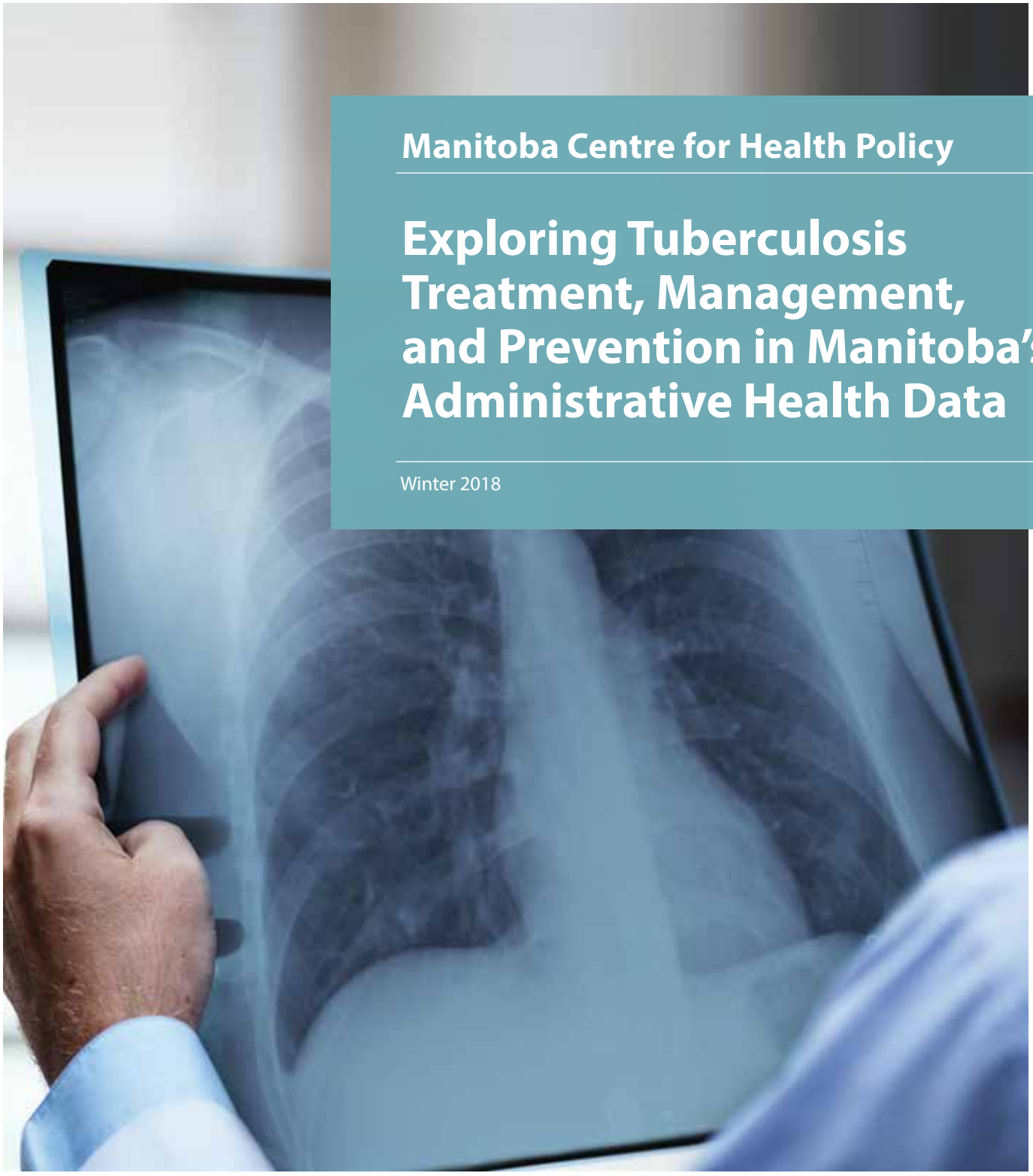

Manitoba Centre for Health Policy

# Exploring Tuberculosis Treatment, Management, and Prevention in Manitoba's Administrative Health Data

Winter 2018


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The Manitoba Centre for Health Policy (MCHP) is located within the Department of Community Health Sciences, Max Rady College of Medicine, Rady Faculty of Health Sciences, University of Manitoba. The mission of MCHP is to provide accurate and timely information to healthcare decision–makers, analysts and providers, so they can offer services which are effective and efficient in maintaining and improving the health of Manitobans. Our researchers rely upon the unique Manitoba Population Research Data Repository (Repository) to describe and explain patterns of care and profiles of illness and to explore other factors that influence health, including income, education, employment, and social status. This Repository is unique in terms of its comprehensiveness, degree of integration, and orientation around an anonymized population registry.

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We thank the Health Research Ethics Board, University of Manitoba, Rady Faculty of Health Sciences, Max Rady College of Medicine, Health Research Ethics Board for their review of this project. MCHP complies with all legislative acts and regulations governing the protection and use of sensitive information. We implement strict policies and procedures to protect the privacy and security of anonymized data used to produce this report and we keep the provincial Health Information Privacy Committee informed of all work undertaken for Manitoba Health, Seniors and Active Living.

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# List of Acronyms

| | |
|---|---|
| **ATC** | Anatomical Therapeutic Chemical |
| **CI** | Confidence Interval |
| **CPL** | Cadham Provincial Laboratory |
| **DIN** | Drug Identification Number |
| **DOPT** | Directly Observed Preventative Therapy |
| **DPIN** | Drug Program Information Network |
| **DSM** | Diagnostic Services Manitoba |
| **FNIHB** | First Nations and Inuit Health Branch |
| **GEE** | Generalized Estimating Equations |
| **HIV** | Human Immunodeficiency Virus |
| **INAC** | Indigenous and Northern Affairs Canada |
| **INH** | Isoniazid |
| **ITBS** | Integrated Tuberculosis Services |
| **LTBI** | Latent Tuberculosis Infection |
| **MCHP** | Manitoba Centre for Health Policy |
| **MHSAL** | Manitoba Health, Seniors and Active Living |
| **NPV** | Negative Predictive Value |
| **OR** | Odds Ratio |
| **PHIN** | Personal Health Identification Number |
| **PPV** | Positive Predictive Value |
| **RIF** | Rifampin |
| **RR** | Relative Rate |
| **TB** | Tuberculosis |
| **WRHA** | Winnipeg Regional Health Authority |

# Executive Summary

Tuberculosis (TB) is a communicable disease that is a major cause of morbidity and mortality. In Canada, Manitoba has one of the highest rates of active (i.e., symptomatic) TB. Latent TB infection (LTBI), when an individual is infected with Mycobacterium tuberculosis but does not have active disease, is also a concern, because individuals with LTBI are more likely to progress to active TB if they do not receive and adhere to treatment.

The World Health Organization's *End TB Strategy*, which was introduced in 2016, has set aggressive targets for reducing the number of TB cases and deaths by 2035. The Strategy identifies local databases, including disease registries and administrative data, as key information sources to achieve progress towards these targets. Specifically, these databases are essential for surveillance, research, and program evaluation that can inform local strategies to end TB.

## Study Purpose and Objectives

Our study purpose was to examine the use of linked TB Registry and administrative data to describe the characteristics and health outcomes of active TB cases and treated LTBI cases in Manitoba. The objectives were to:

1. Describe the completeness and accuracy of information about active TB cases in the Manitoba TB Registry;
2. Validate administrative health data for identifying active TB cases;
3. Examine healthcare use of active TB cases over the disease course and the socio-demographic, comorbidity, and disease characteristics associated with healthcare use;
4. Assess the accuracy and completeness of information about contacts of active TB cases in the Manitoba TB Registry and describe the characteristics and outcomes of contacts; and
5. Explore trends in the treatment of LTBI and the characteristics and outcomes of individuals receiving treatment for LTBI.

# Methods

The Manitoba TB Registry maintained by Manitoba Health, Seniors and Active Living (MHSAL) was acquired into the Manitoba Population Research Data Repository housed at the Manitoba Centre for Health Policy (MCHP). The Manitoba TB Registry was linked (anonymously) with administrative health databases. Patient groups that are the primary focus of the study are:

**Active TB Cohort (n = 1,686):** Includes cases of active TB from the Manitoba TB Registry between April 1, 1999 and March 31, 2014.

**Treated LTBI Cohort (n = 6,217):** Includes cases of treated LTBI ascertained from prescription drug records in Manitoba's Drug Program Information Network (DPIN) database between April 1, 1999 and March 31, 2014.

For Objectives 1 and 2, we described the completeness of the Manitoba TB Registry and agreement between the Manitoba TB Registry and administrative data for multiple characteristics of the Active TB Cohort, such as age of TB cases and laboratory test dates.

For Objective 3, we examined emergency room, acute care, family physician, specialist physician, prescription drug, and homecare service use before and after diagnosis for the Active TB Cohort. The healthcare use of a matched cohort (i.e., matching on age, sex, residence location, and First Nations status) was compared to the healthcare use of the Active TB Cohort.

For Objective 4, we characterized individuals identified as contacts of individuals diagnosed with active TB from the Manitoba TB Registry, and their health outcomes.

For Objective 5, we investigated trends in treatment completion rates for the Treated LTBI Cohort and examined cohort characteristics associated with treatment completion.

# Results and Interpretation

For Objective 1, we found that most of the investigated attributes of the Manitoba TB Registry were complete and agreed with administrative data. These findings reinforce the value of routinely-collected and standardized TB Registry data for TB surveillance and program evaluation.

For Objective 2, we found that TB diagnosis codes in hospital records and physician billing claims had excellent specificity for identifying active TB cases. However, sensitivity and positive predictive value were frequently low, indicating that TB diagnoses in administrative data are not a valid way to identify active TB cases. In jurisdictions where TB Registry data cannot be linked to administrative data, researchers will have difficulty conducting accurate studies about TB outcomes and healthcare use.

For Objective 3, we observed high rates of emergency room, acute care, and family physician use prior to the diagnosis date. This means that TB cases have multiple points of contact with healthcare providers that can facilitate early diagnosis and treatment. High rates of specialist visits and homecare use following diagnosis demonstrate the opportunities to ensure continuity of care. Healthcare use was substantially higher than for a matched disease-free cohort, reinforcing that TB has a large impact on the healthcare system.

For Objective 4, the average number of contacts was highest for First Nations residents living in northern Manitoba and lowest for foreign-born (i.e., residents of Manitoba born outside of Canada) and Canadian-born non-First Nations cases. These findings reflect higher disease prevalence, inadequate social and housing conditions, and the type of TB (i.e., pulmonary TB) predominantly found in northern Manitoba communities.

For Objective 5, treatment completion rates generally increased over time for treated LTBI cases, although the rates varied with the type of treatment. However, regardless of the prescription medication used for treatment, rates never achieved the recommended target of 80% completion, reflecting the challenges associated with having individuals adhere to lengthy treatment courses for LTBI.

# Conclusions and Interpretation

The Manitoba TB Registry contains high-quality information about active TB cases, but there are also gaps in available information for TB surveillance, research, and program evaluation. These gaps could be addressed by reviewing and potentially revising data elements in the Manitoba TB Registry to assess their utility for surveillance, and collecting new data about TB on an ad hoc or routine basis. Linking TB Registry data with administrative data can also provide a comprehensive picture of active TB cases. As well, administrative data can provide information about LTBI treatment, and about multiple determinants of health and healthcare use for active TB cases and treated LTBI cases.

Active TB impacts healthcare service use before and after TB diagnosis and is influenced by socio-demographic, disease, and comorbidity characteristics. Frequent contacts with the healthcare system means that there are multiple opportunities to diagnose active TB and monitor progression of treatment. Improving LTBI treatment completion rates to the recommended target of 80% should help to reduce the size of the LTBI reservoir in affected populations.

# Recommendations

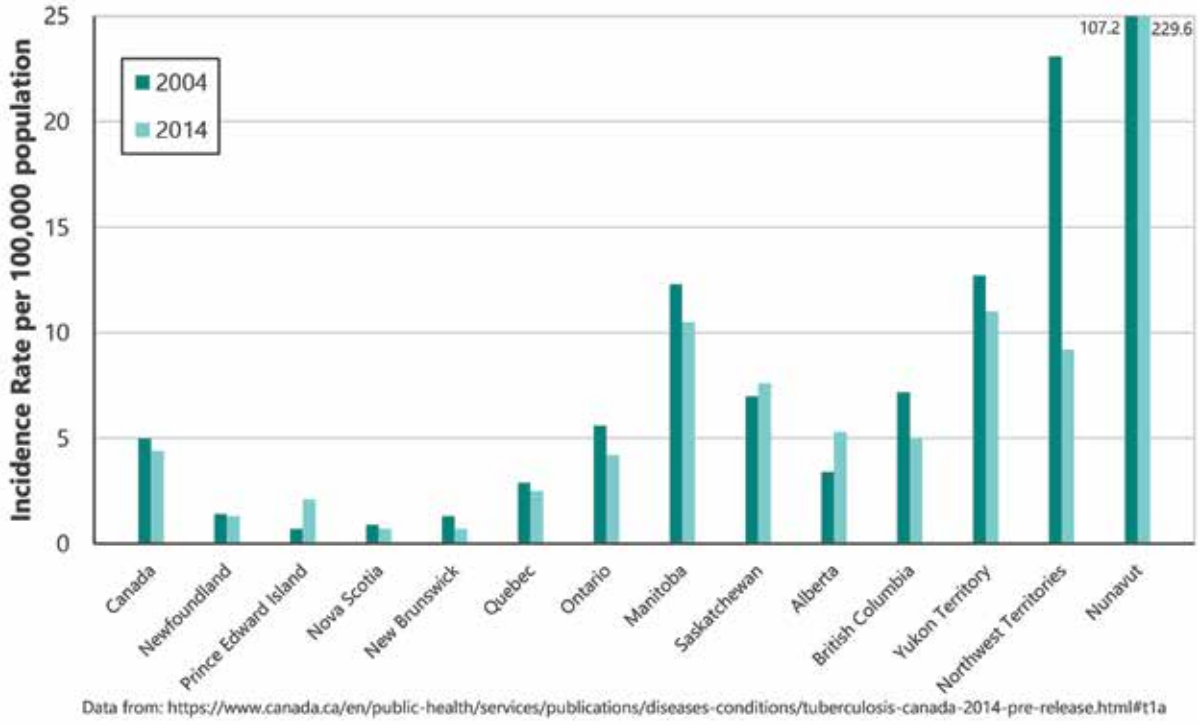
Recommendations arising from this study focus on:

- The value of ongoing commitments to the quality and accessibility of the Manitoba TB Registry for research, surveillance, and program evaluation;
- The benefits of forging and maintaining partnerships to strengthen the data available for TB research, surveillance, and program evaluation;
- Defining and measuring indicators for the evaluation of TB programs and services; and
- The importance of integrating multiple databases to conduct comprehensive studies about health and its determinants that will benefit strategies to end TB in Manitoba.

# Chapter 1:
## Introduction and Background

Tuberculosis (TB) is a communicable disease that is a major cause of morbidity and mortality, and a significant public health concern. In 2014, the most recent year for which national data are available, Manitoba's TB incidence rate was estimated to be 10.5 cases per 100,000 population [1]. While lower than the rate of 12.3 per 100,000 population reported in 2004 (see Figure 1.1), the 2014 rate was substantially higher than the overall national incidence rate of 4.4 cases per 100,000 population and also higher than incidence rates in neighbouring provinces such as Saskatchewan (7.6 incident cases per 100,000 population in 2014) and Alberta (5.3 incident cases per 100,000 population in 2014).

**Figure 1.1: National Reported New Active and Re-Treatment Tuberculosis Incidence Rate**
per 100,000 (all cases) for Canada and Provinces/Territories



Active TB disproportionately impacts Indigenous (i.e., First Nations, Métis, and Inuit) and foreign-born populations [2]. A 2016 report by the Public Health Agency of Canada noted that while Canadian-born Indigenous people made up only four percent of the total Canadian population, they accounted for more than one-fifth (21%) of reported cases of active TB amongst cases with origin information [1]. Accordingly, the incidence rate of active TB amongst the Indigenous Canadian population was estimated to be 20.4 cases per 100,000 population in 2016. Moreover, a 2018 study from British Columbia estimated the incidence rate of active TB amongst recent immigrants to be 24.2 cases per 100,000 population [3]. TB is also a significant issue for individuals with HIV and some chronic conditions, like renal disease [4].

Identifying and treating individuals with active TB is a primary focus for healthcare providers. However, identifying and treating individuals who may have a latent TB infection (LTBI) is also important. LTBI (or 'sleeping TB') arises when an individual is infected with the TB bacterium but the bacterium is dormant and not transmissible. Treatment of LTBI to prevent the development of TB disease is a key strategy for controlling and eliminating TB. Two tests are commonly used to confirm a diagnosis of LTBI: the tuberculin skin test, and the measurement of interferon-γ in whole blood. However, neither is the "gold standard" test for diagnosing LTBI. Individuals with LTBI have an elevated lifelong risk of developing active TB. Individuals at greatest risk of progressing from LTBI to active TB include those who have recently been infected, have HIV, or have chronic conditions that compromise their immune systems.

TB is not only a public health concern, but also has a significant impact on the healthcare system. The most recent national study about healthcare costs associated with TB (in 2004) estimated that total TB-related expenditures that year were $74 million [5]. Moreover, the average cost of treating one case of active TB disease was estimated to be $47,000. TB treatment is a lengthy and complex process that requires multiple medications, frequent monitoring, and follow-up with multiple healthcare professionals. Treatment of individuals with LTBI is less resource intensive and was estimated to cost less than $1,000 per person [5], reinforcing the value of investigating and treating potential cases of LTBI. However, LTBI can also impact the healthcare system; treatment is a lengthy process. Adverse events of treatment, while rare, may contribute to increased healthcare use [6].

## Using Administrative Data for Studies about TB in Canada

The administrative databases in the Manitoba Population Research Data Repository housed at the Manitoba Centre for Health Policy (MCHP) have been used to study the health and healthcare use of individuals diagnosed with many chronic and infectious diseases [7–10]. However, these data have not been used to study TB. Given the disproportionate impact of TB on Indigenous and foreign-born populations, using Manitoba's administrative data to better understand the health and healthcare use of these populations could be particularly beneficial for decision making about TB prevention, treatment, and management programs in Manitoba, as well as across Canada and internationally.

In some Canadian provinces, administrative health data have already been used to estimate the TB disease burden in at-risk populations, identify risk factors for TB, and explore TB's impact on healthcare use. For example, researchers in British Columbia recently published a protocol for a retrospective cohort study involving linkage of multiple administrative and clinical databases to develop a TB risk prediction model for that province's foreign-born population [11]. As part of their investigation, the provincial TB registry was linked to administrative health data to identify TB risk factors and estimate TB incidence rates amongst recent provincial immigrants; a key finding was that TB rates remained high for up to 10 years following entry into the province [3]. As well, multiple demographic characteristics were found to be associated with TB risk. This research highlights the multi-faceted nature of disease risk and the challenges of risk management.

An Ontario study linked administrative data to data from Citizenship and Immigration Canada to examine the effectiveness of the Immigration Medical Surveillance Program for screening new Canadian immigrants for active TB. The researchers found that adherence to ongoing TB surveillance following the initial screening was low, suggesting missed opportunities to prevent future cases of TB [12]. An Alberta study used administrative data to investigate the use of emergency departments amongst TB patients in Edmonton; high use rates prior to TB diagnosis were observed. The authors suggested that emergency department visits provide an opportunity for early disease diagnosis, which is important for controlling future disease risk [13].

Several studies have been conducted using Quebec's TB registry data linked to administrative health databases. For example, one study linked the City of Montreal's TB Resource File to hospitalization data; the linked data were used to examine trends in hospitalization for patients who had confirmed cases of active pulmonary TB (i.e., infectious TB) between 1993 and 2007 [14]. The researchers found that for about two-thirds of the cohort, hospital length of stay was at least 14 days, which was consistent with national recommendations of the time. The authors suggested further studies about the impact of shorter (i.e., < 14 days) hospital stays on patient outcomes, including risk of disease transmission within the community. Another Quebec study used Montreal's TB Resource File to identify predictors of hospitalization and total length of stay for cases of active TB disease [15]; data were extracted from medical charts and public health records. The median length of stay was

17.5 days. Patient characteristics associated with a longer length of stay in hospital included having HIV, renal disease, symptomatic pulmonary smear-positive TB, multi- or poly-TB drug resistance, and being in a teaching hospital. Rubinowicz et al. identified a cohort of individuals being treated for LTBI using Quebec's prescription drug data and linked the data for this cohort to physician billing claims to examine treatment completion rates for patients treated by primary care physicians [16]. The researchers focused on treatment completion rates for isoniazid. The researchers found that only 40.5% of patients completed treatment. Moreover, treatment completion rates were lower for patients who initiated treatment while being cared for by primary care physicians. These studies provide important information about healthcare resource use amongst active TB cases, as well as information about treatment of LTBI and the outcomes of treatment.

Canadian cross-jurisdictional studies about TB have been conducted using provincial TB registry data [17,18]. However, few cross-jurisdictional studies have been conducted using only administrative health data, or using linked TB registry and administrative data. This represents a significant gap in research to describe health and healthcare use of TB populations. Such studies could provide more comprehensive information about the factors that influence disease risk and healthcare use, particularly in at-risk populations.

## TB Programs, Surveillance, and Research in Manitoba

TB services for prevention, management, and patient care in Manitoba are provided via collaborations amongst the Public Health Branch of Manitoba Health, Seniors and Active Living (MHSAL), Health Canada's First Nations and Inuit Health Branch (FNIHB), the Winnipeg Regional Health Authority (WRHA), and Manitoba's other regional health authorities. Responsibility for TB prevention and care was devolved from the province to the health regions beginning in 2005; however, even after this date, case management was still completed by the province and the health regions managed contact follow-up. It was not until April 2011 that there was full devolution of TB case/contact management to all health regions in the province.

In November 2008, the WRHA began providing consultation services for all on-reserve TB cases and contacts under the jurisdiction of FNIHB. Specifically, FNIHB and the WRHA entered into a contribution agreement whereby case and contact consultation services were provided by the WRHA in collaboration with FNIHB for all communities within Manitoba that fall within federal jurisdiction.

In terms of provincial oversight, MHSAL receives and refers reports of laboratory-confirmed or clinical cases of TB to the health regions. MHSAL is also responsible for protocol and policy development, for provincial surveillance, and for funding and providing overall direction for the provincial TB prevention and management program [19].

Information about all laboratory-confirmed and clinically-confirmed cases of active TB is captured in the Manitoba TB Registry. The collection of information is required under legislation because TB is a notifiable communicable disease under Schedule B of the Public Health Act. The Manitoba TB Registry captures detailed information about active TB cases, including demographic and geographic characteristics, contact assessments, bacteriology and x-ray results, course and outcome of treatment, selected measures of healthcare use, and identified drug sensitivities. Appendix 1 provides an overview of the information captured in the Manitoba TB Registry. A provincial protocol provides information about case and contact identification and management and related public health issues [19]. For example, MHSAL provides provincially-funded medications at no cost to individuals who are diagnosed with active TB disease or with LTBI.

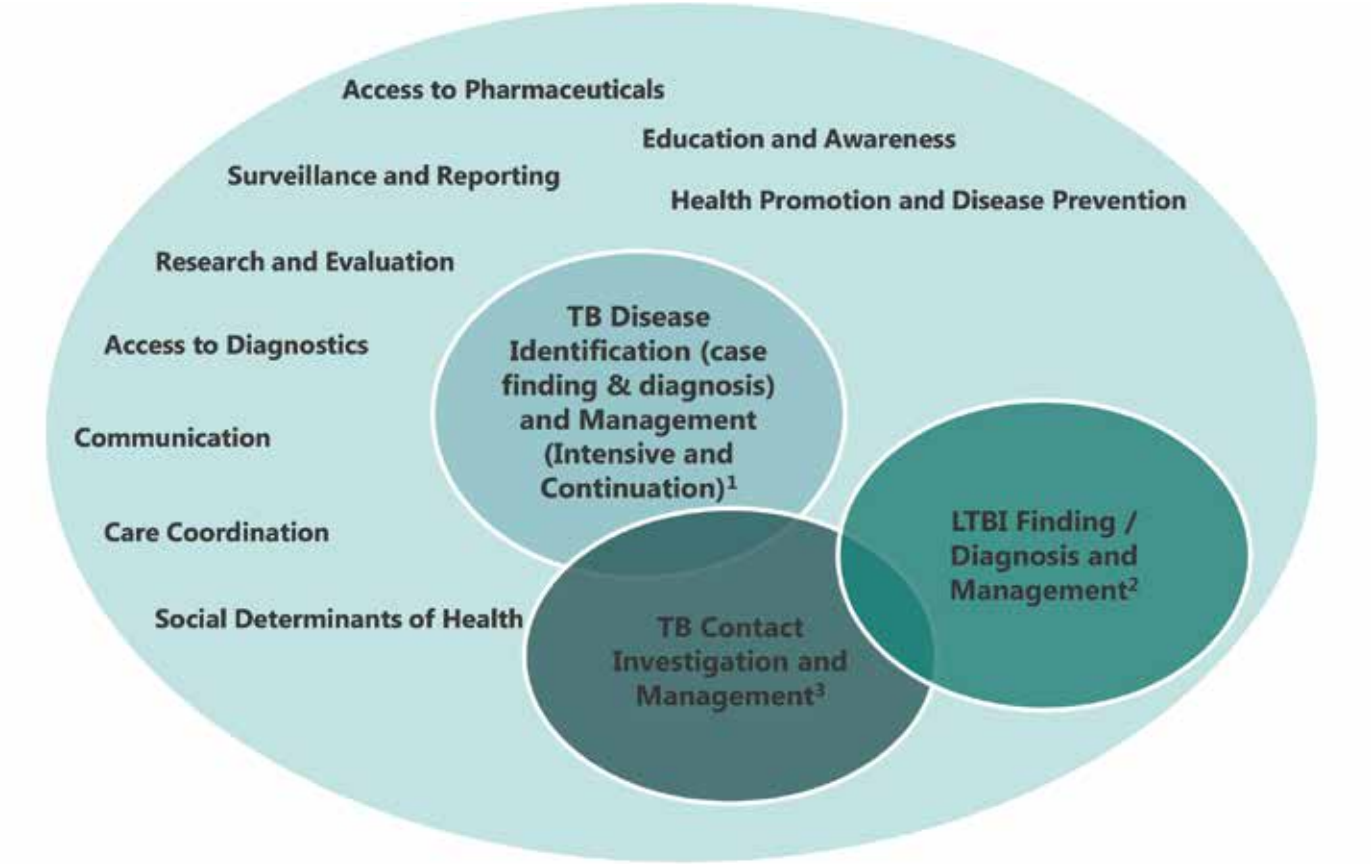
LTBI is not reportable by law. There is no single database that accurately identifies individuals with LTBI in Manitoba; this is true for all Canadian provinces and territories. However, previous Canadian studies and surveillance reports have used prescription drug administrative data, like the data found in Manitoba's Drug Program Information Network (DPIN) database, to identify individuals being treated for LTBI [16,20,21].

The epidemiology of active TB disease in Manitoba, including temporal, geographic, and population-specific trends, has been explored in previous studies [17,22–24]. MHSAL has prepared a provincial surveillance report on active TB from 2000 to 2012, although it has not been publicly released [25]. The province has conducted investigations about diabetes and TB [26], trends and characteristics of TB genotype clusters [27], and treated LTBI in the province. Studies about the health and healthcare use of active TB and LTBI cases have been undertaken within the WRHA, but not for the entire province [28].

# Integrated TB Services in the Winnipeg Regional Health Authority

In 2010, the WRHA established the Integrated TB Services (ITBS) Program. This Program provides a multi-sectoral approach to TB care that focuses on the integration of preventive, primary care, diagnostic, treatment and support services (see Figure 1.2).

**Figure 1.2: Winnipeg Regional Health Authority's Integrated Tuberculosis Services (ITBS) Care Spectrum Conceptual Framework**




[1] TB disease identification and management is the foremost priority area, based on Canadian and World Health Organization recommendations. Some cases of active TB disease are identified outside of a TB contact investigation, and others are identified in a TB contact investigation.

[2] Latent TB infection identification and management includes testing of recent contacts to infectious cases, as well as testing of individuals outside of a TB contact investigation (i.e. screening); e.g. individuals with HIV infection, immigrants and refugees, healthcare workers, etc.

[3] TB contact investigations will identify individuals with active TB disease, latent TB infections, and also individuals who have neither condition.

Performance measurement and program evaluation are standard practices essential to determine whether a strategy is effective in meeting its goals, targets and objectives, and whether ongoing programming is able to adapt and adjust to changing circumstances and needs. In 2013, the ITBS Program established a time-limited Data Management Committee tasked with developing a strategy to measure system performance (evaluation, monitoring and reporting) on key TB indicators. It was recognized at the time that there was no comprehensive provincial TB report that integrated information from across the system for a core set of TB indicators that would facilitate and inform the work of practitioners, program and policy planners and advocacy groups as the new model of TB care evolved in the province.

Front-line and middle management partners who participated on the ITBS Data Management Committee worked with WRHA Decision Support to develop 13 indicators within the spectrum of TB services, including TB disease identification (i.e., clinical and laboratory diagnosis), TB disease management (i.e., patient flow and efficient use of inpatient/outpatient resources), TB contact investigations (i.e., timely assessment of close household TB contacts), and management of latent TB infections (i.e., efficient use of primary care resources). The Data Management Committee consulted several sources, including the Public Health Agency of Canada, FNIHB, and US Centers for Disease Control and Prevention, before deciding on a set of priority performance indicators that might be measurable [29–31].

The Data Management Committee recognized that measuring and analyzing such indicators would require: (a) access to population-based administrative databases linked to the Manitoba TB Registry; and (b) expertise in establishing and managing a central database warehouse

for TB. Therefore, a proposal was submitted to Manitoba Health in December 2014 requesting support from MCHP to determine the feasibility and utility of measuring the 13 proposed TB indicators (Table 1.1).

The development of indicators by the ITBS Data Management Committee to monitor program outputs and outcomes is aligned with activities at national and international levels. For example, the World Health Organization developed a compendium of performance indicators for national and international TB programs; the goal is to facilitate both internal and external measurement and evaluation of TB control programs to improve their quality and effectiveness [32]. As another example, the British Columbia Strategic Plan for Tuberculosis Prevention, Treatment, and Control identifies multiple performance indicators about testing, treatment, contact assessment, screening, and surveillance [33]. While some of these indicators are now being measured, others are still in progress of development.

**Table 1.1: Performance Indicators Developed for the Winnipeg Regional Health Authority's Integrated Tuberculosis (TB) Services Program**

| Performance Area | Indicator |
|---|---|
| **TB Contact Investigation and Management** | #1: Proportion of contacts without complete follow-up within a contact investigation |
| | #2: Proportion of newly-diagnosed active TB cases within a contact investigation |
| | #3: Proportion of newly identified LTBI within a contact investigation |
| | #4: Proportion of contacts with no evidence of TB disease or LTBI within a contact investigation |
| **TB Disease Management** | #5: Proportion of individuals admitted to hospital with a TB diagnosis who were clinically well enough to receive TB care as an outpatient |
| | #6: Average number of days of hospitalization of persons diagnosed with TB disease identified as clinically well enough to receive TB care as an outpatient |
| | #7: Proportion of persons diagnosed with TB disease and prescribed treatment by a Winnipeg Health Region care provider who started treatment for TB disease and completed the prescribed course of TB treatment within 3 months of their target treatment completion date |
| **TB Disease Identification** | #8: Time from date of onset of cough until first visit to healthcare provider for respiratory reason in all persons with culture-confirmed respiratory TB |
| | #9: Time from first visit to healthcare provider for respiratory reason until collection date of first sputum for Acid-Fast Bacilli (AFB) in all persons with culture-confirmed respiratory TB |
| | #10: Number of healthcare visits for respiratory reason between the first visit for respiratory reason and the collection date of first sputum for AFB in all persons with culture-confirmed respiratory TB |
| **LTBI Management** | #11: Proportion of persons diagnosed with LTBI, who are identified as contacts of sputum culture-confirmed TB cases, who start LTBI treatment |
| | #12: Proportion of persons who start LTBI treatment, who are identified as contacts of sputum culture-confirmed TB cases, who complete a full course of treatment for LTBI (at least 80% of doses) |
| | #13: Proportion of persons who start LTBI treatment, who are not identified as contacts of TB cases, who complete a full course of LTBI treatment (at least 80% of doses) |

## Study Purpose and Objectives

The purpose of this study was to examine the use of administrative data for studies about TB and the health and healthcare use of active TB and treated LTBI cases. The objectives were to:

1. Describe the completeness and accuracy of information about active TB cases in the Manitoba TB Registry;
2. Validate administrative health data for identifying active TB cases;
3. Examine healthcare use of active TB cases over the disease course and the socio-demographic, comorbidity, and disease characteristics associated with healthcare use;
4. Assess the accuracy and completeness of information about contacts of active TB cases in the Manitoba TB Registry and describe the characteristics and outcomes of contacts;
5. Explore trends in the treatment of LTBI and the characteristics and outcomes of individuals receiving treatment for LTBI.

## Report Organization

This report is organized as follows. In Chapter 2, we describe the development of the study cohorts that are the basis for analyses to achieve the study objectives. In Chapter 3, we focus on the quality (i.e., accuracy and completeness) of the Manitoba TB Registry (Objective 1), and the validity of Manitoba's administrative health data for ascertaining cases of active TB disease (Objective 2). Chapter 4 explores healthcare use measures for individuals with active TB and compares healthcare use for individuals with active TB to the healthcare use of matched individuals who are disease-, treatment-, and contact-free (Objective 3). Chapter 5 focuses on contacts of individuals with active TB ascertained from the Manitoba TB Registry (Objective 4). Chapter 6 explores treatment completion amongst individuals receiving treatment for LTBI and characteristics of treated LTBI cases (Objective 5).

# Chapter 2:

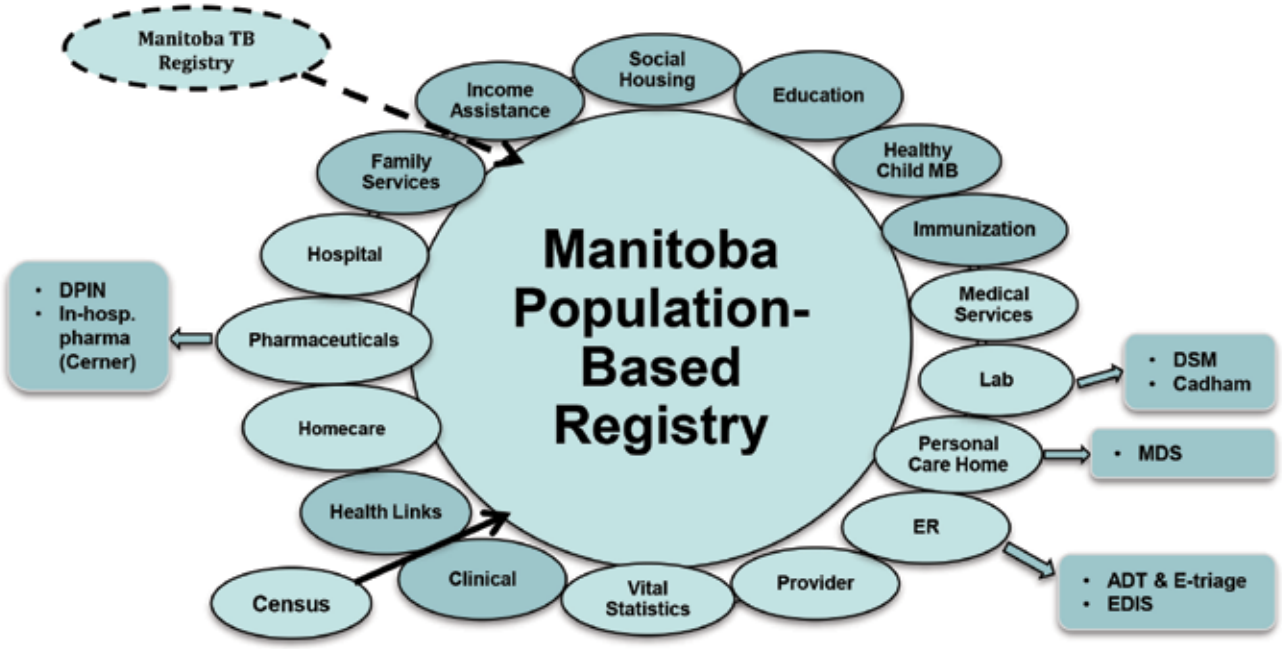
# Developing the Active TB Cohort and Treated Latent TB Infection Cohort

In this chapter, we begin by describing the administrative databases used to conduct the study. Then we describe the methods used to construct a cohort of individuals with active TB and a cohort of individuals receiving treatment for LTBI. These cohorts are used for analyses associated with all of the study objectives outlined in Chapter 1. In addition, we constructed a matched cohort for each of the Active TB and Treated LTBI Cohorts. These cohorts are used for analyses associated with Objective 5.

## Study Databases

The study cohorts were constructed using the Manitoba TB Registry, Manitoba Population-Based Registry (Population Registry), and Drug Program Information Network (DPIN) databases. All of these databases were housed in the Manitoba Population Research Data Repository at the Manitoba Centre for Health Policy (MCHP) at the time of the study (Figure 2.1). Detailed descriptions of these databases in the repository can be found here: (webpage: http://umanitoba. ca/faculties/ health_sciences/medicine/units/community_health_sciences/departmental_units/mchp/resources/ repository/datalist. html).To characterize the study cohorts on socio-demographic measures, we used data from the Population Registry, Indigenous and Northern Affairs (INAC) Status Registry and publicly-available Statistics Canada Census data.

**Figure 2.1: The Manitoba Population Research Data Repository housed at the Manitoba Centre for Health Policy**



The Manitoba TB Registry, which is managed and maintained by MHSAL, contains information about all cases of active TB in the province. It includes demographic and geographic characteristics, contact assessments, bacteriology and x-ray results, course and outcome of treatment, selected measures of healthcare use, and identified drug sensitivities. The population of origin of all active TB cases is identified in the Manitoba TB Registry: First Nations on-reserve, First Nations off-reserve, Canadian-born non-First Nations, and foreign-born (i.e., individuals not born in Canada). The years of data captured in the Manitoba TB Registry provided by MHSAL to MCHP extend from 1993 to 2014.

The Population Registry contains information for all Manitobans registered with the Manitoba Health Services Insurance Plan, including healthcare coverage start and end dates, demographic characteristics, and postal code of residence. The latter was used to assign individuals to health regions and income quintiles. Income quintiles are an area-level measure of socioeconomic status defined using Statistics Canada Census data for total household income from dissemination areas, the smallest geographic unit for which Census data are publicly released by Statistics Canada [34]. Each quintile represents approximately 20% of the total Manitoba population; the methodology is applied separately to urban and rural populations. We combined urban and rural quintiles due to the small number of individuals in some quintiles for the Active TB Cohort.

The INAC Status Registry was created and is managed by the federal department of Indigenous and Northern Affairs. This department determines whether a person is registered as a "Status Indian" under the Indian Act. Registered Status Indians under this system who were residents of Manitoba were distinguished from all other Manitoba residents when describing the study cohorts. This identification via the Indian Act should be noted as a potential limitation; many individuals who identify as First Nations but are not registered under the Indian Act will be included with other Manitoba residents.

The DPIN is an electronic point-of-sale database that contains information about prescriptions filled by community pharmacies (hospital pharmacy data are not captured in DPIN). Each drug approved in Canada is assigned a Drug Identification Number (DIN) by the Health Canada Drugs Program unit; DINs are linked to Anatomical Therapeutic Chemical (ATC) codes in the Drug Product Directory. The ATC classification system, developed by the World Health Organization, is used to classify drugs according to the system or organ that they affect and/or their chemical/therapeutic characteristics [35].

# Developing the Study Cohorts

## Active TB Cohort

The Active TB Cohort was comprised of all active TB cases identified from the Manitoba TB Registry over a 15-year period between April 1, 1999 and March 31, 2014. While the Manitoba TB Registry housed at MCHP contains cases from 1993 to 2014, we limited our attention to the period from 1999 to 2014 for two reasons: (a) Registry data quality appeared to be slightly poorer for earlier years compared to later years, based on the standard data quality report that MCHP produces whenever a new database is added to the Manitoba Population Research Data Repository (see our report's online supplement at http://mchp-appserv.cpe.umanitoba.ca/deliverablesList.html); (b) we were most interested in the treatment and management of recently diagnosed cases, since their care reflects current practices and standards of care; and (c) sufficient observation time was needed after TB diagnosis to characterize the cohort on post-diagnosis healthcare use and outcomes in order to achieve several of the study objectives. At the same time, to ensure we had a sufficient number of active TB cases on which to conduct sub-group analyses, we used a 15-year period to define the cohort.

Individuals excluded from the Active TB Cohort: (a) had an invalid or missing personal health identification number (PHIN) in the Manitoba TB Registry; and (b) did not have a minimum of 365 days of healthcare coverage before the index date and 30 days of coverage after the index date. Individuals could only enter the cohort once, based on their first study index date in the Manitoba TB Registry.

The diagnosis date in the Manitoba TB Registry was the study index date. If an individual did not have a diagnosis date in the Manitoba TB Registry, then the TB Registry entry date was used as a proxy for the diagnosis date.

## Treated LTBI Cohort

The methods to define this cohort were based on the work of Rivest et al., who examined medication completion rates for a cohort of individuals receiving treatment for LTBI using the Régie de l'assurance maladie du Québec database [20]. This database contains information about all prescription dispensations for Québec residents. In addition, input from Manitoba's clinical and public health experts (e.g., co-authors Plourde and Larcombe; epidemiologists from MHSAL) guided the development of the inclusion and exclusion criteria for this cohort.

The Treated LTBI Cohort comprised individuals who had received at least one prescription dispensation for rifampin (RIF) or isoniazid (INH) between April 1, 1999 and March 31, 2014, common antibiotics used to treat LTBI. Individuals could only enter the Treated LTBI Cohort once, based on the first study index date in the prescription drug data. The study index date was the date of the first medication dispensation on or after April 1, 1999.

