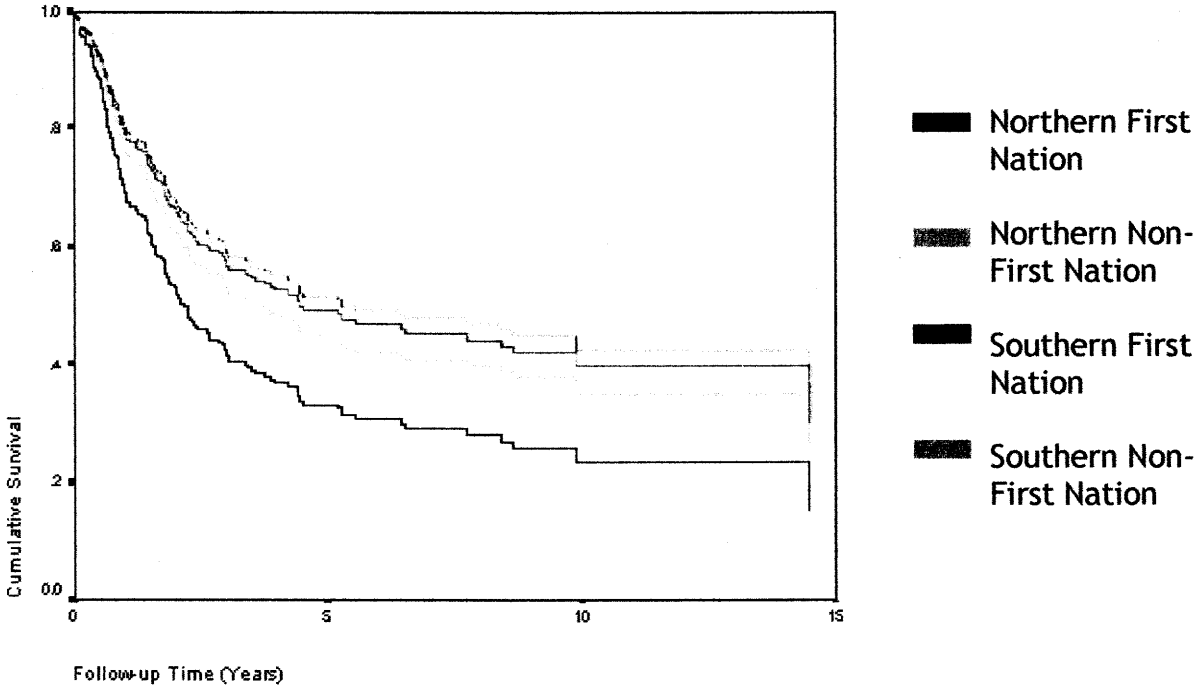
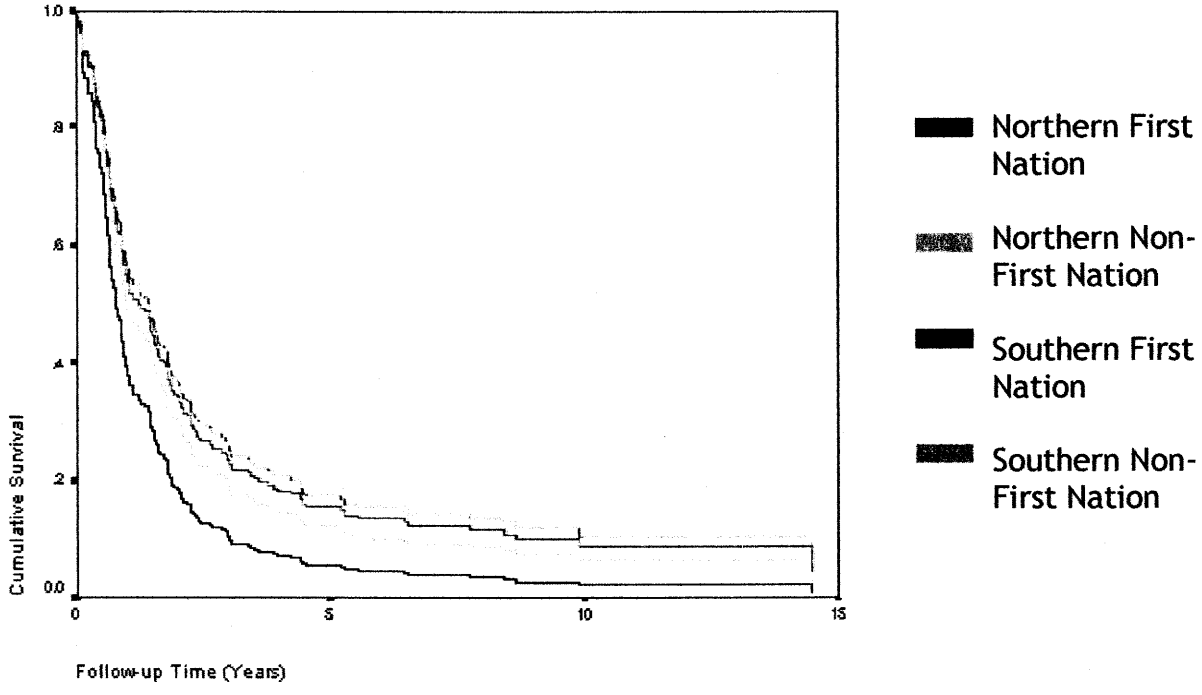


Figure 5.2.4.8 - Age adjusted survival from cancer of the Cervix, TNM Stage IV (death from cervical cancer) 1980 - 1995



5.3 Cancer of the Colon and Rectum

The International Classification of Diseases for Oncology (ICDO) codes for colorectal cancer used were; C18, C19.9,C20.9 and C21.0 to C21.8. The analysis for colorectal cancer was done combining information for both sexes, as the number of cases for each sex individually is quite small.

5.3.1 Distribution of Colorectal Cancer Cases

Table 5.3.1.1 - Distribution of Colorectal Cancer by study group and Dukes stage, 1990-1995

Study Group	Dukes Stage				Total
	A	B	C	D	
Northern FN	-	5 (38.5%)	7 (53.8%)	1 (7.7%)	13 (100.0%)
Northern Non-FN	2 (15.4%)	4 (30.8%)	6 (46.2%)	1 (7.7%)	13 (100.0%)
Southern FN	1 (3.7%)	10 (37.0%)	11 (40.7%)	5 (18.5%)	27 (100.0%)
Southern Non-FN	337 (14.0%)	932 (38.6%)	798 (33.1%)	347 (14.4%)	2414 (100.0%)
Total	340 (13.8%)	951 (38.5%)	822 (33.3%)	354 (14.3%)	2467 (100.0%)

FN = First Nation

920 cases with missing stage data

Table 5.3.1.1 examines the distribution of colorectal cancer cases for each study group by Dukes stage from 1990 to 1995. First it is important to note that in both the northern study groups there are very few cases, 13 in each. For the northern First Nation group there were no cases diagnosed at Dukes stage A. In contrast 14% of those men and women diagnosed with colorectal cancer were diagnosed at Dukes stage A in the southern non-First Nation group. The distribution of Dukes stage B was similar across the four study

groups with 38.5% for the northern First Nation group, 30.8% in the northern non-First Nation group, 37.0% for the southern First Nations, and 38.6% for the southern non-First Nation group. For the northern First Nation group the largest percentage of cases were diagnosed at Dukes stage C.

Table 5.3.1.2 - Distribution of Colorectal Cancer by study group and age, 1990-1995

Study Group	Age Group (Years)			Total
	20 to 49	50 to 64	65 and above	
Northern FN	2 (11.8%)	11 (64.7%)	4 (23.5%)	17 (100.0%)
Northern Non-FN	2 (10.0%)	8 (40.0%)	10 (50.0%)	20 (100.0%)
Southern FN	4 (8.5%)	18 (38.3%)	25 (53.2%)	47 (100.0%)
Southern Non-FN	180 (5.5%)	660 (20.0%)	2463 (74.6%)	3303 (100.0%)
Total	188 (5.6%)	697 (20.6%)	2502 (73.9%)	3387 (100.0%)

FN = First Nation

In table 5.3.1.2 the proportion of colorectal cancer cases diagnosed from 1990 to 1995 by study group and age is presented. Here again before interpreting the information here it is important to keep in mind the differing age structure of the north versus the south of Saskatchewan. For the southern non-First Nation group the highest percentage distribution of colorectal cancer cases was in the age-group 65 and above, with 74.6% of men and women diagnosed with colorectal cancer in this age-group. Similarly in the southern First Nation and the northern non-First Nation groups, the highest proportion of cases were in this oldest age-group. For the northern First

Nation group the highest proportion of colorectal cancer diagnoses were in the 50 to 64 age group.

