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Visual Examination Frequency for People Taking Ethambutol for Tuberculosis

Rapid Review

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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.

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Key Message

- CADTH identified 1 non-Canadian guideline that includes recommendations on the frequency of visual examinations for people with active tuberculosis who take ethambutol as part of their treatment. The guideline recommends testing for visual acuity and colour vision before starting treatment and at every health care visit throughout the course of treatment with ethambutol (recommendations based on clinical experience).

Context and Policy Issues

In Canada, a recommended treatment for active tuberculosis (TB) disease includes a regimen of isoniazid, rifampin, pyrazinamide, and ethambutol.[1] A common adverse effect of ethambutol is eye toxicity (i.e., visual impairment),[1] which can cause changes in visual acuity, visual fields, and colour vision. Given this side effect of ethambutol, there is an interest in knowing whether there is any guidance regarding monitoring for these adverse effects in people taking ethambutol as part of treatment for active TB disease.

In June 2020, CADTH searched the literature for evidence-based guidelines regarding the frequency of visual examination for people taking ethambutol as part of a TB treatment.[2] This report identified 5 evidence-based guidelines that met the inclusion criteria based on their title and abstract. The purpose of the current report is to review the full texts of these guidelines and to summarize and critically appraise the eligible publications.

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

Research Question

What are the evidence-based guidelines regarding the frequency of visual examination for people taking ethambutol as part of a TB treatment regimen?

Methods

Literature Search Methods

A limited literature search was conducted for a previous CADTH report[2] by an information specialist on key resources, including MEDLINE 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 comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts

were ethambutol and visual impairment. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, and guidelines. The search was also limited to English-language documents published between January 1, 2010, and June 4, 2020. Internet links were provided, where available.

Selection Criteria and Methods

The evidence in this report was identified in a previous CADTH report,[2] in which 1 reviewer screened citations and abstracts. For this report, the full-text articles were reviewed by 1 reviewer, and the final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, were duplicate publications, or were published before 2010. Guidelines with unclear methodology were also excluded.

Critical Appraisal of Individual Studies

The included publication was critically appraised by 1 reviewer using the following tool as a guide: the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument.[3] Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Summary of Evidence

Quantity of Research Available

A total of 144 citations were identified in the literature search for the previous CADTH report[2] and 4 potentially relevant publications were retrieved from the grey literature. Five potentially relevant reports were identified and retrieved for full-text review. Of these potentially relevant articles, 4 guidelines were excluded as they did not include recommendations regarding visual examination,[1,4-6] and 1 evidence-based guideline[7] met the inclusion criteria and was included in this report.

Table 1: Selection Criteria

Criteria	Description
Population	People taking ethambutol as part of a tuberculosis treatment regimen
Intervention	Visual examination (e.g., visual field test, colour vision test, dilated fundus and optic nerve examination, visual acuity testing)
Comparator	Not applicable
Outcomes	Recommendations regarding frequency and duration of testing
Study designs	Health technology assessments, systematic reviews, evidence-based guidelines

Summary of Study Characteristics

One evidence-based guideline[7] was identified and included in this report. This guideline was developed by the Singapore Ministry of Health in 2016,[7] and it is intended to be used by health care professionals in Singapore who work with individuals with TB. The population and interventions covered by this guideline (i.e., prevention, diagnosis, and management of TB) were broader than the eligible population and interventions for this report, and recommendations relevant to this report covered testing for visual acuity and colour vision in individuals with TB who will receive or who are receiving treatment with ethambutol. The guidelines were developed by a committee of experts by adapting a previous guideline and a review of relevant literature, but no other details were reported on the methods used to search for evidence or develop the recommendations.[7] The strength of the evidence informing the recommendations was graded from 1++ (highest) to 4 (lowest; expert opinion), and the recommendations were graded from A (highest) to D (lowest) based on the level of evidence. In cases where no relevant evidence (i.e., scientific literature or expert opinion) was identified, recommendations were developed based on the clinical experience of the guideline development group and graded as a "good practice point."

Additional details regarding the study characteristics are provided in tables in Table 2 in Appendix 1.

Summary of Critical Appraisal

This guideline was previously included in a CADTH report[8] on guidelines for the identification of TB. The detailed critical appraisal of the guideline can be found in that report[8] and summarized in Table 3 in Appendix 1. In brief, it was unclear whether this guideline by the Singapore Ministry of Health[7] used a systematic approach to search for and evaluate the evidence because insufficient methodological details were reported in the guideline.

Summary of Findings

The specific recommendations and the strength of the recommendations are provided in Table 4 in Appendix 1.

Guidelines

One evidence-based guideline[7] included recommendations regarding visual examinations for people taking ethambutol as part of a TB treatment regimen.

