

ADDRESSING THE CHALLENGE OF LATENT TUBERCULOSIS INFECTION AMONG INDIGENOUS PEOPLES IN CANADA


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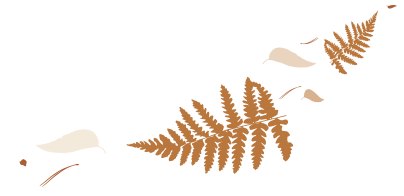


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A coastal landscape featuring a dense field of purple flowers in the foreground, with the ocean and a clear blue sky in the background. The flowers are small and numerous, with yellow centers. The ocean is visible in the distance, with waves breaking. The sky is a clear, bright blue. The overall scene is bright and sunny.

Indigenous peoples' long history of colonization and post-colonial marginalization has resulted in inequities in the socio-economic conditions that are central to the spread of TB.

1.0 INTRODUCTION



Latent tuberculosis infection (LTBI) is an asymptomatic condition that can sometimes progress to active tuberculosis (TB), a disease with serious health consequences. In Canada, the burden of TB is disproportionately high among Indigenous people¹ compared to the general Canadian population, in part due to a greater prevalence of LTBI and the factors that increase the risk of progressing to active TB among this population (Public Health Agency of Canada [PHAC], 2014a). Indigenous peoples' long history of colonization and post-colonial marginalization has resulted in inequities in the socio-economic conditions that are central to the spread of TB. Identifying Indigenous individuals with LTBI, initiating preventative treatment in those who are considered at high risk of progressing to active disease, and fostering adherence² to that treatment are therefore critical for decreasing the unacceptably high rates of TB among affected Indigenous communities.

This report is intended to support researchers, policymakers, program

managers and health practitioners working to address the ongoing high prevalence of TB in many Indigenous communities by increasing their understanding and awareness of some of the challenges faced in addressing LTBI in this population, and highlighting some approaches that may hold promise in addressing these challenges. The report will begin with a brief overview of the context of LTBI among Indigenous populations. This includes a summary of what LTBI is, the factors that place Indigenous people at increased risk of LTBI and progressing to active TB, the prevalence of LTBI among Indigenous people, and how LTBI is currently diagnosed and treated. It will then describe what is known about Indigenous peoples' adherence to treatment for LTBI, and the challenges that exist in addressing high rates of LTBI among specific segments of this population. The final section of this report highlights some of the initiatives and strategies that have shown promise in addressing the challenge of LTBI among Indigenous peoples.

The literature that informs this paper was derived from a broad search of peer and non-peer reviewed literature focusing on TB and Indigenous peoples in Canada generally. These were identified using three academic databases (PubMed Central, Medline, and Google Scholar), using the search terms Aboriginal/Inuit/Métis/First Nation/Native Indian/North American Indian in combination with 'tuberculosis.' Most of the studies identified through this search involved analysing national, regional or local level TB data, reviewing literature or research evidence (three of which involved systematic reviews) or conducting qualitative surveys. While this review was not conducted using systematic search methods, it is fairly comprehensive, with research spanning from 1949 to November 2017. Though the primary focus of this paper is on research focused on Indigenous people in Canada, it may also draw on selected literature related to promising practices to improve TB adherence in other contexts.

¹ The terms 'Indigenous' and 'Aboriginal' are used interchangeably throughout this paper to refer inclusively to the original inhabitants of Canada and their descendants, including First Nations, Inuit and Métis peoples as defined in Section 35 of the Canadian Constitution of 1982. When not referring to all Indigenous peoples collectively, the specific terms 'First Nations', 'Inuit', and 'Métis' will be used.

² The terms 'compliance' and 'adherence' have been used interchangeably to refer to the ability of patients to follow through with health care providers' treatment regimens for LTBI. However, the term 'compliance' can be considered paternalistic, especially in relation to past colonial TB management practices with Indigenous populations, and it suggests a passive role for patients in their health care. The term 'adherence' is more strengths-based as it suggests a more active role for patients in their care and expresses their commitment to taking the actions necessary to improve their health (Wolfe, 2016). As a result, throughout this paper, any usage of the term 'compliance' in the literature will be replaced with the term 'adherence.'



2.0 LATENT TUBERCULOSIS INFECTION



Tuberculosis is an infectious disease caused by an organism called *Mycobacterium tuberculosis* (M.tb) which is spread via aerosol droplets when an infected person coughs, sneezes, or talks (Long & Schwartzman, 2014). It is a preventable and curable disease that primarily affects the lungs, but can affect other parts of the body as well, and result in serious health consequences, including death. TB infection can progress through several stages as described by Tuite and colleagues (2017): the susceptible stage, the infected but asymptomatic stage (LTBI), and the active disease and re-susceptible stages. An active cell-mediated immune system³ is necessary to curtail the spread of M.tb (Cooper, 2009; Long & Schwartzman, 2014).

People with no prior exposure to M.tb may be susceptible to the development of TB because of their naïve immune systems. Once infected, they may not be able to mount a sufficient immune response

against the organism to completely clear it away, causing the bacterium to become stored away, usually in the core of their lungs, from where it can be reactivated (reactivated or secondary TB⁴) or stay dormant for life. This is referred to as the latent TB infection (LTBI) stage, and is characterized by a lack of symptoms. Many cases of secondary TB are not due to reactivation, but rather re-infection. This usually occurs in countries or communities with very high rates of TB where close contact with active TB cases increases the risk of re-infection (Long & Schwartzman, 2014). The active stage of the disease is characterized by coughing, blood tinged sputum,⁵ weight loss and night sweats when the primary site of infection is the lungs. During this stage, individuals are highly infectious. However, only 5-15% of people infected with LTBI will develop the active disease after coming into contact with the organism, while in the remainder of those infected, the condition will remain in a state of latency

(Government of Canada, 2016a; Richardson, Sander, Guo, Greer, & Heffernan 2014; Tuite et al., 2017; Ward, Stewart, Al-Azem, Reeder, & Hoepfner, 2017).

2.1 The determinants of TB infection and disease among Indigenous peoples in Canada

A number of factors contribute to the increased risk of TB infection and disease among Indigenous peoples. These can be grouped into three categories: those associated with the agent, such as virulence of the TB strain; those associated with the host which increase susceptibility to TB, such as genetics or presence of co-morbidities; and those associated with the environment, such as food insecurity and nutritional deficiencies, overcrowded or poor quality living conditions, community isolation, inadequate diagnostic resources and health staff, poverty, and cultural

³ The human body fights diseases in two ways: through the humoral immune system, which produces B cells that mature into plasma cells that secrete antibodies which bind to viruses and attack them; and the cell-mediated immune system, which produces two types of T cells – T helper cells which maximize the capabilities of the immune system by activating other immune cells to destroy infected cells or pathogens, and T killer cells which recognizes and destroy cells infected by viruses (Nauta, 2011).

⁴ Reactivated TB or secondary TB is the development of TB in a host after it has previously been contained.

⁵ Sputum is mucous material from the lungs, brought up by coughing.



Indigenous people, especially on-reserve First Nations and Inuit people, are at greater risk of LTBI and progression to active TB due to a higher prevalence of risk factors.

and historical factors (Canadian Tuberculosis Committee [CTC], 2007; Clark, Riben, & Nowgesic, 2002; Greenwood et al., 2000; Kunitomo et al., 2004; Larcombe et al., 2010; Maud, 2013a; Moore, 1964; Petrelli et al., 2004). These latter factors are often considered to be the social determinants of health. The co-occurrence of these factors can increase the risk of exposure to *M.tb* or leave individuals less resilient in the face of exposure.