Table 5.3.1.3 - Distribution of Colorectal Cancer by study group, Dukes stage, and age, 1990-1995

Study Group		Age Group (Years)			Total
	Dukes Stage	20 to 49	50 to 64	65 and above	
Northern FN	A	-	-	-	-
	B	2 (100.0%)	2 (22.2%)	1 (50.0%)	5 (38.5%)
	C		6 (66.7%)	1 (50.0%)	7 (53.8%)
	D		1 (11.1%)		1 (7.7%)
Total		2 (100.0%)	9 (100.0%)	2 (100.0%)	13 (100.0%)
Northern Non-FN	A	-	1 (16.7%)	1 (16.7%)	2 (15.4%)
	B	1 (100.0%)	2 (33.3%)	1 (16.7%)	4 (30.8%)
	C	-	3 (50.0%)	3 (50.0%)	6 (46.2%)
	D	-		1 (16.7%)	1 (7.7%)
Total		1 (100.0%)	6 (100.0%)	6 (100.0%)	13 (100.0%)
Southern FN	A	-	-	1 (6.3%)	1 (3.7%)
	B	-	4 (44.4%)	6 (37.5%)	10 (37.0%)
	C	1 (50.0%)	5 (55.6%)	5 (31.3%)	11 (40.7%)
	D	1 (50.0%)		4 (25.0%)	5 (18.5%)
Total		1 (100.0%)	9 (100.0%)	16 (100.0%)	27 (100.0%)
Southern Non-FN	A	20 (13.9%)	56 (11.0%)	261 (14.8%)	337 (14.0%)
	B	55 (38.2%)	190 (37.5%)	687 (39.0%)	932 (38.6%)
	C	50 (34.7%)	184 (36.3%)	564 (32.0%)	798 (33.1%)
	D	19 (13.2%)	77 (15.2%)	251 (14.2%)	347 (14.4%)
Total		144 (100.0%)	507 (100.0%)	1763 (100.0%)	2414 (100.0%)

FN = First Nation, "-" = no cases observed

Table 5.3.1.3 examines the distribution of colorectal cancer cases for both sexes diagnosed between 1990 and 1995 by age and Dukes stage. For the two northern groups it is important to note that the number of cases is small, making interpretation difficult. In the 65 and above age-group for the southern non-First Nation group, 39.0% of the colorectal diagnoses were diagnosed at Dukes stage B. This was the highest percentage of cases for the southern non-First Nations group. Similarly for the southern First Nation group in the 65 and above age-group, 37.5% of the diagnoses were diagnosed at Dukes stage B. For the northern non-First Nation group, half of those men and women diagnosed with colorectal cancer in the age-group 65 and above were diagnosed at Dukes stage C.

Table 5.3.1.4 - Distribution of deaths among colorectal cancer patients from colorectal cancer and all causes by study group, 1990-1995

Study Group	Death from colorectal cancer	Death from all causes	Proportion of Colorectal Cancer Deaths
Northern FN	3	6	50.0%
Northern Non-FN	7	11	63.6%
Southern FN	17	29	58.6%
Southern Non-FN	1189	1893	62.8%
Total	1216	1939	62.7%

FN = First Nation

Table 5.3.1.4 describes the distribution of deaths among those diagnosed with colorectal cancer between 1990 and 1995 by study group. For all study groups approximately half or more of those men and women who died with a diagnosis of colorectal cancer, died from colorectal cancer. The lowest proportion (50%) was in the northern First Nation group. The highest

proportion of deaths attributable to colorectal cancer was in both the northern non-First Nation group (63.6%) and the southern non-First Nation group (62.8%). For the southern First Nation group, 58.6% of those women and men who died with a colorectal cancer diagnosis, died from colorectal cancer. It is difficult to ascertain whether the differences observed between study groups are meaningful as the number of cases in the north are quite few.

Table 5.3.1.5 - Distribution of deaths among colorectal cancer patients from colorectal cancer and all causes by study group and Stage, 1990-1995

Study Group	Dukes Stage	Death from colorectal cancer	Death from all causes	Proportion of Colorectal Cancer Deaths
Northern FN	A	-	-	-
	B	-	-	-
	C	1	3	33.3%
	D	1	1	100.0%
Total		2	4	50.0%
Northern Non-FN	A	-	-	-
	B	1	1	100.0%
	C	3	4	75.0%
	D	1	1	100.0%
Total		5	6	83.3%
Southern FN	A	-	-	-
	B	1	3	33.3%
	C	4	6	66.7%
	D	4	5	80.0%
Total		9	14	64.3%
Southern Non-FN	A	36	105	34.3%
	B	178	381	46.7%
	C	347	507	68.4%
	D	258	338	76.3%
Total		819	1331	61.5%

FN = First Nation, "-" = no cases observed

Table 5.3.1.5 describes the distribution of those men and women diagnosed with colorectal cancer between 1990 and 1995 who died either from colorectal cancer or from another cause. Examining the southern non-First Nation group, the expected pattern of distribution is seen. The worse the stage (higher the stage) the higher the proportion of cases die of colorectal cancer. Of those that died with a diagnosis of colorectal cancer at Dukes stage D, 76.3% died from colorectal cancer. This was then followed by Dukes stage C (68.4%), stage B (46.7%), and stage A (34.3%). A similar pattern was seen in the southern First Nation group. The number of deaths in the two northern groups was very small thus making interpretation difficult.

Table 5.3.1.6 - Distribution of deaths among colorectal cancer patients from colorectal cancer and all causes by study group and age, 1990-1995

Study Group	Age Group (Years)	Death from colorectal cancer	Death from all causes	Proportion of Colorectal Cancer Deaths
Northern FN	50 to 64	2	4	50.0%
	65 and above	1	2	50.0%
Total		3	6	50.0%
Northern Non-FN	50 to 64	2	3	66.7%
	65 and above	5	8	62.5%
Total		7	11	63.6%
Southern FN	20 to 49	1	2	50.0%
	50 to 64	7	10	70.0%
	65 and above	9	17	52.9%
Total		17	29	58.6%
Southern Non-FN	20 to 49	7	65	10.8%
	50 to 64	83	305	27.2%
	65 and above	614	1523	40.3%
Total		704	1893	37.2%

FN = First Nation

Table 5.3.1.6 examines the distribution of those men and women who died with a diagnosis of colorectal cancer between 1990 and 1995. For the southern non-First Nation group the largest proportion of deaths attributable to colorectal cancer was in the 65 and above age-group. In the southern First Nation group the 20 to 39 age-group had the highest proportion of colorectal cancer deaths but this was only one case and therefore must be interpreted with caution. Also in this study group the 50 to 64 age-group had 70.0% of the deaths attributable to colorectal cancer. All deaths from colorectal cancer or other causes occurred in the 50 to 64 and 65 and above age-groups in the two northern study groups.

5.3.2 Colorectal Cancer Survival 1990 to 1995

The crude survival for colorectal cancer was calculated using the Kaplan-Meier method. Two end points for survival were used;

1) death from all causes and; 2) death from colorectal cancer.

Figure 5.3.2.1 - Survival from Colorectal cancer (death from all causes) 1990 - 1995

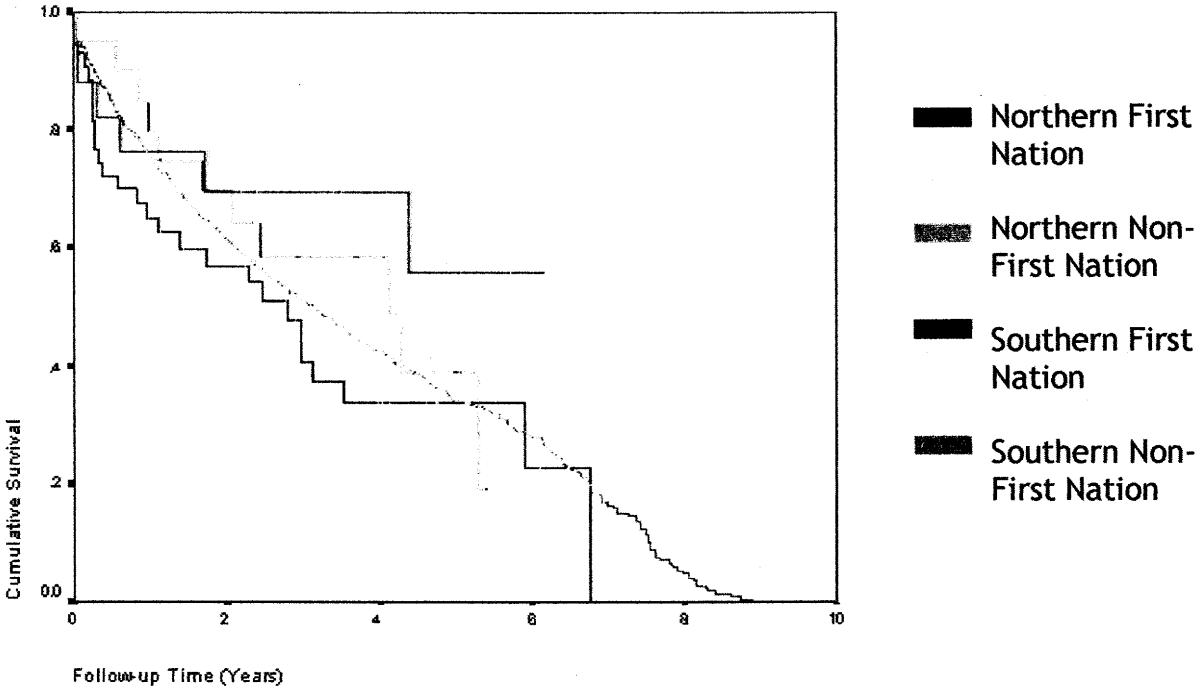


Figure 5.3.2.1 shows the proportion of colorectal cancer patients who remain alive over time, where time zero is the time of diagnosis. By looking at the curves alone, the four study groups survival experience over the first five years after diagnosis is quite different. The northern First Nation group had a five-year survival rate of 56%. The northern non-First Nation group had a survival rate of 39%. The southern First Nation group had a five-year survival of 34%. The comparison group, the southern non-First Nation group, had a

five-year survival rate of 35%. Using the Log Rank test to compare the survival between the four study groups, the four study groups are found to be not significantly different (p = 0.34) where the end point is death from all causes.

