Pre-provision of naloxone to prevent heroin overdose deaths: evidence, myths and UK experience

Professor John Strang
National Addiction Centre, London, UK
Declaration (personal & institutional)

DH, NTA, Home Office, NACD, EMCDDA, WHO, UNODC, NIDA

NHS provider (community & in-patient); also Phoenix House, Lifeline, Clouds House, KCA (Kent Council on Addictions)

Reckitt-Benckiser, Schering-Plough, Genus-Britannia, Napp, Titan, Martindale, Catalent, Auralis, Lundbeck, Astra-Zeneca, Alkermes, UCB, Fidelity, Rusan, Mundipharma Europe, Lannacher, Lightlake & others, including trying to work with possible pharma-manufacturers

UKDPC (UK Drug Policy Commission), SSA (Society for the Study of Addiction); and two Masters degrees (taught MSc and IPAS)

Work also with several charities (and received support) including Action on Addiction, and also with J Paul Getty Charitable Trust (JPGT) and Pilgrim Trust
I’m a doctor, not a lawyer

I’m a doctor, working with my patients
Why does the take-home naloxone issue matter?

Overdose is the major cause of death among drug users – mainly opiates

Most heroin overdoses are witnessed

Most witnesses intervene actively (often wrongly)

Many family members witness overdose
Structure of today’s talk: take-away naloxone and overdose deaths

What is the problem?

When does it occur?

How could naloxone help?

Areas of confusion
Oxygen saturation: IV versus IM

![Graph showing oxygen saturation over time for IV and IM injections. The graph displays the percentage of oxygen saturation (SpO2) on the y-axis and minutes post-injection on the x-axis. The green line represents the IV route, while the yellow line represents the IM route. The graph shows a trend where the IV route maintains a higher oxygen saturation compared to the IM route throughout the observation period.](image-url)
Oxygen saturation: IV versus IM

![Graph showing oxygen saturation over time for IV and IM injections. The graph indicates that IV injection leads to a quicker and more stable oxygen saturation.]
Oxygen saturation: case study

Male, age 49
Intravenous diamorphine (6 years)
This dose = 120 mg
Daily dose = 400mg

Minutes post-injection
SpO2 (%)
WHICH DRUG?
# Drug use prevalence and Drug-related deaths: England & Wales 2011/12 (ONS)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Prevalence in general population (use in last year, age 16-59)</th>
<th>No. of deaths in 2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cannabis</td>
<td>6.9%</td>
<td></td>
</tr>
<tr>
<td>Cocaine</td>
<td>2.2%</td>
<td></td>
</tr>
<tr>
<td>Amphetamine</td>
<td>0.8%</td>
<td></td>
</tr>
<tr>
<td>Ecstasy</td>
<td>1.4%</td>
<td></td>
</tr>
<tr>
<td>Opiates (inc heroin &amp; methadone)</td>
<td>0.3%</td>
<td></td>
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<td>---------------------</td>
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</tr>
<tr>
<td>Cannabis</td>
<td>6.9%</td>
<td>7</td>
</tr>
<tr>
<td>Cocaine</td>
<td>2.2%</td>
<td>112</td>
</tr>
<tr>
<td>Amphetamine</td>
<td>0.8%</td>
<td>62</td>
</tr>
<tr>
<td>Ecstasy</td>
<td>1.4%</td>
<td>13</td>
</tr>
<tr>
<td>Opiates (inc heroin &amp; methadone)</td>
<td>0.3%</td>
<td>1,082</td>
</tr>
</tbody>
</table>
Conclusion number 1: Drugs involved with overdose

HEROIN

Heroin and sedative mixtures
HOW COMMON?
London PAI Study #2: 312 injectors

Personal overdose? - 117 (38%)
Witnessed overdose? - 157 (50%)
Witnessed fatal O/D? - 46 (15%)

(Strang, Griffiths, Powis, Fountain, Williamson and Gossop, Drug and Alcohol Review, 1999)
INTERVENTION OPPORTUNITY?

