University of Alberta

HIV in Aboriginal women in Northern Alberta

by

Sandra E. Shokoples 

A Thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Master of Science

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"Indigenous individuals and peoples are free and equal to all other individuals and peoples in dignity and rights, and have the right to be free from any kind of adverse discrimination, in particular that based on their indigenous origin or identity."

Excerpted from the Draft Universal Declaration on the Rights of Indigenous Peoples, by the United Nations Working Group on Indigenous Populations, reflecting an emerging international consensus on the rights of First Peoples around the world. (August 23, 1993)

This project was undertaken to provide epidemiological evidence to support HIV prevention programs for women and for Aboriginal people.

Abstract

Although only 8.4% of the population of northern Alberta are Aboriginal, 46% of women with human immunodeficiency virus (HIV) in northern Alberta who were seem by the Northern Alberta HIV Program are Aboriginal. The highest numbers of HIV positive women were in the 15-34 year age groups. Of the two major risk factors for women for contracting HIV - heterosexual contact and intravenous drug use (IVDU), more HIV positive Aboriginal women had used IV drugs. There was no statistically significant difference between HIV positive Aboriginal women and non-Aboriginal women in terms of the proportion who had received anti-retrovirals (ARV) or the proportion who had experienced outcomes of low CD4 count, death, or acquired immunodeficiency syndrome (AIDS). HIV positive Aboriginal and non-Aboriginal women continue to become pregnant after being diagnosed as HIV positive. Aboriginal leadership and participation in programs that address the issues of women and of Aboriginal people are necessary to prevent the spread of this epidemic.

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Abbreviations

3TC	lamivudine
ACCESS	Microsoft database software
AIDS	Acquired Immune Deficiency Syndrome
ARV	antiretroviral (drugs)
AZT	zidovudine
CCR5	CD4 coreceptor
CD4	cluster designation 4
CDC	Center for Disease Control – Atlanta, Georgia
CXCR4	CD4 coreceptor
HAART	highly active antiretroviral therapy
HCV	Hepatitis C virus
HIV	Human Immunodeficiency Virus
HIV-1	Human Immunodeficiency Virus type 1
HIV-2	Human Immunodeficiency Virus type 2
HR	hazard ratio
IV	intravenous
IVDU	intravenous drug use
PI	protease inhibitors
RAH	Royal Alexandra Hospital
RHA	Regional Health Authority
SPSS	Statistical Package for Social Science, SPSS Inc.
STD	sexually transmitted disease
T_H cells	T-helper subset of lympocytes
UAH	University of Alberta Hospitals
VL	viral load

Chapter One

1.1: Overview of HIV and AIDS

1.1.1 Introduction to HIV and AIDS

HIV (Human Immunodeficiency Virus) is a human retrovirus that depletes the immune system by destroying T-lymphocytes and macrophages displaying CD4 markers on their surface.[1] AIDS (Acquired Immune Deficiency Syndrome) is the combination of opportunistic infections and malignancies associated with infection with HIV virus. Two types of HIV virus have been identified; HIV-1 and HIV-2.[1,2] HIV-1 has been found worldwide. HIV-2 is presently found predominantly in West Africa and recently in India.[1,3] HIV-1 is presumed to have originated in Africa from a primate source; possibly chimpanzee.[4] It has one major group (group-M) that contains at least 10 clades and two rare groups - O and N. HIV-1, M group, clade B is the predominant virus detected in North America.[1,2]

HIV is transmitted through person-to-person transfer of body fluids, i.e. transfusion of blood products, needle sharing, unprotected sexual contact, and perinatally.[4]

Although the implications of a diagnosis of HIV infection have changed considerably since the advent of potent antiretroviral therapies, patients living with this virus require long-term medical treatment and follow-up. Premature death due to opportunistic infections or malignancies is still the outcome of untreated HIV infection in the vast majority of cases.[1,3,5]

AIDS is the clinical presentation of advanced HIV infection. Depletion of the patient's immune system allows infections by opportunistic pathogens, reactivation of dormant organisms and proliferation of malignant cells.[6]

1.1.2 The HIV virus and its pathogenesis

HIV is a member of the genus Lentivirus of the family Retroviridae. The virus particle consists of a nucleocapsid containing two copies of single-stranded RNA and reverse transcriptase, surrounded by an envelope or membrane partially derived from the host cell.[2,3]

The human immune system consists of cells that produce humoral immunity (the killing of cells through the use antibodies) or cellular immunity (direct killing of infected cells by lymphocytes). CD4+ lymphocytes or T-helper cells are responsible for the regulation of both humoral and cellular immunity through their ability to become activated by non-specific immune system cells such as macrophages that present ingested foreign material on their surface. The CD4+

lymphocytes produce cytokines that activate cell-mediated immunity and stimulate B cells that produce antibody. Loss of CD4+ cells as they become infected by HIV virus results in declining immune function.[7]

HIV enters cellular components of the immune system that express CD4 receptors on their surface through the binding affinity of the viral envelope GP120 glycoprotein for CD4 molecules. CD4 receptors are found on CD4+ lymphocytes, dendritic cells, and macrophages.[2,5] Macrophages and dendritic cells occur at sites of entry for the virus such as mucosal tissue and are the non-specific component of the immune system in tissues such as the brain and lungs.[2,5] Macrophages carry a small number of CD4 molecules on their surface, are relatively resistant to the lytic effects of viral infection and, therefore, can harbor viral particles.[5] Macrophages also contain the CCR5 chemokine co-receptor which allows infection by an HIV virus phenotype (M-tropic) that is present early in infection.[2] CD4 + lymphocytes carry a large number of CD4 molecules and the co-receptor CXCR4 on their surface. They are the cells that are depleted by viral infection.[5] CXCR4 is the co-receptor for the T-tropic phenotype of HIV virus. CD4 negative cells such as astrocytes, spermatozoa and vaginal epithelial cells are infected by HIV through a glycolipid receptor.[2]

The virus binds to the cell, and fusion occurs between the viral membrane and the cell membrane.[5] The viral capsid enters the cell and the virus uncoats, releasing

the viral RNA into the cell. Viral reverse transcriptase copies the single stranded RNA of the HIV virus into double stranded DNA.[5] The viral DNA integrates into the host chromosome, using the viral enzyme integrase, to be transcribed by the host cell to produce virus when the host cell becomes active.[1,8] CD4+ lymphocytes that produce virus eventually die.[7]

Viral RNA is unstable and transcription errors occur at a rate of 10^{-3} to 10^{-4} per nucleotide incorporated.[9] These mutations may produce an individual virus that is not viable or produce a virus that is more fit to survive in the presence of either the host's immune response or antiretroviral drugs (drug resistance).[10] A virus with a mutation that allows it to survive in the presence of the antiretroviral drug being used in treatment will soon become the predominant quasispecies in a patient that continues to receive that drug.[1,11]

Initial exposure to HIV sometimes causes a mononucleosis-like illness. This acute phase occurs days or weeks after exposure during which large numbers of virus particles are produced and infect cells throughout the body. A clinical latent phase follows during which equilibrium is reached between high levels of virus production and high levels of CD4 lymphocyte production and destruction but the patient may be free of symptoms.[2,3,5,6]

AIDS is the clinical manifestation of the ultimate decline in number and function of the cells of the immune system by infection with HIV. The length of the clinical latent phase before the progression to AIDS varies for each patient depending on a combination of viral factors and individual immune response.[12] The Canadian surveillance case definition for AIDS includes laboratory evidence of HIV infection and the presence of clinical conditions indicating immunosuppression including pulmonary tuberculosis, Kaposi's sarcoma, pneumocystis carinii pneumonia (PCP), invasive cervical cancer and recurring pneumonia.[13] Appendix D lists the Canadian surveillance definition for AIDS reporting. HIV virus generally does not cause death directly; morbidity and mortality are usually due to these opportunistic diseases.[2] The median time from HIV infection to AIDS in untreated adults is 10 to 11 years.[2] The median time from HIV infection to AIDS in patients who receive HAART has not yet been established. A wide range of factors including host factors such as overall health status, immune response, tolerance to treatment, type of opportunistic infections, and treatment compliance determine the survival time of HIV positive patients.[2] Patients may be unaware of their seropositivity and not present to a physician until treatment is required for an opportunistic infection or malignancy.

1.1.3 Testing for HIV/AIDS

In northern Alberta, testing for HIV is done by the Provincial Laboratory for Public Health, and Canadian Blood Services. The screening test for HIV consists

of an Enzyme Immunoassay (EIA) to determine the presence of antibodies to the HIV in the blood of the patient. The EIA screening test has a high sensitivity (99%). All reactive EIA screening tests are repeated to ensure that there were no errors in the testing process. False positive results may occur, therefore all positive results from the screening assay are confirmed by performing a Western Blot assay that detects the presence of antibodies to HIV proteins with a high specificity.[2,6] False negative tests can occur in patients during the early days of their infection due to the delay between exposure to the virus and the production of a detectable amount of antibody produced by the body to the virus. This window period is usually three to four weeks.[2] All HIV test results must be given to the patient with counseling about the meaning of a positive or negative result. Patients with a negative test result who are engaged in high risk activities such as intravenous drug use or unprotected sexual contact with multiple partners are informed about the importance and practical aspects of behaviour change and encouraged to be retested for HIV.

The amount of virus or viral load in the blood of an HIV positive patient can be determined by the detection of viral RNA by amplification techniques such as polymerase chain reaction (PCR). PCR can be used for diagnosis during the window period, but is mainly used to monitor the effectiveness of antiretroviral therapy (ARV).[2] High viral loads are associated with poor prognosis and low viral loads (below the limits of detection of the assay) are an indication that the

patient is compliant with their treatment and that the antiviral drugs being used remain effective for the patient.[2] Detection of the virus by PCR is also used to determine the infection status of infants born to HIV infected mothers since the EIA will detect antibodies in the infant that originated in the mother; these antibodies may take 18 months to disappear.[4] Detection of viral RNA in the blood of the newborn allows earliest possible treatment.[4]

Sensitivity testing is used to determine the variation of virus quasispecies that develop in a patient during the course of the their infection in response to antiviral therapy. Its primary use is to predict HIV drug resistance. This relatively new technology allows physicians to change a patient's antiviral regimen in response to a change in the population of virus that emerges as a result of viral mutation and selection in the presence of the drug.[2,10]

Quantitation of the number of lymphocytes containing CD4 receptors (CD4 counts) in both absolute numbers and as a ratio of CD4+ lymphocytes to CD8+ lymphocytes, is performed to determine the status of the patient's immune system as it is affected by the destruction caused by viral infection.[2] As the number of CD4+ cells decreases, the risk of serious opportunistic infections increases. A low CD4 count is used to determine the requirement for initiation of or changes in antiretroviral therapy and prophylaxis for opportunistic infections such as PCP.

1.1.4 Treatment

Treatment of HIV infected patients involves medication to prevent or treat opportunistic infections, medication to provide symptom relief, and antiretroviral drugs. Refer to Appendix E for a list of antiretroviral drugs.

In addition to the diseases that occur in the community, HIV patients with a low CD4 count are susceptible to infections from organisms that are normally benign components of the patient's internal or external environment.[13] Treatment is prescribed prophylactically to prevent opportunistic infections such as PCP, toxoplasmosis, and Mycobacterium avium complex in the absence of a functioning immune system. Treatment is also available for viral infections such as cytomegalovirus, herpes simplex virus, and varicella. Antibiotics, anti-virals, and anti-fungals are a poor substitute for innate immunity however. Bacteria and viruses can become resistant to treatment through genetic changes; fungal infections are difficult to eradicate from the body once established and recur when anti-fungal therapy stops.[7]

Antiretroviral therapy disrupts viral replication by interrupting the activity of enzymes involved in the process of producing virus particles. Nucleoside analogs such as zidovudine (AZT) and lamivudine (3TC) prevent transcription of viral RNA into DNA by inserting nucleotides into the transcribed DNA that terminate the process. Non-nucleoside reverse transcriptase inhibitors such as nevirapine,

delavirdine and efavirenz bind to the viral reverse transcriptase and prevent its activity. Protease inhibitors such as saquinavir, ritonavir and nelfinavir prevent the cleavage of translated viral proteins into functional forms, which prevents virus assembly and release.[2]

Highly active antiretroviral therapy (HAART) is the use of a combination of antiretroviral drugs to increase the potency of treatment and to prevent the development of drug resistance.[14] HAART therapy generally includes at least three antiretroviral drugs. When anti-retroviral drugs are used viral RNA can be reduced to below the level of detection of the viral load assay in a large proportion of patients and some degree of immune function can often be restored.[2,15,16,17] A high degree of patient compliance with the therapy regimen is very important to prevent the emergence and transmission of drug resistant virus.[11]

1.2: The study population

1.2.1 Epidemiology

In 1981 a new pattern of immunosuppression and opportunistic infections was observed in the Los Angeles area among previously healthy young gay men.[6] The outbreak of immunodeficiency was soon found across the United States and by 1982 over 800 cases had been reported. At that time the risk groups identified were homosexual men, intravenous drug users, Haitian immigrants, hemophiliacs, recipients of blood products, sexual partners of those at risk of contracting HIV and children born to high-risk mothers. The etiological agent was isolated in 1983 in Paris and in Bethesda in 1984.[6] HIV was found to have originated in Africa from human contact with other primates. The inevitable encroachment of humans into the ecosystem of other primates in Africa combined with humans' ability to travel and interact with people throughout the world has provided a primary example of viral emergence.[2]

