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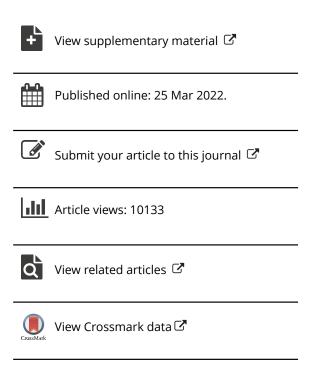
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CANADIAN TUBERCULOSIS STANDARDS—8TH EDITION



Chapter 11: Tuberculosis contact investigation and outbreak management

Elizabeth Rea^{a,b}, Jessika Huard^{c,d} and Robyn Lee^{b,d}

^aTuberculosis Program, Toronto Public Health, Toronto, Ontario, Canada; ^bDalla Lana School of Public Health, University of Toronto, Ontario, Canada; ^cDirection régionale de santé publique, Centre intégré universitaire de santé et de services sociaux du Centre-Sud-de-l'Île-de-Montréal, Montréal, Québec, Canada; ^dNunavik Regional Board of Health and Social Services, Public Health, Kuujjuaq, Québec, Canada

KEY POINTS

- Contact investigation and follow-up is an essential component of tuberculosis (TB) programs in Canada, and of the World Health Organization (WHO) framework for TB elimination in low-burden countries.
- Only pulmonary and laryngeal TB are infectious, with limited exceptions. Contact investigation should be prioritized according to the infectiousness of the source case, extent of exposure and immunologic vulnerability of those exposed; contact investigation should be carried out for both sputum smear-negative and smear-positive cases. Contact investigation is iterative: it should be expanded if initial results indicate that transmission has occurred.
- The objective of contact investigation is to rapidly identify and treat any secondary cases, and to identify contacts with latent TB infection (LTBI) in order to offer preventive treatment. Source-case investigation ("reverse contact investigation") should be done for children under 5 years old with TB disease.
- Household members are consistently at highest risk, even when the index patient has smear-negative disease. In theory, there is no amount of exposure to infectious TB that is absolutely without risk; in practice, almost all transmission occurs with close, prolonged or repeated contact over days or months.
- Clinical assessment, TB screening and follow-up of contacts should follow standard practices; and TB programs should have clearly identified clinical referral pathways.

1. Introduction

Contact investigation and clinical follow-up of those who are infected or have active disease is an essential component of TB programs in Canada, and of the WHO framework for TB elimination in low-burden countries.¹⁻³ Several studies have found contact investigation incorporating treatment of the identified active cases and contacts with LTBI to be cost-effective⁴; in modeling studies, household contact investigation LTBI treatment follow-up may contribute as much

as 18-27% to a decline in active TB incidence over 5-15 years, compared to no contact investigation and follow-up.^{5,6}

Reporting of active TB disease is required in all Canadian jurisdictions; in part, this is to ensure that contact investigation can be carried out quickly, in an organized, collaborative manner. TB programs in North America typically find a median of 4 (average of 6) close contacts for each TB case.^{7,8} The majority of Canadian-born children with TB disease have a known close TB exposure, highlighting the importance of contact investigation, especially in the household.⁹

Contact investigation demands considerable time, expertise and coordination. It is best carried out by public health/ TB program authorities in collaboration with treating clinicians and other providers. Anxiety, stigma and lack of knowledge about TB among those exposed may be major issues. Provision of clear, credible and consistent information about TB and the clinical follow-up plan is essential.

1.1. Glossary of terms

(see Appendix A - Glossary).

2. Objectives of contact investigation

Contact investigation has three main objectives. In order of priority these are:

1. Identify and initiate treatment for secondary cases of active TB disease

Typically, 1-2% of close contacts are found to have active disease at the time of contact investigation; the proportion is about 3.3% for smear-positive pulmonary patients.^{7,10} Early identification and treatment reduces the morbidity and mortality risk of TB disease for these individuals and rapidly reduces the risk of further transmission to others. This objective is particularly critical for contacts who are vulnerable to rapid progression if infected, such as children less than 5 years of age or those with significant immune suppression.^{9,11}

2. Identify and treat the infectious source patient if the index patient is less than 5 years old.

TB disease in a young child (whether pulmonary or extra-pulmonary) is a sentinel event. The younger the child, the more likely this reflects recent transmission, usually from an undiagnosed adolescent or adult in the household, or other caregiver close to the child (see Chapter 9: Pediatric Tuberculosis). 9,12,13 Source-case investigation (also known as "reverse contact investigation") should be carried out when TB disease is diagnosed in any child less than 5 years old. 14,15 Source investigation should also be done when a cluster of tuberculin skin tests (TST) conversions is identified in an institutional setting with no known source patient, and may be considered for patients with pleural TB if TB program resources allow. 16 However, source investigations usually give very low yield; even for patients less than 5 years old a source case is identified in less than half of investigations.¹² Source-case investigation is not advised for individuals of any age with LTBI identified on a routine screening.

3. Identify contacts with LTBI in order to offer preventive treatment.

Without treatment, about 5% of newly infected contacts will develop active disease within two years of exposure. Thus, a well-functioning contact investigation and follow-up program can reduce morbidity and mortality among infected contacts, and over time can contribute substantially to TB elimination.

3. Principles of contact investigation

3.1. Prioritize the work

This is the most important principle. Contact investigation should be prioritized according to the infectiousness of the source case and the extent of exposure and immunologic vulnerability of those exposed. This will allow the TB program to put the most effort into those contacts at most risk.

3.2. Rapidly initiate contact investigation

When notification of a new TB diagnosis is received, the public health authority should ensure that all medical investigations to confirm the diagnosis and determine the degree of infectiousness are under way, and the patient is in home isolation or hospital airborne isolation. Once pulmonary/ laryngeal TB is confirmed (by GeneXpert or other nucleic acid amplification test, by positive smear in regions with little non-tuberculosis mycobacterium infection or by positive culture), or if the clinical suspicion is sufficiently strong to begin TB treatment pending laboratory confirmation, then investigation of household and other high-priority contacts should begin promptly, especially for any children less than 5 years old and immunocompromised individuals (see Chapter 2: Transmission and Pathogenesis of Tuberculosis and Chapter 3: Diagnosis of Tuberculosis Disease and Drug-resistant Tuberculosis). Investigation of contacts beyond the high-priority group (see below) should always await laboratory confirmation of the diagnosis.

Good practice statement

• The initial contact tracing interview should be done within three days of the TB patient being notified to the public health TB team. Screening of high-priority contacts should begin within the next 7 days.

3.3. Assess the risk of transmission

The transmission risk assessment focuses on how infectious the patient is, over what time period, and the duration, proximity and characteristics of the space where exposure

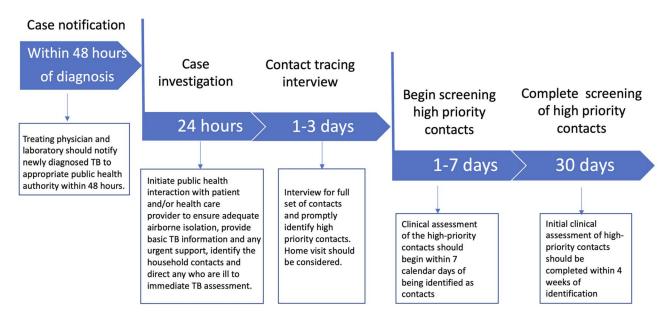


Figure 1. Timelines for contact investigation.



occurred. Factors associated with TB transmission are reviewed in detail in Chapter 2: Transmission and Pathogenesis of Tuberculosis.

3.3.1. Infectiousness of the index patient

The single greatest factor determining the extent of initial contact investigation is the degree of infectiousness of the index patient.17 With limited exceptions, only adolescents and adults with pulmonary and larvngeal TB are infectious and require contact investigation (see also Chapter 2: Transmission and Pathogenesis of Tuberculosis and Chapter 9: Pediatric Tuberculosis). 14,18 Pleural TB should be assumed to include pulmonary involvement until ruled out by sputum results. Sputum-smear status is the most reliable indicator of infectiousness; the "worst" (ie, most positive) result is used to evaluate infectiousness. 19,20 Infectiousness for both drug-resistant TB¹⁰ and patients co-infected with human immunodeficiency virus (HIV) should be evaluated by the usual criteria.

3.3.2. Likely period of infectiousness

There is no clear epidemiologic evidence on when infectiousness begins. Pulmonary TB is generally considered to become infectious at the onset of cough (or worsening of a baseline cough), and this should be the priority timeframe for contact investigation. If no cough or other respiratory symptoms are reported, the onset of other symptoms attributable to TB may be used to estimate the onset of infectiousness. In practice, it is often difficult to know with certainty when symptoms began.

The US Centers for Disease Control and Prevention¹⁴ recommends, based on expert opinion, that patients with smear-positive or symptomatic disease should be considered to have been infectious for three months before onset of respiratory symptoms or the first positive finding consistent with TB, whichever is longer. Asymptomatic, non-cavitary TB with a negative smear should be considered infectious four weeks before the first positive finding consistent with TB.

For contact investigation, the period of infectiousness effectively ends when the index patient is placed in isolation from others (this may be before or after diagnosis; at home with no contacts, or on admission to formal airborne isolation in hospital) or is no longer infectious due to TB treatment, whichever comes first. See also Appendix B: De-isolation review and recommendations.

3.3.3. Degree of exposure to the index patient: duration,

Household members are consistently at highest risk of becoming infected, even from index patients with smear-negative disease, as they have very close contact over extended periods. 10,11,20-24 Beyond this group, there are so many variables in TB transmission that it is difficult to quantify the exact duration of exposure that constitutes a significant risk, and each case should be evaluated on its specific characteristics. 20,22,23,25,26 In theory, there is no amount of exposure to infectious TB that is absolutely

without risk; in practice, almost all transmission occurs with close, prolonged or repeated contact over days or months.

