Interferon-Gamma Release Assay Testing for Latent Tuberculosis Infection

Recommendation

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Ontario Health

Draft Recommendation

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends publicly funding interferon gamma release assay (IGRA) testing for latent tuberculosis infection.

Rationale for the Recommendation

The Ontario Health Technology Advisory Committee made the above recommendation after considering the clinical, economic, and providers' preferences and values evidence reported in the health technology assessment.[1]

The committee indicated that the adoption and implementation of IGRA testing should align with current Canadian Tuberculosis (TB) Standards,[2] issued in 2022 (hereinafter, the Standards), and relevant future updates, which provide recommendations for situations in which IGRA is preferred over a tuberculin skin test (TST) (e.g., BCG-vaccinated immigrants, BCG-vaccinated contacts, and immunocompromised people). Referral for IGRA testing should be at the discretion of a person's treating or primary care physician or an Ontario public health unit. The committee also recognized that access to IGRA testing will enhance equity of access and quality of care for eligible populations.

The committee concluded that IGRA can be considered a good rule-in test for latent TB infection (LTBI) due to its consistently high specificity. Compared with the TST, IGRA has fewer false positive findings (results showing that a person has LTBI when they don't). This was particularly notable in people who have received a Bacille Calmette-Guérin (BCG) vaccine. IGRA may also be informative for people with immunocompromising conditions (e.g., HIV positive, organ transplant) who are at risk for a false-negative finding (results showing a person does not have LTBI when they do) by TST.

The committee considered the published Canadian economic evidence, which found that IGRA testing for LTBI was either cost-effective or cost-saving compared with TST alone in high-risk populations (as identified by the Standards). Publicly funding IGRA testing in high-risk populations in alignment with the current Standards[2] (e.g., BCG-vaccinated immigrants, BCG-vaccinated contacts, and immunocompromised people) could result in total additional costs of between $2.99 million and $18.80 million over the next 5 years, depending on whether the test is used alone or sequentially with TST. However, the committee recognized the potential for savings of at least $1.63 million if IGRA is used in immigrants and individuals identified through contact investigations who have previously received a BCG vaccine (savings due to the reduction of unnecessary medical follow-up evaluations and treatment in people who would have been incorrectly identified by a TST as having LTBI). Conversely, there may be additional costs of $6.26 million or more when IGRA testing is used in immunocompromised people due to the increased appropriate medical evaluations and treatment for those who would have been incorrectly identified as negative (not having LTBI) with TST.

The committee also considered providers' experiences with IGRA testing and TST. Providers shared views that using IGRA will reduce false-positive test results in people who have received the BCG vaccine and there is no inter-reader variability affecting test results. They also noted that TST requires repeat visits to a care provider, one visit to get the test and a second visit to read the results. Patients can face barriers with transportation to/from settings that provide the TST, a need for childcare, or time-off work

to attend repeat visits. Those patients may become lost to follow up or require additional health provider/system time and resources for test follow up. The cost of IGRA testing was also highlighted as a barrier for patients.

Decision Determinants for Interferon Gamma Release Assay Testing for Latent Tuberculosis Infection

Overall Clinical Benefit

Effectiveness

How effective is the health technology/intervention likely to be (taking into account any variability)?

Based on an overview of reviews summarizing the existing evidence on diagnostic accuracy and clinical utility of IGRA for LTBI:

- IGRA was found to have good evidence as a rule-in test for LTBI due to consistently high specificity
- Compared with TST, testing with IGRA may yield fewer false-positive findings. IGRA testing among people at risk for LTBI results in fewer people testing positive than compared with TST. In head-to-head comparisons, a positive IGRA test led to higher rates of identifying people with LTBI who would go on to develop active TB compared with those who had a positive TST finding
- IGRA may be informative for people with immunocompromising conditions who are at risk of a false negative by a TST, as it yields indeterminate findings signaling that further clinical investigation may be needed

Therefore, the evidence supports the use of IGRA testing as a viable option to diagnose LTBI, in accordance with situations outlined in the current Standards.[2]

Safety

How safe is the health technology/intervention likely to be?

