

## Evidence Brief: Evidence on rescue breathing or chest compressions in local naloxone programs



### Key Messages

- The American Heart Association and World Health Organization have written guidelines on resuscitation in opioid overdose using high quality guideline methods
- For overdose response, AHA guidelines recommend compression-only (CO) CPR and WHO guidelines recommend rescue breathing and chest compressions
- There is no new evidence to support using rescue breathing without chest compressions in protocols for naloxone programs
- Bystanders are more willing to perform CO-CPR than conventional CPR

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### Issue and Research Question

In Ontario, implementation of overdose education and naloxone distribution (OEND) programs is rapidly expanding as a response to an increase in opioid-related deaths. Some local public health units have been operating such programs for several years, and now pharmacies and correctional services are settings involved in implementation of these programs in the province. The first OEND programs in North America began approximately 20 years ago<sup>1</sup>, and are currently

available in 7 of the 13 provinces and territories in Canada.<sup>2</sup>

Currently, there is variation in practice internationally on the overdose response protocol that is used in teaching laypersons to respond to opioid-related emergencies. Depending on the program, members of the public who are not certified in Basic Life Support (herein described as “untrained”) may be taught rescue breathing (RB) only, conventional cardiopulmonary resuscitation (C-CPR) (chest compressions and rescue

breathing), or chest compressions only (CO-CPR) within OEND training.

The International Liaison Committee on Resuscitation (ILCOR), an international non-profit association supported by member organization subscription fees, addressed the topic of cardiac or respiratory arrest associated with opioid overdose for the first time in its 2015 International Consensus on CPR and Emergency Cardiovascular Care (ECC) Science with Treatment Recommendations (CoSTR).

ILCOR was formed in 1993, and a primary objective is to collect, review and share international scientific data on resuscitation.<sup>3</sup> Its member organizations include the American Heart Association (AHA), European Resuscitation Council (ERC), Heart and Stroke Foundation of Canada (HSFC), Australian and New Zealand Committee on Resuscitation (ANZCOR), Resuscitation Councils of Southern Africa (RCSA), Inter American Heart Foundation (IAHF), and Resuscitation Council of Asia (RCA).

The HSFC and AHA work collaboratively to develop North American guidelines for CPR and ECC based on the ILCOR consensus process. The current North American guidelines were published in 2015.<sup>4</sup> The algorithm for treating Opioid-Associated Life-Threatening Emergency in Adults recommends using CPR according to the rescuer's level of training prior to administering naloxone. For the untrained lay rescuer (without certification in Basic Life Support), the AHA specifies CO-CPR is preferred, because it is easier to teach and perform, and does not decrease survival compared to C-CPR. Further, the guideline states that "patients who are unresponsive and not breathing normally have a high likelihood of being in cardiac arrest." Hence, for bystanders who call 911 and receive instructions prior to ambulance arrival it is reasonable for emergency dispatchers to assume the patient is in cardiac arrest and guide an untrained rescuer in performing CO-CPR.

However, some groups in Canada and the United States have reviewed the AHA guidance and other literature, and have made alternate conclusions. The Ontario HIV Treatment Network conducted a Rapid Response summary on this topic in August 2016 and concluded that "there is not enough data to strongly recommend prioritizing chest compressions and/or rescue breathing" when responding to an opioid overdose.<sup>5</sup> The New York State Technical Working Group on Resuscitation Training in Naloxone Provision Programs 2016 Report states that given the insufficient data on this topic that "clinical directors will need to determine whether rescue breathing, chest compressions, both or neither is more appropriate for inclusion in their training curricula."<sup>6</sup>

Given the ongoing debate we sought to review the quality of the HSFC/AHA guideline and other recent scientific guidelines on this topic that were based on systematic reviews. We also sought to review any new direct or indirect scientific evidence on effective responses to opioid-related emergencies since the AHA guideline was published that could be used for decision-making if an OEND program were considering an alternate algorithm compared to the HSFC/AHA guideline.

