Take home naloxone in Australia: Past, present and future

Simon Lenton  NDRI
Paul Dietze Burnet
Reminder: heroin-related overdose
(From Darke & Hall, 2003)

- Older, experienced users most at risk
- Being in drug treatment, particularly opioid substitution, is protective
- ODs overwhelmingly involve poly drugs (esp. benzos & alcohol)
- Voluntary (Rx) or enforced (custody) abstinence → ↓ tolerance & ↑ risk
- Deliberate OD is unusual, overwhelmingly most accidental
- In 60% of fatalities person not alone
- There is time to intervene: Over half of fatalities survive for >20-30mins (Darke & Duflou, 2016)
- For every fatal overdose there are 20-30 non-fatal overdoses
- Significant, often permanent effects of non-fatal overdose include:
  - brain damage due to lack of oxygen (hypoxia) (3 – 5 minutes)
  - lung damage or pneumonia from vomit or fluid entering the lungs
  - muscle damage (rhabdomyolysis) due to long periods of unconsciousness
  - serious injury from falling

(Australian Red Cross, 2006; Kerr Dietze, Kelly, 2008)
Reminder: Reducing risk
Evidence-based strategies (Darke & Hall, 2003)

- Increase access and engagement in treatment esp. opioid substitution
- OD prevention protocols for treatment discharge and prison release
- Educating users re OD prevention including:
  - risk of poly drug use (esp. benzos & alcohol)
  - reduction of tolerance following abstinence (esp. Rx & prison)
  - Not using alone
  - Small taste first
- Training in OD management including:
  - Signs of overdose & importance of not leaving them to “sleep it off”
  - Encouragement to call ambulance early
  - BLS and airway management
  - Naloxone for peer administration
- Protocols between police, ambulance, drug user orgs re reducing routine police attendance at OD. (McGregor et al, 2001)
What is naloxone?

- Naloxone Hydrochloride or Narcan® reverses the acute effects of opioids notably the respiratory depression of OD
- Over 4 decades of use in emergency medicine
- In this context shown to be safe, reliable and effective
- Key response to opioid overdose in hospitals and ambulance services
- Has no other effects. Does not produce intoxication
- Can be administered IV, IM, IN
- 2014 WHO endorsed making naloxone available to people likely to witness an overdose
- In Australia it has been a prescription only medication (S4), but after TGA rescheduling in March 2016 it can now also be purchased over-the-counter in pharmacies (S3) [dual listing]
Key Naloxone Literature to date

- Since the mid 1990s calls to make naloxone available to potential overdose witnesses through Take-home Naloxone (THN) programs (e.g. Darke & Hall, 1997; Strang, Darke, Hall, Farrell, & Ali, 1996)
- Beyond question that at a biological level naloxone can reverse the effects of opioid overdose
- Strong evidence that naloxone can be used safely by trained non-medical peers with many thousands of such overdose reversals having been reported (e.g. Mueller, Walley, et al, 2015)
- Suggestive observational evidence that THN programs can significantly decrease overdose death rates at a community level with decreases in overdose death rates coincident on program implementation
- Walley et al (2013) find a significant difference in death rates between cities and towns where THN programs have, or have not been implemented
- Cost-effectiveness: Naloxone distribution to heroin users is likely to reduce overdose deaths, would increase QALYs and be highly cost effective, even under markedly conservative assumptions (Coffin & Sullivan, 2013)
Key Naloxone Literature to date

- Training family members in overdose management and naloxone administration (Williams, Marsden & Strang et al, 2014, Bagley et al., 2015)
- 2014 endorsement of expansion of THN programs by WHO
- Naloxone distribution through syringe service programmes is cost-effective compared with syringe distribution alone. (Uyei et al., 2017)
- The feasibility of THN in the context of release from a correctional setting has been established, but there is a need for rigorous research into health outcomes and program implementation. (Horton et al., 2017)
- The emergence of illicit markets including increased use of prescription opioids and synthetic opioids in particular (e.g., fentanyl derivatives) has posed challenges for THN naloxone programs (Fairbain, Coffin & Walley 2017)
OPIOID USE AND OVERDOSE TREND DATA IN AUSTRALIA
NDSHS recent use of heroin and misuse of prescription opioids

Percent use last 12 m

- Heroin
- Pain-killers/analgesics and opioids (excludes OTC)

IDRS Data

Figure B6: Recent use of morphine, oxycodone, fentanyl and benzodiazepines, nationally, 2000–2016

