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WHEN
A FRIEND
DROPS...

ALCOHOL
& THE AGED

TACKLING
INDIGENOUS
SMOKING

SENT
PACKING
Should clients
be expelled?

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When a friend drops ...

Libby Topp

ALTHOUGH THE NUMBER OF OPIOID OVERDOSES IN AUSTRALIA DROPPED MARKEDLY FOLLOWING THE REDUCTION IN HEROIN AVAILABILITY A DECADE AGO, MISUSE OF PRESCRIBED OPIOIDS CONTINUES TO INCREASE, AND AT LEAST ONE PERSON STILL DIES OF AN OPIOID OVERDOSE EVERY DAY.

Fatal opioid overdose is the leading cause of death among people who use illicit drugs, exceeding deaths caused by HIV, hepatitis C and drug market-related homicides. Non-fatal overdoses are also familiar events for heroin users, who are likely to have not only experienced their own overdoses, but often have also witnessed those of their friends and peers. Opioids include heroin and synthetic drugs such as morphine, and overdose occurs when an opioid binds to the opioid receptors in the brainstem, which regulates breathing. The drug desensitises the brainstem to blood carbon dioxide levels so that breathing mechanisms are not triggered, leading to respiratory (breathing) failure.

Intervening before death

Australian studies indicate that nobody intervenes before death in 70 to 80 per cent of heroin overdose fatalities, despite substantial opportunities to do so. At least 60 per cent of fatal overdoses occur in a home, with somebody else present, and more than an hour after injection. Witnesses call an ambulance only in a minority of fatalities. Their reasons for not doing so include potential costs, previous negative experiences with hospital staff and fear of police involvement.

Overdose reversal

Opioid overdose can be rapidly reversed with naloxone hydrochloride, known more commonly by the trade name Narcan. Naloxone displaces opioids at the brainstem receptors, thus reversing opioid effects such as respiratory depression, sedation and low blood pressure. Naloxone has no other action; it does not result in intoxication and therefore has no abuse potential. Indeed, when given to tolerant opioid users, naloxone instead rapidly triggers opioid withdrawal. Consequently, black market demand and diversion seem unlikely. In the absence of opioids, naloxone has little effect and thus poses no risk to people who are not tolerant to opioids. Classed under Schedule 4 by Australia's Therapeutic Goods Administration –

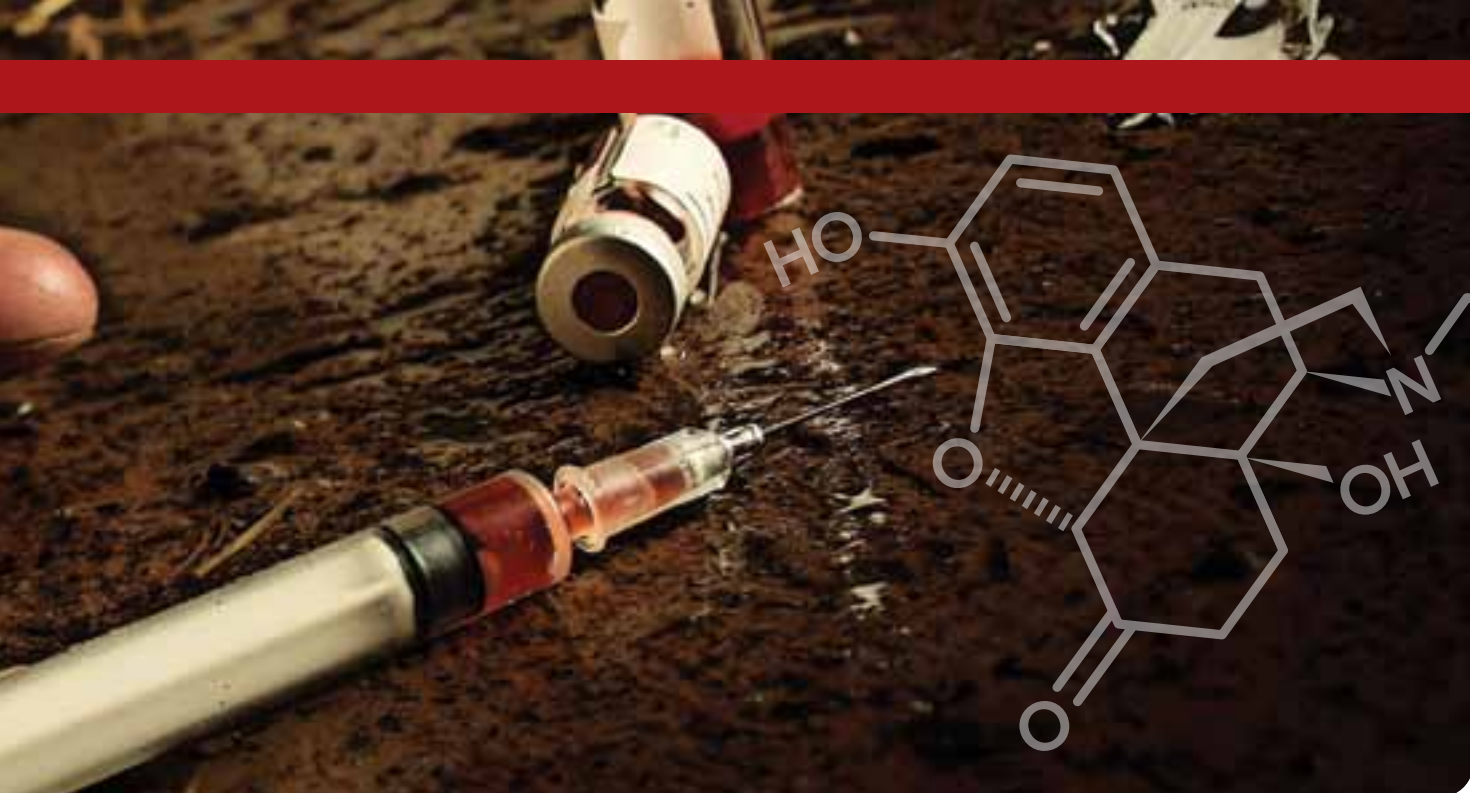
meaning it can only be prescribed by a doctor and then dispensed by a pharmacy – naloxone has been used to safely reverse the effects of opioid intoxication in hospital and pre-hospital (ambulance) emergency settings for decades.

