

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

# Interferon Gamma Release Assay for the Identification of Latent Tuberculosis Infection in People with Previous Bacille Calmette-Guérin Vaccination: Clinical Utility, Cost-Effectiveness, and Guidelines

Service Line: Rapid Response Service  
Version: 1.0  
Publication Date: August 20, 2020  
Report Length: 6 Pages

**Authors:** Diksha Kumar, Mary-Doug Wright, Melissa Severn

**Cite As:** *Interferon Gamma Release Assay for the Identification of Latent Tuberculosis Infection in People with Previous Bacille Calmette-Guérin Vaccination: Clinical Utility, Cost-Effectiveness, and Guidelines*. Ottawa: CADTH; 2020 Aug. (CADTH rapid response report: summary of abstracts).

**Disclaimer:** The information in this document is intended to help Canadian health care decision-makers, health care professionals, health systems leaders, and policy-makers make well-informed decisions and thereby improve the quality of health care services. While patients and others may access this document, the document is made available for informational purposes only and no representations or warranties are made with respect to its fitness for any particular purpose. The information in this document should not be used as a substitute for professional medical advice or as a substitute for the application of clinical judgment in respect of the care of a particular patient or other professional judgment in any decision-making process. The Canadian Agency for Drugs and Technologies in Health (CADTH) does not endorse any information, drugs, therapies, treatments, products, processes, or services.

While care has been taken to ensure that the information prepared by CADTH in this document is accurate, complete, and up-to-date as at the applicable date the material was first published by CADTH, CADTH does not make any guarantees to that effect. CADTH does not guarantee and is not responsible for the quality, currency, propriety, accuracy, or reasonableness of any statements, information, or conclusions contained in any third-party materials used in preparing this document. The views and opinions of third parties published in this document do not necessarily state or reflect those of CADTH.

CADTH is not responsible for any errors, omissions, injury, loss, or damage arising from or relating to the use (or misuse) of any information, statements, or conclusions contained in or implied by the contents of this document or any of the source materials.

This document may contain links to third-party websites. CADTH does not have control over the content of such sites. Use of third-party sites is governed by the third-party website owners' own terms and conditions set out for such sites. CADTH does not make any guarantee with respect to any information contained on such third-party sites and CADTH is not responsible for any injury, loss, or damage suffered as a result of using such third-party sites. CADTH has no responsibility for the collection, use, and disclosure of personal information by third-party sites.

Subject to the aforementioned limitations, the views expressed herein do not necessarily reflect the views of Health Canada, Canada's provincial or territorial governments, other CADTH funders, or any third-party supplier of information.

This document is prepared and intended for use in the context of the Canadian health care system. The use of this document outside of Canada is done so at the user's own risk.

This disclaimer and any questions or matters of any nature arising from or relating to the content or use (or misuse) of this document will be governed by and interpreted in accordance with the laws of the Province of Ontario and the laws of Canada applicable therein, and all proceedings shall be subject to the exclusive jurisdiction of the courts of the Province of Ontario, Canada.

The copyright and other intellectual property rights in this document are owned by CADTH and its licensors. These rights are protected by the Canadian *Copyright Act* and other national and international laws and agreements. Users are permitted to make copies of this document for non-commercial purposes only, provided it is not modified when reproduced and appropriate credit is given to CADTH and its licensors.

**About CADTH:** CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

**Funding:** CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

Questions or requests for information about this report can be directed to [requests@cadth.ca](mailto:requests@cadth.ca)

## Research Questions

1. What is the clinical utility of the interferon gamma release assay for identifying latent tuberculosis infection in people with previous Bacille Calmette-Guérin vaccination?
2. What is the cost-effectiveness of the interferon gamma release assay for identifying latent tuberculosis infection in people with previous Bacille Calmette-Guérin vaccination?
3. What are the evidence-based guidelines regarding the identification of latent tuberculosis infection in people with previous Bacille Calmette-Guérin vaccination?

## Key Findings

One non-randomized study was identified regarding the clinical utility of the interferon gamma release assay for identifying latent tuberculosis infection in people with previous Bacille Calmette-Guérin vaccination. In addition, one evidence-based guideline was regarding the identification of latent tuberculosis infection in people with previous Bacille Calmette-Guérin vaccination. No relevant economic evaluations were identified regarding the cost-effectiveness of the interferon gamma release assay for identifying latent tuberculosis infection in people with previous Bacille Calmette-Guérin vaccination.

## Methods

### Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE All via Ovid, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were interferon gamma release assay and people with a history of Bacille Calmette-Guérin vaccination who may have been exposed to tuberculosis. Search filters were applied to limit retrieval to guidelines for Question 3 only. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2015 and August 3, 2020. Internet links were provided, where available.

### Selection Criteria and Summary Methods

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. The Overall Summary of Findings was based on information available in the abstracts of selected publications. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available, and relevant recommendations were summarized.

This report is a component of a larger CADTH Condition Level Review on tuberculosis. A condition level review is an assessment that incorporates all aspects of a condition, from prevention, detection, treatment, and management. For more information on CADTH's Condition Level Review of tuberculosis, please visit the project page (<https://www.cadth.ca/tuberculosis>).

