

The national and international  
evidence around DRD and naloxone

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# Acute Drug Related deaths

Problems with definitions however DRDs increasing

2-3% heroin users die each year

Death rates among opiate addicts: **20 times the norm** for their age and gender

Addicts released from prison in first two weeks: 29 times more likely to die (male) and 69 times higher (women)

Many countries (incl UK): OD leading cause of death among opioid addicts

50 % opioid users has experienced a non fatal OD at some point in their lives

# Deaths in context.....

**1974- 1992:** poisoning deaths in England & Wales involving heroin and methadone increased tenfold.

**1994-1998:** trend continued with an increase from **276 to 632** in Heroin/ morphine poisoning due to drug dependence

In **1999** reducing drug related deaths became a target within the National Drug Strategy

Advisory Council of the misuse of drugs (ACMD)

**Dec 1999**

'The prevention of drug related deaths not just topical but a matter of pressing urgency'

**2001** Department of Health Target: to reduce DRD by 20% by March 2004

For England the baseline figure was **1.480** drug related deaths  
Target: **1.184**

# Drug Related deaths: the trend

England	1999	2000	2001	2002	2003	2004	2007
Males	1,242	1,262	1,237	1,137	911	1,044	
Females	242	303	291	319	270	295	
<b>Totals</b>	<b>1,484</b>	<b>1,565</b>	<b>1,528</b>	<b>1,456</b>	<b>1,181</b>	<b>1,339</b>	<b>1,539</b>

	1999	2000	2001	2002	2003	2004	Percentage change from 1999 to 2004	
<b>Heroin and Morphine</b>	715	874	840	737	562	693	-3	
<b>Methadone</b>	286	226	199	205	167	194	-32	295
<b>Benzodiazepines</b>	217	190	207	224	195	186	-14	309
<b>Opiates (unspecified)</b>	141	163	154	132	80	106	-25	
<b>Dihydrocodeine</b>	114	98	107	95	77	73	-36	
<b>Cocaine</b>	85	76	86	131	107	139	64	239
<b>Amphetamines (excluding ecstasy)</b>	47	19	25	36	30	33	-30	
<b>MDMA/Ecstasy</b>	23	34	51	47	27	46	100	
<b>Barbiturates</b>	23	16	28	14	18	14	-39	
<b>Codeine</b>	22	27	31	29	31	49	123	

## Drug Related deaths: the trend

71% of all cases were due to opioids (heroin, morphine, methadone, opiates based analgesics) alone or in combination with other drugs

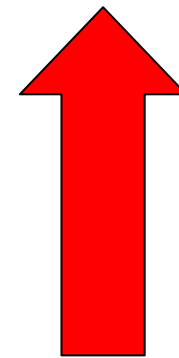
48% fatalities due to Heroin/ morphine alone or in combination with other drugs

Methadone: + 17% to 20% (n= 264 to 295)

Cocaine: + 11% to 16% (n= 174 to 239)

Hypnotics/ sedatives: + 17% to 21% (n= 259-309)

Alcohol combined with other substances: +34% to 38% ( n=525 – 554)



2007

# LEARNING POINTS

DRDs increasing trend

Government struggling to tackle the problem

Patterns being recognised in relation to

- Those involved
- Circumstances of OD
- Causes of death

# OD

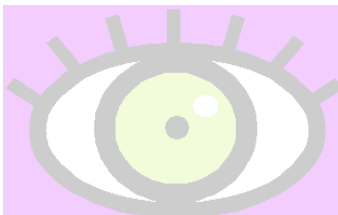
Most OD occur in a three hour period after initial drug intake



Instantaneous death is rare and usually attributable to an anaphylactic reaction



Mechanisms not clear: respiratory depression prime cause



# NON FATAL OPIOID OD

50 % opioid users has experienced a non fatal OD  
at some point in their lives

More than  $\frac{3}{4}$  of those who OD experienced at least one  
morbidity symptom

