

EDITORIALS

Take-home emergency naloxone to prevent deaths from heroin overdose

Time to save lives

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A paradigm shift is occurring in the treatment of heroin overdose. On 5 November the World Health Organization launched guidelines on the community management of heroin and opioid overdose and emergency administration of naloxone by people who are not medically trained.¹ Historically, naloxone has been used only in hospitals and by ambulance workers to reverse the effects of an opioid overdose. Today, several countries are providing emergency naloxone to patients, their families, and other potential non-medical first responders.

This is important because these overdoses contribute substantially to drug related deaths worldwide, with an estimated 69 000 people dying from opioid overdose each year.¹ Of nearly 3000 drug related deaths registered in England and Wales in 2013, more than half (56%) involved opioids.² Last month Scotland (the first country to introduce a national programme to provide naloxone) released results from the first three years of its naloxone programme.³ The proportion of deaths from opioid overdose among people just released from prison (a particularly high risk group) was down substantially from 9.8% (193/1970) in 2006-10 to 6.3% (76/1212) during 2011-13.⁴

Providing emergency naloxone to take home was first seriously mooted in 1996.⁵ Since then policy and practice implications have been explored, with studies of acceptability and feasibility, reports of implementation, and observational studies on the training of staff (medical, nursing and drug workers), at risk populations, family members, and non-medical personnel such as hostel workers and police officers (see web appendix for references). Several countries have clarified that members of the general public may lawfully administer an injection of naloxone for the purpose of saving life.⁶ About 10% of dispensed naloxone is used at overdoses (sometimes for the person prescribed the drug but mostly for someone else), and reports of lives saved are plentiful. However, research on its impact on the number of deaths from overdose is scarce.

In 2012, a United Nations resolution identified the need for more effective prevention of drug overdose, including the use of naloxone.⁷ The same year, the first large scale randomised trial of take-home naloxone (N-ALIVE) started its pilot phase, providing naloxone to former heroin injecting prisoners on their release (1500 released prisoners had been randomised by October 2014).⁸

The new WHO guidelines recommend training first responders in critical interim management of an opioid overdose, including intramuscular injection of naloxone. Importantly, these guidelines are for non-medical as well as medical first responders. They cover the risk of overdose among people working towards recovery in drug-free programmes, people released from prison, and those taking opiate substitutes (such as methadone or buprenorphine) as well as among people out of contact with treatment services.

Schemes to make naloxone available are being implemented around the world. Scotland's national take-home naloxone programme began in 2011, and Wales's scheme started the same year. City and state schemes have recently started in parts of north America, Europe, and Australia. Various countries have clarified the legal status of resuscitation actions by members of the public, including administration of naloxone, with the intention of saving life.⁶

Naloxone's potential for harm must also be considered, even though mild in comparison with the risk of imminent death. No deaths occurred in the 12 hours after naloxone resuscitation among 998 heroin users in San Diego who discharged themselves against advice from ambulance care,⁹ although three deaths in Copenhagen were probably attributable to post-discharge rebound overdose toxicity in a study of 2241 people with opioid overdose who had recovered with naloxone

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Extra references supplied by the author (see <http://www.bmj.com/content/349/bmj.g6580?tab=related#datasupp>)

and were then discharged at the scene.¹⁰ Anecdotally, no increase has been observed in the level of risk taking.

What is the correct naloxone dose for a non-medical first responder to give? Disappointingly this is still unclear and doses given vary greatly: the guiding principle should be, “as little as possible, as much as necessary.” Intramuscular and subcutaneous routes are effective (as well as intravenous) and possibly preferred because the onset of effect is less abrupt.¹¹ Exploratory work with intranasal naloxone is under way.

How should this innovative approach be taken forward? Settings in which people are known to be at high risk (probation hostels; homeless shelters) need naloxone. Critical periods of time (after prison, detoxification, residential rehabilitation, and hospital discharge) need specific attention. Naloxone also needs to be available to families and peers, hostel staff, police officers, and firefighters (both emergency services are already authorised in parts of the US). In addition, all ambulance and drug agency staff need to have naloxone to hand for emergency use. Regulations need to allow naloxone to be available without prescription as part of drug treatment (as with water for injection) or possibly as an over the counter medication. Any patient known to be at risk of death from overdose of heroin or another opioid should carry emergency naloxone, especially at times when contact with treatment or care is associated with transient increased risk—for example, at start and conclusion of opioid substitution treatment, on release from prison, on discharge from hospital or residential care, or on drop out from any of these treatments.¹²⁻¹⁴

Research is still needed to test the extent to which this intervention actually reduces deaths. This poses challenges for study design, not least because the key outcome being measured is a relatively rare event; however, more rigorous scientific studies are now appearing, including time series analyses, cost effectiveness analyses, and randomised controlled trials. The naloxone products also need improvement (for example, as a prefilled syringe containing the correct dose with stake needle). Other possible routes of administration (such as nasal) need development and validation.

These further studies need to be done alongside investigations into optimal dose, comparative routes of administration, and exploration of better mechanisms for wider use of naloxone. These studies are vital, but they must not delay implementation. While we dither, people continue to die from overdose.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare the following interests: JS and PD participated in the WHO guidelines development group. JS and SMB are co-investigators on the N-ALIVE prison release naloxone trial and are on its trial steering and data monitoring committee. JS has received research funding from, and provided consultancy to, drug companies concerning medicinal products potentially applicable in the treatment

of addictions and related complications; this has included arguing for the development of more suitable formulations of naloxone. JS has also conducted research into the potential intervention opportunity of take-home naloxone and has written editorials and commentaries calling for serious consideration of this approach. SB holds GSK shares, has led record linkage work on quantifying drugs related deaths soon after release from prison and after hospital discharge, proposed randomised evaluation of the effectiveness of naloxone for reducing drugs related deaths soon after release from prison, and received an honorarium for a plenary lecture on naloxone. SB serves on Scotland's National Naloxone Advisory Group and was a named, funded statistical consultant on a non-fatal overdose grant for the University of Glamorgan. PD has received an untied educational grant from Reckitt Benckiser related to the postmarketing surveillance of Suboxone (buprenorphine/naloxone) in Australia; he is also the lead evaluator of the Implementing Expanded Naloxone Access in the ACT program in Canberra, Australia. ATMCL is a board member of Reckitt Benckiser and the non-profit treatment provider Hazelden-Betty Ford. He has received a one year unrestricted educational grant from Reckitt Benckiser to provide public education on translation of research into practice.

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