

**CHARACTERISTICS OF TUBERCULOSIS AMONG ABORIGINAL
POPULATIONS: IS THERE A DIFFERENCE IN RATES BY RESIDENCE (ON
AND OFF RESERVE)?**

A Thesis Submitted to the College of Graduate Studies and Research

in Partial Fulfillment of the Requirements

for the Degree of Master of Science

in the Department of Community Health and Epidemiology

University of Saskatchewan

Saskatoon

By Lesley A. McLeod

PERMISSION TO USE

In presenting this thesis in partial fulfillment of the requirements for the Postgraduate degree from the University of Saskatchewan, I agree that the Libraries of the University of Saskatchewan make it freely available for inspection. I further agree that permission for copying of this thesis in any manner, in whole or in part, for scholarly purposes may be granted by the professor, or professors, who supervised my thesis work, or in their absence, by the head of the department or the Dean of the College in which this thesis was done. It is understood that any copying of publication or use of this thesis or parts thereof for financial gain shall not be allowed without my written permission. It is also understood that due recognition shall be given to me, and to the University of Saskatchewan in any scholarly use which may be made of any materials in my thesis.

Requests for permission to copy or make use of material in this thesis in whole or part should be addressed to:

Department Head

Community Health and Epidemiology

College of Medicine

University of Saskatchewan

107 Wiggins Road

Saskatoon, Sk.

S7N 5E5

ABSTRACT

Tuberculosis is a major public health problem in Aboriginal populations. Studies are lacking to evaluate incidence of tuberculosis across residence status. The incidence of tuberculosis in Saskatchewan's Aboriginal population was investigated to determine whether differences existed between off- and on-reserve groups. A retrospective cohort study was performed, using data from the Saskatchewan Tuberculosis Control Program database of on and off reserve residents diagnosed with pulmonary tuberculosis between January 1, 1986, and December 31, 2005. Age, sex and residence-specific incidence rates were calculated with the use of Census populations for 1986, 1991, 1996 and 2001. Multivariate analysis using poisson regression was completed.

There were 1750 cases during the study period; 710 occurred off reserve and 1040 on reserve. 1337 cases were diagnosed in Registered Aboriginals, with the remaining 413 in the non-registered population. The mean age of Aboriginal cases on reserve was 12.92 and 19.98 for off reserve cases. Females were more likely to have tuberculosis on reserve, while males were more likely off reserve. Overall, TB rates both on and off reserve decreased over the study period. The on reserve population maintains greater rates of tuberculosis compared to their off reserve counterparts, after adjustment for age.

Although there is a natural history to infectious disease epidemics such as tuberculosis, it should be a higher priority of government policies and services to further decrease rates. The collection of more accurate population statistics would allow for more in-depth surveillance of TB in Saskatchewan and would contribute to knowledge about how and where to best allocate future resources.

ACKNOWLEDGEMENTS

Funding for this thesis was made possible by a Community and Population Health Research (CPHR) Training Fellowship, courtesy of the Saskatchewan Population Health Evaluation Research Unit (SPHERU), University of Saskatchewan.

I would like to thank my external examiner (Dr. Ibrahim Kahn), my supervisor (Dr. Syed Shah), and my committee members (Dr. Punam Pahwa, Dr. Vernon Hoepfner, and Dr. Sylvia Abonyi) for their guidance, helpful feedback and patience throughout this project. I really appreciate all your time and effort!

I would also like to thank my family for always encouraging me to pursue my education, no matter how long it takes, and for supporting me when I am in doubt of how much longer I can go. To my friends and colleagues; Amy, Maureen, Mark, Christina, and everyone else who shared this process with me, I wish you guys all the best in your future endeavours. I am so grateful that you have been a part of my life!

To everyone else who has shared my triumphs and frustrations these last few years (you know who you are), I really can't thank you enough for your love and support. It was appreciated more than you know!

DISCLAIMER

The analysis performed in this study was based on de-identified data provided by the Saskatchewan Tuberculosis Control Program. The interpretations and conclusions contained in this thesis do not necessarily represent those of the provincial TB Control Program.

TABLE OF CONTENTS

PERMISSION TO USE	i
ABSTRACT	ii
ACKNOWLEDGEMENTS	iii
DISCLAIMER.....	iv
TABLE OF CONTENTS	v
LIST OF TABLES.....	vii
LIST OF FIGURES.....	ix
LIST OF ABBREVIATIONS	x
1.0 INTRODUCTION	1
<i>1.1 Research Questions</i>	<i>4</i>
<i>1.2 Thesis Objectives</i>	<i>4</i>
2.0 LITERATURE REVIEW	6
<i>2.1 Global Burden of TB</i>	<i>6</i>
<i>2.2 TB in Industrialized nations</i>	<i>9</i>
<i>2.3 TB risk factors.....</i>	<i>11</i>
<i>2.4 Status of TB in Saskatchewan</i>	<i>12</i>
<i>2.4.1 Differential TB rates between Aboriginal and Non-Aboriginal people in Saskatchewan</i>	<i>15</i>
<i>2.4.2 Mobility on and off reserve</i>	<i>18</i>
<i>2.5 Government responsibility for aboriginal health services</i>	<i>19</i>
<i>2.6 Gaps in Literature</i>	<i>21</i>
3.0 METHODS.....	22
<i>3.1 Study Design</i>	<i>24</i>
<i>3.1.1 Numerator</i>	<i>25</i>
<i>3.1.2 Exclusion Criteria</i>	<i>25</i>
<i>3.1.3 Denominator.....</i>	<i>27</i>
<i>3.2 Statistical Analysis</i>	<i>28</i>
<i>3.2.1 Descriptive analyses</i>	<i>28</i>
<i>3.2.2 Trend Analysis.....</i>	<i>29</i>
<i>3.2.3 Regression Analysis</i>	<i>30</i>
<i>3.3 Application for Ethics Approval.....</i>	<i>31</i>
4.0 RESULTS.....	32
<i>4.1 Descriptive Statistics</i>	<i>32</i>
<i>4.2 Trend Analysis</i>	<i>41</i>
<i>4.3 Regression Analysis</i>	<i>44</i>

5.0 DISCUSSION.....	47
5.1 Descriptive Epidemiology and Trend Analysis	47
5.1.1 Tuberculosis and Age	47
5.1.2 Tuberculosis and Gender	51
5.1.3 Tuberculosis and Ethnicity	55
5.1.4 Tuberculosis and location of residence	58
5.2 Poisson Regression	62
5.3 Study Limitations and challenges.....	63
5.4 Policy implications	64
6.0 CONCLUSIONS.....	66
REFERENCES	67
APPENDICES	74
APPENDIX A: Glossary of Terms	74
APPENDIX B: Canada Census and Saskatchewan Health population comparison	75
APPENDIX C: Canada Census populations	76
APPENDIX D: Variable List and Descriptions	78
APPENDIX E: Trend Analysis with select reference time periods	82
APPENDIX F: Ethics Approval.....	85

LIST OF TABLES

Table 2.1	22 High Burden Countries (HBCs) of Global TB Incidence.....	6
Table 2.2	Characteristics/Conditions associated with higher risk of TB infection in the U.S.....	9
Table 2.3	Characteristics/Conditions associated with higher risk of TB infection in Canada.....	11
Table 3.1	Proportion of diagnostic classes of all Aboriginal TB cases detected by TB control program, Saskatchewan, 1986-2005.....	25
Table 3.2	Proportion of relapse TB cases in Saskatchewan Aboriginals, by selected variables, 1986-2005.....	26
Table 4.1	Proportion of new pulmonary TB cases in Saskatchewan Aboriginals, by selected variables, 1986-2005.....	32
Table 4.2	Average age-adjusted TB rates in Saskatchewan Aboriginals, by residence.....	34
Table 4.3.1	Average age-adjusted TB rates (95% CI) in Saskatchewan Aboriginal peoples residing on-reserve, stratified by sex, status and age group.....	35
Table 4.3.2	Average age-adjusted TB rates (95% CI) in Saskatchewan Aboriginal peoples residing off-reserve, stratified by sex, status and age group.....	36
Table 4.4	Average age-adjusted TB rates for beginning and end of study period in Saskatchewan Aboriginals (1986/90 and 2001/2005)....	39
Table 4.5	Completion frequencies for pulmonary TB cases in Saskatchewan Aboriginal patients from 2000-2002, stratified by sex, status and location of residence.....	40
Table 4.6.1	Trends in TB incidence rates for on-reserve Aboriginals in 5 year intervals, 1986-2005.....	42
Table 4.6.2	Trends in TB incidence rates for off-reserve Aboriginals in 5 year intervals, 1986-2005.....	42
Table 4.6.3	Trends in TB incidence rates for on and off-reserve Aboriginals in 5 year intervals, 1986-2005.....	42
Table 4.6.4	Summary of TB incidence rate trends in on-reserve Aboriginal populations, Saskatchewan 1986-2005.....	43
Table 4.6.5	Summary of TB incidence rate trends in off-reserve Aboriginal populations, Saskatchewan 1986-2005.....	43
Table 4.6.6	Summary of TB incidence rate trends in on and off-reserve Aboriginal populations, Saskatchewan 1986-2005.....	43

Table 4.7.1	Poisson Regression reduced model for the incidence of tuberculosis in Saskatchewan's Aboriginal population, 1986-2005.....	45
Table 4.7.2	Poisson Regression full model for the incidence of tuberculosis in Saskatchewan's Aboriginal population, 1986-2005.....	46

LIST OF FIGURES

Figure 2.1	Tuberculosis incidence rate in Saskatchewan (per 100,000 population) from 1990-2003.....	12
Figure 2.2	Comparison of incidence rates (per 100,000) of tuberculosis by ethnic origin in Saskatchewan, 1998-2004.....	15
Figure 4.1.1	Age distribution of pulmonary TB cases on-reserve compared with total Aboriginal population (Census 1996), Saskatchewan, 1986-2005.....	37
Figure 4.1.2	Age distribution of pulmonary TB cases off-reserve compared with total Aboriginal population (Census 1996), Saskatchewan, 1986-2005.....	38
Figure 4.2.1	Age-adjusted TB rates on and off reserve, by year, for ages 0-14.....	39
Figure 4.2.2	Age-adjusted TB rates on and off reserve, by year, for ages 15-65+.....	39

LIST OF ABBREVIATIONS

TB	Tuberculosis
WHO	World Health Organization
DOT	Directly Observed Therapy
DOTS	Directly Observed Therapy-Short Course
HBC	High Burden Country
MDR-TB	Multiple Drug Resistant Tuberculosis
HIV/AIDS	Human Immunodeficiency Virus/ Acquired Immunodeficiency Syndrome
IUATLD	International Union Against Tuberculosis and Lung Disease
TST	Tuberculin Skin Test
LTBI	Latent Tuberculosis Infection
PPR	Persons per room
STI	Sexually Transmitted Infection
FNIHB	First Nations and Inuit Health Branch
TU	Tuberculin Unit
ATS	American Thoracic Society
ICD-9	International Classification of Diseases-9 th edition
INAC	Indian and Northern Affairs Canada
SE	Standard Error
DF	Degrees of Freedom
SD	Standard Deviation
CI	Confidence Interval
OR	Odds Ratio
S-DEV	Scaled Deviance
APS	Aboriginal People's Survey

CHAPTER 1:

1.0 INTRODUCTION

Tuberculosis continues to pose a major threat to global public health. The resurgence of this disease in both developing and developed nations has prompted increasing concern, as drug resistance and HIV-coinfection make the disease all the more dangerous and difficult to control (1). It has become evident that in order for nations to implement effective prevention and control programs, further research into underlying factors responsible for infection and progression to TB is needed.

Historically, it has been well documented that significant differences exist in the overall health and well-being of Aboriginal peoples in Canada compared to that of Canadian born non-aboriginals (2, 3). Some etiological factors have included: human biology, individual lifestyles and practices and socio-economic and environmental factors such as income, education and housing (3). Although the differences exist for other illnesses in Canada, they have been well documented for tuberculosis over the years. In Canada, Aboriginal peoples make up approximately 4% of the total population and yet they accounted for 15% of the TB cases reported in 2003 (4). In 2001, the TB rate was 43 times higher for Aboriginal people than the overall Canadian rate at 81.3 cases per 100,000. By comparison, the overall Canadian rate was 7.4 per 100,000 (5). Although there has been a considerable decline over the past 50 years in infectious diseases (including TB) in Aboriginal populations, the rates have now stabilized at a level that remains higher than that of the general Canadian population (3, 4).

As in previous censuses, the highest concentrations of Aboriginal population in 2001 were in the Northern Territories and on the Prairies. The census enumerated

150,040 Aboriginal people in Manitoba and 130,190 in Saskatchewan, in each case about 14% of the province's population. The 156,220 Aboriginal people in Alberta accounted for only 5% of its population (6).

The rate of TB in the province of Saskatchewan is consistently and proportionately higher than the average national rate (4). In 2003, the new active Canadian rate of TB was 4.6 per 100,000. The new active rate for Saskatchewan that year was 8.2 per 100,000. However, the 5-year new active rates (2000-2004) in the Non-Registered and Registered Aboriginal populations of Saskatchewan were 53.5 and 52.2 per 100,000, respectively (7). In 1978, as a general reporting practice, the Saskatchewan TB Control Program began reporting TB case numbers and rates by four categories: Status Indian, Caucasian, Métis and foreign born. Divided in this way, it has become evident that the Aboriginal people in this province (Registered Indians and Métis) have had consistently higher TB rates than the Caucasian group. This difference was reported as early as 1965, the year that the TB program first treated and reported registered Aboriginal cases. However, a relatively new trend in tuberculosis is now evident within Aboriginal groups, which is potentially associated with increasing mobility of people on and off Federal Reserve land. Preliminary data collected by the Saskatchewan TB Control Program from 1986-2005 suggests an increase in the TB rates in those Aboriginal people living off reserve in this province.

Several examples of effective interventions and tuberculosis control can be seen in Canadian, as well as Saskatchewan history. In the mid-1970s, tuberculosis case rates in Canadian Inuit populations were among the highest ever recorded in humans (8). However, intensive interventions and government support in the communities resulted in

one of the fastest decline rates of TB ever reported, suggesting that targeted interventions can be highly effective among at risk populations. Similarly, during the 1980's and 1990's, approximately 50% of TB cases in Saskatchewan occurred in Registered Aboriginal populations living on reserve (7). In 1989, the TB control program implemented DOT (directly observed therapy), a strategy that was later developed and promoted by the World Health Organization (WHO) in 1993 as DOTS¹ (Directly Observed Therapy-Short Course). As a result, drug resistant and relapse TB cases have decreased significantly in Saskatchewan reserve communities (7).

Movement on and off reserve has become increasingly common and in 2005 over half of the Registered Aboriginal population (56%) of Saskatchewan lived off reserve (9). Unfortunately, very little has been done to examine whether this difference in residence makes a difference in health and, in particular, in tuberculosis rates.

This study will be unique in that it will include all people in the province who identify themselves as being Aboriginal. For the purposes of this study, it is important to define the terms I will be using to describe different people within the broad term Aboriginal and to describe in what context these terms are to be used. Although I recognize that several dimensions exist when describing Aboriginal peoples (cultural, biological and legal), I will be using the following definitions of identity as the framework for using these terms. Throughout this study, I will use the term, "Aboriginal" to refer to all those who identify themselves as being of Aboriginal descent. This will include Registered and Non-Registered Aboriginals, as well as Métis and Inuit populations. The term "Registered Aboriginal" will be used to refer to those registered

¹ See Appendix A for definition

under the federal *Indian Act* and “Non-Registered Aboriginal” will include all other Aboriginal people, including Métis, but excluding Inuit. There are different political and health implications that follow the status of these groups and I will be considering these in the context of TB control and prevention.

1.1 Research Questions

- 1) Are there differences in pulmonary TB rates between Aboriginal peoples living on and off reserve between 1986 and 2005?
- 2) What is the trend in pulmonary TB rates over time for both Aboriginal peoples living on and off reserve across the study period?
- 3) Do the variables: year of diagnosis, sex category, age category, location of residence or status category act as significant predictors of TB rates in on and off reserve Aboriginal populations?

