



Australian Drug Policy: Lifesavers -

access to naloxone to reduce opioid overdose-related deaths and morbidity

Anex is a leading national voice in the public health sector. Since our inception as an independent, non-profit organisation in the 1990s, we have worked to increase understanding of, and improve responses to, the problems arising from the use of illicit drugs and the misuse of pharmaceuticals and alcohol.

Anex does not condone drug use, but strives to protect people from drug-related harm when they are at their most vulnerable.

Anex Chief Patron

Emeritus Professor Sir Gustav Nossal AC

Anex Patrons

Professor Margaret Hamilton AO

The Hon. Michael Kirby AC

Emeritus Professor David Penington AC

Correspondence

Anex CEO

Suite 1, Level 2,

600 Nicholson Street

Fitzroy North VIC 3068

Australia

Telephone: 61 3 9486 6399

Facsimile: 61 3 9486 7844

Email: info@anex.org.au

Website: www.anex.org.au

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Use of naloxone hydrochloride for suspected opioid overdose

Naloxone hydrochloride has been used to safely reverse the effects of opioid intoxication in hospitals and by paramedics for decades [1, 2]. Its only action is to reduce the effect of opioids. International experience shows that non-medical personnel can also be trained to safely administer naloxone in opioid overdose situations and in this way potentially further reduce overdose-related death and disability [3, 4].

At present in Australia, naloxone can only be provided to members of the general public via medical prescription. Legal protection has been extended to non-medical personnel who administer it, in the United Kingdom and parts of the United States. Such issues have been discussed for more than a decade in Australia. In the longer term, naloxone could be 'rescheduled' to make it available as an 'over-the-counter, pharmacist involved' purchase in pharmacies, as has been the case in Italy for many years [5, 6].

Needle and syringe program (NSP) personnel are well placed to educate their clients about naloxone, once they themselves have been provided adequate training. Upon completion of training, the NSP workforce, in partnership with willing physicians, could begin distributing naloxone under prescription to opioid users and other potential overdose witnesses. Naloxone should be made available to such potential overdose witnesses through formal programs.

Anex recommends that:

- *Australian Governments should take necessary steps to facilitate the establishment of new pilot programs directed towards opioid overdose treatment with naloxone;*
- *Australian Governments support the education of health care workers and potential overdose witnesses about the use of naloxone in preventing opioid overdose-related mortality and morbidity;*
- *The effectiveness of naloxone programs should be adequately evaluated.*

Background

Opioids are a group of drugs that include opium derivatives such as heroin, as well as synthetic and semi-synthetic pharmaceutical drugs of a similar action. They depress the central nervous system (CNS), thereby reducing the rate of respiration. In an overdose situation, respiration can cease completely. Opioid overdose can lead to permanent brain injury, and other major organ damage. Untreated, opioid overdose can lead to cardiac arrest and death. A significant proportion of, but not all, heroin overdoses are fatal [7]. During Australia's 'heroin glut' [8], more than 1100 fatal opioid overdoses were reported in 1999 [9]. In recent years since heroin availability has reduced, the number of deaths has also significantly reduced. It is estimated that one person per day dies of an opioid overdose, usually involving the injection of heroin [1]. However, of increasing concern is the number of fatal overdoses occurring because of the growing number of people consuming pharmaceutical opioids such as oxycodone and slow release morphine products. This is particularly the case in regional and rural areas.

Naloxone is a drug that is more commonly known by the trade name of Narcan® [10]. Naloxone is a pure opioid antagonist. It reverses the effects of both natural, synthetic and semi-synthetic opioids including codeine, heroin, methadone, morphine, fentanyl and propoxyphene [11].

Naloxone is non-addictive and safe, primarily because it does nothing but counter the depressant effects of opioids. Manufacturers recommend storing naloxone below 25 degrees Celsius and protecting it from light [11], but no other measures are necessary for storage. Indeed, naloxone has been shown to remain viable over a temperature range from -20C to +70C [12]. The liquid form (for injection or for inhalation) has a shelf life of at least two years. Naloxone is not patented in Australia.