Figure 5.3.2.2 - Survival from Colorectal cancer (death from colorectal cancer) 1990 - 1995

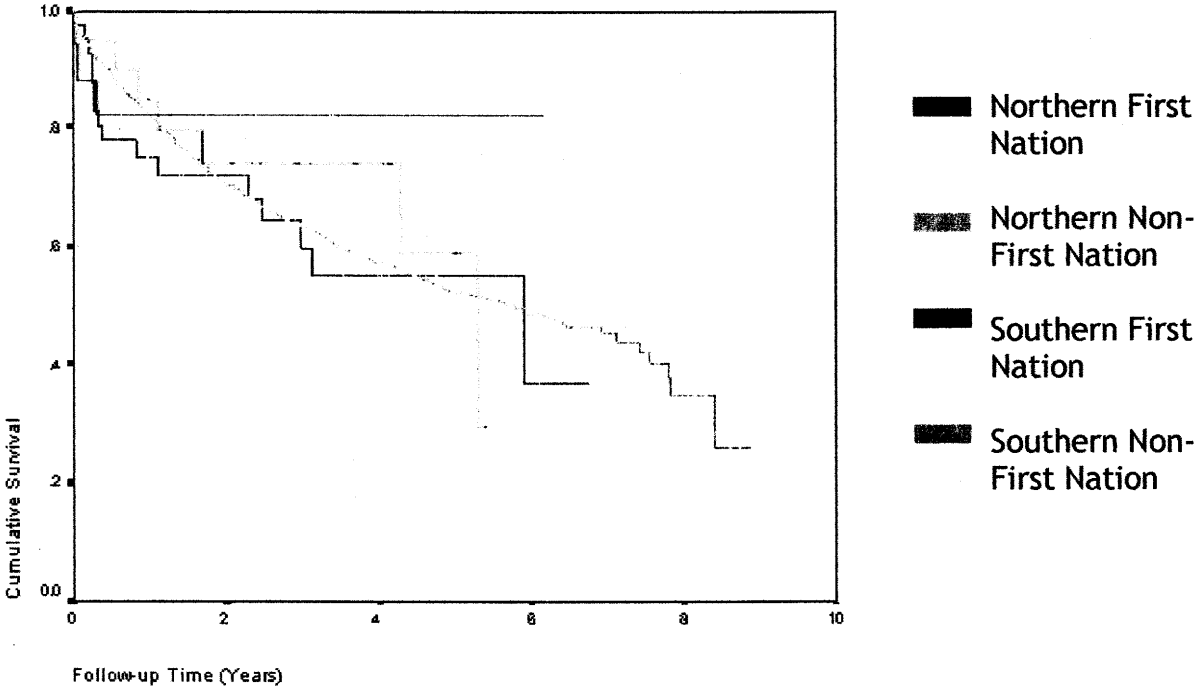


Figure 5.3.2.2 displays the Kaplan Meier survival curves for the four study groups using death from colorectal cancer as the end point. In this instance the four curves have a somewhat similar pattern in relation to one another. The northern First Nation group only had 3 deaths and therefor the survival curve is almost flat. The five-year survival rate for each study group is as follows: northern First Nation 82%, northern non-First Nation 59%, southern First Nation 55%, southern non-First Nation 52%. The 82% five-year survival

rate for the northern First Nation group would seem high, but recall that only 4 of 13 cases died. The Log Rank test comparing the four study groups survival yields a p value of 0.4861 and thus when the end point is death from colorectal cancer the four study groups survival are not significantly different.

5.3.3 Cox Proportional Hazards Model

Similar to the analysis for breast cancer, a Cox's proportional hazards model has been used to compare the relative risk of dying for those diagnosed with cervical cancer. Two analyses have been undertaken here. The first one uses death from all causes as the end point. The second one uses death from colorectal cancer as the end point.

Table 5.3.3.1 - Univariate and Multivariate Relative Risks for Study Groups from Cox's model, colorectal cancer 1990-95 (death from all causes)

Model	Variable	R.R.	95% C.I.	p-value
Study Group alone	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.58	0.26 - 1.30	0.189
	Northern Non-FN	0.88	0.49 - 1.60	0.677
	Southern FN	1.26	0.86 - 1.40	0.237
Age + Study Group	Age	1.03	1.02 - 1.03	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.79	0.35 - 1.75	0.328
	Northern Non-FN	1.08	0.60 - 1.96	0.792
	Southern FN	1.40	0.96 - 2.05	0.082
Stage + Study Group	Dukes Stage			
	A	1.00	-	-
	B	1.38	1.11 - 1.72	0.0037
	C	2.59	2.10 - 3.20	< 0.0001
	D	12.17	9.70 - 15.26	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.58	0.22 - 1.55	0.281
	Northern Non-FN	0.72	0.32 - 1.60	0.417
	Southern FN	0.96	0.56 - 1.66	0.889
Age + Stage + Study Group	Age	1.03	1.03 - 1.04	< 0.0001
	Dukes Stage			
	A	1.00	-	-
	B	1.35	1.09 - 1.68	0.007
	C	2.69	2.18 - 3.33	< 0.0001
	D	13.52	10.77 - 16.98	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.90	0.34 - 2.42	0.843
	Northern Non-FN	0.88	0.39 - 1.96	0.750
	Southern FN	1.15	0.67 - 1.99	0.614

FN = First Nation, RR = Relative Risk, C.I. = Confidence Interval

Table 5.3.3.1 displays the results of the Cox's proportional hazards model analysis where the end point for survival is death from all causes. Four models are presented here. Each model is necessary in order to asses the influence of covariates on the relative risk of dying of colorectal cancer for

each study group in comparison to the reference group, the southern non-First Nation group. The first model has study group alone in the model. With a relative risk of less than one the northern First Nation and northern non-First Nation groups have a better prognosis for colorectal cancer in comparison to the southern non-First Nation group. The southern First Nation group has 1.26 times greater probability of dying of colorectal cancer in comparison to southern non-First Nation group, where the end point is death from all causes. Avery important note here is that these relative risks are not statistically significantly different from the southern non-First Nation group and therefore these differences could take place by chance alone. The second and third models show age and Dukes stage to be strong predictors of colorectal cancer survival controlling for study group. The final model showed similar results to the first or crude model, where the northern First Nation and northern non-First Nation groups both were protective in terms of relative risk in comparison to the southern non-first Nation group. The southern First Nation group had 1.15 times greater risk of dying of colorectal cancer in comparison to southern non-First Nation group when controlling for both stage and age at time of diagnosis, where the end point is death from all causes. All of these relative risks were not significantly different from the southern non-First Nation group.

Table 5.3.3.2 - Univariate and Multivariate Relative Risks for Study Groups from Cox's model, colorectal cancer 1990-95 (death from colorectal cancer)

Model	Variable	R.R.	95% C.I.	p-value
Study Group alone	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.46	0.15 - 1.42	0.177
	Northern Non-FN	0.86	0.41 - 1.81	0.697
	Southern FN	1.17	0.71 - 1.90	0.551
Age + Study Group	Age	1.02	1.01 - 1.02	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.54	0.17 - 1.68	0.286
	Northern Non-FN	0.97	0.46 - 2.03	0.929
	Southern FN	1.25	0.76 - 2.05	0.374
Stage + Study Group	Dukes Stage			
	A	1.00	-	-
	B	1.79	1.25 - 2.57	0.0015
	C	5.02	3.56 - 7.07	< 0.0001
	D	24.33	17.08 - 34.68	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.46	0.12 - 1.86	0.277
	Northern Non-FN	0.94	0.39 - 2.26	0.888
	Southern FN	0.88	0.44 - 1.77	0.719
Age + Stage + Study Group	Age	1.02	1.01 - 1.03	< 0.0001
	Dukes Stage			
	A	1.00	-	-
	B	1.78	1.24 - 2.55	0.0017
	C	5.14	3.64 - 7.24	< 0.0001
	D	25.94	18.19 - 36.99	< 0.0001
	Study Group			
	Southern Non-FN	1.00	-	-
	Northern FN	0.59	0.15 - 2.36	0.453
	Northern Non-FN	1.04	0.43 - 2.51	0.933
	Southern FN	0.98	0.49 - 1.98	0.963

FN = First Nation, RR = Relative Risk, C.I. = Confidence Interval

Table 5.3.3.2 displays the Cox's model for colorectal cancer where the end point for survival is death from colorectal cancer. The first or un-adjusted model shows similar results to the first model presented in table 5.3.3.1. The northern First Nation and northern non-First Nation groups both had relative

risks of less than one, meaning they had a better prognosis after being diagnosed with colorectal cancer than those in the reference group, the southern non-First Nation group. The southern First Nation group had 1.17 times greater probability of dying of colorectal cancer in comparison to southern non-First Nation group, where the end point is death from colorectal cancer. All of these relative risks were not statistically significantly different from the southern non-First Nation group however. The last model (age, stage and study group) showed a relative risk of less than one for both the northern First Nation and southern First Nation groups. The northern non-First Nation group had 1.04 times greater probability of dying of colorectal cancer in comparison to southern non-First Nation group, where the end point is death from colorectal cancer. None of these relative risks were statistically significantly different from the southern non-First Nation group.

