

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Rapid and Simultaneous Tuberculosis and Antibiotic Susceptibility Testing for the Diagnosis of Pulmonary Tuberculosis and Rifampicin Resistance: Diagnostic Accuracy and Cost- Effectiveness

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Research Questions

1. What is the diagnostic accuracy of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of pulmonary tuberculosis compared to smear microscopy?
2. What is the diagnostic accuracy of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of pulmonary tuberculosis compared to mycobacterial cultures?
3. What is the diagnostic accuracy of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of rifampicin resistance compared to culture-based drug susceptibility testing?
4. What is the cost-effectiveness of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of pulmonary tuberculosis or rifampicin resistance?

Key Findings

Three systematic reviews with meta-analysis were identified regarding the diagnostic accuracy of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of pulmonary tuberculosis compared to mycobacterial cultures and rifampicin resistance compared to culture-based drug susceptibility testing. Authors of one of the three systematic reviews with meta-analysis also compared the diagnostic accuracy of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of pulmonary tuberculosis compared to smear microscopy. In addition, four economic evaluations were identified regarding the cost-effectiveness of rapid and simultaneous tuberculosis and antibiotic susceptibility testing for the detection of pulmonary tuberculosis or rifampicin resistance.

Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, 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 tuberculosis and rifampin, and rapid diagnostic and culture or smear microscopy testing for tuberculosis. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2015 and June 9, 2020.

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

Population	People of any age with presumptive pulmonary tuberculosis, presumptive rifampicin-resistant tuberculosis, or presumptive multi-drug resistant tuberculosis
Intervention	Automated real-time nucleic acid amplification test for rapid and simultaneous detection of tuberculosis and rifampicin resistance (e.g., Xpert MTB/RIF)
Comparators	Q1: Smear microscopy (e.g., acid-fast bacilli) Q2: Liquid or solid mycobacterial cultures Q3: Culture-based drug susceptibility testing Q4: Smear microscopy, mycobacterial cultures, or culture-based drug susceptibility testing
Outcomes	Q1-3: Diagnostic accuracy (e.g., sensitivity, specificity, tuberculosis diagnosis, diagnosis of rifampicin resistance, true positive rate, false positive rate) Q4: Cost-effectiveness
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations

Results

Three systematic reviews¹⁻³ with meta-analysis were identified regarding the diagnostic accuracy of rapid and simultaneous tuberculosis (TB) and antibiotic susceptibility testing for the detection of pulmonary TB compared to mycobacterial cultures and rifampicin resistance compared to culture-based drug susceptibility testing. Authors of one of the three systematic reviews² with meta-analysis also compared the diagnostic accuracy of rapid and simultaneous TB and antibiotic susceptibility testing for the detection of pulmonary TB compared to smear microscopy. In addition, four economic evaluations⁴⁻⁷ were identified regarding the cost-effectiveness of rapid and simultaneous TB and antibiotic susceptibility testing for the detection of pulmonary TB or rifampicin resistance. No relevant health technology assessments were identified.

References of potential interest that did not meet the inclusion criteria are provided in the appendix. Due to the volume of relevant literature that was identified from the search results, relevant randomized controlled trials and non-randomized studies are also provided in the appendix.

Overall Summary of Findings

Three systematic reviews¹⁻³ with meta-analysis were identified regarding the diagnostic accuracy of rapid and simultaneous TB and antibiotic susceptibility testing for the detection of pulmonary TB and rifampicin resistance compared to mycobacterial cultures and culture-based drug susceptibility testing. Authors of the first systematic review¹ found that the Xpert MTB/RIF assay was sensitive and specific for detecting pulmonary TB in adults compared to the culture standard. However, the Xpert MTB/RIF assay was found to be of moderate sensitivity and high specificity for TB detection in children.^{2,3} The Xpert MTB/RIF assay was specific and sensitive for detecting rifampicin resistance in both populations.¹⁻³ Authors of one of the three systematic reviews² also compared the diagnostic accuracy of rapid and simultaneous TB and antibiotic susceptibility testing for the detection of pulmonary TB compared to smear microscopy. The Xpert MTB/RIF assay was found to be more sensitive than smear microscopy in detecting pediatric pulmonary TB.² Detailed study findings are included in Table 2.

