CONTEXT AND POLICY ISSUES

Tuberculosis (TB) is an infectious disease caused by strains of mycobacteria, most commonly mycobacterium tuberculosis (MTB), that affects more than two billion people in the world, with poverty, HIV, and TB drug resistance being the main contributors to the resurging global epidemic.1,2 Approximately 95 percent of TB cases occur in developing countries.1,2 Person-to-person transmission of TB occurs via inhalation of airborne particles that generally follow the cough or sneeze of an infected person.3 Following contact with a person with TB infection (called the index case), procedures are needed to investigate the risk of TB transmission, to identify and if necessary to treat the infected cases (called contact TB) in order to limit the transmission of TB.

TB contact investigation is defined as “a procedure for identifying and evaluating people exposed to someone with active TB disease, and providing appropriate treatment to prevent or treat TB, if indicated”. (Alberta Health and Wellness,4 p. 131)

According to the Canadian Tuberculosis Standards, contact investigation has three main objectives. In order of priority these are as follows:

1. Identify and initiate treatment of secondary cases of active TB disease.
2. Identify and treat the source case who infected the index case, if the index case is under 5 years old.
3. Identify contacts with LTBI in order to offer preventive treatment.” (Canadian Tuberculosis Standards,5 p. 295)

The nosocomial transmission of TB in healthcare facilities is a major public health concern. Studies showed that latent TB infection (LTBI) rate among healthcare workers is higher than among general population,6-8 and the incidence is higher in healthcare workers who work in high-risk areas.9 This Rapid Response report aims to review the clinical evidence regarding factors that trigger the need for a contact investigation following patient and staff exposure to a
RESEARCH QUESTIONS

1. What is the clinical evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting?

2. What is the clinical evidence regarding factors that trigger the need for a contact investigation when a staff member is exposed to a patient with an active tuberculosis infection in the hospital setting?

3. What are the evidence-based guidelines regarding best practice for contact investigations when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting?

4. What are the evidence-based guidelines regarding best practice for contact investigations when a staff member is exposed to a patient with an active tuberculosis infection in the hospital setting?

KEY FINDINGS

Evidence from one prospective uncontrolled study suggest a low contagiosity of the index case to staff members in a hospital setting, with age being the only predictor of latent TB infection. Evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting is lacking. Guidelines regarding factors that trigger the need for a contact investigation when a staff member or a patient is exposed to a patient with an active tuberculosis infection in the hospital setting are lacking. The guidelines included in this review describe contact investigation in general that in part may be applicable for hospital setting, and provided recommendations based on low level of evidence.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 2), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and March 28, 2014.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed for relevance. Full texts of any relevant titles or abstracts were
retrieved, and assessed for inclusion. The final article selection was based on the inclusion criteria presented in Table 1.

### Table 1: Selection Criteria

<table>
<thead>
<tr>
<th>Population</th>
<th>Patients and Staff who are exposed to a patient with an active TB infection in the hospital setting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention</td>
<td>Tuberculosis Contact Investigation, Tuberculosis Contact Follow-Up</td>
</tr>
<tr>
<td>Comparator</td>
<td>None/any</td>
</tr>
<tr>
<td>Outcomes</td>
<td>Clinical evidence regarding the factors that determine infection risk and thus trigger when the investigation is needed. (e.g. time period and length of exposure; infectiousness of the patient with TB). Most important factors in triggering the need for an investigation procedure. Comparison of triggers between patients and staff. Guidelines regarding best practice of contact investigation for patients and/or staff.</td>
</tr>
<tr>
<td>Study Designs</td>
<td>Health technology assessments (HTAs), systematic reviews (SRs), meta-analyses (MAs), randomized controlled trials (RCTs), non RCTs, and guidelines.</td>
</tr>
</tbody>
</table>

**Exclusion Criteria**

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2009, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

**Critical Appraisal of Individual Studies**

The quality of the included trials and guidelines was assessed using the Downs and Black, and the AGREE checklists, respectively. Numeric scores were not calculated. Instead, the strengths and limitations of the study are summarized and presented.