HIV infection is a global problem. As of December 2000, 36.1 million people were living with HIV/AIDS worldwide; 16.1 million were women and 1.4 million were children less than fifteen years of age. 920,000 people were living with HIV in North America; 20% were women.[18] In Canada 50,259 positive HIV tests and 18,026 cases of AIDS were reported to the Laboratory Centre for Disease

Control at Health Canada from the beginning of the epidemic in the early 1980s to December 2001.[19]

HIV as a worldwide pandemic has propagated in two patterns. One pattern occurs in developed countries and originally presented in homosexual men and intravenous (IV) drug users (IVDU). This pattern predominated in Canada and the U.S. at the start of the epidemic. The second pattern occurs in developing countries with HIV infecting both men and women in equal numbers and being transmitted heterosexually and perinatally.[20] The epidemic in Canada now has elements of both patterns of transmission with an increasing incidence in IV drug users and heterosexual transmission to women.[21]

The use of highly active antiretroviral therapy (HAART) including the use of protease inhibitors has prolonged the lives of patients with HIV.[14,16] The number of reported AIDS cases and deaths have declined by approximately 80% in industrialized countries as more effective treatments have been implemented, but the decline may have leveled out.[21] No treatment is a cure for HIV. Transmission of HIV appears to be reduced in patients with a low amount of virus in their blood due to effective antiretroviral therapy; however a threshold for preventing transmission has not been established.[22] The effectiveness of antiretroviral therapy has had the side effect of reducing vigilance in high-risk populations which may lead to increased transmission.[14]

The methods of HIV transmission: unprotected sex, IVDU, receipt of blood products containing HIV, and perinatal transmission have been well characterized. Prevention has centred on the mode of transmission prevalent in a given population. The concept of the "risk environment"[23] brings together the social and physical factors of HIV transmission including socioeconomic status, and the sex and drug trade environment.[23,24] In areas where IVDU and heterosexual transmission are predominant, prevention strategies must take into account the lifestyles and circumstances of infected persons in order to identify and prevent transmission to those in similar high risk circumstances.[23,24,25,26]

1.2.2 HIV in women

HIV in women in Canada is on the increase. Nationally women accounted for 14.4% of the population with HIV at the end of 2001.[19] The proportion of women who test positive for HIV per year has been increasing steadily since 1995 reaching 24.9% of new adult HIV positive reports in 2001. Of HIV positive women in Canada, the percentage aged 15-29 has increased from 14.6% for the period up to 1995 to 44.5% in 2001.[19]

The two major risk factors for transmission of HIV to women are heterosexual contact with a person with HIV and intravenous drug use.[21,27] A major concern in this population is the potential for the woman to transmit the infection

to her child perinatally. In the absence of treatment, the risk of transmission of HIV from mother to infant averages twenty to twenty-five percent.[1,12] According to Health Canada, 765 infants have been born to HIV positive women in Canada from 1989 to 1998; 232 of those infants have been confirmed HIV positive.[28] Alberta Health has implemented prenatal screening of women for HIV to allow intervention in the transmission of HIV to infants. The blood collected from women during their routine prenatal screen is tested for HIV unless the woman declines testing.[12,28] In 1999, 13 HIV positive women were identified through prenatal testing.[29]

A number of factors increase the risk of HIV transmission perinatally. These include a high maternal viral load, premature rupture of membranes during delivery, older maternal age and breast feeding.[30] Many studies have shown that antiretroviral therapy can prevent perinatal transmission of HIV.[31,32,33,34,35] The main intervention used to prevent perinatal HIV transmission is early detection through prenatal screening followed by antiretroviral therapy and monitoring of the mother throughout her pregnancy.[12] The protocol used by the Capital Health Authority and Caritas Health Group indicates that women on ARV for HIV should also be placed on IV zidovudine during delivery and ARV should be given to the infant post-natally. Women who are not diagnosed until late in pregnancy, women who have not had ARV, or women who are believed to have had poor compliance to ARV are considered for

delivery by cesarean section and ARV therapy started on both the mother and the infant. Formula feeding instead of breast-feeding is strongly recommended.[12] Research published by Dr. Lee and Dr. Robinson from the Stollery Children's Health Care Centre in Edmonton indicates that 71 babies were born to HIV positive women up to December 31, 1999. Forty-two women who had received ARV during pregnancy and/or during the intrapartum period gave birth to 44 infants; thirty-four of the infants born were not infected, three were infected with HIV and seven had indeterminate HIV status.[35]

1.2.3 HIV in Aboriginal people

The definition of an Aboriginal person for the purpose of this study is a person who identifies themselves as Aboriginal in one of the categories listed in Appendix A.

Health Canada identified in the 1996 census that the mean age of the Aboriginal population is 10 years less than the Canadian mean and that the Aboriginal population is growing rapidly.[36] As of December 31,1998, 24.3% of the Canadian Aboriginal population were women between 15 and 39 years of age.[37]

Health Canada reports on HIV and AIDS cases. A drawback to their data is the unavailability of ethnic status data from Ontario, Quebec, New Brunswick and

Nova Scotia, incomplete reporting of ethnic status in the reports received from other provinces, the possibility that duplicate tests are being reported, and the delay in reporting from the provinces.[42] However, the national data indicates that the incidence of HIV infection in Aboriginal people has been increasing more that that of the general population.[38,39,40,41] In 1998 and 1999, 911 men were reported as being HIV positive; 15% were identified as being Aboriginal.[41] In recent years, the number of Aboriginal women testing HIV positive is equal to or greater than the number of Aboriginal men.[38,39,40,41] Health Canada data also indicates that the annual proportion of Aboriginal persons among those reported to have AIDS has increased from 1% before 1990 to 15% in 1999.[41] AIDS in Aboriginal people continues to increase despite the general decrease in AIDS that has been observed since HAART began to be prescribed.

Twenty percent of the patients seen at the Northern Alberta HIV clinic since the beginning of the epidemic are Aboriginal; 46% of the women seen have been Aboriginal. Health Canada has indicated that 38.9% of women who were reported as HIV positive in Canada between 1998 and 2000 and for whom information on ethnic status was provided were Aboriginal.[42]

Characteristics of Aboriginal populations that place them at risk of contracting HIV include social factors such as poverty, dysfunctional family and childhood experiences, lack of acceptance of HIV as an Aboriginal issue by some

Aboriginal political leaders, low status of women, early age of initiating sexual activity, participation in commercial sex or sex for in exchange for drugs, and biological factors such as increased sexually transmitted diseases, substance abuse, and poor general health.[38,43] Poor general health in Aboriginal communities may be seen in the higher incidence of diseases such as tuberculosis, diabetes, hepatitis, and sexually transmitted diseases, and in shorter life expectancies and higher infant mortality rates than non-Aboriginal Canadians.[44] Once an individual contracts HIV, alienation from the community may lead to lack of care and further high risk activities which may shorten the survival of HIV positive individuals and increase the possibility of transmission to others.[38,43] Poverty, a history of abuse, increased rates of injection drug use, and lack of access to knowledge resources may lead some Aboriginal women to feel that they are not empowered to change risky health behaviors. [38,43,45] In many Aboriginal communities, efforts to correct the problems caused by the erosion of traditional values and disruption of family and community structures suffered by First Nation people are an integral part of HIV/AIDS prevention programs.[38] The social problems that are prevalent in the lives of some First Nations people: teenage pregnancy, substance abuse, and the lack of family structure brought about by residential schools may allow HIV to spread more easily.[46] Characterizing the epidemiology of HIV in Aboriginal people in northern Alberta is important for the targeting and implementation of effective intervention.

1.3: Review of literature pertaining to HIV in Aboriginal women

There are few existing studies contributing to the knowledge of the specific concerns of Aboriginal people with HIV/AIDS and limited data on the incidence of HIV in Aboriginal people residing in Alberta.

In 1998 the Center for Disease Control (United States) reported that 26% of Aboriginal people in the U.S. with HIV/AIDS were women.[47] Research specific to Aboriginals indicates that American Indian and Alaskan women were at higher risk for HIV infection due to needle sharing, high use of cocaine, high number of sexual partners, and trading sex for drugs.[48] A study of a small group of urban Indians in New York emphasized the effect that physical abuse and drug use has on increasing the risk of HIV transmission through unprotected sex.[49] Another study in New York state among low-income, single, sexually active urban Native women found a need for HIV related education to reduce risk behaviour.[50] Surveys done by the Indian Health Service indicate that HIV rates among third trimester Native women in three western states was 4 to 8 times higher than in non-Native women. They also found evidence of the diffusion of HIV to rural areas.[51]

Studies done by Health Canada (Aboriginal Nurses Association) and Alberta Health have been done to attempt to address the special needs of Aboriginal populations and the delivery of AIDS related services. The Health Canada

(Aboriginal Nurses Association) study of Aboriginal women may not be generalizable: the response rate was only 19% and of those that responded, more than 90% were health care workers.[43] The findings of the Alberta Health Study of Metis population was more informative, supplying useful information on attitudes towards sexuality and problems that may be encountered by an HIV/AIDS program directed at preventing the transmission of disease in Aboriginal people.[38] Health Canada has been able to track the increase in the number HIV infections and AIDS cases in Aboriginal people, but their data is underestimated due to the lack of ethnicity information in the reports, misclassification of ethnicity and delayed reporting.[40,41,42] The British Columbia (B.C.) Centre for Excellence in HIV/AIDS has been able to compile descriptive data on the First Nations population infected with HIV in B.C and among injection drug users in Vancouver.[52,53] Data from a Montreal study found a disturbing potential for HIV to be spread rapidly from urban to rural communities.[54] Prior studies on the population of HIV positive patients seen at the Northern Alberta HIV Program showed that up to the end of 1998, Aboriginal people were over represented in the population of people who are HIV positive, a high proportion of Aboriginal people with HIV were women and that IVDU and heterosexual contact were important risk factors for women.[55,56] A qualitative study investigating the cultural factors relating to HIV infection in Aboriginal women found that low self-esteem and survival behaviours developed early in life by Aboriginal women increase their risk of contracting HIV.[45]

In 1998, the Northern Health Research Unit of the University of Manitoba compiled a listing of research being undertaken on HIV/AIDS on Aboriginal people. Their recommendations include more studies on social determinants and risk factors associated with HIV transmission to provide information relevant to preventing the spread of HIV in Aboriginal people.[57]

Chapter Two

2.1 Research objectives

2.1.1 General research objective

The purpose of this project was to characterize the demographic and temporal trends of HIV infection in Aboriginal women of northern Alberta.

The Bureau of HIV/AIDS and STD of the Population and Public Health Branch of Health Canada has identified a rise in AIDS in the Aboriginal population relative to the decline in reported AIDS cases in non-Aboriginal people, but current data on HIV and AIDS in a well defined Aboriginal population is lacking.[40,41] A better understanding of the HIV epidemic in Aboriginal people is essential to the development of prevention strategies and for the planning of treatment services. Information from this study will provide data to further define the issues surrounding HIV in Aboriginal populations. One of the limitations of the national statistics is the under-reporting of ethnic status of the reported HIV positives and AIDS cases.[40,41] The Northern Alberta HIV Program database has captured ethnic status in its patient data. Analysis of this population data will allow the accurate assessment of the HIV/AIDS epidemic in the Aboriginal population in this region.

The geographic distribution of HIV positive Aboriginal patients is important to the development culturally sensitive and population focused prevention and/or support programs. National statistics indicate that intravenous drug use and heterosexual contact are the most prevalent modes of HIV transmission in Aboriginal women.[40,41] Assessment of current trends will assist in the allocation of resources to drug abuse prevention and treatment programs and reinforce the work being dealing with the issues surrounding heterosexual transmission of HIV in this population. Agencies involved with the implementation and funding of HIV support programs and substance abuse treatment centres and women's' shelters will benefit from knowledge of the burden of illness in their area.

The HIV epidemic in northern Alberta has shifted profoundly in the past decade. New infections in Aboriginal people continue to increase disproportionately to those of non-Aboriginal people and more women than men are testing positive for HIV.[55,56] With the implementation of prenatal screening for HIV by Alberta Health and Wellness and HIV becoming a reportable disease to Health Canada in 1998, a more accurate representation of HIV in northern Alberta has become possible.

HIV is a disease that can be prevented, but not cured with the treatments currently available. To address the epidemic among the Aboriginal population effective

education, prevention, and treatment programs are required. Providing the agencies responsible for programs relating to Aboriginal health with current, accurate and pertinent data will enable the implementation and continuation of these programs by providing evidence to support requests for funding. By providing data describing the burden of HIV disease in a defined geographical area, and describing a population for which effective intervention is important, Aboriginal women, community leaders will have a basis for education and community intervention strategies.

2.1.2 The research question

What are the demographic characteristics of, risk factors for, and outcomes of Aboriginal women in northern Alberta diagnosed as HIV positive between 1986 and 1999 and how do these indices compare to those of non-Aboriginal women in northern Alberta diagnosed between 1986 and 1999?