1.2 Thesis Objectives

Despite increasing mobility of Aboriginal people both on and off reserve, very little has been done to examine whether this has an affect on the health and well-being of these people. Some preliminary data, collected by the Saskatchewan Tuberculosis Control Program, suggested that those Aboriginal people living off reserve in Saskatchewan are experiencing greater rates of tuberculosis compared to those living on reserves. This may have implications for the health of Aboriginal peoples in Canada. To meet the mandates of the Canada Health Act and the WHO goal of “Health for All”, it is vital that we examine if and where health disparities exist and how those issues can be addressed. The objectives of this thesis are to: (i) determine whether or not reported cases

of TB differ within the Aboriginal populations of Saskatchewan, stratified by their location of residence (on or off reserve); (ii) determine the trend in TB rates over time in both the on and off reserve Aboriginal populations; and (iii) to examine whether or not any of the variables of interest (year of diagnosis, age, sex, location of residence, and status category) are significant predictors of the tuberculosis rates in the two population groups.

CHAPTER 2:

2.0 LITERATURE REVIEW

2.1 Global Burden of TB

Tuberculosis is currently the world's second most common cause of death from an infectious disease. It has been estimated that 8-9 million people develop tuberculosis and approximately 2-3 million people die from the disease each year (10). Globally, 22 countries bear the greatest burden of TB. These High Burden Countries (HBCs) are home to 80% of the world's cases of tuberculosis (Table 2.1) (11).

TABLE 2.1: The 22 highest burden countries of global TB incidence: cumulative incidence, percentage of population covered by DOTS in 2000 and case detection rate under DOTS in 2000 (11)

	22 high burden countries	Cumulative incidence (%)	Pop. covered in 2000 (%)	Case detection rate under DOTS in 2000 (%)
1	India	21	30	11
2	China	37	68	33
3	Indonesia	44	98	19
4	Nigeria	48	47	12
5	Bangladesh	51	92	24
6	Ethiopia	54	85	29
7	Philippines	57	89.6	45
8	Pakistan	60	9	3
9	South Africa	63	77	67
10	Russia	65	12	2.7
11	Congo	67	70	51
12	Kenya	68	100	43
13	Vietnam	70	99.8	80
14	Tanzania	72	100	45

15	Brazil	73	7	0.8
16	Thailand	74	70	46
17	Uganda	75	100	50
18	Myanmar	76	77	48
19	Mozambique	77	100	40
20	Cambodia	77	99	44
21	Zimbabwe	78	100	52
22	Afghanistan	79	15	9.2

After effective drug treatment was developed for tuberculosis in the 1950s, the priority of TB on the international agenda declined (12). However, after several decades of neglect, tuberculosis has re-emerged as a major public health issue, mostly due to the emergence of HIV and multiple drug resistant TB (MDR-TB) (11). In 1998, the Stop TB global partnership was formed by the WHO and its partners in an effort to promote international cooperation in the fight against TB. The partnership now includes over 150 partners and in March 2000 the “Amsterdam declaration to stop TB” was signed as a result of a Stop-TB initiative. The declaration confirmed commitments to achieve the global targets of TB set by the World Health Assembly and included plans to mobilize resources necessary to expand DOTS and to detect at least 70% of infectious cases by 2005 (11).

Up until recently the true burden of TB in developing countries was unclear, mostly due to the lack of resources necessary for many nations to accurately collect and report such information. However, following the renewed interest in the global TB situation in the early 1990s, the WHO reported that over 95% of the 8 million new TB cases and 2.9 million deaths were occurring in the developing world (11). These

increases seemed to have been fueled by several events, but the HIV epidemic and increasing drug resistance appeared to be the primary contributors in these regions. By 2000, MDR-TB had reached critical levels in specific regions of the world including Estonia, Latvia, and certain regions in Russia and China (13). World TB authorities were alarmed at the increased TB burden on the world's most disadvantaged. As a global problem, it was agreed that something needed to be done. Encouraged by marked improvements made by K. Styblo of the International Union Against TB and Lung Disease (IUATLD) in some of the poorest African countries (14), the WHO began encouraging nations to set goals of 85% cure rates and to focus on case detection only after cure rates were permanently high. Furthermore, member states of the World Health Assembly were urged to intensify their TB control programs following the IUATLD approach, to create national partnerships to promote TB control and to establish the global TB targets discussed previously (cure rate 85%, case detection rate 70%) (11). However, during the second half of the 1990s it became evident through global surveillance that the targets were not within reach due to slow DOTS expansion in the 22 HBCs. As of 2000, there were an estimated 8.2 million new TB cases worldwide, with 60% of all cases occurring in Asia, and sub-Saharan Africa experiencing the highest incidence with 300 cases per 100,000 population. Over 1.8 million people died of TB that year, and 95% of those occurred in developing countries (11). Although the established targets have yet to be met, the DOTS strategy has been expanded significantly over the past decade. As of 2000, 148 out of 210 countries had adopted DOTS, including all 22 HBCs. However, coverage varies greatly and although a nation may have adopted

the DOTS strategy, it does not guarantee diagnosis and treatment for all, leaving many countries struggling to meet their TB control targets (11).

2.2 TB in Industrialized nations

At the turn of the 20th century, TB was a major public health concern in most of the world's nations. In the United States, as in many industrialized nations, improvements in living conditions, public health services and effective treatment regimens resulted in a promising decline in TB rates until the middle of the 1980s (15). The HIV epidemic, financial cutbacks for TB control, multiple drug resistance and increasing immigration from countries with high TB rates have all been implicated in a trend reversal that saw increasing rates of TB for several years in 1980s and 1990s. In 2001 there were 15,989 incident cases of TB in the U.S. (5.8 per 100,000 population), with 49% occurring in the foreign-born population (15). Public health authorities in the United States have identified the following conditions as being associated with a higher risk of TB infection:

TABLE 2.2: Characteristics/conditions associated with higher risk of TB infection in the U.S. (15)
Foreign-born in area with high tuberculosis rates
Use of illicit drugs
Institutionalization or work in: jails and prisons OR Long-term care facilities
Socioeconomic disadvantages
Children of those at high risk

Interestingly, those with aboriginal ancestry are not included as a high risk group in the U.S., although several studies suggest a significantly higher risk for Aboriginal peoples in other industrialized nations such as Australia and Canada (2, 16-18).

In Canada, TB rates are significantly higher in the Prairie Provinces and Territories as compared to other Canadian provinces (4). These regions also have a higher proportion of Aboriginal peoples compared with many other regions of the country (4). Based on a theory proposed by Grigg (19), which will be discussed in greater detail later, the higher rates in Aboriginal peoples may be a result of differences in the phase of the tuberculosis epidemic. As the epidemic in Aboriginal people began much later in Saskatchewan, (approximately 125 years ago, as compared to 500 years ago in the Caucasian population) (20), the peak of the “tuberculosis wave” has been reached much later than those of the non-aboriginal population, who are now on the decline phase of the epidemic.

Reviews from the U.S., Canada and Australia have also identified foreign-born persons as being at a higher risk for TB (15, 16, 18, 21). In Australia in 1995, 75.4% of new TB cases occurred in foreign-born patients, the majority of which came from Vietnam, China, the Philippines, India and Indonesia (18). In the U.S in 2001, 49% of all new TB cases were foreign-born (15) and in Canada, 57.8% of cases were foreign-born in 1995 (21). However, as discussed previously, the TB situation in Canada is not homogeneous and it is interesting to note that data from the provincial control program in Saskatchewan indicates few cases of TB are reported in the foreign-born population (7),

suggesting that tuberculosis in Saskatchewan is primarily experienced by the Aboriginal population.

2.3 TB risk factors

Although, in the global context, Canada has a relatively low rate of TB in the general population, there are some high risk groups that experience consistently higher rates. The risk factors identified in the following list are similar to those identified in the U.S. However, those with Aboriginal ancestry are also at a significantly higher risk in Canada. Table 2.3 was adapted from Long et al (1999) with some additional identified risk factors* that are important in the Saskatchewan context (Khan, pers. com.).

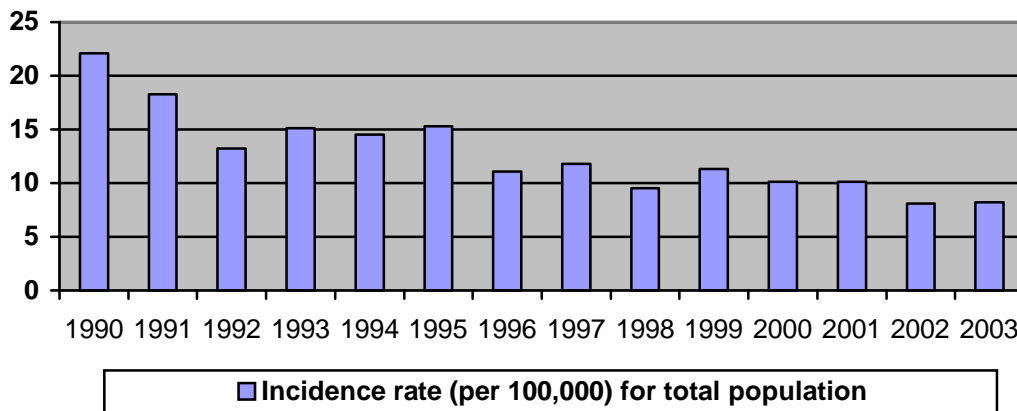
TABLE 2.3: Characteristics/conditions associated with higher risk of TB infection in Canada (21)
Country of origin with high prevalence of TB
Aboriginal Background
Homelessness
Substance abuse
Time spent in a correctional facility
Contact with a person who has TB
Older age
Travel to a high prevalence country
Health care occupation
Other occupational contact with high prevalence group (ie. foreign-born, Aboriginal people)
* Co-morbidities (Diabetes, HIV/AIDS, Hepatitis, etc.)
* Malnutrition
* Care seeking patterns (traditional healers)
* Diagnostic Delays

Study reviews conducted on Australian Aboriginal populations have identified a higher risk for TB. In 1995, 22% of the new TB cases were in Aboriginals, giving a crude incidence rate of 15.5 per 100,000 population compared to 1.33 in the non-aboriginal Australian born population (16, 18). The generally lower economic status among those in the Aboriginal populations exposes them to all risks associated with homelessness and overcrowding, which both have potential implications for TB control (18).

2.4 Status of TB in Saskatchewan

Since 1985, tuberculosis rates in Saskatchewan have generally been decreasing. In 1990, the overall TB incidence rate was 22.1 per 100,000. By 2003, the rate was 8.2 per 100,000 (7). Figure 2.1 shows the general downward trend in incident cases of TB between 1990 and 2003 for the total population in Saskatchewan. Despite the promising decline, the majority of cases remain in the Registered Aboriginal and Métis categories (7).

FIGURE 2.1 Tuberculosis incidence rate in Saskatchewan (per 100,000 population) from 1990-2003 (22)



In 1989, the provincial TB control program began using the DOT strategy with the goal of controlling and preventing tuberculosis in Saskatchewan (23). Directly Observed Therapy (DOT) is the process whereby the ingestion of every dose of medication is observed by a member of the TB health care team (24). DOT is the Canadian standard for TB treatment to prevent drug resistance and relapse cases. As such, successful completion of drug treatment is of the utmost importance. At that time, approximately 50% of TB cases were being found in Aboriginal people living on federal reserves. Since adding DOT and increasing targeted screening on reserve to BCG vaccination for all children on reserve, the overall incidence of TB in Saskatchewan has decreased in the Registered Aboriginal population (7).

The Saskatchewan TB Control Program has since produced a TB Control Manual containing guidelines to be followed in Saskatchewan in the event of suspected and confirmed TB cases (24). Briefly, the manual outlines how the control program manages case detection, diagnosis, treatment, screening programs, prevention and contact tracing within the province. It also details how public health service workers (e.g. family doctors, nurses, community health workers, etc) should participate in controlling TB in their communities. As mentioned previously, the control program in Saskatchewan uses the DOT treatment regimen. Case detection is either passive (patient presents with symptoms) or active (case is detected following screening or contact tracing). For example, in the event that a patient presents to their family physician with symptoms suggestive of tuberculosis, a sputum examination and/or chest X-ray should be performed in order to confirm diagnosis. If positive, this patient would be referred to the TB clinic to be registered in the program and to initiate treatment. Members of the control team

will also initiate contact tracing to prevent further spread of the disease. At this point, a skin test is performed on those people who had been in close contact with the infectious person and appropriate treatment given if more cases are found. A similar procedure will be carried out for a patient discovered following active screening procedures, currently performed for children on reserve, as well as several other high risk groups (e.g. employees in correctional facilities). Overall, major efforts are made to detect and treat active cases of disease and to prevent activation of latent cases by providing treatment of latent TB infection (LTBI). As previously mentioned, completion of treatment is very important and the Directly Observed Therapy regimen has been associated with a significantly improved outcome for both the patient and the control program.

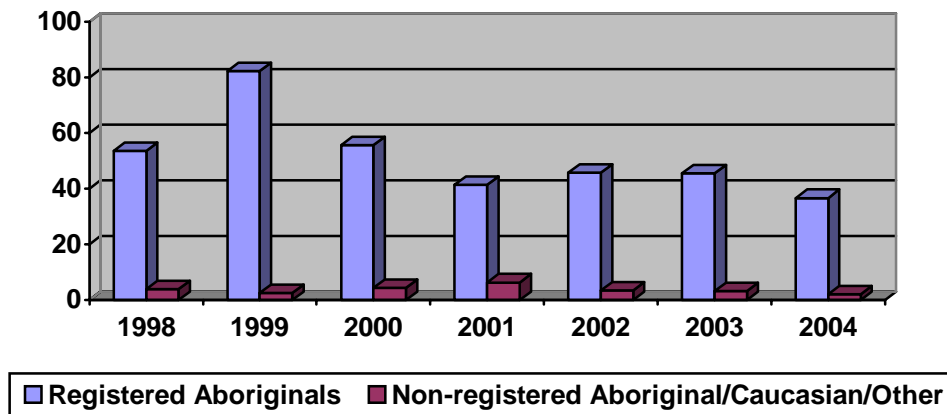
There are several steps in a DOT program and they involve action at many different levels to be a success. Once a patient has been identified and entered into the program, a drug regimen is designed specifically for that individual and the medication is packaged in Saskatoon and distributed. A TB Worker, who is a TB control team member, checks the supply of medication with the Community Health Nurse when it arrives, and ensures that the medications are the correct dosage amounts. Then, the TB Worker sign and Community Health Nurse sign the official medication record, which serves as an objective, accurate assessment of treatment progress. The TB control personnel is responsible for developing a relationship with the patient and patient's family (improves compliance), delivery of medication at a time and place convenient to the client, observing the ingestion of the medication, recording of doses administered, and the return of original packaging and medication record to the TB clinic that serves the area. Of course, this requires a great deal of commitment, organization and resources

and, as is often the case when resources are limited, high risk populations are often targeted in order to most efficiently use what is available. Those populations currently at highest risk of tuberculosis infection in Saskatchewan include: HIV-positive, IV drug users, inner city homeless, Aboriginal, Foreign born and persons over 65 years of age (21).

2.4.1 Differential TB rates between Aboriginal and Non-Aboriginal people in Saskatchewan

In Saskatchewan in particular, Aboriginal people are a higher risk population for TB infection and disease compared to Caucasians. Figure 2.2 shows the incidence of TB in Registered Aboriginal population as compared to all other people in Saskatchewan between 1998 and 2004.

FIGURE 2.2 Comparison of incidence rate (per 100,000) of tuberculosis by ethnic origin in Saskatchewan 1998-2004 (7, 9, 25)



So why do Aboriginal people in this province have consistently higher TB rates when drugs are available to treat the disease and rates in the Caucasian population continue to decrease? Several explanations exist in the literature. According to Grigg (19), these two populations are at different stages of a TB epidemic. The Saskatchewan Indian epidemic began 125 years ago, while the Caucasian epidemic began about 500 years ago. The theory suggests that two important events in North American history resulted in a shift from previously endemic TB in the Aboriginal population to epidemic TB. The first event was the extinction of the bison, the main source of food, clothing and shelter for North American Aboriginals in the early 19th century. This resulted in starvation and changed a way of life that had been used for generations (20, 26). Second, the construction of a trans-Canada railroad through Saskatchewan in the late 19th century required the acquisition of land that was occupied by Aboriginal groups. In exchange for land on which to build the railroad, the government provided Federal Reserve land and the federal treaties were signed. When people moved onto the reserves, a previously nomadic lifestyle became much more sedentary. Instead of smaller family groups residing in traditional tepee for short periods of time, larger groups resided in log houses, with less ventilation for longer periods of time. It is argued that these changes created the conditions that shifted TB into epidemic proportions in the North American Aboriginal population, resulting in different case rates and patterns in the two populations, as they were in different phases of the natural epidemiologic curve. This theory may explain the non-homogeneity of TB in Canadian Aboriginal and Non-Aboriginal populations (20, 27-29).

