National Addiction Centre

Institute of Psychiatry at The Maudsley

King's College London

Take-home naloxone to prevent heroin/opioid overdose deaths: a UK/Australia shared vision

Professor Sir John Strang

National Addiction Centre, King's College London, UK

KING'S HEALTH PARTNERS

Pioneering better health for all

Declarations (personal & institutional)

- NHS provider (community & in-patient); also Phoenix House, Lifeline, Clouds House, KCA (Kent Council on Addictions).
- Dept of Health, NTA, Home Office, NACD, EMCDDA, WHO, UNODC, NIDA.
- Dialogue and work with pharmaceutical companies re actual or potential development of new medicines for use in the addiction treatment field (incl re naloxone products), including (past 3 years) Martindale, Indivior, Mundipharma, Braeburn/Camurus and trial product supply from iGen and Braeburn.
- SSA (Society for the Study of Addiction); UKDPC (UK Drug Policy Commission), and two Masters degrees (taught MSc and IPAS) and an Addictions MOOC.
- Work also with several charities (and received support) including Action on Addiction, J Paul Getty Charitable Trust (JPGT) and Pilgrim Trust.
- The university (King's College London) has registered intellectual property on a buccal naloxone formulation, and JS has been named in a patent registration by a Pharma company as inventor of a novel concentrated naloxone nasal spray.
- Lecture includes data and analyses from collaboration with Pharma.

Overall message

- Proud of what we have achieved
- Humble about how much more we need to do

interplay of advocacy, research and practice

Essential contributors to evolving thinking

- Wayne Hall
- Shane Darke
- Robert Ali
- Simon Lenton
- Louisa Degenhardt
- Paul Dietze
- Victoria Manning
- James Bell
- Nick Lintzeris
- Nico Clarke
- Suzanne /Nielsen
- Michael Farrell


EL SIDA TE ENGANCHA POR LA DROGA
SIETE DE CADA DIEZ ENFERMOS DEL SIDA SON DROGADICTOS
PARTAGER LES SERINGUES
SIDA
C'EST RISQU
LE SIDA
Vögeln nur mit Kondom
ROUTLEDGE

Essential contributors to evolving thinking

- Alex Wodak and the 1991/2 International Harm Reduction Conference committee
- …..

‘Harm Reduction: from Faith to Science’
(3rd International Harm Reduction Conference)
John Strang, Melbourne, March 1992

(1992)

“From the point of view of harm reduction, the case for such interventions seems incontestable. They stand as examples of virtually all benefit and virtually no cost. These surely stand as excellent vanguard projects for a harm reduction movement. **And if your heart is just not into such obvious but uncontroversial harm reduction measures, then why not give some thought to the idea of distribution of supplies of naloxone, the opiate antagonist, to opiate users who may at some later date be able to give a life-saving injection of the drug to a fellow drug user who has inadvertently overdosed.”**

PSYCHOACTIVE DRUGS & HARM REDUCTION

FROM FAITH TO SCIENCE

EDITED BY
NICK HEATHER
ALEX WODAK
ETHAN NADELMANN
& PAT O'HARE

Strang J. (1993). Chapter in 'Psychoactive Drugs and Harm Reduction: From Faith to Science'. Whurr Publishers, London, UK. (eds: Heather N Wodak A., Nadelmann E an O' Hare P.).

Chapter 1
Drug Use and Harm Reduction: Responding to the Challenge

JOHN STRANG

Some thought should also be given to more controversial options – for example, the possible distribution of supplies of naloxone (the opiate antagonist) to opiate users who may at some later date be able to give a life-saving injection of the drug to a fellow drug user who inadvertently overdoses, as has recently been put forward (Strang and Farrell, 1992).

Harm minimisation for drug misusers

(1992)

When second best may be best first

But orthodox medicine must also take up the challenge and explore these new territories. Why don't we already offer injecting drug users testing and vaccination for hepatitis B infection?[19 20] Perhaps a case can be made for distributing ampoules of the opiate antagonist naloxone. Its potential for abuse is nil, the risks are probably minimal, and considerable benefit may accrue if drug users could give emergency doses of antagonist to fellow injectors who inadvertently overdose.