**SUMMARY OF EVIDENCE**

**Quantity of Research Available**

The literature search yielded 411 citations. After screening of abstracts from the literature search and from other sources, 54 potentially relevant studies were selected for full-text review. One trial related to contact investigations following patient and staff exposure to active tuberculosis infections were included in the review. Three guidelines about contact investigation in general that may be applicable for hospital setting were also included.

The PRISMA flowchart in Appendix 1 details the process of the study selection.

**Summary of Study Characteristics**

A detailed summary of the included study is provided in Appendix 2.
Study design

One trial\textsuperscript{12} and three guidelines\textsuperscript{4,13,14} were identified. The trial was a prospective uncontrolled study; the objective of the study was to evaluate an IGRA in comparison to the TST and to identify risk factors for test positivity.\textsuperscript{12} The guidelines are “Alberta Health and wellness: tuberculosis prevention and control guidelines for Alberta (2010)”,\textsuperscript{4} “Guideline for preventing the transmission of mycobacterium tuberculosis across the Consortium of Care (2010) – Newfoundland”,\textsuperscript{13} and the NICE guideline “Tuberculosis: clinical diagnosis and management of tuberculosis, and measures for its prevention and control (2011)”.\textsuperscript{14}

Population

The trial included in-hospital health care workers with exposure to a single index case (TB smear negative, culture positive, with pulmonary involvement) with a mean age of 38 ± 10 years, and mean duration of employment in health care of 14 ± 10 years. The inclusion criteria were an age of 18 years old or above, actual contact with the index case during infectivity, with written and informed consent.\textsuperscript{12}

Interventions and comparators

The trial used QuantiFERON-TB Gold in Tube assay (QFT-GIT) (an interferon-gamma release assay [IGRA]), and Mantoux tuberculin skin test (TST) to detect TB. Contacts were evaluated using a standardized interview and questionnaire, IGRA, TST, and followed with chest X-ray if IGRA results were positive.\textsuperscript{12}

Outcomes

The trial measured time of exposure to index case, QFT-GIT result, TST result, and predictor of QFT-GIT and TST positivity.\textsuperscript{12} The guidelines provided recommendations for tuberculosis treatment, prevention and control for patients with active TB or contact TB, including contact investigation.\textsuperscript{4,13,14} The strength of the evidence and recommendation was graded in the NICE guideline.\textsuperscript{14}

Summary of Critical Appraisal

The included study\textsuperscript{12} had the hypothesis clearly described, method of selection from source population and representation described, main outcomes, interventions, patient characteristics, and main findings clearly described, losses to follow-up described (denied consent or had indeterminate QFT-GIT results), and estimates of random variability and actual probability values provided. The findings from this study can be generalized to the general population under study, but the study rigour was limited due to its observational uncontrolled design.

The following guidelines were not specifically about contact investigation for hospital setting, but were included since they may be applicable to a hospital setting.

The Alberta and Newfoundland guidelines\textsuperscript{4,13} had clear scope and purpose, specific and unambiguous recommendations, with health benefits, side effects and risks stated in the recommendations, and target users of the guideline clearly defined. The method for searching for and selecting the evidence, the methods used for formulating the recommendations, and the procedure for updating the guidelines were unclear. It was unclear whether the guidelines were
piloted among target users, and whether patients’ views and preferences were sought. Potential cost implications of applying the recommendation were not included and level of evidence was not graded.

The NICE guideline\textsuperscript{14} had specific and unambiguous recommendations, with a systematic and clearly described method of searching for and selecting the evidence, and clearly described methods used to formulate the recommendations, with procedures to update the guidelines provided. It was piloted among target users, patients’ view and preferences were sought, and the procedures to update the guideline were provided. It was unclear whether potential cost implications of applying the recommendations were considered.