Another explanation includes differential biological susceptibility. This susceptibility is inherent in the epidemic phase described earlier. In the early phase, people are more susceptible as there has been limited exposure and less chance for immunity to build, while in the later phase, immunity has increased and fewer people are susceptible resulting in fewer cases. More recent evidence suggests that age and status play a role in differential TB rates (30). A study by Ward showed that younger people are at a greater risk for progression from TB infection to active disease. As the Aboriginal population is younger than the general Canadian population, this may play a role in greater case rates in Aboriginal people. Finally, since TB is an airborne infection, the transmission is greater when more people are breathing the same air, or crowding (3, 17). A study conducted in 2002 examined the association between housing density and tuberculosis in Canadian Aboriginal communities (31). The results demonstrated that the TB rates in selected isolated Registered Aboriginal communities were the highest in Saskatchewan (104.3 per 100,000), Alberta (76.2 per 100,000) and Manitoba (74.0 per 100,000), the three Canadian provinces with the highest levels of housing density at 0.8, 0.6 and 0.8 average persons per room (ppr), respectively. The study also showed that average housing density is higher in on-reserve Aboriginals (0.7 ppr) than the non-aboriginal Canadian population (0.4 ppr).

Studies have also suggested that those with substance abuse problems are more likely to have higher rates of sexually transmitted infections (STIs) such as HIV, which decreases immune function and makes sufferers more susceptible to TB after infection (10, 12). It is argued that several things will be needed in order to decrease the levels of TB in Aboriginal populations. These would include targeted surveillance and directly

observed therapy and prophylaxis as well as promotion of community partnerships to address social and environmental issues (3, 17).

2.4.2 Mobility on and off reserve

Studies suggest that whenever there is a lot of movement, the picture of tuberculosis is complicated (19). A study conducted by Cummings et al. (32) suggested that TB patients who moved prior to completing anti-tuberculosis treatment were 5.5 times more likely to default on treatment than those who did not move. Aboriginal mobility on and off reserves is a complicated issue. Between 1966 and 1986, the off reserve Aboriginal population of Saskatchewan quadrupled (5). In 2000, 52% of the Registered Aboriginal population lived off reserve and 48% lived on. As of 2005, 56% of the Registered Aboriginal population in Saskatchewan lived off reserve, with the remaining 44% living on, indicating a trend in the movement of the provincial Aboriginal population off the reserves (9). So why do people move off the reserve? In some studies, Aboriginal people state they have moved in order to participate in the labour force (33, 34). Other studies suggest people move due to increasing populations on reserves too small to support the growth and that may, in turn, create the conditions conducive for the spread of TB (5). In addition, most reserves are rural and have limited resources available for housing and employment (5). It is argued that migration off reserve becomes necessary when the reserve is no longer able to support the existing population (35). Unfortunately, accurate data regarding how many people live on or off reserve at any given time is difficult to collect as transient migration, both on and off reserve, is common among these populations. Many people are forced to leave the reserve to look

for work and find seasonal employment only to return to the reserve when the work term ends (34).

In earlier decades, large numbers of people living in one house, breathing the same poorly ventilated air, were resulting in environments that were at high risk for the spread of TB in these communities. To address this problem, the federal government committed resources for the prevention and control of TB on reserves. Currently in Saskatchewan, although the diagnosis and treatment of all TB cases are handled by provincial authorities, approximately half of the funding for the provincial control program comes from the Saskatchewan government with the other half coming from Health Canada and First Nations and Inuit Health Branch (FNIHB), resulting in a TB control partnership (23). However, with 68% of the combined budgets directed on reserve, or \$48,000/case compared to \$17,000/case directed off reserve (2002-2006), case finding, treatment, as well as increased screening and prevention strategies are less available for those living off reserve (23).

2.5 Government responsibility for aboriginal health services

The amount of movement on and off reserves has serious implications for TB control due to the political jurisdictional boundaries that are in place and a solution to these issues has yet to be found. According to the *Indian Act* signed in 1876, the health services of Registered Aboriginals were the responsibility of the federal government, regardless of their residence (5). Those of Non-Registered, Métis and Inuit origins were the responsibility of the provincial or territorial governments where they lived. In practice today, after a major overhaul of the *Indian Act* in 1951, only those Registered Aboriginals who live on a federal reserve receive additional federally funded health

services (36). If an individual or family decides to move off the reserve, their health services become the responsibility of the provincial government (36).

In Saskatchewan today, the provincial government pays health insurance premiums for everyone, using revenue from taxes. In addition to provincial health services, federal funding for additional non-insured services is available for Registered Aboriginal people that live on a federal reserve (5, 36). The issue of government responsibility remains a very complex political and historical issue. Controversy still remains over the services that should be available to Aboriginal people residing off reserve. The issue was complicated further with the introduction in 1986 of the Indian Health Transfer Policy, the goal of which was to transfer responsibility for health care and services away from federal and provincial governments and to Aboriginal communities themselves (36, 37). The debate continues over whether this is a step in the right direction. Many would argue that it is a beneficial policy allowing for the promotion of Aboriginal autonomy and self-determination, while others argue that it is simply a way for the government to get out of its financial obligations (5).

The debate concerning responsibilities in Aboriginal health services is further evidence of the complexities of Aboriginal identity and jurisdictional issues. Legal definitions of identity may not necessarily be how individuals identify themselves, often leading to conflict and ultimately, poor health outcomes (38). Jurisdictional issues may therefore become confused as population definitions remain vague and fluid. Although differential resource access can not be directly correlated to the Aboriginal TB rates in this study, it has been historically evident that conflicts regarding identity and jurisdiction

need to be resolved in order to improve the general health and well-being of this population.

2.6 Gaps in Literature

Many gaps exist in the published literature surrounding the Aboriginal experience off reserve. Until recently, there has been very little statistical data available on the socio-economic and health status of these people. In addition, statistical complications arose due to several political and legal changes, such as those introduced through Bill C-31 in the 1990's, in which many people who had previously lost legal status under the Indian Act, regained that status. Because of this, population statistics for certain groups have experienced artificial shifts that are difficult to track and to compare trends.

Contemporary literature has begun to emerge that examines the issue of urbanization for Canadian Aboriginal peoples, covering topics such as how urban Aboriginals are perceived by other ethnic groups or other Aboriginals and alternatives for integrating Aboriginal peoples in the Canadian urban setting (39, 40). However, this research is geographically based and is not specific to health care and utilization, limiting the information that can be gained on the population health perspective experienced by urban aboriginals. It also maintains a focus on off reserve Aboriginals that have moved to cities, leaving out those who are still rural but do not reside on a federal reserve. As a result of the difficulties obtaining reliable data, as well as the transient nature of some of the population, very little work has been done which examines the relative differences in the health of those people living off reserve as compared to those living on, and specifically how these differences are manifested in the context of tuberculosis.

CHAPTER 3:

3.0 METHODS

We used TB surveillance data maintained by the Saskatchewan TB control program to conduct this study. This program maintains a computerized database of all individuals with documented tuberculin skin test (TST) results since 1986. Demographic data, such as gender, date of birth, ethnic origin and home address were provided by the individual at the time of testing. For ethnic origin, the individual selected one of: Canadian-born Caucasian, Status Indian, Non-status or Métis, Asian or Other (foreign born). Only those patients who identified themselves as Aboriginal (Status Indian or Non-status/Métis) at the time of diagnosis were included in the study. For the purposes of this study, those identifying themselves as Status Indian were considered Registered Aboriginal and those of Non-status/Métis descent were considered Non-registered Aboriginal.

Tuberculin skin tests were provided for contact tracing and screening of high risk individuals as recommended by Saskatchewan TB control (41). High risk populations that were recommended for screening included First Nations children on reserve at age 2, school entry, and thereafter biannually through grade 6 (kindergarten is school entry). Certain individuals, including day care, health care and correctional centre employees, as well as recent immigrants also received TST screening. Contact tracing was provided to all known contacts with more than 10 hours of exposure in the previous 30 days to an infectious case and/or to potential sources of a primary TB case. Status Indians predominantly received skin tests during on reserve school screening, as well as for contact tracing. Non-status/Métis received TST screening primarily as part of contact tracing and occupational health.

Tuberculin skin testing was completed using 5 tuberculin units (TU) in 0.1ml of tuberculin purified protein derivative, injected intradermally, and read by a TB nurse 48-72 hours later, as recommended (41). A positive tuberculin skin test was defined as induration (localized hardening of soft tissue surrounding injection site) of ≥ 5 mm for individuals known to have had contact with an infectious TB case or for those with HIV/AIDS, and ≥ 10 mm for all other individuals (42).

If an individual had a positive TST, they were assessed by a TB control physician to determine if treatment for disease or preventative therapy would be needed. A unique file number was assigned to all individuals with a positive TST who were assessed by a TB control physician. Cases were updated in the database if an individual with a previously positive TST developed TB disease.

Treatment compliance data was collected meticulously in the early years of the treatment program but not entered into the database. Completion of treatment is defined as taking $>80\%$ of prescribed course of drug therapy (42). For this study, completion data was examined and reported for the years 2000-2002 (complete data), excluding cases that died during treatment.

The TB control program utilizes two designated TB case data entry clerks. The data were entered within 24 hours based on laboratory (smear/culture) results or clinical (start of treatment) results. Each year the director of TB Control reviewed all cases, starting in January of the following year, as part of writing an annual report. During this process the director verified the data using the record and discussion with the treating doctor. For research purposes, more detailed verification was needed, which was conducted by the

director prior to release of data. Data were ready for use within 6 months for case incidence/prevalence reports and 18 months for treatment outcome research.

Tuberculosis disease, in this study, was defined by the Canadian TB Standards (5th Ed.) as *Mycobacterium tuberculosis* complex demonstrated on culture, or in the absence of bacteriological proof, cases clinically compatible with tuberculosis will be used (42). The American Thoracic Society (ATS) classification was used to identify the site of TB cases (43).

3.1 Study Design

We conducted a retrospective cohort study to estimate the incidence of pulmonary tuberculosis for the aboriginal population in the province of Saskatchewan and to compare rates in off and on-reserve population from 1986 to 2005.

The complete list of variables made available to the researcher included: date of diagnosis, patient file number, date of birth, gender (M/F), ethnic origin (I/M), diagnosis postal code, diagnosis health district, regional health authority, on/off reserve, ATS classification (American Thoracic Society classification system), previous diagnosis year (for relapse cases), diagnosis method, date of death, cause of death, compliance, ICD-9 codes (International Classification of Diseases is the classification used to code and classify mortality data from death certificates), test specimen description, and results of smear and culture tests (Positive or Negative).

The patient's date of birth and the date of diagnosis were used to recode a categorical age variable, which was categorized into ages 0-14 and 15+. Gender, ethnic origin, location of residence (on/off reserve), and diagnosis method (active/passive) were also recoded as bivariate categorical variables.

3.1.1 Numerator

All Aboriginals in the province of Saskatchewan with confirmed tuberculosis disease between Jan.1, 1986 and Dec. 31, 2005 were identified from the Saskatchewan TB Control database.

3.1.2 Exclusion Criteria

A breakdown of total TB cases in Saskatchewan Aboriginals from 1986-2005 is presented in Table 3.1. Any individual who was identified as having a relapse case of TB (had a previous date of diagnosis) was not included in this study, as it was felt that relapse cases would artificially inflate case rates. Case frequencies of relapse cases have been included in Table 3.2 for comparison with new, active cases.

TABLE 3.1 Proportion of diagnostic classes of all Aboriginal tuberculosis cases detected by TB control program, Saskatchewan 1986-2005.

Diagnostic Class	Off Reserve (%)	On Reserve (%)
All (n = 2278)	984 (43)	1294 (57)
New Pulmonary (n=1750)	710 (41)	1040 (59)
Smear +, Culture +	210 (30)	168 (16)
Smear +, Culture -	2 (0)	5 (0)
Smear -, Culture +	80 (11)	87 (8)
Smear -, Culture -	47 (7)	77 (7)
No specimen	371 (52)	703 (68)
Relapse Pulmonary (n=120)	67 (56)	53 (44)
Smear +, Culture +	52 (78)	24 (45)
Smear +, Culture -	1 (1)	2 (4)
Smear -, Culture +	11 (16)	12 (23)
Smear -, Culture -	3 (4)	7 (13)
No specimen	0 (0)	8 (15)

Non-pulmonary and Pleural (n=408)	207 (51)	201 (49)
Non-pulmonary	123 (59)	124 (62)
Non-pulmonary, relapse	20 (10)	19 (9)
Pleural	62 (30)	50 (25)
Pleural, relapse	2 (0)	8 (4)

In addition, any individual who was diagnosed with non-pulmonary or pleural tuberculosis was excluded from this study (as per the ATS classification). This was decided as it was felt at the time that pulmonary cases were more of a public health risk as they are infectious via an airborne route. Cases with incomplete demographic information, such as ethnic origin, sex or postal code, were reviewed by the director of the TB Control Program and missing data were filled in using the master database where possible.

TABLE 3.2: Proportion of relapse TB cases in Saskatchewan Aboriginals, by selected variables 1986-2005

	Frequency	Percent (%)
Total	167	100
Sex		
Male	81	48.5
Female	86	51.5
Age		
0-14	7	4.2
15-65+	160	95.8
Status		
Registered Aboriginal	115	68.9
Non-registered Aboriginal	52	31.1
Residence		
On reserve	79	47.3
Off reserve	88	52.7

Sex x Residence		
Male off reserve	43	25.7
Male on reserve	38	22.8
Female off reserve	45	26.9
Female on reserve	41	24.6
ATS classification		
Pulmonary	118	70.7
Non-pulmonary and Pleural	49	29.3

3.1.3 Denominator

In order to maintain up-to-date information on Canadians, the federal government conducts a national census survey every 5 years that attempts to collect data from every person. In addition, other national agencies such as Health Canada and Indian and Northern Affairs Canada (INAC) also collect information on Aboriginal people of Canada. Although the information is important to collect, problems with data noise can arise for several reasons. First, the agencies that collect the information do so independently and use different terms of reference and definitions of identity, making comparison difficult and posing several problems for researchers wishing to look at certain characteristics of any given population. In addition, due to the methods utilized for data collection, many people may be missed and/or may refuse to participate, resulting in an underestimate of population and other variables.

Prior to calculation of TB rates, the source of appropriate denominator populations was determined. There were several advantages and disadvantages to using each source. Those populations collected by the Saskatchewan Health Registration database provided annual statistics that were thought to be more accurate than census populations. In

addition, population statistics collected by this agency had been previously used by the Saskatchewan TB Control Program. However, a specific breakdown for non-registered Aboriginal populations in the province was not available and therefore, rates would only be possible to calculate for Registered Aboriginals. That problem was addressed by Canadian Census data, which is reported in both Status Indian and Non-Status categories. However, the data is only collected every 5 years, meaning case averages would be needed to calculate incidence rates for each year. In addition, there has been criticism regarding the completeness and accuracy of census data.

To address the issue of denominator source, age standardized TB rates were calculated for the Registered Aboriginal populations only from both sources and compared². It was decided that if the census rates did not differ significantly from the presumably more accurate Saskatchewan Health rates in the Registered Aboriginal group, the census populations would be used and non-registered Aboriginal rates could be calculated for the study. It was determined from this process that there was not a significant difference between the rates calculated from census and health registration sources, and therefore, census data for the years 1986, 1991, 1996 and 2001 were used as denominator populations in the calculation of TB rates in this study. See Appendix C for complete census populations used in this study.

3.2 Statistical Analysis

3.2.1 Descriptive analyses

Descriptive analysis included frequency of pulmonary TB cases in Saskatchewan Aboriginal people by year of diagnosis, sex category, age category, location of residence

² See Appendix B for population comparison

(on/off reserve) and status category (registered/non-registered Aboriginal), as well as a table of completion results for the years 2000-2002. Preliminary descriptive statistics were performed using five age categories based on categories reported in other tuberculosis literature. There were small numbers in some age categories leading to unstable estimates and it was decided to present the age in two major categories (0-14 and 15+) for further analysis.

