Overview of studies on the provision of take-home naloxone

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Naloxone is effective to reverse opioid overdose (including synthetic opioids).

Take home naloxone programs are available in at least seven EU Member States and Norway, in USA, Canada and Australia (16 Countries).

Exchanging knowledge on such an intervention enable the potential implementers to take informed decisions.
Objectives

To assess the effect of take home emergency naloxone and educational intervention on:

- knowledge improvement,
- naloxone use,
- management of the overdoses witnessed and
- death from overdose

Overview of the available studies (Cochrane Group on Drugs and Alcohol – Minozzi, S; Ferroni, E et al - EMCDDA)
Randomized controlled trials (RCT), controlled clinical trials (CCT), controlled cohort studies, interrupted time series analysis (ITS), cross sectional studies, case series, any study conducted to evaluate implementation of programs.

We considered studies involving current or former opioid injectors, their relatives and peers.
Methods - Inclusion criteria – population and interventions

All participants were included regardless of age, gender and nationality.

The experimental intervention was:
• take home emergency naloxone accompanied or not by explanatory leaflets, education and training for opioid users, peers and families;

The control intervention was
• intervention-as-usual (e.g. information on the risks of overdose) or no intervention.
Results

1542 references (471 Pubmed; 641 Embase; 302 Web of Science; 46 Cochrane Central; 21 CDAG Register; other sources 2)

Duplicates cleaning 1045 references

70 full text articles

21 studies included

+ 2 ongoing studies
Results

Twenty-one publications about 21 studies were included in the present overview (two publications referred to the same study whereas one publication reported the results of two programs).

1 randomized controlled trial (RCT), 3 were case-series and 17 were pre-post studies.

Furthermore, two ongoing trials were identified.

Of the included studies, fourteen studies were conducted in the USA, six in the UK, one in Canada and one in Germany.

Duration of observation (3 months – 8 years)
<table>
<thead>
<tr>
<th>Intervention</th>
<th>Comparison</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>Training (1 hour) and provision of take home naloxone</td>
<td>Distribution of booklet on overdose risk factors, opioid overdose signs, actions to take in an overdose, and basic information about naloxone</td>
<td>Williams 2013</td>
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<tr>
<td>Training program with the provision of take home naloxone</td>
<td>No comparison</td>
<td>Gaston 2009; Seal 2005 and Strang 2008</td>
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<tr>
<td>Training and intra-nasal naloxone distribution programmes realized at city or regional level</td>
<td>n.a.</td>
<td>Doe-Simkins 2009,</td>
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## Results

<table>
<thead>
<tr>
<th>Population</th>
<th>Outcome</th>
<th>Effects</th>
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</thead>
<tbody>
<tr>
<td>Drug users and their peers</td>
<td>Knowledge about signs of overdose, correct management of patients, naloxone use</td>
<td>N= 8 studies the RCT and all the other uncontrolled studies showed an improvement in knowledge.</td>
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<td></td>
<td>Attitudes: willingness to use naloxone, confidence and acceptability of naloxone</td>
<td>N= 7 studies the RCT showed a significant improvement. The uncontrolled studies: three showed a significant improvement; 1 reported only the post intervention results and 3 did not show improvement.</td>
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<td></td>
<td>Management of overdose</td>
<td>N=12 studies Ambulance call: median 30% of overdose witnessed Recovery position 40% of overdoses (3 studies self-reported) Cardiopulmonary resuscitation (CPR) 61% of overdoses (6 studies, self-reported). Naloxone refill 59.5% of overdose witnessed (range 23%-80%) in the 4 studies active follow up.</td>
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## Results

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<td>Drug users and their relatives and peers</td>
<td>Naloxone administration (% overdoses)</td>
<td>N=11 studies RCT (28%); 2 studies self-report (76% and 50%) 7 studies active follow up median of 67% (range 0-100%). 1 study reported the percentage of participant who administered naloxone (44%) and in one study have reported 17 naloxone administrations during the first eight months, all with successful outcomes.</td>
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<tr>
<td>Communities</td>
<td>Reducing death due to overdose</td>
<td>N=13 studies One ITS overdose fatalities lower both in the communities with high program implementation and in communities with low program implementation when compared with communities without program implementation (high vs no Adj RR: 0.54, 95%CI 0.39-0.76; low vs no: Adj RR 0.73, 96%CI 0.57-0.91). 1 study reported that 83% of the overdoses occurred the study were reversed (no info 17%). In 4 studies lethal overdoses (despite naloxone administration) ranged from zero to 4 %the median 0.8. 6 studies with active follow up lethal overdoses (despite naloxone provision) ranged from 0 to 33%). Three studies reported the total number of overdose reversed (no information are given about number of overdose where naloxone was administered).</td>
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Summary

There is evidence that educational and training intervention with naloxone take home provision can decrease overdose related mortality.

There is weaker but consistent evidence that educational and training intervention with naloxone provision for opioid dependent patients and their peers is effective in improving knowledge and attitudes about the correct use of naloxone and management of witnessed overdose.

There is sparse evidence that people return to refill naloxone provision.
Discussion

Take home naloxone provision is an emergency saving-life intervention.

Public health programs (lay people interventions in critical situations), are complex to assess.

In analogy with public access to defibrillation (PAD) for out of hospital cardiac arrest, factors contributing to the survival rates are difficult to control in an experimental study design.

Nevertheless, even though the evidence in support of PAD is scarce, the available systematic reviews of the literature suggest the implementation of such an intervention (Clare, 2006; Smith, 2007) for the actual or potential reduction of fatal cases.
Discussion

This overview reached similar results of a recently published review (Clark et al 2014) which included a lesser number of studies.

The World Health Organization is launching (5th November) document targeting worldwide countries and some national guidelines are available in the European Countries and can be consulted in the Best Practice Portal.
Milan 1980 - Dario Rizzi, 16 years old