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Once-weekly Isoniazid and Rifapentine for 12 Weeks for the Treatment of Latent Tuberculosis Infection: Clinical Utility and Cost-Effectiveness

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Research Questions

1. What is the clinical utility of once-weekly isoniazid and rifapentine for 12 weeks for the treatment of latent tuberculosis infection?
2. What is the cost-effectiveness of once-weekly isoniazid and rifapentine for 12 weeks for the treatment of latent tuberculosis infection?

Key Findings

Two systematic reviews with meta-analyses, one systematic review with a network meta-analysis, five randomized controlled trials and ten non-randomized studies were identified regarding the clinical utility of once-weekly isoniazid and rifapentine for 12 weeks for the treatment of latent tuberculosis infection. Additionally, two economic evaluations were identified regarding the cost-effectiveness of once-weekly isoniazid and rifapentine for 12 weeks for the treatment of latent tuberculosis infection.

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 latent tuberculosis, Isoniazid and Rifapentine. 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, 2014 and July 21, 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 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. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available.

Table 1: Selection Criteria

Population	People receiving drug treatment for latent tuberculosis infection (LTBI)
Intervention	Once-weekly isoniazid and rifapentine for 12 weeks (3HP)
Comparator	Alternative treatments for LTBI (e.g., isoniazid daily for 6 or 9 months)

Outcomes	<p>Q1. Clinical utility (e.g., eradication of LTBI, treatment completion, rates of discontinuation of therapy, quality of life, acquired drug-resistance, development of active TB infection, need for subsequent treatment, adverse events)</p> <p>Q2. Cost-effectiveness (e.g., cost per health benefit)</p>
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations

Results

Two systematic reviews with meta-analyses,^{1,2} one systematic review with a network meta-analysis,³ five randomized controlled trials⁴⁻⁸ and ten non-randomized studies⁹⁻¹⁸ were identified regarding the clinical utility of once-weekly isoniazid and rifapentine for 12 weeks for the treatment of latent tuberculosis infection. Additionally, two economic evaluations^{19,20} were identified regarding the cost-effectiveness of once-weekly isoniazid and rifapentine for 12 weeks for the treatment of latent tuberculosis infection. No relevant health technology assessments were identified in the literature.

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

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Hamada Y, Ford N, Schenkel K, Getahun H. Three-month weekly rifapentine plus isoniazid for tuberculosis preventive treatment: a systematic review. *Int J Tuberc Lung Dis.* 2018 12 01;22(12):1422-1428.
[PubMed: PM30606313](#)
2. Pease C, Hutton B, Yazdi F, et al. A systematic review of adverse events of rifapentine and isoniazid compared to other treatments for latent tuberculosis infection. *Pharmacoepidemiol Drug Saf.* 2018 06;27(6):557-566.
[PubMed: PM29573031](#)

Systematic Review with Network Meta-Analysis

3. Pease C, Hutton B, Yazdi F, et al. Efficacy and completion rates of rifapentine and isoniazid (3HP) compared to other treatment regimens for latent tuberculosis infection: a systematic review with network meta-analyses. *BMC Infect Dis.* 2017 04 11;17(1):265.
[PubMed: PM28399802](#)

Randomized Controlled Trials

4. Ruan QL, Huang XT, Yang QL, et al. Efficacy and safety of weekly rifapentine and isoniazid for tuberculosis prevention in Chinese silicosis patients: a randomized controlled trial. *Clin Microbiol Infect.* 2020 Jun 15;15:15.
[PubMed: PM32553881](#)

5. Wheeler C, Mohle-Boetani J. Completion rates, adverse effects, and costs of a 3-month and 9-month treatment regimen for latent tuberculosis infection in California inmates, 2011-2014. *Public Health Rep.* 2019 May/Jun;134(1_suppl):71S-79S. [PubMed: PM31059418](#)
6. Sun HY, Huang YW, Huang WC, et al. Twelve-dose weekly rifapentine plus isoniazid for latent tuberculosis infection: a multicentre randomised controlled trial in Taiwan. *Tuberculosis (Edinb).* 2018 07;111:121-126. [PubMed: PM30029896](#)
7. Denholm JT, McBryde ES, Eisen D, et al. SIRACLE: a randomised controlled cost comparison of self-administered short-course isoniazid and rifapentine for cost-effective latent tuberculosis eradication. *Intern Med J.* 2017 12;47(12):1433-1436. [PubMed: PM29224209](#)
8. Villarino ME, Scott NA, Weis SE, et al. Treatment for preventing tuberculosis in children and adolescents: a randomized clinical trial of a 3-month, 12-dose regimen of a combination of rifapentine and isoniazid. *JAMA Pediatr.* 2015 Mar;169(3):247-255. [PubMed: PM25580725](#)

Non-Randomized Studies

9. Alvarez GG, Van Dyk D, Mallick R, et al. The implementation of rifapentine and isoniazid (3HP) in two remote Arctic communities with a predominantly Inuit population, the Taima TB 3HP study. *Int J Circumpolar Health.* 2020 Dec;79(1):1758501. [PubMed: PM32379538](#)
10. Jo KW, Kim JS, Kwon HS, et al. Adverse event and treatment completion rates of a 12-dose weekly isoniazid and rifapentine course for South Korean healthcare workers. *Respir Med.* 2019 Oct - Nov;158:42-48. [PubMed: PM31605920](#)
11. Cruz AT, Starke JR. Completion rate and safety of tuberculosis infection treatment with shorter regimens. *Pediatrics.* 2018 02;141(2):02. [PubMed: PM29363561](#)
12. Macaraig MM, Jalees M, Lam C, Burzynski J. Improved treatment completion with shorter treatment regimens for latent tuberculosis infection. *Int J Tuberc Lung Dis.* 2018 11 01;22(11):1344-1349. [PubMed: PM30355415](#)
13. Arguello Perez E, Seo SK, Schneider WJ, Eisenstein C, Brown AE. Management of latent tuberculosis infection among healthcare workers: 10-year experience at a single center. *Clin Infect Dis.* 2017 Nov 29;65(12):2105-2111. [PubMed: PM29020308](#)
14. McClintock AH, Eastment M, McKinney CM, et al. Treatment completion for latent tuberculosis infection: a retrospective cohort study comparing 9 months of isoniazid, 4 months of rifampin and 3 months of isoniazid and rifapentine. *BMC Infect Dis.* 2017 02 14;17(1):146. [PubMed: PM28196479](#)

