CADTH

CADTH RAPID RESPONSE REPORT:
SUMMARY WITH CRITICAL APPRAISAL

Codeine for Acute Pain for Urological or General Surgery Patients: A Review of Clinical Effectiveness

Service Line:	Rapid Response Service
Version:	1.0
Publication Date:	December 2, 2019
Report Length:	9 Pages

CADTH

Authors: Dave K. Marchand, Caitlyn Ford

Cite As: Codeine for Acute Pain for Urological or General Surgery Patients: A Review of Clinical Effectiveness. Ottawa: CADTH; 2019 Nov. (CADTH rapid response report: summary with critical appraisal).

ISSN: 1922-8147 (online)

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.

Funding: CADTH receives funding from Canada's federal, provincial, and territorial governments, with the exception of Quebec.

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

Abbreviations

CRD	Centre for Reviews and Dissemination
RCT	randomized controlled trial
MeSH	Medical Subject Headings
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses

Context and Policy Issues

Surgical procedures can cause inflammation, tissue injury (e.g., mechanical, thermal, chemical), or nerve injury (e.g., transection, stretching, compression).[1] These types of inflammation or injury result in pain which can be classified as acute (lasting for minutes to several weeks), or chronic (lasting months to years).[2,3] This report will focus on acute pain as a result of urological or general surgery, where urological surgery concerns the male and female urinary tract and the genital organs in males,[4] and general surgery concerns surgical problems outside any specific specialties[4] (e.g., upper and lower gastrointestinal tract, hepatobiliary, pancreatic, soft tissues, hernias[5]).

The goals of therapy for postoperative acute pain include the recognition that the patient is experiencing pain, the anticipation and pre-emptive relief of pain, the rapid reduction of pain intensity, and the general minimisation of discomfort.[1-3,6] Treatment should be continued as long as the patient is experiencing pain.[6] Typically, therapeutic options for postoperative pain control are multimodal and tailored to the patient's characteristics, their needs, and the level of pain associated with the surgery.[1] These factors will determine the type of analgesic technique (i.e., systemic, regional, local), as well as the class of pharmacotherapy (e.g., opioid, non-opioid) that should be privileged. Opioids (e.g., morphine, fentanyl, hydromorphone, oxycodone, codeine) are the most widely used treatment of postoperative pain;[1,3] however, non-opioids (e.g., non steroidal anti-inflammatory drugs, acetaminophen, salicylates) can also be used.[2,3] This being said, opioid prescribing practices have come under scrutiny in recent years as Canada and other jurisdictions battle with an opioid epidemic.[7] Overprescribing by physicians,[8-10] and the diversion of non-consumed supplies, have been recognised as a contributor to the national opioid epidemic.[11] As a result, there has been a desire to optimize opioid prescribing after surgery, when patient and surgical factors make this possible.[8] Specifically, the role of codeine for pain management in urological or general surgery is being questioned and will be the focus of the present report.

In Canada, several formulations of codeine are available for treatment of pain. Codeine primarily agonises the mu receptor.[12,13] It is metabolised in the liver by the cytochrome P450 system, specifically via the CYP2D6 isoenzyme, to various metabolites including morphine,[2,12] which accounts for some of its analgesic effect.[2,12,13] The rate of metabolism by the CYP2D6 isoenzyme is known to vary in the general population,[2,12] which highlights the variety of pain relief that can been observed when codeine is used as a single agent.[2] It is a relatively weak opioid,[13] and may also be used in combination with acetaminophen, where an additive analgesic effect is seen.[2]

Two related CADTH reports, published in 2019, sought clinical effectiveness evidence on codeine for orthopedic surgery[14] and acute pain in pediatrics.[15] The first report identified two relevant systematic review that did not contain any relevant literature,[14] while the second report identified one systematic review, three randomized controlled trials, and one

non-randomized study.[15] The objective of the present report is to investigate the clinical effectiveness of codeine or codeine with acetaminophen for the management of acute pain in adults post urological or general surgery.

Research Questions

1. What is the clinical effectiveness of codeine for patients with acute pain who have undergone general surgery?
2. What is the clinical effectiveness of codeine with acetaminophen for patients with acute pain who have undergone general surgery?
3. What is the clinical effectiveness of codeine for patients with acute pain who have undergone urological surgery?
4. What is the clinical effectiveness of codeine with acetaminophen for patients with acute pain who have undergone urological surgery?

Key Findings

No relevant literature was identified regarding the clinical effectiveness of codeine, with or without acetaminophen, for patients with acute pain having undergone urological or general surgery. Thus, the clinical effectiveness of codeine, with or without acetaminophen, for such patients remains unclear.