Crude and age-adjusted TB rates for both on and off reserve populations were calculated by census year (Objective 1) and expressed as number of cases/100,000 (44), using census data for the denominators and 1996 Saskatchewan total Aboriginal population as a standard population³. Crude rates were obtained using the following

formula: $\frac{(\text{Total Aboriginal cases between 1986 and 1990})/5}{1986 \text{ Aboriginal population off reserve}} \times 100,000$. Age adjusted rates

were calculated by census year, using the 1996 census total Aboriginal population as the standard population and were expressed as cases/100,000. Confidence intervals were calculated in Microsoft Office Excel 2003, as age adjusted rate $\pm (1.96 \times \text{SE})$ where SE = standard error = $\frac{\text{age adjusted rate}}{\sqrt{\text{average annual cases}}}$ (44). In some cells, confidence intervals were

exceptionally wide due to small case numbers. In these situations, confidence intervals were not reported.

3.2.2 Trend Analysis

Tests for trend in incidence rates over time were performed (Objective 2). A Poisson regression model was used to test for evidence of a trend in incidence rates as a function

³ See Appendix C for census populations utilized for study calculations

of calendar year. The GENMOD procedure, with a Poisson distribution, was used to evaluate trends over time (45). The following regression model was used:

$$\text{Ln}(\lambda) = \beta_0 + \beta_1(\text{Year}_{1991-1995}) + \beta_2(\text{Year}_{1996-2000}) + \beta_3(\text{Year}_{2001-2005}) + \beta_4(\text{onoffres}) + \beta_5(\text{sexcat}) + \beta_6(\text{agecat}) + \beta_7(\text{statuscat}) + \varepsilon$$

Here the λ is the tuberculosis incidence rate for 5 year intervals and the natural log transformation ensures that the model-based predictions of rates are constrained to be greater than or equal to zero.

3.2.3 Regression Analysis

Poisson regression analysis was conducted to determine the significance of variables potentially associated with the incidence of tuberculosis (Objective 3). Poisson regression is an analysis technique that is available for modeling dependent variables that describe incidence and assumes that the underlying distribution of the response variable, Y , is distributed as a Poisson random variable (46). The Poisson distribution is the appropriate probability model for counts of rare, independent event (i.e. cases of tuberculosis in Saskatchewan Aboriginals). Although tuberculosis in Aboriginal populations has been shown to be re-emergent in recent literature, it will be considered a rare event, compared to rates previously recorded, and to current rates of some chronic diseases (heart disease, cancer, etc.).

Variables with epidemiologic relevance to tuberculosis were chosen for inclusion into the regression model. These variables included year of diagnosis, age category, sex category, location of residence (on or off reserve) and status category (registered or non-registered). Inclusion into the main effects model was determined by the above variable's statistical significance with the incidence of tuberculosis ($p \leq 0.05$).

Regression analysis performed on the main effects model demonstrated under-dispersion. In the case of poisson regression, under-dispersion occurs when the observed mean is less than the variance, as the assumption in poisson regression is that mean is equal to variance. Over- and under-dispersion⁴ were checked for by examining the Goodness of Fit criteria values for scaled deviance and scaled pearson χ^2 , and their respective degrees of freedom (df). Evidence of under-dispersion ($\chi^2/df < 1$) was observed and was corrected by multiplying each of the model parameters by Pearson's scaling factor. Modeling was performed by using PROC GENMOD (45).

The role of each variable in the main effects model in relation to each other was assessed with the inclusion of interaction terms in the model, first one at a time, then in combinations. The significance of all variables and interaction terms were assessed by performing a test of scaled partial deviance ($S-DEV_p$)⁵.

3.3 Application for Ethics Approval

Ethics approval has been granted for this study by the University of Saskatchewan Behavioural Ethics Board. See Appendix F.

⁴ See Appendix A for definitions

⁵ See Appendix A for definitions

CHAPTER 4:

4.0 RESULTS

There were 2278 total Aboriginal cases of tuberculosis reported to the Saskatchewan TB Control Program between Jan.1, 1986 and Dec. 31, 2005. A total of 528 cases were excluded for failing to meet the inclusion criteria (120 relapse pulmonary cases, 408 new and relapse non-pulmonary and pleural cases). 1750 met the inclusion criteria and were included in the final study analysis.

4.1 Descriptive Statistics

There were 1750 incident cases of pulmonary TB in Saskatchewan's Aboriginal population; 710 occurred off reserve and 1040 occurred in people residing on reserve. There were 1337 cases among the Registered Aboriginals and 413 in the non-registered population. The proportion of new pulmonary TB cases for selected variables was calculated (Table 4.1). See Table 3.2 for comparison with relapse cases.

TABLE 4.1 Proportion of new pulmonary TB cases in Saskatchewan Aboriginals, by selected variables 1986-2005.

	Frequency	Percentage (%)
Sex		
Male	924	52.8
Female	826	47.2
Age		
0-14	1089	62.2
15-65+	661	37.8
Residence		
Off Reserve	710	40.6
On Reserve	1040	59.4
Sex x Residence		

Male off reserve	395	22.6
Male on reserve	529	30.2
Female off reserve	315	18.0
Female on reserve	511	29.2
Status		
Registered Aboriginal	1337	76.4
Non-Registered Aboriginal	413	23.6
Specimen Type		
Gastric washings	703	40.2
Urine	18	1.0
Pleural Fluid	14	0.8
Sputum	628	35.9
Lung Tissue	13	0.7
Bronchial washings	17	1.0
Other	357	20.4
Smear results		
Negative	296	16.9
Positive	389	22.2
No specimen	1065	60.9
Culture results		
Negative	729	41.7
Positive	665	38.0
No specimen	356	20.3
Regional Health Authority		
Athabasca	227	13.0
Keewatin Yatthé	368	21.0
Mamawetan Churchill River	425	24.3
Prairie North	153	8.7
Prince Albert Parkland	155	8.9
Kelsey Trail	155	8.9
Saskatoon	120	6.9

Sunrise	8	0.5
Cypress	16	0.9
Regina Qu'Appelle	111	6.3
Sun Country	12	0.7
Diagnosis method		
Passive	982	56.1
Active	768	43.9

The average age adjusted TB rates were calculated for each census period, by residence (Table 4.2). On-reserve, those in the younger age group (0-14) had greater age-adjusted rates than the 15+ age group, across the entire study period. Off-reserve however, the trend reversed with the older age having higher age-adjusted rates after 1996 (Table 4.2). Overall, the results demonstrate that there is a higher rate of new pulmonary TB cases in Saskatchewan Aboriginal peoples residing on reserve across the study period.

The age adjusted rates of those people diagnosed with TB are described in table 4.3.1 (on reserve) and 4.3.2 (off reserve). The mean age of Aboriginal cases on reserve was 12.92 (SD=18.29) (median age 4, range 0-88 year). The mean age of Aboriginal cases off reserve was 19.98 (SD=19.94) (median age 14, range 0-86).

TABLE 4.2 Average Age-adjusted TB Rates in Saskatchewan Aboriginals, by residence

	Off Reserve		On Reserve	
	Avg. Cases	Age-adjusted Rate/100,000 (95% CI)	Avg. Cases	Age-adjusted Rate/100,000 (95% CI)
1986-1990				
0-14	21	43.21 (30.11-56.11)	47	175.31 (134.70-215.91)
15-65+	21	41.93 (23.99-59.86)	25	94.48 (67.47-121.49)

1991-1995				
0-14	28	39.94 (28.60-51.29)	45	149.68 (110.69-188.68)
15-65+	20	30.08 (18.90-41.26)	11	37.54 (26.60-48.48)
1996-2000				
0-14	11	14.57 (8.64-20.50)	35	94.24 (67.63-120.84)
15-65+	12	16.70 (6.74-26.67)	13	35.68 (23.86-47.50)
2001-2005				
0-14	12	17.15 (10.95-23.35)	19	41.82 (27.24-56.40)
15-65+	17	22.57 (9.80-35.34)	13	26.21 (14.42-37.99)

When further stratified by sex and status category, both males and females in the Registered Aboriginal group on reserve experienced higher age adjusted rates in the 0-14 age group, as compared to the older group. This trend could be seen across the entire study period (Table 4.3.1). The non-registered Aboriginal group on reserve is very small and confidence intervals calculated for age adjusted rates in this group were not reported due to small case numbers.

TABLE 4.3.1 Average age-adjusted TB rates (95% CI) in Saskatchewan Aboriginal peoples residing on-reserve, stratified by status category, sex and age group

	Registered Aboriginal		Non-registered Aboriginal	
	Male (95% CI)	Female (95% CI)	Male (95% CI**)	Female (95% CI**)
1986-1990				
0-14	145.63 (80.49-210.18)	207.31 (128.82-285.80)	0.00	297.42
15-65+	93.98 (41.67-146.28)	97.26 (41.77-152.76)	54.39	61.49
1991-1995				
0-14	176.76 (108.72-250.80)	165.06 (93.43-236.69)	11.21	0.00
15-65+	37.12 (3.91-70.32)	48.89 (11.01-86.77)	6.78	0.00
1996-2000				
0-14	100.25 (55.41-145.09)	83.31 (41.15-25.47)	59.16	800.91
15-65+	34.77 (8.24-61.30)	34.33 (7.31-61.36)	78.77	0.00

2001-2005				
0-14	42.66 (15.09-70.23)	46.86 (17.22-76.50)	11.91	0.00
15-65+	36.47 (11.51-61.43)	18.07 (0.36-35.78)	11.60	11.26

** Not reported due to small case numbers

Off reserve, the Male Registered Aboriginal group shows an increase in rates in the older age group over the last ten years of the study period, compared to the predominance of cases in the younger group between 1986 and 1995 (Table 4.3.2).

Females of the same status, however, demonstrate mixed results, as do the rates in the non-registered Aboriginal group. Once again, when rates on and off reserve are compared, the results demonstrate higher rates across the study period in the on reserve Aboriginal population.

TABLE 4.3.2 Average age-adjusted TB rates (95% CI) in Saskatchewan Aboriginal people residing off reserve, stratified by status category, sex and age group

	Registered Aboriginal		Non-registered Aboriginal	
	Male (95% CI)	Female (95% CI)	Male (95% CI)	Female (95% CI)
1986-1990				
0-14	58.63 (10.91-106.34)	59.37 (14.07-104.66)	34.28 (2.25-66.31)	28.31 (1.23-55.38)
15-65+	55.32 (2.41-108.23)	53.30 (7.49-99.10)	41.02 (10.19-71.85)	29.25 (2.52-55.97)
1991-1995				
0-14	41.92 (5.89-77.96)	32.33 (3.41-61.24)	50.01 (19.90-80.12)	33.70 (9.08-58.32)
15-65+	34.22 (1.49-66.95)	35.50 (3.06-67.94)	39.78 (11.50-68.06)	15.75 (-0.99-32.48)
1996-2000				
0-14	12.15 (-3.22-27.52)	12.36 (-2.66-27.38)	19.77 (-0.65-40.20)	10.74 (-3.45-24.92)
15-65+	17.94 (-3.87-39.74)	12.19 (-3.23-27.62)	20.46 (2.16-38.76)	13.73 (-1.81-29.27)

2001-2005				
0-14	11.01 (-4.25-26.26)	9.00 (-4.15-22.15)	35.79 (5.03-66.56)	17.28 (-2.27- 36.84)
15-65+	26.14 (0.52-51.76)	24.43 (2.10-46.75)	25.93 (4.45-47.41)	14.03 (-1.85-29.91)

In both the on and off reserve groups, the 0-14 age group represents a greater proportion of the total population. For this age group, in particular, there appears to be a higher proportion of under-age cases relative to their proportion of the population (Fig 4.1.1 and Fig 4.1.2).

FIGURE 4.1.1 Age Distribution of pulmonary TB cases on reserve compared with total Aboriginal population (Census 1996), Saskatchewan. 1986-2005

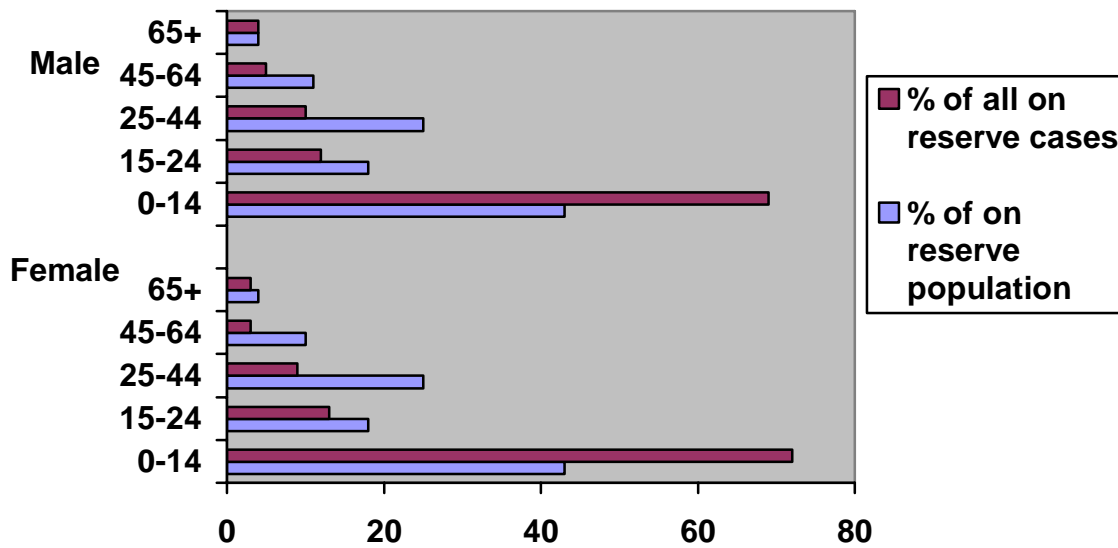
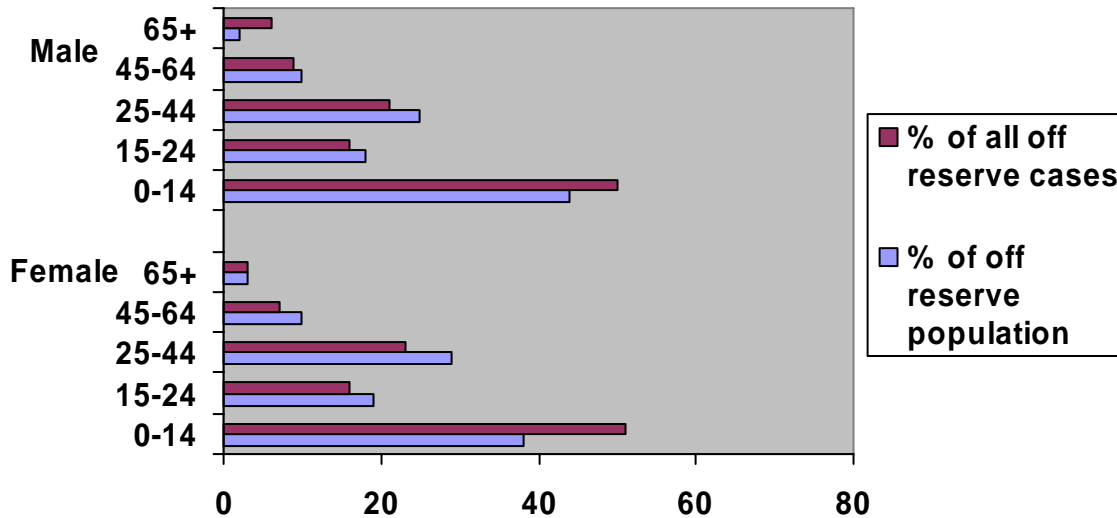


FIGURE 4.1.2 Age Distribution of pulmonary TB cases off reserve compared with total Aboriginal population (Census 1996), Saskatchewan. 1986-2005



The average age adjusted rates for each census period, by residence and age group show an overall convergence of rates toward the end of the study period (2001-05).

However, as mentioned previously, the on reserve population maintains a greater rate of new pulmonary TB cases than the off reserve group in both age groups (Figs 4.2.1-4.2.2).