2.1.3 Specific research objectives

1. To determine the number of Aboriginal women seen each year in northern Alberta. To determine the age distribution of HIV positive Aboriginal women in northern Alberta and compare this with the age distribution of non-Aboriginal HIV positive women in northern Alberta.
2. To determine the geographic distribution of HIV positive Aboriginal women in northern Alberta and compare this with the geographic distribution of HIV positive non-Aboriginal women in northern Alberta. To determine the geographic mobility of HIV positive women.
3. To determine the risk factors for HIV transmission in HIV positive Aboriginal women in northern Alberta compared to those in non-Aboriginal HIV positive women in northern Alberta.
4. To determine whether HIV positive Aboriginal women and non-Aboriginal women in northern Alberta access medical treatment, specifically combination antiretroviral therapy.
5. To compare the prognostic indicators of Aboriginal women and non-Aboriginal women. To determine the outcomes of HIV disease in Aboriginal and non-Aboriginal women in northern Alberta.
6. To determine the number of pregnancies and the number of children born to HIV positive Aboriginal and non-Aboriginal women in northern Alberta.

2.2 Methods

2.2.1 The HIV clinical database

The HIV clinics in Edmonton consist of infectious disease specialists and staff at the University of Alberta Hospital (UAH) and the Sexually Transmitted Disease Clinic of Alberta Health and Wellness (STD clinic). The Northern Alberta HIV Program is a service provided to the infectious disease specialists and patients and consists of a clinical nurse specialist, social worker, dietician, pharmacist, and clerical staff to maintain a database of HIV positive patients and funding for ARV and special testing through a special program of Alberta province-wide services. The physicians and outreach staff work as a team to provide support for HIV positive patients and their families.

HIV positive patients are usually referred to the infectious disease specialists by their general practitioners. The infectious disease specialists provide counseling to patients and their families, treatment for HIV and opportunistic infections, and monitoring of therapy.

The Microsoft ACCESS database of HIV positive patients was implemented to provide cumulative reports to the infectious disease specialists and has been maintained by the HIV outreach program with funding from Health Canada and the Capital Health authority or equivalent since 1991. Each patient has a file in

the database; each visit or contact is recorded for that patient. Patients prior to 1991 were entered into the database retroactively. The majority of the data is entered from the patient's medical charts into the database by a single person at each site (UAH and STD clinic). Telephone contact information may also be entered into the patient's database record. Prior to a patient's appointment with an infectious disease physician or at the physician's request, a report for the patient that includes demographic data and a summary of previous visits is produced and placed in the patient's chart. At this time the accuracy and completeness of data can be reviewed by the physician.

The database is maintained by the Sexually Transmitted Diseases clinic, the HIV clinic at the Royal Alexandra Hospital site, and the HIV outreach program at the University of Alberta Hospital. The database is stored in a file server at the University Hospital site. Access to the database is controlled by password protection; access to the computer terminals is restricted to persons with a key to the office. Referential integrity is set in Microsoft ACCESS to protect against accidental changes and deletion of data and to ensure that the relationships between records in related tables are valid. The database is backed up daily.

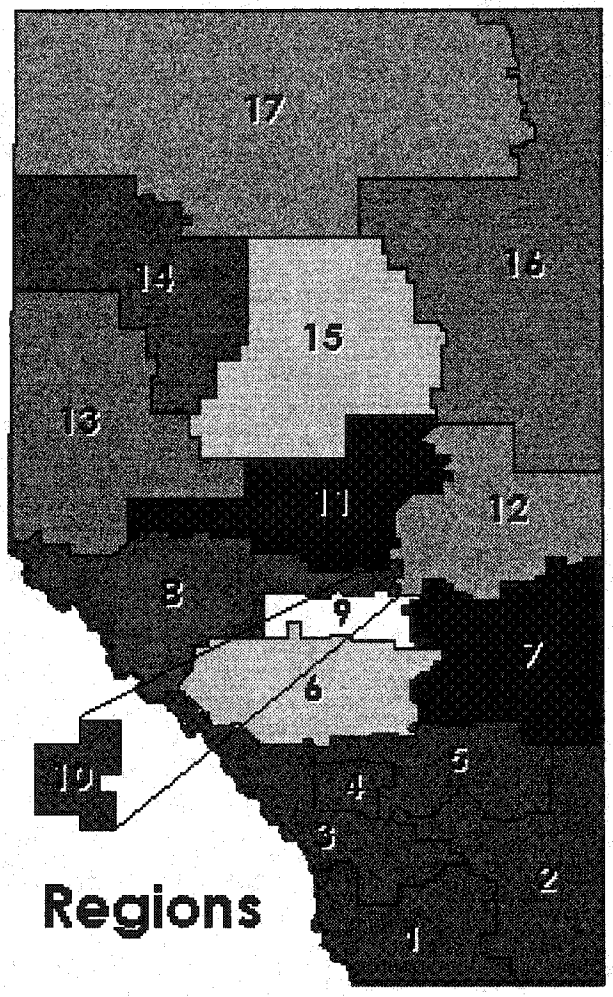
The data used for this analysis were extracted from the database on February 22, 2000. To ensure confidentiality patient names and other personal identifiers were removed from the extracted data.

2.2.2 Study population

The study population consists of Aboriginal women (more than 15 years old) from northern Alberta diagnosed with HIV and seen at HIV referral centres at the University of Alberta Hospital, Royal Alexandra Hospital, and Sexually Transmitted Diseases clinic in Edmonton between January1986 and February 2000. Patients in the database have had their ethnicity documented including five Aboriginal categories: Aboriginal, Aboriginal Inuit, Aboriginal/Metis, or Aboriginal/Treaty. The comparison population is HIV positive non-Aboriginal women from northern Alberta referred to the same centres during the same time period.

The population of northern Alberta is defined as persons living in the province of Alberta in Regional Health Authorities (RHA) 8 to 17 inclusive. The RHA of residence was determined by comparing the patient's current postal code with a cross-reference database of RHA/postal codes. The number of Aboriginal women from northern Alberta who are included in the Northern Alberta HIV Program's clinical database is 91. The comparison population consists of 105 non-Aboriginal women.

Figure 2.1 Map and list of Regional Health Authorities in Alberta



Region 8 - Westview Regional Health Authority
Region 9 - Crossroads Regional Health Authority
Region 10 - Capital Health Authority
Region 11 - Aspen Regional Health Authority
Region 12 - Lakeland Regional Health Authority
Region 13 - Mistahia Regional Health Authority
Region 14 - Peace Health Region
Region 15 - Keeweetinok Lakes Regional Health Authority
Region 16 - Northern Lights Regional Health Authority
Region 17 - Northwestern Health Services Region

2.2.3 Ethics

The clinical database of the HIV Outreach Program has been approved by the University of Alberta Research Ethics Board. This thesis topic has been approved by the University of Alberta Health Ethics Board based on the secondary analysis of patient records. Patient charts were accessed as necessary to obtain missing data. No primary patient contact was made for this study.

To ensure patient confidentiality analysis was performed on non-nominal data extracted from the clinical database.

2.2.4 Measurements

Refer to Appendix B for a list of variables used in the analysis.

The Aboriginal status variable was determined by grouping patients into Aboriginal or non-Aboriginal based on their self-reported status as recorded in the "ethnic status" field of the database. Appendix A contains a listing of the original ethnic status codes used in the database and the grouping used.

The age of the patients at presentation was determined by subtracting the date in the "first seen" field from the patient's birthdate. The age of the patients was grouped into ten year intervals for comparison.

The area of residence was determined by reducing the postal code in the patient's original address to its first two characters. Patients were designated as being from an urban location if their postal code began with T5 or T6. This indicates that the place of residence was Edmonton.[58] Edmonton, containing 30% of the population of Alberta, is considered by Statistics Canada as a census metropolitan area. Patients living outside of Edmonton in northern Alberta were considered to be rural. The postal code for the patient's location at time of diagnosis was obtained from the patient charts. The postal code for the patient's current address was obtained from the address fields of the database.

The risk factors for HIV transmission as identified by the patient were recorded in the database in the "risk factor" field. These were grouped by their common factors: heterosexual contact, IVDU, and receipt of blood products. Refer to Appendix C for the raw data and grouping used. The risk factors for HIV transmission are defined as:

1. Heterosexual sex: unprotected sex with one or more partners,
2. Intravenous drug use (IVDU): use of needles to inject substances of abuse; sharing needles with HIV infected persons,
3. Transfusion: receiving HIV containing blood products.

Women who were at risk because of both unprotected sex and intravenous drug use were included in the analysis as a separate group.

Antiretroviral therapy accessed was obtained from the "drug" field of the database. See Appendix E for a list of antiretroviral drugs and their classification. Patients who had any record of antiretroviral therapy were considered as having accessed therapy. The date that antiretroviral therapy was started was used when considering whether treatment had preceded pregnancy.

The initial CD4 count was extracted from the "CD4" field of the database based on earliest CD4 count recorded. The CD4 count was grouped based on the CDC 1993 classification of infections.[2]

Clinical outcomes were used in addition to death in the survival analysis. This was done because the follow-up time of five years is less than the published median survival time of HIV positive patients.[2] The clinical outcomes chosen are indicators of AIDS defining illness as defined by the CDC and by Health Canada.[13,59,60] This definition includes one of the illnesses listed in Appendix D. A CD4 count of less than 200 was included as an outcome due to its value as a prognostic indicator.[3] Viral load is used in some studies as a prognostic indicator; in this study CD4 count data was more complete because viral load information only became available in late 1996. CD4 count and viral load cannot be used together in the analysis because there is a correlation between high viral load and low CD4 count.[3] The outcome of CD4<200, AIDS or death were extracted from the "CD4", "deathdate", "new events" and "comments" and "last

updated" fields of the database. The date of earliest event was used to determine the time to the outcome. The time variable was determined by subtracting the date of the outcome or, if no outcome had occurred, the date that the record was last updated from the seropositive date. This gave the most accurate representation of the data in the database as opposed to assuming that no patients were lost to follow-up. The data was right censored at the end of the study period (six years) giving a five year interval for analysis. This removed some of the bias associated with individuals entering the study at various times. There were only three women who were followed for more than six years.

Left censoring is appropriate in this population as the date of a seropositive test is not the same as the date of infection with HIV.[61] The survival analysis was limited to patients who were in the database for at least 1 year. This excluded patients who had only recently been recorded in the database, patients who had experienced the outcome before accessing treatment, and patients who were recently diagnosed, but includes the survival time of patients who were known to be living with HIV and being treated at the HIV clinics. This removes bias towards the shorter survival times experienced by patients who may have been living with undiagnosed HIV and are only entered in the database when they access treatment for an AIDS related outcome as defined by this study.

Survival analysis using the Kaplan Meier method was done to determine the frequency of outcome over time. The plots of these occurrences gave a graphical representation and a side by side comparison of the survival of two groups. The survival function is described by the equation $S(t)=P(T>t)$ or the probability that a person will survive beyond a specified time(t). The plot of the survival function gives a continuum of probabilities from t_1 to t_n.[62]

Cox regression analysis was used to determine the relevance of risk type, ethnic status, and treatment with antiretroviral therapy on the outcomes of CD4<200, death, or AIDS defining illness. The Cox model gives a means of interpreting the hazard posed by a set of variables that can be applied to determining an individual's risk of experiencing a given outcome at a specified time. The hazard at time t is the product of the baseline hazard times the exponent to the linear sum of the explanatory variables. The proportional hazards assumption is that the baseline function is independent of the explanatory variables – or is time-independent. A time independent variable does not change over time; in this analysis the variables of ethnic status, risk factor and ARV are defined once for each patient and do not change with time.[62]

Variables were chosen on the basis of their biological plausibility in the model. Protease inhibitors could not be used in the model with ARV as the use of

protease inhibitors is included with treatment with ARV. Variables were entered into the model without a significance level set for an entry criteria.

Two Cox regression models were assessed. The first model used the same variables as the Kaplan-Meier survival analysis. The second model was designed to assess the effects of confounding due to differential severity of disease at the beginning of the follow-up period and therefore the patient's initial CD4 count (from the date the patient was first seen at the Northern Alberta HIV Program) was included in the analysis. No patients were censored in this model before one year or after six years. However patients were excluded who had an initial CD4 count of less than 200 because this variable was the same as one of the criteria used in the outcome. One patient who had transfusion as a risk factor was removed because their inclusion in the model would not result in a significant finding. The time variable was changed to be the time from when the patient was first seen at the Northern Alberta HIV Program to the date that the first outcome had occurred or the date that the patient's data had been last updated.

Based on Schoenfeld's formula [63], this study has 86% power to find a hazard ratio (HR) of 3.0 statistically significant. The power calculation is based on the Aboriginal status and antiretroviral treatment variables. The number of patients used for this calculation was 126 and the number of outcomes used was 25.

Analysis of other variables indicates that because of smaller numbers of patients in the subgroups only large hazard ratios (>6) will be statistically significant.

The number of HIV positive women Aboriginal and non-Aboriginal women in northern Alberta who became pregnant and the number of pregnancies was extracted from the "new events" and "comments" fields of the database. The number of women who had tested positive for HIV before conception was determined from the date of their positive HIV test compared to the date of the birth of their child.

Aboriginal status and risk factors were variables for which data was missing from patients' records in the database. Due to the small number of patients in the analysis, the time was taken to review the patient charts and/or ask the physicians to acquire the missing data. The first recorded address of the patients after their HIV positive diagnosis was also acquired by referring to the charts.

2.2.5 Statistical analysis

Microsoft ACCESS (ACCESS 97, Microsoft Corporation), Instat3 (Graphpad Inc, San Diego, CA), and SPSS Graduate Pack 9.0 (SPSS, Chicago, Illinois) were used for statistical analysis.

For all analyses the results were considered statistically significant if the p-value was less than 0.05.

