Tuberculosis Prevention, Diagnosis, and Care in Manitoba, 2008-2010: A Performance Analysis

by

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ABSTRACT

A cross-sectional study of Manitoba TB Registry data was conducted using a set of performance measures based on the US Centers for Disease Control and Prevention TB Performance Objectives and Targets framework.

The study investigated all cases of TB diagnosed in Manitoba during the period of 2008 to 2010 (inclusive), and their contacts. Seven performance measures (PMs) were analyzed: treatment completion/cure, early diagnosis, HIV testing/reporting, paediatric cases, retreatment cases, contact elicitation, and contact assessment. Ethnic-origin, age, sex, geographic, and treatment history groups were compared on these PMs through log-binomial and robust Poisson regression analyses, implemented through a generalized estimating equations (GEE) modelling approach.

An updated epidemiological profile is provided, along with a baseline of performance in TB prevention, diagnosis, and care in Manitoba. Significant differences were found between Manitoba sub-populations in the PMs. The PM framework developed in this study provided valuable information for TB program planning and evaluation.

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Table of Contents

LIST OF TABLES AND FIGURES

Tables

Figures

Boxes

1. INTRODUCTION

There are 1.7 million deaths worldwide attributable to TB every year and approximately one third of the world's population – 2 billion people – are infected with *Mycobacterium tuberculosis*, the cause of TB disease (Rasanathan, Sivasankara Kurup, Jaramillo, Lonnroth, & Lönnroth, 2011). *M. tuberculosis* is transmitted through the air in droplets expelled during breathing, coughing, sneezing, and talking. These enter the airways and colonize the respiratory system and from there can spread to the rest of the body. *M. tuberculosis* can progress rapidly from infection to active disease, which occurs in about 5% of healthy persons who are initially infected (known as primary disease), or remain dormant as a latent TB infection (LTBI), with a risk of becoming active at a later time (Vynnycky & White, 2010). Both active and latent TB can be treated with anti-tuberculous drugs. Isoniazid, rifampin, and pyrazinamide, are among the first-line medications used for treatment of active disease. Other newer drugs from the class of flouroquinolones are used to treat forms of TB that are resistant to the first line drugs. Drug-resistance is a growing problem for TB prevention, diagnosis and care world-wide.

In 2013 in Canada, there were 1,640 cases of new active or reactivated TB which translates to an annual incidence case rate (IR) of 4.7 per 100,000 population (Public Health Agency of Canada, 2015). Among these cases, 1,146 were foreign-born (69.9%; IR = 14.8/100,000), 309 were Aboriginal[1] (18.8%; IR = 19.9/100,000), and 155 were non-Aboriginal Canadian-born (9.5%; IR = 0.6/100,000) (Public Health Agency of Canada, 2015). Between 2000-2012, Manitoba reported an average of 124 new active or reactivated TB cases per year (range = 98 to 156) (Epidemiology and Surveillance Unit, 2013). For 2013, Manitoba reported

1 Aboriginal is defined by the PHAC as: First Nations (both status and non-status), Inuit, and Metis individuals in Canada.

169 new active or reactivated cases of TB for an IR = 13.4/100,000 population (Public Health Agency of Canada, 2015). The incidence rate of new active or reactivated TB is significantly higher in Manitoba than in Canada generally (Basham, 2012; Public Health Agency of Canada, 2009b). The incidence rates of TB are far higher amongst foreign-born and Aboriginal Manitobans than Canadian-born non-Aboriginal Manitobans.

Provincial TB programs vary across Canad. In Manitoba, the Winnipeg Regional Health Authority (WRHA) Integrated Tuberculosis Services (ITS) organizes TB services under a provincial framework (Whitlock, Shaw, Nowicki, & Mahmud, 2012). By law, all case and contact data are reported to the Manitoba Tuberculosis Registry (the "Registry") maintained by the Communicable Disease Control Unit of the Public Health Division of Manitoba's Ministry of Health. The Registry contains demographic, diagnostic, and treatment data for TB cases and contacts. These data have been used in previous studies, although none of these studies focused on performance measurement (Blackwood, Al-azem, Elliott, Hershfield, & Kabani, 2003; Cook, Manfreda, & Hershfield, 2004; Olson, 1999; Sharma, Wolfe, Hershfield, & Kabani, 2003).

The performance of TB programs is a subject of significant study in the United States, (often employing secondary administrative data similar to the Manitoba TB Registry). The US Centers for Disease Control and Prevention uses performance measurement to monitor city, state, and local TB programs and services and provide targeted assistance to these programs intended to improve them and reach the target of TB elimination (Hughes et al., 2010; US Centers for Disease Control and Prevention, 2010). This study applies a performance measurement framework to TB prevention, diagnosis, and care in Manitoba, with special attention given to ethnic-origin and geographic group differences in performance.

Utilizing the Manitoba TB Registry data this study compares TB prevention, diagnosis, and care performance within Manitoba for the major ethnic-origin groups: (i) foreign-born, (i) First Nations, and (iii) Canadian-born non-First Nations. These groups have been shown to have significantly different incidence rates of TB within Canada. Each group faces a different set of challenges to TB prevention, diagnosis, and care, with the First Nations facing some of the most significant barriers to TB prevention, diagnosis, and care (Jensen et al., 2012).

Study Rationale

In Canada, progress has been made towards the long-standing goal of eliminating TB. Mortality rates declined dramatically starting as early as 1882 with the discovery of *tubercle bacillus,* which was foundational to germ theory, and introduction of quarantine (TB sanatoria), and improved social determinants of health, including nutrition, housing, hygiene, working conditions, up to the mid-1940's. A more rapid decline in mortality from TB occurred with the introduction of chemotherapy to treat TB (1944-1946). By 1977 the speed of decline slowed with mortality rates being substantially lower (Public Health Agency of Canada, 2009a; Wherrett, 1977). A similar decline occurred for TB incidence from the mid-1940's to the late 1990's (Health Canada, 1998). In the later 20th and early 21st centuries, the total number of TB cases per year decreased from 1,994 cases in 1997 to 1,548 in 2007 (which is a 22.4% decline), despite population growth. The annual Canadian TB case rate (per 100,000 persons) declined from 6.7 in 1997, to 4.7 in 2007 (a 29.9% decline) (Public Health Agency of Canada, 2009a).

While this decline shows progress, low and declining rates are not a sign that TB prevention, diagnosis, and care is no longer an important public health threat. As illustrated in

the USA and globally, TB can resurge when budgets are reduced and prevention and control are neglected (Institute of Medicine, 2000). The USA has shown that enhanced TB services are still critical to not only reduce and eventually eliminate TB, but to prevent its resurgence (US Centers for Disease Control and Prevention, 2015b).

In low-incidence countries, such as Canada and the USA, TB programs must have surveillance systems to analyze TB services in terms of their efficacy and effectiveness in order to identify areas of need and make targeted improvements (Cass et al., 2013; McNabb et al., 2004). One type of quantitative evaluation that has evolved for this purpose is *performance measurement* (PM), which was the inspiration for this project. *Performance* can refer to many aspects of a health program. Smith, Mossialos, et al. (2009) describe performance measurement as an accountability tool, allowing stakeholders to use performance information in decision-making and enhancing the accountability of health system managers and providers for the quality of care provided. In this study, *performance* refers to the performance of TB prevention, diagnosis, and care services in terms of how well the program is performing according to a set of quantitative indicators. The indicators selected for this study (and discussed later), while not comprehensive, provide important insights into how well Manitoba TB services were achieving the objectives of TB prevention, diagnosis, and care programs. Furthermore, this study contributes to the recommended "cross-jurisdictional approach for managing tuberculosis among Canada's Aboriginal peoples" (Health Canada, 1998, p. 11) by analysing the data for First Nations in Manitoba, on-reserve, off-reserve, and separately for Winnipeg and for Northern Manitoba, enabling an understanding of performance across jurisdictional and regional lines.

Indeed, First Nation leaders in Canada have called for greater accountability for services

provided to First Nations people, including in tuberculosis prevention, diagnosis, and care (Standing Committee on Health, 2010). Despite the dramatic decline in the rates of TB a large disparity remains in the incidence and prevalence of TB between Aboriginal and non-Aboriginal peoples (Clark & Cameron, 2009; Long et al., 2013). The national Assembly of First Nations (AFN) has identified TB as a key health issue and specifically sees longer delays in diagnosis and treatment for First Nations in Canada (Assembly of First Nations, 2010). Since First Nations are the population most affected by TB in Manitoba it is logical and in keeping with the United Nations Declaration on the Rights of Indigenous Peoples (DRIPS)[2] for First Nations to have access to information about TB services and outcomes in Manitoba via performance measurement initiatives, such as the present study.

In Canada, the federal government is constitutionally responsible for Indigenous peoples, including health care provided to Indigenous peoples. Provincial governments are responsible for healthcare delivery, including public health, and the data generated in the provision of health services. Additionally, mandatory reporting of infectious diseases such as TB exists within every province in Canada, who have health data reporting relationships with the federal government. When provincial and federal responsibilities and jurisdictions are taken into consideration, along with the disproportionate burden of TB on First Nations, as well as the overall move towards self-determination and recognition of First Nations Governments, we begin to see a multi-jurisdictional environment in which TB prevention, diagnosis, and care operates in Manitoba.

In Canada, *National Consensus Conference on Tuberculosis* of 1997 made it clear that all provinces are responsible for ensuring that national standards for TB prevention, diagnosis, and care are met (Health Canada, 1998). However, mechanisms do not exist in most provinces, or

2 Articles 23, 24(2), and 29(3) (United Nations, 2007).

are only now being developed, to measure performance in achieving these standards. The possible exception is Alberta who has made some early strides towards applying a performance measurement framework (Sutherland et al., 2007). The absence of performance measurement of TB programs leaves programs with goals and standards and no system for measuring their achievement. Without a performance measurement framework for on-going evaluation of provincial and federal TB programs, a major gap is created in knowledge about the successes and failures of TB services and goes against best practices in TB program management (Broekmans et al., 2002; Stirling & Enarson, 2007; Taylor, Nolan, & Blumberg, 2005).

Recently, the federal government has set some broad TB prevention, diagnosis, and care targets, and they are: (i) an annual incidence rate of 3.6 cases per 100,000 persons by the year 2015 (Health Canada, 2010), and (ii) "elimination of TB as a public health problem by 2050" (Health Canada & Public Health Agency of Canada, 2014, p. 2). In 2012, the Pan-Canadian Public Health Network released a set of performance measures for Canadian TB prevention, diagnosis, and care programs, although these have yet to be implemented nation-wide (Pan-Canadian Public Health Network, 2012). The performance measures include specific targets for the following dimensions of TB prevention, diagnosis, and care:

- Microbiological diagnosis of active TB disease,
- HIV serologic testing
- Treatment of active TB disease
- Contact follow-up
- Targeted screening for active TB disease and LTBI
- Immigration medical surveillance

When we consider the difference between the federal TB goal of 3.6 per 100,000 and the current rate of TB in Manitoba of 13.4 per 100,000 (Public Health Agency of Canada, 2015), a number of questions emerge. How is the Manitoba TB program performing in terms of prevention, diagnosis, and care? Where are improvements needed, i.e., for what demographic, geographic, and health service population groups? To answer these questions requires a detailed study into the differences in TB risk, incidence, diagnosis, treatment, and outcomes from both population health and health services perspectives. Such a study could reveal areas of variation across population groups and shed light on the reasons for any observed differences, thereby providing knowledge indispensable to planning and evaluating TB prevention and control strategies.

One possible framework to adapt to the Canadian situation was developed by the US Centers for Disease Control and Prevention (US-CDC) for TB prevention, diagnosis, and care program performance measurement (US Centers for Disease Control and Prevention, 2010). This framework has guided US TB programs in efforts to improve services and reduce the incidence of TB, and recent analyses suggest the effort has resulted in service improvements and reduced incidence (Hughes et al., 2010; National Center for HIV/AIDS Viral Hepatitis STD and TB Prevention, 2015). No performance measurement (PM) framework has been applied in Canada, but the US could serve as a template for TB program evaluation. Vital to the process of program improvement are relationships built through the sharing and interpreting of performance information - linked to a desire for transparency and cooperative governance in health care (Smith et al., 2009). In the US case, the CDC collaborates with state and local programs through

the National Tuberculosis Indicators Project (NTIP) based on the quantitative *TB Performance Objectives and Targets for 2015* framework. Applying this framework in Manitoba has merit to demonstrate the feasibility of using performance measurement towards eliminating TB locally and globally.

In keeping with United Nations reporting principles, the expectation is for countries to report statistics by ethnic-origin groups, including health system performance related to TB to address disparity issues. Variations in performance between ethnic-origin groups do not indicate variation in the desire to eliminate TB between groups. For example, adherence to TB therapy is affected by a myriad of social, economic, healthcare, political, and personal factors, which disadvantage one or more of these groups (Orr, 2011b). Attributing the causes of strong or weak performance is, however, complex (Terris & Aron, 2010), and beyond the scope of this study. Studying performance by ethnic origin group improves the potential for results to be useful to the groups represented in the study, which was a key motivation for this research. Moreover (Rasanathan et al., 2011, p. S32):

> "A social determinants perspective bolsters this attention [to primary care system improvements] by adding the requirement to consider the equity of health system performance throughout the continuum of care for TB. Reaching the urban poor whose cases are not detected, and improving adherence to treatment, requires measurement of health system performance by dis-aggregating data. This is necessary to understand which groups are receiving poorer service delivery, or not being reached, so that strategies can be implemented to improve and prioritise services for them."

Study Purpose

The purpose of this study is to understand how well Manitoba TB prevention, diagnosis, and care are performing and where differences lie in performance between ethnic-origin and geographic groups within Manitoba. By using quantitative performance measures to study various aspects of tuberculosis services this study provides a needed snapshot of TB prevention, diagnosis, and care performance in Manitoba. The results of this study identify areas of strong and weak performance in Manitoba and specific performance issues for geographic and ethnic-origin sub-populations. The information generated by this study can inform TB program managers, the public, patients, and affected communities to in their efforts to improve TB prevention, diagnosis, and care in Manitoba.

Research Questions

1. Using the Manitoba TB Registry, how is Manitoba performing in terms of TB prevention, diagnosis, and care?
2. Does performance vary by ethnic-origin, sex, age, and geography, and if so how?
3. Which performance targets are measurable with the Manitoba TB Registry and which are not?

Study Objectives

This project will inform improvements to TB prevention, diagnosis, and care in Manitoba through a quantitative analysis of program performance, and by pilot testing a rigorous indicators framework and laying the foundation for further research. Specific study objectives are:

(a) Establish a baseline of TB prevention, diagnosis, and care performance in Manitoba;

(b) Compare performance across populations in Manitoba; and

(c) Develop a methodology for measuring TB prevention, diagnosis, and care program performance using the Manitoba Tuberculosis Registry.

To this end, the thesis begins with a literature review on TB globally, in Canada and specific to Manitoba, followed by the rationale of performance measurement in TB programming worldwide, specific to the United States, and its relevance to Canada and its provinces. A methodology chapter outlines the study design and analysis approach used, followed by a results chapter. A discussion of the findings and their limitations, followed by recommendations for improving TB prevention, diagnosis, and care in Manitoba and future research on TB and TB program performance, concludes the thesis.

2. LITERATURE REVIEW

The following literature review is divided into two parts. Part I examines the history of tuberculosis (TB) in Canada and Manitoba, the social determinants of TB, the global principles and strategies for TB control and elimination, and modern epidemiology of TB in Canada. Part II reviews specific means by which TB programs attempt to reduce rates of TB through prevention, diagnosis, and care activities. The focus of the review was the methods used to measure performance on these TB program components, with an emphasis on North American experiences with TB and examples of performance measurement in TB.

PART I. TUBERCULOSIS IN CANADA: HISTORY, EPIDEMIOLOGY, AND PRINCIPLES FOR PREVENTION, DIAGNOSIS, AND CARE

Tuberculosis (TB) was declared a global health emergency in 1993 and is pandemic with an estimated 1.7 million deaths annually, constituting the second largest cause of death from infectious diseases, second only to HIV (Coberly & Comstock, 2006; Rasanathan et al., 2011; World Health Organization, n.d., 2009). TB incidence and mortality has declined significantly worldwide and in Canada since the mid-1800's (Vynnycky & White, 2010). Social and medical challenges to eliminating the disease remain, however, along with new challenges (Jensen et al., 2012). Multiple drug-resistant tuberculosis (MDR-TB), the lack of resources for complete case-finding, case-holding, and treatment, HIV-TB co-infection, and the conditions of poverty all serve to keep TB alive globally (Rasanathan et al., 2011).

In Canada, TB is in an endemic state amongst at-risk populations including immigrants from high-incidence countries, the urban poor, and select Inuit and First Nations communities

(Aspler et al., 2010; Coberly & Comstock, 2006; Cowie & Sharpe, 1998; Kulmann & Richmond, 2011). The present context of TB prevention, control, and hopefully elimination, all rest on the degree to which the social, organizational, and medical challenges are met (Rasanathan et al., 2011). For instance, the contribution of the social determinants of health to TB rates is well established (Rasanathan et al., 2011; Wherrett, 1977). In Canada, overcrowded housing is a known risk factor for TB in First Nations and Inuit communities (Standing Committee on Health, 2010).

Another major determinant of health is health care itself. TB prevention, diagnosis, and care programs can influence TB incidence and prevalence through their scope, coverage, and performance in pursuing case-finding, case-holding, treatment via directly observed therapy (DOT), contact-tracing and preventive therapy (Fair, Hopewell, & Pai, 2007). The degree of success in these activities, however, depends on *other* public health activities, including appropriate diagnosis, prompt laboratory reporting and initiation of treatment (Fair et al., 2007). Ultimately, for Canada to reach the goal of eliminating TB by 2050, major advancements in TB services are required including in the area of performance targets, which drive continuous quality improvement through measuring performance and intervening to improve performance.

To understand the context of TB prevention, diagnosis, and care in Manitoba, a wide-ranging search of the available literature, both gray and peer review materials was conducted on a continuous basis between 2010 and 2015, when the present study was completed.

The findings of this literature review are presented as follows: First, the history of TB prevention, diagnosis, and care in Canada and Manitoba is given leading up to present day policy and management structure. Second is a description of the social determinants of TB. Third is a

review and analysis of the epidemiology of TB in Canada, focusing on Manitoba. The main portion of the literature review follows, which concentrates on performance measurement in TB prevention, diagnosis, and care, while detailing experiences and examples of same: emphasizing Canadian and American sources. A summary of the findings is provided to set the stage for the methodology (Chapter 3).

History of TB Prevention, Diagnosis, and Care in Canada

During the 19th century tuberculosis was a major cause of death for both European and Indigenous peoples in Canada, with mortality rates ranging from of 50 to 80 per 100,000 and 600 to 700 per 100,000, respectively, between 1921-1945 (Wherrett, 1977). Tuberculosis is a disease that cost many Canadians their lives particularly First Nations and Inuit peoples (Alvarez, Orr, Wobeser, Cook, & Long, 2014).

The history of TB in Canada is intricately linked with the development of health-care generally. In Canada, between 1900 to 1950, TB was a major cause of death. A disproportionate amount of TB amongst the urban poor, coupled with the lack of urban sanatoria, prompted the need for new forms of health and social service delivery to tuberculous individuals (formerly known as consumptives) in cities (McCuaig, 1999). These services were delivered through dispensaries, which offered examinations, treatments, and social support in the form of the necessities of life (McCuaig, 1999). The establishment of sanatoria solidified and organized a large network of voluntary, medical, and nursing associations with roles in the campaign against TB (McCuaig, 1999). The construction of sanatoria was a key objective of this movement, which institutionalized health care for the first time in many communities (McCuaig, 1999). As

McCuaig (1999) explains:

> "Tuberculosis was a chronic and therefore costly disease that very few Canadians could afford to deal with themselves. The extension of free treatment had more far reaching consequences than the mere government assumption of that particular burden... It was no accident that Saskatchewan, the first to extend free treatment to the tuberculous, was also the first to extend free treatment to sufferers of other chronic and costly diseases." (p. 257)

The development of TB services across Canada was the largest public health campaign in Canadian history, prompting the development of public health boards across the country and in all municipalities, even the early development of publicly funded health care (Wherrett, 1977). TB Sanatoria were established through a long process of health reform to provide tuberculosis care, often led by survivors of TB (McCuaig, 1999; Wherrett, 1977). Municipal, charitable, provincial, and eventually national efforts to combat TB made the construction of sanatoria across Canada possible, and also provided social and economic support for TB patients (due largely to ex-patients' advocacy) who often had to spend years in sanatoria unable to work or be with family, which placed tremendous strain on patients both economically and psychologically (Wherrett, 1977).

Treatment, prior to the development of anti-tuberculosis drugs (1944-46), was provided in sanatoria, which offered fresh-air treatment and surgical options, including collapse treatment (thoracoplasty) and pneumothorax (McCuaig, 1999, pp. 69-80). The removal of infectious individuals from families and communities helped slow the spread of diseases considerably (Mierau, 2005; Wherrett, 1977). The rise of germ theory led to isolation of the TB bacillus by Robert Koch (1882), and initiated research on anti-TB drugs (Wherrett, 1977). What followed

was the development of anti-tuberculosis drugs, namely, streptomycin (1944), para-amino-salicylic acid (PAS) (1946), isonicotinic hydrazide (INH) (1952), and rifampicin (RMP) (1968). These drugs meant that treatment could be expanded beyond sanatoria into the community, which resulted in the new challenge of ensuring completion of the prescribed regimen of chemotherapy (Mierau, 2005; Wherrett, 1977). Mortality rates further declined to <10 per 100,0000 by 1965, which ended the sanatorium era in Canada. With the disease apparently conquered, the focus shifted to new challenges for public health and health care, such as heart disease and cancer (Wherrett, 1977).

The development of TB care in Canada was also implemented for First Nations, Inuit, and Metis peoples, with different responsbilities that developed in a parallel process to the development of these systems generally. A major challenge for First Nations, Metis, and Inuit included the development of Residential Schools, which contributed to the spread of TB amongst First Nations people.

In 1909, Dr. Peter Bryce, the Chief Medical Officer for the Department of Indian Affairs of Canada, and Dr. J.D. Laferty, examined 243 students in 8 Indian Residential Schools in Alberta for TB, finding that 100% of the children had active TB. Bryce described the conditions of the Residential schools, as well as Indigenous health within Canada generally as a "National Crime" (Bryce, 1922). Sanatoria were places that many First Nations and Inuit people in Canada were forcibly sent, without knowing whether they would be able to return, and often never to be seen again by family or friends (Mierau, 2005; Wherrett, 1977).

The history of TB in Canada amongst First Nations, contributes to breakdown in trust and communication today, which must be addressed by TB programs engaging high incidence

communities today (McDonald, 2008). This is a key challenge for TB programs in the modern era. The following sections takes a closer look at the history of TB in Manitoba, with a description of the current management structure.

Manitoba TB Prevention, Diagnosis, and Care

The Sanatorium Board of Manitoba (SBM) was established in 1904 under the S*anatorium Board Act of Manitoba* and had primary responsibility for treating TB patients in Manitoba. The Board oversaw the operation of seven sanatoria until medication reduced the need for long periods of quarantine. Turnover in SBM medical directors in the late 1950's prompted the modernization of the TB program to focus primarily outpatient care in the face of emptying sanatoria (Manitoba Lung Association, 2008; Mierau, 2005). In 2006, Manitoba Health transferred program management from the Manitoba Sanatorium Board to Manitoba Health with service delivery by regional health authorities (Manitoba Health, 2006; Orsini, 2009). This included a restructured program, guided by a steering committee with representatives from the following organizations: Manitoba Health, the First Nations and Inuit Health Branch of Health Canada, the Winnipeg Regional Health Authority, the Burntwood Regional Health Authority, the Lung Association, Manitoba, and the University of Manitoba (Manitoba Health, 2006).

Tuberculosis is a reportable disease under *The Public Health Act* (Manitoba), *Reporting of Diseases and Conditions Regulation* [C.C.S.M c. P210, Regulation 37/2009], which states that any laboratory or health provider who knows or reasonably suspects that a person has or recently had a reportable disease must make a report to Manitoba Health (Minister of Health, 2009).

Manitoba Health enters this information into a central database, including both paper and electronic filing, known as the Manitoba Tuberculosis Registry ("TB Registry"). The history of the Manitoba TB Registry is not clear and has not been the subject of any published studies known to the author at the time of writing. However, numerous mentions are made of it in articles on TB in Manitoba. The TB Registry has served various functions since inception. Presumably, the TB Registry began as a record keeping system for managing TB sanatoria, and then transitioned into a tool for community-based TB prevention, diagnosis, and care. Specific functions the TB Registry has include: case-holding for treatment (now delivered through directly observed therapy (DOT) where locating patients is critical), contact tracing for case-finding and preventive treatment, and epidemiological research. However, there has been limited research using the TB Registry, with only a small number peer-reviewed research articles, two Master theses and a single Ph.D. dissertation on the University of Manitoba's thesis and dissertation database (Blackwood et al., 2003; Al-Azem, 1999; Olson, 1999; Al-Azem, 2006). Manitoba Health reported that work to improve the TB Registry was underway, although the exact nature of these improvements was not reported (Manitoba Health, 2008)

In 2009, Manitoba Health gave overall TB program management roles and responsibiltiies to the Winnipeg Regional Health Authority (WRHA), along with Health Canada's First Nations and Inuit Health Branch also contracted the on-reserve management of TB to the WRHA (Standing Committee on Health, 2010). However, Regional Health Authorities (RHA's), which administer health services in Manitoba, conducting public health programs within their regions. The most recent Manitoba TB Protocol summarizes the collaborative nature of TB prevention, diagnosis, and care services in Manitoba (Manitoba Health, 2014, p. 1):

> "Manitoba Health (MH) Public Health Branch (PHB), Health Canada (HC) First Nations and Inuit Health Branch (FNIHB), Winnipeg Regional Health Authority (WRHA) and other regional health authorities (RHAs) work collaboratively to ensure that tuberculosis (TB) prevention and care are integrated, timely and comprehensive. A transition process was completed in April 2011 whereby all RHAs assumed responsibility for case and contact identification and management for their respective residents, and the WRHA provides consultation to all regions as requested. The WRHA has an agreement with FNIHB whereby the WRHA coordinates case management and contact investigation for First Nations communities."

While multi-jurisdictional partnerships are often advocated for in theory, the practice may fall short of expectations. In 2009, Orsini analyzed the governance of TB prevention, diagnosis, and care in Manitoba, critically assessing its multi-jurisdictional nature and noting the complexity of TB services organizational structure and management in the context of Aboriginal peoples and federalism (Orsini, 2009). One major issue for TB prevention, diagnosis, and care in Manitoba and Saskatchewan (where there are large numbers of First Nation TB cases) is the disparate nature of health programming for First Nations people, which poses special problems in the case of a highly communicable disease such as TB (or pandemic influenza), requiring sustained prevention and control efforts coordinated across jurisdictional boundaries (Orsini, 2009).

The fundamental question that must be asked of any TB program is whether it is achieving its ultimate objectives, regarding outcomes for patients and the population they are part of. In TB programming the overall risk of TB to a population, measured through incidence and prevalence are key to gauging the success of prevention, diagnosis, and care programs.

Modes of influencing the incidence and prevalence of TB in a population include biomedical interventions and investments in the social determinants of health, which are reviewed next.

Modern TB Prevention, Diagnosis, and Care

Tuberculosis (TB) is an airborne infectious disease spread through droplets in the air. The best way to understand TB transmission is through a susceptible, pre-infectious, infectious, recovered/immune, susceptible (SEIRS) model (Vynnycky & White, 2010). Its prevention and control follows three principles: finding and treating active TB cases to prevent transmission and death, finding and treating latent TB patients to prevent (re)activation, and through improving the determinants of health that affect transmission of TB and the transition from infection to disease (BC Communicable Disease Policy Advisory Committee, 2014). The operational aspect of modern TB prevention, diagnosis, and care includes the following: 1) rapid diagnosis of TB, 2) development of TB care plans including a treatment regimen based on sound diagnosis implemented by trained physicians and nurses, 3) pharmacy services, 4) completion of treatment through DOT, 5) contact finding, assessment and treatment, and 6) active surveillance by public health officials. Population-based data systems, regular epidemiological analysis, and annual evaluation, are vital to modern TB programs for planning to make improvements leading to strengthening of the components of TB prevention, diagnosis, and care. A description of these components follows, beginning with anti-tuberculosis drugs.

As for treatment, drugs have various modes of action, and there are different phases of treatment of active TB. The bactericidal phase seeks to reduce the bacterial load of *M. tuberculosis* and isoniazid is the primary drug used to do so. The second phase is the sterilizing phase where destroying the ability of remaining *M. tuberculosis* bacteria to reproduce is the goal,

and rifamycin-derived drugs are primarily used for this purpose (Jindani, Doré, & Mitchison, 2003). The globally recommended initial treatment for drug-sensitive TB now involves a four-drug regimen, including isoniazid (INH), rifampin (RMP), pyrazinamide (PZA), and ethambutol (EMB) (Caminero, Matteelli, & Lange, 2011).

What greatly differentiates modern TB prevention, diagnosis, and care from past sanatoria practices is that this treatment is provided in the community for the majority of patients, with only a small proportion of cases being treated in hospitals for extended periods. The principles of TB prevention, diagnosis, and care promulgated by the US Centers for Disease Control include (Taylor et al., 2005):

- "Early and accurate detection, diagnosis, and reporting of TB cases leading to initiation and completion of treatment.
- "Identification of contacts of patients with infectious TB and treatment of those at risk with an effective drug regimen.
- "Identification of other persons with LTBI at risk for progression to TB disease and treatment of those persons with an effective drug regimen.
- "Identification of settings in which a high risk exists for transmission of *M. tuberculosis* and application of effective infection-control measures." (p. 15).

In 2005, the World Health Organization (WHO) developed a six point Stop TB Strategy (referred to as Stop TB) as the basis for global action against tuberculosis (Raviglione, 2007). Stop TB built upon the success of the direct observed treatment short-course (DOTS) system. The DOTS system was based on the work of Karel Styblo in the 1970's and 1980's that resulted

in what is referred to as the "Styblo model", which set out specific tasks for TB program in the modern era, particularly DOTS (Arnadottir, 2009). DOTS was officially supported by the WHO in 1994 under its *Framework for Effective Tuberculosis Control* (Broekmans et al., 2002). This framework included the following essential elements of Styblo's DOTS system (Broekmans et al., 2002):

- "political commitment to tuberculosis control;"
- "diagnosis based on bacteriology (sputum smear microscopy) and case-finding among symptomatic patients presenting to health services;"
- "standardized short-course chemotherapy provided under proper case-management conditions, including directly observed therapy;"
- "the provision of a regular supply of essential antituberculosis medications;" and
- "the establishment and maintenance of a recording and reporting system with evaluation of treatment outcome." (p. 765).

The Stop TB Strategy addressed those co-infected with HIV and those with drug-resistant TB, and promoted new and effective tools to prevent, detect and treat TB (Raviglione, 2007). More recently, the WHO released its *End TB Strategy,* which remains true to the fundamentals the Stop TB Strategy and DOTS also lays out the following guiding principles for global action to end TB (WHO, 2015):

- Government stewardship and accountability, with monitoring and evaluation.
- Strong coalition with civil society organizations and communities.
- Protection and promotion of human rights, ethics and equity.
- Adaptation of the strategy and targets at country level, with global collaboration.

Currently, treatments are advancing to eliminate TB, with new drugs being developed to treat MDR TB and to improve treatment of drug-sensitive TB with greater effectiveness in the presence of HIV co-infection (Bark et al., 2011). An example of new drugs being developed is TMC207, which is the first-in-class of a new class of drugs known as diarylquinolines – which

has strong bactericidal and sterilizing effects and can be used alone or included in existing drug regimens (Matteelli, Carvalho, Dooley, & Kritski, 2010).

Molecular epidemiological methods have also emerged as a tool to improve contact-tracing through cluster identification and social network analysis. The use of geographic information systems (GIS) and global positioning system (GPS) for mapping of cases and contacts, as well as health services, have provided new methods for understanding the ways TB spreads, in real time (Theron et al., 2015). Connecting these new sources of information to the populations they are studying and *vice versa* is another matter, which requires action on the social determinants of health generally and TB specifically, including strong community engagement and bidirectional information flows between national, regional, and local TB programs and the communities they serve (Theron et al., 2015).

Modern TB prevention, diagnosis, and care strategies can be divided into two categories: TB control strategies and TB elimination strategies. TB control strategies focus on active TB case finding and treatment, whereas TB elimination strategies include the former and augment them with LTBI diagnosis and treatment: seeking to eradicate the much larger pool of TB infection and thereby eliminate TB in the long-term (Broekmans et al., 2002). In addition to strong TB programming, action on the social determinants of health is vital to eliminating TB, with a bio-social model of sustainable development as a key conceptual framework bridging these two dimensions of TB prevention, diagnosis, and care. Although treatment with anti-tuberculosis drugs has proven effective in reducing TB rates, even in the presence of stagnant social and economic conditions, biomedical interventions are not alone sufficient for the elimination of TB. Considering and addressing the social determinants of health is also

important.

Social Determinants of TB

Prior to the discovery of *tubercle bacillus* by Robert Koch in 1886 and thereafter, it is widely recognised that improvements in the social determinants of health (SDOH) contributed to the decline in TB incidence and mortality. The tenet that social determinants matter was central to McKeown's thesis that the contribution of medical interventions to improvements in health is at the very least overstated (Rasanathan et al., 2011). Rising living standards for many people in the world during this time is credited with the reduction in incidence and mortality from an assortment of diseases, including TB. Poor social conditions, however, persist, and therefore TB remains a global challenge today. Considering population growth, and despite declines in incidence and mortality, there are actually more cases world-wide than before, requiring more investment than ever for TB prevention, diagnosis, and care (Rasanathan et al., 2011). Calling for action on the social determinants of health therefore remains necessary.

Crowded living spaces, coupled with malnutrition and inadequate water/sanitation services, elevated and prevalent intermediate risk factors (smoking, alcoholism, comorbidties) amongst the poor, and differences in health services, when taken together, promote infectious diseases like tuberculosis. For instance, a myriad of social determinants are associated with TB. Alcoholism acts on the host compromising immunity and crowded housing creates the conditions for TB to spread (Kulmann & Richmond, 2011; Rasanathan et al., 2011; Standing Committee on Health, 2010). Differential access to diagnostic, treatment, and preventative services also

contributes to disparities in incidence, prevalence, and outcomes of TB (Rasanathan et al., 2011).

In addition, the political, social, and economic forces that determine who is rich and who is poor are also a form of "structural violence", creating the conditions for infectious diseases, like TB, to persist or escalate within oppressed populations (Farmer, 2010). In high-income political/economic zones (e.g., Europe), TB has been referred to as "...the biological expression of social inequity" with its concentration in the urban slums of European big cities (Ali, 2014, p. 2195). To deal with TB as a social disease, a working group of public health officials from 57 European big cities (>500,000 population) developed a consensus statement that includes the following recommendations (van Hest et al., 2014, pp. 3-5):

Box 2.1. Recommendations for Big City TB Control and Social Determinants

Big city TB control programmes should:

1.1. Advocate for sustained political commitment to emphasise the social determinants of health that put subgroups of the population at increased risk of TB;

1.2. Investigate and monitor inequalities and socio-economic deprivation and their links with TB in order to intervene with a comprehensive public health approach;

1.3. Collaborate to promote suitable housing for homeless people in order to prevent transmission of TB and promote cure in this population;

1.4. Provide access to social support for all vulnerable populations, irrespective of their status;

1.5. Identify barriers and promote access to healthcare services for all those at risk of TB.

For most developed nations, as illustrated above, it appears that there are rising inequalities rather than a shrinking of the gap between rich and poor (OECD, 2013), which contributes to the persistence of TB in low-incidence countries. Without action on the social determinants of health as well as full implementation of DOTS, Stop TB, and End TB strategies, the goal of eliminating TB will always remain just that: a goal (Rasanathan et al., 2011). Enhancing living standards for the poor and reducing disparities between classes is complicated and highly political. Regardless of this complexity, it is essential to succeeding in the fight to eliminate TB globally (Fanning, 2011).

An important social determinant of TB is healthcare itself, which varies in terms of performance and across income groups (Rasanathan et al., 2011):

> "In most countries, TB services are integrated into mainstream national health systems. Weaknesses and inequities in health service delivery common in health systems are therefore replicated in the delivery of TB services. While under-researched, poverty and low socioeconomic status are associated with worse treatment outcomes for those with TB." (p. S32).

Of the few Manitoba studies examining TB from a SDOH perspective, Olson's (1999) comparative study of TB amongst First Nations people in Manitoba stratified TB case proportions by income quintiles. Because individual-level data on income of TB cases was not available, income quintiles were calculated at the ecological level and linked to individual cases by postal code. While direct comparisons of socioeconomic status was not possible five equally sized income groups, based on Census reported average household income of the neighbourhood

the case lives in and with each income quintile containing 20% of the population, were calculated to analyze the proportion of TB cases within each (Manitoba Centre for Health Policy, 2012; Olson, 1999). Olson found that the peak proportion of TB cases between 1990-1994 in Manitoba occurred in Quintile 1 (30.5%) [lowest income] and Quintile 3 (25.7%) [medium income]. For Status First Nation Manitobans it was reversed at 24.6% and 43.1%, respectively. For immigrants, the proportion of cases peaked in quintile 1 at 36.9% and again in quintile 2 at 20.6%, which mirrored the pattern observed in the total Manitoba TB case population (Olson, 1999). The distribution of First Nations TB cases in Manitoba according to income quintiles defies the provincial pattern, indicating that TB is circulating more widely across income groups amongst First Nations compared to non-First Nations. Olson suggested that the more important risk factor for TB amongst First Nations is household crowding (the mean number of people per house in houses that reported at least one TB case) rather than income. Although her findings were inconclusive, her approach has merit for further study with new data and methods. The *Determinants of TB Transmission* (DTT) study led by Dr. Richard Long may provide answers to some of these questions. The DTT study is examining TB cases and incidence qualitatively and from a determinants of health approach that includes biological data (Long et al., 2013).

In summary, while innovative approaches to understanding TB has evolved with improved data, the key to eliminating TB still remains the same (Fanning, 2011). To support action sound program evaluation data, reported annually is necessary. In Canada, local public health authorities are required by law to report all cases of TB to the respective provincial/territorial TB programs. Provincial/territorial governments then voluntarily submit reports of TB cases to the federal government. The case reports must meet the case definition for

national-level surveillance to the Canadian TB Reporting System managed by the Public Health Agency of Canada. This system includes select non-nominal information of each active TB case. Data for each case includes demographic, clinical, diagnostic, treatment and outcome details (Alvarez, Archibald, et al., 2014), and provides for epidemiological surveillance of TB in Canada.

Epidemiology of TB in Canada

As a high-income and low-incidence country, the national TB incidence rate is low, which means that TB prevention, diagnosis, and care are not major public health priorities. TB is endemic, primarily affecting people of lower socio-economic status (SES), Aboriginal people, and foreign-born persons from high-incidence countries (Aspler et al., 2010; Cowie & Sharpe, 1998; Public Health Agency of Canada, 2009b; Tapiero & Lamarre, 2003). In 2007, there were 1,519 cases of TB. Disaggregation by ethnic-origin, yielded the following frequency distribution: foreign-born (67%), Aboriginal (20%), and Canadian-born non-Aboriginal (11%) (Public Health Agency of Canada, 2009a). In 2009, the annual TB incidence rate in Canada was 4.7/100,000 overall. The lowest rate was for Canadian-born, non-Aboriginal at 1.0/100,000, then dramatically higher for foreign-born persons at 13.3/100,000, but at its highest for Aboriginal peoples at 27.8/100,000 (Public Health Agency of Canada, 2009b). More recent figures show no major changes in either case rates or distribution (Halverson, Ellis, Gallant, & Archibald, 2014; Public Health Agency of Canada, 2015). However, ongoing trends include slow declines in the rates for most populations and a shift in the composition of the foreign-born TB cases' countries of origin, from established market economies to African and Asian

populations, primarily, where incidence of TB is the highest (Halverson et al., 2014).

Of particular concern is the stagnation of progress in the fight against TB amongst Canadian Aboriginal populations, and a rising trend in TB amongst the Inuit (Alvarez, Orr, et al., 2014). Although overall TB rates for First Nations are significantly higher than foreign-born or Canadian-born non-Aboriginal, rates of TB vary considerably for First Nations from region to region and community to community (Alvarez, Orr, et al., 2014; Long et al., 2013; Phypers, Kunimoto, Behr, Scholten, & Ellis, 2007) while Inuit rates are consistently high and rising, due to the relative concentration of the Inuit population in the Canadian North (Halverson et al., 2014). Furthermore, next to the Canadian North, Manitoba has the second highest rates of TB, overall, and for Aboriginal peoples in particular (First Nations and Inuit Health Branch, 2011; Halverson et al., 2014; Long et al., 2013).

