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SUMMARY WITH CRITICAL APPRAISAL

N-Acetylcysteine Instillation During Bronchoscopy for Patients Requiring Non-Cystic Fibrosis-Related Mucus Secretion Clearance: A Review of Clinical Effectiveness and Guidelines

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Authors: Calvin Young, 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.

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Questions or requests for information about this report can be directed to Requests@CADTH.ca

Abbreviations

CRD	Centre for Reviews and Dissemination
MeSH	Medical Subject Headings
NAC	N-acetylcysteine
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Context and Policy Issues

Bronchoscopy is a commonly-used procedure that allows for the visualization of the lungs and air passages using a bronchoscope, a narrow tube with attached lighting and real-time video equipment.[1] Bronchoscopy may be performed for several reasons, including the diagnosis of disease (e.g., lung cancer, tuberculosis, pneumonia, infections), foreign body removal, stent insertion, and biopsy.[1,2] These procedures may be impeded in cases where the patient is experiencing impaired mucus secretion clearance as a result of various pathologies. Mucolytic agents (a class of drugs which aid in the clearance of mucus in the airways), such as N-acetylcysteine (NAC), may be administered prior to bronchoscopic examination in order to increase visibility and access to the underlying tissue.[3,4] NAC's mechanism of action involves the cleavage of disulfide bonds in heavily cross-linked mucus glycoproteins, resulting in decreased mucus viscosity, thereby facilitating its clearance.[5,6]

The purpose of the current report is to evaluate the clinical effectiveness and evidence-based guidelines regarding NAC instillation during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance. The findings of this review are complimented by two additional reports on the use of NAC in patients requiring mucus secretion clearance (not specific to bronchoscopy), conducted separately by CADTH.[7,8]

Research Questions

1. What is comparative clinical effectiveness of N-acetylcysteine instillation versus saline (normal or hypertonic) during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance?
2. What are the evidence-based guidelines for N-acetylcysteine instillation during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance?

Key Findings

No relevant literature was identified regarding the comparative clinical effectiveness of N-acetylcysteine instillation versus saline (normal or hypertonic) during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance. Additionally, no evidence-based guidelines were identified regarding N-acetylcysteine instillation during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, Embase, the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, 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 acetylcysteine and mucus or mucous secretions. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2014 and July 8, 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	Adult patients without cystic fibrosis requiring mucus secretion clearance during bronchoscopy
Intervention	N-acetylcysteine instillation during bronchoscopy
Comparator	Q1: Saline (normal or hypertonic) Q2: No comparator
Outcomes	Q1: Clinical effectiveness (e.g., safety, lung function, symptom relief, health related quality of life, exacerbations [e.g., requirement for antibiotics], health care utilization, microbiology, mucociliary clearance, sputum measures [e.g., colour, weight, rheology], inflammation) Q2: Evidence-based guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and evidence-based guidelines

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2014. Guidelines with unclear methodology were also excluded.

Summary of Evidence

Quantity of Research Available

A total of 374 citations were identified in the literature search. Following screening of titles and abstracts, 359 citations were excluded and 15 potentially relevant reports from the electronic search were retrieved for full-text review. In addition, one potentially relevant publication was retrieved from the grey literature search for full-text review. Of these 16 potentially relevant articles, all were excluded for various reasons; no publications met the inclusion criteria and were included in this report. Appendix 1 presents the PRISMA[9] flowchart of the study selection. References of potential interest are provided in Appendix 2.

Summary of Findings

No relevant literature was identified regarding NAC instillation during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance; therefore, no summary can be provided.

Limitations

No relevant literature was identified regarding the clinical effectiveness of NAC instillation versus saline (normal or hypertonic) during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance. Additionally, no evidence-based guidelines were identified regarding NAC instillation during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance. This report is limited by the timeframe used for literature searches (extended only to 2014); it is possible that relevant literature was published more than five years ago and was excluded by the current date-limited search.

Conclusions and Implications for Decision or Policy Making

No relevant literature or evidence-based guidelines were identified regarding NAC instillation during bronchoscopy for non-cystic fibrosis patients requiring mucus secretion clearance; therefore, no conclusions regarding the clinical effectiveness or evidence-based guidelines can be provided.

Research examining the comparative clinical effectiveness of NAC instillation during bronchoscopy for non-cystic fibrosis patients is required in order to investigate this potential application of NAC. The lack of published evidence precludes the creation of appropriate guidelines for health care providers who perform bronchoscopy in this patient population.