Objective 1

The frequency distribution of HIV positive women categorized by the year they first attended an HIV clinic was determined. The rate of infection per 100,000 women was determined by dividing the number of HIV positive women by the number of women in regional health authorities 8 to 17 in each year as estimated by Alberta Health and Wellness.[64] This population data is not available prior to 1995 when the regional health authorities were created. The age frequency distribution of Aboriginal and non-Aboriginal HIV positive women in northern Alberta was determined. The age distribution of Aboriginal HIV positive women was compared to the age distribution of non-Aboriginal women by analyzing a contingency table using the Pearson Chi-square.

Objective 2

The number of women living in urban and rural areas was compared by analyzing contingency tables using Fisher's exact test (2-tailed). Postal codes from the most recent recorded address and address when the patient was first seen at the HIV clinic were compared to determine the geographic mobility of this population.

Objective 3

The risk factors for HIV transmission for HIV positive Aboriginal and non-Aboriginal women in northern Alberta were compared using Fisher's exact test (2-tailed).

Objective 4

Accessing therapy and the type of therapy prescribed to Aboriginal and non-Aboriginal women were compared by analyzing a contingency table using Fisher's exact test (2-tailed).

Objective 5

The initial CD4 count of Aboriginal women and non-Aboriginal women were compared by analyzing a contingency table using the Pearson Chi-square.

Occurrence of an outcome was compared between Aboriginal and non-Aboriginal women in the database using Fisher's exact test (2-tailed). Refer to Appendix D for the Canadian criteria for AIDS defining illness.

The survival of Aboriginal women who have tested HIV positive and non-Aboriginal women who have tested HIV positive was compared using Kaplan-Meier survival curves, median and mean survival, and the log-rank test. The effect of treatment with antiretroviral therapy on survival was compared between

Aboriginal and non-Aboriginal women using median and mean survival and the Log rank test.

A Cox regression model that includes the variables risk factor, antiretroviral therapy, and ethnic status was made using the same outcome variable and time interval as the Kaplan-Meier survival analysis. A second model was made to assess the same risk factors while controlling for confounding caused by initial CD4 counts.

Objective 6

The number of HIV positive Aboriginal and non-Aboriginal women in northern Alberta who became pregnant, the number who received antiretroviral therapy during pregnancy and who had tested positive for HIV before conception were compared by analyzing contingency tables using Fisher's exact test.

Chapter Three

3.1 Results: Objective 1

3.1.1 Background

The total number of HIV positive patients seen by infectious disease physicians at the HIV clinics as of February, 2000 was 1275. Of these, 246 patients were Aboriginal (Aboriginal, Inuit, Metis or Treaty), 967 patients were non-Aboriginal and for 62 patients the ethnic status was unrecorded. Two hundred and forty-one patients were female: 110 were Aboriginal, 130 were non-Aboriginal and 1 woman had no recorded ethnic status.

Women who were living outside northern Alberta (Regional Health Authorities 8-17) at the time that they were tested as being positive for HIV antibodies (seropositive) were excluded from the analysis. The excluded patients include 17 Aboriginal HIV positive women and 22 non-Aboriginal HIV positive women. Ten women were from outside Alberta, 20 were from Regional Health Authorities 1-7, and 9 patients had no address recorded.

The total number of HIV positive women who were diagnosed as HIV positive between 1986 and 1999 and who were living in northern Alberta when first seen

at the Northern Alberta HIV clinic was 196. Ninety-one women were Aboriginal and 105 women were non-Aboriginal.

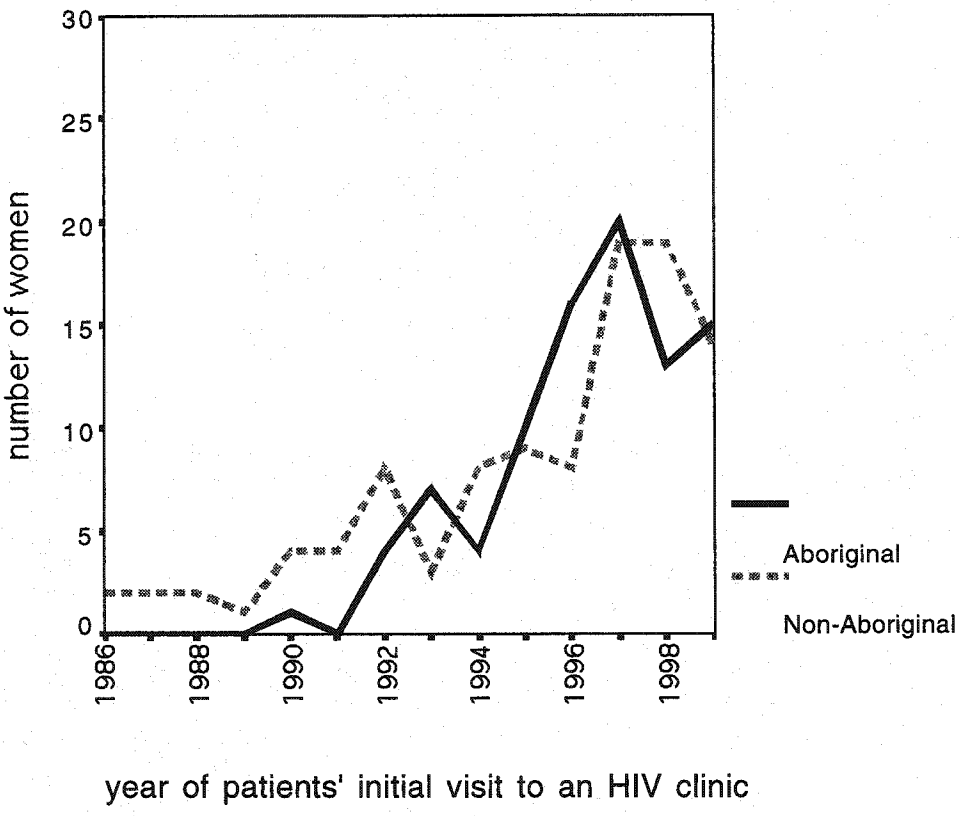
3.1.2 Objective 1: Demographics of HIV positive women in northern Alberta

Table 3.1 Number of new patients per year; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

Year	Aboriginal number (% of Aboriginal)	Non-Aboriginal number (% of non-Aboriginal)	Total number (% of total)	rate /100,000 women
1986-1991	1 (1.1)	15 (14.6)	16 (8.3)	
1992	4 (4.4)	8 (7.8)	12 (6.2)	
1993	7 (7.8)	3 (2.9)	10 (5.2)	
1994	4 (4.4)	8 (7.8)	12 (6.2)	
1995	10 (11.)	9 (8.7)	19 (9.8)	3.0
1996	16 (17.8)	8 (7.8)	24 (12.4)	3.7
1997	20 (22.2)	19 (18.4)	39 (20.2)	6.0
1998	13 (14.4)	19 (18.4)	32 (16.6)	4.9
1999	15 (16.7)	14 (13.6)	29 (15.0)	4.3
Total	90 (100)	103 (100)	193 (100)	

One Aboriginal woman and two non-Aboriginal women were seen in January and February, 2000.
Population data used was from Alberta Health and Wellness [64]

Figure 3.1 Number of HIV positive women by ethnic status and year first seen at the HIV clinics; Northern Alberta HIV Program, August 1986 – December 1999.



The data in table 3.1 shows that few HIV positive women were first seen prior to 1992. From 1992 to 1999 the number of Aboriginal women seen at the HIV clinic has been approximately equal to the number of non-Aboriginal women seen. One Aboriginal woman was first seen in 1990 but the numbers did not begin to increase steadily until after 1992, quickly increasing to the same numbers as non-Aboriginal women seen per year. This is represented graphically in figure 3.1.

The number of women infected with HIV per year peaked in 1997. The rate per 100,000 women could not be calculated prior to 1995 because population counts based on Regional Health Authorities was not available.

Table 3.2 Age distribution; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

Age in years	Aboriginal (% of Aboriginal)	Non-Aboriginal (% of non-Aboriginal)	Total (% of total)
15-24	25 (27.5)	24 (22.9)	49 (25.0)
25-34	42 (46.2)	43 (41.0)	85 (43.4)
35-44	17 (18.7)	28 (26.7)	45 (23.0)
45 and older	7 (7.7)	10 (9.5)	17 (8.7)
Total	91 (100)	105 (100)	196 (100)

* Age at the date of the patient's first visit to the HIV clinic

There is no statistically significant difference in the age distribution of Aboriginal HIV positive women versus non-Aboriginal HIV positive women (p=0.520). Seventy-four percent of Aboriginal HIV positive women and 64 percent of non-Aboriginal HIV positive women were between 15 and 34 years of age when they were first seen at an HIV clinic.

3.2 Results: Objective 2

3.2.1 Objective 2: Geographic distribution of HIV positive women in northern Alberta at time of diagnosis

Table 3.3 Location at time of diagnosis; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

	Aboriginal (% of Aboriginal)	Non-Aboriginal (% of non-Aboriginal)	Total (% of total)
Urban	61(67.0)	83(79.0)	144(73.5)
Rural	30(33.0)	22(21.0)	52(26.5)
Total	91 (100)	105 (100)	196 (100)

Urban= Edmonton (postal codes beginning with T5 and T6)
Rural= all other postal codes in Regional Health Authorities 8-17

The majority of HIV positive women (73.5%) resided in Edmonton when they first attended an HIV clinic. A higher percentage of Aboriginal HIV positive women were living outside of Edmonton; this difference is not statistically significant between Aboriginal and non-Aboriginal HIV positive women ($p=0.074$).

Table 3.4 HIV positive women who have changed address; Northern Alberta HIV Program, August 1986 - February 2000

	Aboriginal (% Aboriginal)	Non-Aboriginal (% non-Aboriginal)	Total (% of total)
rural to urban	4 (12.1)	4 (12.9)	8 (12.5)
urban to rural	1 (3.0)	1 (3.2)	2 (3.1)
moved out of N. Alberta	2 (6.1)	2 (6.5)	4 (6.3)
remained in urban location	21 (63.6)	20 (64.5)	41 (64.0)
remained in rural location	5 (15.2)	4 (12.9)	9 (14.1)
Total	33 (100)	31 (100)	64 (100)

Sixty-four patients changed their address from the time they first visited the clinics to February, 2000. The number of HIV positive Aboriginal and non-Aboriginal women who have moved since their first visit to the HIV clinic is similar. The majority of women who changed their address lived in Edmonton and moved to another area within Edmonton (64.1%).

3.3 Results: Objective 3

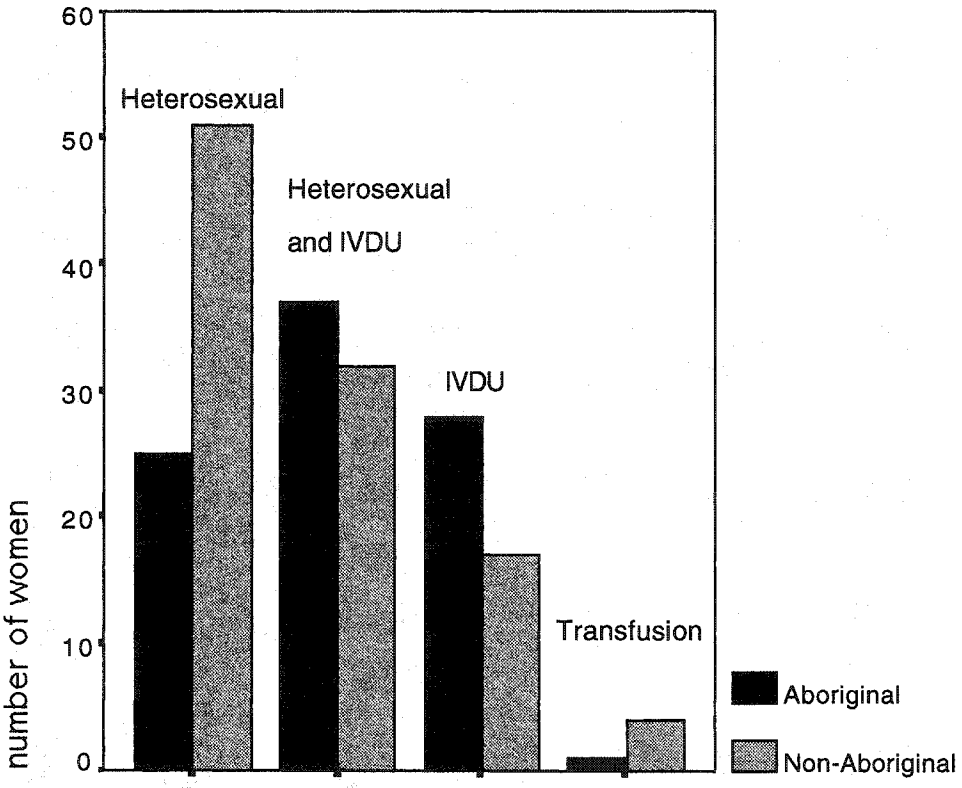
3.3.1 Objective 3: Risk factors of HIV positive women in northern Alberta.

