CANADIAN TUBERCULOSIS STANDARDS

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CHAPTER 13

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CHAPTER 13

TUBERCULOSIS SURVEILLANCE AND SCREENING IN SELECTED HIGH-RISK POPULATIONS

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KEY MESSAGES/POINTS

- Screening for and treatment of latent tuberculosis infection (LTBI) should only be undertaken if the local TB control program already effectively manages active TB cases and their contacts.
- The selection of people for targeted LTBI screening and treatment is based on their risk of prior TB exposure and their risk of reactivation, balanced against the likelihood of safe completion of treatment, including the risk of hepatotoxicity, which increases with age.
- Groups discussed in this chapter that may warrant targeted screening are the foreign-born, people with non-HIV immune suppression and other medical or behavioural risk factors for TB, and long-term visitors to countries with higher TB incidence.
- Other groups that may be considered for targeted LTBI screening are discussed in other chapters and include TB contacts, people with HIV infection, Canadian-born Aboriginal Peoples, children, and employees and users of health care and correctional facilities.
- Most foreign-born groups undergo a mandatory medical examination prior to arrival in Canada, which includes chest radiography to detect active TB. Those found to have active TB must be treated prior to arrival to ensure that they are no longer infectious. Citizenship and Immigration Canada (CIC) requires that individuals with previously treated TB and those with abnormal chest radiographs but without active TB detected in this program undergo TB surveillance after arrival.
- Only a small proportion of all cases of active TB diagnosed in the foreign-born after arrival in Canada are detected during the immigration post-landing surveillance program. This underscores the need for additional screening programs for subgroups of the foreign-born at increased risk of TB reactivation.
- To improve uptake of LTBI screening and treatment in the foreign-born population, investment in TB education programs for patients and providers should be considered together with delivery of care in a culturally sensitive manner with good access to interpreters.

- To improve the likelihood of safe completion of LTBI treatment in vulnerable groups, such as injection drug users and the homeless, it is suggested that patients be assessed to determine coexisting viral hepatitis in order to decrease the possibility of hepatotoxic effects of LTBI treatment. Those at highest risk of reactivation should be considered for special measures to enhance adherence, such as directly observed LTBI treatment and/or incentives and enablers.

INTRODUCTION

The last three decades have seen marked shifts in the epidemiology of TB in Canada. Active disease is increasingly concentrated in specific population subgroups, notably the foreign-born, Aboriginal Peoples and people with medical, social and/or behavioural risk factors, such as HIV infection, homelessness and injection drug use (see Chapter 1, Epidemiology of Tuberculosis in Canada).

While it is recommended that the first priorities in TB control remain the timely detection and treatment of active TB followed by suitable management of contacts at risk, the concentration of TB in specific groups makes it relevant to consider targeted screening. Targeted screening interventions systematically seek to diagnose and treat active TB or LTBI among those at increased risk of infection and/or progression to active disease. In this chapter, the focus is on TB surveillance and screening of immigrants and refugees; people with non-HIV immune suppression and other medical, social or behavioural risk factors for TB; and long-term visitors to higher-incidence countries. Screening and management of active TB and LTBI among TB contacts, people with HIV infection, Aboriginal Peoples, children, and employees and users of health care and correctional facilities are discussed in other chapters.

SURVEILLANCE

Surveillance refers to an ongoing process of (a) systematic collection of pertinent, high-quality data; (b) orderly consolidation and evaluation of these data; and (c) prompt dissemination of the results to those who need to know, particularly those who are in a position to take action.[1]

Generally, the objectives of a surveillance program are to guide health interventions, estimate trends, identify groups at high risk, monitor changes in patterns of transmission, evaluate prevention strategies and suggest hypotheses for further research.

It is important for providers and public health authorities to understand the distribution of TB in Canadian communities and to detect transmission. Moreover, suitable documentation of the outcomes of screening interventions (e.g. contact investigation, chest radiography for immigrants) allows for quality control assessment and informed decision-making about future policies and their potential targets.

In the context of immigration, the term “medical surveillance” refers to the process whereby immigrants and refugees with inactive TB or previous TB treatment detected in the pre-arrival

TB screening program are required by CIC to report to local public health authorities for examination and follow-up.

SCREENING – DEFINITIONS, TOOLS AND GOALS

Screening refers to a process that attempts to discover conditions suitable for early preventive or curative intervention. These conditions may not be sufficiently symptomatic to induce patients to seek medical help on their own. Screening may be justified by the prevalence and/or potential severity of the target condition, when its detection permits intervention that improves outcomes.[2] In the case of active TB, the goal is to reduce unfavourable outcomes and interrupt transmission by instituting prompt and effective treatment. The goal of targeted screening for LTBI is to reduce the likelihood of subsequent progression to active disease among people at increased risk by appropriate initiation, supervision and successful completion of treatment.

Symptom screens and chest radiography are the primary screening tools when the focus is the identification of prevalent, undiagnosed active cases of infectious pulmonary TB (so as to treat and render them noninfectious). Subsequent microbiologic confirmation with sputum smear and culture or other suitable specimens is always recommended (See Chapter 6, Treatment of Latent Tuberculosis Infection).