Statistical comparisons between provinces, however, are rarely made in federal surveillance reports, which obfuscates inter-provincial analysis. In order to better understand TB rates in Canada, nationally and inter-provincially, for each ethnic-origin group, a Poisson regression analysis of TB case rates and trends in the rates, between 1996-2009, was conducted using data available from the Public Health Agency of Canada (Basham, 2012). Parameter estimates were calculated using generalized linear modelling for count data (Poisson distribution with log link), using the natural logarithm of the ethnic-origin group population as an offset term to produce rates. Independent variables included year and province, and the dependent variable in each model was the annual case count for each ethnic-origin group by province, offset by the logarithm of the population count for that year, province, and ethnic-origin group. Three Poisson regression models were developed for each ethnic-origin group using (1) province, (2) year

(1996-2009), and (3) province and year as predictors in the respective models. Model 1 compared provincial TB incidence rates. Model 2 analyzed trends in TB incidence rates over the study period, and model 3 did both, holding either *province* or *year* constant for the comparative and trend analyses. Models were evaluated using *Z*-tests for significance of predictors and chi-square tests for deviance. Mallow's C_p and Akaike's Information Criteria (AIC) were used for model fit.

Adjusted and unadjusted rate ratios (RR's) were calculated for foreign-born, Aboriginal, and non-Aboriginal Canadian-born populations across provinces; the adjusted RR's included the effect of years and province in the models. In Figure 2.1, Adjusted RR's were calculated by exponentiating the parameter estimates for province ($RR = e^{\beta province}$). In Table 2.1., adjusted RR's for trends were calculated by exponentiating the parameter estimates for year ($RR = e^{\beta year}$). The models use Alberta as the control group, which means that Alberta's TB case rate for each ethnic-origin group is the reference for the RR's of other provinces. $RRj = IR_j / IR_J$, where *j* = British Columbia, Manitoba, Ontario, Quebec, Saskatchewan; and *J* = Alberta. Alberta was made the reference group because it was alphabetically first in the list and selected by *R* as the default reference category of province. Confidence intervals (CI's) were calculated by profiling the likelihood function using the confint() function in *R*.

For the period 1996-2009, statistically significant declines in the TB rates amongst the foreign-born and the Canadian-born non-Aboriginal people were found. There was no significant change in the incidence rate for Aboriginal peoples (Basham, 2012). This analysis showed the following. There is disparity in progress towards eliminating TB in Canada, whereby Aboriginal rates are decreasing at the slowest pace compared to non-Aboriginal

populations. Manitoba had the highest rate of TB amongst Canadian-born non-Aboriginal peoples ($RR_{MB/AB} = 2.69$). Manitoba had the highest RR point estimate for foreign-born persons (RR = 1.11), but not statistically significantly higher than British Columbia's rate ($RR_{BC/AB} = 1.04$). Manitoba had the second highest rate of TB amongst Aboriginal peoples in Canadian provinces with $RR_{MB/AB} = 3.26$, next to Saskatchewan's $RR_{SK/AB} = 4.89$ (Figure 2.1, Table 2.1, as displayed in Basham, 2012).

Since this analysis, Saskatchewan has seen a decline in the rate of TB amongst Aboriginals, while Manitoba has not, leaving Manitoba as the *province* with the highest rate of TB in Canada (Halverson et al., 2014; Public Health Agency of Canada, 2015). Taken together, a picture of elevated rates in Manitoba emerges, which prompts the question of why it is so.

Figure 2.1 Ethnic-origin Specific TB Adjusted Rate Ratios: Canada, 1996-2009

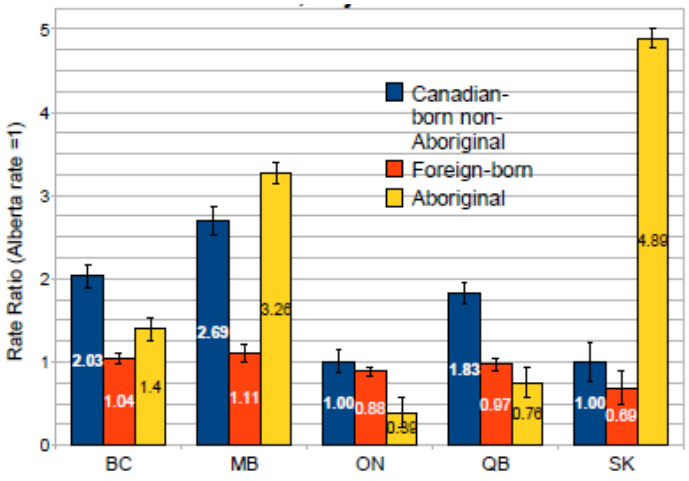


Table 2.1. Ethnic-Origin-Specific Trends in TB Case Rates in Six Canadian Provinces: 1996-2009

Parameter [Intercept and Year are exponentiated]	Aboriginal	Foreign-Born	Canadian-born, non-Aboriginal
Intercept (95% CI) = Alberta rate in 1996	0.000152 (0.000135, 0.000171)	0.000254 (0.00024, 0.00027)	0.000011 (0.0000097, 0.0000126)
Year (95% CI) [multiplicative effect]	0.969 (0.961, 0.977)	0.957 (0.953,0.961)	0.944 (0.936, 0.952)
Null Deviance (d.f.=83)	2599.55	752.62	752.43
Residual Deviance (d.f.=77)	282.89	182.01	152.63

Sig. Codes: * < 0.05, ** <0.01, ***<0.001

Epidemiology of TB in Manitoba

There were 169 new active or reactivated cases of TB in Manitoba in 2013 for a case rate of 13.4 per 100,000. Manitoba's TB case rates, in 2013, by ethnic-origin group were: 51.1 per 100,000 for Aboriginal peoples; 85.3 per 100,000 for First Nations; 20.8 per 100,000 for foreign-born; and 1.4 per 100,000 for non-Aboriginal Canadian-born. Most provinces report between 3 to 12 cases per 100,000 population annually (Public Health Agency of Canada, 2009b), whereas Manitoba's current rate is estimated at 13.4 / 100,000. Manitoba has also experienced a plateau in the rate of TB overall between 1996 and 2009 (Basham, 2012). Manitoba TB cases have a different case distribution than all Canadian TB cases (reported above), being predominantly First Nations cases for decades.

In 2013, Manitoba accounted for 113 of 309 of all Aboriginal TB cases (36.6%) in Canada, and 110 of 200 national First Nations cases (55%) (Public Health Agency of Canada, 2015). As reported by Blackwood et al. (2003), Manitoba has had a different case-distribution

from Canada as a whole with the following ethnic-origin distribution during the period of 1992 to 1999 of Treaty First Nations at 44.4%, foreign-born at 29.4%, and Canadian non-First Nation at 26.2%.

Blackwood et al. (2003) separated urban and rural TB cases in Manitoba for the period 1992-1999 ($N = 855$), and found the following case ethnic-origin distributions for urban cases: Treaty First Nation were 24.8%, 44.7% were foreign-born, and 30.4% were Canadian non-Treaty. For the rural cases 80.2% were Treaty First Nation, 1.3% were foreign-born, and 18.5% were Canadian non-Treaty. The estimated rate of TB for 1992 to 1997 in Manitoba was Treaty First Nations at 48.4 case per 100,000, foreign-born at 22 per 100,000, and Canadian-born non-Treaty at 3.3 per 100,000 (Blackwood et al., 2003).

According to the Public Health Agency of Canada (2009b), TB incidence rates varied across Canada from low (~1 per 100,000) in the Atlantic Provinces to a high (~100 per 100,000) in Nunavut. Most provinces report between 3 to 12 cases a year per 100,000, whereas Manitoba's most recently available rate of TB was 13.4 per 100,000 (Public Health Agency of Canada, 2015). Manitoba has also experience a plateau in the rate of TB overall between 1996 and 2009 (Basham, 2012). Currently Manitoba has the second highest rate of TB in Canada, with Nunavut having the highest (Halverson et al., 2014).

A study of TB incidence rates in the prairie provinces of Canada (Manitoba, Alberta, and Saskatchewan) compared overall TB case rates and culture-positive pulmonary TB incidence rates during 2004-2008 and 2007-2008, respectively, for Aboriginal populations on and off-reserve (Long et al., 2013). After adjusting for age and sex differences between provinces, Long et al. (2013) found significant disparities in the rates between Aboriginal population groups and

between provinces. Manitoba was found to have the highest rates (per 100,000 person years) of culture-positive pulmonary TB, with the highest incidence rates of TB amongst registered First Nations living on-reserve (77.6, 95%CI: 60.8 – 94.5) as opposed to those living off-reserve (53.5, 95%CI: 36.4-70.6), for a combined on and off-reserve incidence rate of 67.4 (95%CI: 55.2-79.5) (Long et al., 2013). Manitoba's First Nations TB incidence rates were significantly higher than Alberta and Saskatchewan (Long et al., 2013). Moreover, Manitoba had the highest overall rate of culture-positive pulmonary TB amongst all Canadian-born (which is everyone except the foreign-born) (Long et al., 2013). The rate was 8.2/100,000 person-years (95%CI: 6.8 - 9.2) and was not significantly different from Saskatchewan, which had the next highest rate of 6.2/100,000 person-years (95%CI: 4.9 – 7.4) (Long et al., 2013).

Within Manitoba, TB incidence has varied amongst First Nations communities, and within the First Nations population as well, based on individual risk factors (Olson, 1999). Differences in methodologies, data sources, population denominators, and the way comparison groups are defined between studies creates confusion about what the true incidence rates are for First Nations in Manitoba (Al-Azem, 1999; Epidemiology and Surveillance Unit, 2013; First Nations and Inuit Health Branch, 2011; Olson, 1999; Welch, 2014; Whitlock et al., 2012).

Table 2.2 illustrates variability in incidence rates estimated by various government reports and scientific studies of TB in Manitoba, providing an overview of population-specific TB rates. Figures were only available for some categories from each source, due to differing methods and objectives of the authors. Table 2.2 shows the incidence rate of TB amongst First Nations as a whole, as well as a flip in the rate ratio between on- and off-reserve, with on-reserve having higher incidence rates from 2004 onward, while off-reserve rates were higher during the 1975 to

1994 study period used by Olson (1999). A slight decline in the estimate from the period of 1975 to 1994 to the 2013 estimates was apparent for foreign-born persons as well as Canadian-born non-First Nations, although not for the province overall. Table 2.2 also shows an apparent "U-shaped curve of concern" (Reichman, 1991, p. 741) of TB incidence for First Nations: being high initially, then declining, and rising again.

Table 2.2 Population-specific TB case rates (per 100,000) of active TB in Manitoba: Various sources

Period Population	1975-1994	1992-1997	1992-1999	2004-2008	2006-2008	2012	2013
First Nations	87.9	44.3	48.4	65.3	-	-	85.3
• On-reserve	39.9	33.7	-	68.8	71.9	116.2	89.1
• Off-reserve	68.8	-	-	59.6	-	58.9	42.7
• Winnipeg	-	56.2	-	-	-	-	-
Foreign-born	25.8	20.0	22.0	-	-	-	20.8
• Winnipeg	-	23.6	-	-	-	-	-
• Outside Winnipeg	-	3.9	-	-	-	-	-
Canadian-born non-First Nations	-	3.5	3.3	-	-	-	1.4
Overall rate	13.7	-	9.2	9.7‡	-	10.9	13.4
Source	(Olson, 1999)	(Al-Azem, 1999)	(Blackwood et al., 2003)	(Long et al., 2013)	(First Nations and Inuit Health Branch, 2011)	(Epidemiology and Surveillance Unit, 2013)	(Public Health Agency of Canada, 2015)

Notes:
**First Nations are Status Indian people registered under the *Indian Act (Canada)*, this does not include the Metis.
‡ "All Canadian-born", which includes First Nations, Metis, Inuit, and Canadian-born non-Aboriginal, and excludes all foreign-born

Drug-Resistant TB in Manitoba

Between 2002-2012, Manitoba has had several drug-resistant cases of TB reported, including two cases of extensively drug resistant (XDR) TB, six cases of multi-drug resistant (MDR) TB, and 60 cases of mono-resistant TB (Table 2.3). Canada-wide, only eight XDR TB cases were reported between 2002-2012, with two being in Manitoba. In other words, during this 10-year period, Manitoba contributed 25% of the total number of XDR TB cases in Canada (Public Health Agency of Canada, 2013).

Table 2.3. Drug Sensitivity Testing Results of M.TB. isolates, Manitoba: 2002-2012

Drug Sensitivity Test Result	Cases (#)	Proportion of Total (%)
Isolates susceptible	1,023	93.77
Mono-resistance	60	5.50
Multi-drug resistant (MDR)	6	0.55
Extensively drug resistant (XDR)	2	0.18
Total	1,091	100

(Based on Public Health Agency of Canada, 2013, Appendix 3, Table 7)

The presence of drug resistant TB in Manitoba, in the wake of a growing global problem of TB drug-resistance, identifies a concern as to whether all patients are completing treatment to prevent drug-resistance. The standard is that all active TB cases should be treated with multi-drug regimens (i.e., no mono-therapy), and all patients with drug-resistant TB should have rigorous contact investigations to ensure contacts are evaluated and treated for latent drug-resistant TB infection (Kliiman, Gunther, & Altraja, 2012).

While guidelines are already in place in many regions regarding drug resistant strains of TB, a recent study of five European low-incidence countries' control practices for MDR/XDR-

TB cases found numerous problems in surveillance (treatment outcomes not documented properly), hospital infection control (facilities and procedures), clinical management (inadequate bacteriological diagnosis, regimen selection and treatment duration); and laboratory support and diagnostic/treatment algorithms (Kliiman et al., 2012). The extent to which these issues are problems in Manitoba is currently unknown. However, performance indicators could help identify issues with programming for drug-resistant TB.

Prior to 1990, no record of drug-resistance was maintained in the Manitoba TB Registry (Olson, 1999). For the period of 1990-1994, 9.9% of TB cases had unknown drug-sensitivity with First Nations having the highest percentage (12.2%) with unknown drug-sensitivity, while 5.7% of foreign-born cases had unknown drug-sensitivity (Olson, 1999). Drug resistance has since increased in Manitoba since Olson's (1999) study, which covered the period of 1990 to 1994 with respect to drug resistant TB. During the period of 1990 to 1994, drug-resistance was present in 3% of the overall number of TB cases in Manitoba, 0.5% in the First Nations population, and 9.2% in the immigrant population (Olson, 1999). In Manitoba, between 2007-2011, 6.58% (34 of 517) of culture-positive TB cases were resistant to isoniazid (INH) and in 2011 2.1% (2/97) were multi-drug resistant (MDR) (Alfa, 2012). A recent report on drug-resistant TB in Canada for 2012 shows a higher percentage of drug-resistant TB than previously, with approximately 8% of TB cases being infected with drug-resistant *M.tuberculosis* strains (Public Health Agency of Canada, 2013).

While the increase in drug-resistance is a real problem, prioritizing drug-resistant forms of TB over strong general TB prevention, diagnosis, and care is inappropriate. The term drug-resistant invokes a 'fear factor', particularly with non-expert policy makers, that may result in

funding being re-directed away from general TB prevention, diagnosis, and care to focus on drug-resistant cases (Khan & Coker, 2014).

PART II. PERFORMANCE MEASUREMENT IN TB PREVENTION, DIAGNOSIS, AND CARE

The preceding sections provided an overview of the history and epidemiology of TB in Canada and Manitoba particularly, including the social determinants of TB. The global principles of TB prevention, diagnosis, and care and strategies for the control and elimination of TB in the modern era were also reviewed. This part of the literature review focused on the methods used to measure performance on these program components. According to McNabb et al. (2004), performance measurement (PM) offers a means of accountability to central government and to the public regarding the use of public resources by TB programs. PM helps identify areas of strong or weak performance and when tracked over time can provide a system for monitoring progress towards TB elimination through analysis of TB prevention, diagnosis, and care processes, systems, and outcomes (McNabb et al., 2004). Prerequisites for conducting PM identified by the European framework for TB elimination in low-incidence countries include disease surveillance using registries that document all cases and at minimum record treatment outcomes. The following are four broad dimensions of performance for TB prevention, diagnosis, and care programs, with some specific examples, stated in the *European framework for tuberculosis control and elimination in countries with a low incidence* (Broekmans et al., 2002):

- "Indicators of government commitment (e.g., availability of national tuberculosis control policy); Coverage of the national policy (e.g., proportion of country implementing national strategy);

- "Indicators of control performance (e.g., proportion of definite cases, proportion of definite pulmonary tuberculosis cases with successful outcome (cure and treatment completion), and proportion of tuberculosis cases with unsuccessful treatment outcomes (death, failure, treatment interruption), assessment of BCG coverage);
- "Indicators of the functioning of the surveillance system (e.g., time trends in tuberculosis notifications, for all and pulmonary cases); Number of cultures and proportion of cultures positive for Tuberculosis complex among all examinations requested for mycobacterial investigation; Number of direct smear microscopy examinations and proportion of positive results; Estimate of patient's and doctor's delay in diagnosis and treatment; Prevalence of multidrug-resistant tuberculosis in new and retreatment tuberculosis cases.
- "Indicators of training, supervision, and other managerial aspects of tuberculosis control." (p. 773).

Included in the *European framework* is a requirement that all TB surveillance systems in low-incidence European countries must capture these indicators to assess progress towards elimination of TB in line with previously established consensus statements on monitoring of TB (Broekmans et al., 2002). Fundamental variables collected from individual TB cases based on these consensus statement are: (i) date of starting treatment, (ii) place of residence, (iii) date of birth, (iv) sex, (v) country of origin, (vi) site of disease, (vii) bacteriological status, (viii) history of anti-tuberculosis treatment, and (viiii) treatment outcome (Broekmans et al., 2002).

From Neglect to Performance Measurement: TB Elimination in the United States

In the United States, federal funding cuts for TB programming, reduced state and local prevention and control efforts, were factors leading to a resurgence in cases during the mid-1980's (Reichman, 1991). Other factors included the rise of HIV/AIDS and the erosion of the

social safety-net (Institute of Medicine, 2000). The sudden rise of TB rates became known as the "U-shaped curve of concern" (Reichman, 1991, p. 741) and was met with intensified efforts to eradicate the disease at enormous cost (Institute of Medicine, 2000). Between 1993-2003 the overall US incidence rate of TB fell 44% due to these intensified efforts and also, to an extent, due to a cohort effect (France et al., 2007). More recently, the period of 2008 to 2009 saw the largest single-year decrease in the rate of TB in the US since data were recorded, decreasing 11.4% from 4.2 cases per 100,000 to 3.8 cases per 100,000 (Winston, Pratt, Armstrong, & Navin, 2010). This decrease was country-wide, with the largest drop in the rate among US-born persons making it improbable that stricter immigration screening contributed to the declining TB rates (Winston et al., 2010). Whether the US can sustain this decrease depends on a several factors, including program performance, financing, and social determinants of health. An examination of the US experience performance measurement of TB prevention, diagnosis, and care follows.

What happened between these periods? The ability to examine TB programs through performance measurement data allowed for in-depth investigation of the association between TB services and changes in the TB incidence and prevalence. Using US-CDC TB performance targets, Hughes *et al.* (2010) analyzed US CDC data for the period of 2004-2009 and reported improved performance for most indicators of TB case management (Hughes et al., 2010). The exception was three of four indicators pertaining to contact investigation and follow-up. The data collected by the CDC's National Tuberculosis Indicators Project (NTIP) thus provided key insights into areas where performance improvements were needed, along with positive feedback on areas of strong performance. Preliminary analyses of epidemiological data by CDC and state TB programs suggested that the decline in case counts was attributable to an actual decline in

incidence, as opposed to under-reporting, changes in immigration, or other potential causes (Winston et al., 2010). With correlation between improved program performance and declining rates nationally, the US-CDC model of PM suggests that focused investment in creating and monitoring national targets, as well as funding their use throughout the country has contributed to the recent, significant, reductions in the incidence of TB in the United States. However, the monitoring of TB program performance alone cannot cause the decline in rates. Rather, the US focus on TB elimination, which includes vigorous contact tracing and treatment and resources to implement strong TB elimination strategies, were likely causes of these declines. Although without a complete examination of the numerous factors contributing to the rate of TB it is impossible to say with any certainty what the true causes of these declines were. The following is an analysis of data from Canada and the US on treatment success and case rates.

Treatment success data published by the WHO confirms that the United States has had more success in treating TB than Canada during the period of 1997 and 2011 (Fig. 2.3) (World Health Organization, 2014). Moreover, the US has had a faster decline in the TB incidence rate than in Canada for the same period, which suggests that the US-CDC approach to TB prevention, diagnosis, and care, which involves rigorous PM, is more effective (Fig. 2.4) (World Health Organization, 2014).

Examining measures used in the United States and those presented for use in Canada is vital to developing a set of valid, informative, actionable, comparable, and contextually-relevant performance measures of TB prevention, diagnosis, and care for Manitoba. The following section looks at a range of indicators from a variety of published sources.

Figure 2.2. Annual TB Treatment Success: Canada and United States, 1997-2011

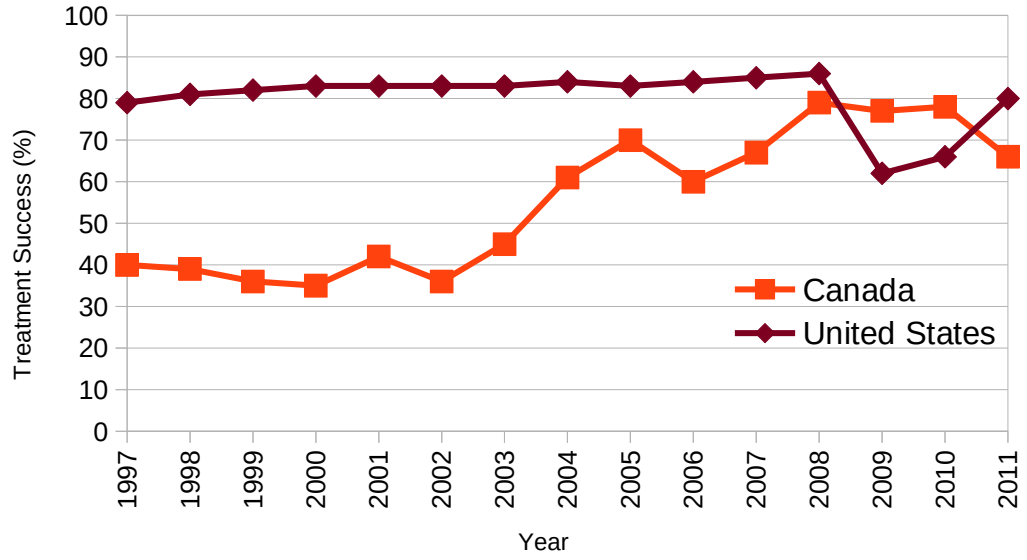
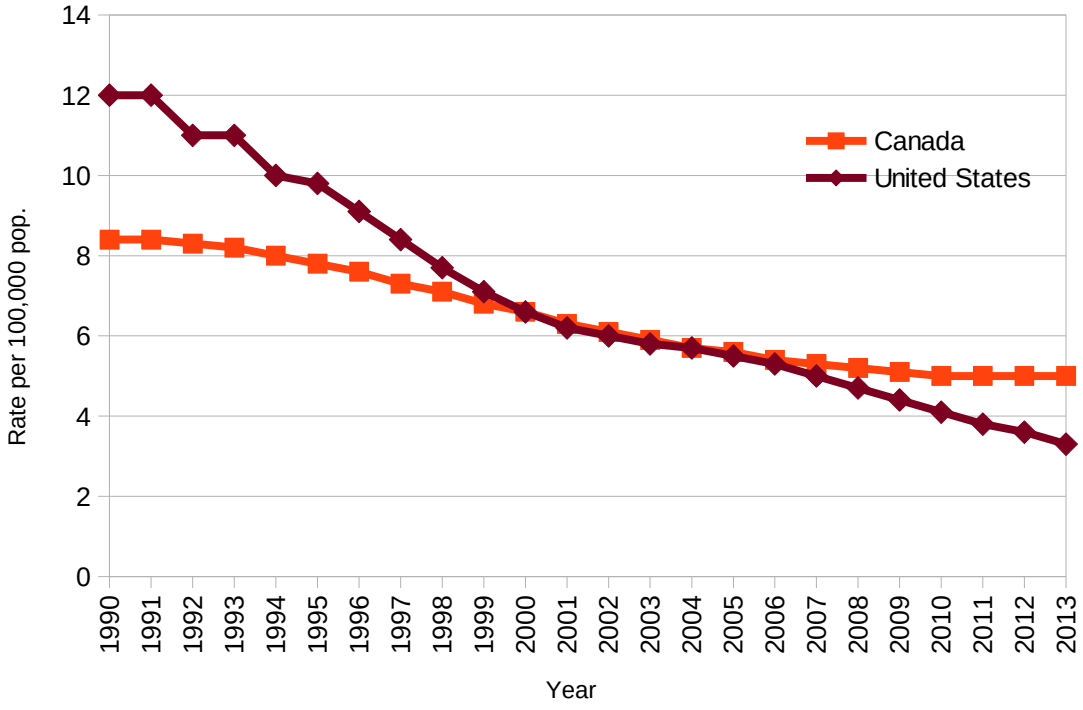


Figure 2.3. Annual TB Case Rate: Canada and United States, 1990-2013



Performance Measures Used in TB Prevention, Diagnosis, and Care

Numerous measures of TB program performance are currently used or under development. Outcome measures, process measures, and system measures are the major categories of PM's (Smith et al., 2009). Below is a review of studies examining TB prevention, diagnosis, and care program performance, primarily from US sources. Where possible, Manitoban and Canadian literature are used to highlight performance measurement potential.

From this review, some performance targets identified measure multiple aspects of TB prevention, diagnosis, and care. One measure is culture conversion from positive to negative, and the time for this to happen. This measure captures several aspects of TB prevention, diagnosis, and care, such as: (a) the bactericidal activity of a particular drug regimen, (b) the adherence of a patient to the regimen, and (c) patient properties, such as immune system function, which itself is made of multiple interacting and synergistic factors, including but not limited to genetic, behavioural, and environmental/social factors.

Performance measures tell us more than how a TB program is performing. Performance measures also reflect underlying social and individual factors about the TB patient population and are population health measures – as illustrated by TB incidence rates and trends in rates. The following are other key measures of TB prevention, diagnosis, and care, including their rationales and selected estimates.

Early Detection of Pulmonary TB: Smear Negative at Diagnosis

Acid-fast bacilli (AFB) smear positive TB cases are more infectious than smear negative TB cases. The proportion of infectious pulmonary cases that are smear positive is a performance

indicator of early detection of TB, which interrupts the progression of disease and transmission to others. The use of this measure by Al-azem (1999) showed, for the period 1992-1997, that 50.8% of active TB cases in Manitoba were smear positive, 40.8% were smear-negative, while 8% had no smear test at all. The proportion of pulmonary TB cases that were smear-negative was an indicator of early detection of pulmonary TB.

Human Immunodeficiency Virus (HIV) Testing & Reporting

In 1992 the Canadian Thoracic Society, Tuberculosis Directors of Canada, Department of National Health and Welfare (now Health Canada) in consultation with the provincial and territorial epidemiologists, AIDS coordinators and HIV caregivers, released a statement on HIV and TB co-infection (Long et al., 2014). This statement included the recommendation that all active TB cases be offered testing for HIV in-line with the principles of informed consent (Long et al., 2014). The reason for this recommendation is the synergistic relationship between TB and HIV, which must be taken into account when developing TB prevention, diagnosis, and care plans (Long et al., 2014). A key motivator for universal HIV testing of TB cases is that susceptibility to TB disease is much greater in HIV infected and other immunocompromised persons, with lower CD4+ cell counts leading to higher progression from infection to disease in a dose-response manner, as well as higher risk of reactivation of disease (Sester, Bumbacea, Duarte, & Lange, 2012). Concern about the opt-out HIV testing potentially overriding patients' informed consent have been expressed, with ethical justifications centred on the personal and public health benefits of testing. Individual care outcomes are better with earlier detection and the prevention of HIV transmission is aided by knowledge of HIV status and subsequent contact

investigation and treatment for HIV and TB. Moreover, there are very limited risks from the actual testing process – although positive test results and the potential ramifications of a diagnosis of HIV must be handled with care, by public health officials, physicians, nurses, and people now living with HIV.

According to Harris et al., (2006) HIV is "the most potent risk factor for progression to active TB disease" (p. 165). For instance, people aged 15-49 years diagnosed with active TB are 19 times more likely to be HIV positive than the general population, and people living with HIV were 20-30 times more likely than the general population to develop TB disease (Diel & Nienhaus, 2012).

Another important reason for HIV testing of TB cases, is that the presence of HIV significantly complicates TB treatment, with the need to incorporate highly active antiretroviral therapy (HAART) into TB care plans. As well, TB is the leading infectious disease causing death amongst people living with HIV/AIDS worldwide, causing 1 in 5 deaths amongst people living with HIV, thus TB care for persons living with HIV is essential (World Health Organization, 2013). Because of the strong links between TB and HIV/AIDS, TB has been classified as an AIDS-defining condition (US-CDC, 2008). Inadequate HIV-testing facilities in sub-Saharan Africa have led to the practice of defining AIDS cases based on death from TB.

In Canada, the prevalence of HIV-TB co-infection is estimated to lie between 1.6% and 19% (Phypers, 2007). Between 1997-1998, only 21.6% of active TB cases recorded in the Canadian Tuberculosis Reporting System (CTBRS) had documented HIV testing (Harris et al., 2006). Yet, all TB cases should be tested for HIV to help practitioners tailor treatment to patients and by recording the results to better understand the epidemiology of the TB/HIV co-infection

(Harris et al., 2006).

In Manitoba, an estimated 41% of TB active TB cases (665/1616) diagnosed between 2000-2012 had an HIV test result recorded. Of the 41% tested, 8% tested positive for HIV, which is (as expected) significantly higher than the prevalence of HIV found in the general population (Epidemiology and Surveillance Unit, 2013). In the Winnipeg health region, 14.1% of TB patients did not have a documented HIV test result, which demonstrates a much better performance result than for Manitoba overall (Whitlock et al., 2012). With an increasing number of TB patients being offered HIV testing there are grounds for optimism when it comes to this measure of TB prevention, diagnosis, and care program performance (Whitlock et al., 2012).

Nevertheless, Manitoba still has a long way to go before achieving a goal of 100% HIV testing of TB cases, and the same is true for Canada overall. In 2004, there were 38 HIV positive TB cases out of a total of 374 TB cases with known HIV status in Canada, which is 10.16% of cases with known HIV status being HIV positive cases (Phypers, 2007). In 2004, Manitoba's proportion of TB cases with known HIV status that were HIV positive was 17.65% and Alberta's proportion was 2.2%.

Table 2.4 summarizes HIV testing outcomes into two categories: HIV status reported (known) and HIV status not reported (unknown). In Table 2.4, Manitoba's proportion of TB cases with known HIV status was 35.4%. Alberta had the highest proportion of TB cases tested for HIV at 83.5%, compared to the national proportion of cases with an HIV test result reported of 23.2% (Table 2.4).

Table 2.4. HIV status reporting of TB cases: Canada, Alberta, and Manitoba: 2004

HIV Status	Canada	Alberta	Manitoba
Reported (#)	376	91	51
Un-Reported (#)	1239	18	93
Total	1615	109	144
HIV Status Known (%	23.3	83.5	35.4

(Based on Phypers (2007)

Contact Investigation and Latent TB Infection Diagnosis and Treatment

A contact is a person who have been exposed to an infectious pulmonary case of TB and that is named by the index or source case during a contact investigation (CI) as someone who is (a) known to the case and (b) who has been in close contact with the case in the recent past (Tian, Osgood, Al-Azem, & Hoeppner, 2013). The goal of the CI is to identify latent and active TB through medical evaluation of contacts with an *a priori* commitment to treatment of those who are positive for active or latent TB. Contact tracing is fundamental to reducing both the incidence of active TB disease as well as the prevalence of latent TB infection in the general population (Tian et al., 2013). Contact tracing is even more important in the presence of one or more of the following: (a) HIV-TB co-infection, (b) multi- or extensive-drug resistant TB (MDR/XDR-TB), and (c) prolonged contact between case and children (Cauthen et al., 1996; Diel & Nienhaus, 2012; Tian et al., 2013). While contact-tracing is vital for these groups, the evidence base is not completely clear when it comes to preventive treatment in the presence of all three risk factors (i.e., an HIV-positive child exposed to an MDR/XDR-TB case (Whittaker, Jones, & Kampmann, 2012). Although new Canadian standards for the treatment of LTBI

provide an evaluation of the evidence for many potential patient characteristics, and offer evidence-based recommendations for treatment of contacts related to potential risk factors for progression to active disease and the ability of prophylactic treatment to prevent of active disease, as well as concerns over adverse events.

TB control strategies focus on the detection, diagnosis, and care of active TB disease while TB elimination strategies focus on, in addition to control of active TB, the detection, diagnosis, and care of persons with latent TB infection (LTBI) (Broekmans et al., 2002). The focus on LTBI is at the heart of TB elimination in low-incidence countries (Broekmans et al., 2002).

LTBI diagnoses are made through the use of: (a) tuberculin skin test (TST), and/or (b) interferon-gamma release assay (IGRA). Neither TST nor IGRA have any ability to detect active disease. TST and IGRA can both identify the presence of tuberculin anti-bodies in people known or suspected to have come into contact with an infectious case of TB (Pai, Kunimoto, Jamieson, Menxies, 2014). Once identified, LTBI can be treated through several course of anti-TB medications, depending on the type of TB the contact has been exposed to. The standard LTBI treatment in Canada consists of 9 months of isoniazid (INH) (Menzies, Alvarez, and Kahn, 2014).. However, when the index case is infected with an INH-resistant strain of TB, the use of rifamycin-based drugs [rifampin (RMP), rifapentine (RFP)] and pyrazinamide is necessary (Menzies, Alvarez, and Kahn, 2014).

The goal of LTBI diagnosis and treatment are to prevent the progression from latent infection to active disease, which benefits both individual and public health. By preventing an LTBI patient from progressing to active TB disease, the possibility of future transmission is

reduced. The sooner people with LTBI or active TB are detected the sooner treatment can be started and the transmission process can be arrested. Measures of CI performance include:

- elicitation of contacts from the index case
- assessment of contacts for LTBI
- offer of treatment for LTBI
- acceptance of treatment for LTBI
- completion of LTBI treatment

An understanding of each is vital to the evaluation of any TB elimination program or strategy. The aggressive detection and treatment of LTBI in the US has likely contributed to the historic declines observed in the US recently (Fanning, 2015, personal comm.). The emphasis on LTBI diagnosis and treatment in Alaska Inuit over the last 40 years compared to the focus on Bacillus Calmette-Guerin (BCG) vaccination in Canadian Inuit, has also been credited with the substantially lower rate of TB in the former at the time of writing (Orr, 2015, personal comm.).

In the US, LTBI infection rates and treatment outcomes are regularly reported on. In Canada, the lack of LTBI diagnosis and treatment reporting is a gap in TB programming and a therefore also a gap in knowledge about TB in Canada. Examples of CI and LTBI performance measurement are described in the following sections.

Hughes *et al.* (2010) report that contact investigation is the weakest area of performance in the US at present. With a goal of 100% of AFB smear-positive TB patients having contacts elicited, the US performance on this indicator was 92.4% in 2002 and 92.2% in 2006, representing an ongoing challenge to LTBI case finding and treatment. Of the 92% of cases who

had contacts elicited above, the US 2015 national target is 93% of these contacts to sputum-smear positive (SS+) patients being evaluated for TB disease or LTBI, with actual performance ranging from 82.2% in 2002 to 79.6% in 2006, showing declining performance (Hughes et al., 2010). Moving to those with identified LTBI, the US national target was 88% starting chemoprophylaxis, and the true proportion was 72.2% in 2002, with a slight but not significant decline to 71.9% in 2006. Finally, the percentage of contacts to sputum smear-positive TB patients who complete LTBI treatment amongst those who start LTBI treatment increased from 59.1% in 2002 to 65.6% in 2006. While this shift is promising there is still a ways to go to reach the national 2015 target of 79% of acceptors completing treatment for LTBI.

In Canada, a study of LTBI treatment completion in Quebec using provincial health insurance pharmaceutical data from the period 2006 to 2010 showed that of those who started isoniazid preventive therapy, only 31.3% obtained a sufficient number of doses (≥270) and of those starting rifampin for treatment of LTBI, 64.9% had obtained the required number of doses (≥120) to achieve treatment completion (Rivest, Street, & Allard, 2013). Another Canadian study looking at LTBI treatment in the inner-city of Edmonton for the years 2005 to 2010 found that 57 of 77 patients (74%) who started treatment also completed treatment (Malejczyk et al., 2014). Of concern, however, is the variation in treatment completion rates across Canada, particularly among and within population groups. To date, no studies have sought to understand these variations and the reasons why such variations occur. Studies of this nature could determine whether contact tracing and a possible treatment gap could be addressed through federal public health support, similar to how the US-CDC assists state and local TB programs.

The other aspect of LTBI treatment is that before one can start treatment, one must first

accept it. Accepting treatment is not required in the case of LTBI. Colson et al. (2011) using a prospective cohort design examined the reasons that 14% of contacts from 12 CDC-funded Tuberculosis Epidemiological Studies Consortium study sites did not accept treatment for their LTBI. They found that having health insurance, having low acculturation, having social support, acknowledging having LTBI, believing the taking LTBI medicines is worth the trouble, and having good communication with providers of TB care, were all statistically significantly associated with increased odds of accepting LTBI treatment (Colson et al., 2011). This study went beyond measuring performance and investigated possible predictors of performance, i.e. the reasons for acceptance of LTBI treatment. It illustrates how one can develop a deeper understanding of the underlying factors associated with TB program performance, which is the key to improving performance and making progress towards eliminating TB.

Treatment Completion

Perhaps the most important indicator of a TB prevention, diagnosis, and care program's success is treatment completion. More so than incidence rates, as TB programs do not have control over the social determinants of TB, but do have control over the *treatment* of TB. Hughes *et al.* (2010) report that 82.9% of newly diagnosed active TB cases in the U.S., for whom 12 months or less of treatment is indicated, completed treatment in 12 months or less in 2004 (Hughes et al., 2010). This figure rose from 83.1% in 2005, to 83.7% in 2006 (Hughes et al., 2010) and to 89.0% in 2013 (National Center for HIV/AIDS Viral Hepatitis STD and TB Prevention, 2015). Treatment completion rates were higher in patients undergoing directly observed therapy (DOT) which has been shown to reinforce adherence to TB treatment regimen

and a key method of monitoring patient progress (Hughes et al., 2010).

Orr (2011) investigated another aspect of DOT/treatment completion, which considered a multitude of contextual and behavioural dynamics. In a two-part literature review on adherence to TB treatment in the context of Canadian Indigenous populations, Orr suggests that "[a]dherence to therapy for TB is unlikely to improve in a substantial way unless Indigenous beliefs about causation and care are incorporated into a program which has meaning for the patient" (Orr, 2011b, p. 138). Further issues related to treatment adherence and completion that must be considered with respect to First Nations include (Orr, 2011a) (pp. 124-5):

- "Poverty"
- "Adherence or non-adherence is a task-specific behaviour, and is not inherent to any particular ethnic or racial group."
- "The word "adherence" may only be applied when agreement to a care plan is initially established between patient and provider(s)."
- "Poor adherence to TB therapy is the most common cause of initial treatment failure and of disease relapse, which in turn contribute to patient morbidity, mortality, the transmission of the disease to others and the development of drug resistance. Adherence to care for TB disease is a necessity for the care of both the individual and society."
- "Canadian practice endorses a patient-centred approach while recognizing individual responsibility within society, as outlined in both the International Standards for Tuberculosis Care (ISTC) and the Patients' Charter."
- "Adherence behaviour is influenced by complex interactions between health system, personal factors and societal factors, rather than directly from individual factors acting independently."

Paediatric Cases

Paediatric cases of TB reveal ongoing transmission within a population (Whittaker et al.,

2012). Because children progress from infection to disease rapidly, it is a clear indication that there is an infectious case in the child's life, and therefore reverse contact tracing takes place, in which the goal is to find the source of infection (i.e., index case), as opposed to their contacts. The goal set by the US for 2015 is to "[d]ecrease the TB case rate for children younger than 5 years of age to less than 0.4 cases per 100,000." (US Centers for Disease Control and Prevention, 2010, p. 1).

During the period of 1991 to 1998, the incidence rate of paediatric TB (cases aged 0-14 years) declined dramatically for First Nations on-reserve in Canada, from 140 cases per 100,000 population, to just under 60 per 100,000 (Clark, 1999). The paediatric TB case rates for Canadian First Nations living on-reserve for the period of 2006 to 2008 was 17.5 per 100,000 for ages 0-4 years, and 11.5 per 100,000 for ages 5-14 years (First Nations and Inuit Health Branch, 2011). In Manitoba, for First Nations living on-reserve, during the longer period of 2000 to 2008, these rates were much higher, with ages 0-4 years having a rate of 22.7 per 100,000, and ages 5-15 years having a rate of 23.9 per 100,000 (First Nations and Inuit Health Branch, 2011). During this same period (2000 to 2008), Saskatchewan First Nations people on-reserve had the highest rates of paediatric TB in Canada, with ages 0-4 years having a rate of 157.8 per 100,000 and ages 5-14 years having a rate of 34.4 per 100,000 (First Nations and Inuit Health Branch, 2011). By 2013, Canada's case rate of TB for children 1-4 years of age was 2.4/100,000, and in Manitoba the case rate was an alarming 12.6/100,000 (Public Health Agency of Canada, 2015). The rate was highest among the general population and First Nations as well, indicating poor performance in controlling the transmission of TB in Manitoba Attention to paediatric TB is therefore essential to prevent the infection of children with TB and thereby reducing the long-

term pool of TB infected persons.