Sydney - 86% had witnessed O/D
Adelaide - 70% had witnessed O/D
London PAI injectors - 50%
(London treatment sample - 83/97%)
Conclusion number 2

Overdose is common hazard

Overdose frequently witnessed
Resusc training and naloxone?

opiates involved?

home context?

peers present?
### Naloxone? - personal O/D

<table>
<thead>
<tr>
<th>Last personal overdose...</th>
<th>Treatment sample (n=142)</th>
<th>Community sample (n=312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever overdosed?</td>
<td>78/142 (55%)</td>
<td>118/312 (38%)</td>
</tr>
<tr>
<td>- involved opiates</td>
<td>72/78 (92%)</td>
<td>102/118 (86%)</td>
</tr>
<tr>
<td>- at own or friends home</td>
<td></td>
<td></td>
</tr>
<tr>
<td>own home</td>
<td>61/78 (78%)</td>
<td>84/118 (80%)</td>
</tr>
<tr>
<td>friends home</td>
<td>43</td>
<td>52</td>
</tr>
<tr>
<td>18</td>
<td></td>
<td>42</td>
</tr>
<tr>
<td>- in company of others</td>
<td>66/78 (85%)</td>
<td>95/118 (81%)</td>
</tr>
<tr>
<td>sexual partner</td>
<td>33</td>
<td>32</td>
</tr>
<tr>
<td>close friends</td>
<td>27</td>
<td>57</td>
</tr>
</tbody>
</table>

(Strang, Powis, Best, Vingoe, Griffiths, Taylor, Welch and Gossop, Addiction, 1999)
### Naloxone? - witnessed O/D

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<th>Witnessing overdoses</th>
<th>Treatment sample (n=142)</th>
<th>Community sample (n=312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever witnessed overdose?</td>
<td>44/48* (92%)</td>
<td>167/312 (52%)</td>
</tr>
<tr>
<td>Witnessed O/D in last year?</td>
<td>13/48 (27%)</td>
<td>81/312 (26%)</td>
</tr>
<tr>
<td>Last overdose witnessed...</td>
<td></td>
<td></td>
</tr>
<tr>
<td>involved opiates</td>
<td>44/44 (100%)</td>
<td>153/159* (96%)</td>
</tr>
<tr>
<td>- O/D by sexual partner</td>
<td></td>
<td></td>
</tr>
<tr>
<td>close friend</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>casual acqu.</td>
<td>32</td>
<td>84</td>
</tr>
<tr>
<td>stranger</td>
<td>1</td>
<td>53</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>

* data collected from only 48
* data missing on 8 cases

(Strang, Powis, Best, Vingoe, Griffiths, Taylor, Welch and Gossop, Addiction 1999)
# Naloxone? - witnessed fatal O/D

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<th>Witnessing fatal overdoses</th>
<th>Treatment sample (n=142)</th>
<th>Community sample (n=312)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever witnessed overdose fatality?</td>
<td>14/48* (29%)</td>
<td>55/312 (18%)</td>
</tr>
<tr>
<td>Last fatal O/D witnessed...</td>
<td>14/14 (100%)</td>
<td>34/38* (89%)</td>
</tr>
<tr>
<td>-involved opiates</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>-death of sexual partner</td>
<td></td>
<td>33</td>
</tr>
<tr>
<td>close friend</td>
<td></td>
<td>15</td>
</tr>
<tr>
<td>casual acquaintance</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>stranger</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* data collected from only 48
** data missing on 8 cases
* data available from only 38 subjects

(Strang, Powis, Best, Vingoe, Griffiths, Taylor, Welch and Gossop, Addiction, 1999)
Conclusion number 3: O/D intervention opportunity?

- opiates involved? - YES
- home context? - YES
- peers present? - YES
Structure of today’s talk:
take-away naloxone and overdose deaths

What is the problem?

When does it occur?

How could naloxone help?

Areas of confusion
When in particular excess?

Post-detox and post-rehab

During methadone early treatment

* Prison release *
Risk of death during and after opiate substitution treatment in primary care: prospective observational study in UK General Practice Research Database

Rosie Cornish, statistician,¹ John Macleod, professor in clinical epidemiology and primary care,¹ John Strang, professor in the psychiatry of the addictions,² Peter Vickerman, senior lecturer in mathematical modelling,¹³ Matt Hickman, professor in public health and epidemiology¹

ABSTRACT

Objective To investigate the effect of opiate substitution treatment at the beginning and end of treatment and according to duration of treatment.

Design Prospective cohort study.

Setting UK General Practice Research Database.