Indigenous people, especially on-reserve First Nations and Inuit people, are at greater risk of LTBI and progression to active TB due to a higher prevalence of risk factors. They are more likely to live in poverty and be food insecure compared to the general population, increasing their vulnerability to LTBI; and are more likely to live in overcrowded or poor quality housing, thus increasing transmission of TB if there is already an active case in the household (Al-Mouaiad Al-Azem, 2006; CTC, 2007; Clark, Riben, & Nowgesic, 2002; Larcombe et al., 2010; Kunitomo et al., 2004; Moore, 1964). They are often highly mobile, which affects the continuity of health service delivery (Snyder & Wilson, 2012), or dispersed across large and remote geographic areas, where access to health care and diagnostic

services may be extremely limited (National Collaborating Centre for Aboriginal Health, 2011). They may distrust mainstream healthcare providers due to perceptions of racism, discrimination, and previous negative experiences with the health care system, including Indigenous peoples' experiences with historic colonial TB practices which saw the forced removal of infected individuals from their communities without explanation and, in many cases, without ever returning home (Al-Mouaiad Al-Azem, 2006; Aspler et al., 2010; Moffatt, Mayan, & Long, 2013; Richardson et al., 2014). These perceptions can result in delayed diagnosis and care, and a greater tendency for TB to be more advanced at presentation. Indigenous people have a highly integrated and communal social structure, which can result in increased transmission of TB (Eisenbeis, 2015; Eisenbeis et al., 2016; Orr, 2013). The Indigenous population profile is younger than the general Canadian population profile, increasing the potential for TB transmission to children and those in child-bearing years (Eisenbeis, 2015). Some research has identified possible genetic and immunological factors that may be increasing the susceptibility of Indigenous people to TB infection (Greenwood et al., 2000; Larcombe et al., 2005, 2008,

2012a/b; 2015; 2017). Additionally, Indigenous populations who were exposed to TB epidemics early after colonization appear to have developed more innate resistance and have lower rates of TB than those who had later exposure (Pepperell et al., 2010, 2011 a/b).

The risk of progressing from LTBI to active TB disease increases when an individual's immunity is lowered through the presence of health conditions such as diabetes, HIV, malnutrition, cancer or treatment with anticancer therapy. It can also increase when individuals have prolonged close contact with someone who has active TB, have a personal history of TB, are homeless, smoke and abuse substances, or are residents of long-term care facilities or health care workers (Ai, et al., 2016; Long & Boffa, 2010). Indigenous people have a higher prevalence of many of the factors that increase the risk of developing active TB. Table 1 lists these risk factors and the corresponding estimated risk; that is, the prevalence of active TB among individuals with a specific risk factor in relation to individuals with no known risk factor. Wherever possible, the prevalence of these risks factors among Indigenous populations is given.

TABLE 1: ESTIMATED RISK OF DEVELOPING ACTIVE TB FOR SELECTED RISK FACTORS

Risk factor	Estimated risk for TB	Prevalence (or incidence) of risk factor among Indigenous peoples
High risk		
Acquired-immunodeficiency syndrome (AIDS)	110-170	Prevalence of AIDS among Indigenous peoples has ranged from a low of 2.4% of all AIDS cases in 1979 to a high of 21.7% of all AIDS cases in 2006, after which rates have experienced slight annual decreases to 13.9% of all AIDS cases in 2008 (Public Health Agency of Canada [PHAC], 2010).
Human immunodeficiency virus infection (HIV)	50-110	Indigenous people have rates of HIV that are approx. 3 times the national average (Government of Canada, 2016b).
Transplantation (related to immune-suppressant therapy)	20-74	Indigenous people are 1.5 times less likely to receive renal (kidney) transplants compared to non-Indigenous people (Canadian Institute for Health Information [CIHI], 2013). ⁶
Chronic renal failure requiring hemodialysis	7-50	Indigenous people are approx. 3 times more likely to experience chronic renal failure requiring hemodialysis than non-Indigenous people (CIHI, 2013). ⁶
Carcinoma of head and neck	11.6	Indigenous people have a non-significant risk of 1.3% more than non-Indigenous peoples (Erickson, Biron, Zhang, Seikaly, & Côté, 2015).
Recent TB infection (<2 years)	15	Indigenous people have rates of TB that are 3.7 times the national average and among the Inuit, the TB rate is 36 times the national average (Gallant et al., 2017), resulting in high rates of active TB in some Indigenous communities. Therefore, more people are likely to have been recently infected and at high risk of progressing to active TB (see for example, Lee et al., 2015).
Moderate risk		
Diabetes Mellitus	2-3.6	First Nations people have rates of diabetes that are 3-5 times the national average (Canadian Diabetes Association, 2017).
Young age when infected (0-4 yrs)	2.2-5	The incidence rate of pediatric TB age 0-4 in Nunavut is 120.8/100000 ² compared to the national average of 2.7 cases/100,000 ⁷ (Gallant, Duvvuri, & McGuire, 2017)
Slightly increased risk		
Heavy alcohol consumption (≥3drinks/day)	3-4	Indigenous people are 1.3 times more likely to have consumed alcohol heavily in the past year compared to non-Indigenous people (Kelly-Scott & Smith, 2015).
Cigarette smoker (1 pack/day)	1.8-3.5	The daily smoking rate among Inuit is three times the national average; 18.7% of Inuit who smoke daily smoke heavily ⁸ (Bougie & Kohen, 2017). Daily smoking among First Nations in the 2008/10 Regional Health Survey is more than twice that of the general Canadian population (First Nations Information Governance Centre, 2012).
Low risk		
Person with positive tuberculin skin test (TST), no known risk factor, normal chest x-ray	1	

Adapted from Canadian Tuberculosis Standards-7th Edition (Menzies, Alvarez, & Khan, 2014, p. 127).

⁶ There is a lack of comparative data on other types of transplants.

⁷ Recall that 80% of the Nunavut population is Indigenous.

⁸ Heavy smoking is smoking more than 25 cigarettes per day.

2.2 Prevalence of LTBI among Indigenous peoples in Canada

In Indigenous populations, TB tends to be localized to selected high incidence First Nations and Inuit communities and urban centres where it is “believed that the reservoir of LTBI is constantly being replenished by ongoing transmission” (Patel, et al., 2017, p. 2). These communities have experienced decades of TB outbreaks and the prevalence of LTBI within these communities is high, increasing the likelihood of TB reactivation and ongoing transmission (Clark & Riben, 1999). Common symptoms of TB like a cough or fever can be misinterpreted

as symptoms of a cold or influenza, resulting in delayed treatment and care. By the time TB is clinically suspected, transmission of the infection may have already occurred in many close contacts of infectious individuals (Ward, Marciniuk, Pahwa, & Hoepfner, 2004). This section examines what is known about the prevalence of LTBI among Indigenous people in Canada.

Surveillance of TB is generally very comprehensive and of high quality in Canada, with public health data existing at the national and provincial levels, and for First Nations (in many cases both off and on reserve), Inuit and Métis specifically (PHAC, 2014). However, while there is a legal requirement to report active TB cases, to provincial/

territorial TB programs, these same reporting requirements do not apply to LTBI (PHAC, 2014b). As a result, data on the prevalence of LTBI among Indigenous populations to guide health interventions is lacking.

In the few studies that have distinguished between prevalence of LTBI and active TB among Indigenous populations, disproportionately high rates of LTBI prevalence have been identified. These have ranged from 12-61% among Indigenous adults (Brassard, Anderson, Schwartzman, Menzies, & Macdonald, 2008b; Clark & Riben, 1999; Correctional Service Canada, 2015; Whyte & Bourgeois, 2012; Yuan, 2007), to 1.3-29% among Indigenous children and youth (Grzybowski, Galbraith, & Dorken, 1976; Nunavut Department of Health and Social Services, 2005 and Saskatchewan TB Control Program as cited in in Yuan, 2007; Smeja & Brassard, 2000; Whyte & Bourgeois, 2012). However, these studies are generally dated, small in scale, or report on only a specific segment of the Indigenous population (e.g. such as prison inmates).

Because active TB disease and LTBI represent opposite ends of the spectrum of the same disease, TB rates in a community can be used as a proxy for determining the prevalence of LTBI. In 2015, there were 1639 cases of active TB in Canada with an incidence rate of 4.6 cases per 100,000 population (Gallant et al., 2017). Seventy-one percent of these were in foreign born-individuals from high TB endemic countries, 17% were in Canadian born-Indigenous people, and 11% were in Canadian born-



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non-Indigenous people (Gallant et al., 2017). In interpreting this data, it is important to note that Indigenous peoples represent approximately 4.9% of the Canadian population (Statistics Canada, 2017).