BMJ
British Medical Journal

Strang & Farrell (1992) BMJ, 304: 1127-1128.

BMJ
British Medical Journal

(1996)

Heroin overdose: the case for take-home naloxone

Home based supplies of naloxone would save lives

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Australia

Non-fatal overdose is an occupational risk of he
and fatal overdose is a common cause of premat
heroin users.[2-4] One of the major contributors
outcome is the inadequacy of heroin users' resp
overdoses of their peers. They may delay calling ar
for fear of the police arriving, and their efforts to r
tose users are often ineffective. The distribution of
opiate users was first mooted in 1992[5] as an inter
would be life saving in such situations.[6] With a r
deaths from heroin overdose it is time to take th
seriously.

Interviews with 320 heroin users in Sydney fou
thirds had had a drug overdose, a third within th
and that 80% had been present at the overdose
user.[7] In Australia the incidence of deaths f
overdose has increased over the past decade while
other drug related causes have fallen. In the Unite
a sharp increase in the numbers of deaths among
has recently been reported from Glasgow.[8]

Naloxone has a long established use in emergen
tion of patients with opiate overdose.[9] Such a trie

(1996)

Papers

Frequency of non-fatal heroin overdose: survey of heroin users recruited in non-clinical settings

BMJ 1996; 313 doi: http://dx.doi.org/10.1136/bmj.313.7054.402 (Published 17 August 1996) Cite this as: BMJ 1996;313:402

Michael Gossop, head of research[a], Paul Griffiths, senior researcher[a], Beverly Powis, research psychologist[a], Sara Williamson, research psychologist[a], John Strang, professor of the addictions[a]

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Addiction (1999) 94(4), 471–478

(1999)

RESEARCH REPORT

Self-reported overdose among injecting drug users in London: extent and nature of the problem

BEVERLY POWIS, JOHN STRANG, PAUL GRIFFITHS, COLIN TAYLOR, SARA WILLIAMSON, JANE FOUNTAIN & MICHAEL GOSSOP

National Addiction Centre, London, UK

Abstract

Aims. *To estimate the extent and nature of overdose and factors associated with overdose among injecting drug users in London.* **Design.** *Three hundred and twelve current injecting drug users were recruited and interviewed in community settings by a team of "privileged access interviewers".* **Measurements.** *A structured questionnaire was used that covered the following areas: demographic characteristics, drug use, injecting behaviour, sharing practices, severity of drug dependence, experience of overdose, injecting-related health problems and treatment history.* **Findings.** *The results showed that experience of overdose was common (38%). A majority (54%) had witnessed someone else overdose. Overdosing was not a solitary experience; over 80% of subjects who had overdosed had done so in the presence of someone else, but only 27% reported ambulances having been called. Factors found to be associated with overdose were: age at which injecting began; gender (women being more likely to experience overdose); use of alcohol; and polydrug*

Addiction (1996) 91(3), 405–411

(1996)

RESEARCH REPORT

Overdose among heroin users in Sydney, Australia: I. Prevalence and correlates of non-fatal overdose

SHANE DARKE, JOANNE ROSS & WAYNE HALL

National Drug and Alcohol Research Centre, University of New South Wales, Australia

Abstract

A sample of 329 heroin users were interviewed regarding their personal experience of non-fatal heroin overdose. Experience of overdose was widespread, with two-thirds of subjects (68%) reporting having overdosed. The median number of life-time overdoses was three, with males and females equally likely to have overdosed. The majority (62%) of most recent heroin overdoses occurred in conjunction with the consumption of other central nervous system depressants (alcohol, benzodiazepines and other opioids). Logistic regression analyses indicated three independent factors associated with having overdosed: longer heroin using careers, greater heroin dependence and higher levels of alcohol consumption. Implications for the reduction in the