**Table 1: Selection Criteria**

<b>Population</b>	People with a history of Bacille Calmette-Guérin vaccination who may have been exposed to tuberculosis
<b>Intervention</b>	Q1, 2: interferon gamma release assay Q3: interferon gamma release assay, tuberculin skin test
<b>Comparator</b>	Q1, 2: Tuberculin skin test Q3: not applicable
<b>Outcomes</b>	Q1: Clinical utility (e.g., detection outcomes, people who obtain screening in accordance with guidelines, patients receiving treatment for infection, need for additional latent tuberculosis infection screening) Q2: Cost-effectiveness (e.g., cost per health benefit) Q3: Recommendations regarding the best practices for screening for latent tuberculosis infection in this population
<b>Study Designs</b>	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, evidence-based guidelines

## Results

One non-randomized study<sup>1</sup> was identified regarding the clinical utility of the interferon gamma release assay (IGRA) for identifying latent tuberculosis infection (LTBI) in people with previous Bacille Calmette-Guérin (BCG) vaccination. In addition, one evidence-based guideline was regarding the identification of LTBI in people with previous BCG vaccination. No relevant economic evaluations were identified regarding the cost-effectiveness of the IGRA for identifying LTBI in people with previous BCG vaccination. No relevant health technology assessments, systematic reviews, or randomized controlled trials were identified.

Additional references of potential interest that did not meet the inclusion criteria are provided in the appendix.

## Overall Summary of Findings

One non-randomized study<sup>1</sup> was identified regarding the clinical utility of the IGRA for identifying LTBI in people with previous BCG vaccination. The authors found that the implementation of QuantiFERON R-TB Gold In-tube testing combined with the tuberculin skin test (TST) significantly reduced rates of tuberculosis diagnosis and preventative therapy among BCG-vaccinated contacts compared to TST alone.<sup>1</sup>

One evidence-based guideline<sup>2</sup> was identified regarding the identification of LTBI in people with previous BCG vaccination. The World Health Organization recommends that either a TST or IGRA should be used to identify LTBI, with BCG vaccination not being a determining factor in selecting a test.<sup>2</sup> As part of the condition level review, the guideline<sup>2</sup> in this report was previously included in a CADTH report<sup>3</sup> on guidelines for identification of tuberculosis. The detailed critical appraisal of this guideline can be found in that report.<sup>3</sup>

No relevant literature was found regarding the cost-effectiveness of the IGRA for identifying LTBI in people with previous BCG vaccination; therefore, no summary can be provided.

## References Summarized

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-Analyses

No literature identified.

### Randomized Controlled Trials

No literature identified.

### Non-Randomized Studies

1. Munoz L, Gonzalez L, Soldevila L, Dorca J, Alcaide F, Santin M. QuantiFERON R-TB Gold In-Tube for contact screening in BCG-vaccinated adults: A longitudinal cohort study. *PLoS ONE*. 2017;12(8):e0183258.  
[PubMed: PM28854216](#)

### Economic Evaluations

No literature identified.

### Guidelines and Recommendations

2. Latent tuberculosis infection: updated and consolidated guidelines for programmatic management. Geneva: World Health Organization; 2018.  
<https://apps.who.int/iris/bitstream/handle/10665/260233/9789241550239-eng.pdf?sequence=1&isAllowed=y> Accessed 2020 Aug 19.  
*See: 4. Testing for latent tuberculosis infection, Considerations for implementation, page 22*

## Appendix — Further Information

### Previous CADTH Reports

3. Identification of Tuberculosis: A Review of the Guidelines. Ottawa: CADTH; 2020 February. (CADTH rapid response report: summary with critical appraisal). <https://www.cadth.ca/sites/default/files/pdf/htis/2020/RC1236%20TB%20identification%20Final.pdf> Accessed 2020 Aug 19.

### Non-Randomized Studies – Mixed Population

4. Crossa A, Kessler J, Harris TG. Enhanced Tuberculosis Infection Treatment Outcomes after Implementation of QuantiFERON R-Gold Testing. *PLoS ONE*. 2015;10(9):e0138349. [PubMed: PM26371760](#)
5. Lee H, Park HY, Jeon K, et al. QuantiFERON-TB Gold In-Tube assay for screening arthritis patients for latent tuberculosis infection before starting anti-tumor necrosis factor treatment. *PLoS ONE*. 2015;10(3):e0119260. [PubMed: PM25746854](#)

### Clinical Practice Guidelines – Methodology Unclear

6. Position statement on interferon- $\gamma$  release assays for the detection of latent tuberculosis infection; 2017. *Communicable Diseases Intelligence*:41(4):E322-E336. [https://www1.health.gov.au/internet/main/publishing.nsf/Content/4A5C7E747C705B0ACA25823C00068704/\\$File/cdi4104-c.pdf](https://www1.health.gov.au/internet/main/publishing.nsf/Content/4A5C7E747C705B0ACA25823C00068704/$File/cdi4104-c.pdf) Accessed 2020 Aug 19.  
*See: Contact investigation in adults, Revised recommendations*
7. Primary Care Guidelines for the Management of HIV/AIDS in British Columbia. Vancouver: British Columbia Centre for Excellence in HIV/AIDS; 2015. [http://www.cfenet.ubc.ca/sites/default/files/uploads/primary-care-guidelines/primary-care-guidelines\\_015-09-15.pdf](http://www.cfenet.ubc.ca/sites/default/files/uploads/primary-care-guidelines/primary-care-guidelines_015-09-15.pdf) Accessed 2020 Aug 19.  
*See: A. Tuberculosis Screening, page 34*