The over-representation of Indigenous peoples in cases of TB is highlighted most clearly using incidence rate data. While Canadian born non-Indigenous people had an incidence rate of 0.6 per 100,000 in 2015, the incidence rate of TB was 15.1 per 100,000 for First Nations, 166.2 per 100,000 for Inuit, and 2.2 per 100,000 for Métis people (Gallant et al., 2017). However, recently there has been a trend in Canada towards micro-epidemics, where the bulk of reported TB cases come from only a few First Nations and Inuit communities experiencing outbreaks (Clark & Riben, 1999; Dawar, Clark, Deeks, Walop, & Ahmadipour, 2003). This suggests there may be a high prevalence of LTBI within these specific communities. Given the geographic isolation of many Inuit and First Nations communities and the high degree of social interaction and mobility among community members, a high prevalence of LTBI within these communities has considerable potential to contribute to the ongoing transmission of TB through reactivation, not only within the Indigenous communities but also within Canada. There is clearly a need for better surveillance which differentiates between latent and active TB, or between primary and reactivated TB, as well as renewed research on the rates of latent TB among Indigenous populations so that high risk communities can be identified for a targeted TB elimination approach.



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2.3 Diagnosing and treating LTBI

The management of LTBI is part of a multi-pronged TB strategy that includes the treatment of TB, case finding, contact tracing, surveillance, screening and education (British Columbia Center for Disease Control [BCCDC], 2011). The 7th edition of the Canadian Tuberculosis Standards notes that the goal of testing for LTBI should be to identify individuals at increased risk for the development of active TB who would benefit from treatment, with the intention that they will receive this treatment (Pai, Kunimoto, Jamieson, & Menzies, 2014). Since only a small proportion of screen-test-positive patients will develop active TB in the future, preventative therapy should only be targeted at individuals who are at high risk of developing active TB disease because of the waste of resources and the increased likelihood of anti-TB drug resistance developing (Ai et al., 2016). The population targeted for LTBI screening include

individuals who have been in contact with persons recently diagnosed with active TB, individuals with impaired immunity at risk of progressing from LTBI to active TB disease, foreign-born persons and visitors from TB endemic areas, and previously untreated people with chest x-ray findings of old healed TB (Greenaway, Khan, & Schwartzman, 2014). Because Indigenous people in some communities have a high prevalence of TB and are considered at increased risk of progressing to active TB, targeted screening for LTBI may be warranted in these communities.

Currently, two screening methods are widely used to identify individuals who may have LTBI: the Tuberculin Skin Test (TST, sometimes called the Mantoux test) and the Interferon Gamma Release Assay (IGRA) test. Both tests detect individual cell-mediated response against TB; however, neither is able to distinguish between LTBI and active TB. The TST involves two visits to a physician or health clinic

– the first to inject a TB protein into the skin and the second to measure the size of the area that has become hardened after 48-72 hours. The IGRA involves a blood test measuring the cell-mediated immune response to substances that stimulate the production of antibodies in response to M.tb. This test does not require the patient to return to the lab and can be completed in 24 hours, but requires greater laboratory infrastructure and technical capacity, and is therefore more expensive (Kiazyk & Ball, 2017). While no gold standard exists for diagnosing LTBI, evidence from systematic reviews and meta-analyses indicates that specific IGRA tests have more diagnostic utility for LTBI in patients on hemodialysis (Ferguson et al., 2015), with end-stage renal disease (Rogerson et al., 2013), and who have received the Bacillus Calmette-Guérin vaccine against TB as young children or have had multiple TB boosters (Doan, et al., 2017; Kiazyk & Ball, 2017; Kwong, Krahn, Cleland, Gordon, & Wobeser, 2016; Mancuso et al., 2017; Trajman, Steffen, & Menzies, 2013). TSTs are preferred for children less than 5 years due to the low sensitivity of IGRAs, and for groups of people who have low rates of returning to have their TSTs read, like homeless individuals (Doan et al., 2017; Moon & Hur, 2013). Both IGRAs and TSTs perform similarly poorly in predicting risk for progressing to active TB (Ai et al., 2016; Auguste et al., 2017; Trajman et al., 2013). Once patients have

tested positive using TST or IGRA, chest x-rays and sputum smears and culture⁹ can be used to exclude active TB disease (Amaratunga, & Alvarez, 2016).

Research has shown that individuals are lost throughout all stages of the cascade of care in the diagnosis and treatment of LTBI, across a range of settings and population groups. The greatest losses have occurred at the stages of initial screening, completing medical evaluation, and starting and completing therapy (Alsdurf, Hill, Matteelli, Getahun, & Menzies, 2016). Some factors that may be contributing to these losses include misconceptions regarding susceptibility to TB, poor TB awareness among health care workers, lack of specialist services, and language/culture barriers (Heuvelings, de Vries, & Grobusch, 2017). The factors associated with the fewest losses have included having immune-compromising medical indications, being part of contact investigations, and using rifamycin-based treatment regimens (Alsdurf et al. 2016). Addressing the high rates of TB among Indigenous people requires focusing on the ways in which losses can be reduced at each stage of the cascade of care, including targeted screening of LTBI, rapid tracing of close contacts of individuals who test positive for TB, as well as timely diagnosis and treatment of active TB disease (Amaratunga, & Alvarez, 2016; Tuite et al., 2017).

Within the context of LTBI, losses in the cascade of care may occur because of the difficulty of convincing someone who has no symptoms to not only seek out testing and a diagnosis, but to accept a lengthy drug treatment which can have potentially harmful side effects, including hepatitis, allergic reactions, peripheral nerve damage, and potentially life-threatening hepatotoxicity (damage to the liver) (Denholm et al., 2014; Kiazyk, & Ball, 2017). In Canada, the recommended drug treatment for LTBI is daily use of Isoniazid, also known as Isonicotinylhydrazide (INH), for six to nine months (Menzies et al., 2014). Concurrent treatment with Pyridoxine or vitamin B6 is also important for individuals who are malnourished, have an alcohol use disorder, are pregnant, or have diabetes, uremia (accumulation of urea because of kidney failure) or other conditions that increase the chances of peripheral nerve damage (BCCDC, 2015; Menzies et al., 2014). Research has shown that rates of treatment acceptance for LTBI are often low, as are treatment completion rates (Pease, Amaratunga, & Alvarez, 2017). Shorter regimens of LTBI have been advocated to address this challenge as treatment completion rates have been higher for such regimens compared to INH monotherapy. These may include using the drug Rifampin alone daily for 4 months or in combination with INH for 3 to 4 months (Menzies et al., 2014; Pease et al.,

⁹ Sputum smears involve examining the mucous that comes from the lung under a microscope for signs of the TB bacteria. It is a simple and inexpensive test that can produce results within hours, however the sensitivity of these tests to detect TB bacteria is relatively low (approx. 50-60%), and even lower among individuals with HIV and TB co-infection. Culture tests involve studying the bacteria by growing it on different substances to find out if the M.tb bacteria are present. It is highly accurate, however, it can take several weeks to get a result and requires skilled personnel and expensive equipment (Kanabus, 2017).



2017; World Health Organization, 2015). Two months of Rifampin and Pyrazinamide have also shown excellent efficacy in experimental studies and randomized trials; however, this regimen has been associated with an unacceptably high rate of severe liver toxicity, and thus its use has been largely abandoned (Lobue, & Menzies, 2010).

Recently, Health Canada has given limited approval to use a weekly course of INH in combination with Rifapentine over a three-month period (known as 3HP) among Inuit from a TB endemic community. While this drug has yet to be approved for widespread use in Canada, it has been found to be effective in some places. For example, a study conducted by Sterling and colleagues (2011) involving 8000 LTBI patients from the United States, Brazil, Canada and Spain found that a directly observed weekly dose of INH in combination with Rifapentine for 12-16 weeks was equally as effective as a 9-month regimen of INH monotherapy in

preventing the development of active TB. This treatment regimen has resulted in lower rates of hepatotoxicity and higher completion rates than other regimens; however, it has been associated with high rates of hypersensitivity reactions (Pease et al., 2017; Sterling et al., 2011). While not severe in most cases, further research is required to assess its safety and effectiveness. The current requirement of 3HP to be administered via directly observed therapy, however, may be a barrier to its uptake in Indigenous communities, which may require some flexibility in terms of who ensures that the patient is adhering to therapy and the context in which this therapy is observed.