When the focus of screening is the detection of LTBI, either the tuberculin skin test (TST) or the interferon gamma-release assays (IGRAs) may be used. Conditions under which either test is preferred and their interpretation are reviewed in Chapter 4, Diagnosis of Latent Tuberculosis Infection. Positive screening tests for LTBI should be followed by chest radiography to address the possibility of subclinical active TB. Chest radiography also identifies abnormalities that are associated with increased reactivation risk.

- The highest priority in TB control programs is to detect and treat active TB cases and to investigate their contacts.
- Screening and treatment for LTBI should only be undertaken if the TB control program effectively manages active TB cases and their contacts.
- Screening for LTBI is only appropriate when available infrastructure and resources allow the monitoring and support needed to achieve safe and complete treatment.[3]

Strong recommendations, based on moderate to strong evidence

TARGETING GROUPS FOR SCREENING

The choice of which groups should be targeted for LTBI screening and treatment should be based on a number of factors, and the assessment is usually performed in various settings by different professionals, such as public health, occupational health, primary care or subspecialty physicians. The most important factors to take into consideration when selecting people as suitable candidates for LTBI screening and treatment are their risk of prior TB exposure (Table 1) and of reactivation, balanced against the risk of hepatotoxicity (see Chapter 6, Treatment of Latent Tuberculosis Infection). The likelihood that individuals will safely complete treatment as prescribed should also be taken into account. Hence, the benefit of screening

programs for LTBI will be greatest in those with a higher probability of infection and/or significant risk factors for reactivation, coupled with a low risk of toxicity and a high probability of treatment completion. LTBI treatment may be particularly beneficial in certain subgroups, such as young children and those with severe immunosuppression, for whom there is increased risk of progression to active disease and also a greater risk of severe forms of the disease, such as miliary TB or TB meningitis (see Chapter 6).

Table 1. Groups with increased risk of TB exposure and latent TB infection[4]

Groups at risk	Prevalence of positive TST	Setting or group usually responsible for screening
Close contacts of an active case of pulmonary TB	Variable, higher than source population	Public health, primary care
Immigrants from countries with high TB incidence Children Adult (lived >20 years in country with high TB incidence)	 15%-23% 53%-61%	Public health, primary care
Injection drug user (TST ≥10 mm) (TST ≥5 mm)	 66% 31%	Primary care, treatment facilities
Homeless	18%-51%	Primary care, shelters, public health
Aboriginal communities* Adults Children	 14%-30% 5%-29%	Public health, primary care
Health care workers*	11%-46%	Occupational health, public health
Residents of long-term care facilities*	6%-25%	Primary care, facility director of care, public health
Residents of correctional facilities*	12%-72%	Inmate health services, public health
Travellers to countries with high TB incidence	Variable	Travel medicine, primary care
Reference Canadian-born non-Aboriginal children Canadian-born non-Aboriginal adults, not BCG vaccinated Canadian-born non-Aboriginal adults, BCG vaccinated Canadian-born non-Aboriginal adults, BCG vaccination nonspecified	 1-3% 7% 65% 13%	Targeted screening not recommended

*BCG status not specified

SCREENING IMMIGRANTS FOR TUBERCULOSIS INFECTION AND DISEASE

OVERVIEW OF IMMIGRATION TO CANADA

Over the course of the last four decades, international migration has increased at an unprecedented rate, the total number of international migrants estimated to be 200 million people.[3] Canada is a leading destination for migrants and receives on average ~250,000 immigrants and refugees annually, who account for almost 20% of the population (2006 Census[5,6]). Over the past 40 years, there has been a major demographic shift in the source countries of new migrants. Before the 1960s, most individuals immigrating to Canada originated from European countries. Since the 1970s, however, most immigrants (>70%) have originated from countries with intermediate or high TB incidence rates in Asia, Africa and Latin America.[5,6]

The two main administrative classifications of migrants arriving in Canada are 1) permanent residents who come to Canada to resettle and 2) temporary residents who are visiting, studying or working in Canada but who maintain their own nationality. Permanent and temporary residents are further classified into several subgroups (see Table 2). In addition, Canada receives more than 35 million international visitors per year.[8] Most groups apply for permission to come to Canada while still living in their countries of origin, an important exception is refugee claimants who apply for status after arrival in Canada.[6]

Table 2. Classification of international migration to Canada (2010)[7]

Immigration category	Annual number of migrants*
Permanent residents	
Economic class (business and economic migrants)	187,000
Family class (family reunification)	60,000
Humanitarian class (refugees resettled from abroad or selected in Canada from refugee claimant population)	25,000
Others	9,000
Total	**281,000**
Temporary residents	
Migrant workers	182,000
International students	96,000
Refugee claimants (those arriving in Canada and claiming to be a refugee)	23,000
Others	81,000
Total	**382,000**
Other migrants	
Irregular migrants (no official migration status)†	~200,000
Visitors	~35,000,000

*Numbers rounded to nearest 1,000. Data from Citizenship and Immigration Canada Facts and Figures 2010.[6]

†Includes those who have entered Canada as visitors or temporary residents and remained to live or work without official status. It also includes those who may have entered the country illegally and did not register with authorities or apply for residence.