Re-Treatment Cases

The goal of TB treatment is to have a lasting cure after a complete course of treatment. When this is achieved the chance of developing drug-resistance is far lower (Kliiman et al., 2012). An individual with current active TB, who has a previous history of treatment, however, has a higher probability of harbouring drug-resistant strains of TB (Kliiman et al., 2012). TB programs should therefore enhance completion rates and compliance with TB treatment to prevent recurrence (Moniruzzaman, Elwood, Wong, Kazanjian, & Fitzgerald, 2009). The performance target for retreatment cases set by Fanning & Orr (2010) is <3% of annual incident cases. Re-treatment cases have two possible origins: (i) reactivation, and/or (ii) reinfection; each of these sources have particular implications for TB prevention, diagnosis, and care programs.

Laboratory Reporting

Another key indicator is laboratory reporting. Silin et al. (2010) analyzed delays in the reporting of TB cases by laboratories to the TB prevention, diagnosis, and care program in New York City's Department of Health and the Division of TB Control for the study period of 2003-2006. They found that 43% of persons living in New York City with confirmed or suspected TB were reported 4 or more days late, with late representing more than 7 days after specimen collection. Another key finding was that follow-up case to laboratories and local public health units to educate them on the importance of documenting all cases led to a significant improvement in documenting cases. The marked improvement was a shift down from 43% with

incomplete documentation to only 20% with incomplete information.

In a California study led by Pascopella et al. (2004), 26.9% of smear-positive and 46.8% of smear-negative patients had a delay in reporting laboratory results back to the specimen submitter. Among patients whose treatment was not started until specimens were collected, those with delayed laboratory reporting were more likely to have delayed treatment than patients with no laboratory reporting delays (odds ratio [OR] of 3.9 and 95% confidence interval [CI] of 1.6 to 9.7 for smear-positive patients and OR of 13.1 and CI of 5.3 to 32.2 for smear-negative patients), which remained significant after adjusting for other risk factors. Overall, these studies suggest that timely laboratory reporting supports timely initiation of treatment, which is crucial to controlling the spread of TB by reducing infectiousness.

Treatment Initiation

The timing of treatment initiation is a measure of TB program performance as well. Pirkis *et al*. (1996) studied the time from symptom onset to treatment initiation (guideline: 30 days) and the time from diagnosis to treatment initiation (guideline: 3 days) at Fairfield Hospital, Victoria, Australia (Pirkis et al., 1996). Using their guidelines (30 days and 3 days, respectively), they found that only 31% of both smear-positive and smear-negative patients initiated treatment within 30 days of onset of symptoms and 86% of smear positive cases initiated treatment within 3 days of their smear-positive status being established through microscopy.

Directly Observed Treatment

Directly observed treatment (DOT) is a process where trained TB workers physically

observe patients swallowing their prescribed TB medications. DOT is an internationally recognized best practice for administering TB medications (Tapiero & Lamarre, 2003). DOT prevents absconding from a treatment regime or alterations of the dose by the patient that may lead to drug-resistance by failing to fully eradicate the *M. tuberculosis* (MTB) in the patient's body.

In terms of program performance, the proportion of patients being managed using DOT is part of secondary prevention; that is, preventing the progression of disease and the emergence of drug-resistance in previously susceptible strains (Sia & Wieland, 2011). There are different ways to measure DOT and adherence to drug regimens, including, for example, attendance for appointments and pill counts (number prescribed / number taken).

Sputum-Culture Conversion

Once treatment has been initiated, additional sputum samples should be taken monthly (until negative) and subjected to microscopy and culture to determine when TB cases with positive sputum culture results for MTB convert to negative, which indicates treatment progress (Sia & Wieland, 2011). Depending on drug-resistance, time to culture conversion can be significantly longer (Qazi et al., 2011). According to the US-CDC performance objectives and targets for 2015, after four (4) months of treatment with anti-tuberculous drugs, sputum cultures should be negative in cases of pan drug-susceptible TB (US Centers for Disease Control and Prevention, 2010). Culture conversion after 2-months is considered a key clinical indicator of treatment efficacy, which makes it a clinically-relevant TB care performance measure (Caminero et al., 2011).

For instance, a recent multicentre Phase 3 US Food and Drug Administration (FDA) trial of new anti-tuberculosis drugs required objective measures of TB treatment success based on patient, public health, and regulatory goals for TB treatment (Bark et al., 2011). By analyzing the alignment of culture conversion with resolution of symptoms it was concluded that culture conversion is an objective bacteriological endpoint for assessment of treatment success in clinical trials (Bark et al., 2011). Furthermore, it was also a valid and useful measurement of a TB prevention, diagnosis, and care program's performance (Caminero et al., 2011).

Other considerations, when examining culture conversion, emerged in a Pakistani study that found that with multi-drug resistant TB, there are significant delays in culture conversion with a median time of 196 days (presumably from treatment initiation, although not stated in the article) and a cumulative probability of culture conversion at four months of treatment of 33% (95% CI: 24% - 46%) (Qazi et al., 2011). Factors influencing time to culture conversion included history of treatment with second-line anti-TB drugs, smear-grade at diagnosis, and smoking (Qazi et al., 2011).

Examples of Performance Measurement in Canadian TB Prevention, Diagnosis, and Care

Performance measures are increasingly being referenced in every imaginable government document. Their use in the health field has expanded rapidly within Canada, including to the area of TB prevention, diagnosis, and care. However, the actual implementation of performance measurement in Canada is far less mature than in the United States or Europe. This section looks at recent efforts in Canada to establish performance measurement in TB prevention and diagnosis within Canada. I begin by describing performance measures included in the Canadian

Tuberculosis Standards, 6th Edition. The 7th Edition of the Canadian Tuberculosis Standards did not contain any performance targets, focusing instead on reviewing and describing the evidence for various aspects of TB prevention, diagnosis, and care, and revising the standards based on this review. After, the United States' implementation of TB program objectives and performance targets through the US Centers for Disease Control and Prevention (US-CDC). An adaptation of these measures to the Canadian context is presented, followed by two provinces (Alberta and British Columbia) who have experimented with performance measurement in TB prevention, diagnosis, and care.

A major way Canada has fostered national collaboration on TB is through the Canadian TB Standards, which are now in their 7th edition. The standards were first published in 1972, with a paediatric supplement that followed in 1974. Subsequent editions were reported in 1981, 1988, 1996, 2000, and 2007. Like the previous editions, chapter authors were recruited from across Canada based on expertise. In the 6th edition, a number of performance indicators were included in two separate chapters. These are not seminal, but are some of the earlier performance measures and targets established in Canada. Box 2.2 presents TB program and laboratory performance standards found in the Canadian Tuberculosis Standards.

Box 2.2. Performance Measures c.f. Canadian Tuberculosis Standards, 6th ed., 2007

TB Laboratories (Wolfe, Antonation, & Sharma, 2007) (p. 32)

-Continued decrease in the national incidence rate of TB disease

-Timeliness of AFB smear, culture and susceptibility testing

-Availability of SOPs, monitoring of proficiency testing results and participation in an approved laboratory accreditation program

-Efficient and complete flow of information for optimal patient care

-Measurement and assessments of training programs

-Evidence-based appropriate funding available for laboratories.

Treatment of TB Disease (Hoeppner, Ward, & Elwood, 2007) (p. 129):

The ideal anti-TB drug regimen and drug delivery system for any patient will result, at a minimum, in the following:

- convert sputum cultures to negative after 4 months of treatment;
- achieve re-treatment rates of less than 3% within 2 years following cessation of treatment;
- achieve acquired drug resistance rates of 0%;
- be cost-effective (since DOT is the optimal mode of drug delivery, intermittent regimens of 120 doses [9 months] or 95 doses [6 months] are recommended);
- be tolerated by the patient (< 5% of patients will discontinue or modify therapy because of adverse effects); and

-achieve at least a 90% cure (negative sputum culture at the end of treatment) or treatment completion (treatment completed but no sputum culture at the end of treatment) rate within 12 months of starting treatment for patients who did not die or transfer out during treatment.

Treatment of LTBI (Hoeppner et al., 2007) (p. 137):

The ideal LTBI treatment regimen and drug delivery program for any patient will achieve, at a minimum, the following:

-result in 80% acceptance of treatment among persons with LTBI at high risk of

-progressing to active TB disease and without contraindications to INH or RMP;

-result in at least 80% of patients completing the required number of doses;

-result in drug discontinuation rates due to adverse effects of less than 5%; and

-result in less than 5 cases of active TB disease per 1,000 adequately treated patients at 2 years of follow up.

In 2010, the US-CDC issued performance objectives for the United States with targets to be reached by 2015 (US Centers for Disease Control and Prevention, 2010). Later the same year, Fanning and Orr presented a set of performance objectives and targets to Health Canada for use in First Nations and Inuit Health (FNIH) jurisdictions (Table 2.5), which were adapted from the US-CDC performance targets to the Canadian context (Fanning & Orr, 2010). In 2012, as noted above, PHAC and its Pan-Canadian Public Health Network, provided guidance on monitoring and evaluation to assess performance of TB prevention and control activities and measure progress towards those targets, which are listed in Appendix IV of their report (Pan-Canadian Public Health Network, 2012).

While few provinces are moving towards adopting performance measurement, Drs. Anne Fanning and Pamela Orr, as early as 2010, advised Health Canada's First Nations and Inuit Health Branch (FNIHB) National Headquarters that they too need to adopt performance categories, such as those based on the US-CDC TB Elimination Program Objectives and Performance Targets (US Centers for Disease Control and Prevention, 2010). The performance measures proposed by Fanning and Orr, were as follows (Table 2.5).

Table 2.5. TB Program Objectives and Performance Targets (Source: Fanning & Orr, 2010)

Objective Categories	Objective and Performance Targets
Completion of Therapy	For patients with newly diagnosed TB for whom 12 months or less of treatment is indicated, increase the proportion of patients who complete treatment within 12 months to 93%
Re-treatment Case	< 3% of cases per year are relapsed (re-treatment) cases*
TB Case Incidence	Decrease the incidence of TB to 3.6/100,000 by 2015
Contact Investigation	Contact list for each infectious case is completed within 7 days of diagnosis of the index case Contacts are assessed and, for those for whom prophylaxis is appropriate**, the prophylaxis is started within 28 days of completion of contact list ≥ 80% client acceptance of offered prophylaxis ≥ 80% completion of prophylaxis among those who accept ≥ 90% of all preventive therapy is given by DOPT
Laboratory Reporting	Sputum smears are reported back to ordering staff/facility within 48 hours of collection
Treatment	95% of patients who are diagnosed (clinically or microbiologically) with TB are started on treatment within 48 hours of diagnosis ≥ 90% of cases are treated by DOT 100% of cases of TB-HIV co-infection are treated by DOT
Sputum Culture Conversion	95% of patients with culture positive sputum will be sputum culture negative within 4 months of treatment initiation
HIV Status	95% of TB cases have HIV testing and have the result reported provincially and federally
Early Diagnosis	Decrease the percentage of pulmonary TB cases that are smear positive to less than or equal to 33% Mean and median time from onset of symptoms to onset of therapy is less than 4 months in 80% of cases
Prevention	100% of HIV positive persons are tested for TB infection/disease ≥ 80% of those at increased risk of TB reactivation due to impaired immunity (other immunosuppressed conditions, diabetes, renal failure as defined by creatinine clearance less than 20 ml/min., immunosuppressant medication, pulmonary silicosis) are tested for LTBI and assessed for possible preventive therapy.

Although the Canadian TB Standards have existed for decades, and the movement to adopt and apply performance measurement is a relatively recent phenomenon. The following illustrates how it has been approached in two Canadian provinces. While Canadian TB performance standards have existed for some time, they have not been regularly monitored or reported on by Canadian TB prevention, diagnosis, and care programs (Orr, 2011a).

In British Columbia, a *Strategic Plan for Tuberculosis Prevention, Treatment, and Control* prioritized a number of actions including enhanced TB surveillance. To this end, the following objectives were developed by British Columbia (BC Communicable Disease Policy Advisory Committee, 2012):

- Formalize a TB surveillance network that enables assessment of performance targets.
- Formalize a process that communicates TB data between the BCCDC, Provincial Health Labs, and regional health authorities in a timely manner.
- Establish a TB surveillance lead in each regional health authority.
- Establish tripartite protocols regarding Aboriginal TB surveillance data management.

In 2014, the BC committee reported that they had met the first objective but others were still a work in progress (BC Communicable Disease Policy Advisory Committee, 2014). The development and measurement of performance indicators, for instance, were slated for completion within 2 to 5 years. The committee had also committed, by 2017, to meet all performance targets listed in the *Guidance for Tuberculosis Prevention and Control Programs in Canada*, as reported above.

Alberta's TB program led the way by using a performance measurement approach in their

report on TB in that province for the period of 2000-2004 (Sutherland et al., 2007). Since then, however, Alberta has not made performance measurement a regular reporting feature. Performance measures reported on by Sutherland et al. (2007) included (p. 34):

- bacteriologic confirmation of disease (at least one sample sent for culture and drug-susceptibility testing prior to treatment initiation);
- initial treatment with multiple drugs;
- timeliness of treatment onset ("90 per cent of anti-tuberculous treatment should start within 72 hours of a smear positive sputum specimen being collected"); and
- HIV screening of active tuberculosis cases ("80 per cent of people with a diagnosis of active tuberculosis will have an HIV test within a two month period around the tuberculosis diagnosis date.")

Also reported were indicators of relevance to TB preventive treatment, and they were: 1) the numbers of *high-risk people* offered preventive therapy and 2) the proportion of people who agreed to undertake preventive therapy who complete treatment (Sutherland et al., 2007). High-risk people (for progression of LTBI to active disease) were defined as those with any of the following conditions: cancer, HIV, diabetes, renal failure, injection drug use, having had a transplant and requiring treatment with tumour necrosis factor (TNF) inhibitors or long term corticosteroid use. Specific targets for these measures were (Sutherland et al., 2007):

- 100% of TST positive high-risk people will be offered preventive treatment unless contraindicated; and
- 75% of those accepting LTBI treatment will complete the course of therapy

Year-to-year changes in the proportion of patients meeting the performance guideline and comparison with the target proportion allowed Alberta's TB program to understand successes and challenges in delivering high-quality TB care. For example, a decline in the proportion of patients started on recommended multi-drug treatment regimens was cause for concern; however, a strong increase in HIV testing of TB cases was a programmatic success (Sutherland et al., 2007). This type of analysis can help programs track their performance over time and strengthen services that are weak, and build on success.

A study demonstrating the merit of performance measurement approach to TB in Alberta was used to evaluate Alberta TB outcomes for culture-positive pulmonary TB cases for those ≥ 15yrs old in two decennial periods, 1989-1998 and 1999 to 2008 (Jensen et al., 2012). They found that there were some improvements in several areas of TB prevention, diagnosis, and care, and that some worsened while no change was noted in others (Jensen et al., 2012). The authors reported statistically significant improvement in the proportions of: 1) Patients treated with DOT (85.89% to 97.4%); 2)Incident paediatric cases (34% to 11%); 3) Contacts assessed for LTBI (79.3% to 89.9%); 4) Completion of preventive treatment for LTBI amongst those accepting treatment (64.5% to 85.2%); and 5) Non-adherent or lost to follow-up (16.3% to 8.3%) (Jensen et al., 2012).

Jensen et al. (2012) also found a statistically significant reduction in the proportion of LTBI cases accepting chemoprophylaxis (73.1% to 63.8%). There was no significant change in the proportion of patients who: (a) completed treatment or were cured (82.1% to 86.8%), (b) died (16% to 11.8%), or (c) transferred out (1.9% to 1.6%) (Jensen et al., 2012). Jensen et al.

concluded that significant progress was made in reducing the rate of TB for Canadian-born non-First Nations, with some progress for First Nations, and no real change in the rate for foreign-born people. With 78.9% of Alberta TB cases amongst the foreign-born this is of high importance for Alberta (Jensen et al., 2012).

Summary of Literature Review

This review demonstrated that national and provincial TB programs have been collecting data that for surveillance purposes but few have used the data they collect to assess performance. According to Orr (2011), the existence of performance measures is not sufficient to eliminate TB. Surveillance data has to be regularly monitored within provincial TB programs, using these performance measures, and reported on publicly.

The performance measurement-informed studies reviewed provided key information regarding where improvements are needed and how programs are performing over time. These studies demonstrated the importance of developing and adopting a local, regional, provincial, and national performance targets approach to TB prevention, diagnosis, and care.

Furthermore, adopting performance measurement tools and systems to analyze TB services allows program to first understand and secondly address the performance of TB prevention, diagnosis, and care efforts within a jurisdiction. Moreover, utilizing descriptive and analytical epidemiological and statistical methods supports the objective assessment of TB prevention, diagnosis, and care based on clearly defined objectives (e.g., treatment completion). When these approaches are combined, the information generated best informs policy development, program improvements, resource allocation to improve TB services, which should

yield – in time – reductions in TB rates. As governments and health authorities restructure their programs to eliminate TB, there is an opportunity to explore new evaluation approaches and to inform how TB Registry data is collected and used.

From this review, evidence-based indicators to gauge program performance have shown promise. The use of performance measurement for TB programs in the United States and Alberta appears to have contributed to the faster decline in rates in those jurisdictions. Given the high rates in Manitoba, a study investigating the merit of performance measures stratified along ethnic-origin and geographical lines is timely to improve efforts to prevent, control, and eliminate TB.

This thesis examines how the Province of Manitoba may adopt what is becoming the norm in TB surveillance and monitoring. Why Manitoba? Manitoba experiences one of the highest incidence rates of TB in Canada (Epidemiology and Surveillance Unit, 2013; Halverson et al., 2014; Public Health Agency of Canada, 2015). This high rate begged the following questions: 1) How is the Manitoba TB program performing in terms of prevention, diagnosis, and care and what efforts should be made for high-risk groups? 2) Are there differences between groups within Manitoba in terms of TB prevention, diagnosis, and care? Blackwood et al. (2003, p. 10) suggest that: "Targeting and intensifying control measures in the immigrant and treaty status Aboriginal sub-populations should be a priority in striving for the goal of tuberculosis elimination in Manitoba." The persistence of TB and the inequality in TB hospitalizations observed in Manitoba illustrates the need for Manitoba Health to adopt performance measurement to monitor TB prevention, diagnosis, and care programs and ensure all cases are managed according to clinical guidelines (Martens, P; Brownell, M; Au, W; MacWiliam, L;

Prior, H; Schultz, J; Guenette, W; Elliott, L; Buchan, S; Anderson, M; Caetano, P; Metge, C; Santos, R; Serwonka, 2010). Manitoba's TB prevention, diagnosis, and care context warrants the use of performance measures that are stratified along ethnic-origin and geographical population group, are relevant to improving TB prevention, diagnosis, and care, and that involve specific populations in the process of eliminating TB through intensified control. The Canadian Tuberculosis Standards and the Pan-Canadian Public Health Network guidance document on TB both support the need for performance measurement in TB prevention, diagnosis, and care at the provincial level.

To this end, a methodology was designed to study TB prevention, diagnosis, and care in Manitoba through a performance measurement framework based on the epidemiology of TB in Manitoba. The PM frameworks reviewed above served as the sources for the performance measures used in the present study. A cross-referenced summary of these measures and their inclusion/exclusion from each of the frameworks is provided below (Table 2.6), which shows the performance measures used in the present study, and the number of times the performance objective is mentioned by key frameworks. In Table 2.6, treatment completion / cure, re-treatment, HIV testing/reporting, contacts elicitation, and contact assessment were mentioned in all frameworks. Incidence rates were mentioned in all but one framework, while paediatric TB was mentioned in only a single framework and case mortality was not mentioned in any. Due to the high rate of paediatric TB in Manitoba, other literature supporting the validity and utility of paediatric TB as a performance measure are included in the bottom right corner of Table 2.6.

Table 2.6. Comparison of TB Performance Measurement Frameworks: Cross-reference of Objectives and Targets

Performance Measures (PMs) Used in Present Study	Canadian Tuberculosis Standards, 6th	United States TB Program Performance Targets (2015)	Proposed TB Program Objectives and Performance Targets for FNIH Jurisdictions	Guidance for TB Prevention and Control Programs in Canada – Appendix IV	PM Included (# of frameworks that mention the PM)
Incidence rates	Reduce incidence rates	2.5 / 100,000	3.6 / 100,000	No	3
Treatment completion / cure	90%	93%	93%	≥90%	4
Early Detection of Pulmonary Cases (smear-negative at Dx)	No	No	<33% smear-positive	No	1
Retreatment Cases	<3% of cases treated within 2-years of treatment ending	<3% cases/year	<3% cases/year	≤3% of cases treated within 2-years of treatment ending	4
HIV testing/reporting	90%	88.7%	95%	>90%	4
Paediatric cases	No	<0.4 cases / 100,000 for children 0-5 years	No	No	1
Case Mortality (crude proportion only)	No	No	No	No	0
Contacts Elicited	Implied; no specific target set	100% of AFB smear-positive	100% of infectious cases	(100% of infectious cases	4
Contacts Assessed	Implied; no specific target set	93% of AFB smear-positive	100% of infectious cases	100% of infectious cases	4
Citation	(Hoeppner et al., 2007; Wolfe et al., 2007)	(US Centers for Disease Control and Prevention, 2010)	(Fanning & Orr, 2010)	(Pan-Canadian Public Health Network, 2012)	(Long, Whittaker, Russell, Kunimoto, & Reid, 2004; Whittaker et al., 2012)

Notes: HIV: human immunodeficiency virus; AFB: Acid-fast bacilli.

3. METHODOLOGY

This chapter provides the analytical plan, data source, variable definitions, and discussion of statistical methods that comprised the methodology of this study. The chapter begins by revisiting the original research questions, describing the study design, population, and the source of data, including how the data source was selected, accessed, and used. This is followed by a discussion of the dependant variables (i.e., performance measures) and the independent variables. for this study. After this discussion is a detailed explanation of the statistical analysis, including the types of modelling used generally and the specific modelling of each performance measure (PM).

Research Questions Revisited

With the understanding gained through the literature review we may now refine the research questions to ask (1) how is Manitoba TB prevention, diagnosis, and care are performing according to the performance measures identified in PM frameworks, and (2) are there differences between ethnic-origin, age, sex, treatment history, or geographic groups in terms of the PMs identified. Sub-questions arising from these two research questions included: What study design will achieve the study aims? How does one calculate these performance measures using the TB data available in Manitoba? Which statistical methods are most appropriate to analyze them? These sub-questions fall under the third research question, which was: Which performance targets are measurable with the Manitoba TB Registry and which are not? This chapter develops a methodology to answer these research questions

Study Design

This study is a cross-sectional analysis of TB prevention, diagnosis, and care in Manitoba. A cross-sectional study design is an observational study design that uses observations collected at a one time point or time period (Mann, 2003). The primary purpose of this design for health research is to provide a snapshot of the study population during that period, particularly the prevalence of conditions or outcomes of interest. Cross-sectional studies in health research often seek to estimate the prevalence of risk or protective factors amongst the population and test for associations between hypothesized risk or protective factors and outcomes or conditions of interest to the researcher. Because both exposure and outcome occur at the same time in a cross-sectional study, the direction of any associations found between variables cannot be ascertained. Estimation of trends is also not possible within a cross-sectional analysis because only one point or period of time is recorded. However, variables such as age, sex, ethnic-origin, which cannot be caused by other variables, are exceptions to this rule.

For the present study, the two aims of this study that motivated the selection of a cross-sectional design were (1) providing a baseline of TB program performance in Manitoba, rather than to determine trends, and (2) pilot testing a performance measurement (PM) framework. These two study aims required the estimation of the *prevalence* or *probability* of each individual performance measure being met, without the requirement for a trend analysis, or being concerned with the direction of the effect (because the key independent variables could not be caused by the outcome). The second aim also motivated the selection of a cross-sectional design, due to its relative simplicity compared to a cohort, even a retrospective cohort, design. Because this study was a pilot of performance measurement on TB data in Manitoba, the investment of

additional time and energy into developing a cohort or case-control analysis would not have been appropriate.

The study design is therefore both descriptive and analytical, providing estimates of performance for the whole province as well as comparing patient groups (age, sex, ethnic-origin, and geographical). The methods, described below, are appropriate to cross-sectional data to study the probability of these patient groups meeting performance objectives and targets that were developed from the various frameworks.

Study Population

The study population included all TB cases diagnosed in Manitoba between January 1, 2008 and December 31, 2010 and reported to the TB Registry. Contacts to these cases were also included in the study population, although without the demographic, diagnostic, and treatment information that was provided for the cases. This is a population-based study because the Manitoba TB Registry is a population-based registry of TB cases and contacts in Manitoba maintained under provincial law requiring the reporting of cases and contacts to Manitoba Health. The case and contact definitions provided below were applied to the performance measures used in this study, based on the inclusion and exclusion criteria for each measure.

> ***Case***: A case is any individual listed in the Client Table of Manitoba TB Registry, which includes cases diagnosed with TB during the period of January 1, 2008 to December 31, 2010.
>
> ***Infectious Pulmonary Case***: an infectious pulmonary case means a case as defined above with at least one pulmonary specimen (sputum or bronchial washings) collected, tested, and recorded in the Laboratory Table that is culture-positive.

Contact: A Contact is a contact event recorded in the Manitoba TB Registry's Contact Table. A person could be listed multiple times for multiple cases, and each time they are listed is considered a separate contact (i.e., contact event).

Contact to an Infectious Pulmonary Case: A contact to an infectious pulmonary case is a contact as defined above, where the case has a culture-positive pulmonary (sputum or bronchial washings) specimen.

Unique Contact: A unique Contact ID Number in the Contact Table is a unique contact – that is, an individual person. Each unique contact (i.e., Contact ID Number) can be listed more than once, representing separate possible transmission events, which are referred to as contacts in this study.

Data Source

In Manitoba, there are two primary TB databases: the Manitoba Tuberculosis Registry ("TB Registry"), operated by Manitoba Health, and the Integrated Public Health Information System (IPHIS) managed by the Winnipeg Regional Health Authority (WRHA).

The TB Registry is the central database for TB case notifications, which are reportable to Manitoba Health by law (Minister of Health, 2009). The TB Registry has been used for previous studies on tuberculosis in Manitoba although not from a performance measurement perspective (Al-Azem, 1999; Blackwood et al., 2003; Olson, 1999). The TB Registry was selected because it contains case and contact information for the whole province of Manitoba, whereas the IPHIS, at least for the study period, contains only the information on Winnipeg TB cases and contacts. This however may have changed with the expansion of the WRHA's role in TB prevention, diagnosis, and care province-wide.

At a meeting of TB data stakeholders organized prior to the initiating the research, there was discussion of the existing TB databases within Manitoba and the requirements for access and use of any data contained in them. In addition to the TB Registry and IPHIS, Health Canada's

First Nations and Inuit Health Branch (FNIH) holds TB case and contact information for First Nation on-reserve health centres, collected during the provision of TB prevention, diagnosis, and care services. After the discussion it was decided that the TB Registry was the most appropriate data source for this project.

Based on the PM frameworks, indicators represented by select fields from the TB Registry were extracted by Manitoba Health staff and transferred to the Centre for Global Public Health at the University. Data requested and transferred included all TB cases and contacts reported to the Manitoba TB Registry during the three-year period starting January 1, 2008 and ending December 31, 2010. These data were the most recent TB case and contact data available at the time the request was planned for which complete follow-up data would exist and would provide a sufficient number of cases to perform multiple regression analysis.

The study data, abstracted from the Manitoba TB Registry by Manitoba Health, arrived as an Excel workbook file containing seven spreadsheets (hereafter referred to as tables). The tables were reviewed for content and ability to merge them for analysis. Tables were merged using the unique Client ID number. The process of merging was guided by analytical questions specific to this study. For example, to estimate the proportion of infectious pulmonary TB cases required the merging of the TB Client Table and the Laboratory Table by sorting the laboratory test results for each patient Client ID number chronologically by specimen collection date, selecting only the first observation for each case/client. To link predictor variables (e.g., demographic information) to the lab test results, the resulting-sorted laboratory table was then merged with the Client Table by Client ID number.

Another approach used to examine the data was to merge all the tables together by Client

ID number, then removing unneeded records afterward. This resulted in a data set of 10,372 rows, representing multiple records due to the many contacts listed in the contact table. This merged dataset was the primary dataset used for analyses, because it ensured complete merging of all variables. Thereafter, cases and contacts could be removed based on the inclusion and exclusion criteria for each performance measure, which are discussed below.

Performance Measures – Towards a Framework

The performance measurement framework for this study was developed through adaptation of existing performance measures used by or recommended for TB programs and studies of specific performance measures or, where available, entire performance improvement projects (Cass, 2013). The resulting performance measurement framework was also designed for the existing Manitoba TB data, which is discussed below. The original documents used to guide this study are a set of objectives and quantitative targets developed by the U.S. Centers for Disease Control and Prevention (US Centers for Disease Control and Prevention, 2010) and an adaptation of these objectives and targets to the Canadian context (Fanning & Orr, 2010). These two frameworks were the catalyst for the study design, and the literature review augmented and refined the performance measures. These performance measures were individually compared to the TB datasets available in Manitoba to develop a method for indicator development and estimation. For instance, a key consideration in accessing this data was the need for understanding performance measurement according to First Nations status. A description of the performance measures used in this study follows, which became the dependant variables in regression analyses described further below.

Dependent Variables

The performance measures are the dependent variables for the statistical analysis. The majority of the originally planned performance targets were not measured in or measurable from the Manitoba TB Registry data supplied for this study. So instead the broader objectives of these measures were adapted to the TB Registry data to create a set of measures that could be analyzed with the data available. A number of derived variables were developed to measure performance towards the objectives listed in the frameworks and could be considered dimensions of program performance (Table 2.6), which were described in the literature review:

1. Treatment completed or patient confirmed cured (negative culture)
2. Early diagnosis (infectious pulmonary cases that are smear *negative* when diagnosed)[3]
3. HIV test result on file
4. Re-treatment cases (cases that have been cases more than once)
5. Case mortality (death before or during treatment) [not modelled]
6. Paediatric cases (cases aged <= 14 years)
7. Contacts elicited (>=1 contact per infectious pulmonary case)
8. Contacts to infectious pulmonary cases who are medically assessed for TB

These measures are described in more detail, including their calculation, inclusion and exclusion criteria, and specific analysis methods, in the *Analysis of Performance Measures* section.

3 Note: this is the inverse of the performance target described by Fanning and Orr (2010).

Independent Variables

An independent variable is one that is not affected by the outcome of interest. Independent variables are selected because they are either known or believed to have an effect on the outcome of interest, or to confound a relationship between a hypothesized predictor variable and the outcome. These types of variables are also known as covariates, used to adjust for differences in case-mix (risk adjustment) and enable fair comparison between key question predictors, which could be categorical or continuous.

As previously noted, several independent variables were selected to both select and compare patient groups for determining if performance standards were met for each performance measure. The inclusion and exclusion process for each performance measure was based on the independent variables used in this study, which are described first in a cursory manner in the following section and in more detail in the Analysis of Performance Measures section.

While the selected factors and blocking criteria do not completely adjust for risk or case-mix, they do help provide more accurate comparisons of performance within and between ethnic-origin groups (Iezzoni, 2010). Further analysis using other factors (e.g., socioeconomic status, health status, health behaviours, etc.) would be needed to provide truly fair comparisons between ethnic-origin groups (Iezzoni, 2010). Unfortunately this kind of analysis was not feasible in the present study, which provides, an analysis of TB prevention, diagnosis, and care performance by ethnic-origin group but does not completely adjust for case-mix, risk factors, and any other potentially confounding variables when comparing performance between groups. Results are a reflection of a several aspects of treatment, including care by the TB prevention, diagnosis, and

care program and its providers and individual patient characteristics.

The following is an outline of the independent variables and identifies their respective, and sometimes multiple, role(s) in the analysis:

1. Age Group
    - Categorical covariate: 0-18 , 19-35, 36-55, 56+ years
    - Dependent variable: 0-14 years ("paediatric") and 15+ years ("adult")
2. Sex
    - Categorical covariate: Male and Female
3. Ethnic Origin
    - Categorical covariate: First Nation, Foreign-born, and Canadian-born non-First Nation
    - Inclusion/Exclusion Criteria:
        - Part II: First Nations
        - Part IV: Northern First Nations
4. Geography
    - Categorical covariate: on-reserve and off-reserve
    - Inclusion/exclusion: Regional Health Authority
        - Part IV: Northern
        - Part III: Winnipeg
5. Bacteriologic status (specimen types, smear result, culture result)
    - Inclusion/exclusion:
        - infectious pulmonary case
            - specimen type
                - Inclusion/exclusion: infectious pulmonary case ("bronchial washings" or "sputum") and sputum-smear positive case ("bronchial washings" or "sputum")
            - smear-result ("positive" or "negative")
                - Dependant variable: Smear-negative at diagnosis (Early Dx)
                - Inclusion/exclusion: smear-negative or smear-positive for contact investigation outcomes analysis
            - culture-result
                - Inclusion/exclusion: infectious pulmonary cases ("culture positive")
6. History of treatment
    - Categorical covariate: history of treatment for TB

Demographic Groups

This study focused on three "ethnic-origin" groups: (1) foreign-born, (2) Canadian-born non-First Nations, and (3) First Nations. These groups are internally diverse and used frequently in studies of TB in Canada (Public Health Agency of Canada, 2009a), the United States (as American Indians or Alaska Natives) (Hughes et al., 2010), and other commonwealth countries (Australia and New Zealand) according to their indigenous identity (Smylie, Anderson, Ratima, Crengle, & Anderson, 2006). How these groups were defined in the present study is outlined below.

Additional groupings include age and sex, which have different epidemiological profiles, and some variance between ethnic-origin groups. Finally, geographic sub-populations (Winnipeg, Northern Manitoba, and First Nations on- and off-reserve) were used to compare performance and are explained below. The inclusion of multiple groups is required to understand differences in the performance of TB prevention, diagnosis, and care services amongst these groups and will provide new insights into the epidemiology and control of TB in Manitoba. The importance of understanding healthcare performance according to ethnic-origin and geographic groups cannot be understated, and was summed up well by Smylie et al. (2006, p. 2030):

> "Although the development of macro healthcare monitoring systems is important, the underdevelopment of local performance measurement systems and marginalisation of Indigenous perspectives undermines effective local primary healthcare services by constraining the extent to which local services can access comprehensive performance data to guide service development. This oversight interferes with the ability of Indigenous communities to achieve the expression of Indigenous cultural

> values in health system development and affects the capacity of the system to contribute to the achievement of the highest attainable standard of health for Indigenous peoples."

Ethnic-Origin Group

The foreign-born includes anyone born outside Canada, whether from a high-incidence or low-incidence country, or be a lower as opposed to higher income individual, etc. Foreign-born persons from high-incidence countries will have higher probability of TB than foreign-born persons from low-incidence countries. In Canada, 80% of foreign-born immigrants are from high-incidence countries (Phypers et al., 2007). The foreign-born are a key sub-population group in the study of TB in low-incidence countries. In the TB registry, this group is captured through the variable *origin,* and cases are already coded as "foreign-born", thus requiring no recoding.

For this study, any person whose *ethnic-origin* is coded "Status First Nations" represented a First Nations person. Although the TB Registry identified Metis and Inuit cases of TB (n= 10), they were removed for two reasons: 1) the study objectives were to estimate First Nations specific performance, and 2) the number of cases was too small to conduct meaningful analysis. First Nations people were known in advance to comprise the majority of TB cases in Manitoba and were therefore the primary group of interest to this study, which required First Nation-specific analysis (Aspler et al., 2010; Fanning, 2011; Orr, 2011a, 2011b; Orsini, 2009).

A Canadian-born non-First Nation case is any case in the Registry who is not foreign-born and is not First Nations. The *origin* variable in the Registry data set is coded to identify this group. Canadian-born non-First Nations have a distinct risk profile, including significantly lower overall rate of TB amongst this group, with those becoming infected with TB usually

living in poverty.

Age Group

Age at diagnosis is an important covariate to produce age-adjusted estimates of performance when comparing groups, and as a stratification variable to compare performance between age groups. For this study, age at diagnosis was modelled as (a) a continuous variable, and (b) a categorical variable. The following age group categories were created:

- 0-18 years
- 19-35 years
- 36-55 years
- 56+ years

An additional paediatric case group (0-14 years) was created to measure the proportion of TB cases that are children and to compare this variable across groups using a dummy variable indicating whether a case is a paediatric case or not.

This measure allowed for age-specific TB rates, which are known varies considerably. Older people tend to have higher risk of TB disease because of greater lifetime exposure potential and a weakening immune system consistent with the ageing process. Interrupting transmission of infection from older to younger age groups is a key for long-term eradication of TB because children, once infected, can be a source of latent infection and new incident disease far into the future (Tapiero & Lamarre, 2003). As well, there is a more rapid progression from infection to disease amongst children and they are at higher risk of complicated forms of TB such as miliary/disseminated TB and TB meningitis (Tapiero & Lamarre, 2003). Reverse contact-tracing is a method of finding active cases, which is employed when a very young child

becomes a case, as the vast majority of children under 3 years will have been infected by an infectious case in the household (Whittaker et al., 2012).

Sex

Sex is an important covariate in comparing TB incidence and prevalence between groups. Being male or female affects the probability of contracting TB, with males being more likely than females, having higher rate of TB than women globally (World Health Organization, 2009). This pattern has been noted in Manitoba (Blackwood et al., 2003). Sex is therefore an important covariate in comparing performance between other groups of interest (e.g., ethnic-origin). While the different risk for TB between the sexes is known in Manitoba, what is not know is where there are differences between men and women in the prevention, diagnosis, and treatment of TB, i.e., in performance. Therefore, sex-based differences in performance of TB program are considered in this study.

Geography

In Manitoba, regional health authorities (RHAs) are geographic administrative and service entities. The Manitoba TB registry includes RHA as a standard field for public health follow-up purposes. In the study period, there were 11 RHA's operating, but since then, the numbers were reduced to five (Manitoba Health, 2012). Coding in the Registry data set already reflected the new RHA designations. They are: Prairie Mountain Health, Northern, Interlake-Eastern, Winnipeg, and Southern. Additional geographic variables included town (the city, town, or reserve that the case resides in) and residence (a variable relevant to First Nations,

indicating whether they are ordinarily resident on-reserve or off-reserve). While contacts to cases tend to fall within the same geographic area as the case, this designation, may not be accurate in all cases. Because the location of the contacts was not recorded in the registry, the assumption of geographic homogeneity between cases and contacts was made due to the way TB spreads. For example, the geographic sub-population unit, the City of Winnipeg and Northern Manitoba, was used for those cases and contacts falling within those regions. Finally, for First Nations (FN), the registry included the residence location, either living on reserve or living off reserve, which allowed for comparisons between those geographic groupings.

Bacterial Status

Bacterial status refers to the specimen(s) collected from cases during diagnosis. Typically, these are sputum samples or bronchial washings, which are of interest in the present study. Cases with at least one pulmonary specimen collected (sputum or bronchial washings) that is culture positive for *Mycobacterium tuberculosis* (MTB) are considered infectious pulmonary cases. Infectious pulmonary cases are analyzed separately, excluding all other cases, to understand performance regarding contact elicitation and assessment as well as early diagnosis. These performance measures require focusing on infectious pulmonary cases in order to provide meaningful results in terms of TB transmission. Bacteriological status, however, was used only as an inclusion or exclusion criteria for analyses, rather than as a predictor or covariate.

Statistical Analysis

The statistical analysis sought to adjust for potentially confounding factors (age, sex) among ethnic-origin and geographic groups using multiple regression techniques. For these analyses, dummy variables were created representing the dependent variables for the study, such as treatment completion or cure (yes = 1, no = 0). The independent variables as noted above were: age group (0-18, 19-35, 36-55, 56+), sex (male or female), ethnic-origin (First Nation, foreign-born, Canadian-born non-First Nation), RHA (Northern, Winnipeg, Other), residency (on-reserve or off-reserve)[4], previous treatment history (1st time case or 2nd time case), and bacteriological status (smear-positive, culture-positive; smear-negative, culture-positive).

While logistic regression has been used in past to analyze cross-sectional data, such as those used in this study, there are numerous problems with the use and interpretation of these results, particularly the odds ratio (OR), which is discussed below. Instead, log-binomial and robust Poisson regression was used, implemented through a generalized estimating equation (GEE) modelling approach. These methods have been shown to be produce estimates that are more realistic and therefore easier to interpret for non-epidemiologists (Spiegelman, 2005). Univariable and multivariable log-binomial and robust Poisson regression analyses yielded unadjusted and adjusted *probability ratios* (PR) of patients meeting performance targets between patient groups and for personal characteristics. All statistical analyses were conducted using SAS 9.4 © for Windows.

Odds Ratios versus Prevalence/Probability Ratios

The choice of a measure of association is critical for researchers seeking to understand observational data. To obtain reliable, interpretable, and implementable, measures of association

4 First Nations only.

one must consider the nature of the data (the distribution of the outcome, the prevalence of the outcome, whether it is longitudinal or cross-sectional, etc) as well as the standard practices in the field. When reviewing available methods for this study we need to consider a measure of association that is best suited to the study data.

Using prevalence/probability ratios (PR) for analyzing and reporting on cohort and cross-sectional data was selected, as it has emerged as a new standard (Skov et al., 1998). Logistic regression, while commonly used to analyze cohort data, is either an error on the part of researchers or a failure to adopt emerging methods (Cummings, 2009). Odds ratio (OR) estimates, along with 95% confidence intervals (95%CI) determine whether variables are associated with increased or decreased odds of meeting a particular performance measure between groups. However, an OR is only a reliable approximation to the relative risk when the outcome of interest is rare in a study population (Cummings, 2009).

