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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Prevention of Tuberculosis Reactivation: Clinical Utility and Guidelines

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Authors: Diksha Kumar, Suzanne McCormack

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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**

Research Questions

1. What is the clinical utility of screening for latent tuberculosis infection in people at risk of tuberculosis reactivation?
2. What is the clinical utility of treating latent tuberculosis infection to prevent tuberculosis reactivation?
3. What are the evidence-based guidelines for the prevention of tuberculosis reactivation?

Key Findings

One network meta-analysis and one non-randomized study were identified regarding the clinical utility of treating latent tuberculosis infection to prevent tuberculosis reactivation. Two evidence-based guidelines were identified regarding the prevention of tuberculosis reactivation. No literature was identified regarding the clinical utility of screening for latent tuberculosis infection in people at risk of tuberculosis reactivation.

Methods

A limited literature search was conducted by an information specialist on key resources including Medline, 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 latent tuberculosis and reactivation. Search filters were applied to limit retrieval to guidelines for Q3 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 June 24, 2020. Internet links were provided, where available.

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).

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Populations	Q1: Individuals at risk of LTBI or TB reactivation Q2: Individuals with LTBI Q3: Individuals with LTBI or who are at risk of LTBI or TB reactivation
Interventions	Q1: Screening for LTBI using the tuberculin skin test or interferon-gamma release assay Q2: Treatment for LTBI Q3: Strategies and approaches to prevent TB reactivation
Comparators	Q1: No screening for LTBI Q2: No treatment for LTBI Q3: Not applicable

Outcomes	Q1: Clinical utility (e.g., patients receiving treatment for LTBI, TB reactivation, adverse effects of treatment) Q2: Clinical utility (e.g., TB reactivation, need for subsequent treatment for active TB, adverse effects of LTBI treatment, anxiety) Q3: Recommendations regarding strategies to reduce TB reactivation
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, evidence-based guidelines

LTBI = latent tuberculosis infection; TB = tuberculosis

Results

One network meta-analysis[1] and one non-randomized study[2] were identified regarding the clinical utility of treating latent tuberculosis infection (LTBI) to prevent tuberculosis (TB) reactivation. Two evidence-based guidelines[3,4] were identified regarding the prevention of TB reactivation. No literature was identified regarding the clinical utility of screening for LTBI in people at risk of TB reactivation. No relevant health technology assessments and randomized controlled trials were identified.

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

Overall Summary of Findings

One network meta-analysis[1] and one non-randomized study[2] were identified regarding the clinical utility of treating LTBI to prevent TB reactivation. The authors of the network meta-analysis[1] found that compared to no treatment, weekly rifapentine-isoniazid regimens were more efficacious in preventing active TB in patients with LTBI. The authors of the non-randomized study[2] found that individuals with LTBI were at a higher risk of developing active TB if they did not undergo treatment.

Two evidence-based guidelines[3,4] were identified regarding the prevention of TB reactivation. A summary of relevant recommendations is presented in Table 2.

No relevant literature was found regarding the clinical utility of screening for LTBI in people at risk of TB reactivation; therefore, no summary can be provided.

Table 2: Summary of Relevant Recommendations

Summary of Recommendations
National Institute for Health and Care Excellence, 2017[3]
• New entrants from high incidence countries should be screened for LTBI (page 51). • New entrants positive for LTBI should be offered treatment if they are aged 65 years or younger and confirmed to be negative for active TB (page 51). • New entrants positive for LTBI who are not offered treatment should be provided with “inform and advise” information (page 51).
United States Preventative Services Task Force, 2016[4]
• Asymptomatic adults at increased risk of TB infection should be screened for LTBI, including individuals who were born in, or are former residents of high incidence countries and individuals who live in, or have lived in, high-risk settings such as homeless shelters and correctional facilities.