Table 3.5 Risk Factors; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

Risk Factor	Aboriginal (% Aboriginal)	Non-Aboriginal (% non-Aboriginal)	Total (% of total)
Heterosexual	25 (27.5)	51 (49.0)	76 (39.0)
Heterosexual and IVDU*	37 (40.7)	32 (30.8)	69 (35.4)
IVDU	28 (30.8)	17 (16.3)	45 (23.1)
transfusion	1 (1.1)	4 (3.8)	5 (2.6)
Total	91 (100)	104 (100)	195 (100)

One patient has no identified risk factor in the database
*Heterosexual and IVDU indicates that the patient had indicated experiencing both risk factors.

Figure 3.2 Distribution of risk factors in Aboriginal and non-Aboriginal HIV positive women; Northern Alberta HIV Program, August 1986 - February 2000



*Heterosexual and IVDU indicates that the patient has indicated experiencing both risk factors.

The primary risk factor for HIV transmission for women is heterosexual transmission (39%). The overall difference in the distribution of risk factors between Aboriginal HIV positive women and non-Aboriginal HIV positive women is statistically significant (p=0.005). There are more Aboriginal HIV positive women with risk factors associated with IVDU compared to non-Aboriginal HIV positive women. Eighty-one percent of women who were

included in the risk category of heterosexual and IVDU are positive for Hepatitis C virus (HCV). HCV is highly associated with IVDU.[66] This may indicate that the main risk factor for the majority of this group is IVDU.

3.4 Results: Objective 4

3.4.1 Objective 4: Accessing treatment

Table 3.6 HIV positive women who have received any antiretroviral therapy (ARV); Northern Alberta HIV Program, August 1986 - February 2000

	Aboriginal (% of Aboriginal)	non-Aboriginal (% of non-Aboriginal)	Total (% of total)
Have received ARV	60 (65.9)	66 (62.9)	126 (64.3)
No ARV received	31 (34.1)	39 (37.1)	70 (35.7)
Total	91 (100)	105 (100)	196 (100)

There is no statistically significant difference between the number of Aboriginal and non-Aboriginal HIV positive women who have received antiretroviral therapy ($p=0.765$). Of the women who did not receive ARV, 82% did not experience an outcome of death, CD4 count of less than 200 or AIDS.

Table 3.7 HIV positive women who have received protease inhibitors (PI); Northern Alberta HIV Program, August 1986 - February 2000

	Aboriginal (% Aboriginal)	non-Aboriginal (% non-Aboriginal)	Total (% of total)
Have received PI	32 (35.2)	48 (45.7)	80 (40.8)
No PI received	59 (64.8)	57 (54.3)	116 (59.2)
Total	91 (100)	105 (100)	196 (100)

There is no statistically significant difference between the number of Aboriginal and non-Aboriginal HIV positive women who have accessed antiretroviral therapy that includes protease inhibitors. ($p=0.147$). Protease inhibitors first became available in late 1996. Of the patients who did not receive protease inhibitors, thirteen women (6 Aboriginal) have not been seen at the clinic since 1996, and sixteen women (4 Aboriginal) died before protease inhibitors became available.

3.5 Results: Objective 5

3.5.1 Objective 5: Survival Analysis.

Twenty-six women have had their death recorded in the database. Four women have a cause of death other than AIDS recorded and three women do not have a cause of death recorded. Causes of death other than HIV related include non-AIDS-defining cancer and homicide.

Table 3.8 Age distribution of deceased HIV positive women; Northern Alberta HIV Program, August 1986 - February 2000

Age in years	Aboriginal (% of Aboriginal)	Non-Aboriginal (% of non-Aboriginal)
15-24	0	1 (6.2)
25-34	7 (77.8)	8 (50.0)
35-44	1 (11.1)	3 (18.8)
45-66	1 (11.1)	4 (25.0)
Total	9 (100)	16 (100)

Table 3.9 HIV positive women who have had outcomes of death, CD4<200 or AIDS; Northern Alberta HIV Program, August 1986 - February 2000

	Aboriginal (% of Aboriginal)	Non-Aboriginal (% of non-Aboriginal)	Total (% of total)
Death, CD4<200 or AIDS	32 (35.2)	36 (34.3)	68 (34.7)
Death, CD4<200 or AIDS not indicated	59 (64.8)	69 (65.7)	128 (65.3)
Totals	91 (100)	105 (100)	196 (100)

34.7% of HIV positive women died or had an AIDS related outcome. In most cases AIDS was indicated in the database before death. No significant difference in the proportion of occurrences of adverse outcomes was found between Aboriginal and non-Aboriginal HIV positive women (p=0.900). Sixty-seven percent of women are living HIV positive without having had an AIDS defining illness.

Table 3.10 Initial CD4 count; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

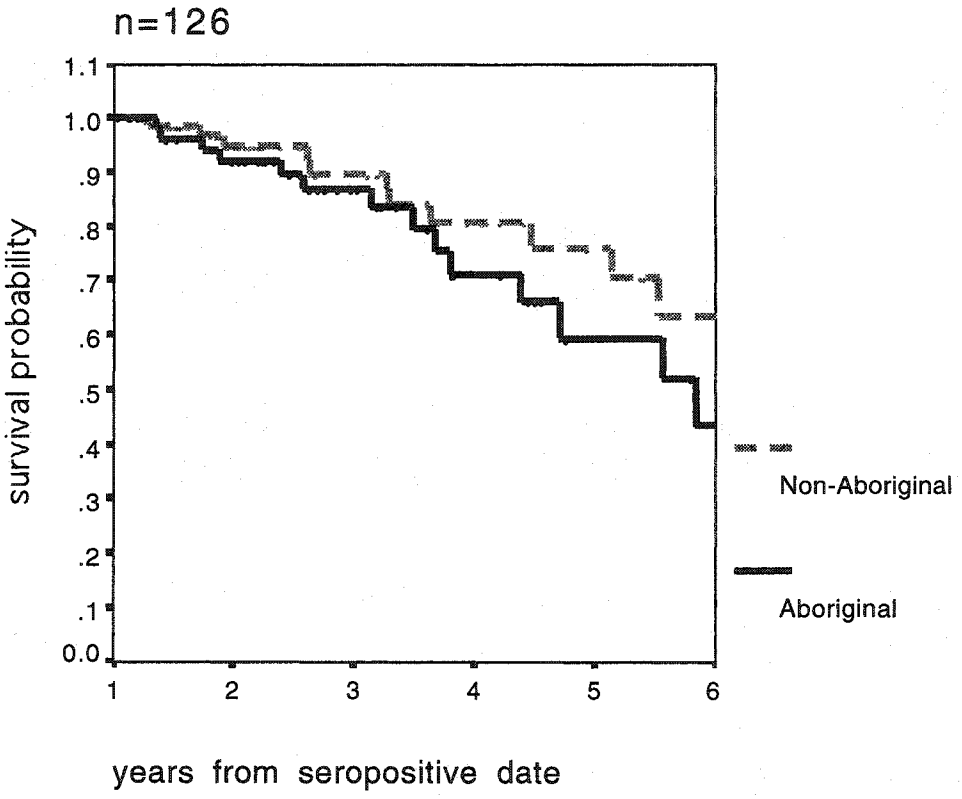
Initial CD4 count (normal:900-1200)	Aboriginal (% of Aboriginal)	Non-Aboriginal (% of non-Aboriginal)	Total (% of total)
<200/μL	15 (17.6)	17 (17.5)	32 (17.6)
200-499/μL	33 (38.8)	26 (26.8)	59 (32.4)
≥500/μL	37 (43.5)	54 (55.7)	91 (50.0)
Total	85 (100)	97 (100)	182 (100)

14/196 patients (6 Aboriginal and 8 non-Aboriginal) had no CD4 count recorded in the database

There is no statistically significant difference in the distribution of initial CD4 counts between Aboriginal and non-Aboriginal women (p=.160). The median CD4 count at initial visit was 450 for Aboriginal women and 530 for non-Aboriginal women. Patients who did not have an initial CD4 count recorded were usually patients with only one or two visits recorded.

Data from the patients who were excluded from the survival due to left censoring was reviewed to ensure that no bias was introduced by their removal. The 70 patients who were excluded from the model had similar baseline characteristics to the126 included in the model.

Figure 3.3 Survival curve of HIV positive Aboriginal and non-Aboriginal HIV positive women who have had an outcome of death, or CD4<200, or AIDS defining illness; Northern Alberta HIV Program, August 1986 - February 2000



The survival curves for HIV positive Aboriginal and non-Aboriginal HIV women were compared for a five year time period beginning one year after their seropositive date. The outcome used was an occurrence of an AIDS defining illness, a CD4 count of less than 200, or death. Twenty-five outcomes occurred during this time period.

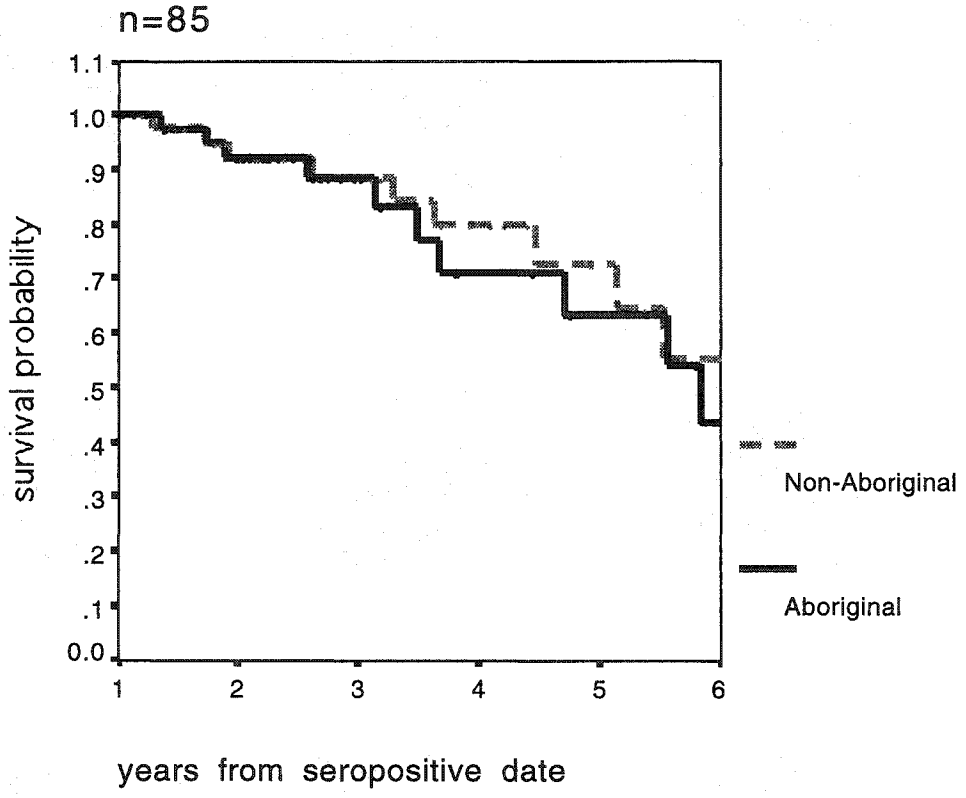
The median survival time is the time at which the cumulative survival proportion is equal to 0.5 or the time at which half of the outcomes in the sample have occurred. The cumulative probability of survival depends on the number of outcomes. The number of outcomes for Aboriginal HIV positive women was 14 and the number of outcomes for non-Aboriginal HIV positive women was 11. The median survival time for Aboriginal HIV positive women was 5.84 years (95% CI 4.14-7.54) and for non-Aboriginal women the median survival time was not reached. The survival curve indicates decreased survival for Aboriginal women compared to non-Aboriginal women however this finding is not statistically significant.

The mean survival time is affected by the amount of data that is censored as patients who are not followed for the full 5 years have a short value for their survival time. The mean survival time for Aboriginal HIV positive women was 4.88 years (CI 4.38-5.38) and the mean survival time for non-Aboriginal HIV positive women was 5.23 years (CI 4.81-5.64). There is overlap of the confidence intervals indicating that there is no difference in time to outcome between the two groups of women.

There is no statistically significant difference in survival time between the two groups. (Log Rank statistic = 1.48 p = 0.224)

3.5.2 Survival of HIV positive women who have taken antiretroviral therapy

Figure 3.4 Survival curve for HIV positive women who have taken antiretroviral therapy; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

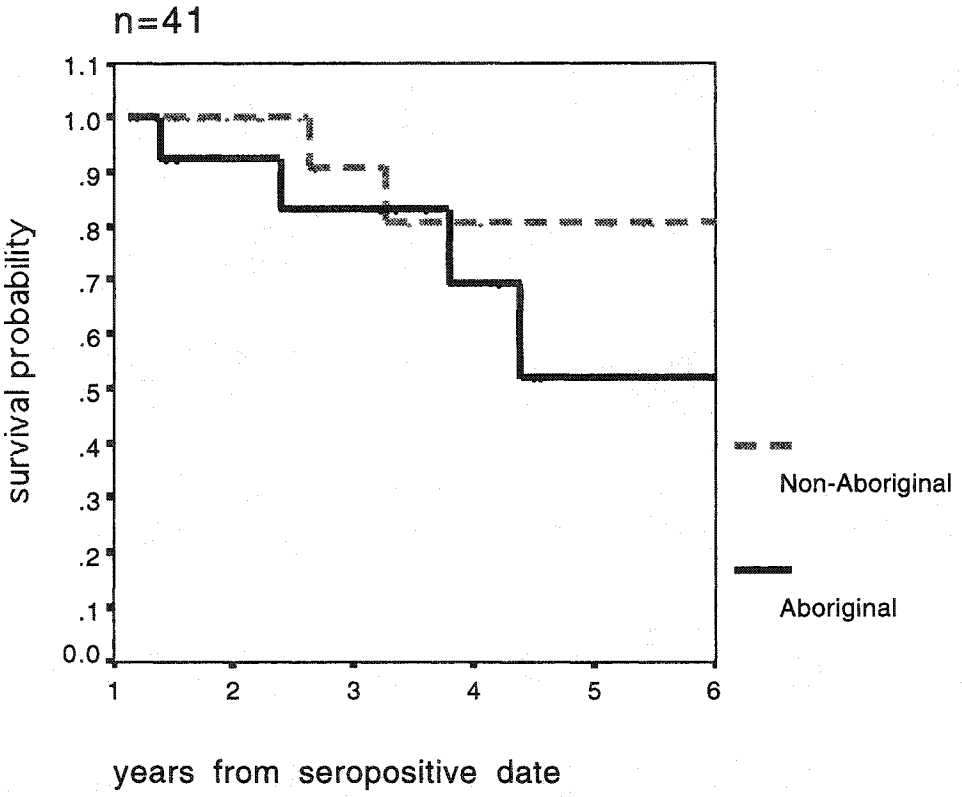


The median survival time for Aboriginal HIV positive women who had taken ARV was 5.84 years (CI 4.26-7.42); for non-Aboriginal HIV positive women the median survival time was not reached (>6 years).