Alternative algorithms within a protocol taught to untrained members of the public to respond to adult cardiac or respiratory arrest where opioids are suspected could include:

- rescue breathing only,
- conventional CPR (includes rescue breathing and chest compressions), or
- neither rescue breathing or chest compressions.

This Evidence Brief asks: *What is the effectiveness of rescue breathing only, conventional CPR, or neither by adult laypersons on survival in suspected opioid-associated resuscitation emergencies among adults in the community, compared to compression-only CPR used with or without naloxone?*

Given that the evidence review for the 2015 AHA guideline did not find direct evidence on this question, we developed secondary questions which would also be informative for program decisions if our updated search also found no articles directly answering this question. We explored the following secondary questions:

- *What is the effectiveness of rescue breathing, conventional CPR, or neither by adult laypersons on survival in resuscitation for any cause among adults in the community, compared to compression-only CPR?*
- *What is the effectiveness of rescue breathing, conventional CPR, compression-only CPR or neither used by adult laypersons on survival in resuscitation for non-cardiac causes among adults in the community, compared to cardiac causes?*
- *What is the willingness of adult laypersons to perform rescue breathing, conventional CPR, or neither in resuscitation for any cause among adults in the community, compared to compression-only CPR?*

It is beyond the scope of this evidence brief to review the most recent literature comparing the effect of rescue breathing and chest compressions on technical aspects of CPR performance (e.g., compression depth); we address the outcomes of survival and willingness to perform CPR.

## Methods

The evidence base for this review consists of review of the published literature, guidelines, grey literature and snowball literature searching. Each of these strategies will be described in turn. The detailed search strategy with key words is available from PHO on request.

PHO Library Services conducted a database search on October 27 2016 in line with a peer-reviewed search strategy. Two databases were searched (Ovid Medline, Embase) using relevant search criteria (subject terms, key words,

English language, from 2013 to 2016). Given time constraints, the search was created to balance sensitivity and specificity. Articles that were clearly off-topic (or out of scope) were removed by the library staff.

Studies were eligible if they were published in the English language, represented primary research findings, and reported on adults with out of hospital cardiac arrest (OHCA) treated by an adult bystander with CPR, and compared CPR including rescue breathing to chest compression only CPR on survival or willingness to perform CPR. Scientific guidelines were eligible if the guideline used a systematic review process to develop the guideline. Title and abstracts were screened for eligibility by two reviewers using standardized criteria, and discrepancies were resolved by consensus. For articles potentially eligible on title and abstract screening, full text articles were retrieved and two reviewers assessed each article for eligibility using the same eligibility criteria and consensus process for discrepancies.

Further, the PHO Library Services used a sample of the included articles to perform snowball searching for additional relevant articles, to determine whether additional searching was necessary to obtain a complete set of relevant publications. This process confirmed the completeness of the original search strategy.

In addition to the database search, PHO Library Services also conducted a grey literature search to identify all relevant scientific guidelines for delivery of rescue breathing or chest compressions with or without naloxone for adults with opioid overdose in the community by untrained adult laypersons. We performed the search by running two keyword searches in a general search engine (Google). The key word search strings included [resuscitation, "rescue breathing," "chest compressions," "heart attack", fentanyl, or overdose guidelines] or [CPR "heart attack," overdose guidelines]. Two reviewers independently reviewed the search results to identify any relevant guidelines that used a systematic literature review to provide its recommendations.

For included articles, relevant information was extracted from each article by one reviewer, and a second reviewer independently extracted the data on 20% of the included articles and compared results with the other reviewer for reliability.

For each identified guideline (n=2), two reviewers independently applied the AGREEII tool to assess the quality of the guidelines, as recommended by the PHO MetaQAT.<sup>7</sup> The AGREEII tool is an internationally recognized quality assessment tool for guidelines.<sup>8</sup> Discrepancies in quality rating were resolved by consensus.

For all other included articles (n=14), two reviewers independently applied a quality appraisal tool appropriate for the study design. The Health Evidence Quality Assessment Tool for Review Articles,<sup>9</sup> was selected to appraise review articles given its applicability to both qualitative and quantitative reviews. The Newcastle-Ottawa Scale (NOS) was selected for nonrandomized studies, including case-control and cohort studies.<sup>10</sup> These tools most closely matched study designs in the available literature and allowed for an objective assessment of overall quality.

