The Epidemiology of Active Tuberculosis Disease in the Winnipeg Health Region, 2013-2016

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FOREWORD

We are pleased to be able to present the second edition of the regional tuberculosis technical surveillance report. As with the first report in 2012, our aim is to provide decision-makers, clinicians and public health practitioners with information on the trends in active tuberculosis in the Winnipeg Health Region, updated to include calendar years 2013 – 2016.

Tuberculosis remains a significant health problem in the Region. One of the major demographic shifts since 2009 has been the proportion of persons with tuberculosis who are foreign-born, having increased from around 50% (2009) to 76% (2016); a trend also noted in other prairie urban centres. Since some foreign-born persons with tuberculosis come from countries with high rates of multidrug-resistant tuberculosis, it is not surprising that Winnipeg is seeing more drug-resistant disease. While drug-resistant tuberculosis was virtually nonexistent in 2012, 17% of all culture-confirmed tuberculosis infections in 2016 were drug-resistant. This worrisome trend must be closely monitored, as it will result in decreasing the effectiveness of treatments and will greatly increase costs of treating tuberculosis.

Although our overall annual number of individuals with tuberculosis have remained essentially unchanged since 2012, with the increase in proportion of foreign-born persons with tuberculosis we have seen a decrease in the proportion and numbers of those who are of Indigenous origin.

Socio-economic disadvantage continues to slow progress in reducing TB rates in the Region. By continuing to document the disproportionate burden of tuberculosis on certain peoples (foreign-born and Indigenous), this report highlights once again the need for well-resourced, sustained and coordinated efforts to address underlying socio-economic causes of the disparities, in addition to ramping up efforts to improve earlier diagnosis and treatment.

We cannot drop our guard. Our Region's approach to the ever-changing challenges of tuberculosis prevention and treatment continues to evolve from the Integrated Tuberculosis Services multidisciplinary preventive, primary care, and acute care approach established in 2010 to a future that will need to include a significant increased engagement in tuberculosis strategic planning with key partners at community, regional, provincial, and federal levels.

Timely, accurate and relevant monitoring and analyzing of surveillance information for tuberculosis is essential for determining healthcare priorities; focusing prevention efforts; identifying challenges that will inform public health practice; and improving the quality of programs and services aimed at reducing the incidence and impact of tuberculosis in the Region.

Sincerely,

Catherine Cook, MD, MSc, FCFP
Vice President, Population and Aboriginal Health

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Vice President, Interprofessional Practice and Chief Nursing Officer

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The authors are grateful also to many other clinicians and public health practitioners internal and external to the Region for their thoughtful review of this report.

For Further Information

You can find this document at http://www.wrha.mb.ca/surveillance.

For comments or inquiries concerning the material in this publication, contact EPI@wrha.mb.ca.

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THE WINNIPEG HEALTH REGION (WHR)

- The largest health region in the province of Manitoba (with a population of roughly 705,240 in 2014, about 60% of the total provincial population).
- Includes the capital city of Winnipeg, and the rural municipalities of East St. Paul and West St. Paul.
- For planning and management purposes, the WHR is divided into 12 Community Areas (Map).
- The Winnipeg Regional Health Authority (WRHA) is responsible for the delivery of acute care, public health and other community services to the residents of the WHR.

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EXECUTIVE SUMMARY

Tuberculosis (TB) continues to be a significant public health problem throughout the world, and remains a cause of morbidity and preventable cause of death in the Winnipeg Health Region (WHR). Data used in this report were obtained from the electronic public health records of the Population and Public Health Program of the Winnipeg Regional Health Authority (WRHA). This regional surveillance report provides the distribution of active TB disease since 2009 and a detailed descriptive analysis of active TB disease for calendar years 2013 to 2016.

Since 2009, there have been 571 cases of active TB disease reported among residents of the WHR. There were 90 cases reported in 2009 and 86 cases reported in 2016. The corresponding age-standardized rates (cases per 100,000 population) decreased from 13.1 in 2009 to 11.4 in 2016. The number of TB cases (and corresponding rates) has fluctuated considerably from year-to-year, having decreased from 2009 to 2014, and then increased again in 2015 and 2016 largely due to increases of TB in foreign-born persons. The regional rates were often similar to or lower than provincial rates (R. Wang & C. Loeppky, personal communication, August 18, 2017) but much higher than the national rate (Gallant, Duvvuri, & McGuire, 2017a).

In the WHR, males were more likely to be affected than females overall and individuals aged 25 to 44 years old represented the largest percentage of reported cases at 37% between 2013 and 2016. TB age-specific rates were lowest among children under 15 years of age and highest in the 15-24 and 25-44 age groups in the WHR, while in Canada the TB rates were highest in the 25-44 and 65+ age groups (Gallant et al., 2017a).

Demographic trends such as increasing migration from endemic countries, recurring outbreaks of TB in northern Manitoba communities, and persistent patterns of socio-economic disadvantage have slowed progress in reducing TB rates in the region. Within the region, the disease burden is unevenly distributed. While the suburban community areas (CAs) of the WHR had stable rates that were lower than the national rate, the inner core CAs (Downtown and Point Douglas) had rates that were five to10 times higher than the suburban CAs. The TB rates in the northern WHR areas (Inkster and Seven Oaks CAs) were roughly three to five times the rates observed for the other suburban areas. Point Douglas CA had the highest age-standardized rate in six of the last eight years, including 2016 (48.9 per 100,000).

Foreign-born and Canadian-born Indigenous populations are disproportionately infected with TB in the WHR. Between 2013 and 2016, the majority of persons with TB (72%) were foreign-born; likely explained by immigration from and travel to high incidence countries. The majority of foreign-born persons with TB were born in a Western Pacific country and had lived in Canada for more than two years. Indigenous peoples made up more than three-quarters (78%) of Canadian-born persons with TB reported in the same time period, highlighting the role of historical disadvantages such as structural racism; intergenerational trauma; poverty; homelessness; poor housing and overcrowding; social and geographic isolation; and inaccessible or inadequate health care services in the TB epidemic in Indigenous peoples.

Of all persons with TB who had a known HIV status (96%) from 2013-2016, 12 (4%) individuals were reported to be HIV-positive. Of those persons with TB who had available information regarding defined risk factors, the percentage of individuals with reported substance

use was 17% and reported homelessness was around 4%. Overall, 17% of persons with TB in this report were identified as having diabetes and 5% were identified as having advanced chronic kidney failure.

Over two-thirds (69%) of individuals in the WHR had respiratory TB from 2013-2016. Respiratory TB was diagnosed more often than non-respiratory TB in both Canadian-born and foreign-born individuals. The percentage of respiratory TB infections with a positive acid-fast bacillus (AFB) smear was 39%; this percentage fluctuated from a low of 35% in 2015 and a high of 45% in 2016. Overall, the majority (87%) of all persons with TB were culture-confirmed.

Of all culture-confirmed infections from 2013-2016, 25 (10%) had a TB strain that was drug-resistant to one or more of the four first-line drugs: isoniazid (INH), rifampin, pyrazinamide, or ethambutol. The percentage of culture-confirmed infections with drug-resistant TB rose from 5% in 2013 to 17% in 2016. Sixteen (6%) of the culture-confirmed infections reported between 2013 and 2016 had isoniazid mono-resistant TB, six (2%) had other drug-resistant TB, and three (1%) had multidrug-resistant (MDR) TB. The majority of drug-resistant infections were found in foreign-born individuals, females, and persons aged 25-54 years.

TB was the underlying cause of death in seven individuals and contributed to but was not the underlying cause of death in nine cases between 2013 and 2016. Nearly all persons (98%) diagnosed between 2013 and 2016 had started treatment at the time of this report. Of the five individuals (2%) who had never started treatment, four were reported as deceased. For those individuals that had ended treatment, eighty-eight percent had completed 100% of treatment at time of this report.

A total of 1,713 unique contacts were named between 2013 and 2016; nearly half (44%) of all contacts named were household contacts. In this time period, the number of times a contact was named by persons with TB ranged between one and 18 times. The average number of contacts named by persons with TB in 2016 was 11.3.

In addition to established strategies such as public health management of persons with TB and their contacts and innovative strategies to address large reservoirs of persons with latent tuberculosis infection, complementary interventions are needed to address inequities in the underlying socio-economic determinants of health.

INTRODUCTION

This document is a statistical report written in a conventional style describing cases and contacts using strict well-defined case and contact definitions. The authors recognize the importance of language in the discourse around tuberculosis, including concerns around the use of impersonal designations like "case" and "contact". Although these terms are used throughout the report to describe "active TB cases", we fully acknowledge that these are persons with TB who are more than just the sum of their disease. Hereafter, the use of "TB case" and "TB contact" is meant to refer to persons who have TB and persons who have close personal contact with persons who have TB.

Tuberculosis (TB), an infectious disease caused by the bacillus *Mycobacterium tuberculosis* (MTB), is a major global public health problem (World Health Organization [WHO], 2016). TB remained one of the top 10 causes of death worldwide in 2015 (WHO, 2017a). Of the estimated 1.7 million TB deaths in 2016 worldwide, 0.4 million deaths were thought to have resulted from TB disease among people living with HIV (WHO, 2017b). There were an estimated 10.4 million new TB cases in 2016 worldwide; of these, an estimated 1 million were children (WHO, 2017b).