EPIDEMIOLOGY AND PREDICTORS OF TB AMONG THE FOREIGN-BORN IN CANADA

Canada is a low-incidence country and had an overall TB disease rate of 4.6 per 100,000 population in 2010.[9] The majority of the 1,577 reported cases (66%) occurred in the foreign-born population, which has an overall 13-fold greater incidence of TB than the non-Aboriginal Canadian-born population (13.3 vs. 1.0 cases/100,000 population), although rates are as high as 500 times greater in certain subgroups of immigrants.[9,10] The strongest predictors of active TB development in immigrant populations are the global region of origin, immigration category (refugees at 2-fold increased risk compared with other immigrants), the presence of underlying medical comorbidities, the time since arrival in Canada and recent travel to countries with a high TB incidence[10-17] (also see Chapter 1, Epidemiology of Tuberculosis in Canada). Refugees and foreign-born children from high-incidence countries are particularly important subgroups to consider for targeted screening, for the reasons listed below.

Refugee populations have consistently been reported to have an approximately 2-fold increased risk of active TB compared with the immigrant population, at least within the first year after arrival.[18-21] This may be due to a higher prevalence of LTBI in the refugee population and crowded conditions that increase the likelihood of recent exposure to TB. [22]

Foreign-born children less than 11 years of age from high-incidence countries do not undergo pre-arrival radiographic screening for TB (see http://www.cic.gc.ca/english/department/partner/pp/pdf/IMEI_Tuberculosis.pdf).[23] For this and several other reasons children may particularly benefit from LTBI screening and treatment. In children less than 5 years of age there is higher likelihood of severe or rapidly progressive disease, such as miliary TB or TB meningitis.[24,25] Furthermore, TB in young children is more often paucibacillary or extrapulmonary and therefore more difficult to diagnose.[24,25] Finally, children with LTBI have many years of life in which active TB may develop and a relatively low risk of hepatotoxicity (see Chapter 9, Pediatric Tuberculosis).

IMMIGRATION TB SCREENING REQUIREMENTS FOR THE FOREIGN-BORN

Pre-entry tuberculosis screening

CIC requires all individuals applying for permanent residency and certain individuals applying for temporary residency to undergo an immigration medical examination (IME) before arrival, which includes a chest radiograph for applicants ≥11 years of age (see Table 3) (see http://www.cic.gc.ca/english/resources/manuals/op/index.asp).[26] The objective of this program is to detect prevalent active TB in migrants prior to arrival in Canada so as to ensure that they are treated and are no longer infectious on arrival. This screening program does not aim to detect or treat LTBI. Once the IME has been completed it is valid for a period of 12 months.[27] Most visitors do not require this examination. CIC's determination of which temporary residents or visitors require an IME is based on their place of origin (a 3-year average incidence rate of all cases of TB of ≥30/100,000 population), the duration of the visit (longer than 6 months) and occupation (workers in close contact with others). For most migrants the IME is performed before departure from the country of origin by a designated medical professional, and the cost is borne by the applicant. The exceptions to this are convention refugees for whom the

examination is provided free and refugee claimants, who claim refugee status after arrival in Canada and undergo an IME shortly after arrival.

Note: In 2009 the World Health Organization changed its method of reporting the global burden of TB and began reporting annual incidence of ALL TB cases per 100,000 rather than annual incidence of smear-positive TB. To reflect this change, the definition of high TB incidence countries/territories has changed from 15 per 100,000 smear-positive TB cases to 30 per 100,000 for all forms of active TB cases (3-year average).[11] The 3-year moving average is used to adjust for unstable rates in some jurisdictions. Furthermore, estimated rates adjusted for under-reporting of cases are used for some countries, rather than the country's reported incidence rate. To view current international incidence rates, see http://www.publichealth.gc.ca/tuberculosis.

Chest x-rays are examined for evidence of active or inactive TB disease by a local radiologist. CIC, in consultation with Canadian TB specialists, grades chest x-rays according to an 18-factor ascending scale of findings characteristic of active TB disease or inactive TB infection.[27] Individuals with certain abnormalities on their chest x-ray must submit three consecutive sputum samples for smear and culture. Those unable to submit sputum will be required to repeat the chest radiography 6 months after the initial one to establish stability. Those found to have active TB must complete a course of treatment consistent with Canadian standards. Before being given permission to enter Canada by CIC, they must submit proof of successful treatment completion, three negative sputum smears and cultures, and stable and/or improving chest x-rays taken over a minimum period of 3 months. In 2011 active TB was identified during 0.09% of 500,992 immigration medical assessments (Dr. Sylvain Bertrand, Citizenship and Immigration Canada, personal communication).

Applicants identified as having inactive pulmonary TB are permitted to enter Canada but are placed under medical surveillance and referred to provincial/territorial public health authorities to report for post-landing surveillance (see below) within 30 days of arrival.

Inactive pulmonary TB is defined as follows:

a) a history of treated active TB and/or

b) an abnormal chest x-ray suggestive of TB and
   i) two chest x-rays taken at an interval of 3 months apart with stable appearance and three negative sputum smears and cultures or
   ii) two chest x-rays taken at an interval of 6 months apart with stable appearance.