Details of the strengths and limitations of the included studies are summarized in Appendix 3.

Summary of Findings

Main findings of included studies are summarized in detail in Appendix 4.

1. What is the clinical evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting?

The literature search did not find clinical evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting.

2. What is the clinical evidence regarding factors that trigger the need for a contact investigation when a staff member is exposed to a patient with an active tuberculosis infection in the hospital setting?

The literature search identified one prospective uncontrolled study that conducted a contact investigation among health care workers in a German hospital after exposure to patient with active TB.\textsuperscript{12} The trial included in-hospital health care workers who were exposed to a single index case (TB smear negative, culture positive, with pulmonary involvement) with a mean age of 38 ± 10 years, and mean duration of employment in health care of 14 ± 10 years. The interferon-gamma release assay QuantiFERON-TB Gold in Tube (QFT-GIT) (Celestis, Carnegie, Australia), and Mantoux tuberculin skin test (TST) were used to detect latent TB infection in exposed health care workers. Outcomes included time of exposure to index case (using a standardized interview and questionnaire), QFT-GIT result, TST result, and predictors of QFT-GIT and TST positivity.

The median cumulative exposure time of exposure to index case was 60 min (range 3 to 4,000 min). Eighty-two subjects (57.3\%) had had close contact to the index case, and among them, 4 subjects (2.8\%) had been exposed for > 40 hours.

QFT-GIT results were positive in 13 subjects (9.1\%), with QFT-GIT-positive subjects being significantly older than test-negative subjects (mean 46 ± 10 vs 37 ± 9 years, \(P = 0.006\)). QFT-GIT-positive subjects had been working in healthcare for a longer period of time than test-negative subjects (mean 21 ± 12 vs 12 ± 8 years, \(P = 0.032\)). There was no statistically significant difference between median cumulative exposure times with regard to the QFT-GIT
results (there was no difference in median cumulative exposure time between the QFT-GIT-positive group and the QFT-GIT-negative group).

TST results were positive in 40 subjects (28.0%), with TST-positive subjects being significantly older than test-negative subjects (mean age 40 ± 9 vs 36 ± 9 years, P = 0.0.036). There was no statistically significant difference between duration of employment in health care and TST results, and no statistically significant difference between median cumulative exposure times and TST results. Discordant results between QFT-GIT and TST results occurred in 27.3% of subjects, most of them in the combination of TST-positive / QFT-GIT-negative, which was associated with TST false positive results with BCG vaccination and foreign origin.

While age was the only predictor of QFT-GIT positivity (the chance of having a positive QFT-GIT result increased 2.7 times with age), no relation was found between QFT-GIT positivity with exposure time, close contact, BCG vaccination, foreign origin, or any other variable such as health care profession (nurses, physicians), or affiliation with pulmonary care.

Further physical examinations and chest X-ray did not show active TB in all 13 subjects with positive QFT-GIT results, and no contact developed active TB over a follow-up period of 2 years after the last exposure to the index case.

The findings from this trial suggest a low contagiosity of the index case to staff members in a hospital setting, with age being the only predictor of latent TB infection.

3. What are the evidence-based guidelines regarding best practice for contact investigations when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting?

The literature search did not find evidence-based guidelines regarding best practice for contact investigations when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting. The following guidelines were about contact investigation in general that in part may be applicable for hospital setting. In general, the guidelines recommended a strict definition of high priority contacts, specific steps to follow for contact investigation without delay, and specific tests to detect infectivity in TB contacts.

The 2010 Alberta guidelines stated in section “Indications for TB contact investigation”: “Whenever a case of active TB disease is strongly suspected or diagnosed (either clinically or with laboratory confirmation) a decision must be made as to whether or not contact investigation is indicated…” (p. 138, 139) The guideline further stated in section “Prioritization of initiation of TB contact investigation in Alberta”: “There are two major considerations in prioritization of contact investigations: likelihood of transmission from the index case, and susceptibility of contacts for rapid progression to active TB disease if transmission has occurred” (p. 140) It noted in section “Systematic approach to TB contact investigation” that successful investigation “requires careful attention to detail in the gathering and evaluation of information. While contact investigation does not always follow this order, the steps outlined below should assist local TB program staff to ensure the necessary information is gathered.