It is not social closeness to the person with TB, but rather, the amount of time in a shared airspace that is the critical issue. For example, IT personnel may report working very closely with team members but spend little time together in shared air space if the work is mainly done electronically; someone who has minimal interaction with the TB patient but works in the neighboring cubicle is at much higher risk. Among household members, those who share a bedroom with the TB patient are at higher risk, independent of other exposure factors.²⁰

For context, 2 large North American studies (each with more than 3,000 contacts) identified 120-250 cumulative hours of exposure as a reasonable threshold for contact investigation. 20,25 Another study found that contacts who had LTBI had a mean of 321 cumulative hours of close exposure to the index patient, compared with 211 hours for uninfected contacts.²³ In school settings, it is generally only students who share classes with an infectious person who are at risk; consistent with the closeness of interactions, schoolchildren are more likely to become infected by a fellow student with TB than by a teacher with TB.27-31 Two Scandinavian studies documented minimal risk of transmission to children in daycare settings with less than 18-24 hours of cumulative exposure to cavitary, smear-positive adult caregivers. 32,33 A transmission study in a Canadian homeless shelter suggested 5 nights (cumulative) in the same room with a cavitary, smear-positive patient as a pragmatic risk threshold for contact investigation.³⁴ As an extreme example, in a progressively expanded outbreak investigation among university students exposed to an index patient with laryngeal and cavitary pulmonary TB, the risk of infection per hour of classroom exposure was more than 1% for several shared classes; some contacts converted with as few as 3-4 hours of exposure per week over the infectious period.³⁵ Rarely, children less than 5 years old have been infected following extremely short exposure (<30 minutes) in a small space with a highly infectious adult.³⁶

3.3.4. Characteristics of the space where exposure occurred

The room size and ventilation where exposure occurred (eg, large cafeterias or lecture halls vs small seminar rooms) may reduce or facilitate transmission: exposure in cramped, ill-ventilated spaces may lead to transmission in much shorter exposure times. Formal ventilation assessment is not generally necessary. However, in hospitals, where ventilation rates can vary greatly, it may be possible to arrange for facility staff to measure air exchanges per hour in the exposure areas. Exposures in areas with lower ventilation can be prioritized, while those with very high ventilation pose much lower risk outside of unprotected aerosolizing procedures (see Chapter 14: Prevention and Control of Tuberculosis Transmission in Healthcare Settings). Smoking tobacco or other substances with others increases transmission risk, particularly in confined spaces.^{37–41} TB transmission is rarely

thought to occur outdoors, but has been occasionally been documented in groups who smoke together regularly.⁴²

Figure 2 illustrates the conjunction of time, proximity and characteristics of the shared air space to assess exposure risk. In this example of exposure in an open-plan office, duration of exposure to the infectious patient was relatively long, but in a large, well-ventilated space. A coworker whose desk is very close nearby has a higher risk of transmission than others sitting far away.

3.4. Contact interview

The interview of an infectious TB patient for contact tracing is one of the most important parts of the investigation. It takes considerable skill and is most successful when done by staff with training/experience in public health interview techniques, including motivational interviewing, and who are familiar with local social patterns. 43-46 The initial interview can also lay the foundation for long-term adherence to TB treatment, and should be approached as an integral component of TB care for the patient. Most TB patients in Canada were born in countries with high TB incidence or in First Nations/Inuit communities (see Chapter 1: Epidemiology of Tuberculosis in Canada), so language and cultural perceptions about TB, TB stigma and health are very important to support the trust and rapport essential for full disclosure. 44,47 Interviews are best carried out in the language the patient is most comfortable with, if necessary through a professional interpreter or an objective third party (not a family member). Face-to-face interviewing, in privacy, is ideal.

Confidentiality of contact investigations should be stressed, but note that legislation may permit or require release of information about the case's diagnosis to specific individuals (including public health authorities). For example, some information may have to be shared in confidence with selected individuals (eg, a school principal) in order

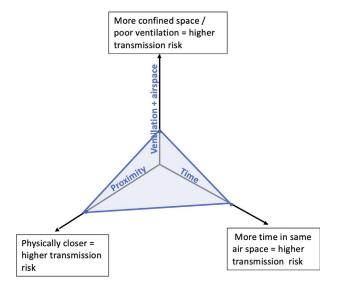


Figure 2. Evaluating exposure risk: Time, proximity, characteristics of the shared air space.

to identify or reach contacts and ensure that they, too, get the medical follow-up they need.

Interviewing is usually best extended over two or more sessions, a week or more apart, as the patient becomes more familiar with public health staff, and the initial stress and anxiety over the diagnosis are resolving. Patients may find it helpful to look at contact lists on their phone, social media, or calendars as a memory aide. Proxy or supplemental interviews with family, close friends, work supervisors, etc. (ideally with patient permission) may be helpful if patients are unable or unwilling to participate. All patients should routinely be asked about the locations where they spend time regularly, as well as names of specific close contacts. Location-based investigation is the basis for social-network approaches discussed below; it is especially critical when highly infectious patients are unable (or unwilling) to name specific contacts in the settings where they spend time. 48-51 Location-based screening will inevitably include some nonexposed individuals, but may be the only way to reach contacts at risk in those settings.

All interviews to identify contacts should include the following:

- Name-based information (including name, alias/nickname, phone, address, email/social media contact, age, nature of interaction):
 - Description of the household/congregate setting; household contacts and their ages (includes anyone who regularly sleeps at the home)
 - Other households the case visits frequently, particularly overnight
 - Close friends, relatives and caregivers who are visited or are present in the home at least once per week (how often, for how long)
 - Close colleagues at work (how often together, nature of interaction)
 - Transportation to work/school (carpool, public transit, etc.)
 - Any contacts who are ill with potential TB symptoms or who have known TB
 - Any contacts who are children, and their ages 0
 - Any contacts who are immunosuppressed (people with HIV, cancer patients, etc)
 - Any major events (eg, weddings, funerals, parties) the case attended while infectious

· Location/site-based information

- Work/school location and description of setting (type of work, size of room, ventilation, lunch/break rooms, etc)
- Place of worship, volunteering, clubs, sports teams, recreation or drop-in programs, hobbies or other locations visited frequently
- Smoking tobacco or other substances (where, who else smokes in the same location at the same time)
- Any other homes, "party sites," places or groups the patient has regularly been in or with while infectious
- Any recent travel or visitors staying at the home within the previous 2 years; if so, obtain details



A site visit to assess the home is best practice, even if the initial interview is carried out in hospital, to assess feasibility of home isolation, identification of additional household contacts, identification of any social/practical issues relevant to treatment adherence, and so forth. Site visits to the school or workplace and other exposure locations are also helpful to make contact-investigation decisions (to assess environmental characteristics such as size, layout, use of the space and ventilation; interviews with a direct supervisor can help to identify potential contacts).52 Discretion is important, as a site visit may precipitate unnecessary anxiety and/or lead to a breakdown of confidentiality and repercussions for the patient. It is advisable to arrange site visits directly with senior personnel, such as a school principal, division manager or occupational health manager, and emphasize the importance of maintaining confidentiality as much as possible (see Site-based Screening, in the following sections).

4. Organized, systematic contact investigation

4.1. Prioritizing contacts

Recommended priorities for initial contact investigation are outlined below. These are guidelines: it is always important to consider the specific circumstances, work from first principles of TB transmission and re-evaluate according to the results of the investigation as they become available. See Appendix 1 for an example of a structured, risk-based tool to guide initial contact investigation.

Contacts can be prioritized according to high, medium and low priority:

- High-priority contacts are those with the most exposure, and those with the highest risk of progression to active TB if infected. They can include:
 - household contacts, who regularly sleep in the same household as the infectious case on an ongoing basis (eg, 3 or more times per week) and can include members of an extended family, roommates, boarders, couch-surfers, etc.;
 - household-like contacts in congregate settings, such as homeless shelters, jails and long-term care facilities (generally, room-mates or cell-mates);
 - caregivers with extensive/daily exposure to the index patient;
 - contacts exposed (ie, without an N95 mask) during bronchoscopy, sputum induction, autopsy or other aerosolizing medical procedures (see Chapter 14: Prevention and Control of Tuberculosis Transmission in Healthcare Settings; and
 - medium-priority contacts who are at high risk of progression of LTBI to TB disease (eg, aged less than 5 years, HIV, dialysis, transplant, silicosis (see Chapter 4: Diagnosis of Tuberculosis Infection).
- · Medium-priority contacts have regular contact with the index case and share air space at least several times weekly but do not sleep in the same household most of the time.

Most social, school and workplace close non-household contacts fall into this group, which may include:

- caregivers with less extensive exposure to the case;
- regular sexual partners;
- close friends;
- extended family;
- daycare and primary/secondary school classroom
- coworkers who work in close proximity, particularly in small rooms;
- homeless/underhoused individuals using the same drop-in program regularly; and
- low-priority contacts who are at high risk of progression of LTBI to TB disease, (eg, aged less than 5 years, HIV, dialysis, transplant, silicosis (see Chapter 4: Diagnosis of Tuberculosis Infection).
- Low-priority contacts are casual contacts who spend time regularly but less frequently with the infectious case. Investigation should be expanded to this group only if there is significant evidence of transmission among closer contacts. This group may include:
 - high school students who share only one course with the TB patient;
 - classmates in very large college/university classes;
 - less exposed colleagues at work;
 - members of a club, team or other social/recreational/ religious group; and,
 - extended family members who are seen occasionally.

As shown in Figure 3, for index patients who are smear-positive or have cavitary disease, the initial group of contacts to investigate should include both high- and medium-priority contacts. For smear-negative index patients, initial contact investigation should include high-priority contacts only; investigation should be expanded to medium-priority contacts only if there is evidence of transmission among the closer contacts.

The specific circumstances should always be considered (see the Risk Assessment section). For example, a choir group meeting once per week to sing close together indoors may pose significant risk53 but a regular outdoor soccer game generally poses little risk.

Expansion of the investigation to low-priority contacts should be only undertaken if there is clear evidence of transmission in the initial investigation, moving in a concentric circle model to the group with next-closest contact (see the section on Expanding Contact Investigation).

4.2. Standard approach to the screening and clinical evaluation of contacts

Clinical assessment, TB screening and follow-up should follow standard practices, and TB programs should have clearly identified clinical referral pathways for contacts (see Chapter 4: Diagnosis of Tuberculosis Infection and Chapter 9: Pediatric Tuberculosis). Participation rates for TB screening may be higher if it is done directly by TB program staff, whether at the home/exposure site, or at a TB clinic.

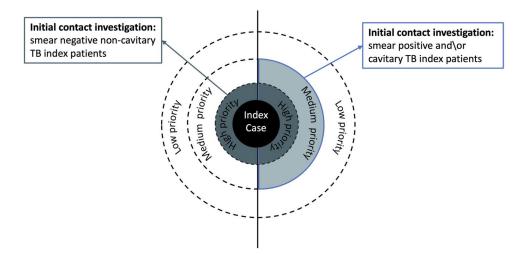


Figure 3. Scope of initial contact investigation.

All identified contacts who have no symptoms of TB disease, and are not already known to have tested positive on a TST or an interferon-gamma release assay (IGRA), should be assessed for LTBI. The results should be interpreted regardless of Bacille Calmette-Guérin (BCG) vaccination status. Similarly, for people whose first-ever TST and/ or IGRA is performed because of the contact investigation, a positive result could reflect infection in the past (remotely) rather than by the recent case. Nevertheless, because of the risk associated with recent exposure, for clinical and public health management, the positive result must be interpreted as a recent infection (see also Chapter 4: Diagnosis of Tuberculosis Infection). If a TST is the screening test for LTBI, high-priority contacts should ideally have both an initial TST immediately and a second TST at least 8 weeks from the last day of exposure, to identify conversion. If LTBI screening is done by IGRA, a single test at 8 weeks after exposure should be done.

In many medium-priority exposure settings, it is most practical to do a single round of screening after 8 weeks from the last exposure. Especially for non-household contacts, participation rates drop significantly between initial and post-8-week screenings as the level of initial anxiety declines, with up to 50% of those whose initial TST is negative lost to follow-up.⁵⁴ Also, as more time elapses before the initial test, it is progressively less likely that conversions will be detectable since many infected contacts may have already converted to a positive TST. Thus, if an initial screening cannot be organized before 4 weeks from the last exposure and loss to follow-up minimized, it is generally more efficient to do a single post-8-week screening. In populations in which many people have prior exposure to TB or BCG vaccination (eg, immigrants from high-incidence countries), this also avoids false TST "conversion" related to boosting. In the rare situation that low-priority contacts are investigated, we suggest only a single test at least eight weeks from the last day of exposure.