The effect of opiate substitution treatment on mortality.
Risk of death during and after treatment

Mortality rate ratio compared to not on treatment

- On treatment (days 1-28)
- On treatment (remaining days)
- Off treatment (days 1-14)
- Off treatment (days 15-28)
- Off treatment

Cornish et al, *BMJ* 2010; 341: c5475
When in particular excess?

Post-detox/rehab

During methadone early treatment

Prison release
Prevalence of drug dependence

Drug dependence prior to prison

- **Opiates & stimulants**
- **Opiates only**
- **Stimulants only**
- **Cannabis only**

Substance Misuse in Prisoners 2002 Singleton N, Farrell M, Meltzer H ONS.
Acute risk of drug-related death among newly released prisoners in England and Wales

Michael Farrell & John Marsden
National Addiction Centre, Division of Psychological Medicine and Psychiatry, Institute of Psychiatry, King's College London, UK

ABSTRACT

Aims To investigate drug-related deaths among newly released prisoners in England and Wales. Design Database linkage study. Participants National sample of 48,771 male and female sentenced prisoners released during 1998–2000 with all recorded deaths included to November 2003. Findings There were 442 recorded deaths, of which 261 (59%) were drug-related. In the year following index release, the drug-related mortality rate was 5.2 per 1000 among men and 5.9 per 1000 among women. All-cause mortality in the first and second weeks following release for men was 37 and 26 deaths per 1000 per annum, respectively (95% of which were drug-related). There were 47 and 38 deaths per 1000 per annum, respectively, among women, all of which were drug-related. In the first year after prison release, there were 342 male deaths (45.8 were expected in the general population) and there were 100 female deaths (8.3 expected in the general population). Drug-related deaths were attributed mainly to substance use disorders and drug overdose. Coronial records cited the involvement of opioids in 95% of deaths, benzodiazepines in 20%, cocaine in 14%, and tricyclic antidepressants in 10%. Drug-related deaths among men were more likely to involve heroin.
Excess mortality ratio for different time periods post-release by cause of death (Singleton, Farrell, Marsden et al 2003)

Excess mortality ratio

Drug-related deaths
Not drug-related

Time since release (weeks)

Up to 1
1 up to 2
2 up to 4
4 up to 8
8 up to 13
13 up to 26
26 up to 52
>=52
Total

Excess mortality ratio

40
35
30
25
20
15
10
5
0
Structure of today’s talk:
*take-away naloxone and overdose deaths*

Where is the problem?

When does it occur?

How could naloxone help?

Areas of confusion
Pre-filled syringe
1 mg per ml, 2 ml syringe
available from: Antigen, Aurum, Mayne £6.30
First mooted:
JS - Keynote on Harm reduction - pushing at the envelope (Melbourne Harm Reduction conference, 1992) (and the linked Heather et al book)

First serious consideration:
First investigated:
Preventing opiate overdose fatalities with take-home naloxone: pre-launch study of possible impact and acceptability

JOHN STRANG, BEVERLY POWIS, DAVID BEST, LOUISA VINGOE, PAUL GRIFFITHS, COLIN TAYLOR, SARAH WELCH & MICHAEL GOSSOP
Why does the take-home naloxone issue matter?

Overdose is the major cause of death among drug users – mainly opiate

Most heroin overdoses are witnessed

Most witnesses intervene actively (often wrongly)

Many family members witness overdose
Training - scope

Training elements

(a) how to recognise overdose
(b) how to manage situation – general
(c) how to give naloxone
British Red Cross
Community Based First Aid Film
Interview Based Inspiration

How to Recognise Opiate Overdose

- Person unconscious, cannot be woken – UNROUSABLE

- CYANOSIS – BLUE lips or tongue

- Not breathing at all or breathing slowly – deep snoring.

- Pin point pupils
**Actions on Discovering Overdose**

A – Ambulance - CALL AMBULANCE

B- Breathing - Check Airway – clear if blocked, Check breathing.