Effective LTBI treatment can substantially reduce the risk of progression to active TB disease. Clinical trials among the general population have shown between 69% and 93% reductions in the risk of progressing to active TB when treated with INH over 6- and 12-month regimens respectively

(Hirsch-Moverman, Daftary, Franks, & Colson, 2008). While no treatment trials directly compare the efficacy and safety of the 9-month Isoniazid regimen with other regimens, some shorter course regimens have been compared to 6 months of INH. None of these were found to be superior in terms of effectiveness but in terms of safety, 3-4 months of Rifampicin and 3-months weekly Rifapentine in combination with INH were found to be safer than the 6-month and 9-month INH regimens (Lobue & Menzies, 2010; World Health Organization, 2015).

Several studies have assessed the effectiveness of preventive therapy for LTBI among Indigenous populations in Canada. For example, Dorken, Gryzbowski and Enarson (1984) evaluated the effectiveness of drug treatments for LTBI among 370 Inuit from Frobisher Bay, comparing them to a control group involving 217 subjects. They found that the risk of progressing to active disease was 0.1% per year in the treated group compared to 1.0% per year in the control group. None of the Inuit patients in Gryzbowski, Galbraith and Dorken's (1976) clinical trial of preventive therapy developed active TB over an estimated three-year observation period. In the Sioux Lookout Zone, the lowest risk of reactivation occurred among those who had received proper drug treatment in the mid-1950s (Young, 1982). Morán-Mendoza and colleagues (2010) found that over a 12-year period in BC, the highest rates of TB were found among First Nations patients who did not adhere to their treatment regimens for LTBI.

2.4 Adherence to LTBI treatment among Indigenous populations

In order to treat LTBI effectively, a mutually agreed upon care plan must be established between patients and healthcare providers, with patients agreeing to adhere to their treatment protocol (PHAC, 2014b). The Canadian TB Standards currently recommends a minimum of 80% adherence with a 9-month regimen of INH (Comstock, 1999; Menzies et al., 2014), while the American Thoracic Society recommends that all prescribed doses of a 9-month regimen of INH be completed within 12 months and all doses of a 4-month regimen of Rifampin must be completed in 6 months to be effective (Munsiff, Nilsen, & Fujiwara, 2008). These recommendations emphasize the total doses of completed drug treatment within the given timeframe as central to the regimen's effectiveness.

Research investigating rates of adherence to LTBI treatment among Indigenous peoples is generally sparse. Most of the studies are dated and focus on selected First Nations or Inuit communities. This body of research shows varying rates of adherence to LTBI treatment among Indigenous peoples, which are often affected by how aggressively patients are followed up. A major limitation to the interpretation of these results is the grouping together of LTBI treatment cases that result from contact tracing (contacts exposed to an active TB source) and those identified for treatment during routine TB screening programs. This is an important consideration

because in the latter case, not everyone who is positively screened for treatment may be aggressively followed up for treatment, unlike individuals exposed to an active TB source.

Table 2 summarizes existing data on rates of adherence with LTBI treatment among Indigenous populations in Canada. Clark and Riben (1999) showed that adherence to drug treatment for LTBI among First Nations on reserve was quite low in most regions, particularly among adults. The highest rates were in Saskatchewan (among children), while the lowest were in Alberta. More recently, Eisenbeis and colleagues (2016) compared adherence to treatment among close contacts of Indigenous on and off-reserve LTBI cases with those of close contacts of non-Indigenous TB cases in Alberta over the period 2001-2010. They highlighted significant differences in the outcomes of contact investigations among the three groups, with close contacts of Indigenous off-reserve cases experiencing the greatest delays in assessment and the lowest rates of completion of assessment and preventive therapy. Urban and off-reserve Indigenous people may face unique barriers in accessing health care that may affect adherence to LTBI treatment, including jurisdictional differences in program delivery, lack of prioritization of TB as a health concern, lack of provincial health insurance cards or personal identification, long wait times, competing health priorities and poverty (Brassard, Anderson, Menzies, Schwartzman, & Macdonald, 2008a; Brassard et al., 2008b; Eisenbeis, et al., 2016). In contrast, Eisenbeis and colleagues

(2016) highlight the assets available in First Nations reserves that can make contact investigations more successful with respect to completing assessment and preventive therapy. These can include: 1) the presence of health care staff imbedded in the community who can easily identify household contacts in TB cases, and who have a strong partnership between the provincial TB program and the federal agency with jurisdiction over public health on reserve and can assist with program delivery; and 2) public health units which provide assistance to facilitate the completion of the assessment process such as transportation to x-ray/lab facilities or clinics.

It should be noted that poor adherence to LTBI treatment is not unique to Indigenous peoples. Treatment completion rates for various drug regimens approved in Canada in randomized trials have ranged from 55% to greater than 95%, with higher completion rates noted for shorter courses of drug treatment and for directly-observed therapy (Menzies et al., 2014). Because these randomized trials were not specific to Indigenous peoples, there is a need to review the literature to identify the unique barriers to LTBI completion among Indigenous peoples in Canada in order to propose effective strategies.



TABLE 2: ADHERENCE TO LTBI TREATMENT AMONG INDIGENOUS POPULATIONS IN CANADA

	Population	Period	Type of treatment	Completion rates	Outcome: the risk of active TB disease	Source
PRE - 1990	370 Inuit individuals from Frobisher Bay placed on a regimen of isoniazid and ethambutol 3x's/week for 18 months	1971-72	Directly observed preventive therapy (DOPT)	More than 90% completion of a supervised 18-month regimen of INH and Ethambutol	The risk of active TB disease in the treatment group was 0.1% per year and in the control group, it was 1% per year.	Dorken, Grzybowski & Enarson (1984)
	102 patients from Cree territory of Mistassini Lake	1981-85 1986- 1991	unspecified	78% compliance with combination therapy and 33.7% compliance with INH therapy.	14 cases of TB: 4 cases prior to 1990 and 10 between 1990 and 1991.	Rideout & Menzies, 1994
1990 - 2000	Indigenous people in BC	1992-94	Daily DOPT compared to twice weekly Self-administered preventive therapy (SAPT)	75.2% of DOPT patients and 60.9% of SAPT patients completed a 6 month regimen; 50.9% of DOPT and 36.6% of SAP patients completed a 12 month regimen	Not measured	Heal, Elwood, & FitzGerald, 1998
	Indigenous peoples from the Prairie provinces	1992-95 1986-1989	6 mths of twice weekly INH and Rifampin by DOPT compared to 1 yr self-administered INH	82% of DOPT patients completed treatment; 19% of SAP patients completed treatment	TB rate was 0.9/1000 years in DOPT group and 9/1000 years in SAP group.	McNab, Marciniuk, Alvi, Tan, & Hoepfner, 2000
	First Nations on reserve in Pacific region	1991-99	DOPT; regimen unspecified	ranged from a high of 100% in 1991 to a low of 50% in 1996	Not reported	Clark & Riben, 1999
	First Nations on reserve in Alberta	1991-99	DOPT; regimen unspecified	ranged from a high of 100% in 1998 to a low of 61% in 1995	Not reported	Clark & Riben, 1999
	First Nations on reserve in Saskatchewan	1991-99	DOPT; regimen unspecified	ranged from a high of 98% in 1992 to a low of 84% in 1997	Not reported	Clark & Riben, 1999
	First Nations on reserve in Manitoba	1991-99	DOPT; regimen unspecified	Ranged from a high of 96% in 1998 to a low of 51% in 1994	Not reported	Clark & Riben, 1999
	First Nations on reserve in Ontario	1991-99	DOPT; regimen unspecified	ranged from a high of 100% (1997, 1998, 1999) to a low of 42% in 1994	Not reported	Clark & Riben, 1999
2000 - 2010	Urban Indigenous persons in Montreal	July 2005- July 2006	unspecified	Only four of 25/164 who tested positive for TB attended their scheduled appointments; two were offered treatment – one refused and one failed to return for a second appointment	Not reported	Brassard et al., 2008b
	Close contacts of Indigenous on and off reserve culture-positive pulmonary TB in Alberta compared to non-Indigenous contacts	2001-2010	unspecified	54% for close contacts of Indigenous cases on reserve; 41% for close contacts of Indigenous cases living off reserve; 37% for non-Indigenous contacts	Not reported	Eisenbeis et al., 2016



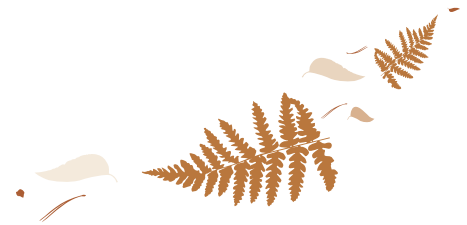


...the challenge of addressing high rates of LTBI in Indigenous communities is also related to a number of factors stemming from the complex interaction between the health system, personal and societal factors, many of which are rooted in a legacy of colonialism

(Orr, 2011a).



