



Canadian Agency for  
Drugs and Technologies  
in Health

## RAPID RESPONSE REPORT: SUMMARY WITH CRITICAL APPRAISAL

**TITLE: Administration of Naloxone in a Home or Community Setting: A Review of the Clinical Effectiveness, Cost-effectiveness, and Guidelines**

**DATE:** 20 June 2014

### CONTEXT AND POLICY ISSUES

Natural or synthetic opioids can be used therapeutically, recreationally, and children may be unintentionally exposed to them.<sup>1</sup> Opioid addiction and abuse is a major medical and social problem all around the world.<sup>1,2</sup> The opioids exert their biologic effects through interactions with multiple opioid receptors ( $\mu$ ,  $\delta$  and  $\kappa$ ). The  $\mu$ -opioid receptor is attributed to respiratory depression - a main hazard of severe opioid overdose which is potentially fatal.<sup>1,3-5</sup>

Opioid antagonists are commonly used as rescue medications to reverse severe opioid-induced respiratory depression.<sup>4,6</sup> Naloxone is a non-selective, short-acting opioid receptor antagonist which acts on the  $\mu$ -,  $\delta$ - and  $\kappa$ -opioid receptors.<sup>2</sup> It has been approved by Health Canada as an opioid antagonist since 1994.<sup>7</sup> The most common use of naloxone is for the treatment of opioid overdose in both hospital and out-patient settings, and in rapid detoxification (being given intravenously [i.v.] when combined with other medications).<sup>2</sup> Other routes of administration include intramuscular, subcutaneous, intranasal and through an endotracheal tube.<sup>1,8</sup>

The administration of naloxone in a home or community setting for overdose prevention may be an attractive option to reduce over-dose related deaths as it appears to be feasible and safe.<sup>9</sup> In Canada, there are at least four cities with local overdose prevention and response programs involving naloxone dispensing, while British Columbia has recently launched a provincial program.<sup>10</sup> Currently in Ontario, naloxone is not listed on the formulary or available through the province's Exceptional Access Program.<sup>11</sup>

The purpose of this review is to assess the evidence of the clinical effectiveness and cost-effectiveness of the administration of naloxone in a community or home setting versus naloxone administered by a health professional. Evidence-based guidelines and recommendations for the dosing of naloxone in this setting will also be discussed.

**Disclaimer:** The Rapid Response Service is an information service for those involved in planning and providing health care in Canada. Rapid responses are based on a limited literature search and are not comprehensive, systematic reviews. The intent is to provide a list of sources of the best evidence on the topic that CADTH could identify using all reasonable efforts within the time allowed. Rapid responses should be considered along with other types of information and health care considerations. The information included in this response is not intended to replace professional medical advice, nor should it be construed as a recommendation for or against the use of a particular health technology. Readers are also cautioned that a lack of good quality evidence does not necessarily mean a lack of effectiveness particularly in the case of new and emerging health technologies, for which little information can be found, but which may in future prove to be effective. While CADTH has taken care in the preparation of the report to ensure that its contents are accurate, complete and up to date, CADTH does not make any guarantee to that effect. CADTH is not liable for any loss or damages resulting from use of the information in the report.

**Copyright:** This report contains CADTH copyright material and may contain material in which a third party owns copyright. **This report may be used for the purposes of research or private study only.** It may not be copied, posted on a web site, redistributed by email or stored on an electronic system without the prior written permission of CADTH or applicable copyright owner.

**Links:** This report may contain links to other information available on the websites of third parties on the Internet. CADTH does not have control over the content of such sites. Use of third party sites is governed by the owners' own terms and conditions.

**RESEARCH QUESTIONS**

1. What is the comparative clinical effectiveness of naloxone administered in a community or home setting versus administered by a health professional?
2. What is the cost-effectiveness of naloxone administered in a home or community setting compared with administration by a health professional?
3. What are the evidence-based guidelines for the administration of naloxone?