The present study adopted instead a robust log-binomial regression and robust Poisson regression approach, as it meets the new standards for corss-sectional and cohort data. For a common (i.e., prevalent) outcome, the relative risk (RR) or prevalence/probability ratio (PR), rather than the OR, is used to make inferences about the probability of an event. Why is this the case? The OR has specific properties that contribute to or detract from its inferential usefulness. It is thus important to understand them in contrast with other measures of association; particularly RR/PR. For example, the OR is symmetrical with respect to the definition of the outcome variable, and whether it is the odds of an event *happening* or an event *not happening*, the resulting OR will be symmetrical around 1.0, meaning that it does not matter how the outcome is defined since the result will be the same (Cummings, 2009). OR estimates also tend

to be more extreme, with estimates farther from 1.0 than PR/RR estimates, suggesting a greater magnitudes of independent variables' effects. Given these basic tenets of OR's a more appropriate measure of association was selected, consistent with the regression methods selected.

The probability or prevalence ratio (PR) of achieving performance was calculated using SAS PROC GENMOD Using SAS PROC GENMOD to implement a generalized linear model (GLM) that is binomially distributed with a log link and sandwich variance estimated (i.e., a robust log-binomial model), or Poisson distributed with a log link and sandwich variance estimator (i.e., robust Poisson model), the probability or prevalence ratio (PR) of achieving performance measures can be calculated. Unlike with the OR, there is an asymmetrical relationship between the risk of and event and the risk of an event not happening. In cases where the outcome was rare and/or convergence was an issue, robust Poisson regression was used instead of log-binomial. Since both models are able to produce estimates of probability ratios, the results from both model types are presented in the same manner.

Log-Binomial Regression

In order to estimate the probability of patients meeting performance targets, log-binomial regression, implemented through a GEE framework, was used. To compare groups, probability ratios or prevalence ratios (PR) were used, based on a series of univariable and multivariable log-binomial regression models. Log-binomial regression is superior to logistic regression when examining cohort or cross-sectional data for several reasons: (1) it directly estimates the proportion of patients meeting performance targets; (2) results in the form of PRs are more easily interpreted than ORs; and (3) it is better suited to data where the outcome of interest is common

(i.e., outcome prevalence >0.10) amongst the study population (Petersen & Deddens, 2008). For this study, the GEE log-binomial model was applied to the merged patient database within which dummy variables were created indicating whether each TB case (i.e., patient) had been treated to the recommended performance standard (Y=1) or not (Y=0), adjusting for known confounding factors (*age* and *sex*) in order to make fair comparisons between-groups. SAS PROC GENMOD was used with cases' unique *client ID numbers* as subjects in the REPEATED statement with an exchangeable correlation structure being specified.

Robust Poisson Regression

When outcomes are highly prevalent (i.e.,outcome prevalence >0.90), and particularly in the presence of outliers and/or continuous covariates (e.g., age), robust Poisson regression – implemented through a generalized estimating equations (GEE) modelling approach – is preferable to log-binomial methods for estimating the PR (Chen, Shi, Qian, & Azen, 2014; Zou & Donner, 2011). Robust Poisson regression, using a GEE approach, was used to estimate the PR of performance outcomes that were either: very common (>0.90) or rare (<0.10). Robust Poisson (RP) was also used when log-binomial failed to converge. This model estimates the log probability that the count, under Poisson distribution, equals 1 (Petersen & Deddens, 2008). Since dummy variables were used, that can only equal 0 or 1, the RP model approximates the binomial (Chen et al., 2014). SAS PROC GENMOD was used with cases' unique client ID numbers specified as subjects in the REPEATED statement and various correlation structures (SAS Institute Inc., 2015).

The exception was the contact assessment performance measure, where contacts were

clustered around cases, which is a realistic modelling assumption given the association between case and contacts generally present in contact investigations, except in rare circumstances. Contacts were grouped using the unique client Id number (each representing a case) to group contacts, correcting the standard error estimates for correlation between contacts of the same case (Zou & Donner, 2011). Independent variables were measured at the case level while the outcome variable, contact assessment complete (Y/N)?, was measured at the contact level.

Analysis of Performance Measures

The performance measures listed above were used as outcome variables, and they were primarily measured as binary outcomes, which were also translated into crude proportions. Binary variables were created based on classifying all patients meeting the inclusion criteria for the performance measure being coded as either "1" (met the performance target) or "0" (did not meet the performance standard). The sum of these indicator variables were then divided by the number of eligible cases for inclusion in the performance measure to find the proportion of patients meeting the measure and establish a performance baseline.

Hypotheses

Hypotheses were generated for each study research question. The hypothesis for each between-groups comparison was that the groups were different in terms of the probability of achieving the performance target. A Type 1 error rate of $\alpha = 0.05$ was used in testing of hypotheses for statistical significance.

Research Question 1: Using the Manitoba TB Registry, how is the Manitoba TB prevention, diagnosis, and care program performing in terms of treatment and outcomes? The hypothesis was that the proportion of TB cases meeting the target would not equal zero [HA1: $p \neq 0$]. The null hypothesis was that the proportion of patients who meet the performance target equaled zero [H01: $p = 0$]. This was quite unlikely for any of the targets, of course, and was used for estimating the true proportion of patients meeting the target and 95% confidence intervals. To compare the proportion of cases or contacts successfully meeting the performance measure between Regional Health Authorities (RHAs) in Manitoba, as Z-test for proportions was used.

Research Question 2: Does performance vary by ethnic-origin, sex, age, and geography, and if so how? The alternative hypothesis was that there were significant differences between patient groups in their probability of achieving the performance target [HA2: $PR_i \neq 1.0$]. The null hypothesis (using a general form, adaptable to each grouping variable) was that there would be no significant difference between patient groups (e.g., on vs. off-reserve First Nations) in terms of their probability of achieving the performance target, which was measured using the probability ratio of groups being compared [H02: $PR_i = 1.0$]. A statistically significant ($\alpha = 0.05$) difference in a group's probability of achieving a performance target were found where that group's 95% CI for the performance measure in question did not include 1.0. For example, when comparing First Nations versus foreign-born on the probability of treatment completion/cure, if the PR = 0.75 with 95% CI: 0.60 – 0.90, then a First Nation case would be considered to have

a statistically significantly lower probability of treatment completion/cure than foreign-born cases. However, if the PR for this comparison was 0.75 with 95% CI: 0.60 – 1.01, then no statistically significant difference existed between First Nations and foreign-born in the probability of treatment completion/cure.

Research Question 3: Which performance measures are measurable using the Manitoba TB Registry and which are not? Using the original performance measurement framework that guided this study (Fanning, Orr, 2010), a working hypothesis was that approximately half of these performance measures would be measurable with the Manitoba TB Registry. The following describes the analysis approach used for each of t6he following performance measures used in this study.

Treatment Completion/Cure

To compare the probability of treatment completion / patient cure, a dummy variable was created combining either treatment complete without culture or cure (i.e., negative culture at end of treatment) into a success (treatment complete = 1), and other values (absconded, treatment failure, death, transferred, missing, or other) into a failure (treatment complete = 0). Robust Poisson regression was used because the outcome was very common (outcome prevalence >0.9). The tables is the results section show the exponentiated differences in the least squares means (i.e., probability ratios). All cases listed in the Registry were used in this analysis.

Early Detection of Pulmonary TB

It is important to detect infectious pulmonary cases of TB earlier rather than later to

prevent the spread of infection as much as possible. In order to determine the proportion of cases detected early, the following formula was used: (S-,C+) / [(S-,C+)+(S+,C+)], where S+ means smear positive, and C+ means culture positive. This measure is often calculated another way, as the proportion of smear positive infectious pulmonary cases. It was decided that measuring the probability of being smear-negative would better fit with the performance measurement concept, as it indicates early rather than late detection of pulmonary TB. Infectious pulmonary TB cases were compared in terms of the probability of early detection/diagnosis of infectious pulmonary TB. Comparisons between groups on the probability of being smear-negative (early detection), were done using Robust Poisson regression, due to non-convergence of the multivariable log-binomial regression model. Only culture-positive infectious pulmonary cases were included in this analysis. An unstructured correlation structure was specified for the GEE models.

HIV Testing and Reporting

Knowing whether a patient is HIV positive can have major ramifications for treatment and should be known for all TB cases. After merging the Client table and HIV table, a dummy variable was created indicating whether an HIV test was on file (*test*=1) or not on file (*test*=0). All cases in the Registry were included in the analysis of this performance measure. This indicator was one of the originally planned performance measures for this study (Table 3.1). For this variable, log-binomial regression was employed. Results from the univariable log-binomial regression of HIV testing/reporting by ethnic-origin, however, were nearly identical to those produced by robust Poisson regression, thus making the choice of model somewhat arbitrary. Log-binomial was considered more technically appropriate, because it forces all estimated

probabilities to fall between 0 and 1, as they should, and it correctly specifies the probability distribution of the outcome variable – unlike robust Poisson, which only approximates the binomial (Petersen & Deddens, 2008).

To more closely examine of the probability of having an HIV test result on file in the Manitoba TB Registry for First Nations, log-binomial regression modelling was used, with resides on reserve (yes/no), age, sex, and treatment history entered into separate models as the sole predictor in each (univariable models) to obtain unadjusted probability ratios (PR). To provide a fair comparison between on- and off-reserve First Nations's multivariable log-binomial regression was used, with age, sex, and previous treatment for TB entered into a single model as covariates along with resides on reserve as the key predictor variable.

For Northern Manitoba First Nations, log-binomial regression was used, although for the multivariable model of this group's early detection rate, the convergence was deemed "questionable" by the SAS System due to the relative Hessian convergence criterion being 0.00426 compared to the limit of 0.001. However, re-running the model using robust Poisson regression produced very similar results. Therefore, the log-binomial model was chosen so as to be consistent with the univariable models and with the other parts of the analysis.

Paediatric Cases

The probability of a case being a paediatric case (child=1) was modelled using log-binomial regression for all parts of the analysis (Manitoba, Manitoba First Nations, Winnipeg, and Northern Manitoba First Nations). Because children would not be expected to be cases more than once, the variable treatment history was not part of the analysis of this variable in any

section. Age was also excluded from the analysis because age defines the outcome of interest. All cases listed in the Registry were used in this analysis.

Re-Treatment Cases

Due to the relatively rare nature of cases being re-treatment cases (π <0.10), the robust Poisson method was chosen to analyze this variable for all study sub-populations. Age was included in the analysis of this variable even though the number of re-treatment cases in the 0-18 years age group was low. This was expected given there would be less risk time to be a case. All cases listed in the Registry were used in this analysis.

Contact Investigation

Contact investigation is relevant primarily in cases of pulmonary or respiratory TB, where the case is infectious (Al-Azem, 2006). Sputum-smear positive cases are the most infectious and the highest priority from public health standpoint. For the contact investigation piece of this study, cases of pulmonary TB, that is, those with sputum or bronchial wash specimens recorded in the Laboratory Table that were culture-positive, were the focus, but all cases were considered. This part of the study used two units of analysis: (1) the case-level, where it is determined whether the case named contacts to a public health practitioner; and (2) the contact level, where a determination was made about whether those contacts identified were assessed for infection or disease.

When the data sets were merged together, the case demographic information was applied to the contacts, and could therefore be used in the analysis. However, care had to be taken with interpreting the results, as the demographic information was not that of the contacts, but rather

the cases. In some instances one might assume ethnic-origin homogeneity amongst contacts (e.g., in a First Nations community there are primarily First Nations people), yet in other scenarios, such as Winnipeg, this assumption could not be sustained, even though there is likely a certain amount of segregation between these groups and a higher likelihood of mixing with people of similar ethnic-origin. Regardless, the limitation of the demographic information of cases being used as a proxy for contacts must be understood prior to interpreting results. However, a recent multicentre study on contact investigation using social network analysis methods found that: "Although many data were missing, the race and ethnicity distribution of the contacts mirrored those of the patients at each respective site" (Cook et al., 2007, p. 1520); lending credit to the present study's approach of using case ethnic-origin as a proxy for contact ethnic-origin.

The analysis of contact investigation data was complicated by several matters, which must be considered before making judgements about performance. For one, contact tracing was done on a case-by-case basis – meaning that if contact tracing was not warranted it might not have been performed. It follows that those cases listed in the contact database were those where a contact investigation was deemed appropriate – i.e., whether the case was infectious or not. Therefore, the assertion could be made that all contacts listed in the Registry should be evaluated for LTBI or active disease.

Analysis of data for all contacts and for those to infectious pulmonary cases allowed for a very brief sensitivity analysis regarding this potential modelling assumption and is discussed for each group. The sensitivity analysis tested the hypothesis that the contacts listed in the contact table were those of infectious pulmonary cases, even if not confirmed by culture-positive sputum

or bronchial washings. The sensitivity analysis compared the total contact list's proportion of contacts with contact assessment completed to the smaller group of contacts of infectious pulmonary cases with contact assessment completed. The proportions of contacts assessed were relatively similar between all cases' contacts and infectious pulmonary cases' contacts, suggesting that those on the contact list were there because they should be. However, the infectious pulmonary cases' contacts were used for the statistical analysis of this performance measure to ensure fair comparison between populations.

For these analyses, two graphical tools were employed to understand the data structure and key epidemiologically descriptive indicators of TB, such as the number of cases and contacts in various regions of Manitoba, indicating the total disease burden. These figures were placed onto a map of the province, defining both the boundaries of the regions and the burden of TB in each region.

Another tool utilized was the flowchart. A flowchart identifies the flow of inputs through a process, ending in various outputs. It is the blueprint of a process, essentially, and can be complex and intricate, or elegant and simple, depending on the process being described. This was done consistent with the advice from Dever (1997) regarding the necessity of using flowcharts in public health management (p. 206):

> "By mapping out the process, group [i.e., public health team] members can gain a shared understanding of it and use their shared understanding to collect data, narrow down the problem, focus discussion of the process, and identify resources."

A flowchart of the merged case and contact data was created at the beginning of the analysis. The flowchart included all cases and contacts listed in the TB Registry during the study period. The graphical tools used in this study (TB by RHA map; TB case and contact flowchart) were shared with committee members and were useful in developing a birds-eye-view of the data that was easily interpreted, and which prompted a series of research sub-questions that had to be answered during the analysis to 1) understand the data, 2) measure performance appropriately, and 3) guide the interpretration of the results.

Contacts Elicited

Because this performance measures is concerned with *infectious* cases of TB, only infectious pulmonary cases (as defined above) were included in the statistical modelling. When confining the analysis to this group the results were much more informative, as differences between groups in the proportion of infectious pulmonary cases influences the level of contact investigation amongst that population. A dummy variable was created to determine if any contacts were elicited from a case or not. Contacts with elicited >=1 contact per case were assigned a "1" and those with no contacts elicited a "0". Comparison between groups was done using univariable and then multivariable robust Poisson regression. Since the proportion of sputum/bronchial washings smear-positive cases with contacts elicited is so high, statistical analysis of this sub-group was not feasible.

Contacts Assessed

Robust Poisson regression analysis, implemented through a generalized estimating equation (GEE) approach, was used to compare the probability of different types of infectious

pulmonary cases' contacts were medically evaluated (i.e., assessed for latent TB infection or active disease). GEE is based on the generalized linear model (GLM) but allows a covariance matrix structure to be estimated from the data, taking into account the correlation between observations within clusters. The GLM part of the model had a Poisson distributed outcome variable (i.e., 0 or 1), with log link function. This allowed adjustment for case characteristics, such as age, sex, and treatment history when comparing ethnic-origin of the cases, as well as comparing Manitoba (and Northern Manitoba) First Nations on- and off-reserve.

For this performance measure, the contacts were grouped into case-based clusters according to the unique client ID number, using the REPEATED statement in SAS PROC GENMOD. This ensures that the standard errors for significance tests were not unreasonably small due to large sample size. In the REPEATED statement, the option of specifying a correlation structure was used for the various sub-populations. Different correlation structures were specified for the four parts of the study: Manitoba population, Manitoba First Nations, Winnipeg, and Northern Manitoba First Nations. Only for Manitoba as a whole, was an unstructured correlation structure feasible, due to having the largest number of cases and contacts. For Manitoba First Nations, an exchangeable correlation structure was specified, which is the second most robust correlation structure. Winnipeg and Northern Manitoba First Nations only had enough cases and contacts to use compound symmetry correlation structures for estimation.

Unfortunately for this study, the exact value definitions from the contact assessment variable were not available. The variable 'contact assessment complete' had the following outcomes: (1) missing value, (2) contact assessment complete – no further follow-up required;

(3) contact assessment complete, ongoing surveillance required (see above dates); and (4) contact assessment complete. Values 2, 3, and 4 were converted into successes (ca=1), and missing values (as either " " or ".") were recoded into failures (ca=0). A similar issue regarding unclear contact assessment definitions was noted in a recent comparison of TB trends in Mexico and the USA, which stated that (Hernández-garduño et al., 2015):

> "in the last Mexican report it is assumed that "contacts examined" means contact investigation..., it is not clearly and specifically defined in this report nor in the current TB Mexican guidelines i.e., it is not mentioned whether "contacts examined" were examined by a physician looking for signs of active TB, whether contacts had a tuberculin skin test (TST) or QuantiFERON done, had a chest X-ray or whether preventive treatment was offered and/ or received". (p. 249).

Although the exact definition of what follow-up was required was not provided with the data, an assumption that these were people who either developed active TB disease or had LTBI could reasonably be made. This assumption was made to estimate the ratio of new active TB cases or latent TB infected contacts to index cases. While not as meaningful as a fully defined measure would be, this ratio provides an indication of TB surveillance, case-finding, and transmission, but could not discriminate between them.

The study plan also called for an analysis of LTBI treatment but the request was not clear enough and data for LTBI diagnosis and treatment outcomes was not included the data received for the study.

Ethics Process

This study was approved by the following oversight bodies: The University of Manitoba Bannatyne Campus Research Ethics Board (REB); the Assembly of Manitoba Chiefs' Health Information and Research Governance Committee (HIRGC); and the Health Information and Privacy Committee (HIPC) of Manitoba, which handles all data requests according to the *Personal Health Information Act* [Manitoba] (PHIA) and is designed to safeguard Manitobans' personal health information. These oversight bodies were satisfied that no individuals would be identifiable, and that there was a sufficient methodology developed for the study of a valid problem with potential benefit to public health in Manitoba. Finally approval to release the Manitoba TB Registry was provided by Manitoba Health Public Health Surveillance Unit, and a data transfer agreement was signed by the University of Manitoba and my thesis advisor, Dr. Brenda Elias in order to house the abstracted TB registry, as requested, at the Centre for Global Public Health at the University of Manitoba for data analysis purposes. Additional requirements for the transfer of the data included naming two data stewards at the Centre and they were: Drs. Jamie Blanchard and Nancy Yu.

Further support was drawn from First Naitons governance resolutions. The First Nations population and communities in Manitoba are some of the most severely affected by TB and are therefore more involved in TB prevention, diagnosis, and care on a day-to-day basis, in Manitoba. This fact demands greater involvement of First Nations in analyzing the performance of TB services in Manitoba. First Nation leaders in Manitoba have called for more information about how TB programs are operating through a resolution passed by the Manitoba Keewatinowi Okimakanak, Inc. (MKO).[5] This resolution demonstrated the importance of this study in

5 A provincial/territorial organization representing 27 northern Manitoba First Nations (www.mkonorth.com).

establishing a baseline for TB prevention, diagnosis, and care performance for First Nations, particularly northern Manitoba First Nations, and to identify variation in performance between-groups.

As per the university and government signed agreement, the data-set was stored on a secure server operated by the University of Manitoba, Faculty of Health Sciences, College of Medicine, Department of Community Health Sciences (CHS) of which the Centre for Global Public Health (CGPH) has a partition fully protected as per an agreement signed by this Centre and Manitoba Health. The data, consistent with the permission granted, would remain under the management of CGPH Information Technology staff for seven years, using documented policies and procedures that are PHIA compliant.

4. RESULTS

This chapter presents the results of a cross-sectional analysis of TB cases diagnosed between January 1, 2008 and December 31, 2010, and their identified contacts, in Manitoba. The findings of this study are organized into four parts representative of the relative burden of TB in the province: (1) Manitoba; (2) First Nations in Manitoba; (3) Winnipeg; and (4) Northern Manitoba.

Part I provides an overview of the province and includes findings on the performance between ethnic-origin groups adjusting for age, sex, and treatment history. Performance measures are further categorized into the following sub-sections: (i) case management; and (ii) contact investigation. Part II is an analysis of TB prevention, diagnosis, and care amongst First Nations. Comparisons between First Nations living on and off reserve were made adjusting for age, sex, and treatment history. Parts III and IV cover the Winnipeg and northern health region, respectively. Together these two regions host the majority of TB cases in Manitoba, and their very different circumstances warranted closer investigation. As well, special attention was paid to contact investigation by Regional Health Authority (RHA) as TB is spread by close proximity to an infected person, making geography and public health response key factors in understanding both the epidemiology and control of TB.

While the study period involves cases diagnosed between 2008-2010, inclusive, the information provided by Manitoba Health extended beyond this period, ranging from 1996 – 2012, allowing for determination of treatment completion, previous HIV testing, and other relevant factors, for the entire 2008-2010 cohort (Table 4.1).

A number of variables had many missing values, and in a couple instances, no values at

all, particularly in the Drug Treatment table. Variations in data entry practice and between health care providers over the study period were possible explanations for any missing data patterns. Full consideration of this was beyond the scope of the present study. The assumption made is that data quality was consistent enough across geographic, ethnic-origin, and other groups to make fair comparisons between them based on the data. Of import to this study were ten cases where no ethnic-origin is noted. These cases were excluded from any analysis using ethnic-origin group as a predictor or stratification variable.

Table 4.1. Manitoba TB Registry Data: Summary of Tables

Table Type	Variables (Columns)	Observations (Rows)	Date Range
Client	17	428	January 25, 2008 – January 7, 2011
Laboratory	10	2,351	January 4, 2008 – May 13, 2012
Drug Reaction	5	1,501	February 7, 2008 – February 1, 2011
Drug Treatment	15	6,412	January 3, 2008 – May 7, 2012
Contact	6	7,442	January 2, 2008 – December 29, 2010
X-Ray	5	1,221	May 29, 2006—March 11, 2014
HIV*	4	250	January 1, 1996 – December 5, 2011
All	54	10,372	January 1, 1996 – May 13, 2012

*Two cases in the HIV tables had 1900 recorded as the year their HIV test was administered, which is an obvious data entry error. Since the date of HIV testing was not a variable of interest in this study, these two cases did not have to be excluded from the analysis.

PART I. MANITOBA

This section presents results for all TB cases in Manitoba. First the demographics of TB cases are summarized, then diagnostic features of TB cases. Performance measure results are presented after, starting with case management indicators and followed by contact investigation indicators.

Demographic description of TB cases in Manitoba

In Table 4.2, between January 1, 2008 and December 31 2010, there were 428 cases of active TB diagnosed in Manitoba and recorded in the TB Registry. The 2008, 2009, and 2010 Manitoba population estimates were 1,197,800, 1,208,600, and 1,220,900, respectively (Manitoba Bureau of Statistics, 2011), for a total of 3,627,300 individuals residing in Manitoba. The overall case rate for TB in this period was 11.8 per 100,00 persons (428 / 3,627,300 * 100,000).

There was significant variation in the age-distribution of TB cases. The majority of TB case in Manitoba were between the ages of 19 and 55. Males made up a significant majority of the TB cases at 57% versus 43% of females ($p<0.05$). For the overall Manitoba population, the majority (59.6%, n = 249) of cases represent Status First Nations people, followed by Foreign-born (29.2%) then all other non-aboriginal Canadians (11.2%). As for geographic distribution, the Winnipeg RHA had the most cases at 52.1% followed by the Northern RHA at 35.8%. Combined, these regions host 87.9% of TB cases (n = 376) in Manitoba. As the map (fig. 4.2) illustrates the Northern Health Region is geographically much larger, covering almost half of the province's landmass, with 27 First Nation communities, several municipalities (Thompson, The

Pas, Flin Flon, Gillam, Lynn Lake, Leaf Rapids) and a myriad of smaller communities. Winnipeg is relatively small geographically, but has a much larger population.

Table 4.2. Descriptive Statistics for Active TB Cases in Manitoba, 2008-2010

Variable	TB Cases (*n*)	TB Cases (%)
Age Group* **	428	100
0-18	63	14.7
19-35	119	27.8
36-55	161	37.6
56+	85	19.9
Sex* **	428	100
Male	244	57
Female	184	43
Ethnic-Origin* **	418[§]	97.7
Canadian-born non-First Nations	47	11.2
First Nation[¥]	249	59.6
On-reserve	171	69.0
Off-reserve	77	31.0
Foreign-born	122	29.19
RHA* **	428	100
Northern	153	35.8
Interlake-Eastern	28	6.5
Southern	10	2.3
Prairie Mountain	14	3.3
Winnipeg	223	52.1

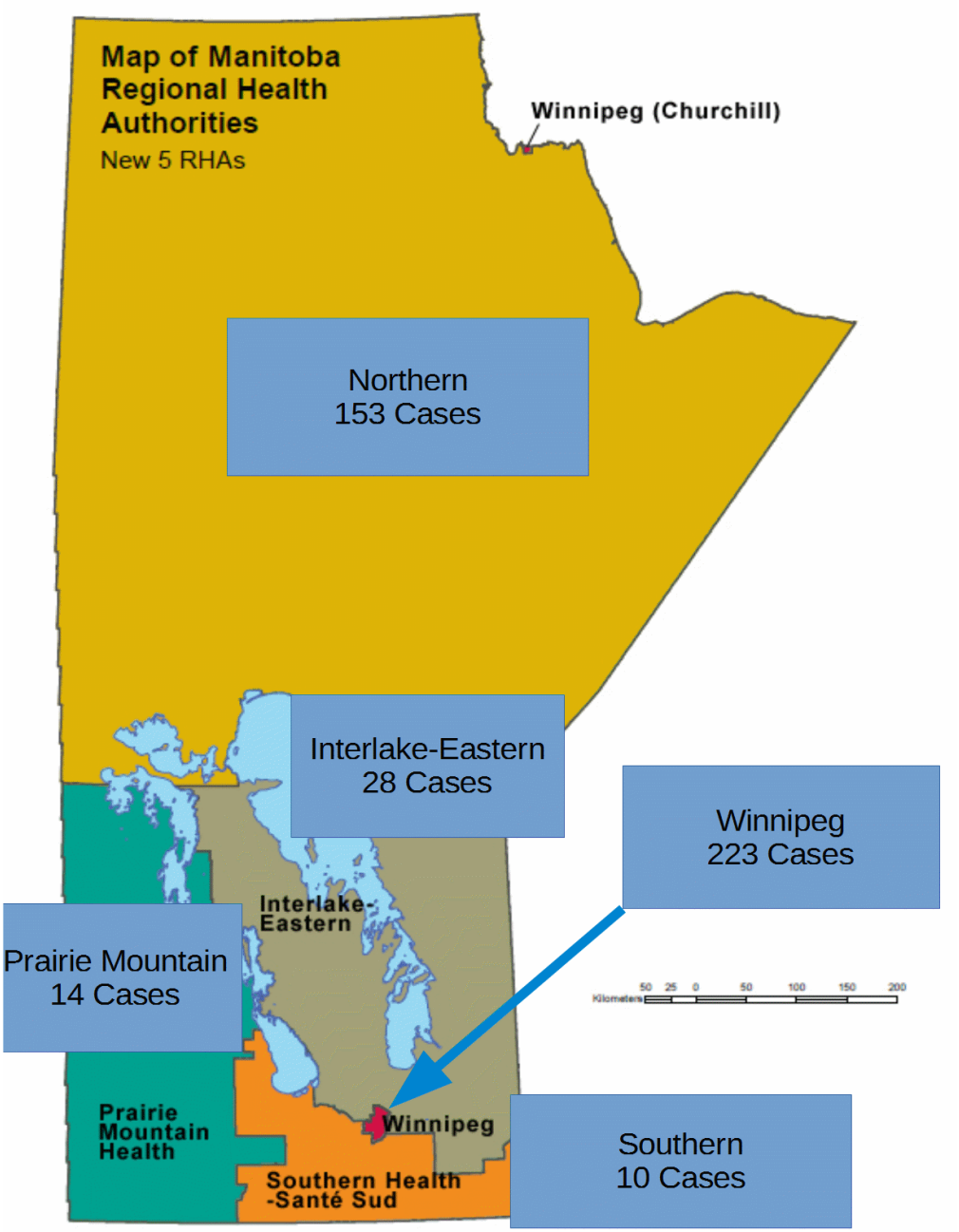
Significance levels: *p<0.05, **p<0.01, ***p<0.001.

RHA: Regional Health Authority.

[§]10 cases with Inuit and Metis origins were removed from all analyses using ethnic-origin as a predictor variable.

[¥] 1 First Nation case didn't have residency information, so the

Figure 4.1. Visual Summary of the Distribution of TB Cases by Manitoba RHAs: 2008-2010



Age, Sex, and Ethnic-Origin Distribution of TB Cases

The average age of TB patients in Manitoba is lowest for First Nations (35 years) and highest for non-First Nation Canadian-born (49 years) (Table 4.4). First Nations in Manitoba have the highest proportion of paediatric TB cases, measured as cases aged <=18 years (Table 4.3). This suggests a significant amount of ongoing transmission within the First Nations population. The majority (76.6%) of Canadian-born non-First Nations cases were 36 years or older, while the majority of foreign-born (63.9%) and Status First Nations (67.8%) cases were between 19-55 years of age. Male TB cases were consistently older than female TB cases across ethnic-origin groups, with the average age of male TB cases in Manitoba being 41 years, and females being 39 years (Table 4.4). These averages were biased towards First Nation TB cases' average ages due to being the group with the largest number of cases.

Table 4.3a Age and Sex Distribution of TB Cases, 2008-2010

Age Group	Female *n* (%)	Male *n* (%)	Total
0-18	34 (54)	29 (46)	63
19-35	53 (45)	66 (55)	119
36-55	61 (38)	100 (62)	161
56+	36 (42)	49 (58)	85
Total	184 (43)	244 (57)	428

Table 4.3b. Ethnic-Origin-Specific Age-Distribution of TB Cases, 2008-2010

Age Group	Canadian-born non-First Nations	Foreign-born	Status First Nations
0-18 years	s	9%	19.7%
19-35 years	s	33.6%	27.3%
36-55 years	40.4%	30.3%	40.2%
56+ years	36.2%	27.1%	12.9%

S: suppressed/cross-suppressed due to small cell counts (<=5)

Table 4.4. Average Age at Diagnosis by Ethnic-origin and Sex of TB Cases, 2008-2010

Ethnic-origin	Sex	Average Age By Sex (Years)	Average Age Overall (Years)
Canadian-born non-First Nation	F	43	49
	M	54	
Foreign-born	F	40	44
	M	47	
First Nations	F	35	35
	M	36	

Clinical and Microbiological Features

Clinical diagnosis is a measure of the severity of disease in patients and generally is only done when the TB disease is at an advanced stage and patients were seriously ill (Olson, 1999). Table 4.5 shows the key clinical and microbiological features of the study population. Of 428 cases of TB diagnosed in Manitoba between 2008 and 2010, 16.4% had a clinical diagnosis and 83.6% of cases had a culture-confirmed diagnosis. Three hundred and nineteen cases (74%) had abnormal chest x-ray results and 65 cases (15%) had normal chest x-ray results. Selecting cases

with sputum or bronchial washings specimens was done to examine the bacterial status of pulmonary TB cases in Manitoba during the study period. In the present study 268 of 428 TB cases (62.6%) were considered *infectious pulmonary cases* of TB, based on the number of cases with culture-positive pulmonary specimens (Tables 4.5, 4.6). Two key epidemiological indicators are the proportion of TB patients co-infected with HIV and drug-resistance. Over half (250 or 58.4%) of 428 TB cases were tested for HIV and 12 (4.8%) of these 250 cases were HIV-positive. Twenty three (6.4%) of 358 TB cases with drug-sensitivity test (DST) results available has isolates that were resistant to isoniazid (INH).

Table 4.5. Clinical and microbiological features of TB Cases: Manitoba, 2008-2010

Feature	Cases (*x*)	Cohort (*n*)	Proportion (%)
Case Criteria			
Clinical Dx*	70	428	16.4
Positive Culture	358	428	83.6
X-Ray Result			
Normal	65	427	15.2
Abnormal	319	427	74.7
Missing/Poor Quality/Not Done	43	427	10.1
Pulmonary*	268	428	62.6
S+ C+	84	316	26.6
S- C+	184	316	58.2
S- C-	48	316	15.2
HIV Status			
Tested for HIV	250	428	58.4
HIV positive**	12	250	4.8
Drug Resistance*			
Resistant to INH	23	358	6.4

*This is an indication of the severity of disease
**Proportion of TB cases that were HIV positive of those tested for HIV.

***Cases with drug resistance pattern.
****Specimen type: sputum and/or bronchial washings

Table 4.6. Smear & Culture Results of TB cases with Sputum/Bronchial Washings specimens: Manitoba, 2008-2010

	Culture Result		
Smear Result	***N***	***P***	**Total**
N	48	184	232
P	0	84	84
Total	48	268	316

Performance Measures for Case Management

This section looks at individual case management performance measures, including treatment completion/cure, early detection (i.e.., infectious pulmonary cases that were smear-negative at diagnosis), HIV testing/reporting, paediatric cases, and re-treatment cases. Case mortality was not modelled statistically, due to small numbers for most of the ethnic-origin groups, and none in younger age categories.

Treatment Completion/Cure

A breakdown of treatment outcomes for TB cases in Manitoba shows that the most common outcome is treatment complete without culture at 77.1% (Table 4.7). Manitoba's overall treatment completion/cure rate combined was 92.1% (77.1 + 15.0 or 394 of 428 cases).

Table 4.7. Treatment Outcomes for TB Cases: Manitoba, 2008-2010

Treatment Outcome	Total	
	#	%
Treatment complete without culture	330	77.1
Cure (negative culture)	64	15.0
Absconded	7	1.6
Treatment to New Jurisdiction / Other	6	1.4
Death	21	4.9
Total	418	100

In table 4.8 no significant difference was found between ethnic-origin groups in the rate of treatment completion/ being cured for TB cases, with all PR estimates very close to 1.0. There were no significant differences between males and females, or for Treatment history, in the unadjusted or adjusted PR models. However, age was significantly associated with treatment completion/cure in both models. Robust Poisson regression analysis, however adjusting for age, sex, ethnic-origin, and treatment history (first or second time being an active case) - showed a significant association between age and treatment completion/cure. As age increased the probability of successfully completing treatment declined, holding other variables constant, with 0-18 and 19-35 year old TB cases having significantly higher treatment completion/cure rates than either 36 years or older. No significant difference between males and females were found in regards to probability of treatment completion / being cured.

Table 4.8. Robust Poisson Regression Analysis of Treatment Completion/Cure: Manitoba, 2008-2010 (cases, n = 428)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin		LCL	UCL		LCL	UCL
Canadian-born vs. foreign-born	1.02	0.92	1.14	1.06	0.95	1.18
Canadian-born vs. Status First Nation	0.98	0.89	1.07	1.02	0.93	1.12
Foreign-born vs. Status First Nation	0.96	0.89	1.02	0.96	0.90	1.03
Sex						
Female vs. Male	1.03	0.97	1.09	1.02	0.97	1.08
Treatment History						
1st time vs. 2nd time Case	1.19	0.93	1.53	1.14	0.89	1.47
Age Groups						
0-18 vs. 19-35	NE	NE	NE	1.00	0.98	1.01
0-18 vs. 36-55	1.13***	1.07	1.19	1.12***	1.06	1.18
0-18 vs. 56+	1.23***	1.11	1.37	1.23***	1.10	1.36
19-35 vs. 36-55	1.13***	1.07	1.19	1.12***	1.06	1.18
19-35 vs. 56+	1.23***	1.11	1.37	1.23***	1.11	1.37
36-55 vs. 56+	1.09	0.97	1.23	1.10	0.98	1.24

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; NE: not estimable due to small cell sizes.

Early Detection of Pulmonary TB

The overall proportion of infectious pulmonary cases that were detected early (i.e., smear-negative at diagnosis) during the study period was 184/ 268 = 68.7% (Table 4.5). In table 4.9 (PR column), a univariate analysis of early detection by ethnic-origin group the data showed that Canadian-born non-First Nations pulmonary TB cases in Manitoba, while 31% less likely, were not significantly less likely to be smear-negative at diagnosis than foreign-born infectious pulmonary TB cases ((1 – 0.69)*100 = 31%). Sex and previous treatment for TB did not predict

smear status at diagnosis. In the unadjusted model, age was significantly related to early detection with the 0-18 year old group being significantly more likely than either the 19-35 or 36-55 year old groups to be smear-negative at diagnosis. After adjusting for sex and previous treatment for TB, age remained a significant predictor of smear-status at diagnosis for pulmonary TB cases, with pulmonary cases aged 0-18 years being 36% and 35% more likely to be smear-negative at diagnosis than pulmonary cases aged 19-35 years and 35-56 years, respectively (Table 4.9).

Table 4.9. Robust Poisson Regression Analysis of Early Detection of Pulmonary TB: Manitoba, 2008-10 (infectious pulmonary cases, n = 266)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. Foreign-born	0.69	0.45	1.06	0.71	0.46	1.09
Canadian-born vs. Status First Nation	0.72	0.48	1.09	0.74	0.49	1.12
Foreign-born vs. Status First Nation	1.04	0.87	1.25	1.04	0.86	1.25
Sex						
Female vs. Male	0.98	0.82	1.16	0.94	0.79	1.12
Treatment History						
1st time vs. 2Nd time Case	0.82	0.64	1.06	0.83	0.65	1.07
Age Groups						
0-18 vs. 19-35	1.40*	1.12	1.76	1.36*	1.08	1.71
0-18 vs. 36-55	1.38*	1.14	1.68	1.35*	1.10	1.66
0-18 vs. 56+	1.24	0.998	1.54	1.23	0.97	1.55
19-35 vs. 36-55	0.99	0.78	1.23	0.99	0.80	1.24
19-35 vs. 56+	0.88	0.69	1.12	0.90	0.71	1.16
36-55 vs. 56+	0.90	0.72	1.11	0.91	0.73	1.14

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

HIV Testing and Reporting

There was no difference between ethnic-origin groups in the likelihood of HIV testing and reporting in the unadjusted and adjusted models. The same was true for sex and treatment history. The point estimates for treatment history, however, suggest that cases without previous TB treatment history were more likely to have HIV test result available than those with a history of treatment for TB (second time cases). Cases between the ages 0-18 years had a 47% higher probability of having a known HIV status than cases 56+ years old. The 19-35 year group was 21% more likely than the 36-55 year age group and 62% more likely than the 56+ year age group to have known HIV status. Cases 18 years old and under were 33% more likely to have HIV test results on file than the 56+ year old group, although this result was not statistically significant ($p>0.05$). Age remained a significant predictor of HIV testing/reporting in the multivariate model, suggesting that age was the most important predictor of having known HIV status for Manitoba TB cases, with the oldest patients being the least likely to have an HIV test on file.

Table 4.10. Log-Binomial Regression Analysis of HIV Test Result On-File: Manitoba, 2008-2010 (cases, n = 428)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.03	0.77	1.38	1.02	0.75	1.38
Canadian-born vs. Status First Nation	0.97	0.74	1.26	0.99	0.74	1.32
Foreign-born vs. Status First Nation	0.94	0.78	1.13	0.97	0.81	1.16
Sex						
Female vs. Male	0.99	0.84	1.17	1.01	0.87	1.18
Treatment History						
1st time vs. 2nd time Case	1.79	0.92	3.45	1.63	0.83	3.18
Age Groups						
0-18 vs. 19-35	0.91	0.73	1.14	0.91	0.73	1.14
0-18 vs. 36-55	1.12	0.89	1.42	1.11	0.87	1.40
0-18 vs. 56+	1.50*	1.10	2.05	1.47*	1.07	2.04
19-35 vs. 36-55	1.23*	1.03	1.48	1.21*	1.01	1.46
19-35 vs. 56+	1.65***	1.25	2.17	1.62**	1.21	2.16
36-55 vs. 56+	1.33*	1.01	1.77	1.33	0.99	1.79

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Paediatric Cases

In table 4.11, no association between sex and being a paediatric case was observed in the unadjusted and adjusted models. Canada-born, however, were twice as likely as foreign-born to be paediatric cases. Foreign-born cases were 78% and 79% less likely than First Nations cases to be children aged 0-14 before (unadjusted $PR_{FB/FN} = 0.22$) and after (adjusted $PR_{FB/FN} = 0.21$) adjusting for sex ($p<0.01$). While significant, this finding was based on a few cases, resulting in a larger variance and wide confidence interval. Canadian-born non-First Nations were only 43%

as likely as First Nations to be paediatric cases. Small case numbers made this estimate statistically non-significant. The actual number of cases were too small to report for foreign-born and Canadian-born non-First Nations separately, for privacy reasons, which may have affected the ability to detect a difference between these groups at the $\alpha = 0.05$ level.