How naloxone is used

Naloxone is used by medical personnel to reverse the effects of opioid overdose in and out of hospital settings (such as ambulance attendances) or in acute settings, that is, hospitals [13, 14]. Each year, hundreds of lives are saved and severe brain injuries prevented by Australian paramedics who carry and use naloxone for people who have an opioid overdose [15].

Naloxone is generally administered by injection either intravenously by medical personal in hospital settings, or intramuscularly by paramedics if in pre-hospital settings [16]. However it can also be administered via a nasal spray device which converts the naloxone liquid into a fine mist, overcoming concerns about possible needle-stick injuries. [17].

Nasal administration has been shown to be as effective as intravenous administration in a retrospective study of paramedics conducted in the United States [18]. The Boston,

Massachusetts, program uses nasal administration rather than injection [4]. Application by nasal spray has been trialled by paramedics in Victoria where it was found to be effective and safe [19]. However, at present, intranasal preparations of naloxone are not licensed in Australia.

Naloxone availability in Australia: Who can use it?

Although being a non-addictive, safe and an indisputably lifesaving drug, naloxone is classified as a Schedule 4 drug by the Therapeutic Goods Administration in Australia [14]. This means that it can only be administered by trained medical staff, such as paramedics, or prescribed by a doctor to a person who would then present the script at a pharmacy [1].

In Australia doctors have generally not prescribed naloxone to lay people, for example, a person who is at risk of opioid overdose or the parents of a person at risk. Naloxone distribution has occurred in the US for more than 12 years without any known legal problems [20].

On 16 December 2011, the Australian Capital Territory (ACT) Government announced that Australia's first program to provide naloxone to trained potential overdose witnesses would commence in 2012. It will be independently evaluated [21, 22]. Under the program, which has commenced, naloxone will be provided under prescription and two hundred people will be trained in the following:

- risk factors for opioid overdose;
- recognising opioid overdose;
- responding to opioid overdose (including resuscitation techniques, calling for an ambulance and the administration of naloxone).

Availability of naloxone to non-medical personnel in other nations

Increasingly, naloxone is being made available to those who can be termed “potential overdose witnesses”. Early pilot studies in the mid-1990s in the Emilia-Romagna region of Italy began making naloxone available to heroin users so that their family or peers could reverse overdose quickly while awaiting emergency medical care to arrive [23]. By 2000, reports were emerging from Germany that drug users when trained to administer naloxone could successfully reverse other peoples' opioid overdoses [24].

The Chicago Recovery Alliance established the first United States program to prescribe injectable naloxone in Chicago in 2001 [25], and by 2010 had distributed naloxone to more than 15,000 potential overdose witnesses, and received reports of more than 1500 successful overdose reversals. By 2011 there were at least 188 specific local programs/projects throughout 15 states and the District of Columbia, with more than 53,000 people trained and more than 10,000 overdose reversals recorded [3, 4, 26, 27]. Programs in the United States have been established under both Democrat and Republican state administrations.

Notably, some programs have been established in rural areas in response to alarming levels of overdose caused by misuse of pharmaceutical opioids rather than heroin. Naloxone is made available to lay people, including drug users themselves, in various injectable and nasal spray formulations [10, 26].

As recently described in the Centers for Disease Control's (CDC) *Morbidity and Mortality Weekly Report*, several US states have enacted 'Good Samaritan' or limited legal liability legislation. This legislation protects any person who prescribes or administers naloxone from a legal liability arising from the use of naloxone, providing the naloxone is given "in good faith" [4]. In Boston City, regulations have been passed by which the city's Board of Health assumes liability for the work of medical and non-medical personnel involved in the program [26]. An example of the protective legislation comes from California:

"The bill would authorize a person who is not otherwise licensed to administer an opioid antagonist in an emergency without fee if the person has received specified training information and believes in good faith that the other person is experiencing a drug overdose. The bill would prohibit that person, as a result of his or her acts or omissions, from being liable for any violation of any professional licensing statute, or subject to any criminal prosecution arising from or related to the unauthorized practice of medicine or the possession of an opioid antagonist" [5].