3.0 BARRIERS TO ADDRESSING THE CHALLENGE OF LTBI AMONG INDIGENOUS PEOPLE



Reducing the high rates of TB in some Indigenous communities is an ongoing challenge because of the high prevalence of undiagnosed and untreated LTBI among Indigenous individuals. This challenge is related not only to the asymptomatic nature of LTBI, but likely also to some unique factors that may be affecting Indigenous people's willingness to undergo testing, initiate treatment, and adhere to their treatment regimen. In part, the challenge of addressing LTBI is related to the prolonged period of LTBI treatment; the difficulty of convincing a patient who is not experiencing any symptoms that he/she should undergo testing, initiate treatment, and complete their prescribed medications; and the side effects of commonly used drugs (Clark & Riben, 1999; FitzGerald et al., 2003; Heal et al., 1998; Menzies et al., 2014). However, the challenge of addressing high rates of LTBI in Indigenous communities is also related to a number of factors stemming from the complex interaction between the health system, personal and societal factors, many of which are rooted in a legacy of colonialism (Orr, 2011a). This section summarizes the literature on potential barriers Indigenous people may face in undergoing testing, initiating treatment, and completing their treatment regimens. While there is little research focused specifically on barriers within the context of Indigenous people with LTBI, it is likely that these barriers are similar to those experienced by Indigenous people seeking out a diagnosis, initiating treatment and completing that treatment for active TB.



3.1 Personal barriers

Personal barriers that may be affecting Indigenous people's willingness to seek out a diagnosis, initiate treatment and complete that treatment regimen are related to their knowledge, attitudes and beliefs about TB, as well as their health status. Several studies assessed the level of knowledge about TB and LTBI among Indigenous people in selected locations and found a strikingly low level of knowledge about the perceived health risks of TB, the severity of TB, and susceptibility to developing active TB (Brassard et al., 2008a; Gibson, Cave, Doering, Ortiz, & Harms, 2005; Jenkins, 1997; Møller, 2005; Rideout & Menzies, 1994). This lack of knowledge can affect an individual's health-seeking behaviours and their commitment to completing their treatment. Research has shown that improving knowledge about TB can improve adherence to treatment for LTBI and TB disease (Orr, 2011a). Additionally, the attitudes and beliefs individuals have about their ability

to take the necessary actions and control over their health and adopt health-promoting behaviours can also prevent individuals from being motivated to seek out a diagnosis, initiate treatment, and complete the treatment (Rideout & Menzies, 1994; Brassard et al., 2008a).

The literature identified several factors that may be contributing to a lack of knowledge about TB and LTBI among Indigenous people. First, the social stigma attached to having TB has created a general silence about the disease, preventing people from talking about it within their communities (Brassard et al., 2008a; Marra, Marra, Cox, Palepu, & Fitzgerald, 2004; Møller, 2005, 2010). For example, in interviews regarding perceptions and knowledge about TB in two Inuit communities, participants held the view that TB afflicted those who broke moral codes of conduct (Møller, 2010). Second, health information on TB is often not culturally appropriate, nor conveyed in ways that are consistent with Indigenous knowledge and ways of learning. In Møller's (2010) study on TB knowledge among Inuit

in Nunavut, more than half of study participants had no recollection of seeing or hearing about TB in their community. Among those who had, they did not consider the information as very valuable because it pertained to symptoms they did not have or they felt the message was conveyed in ways that did not appeal to them. Participants in Møller's (2010) study highlighted the need for culturally-appropriate messaging which reflected Inuit ways of thinking and educating. This included the use of Inuit languages, oral or story-telling methods rather than written ones, and personal rather than abstract approaches (involving relationship building between healthcare providers and clients, or stories of individuals' experiences with TB), as well as incorporating content relevant to the local context.

Another personal barrier that may impede adherence to LTBI therapy is related to health status. Indigenous people experience a disproportionately high burden of illnesses such as HIV, diabetes and renal failure. Such illnesses

can increase the risk and severity of medication side effects and complications of TB disease, lead to increased pill burden or economic burden, result in competing life priorities and demands, or affect one's ability to cope (Orr, 2011a). The high prevalence of alcohol and substance use among Indigenous people can also increase the risk of non-adherence to treatment regimens. Notwithstanding, these factors are part of a complex web of barriers within society and the health care system in limiting adherence to treatment (Orr, 2011a).

3.2 Health care system barriers to LTBI treatment

There are a number of unique health system barriers for Indigenous people that may impede LTBI diagnosis, treatment initiation, and adherence to treatment. These can include:

- marginalization within mainstream society with respect to accessing health care, including ongoing racism and discrimination within the healthcare system, mistrust of non-Indigenous health providers, and lack of health care professionals and services, including diagnostic and laboratory services (Gibson, et al., 2005; Jenkins, 1977; Møller, 2005; Orr, 2011b; PHAC, 2014);
- lack of health provider knowledge about TB, especially in under-resourced rural and remote locations (Clark & Riben, 1999; Marra et al., 2004);
- lack of a provincial health insurance card or personal identification (for example,

among homeless populations) (Brassard et al., 2008a/b; Hwang, 2011);

- lack of a regular family physician and long wait times to access services in urban areas (Brassard et al., 2008a); and
- language and cultural barriers (Gibson et al., 2005).

These factors can result in a delayed diagnosis, lack of follow up with patients, and/or inadequate treatment supervision.

Several studies highlighted the impact of health system barriers on Indigenous peoples' perceptions of, and experiences with, TB. For example, Maud (2013b), in the context of the Métis, shows how past perceptions and stereotypes of Indigenous peoples continue to plague the healthcare system and manifest in differential treatment. This is reflected, for example, in experiences of racism and discrimination in health care settings, as well as in health messages that inadvertently attach blame on individuals for the spread of TB (ie., those focusing on hygiene rather than on structural or systemic issues that contribute to the spread of TB, like malnutrition and overcrowding). Such stereotyping continues to exist in many Indigenous peoples' contemporary experiences within the healthcare system, resulting in poor relationships between patients and their healthcare providers. When these perceptions are experienced within the context of LTBI assessment, diagnosis and treatment, they can contribute to the stigma associated with TB (see for example Brassard et al., 2008a; Gibson et

al., 2005; Macdonald, Rigillo, & Brassard, 2010), affecting patients' willingness to be tested when no symptoms are present, and to initiate and complete treatment for the condition.

Likewise, Møller's (2005) study exploring perceptions of TB among Inuit in Nunavut found that the practices, beliefs and attitudes of Qallunaat (western) healthcare professionals towards Inuit patients likely inspired resistance to TB messages being communicated by representatives of colonizing ideologies. For example, study participants noted that some western-trained health care professionals were disrespectful of Inuit patients and often made derogatory remarks and assumptions about them – using generalizations like “drunks” and “gamblers.” These types of stereotypes can affect Indigenous patients' engagement with healthcare services. To the authors' knowledge, there have been no studies conducted to date that specifically explore the impacts of Indigenous people's experiences with, or perceptions of, mainstream healthcare services on their adherence to LTBI treatment. However, there is a relatively large body of literature that highlights ongoing structural barriers within the healthcare system, including stigma, stereotyping and discrimination, that affect Indigenous peoples' health and well-being (see for example, Allen & Smylie, 2015; Cameron et al., 2014; Denison, Varcoe, & Browne, 2013; Goodman et al., 2017; & Kurtz, Nyberg, Van Den Tillaart, & Mills, 2008). Additionally, a study examining adherence to LTBI preventive therapy among Cree

from Mistassini Lake during the period 1981-91 found that rates of adherence to treatment were much higher during the first five years of the study (75%) compared to the last five years (Rideout & Menzies, 1994). The finding suggests that negative perceptions of western healthcare professionals among the Cree may have contributed to a reduction in patient adherence to treatment in this specific case, as the later period of this study corresponded to a shift in the responsibility for TB treatment follow-up from Indigenous health workers to non-Indigenous nurses in 1985/86. Collectively, these perceptions highlight the critical need for a culturally safe and trusting healthcare environment for Indigenous people in effectively addressing the challenge of LTBI in Indigenous communities.