## Main Findings

The search of the published literature identified 797 articles, from which 33 unique articles met inclusion criteria for our evidence brief on title and abstract screening. On full text review, 15 articles were relevant to our evidence brief objectives. Of these, the only published guideline addressing CPR for opioid overdose was the AHA guideline.<sup>4</sup> The remaining 14 articles were included for relevance to a secondary question (one was relevant to two questions), and none addressed our primary question. These included 2 reviews and one meta-analysis, as well as 11 primary studies with comparisons relevant to our research questions.

The grey literature search found 12 unique potential guidance documents or reports. Upon review, two scientific guidelines met our inclusion criteria for having used a systematic review to develop a formal guideline. One was developed by the AHA, and the other by the World Health Organization.<sup>4,11</sup>

The quality ratings for the published and grey literature guidelines were strong (Lavonas 2015, strong quality, AGREEII 6/7; World Health Organization (WHO) (2014, strong quality, AGREEII 7/7). Of the remaining 14 articles, 10 were rated strong, two were moderate, and two were weak quality.

### Guidelines for overdose response

The AHA guideline for Cardiac or Respiratory Arrest Associated With Opioid Overdose (Part 10) recommends that the rescuer begin CPR if the victim is unresponsive with no breathing or only gasping, and that the CPR technique should be based on the rescuer's level of training. The guideline also states, "Standard resuscitation, including activation of emergency medical services, should not be delayed for naloxone administration." Specific to CPR training level recommendations, Part 5 of the 2015 AHA guideline specifies that untrained lay rescuers should provide CO-CPR because it is easier to teach, remember, and perform.<sup>12</sup> The guideline chapter specific to overdose does not separately comment on the evidence on effectiveness of chest compressions or rescue breathing in adults with opioid-related respiratory or cardiac arrest. Through contact with the chapter authors, we found that a systematic search for evidence on this topic was performed and that no relevant studies were found.

Similarly the scientific guideline from the WHO on *Community management of opioid overdose* (2014)<sup>11</sup> found no studies comparing C-CPR and CO-CPR for opioid overdose in a systematic review of the literature. The guideline recommends both rescue breathing and chest compressions:

- *“In the absence of regular breathing provide rescue ventilation and administer naloxone.”*
- *“If there are no signs of life, commence chest compressions.”*

This guideline differed from the AHA guideline in advising that “the resuscitation approach used should be one that does not delay the initial administration of naloxone.”

### **Survival in OHCA: CO-CPR vs. other**

We found 8 studies with mixed results relevant to the question of CO-CPR compared to other CPR approaches. Overall, four found better outcomes for CO-CPR compared to C-CPR. Two favoured C-CPR for remote populations, and two others favoured C-CPR in a general cohort. Of note, one of these studies also evaluated the effectiveness of ventilation-only CPR and found it inferior to CPR involving chest compressions.<sup>13</sup>

Among these studies, a meta-analysis of observational studies comparing CO-CPR and C-CPR among adults with OHCA found C-CPR could lead to better survival outcomes and return of spontaneous circulation (ROSC) than CO-CPR, but found no difference for neurologic outcome (survival RR 0.95, 95%CI 0.91-0.99; ROSC RR 0.95, 95%CI 0.92-0.99; neurologic outcome at discharge RR 0.97, 95%CI 0.91-1.01) (strong quality).<sup>14</sup>

A narrative review of telephone-assisted CPR (T-CPR) described findings for T-CPR with and without ventilation as part of the review (weak quality).<sup>15</sup> This review found 3 RCTs with CO-CPR having a non-significant trend toward better outcomes compared with conventional T-CPR, and one meta-analysis with significantly improved chance of survival with CO-CPR compared to conventional T-CPR (14% v. 12%, NNT 41).<sup>15</sup>