A 2-step TST (two TSTs done a week apart) is not equivalent to an initial and post-8-week TST. Two-step TSTs are not appropriate in contact investigations (see Chapter 4: Diagnosis of Tuberculosis Infection).

4.3. Contact investigations in special settings

See also Chapter 12: An Introductory Guide to Tuberculosis Care...Serving Indigenous Peoples and Chapter 14: Prevention and Control of Tuberculosis Transmission in Healthcare Settings.

4.3.1. Congregate settings and location-based screening

Screening of medium-priority contacts in schools, workplaces, hospitals, correctional facilities, shelters and other congregate settings is generally most efficiently and effectively carried out on site, especially if the number of identified contacts is large. However, it is critical to coordinate with site leadership and be very organized (see Appendix 2 for a recommended approach).

Unless the investigation is conducted in a systematic, risk-based manner, it may result in hundreds of "contacts" with limited or unknowable exposure and often dismal participation rates. There is often pressure to initiate widespread contact investigation from the outset (eg, to an entire school, including many low-priority contacts). If indiscriminate screening is performed with no accounting of exposure parameters, however, interpretation of results is extremely difficult. Unless the individual has a documented prior TST/ IGRA result it is generally impossible to differentiate between a new versus remote infection in the context of a contact investigation. Contacts with minimal exposure may then be mistakenly identified as recently infected and the investigation expanded yet further.

Anxiety may be minimized by limiting the delay between contacting the site and conducting testing, ensuring that key people at the site get the same information at the same time and holding general education sessions about TB and the investigation plan. Communication from all personnel involved in the investigation should be clear, credible and consistent, especially about the actual level of risk involved and the clinical follow-up plan.



4.3.2. People affected by homelessness

Patients with TB who are homeless or underhoused may also suffer from alcoholism, drug addiction or mental illness, as well as other medical co-morbidities.^{55,56} They often have poor access to health services, resulting in delayed TB diagnosis, worsening of the disease, prolonged infectiousness and thus large numbers of contacts who need to be assessed.⁵⁷⁻⁵⁹ Many homeless shelters and rooming houses (single-room occupancy hotels) are crowded and have poor ventilation, making them high-risk settings for transmission. Where baseline prevalence rates of TST positivity are high, this also means that a large number of contacts will require further assessment and possible LTBI treatment.

Contact information can prove difficult to gather from individuals experiencing homelessness or severe addictions, related to recall, trust and competing priorities; contacts may be difficult to locate and have low participation rates for TB screening. These challenges can be made more manageable by recognizing that such patients are not "business as usual," prioritizing efforts on risk and impact, ensuring person-centered care, collaborating with partners in the homeless/underhoused services sector and allocating adequate resources.⁶⁰ It is generally most productive to try to identify any particularly close friends or longer-term roommates by name, and to focus on location-based investigation for medium-priority contacts.⁶¹⁻⁶³ Homeless individuals may be highly mobile, with many locations exposed. Shelters may have bed logs, which can help to identify roommates; in large shared rooms, prioritize those who spent the most nights with the case and slept closest.34,64 Also questions should be asked regarding time spent at drop-in centers or soup kitchens providing services for the homeless and underhoused (day-use shelters), libraries, bars, "party houses," parks, and so forth. Staff at shelters or social service agencies and close friends or family may be able to identify daily patterns or specific close contacts. If there are gaps in the history during the infectious period, checking for recent hospitalizations or detainment in a correctional facility may identify additional exposures in these settings.

Homeless contacts may have significant challenges following through on TB screening, medical evaluation and treatment for LTBI.65 TB programs should prioritize active case finding in order to curtail additional transmission in this high-risk group, and include LTBI screening if the program will be able to support counseling, follow-up and treatment for infected individuals. Non-judgmental and supportive TB staff, screening activities with the explicit goal of reducing barriers to participation and judicious use of incentives and enablers can help increase participation rates. 66,67 It may be possible to find "missing" contacts through confidential alert lists at key service providers so that if these individuals arrive, public health/TB program staff can connect with them for follow-up, though it is essential that partner agencies do not stigmatize these individuals.

Screening on-site at the exposure location and/or in a single session will usually have more success than arrangements involving extra visits or travel (eg, sputum collection

or a portable chest x-ray machine at a shelter-based screening clinic; a one-stop-shop approach at a hospital TB clinic).67-71 Similarly, IGRA may be preferable to TST for LTBI assessment if blood collection can be done on site. Both tests require individuals to be located twice if the goal is initiation of LTBI treatment, but the timeline for the second visit is not so constrained for IGRA as it is for reading a TST. Active participation and encouragement from trusted staff at the shelter or day program during screening clinics is especially helpful. Persistence and flexibility are critical; someone who is not willing to participate on one day may be willing another time.

4.3.3. Contacts during air travel and other transport

The risk of TB transmission during commercial airplane travel is low, and the value of actively screening airplane contacts is limited.⁷² Nevertheless, the WHO has published guidelines outlining the procedures for notifying contacts exposed on international flights with a total duration of ≥8 hours within the previous three months.⁷³ Notification of people with TB who report a history of air travel while infectious should be made to the Public Health Agency of Canada (PHAC) through the provincial/territorial TB program. The reporting form can be found at https://www. canada.ca/en/public-health/services/diseases/tuberculosis/ health-professionals.html#a6.

The few published reports of contact tracing after exposure to TB on buses and trains indicate that transmission is possible on repeated daily exposure to the infectious individual, or on long-distance/multi-day trips.⁷⁴ Such events appear rare, and usually involve highly infectious patients and specific environmental circumstances (eg, daily school bus travel on a crowded, long-duration route in winter, with closed windows and recirculated air).⁷⁵ Taxi rides for local travel have not been associated with transmission.⁷⁶ There is no evidence to support contact tracing related to local public transportation, particularly given the logistic hurdles and considerable inefficiency of contact tracing in these circumstances.⁷⁷

4.3.4. Contact during residence or travel in a high-TBincidence country

This is covered in Chapter 13: Tuberculosis Surveillance and Tuberculosis Infection Testing and Treatment in Migrants.

4.4. Expanding contact investigation

Contact investigation is iterative; the results of each contact investigation should be reviewed by the public health TB program as they become available, to guide decisions about expansion and/or additional outreach interventions. Recent transmission is considered to have occurred if a secondary case of active TB is identified in any contact, there are clear TST conversions among contacts, the prevalence rate of TST ≥10 mm among contacts is significantly higher than expected (for example, 60% among contacts when the

expected prevalence rate is 40%) or a child contact less than 5 years is infected (without another probable source). See Appendix 3 for a table of LTBI prevalence in various Canadian population groups. A fundamental challenge is that transmission can be very difficult to evaluate when the background rate of positive TST results is unknown or high. This is often the case in Canada, where the majority of patients with TB — and many of their close contacts - are foreign-born, originally from high-TB-incidence countries; it is also the case in Indigenous communities with high rates of TB. Thus, Canadian-born contacts with no high-risk travel, particularly children, may have the clearest results for assessing transmission as they are less likely to have prior TB exposure (see Chapter 4: Diagnosis of Tuberculosis Infection).

When there is evidence of transmission, the investigation should first address any remaining unassessed high-priority contacts, and investigate medium-priority contacts if this has not already been done. Genotyping/whole genome sequencing to compare index and secondary cases should be requested, but further contact tracing should not be delayed pending results. Expansion to low-priority contacts with the next-most level of exposure or who are young children/immunocompromised, in a concentric circle manner, should only be considered if recent transmission is found in medium-priority contacts.

The probability of finding infected individuals among less-exposed contacts, and the likelihood that this group of contacts will follow up on screening and LTBI treatment recommendations, should also be considered in any decision to expand from the initial set of contacts. 7,11,20,25 Contact participation rates tend to be lower in less-close contacts, contacts of less-infectious patients and in adults compared with children. 78,79 For some TB patients, it may not be possible to identify a feasible group of next-most-exposed contacts. Individuals with only transient or occasional exposure (eg, attending the same school or workplace but not in the same classroom or area of the workplace; customers at a store with a staff case) rarely warrant investigation in the absence of a declared outbreak.80

5. Classical TB genotyping, whole genome sequencing and social network analysis: Additional tools for detecting transmission and outbreaks

The following techniques are key programmatic tools for outbreak detection and response, along with standard field epidemiology data.81,82

Mycobacterial interspersed repetitive units: Variable Number Tandem Repeats (MIRU-VNTR) involves counting the number of repeats in up to 24 sites in the Mycobacterium tuberculosis (M. tuberculosis) genome and using this information to generate a signature pattern. If the MIRU-VNTR patterns of isolates from two persons are different, this usually means there was no transmission, while if the patterns are the same, this may support recent transmission

between them, that can then be refuted or confirmed by the epidemiologic investigation. This technique can also be used to help determine whether recurrent TB is a relapse or new infection, and to investigate potential specimen mix-ups in the lab.

Whole genome sequencing: Whole genome sequencing (WGS) provides information on nearly 100% of the M. tuberculosis genome. Single base-pair changes, called single nucleotide polymorphisms (SNPs), in one patient's M. tuberculosis genome can be compared to another's to help rule out transmission, by applying a specific threshold of similarity as measured in SNPs. In Canada, WGS for TB was first applied to an outbreak in British Columbia more than a decade ago.⁵⁰ WGS identified two separate transmission clusters, whereas only one was identified with MIRU-VNTR. WGS has since been applied in a variety of settings, including to investigate transmission among persons experiencing homelessness in Toronto⁸³ and in Northern Canada.^{84–87}

At present, MIRU-VNTR offers some advantages when compared to WGS: MIRU is already performed as part of public health surveillance in Canada; provincial and national laboratories have extensive experience with this method; turnaround times are relatively short (2-4 weeks); and most public health teams have experience in interpreting the results. In regions with high M. tuberculosis genetic diversity due to immigration and importation of global M. tuberculosis lineages, such as major Canadian urban centers, MIRU-VNTR may be sufficient for surveillance of transmission or discrimination of relapse versus reinfection based on the high probability of seeing different M. tuberculosis lineages. However, in many Northern communities, the genetic diversity of M. tuberculosis is extremely low, and all isolates have the same or very similar MIRU-VNTR pattern simply because the relevant strain has been circulating in this population for decades. Hence, MIRU-VNTR is not useful for discriminating recent transmission from reactivation or relapse from reinfection in these settings; WGS is needed.84,87,88 For evaluating TB transmission, WGS can substantially reduce the amount of false clustering⁸⁹ and is demonstrably more consistent with epidemiologic data.⁹⁰ WGS has also been shown to provide higher resolution for discriminating relapse from reinfection. 91-93 However, it is important to emphasize that epidemiological confirmation is always necessary in the interpretation of results of either MIRU-VNTR or WGS.

