Canadian Journal of Health Technologies

Canada's Drug Agency
L'Agence des médicaments du Canada

February 2025 Volume 5 Issue 2

Drugs Health Technologies Health Systems

Health Technology Review

Crushed Buprenorphine-Naloxone Tablets

Key Messages

What Is the Issue?

- Opioid agonist therapy (OAT), including methadone and buprenorphine-naloxone, is the primary approach for managing opioid use disorder (OUD) in Canada and has been shown to reduce withdrawal symptoms and opioid use. Recent Canadian clinical guidelines prioritize buprenorphine-naloxone as the first-line treatment for OUD.
- Buprenorphine-naloxone formulations, available as transmucosal tablets or films, are effective for OUD treatment. However, there is a risk of diversion of the tablet formulation; that is, it can be distributed and used by individuals other than those for whom the drugs were prescribed. Crushing buprenorphine-naloxone tablets before administration has been proposed as a potential strategy to mitigate diversion.

What Did We Do?

- We sought to identify, summarize, and critically appraise available studies, as well as review evidence-based guideline recommendations on the administration of sublingual crushed buprenorphine-naloxone tablets for the treatment of opioid dependency.
- We searched key resources, including journal citation databases, and conducted a focused internet search for relevant evidence published since 2016.
- One reviewer screened articles for inclusion based on predefined criteria.

What Did We Find?

- We did not find any evidence regarding the clinical effectiveness and safety of sublingual crushed buprenorphine-naloxone tablets for treating opioid dependency.
- We did not find any evidence-based guidelines regarding sublingual crushed buprenorphine-naloxone tablets for treating opioid dependency.

What Does It Mean?

- We identified no relevant literature on whether crushing buprenorphine-naloxone tablets effectively prevents misuse and diversion in adults with opioid dependence. As a result, no conclusions could be drawn regarding its effectiveness and safety, and no recommendations could be made.

Key Messages

- Additional research is needed to assess the impact of crushing buprenorphine-naloxone tablets on efficacy, bioavailability, and adverse effects to determine the clinical implications of this practice.

Abbreviations

OAT	opioid agonist therapy
OUD	opioid use disorder

Context and Policy Issues

The opioid crisis, a complex health and social issue, claimed an estimated 12,800 lives in Canada from opioid-related overdoses between January 2016 and March 2019.[1] OUD is a chronic condition with significant consequences for society and individuals, including increased mortality, risk of disease transmission, and poor social functioning.[2] The primary approach for treating OUD in Canada is OAT, which includes methadone- and buprenorphine-based formulations, including the buprenorphine-naloxone combination. OAT is an effective form of treatment for people with opioid dependency, reducing withdrawal symptoms and associated risks while curbing opioid use. Recent Canadian clinical guidelines prioritize buprenorphine-naloxone–based OAT as the first choice for OUD treatment.[3] Buprenorphine, a partial opioid agonist, produces mild euphoria and other opioidlike effects, albeit less intensely. Naloxone, an opioid antagonist, blocks the brain receptors targeted by opioids like heroin and methadone. Buprenorphine-naloxone formulations are available as tablets or films and are usually taken daily or every other day by patients.[4] These transmucosal formulations (tablet and film) are effective in treating OUD. Naloxone in transmucosal formulations is poorly absorbed when taken orally. However, if these formulations are crushed and injected, naloxone blocks the effect of buprenorphine (an opioid), helping deter misuse. Still, diversion of transmucosal tablets, such as selling, sharing, or misusing the prescribed tablets leading to its use by individuals other than those for whom the drugs were prescribed, presents significant challenges in ensuring patients adhere to their treatment.[5,6]

Why Is It Important to Do This Review?

Crushing buprenorphine-naloxone tablets before administration has been suggested as a potential method of reducing diversion, promoting safe and effective use of medication, and lowering the risk of untreated opioid dependence.[7] A 2016 CADTH review[8] addressing a similar research question identified 1 study on crushing buprenorphine tablets, but found no literature or evidence-based guidelines on the administration of crushed buprenorphine-naloxone tablets. Understanding the implications of administering crushed buprenorphine-naloxone tablets for preventing misuse and diversion in adults with opioid dependence along with its effects on efficacy, bioavailability, and adverse events is crucial.

Objective

To support decision-making about the clinical practice of crushing buprenorphine-naloxone before administration to prevent diversion, we have prepared this Rapid Review to summarize and critically appraise the available studies on the efficacy and safety of sublingual crushed buprenorphine-naloxone tablets for treating opioid dependency. This report also aims to review the evidence-based guideline recommendations on the administration of crushed buprenorphine-naloxone tablets for the treatment of opioid dependency.

Research Questions

1. What is the clinical effectiveness and safety of sublingual crushed buprenorphine-naloxone tablets for treating opioid dependency?

2. What are the evidence-based guidelines regarding the administration of sublingual crushed buprenorphine-naloxone tablets for the treatment of opioid dependency?

Methods

Literature Search Methods

An information specialist conducted a literature search on key resources including MEDLINE, Embase, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevancy. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. Search concepts were developed based on the elements of the research questions and selection criteria. The main search concepts were buprenorphine-naloxone, form of administration, and opioid dependence. The search was completed on December 18, 2024, and limited to English-language documents published since January 1, 2016.

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. Articles were included if they were made available since the previous search date and were not included in the 2016 CADTH report.[8] The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Criteria	Description
Population	Adults with opioid dependency
Intervention	Sublingual administration of crushed buprenorphine-naloxone combination tablets (Suboxone and generics)
Comparator	Sublingual administration of uncrushed buprenorphine-naloxone combination tablets (Suboxone and generics)
Outcomes	Clinical effectiveness, safety (including potential for misuse or diversion), evidence-based guidelines
Study designs	Q1: SRs, HTAs, RCTs (phase II, III, IV), nonrandomized studies including single-arm trials Q2: Evidence-based guidelines

HTA = health technology assessments; RCT = randomized controlled trials; SR = systematic reviews.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1.