TB remains a public health concern even in developed countries such as Canada. After decades of decline, national incidence rates of active TB disease have stabilized with some variability within Canadian jurisdictions (Gallant, Duvvuri, & McGuire, 2017b). Challenges with early detection and screening, immigration trends, enduring patterns of socio-economic disadvantage, and the HIV/AIDS epidemic are likely contributors to the persistent burden of TB. Extensive public health resources are required to prevent and manage TB. The cost of treating a non-complicated drug-susceptible case of TB was estimated to be $18,395.16 in 2012 (P. Plourde, personal communication, October 3, 2017). By contrast, the cost of treating MDR TB was estimated to be substantially more (>$100,000.00) due to the likelihood of increased hospitalization and high costs of second-line drugs (P. Plourde, personal communication, October 3, 2017).

TB is an airborne disease and typically transmitted from person to person via inhalation of the MTB bacilli. The WHO has estimated that one-quarter of the world's population is currently infected with the inactive or "latent" form of TB, known as latent TB infection (WHO, 2017b). The tuberculin skin test (TST) and interferon gamma release assay (IGRA) are the main tests available for latent TB infection; however, one of the limitations to these tests is that they cannot determine if the infection is recent or old. Left untreated, 5-10% of individuals infected with MTB will progress to active TB disease at some point in their lifetime. Although the bacteria usually affect the lungs, TB disease can occur anywhere in the body, and concurrent respiratory and non-respiratory forms of the disease are possible. Individuals who have non-respiratory TB disease are generally not infectious to others. Individuals with smear-positive TB are more infectious and their contacts are more likely to have recent infection or TB disease.

Drug-resistant TB is an emerging concern for treatment efforts fuelled by improper dosage or inappropriate regimens, unavailability of anti-tuberculosis drugs or poor quality drugs, and non-adherence to treatment regimens (Centers for Disease Control and Prevention [CDC], 2017). Drug-susceptible TB disease is typically treated with a standard 6-month course of four first-line drugs. Directly observed treatment (DOT) is one method to monitor that the prescribed regimen

is being followed and all doses are taken; it can be used for cases at increased risk for non-adherence or treatment failure or relapse (Menzies & Elwood, 2014, p.97). Key treatment objectives include rapid improvement in the clinical condition of the case preventing morbidity, mortality and transmission; drug-resistance; and relapse of disease after treatment completion.

Key TB elimination interventions include early detection and effective treatment of cases with active TB disease; timely investigation of close contacts; targeted screening; preventive therapy for cases with latent TB infection; and health education (Communicable Disease Control, 2014). There is also growing recognition that interventions need to address both structural and social barriers to TB care and prevention efforts (Dean & Fenton, 2010). Continuous monitoring and reporting of TB trends is essential for assessing disease burden, understanding its determinants, and for evaluating the effectiveness of TB elimination efforts. The objectives of this report are to describe the distribution of active TB disease since 2009 and the epidemiology of active TB disease among residents of the WHR during calendar years 2013 through 2016.

METHODS

Data Sources and Case Definitions

In Manitoba, TB is a notifiable disease under the *Public Health Act* (2006). Reporting requirements and guidelines for patient management and contact investigation are outlined in the provincial Tuberculosis Protocol (Communicable Disease Control, 2014). Laboratory and clinical case reports are submitted by laboratories and health care providers to Manitoba Health; and subsequently referred to Regional Health Authorities for follow-up. Upon receipt of a referral, and for the duration of treatment, regional public health nurses collect standardized case and contact information through client interviews, and by reviewing hospital and laboratory records and other relevant sources of information (e.g., the Manitoba Tuberculosis Registry).

Information collected on each case includes socio-demographic information, such as country of birth and address of residence; clinical information, such as results of radiological and microbial testing, disease site, infection and disease risk factors, and treatment outcomes; and exposure history and contact information. Contact investigations are undertaken by public health nurses to identify and evaluate contacts for latent TB infection and TB disease. Data are entered into and maintained in the region's Public Health Information System (iPHIS) – a Web-based application that facilitates recording and tracking of information on cases with notifiable communicable diseases, and their contacts. This surveillance report provides the distribution of clinical and confirmed active TB disease reported among WHR residents since 2009 and a descriptive analysis of cases for calendar years 2013-2016.

A confirmed case of active TB was defined as an individual with *Mycobacterium tuberculosis* complex (MTBC) infection demonstrated on culture or *M. tuberculosis* detected by direct polymerase chain reaction (PCR) in a respiratory specimen. A clinical case was defined as an individual with evidence of active TB disease but with no culture proof of MTB complex or positive direct PCR (see Appendix A for details). Cases were considered to have occurred in the calendar year when the earliest evidence of TB disease was detected (Appendix A). Using the International Statistical Classification of Diseases (ICD), cases were given an ICD-10 coded final diagnosis field in iPHIS, and classified as having respiratory (A15.* and A16.*) or non-

respiratory (A17.*, A18.*, A19.*) disease. Cases with concurrent respiratory and non-respiratory TB were classified as respiratory cases for the purpose of calculating overall incidence rates. In addition, analyses were performed to provide information on cases with concurrent respiratory and non-respiratory diagnostic sites separately from cases with either respiratory or non-respiratory infections.

Drug susceptibility testing may be performed at time of the diagnosis or if required, during treatment. If multiple isolates were submitted for a case, a resistant result superseded a susceptible result; therefore, the number of results equals the number of culture-positive cases. Drug-resistance was defined as an active case of TB with a strain of MTB that is resistant to one or more of the following drugs: isoniazid (INH), rifampin, pyrazinamide, or ethambutol. Counts are provided for cases of TB that were isoniazid mono-resistant, multidrug-resistant (resistant to at least INH and rifampin), and other drug-resistant (resistant to one or more of the other first-line drugs).

For the purpose of this report, *Indigenous Peoples* is a collective term used to describe First Nations (Status and non-Status), Métis, and Inuit peoples. Due to decommissioning of administrative sources (October 2015) and subsequent reliance on individual self-report, Indigenous status may be incomplete. Cases that were born outside of Canada ("foreign-born") were grouped according to place of birth into one of the six standard WHO regions (WHO, 2017c). Cases were assigned to Community Areas (CAs) using their postal code of residence at the time of diagnosis and the 2014 Manitoba postal code conversion file.

The definition for the renal disease risk factor was based on the definition found in the PHAC Canadian Tuberculosis Reporting System Reporting Form Completion Guidelines Version 1.9 (2011). See Appendix A for problematic substance use and homeless risk factor variable definitions. A case's HIV status was defined at the time of diagnosis; a positive status refers to a positive HIV antibody test or other confirmatory laboratory test (e.g., viral load) at the time of TB diagnosis.

Statistical Methods

Annual crude rates of active TB disease (both laboratory-confirmed and clinical cases) were calculated using the corresponding year's mid-point WHR population as the denominator. Population data (2006-2014) were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. Population counts for 2015 and 2016 were not available at the time of analysis. Therefore, 2015 and 2016 population counts were duplicated from 2014 population counts for all rate calculations.

Rates were age-standardized to the 2006 Canadian population (provided by Statistics Canada), and the associated 95% confidence intervals (95% CIs) were calculated with the Tiwari et al. (2006) formula. The purpose of reporting 95% CIs is to provide a measure of the reliability of the estimated rates; the narrower the confidence interval, the more precise the rate estimate is likely to be. All analyses, including mapping, were undertaken using Stata 13.1 (College Station, TX).

HIGHLIGHTS

Disease Burden

Between January 1, 2009 and December 31, 2016, there have been 571 cases of active TB disease reported among residents of the WHR (Table 1). There were 90 cases reported in 2009 and 86 cases reported in 2016. The corresponding age-standardized rates (cases per 100,000 population) decreased from 13.1 in 2009 to 11.4 in 2016. The number of TB cases (and corresponding rates) has fluctuated considerably from year-to-year, having decreased from 2009 to 2014, and then increased again in 2015 and 2016.