Isolates from all patients in an outbreak share the same MIRU-VNTR pattern. However, with WGS, (particularly for outbreaks with long duration), individual SNPs that accumulate over time in each patient's bacteria can be used to understand transmission within the outbreak. This can better identify source cases⁹⁴ and super spreading events,^{84,86} and help discriminate different chains or sub-groups of transmission.84,86,87 Linkage with corresponding clinical and epidemiological data can then be used to identify associated risk factors and inform targeted interventions. In program evaluation, WGS can be useful in estimating the proportion of cases due to recent transmission versus reactivation; the



proportion of recurrences due to relapse versus reinfection; or the impact of community-wide interventions on transmission.84,92,93,95,131

Given these advantages, WGS is now recognized as the gold standard for identifying TB transmission and discrimination of relapse/reinfection. In recent years, a number of jurisdictions have transitioned to routine WGS for their TB surveillance programs, including the UK,96 USA,97 Netherlands⁹⁸ and the state of Victoria in Australia (Dr. Gonçalves da Silva, personal communication). However, WGS has not yet been widely adopted by TB diagnostic laboratories in Canada because of concerns about cost compared to MIRU-VNTR, need for bioinformatics infrastructure and lengthy turnaround times. Importantly, costs of WGS can be offset by eliminating redundant molecular diagnostic tests. For example, New York State99 estimated an incremental cost for WGS of only US\$60 per isolate in 2017. 99 In the past 2 years, substantial laboratory and bioinformatics analytic capacity has also been developed for genomics of SARS-Cov-2. Given this and the availability of published M. tuberculosis-specific bioinformatics pipelines, 100 this infrastructure seems within reach. Finally, the turn-around time for WGS-based reporting for resistance was as little as 15 days from early culture positivity in New York State99 and Australia.101 A UK-based study found no difference in time to results with MIRU or WGS but estimated that WGS results could have been available 21 days earlier than MIRU results if done under more realistic conditions.100

Hence, we suggest consideration be given to transitioning from classical genotyping methods to WGS for routine surveillance of transmission and for outbreak investigations. This transition would provide most immediate advantages in settings with limited M. tuberculosis strain diversity (i.e., Northern Canada), and could then be applied more widely as costs decrease.

Social network analysis is an extension of traditional field epidemiology; it systematically examines the social relationships between cases and contacts to identify settings and behaviors that characterize transmission events, and can be used to visualize or quantify the strength of these connections. Social network analysis has been used extensively in TB outbreaks, most often together with genotyping/WGS; computer software programs for formal social network analysis are available. 48,50,102-104

6. Management of a TB outbreak

TB outbreaks generally last for several years; as a result, response and control are major undertakings.^{105–109} TB outbreaks take place in settings where 1) widespread transmission is possible, and 2) the exposed population is vulnerable to rapid development of secondary cases. Social determinants of health underlie most outbreaks: inadequate housing (overcrowding, inadequate ventilation) and limited access to healthcare (resulting in delayed diagnosis and

prolonged infectiousness) promote transmission to large numbers of contacts. Among these contacts, young children are especially at risk for progression to TB disease, but other individual risk factors - smoking, poorly controlled diabetes, malnutrition, etc.— are often associated with poverty. Thus, outbreaks are more likely to occur in already-challenged settings, such as among homeless or other marginalized populations and in remote Inuit or First Nations communities. 50,84,109 TB outbreaks are also well-documented in congregate settings, including hospitals and long term care homes, correctional facilities, and shelters. 110-112

Good practice statement

· Because TB outbreaks are uncommon in Canada, consultation with colleagues experienced at managing prior TB outbreaks is strongly advised.

6.1. Definition

An outbreak is the occurrence of more cases than expected over a given time period, with ongoing transmission. Outbreaks may be suspected due to clustering of cases by location, time, behavioral factors or strain genotype. 113,114 Note that cases may increase without ongoing transmission, for example due to changes in migration patterns.

The following is a working definition of outbreaks,¹⁴ intended to help identify and contain rapidly evolving clusters:

- During and because of a contact investigation, 2 or more of the identified contacts are diagnosed as secondary cases of active TB (confirmed by genotyping/WGS if available); or
- any 2 or more cases in TB patients occurring within 1 year of each other are discovered to be epidemiologically linked (and matched by genotyping/WGS if available), but the linkage is recognized outside of a direct contact investigation.

Most situations that have been recognized as TB outbreaks involve chains of many more than 2 secondary cases, or one previously unrecognized link to a secondary case, and extend over several years. A slower cluster of linked cases that spans several years may still require heightened TB program response for an identifiable population group yet not be an "outbreak" by the aforementioned definition.

By definition, once an outbreak is declared, additional cases are usually restricted to those who have the outbreak strain, as confirmed by genotyping/WGS of TB isolates. Note that additional unrelated cases may also be diagnosed within the same population during the outbreak period.

While there is no standard for declaring a TB outbreak over, we suggest a functional timeline of 2 years past the last case, consistent with the highest risk period for close contacts to develop active TB.¹¹⁵

6.2. Goals

The goals of the investigation and management of an outbreak of TB are as follows:

- to promptly identify and treat the source patient(s), to rapidly reduce ongoing transmission;
- to rapidly identify and treat new cases of active TB within the at-risk population;
- to identify people with recently acquired LTBI, and offer treatment; and
- to identify and address underlying causes for the outbreak, as part of TB elimination efforts.

6.3. Managing an outbreak

TB outbreak response involves ongoing assessment for transmission patterns via detailed social network interviews and genotyping/WGS; managing multiple, often overlapping, contact investigations; and active case finding and outreach with the at-risk population.^{67,116,117} At the same time, caseloads for TB patients and for medical follow-up and LTBI treatment of contacts are increased during outbreaks. See Appendix 4 for a more detailed discussion of the recommended components of outbreak response and community-wide screening.

6.3.1. Organization and resources

Assistance from beyond the TB program is usually necessary. Outbreak response within the public health/TB program is often most efficiently organized using an Incident Management System-type structure, with well-defined roles for all those involved. An outbreak coordinating group, chaired by key individuals from the public health/TB program, and including clinical TB experts, hospitals, laboratory and the affected community, is strongly advised.

Good practice statement

Given the scale and duration of most TB outbreaks, it
is critical that there be adequate organization, staffing
and resources for investigation and management from
the beginning of the response efforts.

6.3.2. Community outreach and education

TB outbreaks are anxiety-provoking and may be stigmatizing. Often, they take place in a context of limited or inaccurate information about TB and sometimes, negative cultural/historical associations. All these can prolong the outbreak, as lack of recognition of the significance of their symptoms or fear of receiving a diagnosis of TB among individuals can lead to delay in seeking medical care. It is crucial to begin outreach to the affected community and coordinated media communications as early as possible, with information about TB and the outbreak response. 118

6.3.3. Community-wide screening

In small remote communities, or sometimes in closed settings/well-defined sub-populations, screening the entire affected community may be a useful strategy to consider when local TB resources are not able to manage multiple overlapping cases and contact investigations in an escalating outbreak. It may also be more efficient if a large proportion of the community has already been identified as contacts. This approach has been used recently in Nunavut and Nunavik, and more loosely in urban homeless populations.

6.3.4. Evaluating the outbreak response and identifying fundamental causes

Ongoing evaluation of process and outcomes will help to refine the outbreak response and ensure adequate resources. Both outbreak response and final policy recommendations should address the specific challenges in social determinants of health and/or behavioral risks that fueled the outbreak. In facility-based outbreaks a systematic assessment of conditions (including ventilation) and infection-control policies and practices may also identify concrete areas for improvement (see also Chapter 14: Prevention and Control of Tuberculosis Transmission in Healthcare Settings). Individual cases can be treated and cured, but it is difficult to contain outbreaks or reduce endemically high rates of TB without addressing the fundamental causes.^{1,108}

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References

- 1. Lonnroth K, Migliori GB, Abubakar I, et al. Towards tuberculosis elimination: an action framework for low-incidence coun-EurRespir J. 2015;45(4):928-952. doi:10.1183/09031936.00214014.
- 2. Erkens CG, Kamphorst M, Abubakar I, et al. Tuberculosis contact investigation in low prevalence countries: a European consensus. Eur Respir J. 2010;36(4):925-949. doi:10.1183/09031936.00201609.
- 3. Cole B, Nilsen DM, Will L, Etkind SC, Burgos M, Chorba T. Essential Components of a Public Health Tuberculosis Prevention, Control, and Elimination Program: Recommendations of the Advisory Council for the Elimination of Tuberculosis and the National Tuberculosis Controllers Association. MMWR Recomm Rep. 2020;69(7):1-27. doi:10.15585/mmwr.rr6907a1.
- 4. Dasgupta K, Schwartzman K, Marchand R, Tennenbaum TN, Brassard P, Menzies D. Comparison of cost-effectiveness of tuberculosis screening of close contacts and foreign-born populations. Am J Respir Crit Care Med. 2000;162(6):2079-2086. doi:10.1164/ajrccm.162.6.2001111.
- 5. Kasaie P, Andrews JR, Kelton WD, Dowdy DW. Timing of tuberculosis transmission and the impact of household contact tracing. An agent-based simulation model. Am J Respir Crit Care Med. 2014;189(7):845-852. doi:10.1164/rccm.201310-1846OC.
- 6. Guzzetta G, Ajelli M, Yang Z, et al. Effectiveness of contact investigations for tuberculosis control in Arkansas. J Theor Biol. 2015;380:238-246. doi:10.1016/j.jtbi.2015.05.031.
- 7. Anger HA, Proops D, Harris TG, et al. Active case finding and prevention of tuberculosis among a cohort of contacts exposed to infectious tuberculosis cases in New York City. Clin Infect Dis. 2012;54(9):1287-1295. doi:10.1093/cid/cis029.
- 8. Marks SM, Taylor Z, Qualls NL, Shrestha-Kuwahara RJ, Wilce MA, Nguyen CH. Outcomes of contact investigations of infectious tuberculosis patients. Am J Respir Crit Care Med. 2000;162(6):2033-2038. doi:10.1164/ajrccm.162.6.2004022.
- 9. Morris SK, Giroux RJP, Consunji-Araneta R, et al. Epidemiology, clinical features and outcomes of incident tuberculosis in children in Canada in 2013-2016: results of a national surveillance study. Arch Dis Child. 2021;106(12):1165-1170. doi:10.1136/archdischild-2021-322092.
- 10. Fox GJ, Barry SE, Britton WJ, Marks GB. Contact investigation for tuberculosis: a systematic review and meta-analysis. Eur Respir *J.* 2013;41(1):140–156. doi:10.1183/09031936.00070812.
- 11. Moran-Mendoza O, Marion SA, Elwood K, Patrick D, FitzGerald JM. Risk factors for developing tuberculosis: a 12-year follow-up of contacts of tuberculosis cases. Int J Tuberc Lung Dis. 2010;14(9):1112-1119.
- 12. Lobato MN, Royce SE, Mohle-Boetani JC. Yield of source-case and contact investigations in identifying previously undiagnosed childhood tuberculosis. Int J Tuberc Lung Dis. 2003;7(12 Suppl
- 13. Nordholm AC, Holm LL, Svensson E, Andersen PH, Johansen IS. Tuberculosis Transmission in Danish Children: A Nationwide Register-based Study. Pediatr Infect Dis J. 2019;38(4):340-343. doi:10.1097/INF.0000000000002139.
- 14. National Tuberculosis Controllers A, Centers for Disease C, Prevention. Guidelines for the investigation of contacts of persons with infectious tuberculosis. Recommendations from the National Tuberculosis Controllers Association and CDC. MMWR Recomm Rep. 2005;54(RR-15):1-47.
- 15. World Health Organization. Systematic Screening for Active Tuberculosis: Principles and Recommendations. Geneva, Switzerland: WHO Guidelines Approved by the Guidelines Review Committee; 2013.
- 16. Wingfield T, MacPherson P, Cleary P, Ormerod LP. High prevalence of TB disease in contacts of adults with extrapulmonary TB. Thorax. 2018;73(8):785-787. doi:10.1136/thoraxjnl-2017-210202.