1. Index case medical information review
2. Index case interview
3. Field investigation
4. MTB transmission risk assessment
5. Prioritization of contacts
6. Evaluation of contacts
7. Repeat index case interview if necessary
8. Follow-up of contacts
9. Review of contact investigation findings
10. Evaluation of contact investigation activities” (p. 142, 143)

The 2010 Newfoundland guidelines\textsuperscript{13} stated in section “Identification of contacts”: “High priority contacts include:

- Close contacts
- Contacts at high risk of developing TB disease once infected
- Children < 5 years
- Contacts with medical risk factors
- HIV infection
- Receiving immunosuppressive therapy
- Contacts with exposure during a medical procedure (e.g., bronchoscopy)” (p 39)

The 2011 NICE guidelines\textsuperscript{14} stated in section “Recommendations: “Screening should comprise: D(GPP) (evidence based on expert opinion, formal consensus)

- standard testing for latent TB for those aged 35 or younger, and consideration of BCG or treatment for latent TB infection once active TB has been ruled out
- interferon-gamma test six weeks after the Mantoux test, and consideration of BCG or treatment for latent TB infection once active TB has been ruled out, for those who:
  - are previously unvaccinated and
  - are household contacts of a person with sputum smear-positive TB and
  - are Mantoux negative (<6 mm)
- chest X-ray (if there are no contraindications) for those older than 35, possibly leading to further investigation for active TB” (p. 241) “Casual contacts of people with TB, who will include the great majority of workplace contacts, should not normally be assessed.” (evidence based on non-analytic studies, such as case reports, case series) (p 241, 242)

4. What are the evidence-based guidelines regarding best practice for contact investigations when a staff member is exposed to a patient with an active tuberculosis infection in the hospital setting?

The literature search did not find evidence-based guidelines regarding best practice for contact investigations when a staff member is exposed to another patient with an active tuberculosis infection in the hospital setting.

Limitations

Evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting came from one prospective uncontrolled trial. Evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting is lacking. Guidelines regarding factors that trigger the need for a contact
investigation when a staff member or a patient is exposed to a patient with an active tuberculosis infection in the hospital setting are lacking. Identified guidelines did not provide recommendations specific to the healthcare facilities, and therefore may not be fully generalizable to this setting.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

Evidence from one prospective uncontrolled study suggest a low contagiousity of the index case to staff members in a hospital setting, with age being the only predictor of latent TB infection. No relation was found between QFT-GIT positivity with exposure time, close contact, BCG vaccination, foreign origin, or any other variable such as health care professions (nurses, physicians) or affiliation with pulmonary care. The site of the study was a university hospital in Berlin, Germany, and its findings can be applicable to a Canadian setting. Evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting is lacking. The literature search did not find any evidence regarding a distinction between contact investigations when a staff member is exposed to a patient or when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting. Guidelines regarding factors that trigger the need for a contact investigation when a staff member or a patient is exposed to a patient with an active tuberculosis infection in the hospital setting are lacking.

For TB infections in a health care institutions, the Canadian Tuberculosis Standards, which provide information on TB contact investigation in healthcare settings, but do not provide clinical recommendations, stated “Unless the contact investigation is conducted in an organized, systematic fashion, with the basic principles of transmission in mind, it may result in hundreds of “contacts” with limited or unknowable exposure and often dismal participation and follow-up completion rates […] It is often very useful to measure air exchange rates in specific hospital exposure locations, in order to help prioritize contact follow-up. It is also important to confirm whether there were any unprotected aerosolizing procedures, such as intubation, carried out on the infectious case (i.e. when staff did not use N95 masks). Some types of patients are extremely vulnerable (e.g. transplant patients) and even short exposures may be relevant. Visitors to the case and to room-mates may have significant exposure. Hospital infection control and occupational health departments often take advantage of TB exposures to get staff TST documentation up to date, but within this larger group of staff being tested it is important to distinguish those who have the most actual exposure to the infectious case – particularly if there are conversions detected […] Individuals who are immunosuppressed are at much higher risk of TB disease after infection with TB; thus, TB exposures in specialty services or clinics may pose an especially high risk” (p. 309, 310).