Table 3. Citizenship and Immigration Canada requirements for an immigration medical examination[24]

Entrants to Canada	Criteria
Foreign nationals applying for permanent residency (immigrants and refugees selected abroad)	Mandatory for all.
Foreign nationals claiming refugee status in Canada	Mandatory for all.
Foreign nationals applying for temporary residency (including students, workers and visitors)	Those who will stay in Canada for more than 6 months and who have spent 6 or more consecutive months in a country/territory with high TB incidence, as designated by the Public Health Agency of Canada, during the 1 year immediately preceding the date of seeking entry (application) to Canada.
Foreign nationals applying for temporary residency and seeking to work in certain occupations	Mandatory for all who are seeking to work in an occupation in which the protection of public health is essential regardless of length of stay and country of origin AND for agricultural workers from a country/territory with high TB incidence, as designated by the Public Health Agency of Canada. The occupational list is available at: http://www.cic.gc.ca/english/information/medical/medexams-temp.asp#occupational
Seriously ill foreign nationals	May be requested to undergo an immigration medical examination if an Immigration Canada or Canada Border Services Agency officer has reasonable grounds to believe that the person is medically inadmissible to Canada, regardless of anticipated length of stay in Canada and country of origin.

Post-landing surveillance

CIC's Medical Surveillance Program is designed to refer applicants found in the course of their IME to have previously treated TB or inactive pulmonary TB to the Canadian provincial or territorial public health authorities as soon as possible upon their arrival in Canada. Approximately 2% of those who undergo pre-arrival chest radiographic TB screening are targeted for medical surveillance (Dr. Sylvain Bertrand, Citizenship and Immigration Canada, personal communication). Immigrants requiring medical surveillance receive a Medical Surveillance Undertaking Form (IMM 0535B) and an information handout with instructions on how to contact provincial/ territorial public health authorities upon arrival in Canada. They must report to, or be contacted by, a public health authority within 30 days of entry. For complex inactive pulmonary TB cases, evaluation and follow-up should begin within 7 days (see http://www.cic.gc.ca/english/resources/manuals/bulletins/2011/ob340.asp).

This is a passive surveillance system, and the implementation varies among the different provinces and territories, some having a centralized process and others having a decentralized system. Provincial/territorial public health authorities report to the CIC Medical Surveillance Program as to whether the immigrant has been compliant with the requirement for medical surveillance. Compliance is defined as keeping the first appointment with the clinician or being assessed by a specialist designated by public health. Compliance with surveillance varies by province/territory, averaging ~70% (Dr. Sylvain Bertrand, CIC, personal communication). Participation in the Medical Surveillance Program is a formal "condition of landing." While there is currently no enforcement of participation, CIC will not process any further immigration applications from an immigrant under the Medical Surveillance Program (e.g. to extend a visa or apply to become a citizen) until they have met the program requirement.

Immigrants are responsible for their own health care funding until eligible for provincial/territorial health care insurance, which in some jurisdictions may not be until 90 days after arrival. For those under medical surveillance, this may mean a delay of examination, radiography, other necessary procedures and treatment for LTBI for at least 3 months. Temporary health care for refugees and refugee claimants may be covered by the Interim Federal Health Program, a health care coverage program managed by CIC. This will provide coverage for the IME when done in Canada, screening for and treatment of active TB, if detected, as well as screening for and treatment of LTBI in all groups eligible for the Public Health and Public Safety package. Information on the Interim Federal Health Program is available at http://www.cic.gc.ca/english/refugees/outside/summary-ifhp.asp.

Timely compliance with the requirement for medical surveillance has been shown to improve in the following circumstances:[28]

- Advising the immigrant of the need for medical surveillance before travel to Canada or at the port of arrival
- Providing documents requesting medical surveillance in the language of the immigrant (if not fluent in English or French)
- Provincial/territorial health insurance coverage for medical surveillance immediately upon arrival in Canada with no waiting period
- Pre-screening of individuals by public health staff prior to clinician assessment in order to identify those with symptoms and signs of active TB or those at high risk of rapid progression of LTBI to active disease
- Centralized clinics for assessment, when feasible, allowing staff to become more experienced and efficient
- Extended clinic hours
- Readily available and culturally sensitive interpretation services.

During the initial assessment of these individuals, active TB should be ruled out with special attention to symptoms or signs of active TB. If these are present chest radiography and sputum smears and cultures should be performed as deemed appropriate.[29] For those found not to have active TB, testing for LTBI (TST or IGRA), unless previously known to be positive, should be performed and those identified as having LTBI should be considered for treatment as outlined in

Chapter 6, Treatment of Latent Tuberculosis Infection. Those who have completed an adequate and well-documented course of LTBI treatment can be discharged. The need for and duration of follow-up for those not completing LTBI treatment is unclear. In general, such people should be advised of the potential risk of reactivation and told to return for evaluation if symptoms arise (see also Chapter 6). People who are discharged from follow-up should be advised to seek medical attention promptly if symptoms develop that are suggestive of TB and to tell their health care provider about their history of medical surveillance for TB as a result of their IME. [29]

Post-arrival domestic LTBI screening

There are no routine post-arrival domestic LTBI screening programs for immigrants in Canada. There are, however, published primary care guidelines and several screening programs managed by different organizations, for example, school-based screening, immigrant and refugee clinics, services for migrant workers and targeted screening of certain high-risk migrants.[10,30-45] Undocumented migrants are difficult to access and remain a challenge, as they are not systematically screened in any of the existing programs.