Methods

Literature Search 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 codeine and post-surgical pain. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and any types of clinical trials or observational studies. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and October 30, 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: Adult patients with acute pain who have undergone general surgery Q3,4: Adult patients with acute pain who have undergone urological surgery
Interventions	Q1,3: Codeine Q2,4: Codeine with acetaminophen (e.g., codeine as a single product, plus acetaminophen as a single product)
Comparators	Q1,3: Other opioids, placebo, narcotics, non-opiate adjuncts, non-steroidal anti-inflammatory drugs Q2,4: Acetaminophen only
Outcomes	Q1-4: Clinical effectiveness (e.g., pain control), safety (e.g., adverse events, hospitalizations)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies

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.

Summary of Evidence

Quantity of Research Available

A total of 519 citations were identified in the literature search. Following screening of titles and abstracts, 502 citations were excluded and 17 potentially relevant reports from the electronic search were retrieved for full-text review. In addition, no potentially relevant publication was retrieved from the grey literature search for full-text review. Of these 17 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 Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[16] flowchart of the study selection. References of potential interest are provided in Appendix 2.

Summary of Findings

No relevant literature (health technology assessments, systematic reviews, randomized controlled trials, or non-randomized studies) was identified regarding the clinical effectiveness of codeine, with or without acetaminophen, for patients with acute pain having undergone urological or general surgery; 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

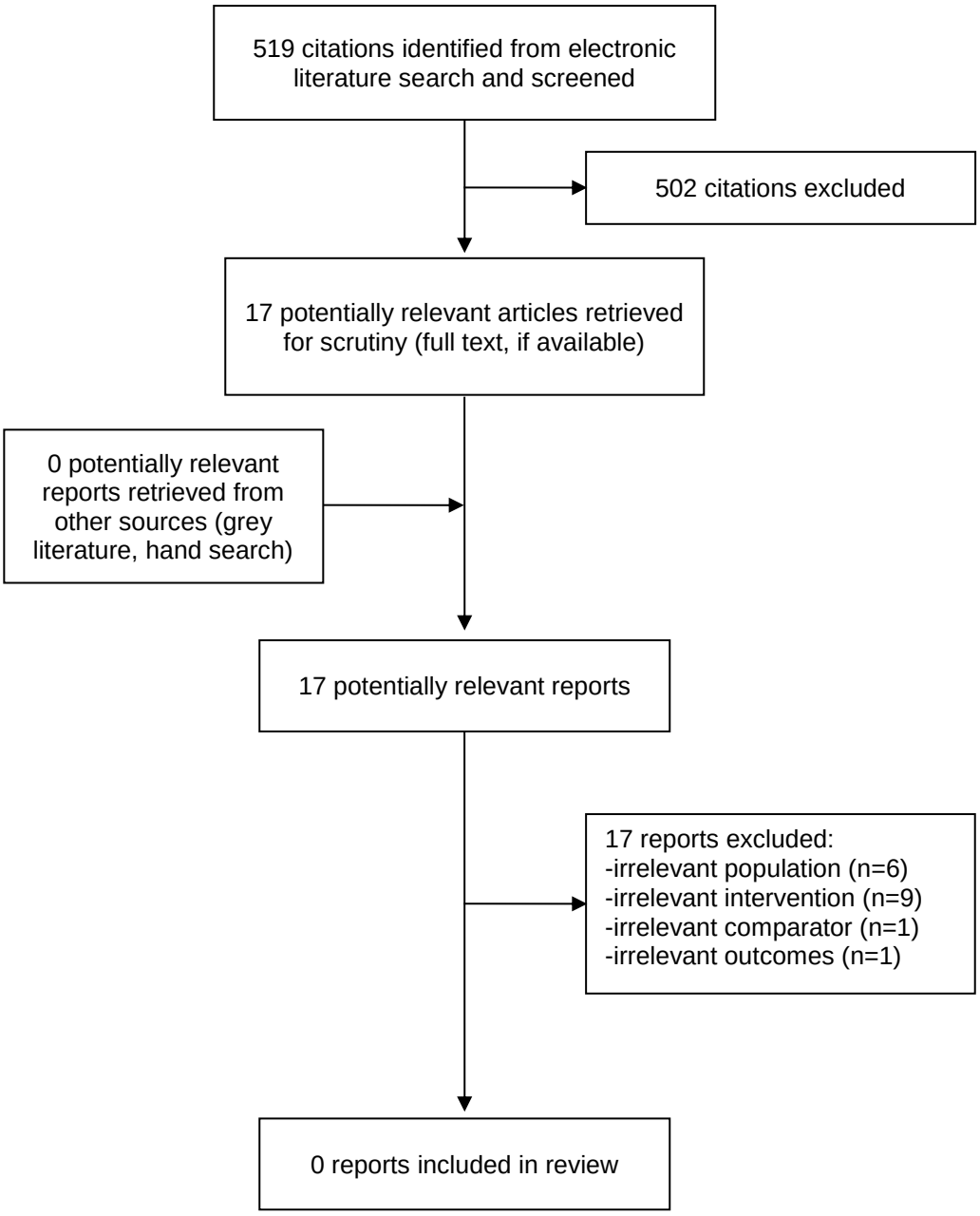
No relevant literature was identified regarding the use of codeine, with or without acetaminophen, for patients with acute pain having undergone urological or general surgery; therefore, no conclusions regarding the clinical effectiveness can be provided. This is similar to the findings of a prior CADTH report on codeine for orthopedic surgery,[14] which was unable to provide any conclusions on clinical effectiveness.