Individuals were excluded from the Treated LTBI Cohort if they: (a) had a diagnosis for leprosy within 30 days prior to the study index date; (b) had a prescription for a medication used to treat chronic bacterial infections within 14 days of their index RIF or INH prescription; (c) received a 2-day or 4-day course of RIF; (d) did not have at least 365 days of healthcare coverage before the index date and 30 days of coverage after the index date; and/or (e) had a prescription for RIF or INH in the 180-day period prior to the study index date. As well, individuals who initiated LTBI treatment with INH and continued treatment with RIF were not included in the Treated LTBI Cohort.

For individuals with an index prescription for INH, prescriptions used to treat active TB or chronic non-TB mycobacterial infections resulted in exclusion from the cohort. These prescriptions included RIF, rifabutin, ethambutol, pyrazinamide, amikacin, capreomycin, cycloserine, linezolid, moxifloxacin, para-aminosalicylic acid, or streptomycin.

For individuals with an index prescription for RIF, prescriptions used to treat active TB or chronic non-TB mycobacterial infections resulted in exclusion from the cohort. These prescriptions included INH, clofazimime, ethambutol, pyrazinamide, amikacin, capreomycin, cycloserine, linezolid, moxifloxacin, para-aminosalicylic acid, or streptomycin, and prescriptions used to treat other chronic bacterial infections (such as methicillin-resistant Staphylococcus aureus) including azithromycin, cefazolin, cefotaxime, cefoxitin, ceftriaxone, cefuroxime, ciprofloxacin, clarithromycin, clindamycin, cloxacillin, cycloserine, dapsone, daptomycin, doxycycline, erythromycin, flucloxacillin, fusidic acid, gentamicin, imipenem, levofloxacin, meropenem, minocycline, mupirocin, sulfamethoxazole/trimethoprim, or vancomycin. These medications were identified in DPIN using ATC codes.

## Matched Cohorts

For Objective 3, we focused on characterizing the healthcare use of the Active TB Cohort. We completed a parallel analysis for the Treated LTBI Cohort, which is reported as supplemental information (see Appendix 4). We selected matched controls for comparison purposes.

To develop the matched cohorts, we worked with a subset of the Active TB Cohort and a subset of the Treated LTBI Cohort. Specifically, we limited our attention to individuals in each of these cohorts who had at least 720 days (i.e., two years) of healthcare coverage following the study index date.

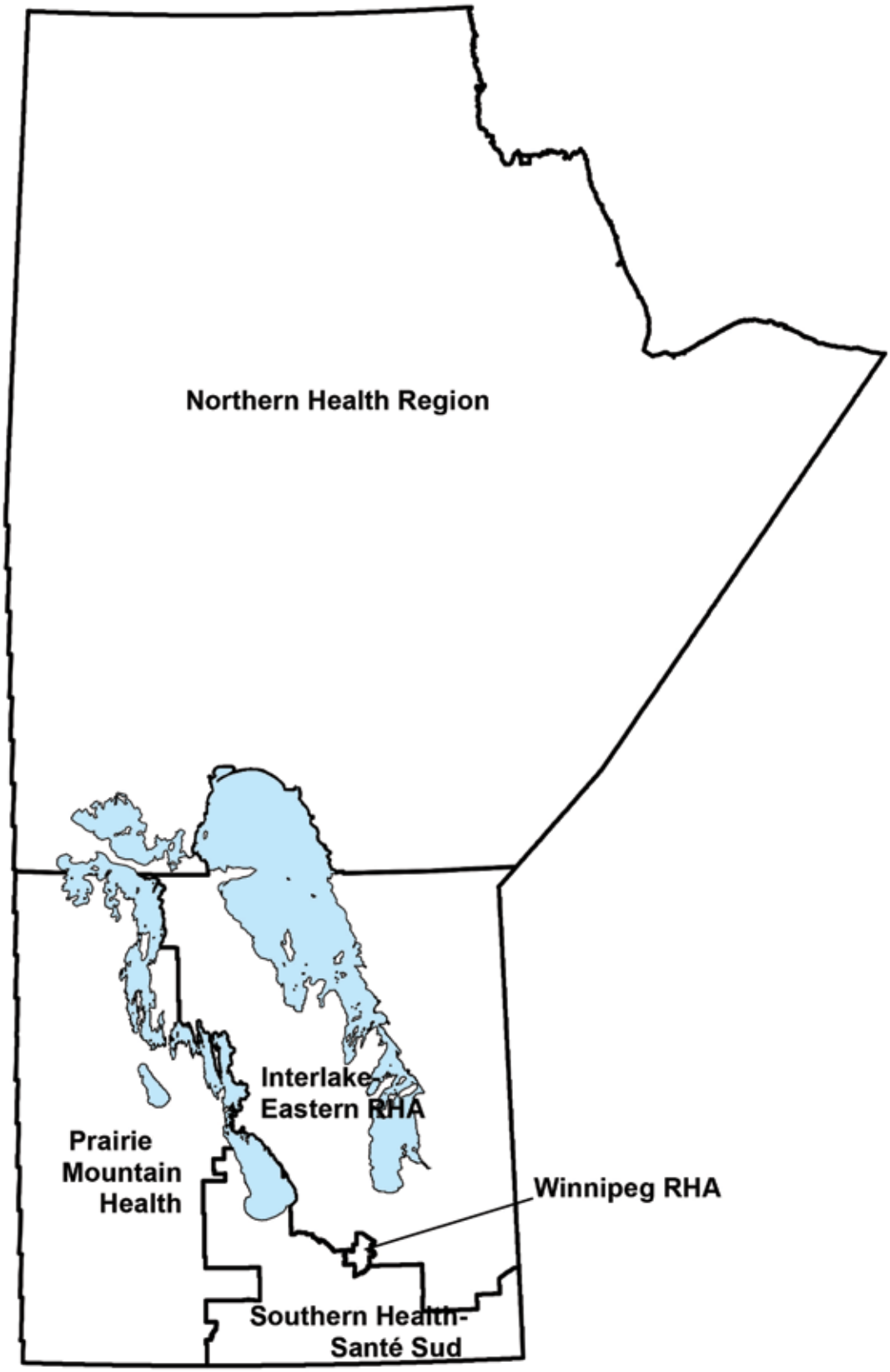
The controls were matched on sex, birth year (within one year of the case birth date), First Nations status, and residence location at the study index date. Residence location was defined using: (a) health region districts, which are subdivisions of health regions (70 in total) defined primarily based on municipal code and some postal codes; and (b) Winnipeg regions called neighborhood clusters (25 in total). Controls were required to have continuous health insurance coverage from 365 days prior to the study index date to 720 days after the index date.

The matched cohorts excluded all individuals who were in the Active TB Cohort, in the Treated LTBI Cohort, or who were identified in the Manitoba TB Registry as a contact of one or more individuals in the Active TB Cohort. Up to five controls were selected for each member of the Active TB and Treated LTBI Cohorts; controls were selected without replacement. First Nations status for matched controls was defined from the INAC Status Registry and supplemented with selected municipality codes (i.e., "A" codes). Children of First Nations mothers, as identified from the Population Registry, were also classified as being of First Nations origin.

# Characterizing the Study Cohorts

All of the study cohorts were described using socio-demographic variables. These included age (0-18 years, 19-44 years, 45-64 years, 65+ years), sex, income quintile (Q1 is the lowest quintile and Q5 is the highest), and health region (Winnipeg health region, non-Winnipeg health region). The non-Winnipeg health regions were classified as rural north (Northern Health Region) and rural south (Interlake-Eastern RHA, Prairie Mountain Health, and Southern Health-Santé Sud); the community of Churchill was assigned to the rural north region (Figure 2.2). We further characterized each cohort on index year period (1999/2000-2003/04, 2004/05-2008/09, 2009/10-2013/14) and Charlson comorbidity score [36]. The comorbidity score was based on data for the 360-day period prior to the study index date and was defined using diagnosis codes in both hospital discharge abstracts and physician billing claims. All other measures were defined as of the study index date. Appendix 2 contains information about the specific diagnoses used to produce the Charlson comorbidity score.

**Figure 2.2: Map of Manitoba's Health Regions**



We also defined specific comorbid conditions for the study cohorts based on validated algorithms defined in previous studies, including diabetes, rheumatoid arthritis, chronic obstructive pulmonary disease, heart disease, HIV, and chronic kidney disease. The diagnosis codes used to ascertain individuals with these conditions in hospital abstracts and physician billing claims are found in Appendix 3. We used the same 360-day period prior to the study index date to ascertain these comorbid conditions for the study cohorts.

For the Active TB Cohort, information from the Manitoba TB Registry was used to define the case criteria for TB diagnosis to determine whether this was a new TB diagnosis or a subsequent (i.e., recurrent) diagnosis and to classify individuals as pulmonary (i.e., infectious) or non-pulmonary TB cases (note: there were no individuals classified as both pulmonary and non-pulmonary; a few cases did, however, have missing information as to whether they were pulmonary or non-pulmonary cases). Non-pulmonary TB involves organs other than the lungs, such as the lymph nodes, abdomen, skin, joints, or bones. The Active TB Cohort was characterized using information about population of origin from the Manitoba TB Registry.

For the Active TB Cohort, Treated LTBI Cohort, and their matched cohorts, we linked to the INAC Status Registry. This linkage was used to distinguish Registered First Nations people from non-First Nations individuals. The limitations of these data as per the Indian Act registered status have been noted earlier in this chapter. It is important to also note that no person can be identified in these data sets and confidentiality is maintained. The socio-demographic, population of origin, Registered First Nations status, and geographic characteristics of the Active TB and Treated LTBI Cohorts and their matched controls were described using means, standard deviations, frequencies, and percentages.

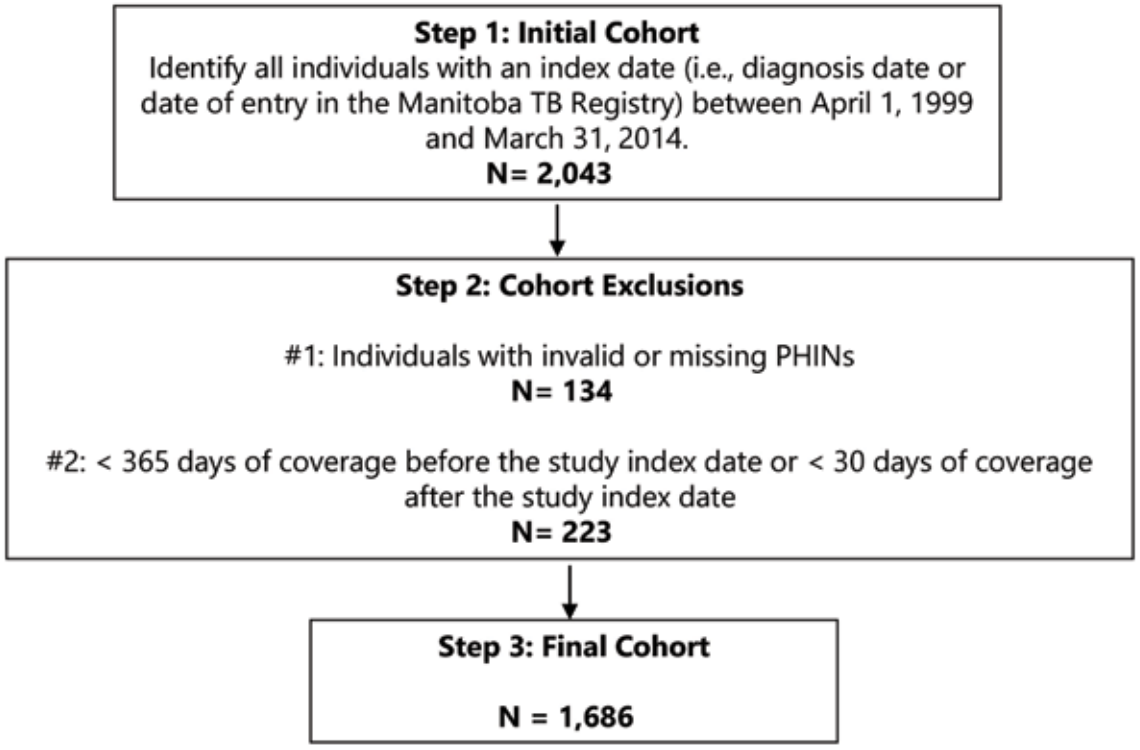
# Results

## Characteristics of the Active TB Cohort

A total of 2,043 individuals had a diagnosis date or entry date in the Manitoba TB Registry between April 1, 1999 and March 31, 2014 (Figure 2.3). After exclusion of individuals with invalid or missing PHINs (6.6%) and incomplete coverage (10.9%), a total of 1,686 individuals comprised the Active TB Cohort.

Of the 357 individuals who were excluded because they had an invalid or missing PHIN or did not meet the coverage requirements, 45.4% were aged 19-44 years, 43.4% were Winnipeg residents, but another 38.9% were missing information about health region. Almost half (40.9%) were foreign-born individuals, although another 6.7% had missing information about population of origin.

**Figure 2.3: Study Flow Chart for the Active TB Cohort**



As Table 2.1 reveals, more than half (55.6%) of the individuals in the Active TB Cohort were male and 15.1% were in the youngest age group (0-18 years). Almost half of the cohort members (47.9%) were aged 19-44 years.

**Table 2.1: Sociodemographic Characteristics of Active TB Cohort**

| | Pulmonary n= 1,027 | | Non-Pulmonary n= 652 | | Overall n= 1,686 | |
|---|---|---|---|---|---|---|
| | Count | Percent | Count | Percent | Count | Percent |
| **Age Group, Years** | | | | | | |
| 0-18 | 78 | 7.6% | 170 | 26.1% | 255 | 15.1% |
| 19-44 | 540 | 52.6% | 268 | 41.1% | 808 | 47.9% |
| 45-64 | 274 | 26.7% | 143 | 21.9% | 417 | 24.7% |
| 65+ | 135 | 13.1% | 71 | 10.9% | 206 | 12.2% |
| **Sex** | | | | | | |
| Male | 614 | 59.8% | 322 | 49.4% | 937 | 55.6% |
| Female | 413 | 40.2% | 330 | 50.6% | 749 | 44.4% |
| **Population of Origin** | | | | | | |
| First Nations on-reserve | 461 | 44.9% | 267 | 41.0% | 733 | 43.5% |
| First Nations off-reserve | 220 | 21.4% | 99 | 15.2% | 320 | 19.0% |
| Foreign-born | 225 | 21.9% | 182 | 27.9% | 408 | 24.2% |
| Canadian-born non-First Nations | 120 | 11.7% | 101 | 15.5% | 221 | 13.1% |
| **Income Quintile** | | | | | | |
| Q1 (Lowest) | 542 | 52.8% | 350 | 53.7% | 894 | 53.0% |
| Q2 | 169 | 16.5% | 110 | 16.9% | 280 | 16.6% |
| Q3 | 79 | 7.7% | 56 | 8.6% | 136 | 8.1% |
| Q4 | 187 | 18.2% | 100 | 15.3% | 289 | 17.1% |
| Q5 (Highest) | 50 | 4.9% | 36 | 5.5% | 87 | 5.2% |
| **Health Region** | | | | | | |
| Rural North (including Churchill) | 464 | 45.2% | 252 | 38.7% | 720 | 42.7% |
| Rural South | 105 | 10.2% | 72 | 11.0% | 178 | 10.6% |
| Winnipeg | 458 | 44.6% | 328 | 50.3% | 788 | 46.7% |

Note: n= 7 individuals could not be classified as pulmonary or non-pulmonary

Almost two-thirds (62.5%) of the Active TB Cohort members were First Nations individuals (on or off-reserve) and 24.2% were foreign-born, based on population origin information in the Manitoba TB Registry. Close to half (42.7%) were from health regions in northern Manitoba and a similar number were residents of Winnipeg health region (46.7%). The lowest income quintile (Q1) accounted for 53.0% of individuals in the cohort; 5.2% were in the highest income quintile (Q5). Three quarters (76.6%) were diagnosed based on a positive culture. Almost all (96.0%) were new cases of active TB.

Using diagnosis information captured in the Manitoba TB Registry, a total of 1,027 individuals (60.9%) were identified as having pulmonary TB. Amongst pulmonary TB cases, 55.6% were male, while amongst non-pulmonary TB cases, 49.4% were male.

The total number of individuals in the Active TB Cohort was relatively consistent across the 15-year study period. A total of 29.3% of all cohort members had an index date in the first five years (fiscal years 1999/2000-2003/04), while 36.4% had an index date in the last five years (fiscal years 2009/10-2013/14). Amongst individuals with a diagnosis of pulmonary TB, 29.4% had a study index date in the first five-year time period and 36.4% had an index date in the last five-year time period, suggesting a slight increase in pulmonary cases over time. Amongst individuals with a diagnosis of non-pulmonary TB, 34.0% had a study index date in the first five-year time period and 31.9% had an index date in the last five years of the study period.

In terms of comorbid characteristics, almost two-thirds (59.8%) of the individuals in the Active TB Cohort had a Charlson comorbidity index score of 0 (most healthy; see

Table 2.2). The most common comorbid conditions that comprise the Charlson index and that were identified in the cohort were chronic pulmonary disease (15.8%), diabetes without complications (14.3%), and cancer (8.1%). Amongst those individuals who had a Charlson index score of zero, 59.0% had non-pulmonary TB and the remaining 41.0% had pulmonary TB. A cancer diagnosis was more prevalent amongst individuals with non-pulmonary TB (12.9%) than amongst individuals with pulmonary TB (5.2%). There were also differences between the two groups of active TB cases on other comorbid conditions that make up the Charlson index, including diabetes without complications, HIV, and renal disease (Table 2.2).

**Table 2.2: Comorbidity Characteristics of Active TB Cohort**

| | Pulmonary | | Non-Pulmonary | | Overall | |
|---|---|---|---|---|---|---|
| | n= 1,027 | | n = 652 | | n = 1,686 | |
| | Count | Percent | Count | Percent | Count | Percent |
| **Charlson Comorbidity Index Score** | | | | | | |
| 0 (Most Healthy) | 592 | 57.6% | 411 | 63.0% | 1,009 | 59.8% |
| 1-2 | 312 | 30.4% | 162 | 24.8% | 475 | 30% |
| 3+ (Less Healthy) | 123 | 12.0% | 79 | 12.1% | 202 | 12.0% |
| **Charlson Comorbid Conditions** | | | | | | |
| Myocardial Infarction | 10 | 1.0% | s | - | 15 | 0.9% |
| Congestive Heart Failure | 26 | 2.5% | 19 | 2.9% | 45 | 2.7% |
| Peripheral Vascular Disease | 12 | 1.2% | 9 | 1.4% | 21 | 1.2% |
| Cerebrovascular Disease | 14 | 1.4% | 12 | 1.8% | 26 | 1.5% |
| Dementia | 10 | 1.0% | 6 | 0.9% | 16 | 0.9% |
| Chronic Pulmonary Disease | 188 | 18.3% | 78 | 12.0% | 267 | 15.8% |
| Connective Tissue Disease-Rheumatic Disease | 18 | 1.8% | 13 | 2.0% | 31 | 1.8% |
| Peptic Ulcer Disease | 16 | 1.6% | 13 | 2.0% | 29 | 1.7% |
| Mild Liver Disease | 41 | 4.0% | 27 | 4.1% | 68 | 4.0% |
| Diabetes without complications | 182 | 17.7% | 59 | 9.0% | 241 | 14.3% |
| Diabetes with complications | 22 | 2.1% | 19 | 2.9% | 41 | 2.4% |
| Paraplegia and Hemiplegia | 7 | 0.7% | s | - | 11 | 0.7% |
| Renal Disease | 35 | 3.4% | 36 | 5.5% | 71 | 4.2% |
| Cancer | 53 | 5.2% | 84 | 12.9% | 137 | 8.1% |
| Moderate or Severe Liver Disease | 7 | 0.7% | 8 | 1.2% | 15 | 0.9% |
| Metastatic Carcinoma | 11 | 1.1% | 8 | 1.2% | 19 | 1.1% |
| HIV/AIDS | 27 | 2.6% | 6 | 0.9% | 33 | 2.0% |

s indicates data suppressed due to small numbers
Note: n= 7 individuals could not be classified as pulmonary or non-pulmonary

## Characteristics of the Treated LTBI Cohort

A total of 10,774 individuals had a prescription for INH or RIF in the study observation period (Figure 2.4); 40.7% of these individuals were excluded based on the criteria used to define the cohort. The vast majority of these exclusions were associated with a prescription for a medication used to treat chronic bacterial infections within 14 days of the index RIF or INH prescription. A total of 175 individuals were excluded because they had a 2- or 4-day course of RIF, which most likely represents post-exposure chemoprophylaxis prescribed for the prevention of invasive meningococcal disease and invasive Haemophilus influenza infections, respectively.

A total of 588 individuals were excluded because they did not meet the coverage requirements (or had a leprosy diagnosis, which was very rare). Amongst these excluded individuals, 57.0% were less than 19 years of age. In fact, a significant number (37.9%) of the excluded individuals were newborns. Almost half (44.4%) of individuals who did not meet the coverage requirements were new residents from outside of Canada.

**Figure 2.4: Study Flow Chart for Treated LTBI Cohort**

**Step 1: Initial Cohort**

Identify all individuals with a prescription of INH or RIF between April 1, 1999 and March 31, 2014
**N = 10,774 individuals**

**Step 2: Exclusions**

#1: For individuals with a prescription for INH only: exclude all individuals with a prescription for RIF, rifabutin, rifapentine, ethambutol, pyrazinamide, amikacin, capreomycin, cycloserine, linezolid, moxifloxacin, para-aminosalicylic acid, or streptomycin that is ± 14 days of the index date
**N = 561 individuals excluded**

#2: For individuals with a prescription for RIF: exclude all individuals with a prescription for INH, clofazimime, ethambutol, pyrazinamide, amikacin, azithromycin, capreomycin, cefazolin, cefotaxime, cefoxitin, ceftriaxone, cefuroxime, ciprofloxacin, clarithromycin, clindamycin, cloxacillin, cycloserine, dapsone, daptomycin, doxycycline, erythromycin, flucloxacillin, fusidic acid, gentamicin, imipenem, levofloxacin, linezolid, meropenem, minocycline, moxifloxacin, mupirocin, para-aminosalicylic acid, streptomycin, sulfamethoxazole/trimethoprim, or vancomycin ± 14 days after (and including) the index date
**N = 3,348 individuals excluded**

#3: Individuals with a prescription for INH or RIF up to 180 days prior to the index date
**N = 60 individuals excluded**

#4: < 365 days of coverage prior to the index date and < 30 days of coverage after the index date or a diagnosis for leprosy ≤ 30 days before the index date *
**N = 588 individuals excluded**

#5: 2-day courses of rifampin was excluded from the "treated LTBI" database because 2-day courses of rifampin are routinely prescribed for chemoprophylactic treatment of close contacts of persons with invasive meningococcal disease.
**N = 111 individuals excluded**

#6: 4-day courses of rifampin was excluded from the "treated LTBI" database because 4-day courses of rifampin are routinely prescribed for chemoprophylactic treatment of close contacts of persons with invasive *Haemophilus influenza* type b disease.
**N = 64 individuals excluded**

**Step 3: Final Cohort**

**N = 6,217 individuals**

* See Appendix 3 for diagnosis codes

Thus, the Treated LTBI Cohort was comprised of 6,217 individuals. Slightly more than half of these individuals (51.2%) were female and more than one-third (39.4%) were less than 19 years of age (Table 2.3). Two-thirds of the cohort members (66.7%) were Registered First Nations individuals based on information contained in the INAC Status Registry (note that we cannot identify individuals in the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations; information about population of origin is only available for active TB cases using information found in the Manitoba TB Registry). More than half (54.5%) of the individuals in this cohort were from the rural north. In addition, almost half of these individuals (48.0%) were in the lowest income quintile and 5.7% were in the highest income quintile.

**Table 2.3: Sociodemographic Characteristics of Treated LTBI Cohort (n = 6,217)**

| | Count | Percent |
|---|---|---|
| **Age Group, Years** | | |
| 0-18 | 2,450 | 39.4% |
| 19-44 | 2,347 | 37.8% |
| 45-64 | 1,164 | 18.7% |
| 65+ | 256 | 4.1% |
| **Sex** | | |
| Male | 3,029 | 48.7% |
| Female | 3,188 | 51.3% |
| **Registered First Nations Status** | | |
| First Nations | 4,149 | 66.7% |
| All Other Manitobans | 2,068 | 33.3% |
| **Income Quintile** | | |
| Q1 (Lowest) | 2,985 | 48.0% |
| Q2 | 1,075 | 17.3% |
| Q3 | 493 | 7.9% |
| Q4 | 1,308 | 21.0% |
| Q5 (Highest) | 356 | 5.7% |
| **Health Region** | | |
| Rural North (including Churchill) | 3,386 | 54.5% |
| Rural South | 766 | 12.3% |
| Winnipeg | 2,065 | 33.2% |

Individuals in the Treated LTBI Cohort were not equally distributed across the 15-year study period. Only 16.7% had an index date in the first five-year period from 1999/2000 to 2003/04, whereas 38.4% had an index date in the last five-year period from 2009/10 to 2013/14, revealing a substantial growth in the number of individuals treated for LTBI over time.

Sociodemographic characteristics of the Treated LTBI Cohort depended on region of residence. Amongst cohort members who were Winnipeg health region residents, one-quarter (24.2%) were in the youngest age group, while amongst non-Winnipeg health region residents, 47.0% were in this age group. Amongst Winnipeg health region residents, 55.1% were female, compared to 49.4% of non-Winnipeg health region residents.

In terms of comorbidity (Table 2.4), over three-quarters (76.5%) of the Treated LTBI Cohort had a Charlson comorbidity index summary score of 0 (most healthy). The most frequently diagnosed Charlson comorbid conditions in the Treated LTBI Cohort were diabetes without complications (8.6%), chronic pulmonary disease (7.5%), and renal disease (3.5%).

**Table 2.4: Comorbidity Characteristics of Treated LTBI Cohort (n= 6,217)**

| | Count | Percent |
|---|---|---|
| **Charlson Comorbidity Index Score** | | |
| 0 (Most Healthy) | 4,759 | 76.5% |
| 1-2 | 1,133 | 18.2% |
| 3+ (Less Healthy) | 325 | 5.2% |
| **Charlson Comorbid Conditions** | | |
| Myocardial Infarction | 34 | 0.5% |
| Congestive Heart Failure | 91 | 1.5% |
| Peripheral Vascular Disease | 65 | 1.0% |
| Cerebrovascular Disease | 51 | 0.8% |
| Dementia | 20 | 0.3% |
| Chronic Pulmonary Disease | 466 | 7.5% |
| Connective Tissue Disease-Rheumatic Disease | 165 | 2.7% |
| Peptic Ulcer Disease | 51 | 0.8% |
| Mild Liver Disease | 135 | 2.2% |
| Diabetes without complications | 533 | 8.6% |
| Diabetes with complications | 88 | 1.4% |
| Paraplegia and Hemiplegia | 14 | 0.2% |
| Renal Disease | 230 | 3.7% |
| Cancer | 142 | 2.3% |
| Moderate or Severe Liver Disease | 20 | 0.3% |
| Metastatic Carcinoma | 26 | 0.4% |
| HIV/AIDS | 32 | 0.5% |

Except for diabetes, comorbid conditions were less common in the Treated LTBI Cohort than in the Active TB Cohort. This is not surprising given the age differences between the two cohorts. For example, HIV/AIDs had a prevalence of 2.6% in the Active TB Cohort, and a prevalence of 0.5% in the Treated LTBI Cohort.

## Characteristics of the Matched Active TB and Disease-Free Cohorts

A total of 1,419 individuals of the 1,686 individuals in the Active TB Cohort had healthcare coverage extending from 365 days prior to the study index date to 720 days following the study index date. These cohort members were matched to a total of 7,078 TB disease-, LTBI treatment-, and TB contact-free individuals, indicating that virtually all active TB cases had the specified five matches.

As expected, the matched controls and active TB cases had the same distribution of age, sex, First Nations status, and residence location, because these characteristics were the basis for matching (Table 2.5). However, there were differences between the two groups on other characteristics that were not used in the matching process. A total of 46.2% of the matched cohort was in the lowest income quintile, compared to 54.6% of the Active TB Cohort. More than three-quarters (79.8%) of the matched cohort had a Charlson comorbidity index score of 0 (i.e., healthy), compared to 62.1% of the Active TB Cohort.

**Table 2.5: Sociodemographic and Comorbidity Characteristics of Matched Active TB and Disease-free Cohorts**

| | Matched Active TB Cohort (n = 1,419) | | Matched Disease-free Cohort (n = 7,078) | |
|---|---|---|---|---|
| | Count | Percent | Count | Percent |
| **Age Group, Years** | | | | |
| 0-18 | 235 | 16.6% | 1,163 | 16.4% |
| 19-44 | 710 | 50.0% | 3,572 | 50.5% |
| 45-64 | 334 | 23.5% | 1,640 | 23.2% |
| 65+ | 140 | 9.9% | 703 | 9.9% |
| **Sex** | | | | |
| Male | 787 | 55.5% | 3,927 | 55.5% |
| Female | 632 | 44.5% | 3,151 | 44.5% |
| **Income Quintile** | | | | |
| Q1 (Lowest) | 775 | 54.6% | 3,267 | 46.2% |
| Q2 | 231 | 16.3% | 1,252 | 17.7% |
| Q3 | 110 | 7.8% | 595 | 8.4% |
| Q4 | 235 | 16.6% | 1,518 | 21.4% |
| Q5 (Highest) | 68 | 4.8% | 446 | 6.3% |
| **Health Region** | | | | |
| Rural North (including Churchill) | 623 | 43.9% | 3,108 | 43.9% |
| Rural South | 151 | 10.6% | 745 | 10.5% |
| Winnipeg | 645 | 45.5% | 3,225 | 45.6% |
| **Charlson Comorbidity Index Score** | | | | |
| 0 (Most Healthy) | 881 | 62.1% | 5,650 | 79.8% |
| 1-2 | 400 | 28.2% | 1,264 | 17.9% |
| 3+ (Less Healthy) | 138 | 9.7% | 164 | 2.3% |
| **First Nations Status** | | | | |
| First Nations | 910 | 64.1% | 4,533 | 64.0% |
| All Other Manitobans | 509 | 35.9% | 2,545 | 36.0% |

## Characteristics of the Matched Treated LTBI and Disease-Free Cohorts

A total of 5,556 individuals amongst the 6,217 individuals in the Treated LTBI Cohort had healthcare coverage extending from 365 days prior to the study index date to 720 days following the study index date. These cohort members were matched to a total of 27,774 TB disease-, LTBI treatment-, and TB contact-free individuals. Similar to the findings for the Active TB Cohort, this indicates that virtually all individuals being treated for LTBI had the specified five matches.

As expected, the Treated LTBI Cohort members and controls had exactly the same distribution for the matching variables of age, sex, First Nations status, and residence location (Table 2.6). Similar to the findings for the Active TB Cohort, a larger percentage of the Treated LTBI Cohort (49.3%) than the matched group (43.5%) was in the lowest income quintile. Similarly, a higher percentage of the matched cohort (84.9%) had a Charlson comorbidity score of zero (most healthy) than the Treated LTBI Cohort (77.7%).

**Table 2.6: Sociodemographic and Comorbidity Characteristics of Matched Treated LTBI and Disease-free Cohorts**

| | Matched Treated LTBI Cohort (n = 5,556) | | Matched Disease-free Cohort (n = 27,774) | |
|---|---|---|---|---|
| | Count | Percent | Count | Percent |
| **Age Group, Years** | | | | |
| 0-18 | 2,258 | 40.6% | 11,218 | 40.4% |
| 19-44 | 2,095 | 37.7% | 10,558 | 38.0% |
| 45-64 | 1,008 | 18.1% | 5,014 | 18.1% |
| 65+ | 195 | 3.5% | 984 | 3.5% |
| **Sex** | | | | |
| Male | 2,689 | 48.4% | 13,445 | 48.4% |
| Female | 2,867 | 51.6% | 14,329 | 51.6% |
| **Income Quintile** | | | | |
| Q1 (Lowest) | 2,739 | 49.3% | 12,068 | 43.5% |
| Q2 | 972 | 17.5% | 4,544 | 16.4% |
| Q3 | 417 | 7.5% | 2,193 | 7.9% |
| Q4 | 1,127 | 20.3% | 6,543 | 23.6% |
| Q5 (Highest) | 301 | 5.4% | 2,426 | 8.7% |
| **Health Region** | | | | |
| Rural North (including Churchill) | 3,113 | 56.0% | 15,559 | 56.0% |
| Rural South | 660 | 11.9% | 3,300 | 11.9% |
| Winnipeg | 1,783 | 32.1% | 8,915 | 32.1% |
| **Charlson Comorbidity Index Score** | | | | |
| 0 (Most Healthy) | 4,317 | 77.7% | 23,569 | 84.9% |
| 1-2 | 986 | 17.7% | 3,853 | 13.9% |
| 3+ (Less Healthy) | 253 | 4.6% | 352 | 1.3% |
| **First Nations Status** | | | | |
| First Nations | 3,824 | 68.8% | 19,114 | 68.8% |
| All Other Manitobans | 1,732 | 31.2% | 8,660 | 31.2% |

# Chapter Summary

In this chapter, we described the data sources used to conduct this study. We described the process of developing the study cohorts that are the basis for analyses that we conduct in subsequent chapters.

We examined the population of origin, sociodemographic and comorbidity characteristics of the study cohorts. Overall, almost half of the Active TB Cohort were young adults under 45 years of age. Consistent with epidemiologic reports about active TB cases in Canada, the majority of individuals in the Active TB Cohort were First Nations individuals living on- or off-reserve and almost one-quarter were foreign-born individuals. More than one-third of the Treated LTBI Cohort was composed of children and youth under 19 years of age and almost half were in the lowest income quintile. More than half of the Treated LTBI Cohort were residents of northern Manitoba.

The process of matching the Active TB Cohort and the Treated LTBI Cohort using the selected matching variables was successful. This facilitates fair comparisons of these two cohorts for subsequent analyses, which focus on differences in healthcare utilization.

# Chapter 3:

# Validating Manitoba TB Registry Data and MCHP's Administrative Health Data

Our study, which linked the Manitoba TB Registry data to administrative health data in the Manitoba Population Research Data Repository housed at MCHP, provides a unique opportunity to examine the accuracy and completeness of the Manitoba TB Registry for conducting population-based studies about the health and healthcare use of active TB cases. Quality of administrative health data and Manitoba TB Registry data is an important contributor to the accuracy of studies that link these two data sources.

The validity of diagnosis codes in administrative data for identifying chronic and acute health conditions has been described in previous research [37]. Diagnosis codes are one of the most important components of administrative data and they have multiple uses. For example, they are used to develop study cohorts, estimate disease incidence and prevalence rates, measure comorbid conditions, and identify health outcomes.

A few studies have conducted validity investigations for TB diagnoses in administrative data. This information is particularly important for researchers and epidemiologists from jurisdictions who have access to administrative data but not to TB Registry data. Cross-jurisdictional studies about TB that rely solely on administrative databases are dependent on administrative data to accurately ascertain TB cases.

Shiff et al. examined the accuracy of diagnosis codes, including TB diagnosis codes, in the pediatric population (i.e., ≤20 years) for ascertaining health conditions [38]. Five conditions were validated in more than one study, including TB, which was examined in two studies. The latter of these two studies looked across multiple age groups to validate definitions for identifying individuals with TB in administrative data. Ronald et al. conducted a systematic review of studies that had used prescription drug administrative data, diagnosis codes, or laboratory data to ascertain patients with TB in administrative data. [39]

In this chapter, we explore the completeness and accuracy of the Manitoba TB Registry and TB case information contained in administrative health data. The objectives were to:

1. Describe the completeness and accuracy of demographic, clinical, and treatment information for active TB cases in the TB Registry; and
2. Validate diagnoses for active TB in administrative health data.

# Overview of Methods

For Objective 1, we examined the completeness and accuracy of the Manitoba TB Registry. This assessment was guided by the information required to report on 13 performance indicators developed by the ITBS Program Data Management Committee. We reviewed the 13 performance indicators for the ITBS Program to identify key concepts on which to assess completeness of the Manitoba TB Registry (Table 3.1). These included contact assessment, treatment of TB, method of case detection (e.g., screening, symptoms), and symptoms of TB.

**Table 3.1: Manitoba TB Registry Data Evaluated for Completeness and Accuracy by Performance Indicator Category**

| Performance Indicator Category | Manitoba TB Registry Table and Field(s) |
|---|---|
| **TB Contact Investigation and Management** | Contact Table: contact_assess_compl; contact_case_num; location_id; place_of_contact; type_of_contact; degree_of_exposure; contact_assess_dt |
| **TB Disease Management** | Hospital Information Table: hospital_code; admitted_dt; discharged_dt |
| **TB Disease Identification** | Symptom Information Table: symptom_entry_id; symptom_id_num; symptom_dt |
| **LTBI Management** | Information about LTBI treatment is not contained in the Manitoba TB Registry |

Completeness (i.e., missing data) for the Manitoba TB Registry is described first. Then, selected elements of the Manitoba TB Registry are compared to their corresponding elements in administrative data sources, to assess the accuracy of the data in the Manitoba TB Registry. We examine demographic, population of origin, healthcare use, and clinical data in this correspondence analysis. This analysis was completed for the Active TB Cohort (see Chapter 2). We report on percent agreement, Cohen's kappa, and Spearman's correlation coefficient. The data sources in the Manitoba Population Research Data Repository housed at MCHP that were used to assess agreement included the Population Registry, hospital discharge abstracts, DPIN records, and Diagnostic Services Manitoba (DSM) and Cadham Provincial Laboratory (CPL) test results.

In addition, we estimated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of population of origin information in the Manitoba TB Registry for the Active TB Cohort. Individuals were classified as First Nations or non-First Nations based on the INAC Status Registry. We combined First Nations individuals living on- and off-reserve into a single First Nations Group. All other individuals in the Active TB Cohort were classified as non-First Nations.

For Objective 2, we estimated the validity of TB diagnoses in administrative data for the entire Manitoba population; we identified all individuals who had continuous health insurance coverage in the Population Registry between April 1, 2010 and March 31, 2015. We focused on this time period in order to describe the validity of TB diagnoses in recent years of administrative data. We used multiple years in order to ensure adequate numbers of TB cases to measure validity with good precision. Validity of TB diagnoses was estimated for new (i.e., incident) cases only; we excluded all individuals who: (a) had a TB diagnosis in the Manitoba TB Registry between April 1, 2010 and March 31, 2011; (b) were identified as a contact of a case with a TB diagnosis between April 1, 2010 and March 31, 2011; and/or (c) had a prescription for any of the following TB-related drugs between April 1, 2010 and March 31, 2011: INH, RIF, pyrazinamide, ethambutol, fixed-dose combinations of these four medications, Tuberculin for Tuberculin Skin Tests (TSTs), rifapentine, or rifabutin. For criterion (b) we used the date of diagnosis or the Manitoba TB Registry entry date of each active TB case to identify contacts for exclusion.

We classified individuals in the Manitoba population who met the inclusion criteria for this analysis into four mutually exclusive groups:

- **Group 1, Active TB Cases:** Individuals in the Manitoba population who met the health insurance coverage criteria and had a diagnosis date or entry date in the Manitoba TB Registry as an active TB case between April 1, 2011 and March 31, 2013 were classified as cases. We set our end date as 2013 in order to allow up to two years of post-diagnosis data for case ascertainment in administrative data.
- **Group 2, Treated LTBI Cases:** Individuals in the Manitoba population who met the health insurance coverage criteria and who had a prescription for RIF or INH between April 1, 2011 and March 31, 2013 and no prescription for a drug used to treat a chronic bacterial infection (as per the development of the Treated LTBI Cohort) and neither a 2-day or 4-day course of RIF (as per the development of the Treated LTBI Cohort) were classified as treated LTBI individuals.
- **Group 3, TB Contacts:** Individuals in the Manitoba population who met the health insurance coverage criteria and were contacts of active TB cases between April 1, 2011 and March 31, 2013 using the TB diagnosis date or TB Registry entry date of the case to ascertain contacts were classified as contacts.
- **Group 4, Disease-, Treatment-, and Contact-Free Individuals:** All other individuals in the Manitoba population who met the health insurance coverage criteria and were not members of Groups 1, 2, or 3, were classified into this latter group.

Subsequently, all individuals in Group 1 were classified as TB cases and all individuals in Groups 2, 3, and 4 were classified as non-cases.

We used the date of first diagnosis, Registry entry, or dispensation of a prescription medication on or after April 1, 2011 to assign individuals to one of these groups. For Group 1, the study index date was the date of TB diagnosis or the entry date in the Manitoba TB Registry for TB cases. For Group 2, the study index date was the date of the first prescription for RIF or INH. For Group 3, the study index date was the case date for a contact of an active TB case. Finally, for Group 4, the study index date was the first healthcare contact between April 1, 2011 and March 31, 2013 or if an individual has no healthcare contacts between these dates, the study index date was a randomly-selected date between April 1, 2011 and March 31, 2013.

We searched each individual's hospital discharge abstracts (inpatient only) and physician billing claims (outpatient only) to identify TB diagnoses. The relevant ICD codes were: ICD-9-CM 010-018 and ICD-10-CA A15-A19. The TB diagnosis could appear in any diagnosis field in the hospital discharge abstract. The date of admission recorded in the hospital discharge abstract was the reference date for comparison with the study index date.

The following accuracy estimates were calculated: sensitivity, specificity, PPV, NPV, Youden's index (sensitivity + [1 – specificity]), and Cohen's kappa; the latter is a chance-adjusted measure of agreement [40,41]. The interpretation of Cohen's kappa is: $\kappa < 0.20$ is poor chance-adjusted agreement, $0.20 \leq \kappa \leq 0.39$ is fair chance-adjusted agreement, $0.40 \leq \kappa \leq 0.59$ is moderate chance-adjusted agreement, $0.60 \leq \kappa \leq 0.79$ is good chance-adjusted agreement, $0.80 \leq \kappa \leq 0.89$ is very good chance-adjusted agreement, and $\kappa \geq 0.90$ is excellent agreement. In addition, 95% confidence intervals were computed for each of these measures, except for Youden's index, because its distributional properties are not well defined.