In summary, clinical evidence regarding factors that trigger the need for a contact investigation when a patient or a staff member is exposed to another patient with an active tuberculosis infection in the hospital setting is limited. Considering the importance of nosocomial TB infections, more clinical trials and evidence-based guidelines specifically focused on contact TB investigation in healthcare facilities are needed.

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REFERENCES


Appendix 1: Selection of Included Studies

411 citations identified from electronic literature search and screened

357 citations excluded

54 potentially relevant articles retrieved for scrutiny (full text, if available)

5 relevant reports retrieved from other sources (grey literature, hand search)

59 potentially relevant reports

55 reports excluded (irrelevant population, interventions or outcomes)

4 reports included in review
Appendix 2: Characteristics of Included Study

<table>
<thead>
<tr>
<th>Trials</th>
<th>Design, Sample Size, Patient Characteristics, Length of Follow-up Conflict of Interest</th>
<th>Intervention</th>
<th>Comparator(s)</th>
<th>Main Study Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ringshausen, 2009, Germany</td>
<td>Prospective observational uncontrolled study 143 in-hospital HCWs with exposure to a single index case (TB smear negative, culture positive, with pulmonary involvement) Mean age: 38 ± 10 years (range 20 – 62) Mean duration of employment in health care: 14 ± 10 years (range 1 – 42) 51.0% of subjects were BCG vaccinated Follow-up time: 2 years No conflict of interest declared</td>
<td>MTB-specific interferon – gamma release assays (IGRAs), using QFT-GIT Mantoux tuberculin skin test (TST)</td>
<td>None</td>
<td>Time of exposure to index case IGRA result TST result Predictor of IGRA and TST positivity</td>
</tr>
</tbody>
</table>

BCG: Bacille Calmette-Guerin; HCW: healthcare worker; QFT-GIT: IGRA QuantiFERON-TB Gold in Tube assay
### Table A2: Summary of Critical Appraisal of Included Study