Sequelae are not rare and represent a public health burden

Pulmonary conditions: oedema and pneumonia

Muscular complications: rhabdomyolysis or crash syndrome

Renal failure from lysis of muscle tissue

Cardiovascular and cognitive problems also described

Physical injuries, burn and assault when unconscious

## OPIOID OD

### Individual risk factors

#### Injecting

bypasses safety mechanisms of adaptation to dose

#### Polydrug Misuse

In particular depressants such as **alcohol and benzodiazepines** tolerance develops to the heroin's impact on breathing but this does not happen with non opioids (survivable doses of heroin can become lethal)

**The more types of drugs used the greater the risk of OD**

Blood morphine and alcohol levels after heroin related deaths have been found to bear an inverse relationship

#### Quality & Quantity of heroin

Taking too much or changes in strength or purity

#### Comorbidity

Psychiatric problems in the form of depression / anxiety accompanied with suicidal thoughts

# OPIOID OD

## Individual risk factors

### What happens with treatment?

? Protective: being on methadone programme

#### Depending on the programme!

Optimisation of the dose: high dose that prevents 'top ups'

Supervised consumption vs. diversion

Relaxed regimes: most OD on methadone in people not being prescribed the drug

Risks increase if drop out of treatment

Drop out of treatment due to changes in tolerance

Ex. Detoxification

Those on methadone less likely to die from OD than premature leavers

'interruptions': ongoing injecting, polydrug misuse

When those patient re-enter treatment the risks are reduced

# OPIOID OD

## Individual risk factors

### Loss of tolerance

Tolerance to heroin's effects on breathing: takes time to develop  
Protection: wanes rapidly after break (2 + days) or reduced use

- **Unsettled lifestyle**
- **Purity variations**
- **Failed attempts to stop**
- **Recreational heroin injecting: irregularity**
- **Imprisonment:** discontinuation of programmes in prison and celebration on release (two weeks after discharge male prisoners 20 times more likely to die)

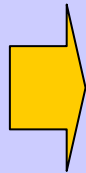
Tolerance: is partly a learned response cued by the environment  
in which the drug is usually taken  
Unfamiliar environment: tolerance lower, heightening the risk of OD  
(weak evidence as other factors cannot be excluded)

**THERE ARE TWO PHASES OF ACTIVITY – PREVENTION AND INTERVENTION**

# LEARNING POINTS

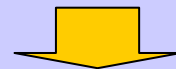
## OD: Predictable

- Polydrug misuse
- Injecting
- Low tolerance
- Out of treatment
- Use alone
- Comorbidity



Prevention is possible

Preventing an OD  
becoming a fatality



Combination of factors involved some  
of them susceptible  
for intervention

# Take Home Naloxone

## BACKGROUND

Most overdoses are:



- witnessed
- occur in residential dwellings
- preventable & users willing to intervene (if trained)



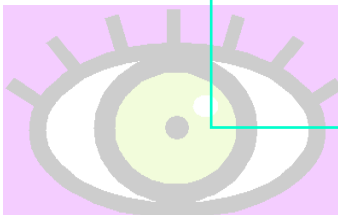
Strang et al 1996  
'Take home naloxone'

International background  
USA pilots



Naloxone: opioid antagonist

No adverse reports  
No abuse potential



# Naloxone



Pure opioid antagonist 'antidote to heroin'

Temporarily reverses effects of an opioid OD



No effect on OD resulting from the use of other drugs

Short acting: wears off quickly



OD can last for 8 hours or more (specially if methadone is involved)

Naloxone can begin to wear off in 20 mins



No potential for abuse

# Effects of Naloxone

- Short acting
- Blocks and reverses the effects of opiates:



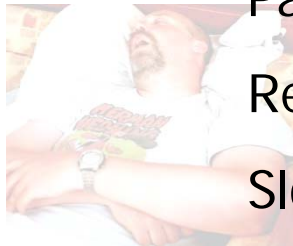
**OPIOIDS**



*Effect*

Stops withdrawals

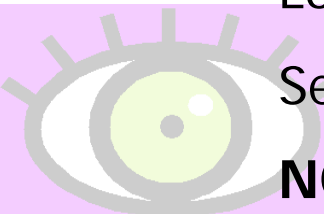
Pain relief



Reduces cough reflex

Slows breathing

Lowers blood pressure



Sedation/coma

**NO OPIATE**

**NALOXONE**



*Effect*

Withdrawals

Feel pain

Cough reflex

Increases breathing

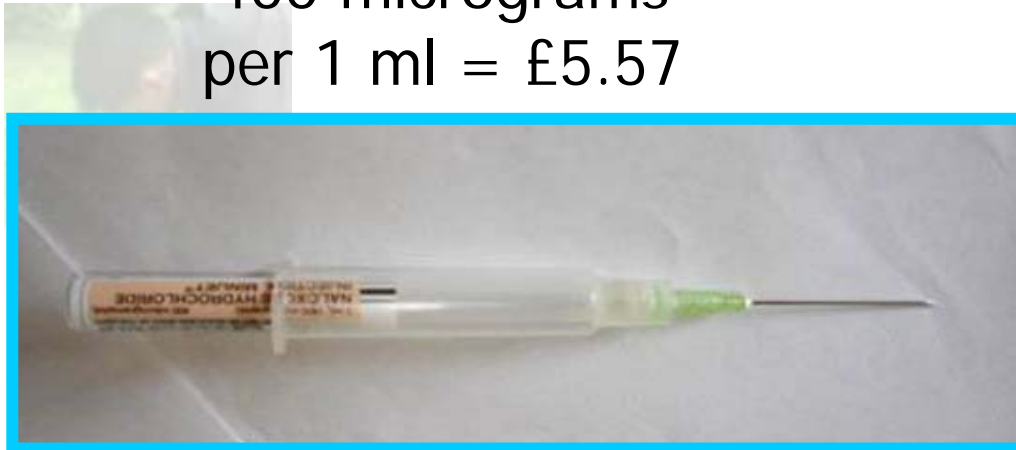
Raises blood pressure

Awake/responsive

**NO EFFECT**

# Mini-jet naloxone

400 micrograms  
per 1 ml = £5.57



To Put Together



Short Needle



Long Needle



Nasal Spray



## Advantages of 'take home' Naloxone

- Prevent opiate overdose death
- Safety
- Lack of abuse potential
- Now approved by MHRA as an emergency medication that can be given by anyone with the intention to save a life (June 2005).
- Relatively easy to administer (Intramuscular)



# Disadvantages of 'take home naloxone'

- Returning to overdose state
- Failure to seek medical attention
- Riskier / increased use due to a 'safety net'
- Needle stick injuries / BBV



## Take home naloxone trials

Study	No. Clients	No. Followed up	No. Client Uses / OD	Outcome
Berlin 1999	124	40 (32%) 16 months	29	No deaths Appropriate in 26/29
Jersey 1999	101	Not reported 16 months	5	No deaths No adverse
San Francisco 2005	24 (12 pairs)	24 (100%) 6 months	15/20	No Deaths No adverse
New York 2006	25	22 (88%) 3 months	10/17	No deaths 1 death (when not used)
<b>NAC England 2006</b>	239	186 (78%) 1-3 months	12/18	No adverse events with naloxone Appropriate Use 1 death – no naloxone
<b>Lanarkshire</b>	19	19 (100%) 2 & 6 months	2	No Deaths No Adverse events
<b>Glasgow 2007/08 (See SDF, 2008)</b>	216	Not reported	10	No Deaths No Adverse events

# Naloxone Projects and Evaluation Studies

**UK: John Strang  
NTA document + Paper in Addiction**

## **The naloxone programme: Investigation of the wider use of naloxone in the prevention of overdose deaths in pre-hospital care**

Commissioned by:

The National Treatment Agency for Substance Misuse

**RESEARCH REPORT**

doi:10.1111/j.1360-0443.2008.02314.x

### **Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses**

**John Strang, Victoria Manning, Soraya Mayet, David Best, Emily Titherington, Laura Santana, Elizabeth Ofor & Claudia Semmler**

National Addiction Centre (Institute of Psychiatry/The Maudsley), Addiction Sciences Building, Denmark Hill, London, UK

# The NAC naloxone project

**Aims: To determine current levels of provision, potential to extend provision & outcomes (reduced fatalities)**

- **Phase 1:** National survey of Tier 3 & 4 drug services, ambulance services, police forces and carer organisations
- **Phase 2:** Development of a training model, national training and cascading of training through to clients
- **Phase 3:** Follow-up study on naloxone provision
- **Phase 4:** Exploration of the medico-legal issues and product development