- 17. Melsew YA, Doan TN, Gambhir M, Cheng AC, McBryde E, Trauer JM. Risk factors for infectiousness of patients with tuberculosis: a systematic review and meta-analysis. Epidemiol Infect. 2018;146(3):345-353. doi:10.1017/S0950268817003041.
- National Institute for Health and Care Excellence. Tuberculosis Guidelines. Accessed October 23, 2021. https://www.nice.org.uk/ guidance/ng33.
- 19. Lohmann EM, Koster BF, Le Cessie S, Kamst-van Agterveld MP, van Soolingen D, Arend SM. Grading of a positive sputum smear and the risk of Mycobacterium tuberculosis transmission. Int I Tuberc Lung Dis. 2012;16(11):1477-1484. doi:10.5588/ijtld.12.0129.
- 20. Reichler MR, Tuberculosis Epidemiologic Studies Consortium Task Order 2 Team, Khan A, Yuan Y, et al. Duration of Exposure Among Close Contacts of Patients With Infectious Tuberculosis and Risk of Latent Tuberculosis Infection. Clin Infect Dis. 2020;71(7):1627-1634. doi:10.1093/cid/ciz1044.
- 21. Bailey WC, Gerald LB, Kimerling ME, et al. Predictive model to identify positive tuberculosis skin test results during contact investigations. JAMA. 2002;287(8):996-1002. doi:10.1001/ jama.287.8.996.
- 22. Acuna-Villaorduna C, Jones-Lopez EC, Fregona G, et al. Intensity of exposure to pulmonary tuberculosis determines risk of tuberculosis infection and disease. Eur Respir J. 2018;51(1):1701578. doi:10.1183/13993003.01578-2017.
- 23. Aissa K, CG94 Study Group, Madhi F, Ronsin N, et al. Evaluation of a model for efficient screening of tuberculosis contact subjects. Am J Respir Crit Care Med. 2008;177(9):1041-1047. doi:10.1164/ rccm.200711-1756OC.
- 24. Romanowski K, Sobkowiak B, Guthrie JL, Cook VJ, Gardy JL, Johnston JC. Using Whole-genome Sequencing to Determine the Timing of Secondary Tuberculosis in British Columbia, Canada. Clin Infect Dis. 2021;73(3):535-537. doi:10.1093/cid/ciaa1224.
- 25. Gerald LB, Tang S, Bruce F, et al. A decision tree for tuberculosis contact investigation. Am J Respir Crit Care Med. 2002;166(8):1122-1127. doi:10.1164/rccm.200202-124OC.
- 26. Migliori GB, Nardell E, Yedilbayev A, et al. Reducing tuberculosis transmission: a consensus document from the World Health Organization Regional Office for Europe. Eur Respir J. 2019;53(6):1900391. doi:10.1183/13993003.00391-2019.
- 27. Roberts JR, Mason BW, Paranjothy S, Palmer SR. The transmission of tuberculosis in schools involving children 3 to 11 years of age. Pediatr Infect Dis J. 2012;31(1):82-84. doi:10.1097/ INF.0b013e31823378c9.
- 28. Caley M, Fowler T, Welch S, Wood A. Risk of developing tuberculosis from a school contact: retrospective cohort study, United Kingdom, 2009. Euro Surveill. 2010;15(11):19510.
- 29. Schepisi MS, Motta I, Dore S, Costa C, Sotgiu G, Girardi E. Tuberculosis transmission among children and adolescents in schools and other congregate settings: a systematic review. New Microbiol. 2019;41(4):282-290.
- 30. Cinquetti S, Dalmanzio M, Ros E, et al. High rate of transmission in a pulmonary tuberculosis outbreak in a primary school, north-eastern Italy. Euro Surveill. 2019;24(24):1900332. doi:10.2807/1560-7917.ES.2019.24.24.1900332.
- 31. Centers for Disease Control and Prevention. Transmission of Mycobacterium tuberculosis in a High School and School-Based Supervision of an Isoniazid-Rifapentine Regimen for Preventing Tuberculosis - Colorado, 2011-2012. Morb Mortal Wkly Rep. 2013;62(39):805-809.
- 32. Dollner H, Ramm CT, Harstad I, Afset JE, Sagvik E. Risk of developing tuberculosis after brief exposure in Norwegian children: results of a contact investigation. BMJ Open. 2012;2(6):e001816. doi:10.1136/bmjopen-2012-001816.
- 33. Gillman A, Berggren I, Bergstrom SE, Wahlgren H, Bennet R. Primary tuberculosis infection in 35 children at a Swedish day care center. Pediatr Infect Dis J. 2008;27(12):1078-1082. doi:10.1097/INF.0b013e31817e83f4.
- 34. Crisan A, Wong HY, Johnston JC, et al. Spatio-temporal analysis of tuberculous infection risk among clients of a homeless

- shelter during an outbreak. Int J Tuberc Lung Dis. 2015;19(9):1033-1038. doi:10.5588/ijtld.14.0957.
- 35. Muecke C, Isler M, Menzies D, Allard R, Tannenbaum TN, Brassard P. The use of environmental factors as adjuncts to traditional tuberculosis contact investigation. Int J Tuberc Lung Dis. 2006;10(5):530-535.
- 36. Luzzati R, Migliori GB, Zignol M, et al. Children under 5 years are at risk for tuberculosis after occasional contact with highly contagious patients: outbreak from a smear-positive healthcare Eurworker. Respir J. 2017;50(5):1701414. doi:10.1183/13993003.01414-2017.
- 37. Oeltmann JE, Oren E, Haddad MB, et al. Tuberculosis outbreak in marijuana users, Seattle, Washington, 2004. Emerg Infect Dis. 2006;12(7):1156-1159. doi:10.3201/eid1207.051436.
- 38. Godoy P, Grupo de Trabajo de Estudios de Contactos de Tuberculosis de Cataluña, Cayla JA, Carmona G, et al. Smoking in tuberculosis patients increases the risk of infection in their contacts. Int J Tuberc Lung Dis. 2013;17(6):771-776. doi:10.5588/ iitld.12.0696.
- 39. Singh M, Mynak ML, Kumar L, Mathew JL, Jindal SK. Prevalence and risk factors for transmission of infection among children in household contact with adults having pulmonary tuberculosis. Arch Dis Child. 2005;90(6):624-628. doi:10.1136/ adc.2003.044255.
- 40. Patra J, Bhatia M, Suraweera W, et al. Exposure to second-hand smoke and the risk of tuberculosis in children and adults: a systematic review and meta-analysis of 18 observational studies. PLoS Med. 2015;12(6):e1001835; discussion e1001835 doi:10.1371/ journal.pmed.1001835.
- 41. Bates MN, Khalakdina A, Pai M, Chang L, Lessa F, Smith KR. Risk of tuberculosis from exposure to tobacco smoke: a systematic review and meta-analysis. Arch Intern Med. 2007;167(4):335-342. doi:10.1001/archinte.167.4.335.
- 42. Rea E, Leung T . Available from Available from A cluster of tuberculosis cases linked to smoking: An under-recognized challenge for tuberculosis elimination . Can Commun Dis Rep. 2018;44(3-4):86-90. 2018-03-01doi:10.14745/ccdr.v44i34a03.
- 43. New Jersey Medical School Global TB Institute. TB interviewing for contact investigation: a practical resource for the healthcare worker. 2008. https://globaltb.njms.rutgers.edu/products/tbinterviewing.htm. Accessed August 25, 2021.
- 44. Ospina JE, Orcau À, Millet J-P, Sánchez F, Casals M, Caylà JA. Community health workers improve contact tracing among immigrants with tuberculosis in Barcelona. BMC Public Health. 2012;12(1):158. doi:10.1186/1471-2458-12-158.
- 45. Miller WR, Rollnick S. Motivational Interviewing: Helping People Change. 3rd ed. New York, USA: Guilford Press; 2013.
- 46. Hohman M, McMaster F, Woodruff SI. Contact Tracing for COVID-19: The Use of Motivational Interviewing and the Role of Social Work. Clin Soc Work J. 2021;49(4):419-410. doi:10.1007/ s10615-021-00802-2.
- 47. Faccini M, Cantoni S, Ciconali G, et al. Tuberculosis-related stigma leading to an incomplete contact investigation in a low-incidence country. Epidemiol Infect. 2015;143(13):2841-2848. doi:10.1017/S095026881400394X.
- 48. Cook VJ, Shah L, Gardy J, Bourgeois AC. Recommendations on modern contact investigation methods for enhancing tuberculosis control. Int J Tuberc Lung Dis. 2012;16(3):297-305. doi:10.5588/ ijtld.11.0350.
- 49. Center for Disease Control. Epidemiologic Notes and Reports: Crack cocaine use among persons with tuberculosis - Contra Costa County, California, 1987-1990. Morb Mortal Wkly Rep. 1991;40(29):485-489.
- 50. Gardy JL, Johnston JC, Ho Sui SJ, et al. Whole-genome sequencing and social-network analysis of a tuberculosis outbreak. N Engl J Med. 2011;364(8):730-739. doi:10.1056/NEJMoa1003176.
- 51. Asghar RJ, Patlan DE, Miner MC, et al. Limited utility of name-based tuberculosis contact investigations among persons using illicit drugs: results of an outbreak investigation. J Urban Health. 2009;86(5):776-780. doi:10.1007/s11524-009-9378-z.