5.3.4 Cox Proportional Hazards Model - Survival Curves

In addition to calculating the adjusted relative risks, the Cox's model also produces survival curves adjusting for covariates. The survival curves for the final model (age, stage, and study group) is presented below. Figures 5.3.4.1 to 5.3.4.4 present the age and stage adjusted survival curves for colorectal cancer, where the end point is death from all causes. The consistent pattern seen here shows the two northern population groups to have very similar survival patterns. The northern First Nation and northern non-First Nation groups survival pattern are almost identical over the four Dukes stages. Both

of these study groups show slightly better survival in comparison to the two southern groups. The southern First Nation group consistently has the worst survival for each Dukes stage. The southern non-First Nation group has a similar survival pattern to the southern First Nation group and is slightly better off in survival.

Figure 5.3.4.1 - Age adjusted survival from colorectal cancer, Dukes Stage A (death from all causes) 1990 - 1995

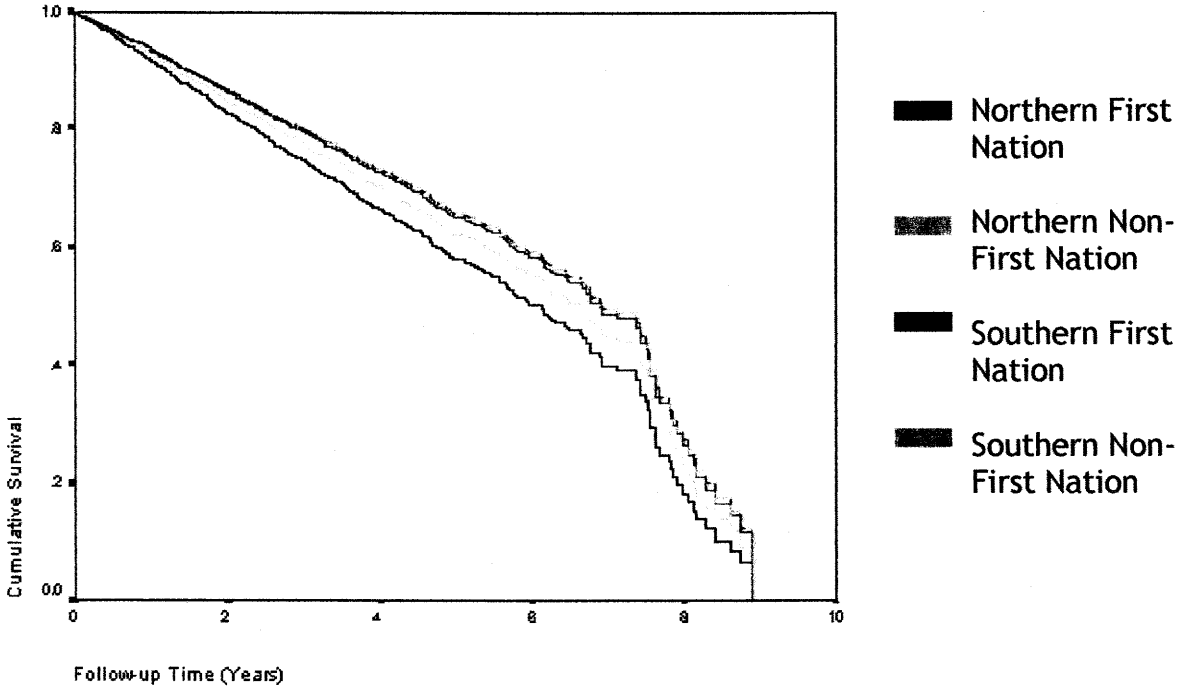


Figure 5.3.4.2 - Age adjusted survival from colorectal cancer, Dukes Stage B (death from all causes) 1990 - 1995

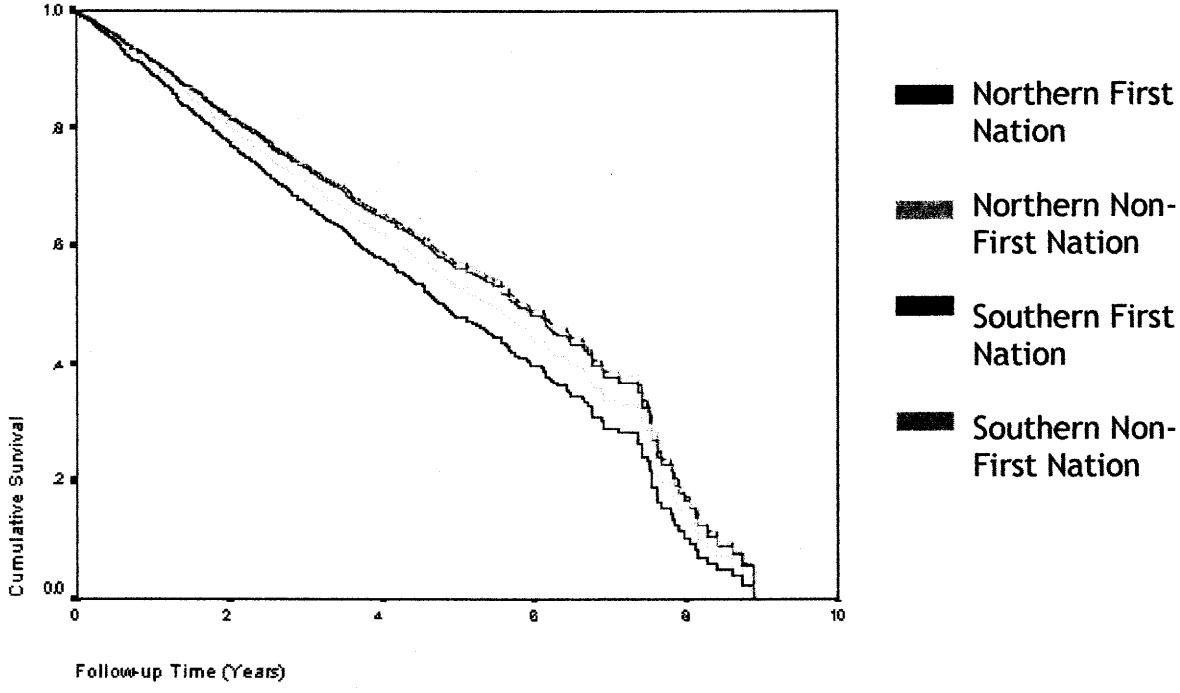


Figure 5.3.4.3 - Age adjusted survival from colorectal cancer, Dukes Stage C (death from all causes) 1990 - 1995