# The naloxone programme: Investigation of the wider use of naloxone in the prevention of overdose deaths in pre-hospital care

FINAL REPORT: June 2007

Commissioned by:

The National Treatment Agency for Substance Misuse

## Recommendations

Drug services

Police

Ambulance

Commissioners

- Training of staff in overdose recognition & management & naloxone use
- Development of protocols, monitoring and record of OD
- To offer training to opiate using clients:  
ex induction pack when substitute prescribing
- Naloxone provision high risk clients: peer based projects to access and train high risk groups

## Phase 1: National Surveys

### **550 Drug Services** (70% response)

- 106,169 clients, 82% opiate users
- 6118 staff, (63%)
- 7% reported 1+ on-site OD (total=83, none fatal)
- 43% reported 1+ off-site OD (total=1139, 23% fatal)
- Availability of naloxone on-site was v. poor (15%)
- Take home naloxone virtually non-existent (1 service)
- 66% staff (n=4,062) interested in OD & N training

Evidence of potential to extend naloxone

# Carers

102 carers attending 4 organisations

- 80% parents, 20% other relative/partner
- 96% of person cared for were opiate users, 87% IDU, 57% in treatment,
- 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...

## Quotes from carers experiences & support for training

- “ My son died of a heroin overdose, I couldn't get to him quick enough, the paramedics couldn't revive him. My daughter is still on drugs” (49 year old mother)
- “ I rushed to the hospital once I heard he had overdosed and stayed for hours. He was the last to be treated because he was a drug user” (27 year old sister)
- “ I was not present when my son collapsed and stopped breathing, ambulance men resuscitated my son. I was not present when my younger son died from accidental overdose, ambulance staff should have naloxone in the ambulance my son could have been saved, training is vital.” (56 year old mother)

# Phase 2: Training

## Aims

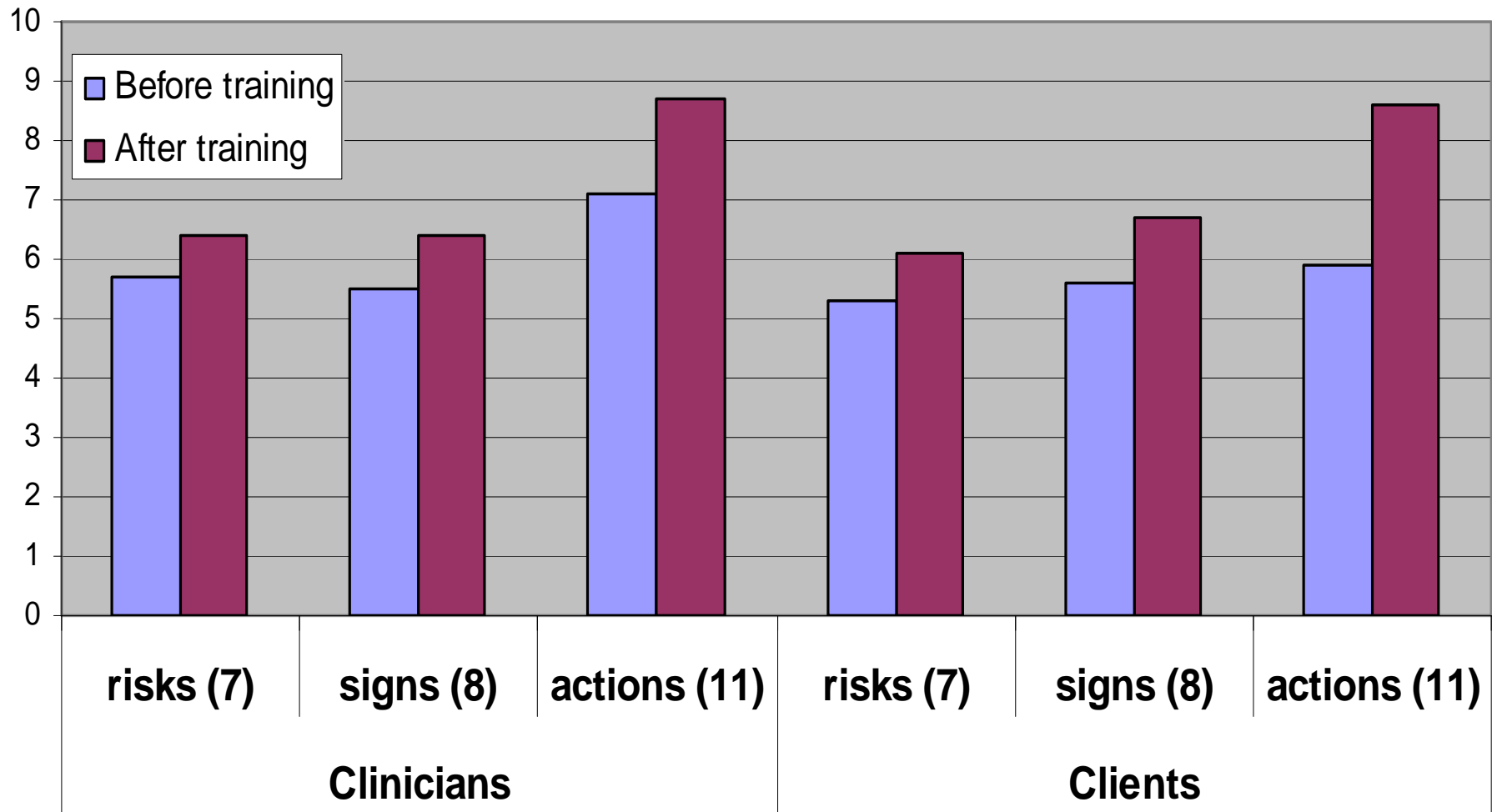
1. Develop a training programme
2. Test the effectiveness of a cascading method
3. Evaluate training to assess changes in clinician & client knowledge in OD management & N administration.