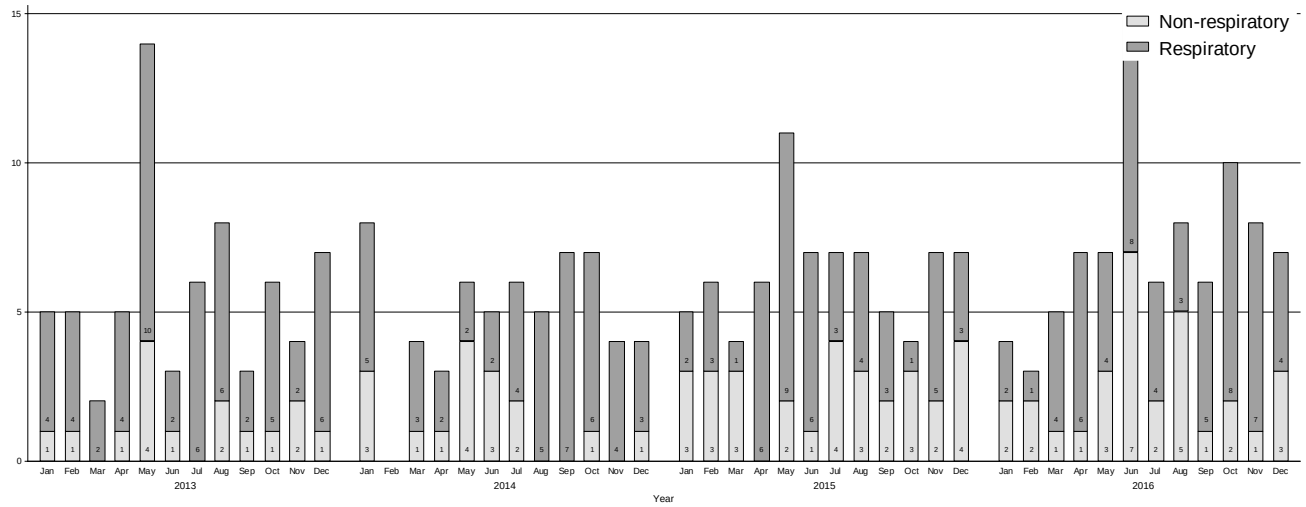
The number of TB cases in the WHR per month ranged between 0 and 15 with an average of 6 cases per month, and no consistent seasonal patterns of disease occurrence were noted over the 2013-2016 time period (Figure 1).

Table 1: Frequency, crude and age-standardized rates (per 100,000) of active TB disease, WHR (2009-2016)

	Number	Crude Rate	Age-Standardized Rate	95%CI
year				
2009	90	13.1	13.1	10.5 - 16.1
2010	73	10.5	10.5	8.2 - 13.1
2011	57	8.0	8.0	6.1 - 10.4
2012	62	8.6	8.6	6.6 - 11.0
2013	68	9.3	9.2	7.2 - 11.7
2014	59	7.9	7.9	6.0 - 10.2
2015	76	10.2	10.1	8.0 - 12.7
2016	86	11.6	11.4	9.2 - 14.1
Total	571	9.9	9.8	9.0 - 10.7

[a]Crude rates are calculated using the corresponding year's mid-point WHR population as the denominator. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. 2015 and 2016 population counts were duplicated from 2014 population counts.
[b]Rates are directly age-standardized to the 2006 Canadian population (provided by Statistics Canada)
[c]95%CI calculated with the Tiwari et al. (2006) formula

Figure 1: Epidemic curve of respiratory and non-respiratory active TB disease by month and year, WHR (2013-2016)



The inner core CAs (Downtown and Point Douglas) had TB rates that were 5 to10 times higher than suburban CAs, ranging from 19.5 per 100,000 in 2014 to 43.1 per 100,000 in 2009 (Table 2). The TB rates in the northern WHR areas (Inkster and Seven Oaks CAs) were roughly three to five times the rates observed for the other suburban areas. In contrast, the TB rates in the suburban CAs of the WHR fluctuated very little and were lower than the national rate.

Table 2: Frequency, crude and age-standardized rates (per 100,000) of active TB disease by community area groupings, WHR (2009-2016)

	Year	No.	Crude Rate	Age-Standardized Rate	95%CI
Inner core (Point Douglas/Downtown)					
	2009	51	42.2	43.1	32.0 - 56.8
	2010	40	32.4	32.3	23.0 - 44.0
	2011	28	22.2	24.0	15.9 - 34.7
	2012	30	23.5	23.2	15.6 - 33.2
	2013	31	24.2	24.5	16.6 - 34.9
	2014	24	18.6	19.5	12.4 - 29.0
	2015	32	24.8	25.0	17.0 - 35.3
	2016	39	30.2	30.5	21.6 - 41.8
North WHR (Seven Oaks/Inkster)					
	2009	19	19.3	19.9	12.0 - 31.0
	2010	11	11.0	11.3	5.6 - 20.2
	2011	13	12.6	12.8	6.8 - 22.0
	2012	13	12.3	12.6	6.7 - 21.5
	2013	18	16.7	17.1	10.1 - 27.0
	2014	16	14.6	14.8	8.4 - 24.0
	2015	21	19.1	19.3	11.9 - 29.5
	2016	25	22.7	23.0	14.9 - 33.9
Rest of WHR (Suburban)					
	2009	20	4.3	4.3	2.6 - 6.6
	2010	22	4.7	4.5	2.8 - 6.9
	2011	16	3.3	3.3	1.9 - 5.3
	2012	19	3.9	3.8	2.3 - 6.0
	2013	19	3.8	3.8	2.3 - 6.0
	2014	19	3.8	3.8	2.3 - 5.9
	2015	23	4.6	4.4	2.8 - 6.6
	2016	22	4.4	4.3	2.7 - 6.6

[a]Crude rates are calculated using the corresponding year's mid-point WHR population as the denominator. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. 2016 population counts were based on 2015 replicated data.
[b]Rates are directly age-standardized to the 2006 Canadian population (provided by Statistics Canada)
[c]95%CI calculated with the Tiwari et al. (2006) formula

In 2016, the inner core (Point Douglas and Downtown CAs) and the northern (Inkster and Seven Oaks CAs) areas of the WHR accounted for three-quarters of all TB cases (Table 2). Compared to the suburban areas, the inner core and northern areas had much higher age-standardized rates (e.g., 48.9 per 100,000 in Point Douglas and 30.2 per 100,000 in Inkster compared to 1.4 per 100,000 in St. Vital) (Table 3 and Figure 4). Point Douglas CA had the highest age-standardized rate in six of the last eight years, including 2016 (48.9 per 100,000).

Table 3: Crude and age-standardized rates of TB disease by community area, WHR (2016)

	Number	Crude Rate	Age-Standardized Rate	95%CI
St. James	5	8.3	8.8	2.9 - 20.4
Assiniboine South	1	2.8	3.5	0.1 - 18.0
Fort Garry	8	9.2	8.9	3.8 - 17.6
St. Vital	1	1.4	1.4	0.0 - 7.9
St. Boniface	0	0.0	0.0	0.0 - 6.2
Transcona	1	2.6	2.9	0.1 - 15.2
River East	3	3.1	3.0	0.6 - 8.7
Seven Oaks	15	19.8	19.6	11.0 - 32.4
Inkster	10	29.1	30.2	14.4 - 55.7
Point Douglas	22	46.4	48.9	30.4 - 74.4
Downtown	17	20.8	20.5	11.9 - 33.0
River Heights	3	5.3	5.4	1.1 - 16.2
Total	86	11.6	11.4	9.2 - 14.1

[a]Crude rates are calculated using the corresponding year's mid-point WHR population as the denominator. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. 2015 and 2016 population counts were duplicated from 2014 population counts.
[b]Rates are directly age-standardized to the 2006 Canadian population (provided by Statistics Canada)
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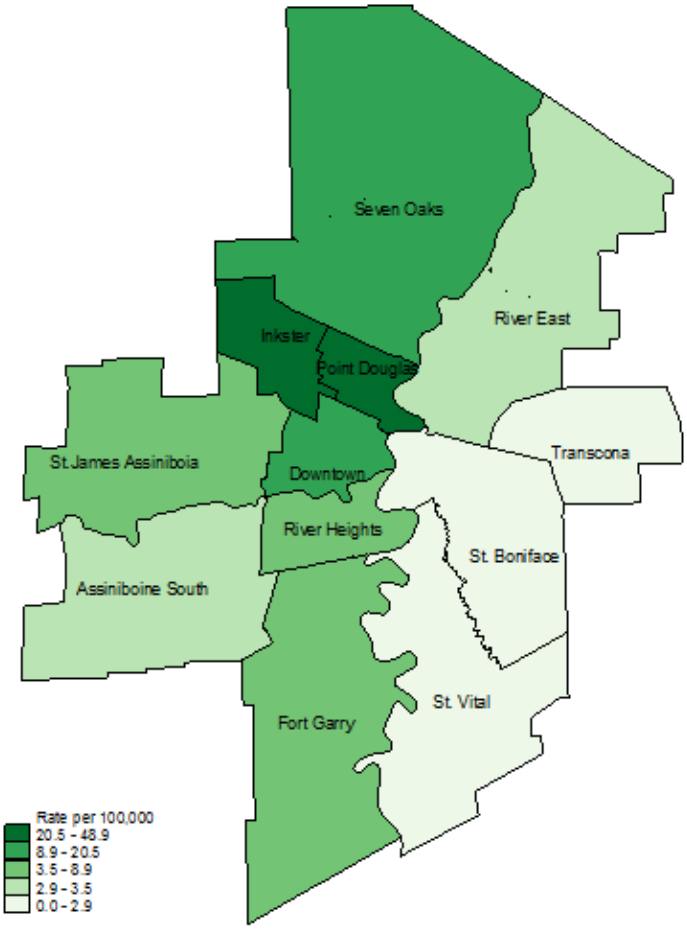
Figure 2: Age-standardized rate (per 100,000) of active TB disease by community area, WHR (2016)



Demographic Characteristics

There were 289 cases with active TB disease reported in the WHR between 2013 and 2016; 68 in 2013, 59 in 2014, 76 in 2015, and 86 in 2016 (Table 4). Approximately half of the cases were male and the highest proportion of cases was in the 25-44 age group at 37% in the time period 2013-2016. Children under 15 years of age represented about 3% of the total number of TB cases.