The CDC funded an evaluation of the Overdose Education and Naloxone Distribution (OEND) program in Massachusetts. It was established in 2006 in 18 towns/suburbs which had recorded five or more fatal opioid overdose deaths in 2004-2006. More than 2800 people were enrolled in the program. Although the evaluation is yet to be peer reviewed and published, the evaluation found that hundreds of overdose reversals were completed [3]. The Massachusetts Public Health Department funded a program to train police officers to resuscitate overdose victims with a nasal naloxone spray. Further, the evaluation showed that, even when many other things were controlled for (ethnicity, poverty, extent of methadone and other drug treatment, etc.) overdose education incorporating naloxone distribution reduces fatal opioid overdose rates and this reduction is related to the intensity and coverage of the OEND [3].

In England, 16 sites were selected in 2009 for a pilot program under which naloxone would be provided to friends, parents and siblings of people at risk of opioid overdose. The program is being administered by England's National Treatment Agency for Substance Misuse [28]. It is targeting "families and carers of opioid misusers" [29], made possible through regulatory reform which, although it can still only be prescribed to a known patient who requires it, permits other lay people to administer naloxone in the event of an overdose [30]. Other programs have saved lives in Wales [31]. In 2012, King's College London is scheduled to commence a large scale randomised controlled trial of naloxone provision to prisoners upon release [32].

Reviews of United States and European Naloxone Distribution Programs (NDPs) reveal several common findings:

1. Lay persons who have been trained by experienced personnel (medical and non-medical) can accurately identify opioid overdose, and can effectively reverse the overdose using naloxone;
2. Naloxone's efficacy in reversing opioid overdose is well documented in the medical literature;
3. Thousands of overdose reversals have been performed by lay people in non-medical settings, with virtually no adverse events (including no severe opioid withdrawal) observed using the formulations and dosages recommended by the NDPs [26];
4. Availability of naloxone does not exacerbate opioid usage in people who are opioid dependent; rather, availability of naloxone is associated with increased likelihood of accessing addiction treatment [25].

Evaluation of the program in San Francisco found that "adverse events" associated with naloxone administration were extremely rare, with very few people reporting that the person to which it was applied reported feeling angry or "dope sick" [33]. It has been found that in the Boston program, which uses nasal administration and involves significant law enforcement training and endorsement, it is a "myth" to claim that naloxone-driven overdose reversal result in violent reactions from people [34].

Naloxone provision to potential overdose witnesses is also occurring in Canada, Germany, Georgia, Russia, Spain, Norway, Afghanistan, China, Kazakhstan, Tajikistan and Vietnam [35].

United Nations' Commission on Narcotic Drugs

Support for further expansion of naloxone distribution programs is growing internationally. In light of evidence from around the world that naloxone provision is safe and effective, in March 2012 the United Nations made the following recommendations:

“opioid overdose treatment, including the provision of opioid receptor antagonists such as naloxone, is part of a comprehensive approach to services for drug users and can reverse the effects of opioids and prevent mortality”,

and,

“Encourages all Member States to include effective elements for the prevention and treatment of drug overdose, in particular opioid overdose, in national drug policies, where appropriate, and to share best practices and information on the prevention and treatment of drug overdose, in particular opioid overdose, including the use of opioid receptor antagonists such as naloxone” [36].

United States Food and Drug Administration

In April 2012 the Food and Drugs Administration (FDA) convened a scientific symposium that brought together leading public health experts and people directly involved in such programs. The US ‘drug czar,’ Gil Kerlikowske, issued a statement on behalf of the White House supporting naloxone provision for fatal overdose prevention, noting that it has been recognised in US official drug strategy policy since 2010 [37].

American Medical Association endorsement

At its Annual Meeting on June 19, 2012, the American Medical Association endorsed and encouraged “the establishment of new pilot programs directed towards heroin overdose treatment with naloxone”. The Association also resolved to “encourage the education of health care workers and opioid users about the use of naloxone in preventing opioid overdose fatalities” [38].