Similarly, a retrospective analysis of RCT data not captured in the literature review above, found lower risk of death after adjustment for confounders among those randomized to CO-CPR in comparison with C-CPR (adjusted hazard

ratio 0.91; 95% CI, 0.83-0.99, P=0.02) (strong quality).<sup>16</sup>

Four studies used nationwide population OHCA data in Japan to compare types of bystander CPR on one-month neurologically favourable survival.<sup>13,17-19</sup> In remote areas, survival was higher with conventional compared with CO-CPR (OR 1.26, 95%CI 1.05-1.51) (strong quality).<sup>18</sup> Survival with ventilation-only CPR was higher than no CPR, but lower than CO-CPR or C-CPR (adjusted OR 1.29, 95% CI 1.01-1.63; OR 0.76, 95%CI 0.59-0.96; OR 0.70, 95%CI 0.55-0.89, respectively) (strong quality).<sup>13</sup> At the population level, neurologically favourable survival attributed to CO-CPR increased from 0.6 to 28.3 per 10 million population (p=0.01), and attributed to any bystander CPR increased from 9.0 to 43.6 (p=0.003) between January 2005 and December 2012 when there was an increase in teaching CO-CPR (strong quality).<sup>17</sup> Finally, an observational study found better outcomes among patients with dispatcher instruction on CO-CPR compared C-CPR (adjusted OR 1.09 95%CI 1.00-1.18) and the addition of rescue breathing provided no neurological benefit in the non-cardiac etiology subgroup (strong quality).<sup>19</sup>

One included study used a methodology of a citation review and document analysis to review the evidence in the AHA and ERC (European Resuscitation Council) 2010 guidelines addressing CO-CPR compared with C-CPR in settings with prolonged EMS response times, and found that there is a possibility of no benefit or harm when CO-CPR is used among the subgroup of individuals in these particular (moderate quality).<sup>20</sup>

### **Survival in non-cardiac OHCA**

None of the three studies we identified found a difference between CO-CPR and C-CPR for non-cardiac causes.

Two studies using national population-based OHCA data in Japan addressed the effectiveness of rescue breathing on neurologically favourable survival in OHCA related to non-

cardiac causes (specifically, respiratory disease). One of these found no difference between three types of bystander CPR on favourable neurological outcomes among 121,081 adults with OHCA in the year 2010 caused by respiratory disease: no CPR, CO-CPR, or C-CPR (reference group; OR 0.68, 95% CI 0.39-1.24; OR 0.68, 95%CI 0.37-1.29) (strong quality).<sup>21</sup> The other was a propensity score-matched cohort study using data from January 1, 2005 to December 31, 2010 comparing neurologically favourable survival at 1 month for patients with OHCA related to respiratory disease between those receiving bystander rescue breathing or no rescue breathing (strong quality).<sup>22</sup> This study found similar outcomes for both groups (0.9 v 0.7%; OR 1.23, 95%CI 0.79-1.93).<sup>22</sup>

A prospective cohort study of 880 patients in Arizona was underpowered to detect a difference in survival among patients with non-cardiac OHCA associated with CO-CPR or C-CPR by bystanders, but found bystanders less likely to perform CO-CPR with respiratory cause (i.e., asphyxia or drowning) rather than cardiac (8.3 v 18.0%,  $p < 0.001$ ) (strong quality).<sup>23</sup>

### **Willingness to provide CPR**

We found four studies comparing the effect of CO-CPR or C-CPR on willingness to provide CPR.<sup>17,24-26</sup> These studies indicate that CO-CPR increases willingness to provide CPR compared to C-CPR.