Nine case ascertainment algorithms were applied to the administrative data; these algorithms were based on different periods of observation time and different administrative data sources. In these algorithms, H refers to an inpatient hospital discharge abstract and P refers to an outpatient physician billing claim. For example, Algorithm 1 classifies an individual as a TB case in administrative data if he/she has at least one hospital discharge abstract with a TB diagnosis code in the one-year period on or after the study index date. Algorithm 3 classifies an individual as a TB case if he/she has at least one hospital discharge abstract or at least one physician billing claim with a TB diagnosis code in the one-year period on or after the study index date.

The first six case ascertainment algorithms are based on either one or two years of data on or after the study index date. The last three case ascertainment algorithms are based on two years of data before or after the study index date.

- Algorithm 1: 1+ H in a one-year period (on or after the index date)
- Algorithm 2: 1+ P in a one-year period (on or after the index date)
- Algorithm 3: 1+ H or 1+ P in a one-year period (on or after the index date)
- Algorithm 4: 1+ H or 2+ P in a one-year period (on or after the index date)
- Algorithm 5: 1+ H or 1+ P in a two-year period (on or after the index date)
- Algorithm 6: 1+ H or 2+ P in a two-year period (on or after the index date)
- Algorithm 7: 1+ H in a two-year period (before and on or after the index date)
- Algorithm 8: 1+ P in a two-year period (before and on or after the index date)
- Algorithm 9: 1+ H or 1+ P in a two-year period (before and on or after the index date)

# Results

## Completeness of the Manitoba TB Registry

Complete information about the assessment of data quality (i.e., missing, valid/invalid, and outlier observations) based on the routine data quality reporting conducted by MCHP is contained in this report's Online Supplement at http://mchp-appserv.cpe.umanitoba.ca/deliverablesList.html. In general, we found that there was little missing or invalid information for most fields in the Manitoba TB Registry. Therefore, we highlight completeness information for only selected elements of the Registry.

Method of case detection, recorded in the case table, was complete for 89.2% of records in the Manitoba TB Registry. The case table contains information about the treatment outcome; this field was missing information for 55.4% of records in the Manitoba TB Registry, which was much higher than for most other fields.

The contact table (Appendix Table 1.5) contains a variable pertaining to whether the contact assessment is complete and requires further follow-up surveillance; we found that there was missing information on this variable for approximately half (i.e., 51.6%) of records in the Manitoba TB Registry. As well, information in the contact table about where the contact occurred was missing for 42.7% of entries in the Registry; again, this was much higher than for the majority of other fields in the Registry. Information about category of place of contact and type of contact both contained less than 1% missing data.

Information about TB treatment is contained in the daily drug table, several Direct Observed Therapy (DOT) tables, drug reaction, and drug summary tables (Appendix Tables 1.7-1.12). In the daily drug table, information about the date an individual started taking a drug was complete for 99.9% of records and information about the date an individual finished taking a drug was complete for 89.1% of records. Information about the reason an individual stopped taking a drug was provided in 81.3% of records. The drug name was complete for 100% of records and drug dosage information was complete for 99.9% of records. Information in the other drug tables was largely complete; for example, drug reaction information was complete for 99.9% of records.

The symptom table (Appendix Table 1.28) records a field containing the type of symptom, which was complete for 99.6% of records, and a field about the symptom onset date, which was complete for 98.9% of records. We further examined the specific types of symptoms that were reported to ascertain if we could identify cough symptoms, as per information required to report on the ITBS performance indicators. Cough was reported for 51 (3.0%) of individuals in the Active TB Cohort when we matched on the case identification number (to ensure that we were matching a single episode of active TB). Thus, there is limited information about cough symptoms in the Manitoba TB Registry.

## Accuracy of the Manitoba TB Registry

**Demographic Characteristics.** We investigated the accuracy of the demographic characteristics of age at the date of diagnosis/TB Registry entry, sex, health region, and six-digit postal code (Table 3.2). We compared the characteristics of the Active TB Cohort (n = 1,686) in the Manitoba TB Registry to those in the Population Registry. The agreement statistics were estimated overall, and then stratified by 5-year time periods and region (Winnipeg and non-Winnipeg).

For year of birth, we observed 99.3% agreement between the Manitoba TB Registry and the Population Registry. Cohen's kappa coefficient was 0.99, which indicates excellent agreement. Percent agreement was consistent over time, and ranged from 98.8% in the five-year period from fiscal years 1999/2000-2003/04 to 99.8% in the five-year period from 2009/10-2013/14. Agreement was 99.4% for residents outside of Winnipeg and 99.2% for residents from Winnipeg. There was no missing information on age in the Manitoba TB Registry for the Active TB Cohort.

The results for sex were similar; there was 99.7% overall agreement between the Manitoba TB Registry and the Population Registry, and the kappa statistic was 0.99. There was little variation by region of residence or by time period in these agreement measures. There was no missing information on sex for the Active TB Cohort.

Percent agreement for the Manitoba TB Registry and the Population Registry on six-digit postal code was lower (69.7%); the kappa statistic was 0.70, which indicates good agreement (Table 3.2). Percent agreement was lower for Winnipeg health region residents (57.6%) than it was for non-Winnipeg residents (80.2%). Moreover, it was lower in the first five years of the study period (1999/2000-2003/04) at 62.4% than it was in the most recent five years of the study period (2009/10-2013/14) at 77.0%. However, the data were largely complete; only 11 individuals in the Active TB Cohort were missing postal code information in the Manitoba TB Registry.

When we compared health region of residence in the Manitoba TB Registry to the corresponding information in the Population Registry, we observed a high percent agreement (93.2%) and the kappa statistic was 0.88 (i.e., very good agreement). The percent agreement was slightly higher for non-Winnipeg residents (94.6%) than for Winnipeg residents (91.6%). Percent agreement was only slightly lower in the first five years (91.8%) than in the last five years (94.1%). There were very few individuals who were missing health region information in the Manitoba TB Registry.

**Population of Origin**. Information on population of origin in the Manitoba TB Registry was compared to the INAC Status Registry. The kappa statistic had a value of 0.94, indicating excellent agreement (Table 3.2). The sensitivity of the Manitoba TB Registry was 0.98 and specificity was 0.98. Percent agreement was high overall, as well as by age group, year, and region. For example, in the 0-18 age group, there was 99.2% agreement between the Manitoba

TB Registry and the INAC Status Registry; in the 45+ age group, the percent agreement was 97.1%. For non-Winnipeg health region residents, the percent agreement was 99.2%, and for Winnipeg health region residents, it was 95.6%.

**Date of Death.** For date of death, the kappa statistic was 0.98, indicating excellent agreement between the Manitoba TB Registry and the Population Registry. There was no variation by region of residence or time period. These statistics were based on data for 76 individuals in the Active TB Cohort who had a date of death recorded in the Manitoba TB Registry during the study observation period.

**Clinical Characteristics.** For case criteria in the Manitoba TB Registry, our comparison was test results reported in DSM data. We excluded active TB cases with a diagnosis date prior to April 1, 2006, because there were no DSM data available for the Active TB Cohort prior to this date. We also excluded all individuals in the Active TB Cohort with DSM specimen collection dates more than 60 days from their diagnosis date. Thus, the results were based on data for 949 individuals. The kappa statistic was estimated as 0.95, which indicates excellent agreement.

For HIV status, we compared the Manitoba TB Registry with serology information from the CPL data, which is the only public laboratory that conducts HIV tests in the province; linkable information about HIV status was captured in the CPL data from 2006 onward. There were a total of 71 individuals in the study cohort who had positive HIV test information in the Manitoba TB Registry. The kappa statistic had a value > 0.99, which indicates excellent agreement.

**Prescription Drug Treatment Initiation.** Dates of prescription drug treatment recorded in the Manitoba TB Registry were compared to dates in DPIN for a selected number of prescription drugs (i.e., vitamin B6; ethambutol; INH; pyrazinamide; RIF). Overall, the dates for initiation of different medications (see Table 3.2) were in close agreement for the two sources. Spearman's correlation coefficient values ranged from 0.93 to 1.00.

**Date of Chest X-Ray.** Dates for chest x-rays recorded in the Manitoba TB Registry were compared to dates in physician billing claims. We looked for a physician billing claim that had a diagnosis code for TB in addition to a tariff code for a radiology service; there were a total of 368 individuals in the Manitoba TB Registry who met these criteria. Spearman's correlation for the dates was very high (0.92).

**Hospitalization.** We examined the accuracy of hospitalization information in the Manitoba TB Registry. Overall, 39.8% of the Active TB Cohort did not have hospitalization information recorded in the TB Registry. We also found that more than 99.0% of individuals who had hospitalization information recorded in the Manitoba TB Registry also had hospital information recorded in the administrative data. Estimates of agreement were high; the correlation between the hospital admission date recorded in the Manitoba TB Registry and hospital discharge abstracts was 0.99. Similarly, the correlation between the hospital discharge date recorded in the Manitoba TB Registry and hospital discharge abstract was 0.99.

We also examined the hospital identifier recorded in the Manitoba TB Registry and compared it to the identifier contained in hospital discharge abstracts. Cohen's kappa statistic was 0.97, which indicates excellent agreement.

**Table 3.2: Estimates of Validity for Selected Elements of the Manitoba TB Registry**

| Measure | TB Registry Data | Reference Standard Data | Statistic Used | Result | N Included |
|---|---|---|---|---|---|
| **Age at TB diagnosis** | Client Table: Birthdt | Age derived from the Population Registry | Spearman correlation coefficient | 1.00 (1.00 - 1.00) | 1,686 |
| **Sex** | Client Table: Orig_Sex | Sex in Population Registry | Kappa | 0.99 (0.99 - 1.00) | 1,686 |
| **Postal Code** | Address Table: Postal_Code | Six-digit postal code from the Population Registry | Kappa | 0.70 (0.68 - 0.72) | 1,675 |
| **Health Region** | Address Table: RHA | RHA as derived from address information in the Population Registry | Kappa | 0.88 (0.86 - 0.90) | 1,683 |
| **Population of Origin** | Client Table: Origin="S" (status First Nation) | INAC Status Registry & A-muncodes and children of First Nations mothers from Population Registry | Kappa | 0.94 (0.93 - 0.96) | 1,682 |
| | | | Sensitivity | 0.98 (0.97 - 0.99) | |
| | | | Specificity | 0.96 (0.94 - 0.97) | |
| | | | PPV | 0.98 (0.96 - 0.98) | |
| | | | NPV | 0.97 (0.95 - 0.98) | |
| | | | Youden's Index | 0.94 | |
| **Date of Death** | Case Table: Death_Dt | Population Registry | Spearman correlation coefficient | 0.99 (0.99 - 0.99) | 76 |
| **Clinical Characteristics** | Case Table: Case_Criteria | Diagnostic Services Manitoba | Kappa | 0.95 (0.92 - 0.97) | 949 |
| **HIV Test Result** | HIV Test Table: HIV_Result | Cadham Provincial Lab Data | Kappa | 1.00 (1.00 - 1.00) | 71 |
| **Prescription Drug Treatment Initiation** | Daily Drug Table: Drug_Start_Dt Drug_Name_ID (INH, EMB, PZA, RIF, or B6) & Direct Observed Therapy Drug List Table: Drug_Start_Dt Drug_Name_ID (INH, EMB, PZA, RIF, or B6) | Prescription Drug Data (DPIN) | Spearman correlation coefficient | | |
| | | | B6 | 0.94 (0.93 - 0.95) | 833 |
| | | | EMB | 1.00 (1.00 - 1.00) | 991 |
| | | | INH | 0.93 (0.93 - 0.94) | 1,333 |
| | | | PZA | 0.99 (0.99 - 0.99) | 1,146 |
| | | | RIF | 0.99 (0.99 - 0.99) | 1,304 |
| **Date of Chest X-Ray** | X-Ray Table: xray_location=1 (chest x-ray) Xray_DT | Physician billing claims Prefix='5' (radiology) | Spearman correlation coefficient | 0.92 (0.90 - 0.93) | 368 |
| **Hospital Admission Date** | Hospital Table: Admitted_Dt | Hospital Discharge Abstracts: Admdt (TB hospitalizations only, any diagnosis field) | Spearman Correlation Coefficient | 0.99 (0.99 - 1.00) | 1,001 |
| **Hospital Discharge Date** | Hospital Table: Discharged_Dt | Hospital Discharge Abstracts (TB hospitalizations only, any diagnosis field) | Spearman Correlation Coefficient | 0.99 (0.99 - 1.00) | 1,001 |
| **Location of Hospitalization** | Hospital Table: Hospital_Code | Hospital Discharge Abstracts (TB hospitalizations only, with TB identified in any diagnosis field) | Kappa | 0.97 (0.94 - 1.00) | 724 |

Note: B6 = Vitamin B6; EMB = Ethambutol; INH = isoniazid; PZA = Pyrazinamide; RIF = Rifampin

## Validity of TB Diagnoses in Administrative Health Data

In this section, we estimate Cohen's kappa, sensitivity, specificity, PPV, NPV, and Youden's index for TB algorithms (i.e., case definitions), which are based on TB diagnoses recorded in hospital discharge abstracts and physician billing claims. Our study cohort for this analysis was comprised of 180 individuals who were classified as TB cases based on information in the Manitoba TB Registry and 1,102,532 individuals in the Manitoba population who were classified as non-cases.

Table 3.3 reports the validity estimates for the entire cohort. The estimates vary substantially based on the data source and the time period used to ascertain TB cases in administrative health data. For Algorithm 1, which ascertained cases/non-cases based on the presence/absence of at least one diagnosis code in hospital discharge abstracts for the one-year period on or after the study index date, the kappa statistic was 0.55. This estimate suggests moderate chance-adjusted agreement between administrative data and the Manitoba TB Registry. Amongst all individuals identified as TB cases in the Manitoba TB Registry in the observation period, slightly less than half were also identified as having a TB diagnosis code in hospital discharge abstracts in the one-year period on or after the study index date (sensitivity = 0.48). Specificity was excellent (>0.99). PPV was 0.68, which suggests substantial misclassification in the administrative data; specifically, this estimate indicates that of all individuals who had a TB diagnosis in hospital discharge abstracts in this one-year period, only about two-thirds of these individuals also had a corresponding TB diagnosis in the Manitoba TB Registry. NPV was very high (i.e., > 0.99). Youden's index was almost equivalent to the estimate for sensitivity because of the very high value of specificity.

**Table 3.3: Validity Estimates for TB Diagnoses in Hospital Records and Physician Billing Claims**

| Algorithm | Cohen's Kappa* | Sensitivity* | Specificity* | Positive Predictive Value* | Negative Predictive Value* | Youden's Index |
|---|---|---|---|---|---|---|
| **Algorithm 1: 1+ H in a one-year period** (after the index date) | 0.55 (0.48 - 0.62) | 0.46 (0.39 - 0.53) | 1.00 (1.00 - 1.00) | 0.68 (0.59 - 0.76) | 1.00 (1.00 - 1.00) | 0.46 |
| **Algorithm 2: 1+ P in a one-year period** (after the index date) | 0.14 (0.12 - 0.16) | 0.89 (0.83 - 0.93) | 1.00 (1.00 - 1.00) | 0.07 (0.06 - 0.09) | 1.00 (1.00 - 1.00) | 0.89 |
| **Algorithm 3: 1+ H or 1+ P in a one-year period** (after the index date) | 0.14 (0.12 - 0.16) | 0.92 (0.87 - 0.95) | 1.00 (1.00 - 1.00) | 0.08 (0.07 - 0.09) | 1.00 (1.00 - 1.00) | 0.92 |
| **Algorithm 4: 1+ H or 2+ P in a one-year period** (after the index date) | 0.36 (0.32 - 0.40) | 0.87 (0.81 - 0.91) | 1.00 (1.00 - 1.00) | 0.22 (0.19 - 0.26) | 1.00 (1.00 - 1.00) | 0.87 |
| **Algorithm 5: 1+ H or 1+ P in a two-year period** (after the index date) | 0.09 (0.08 - 0.10) | 0.94 (0.90 - 0.97) | 1.00 (1.00 - 1.00) | 0.05 (0.04 - 0.06) | 1.00 (1.00 - 1.00) | 0.94 |
| **Algorithm 6: 1+ H or 2+ P in a two-year period** (after the index date) | 0.28 (0.25 - 0.31) | 0.90 (0.85 - 0.94) | 1.00 (1.00 - 1.00) | 0.17 (0.14 - 0.19) | 1.00 (1.00 - 1.00) | 0.90 |
| **Algorithm 7: 1+ H in a two-year period** (before and after the index date) | 0.77 (0.72 - 0.82) | 0.77 (0.70 - 0.82) | 1.00 (1.00 - 1.00) | 0.78 (0.71 - 0.83) | 1.00 (1.00 - 1.00) | 0.77 |
| **Algorithm 8: 1+ P in a two-year period** (before and after the index date) | 0.10 (0.08 - 0.11) | 0.89 (0.84 - 0.93) | 1.00 (1.00 - 1.00) | 0.05 (0.04 - 0.06) | 1.00 (1.00 - 1.00) | 0.89 |
| **Algorithm 9: 1+ H or 1+ P in a two-year period** (before and after the index date) | 0.10 (0.09 - 0.12) | 0.97 (0.94 - 0.99) | 1.00 (1.00 - 1.00) | 0.06 (0.05 - 0.06) | 1.00 (1.00 - 1.00) | 0.97 |

* indicates that these statistical measures have 95% confidence intervals.

For Algorithm 2, which focused on the validity of TB diagnoses in physician billing claims over a one-year period, sensitivity was much higher than for hospital records (0.89) and specificity was very high (>0.99). At the same time, PPV was very low (0.07). This value indicates that amongst all individuals who had a TB diagnosis in physician billing claims in a one-year period, less than 10% also had a TB diagnosis in the Manitoba TB Registry.

Applying Algorithm 3 to the administrative data, which classified individuals as TB cases if they had at least one diagnosis code in hospital records or physician billing claims in the one-year period after the index, a slightly higher sensitivity estimate (0.92) was observed with no loss of specificity (> 0.99). However, PPV was still very low (0.08). The kappa statistic was only 0.14, indicating poor agreement.

Algorithm 4 was similar to Algorithm 3 but required individuals to have at least one hospital record or at least two physician billing claims with a TB diagnosis in a one-year period in order to qualify as a TB case. This algorithm resulted in a modest decrease in sensitivity (0.88), but a large increase in PPV (0.22). This estimate indicates that amongst all individuals who had a TB diagnosis in hospital discharge abstracts or physician billing claims in a one-year period, close to one-quarter of them also had a TB diagnosis in the Manitoba TB Registry.

Algorithms 5 and 6 focused on the two-year period following the TB diagnosis date to ascertain TB cases. These algorithms produced only slight increases in sensitivity (0.94 and 0.90, respectively) when compared to Algorithms 3 and 4. PPV was lower for Algorithms 5 and 6 (0.05 and 0.17, respectively) than for Algorithms 3 and 4.

Algorithms 7, 8, and 9 focused on the two-year period before and after the study index date. Sensitivity was higher for Algorithm 7 (0.77), which was based on diagnosis codes in hospital records in this two-year period, when compared to Algorithm 1, which was based on diagnosis codes in hospital discharge abstract in a single year of data. As well, PPV (0.78) was higher for Algorithm 7 than for Algorithm 1. However, when both hospital records and physician billing claims were used for case ascertainment (i.e., Algorithms 8 and 9) in this two-year period, all validity estimates were virtually identical to the estimates for the other two-year observation periods (i.e., Algorithms 5 and 6).

Additional analyses were conducted; validity estimates were stratified by sex (not shown), age group, and region of residence. There were negligible differences between males and females in the validity of TB diagnosis codes in administrative data. When the validity estimates were stratified by age group (0-18 years, 19-44 years, 45+ years), substantial variation was observed (Table 3.4). Algorithm 1, which required at least one TB diagnosis in hospital discharge abstracts or physician billing claims in a one-year period to classify an individual as a TB case, resulted in sensitivity estimates of 0.25, 0.57 and 0.37 in the three age groups, respectively. The corresponding PPV estimates were 0.40, 0.80 and 0.58, respectively. The highest PPV estimate obtained when the data were stratified by age group was observed in the 19-44 age group for Algorithm 7 (PPV = 0.85).

**Table 3.4: Estimates of Validity of TB Diagnoses in Hospital Records and Physician Billing Claims, by Age Group**

| Algorithm | Age Group | Cohen's Kappa* | Sensitivity* | Specificity* | Positive Predictive Value* | Negative Predictive Value* | Youden's Index |
|---|---|---|---|---|---|---|---|
| **Algorithm 1: 1+ H in a one-year period** (after the index date) | 0-18 | 0.31 (0.12-0.50) | 0.25 (0.12-0.45) | 1.00 (1.00-1.00) | 0.40 (0.20-0.64) | 1.00 (1.00-1.00) | 0.25 |
| | 19-44 | 0.67 (0.58-0.75) | 0.57 (0.47-0.67) | 1.00 (1.00-1.00) | 0.80 (0.69-0.88) | 1.00 (1.00-1.00) | 0.57 |
| | 45+ | 0.45 (0.33-0.57) | 0.37 (0.26-0.49) | 1.00 (1.00-1.00) | 0.58 (0.42-0.72) | 1.00 (1.00-1.00) | 0.37 |
| **Algorithm 2: 1+ P in a one-year period** (after the index date) | 0-18 | 0.08 (0.05-0.12) | 0.88 (0.69-0.96) | 1.00 (1.00-1.00) | 0.04 (0.03-0.07) | 1.00 (1.00-1.00) | 0.87 |
| | 19-44 | 0.18 (0.15-0.22) | 0.89 (0.81-0.93) | 1.00 (1.00-1.00) | 0.10 (0.08-0.12) | 1.00 (1.00-1.00) | 0.88 |
| | 45+ | 0.12 (0.09-0.15) | 0.90 (0.80-0.95) | 1.00 (1.00-1.00) | 0.06 (0.05-0.08) | 1.00 (1.00-1.00) | 0.90 |
| **Algorithm 3: 1+ H or 1+ P in a one-year period** (after the index date) | 0-18 | 0.09 (0.05-0.12) | 0.92 (0.74-0.98) | 1.00 (1.00-1.00) | 0.05 (0.03-0.07) | 1.00 (1.00-1.00) | 0.91 |
| | 19-44 | 0.19 (0.16-0.22) | 0.93 (0.86-0.96) | 1.00 (1.00-1.00) | 0.11 (0.09-0.13) | 1.00 (1.00-1.00) | 0.93 |
| | 45+ | 0.12 (0.09-0.15) | 0.92 (0.82-0.96) | 1.00 (1.00-1.00) | 0.06 (0.05-0.08) | 1.00 (1.00-1.00) | 0.91 |
| **Algorithm 4: 1+ H or 2+ P in a one-year period** (after the index date) | 0-18 | 0.19 (0.12-0.26) | 0.83 (0.64-0.93) | 1.00 (1.00-1.00) | 0.11 (0.07-0.16) | 1.00 (1.00-1.00) | 0.83 |
| | 19-44 | 0.49 (0.42-0.55) | 0.88 (0.79-0.93) | 1.00 (1.00-1.00) | 0.34 (0.28-0.40) | 1.00 (1.00-1.00) | 0.87 |
| | 45+ | 0.32 (0.26-0.39) | 0.87 (0.76-0.93) | 1.00 (1.00-1.00) | 0.20 (0.16-0.25) | 1.00 (1.00-1.00) | 0.87 |
| **Algorithm 5: 1+ H or 1+ P in a two-year period** (after the index date) | 0-18 | 0.06 (0.04-0.09) | 1.00 (0.86-1.00) | 1.00 (1.00-1.00) | 0.03 (0.02-0.05) | 1.00 (1.00-1.00) | 1.00 |
| | 19-44 | 0.13 (0.11-0.15) | 0.94 (0.87-0.97) | 1.00 (1.00-1.00) | 0.07 (0.06-0.09) | 1.00 (1.00-1.00) | 0.93 |
| | 45+ | 0.07 (0.05-0.09) | 0.93 (0.84-0.97) | 1.00 (1.00-1.00) | 0.04 (0.03-0.05) | 1.00 (1.00-1.00) | 0.93 |
| **Algorithm 6: 1+ H or 2+ P in a two-year period** (after the index date) | 0-18 | 0.17 (0.11-0.23) | 0.96 (0.80-0.99) | 1.00 (1.00-1.00) | 0.09 (0.06-0.14) | 1.00 (1.00-1.00) | 0.96 |
| | 19-44 | 0.40 (0.34-0.46) | 0.89 (0.81-0.93) | 1.00 (1.00-1.00) | 0.26 (0.21-0.31) | 1.00 (1.00-1.00) | 0.88 |
| | 45+ | 0.23 (0.18-0.28) | 0.90 (0.80-0.95) | 1.00 (1.00-1.00) | 0.13 (0.10-0.17) | 1.00 (1.00-1.00) | 0.90 |
| **Algorithm 7: 1+ H in a two-year period** (before and after the index date) | 0-18 | 0.43 (0.24-0.62) | 0.38 (0.21-0.57) | 1.00 (1.00-1.00) | 0.50 (0.29-0.71) | 1.00 (1.00-1.00) | 0.37 |
| | 19-44 | 0.86 (0.80-0.91) | 0.86 (0.78-0.92) | 1.00 (1.00-1.00) | 0.85 (0.76-0.91) | 1.00 (1.00-1.00) | 0.86 |
| | 45+ | 0.75 (0.67-0.84) | 0.77 (0.65-0.86) | 1.00 (1.00-1.00) | 0.74 (0.62-0.83) | 1.00 (1.00-1.00) | 0.77 |
| **Algorithm 8: 1+ P in a two-year period** (before and after the index date) | 0-18 | 0.07 (0.04-0.10) | 0.88 (0.69-0.96) | 1.00 (1.00-1.00) | 0.04 (0.02-0.05) | 1.00 (1.00-1.00) | 0.87 |
| | 19-44 | 0.13 (0.10-0.15) | 0.89 (0.81-0.93) | 1.00 (1.00-1.00) | 0.07 (0.06-0.08) | 1.00 (1.00-1.00) | 0.88 |
| | 45+ | 0.08 (0.06-0.10) | 0.92 (0.82-0.96) | 1.00 (1.00-1.00) | 0.04 (0.03-0.06) | 1.00 (1.00-1.00) | 0.91 |
| **Algorithm 9: 1+ H or 1+ P in a two-year period** (before and after the index date) | 0-18 | 0.07 (0.04-0.10) | 0.92 (0.74-0.98) | 1.00 (1.00-1.00) | 0.04 (0.03-0.06) | 1.00 (1.00-1.00) | 0.91 |
| | 19-44 | 0.14 (0.11-0.16) | 0.98 (0.93-0.99) | 1.00 (1.00-1.00) | 0.07 (0.06-0.09) | 1.00 (1.00-1.00) | 0.98 |
| | 45+ | 0.09 (0.07-0.11) | 0.98 (0.91-1.00) | 1.00 (1.00-1.00) | 0.05 (0.04-0.06) | 1.00 (1.00-1.00) | 0.98 |

* indicates that these statistical measures have 95% confidence intervals.

When the validity estimates were stratified by region of residence (Table 3.5), there were differences amongst residents of the rural north, rural south, and Winnipeg health regions. For example, for Algorithm 1, sensitivity estimates were 0.55, 0.41, and 0.36 for individuals in these three regions, respectively. PPV estimates were 0.72, 0.50, and 0.68, respectively. In general, PPV estimates were higher for residents of the rural north than for residents of the rural south and Winnipeg health regions.

**Table 3.5: Estimates of Validity of TB Diagnoses in Hospital Records and Physician Billing Claims, by Health Region of Residence**

| Algorithm | Health Regions | Cohen's Kappa* | Sensitivity* | Specificity* | Positive Predictive Value* | Negative Predictive Value* | Youden's Index |
|---|---|---|---|---|---|---|---|
| **Algorithm 1: 1+ H in a one-year period** (after the index date) | Rural North (including Churchill | 0.62 (0.53-0.71) | 0.55 (0.45-0.65) | 1.00 (1.00-1.00) | 0.72 (0.60-0.81) | 1.00 (1.00-1.00) | 0.55 |
| | Rural South | 0.45 (0.23-0.67) | 0.41 (0.22-0.64) | 1.00 (1.00-1.00) | 0.50 (0.27-0.73) | 1.00 (1.00-1.00) | 0.41 |
| | Winnipeg | 0.47 (0.35-0.58) | 0.36 (0.26-0.47) | 1.00 (1.00-1.00) | 0.68 (0.51-0.80) | 1.00 (1.00-1.00) | 0.36 |
| **Algorithm 2: 1+ P in a one-year period** (after the index date) | Rural North (including Churchill | 0.32 (0.27-0.38) | 0.85 (0.76-0.91) | 1.00 (0.99-1.00) | 0.20 (0.16-0.24) | 1.00 (1.00-1.00) | 0.84 |
| | Rural South | 0.06 (0.03-0.09) | 0.71 (0.47-0.87) | 1.00 (1.00-1.00) | 0.03 (0.02-0.05) | 1.00 (1.00-1.00) | 0.70 |
| | Winnipeg | 0.10 (0.07-0.12) | 0.99 (0.92-1.00) | 1.00 (1.00-1.00) | 0.05 (0.04-0.06) | 1.00 (1.00-1.00) | 0.98 |
| **Algorithm 3: 1+ H or 1+ P in a one-year period** (after the index date) | Rural North (including Churchill | 0.34 (0.28-0.39) | 0.90 (0.83-0.95) | 1.00 (0.99-1.00) | 0.21 (0.17-0.25) | 1.00 (1.00-1.00) | 0.90 |
| | Rural South | 0.06 (0.03-0.09) | 0.76 (0.53-0.90) | 1.00 (1.00-1.00) | 0.03 (0.02-0.05) | 1.00 (1.00-1.00) | 0.76 |
| | Winnipeg | 0.10 (0.07-0.12) | 0.99 (0.92-1.00) | 1.00 (1.00-1.00) | 0.05 (0.04-0.06) | 1.00 (1.00-1.00) | 0.98 |
| **Algorithm 4: 1+ H or 2+ P in a one-year period** (after the index date) | Rural North (including Churchill | 0.49 (0.42-0.56) | 0.82 (0.73-0.88) | 1.00 (1.00-1.00) | 0.35 (0.29-0.42) | 1.00 (1.00-1.00) | 0.82 |
| | Rural South | 0.21 (0.11-0.31) | 0.71 (0.47-0.87) | 1.00 (1.00-1.00) | 0.12 (0.07-0.20) | 1.00 (1.00-1.00) | 0.71 |
| | Winnipeg | 0.30 (0.25-0.36) | 0.97 (0.90-0.99) | 1.00 (1.00-1.00) | 0.18 (0.14-0.22) | 1.00 (1.00-1.00) | 0.97 |
| **Algorithm 5: 1+ H or 1+ P in a two-year period** (after the index date) | Rural North (including Churchill | 0.28 (0.23-0.32) | 0.94 (0.87-0.97) | 0.99 (0.99-0.99) | 0.16 (0.13-0.20) | 1.00 (1.00-1.00) | 0.93 |
| | Rural South | 0.04 (0.02-0.06) | 0.76 (0.53-0.90) | 1.00 (1.00-1.00) | 0.02 (0.01-0.03) | 1.00 (1.00-1.00) | 0.76 |
| | Winnipeg | 0.06 (0.05-0.07) | 1.00 (0.95-1.00) | 1.00 (1.00-1.00) | 0.03 (0.02-0.04) | 1.00 (1.00-1.00) | 1.00 |
| **Algorithm 6: 1+ H or 2+ P in a two-year period** (after the index date) | Rural North (including Churchill | 0.42 (0.35-0.48) | 0.86 (0.78-0.92) | 1.00 (1.00-1.00) | 0.27 (0.23-0.33) | 1.00 (1.00-1.00) | 0.86 |
| | Rural South | 0.14 (0.07-0.21) | 0.71 (0.47-0.87) | 1.00 (1.00-1.00) | 0.08 (0.05-0.13) | 1.00 (1.00-1.00) | 0.71 |
| | Winnipeg | 0.23 (0.19-0.27) | 1.00 (0.95-1.00) | 1.00 (1.00-1.00) | 0.13 (0.10-0.16) | 1.00 (1.00-1.00) | 1.00 |
| **Algorithm 7: 1+ H in a two-year period** (before and after the index date) | Rural North (including Churchill | 0.83 (0.77-0.89) | 0.86 (0.78-0.92) | 1.00 (1.00-1.00) | 0.80 (0.71-0.87) | 1.00 (1.00-1.00) | 0.86 |
| | Rural South | 0.80 (0.66-0.94) | 0.94 (0.73-0.99) | 1.00 (1.00-1.00) | 0.70 (0.49-0.84) | 1.00 (1.00-1.00) | 0.94 |
| | Winnipeg | 0.67 (0.58-0.77) | 0.60 (0.48-0.71) | 1.00 (1.00-1.00) | 0.76 (0.64-0.86) | 1.00 (1.00-1.00) | 0.60 |
| **Algorithm 8: 1+ P in a two-year period** (before and after the index date) | Rural North (including Churchill | 0.29 (0.24-0.34) | 0.86 (0.78-0.92) | 0.99 (0.99-0.99) | 0.17 (0.14-0.21) | 1.00 (1.00-1.00) | 0.85 |
| | Rural South | 0.04 (0.02-0.06) | 0.71 (0.47-0.87) | 1.00 (1.00-1.00) | 0.02 (0.01-0.04) | 1.00 (1.00-1.00) | 0.70 |
| | Winnipeg | 0.06 (0.05-0.08) | 0.99 (0.92-1.00) | 1.00 (1.00-1.00) | 0.03 (0.03-0.04) | 1.00 (1.00-1.00) | 0.98 |
| **Algorithm 9: 1+ H or 1+ P in a two-year period** (before and after the index date) | Rural North (including Churchill | 0.31 (0.26-0.36) | 0.96 (0.89-0.98) | 0.99 (0.99-0.99) | 0.19 (0.15-0.22) | 1.00 (1.00-1.00) | 0.95 |
| | Rural South | 0.06 (0.03-0.08) | 1.00 (0.82-1.00) | 1.00 (1.00-1.00) | 0.03 (0.02-0.05) | 1.00 (1.00-1.00) | 1.00 |
| | Winnipeg | 0.06 (0.05-0.08) | 0.99 (0.92-1.00) | 1.00 (1.00-1.00) | 0.03 (0.03-0.04) | 1.00 (1.00-1.00) | 0.98 |

* indicates that these statistical measures have 95% confidence intervals.

As Table 3.6 reveals, the TB diagnosis codes recorded in Manitoba's hospital discharge abstracts and physician billing claims for the entire population were primarily for pulmonary TB (37.7%), TB of other organs (28.7%), and TB of bones and joints (18.7%). This information was for the period from April 1, 2010 to March 31, 2015.

**Table 3.6: Frequency and Percent of Selected TB Diagnosis Codes in Manitoba's Hospital Records and Physician Billing Claims,** April 1, 2010 to March 31, 2015

| Diagnosis | Count | Percent |
|---|---|---|
| Pulmonary Tuberculosis | 2,552 | 37.7% |
| Tuberculosis of Other Organs | 1,946 | 28.7% |
| Tuberculosis of Bones And Joints | 1,267 | 18.7% |
| Tuberculosis of Genitourinary System | 376 | 5.6% |
| Respiratory Tuberculosis Confirmed | 156 | 2.3% |
| Respiratory Tuberculosis Not Confirmed | 153 | 2.3% |
| Primary Tuberculosis Infection | 108 | 1.6% |
| Other Respiratory Tuberculosis | 108 | 1.6% |
| Tuberculosis of Meninges and Central Nervous System | 67 | 1.0% |
| Miliary Tuberculosis | 18 | 0.3% |
| Tuberculosis of Intestines, Peritoneum, and Mesenteric Glands | 11 | 0.2% |
| Tuberculosis of Nervous System | 6 | 0.1% |

## Chapter Summary

The analyses reported in this chapter reveal that the information contained in the Manitoba TB Registry is largely complete and accurate. We found few fields in the Manitoba TB Registry that were characterized by missing information. We also found that the information contained in the Registry was accurate when compared to administrative data such as hospital records, laboratory test results, and physician billing claims.

Cough was identified as a key concept to measure one of the 13 performance indicators for the ITBS Program; it was captured for less than 5% of individuals in the Active TB Cohort. Thus, it is not possible to measure any performance indicators that require date of cough onset using the Manitoba TB Registry. However, overall there was complete information about symptoms in the Manitoba TB Registry.

The fields we examined for accuracy, including demographic, treatment, and testing information, showed a close agreement when compared to their corresponding elements in administrative health data. Six-digit postal code was the least accurate of the fields that were investigated. This may reflect a lack of updating of residence information in either the Population Registry or the Manitoba TB Registry, or in both sources. TB patients may move between northern and southern Manitoba, and maintenance of accurate up-to-date demographic files is likely impacted by mobility.

The Manitoba TB Registry is the "gold standard" for ascertaining cases of active TB. However, in provinces where TB registry data have not been linked to administrative data, case ascertainment algorithms are needed to develop study cohorts in order to measure the characteristics and outcomes of TB cases. Our study results are therefore useful for developing and recommending one or more case ascertainment algorithms that can be used to define study cohorts in administrative data. Sensitivity and PPV values were low for many of the case ascertainment algorithms that we investigated. The low PPV values indicate that there is substantial misclassification bias in administrative data. Our results are consistent with a recently-published systematic review, which found wide variations in the accuracy of administrative health data for ascertaining TB cases, particularly when using outpatient administrative data (e.g., physician billing claims) for case ascertainment [39]. The authors of this review suggest that caution must be exercised when applying case ascertainment algorithms based solely on diagnosis codes; they may result in under- or over-ascertainment of cases. In addition, we found that variation existed across population sub-groups in the validity of the case ascertainment algorithms, reflecting the fact that individuals defined by age group and region of residence may not all be equally likely to have a diagnosis code for TB recorded in administrative data. Overall, our results suggest that recommending a single algorithm may be difficult. This conclusion is consistent with Ronald et al.'s conclusions [39].

# Chapter 4:

# Healthcare Use for Active TB Cases

The provision of timely and comprehensive healthcare can influence the diagnosis and progression of active TB disease and its spread in communities. When a person with TB contacts the healthcare system, decisions must be made about the commencement of treatment, possibly even before the diagnosis of TB has been verified. Identification and/or treatment of comorbid conditions must often occur alongside TB treatment. The integration of emergency care, acute care, primary care, and supportive care are important considerations. For example, contact with emergency department care can provide an opportunity for early detection. Primary care is essential to ensure completion of treatment, although supportive care (e.g., homecare) also has a role to play in directly observed therapy.

The primary purpose of this component of the study was to examine pre- and post-diagnosis healthcare utilization for active TB cases across multiple healthcare sectors to describe the profile of contacts with the healthcare system during the disease course. The sub-objectives were to:

1. Describe trends in emergency, acute, primary care, specialist, prescription drug and home care use before and after TB diagnosis;
2. Identify patient characteristics associated with pre- and post-diagnosis healthcare use; and
3. Compare the use of healthcare services for active TB cases to that of matched controls.

While this chapter focuses on healthcare use for the Active TB Cohort, a parallel analysis was conducted for the Treated LTBI Cohort. This analysis can be found in Appendix 4.

## Overview of Methods

The analyses conducted in this section were based on the Active TB Cohort, which was defined using the Manitoba TB Registry, and the corresponding matched cohort, which was defined using administrative data. We excluded individuals from the Active TB Cohort who did not have at least 720 days of health insurance coverage following the study index date (i.e., TB diagnosis date or date of entry into the Manitoba TB Registry). A total of 1,419 active TB cases were retained in the analyses of healthcare use. The matched cohort was restricted to individuals who had not been diagnosed with TB, treated for LTBI, or identified as a contact of an active TB case. There was a total of 7,078 individuals in this matched cohort.

Each measure of healthcare use was constructed for 30-day periods prior to (and including) the study index date and then following the study index date. A total of 12 30-day increments were defined for the pre-diagnosis period and 24 30-day increments were defined for the post-diagnosis period. Subsequently, because of small numbers for some measures of healthcare use, we aggregated the data in 60-day increments to ensure confidentiality when presenting graphical summaries of the data.

The healthcare use measures included:

- **Emergency department visits:** a dichotomous measure indicating whether there was at least one visit in a 30-day period. Note that this measure was available from April 1, 2000 to March 31, 2013 for facilities and residents of the Winnipeg health region only.
- **Inpatient hospitalization:** a dichotomous measure indicating whether there was at least one inpatient hospitalization in each 30-day period.
- **Inpatient hospital days:** total number of inpatient hospital days in each 30-day period.
- **Ambulatory family physician visits:** total number of outpatient visits to family physicians in each 30-day period.
- **Ambulatory specialist visits:** total number of outpatient visits to specialist physicians in each 30-day period.
- **Non-TB-related prescription drugs:** number of different prescription drugs in each 30-day period. The 4th level of the World Health Organization's Anatomic, Therapeutic, Chemical (ATC) Classification System was used to distinguish different drugs. The following TB-related drugs were excluded: isoniazid (INH), rifampin (RIF), pyrazinamide, ethambutol, fixed-dose combinations of these four medications, vitamin B6, Tuberculin for TSTs, rifapentine, rifabutin.
- **Homecare visits:** a dichotomous measure indicating whether there was at least one homecare visit in each 30-day period. Note that this measure was available from April 1, 2000 to March 31, 2011 only.

All hospitalizations, hospital days, and physician visits associated with pregnancy and childbirth were excluded when deriving these measures.

Sociodemographic (age group, sex, income quintile, health region of residence, population of origin group), disease (study index year, case criteria, disease recurrence), and comorbidity characteristics were included in the statistical models to test their association with healthcare use. As well, inpatient hospitalization was included as a covariate in the models for family and specialist outpatient physician visits, because an individual cannot seek physician care when in hospital.

Comorbidity was measured using the Charlson Comorbidity Index and was based on the 360 days prior to and including the study index date. In addition, a selected set of comorbid conditions were defined from diagnoses in hospital records and physician billing claims; these included diabetes, rheumatoid arthritis, chronic obstructive pulmonary disease, heart disease, HIV, and chronic kidney disease.

