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CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Pilocarpine for Medication-induced Dry Mouth and Dry Eyes: A Review of Clinical Effectiveness, Cost-Effectiveness, and Guidelines

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Abbreviations

CRD	Centre for Reviews and Dissemination
DED	dry eye disease
MeSH	Medical Subject Headings
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SSRI	Serotonin re-uptake inhibitors

Context and Policy Issues

Xerostomia is defined as dry mouth due to reduced salivary flow.[1] As a result of this, patients may have decreased efficiency in chewing and swallowing and an increased risk of dental disease, such as dental caries (i.e., dental decay).[1] Xerostomia may be caused by medications, chronic disease, and radiotherapy.[2] The prevalence of xerostomia in patients taking medications is higher than in those not taking medications (28% versus 7.5%, respectively).[3] In particular, xerostomia is a potential side effect of psychoactive medications including antidepressants and antipsychotics.[2] For example, patients taking tricyclic antidepressants had a 58% reduction in salivary flow rate compared to patients not taking tricyclic antidepressants, while those taking selective serotonin re-uptake inhibitors (SSRIs) had a 32% reduction compared to patients not taking SSRIs.[4] Treatment for xerostomia includes but is not limited to mouth wash, artificial saliva, moisturizer, and cholinergic drugs (e.g., pilocarpine and cevimeline).[5]

Dry eyes is a condition in which the tears are inadequate to lubricate the eyes, which may lead to symptoms such as scratching, stinging or burning sensation, light sensitivity, and blurred vision.[6] In 2019, it was estimated that 21.3% of Canadian adults may have dry eye disease (DED), which includes medication-induced dry eyes.[7] Oral psychoactive medications can also contribute to dry eye disease.[8] Treatment for dry eyes depends on the cause of the condition and includes punctal plugs for the tear draining ducts, anti-inflammatory drugs, artificial tears, and cholinergic drugs (e.g., pilocarpine and cevimeline).[6]

The purpose of this report is to examine recent literature regarding clinical effectiveness, cost-effectiveness and evidence-based guidelines of pilocarpine for the treatment of psychoactive medication-induced dry mouth or dry eyes.

Research Questions

1. What is the clinical effectiveness of pilocarpine for the treatment of psychoactive medication-induced dry mouth?
2. What is the cost-effectiveness of pilocarpine for the treatment of psychoactive medication-induced dry mouth?
3. What is the clinical effectiveness of pilocarpine for the treatment of psychoactive medication-induced dry eyes?
4. What is the cost-effectiveness of pilocarpine for the treatment of psychoactive medication-induced dry eyes?

5. What are the evidence-based guidelines regarding pilocarpine for the treatment of psychoactive medication-induced dry mouth or dry eyes?

Key Findings

No relevant literature was identified regarding the clinical effectiveness and cost-effectiveness of pilocarpine for the treatment of psychoactive medication-induced dry mouth or dry eyes. Additionally, no evidence-based guidelines were identified regarding pilocarpine for the treatment of psychoactive medication-induced dry mouth or dry eyes.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including Medline and Embase 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 pilocarpine and xerostomia or dry eyes. 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, 2009 and November 25, 2019.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1,2,5: People with psychoactive medication-induced xerostomia (dry mouth) Q3-5: People with psychoactive medication-induced dry eyes
Intervention	Pilocarpine, all formulations
Comparator	Q1-4: Sialagogues (e.g., anethole trithione, cevimeline); Q1,2: Nonpharmacological therapy (e.g., dental care, salivary flow stimulation [e.g., sugarless gum, lozenges], water consumption); artificial saliva, saliva substitutes, oral lubricants Q3,4: Non-prescription artificial tears, ocular lubricants, or viscosity agents (e.g., carboxymethyl cellulose, polyethylene glycol, sodium hyaluronate, petrolatum, carbomer) Q5: Not applicable
Outcomes	Q1: Clinical effectiveness (e.g., oral mucosa health, dental health, salivary flow rate, comfort, quality of life, dysphagia, dysgeusia, side effects) Q2,4: Cost-effectiveness (e.g., cost per quality adjusted life year, cost per clinical outcome) Q3: Clinical effectiveness (e.g., ocular surface health, lacrimal flow rate, ocular comfort, quality of life, side effects) Q5: Evidence-based guidelines on appropriate use and place in therapy
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, economic evaluations, guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1. Guidelines with unclear methodology were also excluded.

Summary of Evidence

Quantity of Research Available

A total of 438 citations were identified in the literature search. Following screening of titles and abstracts, 429 citations were excluded and nine potentially relevant reports from the electronic search were retrieved for full-text review. One potentially relevant publication were retrieved via hand searching for full-text review. Of these potentially relevant articles, all 10 publications were excluded for various reasons, and no publications met the inclusion criteria or were included in this report. Appendix 1 presents the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[9] flowchart of the study selection. Additional references of potential interest are provided in Appendix 2.