Table 4. Socio-demographic characteristics of active TB cases, WHR (2013-2016)

		2013		2014		2015		2016		TOTAL	
		No.	%	No.	%	No.	%	No.	%	No.	%
Sex											
	Female	27	39.7	32	54.2	39	51.3	41	47.7	139	48.1
	Male	41	60.3	27	45.8	37	48.7	45	52.3	150	51.9
Total		68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Age group											
	0-14	2	2.9	3	5.1	1	1.3	3	3.5	9	3.1
	15-24	11	16.2	10	16.9	13	17.1	16	18.6	50	17.3
	25-44	27	39.7	19	32.2	27	35.5	33	38.4	106	36.7
	45-64	18	26.5	19	32.2	23	30.3	21	24.4	81	28.0
	65+	10	14.7	8	13.6	12	15.8	13	15.1	43	14.9
Total		68	100.0	59	100.0	76	100.0	86	100.0	289	100.0

Between 2013 and 2016, the age-standardized rate of TB in females increased from 7.1 per 100,000 to 10.8 per 100,000 (Table 5). The age-standardized rate of TB in males increased slightly from 11.3 per 100,000 in 2013 to 12.3 per 100,000 in 2016. For the region overall, the age-standardized rates (per 100,000) increased from 9.2 in 2013 to 11.4 in 2016.

Table 5: Frequency, crude and age-standardized rates (per 100,000) of active TB disease by sex, WHR (2013-2016)

	Year	No.	Crude Rate	Age-Standardized Rate	95%CI
Female					
	2013	27	7.2	7.1	4.7 - 10.4
	2014	32	8.5	8.6	5.9 - 12.1
	2015	39	10.3	10.2	7.3 - 14.0
	2016	41	10.8	10.8	7.8 - 14.7
Male					
	2013	41	11.4	11.3	8.1 - 15.4
	2014	27	7.4	7.5	5.0 - 11.0
	2015	37	10.1	10.1	7.1 - 13.9
	2016	45	12.3	12.3	9.0 - 16.5
Total					
	2013	68	9.3	9.2	7.2 - 11.7
	2014	59	7.9	7.9	6.0 - 10.2
	2015	76	10.2	10.1	8.0 - 12.7
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[b]Rates are directly age-standardized to the 2006 Canadian population (provided by Statistics Canada)
[c]95%CI calculated with the Tiwari et al. (2006) formula

In the time period 2013-2016, the highest age-specific rates were reported in the 15-24 and 25-44 age groups while the lowest age-specific rates were reported in cases under the age of 15 (Table 6).[1]

[1] In the WHR, pediatric referrals are based on age cutoff of 17 years; a breakdown of the number of cases of pediatric TB using this definition can be found in Appendix B.

Table 6: Frequency and age-specific rates (per 100,000) of active TB disease by age group, WHR (2013-2016)

	2013			2014			2015			2016		
	No.	Age-Specific Rate	95%CI	No.	Age-Specific Rate	95%CI	No.	Age-Specific Rate	95%CI	No.	Age-Specific Rate	95%CI
Age group												
0-14	2	1.6	0.2 - 5.9	3	2.4	0.5 - 7.0	1	0.8	0.0 - 4.5	3	2.4	0.5 - 7.0
15-24	11	10.7	5.4 - 19.2	10	9.7	4.6 - 17.8	13	12.6	6.7 - 21.5	16	15.5	8.8 - 25.1
25-44	27	13.2	8.7 - 19.2	19	9.1	5.5 - 14.2	27	12.9	8.5 - 18.8	33	15.8	10.9 - 22.2
45-64	18	9.2	5.4 - 14.5	19	9.6	5.8 - 15.0	23	11.6	7.4 - 17.5	21	10.6	6.6 - 16.3
65+	10	9.4	4.5 - 17.4	8	7.3	3.2 - 14.4	12	11.0	5.7 - 19.2	13	11.9	6.3 - 20.4
Total	68	9.3	7.2 - 11.8	59	7.9	6.0 - 10.2	76	10.2	8.1 - 12.8	86	11.6	9.3 - 14.3

[a]Crude rates are calculated using the corresponding year's mid-point WHR population as the denominator. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. 2015 and 2016 population counts were duplicated from 2014 population counts.
[b]95%CI calculated with the Tiwari et al. (2006) formula

TB disproportionately affects two groups in the WHR: Indigenous peoples and foreign-born individuals from TB endemic countries. From 2013-2016, 28% of TB cases were Canadian-born with Indigenous peoples making up the majority (78%) (Table 7). Indigenous peoples made up 22% of the total number of TB cases reported in the same time period.

Table 7. Number (%) of cases of active TB disease by place of birth and Indigenous status, WHR (2013-2016)

	2013		2014		2015		2016		TOTAL	
	No.	%	No.	%	No.	%	No.	%	No.	%
Place of birth										
Canada	30	44.1	16	27.1	15	19.7	21	24.4	82	28.4
Elsewhere	38	55.9	43	72.9	61	80.3	65	75.6	207	71.6
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Foreign-born										
Non-recent (>2 Years)	29	76.3	36	83.7	48	78.7	54	83.1	167	80.7
Recent (<=2 Years)	9	23.7	7	16.3	13	21.3	10	15.4	39	18.8
Unknown recency	0	0.0	0	0.0	0	0.0	1	1.5	1	0.5
Total	38	100.0	43	100.0	61	100.0	65	100.0	207	100.0
Canadian Born										
No Indigenous Identifier Reported	4	13.3	7	43.8	1	6.7	6	28.6	18	22.0
Identified/Reported as Indigenous	26	86.7	9	56.3	14	93.3	15	71.4	64	78.0
Total	30	100.0	16	100.0	15	100.0	21	100.0	82	100.0

Note: Due to decommissioning of administrative sources, Indigenous status may be incomplete.

Foreign-born individuals made up about 72% of TB cases (Table 7) from 2013-2016. More than three-quarters (81%) of the foreign-born cases had resided in Canada for more than two years, reflecting the much larger number of these individuals compared to more recent immigrants. Overall, 58% of foreign-born cases were born in a Western Pacific country (e.g., China, Republic of Korea, Philippines), 16% were born in an African country, and 16% were born in a South-east Asian country (e.g., India, Indonesia, Thailand) (Table 8).

Table 8. Number (%) of foreign-born active TB cases by year and region of birth, WHR (2013-2016)

	2013		2014		2015		2016		TOTAL	
	No.	%	No.	%	No.	%	No.	%	No.	%
WHO Regions										
Africa	7	18.4	7	16.3	9	14.8	11	16.9	34	16.4
Americas	1	2.6	0	0.0	2	3.3	3	4.6	6	2.9
South-East Asia	10	26.3	7	16.3	5	8.2	12	18.5	34	16.4
Europe	0	0.0	0	0.0	2	3.3	1	1.5	3	1.4
Eastern Mediterranean	2	5.3	2	4.7	5	8.2	1	1.5	10	4.8
Western Pacific	18	47.4	27	62.8	38	62.3	37	56.9	120	58.0
Total	38	100.0	43	100.0	61	100.0	65	100.0	207	100.0

Clinical Features

About 7% of TB cases were found by investigating contacts of a diagnosed TB case (Table 9). The remaining cases (93%) were detected through a clinical case investigation, most of the time as a result of cases presenting with symptoms suggestive of TB. Roughly two-thirds (69%) of cases had respiratory TB. The percentage of respiratory TB infections with a positive acid-fast bacillus (AFB) smear was 39%; this percentage fluctuated from a low of 35% in 2015 and a high of 45% in 2016. Overall, 87% of all cases were confirmed by culture; 90% of respiratory cases and 80% of non-respiratory cases were culture-confirmed.

Table 9. Number (%) of cases of active TB disease by year and certain clinical features, WHR (2013-2016)

	2013		2014		2015		2016		TOTAL	
	No.	%	No.	%	No.	%	No.	%	No.	%
Investigation Type										
Case Investigation	61	89.7	55	93.2	73	96.1	80	93.0	269	93.1
Contact Investigation	7	10.3	4	6.8	3	3.9	6	7.0	20	6.9
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Respiratory/Non-Respiratory										
Non-respiratory	15	22.1	16	27.1	30	39.5	30	34.9	91	31.5
Respiratory	53	77.9	43	72.9	46	60.5	56	65.1	198	68.5
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
AFB Smear-positive (Resp cases)										
No	33	62.3	27	62.8	30	65.2	31	55.4	121	61.1
Yes	20	37.7	16	37.2	16	34.8	25	44.6	77	38.9
Total	53	100.0	43	100.0	46	100.0	56	100.0	198	100.0
Culture-confirmed (Non-Resp & Resp cases)										
No	7	10.3	8	13.6	13	17.1	10	11.6	38	13.1
Yes	61	89.7	51	86.4	63	82.9	76	88.4	251	86.9
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0

Note: Includes all confirmed and clinical cases diagnosed in the WHR and reporting a valid postal code within the WHR at the time of episode.
AFB: Acid-fast bacillus

Of a total of 289 cases, 245 (85%) had a TB single diagnosis, 39 (13%) had a dual diagnosis, and five (2%) had TB in more than two diagnoses (Table 10). A total of 166 cases (57%) had TB exclusively affecting the respiratory system, and another 32 cases (11%) had TB concurrently affecting respiratory and non-respiratory sites. Therefore, a total of 198 cases had respiratory TB. The remaining 91 cases (31%) had TB exclusively affecting non-respiratory sites.