The average age adjusted rate for 1986-90 period on reserve was 54.32 per 100,000 (95% CI: 32.86, 75.79). For that same period off reserve, the rate was 16.99 per 100,000 (95% CI: 9.69, 24.29). For the period 2001-2005, the average age adjusted rate on reserve was 13.43 per 100,000 (95% CI: 4.20, 11.65) and off reserve was 7.93 per 100,000 (95% CI: 6.01, 20.84) (Table 4.4)

FIGURE 4.2.1 Age adjusted TB rates on and off reserve, by year for ages 0-14

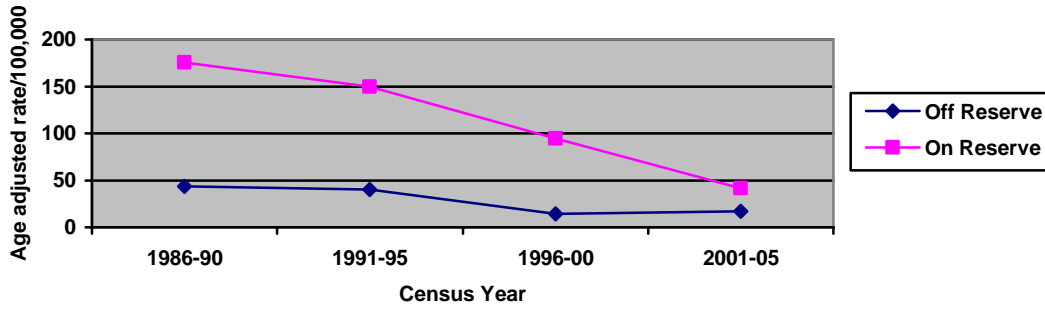


FIGURE 4.2.2 Age adjusted TB rates on and off reserve, by year for ages 15-65+

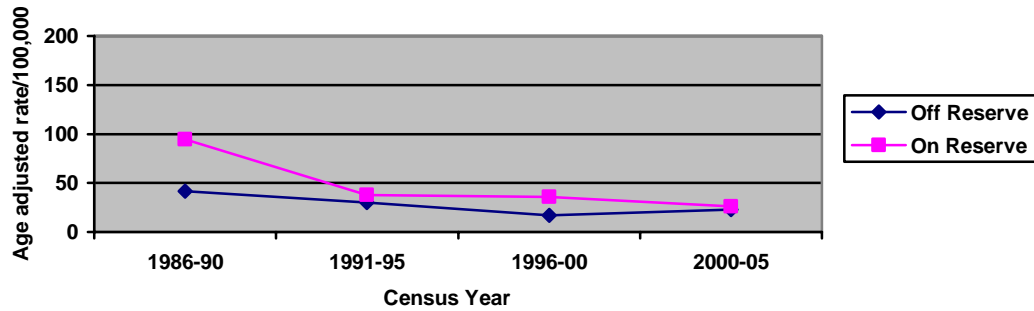


TABLE 4.4 Average age adjusted TB rates for beginning and end of study period in Saskatchewan Aboriginals (1986/90 and 2001/05)

	Average age-adjusted rate/100,000	95% CI
1986-90		
On	54.32	32.86, 75.79
Off	16.99	9.69, 24.29
2001-05		
On	13.43	6.01, 20.84
Off	7.93	4.20, 11.65

As mentioned in the methods section, completion of treatment is a major goal of the DOT regimen in Saskatchewan. Although early in the program, collection of completion data was not entered into the database, Table 4.5 shows that between 2000 and 2002, the vast majority of patients completed 80% or more of their drug treatment, regardless of their location of residence. Note that these data exclude those who died prior to treatment completion. The group with the highest frequency of incompleteness was non-registered females off reserve at 9.5% across the three years of interest.

TABLE 4.5 Completion frequencies for pulmonary TB cases in Saskatchewan Aboriginal patients from 2000-2002, stratified by sex, status, and location of residence.

	Registered Aboriginal		Non-Registered Aboriginal	
	Male (%)	Female (%)	Male (%)	Female (%)
Off Reserve				
No (<80% complete)	1 (5.6)	1 (5.6)	0 (0.0)	2 (9.5)
Yes (>80% complete)	17 (94.4)	17 (94.4)	34 (100)	19 (90.5)
On Reserve				
No (<80% complete)	2 (4.2)	0 (0.0)	0 (0.0)	0 (0.0)
Yes (>80% complete)	46 (95.8)	32 (100)	1 (100)	1 (100)

4.2 Trend Analysis

Results of analysis in TB incidence trends in on and off reserve Aboriginal populations are shown in Tables 4.6.1, 4.6.2, and 4.6.3. Trend analysis using a poisson distribution demonstrates significant decreases in TB incidence rates between 1996-2000 and 2001-2005 compared to the 1986-1990 reference time period, in both the on and off reserve populations ($p=0.0182$ and $p=0.0018$, respectively) (Table 4.6.3). There was no significant decrease in TB incidence rates between the periods 1991-1995 and 1986-1990 in either on or off reserve populations ($p=0.3084$) (Table 4.6.3). A summary of total significant trend results and percent changes are included (Tables 4.6.4, 4.6.5, 4.6.6). Comparisons using other time periods as reference categories are included in Appendix E. Overall, there is a significant decrease in incident pulmonary TB rates in Saskatchewan's Aboriginal population, both on and off reserve. However, the decrease is not as considerable in the off reserve population, compared to that of the on-reserve group.

TABLE 4.6.1 Trends in TB incidence rates for on reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-7.24	0.12	0.00	0.00, 0.00	<0.0001
1986-1990 (ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1991-1995	-0.11	0.17	0.90	0.65, 1.25	0.5256
1996-2000	-0.87	0.20	0.42	0.28, 0.62	<0.0001
2001-2005	-0.70	0.19	0.50	0.34, 0.72	<0.0001

TABLE 4.6.2 Trends in TB incidence rates for off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-5.98	0.17	0.00	0.00, 0.00	<0.0001
1986-1990 (ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1991-1995	-0.42	0.26	0.66	0.40, 1.08	0.0988
1996-2000	-0.80	0.27	0.45	0.27, 0.76	0.0028
2001-2005	-1.50	0.31	0.22	0.12, 0.41	<0.0001

TABLE 4.6.3 Trends in TB incidence rates for on and off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-6.64	0.21	0.00	0.00, 0.00	<0.0001
1986-1990 (ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1991-1995	-0.30	0.30	0.74	0.41, 1.32	0.3084
1996-2000	-0.78	0.33	0.46	0.24, 0.88	0.0182
2001-2005	-1.09	0.35	0.34	0.17, 0.67	0.0018

TABLE 4.6.4 Summary of TB incidence rate trends in on-reserve Aboriginal populations, 1986-2005.

	On Reserve							
	1986-1990		1991-1995		1996-2000		2001-2005	
Reference Period	% change (direction)	p-value	% change (direction)	p-value	% change (direction)	p-value	% change (direction)	p-value
1986-90			10 (→)	0.5256	58 (↓)	<0.0001	51 (↓)	0.0002
1991-95	10 (→)	0.5256			53 (↓)	0.0001	45 (↓)	0.0012
1996-00	58 (↑)	<0.0001	53 (↑)	0.0001			15 (→)	0.4470
2001-05	51 (↑)	0.0002	45 (↑)	0.0012	15 (→)	0.4470		

TABLE 4.6.5 Summary of TB incidence rate trends in off-reserve Aboriginal populations, 1986-2005.

	Off Reserve							
	1986-1990		1991-1995		1996-2000		2001-2005	
Reference Period	% change (direction)	p-value	% change (direction)	p-value	% change (direction)	p-value	% change (direction)	p-value
1986-90			35 (→)	0.0988	55 (↓)	0.0028	78 (↓)	<0.0001
1991-95	35 (→)	0.0988			32 (→)	0.1782	66 (↓)	0.0008
1996-00	55 (↑)	0.0028	32 (→)	0.1782			50 (↓)	0.0346
2001-05	78 (↑)	<0.0001	66 (↑)	0.0008	50 (↑)	0.0346		

TABLE 4.6.6 Summary of TB incidence rate trends in on and off-reserve Aboriginal populations, 1986-2005.

	Total							
	1986-1990		1991-1995		1996-2000		2001-2005	
Reference Period	% change (direction)	p-value	% change (direction)	p-value	% change (direction)	p-value	% change (direction)	p-value
1986-90			26 (→)	0.3084	54 (↓)	0.0182	66 (↓)	0.0018
1991-95	26 (→)	0.3084			38 (→)	0.1549	54 (↓)	0.0267
1996-00	54 (↑)	0.0182	38 (→)	0.1549			26 (→)	0.0267
2001-05	66 (↑)	0.0018	54 (↑)	0.0267	26 (→)	0.0267		

4.3 Regression Analysis

Analysis on the main effects model demonstrated results that were indicative of under-dispersion ($\chi^2/df = 0.1952 < 1$). All model inferences were based on scaled parameter estimates to correct for this. Entering all variables simultaneously (year of diagnosis, age category, sex category, location of residence, and status category) determined that year, age, and location of residence were all significant predictors ($p < 0.0001$). Although the sex category was statistically non-significant ($p = 0.1600$) in the main effects model, it was retained due to its biological significance and to control for potential sources of effect modification and confounding. The status category demonstrated borderline significant results ($p = 0.0572$). Therefore, it was also retained in the main effects model.

Table 4.7.1 displays the results of the Poisson regression main effects model. The year of diagnosis, age category and location of residence were all significantly associated with the incidence of tuberculosis ($p < 0.0001$). Neither sex category, nor status appeared to have significant associations with the incidence of tuberculosis ($p = 0.1600$ and $p = 0.0572$, respectively), but were both kept in the model for the reasons described above.

Several first-order interactions (sex category with location of residence and age category with location of residence), included one at a time, did significantly improve the fit of the overall regression model ($p = 0.0343$ and $p = 0.0152$, respectively). When included in the model together, both interaction terms remained significant (Table 4.7.2). The first-order interaction of year with location of residence resulted in borderline significance and cross-tabs were performed and examined for observable trends, which

resulted in a non-significant finding. No other interactions tested in the model demonstrated any significant association with the incidence of tuberculosis.

In summary, the variables year of diagnosis, status category, and location of residence were all significant predictors of TB rates in the on and off reserve population. The variables sex and age were effect modifiers of location of residence, meaning that the strength of the association between residence and TB rates could be modified by the level of sex (male or female) or age (0-14 or 15+) the researcher is interested in.

TABLE 4.7.1: Poisson regression reduced model for the incidence of tuberculosis in Saskatchewan Aboriginal population 1986-2005 (*n* = 1750)

Main Effects Model (Reduced)					
Parameter	β (estimate)	SE(β)	OR	95% CI	P value
Year category (vs. 1986-90)					
2001-2005	-0.73	0.12	0.48	0.38, 0.61	<0.0001
1996-2000	-0.71	0.12	0.49	0.39, 0.62	<0.0001
1991-1995	-0.19	0.11	0.83	0.67, 1.02	0.0829
Sex category (vs. Female)					
Male	0.12	0.08	1.12	0.96, 1.32	0.1600
Age category (vs. 15+)					
0-14	0.47	0.08	1.60	1.36, 1.88	<0.0001
Residence (vs. on reserve)					
Off Reserve	-0.45	0.10	0.64	0.52, 0.78	<0.0001
Status Category (vs. nonregistered)					
Registered Aboriginal	0.21	0.11	1.24	0.99, 1.54	0.0572

TABLE 4.7.2: Poisson regression final model for the incidence of tuberculosis in Saskatchewan Aboriginal population 1986-2005 (*n* = 1750)

Interaction Model (Full)					
Parameter	β (estimate)	SE(β)	OR	95% CI	P value
Year category (vs. 1986-90)					
2001-2005	-0.73	0.11	0.48	0.39, 0.60	<0.0001
1996-2000	-0.70	0.11	0.50	0.40, 0.61	<0.0001
1991-1995	-0.18	0.10	0.83	0.68, 1.02	0.0702
Sex category (vs. Female)					
Male	-0.05	0.11	0.95	0.76, 1.18	0.6516
Age category (vs. 15+)					
0-14	0.66	0.11	1.94	1.56, 2.43	<0.0001
Residence (vs. on reserve)					
Off Reserve	-0.41	0.15	0.66	0.49, 0.89	0.0059
Status Category (vs. non-registered)					
Registered Aboriginal	0.23	0.11	1.25	1.02, 1.54	0.0340
Onoffreserve x sexcat	0.33	0.16	1.39	1.02, 1.88	0.0344
Onoffreserve x agecat	-0.38	0.16	0.68	0.50, 0.93	0.0155

CHAPTER 5:

5.0 DISCUSSION

The purpose of this study was to describe the epidemiology of incident pulmonary tuberculosis in Saskatchewan's Aboriginal population between 1986 and 2005. In addition, trends in incidence rates over time were identified and a regression model was developed to describe significant variables in the rate differences between the on and off reserve populations.

Overall, the majority of the results generated from this study were consistent with other relevant research findings. The following discussion will describe how our results compared with others, potential reasons for these findings, as well as study limitations and policy implications.

5.1 Descriptive Epidemiology and Trend Analysis

5.1.1 Tuberculosis and Age

Overall this study found a mean age in on-reserve cases of 12.92 (SD=18.29) (median age =4) and 19.98 (SD=19.94) (median age = 14) in off-reserve cases. Between 1986 and 1995, those in the 0-14 age group maintained higher age-adjusted TB rates both on and off reserve, as compared to the 15+ age group. This trend continues through to 2005 in the on-reserve population. However, between 1996 and 2005, the 15+ age group experienced higher age-adjusted rates (compared to the younger group) off-reserve. Overall, the proportion of cases found in the <15 age group both on and off-reserve exceeds their proportion of the total population.

These results are partially consistent with published literature, although different age categories in various studies make direct comparisons difficult. Results from studies conducted in some high burden countries such as South Africa indicate that children <13 years old are being under-diagnosed. A study by Marais et al (47, 48) found children under 13 experienced over half of the tuberculosis recorded in adults but only 13.7% had been diagnosed through the usual methods. This might suggest that those in younger age groups are bearing the greatest burden of TB worldwide, but are being missed by current surveillance and detection protocols in some nations. Marais et al (48) reported an incidence rate of >400/100,000 in children under 13 in Cape Town, South Africa. However, as is similar in many other regions of the world, the treatment of childhood TB is not a priority. This is because, from a TB control point of view, some would argue they represent a “dead-end”. That is, they rarely transmit the disease and contribute little to the maintenance of the epidemic (47). Others would argue that children and young adults do contribute a significant proportion of TB burden and that there are several reasons it is important to study and control paediatric TB. Nelson et al (49) reported that, of the total number of cases estimated worldwide in 2000, 11% of those were children. Starke (50) argues that there are three main reasons why gaining a better understanding of these rates is so important. The first being that children are more prone to developing extra-pulmonary and other more life threatening forms of tuberculosis, compared to adolescents and adults. These can, in turn, produce crippling disease and death in children due to meningitis and disseminated disease. Second, Starke argues that paediatric tuberculosis acts as a public health measure of recent transmission of *Mycobacterium tuberculosis*, as children who develop disease tend to do so rapidly

(weeks-months after primary infection). Therefore, they serve as an indicator of the current rate of TB transmission. Finally, childhood TB rates serve as a measure of future public health because most adults that develop TB disease were infected during childhood. Theoretically then, prophylactic treatment during childhood could prevent most contagious cases of TB disease in adulthood.

Despite several convincing arguments, there is significant evidence to suggest that the accurate surveillance, detection and prompt treatment of paediatric TB is not a priority in many locations. It is difficult to diagnose a child with tuberculosis for several reasons. Problems getting quality sputum samples and results, lack of contact investigation, and adult (contagious) case focused resources all contribute to these difficulties.

In Canada, several studies have provided evidence that children and young adults represent a large proportion of the tuberculosis burden. Long (21) reported that between 1987 and 1995, rates in children under 15 years were on the rise while those in age groups 25-34 and ≥ 65 were decreasing.

Contrary to our results, however, a study of Alberta Registered Aboriginal populations (51) demonstrated the highest age-specific TB rates in the ≥ 65 age group, the same as for the Canadian born non-Aboriginal population of that province. It is unclear why this difference exists between neighbouring provinces. However, it may be related to the incorporation in our study of non-registered Aboriginals and the examination of off-reserve individuals. Those Aboriginal individuals residing off-reserve tend to be younger (52) and therefore, the Alberta study may have yielded similar results with the inclusion of these other groups. In addition, the Saskatchewan TB control program is

more aggressive at case finding among those under age 14, as it has been found that they represent the highest case rates and numbers. The younger patients are found quite often during screening prior to developing active disease (active detection), whereas the older patients are found because they present with symptoms when they are sick (passive detection). In other words, if the method of detection is passive, the patients that are diagnosed are likely to be older.

The difference in the mean age between on and off-reserve cases could possibly be related to the age structure of the two locations. As employment is the most often cited reason for moving off reserve, the 15-34 age range makes up the greatest proportion of those living in these locations and the mean age of the cases is likely to reflect the demographic make-up of that population.