There are no safety concerns related to IGRA testing beyond what is typical for tests that require a blood draw sample.

Burden of Illness

What is the likely size of the burden of illness pertaining to this health technology/intervention?

Latent TB infection affects 23% of the global population and is estimated to affect 22% of the foreign-born population of Ontario. Additionally, the rate of active TB in Canada is estimated to be 4.6 to 5.1 per 100,000 people, reaching 12.7 per 100,00 for Canadian-born Indigenous people.

Need

How large is the need for this health technology/intervention?

There is increasing demand by clinicians to have IGRA testing publicly funded as an option for diagnosing LTBI. Additionally, some patients will have improved accuracy in test results with IGRA testing.

Patient Preferences and Privacy

Patient Preferences and Values

Do patients have specific preferences, values, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment?

Providers explained that IGRA testing is preferred by most of their patients. This is mainly due to IGRA requiring only a single visit to the clinic, while TST requires multiple visits.

Autonomy, Privacy, Confidentiality, and/or Other Relevant Ethical Principles, as Applicable

Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment?

No issues regarding accepted ethical or legal standards were identified.

Equity and Patient Care

Equity of Access or Outcomes

Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?

The full health technology assessment describes the issues around equity in more detail. In brief, 3 primary groups are currently disadvantaged by having only TST publicly funded: those who are BCG-vaccinated, those who are immunocompromised, and those who have difficulties returning for a second medical visit within a restrictive time-frame to have their TST results read.

Patient Care

Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?

Access to IGRA testing would streamline the coordination of care for individuals who have difficulties with TST. IGRA testing would also have public health benefits as it would reduce unnecessary testing and treatment due to false-positive results from the TST, as well as reduce the volume of follow-up visits required to confirm the TB status of contacts.

Cost-Effectiveness

Economic Evaluation

How efficient is the health technology/intervention likely to be?

Based on a systematic review of published Canadian economic studies, IGRA testing (as a single or sequential test to TST) for LTBI was cost-effective or cost-saving compared with TST alone in high-risk populations (as identified by the current Standards[2]). There was high certainty in the currently published body of evidence (Grading of Recommendations, Assessment, Development and Evaluations [GRADE]: High).

Feasibility of Adoption Into Health System

Economic Feasibility

How economically feasible is the health technology/intervention?

For high-risk populations, in alignment with the current Standards[2] (e.g., BCG-vaccinated immigrants, BCG-vaccinated contacts, and immunocompromised people), compared with TST alone, IGRA testing (as a single test or in sequential pathways with TST) could result in total additional costs of between $2.99 million (if IGRA is used alone) and $18.80 million (if IGRA is used sequentially with TST) over the next 5 years. In immigrants and individuals identified via contact investigations who have previously received a BCG vaccine, IGRA testing could save at least $1.63 million due to reductions in unnecessary medical follow-up evaluations and treatment in people who would have been incorrectly identified as positive (false positive) with TST. In immunocompromised people, IGRA testing could result in additional costs of $6.26 million or higher due to increased appropriate medical evaluations and treatment for those who would have incorrectly identified as negative (false negative) with TST.

Organizational Feasibility

How organizationally feasible is it to implement the health technology/intervention?

Interferon gamma release assay testing is currently available in Ontario through private laboratories, as well as at some hospitals. More Ontario hospitals are purportedly interested in providing IGRA testing if the test is publicly funded. The Schedule of Benefits for Laboratory Services might need to be updated with an additional lab fee code specific for the IGRA testing if the test is publicly funded and adopted into the Ontario health care system. Eligibility criteria for public funding of IGRA testing for LTBI would be determined by the Ministry of Health.

References

1. TBD
2. Campbell JR, Pease C, Daley P, Pai, M., & Menzies, D. (2022). Chapter 4: Diagnosis of tuberculosis infection. Can J Respir Crit Care Sleep Med. 6(1):49–65.

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