The data were described using frequencies, means and standard deviations. Plots of trends in healthcare use were produced; these are shown using 60-day increments in order to preserve patient confidentiality since some healthcare events (i.e., hospitalization) are rare in some of the cohort sub-groups in one or more 30-day increments in the study observation period. We show these results for population of origin groups because of their importance in the organization and delivery of TB care.

For count outcome measures, a generalized linear model with a negative binomial distribution and generalized estimating equations (GEEs) were used to model the trend over time. For dichotomous outcome measures, a generalized linear model with a logit function and GEEs was adopted to model the trend. An autoregressive correlation structure was used in each model to account for repeated measurements on the same individual.

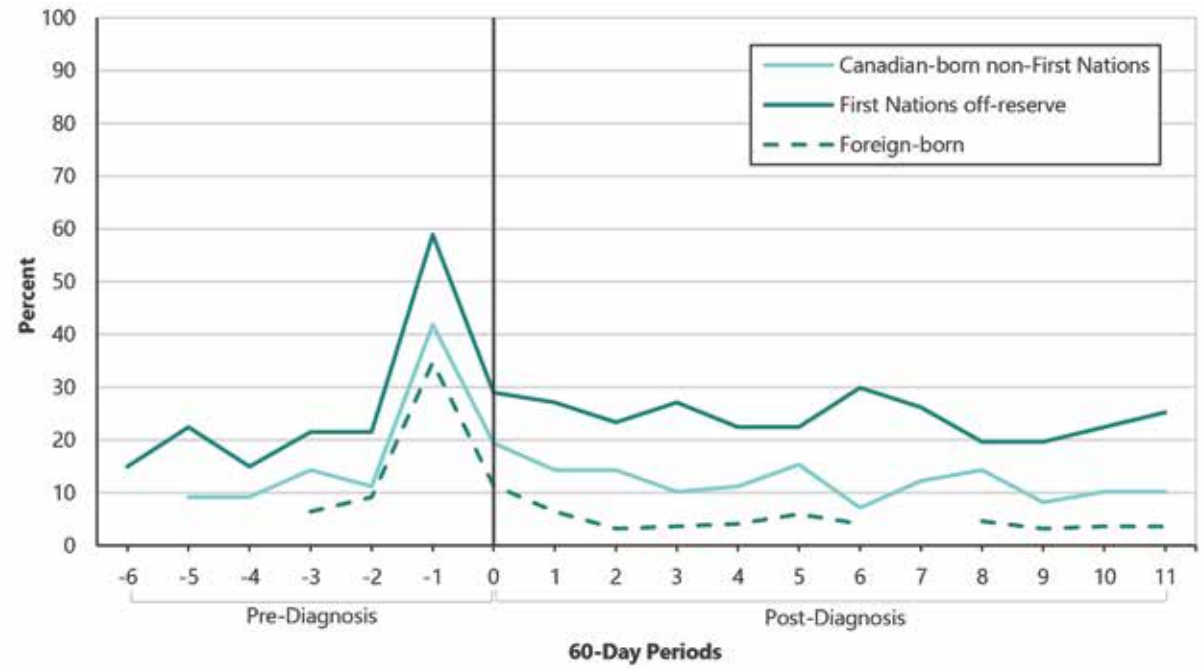
All statistical models included the main effects of age group, sex, income quintile, region of residence, index year, case criteria, disease recurrence, origin group, month, and period (i.e., pre-diagnosis, post-diagnosis). Odds ratios (ORs) and 95% confidence intervals (95% CIs) were produced for the multivariable logistic models. Relative rates (RRs) and 95% CIs were produced for the multivariable negative binomial distribution models. Model fit was evaluated using the scaled deviance.

# Results

## Emergency Department Visits

Emergency department visit data were available for facilities in the Winnipeg health region only. Therefore, the analysis was restricted to residents of this health region. Figure 4.1 describes the emergency department use (i.e., percent of individuals with at least one visit) for active TB cases in 60-day increments before and after the date of diagnosis. Use of emergency departments increased substantially in the months prior to diagnosis and then decreased sharply around the time of diagnosis.

**Figure 4.1: Percent of Active TB Cohort with an Emergency Department Visit Before and/or After TB Diagnosis, Stratified by Population of Origin**
April 1 2001 - March 31 2011

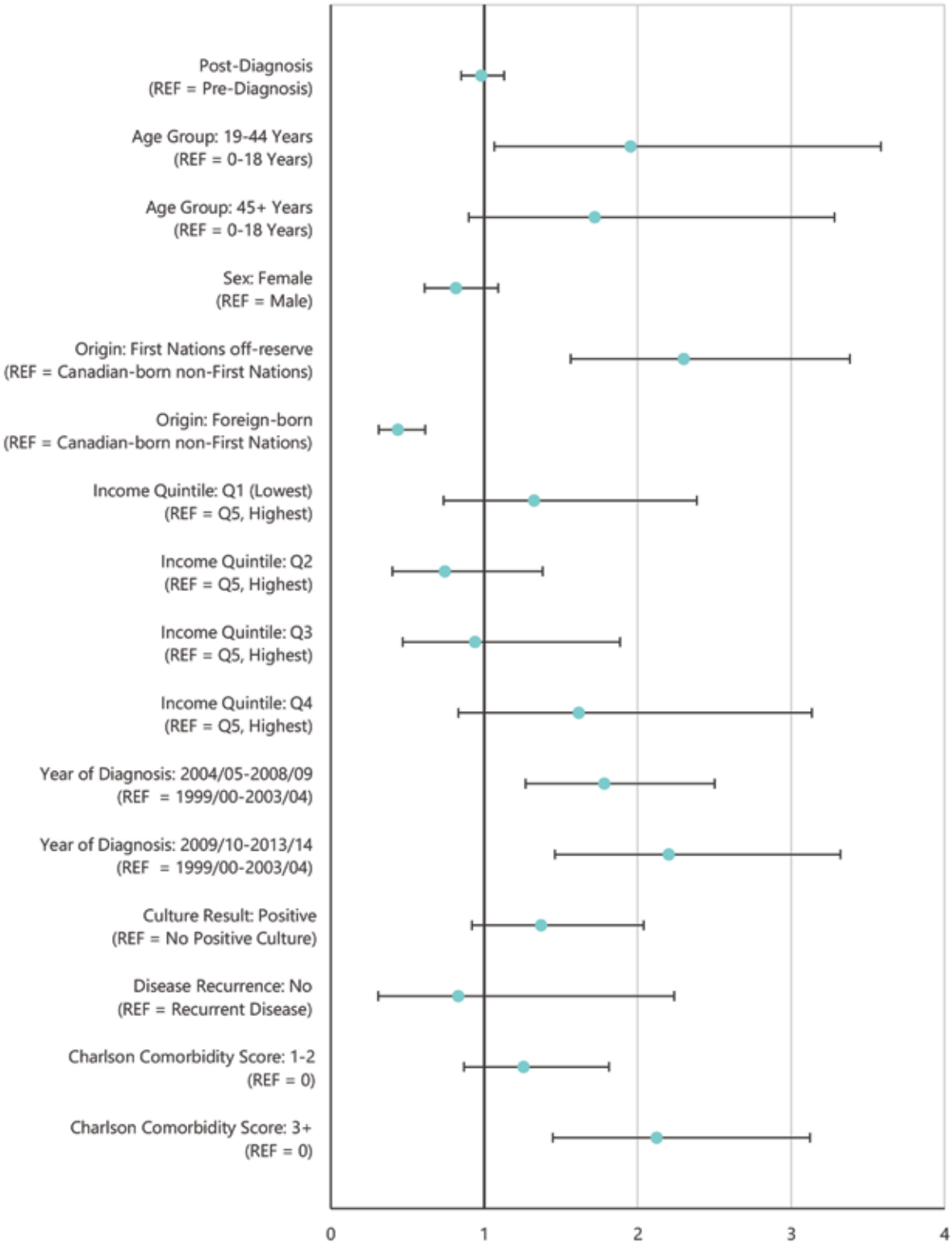



Blank spaces indicate data suppression due to small numbers. Rates for First Nations on-reserve were calculated, but are not shown due to data suppression

Figure 4.2 reports the ORs (and 95% CIs) for the cohort characteristics associated with having an emergency department visit before and/or after TB diagnosis. OR estimates greater than 1 indicate a higher odds of having an emergency department visit than the reference group, while OR estimates less than 1 indicate a lower odds. If the 95% confidence interval does not include 1, then the result is statistically significant.

On average, the odds of an emergency department visit were not significantly different in the post-diagnosis period compared to the pre-diagnosis period (Figure 4.2). The odds of an emergency department visit were higher in the 19-44 years age group than in the youngest age group. The odds were higher for off-reserve First Nations and lower for foreign-born active TB cases than for Canadian-born non-First Nations. There were no differences by income quintile. There were some differences by year of TB diagnosis, with the odds being higher in the two most recent five-year time periods than in the earliest time period. Finally, higher comorbidity amongst active TB cases was associated with a higher odds of an emergency department visit.

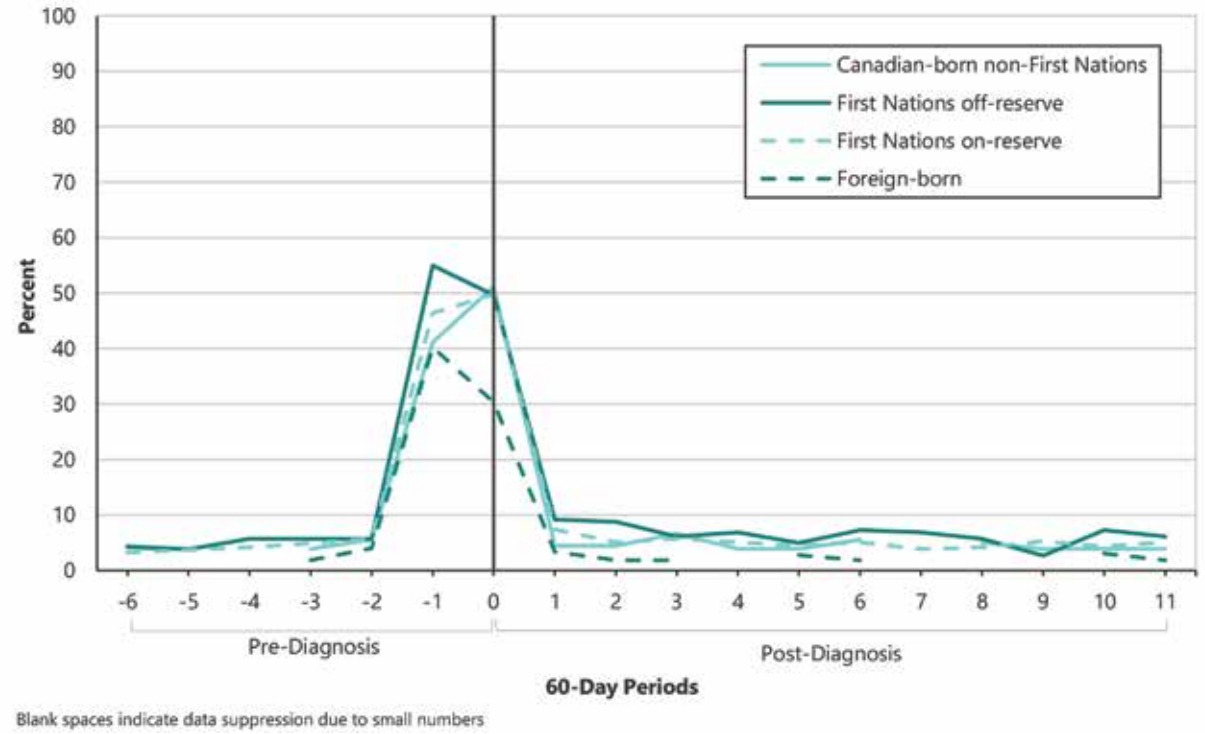
**Figure 4.2: Characteristics of Active TB Cohort Associated with Emergency Department Visits**
Winnipeg Residents Only, Odds Ratio Estimates and 95% CIs



## Inpatient Hospitalizations and Inpatient Length of Stay

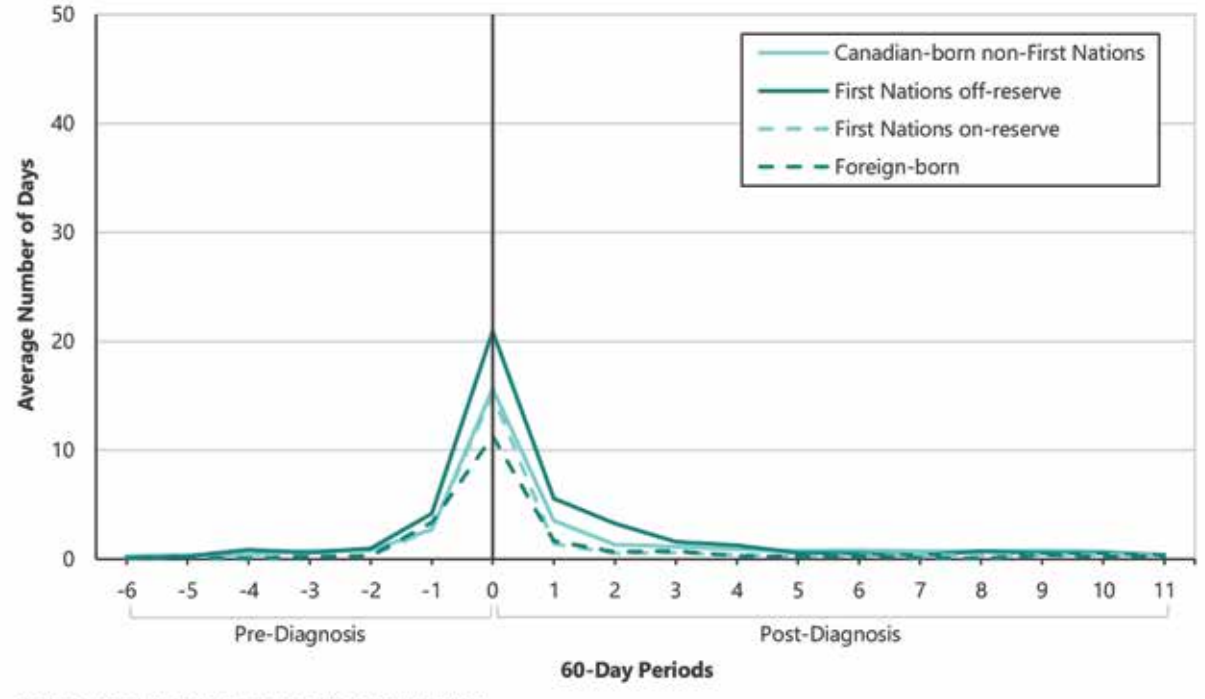
Figures 4.3 and 4.4 show the trends in inpatient hospitalizations and hospital length of stay, respectively. The trends are stratified by population of origin.

**Figure 4.3: Percent of Active TB Cohort with an Inpatient Hospitalization Before and/or After TB Diagnosis, Stratified by Population of Origin**
April 1 1999 - March 31 2013




Blank spaces indicate data suppression due to small numbers

**Figure 4.4: Average Number of Inpatient Hospital Days for Active TB Cohort Before and/or After TB Diagnosis, Stratified by Population of Origin**
April 1 1999 - March 31 2013




Blank spaces indicate data suppression due to small numbers

Overall, inpatient hospitalizations were low in the months prior to diagnosis; no more than 7.0% of individuals in the Active TB Cohort were hospitalized in any given pre-diagnosis month, with the exception of the month prior to diagnosis.

In the month prior to diagnosis, as well as in the month of diagnosis, inpatient hospitalizations were high. Overall, approximately 40-50% of the Active TB Cohort was hospitalized in the month prior to diagnosis and approximately 30-50% was hospitalized in the month of diagnosis. Hospitalization decreased in the month following diagnosis and returned to low pre-diagnosis period rates of hospitalization.

While there were some differences in the percentage of each population of origin group that were hospitalized, the pattern was largely the same across all groups. However, First Nations off-reserve active TB cases were more likely to be hospitalized in the month prior to diagnosis than active TB cases in the other three population origin groups.

Rates of inpatient hospital days showed a similar trend. The average number of inpatient days was less than one per month in the months leading up to the active TB diagnosis date. Overall, in the month that the TB diagnosis occurred, the average number of inpatient days was 12.3 and the median number of days was 13. The average number of hospital days decreased substantially in the months after diagnosis, but still remained higher than in the pre-diagnosis period for a short period of time.

Figures 4.5 and 4.6 provide the results of the statistical analysis for inpatient hospitalizations and inpatient days, respectively. Overall, there was a higher odds of hospitalization following diagnosis than prior to diagnosis. The relative rate of hospital days was also higher following diagnosis than prior to diagnosis. While hospitalization was a rare event in the months following diagnosis, it was still elevated in the post-diagnosis period relative to the pre-diagnosis period for a short period of time. As expected, the odds of hospitalization were higher for older than younger active TB cases. The odds of hospitalization were higher for First Nations on- and off-reserve active TB cases. The rate of inpatient days was not significantly greater for any of the population of origin groups. The odds of hospitalization were lower for foreign-born active TB cases than for Canadian-born non-First Nations cases. Greater comorbidity was associated with a greater odds of hospitalization and a higher rate of hospital days.

**Figure 4.5: Characteristics of Active TB Cohort Associated with Inpatient Hospitalizations**
Odds Ratio Estimates and 95% CIs for Inpatient Hospitalizations*

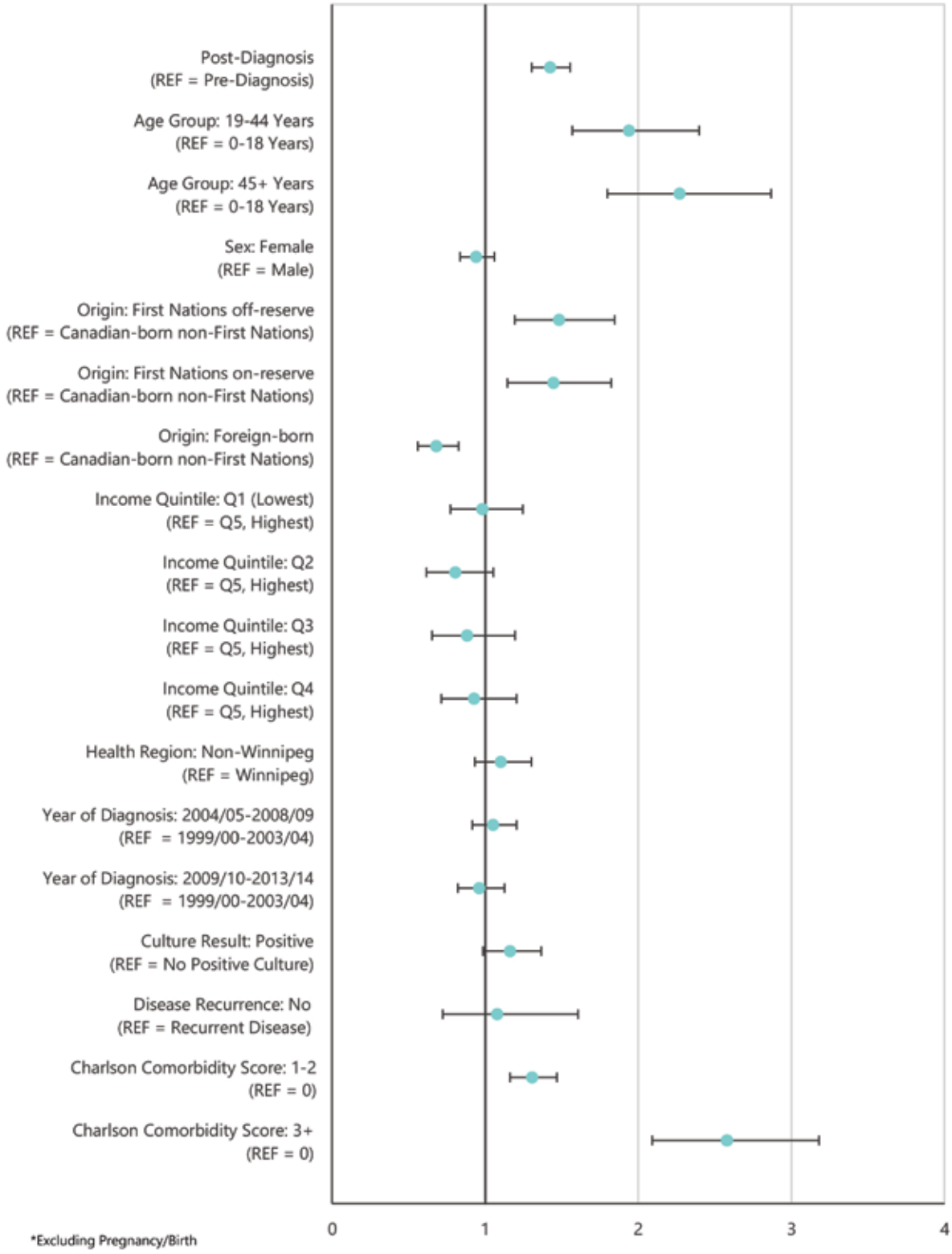
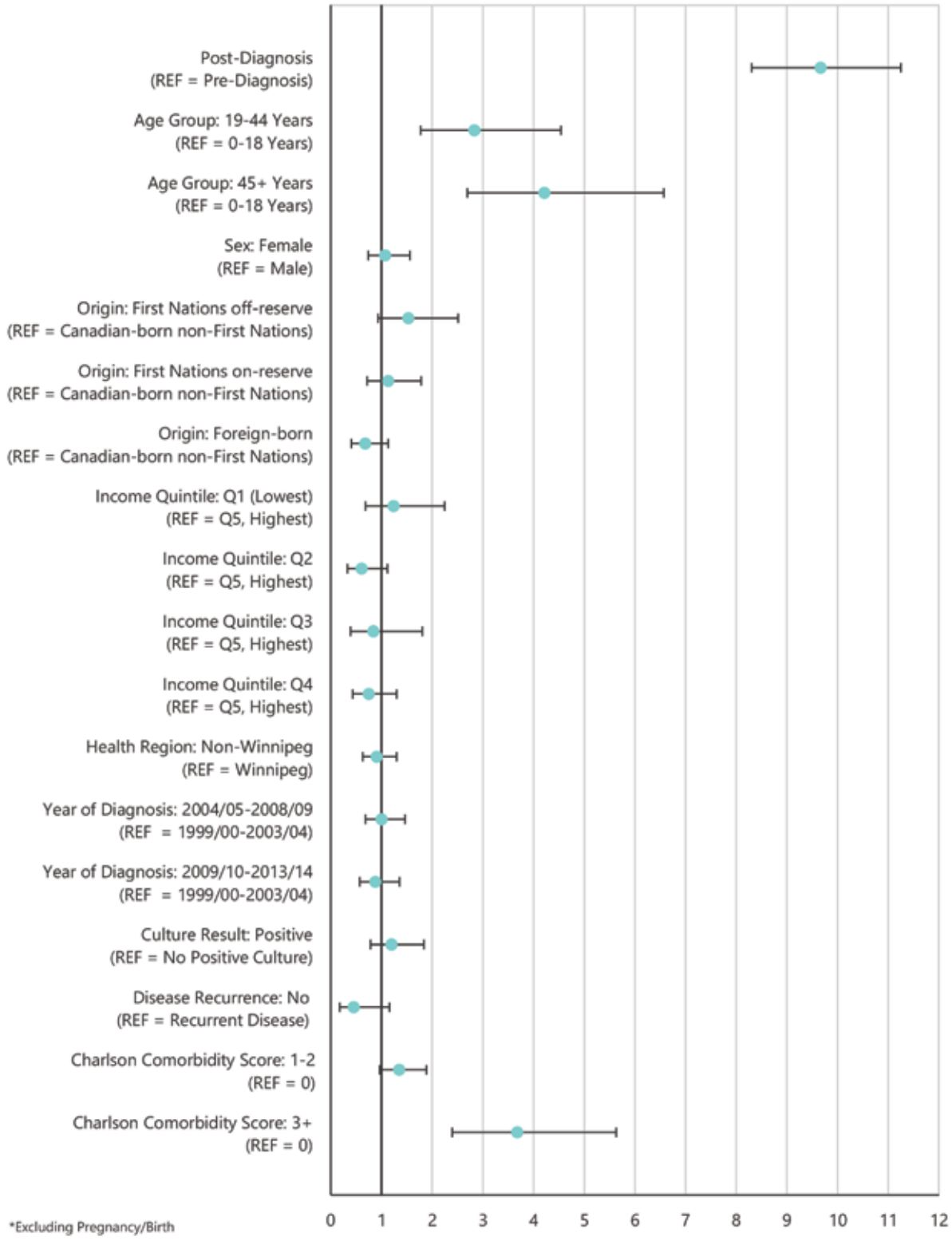


**Figure 4.6: Characteristics of Active TB Cohort Associated with Inpatient Hospital Days***
Relative Risk Estimates and 95% CIs




*Excluding Pregnancy/Birth

## Physician Visits

This section examines the utilization of both family and specialist physician services in the year prior to diagnosis and the two years following diagnosis with active TB. Figures 4.7 and 4.8 depict the trends in family and specialist physician visits over time; the rates shown are per 100 active TB cases. Family physician visit rates were highest immediately prior to diagnosis and then decreased substantially at the time of diagnosis. In contrast, specialist visit rates showed a strong increasing trend leading up to diagnosis, peaked during the month of diagnosis, then decreased gradually in the months following diagnosis before returning to pre-diagnosis levels many months later.

**Figure 4.7: Rate of Family Physician Visits for Active TB Cohort Before and/or After TB Diagnosis, Stratified by Population of Origin**
April 1 1999 - March 31 2013

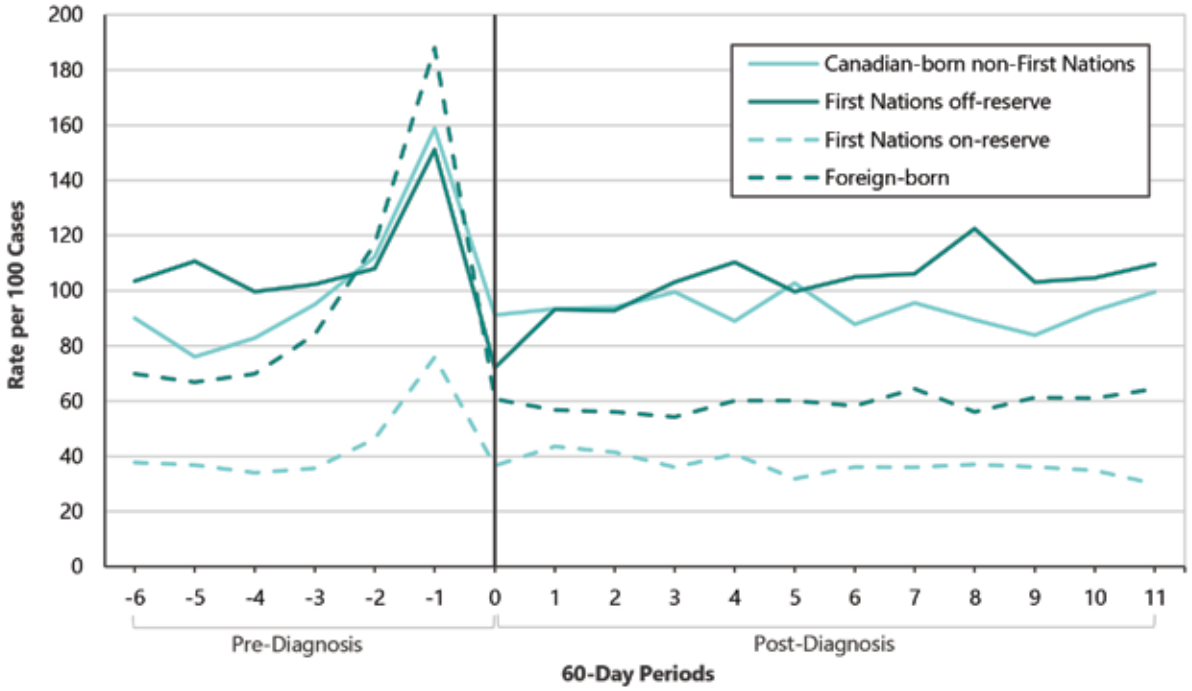
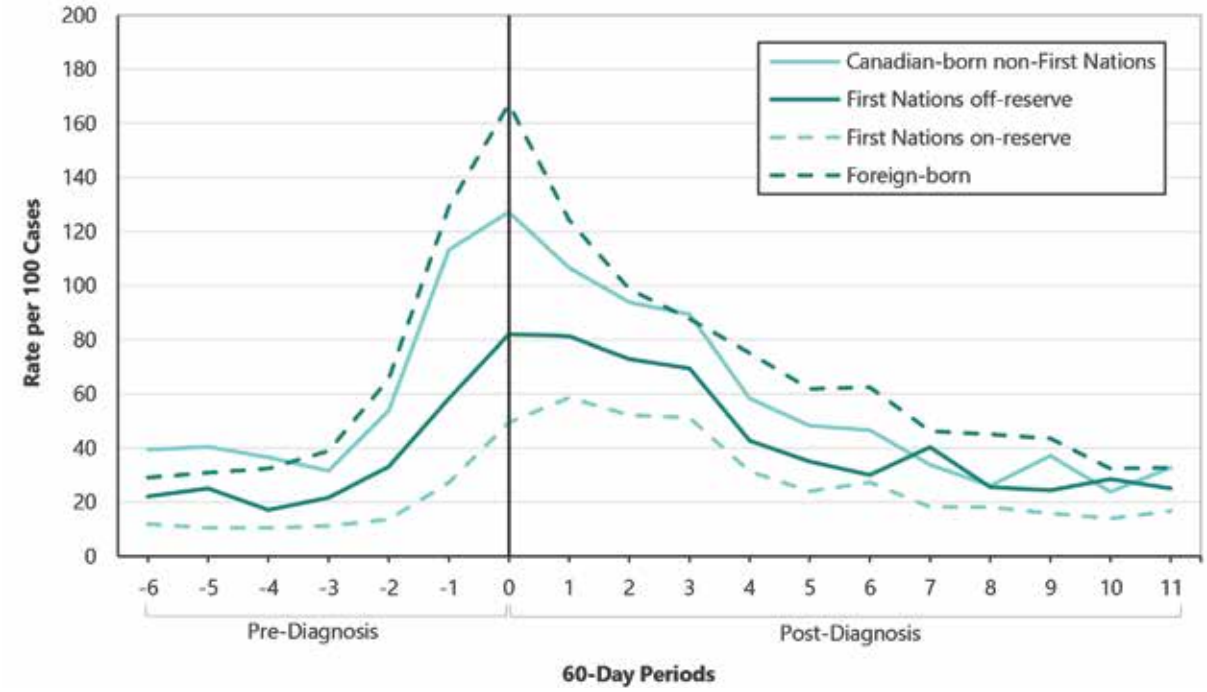



**Figure 4.8: Rate of Specialist Physician Visits for Active TB Cohort Before and/or After TB Diagnosis, Stratified by Population of Origin**
April 1 1999 - March 31 2013

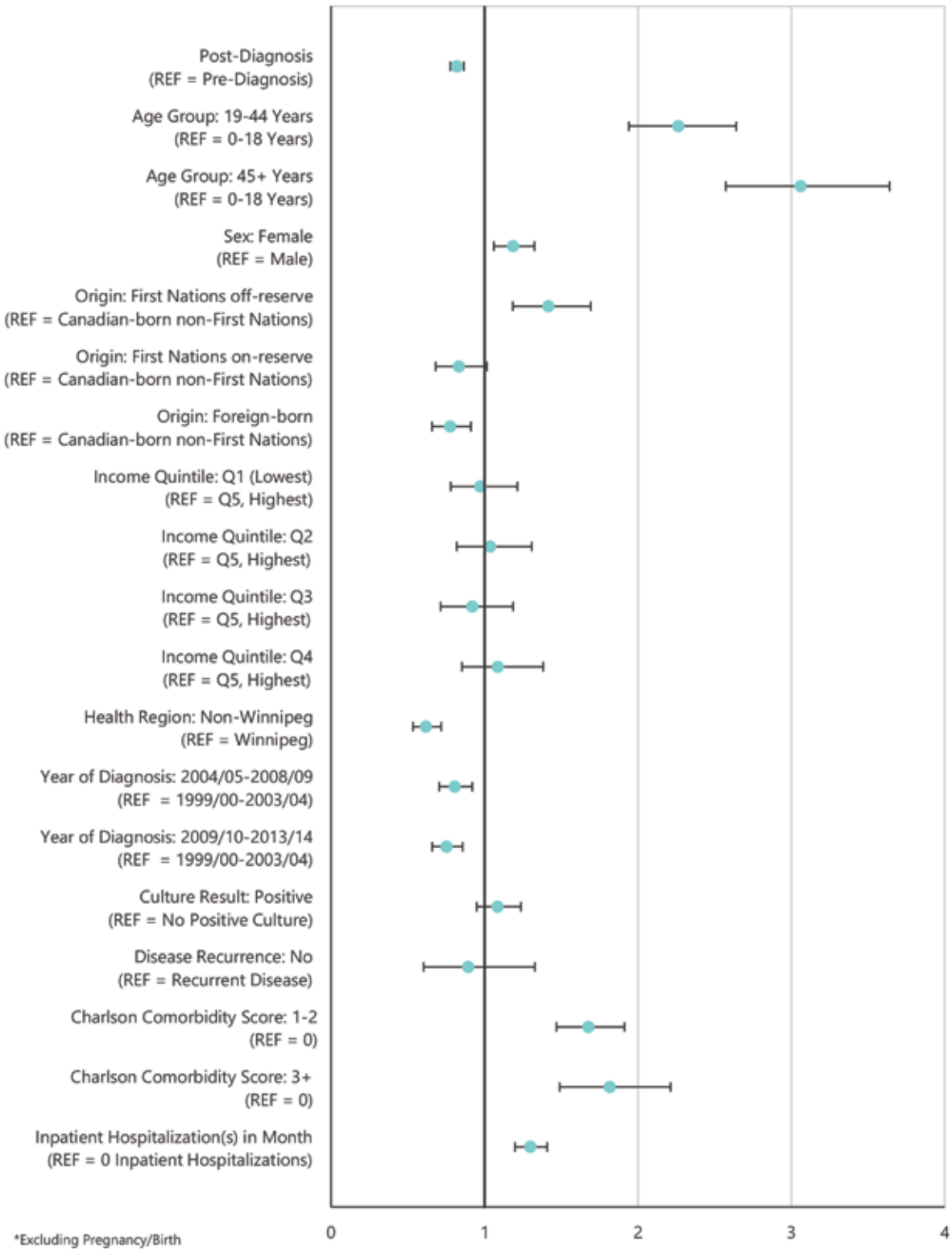


For Canadian-born non-First Nations active TB cases, First Nations off-reserve active TB cases, and foreign-born active TB cases, family physician visit rates were similar in the pre-diagnosis period. The low rates of family physician visits amongst on-reserve First Nations active TB cases may reflect the presence of northern MB nursing stations for primary care on reserves; specifically, the data for northern MB nursing stations may not be consistently captured for all years of the study period in physician billing claims data. However, differences in access to primary care may also account for variations in the trends. After diagnosis, family physician visit rates were much lower for both foreign-born and on-reserve First Nations active TB cases.

With respect to specialist visits in the month of diagnosis, foreign-born active TB cases had the highest rates of utilization and First Nations on-reserve active TB cases had the lowest. Differences amongst the groups persisted throughout the pre- and post-diagnosis periods, but were most pronounced around the time of diagnosis.

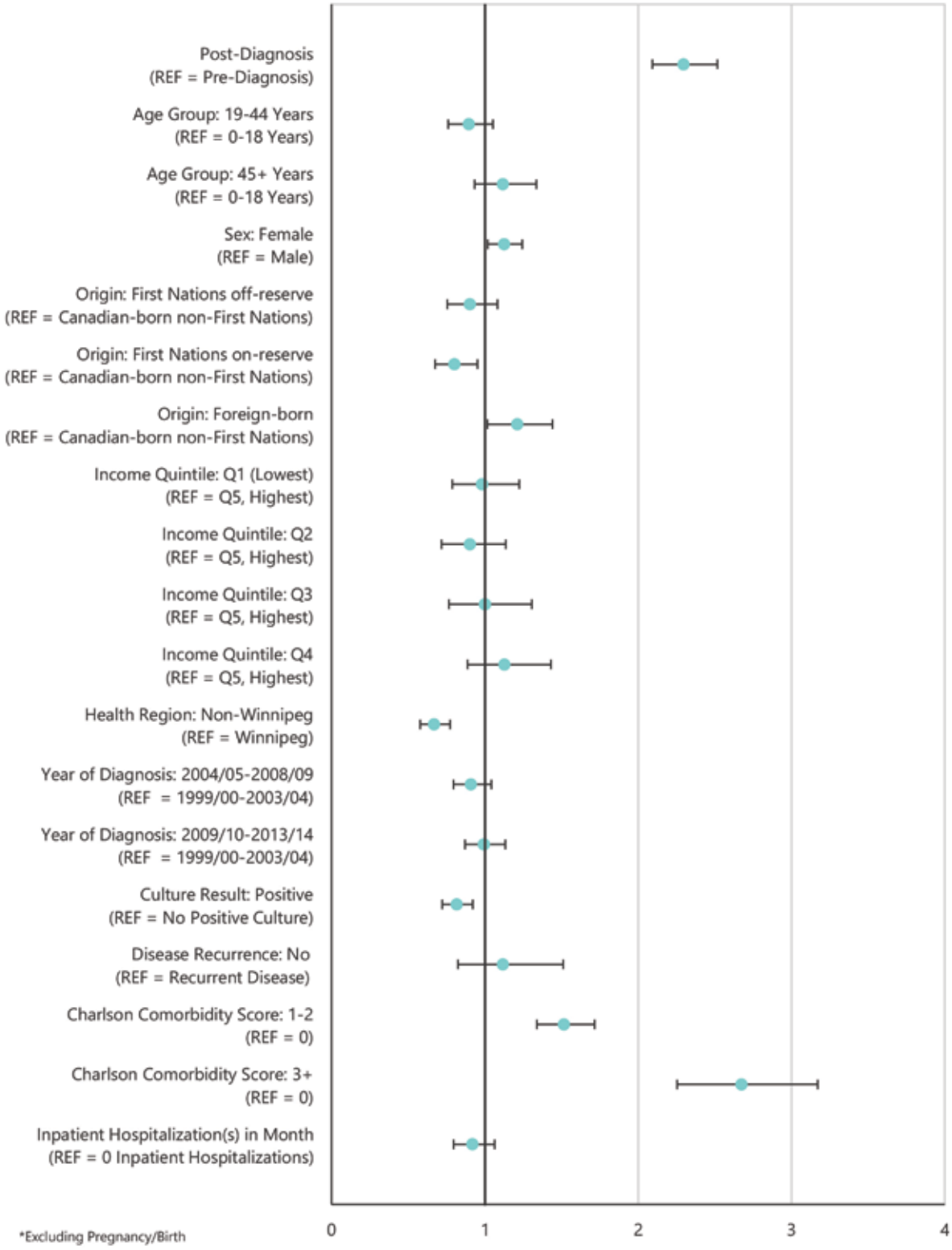
The forest plots in Figures 4.9 and 4.10 reveal that family physician visit rates were significantly lower in the post-diagnosis period than in the pre-diagnosis period. In contrast, specialist physician visit rates were significantly higher in the post-diagnosis period than in the pre-diagnosis period.

**Figure 4.9: Characteristics of Active TB Cohort Associated with Ambulatory Physician Visit Rate***
Relative Risk Estimates and 95% CIs




*Excluding Pregnancy/Birth

**Figure 4.10: Characteristics of Active TB Cohort Associated with Rate of Specialist Physician Visits***
Relative Risk Estimates and 95% CIs




*Excluding Pregnancy/Birth

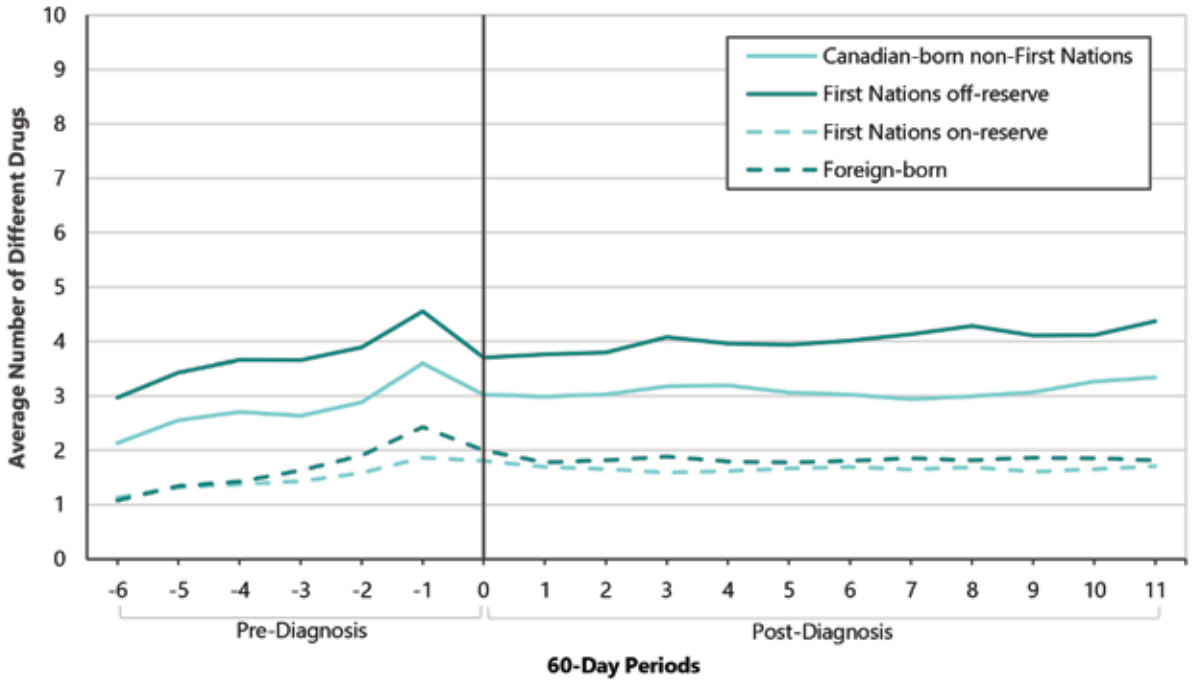
While rates of family physician visits were significantly higher for older than younger active TB cases, age group was not associated with specialist physician visit rates. Rates of both family and specialist physician visits were significantly higher in females than in males. First Nations off-reserve active TB cases had a higher rate of family physician visits when compared to Canadian-born non-First Nations cases. Foreign-born active TB cases had a significantly lower rate of family physician visits and a significantly higher rate of specialist physician visits than Canadian-born non-First Nations. Active TB cases living outside of Winnipeg had lower rates of family physician visits and specialist visits than cases living in Winnipeg.