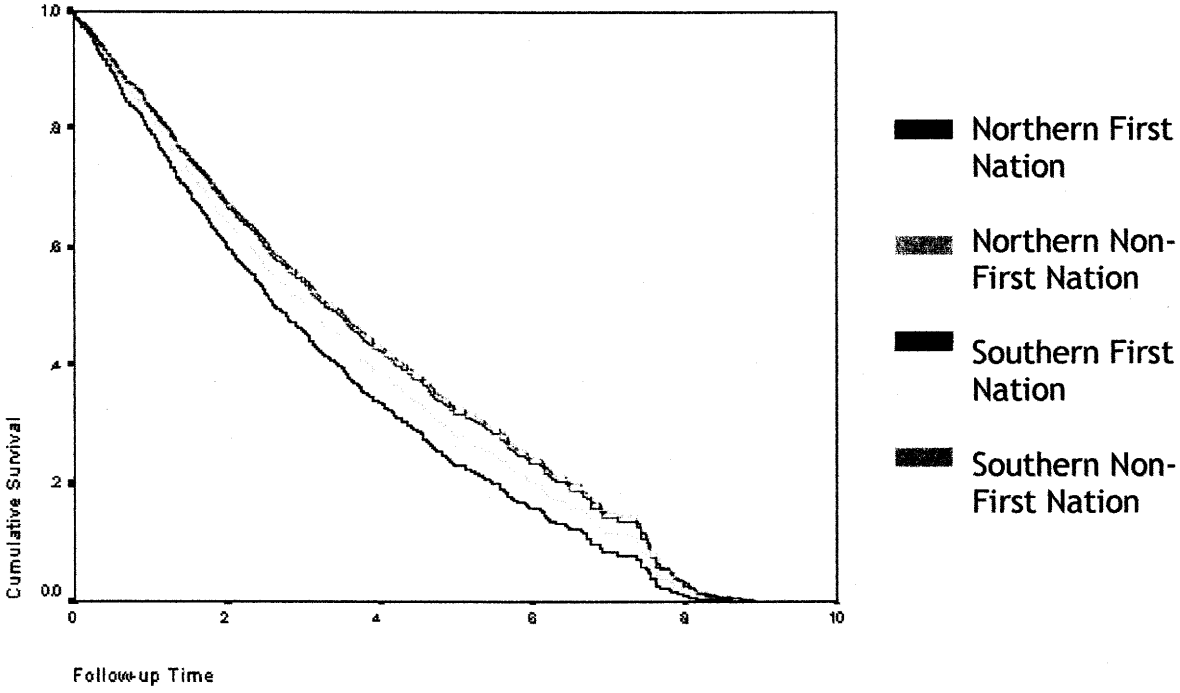


Figure 5.3.4.4 - Age adjusted survival from colorectal cancer, Dukes Stage D (death from all causes) 1990 - 1995

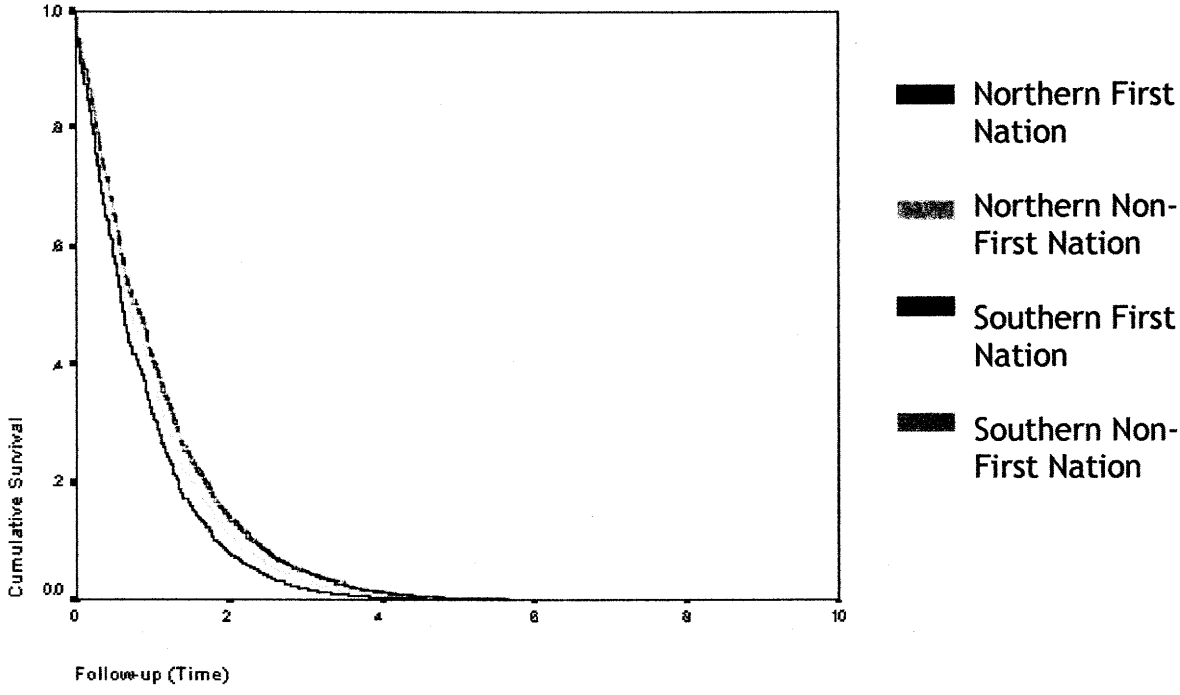


Figure 5.3.4.5 - Age adjusted survival from colorectal cancer, Dukes Stage A (death from colorectal cancer) 1990 - 1995

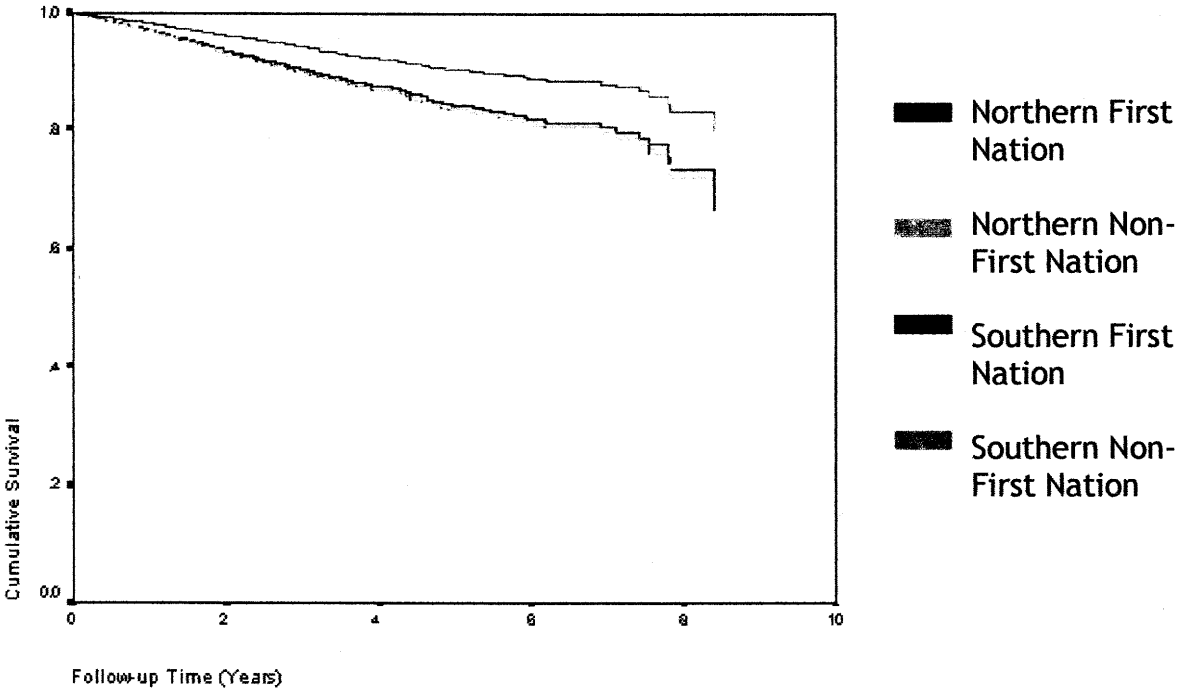


Figure 5.3.4.6 - Age adjusted survival from colorectal cancer, Dukes Stage B (death from colorectal cancer) 1990 - 1995

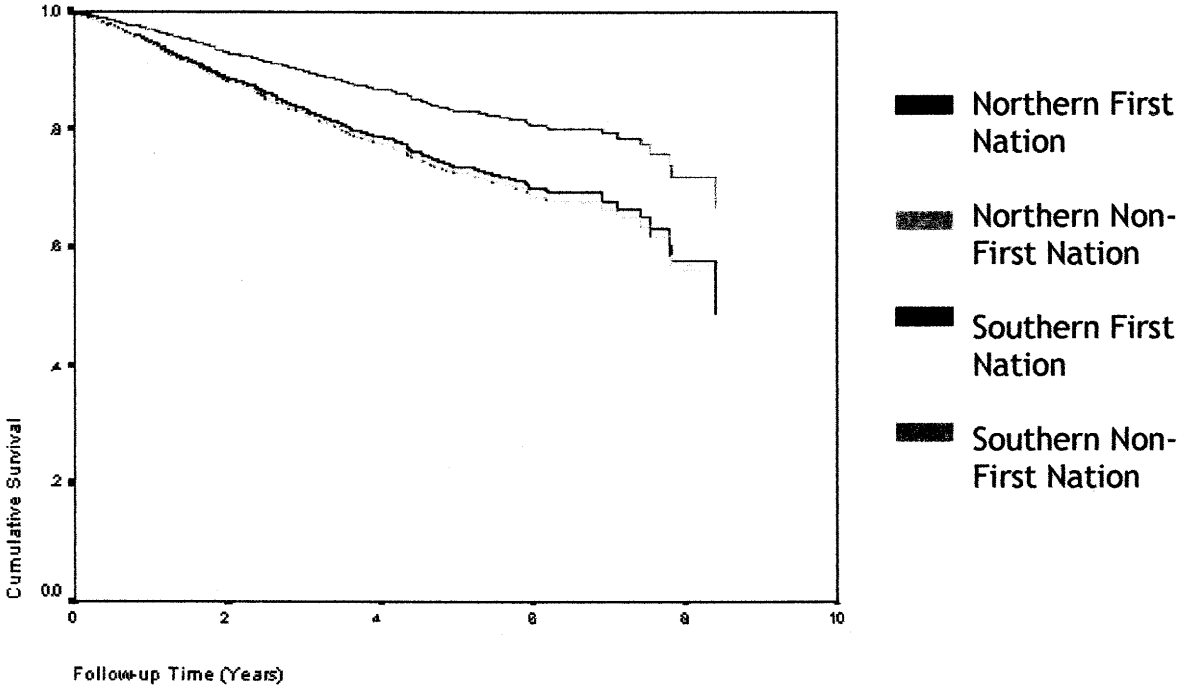


Figure 5.3.4.7 - Age adjusted survival from colorectal cancer, Dukes Stage C (death from colorectal cancer) 1990 - 1995