**KEY FINDINGS**

No relevant literature was identified regarding the comparative clinical and cost-effectiveness of naloxone administered in a home or community setting compared with administration by a health professional. No evidence-based clinical practice guidelines were retrieved in the literature search.

**METHODS**

**Literature Search Strategy**

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, Issue 5), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2009 and May 22, 2014.

**Selection Criteria and Methods**

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to the selection criteria presented in Table 1.

**Table 1: Selection Criteria**

<b>Population</b>	Patients receiving opioids
<b>Intervention</b>	Naloxone administered in a community or home setting (by patient, friends, family, police, or other non-healthcare professional)
<b>Comparator</b>	Naloxone administered by a health professional (e.g. in hospital, clinic, or by EMTs)
<b>Outcomes</b>	Clinical effectiveness: Reduced mortality, reduced morbidity, increased quality of life, ease of use, administration errors, safety Cost-effectiveness Guidelines for administration
<b>Study Designs</b>	Health technology assessments (HTA), systematic reviews (SRs), and meta-analyses (MAs), randomized controlled trials (RCTs), non-RCTs, economic evaluations, evidence-based guidelines.

## Exclusion Criteria

Articles were excluded if they did not meet the selection criteria in Table 1, if they were published prior to January 2009, if they were duplicate publications of the same study, or if they were referenced in a selected systematic review.

## SUMMARY OF EVIDENCE

### Quantity of Research Available

The literature search yielded 227 citations. After screening of abstracts from the literature search and from other sources, 13 potentially relevant studies were selected for full-text review. No relevant health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations, or evidence-based clinical practice guidelines were identified. The majority of citations were excluded as they were review articles, while the remaining citations described take-home naloxone programs that were not compared with administration by a health professional. Policy documents regarding the treatment of naloxone were identified in the grey literature and references are included in Appendix 2.

### Summary of Findings

1. What is the comparative clinical effectiveness of naloxone administered in a community or home setting versus administered by a health professional?

There was no evidence found on the clinical effectiveness of naloxone administered in a community or home setting versus administered by a health professional.

2. What is the cost-effectiveness of naloxone administered in a home or community setting compared with administration by a health professional?

There was no evidence found on the cost-effectiveness of naloxone administered in a home or community setting compared with administration by a health professional.

3. What are the evidence-based guidelines for the administration of naloxone?

No evidence-based clinical practice guidelines were retrieved in the literature search.

## CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No relevant literature was identified; therefore, no conclusions can be presented regarding the comparative clinical and cost-effectiveness of naloxone administered in a home or community setting compared with administration by a health professional. Although no comparative evidence was identified, non-comparative studies suggest high-risk injection drug users are willing to be trained on overdose response strategies to prevent death using take-home naloxone.<sup>12</sup> The non-comparative evidence from two studies<sup>10,12</sup> suggest that the mortality rate for take-home naloxone programs is low, as a program in San Francisco, California reported 6

deaths (2%) among 399 participants<sup>12</sup> while a program in Toronto, Ontario did not report any deaths among 209 participants.<sup>10</sup>

Though limited non-comparative evidence suggest that take-home naloxone programs are associated with a low mortality rate, it remains uncertain whether reported mortality with naloxone take-home programs is comparable to naloxone administration by health care professionals. No evidence-based clinical practice guidelines pertaining to the administration of naloxone were retrieved in the literature search.