EFFECTIVENESS OF TB SCREENING PROGRAMS FOR IMMIGRANTS

Active and inactive TB

Recent estimates of the yield of active TB and inactive TB found in pre-immigration chest radiography screening in migrants to Canada was found to be 0.05% and ~2% respectively.[46] In a recent systematic review and meta-analysis 1.3% of migrants assessed in the post-landing surveillance program in Canada were found to have active TB.[47] Only 67% of those targeted for this surveillance actually completed the screening process, thus highlighting the importance of improving the functioning of these programs.[47] Furthermore, only 2%-15% of all cases of active TB in the foreign-born population in Canada and the United States are detected during required immigration screening programs (post-landing surveillance, refugee claimants or people applying to change immigration status).[48-51] The majority of TB in the foreign-born occurs outside of pre-immigration screening as a result of reactivation of LTBI. Although TB rates among the foreign-born are highest in the first 5 years after arrival (see Chapter 1, Epidemiology of Tuberculosis in Canada), the risk of TB is higher than that of the non-Aboriginal Canadian-born population throughout their lifetime.[13,45,52] The Canadian Thoracic Society believes this highlights the importance of additional screening programs to control TB in the immigrant population.

Latent TB infection

Detecting (for example, with TSTs or IGRAs) and treating LTBI in the immigrant population after arrival is an attractive alternative to chest radiography screening programs. Unfortunately, LTBI screening programs for immigrants perform poorly. In a systematic review and meta-analysis of studies of LTBI screening and treatment in immigrants after arrival in low TB incidence countries (Canada, United States, Spain, Italy and Australia), only 32% of TST-positive immigrants completed LTBI treatment.[53] This suboptimal performance was due to losses and dropouts at all steps of the process: 69.0% completed screening, and 77.0% of those with a diagnosis of LTBI

were offered treatment; of these, 83.0% started treatment, of whom 71.0% completed treatment.[53] Similarly, LTBI screening and treatment in the post-landing surveillance program in Canada and the United States resulted in only 26% of people with a positive TST completing LTBI treatment.[47]

Challenges and barriers to uptake of LTBI screening and treatment in immigrants

Implementing widespread, comprehensive LTBI screening and treatment programs in migrants is challenging for many reasons, the most important of which is the extremely large pool of migrants at risk who are not easily accessible through present health care programs. The potential pool of migrants at risk of reactivation of LTBI to active disease is enormous, given that there are ~6 million migrants living in Canada, ~200,000 new permanent residents and 1.2 million visitors arriving from countries with high TB incidence each year, of whom ~50% have LTBI.[4,7,8] In addition there are 350,000-400,000 new temporary residents, including foreign workers, foreign students, refugee claimants and those in humanitarian groups, arriving each year in Canada.[6] A recent US study highlights the importance of the potential large pool of unscreened people with LTBI at risk of TB reactivation: only 41% of cases of active TB diagnosed within 1 year of arrival occurred in those who had been screened in the pre-landing screening program. The majority of cases occurred in unscreened people, i.e. temporary workers and exchange students (37%), business travellers and tourists (16%) and non-immigrant visitors from Canada and Mexico (7%).[54] In Canada some temporary workers are screened, but most of these other groups are not (Table 3).

Exposure in countries with high TB incidence may also be an important risk factor in immigrants who have been living in Canada for more than 2 years and return home for prolonged periods. Several studies have estimated that 20%-50% of active TB cases in the foreign-born population are due to recent return travel to their countries of origin.[15-17] Accessing this population is a challenge, as only a minority (20%-30%) seek pre-travel advice, and there are no programs to routinely re-evaluate returning travelers.[55-57] Furthermore, people at increased risk of LTBI reactivation who have medical and/or behavioural risk factors are not easily identified, current diagnostic tools do not permit identification of those at higher risk, and the length of LTBI treatment regimens deters completion (see Chapter 4, Diagnosis of Latent Tuberculosis Infection).

Finally, LTBI screening programs for immigrants and refugees encounter many barriers at the level of the patient, provider and infrastructure/institution. Patient-level barriers include the stigma of TB and its association with HIV, linguistic barriers and difficulties coming to appointments because of inconvenient clinic locations or limited clinic hours.[42,58-60] Provider barriers to offering screening to migrants are related to inadequate knowledge of which migrants should be screened or how they should be followed up.[61-63] Poor adherence to treatment for LTBI is associated with barriers similar to those for LTBI screening. They include linguistic barriers, cultural taboos and stigmatization, low education level, perceived low risk of progression from LTBI to active disease, belief that positive results from TSTs are due to BCG (Bacille Calmette-Guérin), reluctance to undergo venipuncture, and economic factors (costs of travel, lack of insurance, delays in obtaining insurance, missed days at work).[58-60,64-66] Until these issues can be addressed, LTBI screening and treatment in Canada after arrival should be focused on migrants at increased risk of active TB.