A nationally representative survey of 428 Canadian adults found willingness to provide CO-CPR compared to C-CPR was significantly greater when the victim was unknown (61.5% v. 39.7%,  $p < 0.001$ ), with fear of disease as a barrier to providing RB (moderate quality).<sup>24</sup> In a population-based observational study in Japan, adults with OHCA received CPR more frequently with dispatcher instruction for CO-CPR compared with C-CPR instruction (70.0% v. 62.1%,  $p < 0.001$ ) (strong quality).<sup>25</sup> At the population level in Japan, there was a significant increase in bystander-initiated CPR overall between 2005 to 2012 (34.6% v. 47.3%,  $p < 0.001$ ) and proportion receiving CO-CPR

(17.4% v. 39.3%,  $p < 0.001$ ) as guidelines shifted in 2010 to instruct CO-CPR (strong quality).<sup>17</sup> A research letter described a survey of 900 adults who completed bystander CPR training, found CPR would significantly increase in the case of an unknown victim and known victim if mouth-to-mouth ventilation (MMV) were removed (85% v 99.8%,  $p < 0.0001$ ; 95.3 v 99.3%,  $p = 0.004$ , respectively) (weak quality).<sup>26</sup>

## **Discussion and Conclusions**

Our review found two current scientific guidelines on bystander response to an opioid-associated emergency, both of which recommend responses that include the use of chest compressions. The AHA guideline recommends CO-CPR for untrained bystanders responding to resuscitative emergencies associated with opioids, and the WHO guideline recommends rescue breathing and chest compressions.

Using a comprehensive search strategy, we also found no new evidence between 2013-2016, including the literature since the AHA guideline was published, to support using an alternative algorithm that includes rescue breathing only for untrained bystander responses to resuscitative emergencies associated with opioids among adults.

The available evidence indicates that RB only is associated with worse outcomes in OHCA than bystander responses that include chest compressions. Moreover, there is no evidence that the addition of RB improves outcomes in OHCA from non-cardiac causes.

Furthermore, CO-CPR is more likely to be performed than C-CPR when a bystander is responding to an adult with OHCA.

There were no studies directly addressing outcomes among adults with resuscitative emergencies associated with opioids, comparing bystander responses with rescue breathing, chest compressions, both or neither. An expert commentary by Douma and Brindley, 2016, offers reasons to promote chest



compressions for overdose.<sup>27</sup> More research is needed to improve specific bystander resuscitation approaches in this population.

We conclude based on the available evidence that bystander CPR for adults is likely to result in better outcomes if the response includes chest compressions. While the available consensus recommendations differ on whether rescue breathing should be performed along with chest compressions for adults with opioid overdose, evidence suggests that rescue breathing may not improve outcomes in OHCA due to non-cardiac causes and that bystanders are more willing to perform CO-CPR than C-CPR.

## Implications for Practice

In community-based overdose education and naloxone distribution programs, the best available evidence supports using the AHA guideline algorithm to instruct untrained bystanders to respond to resuscitative emergencies associated with opioids. This includes instruction on CO-CPR if the client does not have additional certification in Basic Life Support.

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## Specifications and Limitations of Evidence Brief

The purpose of this Evidence Brief is to investigate a research question in a timely manner to help inform decision making. The Evidence Brief presents key findings, based on a systematic search of the best available evidence near the time of publication, as well as systematic screening and extraction of the data from that evidence. It does not report the same level of detail as a full systematic review. Every attempt has been made to incorporate the highest level of evidence on the topic. There may be relevant individual studies that are not included; however, it is important to consider at the time of use of this brief whether individual studies would alter the conclusions drawn from the document.

## Author

Dr. Pamela Leece, Public Health Physician, Health Promotion, Chronic Disease and Injury Prevention

## Contributors

Harkirat Singh, Research Coordinator, Health Promotion, Chronic Disease and Injury Prevention  
Sue Keller-Olaman, Manager, Health Promotion, Chronic Disease and Injury Prevention  
Chetan Mistry, Research Assistant, Health Promotion, Chronic Disease and Injury Prevention

Susan Massarella, Library Information Specialist, Library Services  
Beata Pach, Manager, Library Services

## Reviewers

Dr. Heather Manson, Chief, Health Promotion, Chronic Disease and Injury Prevention  
Dr. Brian Schwartz, Chief, Communicable Disease, Emergency Preparedness and Response

## External Reviewer

Dr. Laurie Morrison, Director, Rescu, St. Michael's Hospital

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Knowledge Synthesis Services, Health Promotion, Chronic Disease and Injury Prevention  
Email: [hpcdip@oahpp.ca](mailto:hpcdip@oahpp.ca)

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