Among single diagnoses, lymph nodes (21%) was the most commonly affected non-respiratory site. Among single, dual and more than two diagnoses (breakdown not shown below), five cases (2%) had a diagnosis of miliary TB and four cases (1%) had a diagnosis of TB of the CNS, both very serious but rare, forms of TB.

Table 10. Number (%) of cases of active TB disease by disease site, WHR (2013-2016)

	TOTAL	
	No.	%
Single diagnosis		
Respiratory	156	63.7
Non-respiratory: Lymph nodes	51	20.8
Non-respiratory: Miliary	1	0.4
Non-respiratory: Other*	37	15.1
Total	245	100.0
Dual diagnosis		
Respiratory (more than one site)	10	25.6
Respiratory & Lymph nodes	14	35.9
Respiratory & CNS	3	7.7
Respiratory & Miliary	3	7.7
Respiratory & Non-respiratory: Other*	7	17.9
Non-respiratory: Other* & Lymph nodes	1	2.6
Non-respiratory: Lymph nodes & Non-respiratory: CNS	1	2.6
Total	39	100.0
More than 2 diagnoses		
Respiratory & Non-respiratory	5	100.0
Total	5	100.0

Note: Other includes genitourinary system, intestines, bones and joints, peritoneum, and mesenteric glands, skin, eye, ear, thyroid, adrenal and spleen
Cases caused by mycobacteria other than tuberculosis (MOTT) may be included in Dual Diagnosis and More than 2 diagnoses categories

Table 11 compares individuals who had respiratory TB (with or without TB in other sites) with those who had TB exclusively at non-respiratory sites ("non-respiratory TB only"). Although cases aged 25-44 represented 37% of total cases, they represented 53% of non-respiratory cases and 29% of respiratory cases. Cases aged 65+ represented 6% of the non-respiratory cases and 19% of respiratory cases despite representing 15% of total cases. While 48% of the cases overall were female, nearly two-thirds (65%) of the non-respiratory cases and less than half (40%) of respiratory cases were females. Foreign-born cases represented 88% of non-respiratory cases while representing 72% of the total number of cases. Of note, older individuals (≥65), males, and Canadian-born TB cases are proportionally over-represented in the respiratory diagnosis category.

Table 11. Number (%) of cases of active TB disease by disease site and socio-demographic characteristics, WHR (2013-2016)

	Non-respiratory		Respiratory		TOTAL	
	No.	%	No.	%	No.	%
Age group						
0-14	2	2.2	7	3.5	9	3.1
15-24	13	14.3	37	18.7	50	17.3
25-44	48	52.7	58	29.3	106	36.7
45-64	23	25.3	58	29.3	81	28.0
65+	5	5.5	38	19.2	43	14.9
Total	91	100.0	198	100.0	289	100.0
Sex						
Female	59	64.8	80	40.4	139	48.1
Male	32	35.2	118	59.6	150	51.9
Total	91	100.0	198	100.0	289	100.0
Place of residence						
Rest of WHR	26	28.6	57	28.8	83	28.7
Core	37	40.7	89	44.9	126	43.6
North WHR	28	30.8	52	26.3	80	27.7
Total	91	100.0	198	100.0	289	100.0
Place of origin						
Canadian born, No Indigenous Identifier Reported	2	2.2	16	8.1	18	6.2
Canadian born, Identified/Reported as Indigenous	9	9.9	55	27.8	64	22.1
Foreign-born	80	87.9	127	64.1	207	71.6
Total	91	100.0	198	100.0	289	100.0

Note: Includes all confirmed and clinical cases diagnosed in the WHR and reporting a valid postal code within the WHR at the time of episode.
Due to decommissioning of administrative sources, Indigenous status may be incomplete.

Disease Risk Factors

Self-reported risk factors for cases between 2013 and 2016 are provided in Table 12. HIV Status was known for 96% of the cases. The remaining cases either refused testing, were not offered a test, or their status was unknown. Twelve (4%) cases were known to be HIV-positive. Diabetes and advanced chronic kidney failure were reported in 17% and 5% of cases, respectively. Substance use was reported in 17% of cases that were asked. The absence of a fixed, regular and adequate night-time residence was reported to be 4% of cases.

Table 12. Number (%) of cases of active TB disease by year and disease risk factors, WHR (2013-2016)

	2013		2014		2015		2016		TOTAL	
	No.	%	No.	%	No.	%	No.	%	No.	%
HIV Status										
Negative	62	91.2	56	94.9	69	90.8	78	90.7	265	91.7
Positive	2	2.9	1	1.7	4	5.3	5	5.8	12	4.2
Test Refused	1	1.5	0	0.0	0	0.0	0	0.0	1	0.3
Test not offered	2	2.9	2	3.4	3	3.9	3	3.5	10	3.5
Unknown	1	1.5	0	0.0	0	0.0	0	0.0	1	0.3
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Diabetes										
No	54	79.4	46	78.0	60	78.9	74	86.0	234	81.0
Yes	12	17.6	13	22.0	14	18.4	10	11.6	49	17.0
Unknown	2	2.9	0	0.0	0	0.0	0	0.0	2	0.7
Missing	0	0.0	0	0.0	2	2.6	2	2.3	4	1.4
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Renal disease										
No	63	92.6	55	93.2	71	93.4	81	94.2	270	93.4
Yes	5	7.4	4	6.8	3	3.9	3	3.5	15	5.2
Missing	0	0.0	0	0.0	2	2.6	2	2.3	4	1.4
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Problematic substance use										
No	51	75.0	49	83.1	60	78.9	68	79.1	228	78.9
Yes	15	22.1	8	13.6	10	13.2	13	15.1	46	15.9
Unknown	1	1.5	2	3.4	4	5.3	3	3.5	10	3.5
Missing	1	1.5	0	0.0	2	2.6	2	2.3	5	1.7
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Homeless										
No	64	94.1	58	98.3	72	94.7	82	95.3	276	95.5
Yes	4	5.9	1	1.7	2	2.6	3	3.5	10	3.5
Missing	0	0.0	0	0.0	2	2.6	1	1.2	3	1.0
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0

Note: Test not Offered is used when there is no indication an HIV test was offered, including cases that die after a few weeks of therapy if they were not offered a test
An Unknown HIV status is defined as a TB cases that was deceased at time of TB diagnosis. POC: Point-of-care testing
Homeless: Lacks a fixed, regular and adequate night-time residence (see Methods). Problematic substance use: A maladaptive pattern of substance use leading to clinically significant impairment or distress (see Methods)
Risk information may be missing because of the timing of death relative to the diagnosing of TB.

Deaths among TB Cases

Of the 289 TB cases included in this analysis, 22 individuals were known to have died by the end of August 2017 (Table 13). TB was the underlying cause of death for seven cases and contributed to but was not the underlying cause of death for an additional nine cases. TB was reported as the underlying cause of death in four cases diagnosed in 2016, corresponding to an approximate case fatality ratio of 5% (Table 13) and a regional mortality rate of 0.5 TB deaths per 100,000 in 2016 (Table 14).

Table 13. Number (%) of deaths among cases diagnosed (2013-2016) with active TB disease by year of death, WHR

	2013		2014		2015		2016		2017YTD		TOTAL	
	No.	%	No.	%	No.	%	No.	%	No.	%		
Cause of death												
TB was underlying cause of death	1	20.0	0	0.0	2	50.0	4	50.0	0	0.0	7	31.8
TB contributed to but was not underlying cause of death	3	60.0	1	33.3	2	50.0	2	25.0	1	50.0	9	40.9
TB was unrelated to cause of death	1	20.0	2	66.7	0	0.0	2	25.0	1	50.0	6	27.3
Total	5	100.0	3	100.0	4	100.0	8	100.0	2	100.0	22	100.0

Table 14. Number (%) of deaths among cases of active TB disease by diagnosis year, WHR (2013-2016)

	2013		2014		2015		2016		TOTAL	
	No.	%	No.	%	No.	%	No.	%	No.	%
Cause of death										
TB was underlying cause of death	1	16.7	0	0.0	2	40.0	4	44.4	7	31.8
TB contributed to but was not underlying cause of death	4	66.7	0	0.0	2	40.0	3	33.3	9	40.9
TB was unrelated to cause of death	1	16.7	2	100.0	1	20.0	2	22.2	6	27.3
Total	6	100.0	2	100.0	5	100.0	9	100.0	22	100.0

Drug-Resistance

Drug-resistant TB is defined as an active case of TB disease that is infected with a strain of MTB that is resistant to one or more of the four first-line drugs: isoniazid, rifampin, pyrazinamide or ethambutol. Between 2013 and 2016, 87% percent of cases were culture-confirmed and sensitivity results were available for all cases. Of these, 25 (10%) cases had a TB strain that was resistant to one or more of the four first-line drugs: 16 (6%) cases had isoniazid mono-resistant TB, six (2%) cases were resistant to one or more of the other first-line drugs, and three (1%) cases had MDR TB (resistant to at least INH and rifampin) (Table 15). All but one of the 25 cases of drug-resistant TB showed initial resistance versus acquired drug-resistance. The percentage of culture-confirmed cases with drug-resistant TB rose from 5% to 17% between 2013 and 2016. Of those culture-confirmed cases with drug-resistant TB, the percentage of cases with isoniazid mono-resistance dropped from 100% in 2013 to 46% in 2016, giving rise to increasing multidrug-resistant TB and other drug-resistant TB in 2015 and 2016.