Strategies to optimize LTBI screening and treatment in the foreign-born

Control of TB in low-incidence settings will need novel strategies to more effectively access all foreign-born groups at risk of LTBI. Improving cultural and linguistic infrastructure may increase the uptake of screening and treatment in the immigrant population.[42,67-69] Several studies show that having a cultural case manager or that matching migrants to a health care provider with similar language or cultural background increased the probability of LTBI treatment completion.[42,64,67] Educating health care providers in identifying migrants at risk is also an important strategy. In a study in which primary care providers were educated about how and whom to screen for TB, the proportion of patients screened for LTBI increased, and the proportion identified with active TB also increased.[61]

Some of the barriers to delivering LTBI treatment may be best addressed by providing it in an integrated primary care setting where a trusting relationship has been established and where several health issues are being managed at the same time. Clinics with longer hours after the usual work day may help people who have difficulties getting time off work to come to clinic visits. Similarly, engaging migrants will require effort on several levels, including care that is tailored to their linguistic and cultural backgrounds, and better pre-travel counselling in the primary care setting.[55-57] Engaging immigrant community resource agencies may be effective.[70] In addition to programmatic improvements, the development of new diagnostic tests that can identify the 10% of people with LTBI whose disease will ultimately reactivate, and shorter LTBI treatment courses would be ideal. Given the magnitude of human migration, the long-term solution will ultimately depend on investment in global TB control to decrease the TB morbidity and exposure in source countries.[71]

SCREENING OF PEOPLE WITH MEDICAL OR BEHAVIOURAL RISKS FOR TB INFECTION AND DISEASE

MEDICAL RISK FACTORS THAT INCREASE TB REACTIVATION

There are several medical conditions and therapies that increase the risk of TB reactivation (see Chapter 6, Treatment of Latent Tuberculosis Infection). Subgroups with an increased prevalence of LTBI (Table 1) who also have medical conditions that increase the risk of LTBI reactivation should be targeted for screening and treatment.[52] Diabetes is a particularly important medical risk factor, as it is more common in certain immigrant groups and the Aboriginal population, and is associated with a 2-3.6 fold increased risk of active TB development.[72] Diabetes affects more than 2 million Canadians and has an overall prevalence of 6%, increasing with age up to a prevalence of 20% in the 75-79 age group.[73] Immigrants from South Asia have a 3-4 fold higher risk of having diabetes as compared with the Canadian-born population, and immigrants from Latin America, the Caribbean and sub-Saharan Africa have about a 2 fold increased risk.[74,75] End-stage renal disease is another important medical risk factor, as it is a common complication of diabetes. Patients receiving hemodialysis are at substantially elevated risk of active TB, with cited relative risks ranging from 10-25 times the background incidence.[76]

There are no systematic evaluations of screening for and treatment of LTBI among people with medical risk factors for active TB, other than HIV. A recent cost-effectiveness analysis suggested that, at a group level, screening and treatment of individuals with these conditions would have little public health impact and would confer limited gains in quality-adjusted survival.[77] This analysis, however, was based on relative risks of reactivation of 2 or less for most of these conditions.

Recommendations for LTBI screening in the foreign- born and those with underlying medical conditions

For the following recommendations see Table 1 for a list of those with an increased prevalence of TST positivity and Table 1 in Chapter 6, Treatment of Latent Tuberculosis Infection, for the conditions that increase the risk of TB reactivation. The recommendations are summarized in Table 4.

- Routine screening of people with a low prevalence of LTBI and medical risk factors with a low relative risk for LTBI reactivation (i.e. a relative risk of <2.0 compared with a healthy individual without known risk factors for reactivation) is not recommended.
  Conditional recommendation, based on moderate evidence

- Foreign-born children up to age 20 should be offered LTBI screening and treatment as soon as possible after arrival.
  Conditional recommendation, based on moderate evidence

- Refugees from countries with high TB incidence should be offered LTBI screening and treatment up until age 50 years, because refugee status is associated with a slightly increased risk of TB reactivation.
  Conditional recommendation, based on weak evidence

- Population groups with increased prevalence of LTBI (such as the foreign-born from countries with high TB incidence) and with conditions presenting a slightly increased risk of reactivation (i.e. refugee status) should be offered LTBI screening and treatment up until age 50 years.
  Conditional recommendation, based on weak evidence

- Population groups with increased prevalence of LTBI and with conditions that pose a moderate risk of reactivation (i.e. diabetes) should be offered LTBI screening and treatment up until age 65 years.
  Conditional recommendation, based on weak evidence

- Everyone with conditions associated with a high risk of LTBI reactivation should be considered for screening (see Table 4).
  Conditional recommendation, based on moderate evidence

- Providing LTBI screening and care to the immigrant population in a culturally sensitive manner with good access to interpreters should be considered.
  Conditional recommendation, based on weak evidence

Table 4. Recommendations of the Canadian Thoracic Society for groups for targeted LTBI screening