## Training Module

- Pre & Post training questionnaires,
- Video & PowerPoint presentation
- Consent form for follow-up interview,
- Information leaflets,
- Naloxone mini-jet / script
- Prescribing protocol (clinicians)

# Changes in knowledge after training

\*\*\*All significant at  $p < 0.001$



# Client confidence in administering naloxone



## Phase 3 Client follow-up study

- 186/239 (78%) follow-up rate
- Mean follow-up = 2.5 months after training
- 70% Male, 83% White British, Mean Age = 36.2 yrs
- First used heroin = 20.7 years
- 60% Maintenance, 30% Other Tx, 10% No Tx
- Average Length of time in Tx = 3 years
- 49% still IV opiate users
- 83% used illicit opiates in past month
- 28% clients trained a partner/carer/friends
- 53% ever experienced an OD (63% >1)
- 76% ever witnessed an OD (83% >1)

# Outcomes = 12 fatalities prevented

- 2 naloxone uses by staff following opioid overdoses
- 2 trained clients had personal overdoses
  - 1 ambulance use, 1 no use - both survived
- 17 clients witnessed 18 Overdoses
- Of 18 OD's - Naloxone given on 12 occasions
  - 10 clients administered naloxone
  - Ambulance gave naloxone to 2 people
  - Of the 6 not given naloxone 1 died.
  - Not used as
    - Instructed not to by 999, Thrown away, Not on person

# Obstacles to naloxone provision

## Among services

- Funding for take home naloxone
- Clinical staff & insurance issues
- Willingness – burden, time, knowledge, confidence

## Among clients

- Patchy uptake & interest in some services (Promotion needed)
- Not receiving naloxone at training
- Complicated device –requires 7 steps

# Where are we now?

- Current provision of take home naloxone is scattered in UK without national guidelines
- High demand for overdose/naloxone training
- Evaluation studies suggest that training works and that it has been effective with particular support for peer training
- Studies are coming up with connection with public health data: reduction in DRDs
- Orange guidelines.....anecdotal....!? What constitutes evidence?

# Conclusion

- Take Home Naloxone can reduce DRD's
- Current provision of take home naloxone is poor
- Low levels of clinician confidence
- High demand for overdose/naloxone training
- Training works
- Lives can be saved
- No evidence of riskier use – most of the 'concerns' appear to be myths and excuses for inaction – harm reduction arguments revisited!
- Needs extending to high risk populations