References

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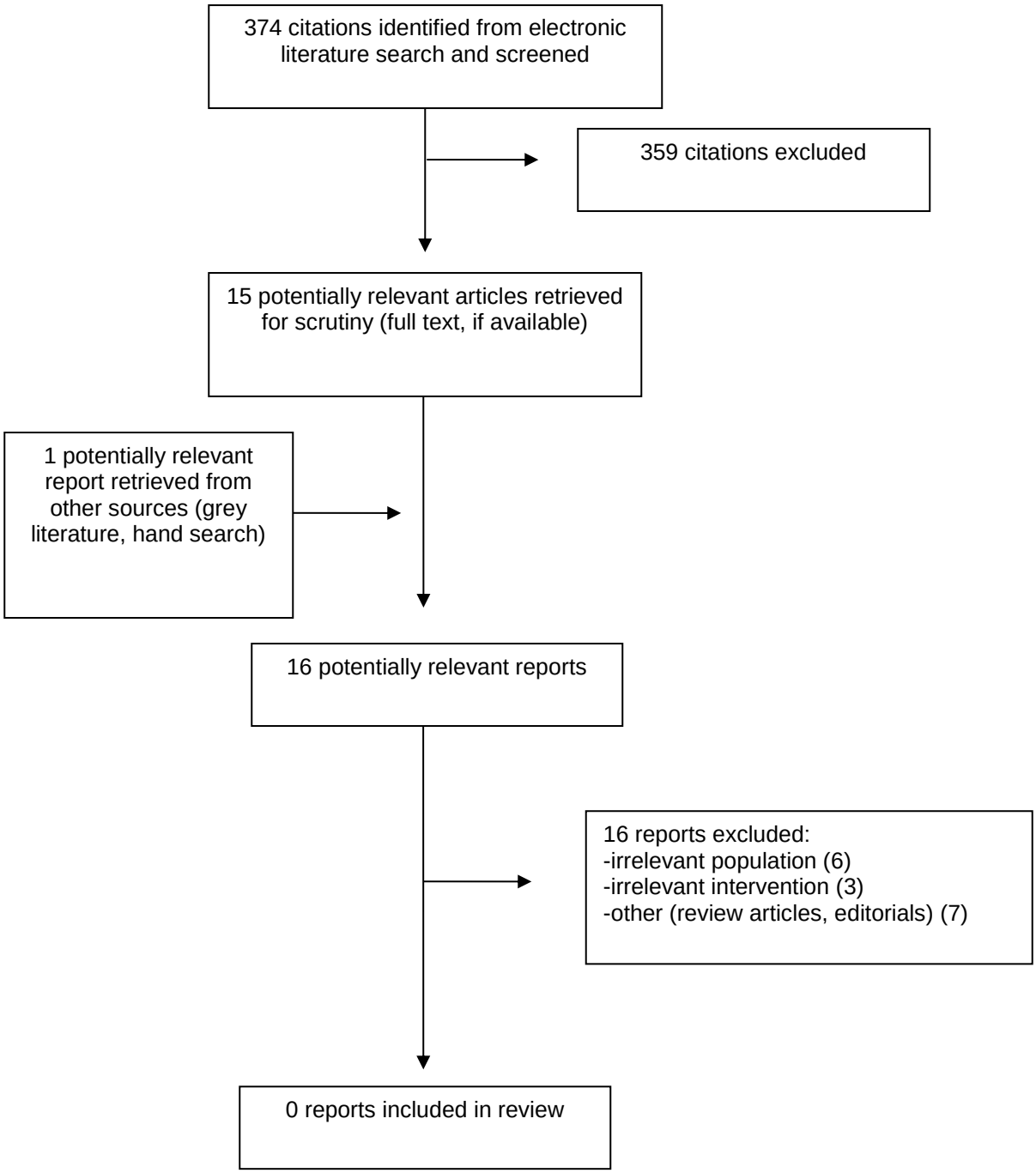
Appendix 1: Selection of Included Studies



Appendix 2: Additional References of Potential Interest

Systematic Reviews and Meta-Analyses

Alternative Population - Patients Not Undergoing Bronchoscopy

Poole P, Sathananthan K, Fortescue R. Mucolytic agents versus placebo for chronic bronchitis or chronic obstructive pulmonary disease. *Cochrane Database Syst Rev*. 2019 05 20;5:CD001287.
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Tarrant BJ, Le Maitre C, Romero L, et al. Mucoactive agents for chronic, non-cystic fibrosis lung disease: A systematic review and meta-analysis. *Respirology*. 2017 08;22(6):1084-1092.
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Review Articles

Pei Y, Liu H, Yang Y, et al. Biological Activities and Potential Oral Applications of N-Acetylcysteine: Progress and Prospects. *Oxid Med Cell Longev*. 2018;2018:2835787.
PubMed: PM29849877

Mokhtari V, Afsharian P, Shahhoseini M, Kalantar SM, Moini A. A Review on Various Uses of N-Acetyl Cysteine. *Cell J*. 2017 Apr-Jun;19(1):11-17.
PubMed: PM28367412