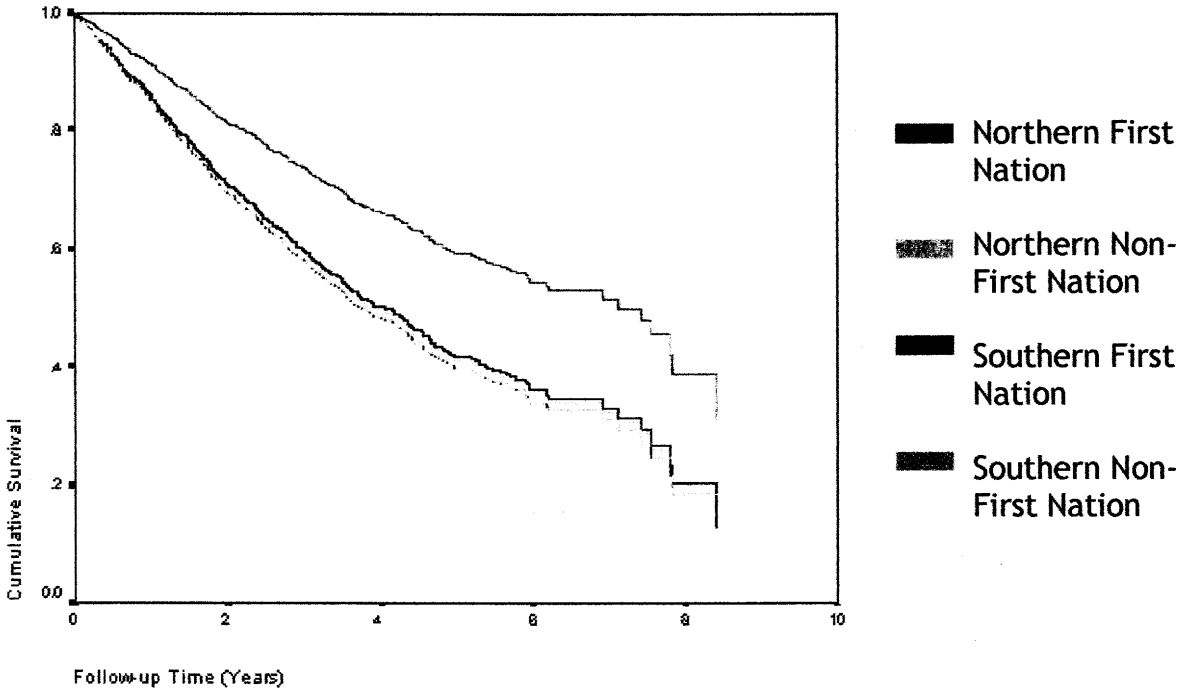
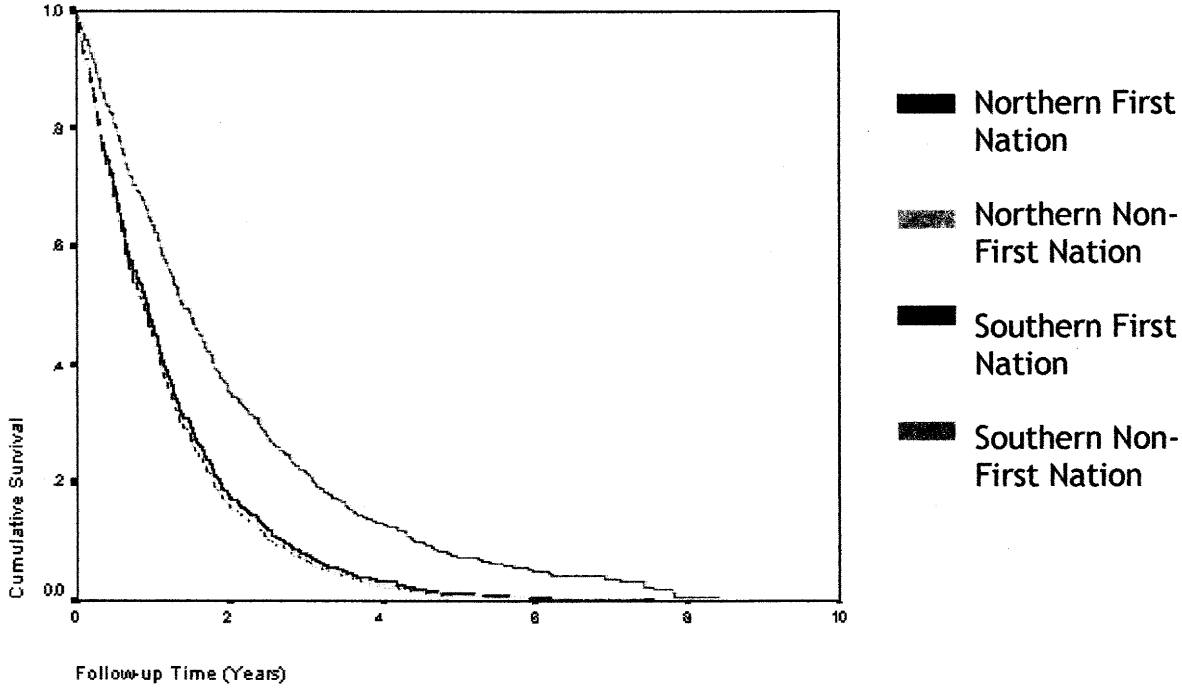


Figure 5.3.4.8 - Age adjusted survival from colorectal cancer, Dukes Stage D (death from colorectal cancer) 1990 - 1995



Figures 5.3.4.5 to 5.3.4.8 are the age and stage adjusted survival curves, where the end point is death from colorectal cancer. Here each figure consistently shows that for each Dukes stage and age adjustment, the northern First Nation group has the best survival pattern in comparison to the other study groups. The survival curves in figures 5.3.4.5 and 5.3.4.6 are relatively flat due to the small number of deaths for those diagnosed at Dukes stage A and B respectively.

6. Discussion and Conclusions

This descriptive study was done to explore and describe cancer survival patterns in northern Saskatchewan First Nations and non-First Nations in comparison to southern Saskatchewan First Nations and non-First Nations. It was also done to explore factors, such as staging at time of diagnosis, that could explain some of the disparity in the survival rates for cervical, colorectal, and breast cancers experienced by northerners (First Nation and non-First Nation) in comparison to southerners northerners (First Nation and non-First Nation). This section will summarize and discuss the results presented in chapter 5. It will begin with some discussion specific to each of breast cancer, cervical cancer and colorectal cancer followed by some summary discussion that is pertinent to all three cancer sites.

6.1 Breast Cancer

The stage specific breast cancer distribution for the northern First Nation and the southern First Nation groups were similar to one another. In addition the stage specific breast cancer distribution for the two non-First Nations groups were also similar to one another. For the two First Nation groups there were a larger proportion of cases diagnosed at TNM stage II versus TNM stage I. In contrast for the non-First Nations groups the distribution of breast cancer cases at TNM stage I and TNM stage II were more similar. This result concurs with research from other studies that concluded

that First Nations groups have more advanced disease at time of diagnosis(5, 40, 44). One possible explanation for this may be that First Nation groups may not have equal geographical access to secondary prevention services in comparison to non-First Nation groups. This explanation may not be the case however. With the difference in the distribution of stage specific breast cancer appearing between First Nations and non-First Nations and not on a geographical basis (north versus south) perhaps geographical access would not explain this difference in stage specific distribution. Further study of geographical differences in access to services could be studied in order to examine this hypothesis. A Geographical Information System (GIS) based study could be carried out looking at physical distances to diagnostic and screening services. Access to secondary prevention strategies can be influenced by knowledge, awareness and attitudes of the individual towards secondary prevention strategies, as well as the appropriateness of the educational messages, and screening program strategies to the group that the program is attempting to reach. For example, one may not feel the need to go to see a health care professional for a regular check-up even if they are feeling well and this could lead to a late stage diagnosis of cancer. Further study into the attitudes and knowledge of First Nations could be done to investigate this further. Another possible explanation of this difference may be willingness to participate in screening programs, which may be influenced by knowledge, awareness and attitudes towards screening (both self screening through self examination and other screening such as clinical examination and

mammography). Some previous studies have shown that First Nation populations are not as willing to participate in screening programs(12, 44). This could in turn mean that when First Nations do go for screening they might have a higher stage of disease. Other factors that may be involved here could be socio-economic status, education level, or cultural beliefs. Further study of these factors is needed to try to pinpoint the factors that could explain why First Nation populations experience a higher proportion of breast cancer cases at TNM stage II versus TNM stage I in comparison to non-First Nation groups. Breast cancer five-year crude survival rates have been calculated for northern First Nations (67%) and northern non-First Nations (71%) for the first time for Saskatchewan. Five-year crude survival rates for the southern First Nation group (69%) and the southern non-First Nation group(77%) have also been calculated and are comparable to rates calculated in the literature(19). A very striking difference was seen in the causes of death among breast cancer patients for the northern First Nation group. Among those northern First Nation breast cancer patients who died, some 90% died from breast cancer. For the other study groups 62% or less died of breast cancer. This observation is further evident in the stage and age adjusted survival curves where the end point is death from breast cancer. In comparison to the survival curves from Cox's model where the end point is death from all causes the northern First Nation survival pattern comes out as being quite different than all three other study groups. Some caution must be used in interpreting this result, as there were few cases in the northern First