Group at risk	Group to be screened	Age limit for screening
1. Close contacts of an active case of pulmonary TB	As soon as possible after diagnosis of the index case (see chapter 12)	Any age
2. Immigrants from countries with high TB incidence	Fibronodular changes on chest x-ray (usually in the context of Post-Landing Surveillance)	Any age
	All children and adolescents as soon as possible after arrival	Up to age 20 years
	Refugees	20-50 years
	Immigrants and refugees with underlying medical comorbidities with the following risk of TB reactivation:* High risk Moderate risk Slightly increased risk	 Any age Up to 65 years Up to 50 years
3. Medical comorbidities*	All individuals regardless of prior TB exposure should be considered for screening if they have certain medical comorbidities that increase risk of TB reactivation (see Table 1 in Chapter 6 for categorization of risk) High risk Moderate risk Slightly increased risk	 Any age Up to 65 years Up to age 50 years
4. Injection drug user OR the homeless	In the presence of underlying medical comorbidities with the following risk of TB reactivation* High risk† Moderate risk Slightly increased risk	 Any age Up to 65 years Up to 50 years
5. Travellers to countries with high TB incidence‡	≥1 month of travel with very high risk contact, particularly direct patient contact in a hospital or indoor setting, but possibly including work in prisons, homeless shelters, refugee camps or inner city slums. ≥3 months of travel to TB incidence country >400,000/100,000 population** ≥6 months of travel to TB incidence country 200-399/100,000 population ≥12 months of travel to TB incidence country 100-199/100,000 population	Up to 50 years if single post-travel TST Any age if documented TST conversion

Table 4. ***Continued***

Group at risk	Group to be screened	Age limit for screening
HIV positive	See Chapter 10	
Aboriginal Peoples	See Chapter 14	
Health care workers	See Chapter 15	
Residents of long-term care facilities	See Chapter 15	
Residents of correctional facilities	See Chapter 15	

For categories 1-3, **conditional recommendation, based on moderate to weak evidence**

For category 4, 5, **conditional recommendation, based on weak evidence**

*Risk of reactivation for different medical comorbidities is outlined in Table 1 of Chapter 6, Treatment of Latent Tuberculosis Infection.

†For those at **high risk**, strongly consider measures to enhance adherence, such as directly observed LTBI treatment with financial incentives. For all others only consider LTBI screening and treatment provided treatment completion and adequate follow-up for hepatotoxicity can be achieved.

‡For those >50 years and at higher risk of prior TB exposure, i.e. foreign-born, current or previous IDU, Aboriginal people, health care workers or those with pre-existing liver disease, consider doing a pre- and post-travel TST to detect recent conversion. In this case, performance of two-step TST pre-travel would enhance the accuracy of testing after travel to detect true conversions from recent infection. For all other travellers, perform a single TST 2 months after return from travel.[78]

**TB incidence expressed as all TB cases/100,000.

Homeless People

The incidence rate of active TB in homeless populations is markedly higher than in their non-homeless counterparts. Despite the challenges in accurately quantifying the number of homeless people, one study estimated the incidence rate of active TB in Toronto's homeless population to be 71 cases per 100,000.[79] Homeless people are also frequently envisioned as Canadian-born individuals; however, recent studies have identified a growing proportion of foreign-born homeless people with active TB.[80] Given the elevated risk of TB drug resistance in many foreign-born populations, this study highlights the risk of drug-resistant disease emerging and propagating within urban shelter systems; hence, adequate infection control measures, including environmental controls in these institutions are recommended (see also Chapter 15, Prevention and Control of Tuberculosis Transmission in Health Care and Other Settings).

The prevalence of LTBI in homeless populations is also markedly elevated relative to non-homeless populations and has been reported as ranging between 18% and 51%.[81] Many homeless people are at increased risk of active TB not only because of repeated TB exposures but also because of the high frequency of medical comorbidities that can compromise their immunity.[82] Among homeless people with active TB, the frequency of HIV coinfection has been reported to range from 5% to 60%.[80,83-85] While LTBI therapy offers the potential to significantly reduce the risk of active TB in homeless people, it is complicated by challenges with adherence to therapy and adverse drug reactions. LTBI treatment completion rates in homeless populations have been reported to be as low as 19%. However, the use of incentives and enablers, and directly observed (preventive) therapy have been used effectively to increase the likelihood of successful treatment completion up to 44%.[86]

Alcohol and/or substance abuse can complicate the treatment of LTBI, not only by affecting adherence to therapy but also by increasing the risk of adverse drug reactions. Concurrent alcohol abuse during LTBI therapy, particularly with isoniazid, markedly increases the risk of hepatotoxicity (up to 4 fold with daily alcohol intake).[87] While LTBI treatment with rifampin is much shorter in duration than isoniazid and is associated with a lower risk of hepatotoxicity,[88] it is important that health care providers carefully assess and exclude active TB before considering its use. This is because the development of rifampin resistance (if individuals are inadvertently treated for LTBI with rifampin when they have subclinical, undetected active TB) would have very serious short-term clinical implications for patients, and could have lasting public health repercussions to those accessing or providing services within the shelter system.[89] Given the potential risk of hepatotoxity due to high rates of associated alcohol use and low rates of treatment completion, efforts to offer LTBI screening and treatment should be reserved for those with a moderate or high risk of TB reactivation.