Table 4.11. Log-Binomial Regression Analysis of Paediatric Case: Manitoba, 2008-2010 (cases, n = 428)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.95	0.45	8.37	2.02	0.47	8.69
Canadian-born vs. Status First Nation	0.43	0.14	1.34	0.43	0.14	1.33
Foreign-born vs. Status First Nation	0.22**	0.08	0.61	0.21**	0.08	0.59
Sex						
Female vs. Male	1.59	0.91	2.79	1.66	0.95	2.88

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Re-Treatment Cases

In table 4.12, the unadjusted comparison between First Nations and Canadian-born non-First Nations was non-significant while the comparison between First Nations and foreign-born showed significantly lower probability of the latter being re-treatment cases compared to the former ($PR_{FB/FN} = 0.95$). After adjusting for age and sex, First Nations were significantly more likely than both Canadian-born non-First Nations and foreign-born cases to be re-treatment cases. Age significantly predicted re-treatment, with no difference between 0-18 and 19-35 or 36-55 year old cases in the probability of re-treatment ($PR_{0\text{-}18 \text{ vs } 19\text{-}35} = 1.01$; $PR_{0\text{-}18 \text{ vs } 36\text{-}55} = 0.97$). However, 0-18 year old cases were significantly less likely than cases aged 56+ to be re-

treatment cases ($PR_{0\text{-}18 \text{ vs } 56+} = 0.93$). Cases aged 19-35 years were significantly less likely to be re-treatment cases than 36-55 year old cases ($PR_{19\text{-}35 \text{ vs } 36\text{-}55} = 0.96$) and 56+ year old cases ($PR_{19\text{-}35 \text{ vs } 56+} = 0.92$).

Table 4.12 Robust Poisson Regression Analysis of Relapse / Re-Treatment Cases: Manitoba, 2008-2010 (cases, n = 428)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.01	0.97	1.06	1.00	0.96	1.05
Canadian-born vs. Status First Nation	0.96	0.91	1.01	0.94*	0.89	0.99
Foreign-born vs. Status First Nation	0.95**	0.92	0.98	0.94**	0.91	0.97
Sex						
Female vs. Male	1.01	0.97	1.05	1.02	0.98	1.06
Age Groups						
0-18 vs. 19-35	1.02	0.98	1.07	1.01	0.96	1.06
0-18 vs. 36-55	0.98	0.93	1.04	0.97	0.92	1.03
0-18 vs. 56+	0.95	0.89	1.02	0.93*	0.86	1.00
19-35 vs. 36-55	0.96*	0.93	1.00	0.96*	0.93	1.00
19-35 vs. 56+	0.93*	0.88	0.99	0.92**	0.87	0.98
36-55 vs. 56+	0.97	0.91	1.03	0.95	0.90	1.02

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Performance Measures for Contact Investigation

Contact investigation has three components: (a) contacts must be named by (i.e., elicited from) a case of infectious TB as close to the time of diagnosis as possible; (b) contacts named in the contact investigation interview must be reached by health care providers to be assessed for latent TB infection (LTBI) or active TB disease; and (c) those newly discovered cases of LTBI or

active TB must be treated (or in some cases of LTBI, assessed in terms of the risks/benefits of therapy). The following analysis only looked at the first two of these components. The third could not be analyzed because treatment information for contacts was not included in the data received.

Overview of Contact Investigation

Figure 4.2 provides an overview of contact tracing numbers, showing the crude numbers and proportions of contacts that were elicited, assessed, and whether further follow-up was required. This includes all cases of TB, not just infectious pulmonary. Of the 428 cases, 318 (74.3%) had contacts elicited. These 311 cases in turn yielded 7,442 contacts (wherein contacts can be contacts twice), as in contact *events*, (see methodology for definition). There were 5,895 contacts evaluated and 95.5% of these did not require follow-up. The remaining 4.5% (n = 266) did require follow-up, although the nature of follow-up required was not indicated in the Contact table.

Figure 4.2. Flow Chart of Cases and Contacts (all cases and contacts)

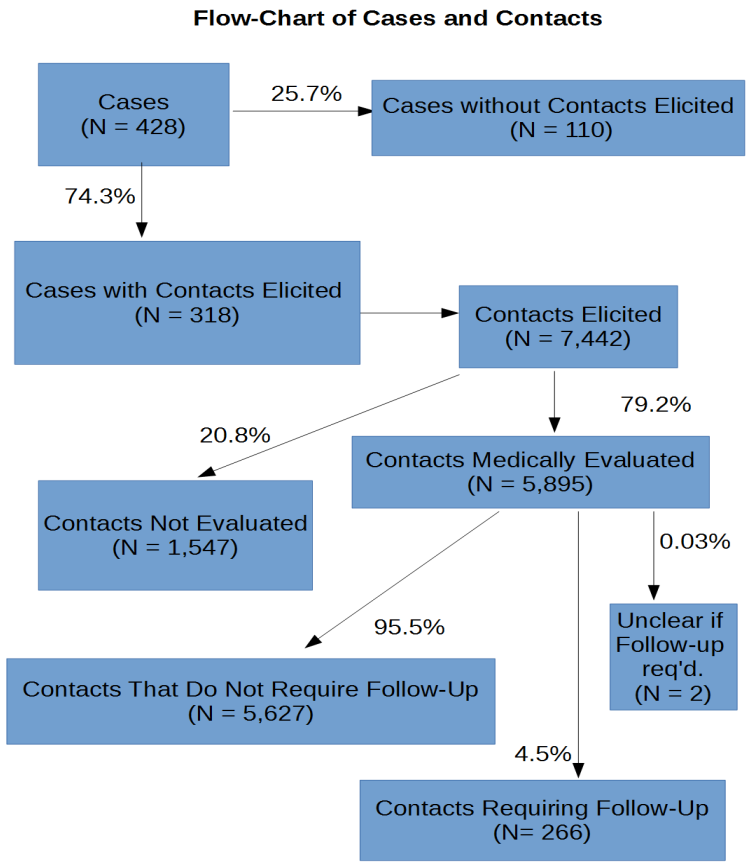
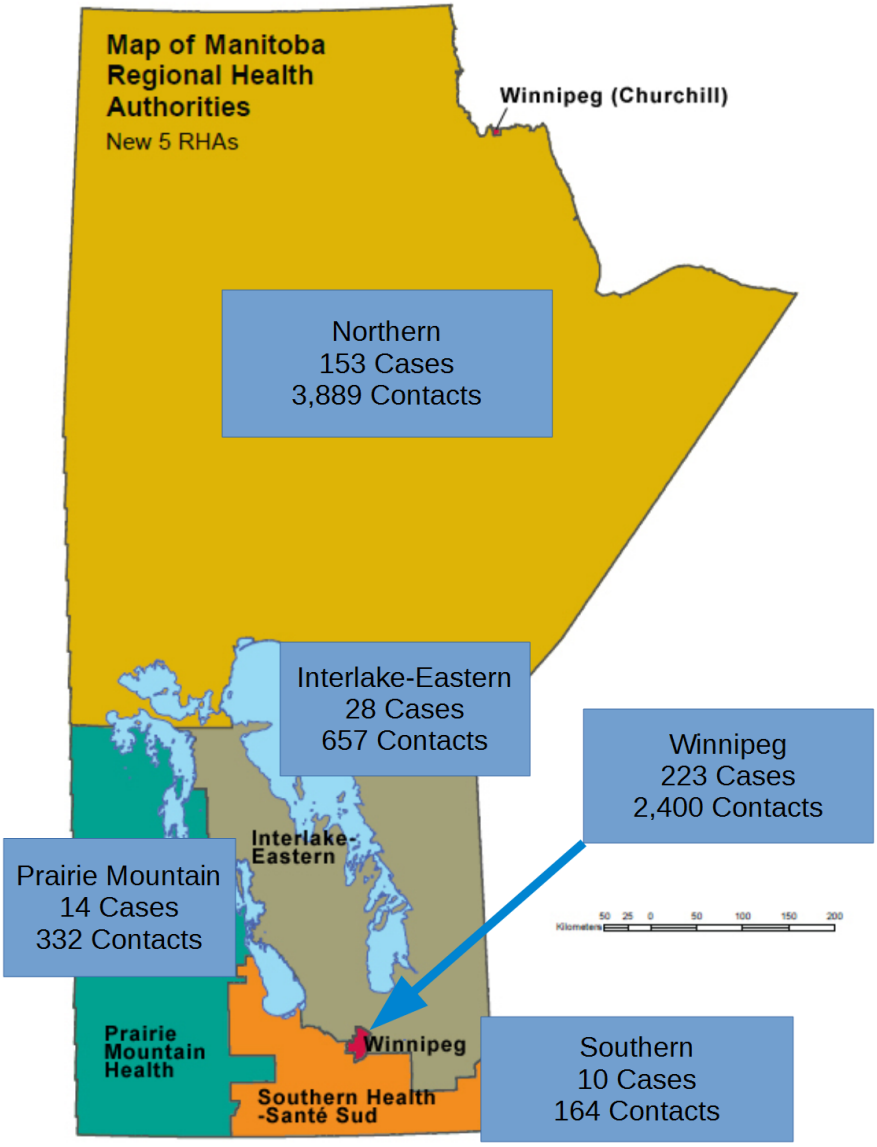


Figure 4.3 shows the geographic distribution of cases and contacts in Manitoba. The north, although having fewer cases than Winnipeg, had the most contacts of any RHA, followed by Winnipeg RHA, Interlake-Eastern RHA, Prairie-Mountain RHA, and finally Southern RHA.

Figure 4.3. Visual Summary of the Distribution of TB Cases and Contacts by Manitoba RHAs: 2008-2010.



Results of Contact Investigation

In table 4.13 there were a total of 428 cases of TB in Manitoba and listed in the Contact Table, even when the case was not associated with any contact(s). As reported in figure 4.2, only 318 of these cases had contact elicited, yielding 7,442 contacts from the contact investigation process. An average of 17 contacts per case was found when considering all 428 cases. Contact assessment was not complete, with only 5,983 of the total number assessed. Of the cases assessed, a net total of 266 contacts required follow-up, which translates into a follow-up rate of 3.57% from the list of all contacts and a ratio of cases requiring follow-up to index cases, which yielded a ratio of 0.622. This essentially means that for every 100 cases of active TB in Manitoba, there were 62 new cases (of either LTBI or active TB) discovered through the contact investigation process, during the study period. As mentioned in the methodology, these figures were assumed to represent either a contact with LTBI, a new active TB case, or a re-infected case if there was a history TB in the contact, although discriminating between these possibilities was impossible with the data provided.

Substantial variation between regions was found in the results of their contact investigations. The Northern RHA (NRHA) has the highest number and proportion of contacts (n = 3,889; π = 5.45%) requiring follow-up out of contacts assessed within the NRHA (n = 3,368), as well as the highest ratio of new active or latent cases with follow-up required to index cases (1.86 new cases of LTBI or active TB found per index case). The NRHA also has the majority of all contacts in the province, with the highest number of contacts per case (25). Interlake-Eastern RHA had the highest proportion of contacts assessed (97.1%), nearing total coverage. The Winnipeg RHA, however, has the lowest proportion of contacts assessed (63.5%).

Table 4.13. Contact Investigation Results: Manitoba Health Regions, 2008-10

	RHA					
	Interlake-Eastern	Northern	Prairie Mountain	Southern	Winnipeg	TOTAL
Cases in Client Table (#)	28	153	14	10	223	428
Contacts in Contact Table (#)	657	3,889	332	164	2,400	7,442
Contacts per Case (avg. #)	23	25	24	16	11	17
Contacts Assessed (%)	97.1	86.6	72.0	77.4	63.5	80.4
Contacts requiring follow-up	23	212	14	s	s	266
Follow-Up Required (% of Assessed)	3.50%	5.45%	4.22%	s	s	3.57%
Ratio of Contacts Requiring Follow-Up to Index Cases (#contacts req. follow-up / #cases)	0.82	1.86	1.00	s	s	0.622

S: Suppressed due to small cell count (<6).

As reported in Figures 4.4 and 4.5, First Nations comprised 79% of the total number of contacts, yet only 60% of the cases. Foreign born, however, made up 29% of cases, and only 13% of the total number of contacts, while Canadian-born non-First Nations made up 11% of cases and 7% of the total number of contacts. This demonstrates *prima facie* differences in TB prevention, diagnosis, and care between these groups in Manitoba, which are explored in more detail below.

Figure 4.4. TB Case Distribution: Manitoba, 2008-2010

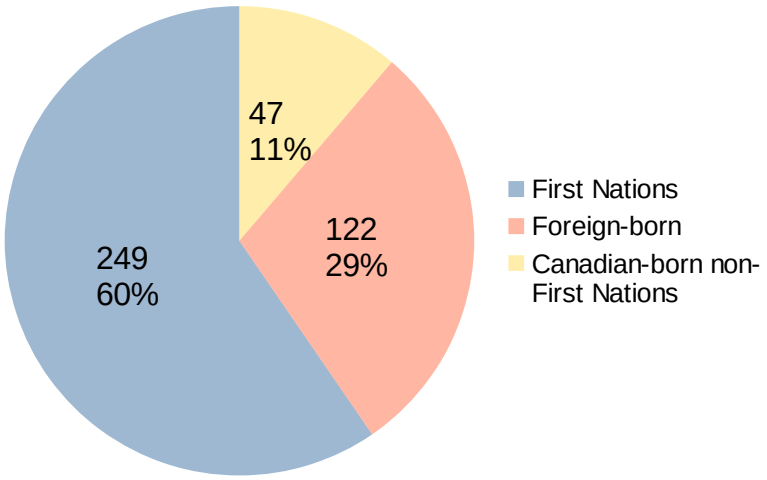
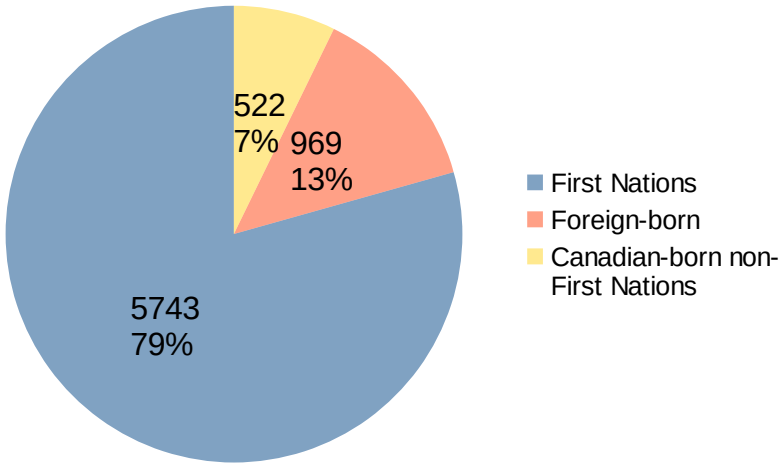


Figure 4.5. TB Contact Event Distribution, by Ethnic-origin of Cases: Manitoba, 2008-2010



In Table 4.14, First Nations cases have a far greater number of contacts, bot in total and average number per case (5,743 contacts / 249 cases = 23 contacts per case) than either foreign-born (969 contacts / 122 cases = 8 contacts per case) or Canadian-born non-First Nations (522 contacts / 47 cases = 11 contacts per case). The proportion of contacts requiring follow-up was also higher amongst First Nations, leading to a greater ratio of latent or active cases (i.e., contacts requiring follow-up) to index cases.

Table 4.14. Results of Contact Investigation based on Ethnic-Origin of Case

Ethnic-Origin of Index Case	Cases (#)	Contacts (#)	Contacts per Case (Avg. #)	Contacts Assessed (%)	Contacts Requiring follow-up (% of assessed)	New Active or Latent Cases Discovered (#)	Ratio of Contacts Requiring Follow-Up to Index Cases (#contacts req. follow-up / #cases)
First Nations	249	5,743	23	81.91	4.93	232	0.935
Foreign-born	122	969	8	60.89	0.51	s	s
Canadian-born non-First Nations	47	522	11	84.67	1.36	S	s
Total	418	7,234	17	79.29	4.20	241	0.577

Note: numbers smaller than in table 4.13 because only cases with ethnic-origin information were included.
S: Suppressed due to cell size <6.

Table 4.15 reports on the contacts elicited and assessed for index cases with *infectious pulmonary TB*, i.e., those with sputum or bronchial washings specimens that were culture-positive and that were smear-positive and smear-negative. The proportion of contacts elicited

and assessed increased when the analysis moved from smear-negative, culture-positive infectious pulmonary cases to smear-positive, culture-positive infectious pulmonary cases.

Table 4.15 Contact Investigation Outcomes by Type of Case

Index Case (infectious pulmonary cases)	Contacts Elicited (% of cases)	Contacts Assessed (% of contacts)
S+, C+	98.85 (86/87)	86.73 (2,496/2,878)
S-, C+	96.13 (174/181)	77.40 (2,997/3,872)
C+	97.01 (260/268)	81.38 (5,493/6,750)

Notes: S+, smear-positive; C+, culture-positive; S-, smear-negative

Contacts Elicited

In Table 4.16, the unadjusted and adjusted model showed no significant difference between any ethnic-origin group or for sex and age. In the unadjusted model, first time cases were 3% (95%CI: 1 – 5%) less likely to have contacts elicited than second time cases. This effect disappeared after adjusting for age, sex, and ethnic-origin**.**

Table 4.16. Robust Poisson Regression Analysis of Contacts Elicited: Manitoba, 2008-2010 (infectious pulmonary cases, n = 268)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.00	0.91	1.10	0.99	0.90	1.09
Canadian-born vs. Status First Nation	0.98	0.90	1.07	0.98	0.89	1.06
Foreign-born vs. Status First Nation	0.98	0.98	1.04	0.98	0.92	1.04
Sex						
Female vs. Male	0.97	0.92	1.02	0.97	0.93	1.02
Treatment History						
1st time vs. 2nd time Case	0.97*	0.95	0.99	0.97	0.95	1.01
Age Groups						
0-18 vs. 19-35	0.95	0.84	1.07	0.95	0.85	1.07
0-18 vs. 36-55	0.95	0.85	1.06	0.96	0.86	1.07
0-18 vs. 56+	0.94	0.84	1.06	0.95	0.85	1.06
19-35 vs. 36-55	1.00	0.95	1.05	1.00	0.96	1.05
19-35 vs. 56+	0.99	0.94	1.04	0.99	0.93	1.06
36-55 vs. 56+	0.99	0.95	1.04	0.99	0.93	1.05

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Contact Assessment

There were a total of 6,750 contacts to pulmonary cases (as defined in Chapter 3) recorded in the Registry during the study period. These contacts were nested into 268 clusters (i.e., pulmonary cases). Only 6,546 contacts had complete case information, reducing the sample size accordingly. These contacts were nested into 268 clusters (i.e., infectious pulmonary cases), because there was a correlation that exists naturally between the index case and their contacts, which must be taken into account when analyzing outcomes at the contact level using case-level information. This was done by specifying a structure for the correlation, creating a generalized

estimating equation (GEE) model that takes into account this correlation.

An unstructured correlation structure was specified, which allowed all clusters to have their own correlations, and was used for all models in this section. However, even when the correlation structure is incorrectly specified, GEE models will still produce reliable estimates (Skov, Deddens, Petersen, & Endahl, 1998). Consequently GEE was an attractive choice for the contact assessment data, given that little was known in advance about the nature of the correlation between contacts to the same index case.

For the adjusted model, 6,546 contacts had complete case information. The GEE algorithm failed to converge. There was insufficient sample size to estimate all the parameters in the model, when estimating the parameter for *treatment history* in the univariable models, and therefore this parameter was marked non-estimable (NE) in the table below.

As reported in Table 4.17, in the unadjusted model, younger cases were more likely to have their contacts assessed than older cases, generally, with the exception of 0-18 year old cases compared to 19-35 year old cases ($PR_{0\text{-}18 \text{ vs. } 19\text{-}35}$ = 0.97, 95%CI: 0.81 – 1.16) and 36-55 year old cases (PR = 1.04, 95%CI: 0.81 – 1.16). However, 0-18 year old cases were 27% (1 – 59%) more likely to have contacts assessed than cases 56 years and older. Similarly, both 19-35 year old cases and 36-55 year old cases also had 31% and 22% higher probabilities of contacts being assessed than cases 56 years and older, respectively.

In the unadjusted model, contacts to foreign-born infectious pulmonary cases, were 19% less likely to be assessed for LTBI or active TB than contacts to Status First Nations infectious pulmonary cases. After adjusting for age, sex, and treatment history, contacts to Status First Nations pulmonary TB cases, as opposed to contacts to foreign-born pulmonary TB cases were

still 18% (95% CI: 1 – 31%) were more likely to be assessed for LTBI or active disease ($p < 0.05$). Age of the index case also remained significantly associated with the probability of contacts being assessed. Contacts to 19-35 years old infectious pulmonary cases had a 32% higher probability than contacts to 56+ year old pulmonary TB cases to be assessed for LTBI or active disease, after adjusting for sex, treatment history, and ethnic-origin. Other age group differences were non-significant in the adjusted model.

Table 4.17. Clustered Robust Poisson Regression Analysis of Contacts Assessed: Manitoba, 2008-2010 (Contacts, n = 6,546, to infectious pulmonary cases, n = 268)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.14	0.87	1.50	1.21	0.94	1.56
Canadian-born vs. Status First Nation	0.93	0.74	1.16	1.00	0.81	1.22
Foreign-born vs. Status First Nation	0.81*	0.68	0.97	0.82*	0.69	0.99
Sex						
Female vs. Male	0.95	0.84	1.08	0.98	0.87	1.10
Treatment History						
1st time vs. 2nd time Case	NE	NE	NE	1.02	0.77	1.36
Age Groups						
0-18 vs. 19-35	0.97	0.81	1.16	0.95	0.79	1.14
0-18 vs. 36-55	1.04	0.87	1.25	1.04	0.86	1.26
0-18 vs. 56+	1.27*	1.01	1.59	1.25	0.98	1.60
19-35 vs. 36-55	1.08	0.95	1.22	1.10	0.96	1.25
19-35 vs. 56+	1.31**	1.09	1.58	1.32**	1.08	1.61
36-55 vs. 56+	1.22*	1.01	1.47	1.20	0.98	1.48

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

PART II. FIRST NATIONS

As reported in this study, Status First Nations constituted 59.6% of the TB cases diagnosed (that have ethnic-origin recorded) and were the majority of TB patients in Manitoba. This finding section reports on all First Nations TB cases in Manitoba, followed by examination of the Northern Health Region.

Data Source

The Manitoba TB Registry was used, with records for Manitoba First Nations TB cases and contacts during the study period selected for this part of the analysis. All cases with an *origin* listed as "Status First Nation" were selected (n = 249) for this analysis.

Demographics

In table 4.18, the sex-distribution of First Nations TB cases in Manitoba is higher among males (58%) than females (42%) and concentrated amongst ages 19-55**.** The proportion of male and female cases was similar for ages 0-18, then favours males for ages 19-35 and 36-55, returning to roughly equal distribution at age 56 years and older.

Table 4.18. Age and Sex Distribution of TB Cases: Manitoba First Nations, 2008-2010

Age Group	Females		Males		Total	
	#	%	#	%	#	%
0-18	25	10.0	24	9.6	49	19.7
19-35	24	9.6	44	17.7	68	27.3
36-55	40	16.1	60	24.1	100	40.2
56+	15	6.0	17	6.8	32	12.8
Total	104	41.8	145	58.2	249	100.00

Clinical and Microbiological Features

Table 4.19 shows that 82% of First Nations cases were diagnosed based on positive culture, while 18% were diagnosed clinically. The majority (73%) of First Nations cases had abnormal chest x-ray readings, while close to 19% had normal readings, and 9% did not have x-rays completed, was of poor quality, or was not reported to the TB Registry. Of the 249 First Nations cases, 165 were considered infectious pulmonary cases (66.3%), and 50 cases were both smear- and culture-positive. One hundred and forty eight cases were HIV tested and had the results reported to the TB Registry. The number of case that were HIV positive was too small to report for privacy reasons. Six cases out of 204 (2.9%) with drug susceptibility test (DST) results for their TB isolates had TB that was resistant to isoniazid (INH). No First Nations cases with DST results were found to have resistance to pyrazinamide (PZA).

Table 4.19. Clinical and Microbiological Features: Manitoba First Nations, 2008-2010

Feature	Cases	Cohort Size	Proportion (%)
Case Criteria			
Clinical Dx*	45	249	18.1
Positive Culture	204	249	81.9
X-Ray Result			
Normal	46	249	18.5
Abnormal	181	249	72.7
Missing/Poor Quality/Not Done	22	249	8.8
Pulmonary[6]	165	249	66.3
S+ C+	50	195	15.4
S- C+	115	195	59.0
S- C-	30	195	25.6
HIV Status			
Tested for HIV	148	249	59.4
HIV positive*	s	148	s
Drug Resistance*			
Resistant to INH	6	204	2.9
Resistant to PZA	0	204	0.0

S: suppressed due to small cell count (<=5)
*This is an indication of the severity of disease
**Proportion of TB cases that are HIV positive of those tested for HIV.
***Cases with drug resistance pattern.

TB Incidence Rates On-Reserve and Off-Reserve

Approximately 70% of First Nations TB patients reside on-reserve and the incidence rates of TB on-reserve were also higher than off-reserve in Manitoba, as well as across Canada. Using the March 2012 Aboriginal Affairs and Northern Development Canada (AANDC) Manitoba First

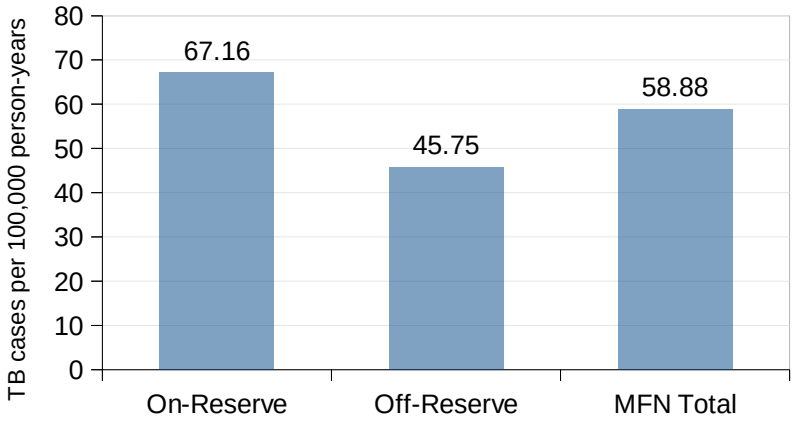
6 Specimen type: Sputum and/or bronchial washings

Nation population counts[7], we can estimate the relative risk of TB on-reserve versus off-reserve. Although this population count is not from the same years as the study period (2008-2010), it is close enough that it is useful for determining relative risk, assuming the growth rates on and off-reserve did not diverge significantly between these two periods.

In Manitoba, the total First Nations (FN) population was 140,975 in 2012, which must be multiplied by three in order to get the denominator for the First Nations incidence rate for this study: 140,975*3 years = 422,925; the numerator is 249 cases of TB diagnosed over the three-year study period. Therefore the First Nations TB incidence rate was 58.88 per 100,000 person-years. Using the same method, the First Nations population on-reserve is 84,874, and the number of cases was 171, making the rate 67.16 per 100,000 person-years[8]. In the report used, the number of First Nations people living off-reserve is not given. By taking the total First Nations population and subtracting the on-reserve population it was deduced that there were 56,101 First Nations people living off-reserve giving us a rate of 77/(56101*3) = 45.75 cases per 100,000 person-years. The relative risk of TB on-reserve versus off-reserve was 1.47 (67.16 / 45.75); thus showing that a 47% higher incidence rate of TB on-reserve than off-reserve (Figure 4.5).

7 https://www.aadnc-aandc.gc.ca/eng/1100100020539/1100100020544 Retrieved: July 16, 2015.
8 171 cases / [84,874 pop. * 3 years] = 67.16 cases / 100,000 person-years

Figure 4.5. Tuberculosis Case Rates: Manitoba First Nations, 2008-2010



Performance Measures for Case Management

Treatment Completion/Cure

In Table 4.20, the unadjusted model(s) showed that there was no association between living on-reserve or off-reserve and treatment completion/cure, with a PR estimate of 1.00 (i.e., equal probability). There were no sex differences found in the unadjusted model. First time cases appeared to be more likely to have completed treatment or to have been cured (PR = 1.27), but the result was not statistically significant. In the unadjusted model, age was a significant predictor of successful treatment completion/cure for First Nations. In the unadjusted model older cases were less likely to complete treatment or be cured than younger cases, with 0-18 and 19-35 year old cases both being more likely to complete treatment or be cured than both the 36-55 and 56+ age groups. In the adjusted model, only cases falling into the age groups 0-18 years and 19-35 years were significantly more likely to complete treatment or be cured than the 36-55 year age group.

There was no association between living on-reserve or off-reserve and treatment

completion/cure, with a PR estimate of 1.00 (i.e., equal probability). First time cases appear to be more likely to have completed treatment or been cured (PR = 1.27). The result, however, was not statistically significant.

In the adjusted model, there was still no significant difference between First Nations living on or off-reserve in terms of treatment completion/cure, either before or after adjusting for age, sex, and treatment history. First time cases were more likely to complete treatment or be cured than second time cases (PR = 1.23), after adjusting for age, sex, and living on- or off-reserve. Again this finding was not statistically significant at the $\alpha = 0.05$ level ($p = 0.537$). Cases falling within the age groups 0-18 years and 19-35 years remain significantly more likely to complete treatment or be cured than the 36-55 year age group in the multivariable model, but not the 56+ age group.

Table 4.20. Robust Poisson Regression Analysis of Treatment Completion/Cure: Manitoba First Nations, 2008-2010 (cases, n = 249)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	1.00	0.93	1.07	1.03	0.95	1.10
Sex						
Female vs. Male	0.99	0.93	1.06	1.00	0.94	1.06
Treatment History						
1st time vs. 2nd time Case	1.27	0.95	1.68	1.23	0.93	1.62
Age Groups						
0-18 vs. 19-35	1.00	NE	NE	1.01	0.98	1.03
0-18 vs. 36-55	1.14***	1.06	1.22	1.13***	1.05	1.22
0-18 vs. 56+	1.14*	1.00	1.30	1.12	0.98	1.28
19-35 vs. 36-55	1.14***	1.06	1.22	1.13***	1.05	1.21
19-35 vs. 56+	1.14*	1.00	1.30	1.12	0.98	1.27
36-55 vs. 56+	1.01	0.87	1.17	0.99	0.85	1.15

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; NE: non-estimable.

Early Detection of Pulmonary TB

In the unadjusted models, as reported in Table 4.21, first time cases were 21% less likely than second time cases to be smear-negative at diagnosis. The difference was not statistically significant. Age group was the sole predictor of being smear negative. The age group 0-18 years was 33% more likely than the 19-35 years group and 37% more likely than the 36-55 years group to be smear-negative at diagnosis. (i.e., have been detected early).

In the adjusted model, first time cases were 25% less likely ($p<0.05$) than second time cases to be smear-negative at diagnosis than second time cases (1 – 0.75*100 = 25%). The age group 0-18 years was 37% and 40% more likely to be smear-negative at diagnosis than 19-35

year old and 36-55 year old cases, respectively.

Table 4.21. Robust Poisson Regression Analysis of Early Detection: Manitoba First Nations, 2008-2010 (infectious pulmonary cases, n = 167)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.87	0.69	1.10	0.88	0.70	1.10
Sex						
Female vs. Male	0.86	0.69	1.07	0.82	0.66	1.03
Treatment History						
1st time vs. 2nd time Case	0.79	0.62	1.01	0.75*	0.58	0.96
Age Groups						
0-18 vs. 19-35	1.33*	1.04	1.72	1.37*	1.04	1.79
0-18 vs. 36-55	1.37**	1.08	1.73	1.40**	1.09	1.81
0-18 vs. 56+	1.19	0.89	1.57	1.25	0.94	1.67
19-35 vs. 36-55	1.03	0.80	1.33	1.03	0.80	1.33
19-35 vs. 56+	0.89	0.66	1.20	0.92	0.69	1.23
36-55 vs. 56+	0.87	0.65	1.15	0.89	0.68	1.17

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

HIV Testing and Reporting

In table 4.22, 59.4% of First Nations TB cases had an HIV test result on file in the TB Registry for the period 2008-2010. A comparison of First Nations living on- and off-reserve showed a significant difference in the proportion of TB cases with known HIV status. In other words, First Nations living on-reserve were significantly more likely to have HIV test results recorded in the TB Registry than were First Nations living off-reserve (Chi-square = 11.83, d.f., = 1, $p < 0.001$).

Table 4.22. Known HIV Status of TB Patients On vs. Off-Reserve: Manitoba First Nations, 2008-10

Location	HIV Test on File # (%)
On-Reserve	114 (66.7)
Off-Reserve	34 (43.6)
First Nations Total	148 (59.4)

In Table 4.23, treatment history was not significantly associated with having an HIV test result reported to the registry. While sex was not significant in the unadjusted model, in the adjusted mode, females First Nations TB cases were 27% more likely to have an HIV testing/reporting than male First Nations TB cases. In both models, First Nations living *off-reserve* had a 34% lower probability of HIV testing/reporting than First Nations living *on-reserve*. In the unadjusted model, age significantly predicted having an HIV test result on file for First Nations, with the age groups 19-35 being significantly more likely to have an HIV test on file than the 56+ age group (APR = 1.61). In the adjusted model, more age groups emerged as significant predictors. The age group 0-18 years was 28% less likely than 19-35 years to have HIV status reported, and cases aged 19-35 years were 30% and 64% more likely than cases, respectfully aged 36-55 years and 56+ years, to have HIV status reported.

Table 4.23. Log-Binomial Regression Analysis of HIV Test Results Reported: Manitoba First Nations, 2008-201 (cases, n = 249)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.65**	0.50	0.86	0.66**	0.51	0.85
Sex						
Female vs. Male	1.06	0.87	1.31	1.27**	1.08	1.50
Treatment History						
1st time vs. 2nd time Case	1.96	0.94	4.09	1.70	0.84	3.44
Age Groups						
0-18 vs. 19-35	0.84	0.64	1.11	0.72**	0.57	0.92
0-18 vs. 36-55	1.04	0.78	1.39	0.94	0.71	1.25
0-18 vs. 56+	1.35	0.86	2.14	1.19	0.75	1.88
19-35 vs. 36-55	1.24	0.98	1.56	1.30**	1.08	1.58
19-35 vs. 56+	1.62*	1.06	2.46	1.64*	1.09	2.47
36-55 vs. 56+	1.30	0.85	2.00	1.26	0.82	1.94

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Paediatric Cases

As reported in table 4.24, First Nations TB cases off-reserve were 58% (95%CI: 4 – 82%) less likely than First Nations cases on-reserve to be paediatric cases ($p<0.05$). Female First Nations TB cases were 85% (95%CI: 2 – 235%) more likely to be paediatric cases than males First Nations TB cases, which was significant in both the unadjusted and adjusted model ($p<0.01$).

Table 4.24. Log-Binomial Regression Analysis of Paediatric Cases: Manitoba First Nations, 2008-2010 (cases, n = 249)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.42*	0.19	0.98	0.42*	0.18	0.96
Sex						
Female vs. Male	1.83**	1.01	3.33	1.85**	1.02	3.35

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Re-Treatment Cases

In table 4.25, no significant difference found for residence and sex in the re-treatment rate. Age however was significant and consistent from the unadjusted to adjusted model. First Nations TB cases aged 19-35 years were, respectfully, 5% and 12% less likely than First Nation cases aged 36-55 years and 56+ years to be re-treatment cases.

Table 4.25. Robust Poisson Regression Analysis of Re-Treatment: Manitoba First Nations, 2008-2010 (cases, n = 249)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	1.04	0.97	1.11	1.03	0.96	1.10
Sex						
Female vs. Male	1.04	0.98	1.10	1.03	0.97	1.10
Age Groups						
0-18 vs. 19-35	1.03	0.97	1.09	1.02	0.96	1.09
0-18 vs. 36-55	0.96	0.90	1.04	0.97	0.90	1.04
0-18 vs. 56+	0.90	0.80	1.02	0.90	0.80	1.02
19-35 vs. 36-55	0.94*	0.88	0.99	0.95*	0.89	0.997
19-35 vs. 56+	0.88*	0.78	0.98	0.88*	0.79	0.99
36-55 vs. 56+	0.93	0.83	1.05	0.94	0.83	1.05

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Performance Measures for Contact Investigation

In this section we examine the results of the contact investigations between First Nations residing on- and off-reserve. Table 4.26 shows a greater number of cases, contacts, and contacts per case amongst First Nations living on-reserve than off-reserve in Manitoba. A clear difference in the proportion of contacts assessed was evident, with on-reserve cases' contacts being assessed 89% of the time and off-reserve cases' contacts being assessed 59% of the time (Table 4.26). Table 4.26 also shows a higher proportion of the contacts to cases on-reserve (5.14%) required follow-up compared to off-reserve cases' contacts (3.96%). There were 199 contacts with follow-up required (FUR) from the on the contact investigations related to cases on-reserve and 33 FUR contacts from the contact investigations related to cases off-reserve (Table 4.26). The ratio of FUR contacts to index cases is 1.16 for on-reserve cases and 0.43 for cases off-reserve.

Table 4.26. Contact Investigation Results for Manitoba First Nations, 2008-2010: On & Off-Reserve

Case Location	Cases (#)	Contacts (#)	Contacts per Case (avg. #)	Contacts Assessed (%)	Follow-Up Required (% of assessed)	Contacts with Follow-up Required (FUR) (#)	# FUR Contacts to # Index Cases (ratio)
On-Reserve (FN only)	171	4,335	25	89.3	5.14	199	1.16
Off-Reserve (FN only)	77	1,408	18	59.2	3.96	33	0.43
Total	248	5,743	23	81.9	4.93	232	0.94

Contacts Elicited

In table 4.27, sex was not a significant predictor in the unadjusted or the adjusted model. Treatment history was significant in the unadjusted model but lost significance in the adjusted model. In the unadjusted model First Nations pulmonary cases living off reserve had a 7% (95%CI: 0.15 – 14%) lower probability of contacts being elicited than First Nations pulmonary cases living on reserve (1 – 0.93 * 100 = 7%). This effect remained statistically significant in the adjusted model and actually increased in magnitude to 8% (1 – 0.92 * 100 = 8%).

Table 4.27. Robust Poisson Regression Analysis of Contacts Elicited: Manitoba First Nations, 2008-2010 (infectious pulmonary cases, n = 167)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.93*	0.86	0.9985	0.92*	0.85	0.99
Sex						
Female vs. Male	0.96	0.91	1.02	0.97	0.93	1.02
Treatment History						
First Time Case vs Second Time Case	0.97*	0.95	0.9995	0.95	0.89	1.00
Age Groups						
0-18 vs. 19-35	0.78	0.55	1.10	0.89	0.76	1.03
0-18 vs. 36-55	0.79	0.56	1.12	0.90	0.77	1.05
0-18 vs. 56+	0.81	0.57	1.16	0.93	0.78	1.10
19-35 vs. 36-55	1.01	0.99	1.04	1.01	0.98	1.04
19-35 vs. 56+	1.04	0.96	1.13	1.05	0.96	1.14
36-55 vs. 56+	1.03	0.94	1.12	1.03	0.95	1.13

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Contact Assessment

A clustered robust Poisson regression analysis of contact assessment was conducted, using a GEE approach, with contacts clustered around cases. There were 5,238 contacts associated with 167 First Nations infectious pulmonary cases, all of which had complete demographic information and were useable in the subsequent analyses. There was an estimated correlation of 0.52 between contacts of the same case, which was derived from the specified exchangeable/working correlation structure.

In table 4.28, only age and residence was significant. In the unadjusted model, contacts to cases off-reserve were 37% less likely to be assessed for LTBI or active TB compared to contacts of cases on-reserve ($p<0.001$). Contacts to cases aged 0-18 years and 19-35 years were 56% and 39% more likely than contacts to cases aged 56+ years to be assessed for LTBI or active TB ($p<0.01$, $p<0.05$, respectively).

In the adjusted model, contacts to First Nations cases living off reserve were 37% (95%CI: 22 – 50%) less likely than contacts to First Nations cases living on reserve to be assessed for LTBI or active TB disease. Contacts to First Nations cases aged 0-18 years, 19-35 years, and 36-55 years were 50%, 40%, and 37% more likely than First Nations cases aged 56+ years, respectively, to have assessment for LTBI or active TB completed.

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Table 4.28. Robust Poisson Regression Analysis of Contact Assessment: Manitoba First Nations, 2008-2010 (infectious pulmonary cases, n = 167; contacts, n = 5,328)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.63***	0.50	0.79	0.63***	0.50	0.78
Sex						
Female vs. Male	0.98	0.84	1.14	1.00	0.88	1.14
Treatment History						
First Time Case vs Second Time Case	1.00	0.76	1.31	0.84	0.65	1.09
Age Groups						
0-18 vs. 19-35	1.24	0.96	1.32	1.08	0.93	1.24
0-18 vs. 36-55	1.16	0.998	1.36	1.10	0.96	1.26
0-18 vs. 56+	1.56**	1.14	2.14	1.50**	1.12	2.02
19-35 vs. 36-55	1.04	0.88	1.22	1.02	0.88	1.1
19-35 vs. 56+	1.39*	1.01	1.91	1.40*	1.03	1.90
36-55 vs. 56+	1.34	0.98	1.84	1.37*	1.02	1.84

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

PART III. WINNIPEG

The Winnipeg Health Region or Winnipeg Regional Health Authority (WRHA) is the largest RHA in Manitoba, serving the City of Winnipeg. The WRHA also provide central leadership in TB prevention, diagnosis, and care throughout Manitoba through a public health unit known as Integrated Tuberculosis Services (ITS). This section describes the results from an analysis of performance measures related to TB cases in the City of Winnipeg (n = 223).