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
</table>
| **Critical appraisal of included studies (Downs and Black.10)** | • hypothesis clearly described  
• method of selection from source population and representation described  
• main outcomes, interventions, patient characteristics, and main findings clearly described  
• losses to follow-up described  
• estimates of random variability and actual probability values provided | • observational uncontrolled study, patients not randomized  
• unclear whether study had sufficient power to detect a clinically important effect |
| Ringshausen,12 2009            | • scope and purpose of the guidelines are clear  
• the recommendations are specific and unambiguous  
• health benefits, side effects and risks were stated in the recommendations  
• target users of the guideline are clearly defined | • unclear about the method for searching for and selecting the evidence  
• unclear about the methods used for formulating the recommendations  
• potential cost implications of applying the recommendation not included  
• unclear whether guideline was piloted among target users  
• unclear whether patients' views and preferences were sought  
• unclear about the procedure for updating the guidelines  
• level of evidence not graded |
| **Critical appraisal of included guidelines (AGREE11)** | • scope and purpose of the guidelines are clear  
• the recommendations are specific and unambiguous  
• health benefits, side effects and risks were stated in the recommendations  
• target users of the guideline are clearly defined | • unclear about the method for searching for and selecting the evidence  
• unclear about the methods used for formulating the recommendations  
• potential cost implications of applying the recommendation not included  
• unclear whether guideline was piloted among target users  
• unclear whether patients' views and preferences were sought  
• unclear about the procedure for updating the guidelines  
• level of evidence not graded |
| Alberta guideline,10 2010      | • scope and purpose of the guidelines are clear  
• the recommendations are specific and unambiguous  
• health benefits, side effects and risks were stated in the recommendations  
• target users of the guideline are clearly defined | • unclear about the method for searching for and selecting the evidence  
• unclear about the methods used for formulating the recommendations  
• potential cost implications of applying the recommendation not included  
• unclear whether guideline was piloted among target users  
• unclear whether patients' views and preferences were sought  
• unclear about the procedure for updating the guidelines  
• level of evidence not graded |
| Newfoundland guideline,13 2010 | • scope and purpose of the guidelines are clear  
• the recommendations are specific and unambiguous  
• health benefits, side effects and risks were stated in the recommendations  
• target users of the guideline are clearly defined | • unclear about the method for searching for and selecting the evidence  
• unclear about the methods used for formulating the recommendations  
• potential cost implications of applying the recommendation not included  
• unclear whether guideline was piloted among target users  
• unclear whether patients' views and preferences were sought  
• unclear about the procedure for updating the guidelines  
• level of evidence not graded |
| NICE guideline,14 2011         | • scope and purpose of the guidelines are clear  
• the recommendations are specific and unambiguous  
• the method for searching for and selecting the evidence are clear  
• methods used for formulating the recommendations are clearly described  
• health benefits, side effects and risks were stated in the recommendations  
• target users of the guideline are clearly defined  
• the guideline was piloted among target users | • unclear whether potential cost implications of applying the recommendation was considered |
Table A2: Summary of Critical Appraisal of Included Study

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Strengths</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>• patients’ views and preferences were sought</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• procedure for updating the guidelines provided</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• level of evidence graded</td>
<td></td>
</tr>
</tbody>
</table>
# Appendix 4: Main Study Findings and Authors’ Conclusions

## Table A3: Main Study Findings and Authors’ Conclusions

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Research question 1</strong> (clinical evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting)</td>
<td>The literature search did not find clinical evidence regarding factors that trigger the need for a contact investigation when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting.</td>
<td>“Our findings suggest a low contagiousity of the particular index case. The frequency of positive QFT-GIT results may in fact reflect the pre-existing prevalence of latent TB infection among the study population. TB transmission seems unlikely and contact tracing not generally warranted after cumulative exposure &lt;40 hours. However, the substantially lower frequency of positive QFT-GIT results compared to the TST may contribute to enhanced TB control in health care.” (p 1e)</td>
</tr>
<tr>
<td>Ringshausen, ² 2009</td>
<td><strong>Time of exposure to index case</strong>&lt;br&gt;Median cumulative exposure time: 60 min (range 3 to 4,000 min) 82 subjects (57.3%) had had close contact to the index case 4 subjects (2.8%) had been exposed for &gt;40 hours <strong>QFT-GIT</strong>: result positive in 13 subjects (9.1%) QFT-GIT-positive subjects were significantly older (mean 46 ± 10 vs 37 ± 9 years for negative result subjects, ( P = 0.006 )) QFT-GIT-positive subjects had been working in health care for a longer period of time (mean 21 ± 12 vs 12 ± 8 years for negative result subjects, ( P = 0.032 )) No statistically significant difference between median cumulative exposure times with regard to QFT-GIT results <strong>TST</strong>: result positive in 40 subjects (28.0%) TST-positive subjects were significantly older (mean age 40 ± 9 vs 36 ± 9 years for negative results subjects, ( P = 0.036 )) No statistically significant difference between duration of employment in health care and TST results No statistically significant difference between median cumulative exposure times and TST results (( P = 0.48 )) <strong>Concordance between QFT-GIT and TST results</strong> Concordance in 72.7% of subjects Discordance in 27.3% of subjects (kappa = 0.15) TST-positivity was associated with BCG vaccination and foreign origin (false positive) <strong>Predictors of test positivity</strong> Age was the only predictor of QFT-GIT positivity (odds ratio 2.7; 95% CI 1.32 – 5.46) No relation between QFT-GIT positivity with BCG vaccination, foreign origin, exposure time per hour, close contact, or any other variable</td>
<td></td>
</tr>
</tbody>
</table>
Table A3: Main Study Findings and Authors’ Conclusions