Naloxone can be injected into veins or muscles. With the appropriate technology, it can also be administered via the nose. Trials among ambulance paramedics indicate no difference in effect between the different routes of administration (Kelly et al. 2005). This will also be tested later this year in a trial of intranasal and intramuscular naloxone at Sydney's Medically Supervised Injecting Centre (MSIC). MSIC Medical Director Dr Marianne Jauncey notes the unique capacity the service has to conduct such research under controlled conditions, and is optimistic that the trial results will add to the momentum behind calls for increased naloxone availability. She notes emphatically, 'It is an absolute disgrace that Australia hasn't introduced controlled naloxone distribution – we are seriously lagging behind in this area!'

Calls for wider naloxone distribution

In the face of increasingly high rates of heroin overdose throughout the 1990s, Australian experts began to call for trials of wider naloxone distribution. The logic was that witnesses such as heroin-using peers or family members could save lives by administering naloxone to reverse an overdose before an ambulance arrived. The momentum behind the proposal waned substantially following the 2001 heroin shortage and the associated decline in overdose rates. For Professor Simon Lenton, Joint Deputy Director

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of Perth's National Drug Research Institute (NDRI) and a longstanding advocate of wider naloxone distribution, the time to reinvigorate the debate is now. 'The fact that overdose rates are currently lower than in the past is no excuse for complacency', he argues. 'We can't wait for the next "glut" in heroin availability and the inevitable spike in overdose rates to consider improving the range of interventions that prevent people dying. Australian drug policy is characterised by a willingness to respond innovatively to reduce harm. Look at the bold pragmatism that led to our early uptake of needle and syringe programs. We need that courageous leadership in the case of naloxone distribution.'

Barriers to wider naloxone distribution

Medico-legal complexities are the major barrier to increasing naloxone distribution, particularly if the proposal involves the provision of a drug for administration to a third party. Patients are not generally prescribed medication to administer to someone else. The prescriber may be concerned that they and/or the lay person who administers naloxone may be sued if the recipient does not recover or acquires a brain injury. However, where naloxone is prescribed to the person to whom it will be administered by a trained companion, these legal concerns no longer apply. Precedents for prescription of medications intended for peer administration have been established, including adrenaline injections for those at risk of anaphylaxis, and glucagon injections for severe insulin reactions among diabetics. In comparison to these drugs, naloxone is relatively safe with fewer associated risks. Early medical literature investigating the effects of naloxone administered in emergency departments and by paramedics indicated that cardiac complications such as seizures and arrhythmias could occur, but extremely rarely, and generally only among people with pre-existing heart conditions. These early reports may also contribute to the reluctance of many doctors to prescribe naloxone for administration by non-medical personnel.