Table 15. Number (%) of culture-confirmed active TB cases showing drug-resistance* by year, WHR (2013-2016)

	2013		2014		2015		2016		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Drug-resistance										
No	58	95.1	48	94.1	57	90.5	63	82.9	226	90.0
Yes	3	4.9	3	5.9	6	9.5	13	17.1	25	10.0
Total	61	100.0	51	100.0	63	100.0	76	100.0	251	100.0
Type of Resistance										
Isoniazid mono-resistant	3	100.0	3	100.0	4	66.7	6	46.2	16	64.0
Multidrug-resistant	0	0.0	0	0.0	1	16.7	2	15.4	3	12.0
Other drug-resistant	0	0.0	0	0.0	1	16.7	5	38.5	6	24.0
Total	3	100.0	3	100.0	6	100.0	13	100.0	25	100.0

*Drug-resistance was defined as resistance to one or more of the following drugs: Rifampin, Pyrazinamide, Isoniazid or Ethambutol

Overall, 10% of both non-respiratory and respiratory cases showed drug-resistance between 2013 and 2016 (Table 16). The proportion of isoniazid mono-resistant TB and other drug-resistant TB was higher in respiratory cases than in non-respiratory cases. Two MDR TB non-respiratory cases and one MDR TB respiratory case were identified.

Table 16. Number (%) of cases of culture-confirmed active TB disease showing drug-resistance by disease site, WHR (2013-2016)

	Non-Respiratory		Respiratory		TOTAL	
	No.	%	No.	%	No.	%
Drug-resistance						
No	66	90.4	160	90.0	226	90.0
Yes	7	9.6	18	10.0	25	10.0
Total	73	100.0	178	100.0	251	100.0
Isoniazid mono-resistant						
No	3	42.9	6	33.3	9	36.0
Yes	4	57.1	12	66.7	16	64.0
Total	7	100.0	18	100.0	25	100.0
Multidrug-resistant						
No	5	71.4	17	94.4	22	88.0
Yes	2	28.6	1	5.6	3	12.0
Total	7	100.0	18	100.0	25	100.0
Other drug-resistant						
No	6	85.7	13	72.2	19	76.0
Yes	1	14.3	5	27.8	6	24.0
Total	7	100.0	18	100.0	25	100.0

*Drug-resistance was defined as resistance to one or more of the following drugs: Rifampin, Pyrazinamide, Isoniazid or Ethambutol

Cases aged 25-44 represented 52% of all cases with drug-resistant TB despite representing only 36% of overall cases (Table 17). Conversely, cases aged 45-64 represented fewer of the drug-resistant cases than their respective proportion of overall cases. The proportion of female cases with drug-resist TB (52%) was slightly higher than the proportion of female cases overall (47%). Nearly all drug-resistant TB cases were born elsewhere (92%) even though only 72% of total cases were foreign-born.

Table 17. Number (%) of culture-confirmed cases of active TB disease showing drug-resistance by socio-demographic characteristics, WHR (2013-2016)

	Drug-susceptible		Drug-resistant		TOTAL	
	No.	%	No.	%	No.	%
Age group						
0-14	5	2.2	0	0.0	5	2.0
15-24	40	17.7	5	20.0	45	17.9
25-44	76	33.7	13	52.0	89	35.5
45-64	68	30.0	3	12.0	71	28.3
65+	37	16.4	4	16.0	41	16.3
Total	226	100.0	25	100.0	251	100.0
Sex						
Female	105	46.5	13	52.0	118	47.0
Male	121	53.5	12	48.0	133	53.0
Total	226	100.0	25	100.0	251	100.0
Place of birth						
Canada	69	30.5	2	8.0	71	28.3
Elsewhere	157	69.5	23	92.0	180	71.7
Total	226	100.0	25	100.0	251	100.0

*Drug-resistance was defined as resistance to one or more of the following drugs: Rifampin, Pyrazinamide, Isoniazid or Ethambutol

Treatment Status

At the time of this report, 98% of cases had started treatment (Table 18). Of all reported cases between 2013-2016, 93% had ended treatment, 6% were still on treatment and 2% had never started treatment.

Table 18. Number (%) of active TB cases by treatment status, WHR (2013-2016)

	2013		2014		2015		2016		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Started Treatment										
No	0	0.0	1	1.7	3	3.9	1	1.2	5	1.7
Yes	68	100.0	58	98.3	73	96.1	85	98.8	284	98.3
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0
Treatment Ended										
Yes	68	100.0	58	98.3	73	96.1	69	80.2	268	92.7
Still on Treatment	0	0.0	0	0.0	0	0.0	16	18.6	16	5.5
No treatment start date	0	0.0	1	1.7	3	3.9	1	1.2	5	1.7
Total	68	100.0	59	100.0	76	100.0	86	100.0	289	100.0

Of the 22 cases with TB who died (all causes of death included), 18 cases had started treatment and all 18 cases had died within one year of treatment start date (Table 19). The average number of days from treatment start date to death date was 58 days (min 6 days, max 270 days). Of the five cases that had never started treatment, four were reported as deceased.

Table 19. Number (%) of active TB cases that died by treatment status, WHR (2013-2016)

	2013		2014		2015		2016		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Started Treatment										
No	0	0.0	1	50.0	2	40.0	1	11.1	4	18.2
Yes	6	100.0	1	50.0	3	60.0	8	88.9	18	81.8
Total	6	100.0	2	100.0	5	100.0	9	100.0	22	100.0
Died within one year of treatment start date										
Yes	6	100.0	1	100.0	3	100.0	8	100.0	18	100.0
Total	6	100.0	1	100.0	3	100.0	8	100.0	18	100.0

Reason treatment ended was reported for all 268 cases whose treatment had ended; of these, 236 (88%) had completed 100% of their treatment, 18 (7%) had died, six (2%) had treatment stopped by their clinician, and five (2%) had transferred out of region (Table 20). Two cases were lost to follow-up and one case ended treatment but had not completed 100% of treatment.

Table 20. Reason treatment ended for active TB cases, WHR (2013-2016)

	No.	
Reason Treatment Ended		
Completed 100%	236	88.1
Completed <100%	1	0.4
Deceased	18	6.7
Incomplete lost to F/U	2	0.7
Clinician stops treatment	6	2.2
Transferred out of region	5	1.9
Total	268	100.0

Note: Cases may have died after completing treatment, during treatment or treatment was stopped because they were palliative.

Ninety-five percent of cases completed treatment within one year; however, treatment duration can vary depending on a number of factors including (but not limited to) drug-resistance and type of TB infection (e.g., bone or CNS) (Table 21).

Table 21. Number (%) of active TB cases by treatment duration, WHR (2013-2016)

	2013		2014		2015		2016		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Completed treatment within 1 year (366 days)										
No	3	5.3	1	1.8	7	10.6	1	1.7	12	5.1
Yes	54	94.7	54	98.2	59	89.4	57	98.3	224	94.9
Total	57	100.0	55	100.0	66	100.0	58	100.0	236	100.0

Note: Treatment duration varies depending on a host of factors including but not limited to drug-resistance and type of TB infection (e.g., bone or CNS).

Contact Investigations

Though there are some exceptions, only respiratory TB is infectious and therefore contact investigations are limited to these cases. A total of 1,912 contacts were named between 2013 and 2016 (Table 22). Overall, nearly half (44%) of all contacts named between 2013 and 2016 were household contacts followed by close non-household (34%) and shelter/rooming house/hotel (7%).

The number of times a unique contact was named ranged between one and 18 times (Table 22). In 2016, a total of 588 contacts were named by active respiratory TB cases with 568 of these being unique. Of the 568 unique contacts, 548 were named once and 20 were named twice. The average number of contacts named by cases in 2016 was 11.3.

Table 22. Number (%) of total and unique contacts named by active respiratory TB cases, WHR (2013-2016)

	2013		2014		2015		2016		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Number of total contacts named	649	100.0	268	100.0	407	100.0	588	100.0	1,912	100.0
Close non-household	220	33.9	75	28.0	134	32.9	225	38.3	654	34.2
Household	271	41.8	182	67.9	204	50.1	176	29.9	833	43.6
Shelter/rooming house/hotel	83	12.8	7	2.6	24	5.9	10	1.7	124	6.5
Other*	75	11.6	4	1.5	45	11.1	177	30.1	301	15.7
Number of unique contacts named	507	100.0	255	100.0	383	100.0	568	100.0	1,713	100.0
Named once	420	82.8	248	97.3	359	93.7	548	96.5	1,575	91.9
Named twice	64	12.6	6	2.4	24	6.3	20	3.5	114	6.7
Named three or more times**	23	4.6	1	0.4	0	0.0	0	0.0	24	1.4

Average number of contacts named per person with active TB in 2015: 9.3

Average number of contacts named per person with active TB in 2016: 11.3

*Other includes: Casual, Correctional Facility, Daycare, Hospital, School/Univ/Coll, Workplace and Other Unspecified

**Number of times a unique contact was named ranged between 3-18

Note: Unique cases and number of contacts (total and unique) are based on respiratory cases with and their contacts only.
If a respiratory case had no contacts named they were not included.
Total does not always add up to all unique contacts

INTERPRETATION

There are a few limitations that are noteworthy. It was not possible to calculate incidence rates of TB for all populations or region/country of birth because reliable up-to-date information on denominator counts (i.e., total number of Indigenous peoples or immigrants residing in the WHR by country of birth) was not available. Limitations for risk factor information include reliance on self-reporting and the potential for subjectivity on the part of the public health nurses collecting the information. Finally, the case numbers in certain subgroup analyses were small; comparisons based on small numbers should be interpreted with caution as they tend to be unreliable. Despite these limitations, this report includes important observations that are discussed below.