This further highlights the lack of evidence regarding the use of codeine for acute post-surgical pain in these circumstances. Research examining the comparative clinical effectiveness of codeine, with or without acetaminophen, for patients with acute pain post urological or general surgery is required in order to investigate this potential application of codeine.

References

1. Mariano ER. Management of acute perioperative pain. In: Post TW, ed. *UpToDate*. Waltham (MA): UpToDate; 2019: https://www.uptodate.com Accessed 2019 Oct 17.
2. Bailey B. Acute Pain. In: Jovaisas B, ed. *Compendium of therapeutic choices*. 7th ed. Ottawa (ON): Canadian Pharmacists Association; 2014.
3. Baumann TJ, Herndon CM, Strickland J. Pain Management. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey LM, eds. *Pharmacotherapy: A pathophysiologic approach*. 9th ed. New York (NY): McGraw-Hill Education; 2014.
4. *Dorland's illustrated medical dictionary.* 32nd ed. Philadelphia (PA): W.B. Saunders Company; 2012.
5. Shafi S, Aboutanos MB, Agarwal SJ, Brown CVR, Crandall M, Feliciano DV, et al. Emergency general surgery: Definition and estimated burden of disease. *The journal of trauma and acute care surgery.* 2013;74(4):1092-1097.
6. Woolf CJ, Chong M-S. Preemptive Analgesia—Treating Postoperative Pain by Preventing the Establishment of Central Sensitization. *Anesth Analg.* 1993;77(2):362-379.
7. Morin KA, Eibl JK, Franklyn AM, Marsh DC. The opioid crisis: past, present and future policy climate in Ontario, Canada. *Subst Abuse Treat Prev Policy.* 2017;12(1):45.
8. Thiels CA, Anderson SS, Ubl DS, Hanson KT, Bergquist WJ, Gray RJ, et al. Wide Variation and Overprescription of Opioids After Elective Surgery. *Ann Surg.* 2017;266(4):564-573.
9. Roberts K, Moser S, Schaffer N, Dubois K, Brummett CM, Collins AC, et al. Prescribing and Consumption of Opioids After Primary, Unilateral Total Hip and Knee Arthroplasty in Opioid Naive Patients. *The Journal of Arthroplasty.* 2019.
10. Tepolt FA, Bido J, Burgess S, Micheli LJ, Kocher MS. Opioid Overprescription After Knee Arthroscopy and Related Surgery in Adolescents and Young Adults. *Arthroscopy.* 2018;34(12):3236-3243.
11. Morris BJ, Mir HR. The opioid epidemic: impact on orthopaedic surgery. *J Am Acad Orthop Surg.* 2015;23(5):267-271.
12. Sweetman SC. *Martindale: The complete drug reference.* 37th ed. London (GB): Pharmaceutical Press; 2011.
13. United States Pharmacopeial Convention. *USP DI. Volume 1 : Drug information for the health care professional.* Greenwood Village (CO): Micromedex; 2005.
14. Codeine for Acute Pain in Patients Undergoing Orthopedic Surgery: A Review of Clinical Effectiveness. *(CADTH Rapid reponse report: summary with critical appraisal)*. Ottawa (ON): CADTH; 2019: https://cadth.ca/sites/default/files/pdf/htis/2019/RC1199%20Codeine%20for%20Orthopaedic%20Pts%20Final.pdf. Accessed 2019 Nov 19.
15. Codeine for Pediatric Patients with Acute Pain: A Review of Clinical Effectiveness. *(CADTH Rapid reponse report: summary with critical appraisal)*. Ottawa (ON): CADTH; 2019: https://cadth.ca/sites/default/files/pdf/htis/2019/RC1200%20Codeine%20for%20Pediatric%20Patients%20Final.pdf. Accessed 2019 Nov 19.
16. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1-e34.

Appendix 1: Selection of Included Studies



CADTH

Appendix 2: Additional References of Potential Interest

Alternative Population – Mixed Types of Surgery

Moore RA, Derry S, Aldington D, Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. *Cochrane Database Syst Rev*. 2015 Sep 28(9):Cd008659.
PubMed: PM26414123

Alternative Intervention – Opioids discussed as a class

Welk B, McClure JA, Clarke C, Vogt K, Campbell J. An Opioid Prescription for Men Undergoing Minor Urologic Surgery Is Associated with an Increased Risk of New Persistent Opioid Use. Eur Urol. 2019 Sep 18.
PubMed: PM31542305