According to Grigg's wave theory of tuberculosis epidemiology mentioned earlier, an asymmetrical curve can be drawn that defines the natural history of tuberculosis within a population (19). The ascending limb of the curve represents the increase in morbidity and mortality in an immune naïve population following the introduction of *M. tuberculosis*. The gradual decline of the curve occurs following the eventual peak in incidence and mortality and shift from non-immune to immune status of the majority of the population. According to this hypothesis, the age of individuals with TB disease will also change over the course of the epidemic. Early in the epidemic, children and young adults are the most susceptible and have the greatest risk of developing disease. They will also be expected to progress from infection to disease quickly due to their non-immune status. As the Saskatchewan Aboriginal population is at a relatively early stage in the tuberculosis epidemic compared to the Canadian-born non-Aboriginal group, the

high rates of TB disease in the younger population is consistent with those expected from Grigg's hypothesis.

As mentioned before, the more aggressive case finding in those under 14 years of age on reserve may also play a major role in the TB age epidemiology found in the Saskatchewan Aboriginal population. It would be an interesting follow-up study to determine whether the age differences found in this analysis would remain if the methods of detection were controlled for.

5.1.2 Tuberculosis and Gender

Gender and tuberculosis has been a well studied area in recent years. Worldwide, the ratio of male to female reported cases is approximately 1.5-2:1 (53, 54). Results from our study were partially consistent with this finding as the crude rate of male cases off-reserve (69.37 per 100,000) was almost 1.5 times that of the off-reserve female crude rate (50.57 per 100,000). However, on-reserve, the crude rate of reported female cases (185.85 per 100,000) was slightly higher than that of the male rate on-reserve (180.95 per 100,000).

As a group, women tend to have longer life expectancy than men of the same socio-economic status (55). However, in many communities, women report more illness and poorer health than men of the same age. The explanation for this paradox lies in the complex relationship between biological factors and social influences. Some examples of biological differences between sexes include the slower maturation of male lungs due to testosterone, chromosomal structure differences that favour female longevity, and female

endogenous hormones that help protect against heart disease (55). There have also been relatively recent changes in social factors that have served to enhance women's inherent biological advantage. Examples include the introduction of birth control measures and enhanced maternity services, as well as the increased post-industrialization role of men as the "bread-winner" in the family, which led to increased occupational deaths compared to women (55).

So why do women often report poorer health outcomes than men? One explanation lies with their longevity. In other words, if an individual lives longer, there is more opportunity for health problems to develop. Other studies have found that women are more likely to suffer reproductive health problems (i.e. cervical and breast cancer, unsafe abortions, etc.) and are more likely to report symptoms of mental illness and stress-related disorders compared to their male counterparts (56).

In terms of tuberculosis rate differences, numerous studies have been conducted to assess the true burden of disease in males and females in different settings (53-55, 57-69). The general consensus on this issue seems to be that there is no consensus regarding the male to female ratio of reported TB cases. Studies conducted in Vietnam, Nepal and Africa found that cases in women are being under-detected due to various barriers associated with being female in those settings (61, 66, 67, 69). For example, Cassels (69) found that through passive case finding, females made up 28% of 159 cases reported in Nepal. However, through active case detection in the same region, 46% of 111 reported cases were female. Other studies have found differences in care seeking and treatment behaviour among men and women (54, 57, 70). Thorson (65) found that, in Vietnam,

more women than men had long-standing cough, delayed seeking care and did not give sputum for diagnosis.

Other studies seem to indicate that higher notification rates in males could partly reflect differences in epidemiology such as differences in exposure and/or risk of infection, and differences in rates of progression to disease. Several studies have found that women of reproductive age have a greater propensity to develop disease after infection with *M. tuberculosis* (progression rate), compared to men of the same age (65, 71, 72). Other studies have identified differential sensitivities to commonly used *M. tuberculosis* detection procedures, resulting in more positive skin tests and/or smear positive results for males (62, 71). Differences in exposure and risk of infection may be attributed, in many cases, to sex differentials in the number of contacts inside and outside the household. It has been hypothesized that males of reproductive age have more frequent external contacts and are, therefore more likely to become exposed to and infected with *M. tuberculosis* (70). Males and females prior to adolescence will theoretically have similar contacts with people outside the house and family, which would explain why the sex difference in notification rates is not generally seen until after age 15.

In summary, theories regarding the sex differentials in pulmonary tuberculosis include: differential biological susceptibility to infection and likelihood of progression to disease following infection, as well as differential sensitivities to various testing procedures. They also include possible under-notification due to various economic, social and cultural factors such as insufficient access to income, legal rights, social status and education.

In the Canadian context, it is well documented that Aboriginal women bear a disproportionate burden of health problems, compared to both non-Aboriginal Canadians as well as Aboriginal men (38, 58). They experience lower life expectancy, higher suicide rates, and higher rates of chronic conditions such as diabetes, heart disease, and cancer on reserve (38). Off reserve, Aboriginal women are more likely than Aboriginal men and the general Canadian population to report fair or poor health (73, 74).

The results found in our study could have several potential explanations in light of the theories mentioned above. As the rates of pulmonary TB in males and females off-reserve are fairly consistent with other studies, explanations could include those epidemiological differences discussed earlier and/or a combination of social factors resulting in the noted male: female ratio. As mentioned in the literature review, more resources are currently allocated for on-reserve screening and case detection in Saskatchewan. There is the possibility that several factors are serving as gender-based barriers to diagnosis and treatment of TB in Aboriginal women off-reserve. More research into this possibility is required to gain better understanding.

On reserve, the reported cases of pulmonary TB in males and females are very similar. One explanation could be the greater attention to active case detection in these communities due to greater resource availability. Another interesting theory has to do with the recently documented interaction between Diabetes mellitus and tuberculosis. A study conducted by Pérez-Guzman et al (75) in Mexico found that the presence of diabetes modifies the male: female ratio in pulmonary tuberculosis. In a group of patients with both diabetes mellitus and pulmonary TB, there was a gradual decline of male predominance in rates with increasing age, until after age 50, female rates became higher

than male. Therefore, if these results can be applied to other populations, the high rate of diabetes in the Aboriginal population on-reserve may be playing a role in the trend reversal of male and female crude rates.

As mentioned previously, gender refers to both, biological differences between sexes, as well as the behaviours, expectations and societal roles that exist within the cultural, social, and political contexts (68). Of course, these contexts can differ markedly between cultures. Therefore, cross-cultural comparisons in this area may serve to identify common and distinctive barriers to TB control and prevention, in order to design and employ a generic research protocol that could be adapted for local use.

5.1.3 Tuberculosis and Ethnicity

The concept of ethnicity has been touched on briefly several times in this thesis, in the context of various health discrepancies between Aboriginal and non-Aboriginal ethnic groups. The notion of ethnicity can be very closely linked to identity, a concept which has had a major impact on the lives of Canadian Aboriginal peoples, and will be discussed in greater detail here.

Issues of identity and status have direct effects upon matters such as membership in an ethnic group, resources allocation, research, politics, epidemiology and identification of health determinants. However, Aboriginal identity is far from being a simple issue: As one researcher stated, “Identity will be a source of pride for some, a source of confusion for others, and will pervade the discussion of any policy or programmatic matters for organizations and governments...” (76).

To establish identity, there are two main approaches; objective and subjective. In the objective method, several attributes are established to identify the boundaries of that identity. These attributes are generally indicators that can be seen or measured objectively, such as hair texture, skin colour, and language (77). The other approach is less structured and is based upon more subjective measures of self. Therefore, using this approach, there are no measurable criteria that would establish an individual's identity as Aboriginal, Métis, Inuit, or other. Using this approach, if a person feels Aboriginal, then he or she is Aboriginal. This approach to identity and status is a lot more fluid and lies in the conceptualization of self at an individual level.

The problem of identity is not one that can be solved, as it is a question with several correct answers, depending on the perspective used. As a result, there has been considerable conflict over the precise status of distinct Aboriginal groups. One result of the issues around definition and identity is that statistical information for the distinct populations (Aboriginal, Métis, Inuit) and research into demographics and/or population health is restricted by inaccurate, incomplete, or complete lack of data, or the inability to extrapolate from sample data sources. For the purposes of this study, legal definitions, as defined by the Federal government were used. However, this is not to imply that these definitions are the only ones, or that they are the most commonly used by the Aboriginal population itself. With this in mind, what little literature that is available comparing distinct Aboriginal groups may have some degree of overlap, depending on the source of the data. It is equally important to note that the category "non-registered Aboriginal" used in this study includes several distinct groups, and may therefore, not be representative of each distinct group.

Although many studies have been conducted comparing the health status of Aboriginal and non-Aboriginal groups, very little research has been done comparing the health status between distinct Aboriginal populations. Our results are mixed, depending on the location of residence. On-reserve registered Aboriginals had a greater overall crude rate (183.70 per 100,000), compared to their non-registered counterparts (163.27 per 100,000). However, off reserve, the opposite was true, with the non-registered crude rate (62 per 100,000) exceeding that in the registered population (56.73 per 100,000). It is unclear at this point why there is a difference in rates between the two status groups. However, according to census data, there were very few non-registered Aboriginals living on-reserve and that may have played a role in skewing the rate calculations for that group.

Being registered under the Indian Act confers the rights and privileges of Indian Status in Canada. There is no similar recognition of status or required registration for Métis. While the constitution Act of 1982 identified Indian, Inuit and Métis as Aboriginal people, the Canadian government only claims responsibility for providing services and programs for registered Aboriginals and Inuit. This categorization has implications for access to services such as TB control, legal rights, and land and has been a source of contention for decades. Qualitative research methods could play a vital role in assessing how the concepts of identity and status impact the health of different Aboriginal groups in Saskatchewan.

The results found in this analysis demonstrate negligible differences in the age-adjusted rates of pulmonary TB between registered and non-registered Aboriginals, both on and off-reserve, although rates in the non-registered population on reserve appear to

vary significantly. This is most likely due to the very low non-registered population on reserve, resulting in skewed rates from small denominators. As previously discussed, the determination of status is a political rather than biological determination. Therefore, the negligible differences in rates by status may be an expected result if biological determinants of TB are the focus.

5.1.4 Tuberculosis and location of residence

The main goal in conducting this study was to compare the pulmonary tuberculosis situation between Aboriginal individuals living on-reserve with those living off. This is a relatively new area of study, despite the fact that the Aboriginal population off-reserve in Canada has been increasing steadily for decades (74). In 2000/2001, Statistics Canada conducted an Aboriginal People's Survey (APS), which collected specific information regarding the health and well-being of all Aboriginal people, including those living off reserve. Although, at that time, there were more Aboriginal Canadians living off-reserve than on, this represented the first national initiative aimed at improving understanding of the health of this group (78).

Reserves are Crown lands that have been set aside for the exclusive use of registered Aboriginals, although some non-registered people will also reside there (79). Although some may argue that reserves represent a reminder of past assimilation practices and colonial domination, they are also a family home to many and serve as a base from which to negotiate political autonomy (79).

However, the question remains, is there a difference in the overall health of those Aboriginal people who live on and off-reserve? If so, which is the healthier group in general? According to Grigg's (19) curve theory of tuberculosis, the flatness of the curve

(i.e. morbidity and mortality rates) and the time required to reach the lowest level of incidence and mortality, are inversely proportional to a population's "degree of urbanization". The term "urbanization", in this context, refers to all factors which increase the opportunity of infection and environmental stress (e.g. crowded living conditions, insufficient food intake, etc.). In these conditions, more of the susceptible population is exposed to *M. tuberculosis*, the wave rises faster and peaks higher, but the selection is also faster so a low level is reached in a shorter time period. This theory could potentially be applied to both on-reserve and urban off-reserve populations (According to 2001 census, 68% of non-reserve Aboriginals lived in urban areas (74)), as conditions such as Grigg described can exist in both situations (e.g. overcrowding, poverty, etc.).

So far, as relevant data on the health of those residing off-reserve remains inadequate, their health status is often extrapolated from health statistics for registered Aboriginals living on-reserve. Some would argue that this method ignores specific issues and needs of those individuals living off-reserve (80). The available information regarding Aboriginal health and location of residence would support the idea that both on and off-reserve populations suffer from many of the same health problems, such as higher rates of some chronic conditions (arthritis, diabetes, hypertension), and lower self-perceived health as compared to the non-Aboriginal population. When we look at health as, not just the absence of disease, but as a state of emotional and spiritual well-being, we can see that both groups experience similar social problems, such as increased rates of alcoholism (22.6% vs. 16.1%), overcrowding, and poverty (44% live below the poverty line), compared to the general Canadian population (78). In 2001, 18% of Aboriginal

people living in Saskatoon lived in crowded (>1 person per room) households, more than 3x the proportion of 5% for the total population (74). In 2002, Clark et al reported that TB rates in Canadian reserves were higher in those communities that were more isolated and had higher housing density (>0.8 persons per room). Overcrowding has been shown in numerous studies to play a role in tuberculosis transmission by increasing the risk of exposure, although we were not able to examine this factor in the current study (31, 81).

Despite some of the stated similarities between these groups, some would question whether certain advantages or disadvantages exist, in terms of health, depending on their location of residence. In 2002, the National Chief of the Congress of Aboriginal People, Dwight Dory stated, “In some ways, Aboriginal peoples off-reserve are in the worst of all possible positions—we carry the unhealthy legacy of Aboriginal policies and dysfunctional backgrounds, without the support and encouragement of the Aboriginal community around us.” He argues that part of the problem is government policy, funding and support is more focused on Aboriginals who live on reserves, while those living off are often forgotten, despite the similar health issues (78).

However, despite the many reported social and cultural advantages (language retention, sense of community) of living on-reserve (39), the trend continues of movement away from the reserves, with employment, education and better living accommodations being the most cited reasons for the move (82). So does the opportunity for greater income and better living conditions necessarily translate to better health outcomes for these populations? Or, in reality, do continued problems with unemployment, increased loss of cultural identity, racism and barriers to adequate housing and culturally appropriate health services continue to result in poor health

outcomes for the off-reserve Aboriginal population? Unfortunately the focus on the health of Aboriginal groups based on geography is still relatively new, and most of these questions can not be answered accurately. The Statistics Canada Aboriginal People's Survey has been a step in the right direction, but follow-ups to this study are needed to identify what, if any, specific challenges continue to exist for the overall health of Aboriginal people in Canada, both on and off-reserve.

Our results indicate that a greater proportion of new pulmonary cases occurred on-reserve over the study period (1040 on and 710 off-reserve, overall). In addition, the trend analysis demonstrated significantly higher rates on reserve compared to those off, across the study period. These results were surprising at first, given that the initial hypothesis, based on preliminary data from the Saskatchewan TB Control Program, was that tuberculosis cases off-reserve were beginning to match or outnumber those reported on. It was determined through closer investigation that, although the number of new pulmonary TB cases off-reserve remain lower than those reported on, the numbers of relapse cases (which were not initially examined in our analysis) are higher in the off-reserve population (52.7% of cases off-reserve vs. 47.3% on-reserve) (Table 3.2). Again, it is unclear at this point what factors may be involved in this trend, as all reported cases in Saskatchewan are treated using the DOT strategy and theoretically, those living in urban centres would have greater access to health services compared to those living in more remote, reserve communities. Follow-up research would be of use here to determine whether relapse cases are, in fact, on the rise in off-reserve Aboriginal populations, and if so, why this might be.

In addition, although also not examined statistically in this study, completion data were gathered for a three year time period (2000-2002) and descriptive frequencies were reported. A quick look at these numbers seems to indicate that the vast majority of patients diagnosed in that time period completed 80% or more of their drug treatment, regardless of their location of residence. This is encouraging information, as it suggests that distance from health services is not acting as a barrier to treatment completion. Whether access to diagnostic and health services is acting as a barrier at the diagnostic level remains to be determined and further research would be of interest in that context.

5.2 Poisson Regression

The purpose of the poisson regression analysis was to investigate the association of location of residence on the incidence of pulmonary tuberculosis in Saskatchewan Aboriginal populations, in combination with other factors of interest, across the study period 1986 to 2005.

The results of the regression analysis indicate that a person's status, the year of their diagnosis, their age and sex, and their location of residence, are all significantly associated with the incidence of pulmonary tuberculosis over the study period. Age and sex proved to have significant interaction effects in our model ($p=0.0344$ and $p=0.0155$, respectively), meaning that the impact of location of residence on the incidence of pulmonary TB is modified by the individual's sex and age. Therefore, an interaction term was added to our model for each effect modifier. Although age and sex are also often suspected confounding variable, the presence of an interaction effect means that the assumption that the effects of these variables on the outcome (TB incidence) is the same,

regardless of the level of the confounder, is violated (83). Therefore, no further tests for confounding were necessary.