Nation group when using death from breast cancer as the end point. With more deaths attributable to breast cancer the poorer survival pattern for the northern First Nation group is expected. This poorer survival pattern may be explained by hypothesizing that there is a greater impact of cancer therapy in the other study groups in comparison to the northern non-First Nation group, therefore those in the other study groups are getting "cured" from breast cancer and eventually die of other causes. Either the therapy available to the northern First Nation population is not as good as the other population groups, or perhaps the willingness to go to and continue with therapy is not the same for the northern First Nation group in comparison to the other population groups. To investigate this further, a study of the type of treatment and attendance of screening programs could be undertaken. One other explanation may be that the death reporting mechanism for the northern First Nation group may not be as accurate for some reason and therefore cancer is used more often on the death certificate as the cause of death than some other more detailed cause. Further investigation of this is necessary to help understand what is the reason for this difference. The most interesting result from the breast cancer analysis comes from the calculation of the relative risk of dying from breast cancer using Cox's model. The relative risk of death increases for each of the First Nations and northern non-First Nations when age is taken into consideration. This shows that survival is even poorer than calculated in the previous study (Irvine,1990) which did not adjust for age. The relative risk of death decreases for each of the First Nations and northern

non-First Nations groups when stage is taken into consideration. This shows that the stage of disease at the time of diagnosis is one of the factors involved in the differences in survival compared to the southern non-First Nations group and may reflect differences in access, availability and utilization of screening (including breast self examination, clinical breast examination, or mammography). From the Cox's model, the age and stage adjusted relative risk for dying from breast cancer for the northern First Nation group was 1.81 in comparison to the southern non-First Nation group, this was statistically significant (p=0.013). Despite adjusting for stage and age, the relative risk was still significant for the northern First Nation group in comparison to the southern non-First Nation group, factors other than stage and age at time of diagnosis must therefore be involved. This result concurs with Gilliland et al and Sugarman et al as they to found some unexplained difference in survival after adjusting for stage, age and other factors (21, 40). Factors such as socio-economic status or treatment access may be tied to this unexplained difference, further study of these factors is necessary.

6.2 Cervical Cancer

The stage specific cervical cancer distribution for the southern First Nation group and southern non-First Nation groups were similar to one another. In these two groups over half of the cervical cancer diagnoses were at TNM stage I. For the two northern groups the distribution between TNM stage I and TNM stage II were similar to each other, but a lower proportion

were in TNM stage I compared to the southern non-First Nations and southern First Nations. The number of cases in the north with staging information was small however. For the southern First Nation group this result is in contrast with research from other studies that concluded that First Nations groups have more advanced disease at time of diagnosis in comparison to non-First Nations (5, 40, 44). Interestingly, although the southern First Nation group had more diagnoses at TNM stage I than any other stage, their survival pattern was worse than all other study groups. The relative risk of death for the southern First Nation group was not significant however. This finding warrants some more investigation, perhaps the influence of treatment should be examined. Cervical cancer five-year crude survival rates have been calculated for northern First Nations (69%) and northern non-First Nations (69%) for the first time for Saskatchewan. Five-year crude survival rates for the southern First Nation group (63%) and the southern non-First Nation group (73%) have also been calculated. The rate calculated by Irvine et al. for all First Nations was 75%, for the north (First Nation and non-First Nation) 66%, and for the entire province 76%(6). In this study both First Nation groups had lower five-year survival rates than the overall First Nation rate from Irvine et al. Their study however, examined all cervical cancer diagnoses from 1967 to 1986, in comparison to this study, which included cervical cancer diagnoses from 1980 to 1995. The crude five-year survival rate calculated in this study includes more recent information and shows a slightly worse survival for First Nations in Saskatchewan recently. In the previous study of cancer survival for

the northern population of Saskatchewan(6), it was suggested that age at time of diagnosis be investigated further as an influence on survival. This study has accomplished this by calculating age and stage adjusted survival using the Cox proportional hazards model. The relative risk of death increases when adjusting for age which suggests that the survival rates are poorer than calculated in the previous study, which did not consider the age differences in the populations. The relative risk of death decreases for each of the First Nations and the northern non-First Nations group when adjusting for stage at time of diagnosis, suggesting that the stage at the time of diagnosis has some influence on the differing survival rates. This may show the potential improvement that is possible with improved screening. Despite adjusting for both stage and age the southern First Nation relative risk is still statistically significant in comparison to the southern non-First Nation group (death from all causes). There are therefore still some unexplained differences in the survival pattern. This concurs with Gilliland et al who also found that after controlling for the distribution of age, gender, stage at diagnosis, histologic grade, and treatment, disparities in survival were not completely explained(40). Factors such as socio-economic related circumstances could further explain this difference, further study into these factors is warranted. As the southern First Nation group has the worst survival pattern when examining stage and age adjusted survival, issues as to why must be asked. Further study into the possible barriers faced by this population group must be carried out. Factors such as willingness to attend treatment, education

about screening and treatment, and cultural beliefs towards secondary prevention strategies could contribute to their poor survival pattern. The question of spending health care dollars on education programs on the benefits of screening and following treatment versus having more comprehensive and rigorous screening and treatment programs should also be asked.

6.3 Colorectal Cancer

The stage specific colorectal cancer distribution for the two First Nation groups and the northern non-First Nation group were similar to one another. In these three groups almost 60% of the colorectal cancer diagnoses were at Dukes stage C and D combined. For the southern non-First Nation group the distribution of colorectal cancer at Dukes stage A and B combined was over 50%. Looking at Dukes stage A, the two First Nation groups (southern and northern) had the lowest proportion of cases followed by the northern non-First nations and the southern non-First Nations. This has implications on the importance of trying to achieve more early diagnoses for these population groups. This could be attained by attempting to increase awareness of the importance of regular check-ups, (i.e. rectal exams) and seeking attention for early symptoms. Caution should be used when interpreting this data as the number of cases in the north and among southern First Nations with staging information was small. For the southern First Nation and northern First Nation groups this result is in accordance with

research from other studies that concluded that First Nations groups have more advanced disease at time of diagnosis in comparison to non-First Nations (5, 40, 44). Colorectal cancer five-year crude survival rates have been calculated for northern First Nations (82%) and northern non-First Nations (59%) for the first time for Saskatchewan. Five-year crude survival rates for the southern First Nation group (55%) and the southern non-First Nation group (52%) have also been calculated. The rate calculated by Tan et al. for the entire province was 54%(6) this is comparable to the rate for southern non-First Nations (the largest population group in the province). Looking at the relative risk of dying the northern First Nation group has the best survival pattern in comparison to the other study groups when examining stage and age adjusted survival. Further study into the possible reasons for this should perhaps be undertaken as colorectal cancer rates have been shown to be rising among First Nations throughout Saskatchewan and northern First Nations on reserve(53).