<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical impact of QFT-GIT test results</td>
<td>No active TB in all 13 subjects with positive QFT-GIT results (by physical examination and chest X-ray)</td>
<td>No contact developed active TB over a follow-up period of 2 years after the last exposure to the index case</td>
</tr>
</tbody>
</table>

Research question 3 (evidence-based guidelines regarding best practice for contact investigations when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting)

The literature search did not find evidence-based guidelines regarding best practice for contact investigations when a patient is exposed to another patient with an active tuberculosis infection in the hospital setting.

The following guidelines aimed to contact investigation in general that may be applicable for hospital setting

**Alberta guideline**

**Responsibility**

"Contact investigation and outbreak management is the responsibility, under the Public Health Act, of local public health staff who work collaboratively with AHS central TB Services or the local outpatient TB clinic and co-ordinate staff in local settings as appropriate." (Alberta guideline, p 131)

They are responsible for

- identifying and evaluating contacts
- providing treatment to contacts found to have active TB disease
- offering treatment to contacts found to have LTBI
- monitoring adherence to prescribed treatment
- ensuring a system is in place to assess completion of treatment” (Alberta guideline, p 132)

The local investigation coordinator(s) should provide the provincial TB Contact Investigation Coordinator with the following:

- information about the whereabouts of named contacts who have moved or live in a different jurisdiction than the case;
- outcomes of all investigation activities as they are completed; evidence of transmission (e.g., identification of additional active cases and/or TST (or IGRA) converters) will necessitate the expansion of the contact investigation;
- reports of compliance with recommendations for contact follow-up and/or treatment.

(Alberta guideline, p 132)

**Indications for TB contact investigation**

"Whenever a case of active TB disease is strongly suspected or diagnosed (either clinically or with laboratory confirmation) a decision must be made as to whether or not contact investigation is indicated. If investigation is indicated, a determination will be made as to who should be included in the initial round of screening (scope) as well as what priority should be assigned to the investigation overall (see Section 4.10.5, Prioritization of contacts, which follows). Initial decision-making is guided by the site of disease and radiology/bacteriology findings at the time of presentation of the index case. The investigation plan may change as additional information becomes available, e.g., through interviews with the case and/or findings from initial round of contact evaluations. For example, if mycobacteriology cultures indicate the case does not have TB, the investigation may be discontinued. Or, if TST conversions or an additional case of active TB disease is found among initial contacts screened, the scope of the investigation may be broadened to include contacts with lesser durations of exposure.” (Alberta guideline, p 138, 139)

**Prioritization of initiation of TB contact investigation**

"There are two major considerations in prioritization of contact investigations.

- likelihood of transmission from the index case, and
- susceptibility of contacts for rapid progression to active TB disease if transmission has occurred
Other factors that may influence prioritization include:
- Index case drug resistance (especially multi-drug or extensively drug-resistant isolates) due to concern about identifying/preventing additional cases of DR-TB
- Number/availability of contacts requiring evaluation at the outset of the investigation (e.g., cases with high numbers of close contacts)
- Public Health response capacity” (p 140)

**Systematic approach to TB contact investigation**

Any successful investigation requires careful attention to detail in the gathering and evaluation of information. While contact investigation does not always follow this order, the steps outlined below should assist local TB program staff to ensure the necessary information is gathered.