5.3 Study Limitations and challenges

There are several limitations to this study. The use of census data in Aboriginal research has been questioned due to potential under-representation of the population (84). If we assume the denominator populations are, in fact, under-estimated, our resulting crude TB rates would be higher than those that actually exist. As previously discussed, the census data was the most complete source of data available for the analysis of interest in this study, and was therefore used as opposed to the other potential sources mentioned previously. One of the greatest challenges for the completion of this study was the immense amount of effort needed to derive population denominators. Often, the census tables were not reported the same from census to census, leaving out some variables of interest in some years, and adding different ones in other years. In addition, the definitions used in the census of Registered vs. Non-registered Aboriginal fluctuated between census years and one could not be sure if people were being double counted or not counted at all.

The use of secondary data, while cost effective and timely, restricted the depth of analysis that was possible for this study. Socio-economic variables such as income, education and housing information would be desirable in order to more comprehensively assess the TB situation in Saskatchewan's Aboriginal populations. In addition, the limited availability of many of the population parameters of interest (i.e number of non-

registered Aboriginals in a given health region) was a barrier to conducting some analysis due to lack of denominator data.

Finally, the exclusion of relapse and non-pulmonary cases of TB was decided at study onset. However, inclusion of these cases in all study analysis (not solely descriptive statistics), may have had an impact on results. For example, as we found a greater number of relapse cases off-reserve compared to on, inclusion of these cases may have supported the initial hypothesis that off-reserve Aboriginals are experiencing an increase in total tuberculosis cases over time, compared to those living on-reserve.

5.4 Policy implications

Upon examination of the results of this study, it would appear that the Saskatchewan TB control program is making improvements in case finding, diagnosis and treatment of pulmonary TB cases in the Aboriginal population of this province. Overall, pulmonary TB rates, both on and off reserve are steadily decreasing, although not to as great of an extent off reserve compared to on. One suggestion may be to increase the aggressiveness of case finding and screening off reserve, although this is a difficult assessment to make without complete and accurate information. Therefore, the single most important recommendation I can make following completion of this study would be to increase surveillance efforts in the province. In order for researchers to obtain a more precise picture of the TB situation in Saskatchewan's Aboriginal population, accurate surveillance data is needed. This requires the collection of population statistics that are reported in a clear, consistent manner across time periods.

Having said that, it is understood that the challenges that face federal, provincial and local agencies charged with such a task, are vast and complications with issues of identity mentioned earlier are sure to arise. It is with good intentions that these recommendations are made, but to what extent can they be implemented at the ground level? It is hoped that in future, various aspects of Aboriginal culture and identity are incorporated in more concrete definitions of identity that can be mutually agreed upon. In addition, the various agencies that collect information on Aboriginal populations need to open up communication lines in order to become more consistent in their reporting of statistics. This will be beneficial to researchers and policy makers alike, as it will provide more focus to certain claims and strengthen the arguments for beneficial policy implementations or changes.

CHAPTER 6:

6.0 CONCLUSIONS

Results from this study indicate that, while the incidence of pulmonary tuberculosis in Saskatchewan's Aboriginal population has decreased over the study period, rates of new cases have remained consistently higher on-reserve compared to those off. Year of diagnosis, status (registered and non-registered Aboriginal), and location of residence had the strongest association with incidence of pulmonary tuberculosis, while age and sex were effect modifiers.

Further research is needed regarding the health status of non-reserve Aboriginals in Saskatchewan and how it differs from those living on reserve. In addition, the collection of more accurate population statistics would allow for more in-depth follow-up studies, both quantitative and qualitative, that include broader determinants of health in the context of the Aboriginal tuberculosis situation in Saskatchewan. By identifying those who are the greatest risk of developing TB disease, and the factors responsible for that risk, resources can be used in the most efficient way to decrease the individual's risk of disease, and to prevent future transmission.

Although there is a natural history to infectious disease epidemics such as tuberculosis, it should be a higher priority of government policies and services to further decrease morbidity and mortality, in spite of falling case rates. Examining both biological and socio-economic variables is important in understanding the epidemiology of TB in Saskatchewan's Aboriginal population.

REFERENCES

1. Yang Z, Kong Y, Wilson F, et al. Identification of risk factors for extrapulmonary tuberculosis. *Clin Infect Dis* 2004;38(2):199-205.
2. Enarson DA. Tuberculosis in Aboriginals in Canada. *Int J Tuberc Lung Dis* 1998;2(9 Suppl 1):S16-22.
3. Young TK. Aboriginal health: not just tuberculosis. *Int J Tuberc Lung Dis* 1998;2(9 Suppl 1):S23-5.
4. Public Health Agency of Canada. Tuberculosis in Canada 2002: Health Canada; 2002.
5. Frideres JS GR. Aboriginal peoples in Canada: Contemporary conflicts. 6th ed ed. Toronto, Canada: Prentice Hall; 2001.
6. Statistics Canada. 2001 Census Profile of Saskatchewan: Government of Canada; 2001. Cat no. 92-377-XIE.
7. Saskatchewan Tuberculosis Control Program. *Saskatchewan Tuberculosis Control Program Annual Reports*. Saskatoon, Canada: Saskatchewan Health, Government of Saskatchewan; 1990-2003.
8. Grzybowski S, Styblo K, Dorken E. Tuberculosis in Eskimos. *Tubercle* 1976;57(4 Suppl):S1-58.
9. Saskatchewan Health. Saskatchewan Health Registration covered population. Accessed Jan. 3, 2006 at http://www.health.gov.sk.ca/mc_dp_covpop2005/ms_office/CovPopBook2005NoFormulas.xls.
10. Frieden TR, Sterling TR, Munsiff SS, Watt CJ, Dye C. Tuberculosis. *Lancet* 2003;362(9387):887-99.
11. Raviglione MC. The TB epidemic from 1992 to 2002. *Tuberculosis (Edinb)* 2003;83(1-3):4-14.
12. Conti AA, Lippi D, Gensini GF. Tuberculosis: a long fight against it and its current resurgence. *Monaldi Arch Chest Dis* 2004;61(1):71-4.
13. Espinal MA. The global situation of MDR-TB. *Tuberculosis (Edinb)* 2003;83(1-3):44-51.

14. WHO. WHO Expert Committee on Tuberculosis. Technical Reports Series no.552 Ninth Report. Geneva, Switzerland: WHO; 1974.
15. Campos-Outcalt D. Tuberculosis: old problem, new concerns. *J Fam Pract* 2003;52(10):792-8.
16. Carnie J, Randall M, Ng MM. Tuberculosis. The old and the new. *Aust Fam Physician* 1998;27(7):615-8.
17. FitzGerald JM, Wang L, Elwood RK. Tuberculosis: 13. Control of the disease among aboriginal people in Canada. *Cmaj* 2000;162(3):351-5.
18. Plant AJ, Krause VL, Condon JR, Kerr C. Aborigines and tuberculosis: why they are at risk. *Aust J Public Health* 1995;19(5):487-91.
19. Grigg ER. The arcana of tuberculosis with a brief epidemiologic history of the disease in the U.S.A. *Am Rev Tuberc* 1958;78(2):151-72 contd.
20. Ferguson R. Tuberculosis among the Indians of the great Canadian Plains. London: Saskatchewan Anti-Tuberculosis League; 1917.
21. Long R, Njoo H, Hershfield E. Tuberculosis: 3. Epidemiology of the disease in Canada. *Cmaj* 1999;160(8):1185-90.
22. Medical Service Branch. Tuberculosis program and epidemiological review. Ottawa: 1999.
23. Hoepfner VH. Personal correspondence. Saskatoon, SK; Oct. 31, 2005.
24. Saskatchewan Tuberculosis Control Program. Saskatchewan Tuberculosis Control Manual: A reference guide to the tuberculosis program in Saskatchewan. Saskatoon, Canada: Saskatchewan Health; 2002.
25. INAC. Registered Indian Population by Age and Sex 1998-2004. Accessed January 16, 2006, at <http://www.ainc-inac.gc.ca/pr/sts/rip>
26. Lux MK. *Medicine that walks: Disease, Medicine, and Canadian Plains Native People 1880-1940*. Toronto, Canada: University of Toronto Press; 2001.
27. Hoepfner VH. Tuberculosis in Saskatchewan Treaty Indians. *Prairie Medical Journal* 1995;65(1):18-20.
28. Hoepfner VH, Marciniuk DD. Tuberculosis in aboriginal Canadians. *Can Respir J* 2000;7(2):141-6.

29. Grzybowski S. Epidemiology of tuberculosis and the role of BCG. *Clin Chest Med* 1980;1(2):175-87.
30. Ward H. Risk factors in the progression from tuberculosis infection to disease. Saskatoon: University of Saskatchewan; 2004.
31. Clark M, Riben P, Nowgesic E. The association of housing density, isolation and tuberculosis in Canadian First Nations communities. *Int J Epidemiol* 2002;31(5):940-5.
32. Cummings KC, Mohle-Boetani J, Royce SE, Chin DP. Movement of tuberculosis patients and the failure to complete antituberculosis treatment. *Am J Respir Crit Care Med* 1998;157(4 Pt 1):1249-52.
33. Canada Mortgage and Housing Corporation. Effects of urban Aboriginal residential mobility. Ottawa; 2002.
34. Cresswell T. *In Place Out of Place: Geography, Ideology and Transgression*. Minneapolis, Minnesota: University of Minnesota Press; 1996.
35. Deprez P SG. *Economic Status of the Canadian Indian: A re-examination* . Winnipeg, Canada: University of Manitoba; 1969.
36. Hawkes DC, ed. *Aboriginal Peoples and government responsibility: Exploring federal and provincial roles*. Ottawa, Canada: Carleton University Press; 1989.
37. Speck D. The Indian Health Transfer Policy: A step in the Right Direction, A revenge of the hidden policy? *Native Studies Review* 1989;5(1):187-214.
38. Waldram JB HD, Young TK. *Aboriginal Health in Canada: Historical, cultural and epidemiological perspectives*. Toronto, Canada: University of Toronto Press; 1995.
39. Peters E. *Aboriginal People in Urban Areas*. pgs:45-70.
40. Peters E. Developing federal policy for First Nations people in urban areas: 1945-1975. *The Canadian Journal of Native Studies* 2001;21:57-96.
41. Health Canada. *Tuberculosis Control: A reference guide to the tuberculosis program in Saskatchewan, 2002*. Saskatchewan: Health Canada FNIHB; 2002.
42. Health Canada. *Canadian Tuberculosis Standards*. 5th ed: Canadian Lung Association; 2000.
43. *Diagnostic Standards and Classification of Tuberculosis in Adults and Children*. This official statement of the American Thoracic Society and the Centers for Disease Control and Prevention was adopted by the ATS Board of Directors, July 1999. This

statement was endorsed by the Council of the Infectious Disease Society of America, September 1999. *Am J Respir Crit Care Med* 2000;161(4 Pt 1):1376-95.

44. Gordis L. Measuring the Occurrence of Disease. In: *Epidemiology*. Philadelphia: W.B Saunders; 2000.

45. SAS Institute Inc. SAS Software Release 9.1. In. 9.1 ed. Cary, NC, USA; 2006.

46. Kleinbaum DG KL, Muller KE, Mizam A. *Statistical Inference: Estimation in Applied Regression Analysis and other Multivariate Methods*. 3rd ed. Pacific Grove: Duxbury Press; 1998.

47. Marais BJ, Gie RP, Schaaf HS, Beyers N, Donald PR, Starke JR. Childhood pulmonary tuberculosis: old wisdom and new challenges. *Am J Respir Crit Care Med* 2006;173(10):1078-90.

48. Marais BJ, Hesselning AC, Gie RP, Schaaf HS, Beyers N. The burden of childhood tuberculosis and the accuracy of community-based surveillance data. *Int J Tuberc Lung Dis* 2006;10(3):259-63.

49. Nelson LJ, Wells CD. Global epidemiology of childhood tuberculosis. *Int J Tuberc Lung Dis* 2004;8(5):636-47.

50. Starke JR. Pediatric tuberculosis: time for a new approach. *Tuberculosis (Edinb)* 2003;83(1-3):208-12.

51. Long R, Sutherland K, Kunimoto D, Cowie R, Manfreda J. The epidemiology of tuberculosis among foreign-born persons in Alberta, Canada, 1989-1998: identification of high risk groups. *Int J Tuberc Lung Dis* 2002;6(7):615-21.

52. Peters E. Geographies of Aboriginal people in Canada. *The Canadian Geographer* 2001;45(1):138-44.

53. Holmes CB, Hausler H, Nunn P. A review of sex differences in the epidemiology of tuberculosis. *Int J Tuberc Lung Dis* 1998;2(2):96-104.

54. Uplekar MW, Rangan S, Weiss MG, Ogden J, Borgdorff MW, Hudelson P. Attention to gender issues in tuberculosis control. *Int J Tuberc Lung Dis* 2001;5(3):220-4.

55. WHO. Sex, Gender and Health. WHO, 1998. (Accessed Jan.6, 2006 at www.WHO.int/docstore/gender-and-health/pages/word/)

56. Paykel ES. Depression in women. *Br J Psychiatry Suppl* 1991(10):22-9.

57. Borgdorff MW, Nagelkerke NJ, Dye C, Nunn P. Gender and tuberculosis: a comparison of prevalence surveys with notification data to explore sex differences in case detection. *Int J Tuberc Lung Dis* 2000;4(2):123-32.
58. Bourassa C., McKay-McNabb K, Hampton M. Racism, Sexism, and Colonialism: The impact on the health of Aboriginal women in Canada. (Accessed Feb 18, 2006, at http://www.canadaconference.ca/pdf/reading_module1cdnwoman.pdf)
59. Chan-Yeung M, Noertjojo K, Chan SL, Tam CM. Sex differences in tuberculosis in Hong Kong. *Int J Tuberc Lung Dis* 2002;6(1):11-8.
60. Diwan VK, Thorson A. Sex, gender, and tuberculosis. *Lancet* 1999;353(9157):1000-1.
61. Eastwood SV, Hill PC. A gender-focused qualitative study of barriers to accessing tuberculosis treatment in The Gambia, West Africa. *Int J Tuberc Lung Dis* 2004;8(1):70-5.
62. Kivihya-Ndugga LE, van Cleeff MR, Ng'ang'a LW, Meme H, Odhiambo JA, Klatser PR. Sex-specific performance of routine TB diagnostic tests. *Int J Tuberc Lung Dis* 2005;9(3):294-300.
63. Martinez AN, Rhee JT, Small PM, Behr MA. Sex differences in the epidemiology of tuberculosis in San Francisco. *Int J Tuberc Lung Dis* 2000;4(1):26-31.
64. Thorson A, Diwan VK. Gender inequalities in tuberculosis: aspects of infection, notification rates, and compliance. *Curr Opin Pulm Med* 2001;7(3):165-9.
65. Thorson A, Hoa NP, Long NH. Health-seeking behaviour of individuals with a cough of more than 3 weeks. *Lancet* 2000;356(9244):1823-4.
66. Thorson A, Hoa NP, Long NH, Allebeck P, Diwan VK. Do women with tuberculosis have a lower likelihood of getting diagnosed? Prevalence and case detection of sputum smear positive pulmonary TB, a population-based study from Vietnam. *J Clin Epidemiol* 2004;57(4):398-402.
67. Thorson A, Johansson E. Equality or equity in health care access: a qualitative study of doctors' explanations to a longer doctor's delay among female TB patients in Vietnam. *Health Policy* 2004;68(1):37-46.
68. Upleker M, Rangan S, Ogden J. Gender and TB control: Towards a strategy for research and action. Geneva: WHO; 1999.
69. Cassels A, Heineman E, LeClerq S, Gurung PK, Rahut CB. Tuberculosis case-finding in Eastern Nepal. *Tubercle* 1982;63(3):175-85.