What needs to occur in Australia to make naloxone available to potential overdose witnesses?

Provision of naloxone under prescription programs

As previously described, naloxone can legally be provided to anyone by medical prescription as long as it is administered to the person for whom it was prescribed. This means that the people that need to be trained are those in contact with persons who have been legally prescribed naloxone. This model is similar to that used for the administration of adrenaline in the management of anaphylaxis in an emergency situation. US programs operate under a prescription model.

Reclassification of naloxone

Naloxone can be rescheduled from a Schedule 4 to either Schedule 3 or Schedule 2 through an application to the Therapeutic Goods Administration. Anex has been informed that no such application has been lodged since naloxone was first scheduled as an S4 drug in 1973 [39]. Reclassification can be done without fees and an application can be lodged by any member of the community.

If naloxone (as a base) was classified as a Schedule 3 (S3) drug, it could be purchased from a pharmacy after consulting a pharmacist. If naloxone was classified as a Schedule 2 (S2) drug, it could be available off-the-shelf so that it could be purchased without the need to consult a pharmacist. Either of these interventions would need to include education of people who consume opioids dangerously and other potential overdose witnesses regarding the availability of naloxone.

Provision via Needle and Syringe Programs and other services

Needle and syringe programs (NSPs) may be the only health services that people who inject opioids access on a regular basis; often they are the only health service that injectors trust.

NSP staff are well placed to provide people at risk of overdose and potential witnesses to overdose, access to naloxone. NSP staff could provide necessary training and advice on how to store naloxone and administer it. This model has proved effective internationally, particularly in the United States [13, 18].

NSP staff should be trained to administer naloxone so that they may reverse overdoses that happen in close proximity to the NSP service.

There are a number of situations where there is a greater risk of drug overdose. For example, death by overdose following incarceration is a major risk; the prison system could begin providing overdose education to inmates, and distributing naloxone to them at discharge, as will occur in the

UK trial [32]. Similarly, drug treatment programs should educate patients that relapse is possible, and that relapse after a period of abstinence carries a high risk of overdose. Treatment programs should educate patients and their families about overdose recognition and prevention, and should make naloxone available to all opioid-addicted patients who choose to attempt abstinence.

Opioid Replacement Therapy (ORT) practitioners

Current doctor-to-pharmacist ORT systems are suitable for making naloxone available to potential overdose witnesses, particularly ORT clients themselves. Opioid overdose is not a problem unique to heroin. The early weeks of methadone treatment, carry a high risk of overdose [40]. Doctors and pharmacists involved in ORT (also known as Opioid Substitution Therapy) are well placed to educate patients and their support networks about the risks of overdose as well as making naloxone available to them when they commence ORT. Having naloxone available in the home is also crucial prevention in the case of accidental ingestion of opioids by a non-tolerant individual.

Family support and consumer organisations

Organisations representing people who consume illicit drugs, known as peer-based organisations, could be involved in naloxone distribution programs. Family drug support bodies are also in an ideal position to facilitate access to naloxone for parents and siblings of people at risk of opioid overdose. Note that both consumer and supporter groups have been involved in the ACT trial that has been developed.

Patients being treated with legally prescribed opioids for chronic and acute pain can also be at risk of accidental overdoses. Any patient who is prescribed opioids should also be educated about the risks of their treatment and have access to naloxone if appropriate. The danger of accidental home ingestion by a non-tolerant individual also exists in relation to prescribed opioids for pain.

Recommendations

Anex recommends that:

- *Australian Governments should take necessary steps to facilitate the establishment of new pilot programs directed towards opioid overdose treatment with naloxone;*
- *Australian Governments support the education of health care workers and potential overdose witnesses about the use of naloxone in preventing opioid overdose-related mortality and morbidity;*
- *The effectiveness of naloxone programs should be adequately evaluated.*

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Suite 1, Level 2,

600 Nicholson Street

Fitzroy North VIC 3068 Australia

Telephone: 61 3 9486 6399 Facsimile: 61 3 9486 7844

Email: info@anex.org.au Website: www.anex.org.au