Data Source

All data tables were merged using the unique Client ID number. A subset of this data representing cases for the Winnipeg RHA were selected for analysis based on the RHA variable provided in the client table. Further sub-setting of this data was done for each performance measure, using the same methods previously explained.

Demographics

In Table 4.29.1, 38.4% of TB cases in Winnipeg during the study period were between 36 and 55 years of age, followed by 32.9% in the age group 19 to 35 years. The pattern distribution was similar for FN with the large number (13.9%) between 36 and 55 years, followed by 6.9% in the 19 to 35 year old group. The foreign-born pattern differed with 22% of cases occurring in the 19 to 35 year old group, followed by 16.7% in the 35 to 55 years old group.

Table 4.29.1. Ethnic-origin-specific Age-Distribution of TB Cases: Winnipeg, 2008-2010

Groups	*Canadian-born non-First Nations*		*Foreign-born*		*First Nations*		*Total*	
Age	#	%	#	%	#	%	#	%
0-18	s	s	s	s	s	s	9	4.2
19-35	s	s	48	22.2	15	6.9	71	32.9
36-55	17	7.9	36	16.7	30	13.9	83	38.4
56+	12	5.6	s	s	s	s	53	24.5
Total	40	18.6	120	55.6	56	25.9	216	100

S: suppressed due to small cell count (<=5)

According to table 4.29.2, among Winnipeg TB cases, the sex distribution was 56% males and 44% females. The distribution of TB cases within the age groups of 0-18 and 19-35 years favoured females, respectively at 59% and 35%. In the older age groups of 36-55 and 56+ years the majority (62%) of cases were males.

Table 4.29.2 Age **and Sex Distribution of Winnipeg TB Cases, 2008-2010**

Age Group	**Female *n* (%)**	**Male *n* (%)**	**Total**
0-18	10 (59)	s	s
19-35	34 (35)	s	s
36-55	33 (38)	53 (62)	86
56+	21 (38)	34 (62)	55
Total	98 (44)	125 (56)	223

S: suppressed due to small cell count (<6)

Clinical and Microbiological Features

In table 4.30, a total of 223 cases were diagnosed in Winnipeg. Of these cases, 192 (86.1%) had a culture confirmed diagnosis while 31 (13.9%) had a clinical diagnosis only. Chest x-ray readings were considered abnormal for 77% of TB cases in Winnipeg, considered normal for 10.4%, and missing, of poor quality, or not done for the remaining 12.6%. Of 223 cases, 135 (60.5%) were infectious pulmonary cases. More than half (56.5%) of Winnipeg TB cases had an HIV test results reported in the TB Registry, and 8% of these cases were HIV positive. Over 7 percent of cases were infected with INH-resistant TB strains.

Table 4.30. Clinical and Microbiological Features of Winnipeg TB Cases, 2008-2010

Feature	Cases	Cohort Size	Proportion (%)
Case Criteria			
Clinical Dx*	31	223	13.9
Positive Culture	192	223	86.1
X-Ray Result			
Normal	23	222	10.4
Abnormal	171	222	77.0
Missing/Poor Quality/Not Done	28	222	12.6
Pulmonary[9]	135	223	60.5
S+ C+	46	160	28.7
S- C+	89	160	55.6
S- C-	25	160	15.6
HIV Status			
Tested for HIV	125	223	56.1
HIV positive*	10	125	8.0
Drug Resistance***			
Resistant to INH	15	192	7.8

*This is an indication of the severity of disease
**Proportion of TB cases that were HIV positive of those tested for HIV.
***Cases with drug resistance pattern.

9 Specimen type: Sputum and/or bronchial washings

Performance Measures for Case Management

Treatment Completion/Cure

In Table 4.31, sex and ethnic origin were not significant predictors of treatment completion/cure in Winnipeg. Age was the only significant predictor. In the unadjusted model, a statistical difference was found between 0-18 and 19-35 years and between 0-18 and 56+ years, with a 25% higher likelihood for each of the younger groups to complete treatment / be cured than the 56+ years age group. Significant differences were also found between 19-35 versus 36-55 years olds and 19-35 versus 56+ year olds.

In the adjusted model, Winnipeg TB cases aged 0-18 years were 11% (95%CI: 3 – 19%) more likely to complete treatment or be cured than cases aged 36-55 years and 26% more likely than cases aged 56+ years; cases aged 19-35 years were 11% (95%CI: 3 – 20%) more likely than cases aged 36-55 years and 27% (95%CI: 10 – 46%) more likely than cases aged 56+ years to complete treatment or be cured.

Table 4.31. Robust Poisson Regression Analysis of Treatment Completion/Cure: Winnipeg, 2008-2010 (cases, n = 223)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.06	0.96	1.16	1.08	0.98	1.19
Canadian-born vs. Status First Nation	1.04	0.94	1.16	1.07	0.96	1.18
Foreign-born vs. Status First Nation	0.99	0.90	1.10	0.99	0.90	1.09
Sex						
Female vs. Male	1.05	0.97	1.13	1.03	0.96	1.12
Treatment History						
1st time vs. 2nd time Case	1.03	0.82	1.30	0.97	0.74	1.26
Age Groups						
0-18 vs. 19-35	1.00	1.00	1.00	1.00	0.98	1.02
0-18 vs. 36-55	1.10**	1.03	1.18	1.11**	1.03	1.19
0-18 vs. 56+	1.25***	1.10	1.43	1.26**	1.10	1.45
19-35 vs. 36-55	1.10**	1.03	1.18	1.11**	1.03	1.20
19-35 vs. 56+	1.25***	1.10	1.43	1.27***	1.10	1.46
36-55 vs. 56+	1.13	0.98	1.32	1.14	0.98	1.33

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001.

Early Detection of Pulmonary TB

In Table 4.32, the unadjusted model showed no treatment history or sex differences in the probability of early detection and diagnosis of infectious pulmonary TB cases in Winnipeg. While Canadian-born non-First Nations were 36% less likely than foreign-born to be smear-negative at diagnosis, the relationship was not statistically significant (Table 4.32). Age was the most important predictor of smear-status for pulmonary cases in Winnipeg. Infectious pulmonary cases aged 0-18 years were significantly more likely than all older age groups to be smear-negative at diagnosis. Infectious pulmonary cases aged 0-18 years were 41%, 43%, and

41% more likely than pulmonary cases aged 19-35, 36-55, and 56+ years, respectively, to be smear-negative at diagnosis (Table 4.32). After adjusting for age, sex, and treatment history, the effect direction of ethnic origin was the same and the relationship was not significant. Infectious pulmonary cases aged 0-18 years were significantly more likely than all older age groups to be smear-negative at diagnosis (Table 4.32). Pulmonary cases aged 0-18 years were 41%, 43%, and 41% more likely than pulmonary cases aged 19-35, 36-55, and 56+ years, respectively, to be smear-negative at diagnosis (Table 4.32). After adjusting for the other variables, age was not a significant predictor of early detection.

Table 4.32. Robust Poisson Regression Analysis of Early Detection – Smear Negative at Diagnosis: Winnipeg, 2008-10 (infectious pulmonary cases, n = 132)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	0.64	0.39	1.03	0.65	0.40	1.07
Canadian-born vs. Status First Nation	0.74	0.44	1.24	0.78	0.45	1.33
Foreign-born vs. Status First Nation	0.16	0.87	1.56	1.19	0.87	1.64
Sex						
Female vs. Male	1.00	0.76	1.30	0.98	0.75	1.29
Treatment History						
1st time vs. 2nd time Case	0.81	0.55	1.17	0.74	0.50	1.09
Age Groups						
0-18 vs. 19-35	1.50*	1.04	2.17	1.32	0.90	1.93
0-18 vs. 36-55	1.45*	1.06	1.99	1.34	0.94	1.90
0-18 vs. 56+	1.37	0.98	1.91	1.31	0.90	1.91
19-35 vs. 36-55	0.97	0.68	1.39	1.02	0.72	1.43
19-35 vs. 56+	0.92	0.63	1.33	1.00	0.69	1.44
36-55 vs. 56+	0.94	0.69	1.30	0.98	0.71	1.36

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; NE: not estimable due to small cell sizes.

HIV Testing/Reporting

In Table 4.33, ethnic-origin, sex and treatment history were not significant predictors of HIV testing/reporting. Only age was a significant predictor, with ages 0-18 years having the highest probability of HIV testing and reporting (unadjusted at 71% and adjusted at 48%). In the unadjusted model, those TB cases aged 0-18 years had a 77% (95%CI: 13 – 176%) higher probability of HIV testing and reporting than cases aged 56+ years. Cases aged 19-35 years had a 65% (95%CI: 15 - 139%) higher probability of HIV testing and reporting than cases aged 56+ years and older. The magnitude of the effect of age group on probability of HIV testing and reporting increased from the unadjusted models to the adjusted model, suggesting an age-sex interaction that should be explored. The PR for the 0-18 year old cases to 56 years and older cases went from 1.77 to 1.88, showing a relationship between age and HIV testing/reporting.

Table 4.33. Log-Binomial Regression Analysis of HIV Testing/Reporting: Winnipeg, 2008-10 (cases, n = 223)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.12	0.84	1.50	1.04	0.77	1.40
Canadian-born vs. Status First Nation	1.30	0.90	1.86	1.24	0.85	1.82
Foreign-born vs. Status First Nation	1.16	0.85	1.59	1.19	0.87	1.63
Sex						
Female vs. Male	0.91	0.72	1.15	0.87	0.69	1.09
Treatment History						
1st time vs. 2nd time Case	2.59	0.76	8.83	2.07	0.60	7.17
Age Groups						
0-18 vs. 19-35	1.07	0.75	1.52	1.09	0.77	1.54
0-18 vs. 36-55	1.27	0.88	1.81	1.23	0.86	1.75
0-18 vs. 56+	1.77*	1.13	2.76	1.88**	1.19	2.96
19-35 vs. 36-55	1.19	0.92	1.53	1.13	0.87	1.48
19-35 vs. 56+	1.65**	1.15	2.39	1.73**	1.17	2.56
36-55 vs. 56+	1.40	0.96	2.03	1.52*	1.03	2.26

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001.

Paediatric Cases

In table 4.34, ethnic origin and sex did not predict whether a case was a paediatric case. Very wide confidence intervals were observed for all PR. For example, while female cases had an equal probability of being a paediatric case as male cases, the very wide confidence interval (APR = 1.02; 95%CI: 0.28 – 3.68) suggested that much caution is required when interpreting this result. For the ethnic-origin groups, it appears as though foreign-born and First Nations cases had similar probabilities of being paediatric cases, while Canadian-born non-First Nations were

more than twice as likely as either First Nations or foreign-born to be paediatric cases. Yet, as noted, the very wide confidence intervals suggest that caution in interpreting these these results is required.

Table 4.34. Log-Binomial Regression Analysis of Paediatric Cases: Winnipeg, 2008-2010 (cases, n = 223)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	2.25	0.53	9.63	2.25	0.51	9.89
Canadian-born vs. Status First Nation	2.10	0.37	12.00	2.10	0.37	12.00
Foreign-born vs. Status First Nation	0.93	0.18	4.95	0.93	0.17	5.05
Sex						
Female vs. Male	1.02	0.28	3.70	1.02	0.27	3.76

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001.

Re-treatment Cases

In the unadjusted model, ethnic-origin was a significant predictor of re-treatment. In the adjusted model Canadian-born non-First Nations cases and the foreign-born cases were both significantly less likely (9% and 11% respectively) to be re-treatment cases than First Nations cases. As for age, cases 0-18 years were less likely than cases 36-55 years and cases 56+ years to be re-treatment cases ($p<0.05$).

In the adjusted model, Winnipeg TB cases aged 0-18 years were significantly less likely than cases aged 56 years and older to be re-treatment cases. Canadian-born non-First Nations and foreign-born both remained significantly less likely than First Nations to be re-treatment cases in Winnipeg after adjusting for age and sex ($p<0.05$).

Table 4.35. Robust Poisson Regression Analysis of Re-Treatment: Winnipeg, 2008-2010 (cases, n = 223)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.02	0.97	1.07	1.01	0.96	1.06
Canadian-born vs. Status First Nation	0.91*	0.83	0.997	0.91*	0.83	0.99
Foreign-born vs. Status First Nation	0.90**	0.83	0.97	0.89*	0.83	0.97
Sex						
Female vs. Male	0.98	0.94	1.03	0.99	0.94	1.04
Age Groups						
0-18 vs. 19-35	0.99	0.96	1.01	0.99	0.94	1.03
0-18 vs. 36-55	0.96*	0.92	0.997	0.98	0.92	1.02
0-18 vs. 56+	0.93*	0.87	0.994	0.93*	0.86	0.9973
19-35 vs. 36-55	0.97	0.92	1.02	0.99	0.94	1.04
19-35 vs. 56+	0.95	0.88	1.01	0.94	0.88	1.01
36-55 vs. 56+	0.98	0.90	1.05	0.95	0.88	1.03

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Performance Measures for Contact Investigation

Contact Elicitation

In the unadjusted model comparing infectious pulmonary cases without a history of treatment for TB (first time cases) to infectious pulmonary cases with a history of treatment for TB (second time cases), a 6% (95%CI: 1 to 9%) lower probability of having contacts elicited during a contact investigation amongst first-time cases (Table 4.36). This estimate became non-significant after adjusting for age, sex, and ethnic-origin. No other hypothesized predictors were statistically significant. However, the PR estimates for both foreign-born and Canadian-born

non-First Nations compared to First Nations suggest that First Nations infectious pulmonary TB cases in Winnipeg were less likely to have contacts elicited than the other two ethnic-origin groups. Although the PRs for comparing First Nations to Canadian-born non-First Nations and foreign-born were not statistically significant and therefore not reliable estimates.

Table 4.36. Robust Poisson Regression Analysis of Contacts Elicited: Winnipeg, 2008-2010 (infectious pulmonary cases, n = 134)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.00	0.90	1.11	0.99	0.89	1.10
Canadian-born vs. Status First Nation	1.03	0.91	1.18	1.04	0.91	1.19
Foreign-born vs. Status First Nation	1.04	0.93	1.15	1.05	0.92	1.20
Sex						
Female vs. Male	0.96	0.88	1.05	0.97	0.90	1.05
Treatment History						
1st time vs. 2nd time Case	0.94**	0.91	0.99	0.93	0.85	1.02
Age Groups						
0-18 vs. 19-35	0.94	0.74	1.21	0.94	0.72	1.22
0-18 vs. 36-55	0.94	0.74	1.20	0.94	0.74	1.21
0-18 vs. 56+	0.91	0.72	1.16	0.93	0.74	1.16
19-35 vs. 36-55	1.00	0.90	1.11	1.00	0.90	1.11
19-35 vs. 56+	0.97	0.88	1.07	0.98	0.88	1.09
36-55 vs. 56+	0.97	0.90	1.06	0.99	0.90	1.08

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Contact Assessment

There were 2,118 contacts associated with 134 infectious pulmonary cases of TB in Winnipeg. Most contacts, 2,058 or 97.2%, had information from the cases available for this

analysis. In Table 4.37, the exchangeable/working correlation structure had an estimated (from multivariable model) correlation within clusters of 0.90 (i.e., 90%), suggesting similarity in contact assessment amongst the contacts of a particular case. In the unadjusted and adjusted models, no significant differences were observed for this performance measure. In both models, while Winnipeg First Nations infectious pulmonary TB cases' contacts appeared to have had a lower probability of being assessed than the other two ethnic-origin groups, the point estimates were not statistically significant.

Table 4.37. Clustered Robust Poisson Regression Analysis of Contact Assessment: Winnipeg, 2008-2010 (infectious pulmonary cases, n = 134; contacts, n = 2,058)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Ethnic-origin						
Canadian-born vs. foreign-born	1.02	0.72	1.44	1.00	0.71	1.39
Canadian-born vs. Status First Nation	1.27	0.84	1.94	1.28	0.84	1.94
Foreign-born vs. Status First Nation	1.25	0.89	1.77	1.28	0.89	1.86
Sex						
Female vs. Male	0.88	0.66	1.17	0.87	0.66	1.15
Treatment History						
1st time vs. 2Nd time Case	1.05	0.59	1.87	0.89	0.49	1.62
Age Groups						
0-18 vs. 19-35	0.80	0.44	1.47	0.76	0.42	1.40
0-18 vs. 36-55	1.07	0.58	1.97	1.03	0.55	1.94
0-18 vs. 56+	0.98	0.53	1.80	1.06	0.56	1.99
19-35 vs. 36-55	1.33	0.96	1.85	1.36	0.99	1.85
19-35 vs. 56+	1.21	0.87	1.70	1.39	0.999	1.92
36-55 vs. 56+	0.91	0.64	1.30	1.02	0.71	1.47

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; LCL: lower confidence limit; UCL: upper confidence limit.

PART IV. NORTHERN MANITOBA

In Northern Manitoba, the study population was 153 cases of TB diagnosed between January 1, 2008 and December 31, 2010, and included this cohort's treatment and outcomes up to 2012. The 3,889 contacts associated with these cases were analyzed in the contact investigation section. The region's case distribution was primarily Status First Nations. A small number of cases were non-First Nations (n = 4), which was too small for analysis purposes. Therefore only First Nations TB cases were analyzed (*n* = 149), which made this part specific to Northern Manitoba First Nations.

Data Source

All tables were merged together using the unique (anonymized) Client ID number. A subset of this data representing cases for the Northern RHA were selected for analysis based on the RHA variable provided in the client table. Further sub-setting of this data set was done for each performance measure, using the same methods previously explained

Geography of Northern Manitoba

The Northern Manitoba RHA boundaries define the case population for this region. Within these boundaries there are a wide-range of communities, from First Nations to the City of Thompson (see Appendix 4). Communities vary by size, demographics, health services, accessibility, culture/language, infrastructure, housing, and natural resources. TB burden varies between these communities, with most of them having no cases of TB, while others having numerous cases of TB during the study period. However, an examination of TB by community

was not part of the analysis plan and therefore these differences could not be described by the present study.

Demographics

In Northern Manitoba, the age distribution of TB was 22.2% in the 0-18 year age group, 28.9% in the group 19-35 years of age then higher at 38.9% for 36-55 year old cases. After 56 years, the percentage dropped to 10.1%. The majority of cases were male (58.4%). The smallest age-sex group amongst Northern First Nations TB cases was females 56+ years, with only 4.7% of cases falling into this category. Sixteen percent of cases were females 36-55 years of age. Only 9.4% of cases were females aged 19-35 compared to 19.5% of cases being males of the same age group. Males cases aged 36-55 years had the largest percentage of any age-sex group with 22.8% of cases falling into this category.

Table 4.38. Age and Sex Distribution of First Nations TB Cases in Northern Manitoba, 2008-2010

Age Group	Females		Males		Total	
	#	%	#	%	#	%
0-18	17	11.4	16	10.7	33	22.1
19-35	14	9.4	29	19.5	43	28.9
36-55	24	16.1	34	22.8	58	38.9
56+	7	4.7	8	5.4	15	10.1
Total	62	41.6	87	58.4	149	100

Clinical and Microbiological Features

In Table 4.39, Northern Manitoba First Nations had a high proportion of cases with a clinical diagnosis (20.81%) and 79.1% had a positive culture. An abnormal chest x-ray reading was found for 71% of cases, while only 6.7% had missing, poor quality or no x-ray result, and 21.5% of cases had a reading of normal. The proportion of cases that were infectious pulmonary cases was 65%. Sixty-three percent were tested for HIV with the results reported to the Manitoba TB Registry. The number of TB cases that were HIV positive was very low and had to be suppressed in the table, as were the number of drug resistant cases.

Table 4.39. Clinical and Microbiological Features of First Nations TB Cases in Northern Manitoba, 2008-2010

Feature	Cases	Cohort Size	Proportion (%)
Case Criteria			
Clinical Dx*	31	149	20.8
Positive Culture	118	149	79.2
X-Ray Result			
Normal	32	149	21.5
Abnormal	107	149	71.8
Missing/Poor Quality/Not Done	10	149	6.7
Pulmonary[10]	97	149	65.1
S+ C+	27	116	23.3
S- C+	70	116	60.3
S- C-	19	116	16.4
HIV Status			
Tested for HIV	94	149	63.1
HIV positive*	s	149	s
Drug Resistance***			
Resistant to INH	s	118	s
Resistant to PZA	s	118	s

*This is an indication of the severity of disease
**Proportion of TB cases that were HIV positive of those tested for HIV.

10 Specimen type: Sputum and/or bronchial washings

***Cases with drug resistance pattern.

Performance Measures for Case Management

Treatment Completion/Cure

In Table 4.40, there were no significant difference in the rate of treatment completion/cure between cases residing on- or off-reserve, between male and female cases, between first time cases and second time cases in Northern Manitoba. There were, however, significant age differences in the unadjusted and adjusted models. In both models, cases in the age groups 0-18 years old and 19-35 years old had a 9% and 7% greater chance, respectively, of completing treatment or being cured than cases aged 36-55 years.

Table 4.40. Robust Poisson Regression Analysis of Treatment Completion/Cure: Northern Manitoba First Nations, 2008-2010 (cases, n = 149)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	1.06	1.02	1.10	1.03	0.995	1.07
Sex						
Female vs. Male	0.97	0.90	1.04	0.98	0.92	1.06
Treatment History						
1st time vs. 2nd time Case	1.46	0.92	2.31	1.41	0.89	2.22
Age Groups						
0-18 vs. 19-35	1.00	1.00	1.00	1.02	0.99	1.05
0-18 vs. 36-55	1.09*	1.01	1.18	1.09*	1.01	1.18
0-18 vs. 56+	1.15	0.95	1.41	1.11	0.92	1.33
19-35 vs. 36-55	1.09*	1.01	1.18	1.07*	1.00	1.15
19-35 vs. 56+	1.15	0.95	1.41	1.09	0.90	1.31
36-55 vs. 56+	1.05	0.85	1.31	1.01	0.83	1.24

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; NE: not estimable due to small cell sizes.

Early Detection of Pulmonary TB

In Table 4.41, the unadjusted and adjusted models yielded no significant associations for on-reserve or off-reserve residency, sex, first-time versus second-time cases, or age.

Table 4.41. Robust Poisson Regression Analysis of Early Detection of Pulmonary TB: Northern Manitoba First Nation, 2008-2010 (infectious pulmonary cases, n = 97)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.87	0.58	1.32	0.87	0.57	1.33
Sex						
Female vs. Male	0.95	0.73	1.24	0.92	0.70	1.20
Treatment History						
1st time vs. 2Nd time Case	0.83	0.60	1.15	0.91	0.63	1.31
Age Groups						
0-18 vs. 19-35	1.35	0.88	2.06	1.39	0.88	2.18
0-18 vs. 36-55	1.04	0.73	1.47	1.07	0.73	1.55
0-18 vs. 56+	0.98	0.65	1.48	1.02	0.66	1.59
19-35 vs. 36-55	0.77	0.55	1.07	0.77	0.56	1.07
19-35 vs. 56+	0.73	0.49	1.08	0.74	0.49	1.12
36-55 vs. 56+	0.94	0.69	1.30	0.96	0.69	1.34

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

HIV Testing/Reporting

In Table 4.42, Northern Manitoba First Nations TB cases residing on-reserve had a much higher probability of HIV testing and reporting than cases living off-reserve. After adjusting for age, sex and treatment history, northern First Nations cases living off-reserve were 58% (95%CI: 17 – 78%) less likely than First Nations cases living on-reserve to have HIV testing and results

reported to the TB Registry (1 – 0.42 * 100 = 58%). Age was not significant in the unadjusted model. However, after adjusting for sex, residency and treatment history, TB cases between the ages of 19-35 years were 38% (95%CI: 1 to 90%) more likely than cases aged 36-55 years to have HIV test results on-file in the registry.

The probability of HIV testing/reporting for First Nations in Northern Manitoba followed a pattern previously observed in this study: an initial increase in probability of HIV testing/reporting with increasing age, from 0-18 to 19-35, then a decreasing probability of HIV testing/reporting as age increased further (36-55 and 56+ years). This was observed through the adjusted model's least-squares probability estimates for the various age groups: 0-18 (π = 36%) 19-35 (π = 49%), 36-55 (π = 35%), and 56+ (π = 33%), where π is the probability of an HIV test result being recorded in the TB Registry.

Table 4.42. Log-Binomial Regression Analysis of HIV Testing/Reporting: Northern Manitoba First Nations, 2008-2010 (cases, n = 149)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.44*	0.22	0.87	0.42*	0.21	0.83
Sex						
Female vs. Male	1.04	0.81	1.33	1.25*	1.05	1.50
Treatment History						
1st time vs. 2Nd time Case	1.45	0.69	3.03	1.47	0.70	3.08
Age Groups						
0-18 vs. 19-35	0.75	0.54	1.05	0.73*	0.55	0.97
0-18 vs. 36-55	0.98	0.68	1.41	1.01	0.72	1.43
0-18 vs. 56+	1.08	0.62	1.88	1.09	0.63	1.89
19-35 vs. 36-55	1.31	0.998	1.72	1.39**	1.10	1.74
19-35 vs. 56+	1.44	0.87	2.38	1.50	0.92	2.43
36-55 vs. 56+	1.10	0.65	1.85	1.08	0.64	1.81

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Paediatric Cases

In Table 4.43, there was no significant difference between Northern Manitoba First Nations cases on- and off-reserve regarding the probability that a case was a paediatric case. Important sex differences, however, were found. In both models, Northern First Nations female TB cases had a significantly higher probability (132%; 95%CI: 9 – 396%) of being paediatric cases than male First Nations TB cases after adjusting for residency (i.e., regardless of living on or off-reserve). Because the estimated PR was based on a small number of cases, the confidence interval (CI) was quite wide. However, the CI did not cross 1.0 and was significant (p<0.05).

Table 4.43. Log-Binomial Regression Analysis of Paediatric Cases: Northern Manitoba First Nations, 2008-2010 (cases, n = 149)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	1.29	0.49	3.39	1.20	0.47	3.06
Sex						
Female vs. Male	2.34*	1.09	5.00	2.32*	1.09	4.96

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Re-treatment Cases

In Table 4.44, there were no sex differences in the probability of being re-treatment cases amongst Northern First Nations TB cases. There were, however, residency (on/off-reserve) and age differences. In the unadjusted model, First Nations TB cases living off-reserve were 6% (95%CI: 3% - 10%) less likely than those living on-reserve to be re-treatment cases. After adjusting for sex and age, First Nations TB cases living off-reserve were 7% (95%CI: 3% - 11%) less likely than First Nations TB cases living on-reserve to be re-treatment cases. Age was also a significant predictor of re-treatment. In both unadjusted and adjusted models, cases that were between 19-35 years of age were significantly less likely to be a re-treatment case than cases aged either 36-55 or 56 years and older.

Table 4.44. Robust Poisson Regression Analysis of Re-Treatment: Northern Manitoba First Nations, 2008-2010 (cases, n = 149)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.94*	0.90	0.97	0.93*	0.89	0.97
Sex						
Female vs. Male	1.06	0.98	1.15	1.05	0.98	1.14
Age Groups						
0-18 vs. 19-35	1.06	0.98	1.15	1.06	0.97	1.15
0-18 vs. 36-55	0.99	0.90	1.09	0.99	0.89	1.10
0-18 vs. 56+	0.88	0.73	1.06	0.89	0.74	1.06
19-35 vs. 36-55	0.94*	0.88	0.99	0.94*	0.89	0.99
19-35 vs. 56+	0.83*	0.70	0.99	0.84*	0.71	0.99
36-55 vs. 56+	0.89	0.75	1.07	0.90	0.75	1.06

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001

Performance Measures for Contact Investigation

Contact Elicitation

In Table 4.45, there were no significant differences in the probability of contacts being elicited for First Nations infectious pulmonary TB cases by sex, age or treatment history. All comparison groups had similar probabilities of contacts being elicited, with most PR's close to 1.0.

Table 4.45. Robust Poisson Regression Analysis of Contacts Elicited – Northern First Nations, 2008-2010 (infectious pulmonary cases, n = 97)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.93	0.80	1.07	0.94	0.84	1.05
Sex						
Female vs. Male	0.97	0.91	1.03	0.98	0.94	1.02
Treatment History						
1st time vs. 2nd time Case	0.99	0.97	1.01	0.98	0.95	1.02
Age Groups						
0-18 vs. 19-35	0.90	0.73	1.11	0.91	0.77	1.09
0-18 vs. 36-55	0.90	0.73	1.11	0.91	0.77	1.09
0-18 vs. 56+	0.90	0.73	1.11	0.91	0.77	1.08
19-35 vs. 36-55	1.00	1.00	1.00	1.00	0.99	1.01
19-35 vs. 56+	1.00	1.00	1.00	1.00	0.99	1.02
36-55 vs. 56+	1.00	1.00	1.00	1.00	0.99	1.02

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; NE: not estimable due to small cell sizes.

Contact Assessment

There were 3,397 contacts associated with the 97 infectious pulmonary cases amongst Northern Manitoba First Nations, all of which had complete case information for the analysis. The multivariable model's within-cluster correlation of the responses of contacts to the same case was 0.57.

A pattern of off-reserve infectious pulmonary cases living off-reserve having a lower probability of their contacts being assessed than those living on-reserve was again observed (Table 4.46). The crude proportion of contacts to Northern First Nations cases on-reserve that were assessed was 92%, and for contacts to Northern First Nations cases off-reserve only 59%. After adjusting for age, sex, and treatment history of the case, the probability that a contact of an infectious pulmonary case living off-reserve will be assessed was 31% (95%CI: 5 – 49%) lower than a contact of an infectious pulmonary case living on-reserve. In other words, a contact of a Northern First Nations infectious pulmonary case of TB living off-reserve was only 69% as likely as a contact of one living on-reserve to be assessed for LTBI or active TB (Table 4.46). Treatment history, while significant in the unadjusted model, was not significant in the adjusted model.

Table 4.46. Clustered Robust Poisson Regression Analysis of Contact Assessment: Northern First Nations, 2008-2010 (infectious pulmonary cases, n = 97; contacts, n = 3,397)

Predictor	PR	95% Confidence Interval		Adjusted PR	95% Confidence Interval	
Residence						
Off-Reserve vs On-reserve	0.69*	0.51	0.95	0.69*	0.50	0.94
Sex						
Female vs. Male	1.08	0.95	1.22	1.11	0.99	1.26
Treatment History						
1st time vs. 2nd time Case	0.86***	0.80	0.94	0.91	0.80	1.03
Age Groups						
0-18 vs. 19-35	1.06	0.89	1.26	1.06	0.89	1.26
0-18 vs. 36-55	1.07	0.90	1.27	1.07	0.90	1.27
0-18 vs. 56+	1.13	0.86	1.49	1.13	0.86	1.49
19-35 vs. 36-55	1.01	0.86	1.17	1.01	0.86	1.17
19-35 vs. 56+	1.07	0.82	1.39	1.07	0.82	1.39
36-55 vs. 56+	1.06	0.82	1.38	1.12	0.84	1.49

Sig. Levels: *p<0.05, **p<0.01, ***p<0.001; NE: not estimable due to small cell sizes.

5. DISCUSSION & CONCLUSIONS

The goal of this study was to analyze TB prevention, diagnosis, and care in Manitoba through the lens of performance measurement. Study objectives included 1) assessing the ability to measure performance with Manitoba TB Registry data, 2) developing a method to best analyze performance using existing registry data, and 3) reporting the results. This final chapter is divided into two parts: Part I summarizes and discusses the results from this study in the context of other research and makes some comparisons with other jurisdictions, in order to answer the original research questions Part II discusses these results to form general conclusions and makes recommendations for TB prevention, diagnosis, and care in Manitoba based on these conclusions and then ideas for future research.

PART I: RESEARCH QUESTIONS AND HYPOTHESES ADDRESSED

A major research questions addressed was how well TB prevention, diagnosis, and care were performing in Manitoba, generally and for First Nations, hypothesizing that performance would be lower for First Nations in Manitoba compared to other groups. How best to measure this performance and how to do so with existing data was addressed and is discussed below.

(i) How is Manitoba TB prevention, diagnosis, and care performing?

To directly address this question two summary tables were produced to provide an overview of the crude results for each performance measure. Table 5.1 reports on performance generally, then by each ethnic-origin group. Table 5.2 examines performance by Regional Health Authorities. A third table (Table 5.3) was produced to show how Manitoba compared to the

United States using select TB performance objectives and targets for 2015, set by the US-CDC and that were measurable using the Manitoba TB Registry, inserting the most current figures available from the US. Following these tables is a discussion of the findings starting with Table 5.1.

Table 5.1. Summary of TB prevention, diagnosis, and care Performance Measures by ethnic-origin: Manitoba, 2008-2010

Performance Measure	Manitoba		Canadian-born non-First Nation	Foreign-born
Treatment Completion/cure (% of cases)	92.06 (394/428)		91.5 (43/47)	89.4 (109/122)
Early diagnosis (% of infectious pulmonary cases that are smear negative at Dx)	67.7 (180/266)		50.0 (12/24)	72.5 (50/69)
HIV test on file (% of cases)	58.41 (250/428)		57.5 (27/47)	55.7 (70/122)
Re-treatment (% of cases)	4.21 (18/428)		*	*
Case Mortality (% of cases that die before or during treatment)	4.91 (21/428)		*	6.56 (8/122)
Incident Paediatric Cases (% <=14 years of age)	10.28 (44/428)		*	*
Contacts Elicited				
Contacts Elicited (% of all cases that have >=1 contact)	74.3 (318/428)		74.5 (35/47)	68.0 (83/122)
Contacts elicited (% of infectious pulmonary cases)ǂ	97.0 (260/268)		95.8 (23/24)	95.8 (68/71)
Contacts Assessed				
Contact Assessment Completed (% of all contacts)	79.2 (5,895/7,442)		84.7 (442/522)	60.9 (590/969)
Contact Assessment (% of contacts to infectious pulmonary cases)	81.4 (5,493/6,750)		87.5 (404/462)	62.7 (530/846)

* Suppressed due to small cell size.
ǂ Specimen Type: Sputum or bronchial washings.

Table 5.2. Summary of TB prevention, diagnosis, and care Performance Measures in Selected Health Regions: Manitoba, 2008-2010

Performance Measure	Manitoba	Winnipeg RHA	Northern RHA	Other RHA[11]
Treatment Completion/cure (% of cases)	92.1 (394/428)	91.5 (204/223)	94.8 (145/153)	86.5 (45/52)
Early diagnosis (% of infectious pulmonary cases that are smear negative at Dx)	67.7 (180/266)	63.6 (84/132)	71.3 (72/101)	72.7 (24/33)
HIV test on file (% of cases)	58.4 (250/428)	56.1 (125/223)	62.1 (95/153)	57.7 (30/52)
Re-treatment (% of cases)	4.21 (18/428)	4.04 (9/223)	5.88 (9/153)	0.00 (0/52)
Case Mortality (% of cases that die before or during treatment)	4.91 (21/428)	6.73 (15/223)	*	*
Incident Paediatric Cases (% cases <=14 years of age)	10.28 (44/428)	4.04 (9/223)	15.69 (24/153)	21.25 (11/52)
Contacts Elicited				
Contacts Elicited (% of cases that have >=1 contact)	74.3 (318/428)	72.7 (162/223)	77.1 (118/153)	73.1 (38/52)
Contacts elicited (% of infectious pulmonary cases)‡	97.0 (260/268)	94.8 (127/134)	99.0 (100/101)	100.0 (33/33)
Contact Assessment				
Contact Assessment Completed (% of all contacts)	79.2 (5,895/7,442)	63.5 (1,525/2,400)	86.6 (3,366/3,889)	87.0 (1,004/1,153)
Contact Assessment (% of contacts to infectious pulmonary cases)	81.4 (5,493/6,750)	65.5 (1,388/2,118)	88.9 (3,163/3,560)	87.8 (942/1,072)

*Suppressed due to small cell size

‡ Specimen Type: Sputum or bronchial washings.

11 Other RHA: Interlake-Eastern RHA, Prairie Mountain RHA, and Southern RHA.

Table 5.3. US-CDC 2015 TB Performance Objectives and Targets: A Comparison of Manitoba and the United States on Selected Targets

Objective	Target	Manitoba 2008-2010	United States 2013
Case Rate	New active or reactivated cases per 100,000 population per year = 2.5	11.8	3.0
Completion of Treatment	For patients with newly diagnosed TB for whom 12 months or less of treatment is indicated, increase the proportion of patients who complete treatment within 12 months to 93.0%.	92.1%[12]	89.0%
Contact Investigation •Contact Elicitation	•Increase the proportion of TB patients with positive acid-fast bacillus (AFB) sputum-smear results who have contacts elicited to 100.0%.	98.85%	NA
•Evaluation	•Increase the proportion of contacts to sputum AFB smear-positive TB patients who are evaluated for infection and disease to 93.0%.	82.56%	NA
Known HIV Status	Increase the proportion of TB cases with positive or negative HIV test result reported to 88.7%.	58.4%	88.5%

NA: Not available.
Note: The Manitoba TB program met several of the US-CDC's 2015 performance targets, with the exception of case rate, HIV testing/reporting, and contact assessment which fell short.

Case Rates

The incidence rate of TB, which is the total number of new cases in a population over a period of time, is the ultimate indicator showing progress towards eliminating TB. Because only those cases that were reported to Manitoba Health and/or Health Canada were observable in a secondary data analysis study, the incidence rate is approximated by the *case rate*, which is the number of new or reactivated cases of TB reported for the population during the time period

12 This result was for all cases of TB, and does not consider time to completion of treatment/cure.

under consideration. The goal of elimination is less than one sputum-smear positive case per 1.000,000 population (Tadolini & Migliori, 2012).

Manitoba's crude annual case rate for the study period (2008 to 2010) was 11.8 cases per 100,000 person-years (Table 5.3). The crude rate calculated by this study was higher than the Canadian national case rate of 4.2 per 100,000 and was above Manitoba's case rate of 8.6 per 100,000, reported for 2007 (Public Health Agency of Canada, 2009a). In 2010, Manitoba's rate was 10.8 per 100,000 (when divided by the Manitoba population for that year, n = 1,220,900). In comparison to the United States, Manitoba's case rate for the period 2008-2010 was ~3.2 times higher than the USA's case rate of 3.6 cases per 100,000 reported for 2010 (Centers for Disease Control and Prevention, 2011). By 2013, the USA had reduced their TB rate to 3.0/100,000, and had a 2015 target of 2.5 cases per 100,000 (National Center for HIV/AIDS Viral Hepatitis STD and TB Prevention, 2015). Back in 1997, Canada set a target of reducing the incidence rate of new active and reactivated TB cases by 5% annually. Unfortunately, Canada failed to achieve this target. Instead, Canada achieved an average 3.3% annual reduction in the TB case rate between 1997 and 2007 (Public Health Agency of Canada, 2009a). Manitoba, however, has never set case rate targets. In 2004, Manitoba had the highest TB case rate for all provinces in Canada, at 12.3 cases per 100,000, but a lower case rate than the northern territories of Nunavut (108 per 100,000), the Northwest Territories (23.4 per 100,000), and the Yukon (12.9 per 100,000) (Ellis, Gallant, Scholten, & Dawson, 2007).

Using only these two points, 12.3 (2004) and 11.8 (2008-2010), then subtracting the latter from the former, we find a decline of 0.5 cases per 100,000 over a 5 year period. The use of this study's case rate (11.8 per 100,000) was justified based on a recent report from Manitoba Health

showing rates of 11.8, 12.8, and 10.7 per 100,000, in 2008, 2009, and 2010, respectively, which produce an average rate of 11.76: confirming the rate calculation in this study.

We calculated the annual rate of decline in the incidence rate by inputting this difference into the following formula. Annual rate of decline in incidence rate = $(IR_{t0} - IR_{t1}) = IR_{difference} / x = b_{YEAR}$, where: x = number of *years* in period, b_{YEAR} = annual rate of change, $IR_{difference}$ = the difference in the incidence rate between the first and second time periods' incidence rates, denoted by IR_{t0} and IR_{t1} respectively. Using this formula the rate of decline in the TB case rate in Manitoba from 2004 to 2008/10 was: (12.3 - 11.8) / (2009 - 2004) = (0.5 cases per 100,000) / (5-year period) = 0.1 cases per 100,000 over the five-year period of 2004 to 2008/10 (using 2009 as the mid-point for determining the number of years). This rate of decline shows that much less progress in reducing TB incidence rates was made in Manitoba than either Canada or the USA during the same time period.

Treatment Completion / Cure

On a positive note, treatment completion for this period appears high in Manitoba with a little more than nine out of ten cases (92.1%) completing treatment or being cured. The US national average was 89.0% of TB cases completing treatment in a 12 month period or less, thus showing comparatively that Manitoba is performing slightly better and is just short of the new 2015 performance objective of 93% (National Center for HIV/AIDS Viral Hepatitis STD and TB Prevention, 2015). While Manitoba appears favourable in this comparison, this study did not assess time to completion of treatment (e.g., a 12 month period or less reported in the US), thus limiting what we can construe as a success in this comparison. In Canada, the Public Health

Agency "pre-release" of the *Tuberculosis in Canada, 2013* reported that 1,409 of 1,699 TB cases (82.9%) had either completed treatment or were cured, showing that the overall Canadian rate had not changed since 2007 (82%) (Ellis et al., 2009; Public Health Agency of Canada, 2015). By 2012, Manitoba reported that 88.8% of cases completed treatment or were cured, and in 2013, that number jumped to 92.6% (Public Health Agency of Canada, 2014, 2015). The variations between these years may be due to relatively large case fluctuations from year to year.