**PREPARED BY:**

Canadian Agency for Drugs and Technologies in Health

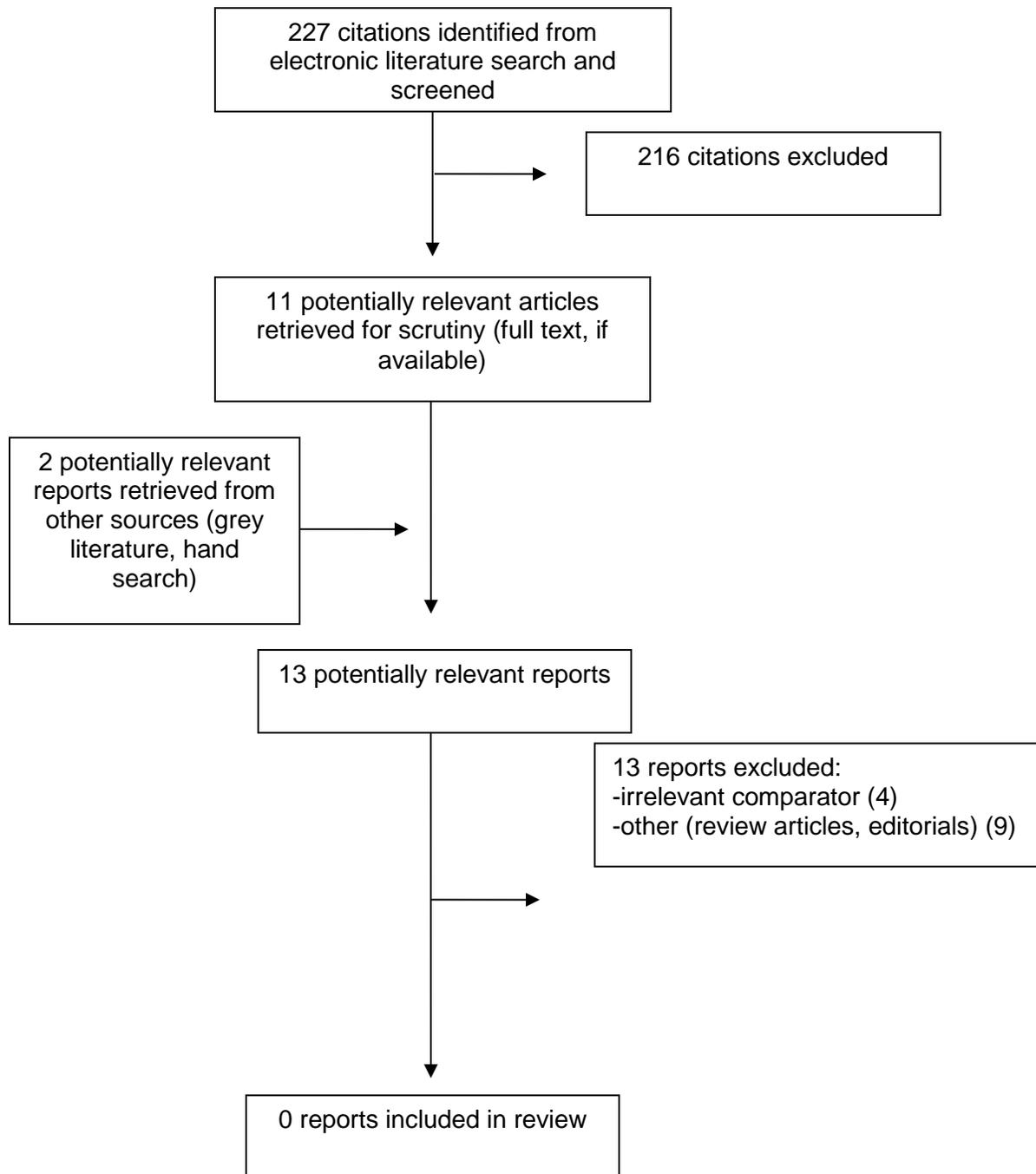
Tel: 1-866-898-8439

[www.cadth.ca](http://www.cadth.ca)