Countering concerns

Lenton and Hargreaves (2000) canvassed the concerns around wider naloxone distribution, posing the following counter-arguments:

- Some users might engage in **riskier opioid use** if naloxone is available. This seems unlikely considering the unpleasant effect of naloxone in precipitating withdrawal among dependent opioid users.
- **Polydrug use**, particularly alcohol and benzodiazepines, is common in overdoses involving heroin. This should not preclude naloxone use. Reversal of the opioid effect could prevent fatalities, minimise associated morbidity, and provide time in which to administer other interventions.
- **Intoxicated administration:** the overdose witness who administers naloxone may often themselves be intoxicated. However, this is likely regardless of which intervention they attempt, and naloxone administration is no more complex than the ideal first responses of calling an ambulance and administering rescue breathing.
- Naloxone's **shelf life** is 18–24 months. A trial would determine whether users replace expired stock.
- Naloxone's **half life** is about 30–90 minutes, raising the possibility that re-sedation may occur, particularly when longer-acting opioids such as methadone have been used, or additional drugs are consumed following naloxone administration. Administration of subsequent doses of naloxone may be necessary, although emergency medicine experience suggests this is rare.
- **Solitary heroin users:** using heroin alone is a risk factor for overdose, as is allowing other users to 'sleep off' their intoxication. Naloxone could not impact on the death rate among solitary users. The dangers of solitary drug use and failing to monitor sleeping drug users must be addressed in educational programs around overdose and use of naloxone.

'IT IS AN ABSOLUTE DISGRACE THAT AUSTRALIA HASN'T INTRODUCED CONTROLLED NALOXONE DISTRIBUTION – WE ARE SERIOUSLY LAGGING BEHIND IN THIS AREA!'

- The primary concern is around the potential of naloxone to **undermine other overdose strategies**, particularly calling an ambulance. Some evidence backs the legitimacy of this possibility. Lenton and Hargreaves (2000) emphasise that naloxone must be considered an additional intervention, rather than an alternative, to those already used. Distribution programs must be accompanied by comprehensive educational programs which stress that naloxone is just one part of an effective emergency response to opioid overdose, which also includes calling an ambulance and rescue breathing.
- Likewise, in response to more recent concerns that naloxone might compromise entry into opioid substitution therapy, Simon Lenton willingly acknowledges that education programs accompanying naloxone distribution must emphasise that engagement in treatment offers the single most effective protection against overdose. 'Education must make clear that naloxone is an intervention to be used as well as, not instead of, our current strategies,' he says.

Evidence accumulates

Generally, controlled trials are considered 'gold standard' evidence demonstrating the impact of medical innovations. This recognition underlay the calls in the late 1990s for trials of naloxone distribution. However, randomised controlled trials are less feasible with many public health interventions, including some in the alcohol and other drugs field such as needle syringe programs. Furthermore, since 2000, many countries have implemented state-sanctioned distribution programs in the absence of such trials, including Canada, Germany, Russia, Spain, Norway, China, Vietnam, the UK and parts of the US. Evidence arising from this program implementation demonstrates that:

- opioid users, peers, family members and outreach workers can be trained to recognise signs of overdose and appropriately administer naloxone
- very few adverse outcomes have been reported
- naloxone programs can facilitate outreach, empower users and increase willingness to seek treatment
- most concerns about the intervention – including the possibility of unsafe naloxone administration, re-intoxication or riskier drug use – appear to have been unfounded
- naloxone is safely administered through many programs operating under a range of models, and has helped save many lives (Lenton et al. 2009).

For Simon Lenton and others, this extensive implementation evidence means that the need for a controlled trial has now past, and Australia should instead move straight to establishing distribution programs. He once again points persuasively to the needle syringe program (NSP) analogy. 'The foresight that saw the introduction and scaling up

of NSPs in Australia before rigorous evidence of their effectiveness from controlled trials was available is the approach we need with naloxone. In fact there still isn't a randomised controlled trial demonstrating that NSPs work, yet nobody doubts that they do. International evidence clearly indicates that naloxone is a safe and effective intervention. It astounds me that we are lagging so far behind in international terms in implementing it.'

What do consumers think?