In 2010, Dr. W. Libich claimed that the current Manitoba TB program is treating 100% of infectious TB cases (Libich, 2010). From the findings of this study, a high level of treatment completion and cure for all groups in Manitoba is apparent yet short of the 100% mark. It is also important to note that cases that died during or before treatment, or who transferred to a new jurisdiction, were also included in the failure group (i.e., did not complete treatment/were not cured). So, removing these cases from the denominator may result in an increased proportion completing treatment/being cured.

Early Detection of Pulmonary TB

The target for this performance measure was to "decrease the percentage of pulmonary TB cases that are smear positive to less than or equal to 33%" (Table 3.1). Of 268 infectious pulmonary TB cases in Manitoba, during the period of 2008 to 2010, 184 (68.7%) were smear-negative, and 84 (31.3%) were smear-positive, which means that this performance target has been met. In Canada, 56% of 1,002 infectious pulmonary cases were smear-positive in 2007, and in Manitoba 47% of culture-positive pulmonary were reported as smear-positive (Ellis et al., 2009). Manitoba was performing better than Canada on early detection at that time period as

well. However, this does not adjust for other factors that may affect this proportion.

While this measure was not part of the US-CDC TB Performance Objectives and Targets for 2015, the 2012 US proportion of smear-positive infectious pulmonary cases was 54.2% and in Canada it was 52.2% of infectious pulmonary cases being smear-positive, only slightly lower than the US proportion (World Health Organization, 2014). These figures suggest that there is some progress in Canada on early detection but a gap still remains between the target and actual performance.

Discrepancies between the Canadian and Manitoban figures may be due to differences in data sources and methods, rather than time period. If not, the finding in this study would constitute a substantial decrease in the proportion of cases that were smear-positive in Manitoba. Regardless, this study has shown that Manitoba met the target for early detection of infectious pulmonary TB. Manitoba also appears to be performing better than the US and Canada on this particular performance measure.

HIV Testing and Reporting

The target for HIV testing and reporting is 95%, and Manitoba only achieved 58.4% of TB cases with HIV testing and reporting. This rate fell well below the United States national average of 88.5% of TB cases having known HIV status in 2011 and the 2015 target of 88.7% (National Center for HIV/AIDS Viral Hepatitis STD and TB Prevention, 2015). That being said, Manitoba's proportion of cases with known HIV status has increased since 2004, when it was reported at 35.4%, which was much higher than the Canadian national proportion of TB cases with known HIV status recorded at 23.2% (Phypers, 2007). The way these rates were calculated

however is subject to some debate.

Canada-wide HIV testing and reporting for TB cases during the period of 1997 to 1998 was 21.6% of 3,767 TB cases reported to the Canadian Tuberculosis Reporting System (CTBRS). However, only 18.7% actually had the *result* of the HIV test reported to the CTBRS (Harris et al., 2006). In 2004, this number did not increase substantially with only 23% of 1,613 cases of TB having HIV test results on file (Skinner, 2010). A report from the former Canadian Tuberculosis Committee (CTC), however, showed a different trend in HIV testing of TB cases in Canada, with a graph displaying a steady increase in the proportion of TB cases with recorded HIV test results – from 5.7% in 1997 to 23.2% in 2004 (Phypers, 2007). While a performance baseline prior to this study is difficult to determine, complete HIV testing and reporting of TB cases in Manitoba was not achieved by Manitoba within the study period. This suggests that new initiatives are needed to enhance performance on this measure of TB prevention, diagnosis, and care. An opt-out policy on HIV testing of TB cases is something that that has been shown to enhance HIV testing rates (Long et al., 2014).

Alberta made significant progress through and opt-out policy of HIV testing TB cases. The Alberta government set a target of 80% of TB cases with reported HIV results for 2004. Between 2000 and 2002, 40-50% of Alberta TB cases had known HIV status, and in 2003 and 2004, the percentage dramatically increased to 80-90% (Sutherland et al., 2007). The reason for this rapid increase? In 2003, Alberta instituted an 'opt-out' HIV testing policy for TB cases, meaning that it is provided universally as part of the standard TB care package (Sturtevant et al, 2009). The successes of this policy in increasing HIV-TB case finding has been demonstrated recently (Long et al., 2014).

The opt-out policy means that HIV testing of patients "became routine unless the patient specifically chose not to be tested" (Sturtevant et al., 2009, p. 116). A two stage procedure is used in clinical settings to implement the 'opt-out' policy: "1) patients are briefly informed about the connection between HIV and TB and the clinical and prevention benefits of being tested and 2) the routine testing of TB patients for HIV unless their provider is actively informed of the patient's decision not to be tested." (Long et al., 2014, pp. 1-2).

Because opt-out is universal (i.e., it is done for everyone), getting tested is less stigmatizing and time consuming than a risk factor-based approach, which implies a decision-making algorithm based on a review of each patient for presence of risk factors for HIV (Sturtevant et a., 2009). Moreover, the risk factor approach may also miss many cases that do not fit existing risk profiles (Sturtevant et al., 2009). Risk factor-based testing tends to focus on intravenous drug users (IVDU) and men who have sex with men (MSM). It is predicted in the not too distant future that such an approach will miss the majority of HIV cases, when the risk has shifted to non-IVDU and heterosexual people of both sexes (Sturtevant et al., 2009). Sturtevant et al. (2009) argued that "poor compliance [with the recommendation of universal HIV testing of TB cases] and the separate of counselling and testing from routine medical care are now difficult to defend, as is ignorance of the relationship between HIV and TB" (p. 116). Manitoba might consider a similar 80% target for HIV testing of TB case and an opt-out policy of HIV testing TB cases as well in order to achieve the target, learning from Alberta's success in this area.

An important TB epidemiological consideration is the number of cases that test positive for HIV. In Manitoba, 4.8% of TB cases tested for HIV were HIV positive, during the period of

2008 to 2010. The estimated prevalence of HIV in Manitoba, in 2011, was 173.8 cases per 100,000 people, or 0.1738% of the population being people living with HIV (CATIE, 2015). The crude HIV prevalence ratio for TB cases to the general population of Manitoba using the Manitoba TB case prevalence of HIV and the Manitoba population HIV prevalence is 4.8/0.1738 = 27.62, meaning that HIV was approximately 27 times more prevalent amongst TB cases than the general population in Manitoba. During the period of 2000 to 2008, 5.1% of Manitoba First Nations TB cases living on reserve were HIV positive according to the Manitoba regional office of Health Canada (First Nations and Inuit Health Branch, 2011).

A question these findings raise is "what is the actual prevalence of HIV in Manitoba?". Two *different* figures, for instance, were provided by the Manitoba HIV Program, based on point-of-care testing for HIV at the Winnipeg Health Sciences Centre and the Nine Circles Community Health Centre, respectively 1.4% and 0.932% (Manitoba HIV Program, 2012). Using these figures we can calculate two new HIV prevalence ratios, the first being 3.43 (4.8/1.4) and the second 5.15 (4.8/0.932). These figures likely give a more accurate depiction of the true prevalence ratio between TB cases and the general population. Regardless of which is used, the message is clear: HIV is far more prevalent amongst TB cases than the general population, which must be considered in epidemiological analyses of TB, and screening of TB cases for HIV (and *vice versa*). HIV testing and reporting for TB cases is therefore an important performance measure for TB programs.

Paediatric Cases

During the study period (2008 to 2010), 10% (44 / 428) of TB cases were paediatric cases

(age <=14 years), which is very close to the finding of 10.2% of cases being aged <15 years from a study of 2007-2008 that included Manitoba (Long et al., 2013). Long et al. (2013) also found that Saskatchewan had the highest proportion of paediatric TB cases, at 30.3% of all TB cases being aged <15 years, compared to other prairie provinces. However, despite a lower *proportion* of cases being paediatric cases in Manitoba, when compared to Saskatchewan, Manitoba had a higher paediatric TB *rate* than any other province in Canada, and this rate was particularly high amongst First Nations (First Nations and Inuit Health Branch, 2011; Public Health Agency of Canada, 2015).

So how does Manitoba compare to other countries in terms of paediatric TB? In the European Union, during the same time period, the proportion of TB cases that were paediatric (under 14 years of age) was 4.3% (Whittaker et al., 2012). Although, there was no numerical performance target set for this measure at the outset of this study, Whittaker et al. (2012) suggested that a decline in the incidence and proportion of children under five "who are mostly infected in their households" would be a sign of decreased transmission within a population (p. 207).

In the US, the 2015 target for paediatric TB is an incidence rate below 0.4 cases per 100,000 children under 5 years of age (US Centers for Disease Control and Prevention, 2010). Based on the Public Health Agency of Canada reports of age-specific TB incidence rates for Manitoba (ages 1-4 years = 12.6 per 100,000 in 2013) and Health Canada's estimate of paediatric TB amongst First Nations on-reserve in Manitoba (0-4 years = 22.7 per 100,000 for 2000 to 2008), Manitoba is no where near reaching the US performance target for paediatric TB (First Nations and Inuit Health Branch, 2011; Public Health Agency of Canada, 2015). An updated US

performance target for TB incidence in children <5 years old is 0.3 cases per 100,000 (US Centers for Disease Control and Prevention, 2015a). While paediatric cases under five was not examine were not examined, the data suggested and was confirmed by other studies that Manitoba's proportion of TB cases 14 years of age or younger was high during this study period.

Consequently, there is a need for creative and swift action to address paediatric TB in Manitoba, especially amongst First Nations living on-reserve. Whenever a child is found to have active TB, the source case must be identified through reverse contact-tracing. Once the source case is identified, a rigorous contact investigation is needed to determine if any other children have possibly been exposed and to ensure preventive therapy for LTBI is available where exposure has been confirmed. Priorities for dealing with paediatric TB include the prevention of infection in children, through more vigorous and effective efforts to detect and treat TB in the adults in proximity to children (reverse contact tracing), and the secondary prevention of disease through more rapid and effective assessment and treatment of exposed children (Orr, 2015). The high rate of paediatric TB in Manitoba reflects unchecked and ongoing TB transmission, which in turn points to failures in current methods of prevention, detection, and care. In particular we need to prioritize contact tracing and therapy of LTBI and active TB in child contacts and adult contacts in close proximity to children.

Re-Treatment Cases

The performance target for this indicator was <3% of TB cases per year being re-treatment cases (Table 2.5). The re-treatment proportion for Manitoba was 4.21% (18/428), which falls short of the target. That being said, it is an improvement from previous figures

reported earlier. During the period of 1992 to 1997, the proportion of cases that were re-treatment in Manitoba was 9.2% (Al-Azem, 1999). In Canada, during the period of 2001 to 2006, 8% of the 9,976 TB cases reported nationally were re-treatment cases (Public Health Agency of Canada, 2009a). It appears that Manitoba is performing better on this measure than Canada as a whole. In British Columbia, however, the proportion of cases classified as recurrent between 1990-2006 was only 2.2% (95% CI: 1.8%, 2.7%), exceeding the national and Manitoba's average. The risk factors identified for recurrence in BC included being of "foreign-born" origin (Adjusted Hazard Ratio, AHR: 2.43, 95% CI: 1.21, 4.88), having prior incomplete TB treatment (AHR: 2.50, 95% CI: 1.27, 4.93), and non−adherence to treatment (AHR: 3.86, 95% CI: 1.90, 7.87) during the primary episode (Moniruzzaman et al., 2009). Amongst First Nations in British Columbia, (Canada), the relative contribution of re-activation of disease appears to have increased while the annual risk of infection has decreased. In other words, a focus on reactivation as a performance indicator is a critical public health activity in that province (Clark & Vynnycky, 2004), and may be relevant to Manitoba.

Contact Investigation

In this study, the original performance target required the creation of contact lists for all infectious cases created within seven days of diagnosis. However, the data requested and abstracted from the Manitoba TB Registry was not sufficient to permit that analysis. Other data may exist in the registry to allow measurement of that performance measure. Why is this measure important for future studies? The proportion of infectious cases that have contact lists created and that have contacts assessed, are at the heart of TB elimination strategies (Broekmans

et al., 2002). For instance, the original performance target called for the creation of contact lists for all infectious cases created within seven days of diagnosis (Table 2.5). In Saskatchewan, they have a performance target that contact investigations are conducted within 30 days for 95% of all active TB cases. The actual proportion achieved between 2001-2006, however, was only 16% between 2001-2006 (Tian et al., 2013). Determining the time of contact list creation and completion was not possible with the data provided for the present study. The results from this study demonstrate significant variation in the assessment of contacts and in the elicitation of contacts between groups. Much more variation was present in contact assessment than contact elicitation, which is discussed below.

Contact Elicitation and Assessment

The US-CDC goal was to have 100% of AFB smear-positive cases having contacts elicited. In Manitoba, a very high proportion (98.85%) of AFB smear-positive cases named contacts during the contact investigation process within this study period. Since it would be extremely rare for a person to have no close contacts whatsoever, the assumption is that there should always be contacts elicited from these cases. From this study, the proportion of culture-positive infectious pulmonary cases of TB with contacts elicited was 97%.

In terms of contact assessment, 79.21% of contacts listed in the Manitoba TB Registry's contact table during the study period were assessed for TB. Of these, 4.5% required “ongoing surveillance” (which could be assumed to mean LTBI positive or active TB, although the exact definition of this value was not known). A similar problem with vague definitions in TB patient registry data was noted by Hernández-Garduño et al. (2015) in their comparison of TB trends in

Mexico and the USA, regarding the term "contact evaluation", which did not specify the type of evlaution performed (e.g., TST, x-ray, etc) (p. 249). For contacts of highly infectious pulmonary (smear-positive) cases, a high rate of contact assessment was expected, as there would be a high probability of transmission from these cases to their family, friends, and community contacts. In Manitoba, the proportion of contacts of pulmonary smear-positive, culture-positive cases that were assessed for LTBI or active disease was 86.73%, which was higher than the overall proportion of contacts assessed.

(ii) Does performance vary by ethnic-origin, age, sex, and geography? If so, how?

Performance tends to vary *to some extent* across ethnic-origin, age, sex, and geography. In the present study, some performance measures varied significantly between ethnic-origin groups, geographic areas (RHAs and on/off-reserve residence), males and females, and by age, while others did not. Differences between some of these groups may be due to either different case-mix or actual differences in the effectiveness of TB services, which was not fully quantified in this study. The question of whether performance varied by ethnic-origin group, specifically whether there was poorer performance for First Nations patients, was a motivator for this research. This study showed that First Nations cases experienced similar and in some cases better treatment than the other two ethnic origin groups. Relatively similar performance on the majority of performance measures between ethnic-origin groups, which was a re-assuring finding.

That being said, wide variation was found between geographically diverse patient populations in the performance of TB prevention, diagnosis, and care outcomes. For instance,

Winnipeg was fairing relatively poorly compared to Northern Manitoba in terms of contact investigation. Manitoba First Nations living on-reserve had a much higher rate of contact assessment and HIV testing/reporting than First Nations people living off reserve. There was a far greater TB incidence rates for First Nations living on reserve than First Nations living off reserve. As well, we found a significantly higher proportion of paediatric TB cases on reserve, suggesting that there was a problem in controlling the spread of TB on-reserve. This finding is key, as it impacts the realization of performance targets generally like short-term infection control and long-term case rates.

Case Rates

TB incidence is dependant upon bacterial, environmental, and individual factors. Globally, age is a key factor in the incidence rate of TB, with far greater incidence amongst older people, with longer lifetime exposure risk and declining immunity. Manitoba TB cases follow the global pattern of higher TB incidence later in life. Males make up the majority of TB cases in Manitoba, as would be expected, given the national TB case proportion of 55% males between 2002-2012, which is consistent with the global sex-distribution of TB (WHO, 2009; Public Health Agency of Canada, 2015).

Research has shown that the TB case rate amongst First Nations (Manitoba or Canada), regardless of how it was calculated, was consistently higher than either Canadian-born non-First Nations or the foreign-born (Al-Azem, 1999; Blackwood et al., 2003; Epidemiology and Surveillance Unit, 2013; Olson, 1999; Public Health Agency of Canada, 2015; Sharma et al., 2003). In the present study, the TB case rate calculated for First Nations living on-reserve

(67.16 per 100,000) was higher than that of First Nations living off-reserve (45.75 per 100,000), with a crude $RR_{on/off\text{-}reserve}$ of 1.47, showing that the case rate on-reserve was 47% higher than the rate for First Nations off-reserve. This finding confirmed the Canadian national pattern whereby, for 2013, the crude case rate ratio (RR) of on-reserve was 28.8/100,000 versus the off-reserve 10.6/100,000, yielding an $RR_{on/off\text{-}reserve}$ of 2.72 (Public Health Agency of Canada, 2015).

A different on-reserve TB case rate for Manitoba First Nations (71.9/100,000) was found for the period of 2006 to 2008 by Health Canada (First Nations and Inuit Health Branch, 2011). The TB incidence rate estimates produced for on-reserve (83.3/100,000) and off-reserve (68.1/100,000) First Nations in Manitoba, during the period of 2007 to 2008, yields an incidence rate ratio (IRR) of 1.22, for all cases of TB. Culture-positive pulmonary TB was more pronounced on-reserve (77.6/100,000) than off-reserve (53.5/100,000) yielding an IRR of 1.45 or a greater risk of TB, particularly pulmonary TB, on-reserve than off-reserve for First Nations in Manitoba (Long et al., 2013).

Different methodologies and data sources likely led to these differences, which suggests that we currently are not able to estimate a correct incidence rate ratio. We can also speculate that what may drive these differences is the way case demographics were defined in terms of an often mobile population between on- and off reserve. A future challenge, therefore, is producing comparable figures, while improving how active TB and LTBI surveillance is conducted across political jurisdictions and geographies.

For instance, Manitoba case rates were higher on-and-off reserve than for other First Nations in Canada (First Nations and Inuit Health Branch, 2011; Public Health Agency of Canada, 2015). The association between household crowding, measured by persons-per-room,

community income levels, and isolation and TB notification rates in Canadian First Nations has already been established (Clark, Riben, & Nowgesic, 2002) and likely explains the persistence of elevated TB rates observed in this study. For First Nations people living on-reserve in Manitoba, particularly northern Manitoba, household crowding is a persistent problem (Alvarez, Orr, et al., 2014). If there is little movement to address the social determinants of TB, it is likely that Manitoba will continue to struggle in their efforts to eliminate TB. Using the case rate to monitor change is therefore key to tracking progress and should be given appropriate attention in relation to target-setting.

In Alaska, where TB rates were comparable to those of Manitoba, a reporting framework based on the US-CDC performance objectives and targets model, was adopted and contains specific case rate targets for 2015 (Section of Epidemiology, 2014). They were 1) U.S.-born persons who are not Alaska Native to less than 0.7 cases/100,000; 2) Alaska Native persons to less than 20 cases/100,000; 3) Foreign-born persons to less than 20 cases/100,000; 4) U.S.-born non-Hispanic blacks to less than 5.0 cases/100,000; and 5) Children younger than 5 years to less than 3.6 cases/100,000 population. In Table 5.4, Manitoba were compared to Alaska's targets for 2012 (for which data is available) to and found that Manitoba has met 2 out of 4 targets, while Alaska achieved 3 of 4 targets. Both, however, were far from meeting the indigenous (Alaska Native or First Nation) case-rate target. As well, Manitoba's childhood TB rate was substantially higher than that of Alaska, which reached their target on childhood TB rates. From this comparison, we see that paediatric TB is a problem in Manitoba, and the rate of TB amongst First Nations in Manitoba is higher than amongst Alaska Natives. These findings suggest that targeted interventions with these populations, particularly for paediatric TB amongst First

Nations, is a promising area for preventative action towards eliminating TB.

Table 5.4. Alaska's 2012 Case Rate Targets (per 100,000 pop.) Adapted to Manitoba

Population Group	Alaska's Performance Target for 2012	Alaska Case Rates (2012)	Manitoba Case Rates (2012)	Manitoba Case Rates (2013)	Did Manitoba Meet Target?
U.S.-born persons who are not Alaska Native (Canadian-born, non-Aboriginal)	1.5	0.4	0.8	1.4	Yes
Alaska Native persons (Manitoba First Nations)	25	43	66.0	85.3	No
Foreign-born persons	25	24	20.7	20.8	Yes
Children younger than 5 years of age (Manitoba children 1-4 years)	< 5	4	12	12.6	No

(Public Health Agency of Canada, 2014, 2015; Section of Epidemiology, 2014)

A case rate target system, such as that used by Alaska, and virtually all US States, enables tracking progress towards TB elimination for specific populations and could be used in Manitoba to focus attention on populations with distinct risk profiles. Alaska has set progressively lower case-rate targets, and Manitoba, along with other provinces, could do the same. A consideration is that year to year changes in case rates are common. There are long term factors embedded in the case rate, such as the prevalence of TB and LTBI, housing, nutritional, and other socio-economic factors, alcohol, smoking, and substance abuse behavioural factors; and the combined efforts of TB prevention, diagnosis, and care programs. Therefore, fluctuations in the case rate over a short period of time reflect more than the efforts of TB prevention, diagnosis, and care programs. Long-term population health trends and the social determinants of health cannot be ignored when examining case-rates and/or setting case rate

targets. Caution is warranted when interpreting case rates over short periods of time. However, when we examine rates over longer periods of time, important trends can be revealed.

The TB incidence rate for First Nations in Manitoba declined from an initially high point of 87.9 per 100,000 during the period of 1974-1994, to a low-point of 44.3 per 100,000 in 1992-1997, then rose to 65.3 per 100,000 in 2004-2008, and continued to rise, reaching 85.3 per 100,000 in 2013 (Table 5.5). A similar table created for the overall rate of TB in Manitoba suggests the same pattern over time: starting high, declining, and then increasing back to the original rate, although not as pronounced, given the lower rate of TB overall compared to the rate for First Nations alone (Table 5.6).

Table 5.5. TB Incidence Rate: Manitoba First Nations, 1975/1994-2013

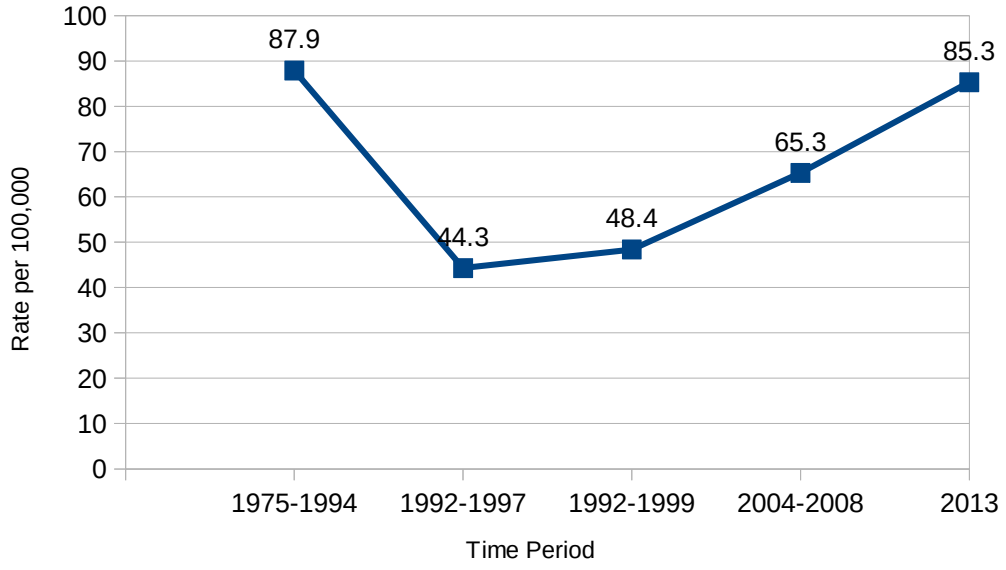
	1975-1994	**1992-1997**	**1992-1999**	**2004-2008**	**2013**
Manitoba First Nations TB Incidence Rate (per 100,00)	87.9	44.3	48.4	65.3	85.3
Source	(Olson, 1999)	(Al-Azem, 1999)	(Blackwood et al., 2003)	(Long et al., 2013)	(Public Health Agency of Canada, 2015)

Table 5.6. TB Incidence Rate: Manitoba, 1975/1994 – 2013

	1975-1994	**1992-1999**	**2004-2008**	**2012**	**2013**
Overall rate	13.7	9.2	9.7	10.9	13.4
Source	(Olson, 1999)	(Blackwood et al., 2003)	(Long et al., 2013)	(Epidemiology and Surveillance Unit, 2013)	(Public Health Agency of Canada, 2015)

Figure 5.1 is a plot of the TB rate for First Nations that shows a U-shaped trend in the incidence rate of TB amongst First Nations in Manitoba, which should cause concern for TB program managers and policy-makers in both the provincial and federal health systems. This type of "U-shaped curve of concern" in US TB rates in the 1980's prompted major re-investment in TB prevention, diagnosis, and care (Reichman, 1991, p. 741), which has since proven effective through sustained reductions in the incidence of TB within the US (Winston et al., 2010; Hernández-Garduño et al., 2015).

Figure 5.1. U-Shaped Curve of Concern in TB Incidence Rate: Manitoba First Nations, 1975-2013.



In addition to the incidence rates, another epidemiological consideration is overall distribution of TB cases by ethnic-origin. In Manitoba, the proportion that were Canadian-born non-First Nations TB cases has declined from 26.2% in the 1992-1998 period to 11.2% in the 2008-2010 period (present study) (Blackwood et al., 2003). This finding suggests that progress was made in reducing TB incidence in this population, or that there may be a cohort-effect.

Concurrently, the proportion of patients that were First Nations and foreign-born had increased. The shift in case distribution is something that must be taken into account when planning for performance improvements. A cultural and ethnic-origin-specific approach, regarding ethnic-origin of cases and their contacts as distinct population groups, as adopted in this study, is needed to reach these populations and work together towards TB elimination.

Manitoba has had consistently high case rates compared to other Canadian jurisdictions. Elevated rates over long-periods of time cannot be attributed to annual variability due to small numbers (Libich, 2010); and high rates over time suggests that TB is in an endemic state in Manitoba that requires enhanced interventions.

Treatment Completion / Cure

For treatment completion and cure, no significant differences were detected between ethnic-origin groups either in Manitoba or in Winnipeg specifically, which suggests health equity between ethnic-origin groups when it comes to initial treatment outcomes. This means that a First Nations case, a foreign-born case, and a Canadian-born non-First Nations case all have equal probability of completing treatment for TB and/or being cured, after adjusting for age, sex, and treatment history. In all analyses, however, younger age groups were more likely than older age groups to complete treatment or be cured. For the whole province or northern Manitoba, there was no significant difference between First Nations residing on-or-off reserve in the treatment completion/cure rate. On-reserve, 93.57% of First Nations TB cases completed treatment or were cured, as were an almost identical proportion of TB cases off reserve (93.59%). This finding is consistent with previous studies. Health Canada's First Nations and

Inuit Health Branch (2011), for instance, reported that during the period of 2000-2008, 92.3% of on-reserve Manitoba First Nations TB cases completed treatment without culture or had negative culture (i.e., were cured) at the end of treatment.

So what may account for the age difference in treatment completion/cure? A Spanish study of TB treatment outcomes found that for TB cases age 64 years and older they were significantly more likely to die during the course of treatment (Caylà et al., 2004). In a multivariate analysis to find predictors of death during treatment, statistically significant risk factors for death during treatment included: age >64 years, HIV+ status, being an alcoholic, and being hospitalized (Cayla et al., 2004). Non-significant factors in this multivariate analysis were: homelessness, drug addiction, and DOT (Cayla et al., 2004). However, when looking at the outcome of default, instead of death, the risk factors were different. Default, in Cayla et al.'s (2004) study, was defined as "a patient for whom it was known, through supervised treatment or periodic controls, that they had not received tuberculosis treatment for over 1 month, or who had not attended follow-up appointments prescribed by the physician in charge" (p. 459). Being drug-addicted, an immigrant, or between 18-64 years of age, all became independent risk factors in a multivariate analysis of treatment default.

The scope of this study and the small numbers, however, did not allow for the modelling of case fatality or for default individually. Nevertheless, these findings suggest that the pattern of non-completion of treatment for older age groups when compared to younger age groups follow this pattern. Other factors, such as drug addiction, homeless, and HIV status were not included in the present study, but could be included in future research on the subject of treatment completion.

Early Detection of Pulmonary TB

For Manitoba overall and for First Nations, age was a significant predictor of early detection of pulmonary TB regardless of ethnic-origin and sex, with 0-18 year old cases being more likely than older cases to be smear-negative (Parts I and III). This result, however, likely reflects physiologic differences between children and adults with respect to sputum production, rather than early detection (Whittaker et al., 2012). Age was not a factor in either Winnipeg or in northern Manitoba in the probability of infectious pulmonary cases being smear negative. Indeed there were no significant predictors of early detection for First Nations in northern Manitoba.

For First Nations cases living on-reserve, the proportion of cases that were infectious pulmonary cases was 53.8%. This finding was lower than the 61.4% considered pulmonary by Health Canada during the period of 2000 to 2008 amongst Manitoba First Nations TB cases living on-reserve (First Nations and Inuit Health Branch, 2011). The northern Manitoba RHA had the second highest proportion, 71.3%, of infectious pulmonary cases detected early (i.e., smear-negative at diagnosis). Winnipeg had the lowest proportion of infectious pulmonary cases detected early, with 63.6% being smear-negative at diagnosis. To determine if there was a significant difference between these two proportions (WRHA and NRHA), a post-hoc two-tailed z-test was conducted.[13] Results showed that the two proportions were not significantly different (difference in proportion = 0.077 [95%CI: -0.0449 to 0.1989], p = 0.217).

In Manitoba overall and Winnipeg specifically, Canadian-born non-First Nations were less likely, although not significantly, to be smear-negative at diagnosis than foreign-born or First Nations (p>0.05). Disaggregation of results by ethnic-origin allowed us to test whether early

13 http://epitools.ausvet.com.au/content.php?page=z-test-2

detection varied between groups. It appears that Canadian-born non-First Nations infectious pulmonary cases were less likely to be detected early; however, my study did not have enough power to detect a difference at the $\alpha = 0.05$ level. This apparent difference should, however, be studied in future research.

HIV Testing and Reporting

Because the data on HIV testing is limited to that reported to the Manitoba TB Registry, only a measure of the probability of HIV testing *and* reporting, combined, not testing alone, was analyzed. This means that this measure is only a proxy for testing. This issue is noted here but discussed in more detail later.

Significant geographic variation was noted in HIV testing and reporting amongst TB cases in Manitoba, by RHA and on-and-off reserve residence. There were no ethnic-origin between-group differences in the probability of HIV testing and reporting. The probability of HIV testing/reporting appeared to follow a dome-shaped pattern with age group in each part of the analysis. Those aged 0-18 years were the least likely to be tested, those 19 to 35 years were the most likely, and then the probability became less in each subsequent age group 36-55 and 56+ years. This age and HIV testing/reporting relationship was consistent throughout the analysis.

One question this pattern raises is what should HIV testing look like for the younger, middle-aged and older age groups given the distribution of reported HIV cases in Canada and the target of 95% testing, and goal of 100% testing. When considering that HIV information is vital to the treatment of TB, and that the risks of HIV testing were generally low, there is a strong

prima facie argument for an equal probability of testing for all age groups. However, given that the current system of testing TB cases is based on risk factors for HIV, which includes age group consideration, it was not expected that an equal probability of HIV testing would be found amongst the age groups.

Amongst First Nations TB cases in Manitoba, cases living off-reserve were 34% (95%CI: 15 – 49%) less likely than cases living on-reserve to have HIV testing/reporting, after adjusting for age, sex, and treatment history. However, cases living on-reserve in northern Manitoba were 58% (95%CI: 17 – 78%) more likely than cases living off-reserve in northern Manitoba to have a HIV test result recorded in the Manitoba TB Registry ($p<0.05$). This finding demonstrates a need for enhanced HIV testing and reporting off-reserve, both generally and in northern Manitoba. Manitoba First Nations TB cases living on-reserve had better than average performance on this measure. That being said, this research shows that the target of 95% of TB cases being tested for HIV, and having the result of this test reported provincially and federally was not achieved in either on- or off-reserve settings; that is, only 66.7% of on-reserve and 43.6% off-reserve First Nations TB cases have had an HIV test conducted and the results reported to the registry.

The proportion of northern Manitoba First Nations TB cases with HIV testing/reporting was somewhat higher at 63%, when compared to the Manitoba First Nations average (59.4%). However, these proportions were not significantly different at the $\alpha = 0.05$ level, according to a two-tailed Z-test for difference between proportions ($p = 0.46$)[14]. My findings differed from a Health Canada report for the period of 2000 to 2008 (First Nations and Inuit Health Branch, 2011). In that report, 32.7% of TB cases on reserve in Manitoba had a known HIV test result.

14 http://epitools.ausvet.com.au/content.php?page=z-test-2&p1=.594&p2=.631&n1=249&n2=149&Conf=0.05&tails=2&samples=2

Those cases were TB cases with an HIV result that was reported *federally* and entered into FNIH's database, which is separate from the Manitoba TB Registry. The discrepancy is likely due to differences in HIV test result reporting to the separate federal and provincial databases. However, the performance target of 95%, as supported by Fanning and Orr (2011), makes it clear that HIV test results should be reported to both provincial and federal databases to enable both provincial and national monitoring and research of TB and HIV.

For instance, if under-reporting constitutes part (but not all) of the proportion of TB cases without HIV tests and results reported, enhanced surveillance, such as integration of databases might increase the number of test results that are reported. However, to increase testing for HIV amongst TB cases, an 'opt-out' policy for HIV testing of TB cases could be a very effective option. HIV testing and reporting incentives for TB patients, providers, and programs might also be considered, although the design of incentives must be done with care (Conrad, 2009).

There are a number of key reasons that enhanced surveillance of TB/HIV co-infection is desirable at both national and provincial levels. They are: (1) to address inter-provincial travel by cases with HIV/TB co-infection, which introduces a public health risk to another province and that a national database would enable provincial public health officials to identify and ensure proper treatment for these cases; (2) for accurate national reporting on the incidence, prevalence, and treatment of HIV/TB co-infection in Canada; and (3) to facilitate national research on HIV/TB co-infection in the search for more effective prevention, control, and treatment interventions – from policy to pharmaceuticals (Sturtevant et al., 2009; Long et al., 2014).

The consideration of geographic distribution of TB/HIV co-infection is also a concern within provinces. In Winnipeg, the present study showed that the proportion of TB cases with

known HIV status (56%) was lower than the Northern RHA (62%) and all other RHA's (58%), although the difference between WRHA and Northern RHA was not significant (2-tailed z-test statistic = 1.2, $p = 0.249$).[15] Meanwhile, the Winnipeg Regional Health Authority maintains its own database of TB cases (the *Integrated Public Health Information System*) and using this system reports a much higher proportion (90.6%) of TB patients with HIV test results on file in Winnipeg in 2010 (Whitlock et al., 2012). Discrepancies between the figures in the Manitoba TB registry and IPHIS is a cause for concern and should be the subject of future research on performance of TB prevention and control in Manitoba.

Paediatric Cases

Significant variation was found between ethnic-origin groups, geography, and sex. Foreign-born cases, for instance, were only 21% (95%CI: 8% - 58%) as likely as First Nations cases to be paediatric cases. First Nations living in Manitoba had the highest proportion of paediatric TB cases (14.9%) in the study period, measured as cases aged <=14 years. This proportion has increased by 55% since 1992 to 1997, when the proportion of TB cases 0-14 years was 5.3% of foreign-born, 6.7% of Canadian-born non-First Nations, and 9.6% of First Nations (Al-Azem, 1999). This increase shows a persistent and growing problem of childhood TB amongst Manitoba First Nations, particularly on-reserve. First Nations TB cases living *off-reserve* were only 42% (95%CI: 4 – 82%) as likely than First Nations TB cases living *on-reserve* to be children with TB. Why is there a higher probability of TB cases being children on-reserve than off-reserve? The answer lies in the probability of being infected. Because there is a faster progression from infection to disease amongst children, the higher probability of cases on-

15 http://epitools.ausvet.com.au/content.php?page=z-test-2&p1=.5605&p2=.6209&n1=223&n2=153&Conf=0.05&tails=2&samples=2

reserve being children indicates a greater problem of transmission on-reserve compared to off-reserve. This research was, however, unable to answer this question.

Female First Nations TB cases were significantly more likely than male First Nations TB cases to be children, despite having an even age-sex distribution of cases 85% (95%CI: 2 – 235%). This relationship became more pronounced within Northern Manitoba where female First Nations TB cases were 132% (95%CI: 9 – 396%) more likely than male First Nations TB cases to be paediatric cases. Why the higher ratio of females to males amongst First Nations paediatric cases? Why is this imbalance more pronounced in northern Manitoba? A study of childhood TB cases aged 0-14 years in Himachal Pradesh, India, found a similarly high ratio of females (65%) to males (35%) was during the period of 2000 to 2010 and suggested reasons for the higher proportion among girls were neglect of female children, poorer nourishment, confinement to the home (indoor) for chores, etc. (Mazta, Kumar, & Kumar, n.d.). Another study conducted in Bangalore Mahanaga, India found a low ratio of males to females (0.6/1.0) amongst paediatric TB cases and reached similar conclusions about the causes of this imbalance (Sharada & Nelliyanil, 2009). The question this research raises is whether First Nations girls in Manitoba spend more time in their household environments than First Nations boys, where there is greater potential for TB transmission from an infectious household member. More importantly, what protective factors can be identified and implemented to reduce the burden of paediatric TB in Manitoba First Nations?

In terms of geography, the lowest proportion of paediatric TB cases was in Winnipeg ($\pi_{Winnipeg}$) at 4% of cases, which is followed by a dramatically higher proportion in the Northern RHA (π_{North}) at 16%, and then all other RHAs ($\pi_{Other\ RHAs}$) at 21%. The difference in the

proportion of TB cases that were paediatric between the Winnipeg RHA and Northern RHA [$\pi_{North} - \pi_{Winnipeg}$ = 0.1165 (95%CI: 0.0583 - 0.1747)] was statistically significant (using a post-hoc two-tailed z-test at $p<0.0001$).[16] The difference between the Northern RHA and other RHA's proportion of paediatric cases [$\pi_{Other\ RHAs} - \pi_{North}$ = 0.0556 (95%CI: -0.0629 - 0.1741)], was not statistically significant when compared with a two-tailed z-test for difference in proportions (p = 0.3576).[17] This means that the North and other RHA's face a comparable burden of paediatric TB as a proportion of cases, although not absolutely in terms of the number of incident paediatric cases, which is higher in the Northern RHA.

For the Winnipeg TB cohort, a small number of paediatric cases produced wide confidence intervals for comparisons between ethnic-origin groups, meaning that, the estimates were not stable. However, the point estimates suggest that First Nations have the highest probability of being paediatric cases in Winnipeg, but the results were not statistically significant. Having the highest PR estimate, however, suggests that vigilance is required to decrease the burden of paediatric TB amongst First Nations cases in Winnipeg as well on-reserve.

Re-Treatment Cases

As expected, age was significantly associated with re-treatment rates, with younger age groups being less likely than older age groups to be re-treatment cases Some variation between ethnic origin groups and geography were found. For instance, 6.4% of First Nations cases were re-treatment cases. Figures for both Canadian-born non-First Nations and the foreign-born were

16 http://epitools.ausvet.com.au/content.php?page=z-test-2&p1=.0404&p2=.1569&n1=223&n2=153&Conf=0.05&tails=2&samples=2
17 http://epitools.ausvet.com.au/content.php?page=z-test-2&p1=.2125&p2=.1569&n1=52&n2=153&Conf=0.05&tails=2&samples=2

too small to report (i.e., <5 cases). Despite the actual numbers or proportions of re-treatment to be reported for the various independent variables, due to small cell sizes (<=5 cases), the use of regression methods, i.e., robust Poisson regression, allowed us to report on probabilities between groups, without having to report the actual cell counts used in model estimation. This is an advantage of the modelling approach used in this study.

The analysis found that the overall re-treatment proportion was 4.21%, and that First Nations carried a significantly greater burden of re-treatment. Foreign-born and Canadian-born non-First Nations cases were 6% less likely to be re-treatment cases than First Nations. Manitoba First Nations TB cases aged 19-35 years were less likely to be re-treatment cases as opposed to First Nations TB cases aged 56+ years, who were more likely to become such cases, which mirrors the pattern observed for all Manitoba TB cases.

While it was not possible to investigate the cause for re-treatment cases, recent research on TB elimination for the Canadian First Nations population showed a steady decline in the annual rate of infection but an increasing contribution of *reactivation* to the incidence rate (Clark & Cameron, 2009; Clark & Vynnycky, 2004). This emerging pattern suggests that endogenous reactivation may become the primary source of recurrent TB cases as opposed to exogenous reinfection (Clark and Cameron, 2009; Clark & Vynnycky, 2004). This research tells that understanding and acting on both sources of re-treatment will be key to eliminating TB.

In Northern Manitoba, First Nations TB cases off reserve were significantly less likely than the on reserve counterparts to be re-treatment cases. So what is it about the reserve environment that may contribute to re-treatment? One possible explanation is that there is a higher probability of re-infection due to persistent poverty and household overcrowding, which

characterizes many northern communities, particularly remote communities and those with the highest TB burden (Clark, Riben, and Nowgesic, 2002).