Colonial experiences, including suppression of Indigenous languages and cultures, and the loss of land rights and self-determination, have contributed to social, economic and cultural marginalization that is at the root of many of the health disparities experienced by Indigenous peoples (Czyzewski, 2011; Patel et al., 2017).

3.3 Societal barriers to LTBI treatment

Many societal barriers have their roots in Indigenous peoples' intergenerational and ongoing experiences with colonialism. Colonial experiences, including suppression of Indigenous languages and cultures, and the loss of land rights and self-determination, have contributed to social, economic and cultural marginalization that is at the root of many of the health disparities experienced by Indigenous peoples (Czyzewski, 2011; Patel et al., 2017). Challenges such as poverty, malnutrition, crowded or substandard housing, substance abuse, homelessness, psychiatric disorders, and ongoing racism and discrimination contribute

to increased prevalence of TB and LTBI and may influence LTBI diagnosis and treatment. In the face of multiple pressing challenges, TB may be considered a lower priority, especially when no symptoms are present (Abonyi et al., 2017). McMullin and colleagues (2012) poignantly describe the enduring impacts of colonization on the transmission of TB among Cree TB patients from the Canadian Prairies. Past and continuing experiences with oppression and adversity have contributed to overwhelming feelings of individual and collective apathy and despair about the hold TB had on Indigenous peoples, which manifested as "Old Keyam," or a sense of "what does it matter?" or "I do not care." These types of attitudes can influence patients' responses to TB and biomedical



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Indigenous TB patients were forcibly removed from their families and communities and placed into sanatoria far from home, often for extended periods of time, where they faced foreign medical treatment, a foreign language and culture, and uncertainty about their treatment or about when they might return home.

treatment, highlighting the need to reshape Indigenous peoples' TB experience into a more positive one, by returning to them some measure of hope and control over their health and their ability to affect change.

Another aspect of colonialism that continues to influence the thoughts and behaviours of Indigenous TB patients is the legacy of historic TB prevention and treatment policies and practices (Gibson et al., 2005; Møller, 2005, 2007, 2010). During the 1940s and 50s, the federal government adopted a TB prevention and treatment strategy involving placement of patients with active TB into sanatoria. While the use of sanatoria was considered standard practice for treating all TB patients during this period, for Indigenous people, these were viewed as sites of removal and exclusion from Indigenous cultures and practices of healing, from communities and from families (Moffatt et al., 2013). Indigenous TB patients were forcibly removed from their families and communities and

placed into sanatoria far from home, often for extended periods of time, where they faced foreign medical treatment, a foreign language and culture, and uncertainty about their treatment or about when they might return home. Many Indigenous people died of their illness, others lost connection to their communities and never returned, and still others returned to their communities but faced challenges reintegrating (Moffatt et al., 2013). This strategy took a heavy toll on Indigenous individuals, families and communities. Several qualitative studies have shown how the trauma associated with the sanatorium experience has contributed to the development of fear and mistrust with mainstream health care (Gibson et al., 2005; Hodgson, 2008; Moffatt et al., 2013; Møller, 2005, 2007, 2010). Current strategies to control and treat TB bear some similarity to those of the sanatorium experience, including relocation from home and temporary periods of isolation in hospitals to treat active TB cases, uncertainty about the time frame

for treatment, and the invasiveness of the practice of contact tracing, whereby patients with TB are asked to identify their close contacts, a practice which can be fearful and stigmatizing given the historical practice of removing infected individuals from their homes and communities (Komarnisky, Hackett, Abonyi, Heffernan, & Long, 2015).

Those societal barriers, when viewed within a colonial context, highlight the need for strategies that address the socio-economic conditions in which Indigenous people live, as well as foster self-determination over all aspects of Indigenous peoples' daily lives, including in the development of TB prevention and care initiatives and strategies. These must be driven by Indigenous peoples and communities so they are not viewed as simply another extension of colonial policies and practices, thus engendering resistance to LTBI screening and treatment practices.



4.0 STRATEGIES TO ADDRESS BARRIERS TO LTBI TREATMENT



In 2008, Hirsch-Moverman and colleagues undertook a systematic review of studies on strategies to foster adherence to treatment for LTBI. They found that no single intervention consistently showed effectiveness and concluded that a ‘one-size fits all’ approach was not likely to succeed across all settings. Instead, a number of strategies are needed. The literature highlights several interventions that may lead to improved LTBI treatment by addressing potential barriers for Indigenous peoples at the personal and health care system levels, and within the broader social context. These interventions may cross multiple levels of barriers.

4.1 Personal-level strategies

Interventions at the personal level include ways of improving Indigenous peoples’ knowledge of TB and how to care for it from both Indigenous and western scientific health beliefs and practices, as well as ways of enhancing programs to overcome individual barriers to diagnosis and treatment and address the cultural, social and historical realities of Indigenous peoples. Examples include:

- Bringing care closer to the patient, such as administering treatment at the patient’s place of residence or place of

choosing (Alvarez et al., 2014a, 2014b; Heal et al., 1998) and using IGRA testing whenever it makes sense to do so, as this method has the potential to make more test results available to patients compared to TSTs (see, for example Alvarez et al.’s [2014c] comparison of IGRAs and TSTs in a remote Inuit community);

- Using incentives like food, vouchers or financial compensation to encourage patients to attend their scheduled appointments (Alvarez et al., 2014b; Brassard, 2008b, de Bibiana et al., 2011). While research on the use of incentives has shown mixed results, certain types of incentives used in certain situations have resulted in improvements to adherence to LTBI treatment, especially if used in conjunction with patient education (see for example Brassard et al., 2008b; Lutge, Wiysonge, Knight, Sinclair, & Volmink, 2015; and Volmink & Garner, 1997). There is a clear need for additional research on what incentives work best for Indigenous peoples and under what circumstances.
- Providing culturally appropriate health education to Indigenous peoples about TB, latent

infections and treatment – administered creatively (Alvarez et al., 2014a) and in combination with other methods (Alvarez et al., 2014b);

- Working with Indigenous patients to establish a care plan that meets their needs and is mutually acceptable to patients and healthcare providers (PHAC, 2014b);
- Assisting patients in dealing with life priorities, such as developing reminder and follow-up mechanisms, simplifying protocols, reducing referral times, rigorously tracking migrating patients, using harm reduction methods so that treatment does not compete with addictions, and engaging family and community supports, mentors and sponsors (Alvarez et al., 2014a); and
- Treating patients with dignity and respect, creating a safe space for disclosure, asking patients about their social challenges in a sensitive and caring way, allocating extra time to address their complex health and social needs, knowing about local referral resources and referring patients, and helping patients access benefits and support services (Andermann, 2017).



Very few studies described interventions applicable to the social context of the individual, such as providing assistance with childcare, transportation and shelter. Given the socio-economic circumstances in which many Indigenous people live and the multiple challenges they face to health and well-being, these factors may be important considerations in improving their adherence to LTBI treatment; however this is an area where further research is required.