- 52. Duarte R, Neto M, Carvalho A, Barros H. Improving tuberculosis contact tracing: the role of evaluations in the home and workplace. Int J Tuberc Lung Dis. 2012;16(1):55-59. doi:10.5588/ ijtld.10.0511.
- 53. Mangura BT, Napolitano EC, Passannante MR, McDonald RJ, Reichman LB. Mycobacterium tuberculosis miniepidemic in a church gospel choir. Chest. 1998;113(1):234-237. doi:10.1378/ chest.113.1.234.
- 54. Tian Y, Osgood ND, Al-Azem A, Hoeppner VH. Evaluating the effectiveness of contact tracing on tuberculosis outcomes in Saskatchewan using individual-based modeling. Health Educ Behav. 2013;40(1_suppl):98S-110S. doi:10.1177/1090198113493910.
- 55. The Homelessness Services Association of BC, Urban Matters, BC Non-Profit Housing Association. 2018 Report on Homeless Counts in B.C. 2018. https://www.bchousing.org/publications/2018-BC-Homeless-Counts.pdf. Accessed August 17, 2021.
- 56. Public Health Ontario, Berenbaum E. Homelessness and Health Outcomes: What are the associations?. 2019. https://www.publichealthontario.ca/-/media/documents/E/2019/ eb-homelessness-health.pdf. Accessed August 17, 2021.
- 57. Khan K, Rea E, McDermaid C, et al. Active tuberculosis among homeless persons, Toronto, Ontario, Canada, 1998-2007. Emerg Infect Dis. 2011;17(3):357-365. doi:10.3201/eid1703.100833.
- Tan de Bibiana J, Rossi C, Rivest P, et al. Tuberculosis and homelessness in Montreal: a retrospective cohort study. BMC Public Health. 2011;11:833. doi:10.1186/1471-2458-11-833.
- 59. Deiss RG, Rodwell TC, Garfein RS. Tuberculosis and illicit drug use: review and update. Clin Infect Dis. 2009;48(1):72-82. doi:10.1086/594126.
- 60. Fraser Health Health Equity and Population Health Unit. Recommendations for TB Management among Populations Experiencing Homelessness. 2020. https://www.fraserhealth.ca/-/ media/Project/FraserHealth/FraserHealth/Health-Professionals/ Clinical-resources/resources-for-community-organizations/20_11 _17--Report-on-TB-Research-for-Homeless-Outbreak.pdf. Accessed August 17, 2021.
- 61. Baxter S, Goyder E, Chambers D, Johnson M, Preston L, Booth A. Interventions to improve contact tracing for tuberculosis in specific groups and in wider populations: an evidence synthesis. Health Serv Deliv Res. 2017;5(1):1-102. doi:10.3310/hsdr05010.
- 62. Tibbetts KK, Ottoson RA, Tsukayama DT. Public Health Response to Tuberculosis Outbreak among Persons Experiencing Homelessness, Minneapolis, Minnesota, USA, 2017-2018. Emerg Infect Dis. 2020;26(3):420-426. doi:10.3201/eid2603.190643.
- 63. Li J, Driver CR, Munsiff SS, Fujiwara PI. Finding contacts of homeless tuberculosis patients in New York City. Int J Tuberc Lung Dis. 2003;7(12 Suppl 3):S397-S404.
- 64. Munn MS, Duchin JS, Kay M, Pecha M, Thibault CS, Narita M. Analysis of risk factors for tuberculous infection following exposure at a homeless shelter. Int J Tuberc Lung Dis. 2015;19(5):570-575. doi:10.5588/ijtld.14.0648.
- 65. Yun LW, Reves RR, Reichler MR, et al. Outcomes of contact investigation among homeless persons with infectious tuberculosis. Int J Tuberc Lung Dis. 2003;7(12 Suppl 3):S405-S11.
- 66. Heuvelings CC, de Vries SG, Greve PF, et al. Effectiveness of interventions for diagnosis and treatment of tuberculosis in hard-to-reach populations in countries of low and medium tuberculosis incidence: a systematic review. Lancet Infect Dis. 2017;17(5):e144-e158. doi:10.1016/S1473-3099(16)30532-1.
- 67. Hamilton K, Tolfree R, Mytton J. A systematic review of active case-finding strategies for tuberculosis in homeless populations. Int J Tuberc Lung Dis. 2018;22(10):1135-1144. doi:10.5588/ ijtld.17.0784.
- Jit M, Find and Treat Evaluation Team, Stagg HR, Aldridge RW, et al. Dedicated outreach service for hard to reach patients with tuberculosis in London: observational study and economic evaluation. BMJ. 2011;343:d5376 doi:10.1136/bmj.d5376.
- 69. Lofy KH, McElroy PD, Lake L, et al. Outbreak of tuberculosis in a homeless population involving multiple sites of transmission. Int J Tuberc Lung Dis. 2006;10(6):683-689.

- 70. Paquette K, Cheng MP, Kadatz MJ, Cook VJ, Chen W, Johnston JC. Chest radiography for active tuberculosis case finding in the homeless: a systematic review and meta-analysis. Int J Tuberc Lung Dis. 2014;18(10):1231-1236. doi:10.5588/ijtld.14.0105.
- 71. Jensen SG, Olsen NW, Seersholm N, et al. Screening for TB by sputum culture in high-risk groups in Copenhagen, Denmark: a novel and promising approach. Thorax. 2015;70(10):979-983. doi:10.1136/thoraxjnl-2015-207162.
- 72. Kotila SM, Hallstrom Jansen PL, Helbling N, Abubakar P. I. Systematic review on tuberculosis transmission on aircraft and update of the European Centre for Disease Prevention and Control risk assessment guidelines for tuberculosis transmitted on aircraft (RAGIDA-TB). Euro Surveill. 2016;21(4):30114. doi:10.2807/1560-7917.ES.2016.21.4.30114.
- 73. World Health Organization. Tuberculosis and Air Travel: guidelines for Prevention and Control. 3rd ed. Geneva: World Health Organization; 2008.
- 74. Mohr O, Askar M, Schink S, Eckmanns T, Krause G, Poggensee G. Evidence for airborne infectious disease transmission in public ground transport-a literature review. Euro Surveill. 2012;17(35):20255. https://doi.org/10.2807/ese.17.35.20255-en
- 75. Phillips L, Carlile J, Smith D. Epidemiology of a tuberculosis outbreak in a rural Missouri high school. Pediatrics. 2004;113(6):e514-e519. doi:10.1542/peds.113.6.e514.
- 76. Powell K, Lamb MM, Sisk MK, et al. Passenger contact investigation associated with a transport driver with pulmonary tuberculosis. Public Health Rep. 2012;127(2):202-207. doi:10.1177/003335491212700209.
- 77. Mohr O, Schink SB, Eckmanns T, Krause G. Tuberculosis in public ground transport - is there enough evidence to justify contact tracing? Expert Rev anti Infect Ther. 2015;13(1):1-3. do i:10.1586/14787210.2015.985656.
- 78. Reichler MR, Reves R, Bur S, et al. Evaluation of investigations conducted to detect and prevent transmission of tuberculosis. JAMA. 2002;287(8):991–995. doi:10.1001/jama.287.8.991.
- 79. Eisenbeis L, Gao Z, Heffernan C, Yacoub W, Long R, Verma G. Contact investigation outcomes of Canadian-born adults with tuberculosis in Indigenous and non-Indigenous populations in Alberta. Can J Public Health. 2016;107(1):e106-e111. doi:10.17269/ cjph.107.5255.
- 80. Borgen K, Koster B, Meijer H, Kuyvenhoven V, van der Sande M, Cobelens F. Evaluation of a large-scale tuberculosis contact investigation in the Netherlands. Eur Respir J. 2008;32(2):419-425. doi:10.1183/09031936.00136607.
- 81. Auld SC, Shah NS, Cohen T, Martinson NA, Gandhi NR. Where is tuberculosis transmission happening? Insights from the literature, new tools to study transmission and implications for the elimination of tuberculosis. Respirology. 2018;23(9):807-817. doi:10.1111/resp.13333.
- 82. Doroshenko A, Pepperell CS, Heffernan C, et al. Epidemiological and genomic determinants of tuberculosis outbreaks in First Nations communities in Canada. BMC Med. 2018;16(1):128. doi:10.1186/s12916-018-1112-9.
- 83. Mehaffy C, Guthrie JL, Alexander DC, Stuart R, Rea E, Jamieson FB. Marked microevolution of a unique Mycobacterium tuberculosis strain in 17 years of ongoing transmission in a high risk population. PLoS One. 2014;9(11):e112928. doi:10.1371/journal.
- 84. Lee RS, Radomski N, Proulx JF, et al. Reemergence and amplification of tuberculosis in the Canadian arctic. J Infect Dis. 2015;211(12):1905-1914. doi:10.1093/infdis/jiv011.
- 85. Lee RS, Radomski N, Proulx JF, et al. Population genomics of Mycobacterium tuberculosis in the Inuit. Proc Natl Acad Sci Usa. 2015;112(44):13609-13614. doi:10.1073/pnas.1507071112.
- 86. Alvarez GG, Zwerling AA, Duncan C, et al. Molecular Epidemiology of Mycobacterium tuberculosis To Describe the Transmission Dynamics Among Inuit Residing in Iqaluit Nunavut Using Whole-Genome Sequencing. Clin Infect Dis. 2021;72(12):2187-2195. doi:10.1093/cid/ciaa420.

- 87. Guthrie JL, Strudwick L, Roberts B, et al. Whole genome sequencing for improved understanding of Mycobacterium tuberculosis transmission in a remote circumpolar region. Epidemiol Infect. 2019;147:e188. doi:10.1017/S0950268819000670.
- Nguyen D, Proulx JF, Westley J, Thibert L, Dery S, Behr MA. Tuberculosis in the Inuit community of Quebec, Canada. Am J Respir Crit Care Med. 2003;168(11):1353-1357. doi:10.1164/rccm.200307-910OC.
- 89. Wyllie DH, Davidson JA, Grace Smith E, et al. A Quantitative Evaluation of MIRU-VNTR Typing Against Whole-Genome Sequencing for Identifying Mycobacterium tuberculosis Transmission: A Prospective Observational Cohort Study. EBioMedicine. 2018;34:122-130. doi:10.1016/j.ebiom.2018.07.019.
- Jajou R, de Neeling A, van Hunen R, et al. Epidemiological links between tuberculosis cases identified twice as efficiently by whole genome sequencing than conventional molecular typing: A population-based study. PLoS One. 2018;13(4):e0195413. doi:10.1371/journal.pone.0195413.
- 91. Bryant JM, Harris SR, Parkhill J, et al. Whole-genome sequencing to establish relapse or re-infection with Mycobacterium tuberculosis: a retrospective observational study. Lancet Respir Med. 2013;1(10):786-792. doi:10.1016/S2213-2600(13)70231-5.
- 92. Guerra-Assuncao JA, Houben RM, Crampin AC, et al. Recurrence due to relapse or reinfection with Mycobacterium tuberculosis: a whole-genome sequencing approach in a large, population-based cohort with a high HIV infection prevalence and active follow-up. J Infect Dis. 2015;211(7):1154-1163. doi:10.1093/infdis/jiu574.
- 93. Witney AA, RIFAQUIN Study Team, Bateson AL, Jindani A, et al. Use of whole-genome sequencing to distinguish relapse from reinfection in a completed tuberculosis clinical trial. BMC Med. 2017;15(1):71. doi:10.1186/s12916-017-0834-4.
- 94. Roetzer A, Diel R, Kohl TA, et al. Whole genome sequencing versus traditional genotyping for investigation of a Mycobacterium tuberculosis outbreak: a longitudinal molecular epidemiological study. PLoS Med. 2013;10(2):e1001387. doi:10.1371/journal. pmed.1001387.
- 95. Tyler AD, Randell E, Baikie M, et al. Application of whole genome sequence analysis to the study of Mycobacterium tuberculosis in Nunavut, Canada. PLoS One. 2017;12(10):e0185656. doi:10.1371/journal.pone.0185656.
- 96. Walker TM, Cruz ALG, Peto TE, Smith EG, Esmail H, Crook DW. Tuberculosis is changing. Lancet Infect Dis. 2017;17(4):359-361. doi:10.1016/S1473-3099(17)30123-8.
- 97. Centers for Disease Control and Prevention. Whole Genome Sequencing. https://www.cdc.gov/tb/programs/genotyping/ Tuberculosis_WGS_Training_Module.pdf. Accessed August 1,
- 98. Allix-Béguec C, CRyPTIC Consortium and the 100,000 Genomes Project, Arandjelovic I, Bi L, Beckert P, Bonnet M, Bradley P, Cabibbe AM. Prediction of susceptibility to first-line tuberculosis drugs by DNA sequencing. N Engl J Med. 2018;379(15):1403-1415. doi:10.1056/NEJMoa1800474.
- 99. Shea J, Halse TA, Lapierre P, et al. Comprehensive Whole-Genome Sequencing and Reporting of Drug Resistance Profiles on Clinical Cases of Mycobacterium tuberculosis in New York State. J Clin Microbiol. 2017;55(6):1871-1882. doi:10.1128/JCM.00298-17.
- 100. Pankhurst LJ, COMPASS-TB Study Group, Del Ojo Elias C, Votintseva AA, et al. Rapid, comprehensive, and affordable mycobacterial diagnosis with whole-genome sequencing: a prospective study. Lancet Respir Med. 2016;4(1):49-58. doi:10.1016/ S2213-2600(15)00466-X.
- Martinez E, Bustamante A, Menon R, et al. Whole-genome sequencing of Mycobacterium tuberculosis for rapid diagnostics: feasibility of a decentralised model. Lancet Respir Med. 2016;4(4):e13-4-e14. doi:10.1016/S2213-2600(16)00092-8.
- 102. Andre M, Ijaz K, Tillinghast JD, et al. Transmission network analysis to complement routine tuberculosis contact investigations. Am J Public Health. 2007;97(3):470-477. doi:10.2105/ AJPH.2005.071936.