C – reCovery - If breathing, place in recovery position – if not breathing, begin basic life support

Administer naloxone
How to inject Naloxone – intramuscular (into muscle)

Remove syringe from box and packet

Attach needle to syringe

Inject into the outer thigh, upper arm or outer part of buttock

Hold needle 90 degree above skin

Insert needle into muscle (needs pressure)

Slowly and Steadily push plunger all the way down

Put syringe back in box. Don’t cover needle
Target audience

Anyone with possibility/probability of being in the house with opiate user at time of overdose

(family member; (parent, partner, sib, son/daughter); flatmate etc)

n.b. not just those in treatment
Possible target populations (Training)

Non-medic drug workers
Key agency personnel
Patients
Carers
Wider clients (e.g. NSX, etc)
Users (i.e. not linked to patient status)

Strang, Kelleher et al, BMJ, 2006
Family carers and the prevention of heroin overdose deaths: Unmet training need and overlooked intervention opportunity of resuscitation training and supply of naloxone

JOHN STRANG, VICTORIA MANNING, SORAYA MAYET, EMILY TITHERINGTON, LIZ OFFOR, CLAUDIA SEMMLER, & ANNA WILLIAMS

National Addiction Centre (Institute of Psychiatry/The Maudsley), Denmark Hill, London, UK
Carers – the overlooked intervention workforce

102 carers attending 4 organisations

- 80% parents, 20% other relative/partner
- 96% of opiate users, 87% IDU, 57% in Tx,
- 1/3 used in presence of carer, 47% had past OD
- 20% of carers had witnessed an OD
- 5 had lost user to fatal OD (3 children 2 partners)
- 16% would ‘panic’ or ‘not know what to do’
- 83% expressed an interest OD management & N training

Evidence of potential to extend naloxone…
Does the naloxone ever get used?

Initial experience ……

Berlin/Jersey – about 10% used within a year
New Mexico, USA – 2/100 within few months
Chicago, USA – 52/550

Dettmer, Saunders and Strang, BMJ, 2001
Baca et al, BMJ, 2001
Bigg, BMJ, 2002
The MRC N-ALIVE Pilot Trial: NALoxone InVEstigation

N-ALIVE Chief Investigators

Prof. John Strang, Prof. Mahesh Parmar, Prof. Sheila Bird

N-ALIVE CTU Trial Team

Dr. Angela Meade, Laura Nichols, Lizzie Armstrong, Tracey Pepple

Funding and support: MRC with research support from MHRN.
N-ALIVE trial – pilot & main phase

N-ALIVE research trial to test/prove reduced deaths post-release

Pilot – current, ongoing (n=>500)
Main study – n=30,000 (15k + 15k)
Background

Heroin-related deaths account for 8% of all UK deaths in individuals aged 15-44 yrs.

One in 200 prisoners with history of heroin use by injection dies from a drugs-related death (DRD) within 2–4 weeks of leaving prison.

Current approaches have not prevented high rate of post-release overdose deaths.
Take-Home Emergency Naloxone to Prevent Heroin Overdose Deaths after Prison Release: Rationale and Practicalities for the N-ALIVE Randomized Trial

John Strang, Sheila M. Bird, and Mahesh K. B. Parmar

ABSTRACT The naloxone investigation (N-ALIVE) randomized trial commenced in the UK in May 2012, with the preliminary phase involving 5,600 prisoners on release. The trial is investigating whether heroin overdose deaths post-prison release can be prevented by prior provision of a take-home emergency supply of naloxone. Heroin contributes disproportionately to drug deaths through opiate-induced respiratory depression. Take-home emergency naloxone is a novel preventive measure for which there have been encouraging preliminary reports from community schemes. Overdoses are usually witnessed, and drug users themselves and also family members are a vast intervention workforce who are willing to intervene, but whose responses are currently suboptimal. The research questions the 1% rule with the common knowledge that it is often the time of change and end of society intervention.
Structure of today’s talk:
**take-away naloxone and overdose deaths**

Where is the problem?

When does it occur?

How could naloxone help?

Areas of confusion
Possible concerns

Short half-life - does naloxone last long enough?
What about date-expiry?
Safety net - might it increase risk-taking?
Might witnesses be less likely to call ambulance?
Are witnesses sufficiently skilled?
Will the naloxone be available?
Might family be afraid to give injection?
Next steps – ‘to do’ list

Improve naloxone (route, device, drug)

Extend to other populations
- Non-medical drug workers (health)
- High-risk population agency staff (hostels)
- Carers
- High risk clients (not in Tx, prison release hostels)

Implementation inertia – ‘Just do it’
Thank you