A later year of TB diagnosis was associated with lower rates of family physician visits. A positive culture was associated with a lower rate of specialist physician visits. Greater comorbidity was associated with higher rates of both family and specialist physician visits. Finally, having an inpatient hospitalization was associated with a higher rate of family physician visits when compared to not having an inpatient hospitalization.

## Non-TB Prescription Drug Use

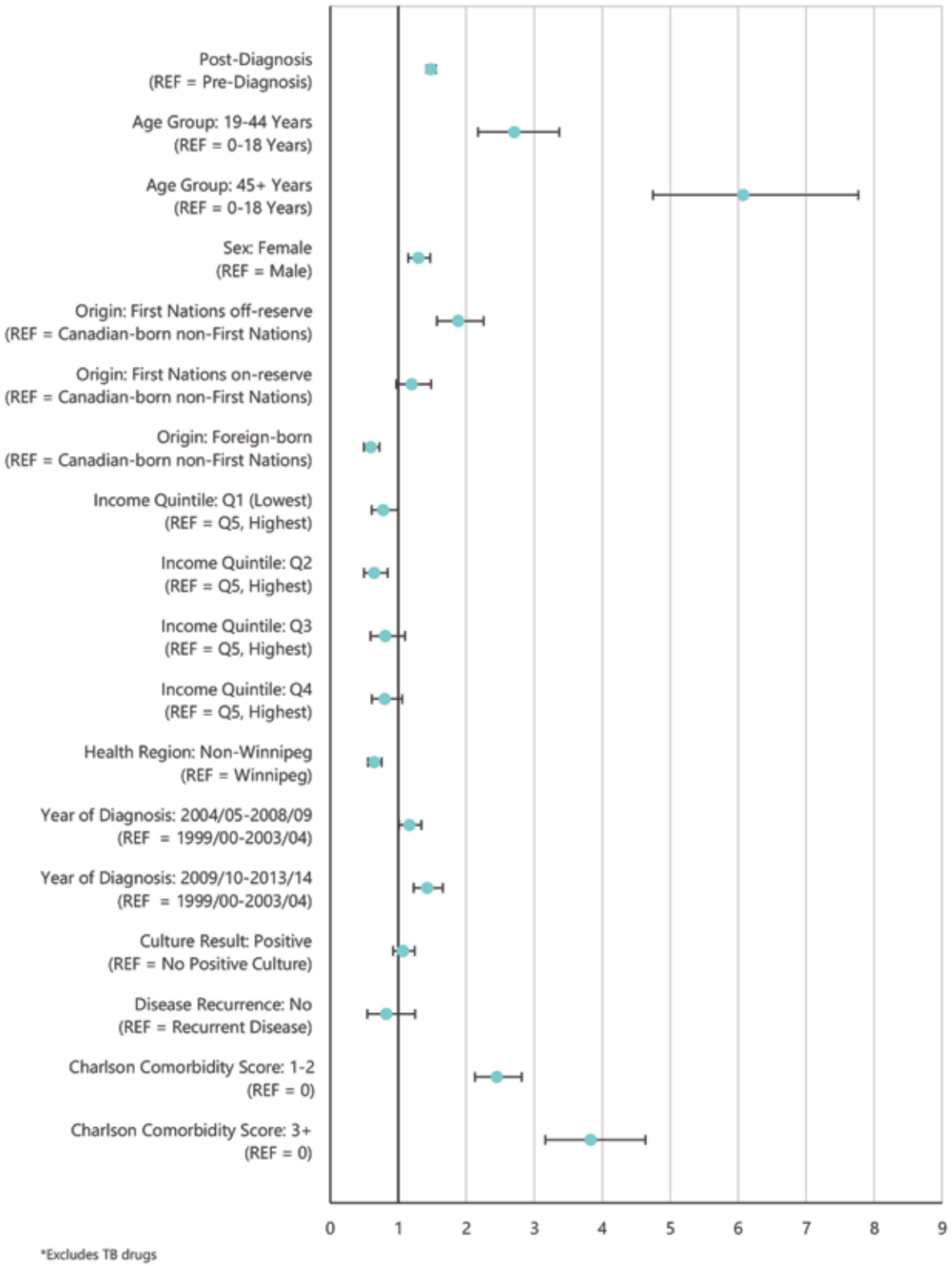
A modest increase in the average number of different non-TB prescription drugs used (e.g., anti-hypertensives, anti-depressants) was observed over the three-year observation period, with a small peak in use just prior to active TB diagnosis (Figure 4.11). Trends in the average number of different non-TB prescription drugs used across the observation period were highest for First Nations off-reserve active TB cases, followed by Canadian-born non-First Nations TB cases. They were similar for First Nations on-reserve and foreign-born active TB cases.

**Figure 4.11: Non-TB Prescription Drug Use for Active TB Cohort Before and/or After TB Diagnosis, Stratified by Population of Origin**
April 1 1999 - March 31 2013




As Figure 4.12 reveals, rates of non-TB prescription drug use were slightly higher in the post-diagnosis period than in the pre-diagnosis period. This pattern may reflect overall increases in prescription drug use in Manitoba over time. Age, sex, and comorbidity were associated with prescription drug utilization. A later year of TB diagnosis was associated with a higher rate of prescription drug utilization than an earlier year of TB diagnosis. A non-Winnipeg health region of residence was associated with slightly lower prescription drug use than a Winnipeg health region of residence location. First Nations off-reserve active TB cases had a higher rate of prescription drug use and foreign-born active TB cases had a lower rate of prescription drug use when compared with Canadian-born non-First Nations TB cases.

**Figure 4.12: Characteristics of Active TB Cohort Associated with Average Number of Different Non-TB Prescription Drugs***
Relative Risk Estimates and 95% CIs

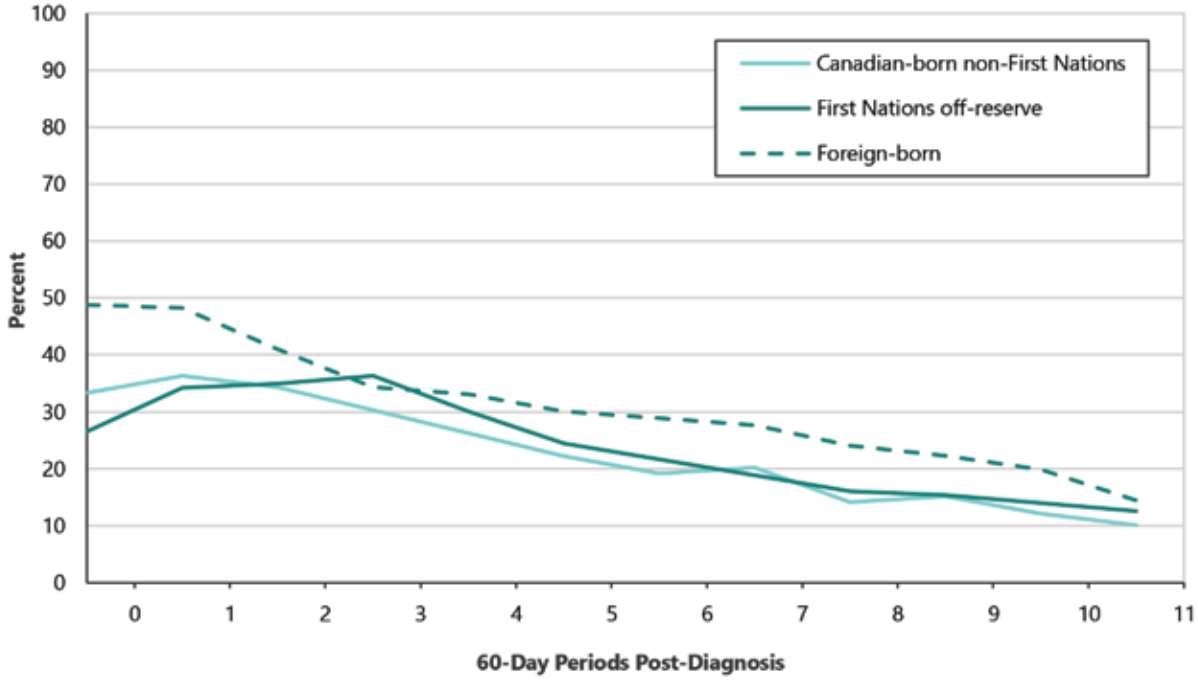



*Excludes TB drugs

## Homecare Use

Homecare use was very low in the months prior to TB diagnosis, so Figure 4.13 contains results only for the two-year post-diagnosis period. Homecare data for First Nations individuals living on reserve are held by the First Nations and Inuit Health Branch and are not available in the Manitoba Population Research Data Repository housed at MCHP, and therefore First Nations on-reserve active TB cases were not included in this analysis.

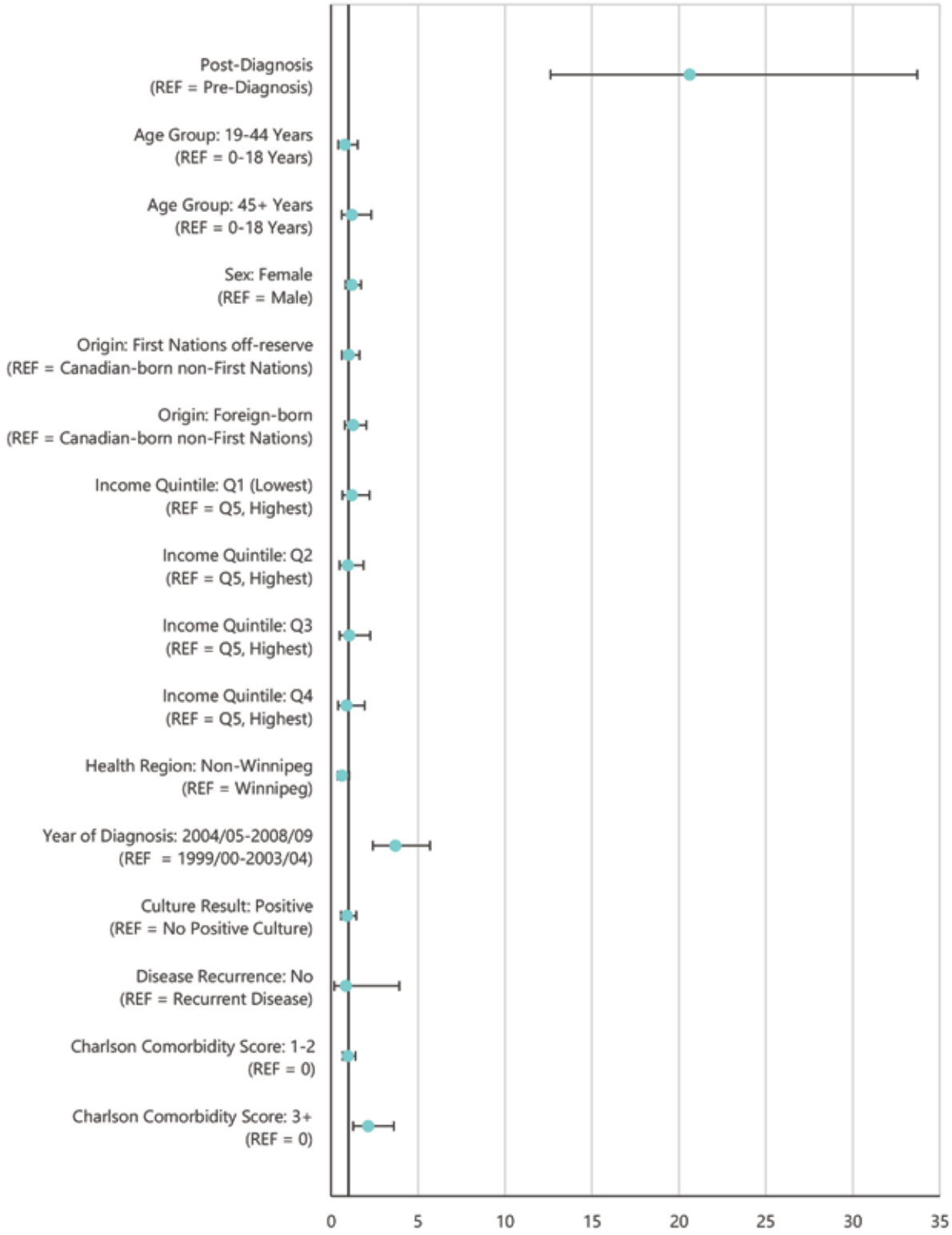
**Figure 4.13: Rate of Homecare Visits for Active TB Cohort After TB Diagnosis, Stratified by Population of Origin**
April 1 2001 – March 31 2009




Rates of homecare visits were slightly higher for foreign-born active TB cases than for other origin groups around the time of TB diagnosis. However, the differences amongst the foreign-born, First Nations off-reserve, and Canadian-born non-First Nations active TB cases were small in the post-diagnosis period.

As the results in Figure 4.14 reveal, homecare use was higher amongst active TB cases with higher rates of comorbidity. Use was also higher in later study years than earlier study years.

**Figure 4.14: Characteristics of Active TB Cohort Associated with Rate of Homecare Visits**
Odds Ratio Estimates and 95% CIs



## Comparisons between the Active TB Cohort and Matched Cohort

Two sets of analyses were used to explore differences in healthcare use between the Active TB Cohort and matched cohort. In the first, we compared rates of healthcare use for the two cohorts, stratified by First Nations status as defined by the INAC Status Registry. In Table 4.1, values greater than 1 for the relative rate (RR) estimates indicate that the Active TB Cohort had higher utilization than the matched cohort, while values less than 1 indicate that the Active TB Cohort had lower utilization. The 95% CIs provide information about whether these differences were statistically significant.

The Active TB Cohort had substantially higher emergency department use than the matched cohort; this was true for First Nations as well as for all other Manitobans. In fact, the rates of emergency department use for First Nations individuals in the Active TB Cohort were almost three times higher than for First Nations individuals in the matched cohort, and for all other Manitobans in the Active TB Cohort, rates were about two times higher than for all other Manitobans in the matched cohort.

For both hospitalizations and hospital days, the rates of use for the Active TB Cohort were much higher than for the matched cohort. This was particularly true for hospital days; the rates were more than 10 times higher for First Nations individuals in the Active TB Cohort than for First Nations individuals in the matched cohort. Similarly, the rates were more than seven times higher for all other Manitobans in the Active TB Cohort than for all other Manitobans in the matched cohort.

The smallest differences between the Active TB Cohort and the matched cohort were in the number of different non-TB prescription medications; rates were only about 20% higher for First Nations individuals and were not significantly different from all other Manitobans.

Table 4.2 provides a different perspective on healthcare use, comparing the rates of use for First Nations individuals relative to all other Manitobans in the Active TB Cohort and the matched cohort. These results are used to explore whether there are differences in accessibility between First Nations and all other Manitobans, and whether these differences have a differential impact in individuals with TB compared to the rest of the population. As Table 4.2 reveals, the size of the RR estimates was similar in both the Active TB Cohort and the matched cohort. The largest difference was for the number of different non-TB prescription medications, where the RR was 2.08 in the Active TB Cohort, but much smaller (i.e., 1.68) in the matched cohort. This indicates that in the Active TB Cohort the number of different prescription medications was about two times higher for First Nations individuals than for all other Manitobans, while in the matched cohort the number of different prescription medication was only about two-thirds higher. Similarly, emergency department visits were more than three times higher for First Nations individuals than for all other Manitobans in the Active TB Cohort, but in the matched cohort they were only about 2.3 times higher.

**Table 4.1: Healthcare Use for Active TB Disease Cohort Relative to Matched Cohort, Stratified by First Nations Status**

| Measure of Healthcare Use | First Nations Status | All Other Manitobans |
|---|---|---|
| | Estimate (95% Confidence Interval) | Estimate (95% Confidence Interval) |
| Emergency Department Visits[a] | **2.91 (2.49 - 3.41)** | **2.03 (1.65 - 2.50)** |
| Inpatient Hospitalizations[a] | **4.52 (4.08 - 5.01)** | **5.08 (4.25 - 6.06)** |
| Inpatient Hospital Days[b] | **10.26 (8.49 - 12.39)** | **7.46 (5.08 - 10.95)** |
| Ambulatory Physician Visits[b] | **1.19 (1.09 - 1.30)** | **1.11 (1.01 - 1.22)** |
| Specialist Physician Visits[b] | **2.51 (2.27 - 2.78)** | **2.03 (1.81 - 2.27)** |
| Number of non-TB Drugs[b] | **1.16 (1.06 - 1.28)** | 0.94 (0.84 - 1.05) |
| Homecare[a] | 2.20 (0.95 - 5.07) | **5.43 (3.23 - 9.13)** |

**Bold** relative rates and odds ratios indicate values that are statistically significant at $\alpha = 0.05$
Note: [a] indicates an Odds Ratio and [b] indicates a Relative Rate

**Table 4.2: Healthcare Use for First Nations Relative to All Other Manitobans, Stratified by Cohort**

| Measure of Healthcare Use | Active TB Disease | Matched Cohort |
|---|---|---|
| | Estimate (95% Confidence Interval) | Estimate (95% Confidence Interval) |
| Emergency Department Visits[a] | **3.33 (2.64 - 4.21)** | **2.32 (2.00 - 2.70)** |
| Inpatient Hospitalizations[a] | **1.71 (1.46 - 2.00)** | **1.92 (1.60 - 2.31)** |
| Inpatient Hospital Days[b] | **1.70 (1.24 - 2.34)** | 1.24 (0.81 - 1.89) |
| Ambulatory Physician Visits[b] | **1.47 (1.29 - 1.67)** | **1.36 (1.26 - 1.48)** |
| Specialist Physician Visits[b] | **0.84 (0.74 - 0.95)** | **0.68 (0.60 - 0.77)** |
| Number of non-TB Drugs[b] | **2.08 (1.80 - 2.39)** | **1.68 (1.52 - 1.86)** |
| Homecare[a] | **0.36 (0.15 - 0.85)** | 0.89 (0.50 - 1.58) |

**Bold** relative rates and odds ratios indicate values that are statistically significant at $\alpha = 0.05$
Note: [a] indicates an Odds Ratio and [b] indicates a Relative Rate

# Chapter Summary

We examined trends in healthcare use before and after diagnosis of active TB, and characteristics of active TB cases associated with healthcare use. Assessing the utilization of healthcare resources for TB contributes to effective planning within the healthcare system.

Substantially elevated use was observed for many healthcare services around the time of diagnosis, reflecting that TB is a resource-intensive condition. Homecare use and specialist physician use were higher after diagnosis, reflecting the long-term follow-up of individuals being treated for active TB. The characteristics of active TB cases associated with use (e.g., age and comorbidity) were often the same as those characteristics associated with use in the general population.

Variations in rates across population of origin groups may reflect inequities in access, incomplete data capture, or both. Visits to northern MB nursing stations on reserve are not consistently captured in physician claims databases, and homecare use information for on-reserve First Nations individuals is not captured in provincial administrative databases held in the Manitoba Population Research Data Repository housed at MCHP. Other allied health services are also not captured in the administrative databases.

Frequent contacts with the healthcare system, particularly those made early in the disease course, are important for early detection and treatment initiation [13]. Hospitalization, while sometimes viewed as a control measure for TB infections, also results in an increased risk of nosocomial infection, disruption of personal and family life, and the potential for increased use of unnecessary medications and tests [42].

# Chapter 5:

## Contacts of Active TB Cases

The identification and prompt assessment of persons who are defined as contacts of persons with active TB disease is the second highest priority of TB programs, after prompt respiratory precautions and treatment of active TB disease. TB is listed under Schedule A of the Public Health Act Reporting of Diseases and Conditions Regulation as a disease requiring contact notification. Contacts are all persons to whom an infectious case (i.e., source case) has been in proximity.

Prompt investigation of contacts of infectious TB cases, especially close contacts (i.e., contacts with whom a case regularly shares breathing space), who are at a higher risk of becoming infected with TB and of progressing to active TB disease, is paramount to the successful containment of TB transmission. The sooner one can assess close household contacts of infectious TB cases, the sooner one can diagnose and treat any contacts who may have latent TB infection or early symptomatic active TB disease, resulting in reduction or elimination of further person-to-person spread of TB.

Recommended contact investigation activities, as provided in Manitoba's provincial TB protocol are [19]:

1. Assessment of information regarding the source case within reasonable time of receipt of notification of the case.
2. Initial interview of infectious source case to determine who the contacts are. The protocol notes that ideally this interview should occur within one business day of notification of the case.
3. Assessment of close contacts. The provincial protocol indicates that this should begin within seven working days of the contact being identified (this assessment should begin within three working days if the contact is known to be less than five years of age or to have high risk of disease progression if infected). This assessment may be delayed where diagnosis of the source case is presumptive (i.e., not yet confirmed), except for contacts who are children or have high risk of disease progression if infected where active TB disease is strongly suspected in source case.
4. Review of assessment of contacts to determine if contact investigation should be expanded to include lower-risk contacts. The provincial TB protocol indicates that this should occur within five working days, whenever possible, of completing assessment of the previous cohort of contacts.
5. Consideration of expansion of contact investigation if evidence of transmission has been identified among the previous cohort of contacts, as resources permit.

6. Consideration of repeating steps 4 and 5 for lower-risk contacts, as resources permit.
7. Prevention of progression to active TB disease among contacts found to have LTBI. This can be achieved through the use of a single antibiotic medication, usually INH given for nine months or RIF for four months (adults) or six months (children). All children exposed to a person with active TB should have a symptom enquiry and TST.

The objective of this component of our study was to assess the accuracy and completeness of information about contacts of active TB cases in the TB Registry and describe the characteristics of contacts. The sub-objectives were:

1. Examine the accuracy and completeness of information about contacts of active TB cases in the Manitoba TB Registry; and
2. Describe the sociodemographic characteristics, comorbidity characteristics, and outcomes among contacts of persons with active TB disease.

## Overview of Methods

To achieve our objective, we first developed an All Contact Cohort that included all contacts of individuals in the Active TB Cohort. Recall that the Active TB Cohort was composed of individuals with a TB diagnosis date or Manitoba TB Registry entry date between April 1, 1999 and March 31, 2014. The All Contact Cohort was used to describe the frequency of contacts, duration of contact assessment, and quality of information about contacts in the Manitoba TB Registry. It is important to note that this cohort does not contain unique individuals, because an individual could be a contact for more than a single case of active TB.

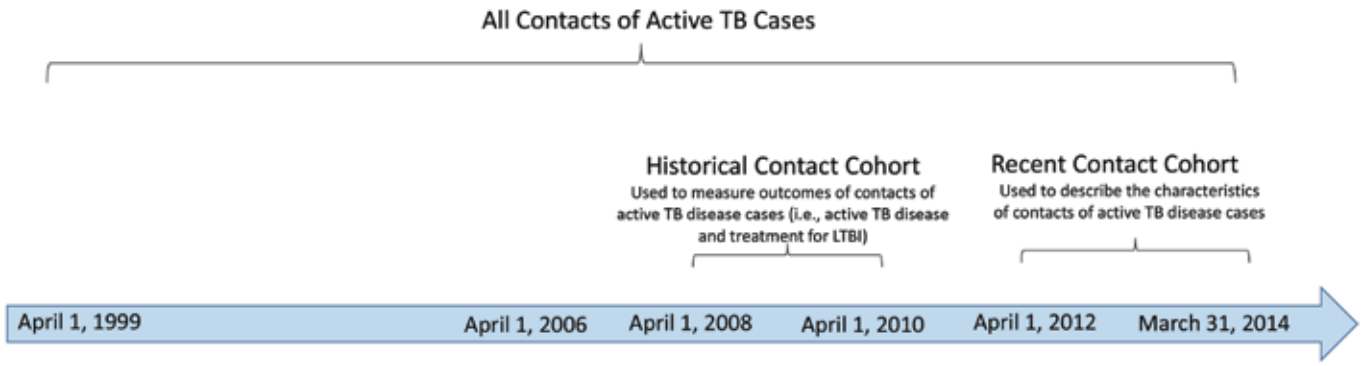
We subsequently constructed two cohorts composed of unique individuals. The first was the Recent Contact Cohort. It captured contacts of recent active TB cases. Given that contact assessments may change over time in response to policy changes or resource availability to conduct investigations, we developed this cohort to give the most current perspective on contact assessment information in the Manitoba TB Registry. To develop this cohort, we selected cases from the Active TB Cohort who had a study index date between April 1, 2012 and March 31, 2014. We excluded all active TB cases who did not have infectious (i.e., pulmonary) TB, based on diagnosis information in the Manitoba TB Registry. As well, we excluded all active TB cases who were less than 10 years of age, who are typically not considered infectious; cases with infectious TB are most likely to have a contact assessment. All contacts who did not have a valid PHIN were also excluded.

The second cohort of unique individuals was the Historical Contact Cohort. We used this cohort to investigate the process of disease transmission from active TB cases to contacts. Specifically, this cohort was used to examine rates of active TB disease and treatment for LTBI amongst the contacts of individuals with active TB. We selected individuals from the Active TB Cohort who had a study index date between April 1, 2008 and March 31, 2010, and excluded all active TB cases who did not have infectious TB, based on diagnosis information in the Manitoba TB Registry, as well as all active TB cases less than 10 years of age. All contacts who did not have a valid PHIN were also excluded.

Sociodemographic characteristics of the Recent Contact Cohort and Historical Contact Cohort were ascertained from administrative health data. Comorbidity characteristics of the cohorts were identified from administrative data in the year prior to the study index date, that is, the diagnosis date or TB Registry entry date for TB cases.

The Historical Contact Cohort included contacts of all cases with a new diagnosis for active TB over the period from April 1, 2008 to March 31, 2014. To identify new cases, we excluded all cases who had a previous TB diagnosis, looking as far back as April 1, 2006 to make this assessment. Similarly, we identified all individuals who were under treatment for LTBI over the period from April 1, 2006 to March 31, 2014; then we limited our attention to incidence of treated LTBI (i.e., initiation of new treatment) over the period from April 1, 2008 to March 31, 2014 (Figure 5.1).

**Figure 5.1: TB Cohorts Defined from the Manitoba TB Registry to Investigate Contact Characteristics**



The Population Registry, hospital discharge abstracts, physician billing claims, prescription drug records, and INAC Status Registry were used to characterize the contact cohorts and their outcomes. Multivariable Cox proportional hazards regression models were used to test a number of factors associated with initiation of treatment for LTBI and diagnosis of active TB in the Historical Contact Cohort. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test. Hazards ratios (HRs) and 95% confidence intervals (95% CIs) were estimated.

# Results

Between April 1, 1999 and March 31, 2014, there was a total of 22,583 contacts in the All Contact Cohort. Of this number, 16,071 (71.2%) had information about population of origin in the Manitoba TB Registry or First Nations Status in the INAC Status Registry; 14,914 (92.8%) contacts were identified as First Nations, 582 (3.5%) were identified as foreign-born and 575 (3.5%) were identified as Canadian-born non-First Nations contacts. Almost three-quarters of contacts who were identified as First Nations were from northern Manitoba health regions (10,699; 71.7%).

Given that there were a total of 1,686 individuals in the Active TB Cohort and 22,583 contacts, this represents an average of 22.0 contacts per active TB case during the study observation period. However, the average varied substantially based on the population of origin and geographic location of the active TB cases. The average was highest for First Nations active TB cases. Specifically, amongst cases identified as having a First Nations on-reserve origin, the average number of contacts was 30.1 (median = 23). An average of 22.5 contacts (median = 17), was identified for individuals in the Active TB Cohort who had a First Nations off-reserve origin. In foreign-born persons, the average number of contacts was 11.6 (median = 7). For Canadian-born non-First Nations cases, the average number of contacts was 17.1 (median = 11).

When we limited our attention to contacts of cases with infectious TB in the Active TB Cohort (n = 982), we identified a total of 16,728 contacts. Slightly more than one-third (35.8%) of these contacts had no information about population of origin in the Manitoba TB Registry. More than half of these contacts (57.8%) were identified as First Nations contacts. Smaller numbers were identified as foreign-born contacts (3.3%) and Canadian-born non-First Nations contacts (3.0%). Amongst those contacts for whom we could identify location of residence, 67.5% were non-Winnipeg health region residents.

We examined the Manitoba TB Registry for information about completeness of contact assessment. In the first five years of the study cohort (i.e., fiscal years 1999/2000-2003/04), information about contact assessment was missing for 97.4% of the cases. In the last five years of the study cohort (i.e., 2009/10-2013/14), 78.8% of contacts were noted to have a complete assessment with no further follow-up required and 0.5% were noted to have a complete assessment with ongoing surveillance required.

We compared the Manitoba TB Registry and the Population Registry for agreement between the two sources on a contact's sex, date of birth, postal code, and health region of residence. The results indicated generally good agreement; there was 98.6% agreement on sex, 95.4% agreement on date of birth, 93.4% agreement on health region of residence, and 77.2% agreement on six-digit postal code.

Further analysis was conducted on contact assessment duration. The Manitoba TB Registry does not contain information about the start date of contact assessment, so we used the study index date (i.e., date of TB diagnosis or date of TB Registry entry) as a proxy for the start date. We calculated the number of days between the study index date and the contact assessment date. This calculation was made for all active TB cases with at least one contact identified from the Manitoba TB Registry (n = 528 active TB cases). The mean was 367 days and the median was 340 days. This time is substantially longer than the expected time from TB diagnosis in an active TB case to follow-up of the initial contact; specifically, national guidelines recommend that investigation of high-priority TB contacts begin within seven working days of their being identified as contacts and be completed within one month [43]. A recently published evaluation of Alberta's TB program that provided an extensive analysis of TB contact investigations did not report on mean length of time between the diagnosis of active TB in the index case and completion of contact assessment [44]. In our study, the number of days between the study index date and the contact assessment date may not be an accurate measure of the true duration of the contact assessment.

## Characteristics of the Recent Contact Cohort

A total of 2,608 individuals were included in the Recent Contact Cohort (Table 5.1). Approximately three-quarters of these contacts were under the age of 45 years. As well, three quarters of these contacts were identified as First Nations individuals; most were from northern Manitoba. A high percentage of contacts (30.8%) were from one of the higher income quintiles (i.e., Q4). Almost half of the contacts were considered home (i.e., household) contacts (43.1%). Very few comorbid conditions were identified in contacts, with the exception of diabetes which was reported in 8.8% of recent contacts.

## Characteristics of the Historical Contact Cohort

There were 3,270 individuals in the Historical Contact Cohort (Table 5.1). As expected, the age distribution was similar to that in the Recent Contact Cohort, with about three-quarters under the age of 45 years. However, there were slightly fewer (31.9%) under the age of 19 years.

**Table 5.1: Sociodemographic Characteristics of Recent and Historical Contacts of Infectious Pulmonary Active TB Cases**

| | Recent Contacts (n=2,608) | | Historical Contacts (n=3,270) | |
|---|---|---|---|---|
| | Count | Percent | Count | Percent |
| **Age Group, Years** | | | | |
| 0-18 | 959 | 36.8% | 1,043 | 31.9% |
| 19-44 | 1,008 | 38.7% | 1,378 | 42.1% |
| 45-64 | 549 | 21.1% | 684 | 20.9% |
| 65+ | 92 | 3.5% | 165 | 5.0% |
| **Sex** | | | | |
| Male | 1,436 | 55.1% | 1,591 | 48.7% |
| Female | 1,172 | 44.9% | 1,679 | 51.3% |
| **Health Region** | | | | |
| Rural North (including Churchill) | 1,651 | 63.3% | 1,509 | 46.1% |
| Rural South | 247 | 9.5% | 503 | 15.4% |
| Winnipeg | 710 | 27.2% | 1,258 | 38.5% |
| **Income Quintile** | | | | |
| Q1 (Lowest) | 1,115 | 42.8% | 1,440 | 44.0% |
| Q2 | 337 | 12.9% | 1,027 | 31.4% |
| Q3 | 198 | 7.6% | 262 | 8.0% |
| Q4 | 803 | 30.8% | 340 | 10.4% |
| Q5 (Highest) | 155 | 5.9% | 201 | 6.1% |
| **Registered First Nations Status** | | | | |
| First Nations | 1,960 | 75.2% | 2,314 | 70.8% |
| All Other Manitobans | 648 | 24.8% | 956 | 29.2% |
| **Contact at Home** | | | | |
| Yes | 1,123 | 43.1% | 1,287 | 39.4% |
| No | 1,485 | 56.9% | 1,983 | 60.6% |
| **HIV Diagnosis** | | | | |
| Yes | 6 | 0.2% | 14 | 0.4% |
| No | 2,602 | 99.8% | 3,256 | 99.6% |
| **COPD Diagnosis** | | | | |
| Yes | 74 | 2.8% | 160 | 4.9% |
| No | 2,534 | 97.2% | 3,110 | 95.1% |
| **Heart Diagnosis** | | | | |
| Yes | 22 | 0.8% | 52 | 1.6% |
| No | 2,586 | 99.2% | 3,218 | 98.4% |
| **Diabetes Diagnosis** | | | | |
| Yes | 230 | 8.8% | 364 | 11.1% |
| No | 2,378 | 91.2% | 2,906 | 88.9% |
| **Chronic Kidney Disease Diagnosis** | | | | |
| Yes | 29 | 1.1% | 51 | 1.6% |
| No | 2,579 | 98.9% | 3,219 | 98.4% |
| **Rheumatoid Arthritis Diagnosis** | | | | |
| Yes | 15 | 0.6% | 32 | 1.0% |
| No | 2,593 | 99.4% | 3,238 | 99.0% |

In the Historical Contact Cohort, 70.8% were identified as First Nations individuals. A larger percentage of historical contacts than recent contacts originated from Winnipeg, possibly due to a growing number of foreign-born active TB cases being diagnosed in Winnipeg in more recent years (which often have fewer contacts).

The income quintile distribution of individuals in the Historical Contact Cohort was more consistent with the expectation of higher numbers of contacts in the lowest income quintiles (i.e., 44.0% in Q1) and low numbers of contacts in the highest income quintiles (i.e., 6.1% in Q5). About the same percentage of historical as recent contacts were identified as household contacts (39.4%). Similarly to recent contacts, very little comorbidity was identified in historical contacts, once again with the exception of diabetes, which was reported in 11.1% of historical contacts.

## Onset of Active TB and Treatment Initiation for LTBI in the Historical Contact Cohort

Previous research has shown that for close contacts (e.g., household contacts) of persons with active TB disease, up to 2% will develop active TB disease within the course of the TB contact investigation and between 20% and 35% will have LTBI [44,45]. In our study, all contacts of active TB cases were evaluated for these outcomes between April 1, 2008 and March 31, 2014.

Overall, 115 (3.6%) individuals in the Historical Contact Cohort, which was used to investigate disease transmission from active TB cases, developed active TB (Table 5.2). The percentage of males who developed active TB was higher (3.9%) than the percentage of females (3.2%). Active TB disease was higher in the 19-44 age group (4.3%) than in other age groups for the Historical Contact Cohort. Residence in rural Manitoba and First Nations origin were significantly associated with subsequent development of active TB disease in contacts. The percentage of active TB disease in First Nations historical contacts was 4.6% compared to 1.0% in non-First Nations historical contacts. The percentage of active TB disease in household contacts (4.9%) was also higher than in non-household contacts (2.7%). Of note, the highest percentage of active TB disease was measured in contacts with diabetes (6.1% vs 3.2% in contacts without diabetes).

**Table 5.2: Diagnosis of Active TB and Treatment for LTBI Amongst Historical Contacts of Active Infectious Pulmonary TB Cases (n = 3,270)**

| | Active TB | | Treated LTBI | |
|---|---|---|---|---|
| | Count | Percent | Count | Percent |
| **Age Group, Years** | | | | |
| 0-18 | 34 | 3.3% | 256 | 25.3% |
| 19-44 | 58 | 4.3% | 185 | 13.7% |
| 45-64 | 20 | 3.0% | 90 | 13.4% |
| 65+ | s | - | 14 | 8.6% |
| **Health Region** | | | | |
| Rural North (including Churchill) | 59 | 4.0% | 304 | 21.1% |
| Rural South | 25 | 5.0% | 125 | 24.9% |
| Winnipeg | 31 | 2.5% | 116 | 9.2% |
| **Registered First Nations Status** | | | | |
| First Nations | 105 | 4.6% | 485 | 21.6% |
| All Other Manitobans | 10 | 1.0% | 60 | 6.3% |

s indicates data suppressed due to small numbers

Overall, 545 (17.1%) individuals in the Historical Contact Cohort initiated treatment for LTBI in the observation period (Table 5.2). This percentage was highest amongst individuals less than 19 years of age and lowest amongst individuals over 65 years, as would be expected given that contacts of active TB disease who are children under five years are the highest priority for offering LTBI treatment and adults over 65 years are much more likely to have drug intolerances.

First Nations individuals in the Historical Contact Cohort were more likely to initiate treatment for LTBI. More than one-fifth (21.6%) of First Nations contacts initiated treatment compared to 6.4% of all other Manitoban contacts. In addition, 19.9% of contacts within the lowest income quintile (Q1) and 19.1% of individuals in the next lowest quintile (Q2) initiated LTBI treatment. In contrast, only 8.6% of individuals in the highest income quintile (Q5) initiated LTBI treatment.

Individuals who were identified as household contacts were more likely to initiate LTBI treatment (22.5%) than non-household contacts (13.6%). Individuals in the Historical Contact Cohort who had a diagnosis of diabetes were as likely to initiate LTBI treatment (16.4%) as those who did not have a diagnosis of diabetes (17.1%).

Multivariable Cox proportional hazards regression models (Table 5.3) revealed an association between the development of active TB in members of the Historical Contact Cohort who were identified as First Nations, household contacts, and had a diagnosis for HIV or diabetes. Patient characteristics not associated with the development of active TB disease in the Historical Contact Cohort included age and sex, region of residence, income quintile, and other comorbid conditions such as chronic renal, cardiac, and respiratory disease.

**Table 5.3: Hazard Ratios and 95% Confidence Intervals for Diagnosis of Active TB Amongst Historical Contacts of Active Infectious Pulmonary TB Cases (n = 3,270)**

| | Hazard Ratio | 95% Confidence Interval |
|---|---|---|
| **Age Group, Years (Ref=19-44)** | | |
| 0-18 | 0.75 | 0.48 – 1.17 |
| 45-64 | 0.74 | 0.43 – 1.26 |
| 65+ | 0.51 | 0.15 – 1.68 |
| **Sex (Ref=Female)** | | |
| Male | 1.28 | 0.89 – 1.85 |
| **Health Region (Ref=Winnipeg)** | | |
| Rural North (including Churchill) | 1.04 | 0.63 – 1.73 |
| Rural South | 1.50 | 0.85 – 2.66 |
| **Registered First Nations Status (Ref=All Other Manitobans)** | | |
| First Nations | 4.26 | **1.99 – 9.11** |
| **Income Quintile (Ref=Q1 (Lowest))** | | |
| Q2 | 0.77 | 0.50 – 1.19 |
| Q3 | 1.84 | 0.87 – 3.89 |
| Q4 | 0.76 | 0.36 – 1.61 |
| Q5 (Highest) | 0.59 | 0.18 – 1.93 |
| **Home Contact (Ref=No)** | | |
| Yes | 1.67 | **1.15 – 2.42** |
| **HIV Diagnosis (Ref=No)** | | |
| Yes | 9.32 | **3.24 – 26.76** |
| **Chronic Kidney Disease (Ref=No)** | | |
| Yes | 2.17 | 0.67 – 7.05 |
| **Heart Disease (Ref=No)** | | |
| Yes | 0.57 | 0.08 – 4.19 |
| **Diabetes (Ref=No)** | | |
| Yes | 1.79 | **1.07 – 3.00** |

**Bold** hazard ratios are statistically significant at $\alpha = 0.05$

Amongst individuals in the Historical Contact Cohort (Table 5.4), the likelihood of LTBI treatment initiation was high for individuals less than 19 years of age, individuals living in the rural north or rural south, and individuals who were household contacts. Historical contacts within the highest income quintiles had a significantly lower likelihood of initiating treatment for LTBI.

**Table 5.4: Hazard Ratios and 95% Confidence Intervals for Treatment of LTBI Amongst Historical Contacts of Active Infectious Pulmonary TB Cases (n = 3,270)**

| | Hazard Ratio | 95% Confidence Interval |
|---|---|---|
| **Age Group, Years (Ref=19-44)** | | |
| **0-18** | **1.81** | **1.49 – 2.20** |
| **45-64** | 1.15 | 0.89 – 1.49 |
| **65+** | 0.87 | 0.50 – 1.50 |
| **Sex (Ref=Female )** | | |
| **Male** | 1.14 | 0.96 – 1.35 |
| **Health Region (Ref=Winnipeg)** | | |
| **Rural North (including Churchill)** | **1.57** | **1.22 – 2.03** |
| **Rural South** | **2.05** | **1.55 – 2.70** |
| **Registered First Nations Status (Ref=All Other Manitobans)** | | |
| **First Nations** | **2.18** | **1.56 – 3.05** |
| **Income Quintile (Ref=Q1 (Lowest))** | | |
| **Q2** | 0.96 | 0.79 – 1.16 |
| **Q3** | 0.94 | 0.61 – 1.45 |
| **Q4** | **0.68** | **0.48 – 0.97** |
| **Q5 (Highest)** | **0.52** | **0.31 – 0.88** |
| **Home Contact (Ref=No )** | | |
| **Yes** | **1.57** | **1.32 – 1.87** |
| **HIV Diagnosis (Ref=No )** | | |
| **Yes** | 1.86 | 0.59 – 5.83 |
| **Chronic Kidney Disease (Ref=No)** | | |
| **Yes** | 0.38 | 0.12 – 1.19 |
| **Heart Disease (Ref=No )** | | |
| **Yes** | 0.34 | 0.08 – 1.36 |
| **Diabetes (Ref=No)** | | |
| **Yes** | 1.11 | 0.83 – 1.49 |

**Bold** hazard ratios are statistically significant at $\alpha = 0.05$

## Chapter Summary

In this chapter, we explored the characteristics of contacts of active TB cases and their outcomes. Both the Manitoba TB Registry and administrative data (i.e., hospital records, physician claims, prescription drug records) were used to conduct this component of the study.