Prior to Starting Treatment

The guideline from the Singapore Ministry of Health recommends that adults should have their visual acuity and colour vision checked before starting a TB treatment regimen that includes ethambutol; this recommendation is considered a "good practice point" because it is based off the clinical experience of the guideline development group (i.e., no supporting evidence).[7]

During Treatment

The guideline from the Singapore Ministry of Health recommends that adults who are taking ethambutol as part of their TB treatment regimen should have their visual acuity and colour vision checked at each visit; this recommendation is considered a "good practice point" because it is based off the clinical experience of the guideline development group (i.e., no supporting evidence).[7]

Limitations

The findings in this report are limited by the quantity and quality of the evidence. One guideline[7] was identified that included 2 relevant recommendations; however, the guideline did not report the methods used to search for evidence or to develop the recommendations, limiting the reliability of the guideline. In addition, the relevant recommendations were based on the clinical experience of the members of the guideline development group rather than evidence from the literature, which reduces the certainty of the recommendations. It was not reported in the guideline whether a literature review was conducted on visual examination in people taking ethambutol, thus it is unknown whether the decision to base these recommendations on the clinical experience of the guideline development group was due to a lack of available evidence on the topic (e.g., literature review did not identify any relevant evidence) or for another reason.

The guideline[7] identified in this report is meant to apply to Singapore, and the recommendations were based off the clinical experience of the members of the guideline development group. Therefore, it is unknown whether the recommendations are generalizable to the Canadian clinical practice.

Conclusions

This report comprised 1 low-quality evidence-based guideline that included 2 recommendations regarding visual examinations in people taking ethambutol as part of a TB treatment regimen. Overall, in adults with TB, testing for visual acuity and colour vision was recommended before starting treatment with ethambutol and at every health care visit throughout the course of treatment with ethambutol. However, these recommendations are based solely off the clinical experience of the guideline development group with no supporting scientific evidence, and this limitation should be considered when interpreting the findings of this report.

References

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Appendix 1: Characteristics of Included Publications

Table 2: Characteristics of Included Guideline

Intended users, target population	Relevant interventions and outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendation development and evaluation	Guideline validation
Singapore Ministry of Health (2016)[7]					
Intended users: Health care practitioners **Target population:** Individuals with TB	**Interventions:** Visual acuity, colour vision **Outcomes**: Not reported	Developed by adapting existing guidelines and a review of relevant literature. No other details provided.	Methods for assessing the evidence were not reported. "Level of evidence: 1++ = High quality meta-analyses, SRs of RCTs, or RCTs with a very low risk of bias 1+ = Well conducted meta-analyses, SRs of RCTs, or RCTs with a low risk of bias 1– = Meta-analyses, SRs of RCTs, or RCTs with a high risk of bias 2++ = High quality SRs of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal 2+ = Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal 2– = Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal 3 = Non-analytic studies, e.g., case reports, case series 4 = Expert opinion (p. 2)."	Recommendations were appraised by scoring the strength of the evidence, and grade of recommendation (no other details provided) Grade of recommendation: A = At least 1 study with evidence level 1++, or a body of evidence that is primarily rated at 1+, with consistency in the results B = Body of evidence with studies rated 2++, with consistency in results C = Body of evidence rated 2+, with consistency of results D = Evidence rated as level 3 or 4 GPP = Recommended best practice based on the clinical experience of the guideline development group	Not reported

GPP = good practice point; RCT = randomized controlled trial; SR = systematic review; TB = tuberculosis.

Table 3: Strengths and Limitations of the Included Guideline Using AGREE II[3]

Item	Singapore Ministry of Health (2016)[7]
Domain 1: Scope and purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	No
3. The population (e.g., patients, public) to whom the guideline is meant to apply is specifically described.	Partially
Domain 2: Stakeholder involvement	
4. The guideline development group includes individuals from all relevant professional groups.	Partially
5. The views and preferences of the target population (e.g., patients, public) have been sought.	No
6. The target users of the guideline are clearly defined.	Yes
Domain 3: Rigour of development	
7. Systematic methods were used to search for evidence.	No
8. The criteria for selecting the evidence are clearly described.	No
9. The strengths and limitations of the body of evidence are clearly described.	Partially
10. The methods for formulating the recommendations are clearly described.	No
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	No
12. There is an explicit link between the recommendations and the supporting evidence.	Partially
13. The guideline has been externally reviewed by experts before its publication.	No
14. A procedure for updating the guideline is provided.	Yes
Domain 4: Clarity of presentation	
15. The recommendations are specific and unambiguous.	Yes
16. The different options for management of the condition or health issue are clearly presented.	Yes
17. Key recommendations are easily identifiable.	Yes
Domain 5: Applicability	
18. The guideline describes facilitators and barriers to its application.	No
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No
20. The potential resource implications of applying the recommendations have been considered.	No
21. The guideline presents monitoring and/or auditing criteria.	Partially
Domain 6: Editorial independence	
22. The views of the funding body have not influenced the content of the guideline.	No
23. Competing interests of guideline development group members have been recorded and addressed.	No

AGREE = Appraisal of Guidelines for Research and Evaluation.

Table 4: Summary of Recommendations in Included Guideline

Recommendations and supporting evidence	Quality of evidence and strength of recommendations
Singapore Ministry of Health (2016)[7]	
Recommendation 1: "Before starting tuberculosis treatment, baseline liver enzymes should be performed in those over 15 years old. Adult patients to be commenced on ethambutol must have their visual acuity and colour vision checked at baseline (p. 50)." No supporting evidence reported.	Recommendation 1: Good practice point
Recommendation 2: "The patient's weight should be documented at each visit and the drug dosages adjusted accordingly. Adult patients on ethambutol must have their visual acuity and colour vision checked at each visit. Those with risk factors for drug-induced hepatitis must be closely monitored (p. 64)." No supporting evidence reported.	Recommendation 2: Good practice point