Source: IDRS participant interviews.
* Data collection started in 2001 for morphine, 2005 for oxycodone and 2013 for fentanyl.
Self report heroin purity IDRS respondents

Source: IDRS participant interviews.
Note: The response 'Don't know' was excluded from analysis.
Figure 56: The prevalence of heroin overdose among participants, 2000–2016

Source: IDRS participant interviews.
* Among those who had ‘ever’ overdosed on heroin.
Note: Data may differ to previous national and jurisdictional reports due to the method of data analysis.
Number of accidental deaths due to opioids among those aged 15-54 years, Australia, 1988-2012

(Roxburgh & Breen, 2017)
Rate Opioid-related deaths Australia

Rate per 100,000 pop. of accidental deaths due to opioids among those aged 15-54 years, Australia, WA, 1988-2013

(From Roxburgh & Breen, 2017)
Rate Opioid-related deaths by drug type
Australia 2001-2013

(Roxburgh, Hall, Dobbins, et al., 2017)
Rate Opioid-related deaths and grams prescribed Australia

(Roxburgh, Hall, Dobbins, et al., 2017)
Rate Opioid-related deaths  Australia

Rate of accidental deaths due to opioids per million persons by 10 year age group, Australia 1988-2013

(Roxburgh & Breen, 2017)
Australian Naloxone developments

Working together: Expanding the availability of naloxone for peer administration to prevent opioid overdose deaths in the Australian Capital Territory and beyond

SIMON LENTON, PAUL BEEZER, ANNA OLSEN, NICOLE WISSING, DAVID McGRATH & CARRIE FORLIE

"National Drug Research Institute, Faculty of Health Sciences, Curtin University, Perth, Australia; "Centre for Population Health, School of Population Health, The University of Melbourne, Melbourne, Australia; "National Capital Authority, Department of Health & Disability Services, ACT Government, Canberra, Australia; "Australian Capital Territory Health and Hospitals, Health & Hospitals ACT Government, Canberra, Australia; and "National Drug Research Institute, Curtin University, Australia"

Abstract

Since the mid-1990s, there have been calls to make naloxone, a prescription-only medication in many countries, available over the counter in some form. Since the early 2000s, naloxone has developed as a form of administration. Numerous studies have found that naloxone provides a range of benefits, including increased healthcare access, reduced drug-related harms and improved treatment outcomes. In Australia, the government has made naloxone available over the counter for the treatment of opiate overdose deaths. Despite that, the availability of naloxone for over-the-counter administration has been limited in other jurisdictions. In this study, the authors describe the development of a new naloxone program in the Australian Capital Territory (ACT). Over the last 10 years, the program has expanded to cover all four ACT jurisdictions. The program is supported by the Australian Capital Territory government, and the researchers are currently exploring the potential for further expansion.

Introduction

Naloxone is an opioid antagonist drug that reverses the effects of heroin and other opioid drugs. It does not cause addiction. It has been used for over 40 years in emergency medicine and medication [1]. Naloxone in emergency settings is now covered under the Australian Capital Territory (ACT) Drug Act 1994, as a Schedule 5 drug and is currently available through a special arrangement with the Australian Capital Territory government.

In the mid-1990s, calls were made to make naloxone available to opioid users and their peers and families to prevent overdose deaths through "naloxone training programs." Such programs have been implemented in many countries, including the UK, the USA, Canada, Germany, and Australia. The programs are designed to improve the availability of naloxone for the treatment of opioid overdose deaths and to increase healthcare access and treatment outcomes.

In the Australian Capital Territory, the government launched the Naloxone Program in 2008, which provided naloxone to opioid users and their peers and families. The program was expanded in 2014 to include all four ACT jurisdictions. The program is supported by the Australian Capital Territory government, and the researchers are currently exploring the potential for further expansion.

Australia reschedules naloxone for opioid overdose

The Therapeutic Goods Administration (TGA) has rescheduled naloxone for the treatment of opioid overdose deaths. The TGA is a government agency responsible for regulating medicines and medical devices in Australia. The TGA's decision was based on the availability of naloxone for the treatment of opioid overdose deaths and the potential for further expansion.

The TGA decision was made after a review of the available evidence and consultation with stakeholders. The TGA considered the benefits of naloxone for the treatment of opioid overdose deaths, including increased healthcare access and treatment outcomes, and the potential for further expansion.