While there are many contacts identified in the Manitoba TB Registry, indicating that contact investigations are extensive, it can be challenging to identify contacts; individuals may be contacts as well as active TB cases, depending on which year(s) of data are under investigation.

There is only a single date pertaining to contact assessment in the Manitoba TB Registry; in the TB Registry data dictionary, it is labelled as the date the contact assessment is done. We examined the duration of time from the study index date (i.e., date of active TB diagnosis or entry into the Manitoba TB Registry) to the contact assessment date as a proxy measure for the duration of the contact investigation period. Pan-Canadian Public Health Network guidelines for tuberculosis control programs recommend that follow-up lists of TB contacts be completed within seven days of the diagnosis of an infectious TB case, and that assessment of close contacts be completed and LTBI treatment started, if indicated and not contraindicated or refused, within 28 days of the diagnosis of infectious TB [29]. Our search for relevant literature did not identify any Canadian studies that evaluated the feasibility of attaining these benchmarks. The duration of time between the study index date and the contact assessment date in the Manitoba TB Registry seems implausible as an accurate measure of the duration of the contact investigation based on these guidelines.

We also described the average and median number of contacts per active TB case. We found that these numbers were higher amongst First Nations on-reserve individuals and lower for foreign-born and Canadian-born non-First Nations active TB cases. These figures are consistent with those from Alberta and other jurisdictions, which have shown a higher number of contacts amongst First Nations than amongst non-First Nations active TB cases [46–48]. Contact investigation is considered a high-priority screening activity for TB programs in higher-income countries. A higher average/median number of contacts in First Nations on-reserve individuals may reflect more thorough contact investigations in on-reserve communications and/or greater numbers of contacts amongst First Nations on-reserve TB cases. Contact rates are influenced by a multitude of factors, including geographic mobility, clustering of individuals (e.g., within private households as well as within public spaces such as on public transportation and shelters), infectiousness (which is influenced by such factors as the type of outbreak-causing strain of the bacterium and access to healthcare), and susceptibility to disease, which includes both TB-specific factors (e.g., the immune response to TB) and extrinsic factors (e.g., smoking and other indoor air pollution) [49].

Lastly, by linking the Manitoba TB Registry with the administrative health data, we were able to measure the rate of active TB disease onset amongst contacts of active TB cases and the factors associated with disease onset, as well as the rate of treatment initiation for contacts with LTBI and the factors associated with treatment initiation. A recent systematic review found that initiation of treatment varied widely in case contacts, from 40-85% [50]. Unfortunately, we are not able to estimate the rate in our cohort because we do not know the number of people with LTBI; we only know the total number of contacts. At the same time, outcome data can be useful for comparative investigations over time or across populations (e.g., urban vs. rural) to better understand the factors that drive disease transmission and the factors that influence initiation of treatment amongst individuals with LTBI.

# Chapter 6:

# Treatment Completion for Latent TB Infections

Once a person who has been exposed to TB becomes infected, the only way to detect this infection is via screening programs that offer testing for LTBI. Screening for LTBI is a well-recognized means of TB disease prevention and containment. Examples of individuals who should be offered testing for LTBI include close household contacts of persons with active TB disease, persons who come from communities with a high incidence of TB (such as northern Indigenous communities, newcomers to Canada who are refugees, persons with HIV infection, persons with chronic renal disease on dialysis, and persons who are being treated with immunosuppressive therapies). Such individuals may have a high risk of LTBI and/or progression to active TB disease, and are most likely to benefit from treatment. When such individuals are offered treatment for LTBI, ideally they will accept and complete therapy.

The recommended benchmark for accepting and completing LTBI treatment is 80% [44]. Since LTBI is not a reportable disease in Manitoba, we do not know how many individuals have LTBI. Using prescription drug data, it is possible to determine how many individuals start LTBI treatment and how many complete treatment [16,20]. LTBI treatment completion rates, when they have been measured elsewhere in Canada and the USA, have ranged from 31-76% [6,16,20,44,51–53]. LTBI treatment acceptance rates are not frequently measured, but in a recent review of TB programs in Alberta they were reported as 80% [44].

The objective of this component of the study was to explore trends in the treatment of LTBI and the characteristics of individuals receiving treatment for LTBI. We conducted this analysis for different prescription medication regimes for LTBI.

## Methods

For the Treated LTBI Cohort, we examined completion of the prescribed treatment course using DPIN data in the Manitoba Population Research Data Repository housed at MCHP. This analysis was conducted for all cohort members who had at least 365 days of health insurance coverage following the study index date. Each individual in the Treated LTBI Cohort was assigned to one of two mutually exclusive groups: (a) INH Treatment Group: first prescription on or after the study index date was for INH; or (b) RIF treatment group: first prescription on or after the study index date was for RIF.

In Canada, nine months of daily self-administered INH or four months of daily self-administered RIF are currently recommended for the treatment of LTBI [43]. We used the DPIN data to identify members of the Treated LTBI

Cohort who were dispensed INH for 270 days or more within a 365-day period; the individuals who met this criterion were defined as having completed INH treatment (INH270). Since completion of six months of INH has also been considered a full course of treatment, albeit less efficacious than a nine-month treatment course, a second analysis of cohort members who were dispensed INH for 180 days or more within a 270-day period were also identified as having completed INH treatment (INH180) [43]. Individuals who were dispensed RIF for 120 days or more within a 180-day period were defined as completing RIF treatment (RIF120).

The percentage of individuals who completed treatment based on the previously described criteria was calculated: INH270, INH180, and RIF120. The sociodemographic characteristics and Charlson comorbidity index scores of completers and non-completers were described. Note that population of origin information was only available from the INAC Status Registry for the Treated LTBI Cohort. Therefore, individuals in the cohort could only be classified as First Nations and non-First Nations. Also, a limitation of this analysis is that it is based on dispensed medications; it is impossible to know if a medication that has been dispensed has actually been taken.

Multivariable logistic regression models were used to test the association of cohort covariates with treatment completion. Model fit was evaluated using the Hosmer-Lemeshow goodness-of-fit test. Odds ratios (ORs) and 95% CIs were estimated.

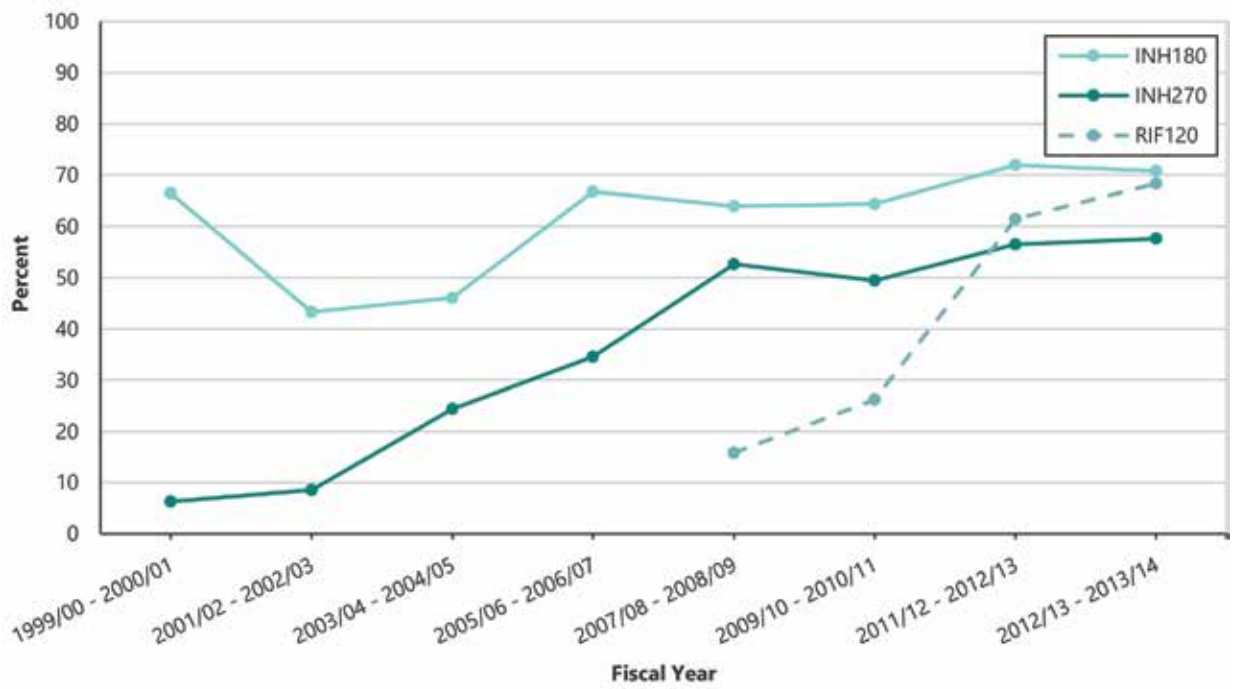
# Results

## LTBI Treatment Completion

The sub-group of the Treated LTBI Cohort that was used to measure treatment completion rates consisted of 5,514 individuals who started treatment between April 1, 1999 and March 31, 2013. Using INH180 or RIF120 treatment regimens, 3,322 (60.2%) of individuals completed treatment (Table 6.1). Given that we did not know the planned prescribing regimen, we considered both INH180 and INH270 for calculating treatment completion for all individuals dispensed INH as their index LTBI treatment. Individuals who initiated LTBI treatment with INH and who were subsequently switched to treatment with RIF were not included in the Treated LTBI Cohort.

INH180 showed higher treatment completion rates (63.8%) than other treatments; these rates remained stable from 2005-2014 (Figure 6.1). INH270 treatment completion was initially low (40.4%) but increased significantly over the 15-year study period, particularly after 2007 where treatment completion rates stabilized at around 50-60%. RIF120 treatment completion was the lowest overall (27.0%), but the rate increased significantly after 2011, up to nearly 70% by the end of the study observation period.

**Figure 6.1: Treatment Completion Rates by Type of Medication in the Treated LTBI Cohort in Manitoba, 1999-2014**




Note: INH180 = 180 day supply of isoniazid dispensed within 270 days of index date; INH270 = 270 day supply of isoniazid dispensed within 365 days of index date; RIF120 = 120 day supply of rifampin within 180 days of index date
Blank spaces indicate data suppression due to small numbers

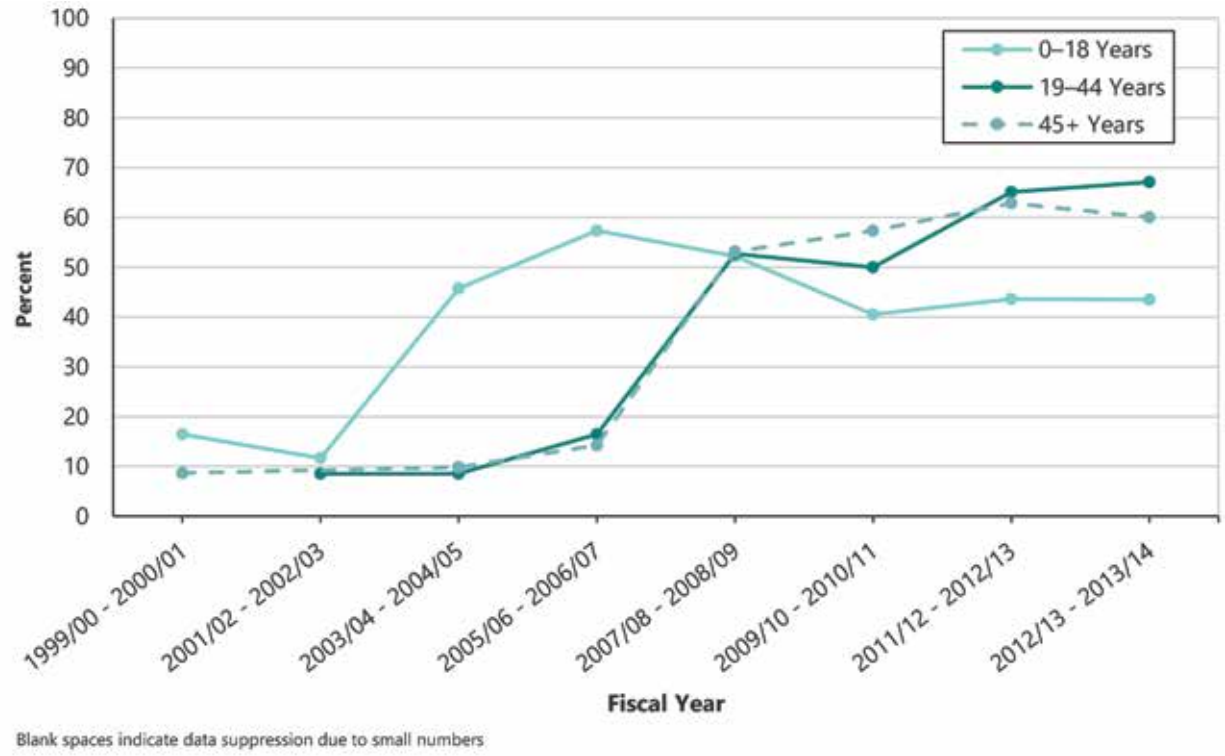
**Table 6.1: Treatment Completion Rates by Type of Medication and Socio-Demographic Characteristics for the Treated LTBI Cohort in Manitoba, 1999-2014**

| | INH180 | | | INH270 | | | RIF120 | | |
|---|---|---|---|---|---|---|---|---|---|
| | N=4,985 | | | N=4,985 | | | N=529 | | |
| | Treatment Complete | Total | Rate | Treatment Complete | Total | Rate | Treatment Complete | Total | Rate |
| **Sex** | | | | | | | | | |
| **Female** | 1,613 | 2,586 | 62.4% | 1,017 | 2,586 | 39.3% | 73 | 275 | 26.5% |
| **Male** | 1,566 | 2,399 | 65.3% | 998 | 2,399 | 41.6% | 70 | 254 | 27.6% |
| **Age Group, Years** | | | | | | | | | |
| **0-18** | 1,262 | 1,842 | 68.5% | 854 | 1,842 | 46.4% | 10 | 84 | 11.9% |
| **19-44** | 1,273 | 2,086 | 61.0% | 746 | 2,086 | 35.8% | 67 | 180 | 37.2% |
| **45-64** | 574 | 936 | 61.3% | 364 | 936 | 38.9% | 55 | 169 | 32.5% |
| **65+** | 70 | 121 | 57.9% | 51 | 121 | 42.1% | 11 | 96 | 11.5% |
| **Region of Residence** | | | | | | | | | |
| **Rural North (including Churchill)** | 1,840 | 2,848 | 64.6% | 1,155 | 2,848 | 40.6% | 35 | 85 | 41.2% |
| **Rural South** | 311 | 499 | 62.3% | 206 | 499 | 41.3% | 45 | 184 | 24.5% |
| **Winnipeg** | 1,028 | 1,638 | 62.8% | 654 | 1,638 | 39.9% | 63 | 260 | 24.2% |
| **Registered First Nations Status** | | | | | | | | | |
| **First Nations** | 2,236 | 3,506 | 63.8% | 1,424 | 3,506 | 40.6% | 47 | 121 | 38.8% |
| **All Other Manitobans** | 943 | 1,479 | 63.8% | 591 | 1,479 | 40.0% | 96 | 408 | 23.5% |
| **Income Quintile** | | | | | | | | | |
| **Q1 (Lowest)** | 1,554 | 2,489 | 62.4% | 976 | 2,489 | 39.2% | 42 | 153 | 27.5% |
| **Q2** | 579 | 866 | 66.9% | 375 | 866 | 43.3% | 26 | 101 | 25.7% |
| **Q3** | 218 | 348 | 62.6% | 134 | 348 | 38.5% | 30 | 95 | 31.6% |
| **Q4** | 683 | 1,042 | 65.5% | 448 | 1,042 | 43.0% | 30 | 98 | 30.6% |
| **Q5 (Highest)** | 145 | 240 | 60.4% | 82 | 240 | 34.2% | 15 | 82 | 18.3% |
| **Charlson Comorbidity Index** | | | | | | | | | |
| **0 (Most Healthy)** | 2,535 | 3,887 | 65.2% | 1,599 | 3,887 | 41.1% | 90 | 303 | 29.7% |
| **1-2** | 520 | 899 | 57.8% | 328 | 899 | 36.5% | 41 | 153 | 26.8% |
| **3+ (Less Healthy)** | 124 | 199 | 62.3% | 88 | 199 | 44.2% | 12 | 73 | 16.4% |
| **Year of Treatment Initiation** | | | | | | | | | |
| **1999-2003** | 418 | 820 | 51.0% | 65 | 820 | 7.9% | 9 | 171 | 5.3% |
| **2004-2008** | 1,439 | 2,236 | 64.4% | 914 | 2,236 | 40.9% | 15 | 147 | 10.2% |
| **2009-2014** | 1,322 | 1,929 | 68.5% | 1,036 | 1,929 | 53.7% | 119 | 211 | 56.4% |
| **Overall Total** | 3,179 | 4,985 | 63.8% | 2,015 | 4,985 | 40.4% | 143 | 529 | 27.0% |

Note: INH180 = 180 day supply of isoniazid dispensed within 270 days of index date; INH270 = 270 day supply of isoniazid dispensed within 365 days of index date; RIF120 = 120 day supply of rifampin dispensed within 180 days of index date.

INH270 treatment completion rates were low, which is most likely due to the challenges in completing a 9-month course of INH, such as side effects leading to treatment discontinuation. The low INH270 treatment completion rates in individuals under 19 years of age from 2009/10-2013/14 (Figure 6.2) are not easily explained, given that there were no age-related differences in INH180 treatment completion rates during that same time period (Figure 6.3) and given a longstanding policy in Manitoba to provide Directly Observed Preventative Therapy (DOPT) in children. Noteworthy, though, is the reversal in treatment completion rates for both INH270 and INH180 in First Nations individuals, which were higher from 2004/05-2009/10 (Figures 6.4 and 6.5) and have more recently been 10-20% lower than for non-First Nations individuals. Further analysis could facilitate the interpretation of why INH270 treatment completion rates in First Nations persons have plateaued at about 50% since 2008/09 (Figure 6.4), while during the same period treatment completion rates in all other Manitobans increased from 40% to 70%. This finding is also difficult to explain given the policy in Manitoba to deliver treatment for LTBI using DOPT in First Nations individuals living in northern communities.

**Figure 6.2: Treatment Completion Rates for Treated LTBI Cohort for a 270-day supply of Isoniazid, Stratified by Age Group**




Blank spaces indicate data suppression due to small numbers

**Figure 6.3: Treatment Completion Rates for Treated LTBI Cohort for a 180-day supply of Isoniazid, Stratified by Age Group**

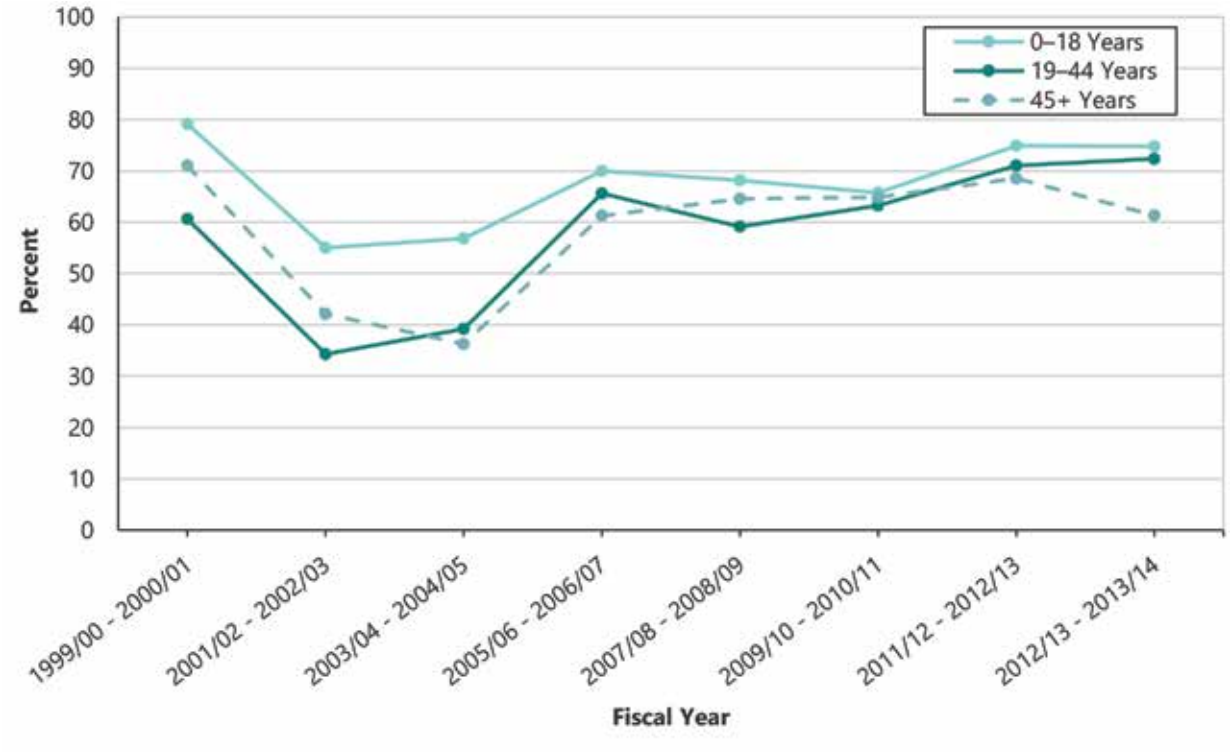
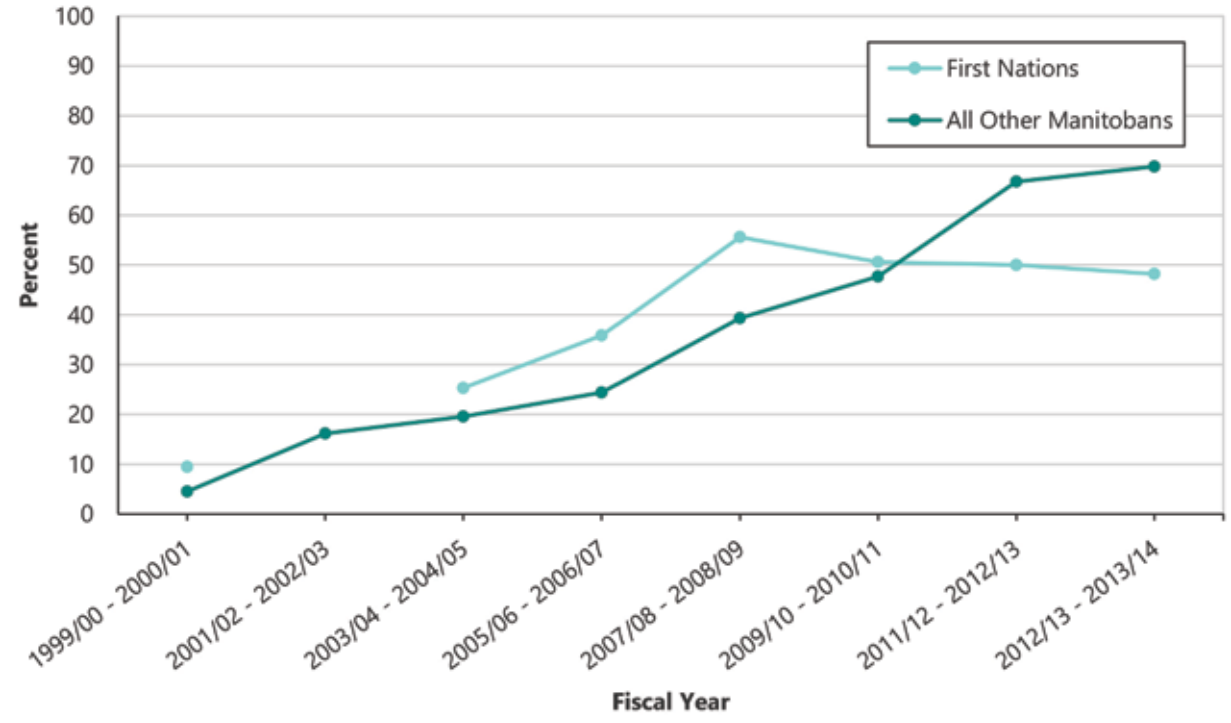
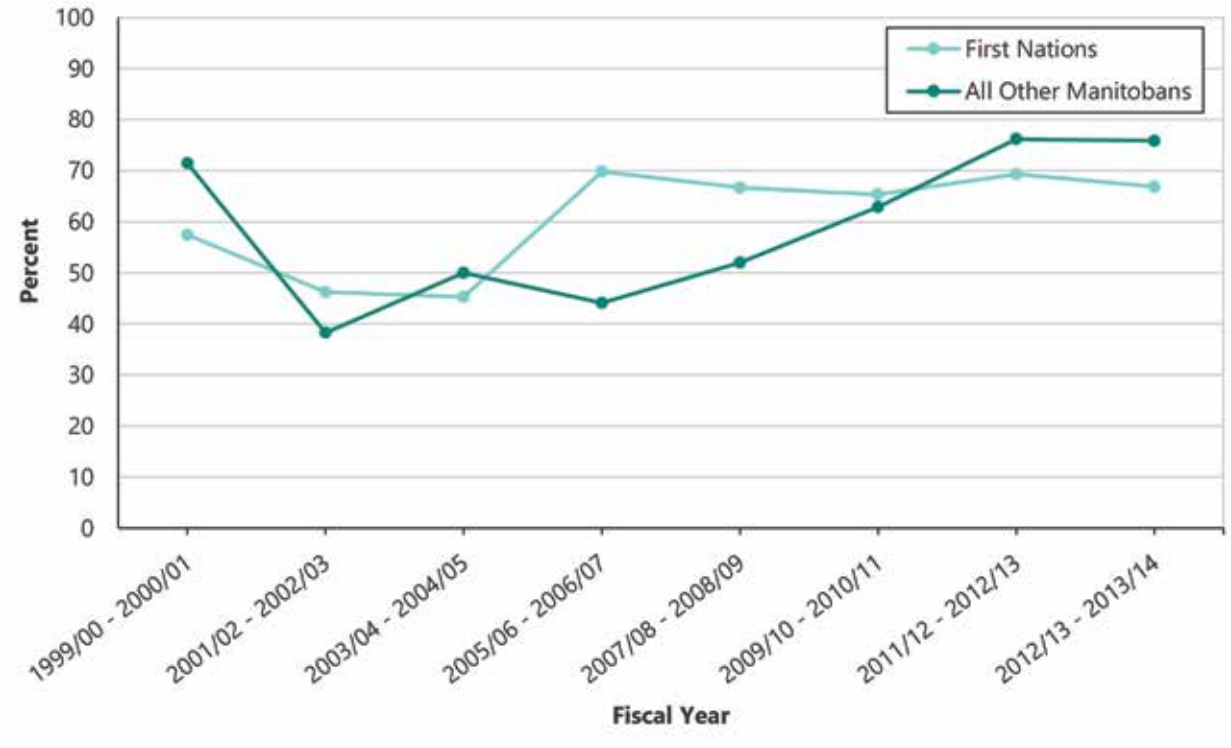



**Figure 6.4: Treatment Completion Rates for Treated LTBI Cohort for a 270-day supply of Isoniazid, Stratified by First Nations Status**




Blank spaces indicate data suppression due to small numbers

**Figure 6.5: Treatment Completion Rates for Treated LTBI Cohort for a 180-day supply of Isoniazid, Stratified by First Nations Status**




As Table 6.2 reveals, the odds of INH180 and INH270 completion was higher in individuals under 19 years of age compared to adults aged 19-44 years (68.5% vs 61.0%; HR 1.4; 95% CI 1.2-1.6). This may be a reflection of the policy in Manitoba to use DOPT for all LTBI treatment in children. The lower odds of completing INH180 in First Nations persons is difficult to explain given that there also exists a practice in Manitoba to use DOPT for all LTBI treatment in First Nations persons living in northern communities. Sex, region of residence (i.e., rural vs urban; north vs south), income quintile, and presence of comorbid conditions were not significantly associated with treatment completion (Table 6.2).

Treatment completion significantly improved over time; rates were highest for INH180 (68.5%) in the most recent 5-year cycle (2009-2014) vs 51.0% in 1999-2003 and 64.4% in 2004-2008. The odds ratio for INH180 treatment completion was about two times larger in 2009-2014 than in 1999-2003 (Table 6.2). For INH270 and RIF120, the odds were even higher in 2009-2014 than in 1999-2003.

**Table 6.2: Adjusted Odds Ratios for the Factors Associated with Treated LTBI Cohort Treatment Completion in Manitoba, 1999/2000-2014/15**

| | INH180 N=4,985 | | INH270 N=4,985 | | RIF120 N=529 | |
|---|---|---|---|---|---|---|
| | Odds Ratio | 95% Confidence Interval | Odds Ratio | 95% Confidence Interval | Odds Ratio | 95% Confidence Interval |
| **Sex (Ref=Female)** | | | | | | |
| **Male** | 1.11 | 0.98 - 1.24 | 1.05 | 0.93 - 1.18 | 0.99 | 0.61 - 1.59 |
| **Age Group, Years (Ref=19-44)** | | | | | | |
| **0-18** | **1.37** | **1.19 - 1.57** | **1.55** | **1.35 - 1.79** | 0.53 | 0.22 - 1.27 |
| **45-64** | 1.02 | 0.86 - 1.21 | 1.04 | 0.87 - 1.25 | 0.86 | 0.49 - 1.51 |
| **65+** | 0.86 | 0.58 - 1.28 | 1.10 | 0.73 - 1.67 | **0.40** | **0.17 - 0.92** |
| **Region of Residence (Ref=Winnipeg)** | | | | | | |
| **Rural North (including Churchill)** | 1.11 | 0.92 - 1.35 | 0.97 | 0.79 - 1.19 | 1.80 | 0.76 - 4.31 |
| **Rural South** | 1.03 | 0.82 - 1.29 | 1.05 | 0.83 - 1.33 | 0.88 | 0.50 - 1.53 |
| **Registered First Nations Status (Ref=All Other Manitobans)** | | | | | | |
| **First Nations** | **0.80** | **0.65 - 0.97** | 0.85 | 0.69 - 1.04 | 1.02 | 0.47 - 2.21 |
| **Income Quintile (Ref=Q5 (Highest))** | | | | | | |
| **Q1 (Lowest)** | 1.03 | 0.78 - 1.37 | 1.12 | 0.82 - 1.53 | 1.18 | 0.51 - 2.72 |
| **Q2** | 1.22 | 0.90 - 1.65 | 1.22 | 0.88 - 1.70 | 1.63 | 0.68 - 3.87 |
| **Q3** | 1.03 | 0.73 - 1.45 | 1.00 | 0.69 - 1.46 | 1.79 | 0.76 - 4.20 |
| **Q4** | 1.13 | 0.84 - 1.53 | 1.26 | 0.91 - 1.75 | 1.45 | 0.61 - 3.46 |
| **Charlson Comorbidity Index (Ref=3+ (Less Healthy))** | | | | | | |
| **0 (Most Healthy)** | 0.97 | 0.71 - 1.34 | **0.70** | **0.50 - 0.98** | 2.17 | 0.96 - 4.89 |
| **1-2** | 0.78 | 0.57 - 1.09 | **0.64** | **0.46 - 0.90** | 1.37 | 0.59 - 3.19 |
| **Year of Treatment Initiation (Ref=1999-2003)** | | | | | | |
| **2004-2008** | **1.67** | **1.41 - 1.98** | **7.96** | **6.06 - 10.46** | 1.95 | 0.79 - 4.83 |
| **2009-2014** | **2.05** | **1.73 - 2.43** | **13.46** | **10.28 - 17.63** | **21.32** | **9.91 - 45.85** |

Note: INH180 = 180 day supply of isoniazid dispensed within 270 days of index date; INH270 = 270 day supply of isoniazid dispensed within 365 days of index date; RIF120 = 120 day supply of rifampin dispensed within 180 days of index date.

**Bold** odds ratios indicate values that are statistically significant at $\alpha = 0.05$

## Chapter Summary

This chapter examined completion of the course of treatment for prescription medications in the Treated LTBI Cohort. Three different treatment regimes were investigated: INH over 180 days, INH over 270 days, and RIF over 120 days. For the RIF 120-day course of treatment, there was a substantial increase in completion rates over time, particularly in the last two years of the study observation period. Similarly, treatment completion rates for both INH regimens (but especially the longer 270-day treatment course) improved over time.

Both expected and unexpected variations in treatment completion were noted by patient characteristics of age, population of origin, Charlson comorbidity score, and year of treatment initiation. Higher treatment completion rates in children are likely explained by the universal delivery of LTBI treatment using DOPT in children. But by the same explanation, one would have expected higher treatment completion rates in First Nations persons, given that DOPT is also widely used in northern remote communities.

LTBI treatment completion rates of 30-70% are consistent with treatment completion rates that have been reported in Canada, the US, and Europe [16,20,50,51]. That INH treatment completion rates in Manitoba have gradually improved since 2005 likely reflects the restructuring of TB services that took place in this province between 2005 and 2010, marked by an increasing focus on LTBI treatment as a key step towards achieving TB elimination. The use of RIF for the treatment of LTBI was very limited prior to 2010 and likely restricted to individuals for whom difficulties were anticipated for the completion of INH. Hence, the low use of RIF prior to 2011 is not unexpected. Since 2012, there have been efforts to promote increasing use of RIF for the treatment of LTBI, accompanied by improved infrastructure to assist individuals in adhering to LTBI treatment. This likely explains the dramatic increase in RIF treatment completion rates between 2007 and 2014.

# Chapter 7:

# Summary, Conclusions, and Recommendations

## Summary and Conclusions

The World Health Organization's *End TB Strategy*, which was initiated in 2016, aims to end the global TB epidemic. More specifically, the goals of the strategy include reducing the number of TB deaths by 95% and the number of new TB cases by 90% between 2015 and 2035 [54]. A key component of this strategy is high-quality, timely, and relevant data to support local decision making [55]. Three types of data are identified as critical to the success of this strategy: (1) existing, routinely-collected data, such as the data found in the Manitoba TB Registry; (2) new data elements that can be used to expand and enhance existing, routinely-collected data sources, such as detailed risk factor measures incorporated into the Manitoba TB Registry; and (3) new, targeted data sources [55]. The latter could include such data types as "omics" data (e.g., genomics, proteomics) to better understand drug resistance in TB, surveys to better understand barriers to seeking or obtaining care, or detailed contact investigation information to better understand transmission patterns. New targeted data sources are intended to provide enhanced information about the dynamics of active TB disease transmission, treatment, and outcomes. An important attribute of the *End TB Strategy* is to ensure that local decision makers are engaged and have access to data to target locations with high case rates.

Achievement of the *End TB Strategy* goals also requires a focus on collaborations across government, communities, First Nations, healthcare providers, and industry partners. There is an emphasis on engagement and partnerships to achieve the Strategy goals.

Given this context, our study addresses a timely topic. Our purpose was to investigate the use of administrative data, linked with Manitoba TB Registry data, to study active TB disease and treatment for LTBI. The objectives were to describe the completeness and accuracy of selected elements of the Manitoba TB Registry, examine the validity of case definitions to ascertain active TB cases from hospital discharge abstracts and physician billing claims, examine pre- and post-diagnosis trends in healthcare use and factors that affect use, explore the characteristics and outcomes of contacts of active TB cases, and report on the treatment of LTBI.

This research was motivated in part by indicators developed by the WRHA's Integrated TB Services Program Data Management Committee for program evaluation. These indicators encompass TB disease identification and management, contact investigations, and LTBI management. All of these program elements are important to the *End TB Strategy*. We provide information about the availability and quality of data resources in Manitoba for measuring concepts relevant to the performance indicators.

Two study cohorts were the focus of our study; the first included active TB cases identified from the Manitoba TB Registry over a 15-year period. The second included individuals receiving treatment for LTBI over a 15-year period; the latter group was identified from prescription drug records and was based on a previously published methodology. The composition of the Active TB Cohort illustrates the disproportionate impact of TB on First Nations populations in northern Manitoba and foreign-born individuals in Winnipeg. As well, the Treated LTBI Cohort demonstrates the disproportionate impact of LTBI on young First Nations individuals. Close to 85% of cases in the Treated LTBI Cohort were from the most recent 10 years of our 15-year study period. An increase in the number of treated cases over time might mean that the pool of untreated LTBI cases is also increasing. However, an increase in the number of treated cases might also mean that a greater proportion of the total number of LTBI cases in the population are being treated. The data sources used in this study cannot provide us with an accurate estimate of the incidence of LTBI in the Manitoba population. Estimating LTBI incidence and prevalence in the population, which is important for measuring progress to eradicate TB, is a complex process that takes account of such factors as the annual risk of TB infection, demographic characteristics (and projections), HIV prevalence, and proportion of TB that is smear positive. The most recent LTBI prevalence estimate for the Americas (i.e., North and South America, including Canada), is 11.0% of the total population [56]; no estimate is provided for Indigenous populations in the Americas. In the population less than 15 years of age, the estimated LTBI prevalence is 2.3%.

Existing routinely-collected data are central to the *End TB Strategy*. Our exploration of the Manitoba TB Registry reveals that it contains information on active TB cases that is largely complete. The accuracy of the data elements that we investigated was high when compared to administrative health data; we examined data elements related to sociodemographic characteristics, dates of treatment, and delivery of healthcare services in coming to this conclusion. Information about quality is important to establish the credibility of the data for surveillance reports, research, and program evaluations, and to ensure that accurate data are provided to decision makers.

Despite the high degree of completeness and accuracy of the Manitoba TB Registry, improvement and expansion of the Registry is an important consideration to maintain its value for surveillance and research. Less than 5% of individuals in the Active TB Cohort had onset of cough information recorded amongst their symptoms, despite this symptom's potential importance for evaluation of timeliness of diagnosis. Previous studies from Ontario and Quebec have used information about symptoms, specifically time from symptom onset to treatment, in order to estimate the duration of potential delays in diagnosis and treatment and factors associated with the length of the delays [57,58].

Moreover, we found that contact assessment information in the Manitoba TB Registry was not easy to interpret. It does not appear possible to conclusively measure the time from initiation to completion of a contact investigation. We found, as expected, that contacts are often associated with more than one person with active TB over time. This may result in difficulties to evaluate completeness of contact investigations, especially for TB outbreaks in northern community settings. As Theron et al. note, collection of specialized local data may be beneficial in such situations [55]. Collection and use of relevant data, at local and wider levels, is an integral part of the *End TB Strategy*.

Routinely-collected administrative data also have a role to play in contributing to the end of the TB epidemic, by providing information about risk factors, healthcare outcomes, and treatment of LTBI. However, we found that these data are not sufficiently sensitive or do not have sufficiently high positive predictive value to accurately ascertain cases of active TB. Our findings are consistent with those reported in a recent systematic review [39].

In addition to reporting on the quality of routinely-collected data, in this study we addressed a number of substantive objectives. These focused on healthcare utilization for active TB, LTBI treatment completion rates, and characteristics of contacts.

With respect to the first of these topics, active TB places a substantial burden on the healthcare system. Active TB cases were frequently hospitalized before and around the time of diagnosis. First Nations individuals living both on- and off-reserve had a greater likelihood of hospitalization than other Manitoba residents; one potential reason may be a lack of access to outpatient care (i.e., general practitioner and specialist outpatient care). Overall, we did find that active TB cases with greater comorbidity and who were older were more likely to be hospitalized.

However, administrative data are not useful for assessing appropriateness of healthcare use. Our study identified that active TB cases have frequent contacts with the healthcare system; this in turn suggests that there are a number of diagnostic opportunities. However, given that TB can initially present with non-specific symptoms like fatigue and weight loss, or with symptoms that mimic more common diagnoses like pneumonia, some of these opportunities may be missed. This could lead to delays in the diagnosis of TB, as has been highlighted in recent media reports [59].

Inequities in rates of healthcare use for First Nations and foreign-born populations when compared with Canadian-born non-First Nations have multiple contributing factors. Other studies have documented a lack of access to primary and specialist healthcare as evidence of inequities [60]. It is important for these inequities in healthcare use to be documented and not confounded by a lack of data. For example, physician billing claims do not consistently capture data from nursing stations in northern

communities, and data on federally funded homecare on-reserve are not available in the Manitoba Population Research Data Repository at MCHP.

Our study revealed that while the Manitoba TB Registry contact assessments can be extensive, it does not appear possible to measure their timeliness. Finally, we observed modest LTBI treatment completion rates of 50-60% for INH and 60-70% for RIF. Thus, there is substantial room for improvement to reach the benchmark of 80% as suggested by the WRHA Integrated TB Services Data Management Committee. These results suggest that there is a need for access to better/newer treatments such as the regimen of twelve once-weekly doses of rifapentine/INH.

## Performance Indicator Measurement

WRHA Integrated TB Services worked with front line TB healthcare providers over several months in 2014 to develop locally relevant performance indicators within the domains of the diagnosis of TB, active TB disease management, LTBI management, and TB contact investigations. Table 7.1 lists the performance indicators developed by the WRHA Integrated TB Services Data Management Committee and comments on the feasibility of measuring these indicators based on the outcomes of this study.