LTBI = latent tuberculosis infection; TB = tuberculosis

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-Analyses

1. Zenner D, Beer N, Harris RJ, Lipman MC, Stagg HR, van der Werf MJ. Treatment of Latent Tuberculosis Infection: An Updated Network Meta-analysis. *Ann Intern Med*. 2017;167(4):248-255. https://pubmed.ncbi.nlm.nih.gov/28761946/

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

2. Zenner D, Loutet MG, Harris R, Wilson S, Ormerod LP. Evaluating 17 years of latent tuberculosis infection screening in north-west England: a retrospective cohort study of reactivation. *Eur Respir J*. 2017 07;50(1):07.
PubMed: PM28751410

Guidelines and Recommendations

3. National Institute for Health and Care Excellence. Tuberculosis. (NICE guideline NG33); 2017. https://www.nice.org.uk/guidance/ng33/resources/tuberculosis-pdf-1837390683589
See: 1.6.2 Opportunistic case finding, page 51

4. Latent Tuberculosis Infection: Screening. Rockville (MD): U.S. Preventive Services Task Force. 2016.
https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/latent-tuberculosis-infection-screening

Appendix — Further Information

Previous CADTH Reports

5. Screening for Latent Tuberculosis Infection in Post-Secondary Institutions: Clinical Utility, Cost-Effectiveness, and Guidelines. *(CADTH Rapid response report: summary of abstracts)*. Ottawa (ON): CADTH; 2020. https://cadth.ca/screening-latent-tuberculosis-infection-post-secondary-institutions-clinical-utility-cost

6. Latent Tuberculosis Infection Testing in People with Compromised Immunity Prior to Biologic Therapy: Diagnostic Accuracy, Clinical Utility and Guidelines. *(CADTH Rapid response report: summary of abstracts)*. Ottawa (ON): CADTH; 2020. https://cadth.ca/latent-tuberculosis-infection-testing-people-compromised-immunity-prior-biologic-therapy-diagnostic

7. Occupational Screening for Latent Tuberculosis: Clinical Utility, Cost-Effectiveness, and Guidelines. *(CADTH Rapid response report: summary of abstracts)*. Ottawa (ON): CADTH; 2020. https://cadth.ca/occupational-screening-latent-tuberculosis-clinical-utility-cost-effectiveness-and-guidelines

Systematic Reviews and Meta-Analyses – Unknown Comparator

8. Greenaway C, Pareek M, Abou Chakra CN, et al. The effectiveness and cost-effectiveness of screening for latent tuberculosis among migrants in the EU/EEA: a systematic review. *Euro Surveill*. 2018 04;23(14):04. PubMed: PM29637889

Non-Randomized Studies – No Comparator

9. Al-Taweel T, Strohl M, Pai M, et al. A Study of Optimal Screening for Latent Tuberculosis in Patients with Inflammatory Bowel Disease. *Dig Dis Sci*. 2018 10;63(10):2695-2702. PubMed: PM29968143

10. Ramos GP, Stroh G, Al-Bawardy B, Faubion WA, Papadakis KA, Escalante P. Outcomes of Treatment for Latent Tuberculosis Infection in Patients With Inflammatory Bowel Disease Receiving Biologic Therapy. *Inflamm Bowel Dis*. 2018 09 15;24(10):2272-2277. PubMed: PM29718223

Review Articles

11. Ai JW, Ruan QL, Liu QH, Zhang WH. Updates on the risk factors for latent tuberculosis reactivation and their managements. *Emerg Microbes Infect*. 2016 Feb 03;5:e10. PubMed: PM26839146

Additional References

12. Canadian Paediatric Society. Approaches to detecting tuberculosis in children and youth. 2018. https://www.cps.ca/en/documents/position/approaches-to-detecting-tuberculosis-in-children-and-youth

13. European Centre for Disease Prevention and Control. Review of reviews and guidelines on target groups, diagnosis, treatment and programmatic issues for implementation of latent tuberculosis management. Stockholm (SE): ECDC; 2018 https://www.ecdc.europa.eu/sites/default/files/documents/October-2018-Review-guidelines-latent-TB-management.pdf

14. Kiazyk S, Ball TB. Latent tuberculosis infection: An overview. *Can Commun Dis Rep*. 2017;43(3-4):62-66. https://pubmed.ncbi.nlm.nih.gov/29770066/

15. Krause V, National Tuberculosis Advisory C. Policy recommendation: latent tuberculosis infection screening and treatment in children in immigration detention. *Commun Dis Intell Q Rep*. 2015 Dec 31;39(4):E597-598. PubMed: PM26779733

16. Public Health England. Tuberculosis (TB): collaborative strategy for England. 2015. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/403231/Collaborative_TB_Strategy_for_England_2015_2020_.pdf
See: A8 Systematically implement new entrant latent TB (LTBI) screening, page 30