The mean survival time for Aboriginal HIV positive women who had taken ARV was 4.94 years (CI 4.36-5.52); for non-Aboriginal HIV positive women the mean survival time was 5.10 years (CI 4.59-5.62).

The overlapping confidence intervals for the mean survival times and the overlapping of the survival curves indicate that there is no significant difference between the survival of Aboriginal and non-Aboriginal HIV positive women who have received antiretroviral therapy. The smaller number of patients in the subgroup means that it would be difficult to detect a difference in the two populations.

Figure 3.5 Survival curve for HIV positive women who have not taken antiretroviral therapy; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000



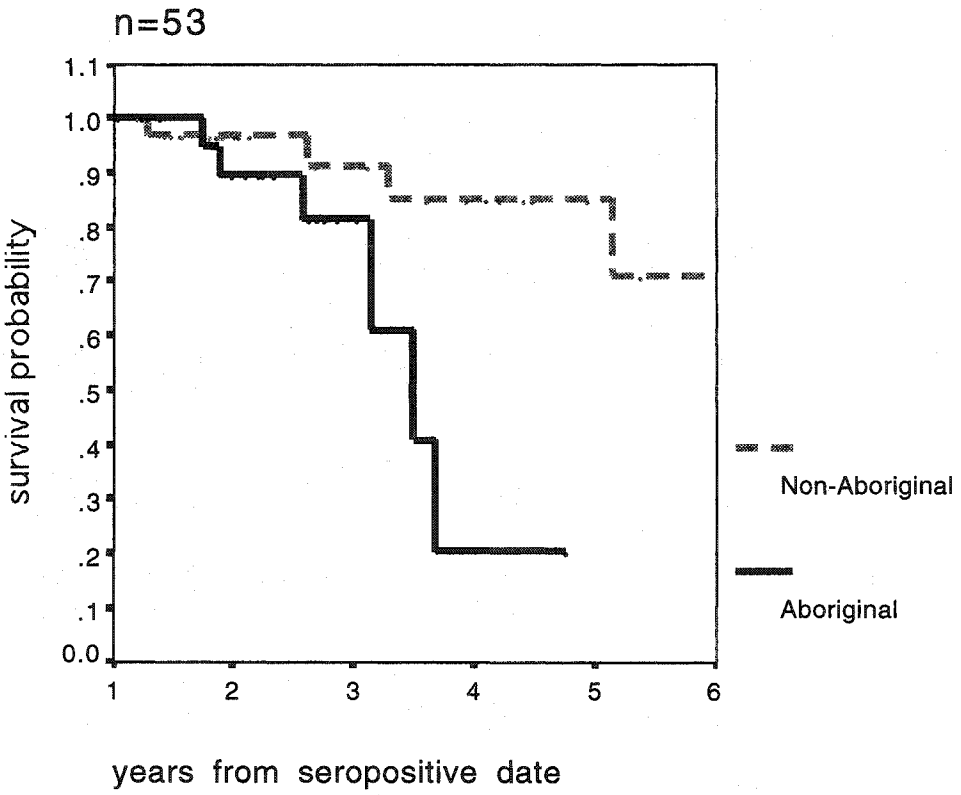
The subgroup of women who had not received antiretroviral therapy had a small number of outcomes (n=6) and the median survival time was not reached in both the Aboriginal women and non-Aboriginal women sub-group.

The mean survival time for Aboriginal HIV positive women who had not taken ARV was 4.74 years (CI 3.76-5.72); for non-Aboriginal HIV positive women the mean survival time was 5.43 years (CI 4.70-6.17).

There is no statistically significant difference in survival between Aboriginal and non-Aboriginal HIV positive women whether they were on antiretroviral therapy or not. (Log rank statistic = 1.06, p=0.304) The ability of the analysis to detect a difference between the two groups was adversely affected by the small numbers of patients in the subgroups.

3.5.3 Survival of HIV positive women who have taken protease inhibitors

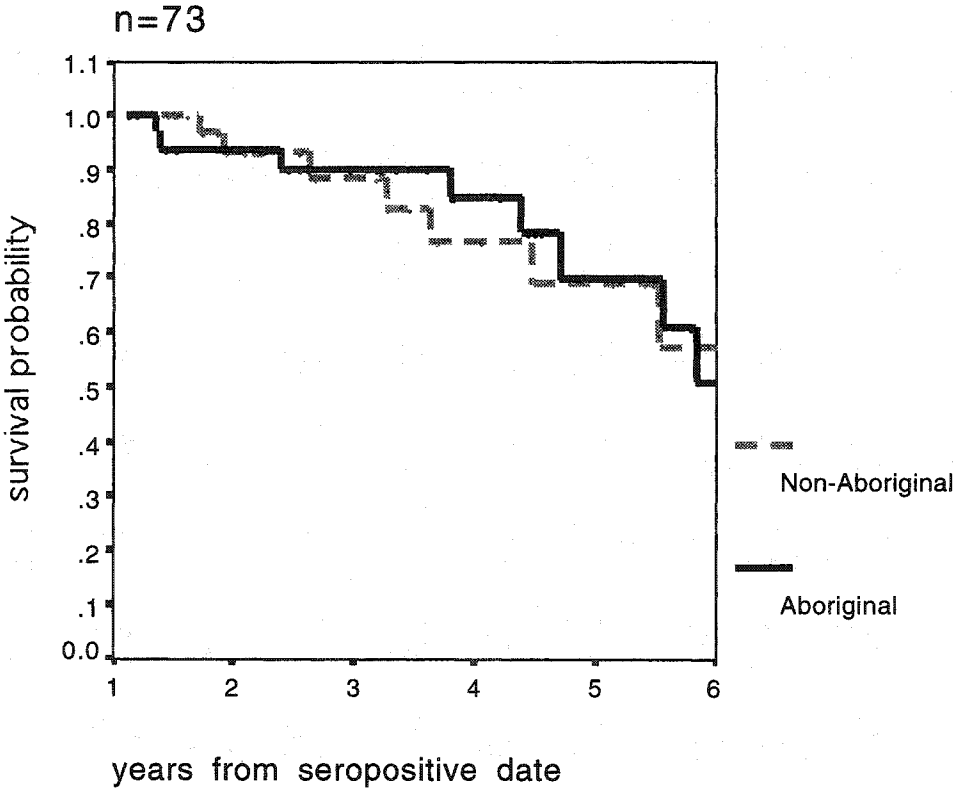
Figure 3.6 Survival curve for HIV positive women who have taken protease inhibitors; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000



The median survival time of Aboriginal HIV positive women who had taken protease inhibitors was 3.50 years (CI 2.78-4.22); for non-Aboriginal HIV positive women the median survival time was not reached (>6 years).

The mean survival time of Aboriginal HIV positive women who had taken protease inhibitors was 3.47 (CI 2.89-4.04); for non-Aboriginal HIV positive women the mean survival time was 5.39 years (CI 4.83-5.95)

Figure 3.7 Survival curve for HIV positive women who have not taken protease inhibitors; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000



The median survival time of Aboriginal and non-Aboriginal HIV positive women who had not taken protease inhibitors was not reached (>6 years).

The mean survival time of Aboriginal HIV positive women who had not taken protease inhibitors was 5.20 (CI 4.68-5.73); for non-Aboriginal HIV positive women the mean survival time was 5.09 years (CI 4.50-5.69)

There is no statistically significant difference in survival between Aboriginal and non-Aboriginal HIV positive women whether they were on antiretroviral therapy containing protease inhibitors or not. (Log rank statistic =1.98, p=0.159) The survival curve for patients who have taken protease inhibitors indicates that Aboriginal women have a reduced survival, however the number of outcomes in this analysis is small.

3.5.4 Cox regression models

Table 3.11 Cox regression model using the dependent variable of survival from time of recorded seropositivity to outcome; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000.

	Univariate			Multivariate		
variable	**HR**	**95%CI**	**p-value**	**HR**	**95% CI**	**p-value**
ARV (therapy vs no therapy)	1.30	0.52-3.29	0.58	1.81	0.67-4.90	0.24
Risk factors*			0.15			0.10
H	1			1		
HI	1.06	0.45-2.39	0.900	1.05	0.45-2.43	0.91
I	0.14	0.02-1.10	0.06	0.11	0.01-0.90	0.04
Ethnic status (Aboriginal vs non-Aboriginal)	1.62	0.74-3.59	0.23	1.84	0.82-4.16	0.14

*Risk groups as compared to risk factor for heterosexual contact
H= Heterosexual contact only
HI= Heterosexual contact or intravenous drug use (IVDU)
I= IVDU

The patients, outcome and time variables used in this Cox regression model are the same as in the Kaplan Meier survival analysis. Log minus log plots of each variable indicated that the proportional hazards assumption is valid.[62]

The multivariate model gives a significant change in –2 Log likelihood from the starting model (p=0.025) indicating that at least one of the variables in the model contributes to the prediction of the outcome.

In this model HIV positive women who are Aboriginal have 1.84 times the risk of having an outcome of death, CD4<200, or AIDS compared to non-Aboriginal HIV positive women after controlling for the variables of ARV and risk factors. This finding is not statistically significant.(p=0.14)

In this model IVDU is found to lower the risk of an adverse outcome compared to heterosexual risk factors (HR=0.11) after controlling for the variables of ARV and ethnic status. This finding is statistically significant. (p=0.04)

HIV positive women who have had ARV have 1.81 times the risk of having an outcome of death, CD4 <200, or AIDS compared to HIV positive women who have not taken ARV after controlling for the variables of ethnic status and risk factors. This finding is not statistically significant.(p=0.24) However a finding of increased risk for patients undergoing treatment is not biologically logical. To investigate this finding further, a second model was made using the same variables but using the CD4 count of the patient when first seen at the HIV clinic to control for the effect of the patient's stage of disease at presentation.

Table 3.12 Cox regression model using the dependent variable of survival from the date that the patient was first seen to the occurrence of the outcome, controlling for initial CD4 count; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000.

	Univariate			Multivariate		
variable	**HR**	**95%CI**	**p-value**	**HR**	**95% CI**	**p-value**
ARV (therapy vs no therapy)	1.56	0.63-3.86	0.34	0.86	0.31-2.44	0.78
Risk factors*			0.09			0.08
H	1			1		
HI	1.48	0.69-3.2	0.31	1.67	0.74-3.78	0.22
I	0.17	0.02-1.10	0.09	0.21	0.02-1.679	0.14
Ethnic status (Aboriginal vs non-Aboriginal)	1.71	0.82-3.56	.15	1.17	0.53-2.6	0.69
initial CD4 count^	0.997	0.996-0.999	0.002	.998	.996-.999	.011

*Risk groups as compared to risk factor for heterosexual contact
H= Heterosexual contact only
HI= Heterosexual contact or intravenous drug use (IVDU)
I= IVDU
^CD4 count that was done at the patient's first visit; continuous variable

The addition of the initial CD4 count to the model, after excluding the patients with CD4 counts of less than 200 and the use of the time variable of time from first visit to the outcome or when the patient's record was last updated, has had little effect on the variables of risk factor and ethnic status compared to the first Cox regression model.

The multivariate model gives a significant change in –2 Log likelihood from the starting model (p=0.002) indicating that at least one of the variables in the model contributes to the prediction of the outcome.

In this model HIV positive women who are Aboriginal have 1.17 times the risk of having an outcome of death, CD4<200, or AIDS compared to non-Aboriginal HIV positive women after controlling for the variables of ARV, risk factors and initial CD4 count. This finding is not statistically significant.(p=0.69)

In this model IVDU is found to lower the risk of an adverse outcome compared to heterosexual risk factors (HR=0.21) after controlling for the variables of ARV, ethnic status and initial CD4 count. This finding is not statistically significant. (p=0.14)

HIV positive women who have had ARV have 0.86 times the risk of having an outcome of death, CD4 <200, or AIDS compared to HIV positive women who have not taken ARV after controlling for the variables of ethnic status, initial CD4 count, and risk factors. This finding is not statistically significant.(p=0.78)

3.6 Results: Objective 6

3.6.1 Objective 6: HIV and pregnancy

Nineteen percent (38/196) of HIV positive women seen were pregnant or became pregnant during the study period (21 Aboriginal and 17 non-Aboriginal).