- 103. Munang ML, Browne C, Evans JT, et al. Programmatic utility of tuberculosis cluster investigation using a social network approach in Birmingham, United Kingdom. Int J Tuberc Lung Dis. 2016;20(10):1300-1305. doi:10.5588/ijtld.16.0161.
- 104. Packer S, Green C, Brooks-Pollock E, Chaintarli K, Harrison S, Beck CR. Social network analysis and whole genome sequencing in a cohort study to investigate TB transmission in an educational setting. BMC Infect Dis. 2019;19(1):154. doi:10.1186/ s12879-019-3734-8.
- 105. Mitruka K, Oeltmann JE, Ijaz K, Haddad MB. Tuberculosis outbreak investigations in the United States, 2002-2008. Emerg Infect Dis. 2011;17(3):425-431. doi:10.3201/eid1703.101550.
- 106. Maguire H, Brailsford S, Carless J, et al. Large outbreak of isoniazid-monoresistant tuberculosis in London, 1995 to 2006: case-control study and recommendations. Euro Surveill. 2011;16(13):19830.
- 107. Powell KM, VanderEnde DS, Holland DP, et al. Outbreak of Drug-Resistant Mycobacterium tuberculosis Among Homeless People in Atlanta, Georgia, 2008-2015. Public Health Rep. 2017;132(2):231-240. doi:10.1177/0033354917694008.
- 108. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City-turning the tide. N Engl J Med. 1995;333(4):229-233. doi:10.1056/NEJM199507273330406.
- 109. Cheng JM, Hiscoe L, Pollock SL, Hasselback P, Gardy JL, Parker R. A clonal outbreak of tuberculosis in a homeless population in the interior of British Columbia, Canada, 2008-2015. Epidemiol Infect. 2015;143(15):3220-3226. doi:10.1017/ S0950268815000825.
- 110. Khalil NJ, Kryzanowski JA, Mercer NJ, Ellis E, Jamieson F. Tuberculosis outbreak in a long-term care facility. Can J Public Health. 2013;104(1):e28-32-e32. doi:10.1007/BF03405650.
- 111. Roycroft E, Fitzgibbon MM, Kelly DM, et al. The largest prison outbreak of TB in Western Europe investigated using whole-genome sequencing. Int J Tuberc Lung Dis. 2021;25(6):491-497. doi:10.5588/ijtld.21.0033.
- 112. Gandhi NR, Weissman D, Moodley P, et al. Nosocomial transmission of extensively drug-resistant tuberculosis in a rural hospital in South Africa. J Infect Dis. 2013;207(1):9-17. doi:10.1093/
- 113. Noppert GA, Yang Z, Clarke P, Davidson P, Ye W, Wilson ML. Contextualizing tuberculosis risk in time and space: comparing time-restricted genotypic case clusters and geospatial clusters to evaluate the relative contribution of recent transmission to incidence of TB using nine years of case data from Michigan, USA. Ann Epidemiol. 2019;40:21-27 e3. doi:10.1016/j.annepidem.2019.10.001.
- 114. Center for Disease Control. Self-study modules on Tuberculosis: Module 9 outbreak detection and response. 2014. https://www. cdc.gov/tb/education/ssmodules/pdfs/module9.pdf. Accessed September 3, 2021.
- 115. Hatherell HA, Didelot X, Pollock SL, et al. Declaring a tuberculosis outbreak over with genomic epidemiology. Microb Genom. 2016;2(5):e000060 doi:10.1099/mgen.0.000060.
- 116. Castilla J, Palmera R, Navascues A, et al. Population-based contact investigation of a cluster of tuberculosis cases in a small village. Epidemiol Infect. 2009;137(10):1426-1435. doi:10.1017/ S0950268809002246.
- 117. Gupta RK, Lipman M, Story A, et al. Active case finding and treatment adherence in risk groups in the tuberculosis pre-elimination era. Int J Tuberc Lung Dis. 2018;22(5):479-487. doi:10.5588/ijtld.17.0767.

- 118. Kerr EM, Vonnahme LA, Goswami ND. Impact of Targeted Local Interventions on Tuberculosis Awareness and Screening Among Persons Experiencing Homelessness During a Large Tuberculosis Outbreak in Atlanta, Georgia, 2015-2016. Public Health Rep. 2020;135(1_suppl):90S-99S. doi:10.1177/0033354920932644.
- Jacobs S, Warman A, Richardson R, et al. The tuberculin skin test is unreliable in school children BCG-vaccinated in infancy and at low risk of tuberculosis infection. Pediatr Infect Dis *J.* 2011;30(9):754–758. doi:10.1097/INF.0b013e31821b8f54.
- 120. Pease C, Zwerling A, Mallick R, et al. The latent tuberculosis infection cascade of care in Igaluit, Nunavut, 2012-2016. BMC Infect Dis. 2019;19(1):890. doi:10.1186/s12879-019-4557-3.
- 121. Rennert-May E, Hansen E, Zadeh T, Krinke V, Houston S, Cooper R. A Step toward Tuberculosis Elimination in a Low-Incidence Country: Successful Diagnosis and Treatment of Latent Tuberculosis Infection in a Refugee Clinic. Can Respir J. 2016;2016:7980869. doi:10.1155/2016/7980869.
- 122. Warrington P, Tyrrell G, Choy K, Eisenbeis L, Long R, Cooper R. Prevalence of latent tuberculosis infection in Syrian refugees to Canada. Can J Public Health. 2018;109(1):8-14. doi:10.17269/ s41997-018-0028-7.
- 123. Minodier P, Lamarre V, Carle ME, Blais D, Ovetchkine P, Tapiero B. Evaluation of a school-based program for diagnosis and treatment of latent tuberculosis infection in immigrant children. J Infect Public Health. 2010;3(2):67-75. doi:10.1016/j. jiph.2010.02.001.
- 124. Lim R, Jarand J, Field SK, Fisher D. Is Universal Screening Necessary? Incidence of Tuberculosis among Tibetan Refugees Arriving in Calgary, Alberta. Can Respir J. 2016;2016:8249843. doi:10.1155/2016/8249843.
- 125. Correctional Service Canada. Infectious Disease Surveillance in Canadian Federal Penitentiaries 2007-2008. 2008. https://www. csc-scc.gc.ca/publications/005007-7602-eng.shtml. Accessed October 4, 2021.
- 126. Romanowski K, Rose C, Cook VJ, et al. Effectiveness of Latent TB Screening and Treatment in People Initiating Dialysis in British Columbia, Canada. Can J Kidney Health Dis. 2020;7:205435812093710. doi:10.1177/2054358120937104.
- 127. Gitman M, Vu J, Nguyen T, Chen C, Rotstein C. Evaluation of a routine screening program with tuberculin skin testing on rates of detection of latent tuberculosis infection and prevention of active tuberculosis in patients with multiple myeloma at a Canadian cancer centre. Curr Oncol. 2020;27(3):e246-e250. doi:10.3747/ co.27.5577.
- 128. Georgia Department of Health. Guidelines for Preventing and Controlling Tuberculosis in Atlanta Homeless Housing Facilities. 2016. https://dph.georgia.gov/sites/dph.georgia.gov/files/TB%20 guidelines_5.26.16_EK_FINAL_v2.pdf. Accessed August 27, 2021.
- 129. Dehghani K, Lan Z, Li P, et al. Determinants of tuberculosis trends in six Indigenous populations of the USA, Canada, and Greenland from 1960 to 2014: a population-based study. Lancet Public Health. 2018;3(3):e133-e142. doi:10.1016/S2468-2667(18)30002-1.
- 130. San Francisco Department of Public Health. San Francisco Shelter Client TB Screening Guidelines. Accessed August 20 2021. https://www.sfcdcp.org/tb-control/tuberculosis-informatio n-for-medical-providers/shelter-client-screening-guidelines/.
- 131. Uppal A, Nsengiyumva NP, Signor C, et al. Active screening for tuberculosis in high-incidence Inuit communities in Canada: a cost-effectiveness analysis. CMAJ. 2021;193(43):E1652-E1659. doi:10.1503/cmaj.210447.



Appendix 1. Example of a structured, risk-based tool for initial contact investigation

Please see the Online Supplemental Material for an example of a structured, risk-based tool for initial contact investigation.

This Toronto Public Health tool was developed in a southern urban Canadian setting; it may not be suitable for all contexts. For more information, contact targettb@toronto.ca. If adapted, please acknowledge Toronto Public Health.