6.4 Summary Discussion

This study provides a measure of cancer survival for the northern First Nation and northern non-First Nation population groups for the province of Saskatchewan. In the past, survival rates for the north of Saskatchewan have been calculated for all residents of the north, grouping First Nations and non-First Nations together. By dividing the north into First Nation and non-First Nation, a more complete understanding of the breast, cervical and colorectal

cancer distribution and survival patterns have been shown. As Gillis et al point out it is important to separate out First Nation and non-First Nation information in the north to help understand fully the health status of these two unique population groups in a unique geographical setting(5). This study confirms in the Saskatchewan setting what the literature has pointed out, both stage of cancer at time of diagnosis and age at time of diagnosis of cancer are strong predictors of survival. The Cox proportional hazards model analysis provides relative risk estimates that are highly significant with narrow confidence intervals for both stage at diagnosis and age. This then shows that for a more accurate estimation of the relative risk of dying from cancer, it is worthwhile to control for factors such as age of cancer patient at time of diagnosis and cancer stage at time of diagnosis. With regard to the impact of stage of diagnosis on survival and access to secondary prevention strategies, the findings of this study concur with those of Gilliland et al(40). They also found that the stage adjusted relative risk estimate was slightly better than the crude model however, they also found that there was still some unexplained differences in the survival patterns between population groups, as did this study. The results in this study however, were not found to be significant for cervical and colorectal cancers, but these two sites had very small number of cases and perhaps after more follow-up time the relative risks may prove to be significant. Other factors that could influence survival could be; type of treatment, participation in screening, cancer histology, and socio-economic status, all factors that have also been pointed out in the

literature(38, 40). It has been shown that when examining the survival curves and relative risks for all sites (end point death from underlying cancer); for breast cancer the northern First Nation group had visibly worse survival than the other three study groups (statistically significant), for cervical cancer the southern First Nation group had visibly worse survival than the other three study groups (borderline significant), and for colorectal cancer the northern First Nation group had a visibly better survival pattern than the three other study groups (not statistically significant). Unexplained differences in survival must be examined, factors such as socio-economic status and attitudes and knowledge of secondary prevention strategies could be examined to further understand these unexplained differences. In addition, cancer treatment issues for the northern First Nation Group (breast cancer), southern First Nation group (cervical cancer), and issues as to why the survival pattern is better for the northern First Nation group for colorectal cancer could also be examined. For colorectal and cervical cancers it must again be pointed out that the number of cases were small and perhaps with a longer follow-up time the results could be more interpretable.

Three main themes come out of this thesis; 1. the proportion of cancer cases in early stage of disease is low for First Nation Groups and northerners in comparison to southerners and non-First Nations this concurs with finding in the literature(21, 40); 2. for each cancer site the relative risk of dying increases for each study group in comparison to the southern non-First Nation group when controlling for age, this allows for a more accurate indication of

the true survival pattern for these groups as compared to studies in the past(6); 3. the role of adjusting for stage of disease and age at time of diagnosis with relation to survival and relative risk has been brought out. It is important to improve access to screening, and make screening programs appropriate to the geography, language and culture of First Nations populations, this is evidenced by differences in the proportion of diagnoses at later stages as well as relative risks calculated adjusting for stage at time of diagnosis. Although adjusting for these factors has been shown to be valuable in terms of a more accurate reflection of the true survival patterns of the population groups, unexplained differences are still present and need to be investigated.

6.5 Study Limitations

This study provides important information about severity of disease at time of diagnosis of cancer through stage distribution and stage adjusted survival analyses. These analyses are useful in helping understand the cancer experience of the northern people of Saskatchewan, however, more information is required to help understand the differences in survival and relative risk between the north and the south. More accurate staging information is required for other cancer sites so that similar studies can be carried out for other cancer sites such as cancer of the lung. Information on other covariates such as cancer histology, grading and type of treatment are required to try and help explain differing survival patterns between First Nations and non-First Nations, both in the north and the south. Other

information on attitudes and knowledge towards secondary prevention strategies and issues of socio-economic status must also be investigated. There are few cases in some of the analyses done here thus risking a chance of stating no significant differences when in fact there could be some differences with a larger number of cases. A longer follow-up time is needed to capture more cases for survival analysis. With more cases a more precise estimate of the relative risk of dying of cancer for each study group can perhaps be obtained.

6.6 Future Work

To better understand the cancer distribution and survival patterns among northern First Nation and northern non-First Nation populations further study needs to be under taken. Factors such as treatment, cancer histology, and cancer grading and their effect on survival should be studied. Other factors such as attitudes and knowledge of secondary prevention strategies should also be examined. The role of socio-economic status may also be important and therefore be further examined as well.

6.7 Conclusions

It is the hope of this author that this study can supply some information to the people of the north and First Nations in Saskatchewan to help better understand and pose further questions about their health status with respect

to cancers of the breast, cervix and colon and rectum. With continued interest and study of northern and First Nations populations perhaps the health inequalities they have experienced in the past can be better understood and even rectified.

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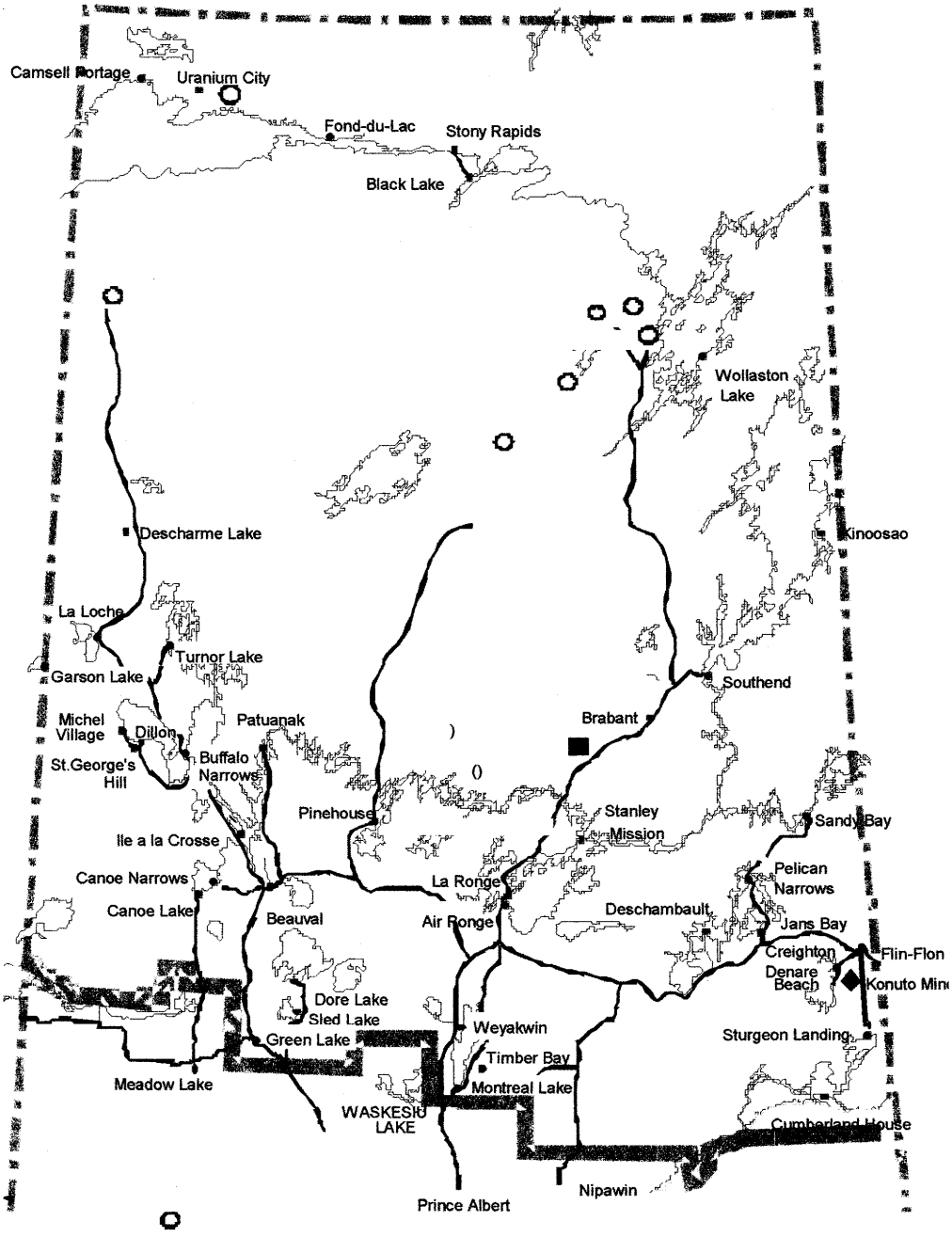
Appendix A: Map of Northern Saskatchewan



Appendix B:"Northern" Covered Population, 1992

First Nation Bands in Northern Saskatchewan

Band	Residence Code
Clearwater Dene First Nation	74880 (Big C Band)
Canoe Lake First Nation	74680
Cumberland House First Nation	72582
English River First Nation	75180
Fond du Lac First Nation	75082
Hatchet Lake First Nation	72882
Lac La Ronge Indian Band	72482
Montreal Lake First Nation	72682
Peter Ballantyne Cree Nation	72082
Buffalo River First Nation	74780 (Peter Pond Lake Band)
Black Lake First Nation	74982 (Stony Rapids Band)
Birch Narrows First Nation	74580 (Turnor Lake Band)

Communities in northern Saskatchewan with residence codes other than First Nation Bands

Community	Residence Code
Air Ronge	80470
Beauval	80370
Buffalo Narrows	80270
Camsell Portage	80170
Canoe Narrows	80371
Creighton	80530
Cumberland House	80570
Denare Beach	80571
Dillon	80271
Flin Flon/Creighton Unorg. area	80575
Fond du Lac	80172
Ile a la Crosse	80374
La Loche	80272
La Ronge	80430
Patuanak	80375
Pelican Narrows	80572
Pinehouse	80472
Sandy Bay	80573

Southend	80473
Stanley Mission	80474
Stony Rapids	80173
Sturgeon Landing	80574
Timber Bay	80475
Turnor Lake	80273
Uranium City	80175
Weyakwin	80471
Wollaston Lake	80174