**Table 7.1: Assessment of Feasibility of Measuring Integrated TB Services Performance Indicators**

| Performance Indicator | Comments on Feasibility of Measurement |
|---|---|
| **#1: Proportion of contacts without complete follow-up within a contact investigation** | It is feasible to identify active TB cases who have a contact investigation using the Manitoba TB Registry. |
| **#2: Proportion of newly-diagnosed active TB cases within a contact investigation** | However, there is only a single contact assessment date provided in the Manitoba TB Registry and it is unclear what this date measures. Therefore, it is not currently feasible to accurately identify the start and end dates of a contact investigation. |
| **#3: Proportion of newly identified LTBI within a contact investigation** | Neither the Manitoba TB Registry nor the Population Research Data Repository contain information about LTBI cases. Therefore it is not feasible to measure indicators about LTBI cases within a contact investigation. |
| **#4: Proportion of contacts with no evidence of TB disease or LTBI within a contact investigation** | Contacts in the Manitoba TB Registry may be associated with more than one active TB case over time. Therefore, for each case, it is often not feasible to measure the proportion of contacts who develop active TB disease in a contact investigation. However, the overall proportion of contacts who develop active TB disease can feasibly be measured. |
| **#5: Proportion of individuals admitted to hospital with a TB diagnosis who were clinically well enough to receive TB care as an outpatient** | The Population Research Data Repository contains complete and accurate information about hospitalization. It is feasible to measure hospital admission and length of stay for active TB cases. However, the Repository does not contain information about appropriateness of hospital admission for persons with active TB disease. |
| **#6: Average number of days of hospitalization of persons diagnosed with TB disease identified as clinically well enough to receive TB care as an outpatient** | |
| **#7: Proportion of persons diagnosed with TB disease and prescribed treatment by a Winnipeg Health Region care provider who started treatment for TB disease and completed the prescribed course of TB treatment within 3 months of their target treatment completion date** | The Manitoba TB Registry contains a "treatment outcome" field that is relevant to the measurement of this indicator. However, we identified that this field was completed for only 44.6% of records in the Manitoba TB Registry. Therefore, it is not feasible to measure this indicator. |

**Table 7.1 Cont'd: Assessment of Feasibility of Measuring Integrated TB Services Performance Indicators**

| Performance Indicator | Comments on Feasibility of Measurement |
|---|---|
| **#8: Time from date of onset of cough until first visit to healthcare provider for respiratory reason in all persons with culture-confirmed respiratory TB** | The Manitoba TB Registry contains information about symptoms. However, information about cough symptoms may be underreported, because it was identified for less than 5% of active TB cases. We were not able to validate the accuracy of symptom information in the Manitoba TB Registry because there is no reference data source. Therefore it is not feasible to measure indicator 8. |
| **#9: Time from first visit to healthcare provider for respiratory reason until collection date of first sputum for Acid-Fast Bacilli (AFB) in all persons with culture-confirmed respiratory TB** | Data on emergency department visits, physician visits, and hospitalizations are contained in the Population Research Data Repository; diagnosis information in physician billing claims and hospital discharge abstracts can be used to identify respiratory diagnoses. However, physician billing claims do not consistently capture all visits to nursing stations in northern Manitoba communities. Thus, it is not feasible to accurately ascertain the first visit to a healthcare provider for a respiratory reason for all Manitoba residents. Emergency department records in the Population Research Data Repository are only available for the Winnipeg health region, which further limits the feasibility of accurately identifying the first visit to a healthcare provider for a a respiratory reason. Information about AFB and culture can be feasibly identified from the Manitoba TB Registry. |
| **#10: Number of healthcare visits for respiratory reason between the first visit for respiratory reason and the collection date of first sputum for AFB in all persons with culture-confirmed respiratory TB** | |
| **#11: Proportion of persons diagnosed with LTBI, who are identified as contacts of sputum culture-confirmed TB cases, who start LTBI treatment** | It is not feasible to identify individuals with LTBI in the Manitoba TB Registry or the Population Research Data Repository. However, individuals receiving treatment for LTBI can be ascertained from DPIN data. The number of days of dispensed medications for INH or RIF in DPIN data can feasibly be used to measure treatment completion rates for the treated LTBI cohort. As well, it is feasible to identify individuals who are contacts of TB cases using the Manitoba TB Registry, with the limitations noted above. |
| **#12: Proportion of persons who start LTBI treatment, who are identified as contacts of sputum culture-confirmed TB cases, who complete a full course of treatment for LTBI (at least 80% of doses)** | |
| **#13: Proportion of persons who start LTBI treatment, who are not identified as contacts of TB cases, who complete a full course of LTBI treatment (at least 80% of doses)** | |

It is not possible to measure all indicators proposed by the Integrated TB Services Data Management Committee using information available in either the Manitoba TB Registry or administrative data, or via linkage of the two data sources. Enhancements to the Manitoba TB Registry, such as additional information about contacts of active TB cases and/or additional information from administrative databases (e.g., alternate level of care bed days at admission) need to be captured in order to measure these indicators.

## Study Recommendations

Valid and accurate data about active TB and LTBI are critical to the health of Manitobans. A number of recommendations arise based on the findings of this study. These recommendations pertain to data quality and validity, access to data, partnerships to strengthen TB data, and the role of data to support decision making to reduce and ultimately eliminate TB in Manitoba.

First, we acknowledge the high quality of the Manitoba TB Registry and the importance of this data resource for TB surveillance, program evaluation, and research. We recommend that investment in the Manitoba TB Registry continue and that expansion of this investment be made a priority. Timely and accurate data entry and continual data quality evaluation is essential to ensure the Registry provides valid and complete information about active TB for both provincial and national reporting and decision making. Monitoring of existing data fields and, where needed, improvement of key data fields, particularly around the onset of symptoms, contact investigations, and use of healthcare services, will help to ensure that the Manitoba TB Registry remains useful and relevant to measure the health and healthcare use of active TB cases. Creation of a data dictionary that documents specific details about data capture and changes in data capture methodology over time is critical to ensuring consistent usability of historical and current data. Electronic data capture, such as automated extraction from electronic medical records, should be an important consideration to facilitate the seamless integration of data into the Registry. Oversight of the Manitoba TB Registry would benefit from the broadening of partnerships. Specifically, the establishment of a technical working group that engages with partners, including First Nations and all Manitoba health regions, is key to guide future development of the Manitoba TB Registry to meet the needs for information across the province. A technical working group would help to ensure relevant data collection by all partners, including First Nations, and could facilitate access to the data for these partners as well as other stakeholders. This technical working group could identify a minimum dataset required for routine surveillance and program evaluation [61]. It could also facilitate the production and use of reports that provide information about active cases and their contacts with an emphasis on how these reports could meet local needs.

Second, while we acknowledge the important contributions that administrative data make to understanding the health and healthcare use of active TB disease cases, we do not recommend using diagnostic information in hospital discharge abstracts and physician billing claims to ascertain active TB cases. These data are likely to result in substantial misclassification bias. It is preferable to use TB Registry data to ascertain active TB disease cases, and to link TB Registry data to administrative data to investigate outcomes in administrative data. While this linkage has been achieved in Manitoba, this may not be possible for all jurisdictions. Cross-jurisdictional studies may instead need to use administrative data for case ascertainment to ensure a consistent methodology is adopted across locations in the study. In such situations, we recommend conducting sensitivity analyses that utilize more than one algorithm to ascertain cases of active TB disease in administrative data. With respect to LTBI cases, we again acknowledge that administrative data play a useful role for identifying treated cases, but recognize that these data will miss untreated cases of LTBI. Thus, we recommend the exploration of additional sources of data, including both active and passive surveillance systems, to monitor LTBI [62].

Third, we recommend that the WRHA Integrated TB Services Data Management Committee (or its successor committee) review and modify its proposed performance indicators so that they can feasibly be implemented to evaluate current programs and services. However, the Committee should also consider the role that it can play to advocate for the addition of new data elements, or more comprehensive collection of existing data elements in the Manitoba TB Registry to move its performance measurement goals forward. We also recommend that Integrated TB Services work in collaboration with custodians of the Manitoba TB Registry, First Nations communities and organizations, and local data partners to identify databases that could be integrated with existing data resources to measure program and service indicators for the entire province. Such an approach may benefit the formation of authentic partnerships amongst First Nations, clinicians, healthcare planners and data custodians to ensure effective measures to end TB. As well, new data may need to be collected and new analytic techniques may be adopted to better use existing data. A recent study emphasized the value of alternative contact assessment data sources, such as locally-developed questionnaires, to ensure effective TB control in high-risk communities [63].

Finally, we recommend that WRHA Integrated TB Services, provincial surveillance epidemiologists, researchers, and partners carefully consider how linkage of databases can lead to research that will support decisions to improve patient care and treatment. The *End TB Strategy* and other sources emphasize the importance of obtaining data about vulnerable populations such as individuals with substance abuse issues or who are homeless, the social determinants of health, primary care delivery, new diagnostics, drugs, and vaccines to facilitate decision making [54,55,64]. Bringing together new databases, including social databases housed at MCHP that capture information about housing, education, and social service use, and clinical databases with information about new diagnosis techniques or efficacy of new medications, will strengthen the environment for innovations. At the same time, we caution that First Nations populations are not always well represented in social databases. Thus, data sharing and new data collection initiatives around social databases are needed to ensure that through data linkage, a rich collection of information is available for the entire population.

In conclusion, the World Health Organization's *End TB Strategy* emphasizes both the value of data and the engagement of partners to reduce the number of TB cases and deaths. In the Manitoba environment, this strategy can be most effective by an emphasis on the use of existing data resources, consideration of the value of new resources, and meaningful involvement of partners, including First Nations, to end TB.

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# Appendix 1: Contents of the Manitoba Health (MH) Tuberculosis Registry

**Appendix Table 1.1: MH Tuberculosis Registry - Client Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Individual client ID number |
| FILEPHIN | MH Scrambled PHIN |
| **Numerical** | |
| SURVEILLANCE | surveillance |
| TREATY_NUMBER | **Treaty number for status clients** |
| YEAR_ARRIVED | If foreign born, year client arrived in Canada |
| YEAR_OF_BIRTH | Client year of birth |
| **Code Number** | |
| BIRTH_COUNTRY | Country in which client was born |
| MED_SVCS_BRCH_NUM | If status, medical services branch number |
| RES_CTRY_FIVE_YEAR | Country in which client resided five years ago |
| **Character** | |
| ACTIVE_FILE | Active TB file |
| BCG | Year of BCG, or may be a comment such as "scar" indicating BCG even if year not known |
| CHART_NUM | **Hospital chart number** |
| DECLINED | Client declined treatment |
| FILEPHINTYPE | MCHP Method to determine FILEPHIN |
| IMMIGRANT_CLASS | Status of immigrant - refugee, landed immigrant etc. |
| IMMIGRANT_OTHER_SPEC | Other notes: student for visitor |
| LTBI_FILE | Latent TB file |
| MARITAL_STATUS | Marital status |
| NON_COMPLIANCE | Client not complying with treatment |
| ON_SURVEILLANCE | Is client on surveillance? |
| ORIG_SEX | Original sex values |
| ORIGIN | origin - Canadian born, foreign born, Inuit etc. |
| OTHER_ABORIGINAL_SPEC | Note whether member of band outside of Manitoba. |
| SEX | Sex (MCHP) |
| SURVEILLANCE_COMPLETE | Is surveillance complete? |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| ADDED_DT | Date client data added to database |
| BIRTHDT | Client date of birth |

**Bold** type indicates suppressed values

**Appendix Table 1.2: MH Tuberculosis Registry - Address Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| ADDRESSENTRYID | Automatically generated number for each unique address entry |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| **Code Number** | |
| HEALTH_UNIT | Number which corresponds to health unit |
| MUNICIPALITY | Number which corresponds to municipality |
| RESERVE | Number which corresponds to reserve name |
| RHA | Number which corresponds to regional health authority |
| **Character** | |
| POSTAL_CODE | 6 digit postal code |
| PROVINCE | name of province |
| RESIDES_ON_RESERVE | Yes/no |
| TOWN | Name of city/community/town |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| ADDED_DT | Date address added |
| ENDED_DT | Date address ended |

**Appendix Table 1.3: MH Tuberculosis Registry - Case Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CASE_IDENTIFIER | 7 digit number that combines year of diagnosis and case number in that |
| CASEENTRYID | Automatically generated number for each unique address entry |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| TB_DOCTOR | Unique identifier that links to physician name and location of practice |
| **Numerical** | |
| CASE_ID_NUM | Specific case #1 = first case, #2 = second case etc. |
| CASE_MANAGEMENT | How case has been managed |
| CASE_MANAGEMENT_RHA | Number corresponding to the RHA that is responsible for managing the |
| CENSUS_DISTRICT_NUM | Census district number |
| PREV_TB_YEAR | Year in which client previously diagnosed with TB if this is not case number |
| **Code Number** | |
| METHOD_OF_DETECTION | Method by which this case was detected. Options include 'symptoms', 'screening' etc. |
| PREV_TB_CTRY | Country in which client was previously diagnosed with TB |
| **Character** | |
| CASE_CRITERIA | Positive culture (1), no positive culture (2), unknown (9) |
| DEATH_DIAGNOSIS_FACTOR | If client is deceased, three options as to whether TB was contributing factor |
| EXTENDED_CARE | extended_care |
| REPORTING_PROVINCE | Province from which the TB case originated |
| TREATMENT_OUTCOME | Options are 1-9. example death during treatment, treatment complete, absconded etc. |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| CASE_COPY_DT | date_case_copy |
| CASE_MANAGEMENT_DT | date_case_management |
| DEATH_DT | Date of death if clients deceased |
| DIAGNOSED_DT | Date current case was diagnosed |
| REPORTED_DT | Date current case was reported to TB unit |

**Appendix Table 1.4: MH Tuberculosis Registry - Client Visit Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| CLINICVISITENTRYID | ClinicVisitEntryID |
| **Numerical** | |
| CASE_ID_NUM | Specific case number. 1 = first case, 2 = second case etc. |
| **Code Number** | |
| CLINIC_ID_NUM | Specific clinic identifier where client was treated |
| REASON_FOR_APPT | Reason for appointment |
| **Character** | |
| FIELD_REQUEST | Field request (yes/no) |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| APPOINTEMNT_DT | Time of appointment |
| CLINIC_APPT_DT | Appointment date |

**Appendix Table 1.5: MH Tuberculosis Registry - Contact Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CASE_ID_NUM | This is the specific case number of the 'Case' (the client ID number) |
| CLIENT_ID_NUM | Indidvidual clent ID number |
| CONTACT_ID_NUM | Individual contact ID number |
| CONTACTENTRYID | Automatically generated number for each unique contact entry |
| **Numerical** | |
| CONTACT_ASSESS_COMPL | Whether contact assessment is complete and if further follow up/surveillance is required |
| CONTACT_CASE_NUM | This is the specific case number of the contact, if the contact also becomes a case |
| **Code Number** | |
| LOCATION_ID | Specific location where contact occurred |
| PLACE_OF_CONTACT | Category of place of contact such as school, daycare, hospital etc. |
| TYPE_OF_CONTACT | Type of contact |
| **Character** | |
| DEGREE_OF_EXPOSURE | Degree of exposure to case |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| CONTACT_ASSESS_DT | Date contact assessment done |

**Appendix Table 1.6: MH Tuberculosis Registry - Contact List Comment Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Individual client ID number |
| CONTACTLISTCOMMENTENTRYID | ContactListCommentEntryID |
| **Numerical** | |
| CASE_ID_NUM | This is the specific case number of the "case" (the client ID number) |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.7: MH Tuberculosis Registry - Daily Drug Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DAILYDRUGENTRYID | DailyDrugEntryID |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| DRUG_ISSUED_COUNT | Number of pills issued |
| DRUG_TAKEN_COUNT | Number of pills taken |
| **Code Number** | |
| DRUG_STOP_REASON | Reason drug stopped |
| **Character** | |
| DRUG_DOSAGE | Drug dosage |
| DRUG_NAME_ID | Drug name |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| DRUG_ISSUE_DT | Date drug issued |
| DRUG_RENEWAL_DT | Date drug renewed |
| DRUG_START_DT | Date drug started |
| DRUG_STOP_DT | Date drug ended |

**Appendix Table 1.8: MH Tuberculosis Registry - Direct Observed Therapy Drug Doses Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DOTDRUGDOSESENTRYID | DOTDrugDosesEntryID |
| **Numberical** | |
| CASE_ID_NUM | Specific case number |
| DRUG_ID_NUM | ID number of drug, link to drug name and dosage |
| DRUG_YEAR | Year in which drug dispensed |
| **Code Number** | |
| DRUG_MONTH | Month in which drug dispensed |
| **Character** | |
| DAY1 | Day as to where drug was dispensed |
| DAY2 | Day as to where drug was dispensed |
| DAY3 | Day as to where drug was dispensed |
| DAY4 | Day as to where drug was dispensed |
| DAY5 | Day as to where drug was dispensed |
| DAY6 | Day as to where drug was dispensed |
| DAY7 | Day as to where drug was dispensed |
| DAY8 | Day as to where drug was dispensed |
| DAY9 | Day as to where drug was dispensed |
| DAY10 | Day as to where drug was dispensed |
| DAY11 | Day as to where drug was dispensed |
| DAY12 | Day as to where drug was dispensed |
| DAY13 | Day as to where drug was dispensed |
| DAY14 | Day as to where drug was dispensed |
| DAY15 | Day as to where drug was dispensed |
| DAY16 | Day as to where drug was dispensed |
| DAY17 | Day as to where drug was dispensed |
| DAY18 | Day as to where drug was dispensed |
| DAY19 | Day as to where drug was dispensed |
| DAY20 | Day as to where drug was dispensed |
| DAY21 | Day as to where drug was dispensed |
| DAY22 | Day as to where drug was dispensed |
| DAY23 | Day as to where drug was dispensed |
| DAY24 | Day as to where drug was dispensed |
| DAY25 | Day as to where drug was dispensed |
| DAY26 | Day as to where drug was dispensed |
| DAY27 | Day as to where drug was dispensed |
| DAY28 | Day as to where drug was dispensed |
| DAY29 | Day as to where drug was dispensed |
| DAY30 | Day as to where drug was dispensed |
| DAY31 | Day as to where drug was dispensed |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.9: MH Tuberculosis Registry - Direct Observed Therapy Drug List Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DOTDRUGLISTENTRYID | Auto generated identification number |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| DRUG_ID_NUM | ID number of drug |
| DRUG_TOTAL_PLANNED | Number of doses planned |
| DRUG_TOTAL_TAKEN | Number of doses taken |
| **Code Number** | |
| DRUG_FREQUENCY | Frequency by which drug is to be taken (once per week etc.) |
| DRUG_STOP_REASON | Reason drug stop |
| **Character** | |
| DRUG_DOSAGE | Drug dosage in mgs |
| DRUG_NAME_ID | Short form of drug name |
| REGIMEN_NUM | Regimen number |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| DRUG_START_DT | Date drug started |
| DRUG_STOP_DT | Date drug ended |

**Appendix Table 1.10: MH Tuberculosis Registry - Direct Observed Therapy Drug Master Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DOTDRUGMASTERENTRYID | Auto generated identification number |
| **Code Number** | |
| CASE_ID_NUM | Specific case number |
| DRUG_ID_NUM | ID number of drug |
| **Character** | |
| DISPENSING_LOCN | Where drug was dispensed |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.11: MH Tuberculosis Registry - Drug Reaction Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DRUGREACTIONENTRYID | Auto generated identification number |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Character** | |
| DRUG_NAME | Name of drug to which reaction was tested |
| TEST_RESULT | Outcome of test (S - sensitive, R - resistant, U - Unknown) |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| TEST_DT | Date of drug reaction test |

**Appendix Table 1.12: MH Tuberculosis Registry - Drug Summary Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DRUGSUMMARYENTRYID | Auto generated identification number |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| DAILY_PLANNED | Number of doses planned for daily regimen |
| DAILY_TAKEN | Actual number of daily regimen doses taken |
| DOT_PLANNED | Number of doses planned for Direct Observed Therapy |
| DOT_TAKEN | Actual number of doses taken on Direct Observed Therapy |
| INPATIENT_PLANNED | Number of doses planned for inpatient |
| INPATIENT_TAKEN | Actual number of doses taken as inpatient |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.13: MH Tuberculosis Registry - Diagnosis Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| DIAGNOSISENTRYID | DiagnosisEntryID |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Code Number** | |
| ICD9_CODE | Diagnosis ICD9 code |
| PRIME_DIAG | Whether this diagnosis is the primary diagnosis (Y/N) |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.14: MH Tuberculosis Registry - Hematology Result Information**

| Variable Name | Variable Label |
|---|---|
| Identification Number | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| HEMATOLOGYRESULTENTRYID | Auto generated identification number |
| TEST_ID_NUM | identification number of test. Links to test_number in hematology test table |
| Numerical | |
| CASE_ID_NUM | Specific case number |
| Character | |
| HEM_RESULT | Test result |
| HEM_SPECIMEN_CODE | Type of test for specimen |
| Date | |
| ACQDT | Date record was acquired at MCHP |
| RESULT_DT | Test result date |

**Appendix Table 1.15: MH Tuberculosis Registry - HIV Information**

| Variable Name | Variable Label |
|---|---|
| Identification Number | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| HIVENTRYID | Auto generated identification number |
| Numerical | |
| CASE_ID_NUM | Specific case number |
| Character | |
| HIV_RESULT | HIV test result |
| Date | |
| ACQDT | Date record was acquired at MCHP |
| TEST_DT | Date of HIV test |

**Appendix Table 1.16: MH Tuberculosis Registry - Hospital Information**

| Variable Name | Variable Label |
|---|---|
| Identification Number | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| HOSPITALENTRYID | Auto generated identification number |
| Numerical | |
| CASE_ID_NUM | Specific case number |
| Character | |
| COMMENT | case management comments |
| HOSPITAL_CODE | Name of hospital |
| Date | |
| ACQDT | Date record was acquired at MCHP |
| ADMITTED_DT | Date client admitted to hospital |
| DISCHARGED_DT | Date client discharged from hospital |

**Appendix Table 1.17: MH Tuberculosis Registry - Immigrant Tracking Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| IMMIGRANTTRACKINGID | ImmigrantTracking ID |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| APPOINTMENT_DT | Appointment date |
| FIRST_LETTER_DT | Date first letter sent |
| FOLLOW_UP_REQD_DT | Date follow up required |
| ORIGINIAL_NOT_DT | Date unit notified of immigrant |
| SECOND_LETTER_DT | Second letter date (if needed) |

**Appendix Table 1.18: MH Tuberculosis Registry - Inpatient Drug Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| INPATIENTDRUGENTRYID | Auto generated identification number |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| DRUG_TAKEN_COUNT | Count of drugs taken |
| **Code Number** | |
| DRUG_FREQUENCY_ID | Frequency by which drug is to be taken (once per week etc.) |
| DRUG_STOP_REASON | Reasons of stopping taking medication |
| **Character** | |
| COMMENT | Case management comments |
| DRUG_DOSAGE | Amount of drug dosage |
| DRUG_NAME_ID | Drug name |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| DRUG_START_DT | Start date of drugs |
| DRUG_STOP_DT | Stop date of drugs |

**Appendix Table 1.19: MH Tuberculosis Registry - Other Diseases Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| OTHERDISEASESENTRYID | Auto generated identification number |
| **Code Number** | |
| DISEASE_ID_NUM | Any other diseases client has been diagnosed with by specific disease |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.20: MH Tuberculosis Registry - Other Test Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individaul client ID number in client table |
| LAB_NUM | Unique number of lab test sent to |
| OTHERTESTENTRYID | Auto generated identification number |
| SOURCE_PATIENT_NUM | Surveillance number |
| TEST_ID_NUM | Unique ID number for test |
| TEST_NUMBER | Unique number of test |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Code Number** | |
| LOCATION_ID_NUM | Location of client |
| SPECIMEN_TYPE | Type of specimen |
| **Character** | |
| COMMENT | Case management comments |
| CULTURE_RESULT | Rssult of culture: N - negative, P - positive |
| MIRU | MIRU |
| SMEAR_RESULT | Result of smear: N - negative, P - positive |
| STRAIN | Strain |
| TEST_REASON | Reason for test - contact or TB survey |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| OTHER_TEST_DT | Date of other test |
| SPECIMEN_COLLECTION_DT | Date of specimen collection |
| SURVEY_DT | Date of survey |

**Appendix Table 1.21: MH Tuberculosis Registry - Sources Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in the client table |
| SOURCE_CASE_NUM | Souce case number |
| SOURCE_ID_NUM | Source ID number |
| SOURCESENTRYID | SourcesEntryID |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.22: MH Tuberculosis Registry - Study Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| STUDY_ID | Study identification number. Links to study name, description and start |
| STUDYENTRYID | Auto generated identification number |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| STUDY_ARM_NUMBER | Study arm of the study |
| STUDY_NUMBER | Study number to which study arm links |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.23: MH Tuberculosis Registry - Study Master Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| STUDY_ID | Study identification number. Links to study name, description and start |
| **Numerical** | |
| STUDY_ARM_NUMBER | Study arm of the study |
| STUDY_NUMBER | Study number to which study arm links |
| STUDY_START_YEAR | Year in which study started |
| **Character** | |
| STUDY_ARM_DESCRIPTION | Description of study arm |
| STUDY_ARM_NAME | Name of study arm |
| STUDY_DESCRIPTION | Brief description of study |
| STUDY_NAME | Name of study |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |

**Appendix Table 1.24: MH Tuberculosis Registry - Surveillance Follow-up Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| SF_CLIENTID | Links to main client id table. Each client should have one unique identifier |
| SURVEILLANCEFOLLOWUPENTRYID | Auto generated identification number |
| **Numerical** | |
| SF_CASEID | Links to main case identification via client ID |
| SF_REVIEWYEARS | Number of years in which surveillance is to take place |
| SF_XRAYYEARS | Number of years for x-rays |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SF_8WEEKTESTDUE_DT | 8 week test due date |
| SF_REVDT1 | Surveillance dates |
| SF_REVDT2 | Surveillance dates |
| SF_REVDT3 | Surveillance dates |
| SF_REVDT4 | Surveillance dates |
| SF_REVDT5 | Surveillance dates |
| SF_REVDT6 | Surveillance dates |
| SF_REVDT7 | Surveillance dates |
| SF_REVDT8 | Surveillance dates |
| SF_REVDT9 | Surveillance dates |
| SF_REVDT10 | Surveillance dates |
| SF_REVDT11 | Surveillance dates |
| SF_REVDT12 | Surveillance dates |
| SF_XRAYDT1 | X Ray due dates |
| SF_XRAYDT2 | X Ray due dates |
| SF_XRAYDT3 | X Ray due dates |
| SF_XRAYDT4 | X Ray due dates |
| SF_XRAYDT5 | X Ray due dates |
| SF_XRAYDT6 | X Ray due dates |

**Appendix Table 1.25: MH Tuberculosis Registry - Survey Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Links to individual client ID number in client table |
| SOURCE_CASE_ID_NUM | ID number of source case if that is reason for survey |
| SURVEY_ID | Identification number of this survey |
| SURVEYENTRYID | SurveyEntryID |
| **Numerical** | |
| CASE_ID_NUM | Case ID number of this client if this client became a case |
| SOURCE_CASE_NUM | Case number of source case |
| SURVEYCOMPLETIONSTATUS | SurveyCompletionStatus |
| **Code Number** | |
| LOCATION_ID_NUM | Location where survey took place |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SURVEY_DT | Date of survey |
| SURVEYCOMPLETION_DT | Date survey completed |

**Appendix Table 1.26: MH Tuberculosis Registry - Survey Comment Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| SOURCE_ID_NUM | ID number of source case if that is reason for survey |
| SURVEYCOMMENTENTRYID | SurveyCommentEntryID |
| **Numerical** | |
| SOURCE_CASE_NUM | Case number of the source case |
| **Code Number** | |
| SURVEY_LOCATION | Location where survey took place |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SURVEY_DT | Date of survey |

**Appendix Table 1.27: MH Tuberculosis Registry - Survey Master Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| SURVEY_ID | ID number of this survey |
| SURVEY_SOURCE_CASE | Links to "source case number" in survey table |
| SURVEY_SOURCE_NUM | Links to "survey source case id number" in survey table |
| **Code Number** | |
| SURVEY_NAME | Links to survey table where this field is called survey location ID |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SURVEY_DT | Date of survey |

**Appendix Table 1.28: MH Tuberculosis Registry - Symptom Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| SYMPTOMENTRYID | SymptomEntryID |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Code Number** | |
| SYMPTOM_ID_NUM | Type of symptoms: ex cough, loss of appetite etc. |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SYMPTOM_DT | Symptom onset date |

**Appendix Table 1.29: MH Tuberculosis Registry - Tuberculin Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| SOURCE_PATIENT_NUM | ID number of source case if that is reason for survey |
| TUBERCULINENTRYID | TuberculinEntryID |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Code Number** | |
| LOCATION_ID_NUM | Location where survey took place |
| **Character** | |
| TEST_REASON | Reason for test: contact or TB survey |
| TEST_RESULTS | Test result |
| TUBN_DUPLICATE | Tuberculin duplicate |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SURVEY_DT | Date of survey |
| TEST_DT | Date of test |

**Appendix Table 1.30: MH Tuberculosis Registry - Visual Test Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| TEST_ID_NUM | Unique number of test |
| VISUALTESTENTRYID | Auto generated identification number |
| **Numerical** | |
| CASE_ID_NUM | Specific case number |
| **Character** | |
| TEST_RESULT | Test result |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| TEST_DT | Date of visual exam |

**Appendix Table 1.31: MH Tuberculosis Registry - X-ray Information**

| Variable Name | Variable Label |
|---|---|
| **Identification Number** | |
| CASE_ID_NUM | Specific case number |
| CLIENT_ID_NUM | Link to individual client ID number in client table |
| SOURCE_PATIENT_NUM | ID number of source case if that is reason for survey |
| XRAY_NUMBER | Unique identifier for Xray |
| XRAYENTRYID | Auto generated identification number |
| **Code Number** | |
| LOCATION_ID_NUM | Location where survey took place |
| XRAY_LOCATION | Location on body where Xray taken |
| XRAY_SUBMITTED_FROM | Location from which Xray submitted |
| **Character** | |
| XRAY_CAVITARY | Cavitary, Non-cavitary or not specified |
| XRAY_DUPLICATE | Whether or not Xray is a duplicate |
| XRAY_REASON | Reason for Xray: Contact or TB survey |
| XRAY_RESULT | X Ray result: Normal, Abnormal, Spoiled etc. |
| XRAY_STORAGE_LOCN | Location where Xray stored |
| **Date** | |
| ACQDT | Date record was acquired at MCHP |
| SURVEY_DT | Date of survey |
| XRAY_DT | Date of XRay |
| XRAY_REQUEST_DT | Date of Xray request |

# Appendix 2: ICD Diagnosis Codes for the Charlson Comorbidity Index

| Comorbid Condition | ICD-9-CM Diagnosis Codes | ICD-10-CA Diagnosis Codes |
|---|---|---|
| Myocardial Infarction | 410, 412 | I21, I22, I25.2 |
| Congestive Heart Failure | 398.91, 402.01, 402.11, 402.91, 404.01, 404.03, 404.11, 404.13, 404.91, 404.93, 425.4–425.9, 428 (hosp), 398, 402, 425, 428 (med) | I09.9, I11.0, I13.0, I13.2, I25.5, I42.0, I42.5–I42.9,I43, I50, P29.0 |
| Peripheral Vascular Disease | 093.0, 437.3, 440, 441, 443.1–443.9, 447.1, 557.1, 557.9, V43.3 (hosp) 440, 441, 443, 447, 557 (med) | I70, I71, I73.1, I73.8, I73.9, I77.1, I79.0, I79.2, K55.1, K55.8, K55.9, Z95.8, Z95.9 |
| Cerebrovascular Disease | 362.34, 430–438 (hosp) 430–438 (med) | G45, G46, H34.0, I60–I69 |
| Dementia | 290, 294.1, 331.2 (hosp) 290, 294, 331 (med) | F00–F03, F05.1, G30, G31.1 |
| Chronic Pulmonary Disease | 416.8, 416.9, 490–505, 506.4, 508.1, 508.8 (hosp) 416, 490–496, 500–505 (med) | I27.8, I27.9,J40–J47, J60–J67 J68.4, J70.1, J70.3 |
| Connective Tissue Disease-Rheumatic Disease | 446.5, 710.0–710.4, 714.0–714.2, 714.8, 725 (hosp) 446, 710, 714, 725 (med) | M05, M06, M31.5, M32–M34, M35.1, M35.3, M36.0 |
| Peptic Ulcer Disease | 531–534 | K25–K28 |
| Mild Liver Disease | 070.22, 070.23, 070.32, 070.33, 070.44, 070.54, 070.6, 070.9, 570, 571, 573.3, 573.4, 573.8, 573.9, V42.7 (hosp) 070, 570, 571, 573 (med) | B18, K70.0–K70.3, K70.9, K71.3–K71.5, K71.7, K73, K74, K76.0, K76.2–K76.4, K76.8, K76.9, Z94.4 |
| Diabetes without Chronic Complications | 250.0–250.3, 250.8, 250.9 (hosp) 250 (med) | E10.0, E10.1, E10.6, E10.8, E10.9, E11.0, E11.1, E11.6, E11.8, E11.9, E12.0, E12.1, E12.6, E12.8, E12.9, E13.0, E13.1, E13.6, E13.8, E13.9, E14.0, E14.1, E14.6, E14.8, E14.9 |
| Diabetes with Chronic Complications | 250.4–250.7 (med n/a) | E10.2–E10.5, E10.7, E11.2–E11.5, E11.7, E12.2–E12.5, E12.7, E13.2–E13.5, E13.7, E14.2–E14.5, E14.7 |
| Paraplegia and Hemiplegia | 334.1, 342, 343, 344.0–344.6, 344.9 (hosp), 334, 342–344 (med) | G04.1, G11.4, G80.1, G80.2, G81, G82, G83.0–G83.4, G83.9 |
| Renal Disease | 403.01, 403.11, 403.91, 404.02, 404.03, 404.12, 404.13, 404.92, 404.93, 582, 583.0–583.7, 585, 586, 588.0. V42.0, V45.1, V56 (hosp), 403, 582, 583, 585, 586, 588, V56 (med) | I12.0, I13.1, N03.2–N03.7, N052–N05.7, N18, N19, N25.0, Z49.0–Z49.2, Z94.0, Z99.2 |
| Cancer | 140–172, 174–195.8, 200–208, 238.6 (hosp), 140–172, 174–195, 200–208, 238 (med) | C00–C26, C30–C34, C37–C41, C43, C45–C58, C60–C76, C81–C85, C88, C90–C97 |
| Moderate or Severe Liver Disease | 456.0–456.2, 572.2–572.4, 572.8 (hosp), 456, 572 (med) | I85.0, I85.9, I86.4, I98.2, K70.4, K71.1, K72.1, K72.9, K76.5–K76.7, |
| Metastatic Carcinoma | 196–199 | C77–C80 |
| HIV/AIDS | 042–044 | B20–B22, B24 |

# Appendix 3: ICD Diagnosis Codes to Identify Select Comorbid and Chronic Conditions in the Study Cohorts

| Disease | ICD-9-CM | ICD-10-CA |
|---|---|---|
| **Diabetes** | | |
| Diabetes mellitus | 250 | |
| Insulin-dependent diabetes mellitus (type 1) | | E10 |
| Non-insulin-dependent diabetes mellitus (type 2) | | E11 |
| Malnutrition–related diabetes mellitus | | |
| Other specified diabetes mellitus | | E13 |
| Unspecified diabetes mellitus | | E14 |
| **Arthritis** | | |
| Rheumatoid arthritis | 714 | M05 |
| Osteoarthritis | 715 | M15-M19 |
| Connective tissue disorders | 446 | M07, M10, M11-M14, M30-M36 |
| Polyarteritis nodosa and allied conditions | 710 | |
| Diffuse diseases of connective tissue | 720 | |
| Ankylosing spondylitis | 274 | |
| Gout | 711-713, 716, 717, 718, 719 | M00-M03, M20-M25, M65-M79 |
| Other arthritis and related conditions. | 721, 725-729, 739 | |
| **Chronic obstructive pulmonary disease (COPD)** | | |
| | 490-496 | J44 |
| **Heart disease** | | |
| Acute myocardial infarction | 410 | I20-25 |
| Other acute and subacute forms of ischemic heart disease | 411 | |
| History of myocardial infarction | 412 | |
| Angina pectoris | 413 | |
| All other forms of chronic ischemic heart disease | 414 | |
| Ischemic Heart Disease | 414 | |
| **HIV** | | |
| | 42 | B20-24 |
| **Renal failure** | | |
| Acute renal failure | 584 | N17 |
| Chronic kidney failure | 585 | N18 |
| End-stage Renal Disease | 585.6 | |
| Unspecified Kidney failure | 586 | N19 |
| **Leprosy** | | |
| | 30 | A30 |

Source: ICD-10-CA: https://www.cihi.ca/en/icd_10_ca_vol1_2009_en.pdf
ICD9: http://icd9cm.chrisendres.com/

Note: A diagnosis of leprosy is ascertained from either hospital discharge abstracts (any diagnosis field) or physician billing claims. The date of hospital admission was used as the diagnosis date if the source of case ascertainment is hospital discharge abstracts

# Appendix 4: Healthcare Use for Treated LTBI Cohort

This section examines the healthcare use of the Treated LTBI Cohort, which was identified using prescription drugs records in the Manitoba Population Research Data Repository housed at MCHP.

The sub-objectives of this component of the study are to:

1. Describe trends in emergency, acute, primary, specialist, and prescription drug healthcare use before and after initiation of treatment for LTBI;
2. Identify predictors of pre- and post-treatment initiation of healthcare use; and
3. Compare the use of healthcare services for treated LTBI cases to that of matched controls.

## Overview of Methods

The analyses conducted in this section were for the Treated LTBI Cohort and the corresponding matched cohort. We excluded all individuals who did not have at least 720 days of coverage following the study index date (i.e., initiation of prescription drug treatment for LTBI), so that we could characterize healthcare use over time. There were a total of 5,556 individuals in the Treated LTBI Cohort who met this criterion. The matched cohort was restricted to individuals who had not been diagnosed with TB, treated for LTBI, or identified as a contact of an active TB case. There were a total of 27,774 individuals in this cohort.

The same measures of healthcare use were defined for the Treated LTBI Cohort as were previously defined for the Active TB Cohort (see Chapter 4). However, we excluded the homecare measure because of low rates of homecare use before and after initiation of LTBI treatment. Thus, the healthcare use measures that we focused on were:

- **Emergency department visits:** a dichotomous measure indicating whether there was at least one visit in each 30-day period. Note that this measure was available from April 1, 2000 to March 31, 2013 only, for facilities and residents in the Winnipeg health region.
- **Inpatient hospitalization:** a dichotomous measure indicating whether there was at least one inpatient hospitalization in each 30-day period.
- **Inpatient hospital days:** total number of inpatient hospital days in each 30-day period.
- **Ambulatory family physician visits:** total number of outpatient visits to family physicians in each 30-day period.
- **Ambulatory specialist visits:** total number of outpatient visits to specialist physicians in each 30-day period.
- **Non-TB-related prescription drugs:** number of different prescription drugs in each 30-day period. The 4th level of the World Health Organization's Anatomic, Therapeutic, Chemical (ATC) Classification System was used to distinguish different drugs. The following TB-related drugs were excluded: isoniazid, rifampin, pyrazinamide, ethambutol, fixed-dose combinations of these four medications, vitamin B6, Tuberculin for TSTs, rifapentine, rifabutin.

Each measure was constructed for 30-day increments prior to (and including) the study index date and then following the study index date. A total of 12 30-day increments were defined for the pre-treatment initiation period and 24 30-day increments were defined for the post-treatment initiation period. All hospitalizations, hospital days, physician visits, and emergency room visits associated with pregnancy and childbirth were excluded when computing each measure.

Sociodemographic (age group, sex, income quintile, health region of residence, First Nations origin), year period of treatment initiation, and comorbidity characteristics were included in the statistical models to test their association with healthcare use. As well, inpatient hospitalization was included in the models for family and specialist physician visits.

The First Nations origin variable had two categories – First Nations and all other Manitobans. This classification was based on information in the INAC Status Registry. Recall that the more detailed categorization of First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations is only available for the Active TB Cohort because this information is found in the Manitoba TB Registry.

Comorbidity was measured using the Charlson Comorbidity Index and was based on the 360 days prior to and including the study index date. In addition, a selected set of comorbid conditions were defined from diagnoses in hospital records and physician billing claims; these included diabetes, rheumatoid arthritis, chronic obstructive pulmonary disease, heart disease, HIV, and chronic kidney disease.

The data were descriptively analyzed using frequencies, means and standard deviations. Plots of trends in healthcare use were produced; these are shown using 60-day periods.

For the count outcome measures, a generalized linear model with a negative binomial distribution and generalized estimating equations (GEEs) were used to model the trend over time. For the dichotomous outcome measures, a generalized linear model with a logit function and GEEs was adopted to model the trend. An autoregressive correlation structure was used in each model to account for repeated measurements of healthcare use on the same individual.

All statistical models included the main effects of age group, sex, income quintile, region of residence, index year, comorbidity category, origin group, month, and period (i.e., pre-diagnosis, post-diagnosis). Odds ratios (ORs) and 95% confidence intervals (95% CIs) were produced for the multivariable logistic models. Relative rates (RRs) and 95% CIs were produced for the multivariable negative binomial distribution models. Model fit was evaluated using the scaled deviance.

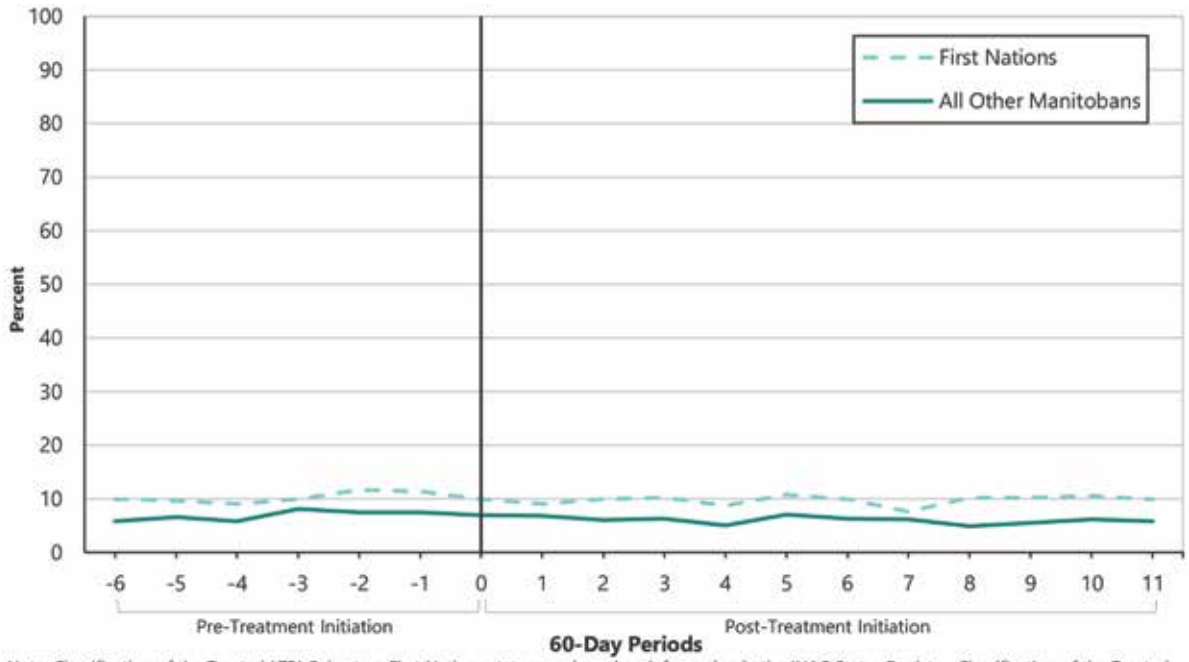
# Results

## Emergency Department Visits

Emergency department visit data were only available for facilities in the Winnipeg health region, and therefore will not reflect total use of emergency departments in the province. Thus, we limited our attention to the Winnipeg health region population when describing use rates.