Summary of Findings

No relevant studies or evidence-based guidelines were identified regarding the clinical effectiveness, cost-effectiveness, or recommendations regarding the use of pilocarpine for the treatment of psychoactive medication-induced dry mouth or dry eyes; therefore, no summary can be provided.

Limitations

The primary limitation of this report was that there was no relevant evidence identified to answer the research questions.

Conclusions and Implications for Decision or Policy Making

No relevant studies or evidence-based guidelines were identified regarding the clinical effectiveness, cost-effectiveness, or recommendations regarding the use of pilocarpine for the treatment of psychoactive medication-induced dry mouth or dry eyes. Future studies may help reduce uncertainty in the clinical effectiveness and cost-effectiveness of pilocarpine, and inform the development of evidence-based guidelines regarding the use of pilocarpine, for the treatment of dry mouth and dry eyes.

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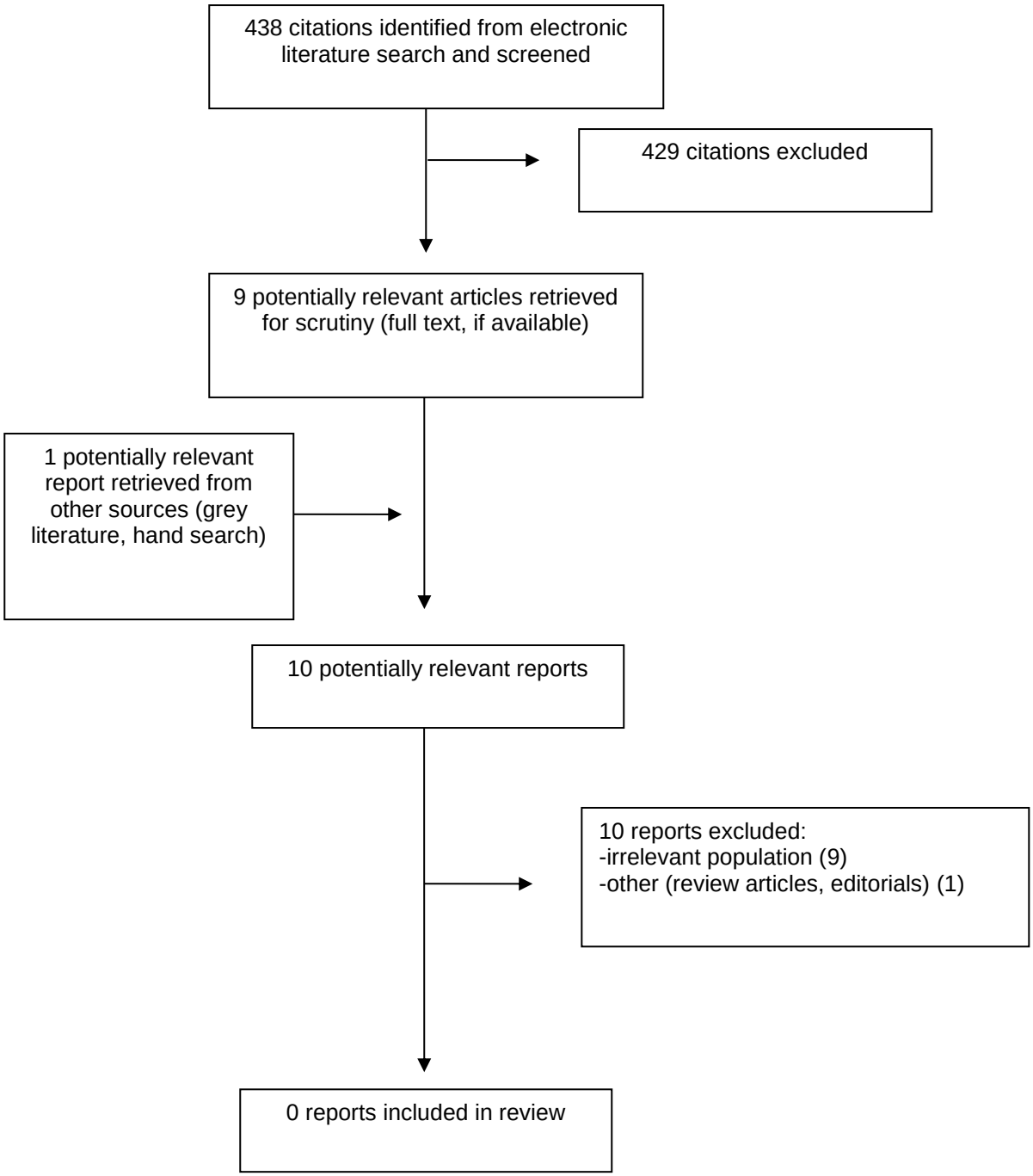
Appendix 1: Selection of Included Studies



Appendix 2: Additional References of Potential Interest

Systematic Review – No Comparator

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Narrative Reviews

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