Between 2009 and 2016, the WHR rates of reported active TB were very similar to overall provincial rates; the WHR's rates were lower but followed the same overall trend. As the rate of TB has fluctuated year-to-year over the last 8 years, it is not yet evident that a long-term decline in disease incidence is forthcoming. Hence progress towards TB elimination in the Winnipeg Health Region remains elusive. After decades of steady decline, annual rates of active TB in Manitoba and the WHR have remained around 11 per 100,000 and 10 per 100,000, respectively. Over the last decade, Manitoba has consistently reported higher rates of active TB than the national rate, which has averaged just under five per 100,000 (Gallant et al., 2017a). In 2015, Manitoba's TB rate was second only to Nunavut.

Overall, the demographic breakdown of TB cases in the WHR was consistent with that observed elsewhere in Canada. Males were more likely to be affected than females overall. In the WHR, TB age-specific rates were highest in the 15-24 and 25-44 age groups while in Canada the TB

rates were highest in the 25-44 and 65+ age groups. TB rates were lowest among children aged 0-14 years.

TB disease burden is not distributed equally within the region. Between 2009 and 2015, the suburban areas of the WHR had stable rates that were lower than the national rate. By comparison, the inner core and northern areas of the WHR had disease rates that were 4-9 times and 2-4 times the national rate, respectively. The residents of these areas are more likely to belong to population groups at higher risk of socio-economic disadvantage: Indigenous peoples, and immigrants and refugees. Like elsewhere in Canada, these populations are disproportionately affected by TB (Public Health Agency of Canada [PHAC], 2015). In 2012, the rate of TB in Canadian-born non-Indigenous people was 0.7 per 100,000 population compared to 29.2 per 100,000 population in Canadian-born Indigenous people and 13.4 per 100,000 in the foreign-born population (PHAC, 2015).

Foreign-born individuals, who constituted approximately 22% of the 2011 WHR population (Statistics Canada, 2013a), made up about 72% of the reported active TB cases. Nationwide, foreign-born individuals compromised about 24% of the Canadian population in 2012 and made up 65% of the total number of active TB cases reported (PHAC, 2015). Prior to the 1970s, Canadian immigrants were primarily born in Europe (Statistics Canada, 2013b). While a larger share of immigrants and refugees have been settling in the three biggest provinces, more recently, the share has been declining. The geographic distribution of new immigrants has shifted in favour of the Prairie provinces (Statistics Canada, 2012). However, as the rate of international migration to Manitoba continues to increase, both the number of foreign-born TB cases and the proportion they represent of all cases are expected to increase, especially as migrants to Manitoba (and the WHR) now tend to originate from high-incidence regions such as the Western Pacific and South-east Asia (Manitoba Labour and Immigration, 2015).

Non-recent foreign-born individuals made up 81% of the WHR foreign-born cases highlighting the need for care providers to think TB when assessing symptomatic foreign-born persons that are not recent newcomers to Canada (particularly those who were exposed in countries with high TB incidence). The majority of TB in foreign-born individuals in Canada occurs after pre-immigration screening due to latent TB infection reactivation (Greenaway, Khan, & Schwartzman, 2014). Some studies have shown that roughly 20% and as high as 56% of foreign-born cases may have acquired TB during recent travel to their home countries with high incidence of TB (Ormerod, Green, & Gray, 2001; Kik et al., 2011). TB rates in foreign-born individuals are highest in the first five years post-immigration; however, their lifetime risk of TB remains higher than non-Indigenous Canadian-born individuals underscoring the need for additional screening in certain immigrant populations (Greenaway et al., 2014).

Indigenous peoples, who constituted about 11% of the 2011 WHR population (Statistics Canada, 2013a) made up 22% of the total number of cases reported between 2013-2016, and roughly three-quarters of Canadian-born cases reported in the same time period. The TB picture in the WHR differs from the Manitoba picture as most TB in Manitoba outside of the WHR occurs in northern Indigenous communities (Manitoba Health, Healthy Living and Seniors, 2015). Nationwide, Indigenous peoples comprised about 4% of the Canadian population in 2012 and accounted for 22% of reported cases (PHAC, 2015). The social determinants of health (e.g.,

intergenerational historical trauma, racism, poverty, homelessness, poor housing conditions and overcrowding; social and geographic isolation; and inaccessible or inadequate health care services) have been long recognized among the root causes of the TB epidemic in Indigenous peoples and other disadvantaged populations (Stop TB Partnership, 2017).

The higher rates of TB in Indigenous populations also reflect the increased prevalence of latent TB infection due to a higher likelihood of exposure to infectious TB coupled with medical risk factors for progression to active TB disease, such as diabetes and advanced chronic kidney failure. Overall, 17% of the TB cases in this report were identified as having diabetes and 5% were identified as having advanced chronic kidney failure. Diabetes and chronic renal failure among some immigrant groups and Indigenous peoples are notable medical risk factors. The prevalence of diabetes among First Nations peoples is estimated to be three to five times higher than the overall Canadian population (PHAC, 2013). Similarly, Indigenous peoples are reported to have a two and a half to four times higher age-standardized incidence of chronic renal failure than the national rate (Alvarez, Orr, Wobeser, Cook, & Long, 2014).

For those cases infected with latent TB infection, HIV is the most significant risk factor for the development of active TB (Menzies, Alvarez, & Khan, 2014). While the national guidelines recommend that HIV testing be offered to all TB cases, HIV testing may not have been offered if the case died soon after diagnosis. In this report, 4% of all cases with a known HIV status were positive. In 2012 in Canada, the percentage of HIV-positive cases was 8% (PHAC, 2015). HIV is increasing in incidence and prevalence in Indigenous populations (Alvarez et al., 2014).

The prevalence of latent TB infection is substantially higher in homeless populations relative to non-homeless populations (Greenaway et al., 2014). The incidence of active TB in homeless populations is also considerably higher than in non-homeless populations often due to repeated exposure and compromised immune systems (Greenaway et al., 2014). Seventeen percent of active TB cases in the WHR reported problematic substance use. Substance use is a behavioural risk factor for TB (Oeltmann, Kammerer, Pevzner, & Moonan, 2009); In a study of TB and substance use in the US, 19% of patients reported substance use and these patients were more contagious and remain contagious longer (Oeltmann et al., 2009). In a review of substance use and TB, treatment barriers including poor adherence and delays in seeking care; TB knowledge and attitudes; high prevalence of latent TB infection; physiological effects of substance use (e.g., effects on the immune system or increased liver toxicity from TB medications interacting with certain substances like alcohol); and associated environment and risk behaviours are all important challenges in this high-risk population (Deiss, Rodwell, & Garfein, 2009).

TB drug-resistance is a global public health concern and although not yet a major problem in Canada, it is slowly increasing. In 2015, of the 139 TB isolates reported to be resistant nationally, 10% were resistant to at least one of the four first-line drugs (PHAC, 2017). Moreover, 8% of isolates tested were resistant to isoniazid and of the isolates reported to be resistant, 74% were isoniazid mono-resistant. In Canada, the major risk factors for drug-resistant TB are foreign birth and persons who have previously been treated for active TB (Long, Avendano, & Kunimoto, 2014). Drug-resistant strains of MTB that are resistant to first-line anti-tuberculosis drugs prove difficult to treat as second line anti-tuberculosis drugs are limited and TB management is consequently more complicated. Challenges to treatment efforts are

compounded by the economic and social costs of treating a case with drug-resistant TB. Therefore, the increasing MDR TB trend in Winnipeg seen in 2015 and 2016 is worrisome.

Nearly all cases (98%) had started treatment at time of report. Of the five cases (2%) who had never started treatment, four were reported as deceased. Eighty-eight percent of cases had completed 100% of their treatment at time of this report. Eighteen cases died during treatment, six cases had treatment stopped by the clinician, and two cases were reported as lost to follow-up. Excluding those who were deceased and those who transferred out of the region whose treatment could not be followed, 236 out of 245 individuals completed TB treatment, meeting the region's desired 95% treatment completion benchmark.

In the WHR, 7% of cases were detected through a contact investigation between 2013 and 2016 while the national figure was 14% in 2012 (PHAC, 2015). Of the cases reported between 2013 and 2016, about two-thirds of cases had respiratory TB compared to 76% of all cases reported between 2005 and 2015 nationally (Gallant et al., 2017b). Individuals who have non-respiratory TB disease are generally not infectious to others; however, there is often a delay in diagnosis and initiation of treatment in these cases.