15. Simkins J, Abbo LM, Camargo JF, Rosa R, Morris MI. Twelve-week rifapentine plus isoniazid versus 9-month isoniazid for the treatment of latent tuberculosis in renal transplant candidates. *Transplantation*. 2017 06;101(6):1468-1472.
[PubMed: PM27548035](#)
16. Huang YW, Yang SF, Yeh YP, Tsao TC, Tsao SM. Impacts of 12-dose regimen for latent tuberculosis infection: treatment completion rate and cost-effectiveness in Taiwan. *Medicine*. 2016 Aug;95(34):e4126.
[PubMed: PM27559940](#)
17. Bliven-Sizemore EE, Sterling TR, Shang N, et al. Three months of weekly rifapentine plus isoniazid is less hepatotoxic than nine months of daily isoniazid for LTBI. *Int J Tuberc Lung Dis*. 2015 Sep;19(9):1039-1044, i-v.
[PubMed: PM26260821](#)
18. Lines G, Hunter P, Bleything S. Improving treatment completion rates for latent tuberculosis infection: a review of two treatment regimens at a community health center. *J Health Care Poor Underserved*. 2015 Nov;26(4):1428-1439.
[PubMed: PM26548690](#)

Economic Evaluations

19. Doan TN, Fox GJ, Meehan MT, et al. Cost-effectiveness of 3 months of weekly rifapentine and isoniazid compared with other standard treatment regimens for latent tuberculosis infection: a decision analysis study. *J Antimicrob Chemother*. 2019 01 01;74(1):218-227.
[PubMed: PM30295760](#)
20. Johnson KT, Churchyard GJ, Sohn H, Dowdy DW. Cost-effectiveness of preventive therapy for tuberculosis with isoniazid and rifapentine versus isoniazid alone in high-burden settings. *Clin Infect Dis*. 2018 09 14;67(7):1072-1078.
[PubMed: PM29617965](#)

Appendix — Further Information

Previous CADTH Reports

21. Kumar D, Loshak H. Treatment of latent tuberculosis infection after re-exposure: guidelines [CADTH rapid response report: summary of abstracts]. Ottawa (ON): CADTH; 2020 Jul:
<https://www.cadth.ca/sites/default/files/pdf/htis/2020/RB1505%20Tx%20After%20TB%20Re-exposure%20Final.pdf> Accessed 2020 Jul 30.
22. Brett K, Dulong C, Severn M. Treatment of tuberculosis: a review of guidelines [CADTH rapid response report: summary with critical appraisal]. Ottawa (ON): CADTH; 2020 Mar:
<https://cadth.ca/sites/default/files/pdf/htis/2020/RC1237%20TB%20treatment%20guidelines%20Final.pdf> Accessed 2020 Jul 30.
23. Li KX, Ryce A. Strategies for the management of latent or previously treated tuberculosis: clinical effectiveness, cost-effectiveness, and guidelines [CADTH rapid response report: summary of abstracts]. Ottawa (ON): CADTH; 2018 Dec:
<https://www.cadth.ca/sites/default/files/pdf/htis/2018/RB1290%20Management%20of%20Latent%20Tuberculosis%20Final.pdf> Accessed 2020 Jul 30.

Systematic Review

Methodology Not Specified

24. Njie GJ, Morris SB, Woodruff RY, Moro RN, Vernon AA, Borisov AS. Isoniazid-rifapentine for latent tuberculosis infection: a systematic review and meta-analysis. *Am J Prev Med.* 2018 08;55(2):244-252.
[PubMed: PM29910114](#)

Randomized Controlled Trial

Alternative Intervention

25. Gao L, Zhang H, Xin H, et al. Short-course regimens of rifapentine plus isoniazid to treat latent tuberculosis infection in older Chinese patients: a randomised controlled study. *Eur Respir J.* 2018 12;52(6):12.
[PubMed: PM30361241](#)

Study Design Not Specified

26. Juarez-Reyes M, Gallivan M, Chyorny A, O'Keeffe L, Shah NS. Completion rate and side-effect profile of three-month isoniazid and rifapentine treatment for latent tuberculosis infection in an urban county jail. *Open Forum Infect Dis.* 2016 Jan;3(1):ofv220.
[PubMed: PM26885547](#)

Review Articles

27. Huaman MA, Sterling TR. Treatment of latent tuberculosis infection-an update. *Clin Chest Med.* 2019 12;40(4):839-848.
[PubMed: PM31731988](#)

Additional References

28. Ontario Agency for Health Protection and Promotion (Public Health Ontario). Use of rifapentine and isoniazid combination therapy for the treatment of latent tuberculosis infection in Ontario. Toronto (ON): Public Health Ontario; 2018 Oct:
<https://www.publichealthontario.ca/-/media/documents/R/2018/rifapentine-isoniazid-combination-latent-tuberculosis-ontario.pdf?la=en> Accessed 2020 Jul 30.