The TGA's decision has been welcomed by Australian health professionals and advocacy groups. The TGA's decision is an important step towards the availability of naloxone for the treatment of opioid overdose deaths and the prevention of overdose deaths.
Australian THN Programs


- NSW projects: commenced July 2012 with OPEN trial Kirketon Rd Centre and Langton Centre, service run, ongoing. Evaluation 83 followed up, 30 reversals (Chronister, Lintzeris, Jackson, et al. 2016). Now KRC, SESLHD, MSIC ISLHD. Across all NSW programs over 1000 trained and supplied THN, 175 anecdotal reversals reported.

- In November 2012 DASSA in SA commenced a prescription naloxone program in Adelaide which aimed to train and provide naloxone to 100 participants.
Australian THN Programs cont.


- In Jan 2013 THN Integrated into the Victorian Drug Strategy, with distribution commencing in August through collaborations between Harm Reduction Victoria & other agencies. 27 reversals among 99 followed up To June 2015. As at July 2017 HRV reported 1072 trained & provided THN + approx. 400 workers trained. Approx. 143 additional reversals reported.

- Jan 2014 Small trial started in Qld via N. Metro Hospital & Health Service. Now NSP staff + opportunistic BI. To date 50+ participants trained & supplied THN. Some 5 Reversals.

- Across evaluations in Australia we have some 358 participants trained and formally followed up with 142 (40%) reversals using THN reported. There are over 2500 additional trainings & provision to PWID with 359 anecdotal reports of reversals.
National Naloxone Reference Group

• Auspiced by the Burnet’s Centre for Research Excellence into Injecting Drug Use (CREDIU)
• Grew out of people involved in early programs following I-ENAACT.
• Now includes reps from 5 jurisdictions which have THN
• Multidisciplinary including drug user group representatives
• Share program information, program materials, and evaluation materials and generally support each other.
• Co-ordinate and advocate (e.g. supporting rescheduling, new product availability such as prenoxad)
Knowledge of Naloxone & THN programs

Data were obtained from cross-sectional surveys of a total of 2088 Aust. PWID conducted annually as part of the Illicit Drug Reporting System from 2013-2015. Specific questions about THN added to the survey in 2013.

Naloxone training evaluation

Does take-home naloxone training implemented in Australia improve knowledge about overdose and overdose response?

Four sites:
- Sydney (OPEN, n=67)
- Canberra (I-ENAACT, n=183)
- Melbourne (DOPE, n=280)
- Perth (WAPNP, n=153)

Group-based training of varied length on overdose:
- Knowledge
- Response
- Naloxone and its use

Pre-post questionnaires using modified OOKS and OOAS

Common items available for OOKS domains analysed:
- Risks for overdose
- Signs of overdose
- Responses to overdose

**Figure 1:** Pre-post changes in available risks (a), signs (b), actions (c) and overall (d) items adapted from the OOKS, by program city.

1a: OOKS Risks mean pre and post training by location

1b: OOKS signs pre and post training by location

1c: OOKS actions pre and post training by location

1d: Overall OOKS scores pre and post training by location
Summary

• High levels of knowledge prior to training
• Increase in correct answers after training
• No substantial differences between sites (despite program differences)
• Largest gains in knowledge observed in overdose signs and actions including naloxone – possible focus for training?

A changing landscape

THN programs in Australia have been affected by:

- Feb 2016 naloxone became available OTC after successful rescheduling application (dual listing)
- March 2016 UCB Australia notified that ceasing to provide Naloxone 400mcg Minijet®
- Depending on supply programs reverted to ampoules
- November 2016 Martindale Prenoxad product granted temporary supply approval by TGA after advocacy by NNRG members
- Fit for purpose 2mg (5 x 0.4mg markings), needles, instructions, disposal container
- April 2017 Prenoxad listed under PBS capping max price at $38.80 (vs $73.52) and provided for approx. $6 to concession card holders.
- Prenoxad can be prescribed by nurse practitioner as well as physician
Scale-up issues

(i) OTC availability important but hasn’t solved issues for community programs reaching marginalised opioid users

(ii) Naloxone for Intranasal administration

(iii) Provision for workers

(iii) Evolving opioid market - Lessons from the North American experience
Scale-up issues cont.

(i) Facilitating provision through community services (NSP’s etc).

In both UK and US states legislative or regulatory changes have been taken to allow approved program trainers, who are not licensed medical personnel, to dispense naloxone rescue kits to participants who have successfully completed brief training.