Given that contact investigations are labour intensive, contact prioritization is recommended, evaluating contacts that are more likely to have recent latent TB infection, are at higher risk of progressing to active TB if they are infected, or have already progressed to active TB. The likelihood of latent TB infection depends on a variety of factors, including but not limited to the case infectiousness as well as intensity, frequency and duration of exposure (CDC, 2005). In this report, nearly half of all contacts named were household contacts and the number of times a contact was named by cases ranged between one and 18 times. It has been reported that 20-30% of contacts have latent TB infection (CDC, 2005) and it has been reported that 1-2% of close contacts are found to have active TB disease (Rea & Rivest, 2014). As latent TB infection is not reportable to public health, a complete picture of latent TB infection in the region has not been presented here. Outcomes of public health contacts investigations have been flagged as a priority sub-section in future reports. In this report, the average number of contacts named by cases in 2016 was 11.3. In the United States, an average of 10 contacts are named per case (CDC, 2005) and TB programs in North America generally find cases name an average of six close contacts (Rea & Rivest, 2014). For these reasons, contact investigations remain a vital priority of TB programs.

CONCLUSIONS

TB remains a public health problem in the WHR and is primarily a disease of certain neighborhoods and specific populations (Indigenous peoples and immigrants and refugees from high-incidence countries).

Established strategies such as early detection and treatment of TB infections, and public health management of persons with TB and their contacts are central to TB elimination efforts. In addition, innovative strategies to address large reservoirs of latent TB infection in immigrants/refugees and Indigenous peoples will be required to reach the goal of TB elimination in the Winnipeg Health Region, including using new technologies in testing and treatment; and updating screening approaches.

Furthermore, disease surveillance activities should be enhanced with epidemiological investigations aimed at understanding the local characteristics and determinants of TB transmission and progression to active disease in each high-risk population or neighborhood. The accessibility, acceptability and effectiveness of disease elimination activities should be continuously monitored.

The significant disparities in the burden of TB documented in this report add to the growing evidence of socially-determined health inequities. In addition to individual level TB infection and disease-focused interventions, complementary culturally relevant community-based interventions will be needed to address inequities in the underlying socio-economic determinants of health.

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APPENDICES

APPENDIX A: ACTIVE TUBERCULOSIS CASE DEFINITIONS AND DEFINITIONS OF KEY VARIABLES

CASE DEFINITIONS

I. **Laboratory-Confirmed Case:** M. tuberculosis detected by direct polymerase chain reaction (PCR) in a respiratory specimen; or MTBC (excluding M. bovis BCG strain, which has been largely eradicated) with or without co-detected mycobacteria other than tuberculosis (MOTT) identified on culture from an appropriate clinical specimen (e.g., sputum, tissue biopsy, respiratory, gastric lavage).

II. **Clinical Case:** In the absence of a positive culture or positive direct PCR, a TB expert has indicated TB disease is likely present, based on one or more of the following:
   - Common signs and symptoms of respiratory TB, which include cough of at least three weeks' duration. This cough is initially dry but after several weeks to months will become productive. Fever and night sweats are common but may be absent in the very young and elderly. Hemoptysis, anorexia, weight loss, chest pain (pleuritic pain) and other symptoms are generally manifestations of more advanced disease.
   - Positive AFB smear.
   - Chest radiographic changes compatible with active TB disease (e.g., pulmonary infiltrates, volume loss due to destruction of the lung tissue and cavitations in the upper segments of the lung lobes). These are the classic triad findings, mainly seen in non-immunocompromised adults.
   - Pathologic or post-mortem evidence of active TB disease.
   - Favourable response to a therapeutic trial of anti-TB drugs.

To assign cases to a calendar year, the earliest reliable date of evidence of TB disease ("epidate") was used regardless of whether the case was clinical or laboratory-confirmed.

More specifically, the *epidate* was defined as the earliest of the following dates:
   - Specimen collection date of the first positive acid-fast bacillus (AFB+ve) smear; or, in the case of lab-confirmed cases with no AFB+ve results, the first positive culture; or
   - Clinician's report of TB disease (first date associated with clinical diagnosis)

HEIRARCHY OF CLASSIFICATION

For the purpose of calculating incidence rates, an individual with active TB disease diagnosed concurrently with both respiratory and non-respiratory sites was classified as a respiratory case of TB, with assigned epidate being the earliest date of evidence of TB disease (even when associated with non-respiratory TB).

Diagnostic classification of active TB disease
Cases were classified as respiratory or non-respiratory based on the ICD-10-coded final diagnosis (Table A1).

Table A1. ICD10 Codes by Diagnostic Classification

Respiratory	Non-respiratory			
	Miliary	CNS	Peripheral Lymph Nodes	Other
A15.*, A16.* Smear Positive if A15.0, A15.00, A15.01	A19.*	A17.*	A18.2	All other A18 codes†

* A15.* refers to all ICD-10 codes that start with A15 and so on;
† other sites (includes tuberculosis of intestines, peritoneum and mesenteric glands, bones and joints, genitourinary system, skin, eye, ear, thyroid, adrenal and spleen).

VARIABLE DEFINITIONS

Geographic area definition
Cases were assigned to Community Areas (CAs) using their postal code of residence at the time of diagnosis and the 2014 Manitoba postal code conversion file; and, subsequently grouped by CA pairings. Community area pairings were defined as: inner core (Point Douglas and Downtown CAs); north WHR (Inkster and Seven Oaks CAs); and suburban WHR (inclusive of the rest of the WHR CAs).

Risk Factor definitions
Regional public health nurses entered risk factors into iPHIS as the information became available through ongoing case interview/management (e.g., nurses' clinical judgment in assessing clients' social risk factors, social risk information volunteered by the client, or laboratory results).

The codes for HIV Status are the same as those found in iPHIS. HIV Status in iPHIS is defined as status at time of diagnosis. A *positive* HIV status is defined as a positive antibody test or other confirmatory HIV laboratory test (e.g., viral load) at time of TB diagnosis. A *negative* HIV status is defined as negative TB antibody test result on or after the date of the client's TB diagnosis. An *unknown* status is defined as a TB case that was deceased at time of TB diagnosis. A status of *test not offered* is used when there is no indication a test was offered, including cases that die after a few weeks of therapy if they were not offered a test. The status *test refused* is used when the client has refused HIV testing at time of TB diagnosis. The status *POC-non-reactive* refers to point-of-care testing.

The following social risk factor definitions were adopted by the nurses:

Problematic substance use: use that begins to have negative consequences for individuals, friends, family or society.
http://drugpolicy.ca/wp-content/uploads/2013/01/CDPC2013_en.pdf

Homeless: Lacks a fixed, regular and adequate night-time residence and has a night-time residence that is:

- A supervised publicly or privately operated shelter designed to provide temporary living accommodations;
- An institution that provides a temporary residence for individuals intended to be institutionalized;
- A public or private place not designed for, or ordinarily used as, a regular sleeping accommodation for human beings. (This does not include prisoners. It is interpreted to include only those persons who are literally homeless, i.e. on the streets or in shelters and persons who face imminent eviction, within a week, from a private dwelling or institution and who have no subsequent residence or resources to obtain housing)
  http://www.nationalhomeless.org/publications/facts/Whois.pdf

Indigenous and Foreign-born definitions

Indigenous status and country of birth were determined as per individual self-report. For the purpose of this report, Indigenous is a collective term used to describe First Nations (Status and non-Status), Métis, and Inuit peoples. The classification of Indigenous was derived from the Status and/or Band Code fields in iPHIS. Cases that were born outside of Canada ("foreign-born") were grouped according to place of birth into one of the six standard WHO regions (WHO, 2017c). The classification of foreign-born was derived from the Birth Country field in iPHIS, which is populated when a public health nurse is made aware of immigration details (e.g., arrival date).

APPENDIX B: NUMBER OF PEDIATRIC CASES USING WHR DEFINITION

Table B1. Pediatric (<=16 years) and adult (17+) age-specific rates of TB by year, WHR (2013-2016)

	2013			**2014**			**2015**			**2016**		
	No.	Age-Specific Rate	95%CI	No.	Age-Specific Rate	95%CI	No.	Age-Specific Rate	95%CI	No.	Age-Specific Rate	95%CI
WRHA Pediatric Definition (16 and under)												
Not a pediatric case	65	11.0	8.5 - 14.0	56	9.3	7.0 - 12.1	75	12.5	9.8 - 15.6	81	13.5	10.7 - 16.8
Pediatric case	3	2.1	0.4 - 6.2	3	2.1	0.4 - 6.2	1	0.7	0.0 - 3.9	5	3.5	1.1 - 8.2
Total	68	9.3	7.2 - 11.8	59	7.9	6.0 - 10.2	76	10.2	8.1 - 12.8	86	11.6	9.3 - 14.3

[a]Crude rates are calculated using the corresponding year's mid-point WHR population as the denominator. Population data were derived from the Manitoba Health Insurance Registry and provided (in electronic format) by Manitoba Health in 2015. 2015 population counts were based on projected data.
[b]95%CI calculated with the Tiwari et al. (2006) formula