In Winnipeg, a similar pattern with younger cases being less likely than older cases to be re-treatment cases due to the fact that younger cases have less risk time relapse or be retreated was observed. As well, Winnipeg First Nations cases were significantly more likely to be re-treatment cases than Winnipeg based foreign-born or Canadian-born non-First Nations ($p<0.05$). This magnitude of both the adjusted PRs comparing (a) First Nations to foreign-born and (b) First Nations to Canadian-born non-First Nations, exceeded the magnitude of the adjusted PRs for these differences in the Manitoba-wide analysis, suggesting that Winnipeg has a problem regarding relapse among First Nations residents. Unfortunately, figures for re-treatment were not available in the latest report from the WRHA (Whitlock et al., 2012).

Performance Measures for Contact Investigation

The proportion of contacts assessed that require additional follow-up (i.e., LTBI or active TB) demonstrates transmission of TB within Manitoba and the value of contact tracing in controlling the spread of infection. The very low proportion of contacts assessed that require follow-up in Winnipeg, resulting in suppression due to small numbers, indicates that contact tracing is likely an area of weakness in Winnipeg's TB prevention, diagnosis, and care system.

Contact Elicited

In this study, there was a low number of sputum AFB smear-positive cases that did not have contacts elicited. Consequently, the analysis could not compare sub-populations in terms of

the proportion of AFB smear-positive infectious pulmonary cases with and without contacts elicited. An adequate sample of sputum/bronchial washings culture-positive cases (i.e., pulmonary cases) was available to conduct a meaningful analysis of contact elicitation.

There were no significant differences in the probability of contacts being elicited from an infectious pulmonary cases between ethnic-origin groups in Manitoba. The null hypothesis was not rejected for this comparison of contact elicitation. In other words, cases of infectious pulmonary TB in Manitoba from different ethnic-origin groups have an equal probability of contacts being elicited. The performance measure for contact elicitation, however, included only culture-positive infectious pulmonary cases. Although an apparent difference between foreign-born and First Nations was found when using all cases ($PR_{FB/FN}$ = 0.85; 95%CI: 0.73 – 0.97), it was statistically non-significant (PR = 0.98; 95%CI: 0.92 – 1.04), when only infectious pulmonary cases were analyzed. This finding showed how a performance measure is sensitive to the case-mix between groups, specifically regarding infectiousness.

Within the Manitoba First Nations population overall there were some notable differences. First Nations infectious pulmonary cases off-reserve were 8% (95%CI: 1 – 14%) less likely than First Nations infectious pulmonary cases on-reserve to had contacts elicited. In Northern Manitoba, however, there was no difference between these groups, which raised the questions why were First Nations off-reserve less likely to have had contacts elicited and why is it that northern on and off reserve residents had an equal chance of having contacts elicited?

In Winnipeg, the lowest proportion of all cases and pulmonary cases to have contacts elicited, respectfully 72.6% and 94.8%. In other words, seven Winnipeg pulmonary cases did not have contacts elicited. One possible explanation for the lower number in the Manitoba TB

Registry is that, the WRHA maintains a separate database for contact investigations and was not fully reporting contacts elicited to the Manitoba TB Registry. Although there is no reason to believe that some contacts be reported to the Registry and others not. However, this is a potentiality that should be explored.

Contact Assessment

Contact assessment, as defined in this study, means that the contact had a record of contact assessment in the Manitoba TB Registry, (contact assessment completed), or a missing value for the contact assessment variable (contact assessment not completed). Contact assessment involves, generally, the medical assessment of a contact or the administration of a tuberculin skin test (TST). However, the exact kind of assessment was not stated in the Contact Table used in this study. This performance measure was applied to cases of infectious pulmonary TB, whose contacts should always be assessed for LTBI or active TB.

In Manitoba, the foreign-born had the lowest level of contact assessment overall (61%), which to some extent reflects the different TB profile of this population; that is, a lower frequency of pulmonary or respiratory TB than either First Nations or Canadian-born, non-First Nations (Cowie and Sharpe, 1998). When the analysis was confined to culture-positive pulmonary cases' contacts, the foreign-born still had a lower proportion of contacts assessed (64%) than First Nations (79%) or Canadian-born non-First Nations (80%).

When analysis was conducted on infectious pulmonary cases' contacts and then adjusted for age, sex, and treatment history, contact assessment levels for foreign-born cases in Manitoba were still significantly lower than First Nations cases (PR = 0.82, 95%CI: 0.69 – 0.99) and the

estimate for Canadian-born non-First Nations cases compared to foreign-born cases suggested a higher probability of the former's contacts being assessed than the latter but the difference was not statistically significant ($\alpha = 0.05$).

Contacts to First Nations cases living on reserve have a much higher likelihood of contact assessment than contacts to First Nations cases living off reserve. The difference is most likely due to the centralized nature of health-care in small communities such as reserves, and the relative ease of tracing contacts. The fact that there is only one health centre in many First Nations communities in Manitoba means that staff there generally know who residents are and where to find them, thus making it easier to follow-up with contacts named in contact investigation interview.

Interestingly, younger First Nations cases were more likely to have their contacts assessed than cases over the age of 56. Reasons for this age difference were unclear. Moreover, the finding that only 60% of contacts to First Nations TB cases off-reserve were assessed for LTBI or active TB (Table 4.26) raises the question on what is driving the contact investigation difference for First Nations living off-reserve, and in Winnipeg. The reasons behind these differences, and attempts to bring TB program factors that work on-reserve to off-reserve populations may provide better outcomes for Manitoba First Nations people living off-reserve.

In Northern Manitoba, no significant difference were observed between First Nations residing on reserve or off reserve pulmonary cases in terms of contacts being elicited. That being said, the rate at which these contacts were *assessed* for LTBI or active disease was strikingly higher on reserve than off reserve, following the general pattern observed for First Nations overall. Again this finding raises the question how are contact assessments being done for First

Nations living off reserve

Cook et al. (2013) first lamented the lack of published data on contact investigation (CI) outcomes in Aboriginal communities in Canada. They then hypothesized that there is a lower rate of CI in Aboriginal populations and queried whether supplementing traditional CI methods (CI interviews and follow-up with phone calls, letters, etc) with modern CI methods (genotyping, social network analysis, and geographic information systematic) may improve CI in these populations (Cook, Shah, & Gardy, 2012). This research discovered greater CI success for First Nations living on reserve than off reserve. Perhaps these methods suggested by Cook et al. (2013) should be considered, not simply in First Nations communities, but province-wide, where they could improve CI for all Manitobans.

These findings raised the question of why contact assessment is less likely in Winnipeg. Possible reasons include challenges of contact tracing in a large city, as opposed to smaller First Nations communities, where the majority of non-Winnipeg TB cases occur. In this study, no significant differences were found in the probability of contact assessment being completed between ethnic-origins, age groups, treatment history, and sex in Winnipeg. While estimates suggest that First Nation cases' contacts were the least likely to be assessed, the probability ratio (PR) was not significant. If not ethnic-origin, then could other factors be involved such as socio-economic status? This finding of no difference suggests an equitable chance of being assessed. The overall proportion of contacts assessed in Winnipeg, however, fell below 60% and equity at a low level is not a sign of good performance. Regardless of group, the data suggests that region-wide performance improvement appears needed for the Winnipeg region. Perhaps the CI methods suggested by Cook et al. (2013) as already noted should be considered.

Costs of Contact Investigation

Using 2004 Canadian dollar cost estimates of conducting contact investigations (CI) in Canada, we can find the approximate cost of contact investigation in Manitoba (Menzies, Lewis, Oxlade, & Lewis, 2008). At $300 per contact assessed Manitoba would have spent $1,768,500 medically evaluating contacts of TB cases in Manitoba during the study period.[18] Since contact tracing follows the Manitoba TB Protocol, we can assume that those contacts assessed fell within the criteria listed therein.

A recent outbreak in an Alaskan village was reported to cost over $1M USD between initial report of first case in March 2013 and the outbreak response concluding in February 2014. A total of 10,900 hours of work, uncovered 17 cases of active TB and 60 people with LTBI, further demonstrating the expense associated with contact investigation and the importance of early detection to prevent spread of TB (Frasene & Cooper, 2015).

In the present study, the number of contacts requiring follow-up discovered through CI (*n* = 266) demonstrated the value of CI, but also suggests that there is a major deficit in finding LTBI through this process, given that approximately one in five contacts listed in the contact table were not assessed. There is a strong likelihood that a number of active TB cases, and a greater number of people with LTBI, were undetected due to incomplete contact assessment. Improvements to CI processes, such as ensuring all contacts to infectious pulmonary cases are evaluated for TB, and based on that evaluation, offered (where appropriate) and complete LTBI treatment, are necessary for elimination of TB in Manitoba (Broekmans et al., 2002).

18 Menzies et al. (2008, p. 394). With 5,895 contacts assessed for TB * $300/contact = $1,768,500 CDN$

(iii) Which Performance Measures were Measurable with the Manitoba TB Registry and which were not?

For this study, a number of potential performance measures were identified for investigation with efforts made to stay true to the original performance objectives, even when the indicator definitions were somewhat or largely different. Initially it was projected that half of the original 18 indicators would be measurable. In this study, eight (8) performance measures were analyzed, covering 6 of the 10 categories, which was reasonably close to the initial estimate. A key determinant of measurement is whether the data accessed has the measure in question. For this study, the data fields requested allowed for the construction of the performance measures. Because it was not feasible to look at the data before receiving it, there was limited *a priori* knowledge of the data structure, as there was no registry field code manual to guide the request. Only an index of the fields of the TB Registry was available, without any information on data quality or the definition of the possible values of the fields in the Registry. There is a strong likelihood that the registry may have more fields to create the additional performance measures in our list. A lesson learned from this study is that data management systems, if not organized for transparency, make performance measurement difficult.

A major gap in this analysis was the lack of contact treatment data, which would (or at least should) be able to answer questions such as: what is the proportion of contacts that are diagnosed as LTBI and active disease, separately? What proportion of latently-infected contacts are offered preventive treatment? What proportion of LTBI cases accepting treatment complete the treatment? These and other related questions are critical to TB elimination in low-

incidence countries and if answered would provide a more complete picture of the performance of TB prevention, diagnosis, and care within Manitoba. They should be the subject of future research.

PART II: CONCLUSIONS AND RECOMMENDATIONS

The final part of this study considers the significance of the study first, followed by a discussion of what the results suggest about TB program management in Manitoba. Policy and program recommendations for TB prevention, diagnosis, and care in Manitoba are made based on the findings, while addressing the strengths and limitations of the study. Finally, ideas for future research on TB in Manitoba are presented along with the overall conclusions from this study.

Significance of Study

This study provided the first look at the Manitoba TB program through a performance measurement lens. A contribution from this research was the development of a method to analyze performance using an existing TB Registry. The analytical approach was trialed and can be revised and expanded in future studies. The log-binomial and robust Poisson statistical methods employed illustrate methods for quantifying the probability (rather than the odds) of TB performance standards being met for various sub-populations. The analysis and results were divided into parts for ease of use by health-care agencies and the populations they serve. Eight performance measures were investigated and future studies can assess the other measures recommended to gauge performance. As well, the study provided insight into the value and

importance of collecting performance measures, consolidating them for ease of use, making the data accessible, through easily interpreted probability-based statements and to trial novel approaches for TB prevention and control.

What the findings suggest about past TB prevention, diagnosis, and care program management in Canada and in Manitoba

According to Lonnroth (2015), Canada has made below-average progress towards eliminating TB when compared to 32 low-incidence countries worldwide for the period of 2000 to 2012. Canada experienced an average annual percent change (APC) in TB incidence rate of -2.2%, compared to an unweighted average APC of -3.0% for all 32 low-incidence countries, and APC of -5% for the United States (Lonnroth et al., 2015). In a survey conducted in 2014 of national TB programs, Canada did not have a national TB program, a specific TB budget, an individual case-based electronic database, or special incentives/enablers for TB patients (Lonnroth et al., 2015). Canada also was not able to report on the number of cases discovered through contact investigation or by ethnic minority or indigenous population screening, HIV/AIDS case screening, prison screening, or screening of healthcare workers (Lonnroth et al., 2015). Moreover, no national policy exists in Canada for TB screening of (i) HIV/AIDS cases, (ii) health-care workers, or (iii) ethnic-minorities/indigenous populations (Lonnroth et al., 2015), although they are all recommended in the Canadian Tuberculosis Standards (Alvarez, Archibald, et al., 2014).

The extent to which these issues translate to Manitoba is unclear. While efforts are being made nationally via the Public Health Agency of Canada to coordinate communicable disease reporting by the provinces and territories, leadership is still required by our provinces and

territories, and the health authorities within, to develop and collaborate through a framework to eliminate TB. As this study demonstrated, the performance elements of a framework can be evaluated using a performance measurement approach. The next step for our public health agencies is to develop a coherent TB strategy that includes performance measurement, and that this strategy operate across jurisdictions - federal, provincial, First Nations, and locally at the regional health authority level.

As of late, Health Canada's First Nations and Inuit Health Branch has produced a strategy to combat TB amongst First Nations on-reserve and Inuit communities in Canada, and this strategy focuses on partnerships with provincial programs, as well as First Nations having a partnership role in the design and delivery of programs for First Nation communities (Rees, 2012). However, the provincial program is truly the backbone of TB prevention, diagnosis, and care in Manitoba, requiring to a large extent, a provincial strategy for eliminating TB. Combined efforts for TB program planning in Manitoba have been described in a matrix of roles and responsibilities for TB in Manitoba (Manitoba Health - Public Health Division, 2014).[19] However, under this matrix, First Nations do not have either specific roles or responsibilities for TB programming in Manitoba. Moreover, a matrix of responsibilities is not a strategy. Consequently, First Nations-specific roles, responsibilities, and strategic support is required to make progress against TB in Manitoba.

First Nation authorities, particularly those residing in the north, face several challenges to TB prevention, diagnosis, and care. They also have unique strengths to draw upon to realize an operational strategy to eliminate TB. Challenges include over-crowded and poorly ventilated housing, isolation, and limited access to physician, nursing, and pharmacy services. In the north,

19 https://www.gov.mb.ca/health/publichealth/cdc/protocol/tb_rolesmatrix.pdf

the centralized nature of healthcare, with generally only one health centre, is an asset, and when supported further can increase performance. Local health centres have the ability to track cases and contacts in the community due to small populations in a concentrated geography, which increases the opportunities for public health programs to engage patients, although with limited resources. Off reserve, a regional healthcare system serving a large dispersed population like Winnipeg makes contact investigations and other public health interventions more complex, increasing the likelihood of poor performance.

To increase continuity of TB care province-wide, strong linkages between communities and urban centres like Winnipeg should be built into the design of TB programs, specifically those that target First Nations patients, their families, and social networks. A TB program, or program component, that is province-wide, but First Nations-specific, is an option that deserves consideration. Involving First Nations health leadership and management in the design and delivery of TB services could offer First Nations a real role in the fight against TB within their communities: both urban and rural. First Nation organizations have the necessary community involvement to link the two worlds, enabling effective follow-up and community action to prevent, diagnose, and care for TB across large geographic regions through preexisting and culturally relevant structures. Such an approach would also recognize First Nations rights to self-governance and self-determination in the field of health, which could contribute positively to other First Nation-led initiatives outside, but related to, the realm of TB prevention, diagnosis, and care. A synergistic relationship exists between the number of initiatives and the impact of those initiatives, as the overall capacity to address health issues expands and a First Nations health system is developed over time.

This study showed that despite high incidence rates of TB for First Nations, particularly on-reserve, the performance of the system was similar or even better, when compared to off-reserve cases. Theoretically, greater volume if addressed appropriately could lead to better outcomes on-reserve, whereby practice makes perfect. Although perfecting the practice of TB care is not the goal of TB programs, improvements in TB care performance are needed to make sustained reductions in incidence and prevalence of TB. Bringing strong performance factors from on-reserve settings to off-reserves settings, where feasible, would therefore make sense. Perfecting TB treatment, however, is only one goal. Equally if not more important is reducing the incidence and prevalence of TB, with good treatment as a component of a holistic strategy to eliminate TB that includes action on the social determinants of health.

Moving from TB Control to TB Elimination in Manitoba

At the Global STOP-TB Indigenous Experts Meeting held in Toronto (Mcdonald, 2008), 130 indigenous health experts from 50 countries discussed global action towards indigenous TB prevention and control. An important observation made was local ideas can lead to local solutions, which can be a guiding principle for any for any TB program. One example of a locally driven solution was an approach taken in the Northwest Territories (NWT) that has relevance to provincial indigenous populations (Mcdonald, 2008, pp 16-17):

> "In 1998 TB programming became the responsibility of the territorial government. An external review of the NWT TB control activities was conducted in the fall of 2000 and 26 recommendations were made to improve the NWT program. The goal of the program was to reduce the incidence rate of active TB in NWT to less than 5/100,000 per year. Reporting

> is centralized and TB registry uses a database tool called iPHIS. There are annual progress reports and TB summaries reported in EpiNorth. Two areas of focus are key – increased active case findings and adding emphasis on the identification and treatment of latent infection. The key messages are, although TB rates are decreasing, there is a need to keep resources dedicated to TB control because "one case can become an outbreak." There is a need to develop and keep TB/public health expertise in the NWT and to enhance public health capacity at the health authority level...
>
> To address the problem community interventions were undertaken. They consisted of an intervention plan that was coordinated with Chief and Council, training of CHR's [community health representative] to deliver TB programs, regular physician visits, public education on TB (using plain language) and temporary community bans of alcohol and alcohol based solvents (one month to one year) including notification of surrounding communities and airlines of temporary bans."

A community and household focus, which is integral to successfully eliminating TB, necessitates First Nations becoming a leading element in TB prevention, diagnosis, and care in Manitoba. The dual personal and public nature of TB care, involving daily DOT, and requiring participation from household members and other close contacts, friends and family, in the investigation, diagnosis, and treatment processes, mean that communities with high incidence of TB must be involved in the program, including its design, delivery, and evaluation. Strong community ties and First Nations leadership in programming can increase the likelihood of better outcomes, resulting in interventions locally adapted and administered. Supporting a variety of program improvement models would enable a better understanding of successful program attributes with the ability to experiment with innovative approaches. Being flexible and allowing

for diverse approaches is ideal since local solutions work best and can be implemented promptly, thereby leading to social mobilization and political commitment (Mcdonald, 2008). With close to two-thirds of TB cases in Manitoba being First Nations people, the program stakeholders at the community level are overwhelmingly First Nations, thus making a good case for program administration to rest with First Nations.

Integrating public health programs while maintaining central control over day-to-day operations of each program, by employing a syndemic model and incorporating a performance measurement and management approach has led to success in New York (Drobnik et al., 2014; New York City Department of Health and Mental Hygiene, 2015; Silin, Laraque, Munsiff, Crossa, & Harris, 2010). A syndemic model considers multiple overlapping epidemics that contribute to each other in a synergistic manner. An integrated approach, based on syndemic modelling, as illustrated in New York could be adapted to Manitoba or other provinces.

Another possible approach is for Health Canada FNIH to contract TB services to a First Nations-controlled organization that can serve First Nations populations in Manitoba specifically. The organization could be an existing one or one that is created solely for TB prevention, diagnosis, and care. An important lesson learned from other regionally specific Health Canada program devolved models, such as the diabetes and maternal-child health, is that while these programs appear to have yielded successful outcomes in the piloted communities, these programs have not been scaled up to reach all First Nations communities, on or off reserve. To serve all First Nations communities, on-and off-reserve, a full commitment is required. Project-based funding is not a sustainable solution for long-standing public health problems, such as TB.

Another consideration is that First Nations governance over programs applies the

principles of self-determination and self-governance proclaimed in the UN Declaration on the Rights of Indigenous Peoples. In British Columbia, the First Nations Health Authority is directly involved in their TB strategy, but is not yet in control of the program, and information specific to the progress is not yet available. For Manitoba to lead TB elimination for First Nations, creating a dedicated First Nations public health organization and integration with other public health programs on- and off-reserve using a syndemic lens may be the way of the future.

Either way, new investments towards TB elimination are needed in Manitoba that target high incidence groups and communities, while promoting high standards of care for all cases and contacts. New organizational structures that reflect both the nature of the disease, a syndemic model, and First Nations as primary stakeholders could enable a process of performance improvement. The following is a number of recommendations to consider TB elimination in Manitoba.

Recommendations for TB Prevention, Diagnosis, and Care in Manitoba

1. Create a Manitoba-wide TB elimination strategy, that is based on ethnic-origin, geographic, and cultural distinctions, has performance measurement embedded within it, and creates a strong partnership approach through organizational development.
2. Full participation of First Nations in programs for TB prevention, diagnosis, and care, including all stages from design to implementation to evaluation. This could be achieved in a number of ways that warrant consultation with First Nations communities and organizations in Manitoba. New models of First Nations health care have emerged in Manitoba, such as the Diabetes Integration Project. These models work based on

accountability to their constituent communities, providing a solid foundation for actions that serve their membership and develop partnerships between communities. Similar strides could be made in TB prevention, diagnosis, and care and should capitalize on successful and proposed First Nations initiatives. Provincial and federal funding to support and sustain such a shift is a critical requirement to ensure success.

    - There are First Nations organizations in Manitoba closely linked with First Nations people living on- and off-reserve, operating locally, regionally, and province-wide, that could be key partners in improving TB prevention, diagnosis, and care. These organizations could have a variety of roles and responsibilities that should be included in a provincial TB elimination strategy.

3. Engage all groups experiencing elevated TB rates and establish performance targets for community engagement, as this has proven to be effective in improving other areas of performance by tailoring programs to the needs of the populations served (Getahun & Joseph, 2012).
4. Specific case rate targets should be set at provincial, regional, and community levels, to measure progress towards eliminating TB in Manitoba. Communities with high incidence and prevalence of TB can be identified and interventions designed to improve or expand TB services, and the effectiveness of these interventions can be assessed through changes in the case rate annually.
5. Establish an 'opt-out' policy regarding HIV testing of TB cases, that all TB care providers offer, and document the offering of, HIV testing for each case of TB (Long et al., 2014). HIV testing is initiated by provider as part of routine TB care, unless patients actively

notifies the provider that they do not want to be tested, and refusal of this test by the patient is recorded, along with the reason for refusal where applicable. Additionally, HIV testing of contacts to infectious TB cases may be a reasonable extension of this program, because HIV is key factor for progression from infection to disease (Skinner, 2010).

6. Improve contact tracing and conduct a performance analysis of LTBI treatment data to fully understand contact tracing within Manitoba, including the identification, assessment, diagnosis, and care of contacts to infectious pulmonary cases of TB. This is a vital component of any TB elimination strategy.
    - Where performance on contact tracing appears to be low, (in Winnipeg, for foreign-born people, First Nations off-reserve), as found in the analysis of contact assessment data, develop solutions in partnership with the organizations representing these groups.
    - Adopting state-of-the-art contact investigation (CI) methods (Social Network Analysis, genotyping, and GIS) should be made part of routine and outbreak CI to increase understanding of TB transmission and to target interventions.
        - TB outbreaks amongst First Nations peoples in Manitoba routinely cross geopolitical boundaries: a fact that must be taken into account by TB service providers, public health officials, and policy-makers (Al-Azem, 2006).
7. Address high levels of paediatric TB amongst Manitoba First Nations, particularly on-reserve, in northern Manitoba, and for female children. A strategy against paediatric TB in Manitoba could include prioritizing the earlier detection of adult cases in proximity to children, reverse contact tracing to find infectious adult cases, improved infection control

procedures on-reserves, and the improved diagnosis and treatment of LTBI in children, particularly in northern First Nations. A longer time-period analysis of all paediatric cases in Manitoba, including their source cases' demographics and relationship to the paediatric case, and possibly a case-control design to find risk factors for paediatric TB, with a focus on designing future prevention efforts, would facilitate the design of a sub-strategy against paediatric TB.

8. Closer monitoring of older TB patients s recommended to enhance treatment completion rates and to reduce death rates.
9. As for social and environmental determinants, action is required on both the biomedical and social determinants of health. Improved housing is one of many areas of need amongst First Nations in Manitoba. There is a socioeconomic dimension to TB that should be studied and acted upon in Manitoba, including the potential for lost employment, stigma, and other consequences of a TB diagnosis. A holistic strategy against TB must incorporate these socio-economic impacts of TB on patients, their families and their communities. The biosocial sustainable development model for TB elimination developed by Ortblad et al. (2015) might be a useful approach for Manitoba.

Strengths and Limitations

This study's strengths and limitations are related to the study design and the Manitoba TB Registry itself. A retrospective database review study involves a reliance on the information collected during the process of providing TB services and then only that information that is reported to Manitoba Health's TB Registry. Researchers accessing registry data are constrained

by the way the data is collected and managed which may impede ways to verify the information collected and entered. While reporting is mandatory by law, it was unclear how reporting was managed during the study period.

Accessing and relying on administrative data for research therefore comes with disadvantages. In this study, data fields were requested but there was only limited information describing the registry fields. Another limitation is that a retrospective analysis can only examine past performance in the time period examined (not historical) and results may not reflect current practices The study could only estimate associations between variables and not the causes of these associations. Without paper copies of all TB case and contact files, it was not possible to verify the accuracy of the data. We were not able to check if there were any differences in the way various health care providers recorded data on the paper forms, or the accuracy of the data entered into the TB Registry.

Another limitation was the short study time period that limited the number of TB cases and contacts. Rather than a snapshot of performance, a longer time period would have allowed for an assessment of performance over time, i.e. performance trends. A key shortcoming was not investigating all combinations of adjustable factors. However, the consistency of the analysis with research questions is a strength created at the expense of more rigorous examination of the data. While this study revealed differences in performance amongst groups, the actual reasons for these differences were not explored and cannot be inferred from this study. SES as a potential predictor was not available in the registry so it was not possible to investigate its role in performance measurement. A separate foreign-born part of the analysis was contemplated

although the diverse nature of this population group as well as the inclusion of foreign-born as a key predictor variable in Manitoba's and Winnipeg's respective parts made this impractical.

There is some debate on the reliability or accuracy of the on and off reserve variable values. A cause of concern is the higher mobility amongst First Nations than other Manitobans. In the present study, with the given data, there was no way to validate the variable residing on reserve (Yes/No). This does not mean that our results of better TB program performance on-reserve than off-reserve, despite higher overall incidence of TB, are unreliable. To the contrary, the data from a population-wide registry of TB cases and the statistical analysis performed incorporated a certain amount of random variation into the modelling. Consequently, a degree of confidence that the results produced (e.g., where statistically significant) would have accounted for such possible inaccuracies. A far greater limitation is the minimal amount of information available about cases and the retrospective design of this study had precluded a complete case-mix adjustment between geographic and ethnic-origin groups. Unfortunately, the treatment of LTBI, which is a vital piece of the elimination puzzle, was not part of this analysis either. The lack of a TB Registry data dictionary was another limitation as well (Yu, 2015). Better documentation of contact investigation variables and the values assigned to these variables in the TB registry databases would have improved reporting on contact investigation outcomes and created the opportunity for more a more intricate research design.

Future research on TB program performance in Manitoba

Extending from this study, future research could explore the reasons for strong and weak performance in TB services and outcomes. Specifically, the reasons for poor performance in the

following areas should be investigated: contact assessment, HIV testing/reporting, case-rates, and paediatric TB. Studies in strong performance are also warranted in the areas of treatment completion/cure and contact elicitation. Research investigating the reasons for varying levels of performance, moving into the realm of intervention research, would be an important next step. For example, research that is "...focused on interventions to overcome personal and family barriers to TB adherence, to increase self-efficacy and sense of coherence and to mobilize family and community support for TB patients" (Orr, 2011b, p. 138).

As well, there is a need to examine the treatment of contacts with LTBI, using a longer time period and by incorporating information from other sources (e.g., HIV/AIDS Registry). A longitudinal analysis of performance could identify trends in both epidemiology and control and how they influence each other. Future research into TB program performance should also consider data collected via the Winnipeg Regional Health Authority (WRHA)'s Integrated Public Health Information System (IPHIS). As well, an ongoing cohort study into program performance would allow continual monitoring of TB services as patients are provided care. Patient perspectives of TB service should also be included to inform policy, planning, and programming. Equally as important, ongoing analysis of performance is needed to determine trends and to provide enhanced public reporting of TB care. Operations research is needed to understand medication dosing, delivery, adherence, and outcomes (Fanning, 2006).

In addition, research is required to identify the financial burden of TB care on the patients, where for example, leaving a remote First Nation to reside in Winnipeg for prolonged treatment will negatively affect a patient and family's ability to earn income. Costs to patient can be catastrophic, when considering that any accompanying family members may end up having to

pay much of their own costs. Prolonged inability to work or permanent disability from TB is possible, and there is no research about these externalized costs of TB care. As a result, financial burdens are greatest for those already poor, and in some cases, TB can be a cause of that impoverishment or its continuation. A recent review study of costs to TB patients and their families found an unweighted average total cost of $847 international dollars, which are US dollars converted to international contexts (Tanimura, Jaramillo, Weil, Raviglione, & Lonnroth, 2014). Financial burdens are greatest on those already poor, and in some cases, TB can be a cause of impoverishment.

Research linking the Manitoba TB Registry to other patient databases is therefore needed, for example. One linkage would be to sexually transmitted infections (STI) and HIV data held by Manitoba Health for surveillance. Data linkage studies would allow the study of STI, HIV, and TB syndemics, as demonstrated by the New York infectious disease syndemic study that demonstrated a need for sustained surveillance and action on TB, HIV, syphilis, chlamydia, and viral hepatitis (Drobnik et al., 2014). Research linking the Manitoba TB Registry to other patient databases are needed, for example STI and HIV, which would allow the study of STI, HIV, and TB syndemics.

Also needed are action research studies using novel approaches to both intervene in the epidemic and also produce scientific knowledge in the process (e.g., such as the TAIMA-TB model implemented in Iqaluit). This type of research could identify people at risk of TB and implement targeted screening to find people with LTBI and offer treatment to them, and also active TB cases that were undiscovered by regular programming (Alvarez et al., 2015). Also studies need to look the disease burden with those already identified with having TB. A recent

study conducted by the US Indian Health Services (IHS) sampled 596 reported TB cases from 24 IHS Service Units (SU) and examined their medical charts to verify TB cases reported to the state. They found that 31.6% of the 503 who were tested for diabetes, had diabetes (Podewils et al., 2014). This rate was almost twice the prevalence of diabetes (16.1%) amongst the American Indian/Alaska Native (AI/AN) population generally (US-IHS, 2012).

In short, future studies are needed, linking administrative, clinical, surveillance and survey data, to gain a greater understanding of cases, including their co-morbidities, health behaviours, socio-economic status, and the health care infrastructure and services they access, as well as opportunities for intervention. Indeed, complex patients and resource-limited settings can both bias a performance analysis if not adjusted for using data on individual and community level factors and multilevel statistical modelling (Terris & Aron, 2010). Future studies of TB program performance should consider individual, compositional and contextual factors, and by way of multilevel modelling we would have a better understanding of what predicts performance.

Concluding Remarks

This study sought to evaluate Manitoba TB prevention, diagnosis, and care using a performance measurement approach currently being employed in the United States and considered in other Canadian provinces. A group of performance measurements, derived from the US framework and adapted to the Registry data, were analyzed using log-binomial, robust Poisson regression, and GEE statistical analysis techniques. Applying a performance measurement approach to provinces or regions like Manitoba with high TB incidence and

prevalence rates has merit. The results of this study showed the viability of such an approach and that performance measurement can act as a catalyst for improvements to TB prevention, diagnosis, and care in Manitoba, through both creative and proven intervention models.

In Manitoba, because First Nations, particularly those residing in the north, are the most affected by TB, the study suggests that performance measures analysis is a tool that may improve programs to serve this demographic, particularly if the analysis is done in a way that is transparent and accessible to First Nations health authorities.

According to Tapiero and Lamarre (2003), eliminating TB in a low-incidence country requires maximizing the clinical and public health management of TB cases and contacts, while concurrently acting on the social determinants of TB and networking with high-incidence countries to reduce the incidence and prevalence of TB globally.

In the absence of a national TB program in Canada (Lonnroth et al., 2015) provincial and First Nation leadership is necessary to drive improvement to TB programming in Manitoba. Performance improvements and the setting of objectives and targets could be taken on provincially and via First Nations, with a process for collaboration, funding, and community involvement. Consideration of a First Nations-led or "co-led" model is in order, given that two thirds of TB cases in Manitoba are First Nations people. While centralized control is important for accountability, strong and sustained community engagement, not simply consultation, are required for TB elimination. Equally important is the need to address the social determinants of health and TB in Manitoba, particularly in the First Nations population, followed by real action as part of an overall TB elimination strategy. A bio-social sustainable development approach (Ortblad et al., 2016), employing performance measurement, could guide this strategy.

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APPENDICES

Appendix 1 - Approval from University of Manitoba Health Research Ethics Board (HREB)

UNIVERSITY OF MANITOBA | BANNATYNE CAMPUS
Research Ethics Board

P126-770 Bannatyne Avenue
Winnipeg, Manitoba
Canada R3E 0W3
Telephone 204-789-3255
Fax 204-789-3414

HEALTH RESEARCH ETHICS BOARD (HREB)
CERTIFICATE OF ANNUAL APPROVAL

PRINCIPAL INVESTIGATOR:	INSTITUTION/DEPARTMENT:	ETHICS #:
Christopher A. Basham	U of M/Community Health Sciences	HS16469 (H2013:213)
HREB MEETING DATE (If applicable):	**APPROVAL DATE:** May 7, 2015	**EXPIRY DATE:** **May 22, 2016**
STUDENT PRINCIPAL INVESTIGATOR SUPERVISOR (If applicable): Dr. Brenda Elias		

PROTOCOL NUMBER:	PROJECT OR PROTOCOL TITLE:
NA	Tuberculosis Control in Manitoba, 2008-10: A Performance Analysis
SPONSORING AGENCIES AND/OR COORDINATING GROUPS:	

Submission Date of Investigator Documents:	HREB Receipt Date of Documents:
May 4, 2015	May 4, 2015

REVIEW CATEGORY OF ANNUAL REVIEW: **Full Board Review** ☐ **Delegated Review** ☒

THE FOLLOWING AMENDMENT(S) and DOCUMENTS ARE APPROVED FOR USE:

Document Name(if applicable)	Version(if applicable)	Date

Annual approval

*Annual approval implies that the most recent **HREB approved** versions of the protocol, Investigator Brochures, advertisements, letters of initial contact or questionnaires, and recruitment methods, etc. are approved.*

Consent and Assent Form(s):

CERTIFICATION
The University of Manitoba (UM) Health Research Board (HREB) has reviewed the annual study status report for the research study/project named on this ***Certificate of Annual Approval*** as per the category of review listed above and was found to be acceptable on ethical grounds for research involving human participants. Annual approval was granted by the Chair or Acting Chair, UM HREB, per the response to the conditions of approval outlined during the initial review (full board or delegated) of the annual study status report.

HREB ATTESTATION
The University of Manitoba (UM) Health Research Board (HREB) is organized and operates according to Health Canada/ICH Good Clinical Practices, Tri-Council Policy Statement 2, and the applicable laws and regulations of Manitoba. In respect to clinical trials, the HREB complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations of Canada and carries out its functions in a manner consistent with Good Clinical Practices.

QUALITY ASSURANCE
The University of Manitoba Research Quality Management Office may request to review research documentation from this research study/project to demonstrate compliance with this approved protocol and the University of Manitoba Policy on the Ethics of Research Involving Humans.

CONDITIONS OF APPROVAL:

1. The study is acceptable on scientific and ethical grounds for the ethics of human use only. ***For logistics of performing the study, approval must be sought from the relevant institution(s).***
2. This research study/project is to be conducted by the local principal investigator listed on this certificate of approval.
3. The principal investigator has the responsibility for any other administrative or regulatory approvals that may pertain to the research study/project, and for ensuring that the authorized research is carried out according to governing law.
4. **This approval is valid until the expiry date noted on this certificate of annual approval. A Bannatyne Campus Annual Study Status Report** must be submitted to the REB within 15-30 days of this expiry date.
5. Any changes of the protocol (including recruitment procedures, etc.), informed consent form(s) or documents must be reported to the HREB for consideration in advance of implementation of such changes on the **Bannatyne Campus Research Amendment Form.**
6. Adverse events and unanticipated problems must be reported to the REB as per Bannatyne Campus Research Boards Standard Operating procedures.
7. The UM HREB must be notified regarding discontinuation or study/project closure on the **Bannatyne Campus Final Study Status Report.**

Sincerely,

[redacted]

John Arnett, PhD., C. Pysch.
Chair, Health Research Ethics Board
Bannatyne Campus

Please quote the above Human Ethics Number on all correspondence.
Inquiries should be directed to the REB Secretary **Telephone:** (204) 789-3255/ **Fax:** (204) 789-3414

Appendix 2 - Approval from Assembly of Manitoba Chiefs' Health Information and Research Governance Committee (AMC-HIRGC)

ASSEMBLY OF MANITOBA CHIEFS SECRETARIAT INC.

2nd Floor · 275 Portage Avenue · Winnipeg, Manitoba · R3B 2B3 · Telephone: (204) 956-0610 · Fax: (204) 956-2109

May 5, 2014

Andrew Basham
[redacted]

Dear Mr. Basham:

Re: Tuberculosis Control in Manitoba, 2008-2010: A Performance Analysis

Thank you for your submission to the Assembly of Manitoba Chiefs Health Information Governance Committee (AMC HIRGC). Your Research Application has been reviewed and the committee agreed to support your research study to understand the performance of Manitoba tuberculosis (TB) control services using a quantitative framework.

A progress report is expected to be received annually and upon completion of the project.

Please note any proposed presentations or publications regarding this data must be sent for review to AMC HIRGC prior to the event or publication. AMC will respond in a timely manner.

If you have any further questions please contact Leanne Gillis at lgillis@manitobachiefs.com.

Miigwech.

ASSEMBLY OF MANITOBA CHIEFS

[redacted]
Kathi Avery Kinew, M.S.W., Ph.D
Manager, Social Development & Research Initiatives

HEAD OFFICE: Swan Lake First Nation · Unit 9-4820 Portage Avenue· Headingley, MB R4H 1C8 · Telephone: (204) 956-0610

Appendix 3 - Approval from Manitoba Health Information and Privacy Committee (HIPC)

Manitoba
Health, Healthy Living and Seniors
Health Information Management
4040-300 Carlton Street, Winnipeg, Manitoba, Canada R3B 3M9
T 204-786-7139 **F** 204-944-1911
www.manitoba.ca

September 8, 2014

[redacted]

HIPC No. 2014/2015 – 10
File number to be quoted on correspondence

Dear Christopher,

RE: Tuberculosis Control in Manitoba, 2008-2010: A Performance Analysis

Thank you for submitting the requested documentation and clarification for the above named project. The Health Information Privacy Committee has now ***approved*** your request for data for this project.

Any significant changes to the proposed study design should be reported to the Chair/HIPC for consideration in advance of their implementation. Also, please be reminded that any manuscripts and presentation materials resulting from this study must be submitted to Manitoba Health, Healthy Living and Seniors for review. Specifically, manuscripts must be submitted *at least **30** calendar days* prior to the intended publication and presentation materials must be submitted *at least **10** calendar days* prior to the presentation.

Please note that a Researcher Agreement will need to be completed before work on this project can commence. This will be initiated by Manitoba Health, Healthy Living and Seniors (MHHL). If you have any questions or concerns, please do not hesitate to contact Joy Wei, Committee Coordinator at (204)786-7204.

Yours truly,

[redacted]

Dr. Biehl, MD, FRCP
Chair, Health Information Privacy Committee

c.c. D. Malazdrewicz

Manitoba
spirited energy

Appendix 4 – Northern Health Region Communities List[20]

1. Brochet/Barren Lands First Nation
2. Cranberry Portage
3. Cormorant
4. Cross Lake/Cross Lake First Nation
5. Easterville/Chemawawin First Nation
6. Flin Flon
7. Garden Hill First Nation
8. Gillam/Fox Lake First Nation
9. God's River/Manto Sipi Cree Nation
10. God's Lake Narrows/God's Lake Narrows First Nation
11. Grand Rapids/Misipawistik Cree Nation
12. Granville Lake
13. Herb Lake Landing
14. Ilford/War Lake First Nation
15. Island Lake
16. Lac Brochet/Northlands Denesuline
17. Leaf Rapids
18. Lynn Lake
19. Marcel Colomb/Black Sturgeon
20. Moose Lake/Mosakahiken Cree Nation
21. Nelson House/Nisichawayasihk Cree Nation
22. Norway House/Norway House Cree Nation
23. Oxford House/Bunibonibee
24. Pikwitonei
25. Pukatawagon/Mathias Colomb Cree Nation
26. Red Sucker Lake First Nation
27. St. Theresa Point First Nation
28. Shamattawa/Shamattawa First Nation
29. Sherridon/Cold Lake
30. Snow Lake
31. South Indian Lake/O-Pipon-Na-Piwin
32. Split Lake/Tataskweyak Cree Nation
33. Tadoule Lake/Sayisi Dene
34. Thicket Portage
35. The Pas/Opaskwayak Cree Nation
36. Thompson
37. Wabowden
38. Wanless
39. Wasagamack First Nation
40. York Landing/York Factory Cree Nation

20 http://www.northernhealthregion.ca/default.aspx?cid=134&lang=1 Retrieved July 21, 2015.