- The homeless should be offered LTBI screening and treatment up to age 65 if they have an underlying medical condition that confers moderate risk of reactivation or at any age if there is a medical condition that confers a high risk of reactivation.
  Conditional recommendation, based on weak evidence

- Homeless people with medical conditions associated with a high risk of reactivation should be considered for special measures to enhance adherence, such as directly observed LTBI treatment and/or incentives and enablers.
  Conditional recommendation, based on weak evidence

Injection Drug Users

Injection drug use is associated with a heightened prevalence of LTBI[90-92] and with blood-borne pathogens. In particular, chronic hepatitis C infection has been identified with high frequency in studies of injection drug users (IDUs), prevalence rates exceeding 60%.[93,94] Chronic infection with hepatitis B is also frequent among IDUs,[84] and although concurrent infection with hepatitis B, C and/or HIV is less common, these viral infections in combination can accelerate the course of liver disease and consequently present heightened risks of hepatotoxicity to those receiving LTBI treatment. Despite the increased risk of drug toxicity, many studies have shown that LTBI treatment can be safely administered to IDUs provided that their liver function tests and clinical status are carefully and regularly monitored.[95-97] While asymptomatic, low-grade elevations in liver function tests are not uncommon in individuals with viral hepatitis, a significant proportion of these people are still able to safely complete LTBI therapy. People with LTBI who have experienced complications with isoniazid or have a high baseline risk of hepatotoxicity could be considered for treatment with rifampin once the presence of active TB has been carefully excluded.

The benefits of LTBI therapy can be substantial, particularly for IDUs with HIV infection or other forms of immunosuppression. However, treatment adherence among currently active IDUs may be suboptimal and consequently can decrease the overall effectiveness of treatment. A systematic review of LTBI therapy among IDUs in Canada and the United States revealed that treatment completion rates ranged between 39% and 70%.[98] As with other vulnerable populations, incentives and enablers and/or directly observed therapy for LTBI can increase the

likelihood of successful treatment completion.[98] Two US-based studies modeling the health and economic effects of programs dedicated to LTBI treatment in IDUs have shown that such programs can be cost-effective.[99,100] Given the potential risk of hepatotoxity due to a high rate of associated alcohol use and/or coinfection with viral hepatitis, and low rate of treatment completion, efforts to identify and offer LTBI screening and treatment should be reserved for those with a moderate or high risk of TB reactivation.

- Current or past intravenous drug users should be offered LTBI screening and treatment up to age 65 if they have an underlying medical condition associated with moderate risk of reactivation, and should be offered screening at any age if they have a medical condition associated with a high risk of reactivation.
  Conditional recommendation, based on weak evidence

- Those at highest risk of reactivation should be considered for special measures to enhance adherence, such as directly observed LTBI treatment and/or incentives and enablers.
  Conditional recommendation, based on weak evidence

Travellers

Travellers to countries with higher TB incidence are at risk of acquiring infection during travel. The risk increases with longer duration of travel and higher TB incidence in the destination country, and is also affected by the type of travel and the work done (if any) in these countries. Long-term travellers to countries with higher TB incidence have a similar risk of acquiring infection during their visit as the local population.[101] Risk is particularly elevated for travellers who work in health care.[101] Similarly, immigrants who return to their home countries to visit friends and relatives are at risk of exposure to TB infection and development of disease. Two U.K. studies in immigrants from the Indian subcontinent estimated that ~20% of cases of TB in the U.K. were due to recent travel to their countries of origin.[16,17] More recently, 56% of TB cases in the Moroccan immigrant population in the Netherlands were associated with recent travel to Morocco.[15]

The Committee to Advise on Tropical Medicine and Travel (CATMAT) has published guidelines on risk assessment and prevention of TB in travellers, including screening for and treatment of LTBI in travellers who make prolonged or high-risk trips.[78] These are summarized in Table 4 but have been modified to reflect the change in the definition of a high TB incidence country, from 15/100,000 smear-positive cases to 30/100,000 population of ALL TB cases. See http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/acs-dcc-5/index-eng.php for additional information. For most travellers judged to require screening for LTBI, a single post-trip TST or IGRA (see Chapter 4) should be sufficient.[102] For individuals who are expected to undergo serial or repeated testing (e.g. health care workers), a pre-travel two-step TST is recommended (and IGRA is NOT recommended, see Chapter 4). Pre-travel testing is also recommended for people in whom the distinction between conversion and longstanding infection is particularly important, e.g. those at increased risk of treatment toxicity because of older age, alcohol consumption or liver disease. **Conditional recommendation, based on weak evidence**

CONCLUSIONS AND RECOMMENDATIONS

The selection of people as suitable candidates for targeted LTBI screening and treatment is based on consideration of their risk of prior TB exposure and of reactivation, balanced against their risk of hepatotoxic effects and the likelihood of safe completion of treatment. To improve uptake of LTBI screening in immigrants, investment in TB education programs for patients and providers and in infrastructure is suggested, as well as programs that can be offered in a culturally sensitive manner with good access to interpreters. In the homeless population and injection drug users, patients with LTBI should be assessed for hepatitis comorbidities that may increase hepatotoxicity; incentives, enablers and directly observed therapy should be considered to achieve LTBI treatment completion for those who have immunosuppressive illness or are HIV positive. For a summary of specific recommendations for each group see Table 4.

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