Four economic evaluations⁴⁻⁷ were identified regarding the cost-effectiveness of rapid and simultaneous TB and antibiotic susceptibility testing for the detection of pulmonary TB or rifampicin resistance. The authors of the first economic evaluation⁴ found that the Truenat assay was more cost-effective than smear microscopy in terms of cost per life-of-year saved. Furthermore, two economic evaluations^{5,6} concluded that the Xpert MTB/RIF assay was more cost-effective than smear microscopy in terms of cost per disability-adjusted life year averted. Finally, the authors of the last economic evaluation⁷ calculated the cost per diagnosis of Xpert MTB/RIF.

Table 2: Summary of Findings of the Included Systematic Reviews and Meta-Analyses

Main Study Findings	Authors' Conclusion
Horne, 2019¹	
<p>Xpert MTB/RIF for detecting PTB in adults</p> <ul style="list-style-type: none"> • Pooled sensitivity = 85% • Pooled specificity = 98% <p>Subgroup of smear-positive adults</p> <ul style="list-style-type: none"> • Pooled sensitivity = 98% <p>Subgroup of smear-negative, culture-positive adults</p> <ul style="list-style-type: none"> • Pooled sensitivity = 67% <p>Subgroup of HIV-negative adults</p> <ul style="list-style-type: none"> • Pooled sensitivity = 88% • Pooled specificity = 98% <p>Subgroup of HIV-positive adults</p> <ul style="list-style-type: none"> • Pooled sensitivity = 81% • Pooled specificity = 98% <p>Xpert MTB/RIF for detecting rifampicin resistance</p> <ul style="list-style-type: none"> • Pooled sensitivity = 96% • Pooled specificity = 98% 	<p><i>“We found Xpert MTB/RIF to be sensitive and specific for diagnosing PTB and rifampicin resistance, consistent with findings reported previously. Xpert MTB/RIF was more sensitive for tuberculosis in smear-positive than smear-negative participants and HIV-negative than HIV-positive participants.”</i></p>
Detjen, 2015²	
<p>Xpert MTB/RIF for detecting pediatric PTB using sputum samples</p> <ul style="list-style-type: none"> • Pooled sensitivity = 62% • Pooled specificity = 98% <p>Sensitivity was 36-44% higher than sensitivity for smear microscopy</p> <p>Xpert MTB/RIF for detecting pediatric PTB using gastric samples</p> <ul style="list-style-type: none"> • Pooled sensitivity = 66% • Pooled specificity = 98% <p>Xpert MTB/RIF for detecting pediatric rifampicin resistance</p> <ul style="list-style-type: none"> • Pooled sensitivity = 86% • Pooled specificity = 98% 	<p><i>“Compared with microscopy, Xpert offers better sensitivity for the diagnosis of pulmonary tuberculosis in children... Although Xpert helps to provide rapid confirmation of disease, its sensitivity remains suboptimum compared with culture tests.”</i></p>
Wang, 2015³	
<p>Xpert MTB/RIF for detecting pediatric PTB</p> <ul style="list-style-type: none"> • Sensitivity = 65% • Specificity = 99% • Pooled diagnostic odds ratio = 164.09 <p>Xpert MTB/RIF for detecting pediatric rifampicin resistance</p> <ul style="list-style-type: none"> • Pooled sensitivity = 94% • Pooled specificity = 99% 	<p><i>“The Xpert MTB/RIF is sensitive and specific for diagnosing paediatric pulmonary TB. It is also effective in detecting rifampicin resistance.”</i></p>

PTB = pulmonary tuberculosis

References Summarized

Health Technology Assessments

No literature identified.

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Economic Evaluations

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Appendix — Further Information

Health Technology Assessment – Unclear Reference Standard

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