We now have an Australian example:

- Lintzeris et al, have received Approval from NSW Health for a ‘credentialed health worker’ to supply the Schedule 3 product Naloxone for injection for the purposes of the **NSW Health Overdose Response and Take Home Naloxone Project**
  - ‘credentialed health worker’ can be a registered nurse or allied health worker (could be NSP staff) who have completed prescribed training.
  - Plan is to apply to expand beyond the scope of the trial in NSW and
  - Protocol has been shared with other jurisdictions as a model which could be modified and adopted.
(iv) Provision for workers.

- There is an obvious case for providing training and naloxone to those who are likely to witness overdoses as part of their employment.

- These include: peer outreach workers, needle exchange staff, drug treatment workers, staff at shelters and other emergency accommodation services, police and other emergency services workers, etc.

- Particularly now that naloxone is available as scheduled 3 (OTC) medicine and IM injection practice associated with the use of an adrenaline auto-injector has been adopted as part of First AID training courses in this country.

- A mechanism for supplying naloxone to workers needs to be identified.
Intranasal naloxone

- We still don’t have an approved IN product in Australia
- Until recently, most THN products used Mucosal Atomizer Devices (MAD) with existing preparations
- Adaptpharma developed and licensed a 4mg product (equivalent to 2mg IM, from their PK data) in the USA
  - 2mg version licensed in Canada
  - No plans for Australia
- Competitor product Nyxoid by Mundipharma (1.8mg in 0.1ml) just now approved in EU
  - Exploration of Australian market underway
- Don’t know how these preparations work in real-world settings!
(iii) N. American experience - prescription opioids

From Fairbairn, Coffin & Walley, 2017

- The rise in opioid prescribing in the US from early 2000s resulted in 4 fold increase in opioid overdoses in 10yrs
- Reformulation of oxycodone to make it harder to inject slowed the rise in deaths
- ‘Epidemic’ saw increased support for prescription monitoring programs and expansion of THN programs
- Examples of THN reducing OD rates in locations where prescription opioid misuse was prevalent (e.g. Project Lazarus 70% reduction in 2009-2010)
- Naloxone co-prescribing found acceptable and effective with reductions in ED visits for opioid related overdose events (Behar et al, 2016; Coffin et al., 2016)
- Co-prescribing of naloxone encouraged for chronic pain patients (2016)
N. American experience - fentanyl and other synthetic opioids
From Fairbairn, Coffin & Walley, 2017

- With the changes in prescription opioid access & formulations, heroin OD rates rapidly tripled
- Emergence of synthetic opioids in traditional heroin and prescription opioid markets have posed new challenges for naloxone-based interventions
- Fentanyl 40x more potent than heroin, relatively easy to manufacture and is thus attractive to those involved illicit drug importation & distribution
- It is rapid acting and has a duration of action of only 30-60 mins as opposed to 4-5 hours for heroin
- Fentanyl tainted “street heroin” largely impacted locations in N. America with white powder heroin market
- In some regions accounting for majority of opioid overdoses, e.g. 74% of deaths in Massachusetts in 2016 and similar in BC (see over)
- Counterfeit pills (e.g. oxycodone) containing fentanyl have added to market confusion (issue for naive consumption + longer onset & action if taken orally)
- Authorities struggling to adapt OENDs and SIFs to this new landscape
N. American experience - fentanyl and other synthetic opioids
From Fairbairn, Coffin & Walley, 2017

- Implications for Naloxone programs:
  - Erratic drug supply – presence of fentanyl in street heroin produces rapid variations in potency
  - 15+ analogues of fentanyl. One, Carfentanyl is 100 times more potent than fentanyl. It has been found in urine drug screens in Canada

- Even where fentanyl is in the illicit heroin market THN programs have proved helpful (Somerville et al, 2017):
  - User ed. re rapid onset (within seconds or minutes)
  - small taste first
  - monitoring by others
  - not mixing with other CNS depressants
  - Multiple doses of naloxone being required
  - Need for OD prevention ed at any opportunity

- Dose
  - optimal dose ranges for Naloxone with fentanyl OD are not yet clear
  - But is likely to be larger (e.g. 2mg IM)
  - More research needed on optimal dose and delivery systems for synthetic ODs
Summary & conclusions

- We have 4 jurisdictions which have implemented and evaluated THN programs.
- These have been successful at changing knowledge and behavior and resulted in successful overdose reversals and lives saved.
- However they are small scale and needed in each state.
- We now have naloxone available OTC.
- We have a model to provide THN direct to clients of community agencies which needs to be implemented in other jurisdictions.
- We hope to have a IN product available in Australia in next 18 months.
- We have a NNRG but no resourcing for it nationally.
- If we see continuing increases in synthetic opioid use this will pose challenges for overdose prevention and management including THN.