4.2 Health care system level strategies

Much of the focus of suggested strategies to address barriers to LTBI treatment within the health care system involves ways of improving relationships between health care providers and clients. Many of these strategies require changes at the organizational level and within the broader societal context in which care is provided, such as a reducing stigma related to TB, as well as

ending racism and discrimination towards Indigenous TB patients. Examples include:

- Providing flexible care that is emotionally/culturally accessible, patient centered (Frieden & Sbarbaro, 2007) and makes patients feel valued and respected (Hirsch-Moverman et al., 2008; Macdonald, Rigillo, & Brassard, 2010; Rideout & Menzies, 1994). Some examples include providing care that does not interfere with land-based (ie. hunting) and ceremonial activities (FitzGerald et al., 2000; Rideout & Menzies, 1994); having community health workers initiate a buddy system (family or friend) to help ensure that patients take their medications (Rideout & Menzies, 1994); bringing LTBI screening initiatives to the patient's door (Alvarez et al., 2014b); and if DOPT or partial DOPT is used, doing so in a location convenient for the patient (Heuvelings et al., 2017);

- Addressing program barriers related to stigma, including zero tolerance policies on use of drugs and alcohol when accessing care, negative attitudes of staff, contact tracing, as well as language and cultural barriers by using interpreters from the same community as patients (Craig, Daftary, Engel, O'Driscoll, & Ioannaki, 2017);
- Finding ways to improve screening uptake by at-risk Indigenous people through such means as a mobile x-ray unit or providing local access to IGRAs in communities with limited access to healthcare services; active referral to a TB clinic by providing a phone number, making an appointment, organizing transport and sending reminders; having TB education be provided by community health workers; and improving cooperation between service providers (Heuvelings et al., 2017; Alvarez et al., 2014c);
- Considering adding chart reminders or recall systems to flag patients at risk, using alternative models of care such as outreach, using patient navigators to assist patients on their journey through health systems, and considering participatory approaches that engage other clinicians in your practice to create a culture of reflection and a more 'upstream approach' (Andermann, 2017, p. 127);
- Ensuring health staff are knowledgeable (Alvarez et al., 2014a; Fitzgerald et al., 2000) and sensitive to the historical and current concerns of their

patients in the context of implementing TB control programs (Fitzgerald et al., 2000; Macdonald et al., 2010; Maud, 2013b; Orr, Case, Mersereau, & Lem, 2007);

- Increasing the number of Indigenous people working in the health care field (Komarnisky et al., 2015);
- Recruiting and training local TB health liaison workers to work alongside health professionals in clinical settings or in the community who function as educators, advocates, and cultural brokers (Alvarez et al., 2014a; Alvarez et al., 2014b; Gibson et al., 2005);
- Showing positive acts of kindness and professionalism (Macdonald et al., 2010), and

providing non-judgmental care to encourage positive health behaviors in LTBI patients (FitzGerald et al., 2000; Macdonald et al., 2010; Maud, 2013b);

- Developing a shared understanding of the causes, treatment and meaning of TB to overcome cultural dissonance with Western medicine (Orr, 2011a) and incorporating Indigenous beliefs about causation and cure into TB programs, including Indigenous healing practices (Alvarez et al., 2014a);
- Adopting culturally appropriate health messaging that is not only translated into the appropriate language, but is conveyed in ways which are consistent and resonate with

Indigenous knowledge and ways of learning (such as oral rather than written messaging) (Møller, 2010);

- Adopting a “patient-centered approach to administration of drug treatment, based on the patient’s needs and mutual respect between the patient and the provider” that is gender-sensitive, age-specific and “draws on the full range of recommended interventions and available support services, including patient counseling and education” (World Health Organization, 2006, p. 3);
- Using measures to assess adherence that are tailored to the patient’s circumstances and are mutually acceptable to both patient and provider (World Health Organization, 2006);



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- Addressing the ‘service gap’ which exists for Indigenous people in accessing health services off reserve to ensure they complete their TB assessments and preventive therapy (Eisenbeis et al., 2016) by streamlining health services for Indigenous people under one roof to provide an integrated model of care to facilitate LTBI diagnosis, treatment and care; helping to increase awareness about Indigenous issues among health providers (MacDonald et al., 2010); and addressing jurisdictional issues regarding service provision and cross-jurisdictional health services coordination and communication;
- Fostering increased communication and coordination between federal/provincial/territorial governments, Indigenous organizations and health jurisdictions to facilitate improved LTBI care and follow-up by addressing the challenge of high mobility among Indigenous people from reserves to urban centres (PHAC, 2014b);
- Addressing the social situations and health-system issues that contribute to losses in the cascade of diagnosis and treatment of LTBI (Alsdurf et al., 2016); and
- Encouraging strong community engagement in TB prevention and care initiatives and strategies (Inuit Tapiriit Kanatami, 2013).

4.3 Social context strategies

Andermann (2017) argues there is a need to recognize that social determinants contribute to the emergence and persistence of disease outbreaks like TB in Indigenous communities. While conventional approaches to addressing communicable disease outbreaks are necessary, they are insufficient in the context of Indigenous health. A ‘syndemics’ conceptual framework, which considers the social, economic, environmental and political context of Indigenous peoples’ lives, is needed to leverage action at multiple levels to tackle the root causes of poor health and inform more effective strategies for improving Indigenous health. Some of the strategies identified in the literature that address the context of Indigenous peoples’ lives overlap with those identified at the individual and health care system levels. These interventions include more holistic strategies aimed at overcoming socio-economic marginalization and improving the health and well-being of entire communities, which reflect, in part, an Indigenous holistic worldview with its emphasis on the interconnectedness of the body, mind, soul and spirit (Tollefson et al., 2013). Examples include:

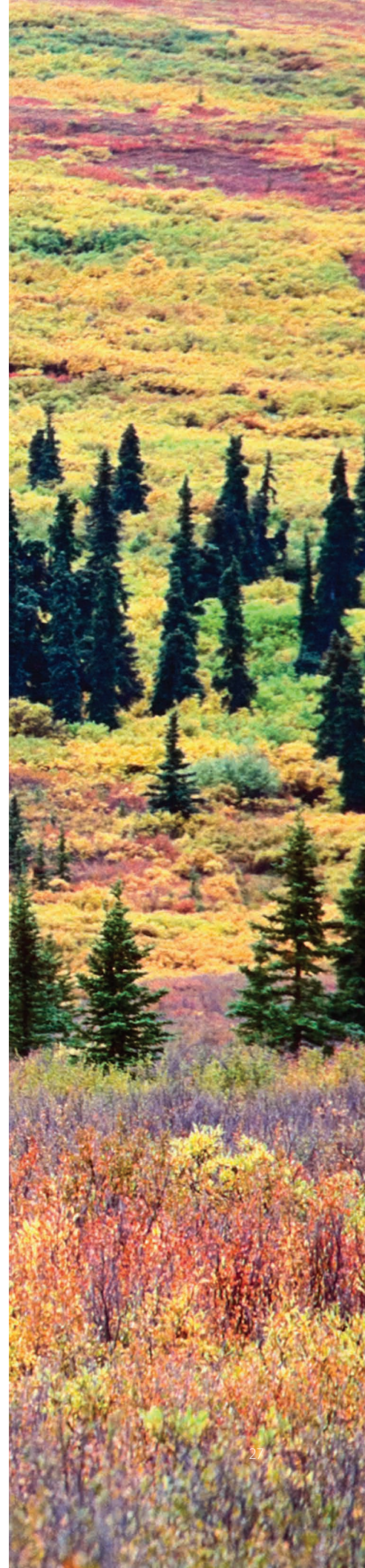
- Providing mental health supports and addressing substance abuse (FitzGerald et al., 2000; McMullin et al., 2012);
- Improving socio-economic status and housing conditions (Clark et al., 2002; FitzGerald et al., 2000; McMullin et al., 2012; Alvarez et al., 2014a);

- Assisting TB patients in finding stable housing (Eisenbeis, 2015);
- Providing better community and social supports (McMullin et al., 2012);
- Subsidizing nutritious food, creating economic opportunities, providing Indigenous-centred educational curriculum, and providing better health care services (Kulmann & Richmond, 2011; McMullin et al., 2012);
- Focusing on the social determinants of health in TB policy (Kulmann & Richmond, 2011; Alvarez et al., 2014a);
- Building respectful relationships to work within and across high incidence Indigenous and non-Indigenous communities, in ways which bridge jurisdictional lines and truly engage communities as partners (Andermann, 2017; Patel et al., 2017);
- Since TB is a “biological expression of social inequality” for Indigenous peoples, addressing not just socioeconomic and connectivity deficits, but also Indigenous-specific determinants related to colonization, loss of language and culture, and disconnection from the land (Patel et al., 2017, p. 12);
- Utilizing decolonizing measures such as embracing Indigenous ways and values in educational, health and political matters (Møller, 2010);
- Using the Truth and Reconciliation Commission’s Calls to Action as a starting

point in promoting greater Indigenous self-determination in child welfare, economic development, justice, culture and education, to close health gaps (Andermann, 2017);

- Developing appropriate programs for community-based healing and reconciliation (Møller, 2010); and
- Developing intersectoral partnerships to address the social determinants of health (Inuit Tapiriit Kanitami, 2013).