Surveys of people who use heroin consistently demonstrate their positive attitudes towards naloxone distribution. High proportions of samples in Australia, the UK and the US report that they would administer naloxone to an overdose victim, accept naloxone treatment from a peer, carry it with them if trained in its use, and that they would have administered it to the victim of their last witnessed overdose if it was available. They also report high rates of willingness to undertake training in overdose prevention and naloxone administration. Reasons include beliefs that peer naloxone distribution may reduce morbidity and mortality by reducing delays to treatment, preservation of ambulance services for other medical emergencies, avoidance of authority involvement, improved response to overdose with resuscitation training, empowerment of people who use heroin to help others, and reduction of the longstanding physical and psychological impact of personal and witnessed overdose (Kerr et al. 2008).



Moving forward: Models for the wider distribution of naloxone

International evidence indicates that distribution of naloxone to potential opioid overdose witnesses saves lives, in the absence of the adverse outcomes many once feared might eventuate. People who use drugs generally hold positive attitudes towards the idea and express a willingness to undertake training. Yet the drug is still scheduled only for use by medical personnel or requiring a prescription from doctors who may be hesitant to provide one.

What, then, are the options for Australian policy makers?

RESCHEDULING

Naloxone is an S4 drug, meaning it must be prescribed by a doctor and dispensed by a pharmacy. Professor Simon Lenton suggests that ideally, naloxone should be rescheduled to S3 so that it could be sold over the counter, as has been the case in Italy for more than two decades.

Naloxone is no longer under patent, meaning there is little financial incentive for a pharmaceutical company to pursue rescheduling, but rescheduling could still occur under provisions which allow state health authorities, professional associations or the National Drugs and Poisons Schedule Committee to initiate the process.

OTHER STRATEGIES

While calling for key stakeholders to support rescheduling initiatives, Lenton argues that other less complex and protracted methods of increasing naloxone availability should be implemented in the meantime. 'Whether or not we reschedule naloxone, there is a case for its distribution for non-medical administration as part of overdose prevention training to frontline workers such as NSP and outreach staff. It should also be made available to groups known to be at highest risk of overdose due to reduced tolerance. These include newly released prisoners and people leaving abstinence-oriented treatment programs.' Indeed, the British Government is currently considering the proposal put by their Advisory Council on the Misuse of Drugs in April 2011 to provide prison inmates with naloxone on their release.

Two important strategies would increase access to naloxone while rescheduling initiatives are considered. The first is the enactment in all Australian states and territories of 'Good Samaritan' legislation to legally protect laypeople using naloxone in emergency situations, making them exempt from civil liability regardless of the outcome. Such laws exist in the UK and in some parts of the US (Lenton et al. 2009).

Indeed, Good Samaritan laws now operate in many Australian jurisdictions, although some of these (e.g. NSW and the ACT) require amendment as they expressly exclude persons who are affected by a mind-altering substance.

The second strategy is the establishment of prescription programs similar to those implemented internationally, under which people who use heroin are provided with a prescription for naloxone by a doctor (and under some models, a nurse), along with comprehensive training in the prevention, recognition and management of overdose, as well as in naloxone administration and follow-up care for the drug use and potential overdose witnesses such as their peers, families and/or outreach workers. These programs, with their many years of combined experience, provide Australia with a range of models to choose from. Lenton believes that, following 12–18 months of the monitoring and evaluation of such programs in Australia, the resulting evidence of the efficacy and safety of naloxone distribution in our own setting will support moves towards the ultimate goal of rescheduling.

ACT LEADS THE WAY

Progress towards such a program is well underway in the ACT. Following strong advocacy by the Canberra Alliance for Harm Minimisation and Advocacy (CAHMA), Anex and other influential stakeholders, the ACT Health Minister made public statements supportive of the provision of naloxone to opioid users. The ENAACT (Expanding Naloxone Availability in the ACT) Committee includes representatives of CAHMA, the Alcohol Tobacco and Other Drug Association ACT, ACT Health, the ACT Division of GPS, the ACT Ambulance Service, the Pharmacy Guild, Family Drug Support and researchers from the Burnet Institute and the National Drug Research Institute, along with other stakeholders. It aims to provide expert guidance and support to stakeholders to develop a program of expanded naloxone availability in the ACT.

ENAACT has commenced designing a distribution program that will involve the roll-out to 200 people who use opioids of a naloxone prescription and delivery through NSP workers of associated education and training programs around overdose and naloxone administration. Evaluation and communication strategies are also being planned.

For Simon Lenton, such progress ensures that the question of wider distribution of naloxone in Australia has finally become one of when, rather than if.

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