## REFERENCES

1. Stolbach A, Hoffman RS. Opioid intoxication in adults. 2012 Jun 27. In: UpToDate. Version 20.7. Waltham (MA): UpToDate; 1992 - .
2. van Dorp E, Yassen A, Dahan A. Naloxone treatment in opioid addiction: the risks and benefits. *Expert Opin Drug Saf*. 2007 Mar;6(2):125-32.
3. National Guideline Clearinghouse. Rockville (MD): National Guideline Clearinghouse; c2009 -. Guideline summary: Practice guideline for the treatment of patients with substance use disorders; 2007
4. Goodman AJ, Le Bourdonnec B, Dolle RE. Mu opioid receptor antagonists: recent developments. *ChemMedChem*. 2007 Nov;2(11):1552-70.
5. Dahan A, Aarts L, Smith TW. Incidence, reversal, and prevention of opioid-induced respiratory depression. *Anesthesiology*. 2010 Jan;112(1):226-38.
6. Centers for Disease Control and Prevention (CDC). Community-based opioid overdose prevention programs providing naloxone - United States, 2010. *MMWR Morb Mortal Wkly Rep* [Internet]. 2012 Feb 17 [cited 2012 Aug 10];61(6):101-5. Available from: <http://www.cdc.gov/mmwr/pdf/wk/mm6106.pdf>
7. Health Canada. Notice of compliance (NOC) database. Ottawa: Health Canada; 1994 -; 2012
8. Baca CT, Grant KJ. Take-home naloxone to reduce heroin death. *Addiction*. 2005 Dec;100(12):1823-31.
9. Bailey AM, Wermeling DP. Naloxone for opioid overdose prevention: pharmacists' role in community-based practice settings. *Ann Pharmacother*. 2014 May;48(5):601-6.
10. Leece PN, Hopkins S, Marshall C, Orkin A, Gassanov MA, Shahin RM. Development and implementation of an opioid overdose prevention and response program in Toronto, Ontario. *Can J Public Health*. 2013 May;104(3):e200-e204.
11. Eggertson L. Take-home naloxone kits preventing overdose deaths. *CMAJ*. 2014 Jan 7;186(1):17.
12. Enteen L, Bauer J, McLean R, Wheeler E, Hurliaux E, Kral AH, et al. Overdose prevention and naloxone prescription for opioid users in San Francisco. *J Urban Health* [Internet]. 2010 Dec [cited 2014 Jun 19];87(6):931-41. Available from: [http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3005091/pdf/11524\\_2010\\_Article\\_9495.pdf](http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3005091/pdf/11524_2010_Article_9495.pdf)

APPENDIX 1: Selection of Included Studies



## APPENDIX 2: Additional References of Potential Interest

### Policy Documents

1. Guidelines for administration of naloxone (narcane) for opioid induced respiratory depression [Internet]. Doncaster (UK): Doncaster and Bassetlaw Hospitals NHS Foundation Trust; 2010. [cited 2014 Jun 19]. Available from: [http://www.dbh.nhs.uk/Library/Pharmacy\\_Medicines\\_Management/Formulary/Formulary\\_S4/Guidelines%20for%20Administration%20of%20Naloxone-1.pdf](http://www.dbh.nhs.uk/Library/Pharmacy_Medicines_Management/Formulary/Formulary_S4/Guidelines%20for%20Administration%20of%20Naloxone-1.pdf)
2. Patient group direction for the administration of naloxone injection in suspected or known opioid overdose for patients aged 12 years and over by nurses and midwives working within NHS Grampian [Internet]. Aberdeen (UK): NHS Grampian; 2012 Aug. [cited 2014 Jun 19]. Available from: [http://www.nhsgrampian.org/grampianfoi/files/Nalox\\_520\\_0712.pdf](http://www.nhsgrampian.org/grampianfoi/files/Nalox_520_0712.pdf)

### Health Technology Assessments

3. Naloxone for use in long-term care and palliative care: clinical effectiveness, safety, and guidelines [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2013 Dec 16. [cited 2014 Jun 19]. (Rapid response report: reference list). Available from: <http://www.cadth.ca/media/pdf/htis/dec-2013/RA0654%20Naloxone%20in%20LTC%20final.pdf>
4. Naloxone for respiratory depression in patients with drug or addiction issues: a review of the evidence on safety and guidelines [Internet]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2012 Sep 5. [cited 2014 Jun 19]. (Rapid response report: summary with critical appraisal). Available from: <http://www.cadth.ca/media/pdf/htis/aug-2012/RC0386%20Naloxone%20for%20respiratory%20depression%20Final.pdf>