While many of these suggested strategies have not been tested for effectiveness in Indigenous communities, they are considered by many Indigenous and non-Indigenous health researchers to be necessary for addressing the underlying causes of health disparities for Indigenous peoples and overcoming barriers that limit health care access and Indigenous peoples’ engagement in their care. However, approaches must be tailored to the individual realities and needs of Indigenous peoples (Rideout & Menzies, 1994; Tollefson et al., 2013). This can include addressing issues related to patient-client relationships, marginalization with the health care system, culturally appropriate health care information, locally available supports and resources, as well as to the socio-economic conditions that contribute to the high prevalence and spread of TB in endemic Indigenous communities.





4.4 Promising Strategies

This section highlights three strategies that hold promise for improving LTBI diagnosis, treatment initiation and completion among Indigenous peoples, each incorporating a different approach. The approaches include a public health campaign in Nunavut, an innovative health service delivery model in Alberta, and the use of mobile phone technologies.

The first example of a promising practice is the TAIMA (Stop) TB campaign, a TB awareness and prevention campaign initiated in Iqaluit, Nunavut over the period January 2011 to February 2013. The campaign involved a public health information component to raise knowledge about TB, as well as a targeted door-to-door screening and testing component delivered in high risk neighborhoods to identify and refer infected individuals for treatment (Alvarez et al., 2015). The campaign was designed in collaboration with

Inuit organizations, community members and local TB health care professionals. Both the health promotion content and mode of delivery were culturally appropriate, including consideration for the historical context of Inuit people's lived experiences with TB and the community context, translation of materials into Inuktitut, having community voices convey the key messages in videos, and training local community members in TB education so they can work alongside nursing staff for the door-to-door component of the campaign. Preventive treatment consisted of nine months of twice-weekly administered INH, use of DOPT, and the transfer of individuals with active TB to the Iqaluit Public Health TB program for treatment (Alvarez et al., 2014b). Additionally, LTBI patients were given the option of having medications delivered to their homes or to any other location they deemed convenient.

An evaluation of the campaign showed that it was successful on

several fronts. Awareness of TB increased, with the number of people coming to the public health clinic doubling over the duration of the campaign. As well, the campaign contributed to 34% of the new LTBI diagnoses identified over this period (Alvarez et al., 2014b). Compared to individuals identified for LTBI through the traditional screening program, a greater proportion of those identified with LTBI through this targeted campaign initiated DOPT (61% compared with 47%), and a similar proportion (68%) completed treatment. However, while the evaluation highlighted the potential of this type of campaign to decrease TB rates in high risk communities, it also underscored the need for sustained yearly TB awareness campaigns, as the number of people visiting the local clinic for TB screening returned back to normal levels after the four-month targeted campaign.

The second example of a promising practice is the establishment of a 'virtual' public health TB clinic in


rural Alberta. It was established in 1999 as part of a restructuring of Alberta's TB program into two specially ventilated 'outpatient' clinics serving the urban centres of Edmonton and Alberta, and the virtual clinic located in Edmonton which serves all non-major metropolitan and on-reserve First Nations cases and their contacts (Long, Heffernan, Gao, Egedahl, & Talbot, 2015). This virtual clinic took into account the geographic, demographic and historical realities of Indigenous people in rural Alberta by introducing a mechanism whereby Status Indians and other rural residents of Alberta could be managed on-site rather than having to travel long distances for treatment (Jensen et al., 2012). Staffed by dedicated public health nurses and university-based TB physicians, the virtual clinic receives an average of 20-40 referrals per week via courier or express mail along with radiographs. Each referral generates a directive by a TB physician which is then acted on by local providers (Jensen et al., 2012). Since the establishment of the clinic, there have been no major outbreaks of TB, suggesting that such a clinic can help detect and reduce transmission in traditionally underserved rural areas (Jensen et al., 2012). An evaluation comparing this virtual clinic with the face-to-face encounters of the two

“outpatient” TB clinics showed that the virtual clinic did equally as well as the face-to-face encounters in terms of patient outcomes, with performance that was comparable on 22 indicators, superior on three indicators, and inferior in three indicators (Long et al., 2015). The evaluation highlighted the potential of a virtual model in addressing issues around equitable service delivery and declining expertise.

Mobile phones are emerging as effective public health interventions in relation to HIV treatment (Denkinger et al., 2013), as well as treatment for active and latent TB (Belknap et al., 2017; Chuck, Robinson, Macaraig, Alexander, & Burzynski, 2016; Liu et al., 2015). In the latter, they have been used as a video replacement for directly observed therapy, as a short messaging service to remind patients of upcoming visits with health providers, and as an device that tracks adherence to preventive therapy for LTBI by detecting pill usage and transmitting the

information. While mobile phones have not yet been used with Indigenous populations to support adherence to their LTBI treatment, this is a promising strategy for future consideration. Not only is it a way of reducing costs, it also addresses a number of barriers that may affect LTBI treatment for Indigenous peoples, including lack of access to health services, healthcare worker shortages, and lack of cultural safety and support, among others. However, the feasibility of implementing such a strategy must be explored more thoroughly, especially within the context of geographically remote areas where cell or internet services may not be optimal.

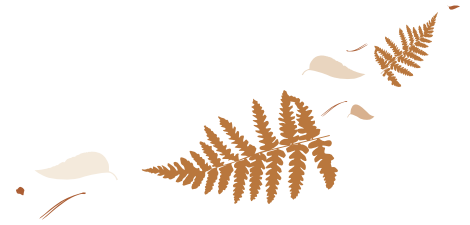




...the challenge of addressing LTBI in Indigenous communities will also require taking actions that address the ongoing legacies of colonialism that have had destructive impacts on Indigenous peoples' health, as outlined in the Truth and Reconciliation Commission [TRC] of Canada's (2015) Calls to Action.

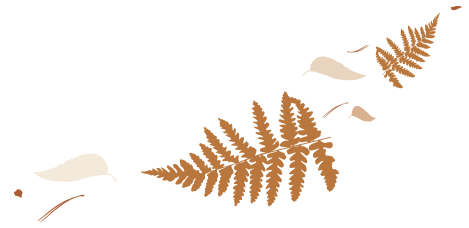


5.0 CONCLUSIONS



The goal of reducing TB among Indigenous peoples is feasible, but it requires sustained and consistent community-wide participation in communities with high rates of LTBI who are at high risk of progressing to TB disease, as well as innovative interventions and education campaigns (Clark, & Cameron, 2009; Demmer, 2011; Lee et al., 2015). It requires addressing any barriers that potentially inhibit Indigenous people from undergoing screening and diagnosis for LTBI in a timely way, initiating preventative treatment, and adhering to that treatment regimen. While some of these barriers relate to the lengthy duration of the treatment and possible side effects, especially in the absence of symptoms, others result from the legacy of colonialism, including fear of social isolation, mistrust in mainstream healthcare systems, personal life challenges, as well as social marginalization. Given these barriers, the challenge of addressing LTBI in Indigenous communities will also require taking actions that address the ongoing legacies of colonialism that have had destructive impacts on Indigenous peoples' health, as outlined in the Truth and Reconciliation Commission [TRC] of Canada's (2015) *Calls to Action*. Specifically, the TRC called on all levels of government to work together to identify and close the gaps in health outcomes between Indigenous and non-Indigenous communities (Call to Action #19), by tracking progress related to LTBI and ensuring appropriate health services are available; increasing the health of Indigenous professionals working in the health-care field (Call to Action #23i); and ensuring all healthcare professionals are provided with cultural competency training (Call to Action #23iii). Additionally, the TRC called on the federal government to recognize, respect and address the distinct health needs of of-reserve Indigenous peoples (Call to Action #20). These actions towards reconciliation would help reduce many of the key structural barriers that exist in addressing LTBI in Indigenous communities.

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