As Appendix Figure 4.1 reveals, emergency department use for treated LTBI cases increased slightly around the time of treatment initiation, but largely remained constant throughout the study observation period.

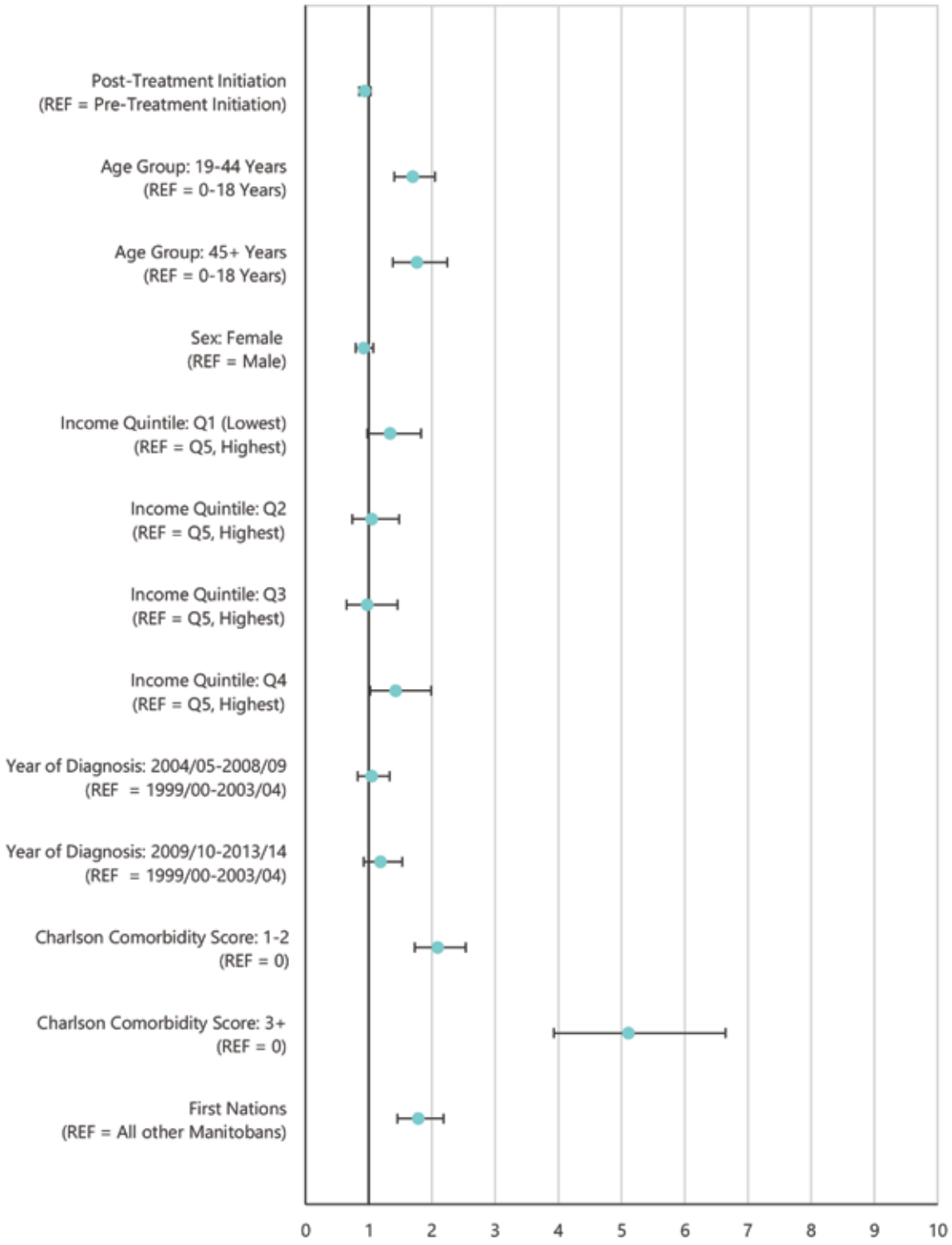
**Appendix Figure 4.1: Percent of Treated LTBI Cohort with an Emergency Department Visit Before and/or After Treatment Initiation, Stratified by First Nations Status**
Winnipeg Residents Only, April 1 2001 - March 31 2011




Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

The forest plot in Appendix Figure 4.2, which focuses on the predictors of emergency department use in the Treated LTBI Cohort, reveals that, on average, there was no difference in the odds of an emergency department visit in the post-treatment initiation period when compared to the pre-treatment initiation period. As expected, the odds of an emergency department visit were higher in older age groups than in the youngest age group. There were no differences in use by income quintile. The odds of an emergency department visit were higher for First Nations than for non-First Nations cohort members. Finally, higher comorbidity amongst individuals in the Treated LTBI Cohort was associated with higher odds of an emergency department visit.

**Appendix Figure 4.2: Characteristics of Treated LTBI Cohort Associated with Emergency Department Visits**
Winnipeg Residents Only, Odds Ratio Estimates and 95% CI

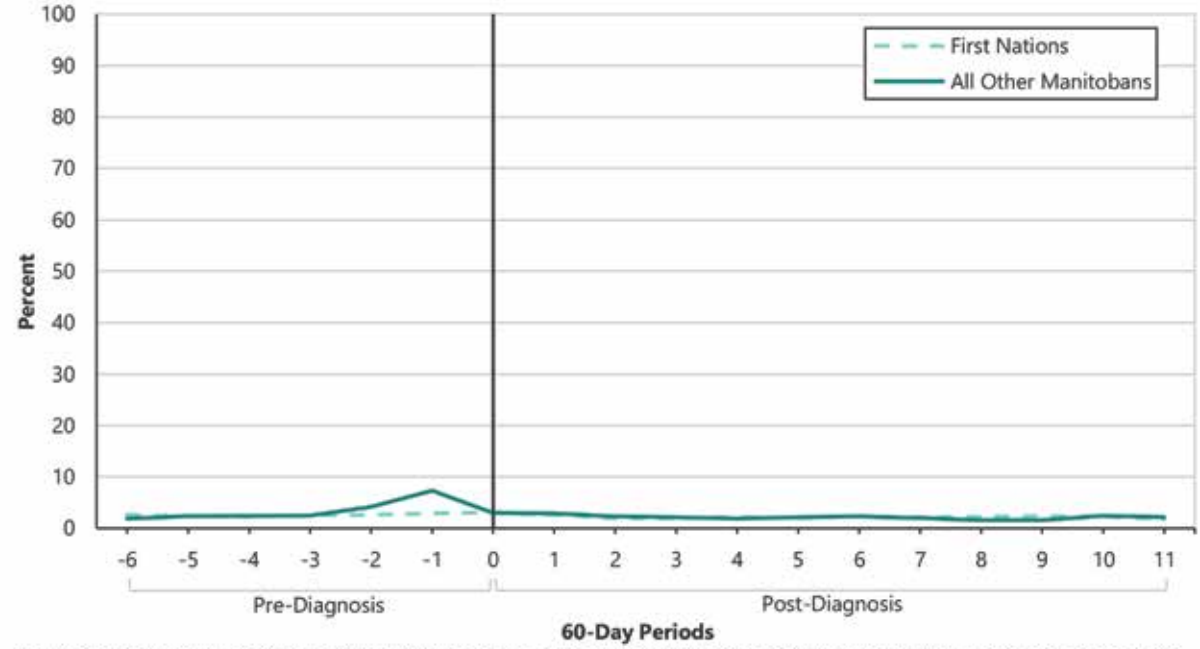



Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

## Inpatient Hospitalizations and Inpatient Length of Stay

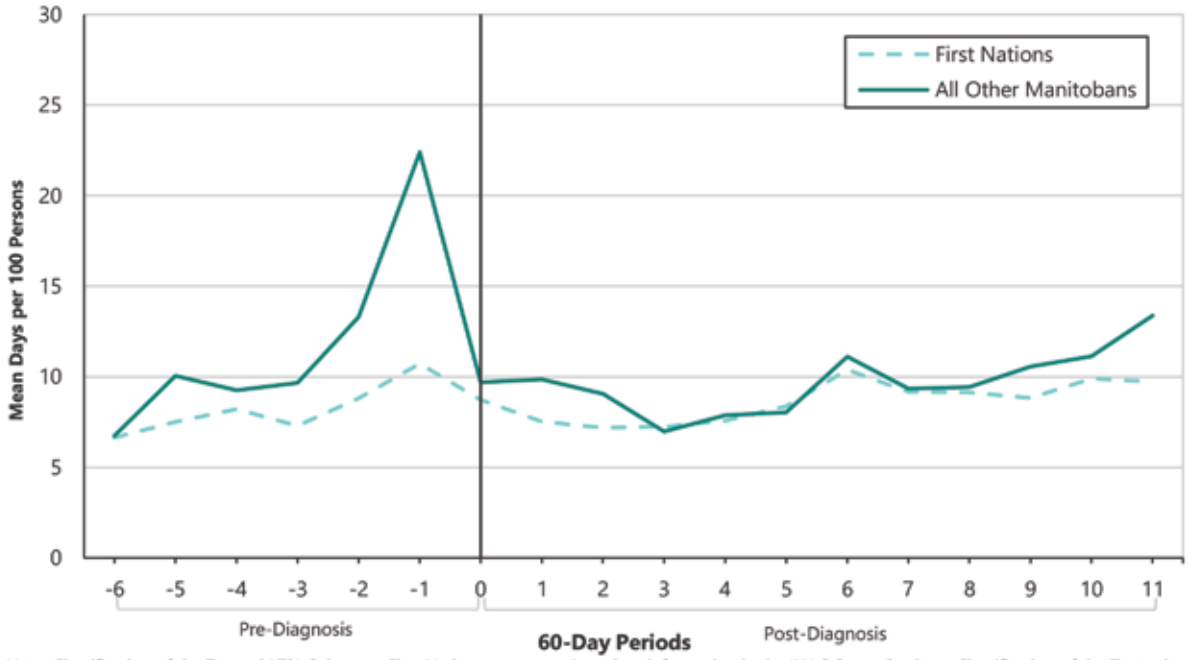
Appendix Figures 4.3 and 4.4 show the trend in inpatient hospitalizations and number of inpatient hospital days, respectively. These trends are shown for the year prior to the initiation of treatment for LTBI and in the two-year period following initiation of treatment.

**Appendix Figure 4.3: Percent of Treated LTBI Cohort with an Inpatient Hospitalization Before and/or After Treatment Initiation, Stratified by First Nations Status**
April 1 1999 - March 31 2013




Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

**Appendix Figure 4.4: Average Number of Inpatient Hospital Days for Treated LTBI Cohort Before and/or After Treatment Initiation, Stratified by First Nations Status**
April 1 1999 - March 31 2013



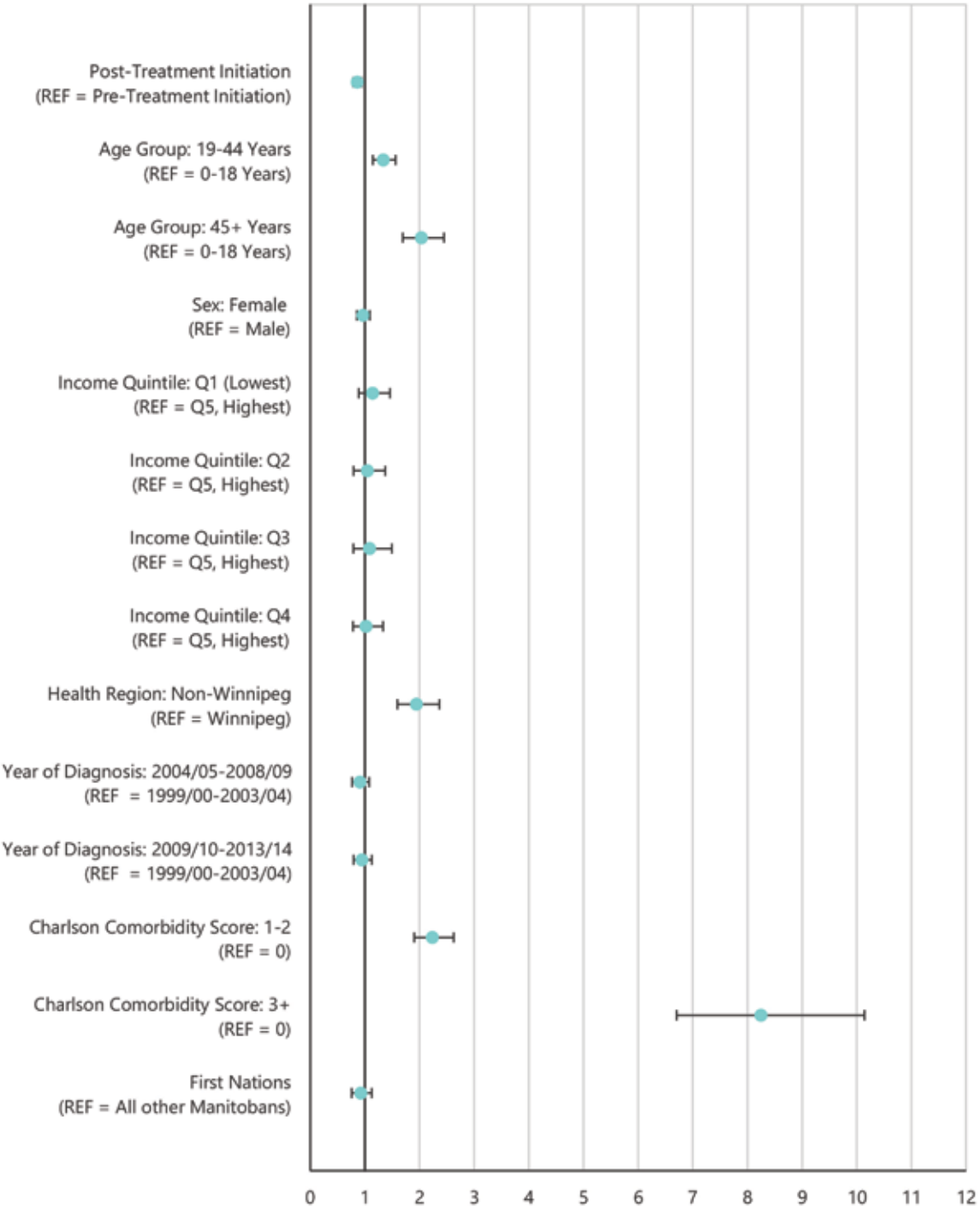

Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

Overall, inpatient hospitalizations remained low for both First Nations and non-First Nations individuals in the Treated LTBI Cohort throughout the study period. There was a slight increase in hospitalizations just prior to the initiation of treatment for non-First Nations members of the cohort, but the percentage of the cohort that was hospitalized in this time period remained below 10%. The number of hospital days showed a similar trend (Appendix Figure 4.4).

The forest plot in Appendix Figure 4.5 provides the results of the statistical analysis for inpatient hospitalizations. The odds of hospitalization were lower in the post-treatment initiation period than in the pre-treatment initiation period. Age and comorbidity were associated with a higher odds of hospitalization, as was a non-Winnipeg residence location. Other covariates were not associated with the odds of hospitalization.

**Appendix Figure 4.5: Characteristics of Treated LTBI Cohort Associated with Inpatient Hospitalizations***

Odds Ratio Estimates and 95% CIs



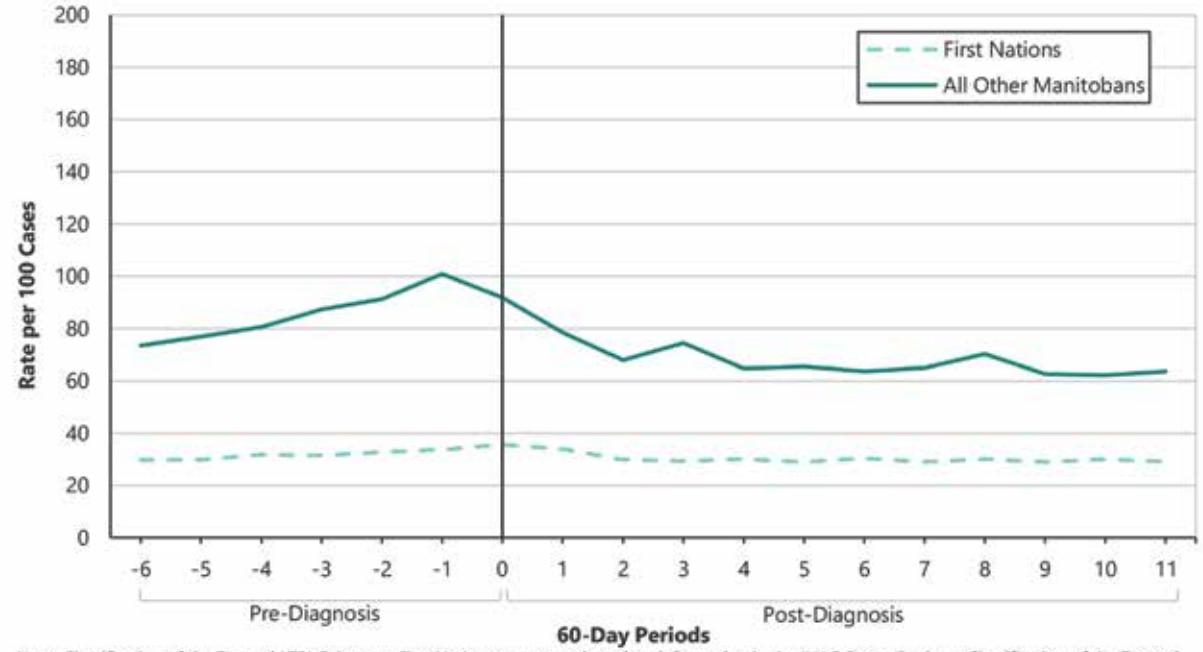

*Excluding Pregnancy/Birth

Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

## Physician Visits

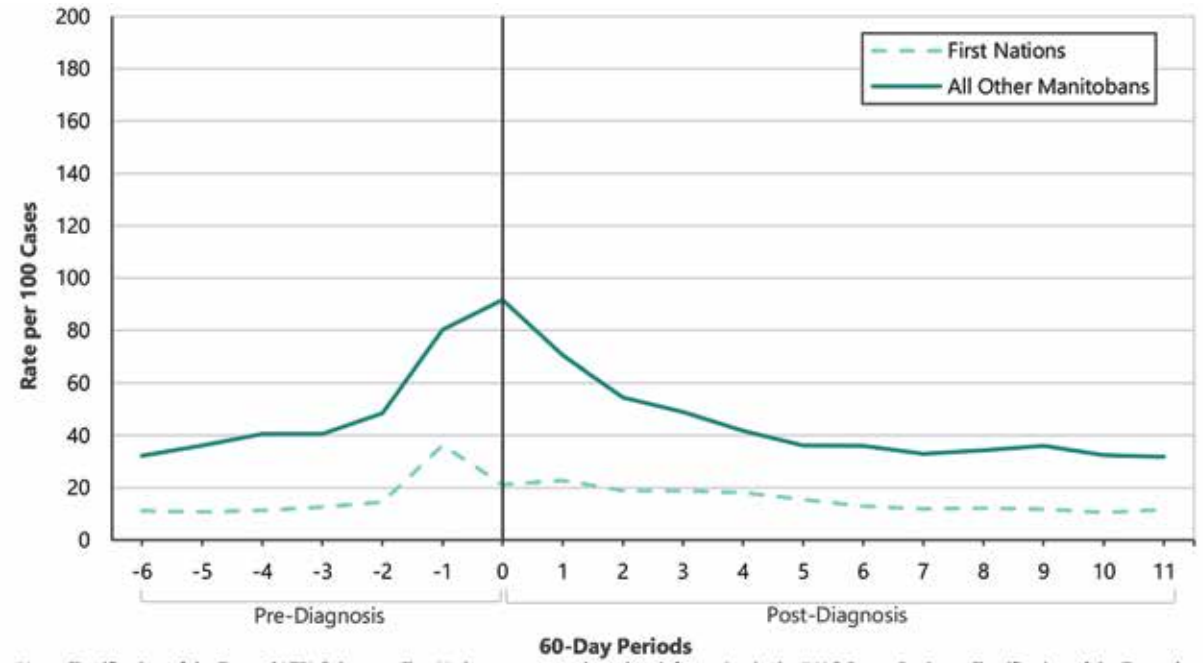
This section examines the utilization of both family and specialist physician services on an outpatient basis in the year prior to initiation of treatment for LTBI and in the two years following initiation of treatment for LTBI. Appendix Figures 4.6 and 4.7 contain results for the trends in family and specialist physician visits over time; the rates shown are per 100 individuals who initiated treatment for LTBI.

**Appendix Figure 4.6: Rate of Family Physician Visits for Treated LTBI Cohort Before and/or After Treatment Initiation, Stratified by First Nations Status**
April 1 1999 - March 31 2013




Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

**Appendix Figure 4.7: Rate of Specialist Physician Visits for Treated LTBI Cohort Before and/or After Treatment Initiation, Stratified by First Nations Status**
April 1 1999 - March 31 2013

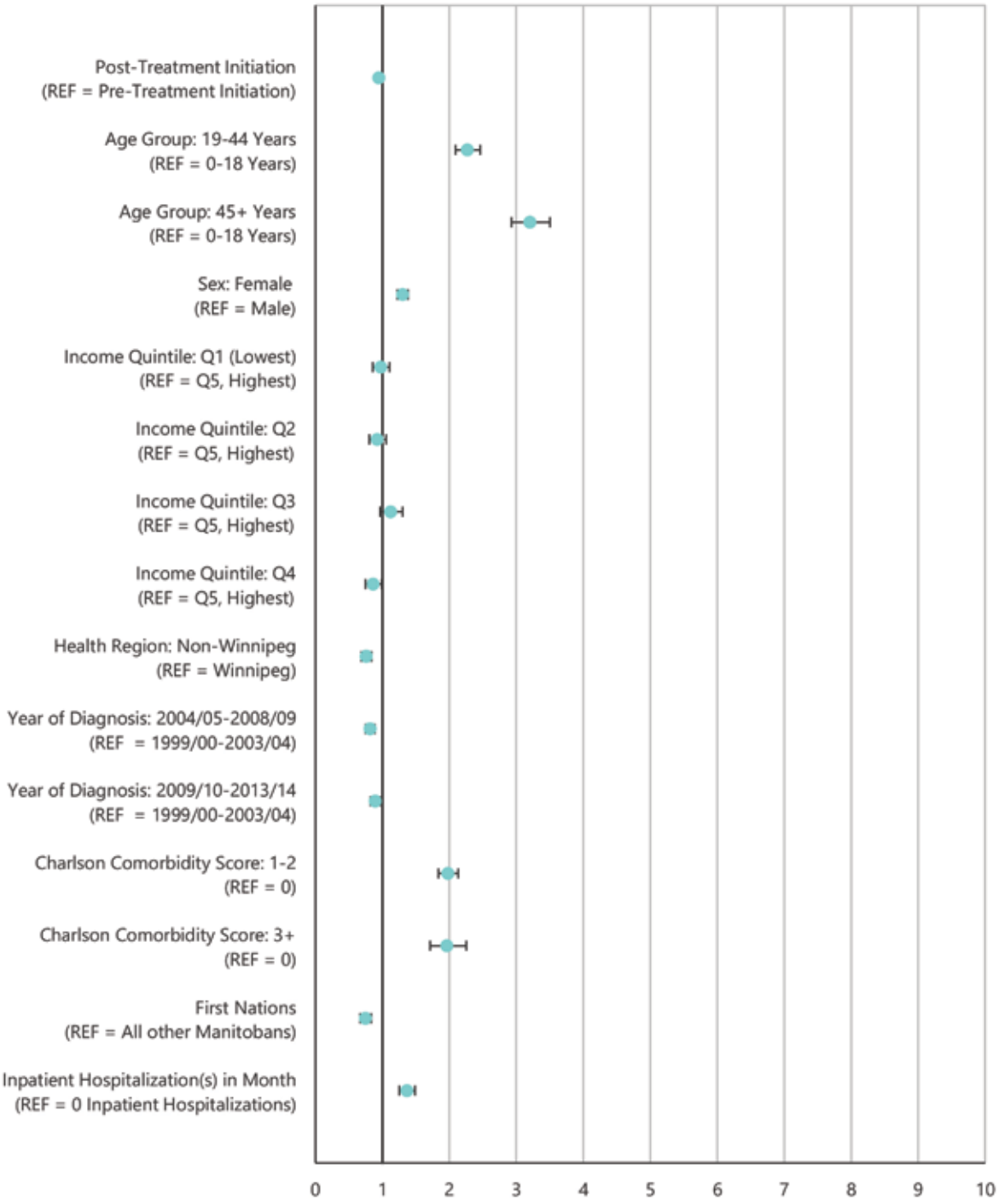



Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

Family physician visit rates were highest immediately prior to initiation of treatment and then decreased over approximately four months following initiation of treatment for non-First Nations cohort members. For First Nations cohort members, family physician visits were less frequent than for all other Manitobans throughout the study period and did not show a substantial increase around the time of treatment initiation. In contrast, specialist visit rates increased just prior to treatment initiation for First Nations cohort members and at the time of treatment initiation for non-First Nations cohort members before decreasing.

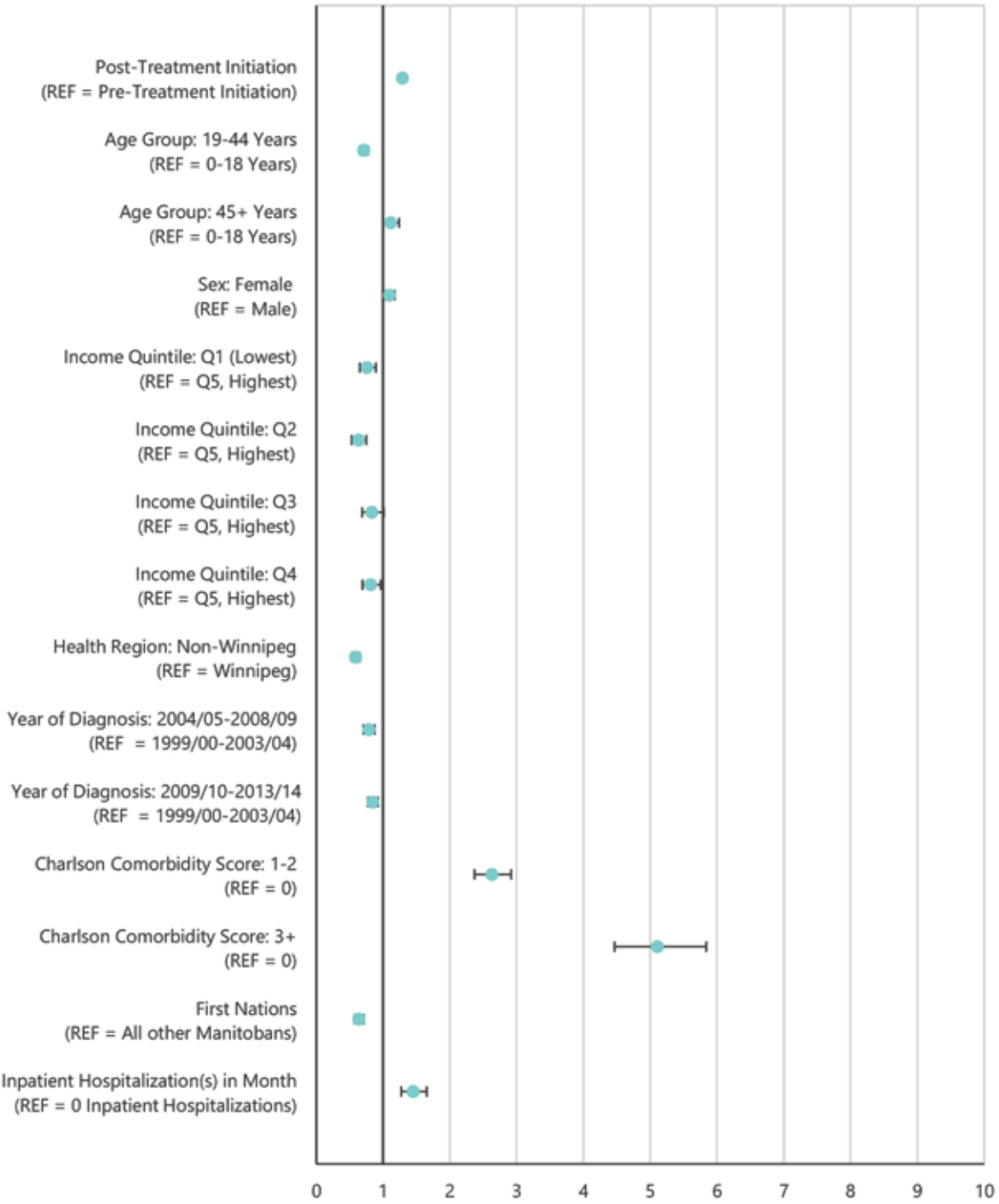
The forest plot for family physician visits (Appendix Figure 4.8) revealed that age, sex, and comorbidity were associated with higher visit rates, as was the presence of an inpatient hospitalization. A non-Winnipeg residence location, First Nations status, and a later year of treatment initiation were associated with lower visit rates. The forest plot for specialist physician visits (Appendix Figure 4.9) revealed that visit rates were higher in the post-treatment initiation period than in the pre-treatment initiation period. The effect of age was mixed; relative to the youngest cohort members, those in the 19-44 years age group had a lower rate of specialist visits, while cohort members in the 45+ years age group had a slightly higher rate of specialist visits. Comorbidity was strongly associated with a higher rate of specialist visits. Lower income quintile, a non-Winnipeg residence location, First Nation status and a later year of treatment initiation were all associated with a lower rate of specialist physician visits.

**Appendix Figure 4.8: Characteristics of Treated LTBI Cohort Associated with Ambulatory Physician Visit Rate***
Relative Risk Estimates and 95% CIs




*Excluding Pregnancy/Birth
Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

**Appendix Figure 4.9: Characteristics of Treated LTBI Cohort Associated with Rate of Specialist Physician Visits***
Relative Risk Estimates and 95% CIs

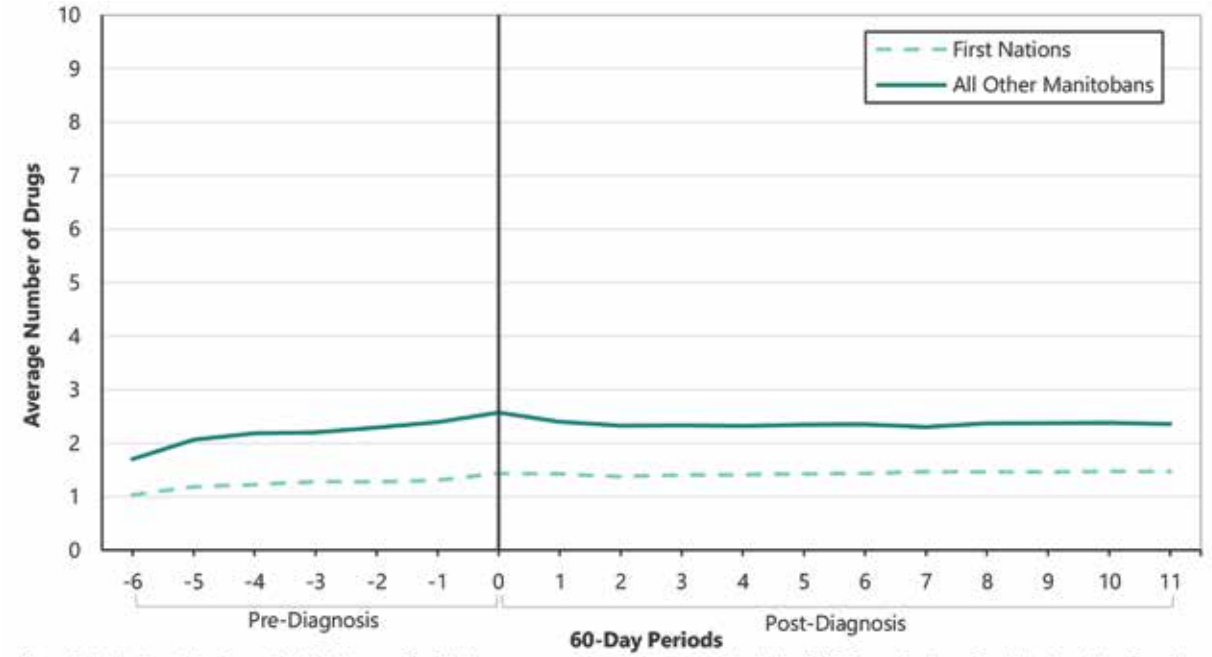



*Excluding Pregnancy/Birth
Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

## Non-TB Prescription Drug Use

The number of non-TB prescription drugs used showed little change over the study period for the Treated LTBI cohort (Appendix Figure 4.10). However, utilization rates were lower for First Nations cohort members than for all other cohort members.

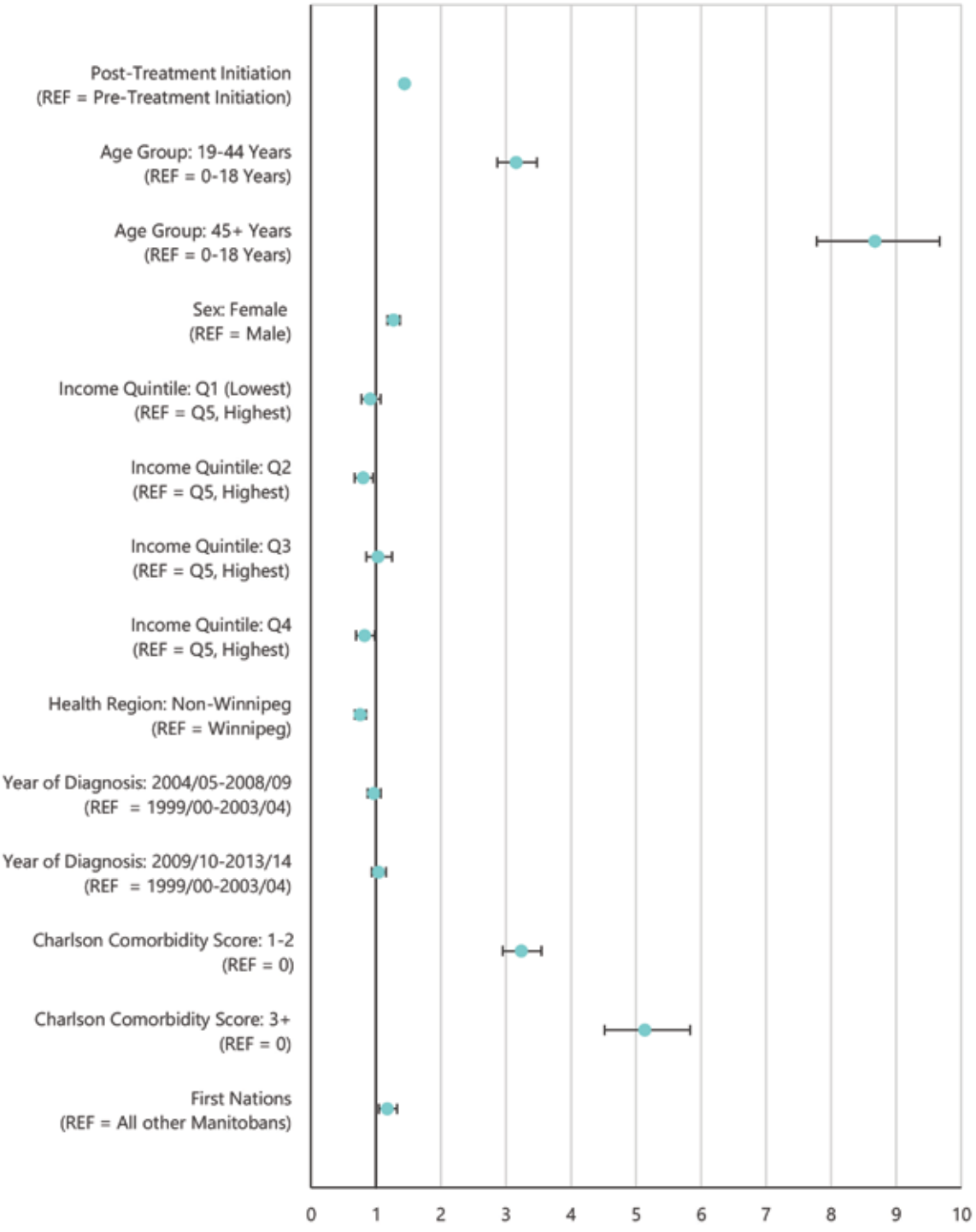
**Appendix Figure 4.10: Non-TB Prescription Drug Use for Treated LTBI Cohort Before and/or After Treatment Initiation, Stratified by First Nations Status**
April 1 1999 - March 31 2013




Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

As the forest plot in Appendix Figure 4.11 reveals, rates of non-TB prescription drug use were slightly higher overall in the post-treatment initiation period than in the pre-treatment initiation period. Age, sex, and comorbidity were also associated with a higher RR of drug utilization, as was First Nations status. A non-Winnipeg residence location was associated with a slightly lower RR of prescription drug utilization than a Winnipeg residence location.

**Appendix Figure 4.11: Characteristics of Treated LTBI Cohort Associated with Average Number of Different Non-TB Prescription Drugs***
Relative Risk Estimates and 95% CIs




* Excludes TB drugs
Note: Classification of the Treated LTBI Cohort on First Nations status was based on information in the INAC Status Registry. Classification of the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations was not possible; this detailed information about population of origin is only available for active TB cases using the Manitoba TB Registry.

## Comparisons between the Treated LTBI Cohort and Matched Cohort

Analyses were conducted to explore differences in healthcare use between the Treated LTBI and Matched Cohort. We compared rates of healthcare use for the two cohorts, stratified by First Nations status as defined from the INAC Status Registry. Recall that we cannot identify individuals in the Treated LTBI Cohort as First Nations on- and off-reserve, foreign-born, and Canadian-born non-First Nations; information about population of origin is only available for active TB cases using the Manitoba TB Registry. In Appendix Table 4.1, values greater than 1 for the RR estimates indicate that the Treated LTBI Cohort had higher utilization than the matched cohort, while values less than 1 indicate that the Treated LTBI Cohort had lower utilization. The 95% confidence intervals provide information about whether these differences were statistically significant.

For hospitalizations, rates were higher for the Treated LTBI Cohort than for the matched cohort and were similar, regardless of population group. For family physician visits, there was no statistically significant difference between the Treated LTBI Cohort and the matched cohort in visit rates amongst First Nations individuals. However, amongst all Manitobans, the visit rate was 27% higher in the Treated LTBI Cohort than in the matched cohort.

Appendix Table 4.2 compares the rates of use for First Nations individuals relative to all other Manitobans in each of the Treated LTBI Cohort and the matched cohort. As this table reveals, the size of the RR estimates was similar in both cohorts. The differences in healthcare use between First Nations and other Manitobans were statistically significant for most of the measures that were investigated.

**Appendix Table 4.1: Healthcare Use for Treated LTBI Disease Cohort Relative to Matched Cohort, Stratified by First Nations Status**

| Measure of Healthcare Use | First Nations Status | All Other Manitobans |
|---|---|---|
| | Relative Rate (95% Confidence Interval) | Relative Rate (95% Confidence Interval) |
| Inpatient Hospitalizations[a] | **1.60 (1.51 - 1.69)** | **1.90 (1.77 - 2.04)** |
| Ambulatory Physician Visits[b] | 0.97 (0.92 - 1.01) | **1.27 (1.21 - 1.34)** |
| Specialist Physician Visits[b] | **1.60 (1.51 - 1.69)** | **1.90 (1.77 - 2.04)** |
| Number of non-TB Drugs[b] | 0.95 (0.91 - 1.00) | **1.27 (1.18 - 1.36)** |

**Bold** relative rates and odds ratios indicate values that are statistically significant at α = 0.05
Note: [a] indicates an Odds Ratio and [b] indicates a Relative Rate

**Appendix Table 4.2: Healthcare Use for First Nations Relative to All Other Manitobans, Stratified by Cohort**

| Measure of Healthcare Use | Treated LTBI Cohort | Matched Cohort |
|---|---|---|
| | Relative Rate (95% Confidence Interval) | Relative Rate (95% Confidence Interval) |
| Inpatient Hospitalizations[a] | **0.69 (0.64 - 0.75)** | **0.82 (0.77 - 0.88)** |
| Ambulatory Physician Visits[b] | **0.81 (0.76 - 0.88)** | **1.07 (1.02 - 1.12)** |
| Specialist Physician Visits[b] | **0.69 (0.64 - 0.75)** | **0.82 (0.77 - 0.88)** |
| Number of non-TB Drugs[b] | **1.14 (1.04 - 1.24)** | **1.51 (1.43 - 1.60)** |

**Bold** relative rates and odds ratios indicate values that are statistically significant at α = 0.05
Note: [a] indicates an Odds Ratio and [b] indicates a Relative Rate

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