70. Hudelson P. Gender differentials in tuberculosis: the role of socio-economic and cultural factors. *Tuber Lung Dis* 1996;77(5):391-400.
71. Fine P. Immunities in and to tuberculosis: implications for pathogenesis and vaccination. In: Porter JDH MK, ed. *Tuberculosis back to the future*. Chichester: Wiley and Sons; 1993:53-78.
72. Murray CJ. Social, economic and operational research on tuberculosis: recent studies and some priority questions. *Bull Int Union Tuberc Lung Dis* 1991;66(4):149-56.
73. Prairie Women's Health Centre of Excellence. *Living Well: Aboriginal Women, cultural identity and wellness - A Manitoba Community Project*. Winnipeg; 2004.
74. O'Donnell V, Tait H, Statistics Canada. Housing Family and Social Statistics Division. *Aboriginal Peoples Survey, 2001 : initial findings : well-being of the non-reserve Aboriginal population*. Ottawa: Statistics Canada; 2003.
75. Perez-Guzman C, Vargas MH, Torres-Cruz A, Perez-Padilla JR, Furuya ME, Villarreal-Velarde H. Diabetes modifies the male:female ratio in pulmonary tuberculosis. *Int J Tuberc Lung Dis* 2003;7(4):354-8.
76. Lamouche J. *Environmental Scan of Métis Health Information, Initiatives and Programs*. 2002.
77. Frideres JS GR. Chap 1: The legacy of Canadian Colonialism - Aboriginal Identity. In: *Aboriginal Peoples in Canada: Contemporary conflicts*. Toronto: Pearson Education Canada Inc.; 2001:17-20.
78. Sibbald B. Off-reserve Aboriginal people face daunting health problems: *StatsCan. Cmaj* 2002;167(8):912.
79. Adelson N. The embodiment of inequity: health disparities in aboriginal Canada. *Can J Public Health* 2005;96 Suppl 2:S45-61.
80. Wigmore M, McCue D. No information on a forgotten people: how healthy are Native people in Canada when they live off reserve. *Arctic Med Res* 1991;Suppl:90-3.
81. Cantwell MF, McKenna MT, McCray E, Onorato IM. Tuberculosis and race/status in the United States: impact of socioeconomic status. *Am J Respir Crit Care Med* 1998;157(4 Pt 1):1016-20.
82. Anderson AB, Bridges and Foundations Project on Urban Aboriginal Housing., University of Saskatchewan., Social Sciences and Humanities Research Council of Canada., Canada Mortgage and Housing Corporation., Community-University Research Alliance. *Migration and mobility between reserve and city : a survey of Whitecap*

Dakota/Sioux First Nation residents in Saskatoon. Saskatoon, Sask.: University of Saskatchewan; 2004.

83. Hosmer DW LS. Applied Logistic Regression. First ed. New York: Wiley-Interscience; 1989.

84. Wright R. Using Census Data to Examine Aboriginal Issues: A Methodological Note. Glasgow, Scotland: University of Glasgow.

85. Stokes M. Categorical Data Analysis using the SAS System. In: Poisson Regression: Wiley and Sons; 2001:350-60.

86. The Five Elements of DOTS. WHO, 2006. (Accessed May 2, 2007, 2006, at <http://www.who.int/tb/dots/whatisdots/en/index.html>)

APPENDICES

APPENDIX A: Glossary of Terms

Over-dispersion: Occurs when the observed variance is larger than the nominal variance for a particular distribution. It occurs with some regularity in the analysis of proportions and discrete counts. Because their distributions are fixed by the mean, this is not surprising in distributions like binomial and poisson. When present, over-dispersion can have a major impact on inferences and needs to be accounted for (85).

Under-dispersion: Occurs when the observed variance is smaller than the nominal variance for a particular distribution. It occurs with some regularity in the analysis of proportions and discrete counts. Because their distributions are fixed by the mean, this is not surprising in distributions like binomial and poisson. When present, under-dispersion can have a major impact on inferences and needs to be accounted for (85).

Scaled Partial Deviance: Partial Deviance is analogous to the partial F-test used in ANOVA and multiple regression, and a -2 log likelihood test in Logistic regression: $DEV_{\text{reduced model}} - DEV_{\text{full model}}$. Scaled partial deviance is used in the event of over- or under-dispersion and is similar to partial deviance. However, the magnitude of the deviance is changed due to the multiplication of a constant $\theta = \chi^2/df$ (85).

DOTS: The DOTS strategy was designed for third world TB. It included government commitment to TB case finding with quality assured bacteriology, standard short course regimens with directly observed therapy, effective drug supply and management, monitoring treatment and evaluating outcomes (86).

APPENDIX B: Canada Census and Saskatchewan Health population comparison

Report

sex and residence combinations		Average Adjusted Rate (Saskhealth)	Average Adjusted Rate (Census)
Male off reserve	Mean	9.9853	8.9676
	N	20	20
	Std. Deviation	4.57826	4.49065
female off reserve	Mean	12.8738	12.2218
	N	20	20
	Std. Deviation	14.07322	14.32455
Male on reserve	Mean	14.5575	16.7600
	N	20	20
	Std. Deviation	5.82917	6.59195
female on reserve	Mean	14.8785	17.4016
	N	20	20
	Std. Deviation	8.65764	9.19410
Total	Mean	13.0737	13.8378
	N	80	80
	Std. Deviation	9.09291	9.85010

APPENDIX C: Canada Census populations

Total Aboriginal

	Male off reserve	Male on reserve	Female off reserve	Female on reserve
1986-90				
0-14	10005	5810	9980	5720
15-65+	13530	7745	15685	7085
1991-95				
0-14	14790	6635	13925	6350
15-65+	17565	9070	21265	8240
1996-2000				
0-14	16710	8360	15970	7905
15-65+	21250	11130	25560	10425
2001-2005				
0-14	14395	9970	14365	9570
15-65+	20655	13825	24750	13600

Registered Aboriginal

	Male off reserve	Male on reserve	Female off reserve	Female on reserve
1986-90				
0-14	4355	5655	4275	5575
15-65+	4250	7535	6005	6900
1991-95				
0-14	5460	5870	5710	5330
15-65+	6870	7385	7975	7445
1996-2000				
0-14	8695	8215	8090	7765
15-65+	8115	10840	12115	10270
2001-2005				
0-14	8000	9250	7690	8835
15-65+	8565	12840	11590	12590

**Non-Registered
Aboriginal**

	Male off reserve	Male on reserve	Female off reserve	Female on reserve
1986-90				
0-14	5650	155	5705	145
15-65+	9280	210	9680	335
1991-95				
0-14	9330	765	8215	1020
15-65+	10695	1685	13290	795
1996-2000				
0-14	8015	145	7880	140
15-65+	13135	290	13445	160
2001-2005				
0-14	6395	720	6675	735
15-65+	12090	985	13160	1010

1996 Total Aboriginal (Standard Population)

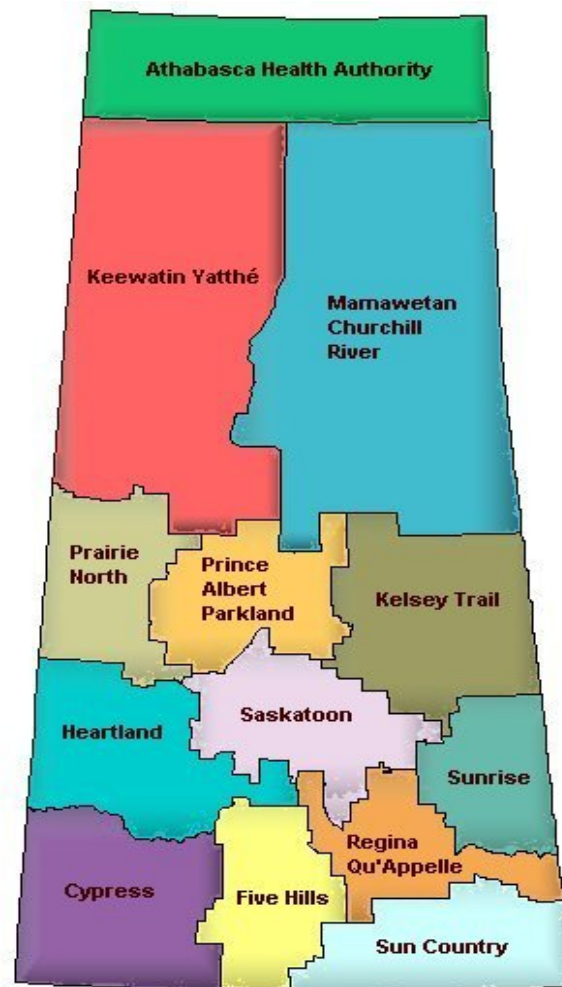
	Off Reserve	On Reserve
0-14	32,680	16,265
15-65+	46,810	21,555

APPENDIX D: Variable List and Descriptions

The outcome of interest was the rate of pulmonary tuberculosis and the variables examined included the following:

- 1. Diagnosis Date:** Date recorded when lab either received culture or when drug treatment begins for pulmonary TB by the Saskatchewan TB control program
- 2. Patient Age:** Ages of patients were categorized as follows – 0-14, 15+ and were categorized as 0-14 = 1 and 15+ = 2
- 3. Patient Gender:** Gender is a categorical variable where male = 1 and female = 2
- 4. Location of Residence:** Patients will be placed in two groups; those who were living off a federal reserve at the time of diagnosis (Off=0) and those who were living on (On=1).
- 5. Status:** Exposure variable was categorized into registered and non-registered Aboriginal (as per previously described definition). Those of non Aboriginal ancestry will not be included in this study. Registered Aboriginal = 1; Non-registered Aboriginal = 2.

6. Regional Health Authorities (RHA): RHA in which patient resides at time of diagnosis. There are currently 13 RHAs in province (categorical variable)



(1=Athabasca; 2=Keewatin Yatthe; 3=Mamawetan Churchill River; 4=Prairie North; 5=PA Parkland; 6=Kelsey Trail; 7=Heartland; 8=Saskatoon; 9=Sunrise; 10=Cypress; 11=Five Hills; 12=Regina Qu'Appelle; 13=Sun Country)

7. Diagnostic method: Categorical variable indicating whether active (health authorities actively looked for cases i.e. screening or contact tracing) or passive (diagnosis made when patient seeks medical services i.e. symptom presentation) diagnosis was used for case detection. Passive = 1; Active = 2.

8. Mortality data: Indicates whether patient died as a result of pulmonary TB. Yes = 1; No = 2.

9. Treatment compliance: Refers to the patient's and health care provider's ability to follow management guidelines appropriately. It refers to the # of doses taken/# of doses prescribed. A completion rate of <80% is considered NOT complete (Continuous variable)

10. ICD-9 Codes: Hospital diagnostic codes indicating the diagnosis of pulmonary TB for each patient. The ICD-9 codes for pulmonary TB are as follows:

011.0 Tuberculosis of lung, infiltrative

011.1 Tuberculosis of lung, nodular

011.2 Tuberculosis of lung with cavitation

011.3 Tuberculosis of bronchus

Excludes: isolated bronchial tuberculosis (012.2)

011.4 Tuberculous fibrosis of lung

011.5 Tuberculous bronchiectasis

011.6 Tuberculous pneumonia [any form]

011.7 Tuberculous pneumothorax

011.8 Other pulmonary tuberculosis

011.9 Unspecified

11. Specimen Description: Provides information about the type of clinical specimen that was collected for the diagnosis of TB. gastric washing=1; urine=2; pleural fluid=3; sputum=4; vaginal tissue=5; lung tissue=6; liver tissue=7; lymph node=8; bronchial washing=9; breast tissue=10, conversion other=11; ear, nose, throat=12; brain tissue=13; bone/joint tissue=14; undefined=15

12. Smear microscopy results: Smear microscopy is the term used to describe the examination of patient specimens under the microscope to determine the presence

of acid-fast bacilli (ie. *M. tuberculosis*). A smear is usually used to determine TB infectiousness, but initially, before formal culture confirmation, a positive result may be due to infection with mycobacteria other than *M. tuberculosis*. Negative smear = 1; Positive = 2

13. Culture results: The presence or absence of *M. tuberculosis* when grown on culture medium. Negative culture = 1; Positive culture = 2.

APPENDIX E: Trend Analysis with select reference time periods

Reference Time Period – 1991-1995

Trends in TB incidence rates for on reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-7.34	0.11	0.00	0.00, 0.00	<0.0001
1991-1995(ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1986-1990	0.11	0.17	1.11	0.80, 1.54	0.5256
1996-2000	-0.76	0.20	0.47	0.32, 0.69	0.0012
2001-2005	-0.60	0.18	0.55	0.38, 0.79	0.0001

Trends in TB incidence rates for off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-6.40	0.19	0.00	0.00, 0.00	<0.0001
1991-1995(ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1986-1990	0.42	0.26	1.53	0.92, 2.52	0.0988
1996-2000	-0.38	0.28	0.68	0.39, 1.19	0.1782
2001-2005	-1.08	0.32	0.34	0.18, 0.64	0.0008

Trends in TB incidence rates for on and off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-6.94	0.22	0.00	0.00, 0.00	<0.0001
1991-1995(ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1986-1990	0.30	0.30	1.36	0.76, 2.43	0.3084
1996-2000	-0.48	0.34	0.62	0.32, 1.20	0.1549
2001-2005	-0.79	0.35	0.46	0.28, 0.91	0.0267

Reference Time Period – 1996-2000

Trends in TB incidence rates for on reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-8.11	0.16	0.00	0.00, 0.00	<0.0001
1996-2000(ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1991-1995	0.76	0.20	2.14	1.45, 3.17	0.0001
1986-1990	0.87	0.20	2.38	1.60, 3.55	<0.0001
2001-2005	0.17	0.22	1.18	0.77, 1.81	0.4470

Trends in TB incidence rates for off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-6.78	0.21	0.00	0.00, 0.00	<0.0001
1996-2000(ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1991-1995	0.38	0.28	1.46	0.94, 2.54	0.1782
1986-1990	0.80	0.27	2.23	1.31, 3.77	0.0028
2001-2005	-0.70	0.33	0.50	0.26, 0.95	0.0346

Trends in TB incidence rates for on and off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-7.42	0.26	0.00	0.00, 0.00	<0.0001
1996-2000(ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1991-1995	0.48	0.34	1.61	0.83, 3.14	0.1549
1986-1990	0.78	0.33	2.19	1.14, 4.20	0.0182
2001-2005	-0.31	0.38	0.74	0.35, 1.56	0.4261

Reference Time Period – 2000-2005

Trends in TB incidence rates for on reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-7.94	0.14	0.00	0.00, 0.00	<0.0001
2001-2005 (ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1996-2000	-0.17	0.22	0.85	0.55, 1.30	0.4470
1991-1995	0.60	0.18	1.82	1.27, 2.60	0.0012
1986-1990	0.70	0.19	2.02	1.39, 2.92	0.0002

Trends in TB incidence rates for off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-7.48	0.26	0.00	0.00, 0.00	<0.0001
2001-2005 (ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1996-2000	0.70	0.33	2.01	1.05, 3.82	0.0346
1991-1995	1.08	0.32	2.93	1.57, 5.48	0.0008
1986-1990	1.50	0.31	4.47	2.45, 8.16	<0.0001

Trends in TB incidence rates for on and off reserve Aboriginals in five year intervals, 1986-2005.

Time period	β	SE (β)	OR	95% CI	p-value
Intercept	-7.73	0.28	0.00	0.00, 0.00	<0.0001
2001-2005 (ref)	0.00	0.00	1.00	1.00, 1.00	0.0000
1996-2000	0.31	0.38	1.36	0.64, 2.88	0.4261
1991-1995	0.79	0.35	1.20	1.10, 4.40	0.0267
1986-1990	1.09	0.35	2.97	1.50, 5.90	0.0018

APPENDIX F: Ethics Approval



Office of Research Services

Dr. Valerie Thompson, Chair
Behavioural Research Ethics Board
University of Saskatchewan
Room 210 Kirk Hall, 117 Science Place
SASKATOON SK S7N 5C8 CANADA
Phone: 966-2084 Fax: 966-8597
Email: Valerie.thompson@usask.ca

MEMORANDUM

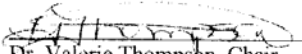
To: Dr. Syed Shah, Lesley McLeod
Date: December 13, 2005
Re: Characteristics of Tuberculosis among the Aboriginal Populations in Saskatchewan: Is there a Difference in Rates by Residence (on and off reserve)?

The study entitled, "Characteristics of Tuberculosis among the Aboriginal Populations in Saskatchewan: Is there a Difference in Rates by Residence (on and off reserve)?" is exempt from the Research Ethics Board review process. This decision is based on the information provided in your ethics application in December 7, 2005.

Article 3.3 of the Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (1998) specifies that REB review and approval is not required to conduct a secondary analysis of data that cannot be linked to individuals, and for which there is no possibility that individuals can be identified in any published reports.

It should be noted that though your project is exempt of ethics review, your project should be conducted in an ethical manner (i.e. in accordance with the information that you submitted). It should also be noted that any deviation from the original methodology and/or research question should be brought to the attention of the Behavioural Research Ethics Board for further review.

Sincerely,


Dr. Valerie Thompson, Chair
Behavioural Research Ethics Board