Appendix 2. Recommended approach for sitebased screening

- Identify a single senior individual from the site who will act as a liaison and be responsible for organizational aspects of the contact investigation on site, usually a school principal, workplace manager or occupational health manager, etc.
- Some exposures may involve multiple sites (eg, an individual transferred between hospitals or correctional facilities); initial planning should involve key individuals across all affected sites to ensure a consistent approach to risk-assessment and contact follow-up.
- Protect the confidentiality of the index case (investigations should be carried out in compliance with the relevant legal/ legislative requirements; provincial/territorial legislation may permit or require disclosure in specific circumstances). This may not be easy; there may be considerable pressure to disclose details and, in many situations, others may be able to guess the identity of the case. Particularly if the identity of the case is widely known or suspected, enlist the help of setting personnel (eg, the principal or manager) to plan for successful reintegration of the TB case once noninfectious.
- Visit the site beforehand to get a sense of the environment and organize the screening arrangements; get input from

- the setting's liaison person to ensure that screening is carried out at a time and in a way that offers the best opportunity for contacts to come to the screening.
- Ensure that adequate TB staffing will be available for the
- Include key players at the site, such as occupational health services, human resources or other administrative staff, as well as union health and safety representatives, in planning and communication; they may benefit from information about TB ahead of a general information session, as others will likely look to them for advice.
- Prepare a communication plan; identify one individual who will be responsible for media and communications to the general public if necessary; alert public health communications staff.
- Provide written information about TB and the contact follow-up plan, and offer general information/education sessions, for all parents/employees/residents prior to the screening sessions; if the number of contacts is relatively small, a separate session specifically for them may be helpful.
- Identify the referral plan for contacts who are TST-positive or symptomatic; manage all contacts referred for medical evaluation consistently, ideally by a limited number of health care providers working in coordination with public health. It can be confusing and alarming for a group of contacts if the work-up and treatment advice are inconsistent from person to person.
- Ensure the results of the medical evaluation are provided promptly to the appropriate public health authority. The public health TB program should review the outcomes of the investigation promptly to determine if there is evidence of transmission and, if so, assess if there is an identifiable next-closest group of contacts to whom the investigation can feasibly be expanded.

Appendix 3. Expected range of LTBI prevalence in various Canadian populations

	Prevalence of LTBI (%)	Type of test	Publication year
Close contacts born in Canada/US ²⁰	31.0	TST (≥5 mm)	2020
Close contacts born outside Canada/US ²⁰	75.6	TST (≥5 mm)	2020
First Nations schoolchildren on reserve, routine school screening (at low risk of TB	BCG in infancy 5.7	TST (≥10 mm)	2011
exposure) ¹¹⁹	no BCG 0.2		
Kindergarten children, routine school screening, Iqaluit, Nunavut 120	11.4	TST (≥10 mm)	2019
Government-assisted refugees ¹²¹	36.0	TST (≥10 mm)	2016
Refugees, medium-incidence origin (about 20/100,000) ¹²²	9.0	IGRA	2018
Migrant children, school-based screening ¹²³	22.8	TST (≥10 mm)	2010
Refugees, very high-incidence origin (>300/100,000) ¹²⁴	51.0	IGRA	2016
Federal inmates ¹²⁵	17.6	TST (≥10 mm)	2008
Dialysis patients, routine screening ¹²⁶	11.5	IGRA	2020
Hematologic cancer patients, routine screening ¹²⁷	8.2	TST (≥10 mm)	2020

Abbreviations: LTBI, latent tuberculosis infection; TST, tuberculin skin tests; TB, tuberculosis; BCG, Bacille Calmette-Guerin; IGRA interferon-gamma release assay

Appendix 4. Components of outbreak response and community-wide screening

The components recommended for TB outbreak response are similar to those for site-based screening in congregate settings, but much expanded in scope and duration:

- An identified outbreak manager, appointed for the duration, with overall responsibility for management and coordination of the outbreak response.
- Public health/TB program nursing staff to coordinate initial work-up and case-management for patients with TB, define infectiousness, coordinate contact investigation and active case finding clinics and provide consultation and communication with others in the field.
- Sufficient field staff to carry out the contact investigation and follow-up, and active case-finding clinics; for outbreaks involving multiple remote communities, mobile specialized teams may be an effective strategy to support local staff.
- Information technology (IT)/database and epidemiologic support. Contact investigation and management in a TB outbreak is very data-intensive. Dedicated epidemiology support is essential for development of effective data-collection strategies and rapid, thoughtful evaluation of the aggregate results as they become available. Tracking hundreds of contacts, often through multiple sites and assessments, demands electronic data collection tools, a good database and IT support.
- Timely WGS is strongly recommended for all TB outbreaks, to confirm case linkages and thereby help focus the response on high-risk locations/populations; analysis of these results and interpretation alongside the epidemiologic investigation data requires strong ongoing collaboration with the supporting laboratory.
- Clear written protocols for all components of the public health outbreak response, including contact investigation, screening clinics, contact management and referral. Clinical protocols for suspected or confirmed TB disease and for contacts should be agreed on by all participating health care partners.
- Training and education on TB for public health staff redeployed to help with outbreak response.
- Education and outreach to health care and social-services partners:
 - Staff in partner organizations may not be experienced in TB work; training and education about TB and TB-related infection control, presentation at medical rounds, etc., at all the organizations involved in the response plan is helpful. In outbreaks among homeless and other marginalized populations, this should include staff at shelters and other homeless services and other low-threshold types of care as they are often critical for early detection of individuals with TB.
 - Ongoing communication to the partner organizations/ sectors will help to raise the index of clinical suspicion for TB, provide up-to-date information about the outbreak and help decrease barriers to care, including early hospitalization for individuals being investigated for active TB when necessary. These patients should not return to congregate settings until infectious TB has been ruled out.
- Consistent, coordinated clinical and diagnostic supports with expertise in TB:
 - Prompt, local access to good-quality chest radiography.

- Identified medical consultants with expertise in TB to review chest radiology, evaluate patients for TB, hospitalize patients if necessary and manage active TB and contact follow-up in a consistent, timely manner; for remote communities, telemedicine links (including review of digital radiology) can be extremely effective.
- Hospital facilities that can provide airborne isolation rooms, diagnostic examinations and treatment without delay.
- Links to public health laboratories for specialized supports and consultation (arrangements to handle larger numbers of specimens; genotyping and interpretation,
- Rapid and safe transportation of specimens and, if necessary, patients.
- Written protocols for clinical work-up and management of active TB patients and contacts to ensure a consistent approach across all partners.
- Active case-finding: In outbreaks in congregate settings such as shelters, long-term care facilities or prisons, ongoing symptom screening and cough logs may be useful case detection tools. 128 As discussed in the main chapter, screening should ideally be on-site for congregate settings (via sputum and/or chest x-ray) to maximize access and participation. If the outbreak involves transient or highly mobile individuals, active case-finding on an ongoing basis over an extended period of time may be the only way to ensure that most contacts are identified and screened. It may be possible to follow infected contacts who refuse or are not eligible for treatment of LTBI through periodic clinical assessment for two years after exposure, in order to detect early TB disease.
- Outreach plan and staff to carry it out: information about TB, the outbreak response and TB screening should be in languages, formats and venues that are easily accessible to the at-risk community. Standard materials may need to be adapted to the cultural and practical setting, ideally with input from community members. Consider posters, videos, internet, local radio or other media, as well as community meetings and presentations through local community groups or services. Community champions and peer outreach may be helpful to reduce the level of anxiety and enhance participation in screening.
- Sufficient TB case-management and treatment support staff to provide complete treatment for all patients with active TB disease and LTBI. At least one year's additional staffing after the outbreak is over may be required. For outbreaks involving patients who move between communities, extra effort should be made to coordinate ongoing TB care between jurisdictions and ensure treatment completion.
- Logistical support for staffing, supplies, transportation, etc.
- Communications personnel to provide regular updates to the media and community on the status of the investigation.
- Program and epidemiology staff and resources to carry out evaluation of outxbreak response.

Community-wide screening seeks to rapidly reduce prevalent infectious TB via active case-finding in an entire population, and usually also to identify and treat the pool of recent contacts with LTBI. It can also help reduce individual stigma, which can be a real stumbling block for contact investigation



and follow-up in smaller communities. As an outbreak-response strategy, it is only practical in small, well-defined populations such as remote northern communities, closed settings or more loosely in homeless outbreaks. It is usually done as a single high-intensity event over 6-8 weeks as a "catch-up" effort, particularly in situations where it is difficult to rapidly assess individual level of contact in a close-knit community, or a majority of the community has already been identified as contacts. It has also been used in repeated lower-intensity cycles (eg, annually) as part of a TB elimination strategy in communities with ongoing high TB rates or repeated outbreaks. This approach needs fewer outside staff and smaller working space, but for a longer commitment. 129,130 A recent study using Nunavik data found both single and repeated community-wide screening strategies to be cost-effective in high-incidence remote communities with frequent outbreaks. 131

Community-wide screening takes considerable planning and resources beyond usual program operations; the decision to proceed should be made only after consideration of the broad local health and community context. TB programs should first consider the healthcare capacity and effectiveness of the current outbreak response. Local staff turnover and lack of TB expertise may be a contributing factor and are common challenges in remote communities; it may be sufficient to supplement the local health care team with additional TB-specific nurses, epidemiologic support, among others, for an extended period to manage the increased TB case/contact needs. If this is neither feasible nor sufficient, then community-wide screening may be a realistic strategy.

Community-wide screening should not be undertaken without consultation with and agreement of community leaders, and all components of the healthcare system (local health center, referral hospital, regional health authority, etc). It is essential to ensure that resources are adequate to balance TB and LTBI care needs resulting from the community-wide screening with other healthcare needs in the community; a community-wide screening almost always means pulling TB resources from elsewhere in the system and diverting local healthcare resources from other conditions, some of which may also be in crisis (eg, mental health, addictions, other

In addition to the general outbreak response components recommended above, community-wide screening in remote communities requires consideration of additional logistics:

- Lead time for a community-wide screening in a remote community is generally 3-6 months. An advance team may be needed to arrange/negotiate logistics.
- Accommodation and workspace for visiting staff are usually constrained in small remote communities.
- Clinic site arrangements and set-up: there is usually not enough room in the local health center or hospital; try community centers, school gyms, sewing centers or other large spaces that can be converted to clinic space for several weeks/months. Screening clinic locations need to have adequate ventilation (especially considering there may be active TB cases), running water and toilets, electricity, phone and, ideally, internet access. If a clinic site has to be renovated - which may be a longer-term investment for the community - then construction personnel, building supplies, temporary barriers and office equipment have to be sourced and transported if not locally available.
- Purchasing, transportation, and inventory systems for clinic equipment are needed. These include infection prevention and control supplies, testing equipment and supplies, such as chest x-ray equipment, GeneXpert (a rapid molecular test), TST/IGRA supplies, sputum-induction supplies, etc. Comprehensive planning is critical. In remote communities, use of GeneXpert may shorten time to diagnosis dramatically compared to transporting of sputum specimens to a lab for smear and culture, though both approaches are necessary. Make independent arrangements so as not to stress the local health center's supply chain. Confirm arrangements for transport of specimens and lab/radiology support, calibration of equipment on set-up and disposal of medical waste.
- Data collection and management: arrange computers and IT support, internet access if possible, connectivity/access to other essential healthcare databases/EMR, radio, phones. Paper versions of forms and records should be available if internet connectivity is unreliable.
- Clinic timing: aim for a period when the largest number of people will be in community; this is often winter.
- Outreach: since the goal is complete community coverage, accurate denominator information is needed; in remote communities this is generally available through the community mayor or housing office. Extensive outreach prior to and during the screening is vital for success, including local champions, local radio/social media, community meetings and door-to-door campaigns providing information and invitations to participate.