Summary of Evidence

Quantity of Research Available

A total of 490 citations were identified in the literature search. Following the screening of titles and abstracts, all 490 citations were excluded. No potentially relevant publications were retrieved from the grey literature search for full-text review. Appendix 1 presents the PRISMA[9] flow chart of the study selection.

Summary of Findings

We did not find any evidence regarding the clinical effectiveness and safety of sublingual crushed buprenorphine-naloxone tablets for treating opioid dependency. We also did not find any evidence-based guideline recommendations on sublingual crushed buprenorphine-naloxone tablets for treating opioid dependency.

Limitations

No evidence was identified regarding sublingual administration of crushed buprenorphine-naloxone tablets.

Conclusions and Implications for Decision- or Policy-Making

No relevant literature was identified to answer the research questions; therefore, conclusions could not be provided about clinical effectiveness and safety or recommendations on sublingual crushed buprenorphine-naloxone tablets. Similar to the 2016 report,[8] no conclusion can be drawn regarding whether crushing buprenorphine-naloxone tablets could serve as an effective strategy to prevent misuse and diversion in adults with opioid dependence. Future areas of research may include examining the impact of crushing buprenorphine-naloxone tablets on the drug's efficacy, bioavailability, and adverse effects to determine the clinical implications of this practice. Additional considerations for future research may include effective practices to deter and reduce opioid diversion.

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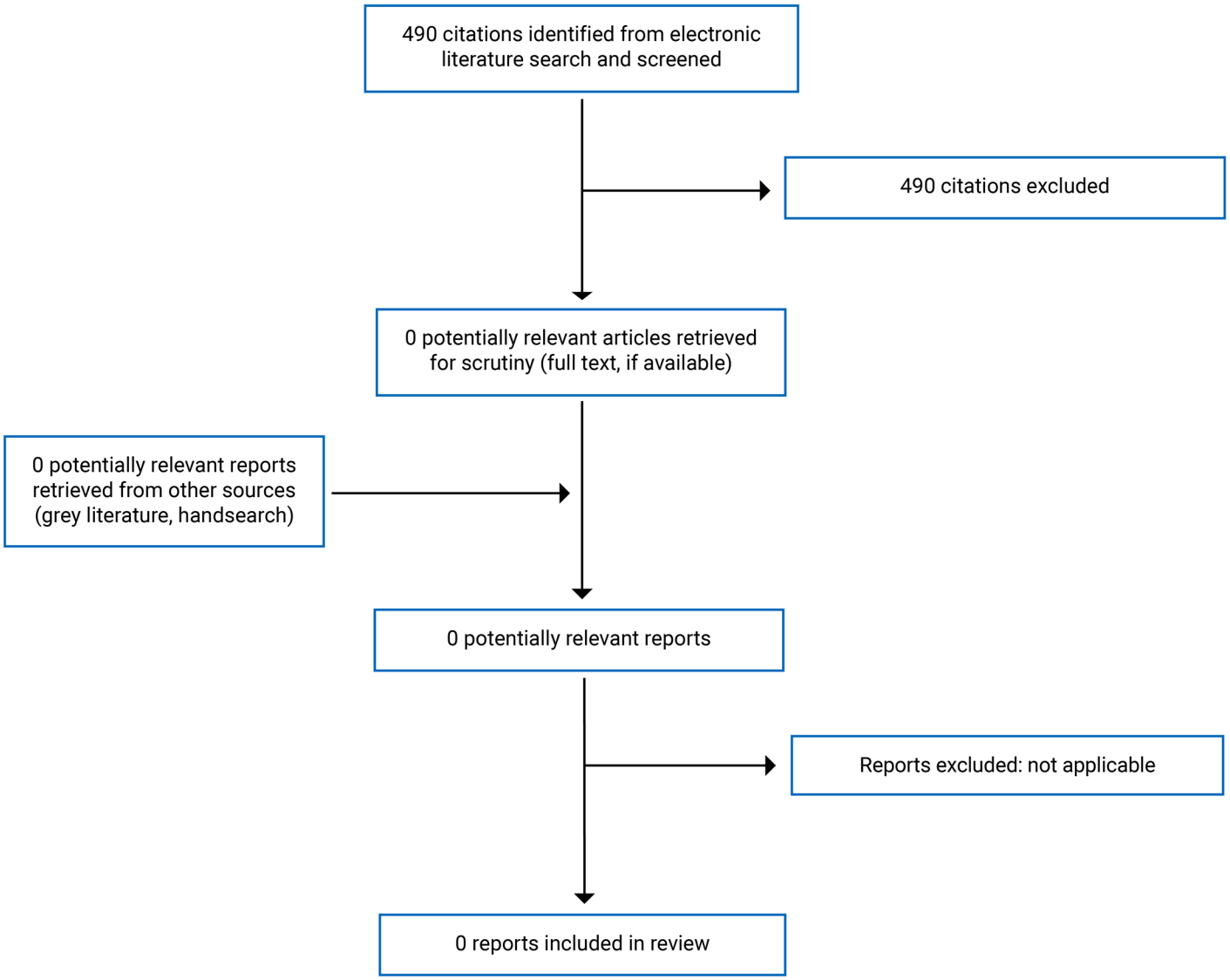
Appendix 1: Selection of Included Studies

Figure 1: PRISMA[9] Flow Chart of Study Selection



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Drugs. Health Technologies and Systems. Médicaments, technologies de la santé et systèmes.

ISSN: 2563-6596

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