Table 3.13 Age of pregnant women at the time of pregnancy; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

Age group	Aboriginal (% Aboriginal)	non-Aboriginal (% non-Aboriginal)	Total (%)
15-24	11 (52.4)	6 (41.2)	17 (44.7)
25-34	8 (38.1)	9 (47.1)	17 (44.7)
35-44	2 (9.5)	2 (11.7)	4 (10.5)
Total	21 (100)	17 (100)	38 (100)

The age distribution of the HIV positive women who were pregnant shows that Aboriginal women were younger when they become pregnant; this difference does not achieve statistical significance.(p=0.515)

Table 3.14 Number of pregnancies; HIV positive women, Northern Alberta HIV Program, August 1986 - February 2000

	Aboriginal (% of Aboriginal)	Non-Aboriginal (% of non-Aboriginal
single pregnancy	17 (80.9)	18 (94.7)
more than one pregnancy	4 (19.1))	1 (5.3)
after serostatus was known		
single pregnancy	10 (83.3)	8 (88.9)
more than one pregnancy	2 (16.7)	1 (11.1)

includes pregnancies that did not progress to full term

The majority of women became pregnant only once. There is no statistically significant difference between the number of HIV positive Aboriginal and non-Aboriginal HIV positive women (p=0.3551) who had single or multiple pregnancies although more Aboriginal HIV positive women had more than one child. There is no statistically significant difference between the number of single or multiple pregnancies of HIV positive Aboriginal and non-Aboriginal HIV positive women after they became seropositive (p=1.000).

Of the thirty-eight women who were pregnant, 74% of women (17 Aboriginal and 11 non-Aboriginal) received antiretroviral therapy. Six women did not receive antiretroviral therapy (4 Aboriginal and 6 non-Aboriginal) during their pregnancy.

Four patients who were diagnosed prior to 1995 were first seen at the HIV clinic after their child had been delivered, three others did not deliver and one patient had only recently been included in the database. The reason that two patients did not receive ARV during their pregnancy was not recorded in the database; reasons may be refusal of treatment, or lack of recording of ARV given in the delivery room in the database. There is no statistically significant difference between HIV positive Aboriginal and non-Aboriginal HIV positive women in the access to treatment during pregnancy. ($p = 1.000$) The outcomes of the infants born to these thirty-eight women were not completely recorded in the database.

Chapter Four

4.1 Discussion

Although only 8.4 % of the population of northern Alberta are Aboriginal (1996 census data) [65], 20% of the HIV positive patients referred to Infectious Disease physicians is Aboriginal; 46% of the women with HIV in northern Alberta are Aboriginal. In the November 1997 and April 2000 bulletins from the Bureau of HIV/AIDS and STD, Health Canada highlighted a disproportionate increase in the incidence of HIV/AIDS in Aboriginal people. They identified the population as young, women, and predominantly IVDU.[40,41] Our data confirms that the number of Aboriginal women is disproportionately high compared to non-Aboriginal women in the population and that heterosexual transmission and IVDU are the major modes of transmission in this population.

Health Canada has only been collecting ethnic status data on HIV positive patients since 1998 and has been able to obtain ethnic status information for less than 30% of HIV positive tests reported.[42] The HIV Outreach Program database is very complete and accurate with regard to ethnic status (see Appendix A) and has been collected prior to the time frame of Health Canada's data. We are able to confirm the proportion of HIV positive Aboriginal women reported by Health Canada in May 2001.[42] In addition, we have identified that this change in the epidemic began in northern Alberta in 1992.

The number of HIV positive women has risen steadily since 1992. This is a similar trend to that seen nationally.[41] Figure 3.1 shows a small decrease in the incidence of HIV in women in 1999; Health Canada's data shows that the number of women who have tested positive for HIV in Canada reached a high point in 1996 with 543 cases, decreased for 1997 (455 cases), then rebounded to 543 cases by 1999.[19] The decreasing trend seen in figure 3.1 may reflect a delay in data entry, a delay in seeing patients who were diagnosed as HIV positive in 1999 or a decrease in the number of new cases of HIV in women in northern Alberta. However, according to the Provincial Laboratory of Public Health, there had been no substantial decline in the number new cases of HIV in women for 1999 [67] therefore a delay may be occurring between the time that the patient is diagnosed as being HIV positive and the time that they are seen by an infectious disease physician.

The majority of the women seen at the HIV clinic are between 15 and 34 years of age. The Alberta Routine Prenatal Screening Program identified 13 HIV positive women through prenatal testing in 1999.[29] As prenatal screening continues, an age bias towards women in their child-bearing years may result.

Seventy-three percent of HIV positive women in northern Alberta live in Edmonton. According to Alberta Health, 62% of women in Regional Health

Authorities 8-17 live in the Capital Health region (including Edmonton and surrounding areas) [64] therefore this number indicates a disproportionate number of HIV positive women living in an urban setting. The percentage of people living in the Capital Health region who are Aboriginal is small (5.5%) compared to the other health regions in northern Alberta.[65] The increased proportion of HIV positive Aboriginal women in Edmonton is most likely due to the presumed higher rates of HIV and HIV transmission in urban areas.

The geographic location of the patient when they first test positive for HIV may not be the same as the location of the patient when they contracted HIV. I suspect that in many instances they are the same; the activities that spread the virus such as IVDU and prostitution, and the best place to have the HIV screening test performed anonymously are both in Edmonton. By the time of the patient's initial visit to the HIV clinic they may have already relocated to be closer to treatment. The HIV clinics record the patient's address for the purpose of contacting the patient, therefore data on all previous residences, both permanent and transient, which would be important epidemiologically is not recorded.

Are there communities in which women with HIV have not yet been tested? A sentinel surveillance study done in two Edmonton emergency rooms in 1998 found that 86% of patients who tested as HIV positive had been previously tested,[68] but routine testing done in a rural community detected a cluster of 16

cases of HIV of which 12 were women who were previously untested and who acquired HIV heterosexually.[55] The stigma associated with testing positive for HIV while living in a close knit community has been identified as a major obstacle to gaining control of the epidemic in Aboriginal Canadians.[69,70,71] Screening programs that target a broad population such as prenatal testing can remove some of the stigma of having the screening test done and remove the likelihood that an untested pool of HIV positive people will remain unknown.[12,72,73]

A pattern of geographic mobility of HIV positive women between urban and rural areas has not been established by this study. Although a third of patients have moved during the time they were being treated, only 8 patients moved out of Edmonton and 6 moved into Edmonton. Although Hogg, et al. found that geographic mobility occurs rarely in patients with AIDS, this may not be the case with persons who are seropositive who have not yet progressed to AIDS.[74] People who are HIV positive, asymptomatic, and are unaware of their serostatus pose the greatest health risk.[75] A concern in northern Alberta is the spread of HIV to rural communities.[43,45,55,76] The potential for explosive spread of HIV in a rural setting was identified by Native community based organizations in Montreal and in British Columbia.[54,69] Alberta's cities and larger towns are logical stepping stones for HIV to progress to other rural areas. A study of the sexual partnering and risk of HIV/STD transmission among Aboriginals in

Ontario found that 22% of Aboriginal people interviewed had partners both within and outside of their community of residence thus resulting in a possible "sexual bridge" between communities.[77] Dr. G. Predy, Medical Officer of Health for the CHA, cites male oilfield workers from northern worksites who spend time in Edmonton as a contributing factor in an increase in STDs in Edmonton.[78] It is also possible that this population is moving STDs such as HIV from Edmonton into northern communities as workers return home after working in the city.

Risk factors are reported by the patient and subject to recall bias. This bias is reduced at the HIV clinics because patients are treated in a non-judgmental way that encourages open dialogue about risk factors. In cases where HIV was transmitted unknowingly through sexual contact, the patient may not have any risk factors such as those related to drug addiction or prostitution. Among HIV positive women, both heterosexual contact and IVDU are primary risk factors for HIV transmission. The proportion of Aboriginal women with risk factors of IVDU is higher than non-Aboriginal women. The British Columbia Centre for Excellence in HIV/AIDS has observed a link between IVDU and HIV in Aboriginal people living in Vancouver in a cross-sectional study.[53] This study also found that Aboriginal people are over represented among users of intravenous drugs.[53] The British Columbia Positive Women's survey found an association between past and present physical and sexual abuse and the use of IV

drugs, however this study does not investigate ethnic status in this context.[79] The United Nations Commission on the Status of Women has identified a link between violence against women associated with women's subservience in many societies and the transmission of HIV to women.[80]

IVDU or the combination of IVDU and heterosexual contact are risk factors for a large proportion of the HIV positive women in this study. Many IVDU are addicts with multiple possible instances for transmission, but HIV can be transmitted through a single incident of needle sharing. Women have indicated that they have had both unprotected sex and used injection drugs. Drug use is associated with decreased use of condoms, therefore this risk factor has a direct effect on the ability of HIV positive women to avoid pregnancy in addition to HIV.[81]

Heterosexual contact could mean multiple sexual partners as in prostitution or a single HIV infected contact. Heterosexual transmission from unprotected sex has implications for pregnancy as well as contracting HIV. Prevention programs that advocate condom use are designed to prevent unwanted pregnancies and stop sexual and vertical transmission of HIV.[7]

Equal numbers of HIV positive Aboriginal women and non-Aboriginal women have been prescribed antiretroviral therapy during their infection. This is an encouraging indication of the equal availability of care in northern Alberta.

Thirty-four percent of women have not received antiretroviral therapy after being diagnosed with HIV. Patients may not yet require antiretroviral therapy, may refuse treatment, or may not pursue further care. As one doctor phrased it some "newly infected patients are struggling with the terrible triad of mental illness, drug abuse, and HIV infection".[82] Patients struggling with addiction have a poor outcome when infected with HIV which may be due to poor compliance.[83] Patients who do not return to the clinic for monitoring and refills of their medications are especially difficult to treat effectively. In order for a patient to be prescribed HAART they must be able to be compliant with the medication and the physician follow-up. Lapses in treatment can lead to treatment resistant virus populations and the inability of the clinic to provide any further drug to treat the virus.[10] The treatment regimens and side effects can be difficult to deal with for many HIV patients.[7] Since both HIV positive Aboriginal and non-Aboriginal women were equally likely to receive ARV, the factors that influence the patient's treatment, such as substance abuse, poor social conditions, and poor mental health could influence both groups. Neither group was found to be younger or at a better stage of their illness when they were first seen at the clinic.

Twenty-six women had their deaths recorded in the database. Most of these deaths were AIDS related and occurred in patients who were among the first to be diagnosed with HIV. During that time, women may have been tested at a later stage in their infection.

The similarity in the distribution of the outcomes for the survival analysis, indicates that ethnicity is not a prognostic indicator. In this analysis, Aboriginal women have the same survival or slightly lower survival than non-Aboriginal women. Ethnicity would effect survival if one group was able to access better treatment, treatment was affected by cultural traditions, or there were genetic predispositions to progression to AIDS. Survival is mainly affected by patient factors that are experienced in varying degrees by both groups of women such as mental illness, substance abuse, physical and sexual abuse, and general health as effected by socio-economic status.[82] However since women have only recently been diagnosed with HIV, this study does not include sufficient follow-up time to determine definitively if Aboriginal women have decreased survival times.

Protease inhibitors are a relatively recent addition to antiretroviral treatment. HAART is combination antiretroviral therapy that may or may not include protease inhibitors.[15,16] Protease inhibitors were used in this study as an indication that the patient was either capable of following a HAART regimen or that the patient was at stage of disease where combination therapy was necessary. The database contains patients that were seen before protease inhibitors were prescribed and some patients have not had protease inhibitors added to their treatment. Although it appears as though Aboriginal women fare worse on protease inhibitors and better without protease inhibitors, this may be due to the

small numbers of patients in the subgroups, the small number of outcomes, the short length of time many patients have been taking PI, some Aboriginal patients are not compliant with their treatment or that the patients were very ill before PI therapy was initiated. Patient compliance could not be assessed in this analysis.

The protective effect of IVDU may be explained by the increased surveillance of high risk populations. These patients know that they are at risk of contracting HIV and are aware of others that have the disease. This level of awareness and heightened monitoring ensures that patients will be detected early in their infection. This not only allows for early treatment of the disease thereby decreasing the likelihood of an outcome occurring, but also increases the length of follow-up at the HIV clinic. This is in contrast to those women who do not have high-risk lifestyle and do not discover their serostatus until they deliver a baby or become ill.

In the first Cox regression model, ARV was associated with an increased (but not statistically significant) risk of experiencing an outcome. This may be due to the patients receiving ARV having more severe disease at diagnosis. The second Cox regression model, which uses initial CD4 count as a measure of disease severity, indicates treatment with ARV is associated with a more plausible but still non-significant decrease risk of an outcome.