1. Index case medical information review
2. Index case interview
3. Field investigation
4. MTB transmission risk assessment
5. Prioritization of contacts
6. Evaluation of contacts
7. Repeat index case interview if necessary
8. Follow-up of contacts
9. Review of contact investigation findings
10. Evaluation of contact investigation activities

The process of contact investigation should begin as soon as a case is strongly suspected or diagnosed. An initial list of known contacts should be submitted to AHS central TB Services or the local outpatient TB clinic on the Tuberculosis Contact List (see Appendix G) within seven days (one calendar week) of notification of the case.” (p 142, 143)

**Assigning Priorities to Contacts**

*Priorities are based on the likelihood of infection and hazards to the contact if infected. Priority is directed to those who:*
- Have recent M. tuberculosis infection (most likely to benefit from treatment)
- Are most likely to develop TB disease if infected or could suffer severe morbidity if they develop TB disease

**High priority contacts include:**
- Close contacts
- Contacts at high risk of developing TB disease once infected
- Children < 5 years
- Contacts with medical risk factors
- HIV infection
- Receiving immunosuppressive therapy
- Contacts with exposure during a medical procedure (e.g., bronchoscopy)

A graduated approach to contact investigations (i.e., a concentric circles model) is used (Appendix Section 5-B). Testing of the first circle of contacts should begin within 7 working days of their being identified as contacts. When there is evidence of transmission in the first group of close contacts, the likelihood of further transmission increases, and it is prudent to expand the testing to include those with less contact.
<table>
<thead>
<tr>
<th>First Author, Publication Year</th>
<th>Main Study Findings</th>
<th>Authors’ Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medium and low risk casual contacts:</td>
<td>The following factors would indicate recent transmission: • a secondary case of tuberculosis • a higher infection rate among contacts than what would be expected in this community e.g. skin test conversion in contacts • evidence of transmission to young children</td>
<td>Testing of the medium-priority contacts should be done by 14 days after being listed as contacts. (p 39, 40)</td>
</tr>
<tr>
<td>NICE guideline, 2011</td>
<td>Contact tracing</td>
<td>Once a person has been diagnosed with active TB, the diagnosing physician should inform relevant colleagues so that the need for contact tracing can be assessed without delay. Contact tracing should not be delayed until notification. D(GPP)* Screening should be offered to the household contacts of any person with active TB, irrespective of the site of infection. Household contacts are defined as those who share a bedroom, kitchen, bathroom or sitting room with the index case. Screening should comprise: D(GPP) - standard testing for latent TB for those aged 35 or younger, and consideration of BCG or treatment for latent TB infection once active TB has been ruled out - interferon-gamma test six weeks after the Mantoux test, and consideration of BCG or treatment for latent TB infection once active TB has been ruled out, for those who: – are previously unvaccinated and – are household contacts of a person with sputum smear-positive TB and – are Mantoux negative (&lt;6 mm) - chest X-ray (if there are no contraindications) for those older than 35, possibly leading to further investigation for active TB. For people with sputum smear-positive TB, other close contacts should be assessed. These may include boyfriends or girlfriends and frequent visitors to the home of the index case. Occasionally, a workplace associate may be judged to have had contact equivalent to that of household contacts, and should be assessed in the same way. D(GPP)* Casual contacts of people with TB, who will include the great majority of workplace contacts, should not normally be assessed. C ** (p 241, 242)</td>
</tr>
</tbody>
</table>

**Research question 4 (evidence-based guidelines regarding best practice for contact investigations when a staff member is exposed to a patient with an active tuberculosis infection in the hospital setting)**

The literature search did not find evidence-based guidelines regarding best practice for contact investigations when a staff member is exposed to another patient with an active tuberculosis infection in the hospital setting.

AHS: Alberta Health Services; **C: level of evidence 3 (evidence based on non-analytic studies, such as case reports, case series); * D (GPP): level of evidence 4 (evidence based on expert opinion, formal consensus). DPP: good practice point, a recommendation based on the experience of the Guideline Development Group; DR-TB: drug-resistant tuberculosis; IGRA: interferon gamma-release assay; LTBI: latent tuberculosis infection; QFT-GIT: QuantiFERON-TB Gold in Tube assay; TB: tuberculosis; TST: tuberculin skin test