HIV positive women continue to have unprotected sex placing unborn children and partners at risk. Twenty-one women conceived children after their serostatus was known. Women who continue to engage in high-risk behaviour after being diagnosed with HIV may be due to lack of education, lack of power to control the use of condoms in their sexual relationships, continued illicit drug use, or depression, other mental illness, or personal choice and risk assessment that influences the patient's ability to behave responsibly.[81,82,83 ,84,85,86]

Seven pregnant women had no antiretroviral therapy recorded. These patients were either diagnosed after delivery, refused treatment, or the protocol for treatment for HIV during pregnancy was not yet in place. Studies done in 1994 found that antiretroviral therapy is effective in preventing the transmission of HIV to infants during birth.[31,32,33,34,35,87,88] The effectiveness of this intervention is the incentive for routine prenatal testing.[70] However any HIV testing must be undertaken with the consent of the patient. Alberta Health's initial investigations following the implementation of prenatal screening found that Aboriginal women were almost twice as likely as non-Aboriginal women to refuse testing.[29] This may be occurring in the smaller communities where the stigma of being HIV positive is greatest.[5,43,45] They also found that teenagers, Aboriginal women and women with low socio-economic status present later in their pregnancies for HIV screening.[29]

Children born to HIV positive mothers come under the care of the pediatric infectious disease physicians. Data published by Dr. Joan Robinson indicates than between January 1, 1998 and December 31, 1999, 71 children were born to HIV infected mothers in northern Alberta. Thirty-five mothers that received antiretroviral therapy both during pregnancy and during delivery had 31 HIV negative children (five children have indeterminate status). Five children who were HIV positive were born to mothers who had incomplete or no antiretroviral therapy. Sixty-eight percent of the children born to HIV positive mothers were Aboriginal. The children's ethnic status was not linked to their HIV status in this report.[35]

Statistics Canada has identified a rapid growth rate in the Aboriginal population with a 70% higher ratio of children under five years of age for each woman of childbearing age.[36] The implementation of prenatal HIV testing will hopefully prevent many HIV positive pregnancies and allow for effective treatment.

4.2 Strengths of the study

The infectious disease physicians at the University Hospital, Royal Alexandra Hospital and the Sexually Transmitted Disease Clinic are the primary providers of care for people infected with HIV. They are experienced in all aspects of the care of the HIV infected individual. Their relationship with their patient ensures that

sensitive information such as risk factors and ethnic status are complete and accurate.

Almost all of the patients with HIV in northern Alberta are recorded in the HIV database. The database was comprehensive in its coverage of the treatment and outcome of its patients. Three clinics contributed patient data to the database, which gives a complete and accurate representation of the population of HIV positive women in northern Alberta. The accurate and complete recording of the ethnic status of patients in the database was instrumental in the ability to pinpoint a group of people to whom specific and culturally sensitive intervention strategies can be directed that can have a large impact on the number of new HIV cases.

The use of a retrospective cohort study allowed for the investigation of multiple exposures and outcomes in this study population over a period of five years.

The database is patient focused; therefore data stored is unique for each patient. The data is not distorted by duplicate records due to anonymous testing, as would be the case with a laboratory database.

4.3 Limitations of the study

The Northern Alberta HIV Program database was designed to collect clinically relevant information about each patient and present it in cumulative chart form to enable physicians to easily recap data on a patient without going through the entire chart. To this end, the data contains many repeated measures, and information was entered in catch-all fields such as "comments". Data entered into the database, especially in the "comments" and "new events" fields depends on the understanding and thoroughness of the person performing the data entry. Many fields were missing data (such as ethnic status) that was crucial to this analysis. Every effort was made to access charts to fill in missing data.

The total number of HIV positive women in northern Alberta who were used in the analysis was 196. This gives very small numbers when subgroups are considered. This limits the data to finding very large differences as being statistically significant.

The patients in the HIV outreach database represents a cohort of high-risk patients who have been tested for HIV and who have followed through with accessing the HIV clinic. Except for prenatal testing and blood donations, patients do not undergo screening for HIV unless they are educated about the risk factors and

recognize themselves as being at risk. For this reason, the results of this study cannot be generalized to all Aboriginal women.

The number of HIV positive women who did not seek care and therefore were not recorded in the database could not be determined. Correlation between positive laboratory reports and patient database records was not useful as many patients were tested anonymously. Some HIV positive tests may have been done on women who did not live in Northern Alberta.

4.4 Recommendations and future research

The disproportionately high numbers of HIV positive Aboriginal women found in this study suggests that resources be allocated to urban HIV initiatives such as needle exchanges, urban safe houses and Friendship centers, and culturally sensitive education programs[24,65,68,89]. Leadership from within the Aboriginal community is essential to the success of culturally sensitive interventions.[69,70] Appropriate social services including those addressing housing, mental health, addiction, discrimination, and employment counseling for all HIV positive patients must continue to be available.[89] Creative approaches to enable effective provision of ARV to Aboriginal and other marginalized HIV positive groups are needed, especially for support of treatment programs for pregnant HIV positive women who do no access prenatal care.

As the number of asymptomatic HIV patients increases, there is evidence that transmission rates may increase due to the misconception that HIV is curable.[14] Agencies that are involved with surveillance, intervention, and education must continue to be supported to prevent a future increase the number of HIV cases.[90]

A study that gathers data specific to treatment effects and outcomes of HIV positive women would best address issues of treatment effectiveness in various subgroups of patients. The ideal study would be a prospective cohort study in which the database was designed for optimal collection of data pertinent to the study, then the chart review carried out to collect the data in formats conducive to the analysis. Further studies that should be undertaken include studies of patient compliance, case control studies in which the patients are matched for stage of illness at diagnosis with HIV, effectiveness of interventions in Aboriginal communities, and follow-up of children with HIV. Evaluation of the impact of prenatal testing and the reporting of HIV to Alberta Health on the incidence of HIV should be done.

The clinical database at the HIV clinic should continue to collect detailed demographic data on HIV positive patients in order to track the epidemic. The database should be designed to include fields that capture data categorically rather

than free text. Patient data should be collected to address specific research questions such as those aimed at treatment, socioeconomic, and cultural effects on the course of HIV disease.

4.5 Conclusion

This study of HIV positive women in northern Alberta found that Aboriginal women are over represented in the HIV positive population, that the majority of the women are young, and that most HIV positive women live in an urban area. The risk factors for women contracting HIV are predominantly unprotected sex and IVDU. Aboriginal women are more likely to be intravenous drug users than non-Aboriginal women. The survival models used in this study are not based on incident cases and should not be considered as predictive for the variables included. HIV positive women continue to engage in high-risk activities including unprotected sex, which places unborn children at risk. Routine prenatal screening has been identified by Alberta Health as one of many strategies to prevent HIV.[89]

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Appendix A

Ethnic Status

Ethnic status was determined by the Infectious disease physician as self-reported by the patient.

Status as recorded in database	grouped status used for study
Aboriginal	Aboriginal
Aboriginal/Inuit	Aboriginal
Aboriginal/Metis	Aboriginal
Aboriginal/Treaty	Aboriginal
Black	non-Aboriginal
Black/Endemic	non-Aboriginal
Caucasian	non-Aboriginal
Caucasian/Endemic	non-Aboriginal
Hispanic	non-Aboriginal
Hispanic/Endemic	non-Aboriginal
Indo-Asian	non-Aboriginal
Indo-Asian/Endemic	non-Aboriginal
Oriental	non-Aboriginal
Oriental/Endemic	non-Aboriginal

Appendix B

List of Database Fields

Name	Description	Original/ Derived	formula
ab	grouped ethnic status	derived	see appendix A
agedeath	age at date of death	derived	death date – birth date
agefirst	age at first seen date	derived	first seen date - birth date
agegrp	grouping of age at first seen	derived	15 year groupings
agepos	age when patient tested positive for HIV	derived	seropositive date - birthdate
AIDS	AIDS defining illness any time	derived	coded as Y if AIDS related illness was recorded in new events field
aidsdead	patient died from AIDS	derived	coded as Y if AIDS related illness was recorded in new events field
arv	antiretrovirals	derived	coded as Y if antiretroviral was recorded in drug field
birthdat	birth date	original	
CD4	CD4 count result	original	
CD41st	CD4 count at first visit	derived	extracted from CD4 count and visit date
CD41stg	grouping of CD4 count	derived	
CD4200	CD4 count was <200 at any visit	derived	extracted from CD4 count
censored	date of outcome or last update	derived	combined from date death, dateoutc, and last update
changed	patient changed address	derived	coded as Y if current postal code and first seen postal code were different
comments	free text field	original	
curur	current postal code indicates urban or rural	derived	U if Edmonton postal code, R if other
dateoutc	first date of CD4, AIDS, death	derived	extracted from visit date

death	patient died y/n	derived	Y= deathdate was recorded
deathdat	date of death	original	
drug	drugs prescribed	original	
enddate	date that data was extracted	derived	February 22, 2000
ethnicst	ethnic status	original	
firstsee	date of patient's first contact with infectious disease physician	original	
HCV	1=pos,0=neg, 3=not tested	derived	
lastupda	date that patient record was last updated	original	
new events	free text field	original	
no.preg	number of pregnancies after seropositive date	derived	extracted from comment and new events fields
oldrha	rha of first address recorded in chart	derived	comparison of pcfirst with rha/postal code lookup database
outcome	CD4<200, death or AIDS	derived	if Y was recorded in AIDS, or CD4200
pcfirst	postal code when first seen	derived	determined from patient charts
pcode	current postal code	original	
pi	protease inhibitors	derived	coded as Y if a protease inhibitor was recorded in drug field
pregaft	patient was pregnant after seropositive date	derived	extracted from comment and new events fields
pregage	age when patient was pregnant	derived	pregnancy date-birthdate
pregany	any pregnancy recorded in the database (y/n)	derived	extracted from comments and new events fields
pregarv	Y if drugdate was during pregnancy time	derived	determined from visit date when pregnant and visit date of drug recorded
ptnid	patient identification number	original	
risk	grouped risk factors	derived	see appendix C
riskbeha	risk behavior	original	
seroposi	date patient was seropositive	original	

serour	seropositive postal code indicates urban or rural	derived	U if Edmonton postal code, R if other
sex	male or female	original	
time1see	time from first visit to outcome, occurrences of outcome at first visit removed	derived	dateoutc-first seen
time5	time to outcome or censoring 5<t<1	derived	datecensored– seropositve date
urfirst	postal code of first recorded address indicates urban or rural	derived	U if Edmonton postal code, R if other
visitdat	date of patient's visit	original	
year	year first seen	derived	extracted from first seen date

*original: fields in the HIV Outreach ACCESS database.
derived: fields calculated or extracted using SPSS

Appendix C

Risk Factors

Risk behaviours as recorded by the infectious disease physician as reported by the patient.

database risk factor	recoded risk factor	Description
H,H?,	H	Heterosexual contact
HI,IH,IH?,HI?,I?H	HI	Heterosexual contact and intravenous drug use
I, I?, ?IB,BI,IB,IG	I	intravenous drug use
HT,T,T?,TH	T	tranfusion related

H= Heterosexual
B=Bisexual
G=Homosexual
I= Intravenous drug use
T=Received blood products

Appendix D

1993 Canadian surveillance AIDS case definition for adults:

1. a definitive diagnosis of one of the following clinical conditions:

Candidiasis of the esophagus, bronchi, trachea or lungs
Lymphoid interstitial pneumonia and/or pulmonary lymphoid hyperplasia affecting a child <13 years of age
Progressive multifocal leukoencephalopathy (PML)
Toxoplasmosis of brain affecting a patient >1 month of age
Pneumocystis carinii pneumonia (PCP)
Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary
Lymphoma, primary, of brain affecting a patient <60 years of age
Kaposi's sarcoma (KS)
Herpes simplex; chronic ulcer(s) > 1 month; or bronchitis, pneumonitis, or esophagitis
Cytomegalovirus disease (other than liver, spleen, or nodes)
Pulmonary tuberculosis
Cryptococcosis, extrapulmonary
Cryptosporidiosis, chronic intestinal, > 1 month

2. laboratory evidence for HIV infection and any disease from above or any of the following definitively diagnosed clinical conditions:

Recurrent or multiple bacterial infections of the following types affecting a child <13 years of age: septicemia, pneumonia, meningitis, bone or joint infection, or abscess of an internal organ or body cavity (excluding otitis media or superficial skin or mucosal abscesses), caused by Haemophilus, Streptococcus, or other pyogenic bacteria
Coccidioidomycosis, disseminated or extra pulmonary
Encephalopathy, HIV related
Histoplasmosis, disseminated or extrapulmonary
Isospariasis, chronic intestinal > 1 month
Kaposi's sarcoma at any age
Lymphoma of the brain at any age
Lymphoma, Burkitt's (or equivalent term), other non-Hogkin's lymphoma of B-cell or unknown immunological phenotype, immunoblastic sarcoma
Mycobacterium tuberculosis, any site (pulmonary or extrapulmonary)
Mycobacterium, other or unidentified species, disseminated or extrapulmonary
Recurrent Salmonella septicemia
HIV wasting syndrome
Cytomegalovirus retinitis (with loss of vision)
Pneumonia, recurrent
Salmonella septicemia, recurrent
Cervical cancer, invasive

Appendix E

Antiretroviral drugs[4]

Nucleoside Analog Reverse transcriptase inhibitors	
	Zidovudine
	Lamivudine
	Didanosine
	Zalcitabine
	Stavudine
	Abacavir
Non-Nucleoside Analog Reverse transcriptase inhibitors	
	Nevirapine
	Delavirdine
	Efavirenz
Protease Inhibitors	
	Saquinavir
	Ritonavir
	Indinavir
	Nelfinavir
	Amprenavir
Nucleotide Reverse Transcriptase Inhibitors	
	Adefovir
Ribonucleotide Reductase Inhibitors	
	Hydroxyurea