Addiction (1998) 93(5), 701–711

(1998)

RESEARCH REPORT

Experience of non-fatal overdose among heroin users in Adelaide, Australia: circumstances and risk perceptions

CATHERINE McGREGOR,[1] SHANE DARKE,[2] ROBERT ALI[1] & PAUL CHRISTIE[1]

[1]*Drug and Alcohol Services Council of South Australia &* [2]*National Drug and Alcohol Research Centre, University of New South Wales, Australia*

Abstract

Aims. *To ascertain the prevalence and risk factors for non-fatal overdose among heroin users to assist in the development of an effective intervention.* **Design.** *Cross-sectional design.* **Setting.** *Community setting, principally metropolitan Adelaide.* **Participants.** *Current heroin users (used heroin in the previous six months).* **Measurements.** *A structured questionnaire including the Severity of Dependence Scale.* **Finding.** *Of 218 current South Australian heroin users interviewed in 1996, 48% had experienced at least one non-fatal overdose their life-time (median: two overdoses), and 11% had overdosed in the previous 6 months. At some time, 70% had been present at someone else's overdose (median: three overdoses). At the time of their*

Addiction (1996) 91(3), 413–417

(1996)

RESEARCH REPORT

Overdose among heroin users in Sydney, Australia: II. Responses to overdose

SHANE DARKE, JOANNE ROSS & WAYNE HALL

National Drug and Alcohol Research Centre, University of New South Wales, Australia

Abstract

A sample of 329 heroin users were interviewed about their experiences at other peoples' heroin overdoses. The overwhelming majority (86%) had witnessed a heroin overdose, on a median of six occasions. Heroin users were reluctant to seek medical attention, with an ambulance being called on only half (56%) of the most recent overdose occasions. At only 17% of most recent overdoses was calling an ambulance the first action taken. Males reported taking significantly longer than females to call an ambulance. Nearly half (44%) of subjects reported that there were factors that had delayed or stopped them seeking medical assistance, the most common impediment being a fear of police involvement. The importance of interventions to encourage help-seeking at overdoses are discussed.

Addiction

(1999)

Addiction (1999) 94(2), 199–204

RESEARCH REPORT

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

National Addiction Centre (The Maudsley/Institute of Psychiatry), London, UK

Abstract

Aims. *Before proceeding with the introduction of an overdose fatality prevention programme including teaching in cardio-pulmonary resuscitation and distribution of naloxone, a pre-launch study of treatment and community samples of injecting drug misusers has been undertaken to establish (i) the extent of witnessing overdoses, (ii) the acceptability of naloxone distribution and training; and (iii) the likely impact of such measures.* **Design and setting.** *Structured interview of two samples: (a) a community sample of injecting*

(2000)

Drug and Alcohol Review (2000) 19, 365–369

EDITORIAL

A trial of naloxone for peer administration has merit, but will the lawyers let it happen?

SIMON LENTON & KIM HARGREAVES

National Drug Research Institute,
Curtin University,
GPO Box U1987, Perth,
Western Australia 6845, Australia

BMJ
British Medical Journal

(2001)

Take home naloxone and the prevention of deaths from opiate overdose: two pilot schemes

Kerstin Dettmer, Bill Saunders, John Strang

Doctors routinely give naloxone during emergency resuscitation after opiate overdose. The distribution of naloxone to opiate addicts has recently been addressed,[1–4] and a survey of drug users shows extensive support for the provision of supplies to take away.[4] We present the preliminary results of two pilot schemes to provide take home naloxone to opiate users.

Methods and results

The Berlin project

In January 1999 drug users in Berlin were given naloxone to take home. Opiate misusers attending a healthcare project (operating from a mobile van or ambulance) were offered training in emergency resuscitation after overdose, provided with naloxone (two 400 µg ampoules), needles, syringes, an emergency handbook, and information on naloxone. They were asked to report on any use of the drug. After 16 months, 124 opiate misusers had received training in resuscitation and were provided with supplies of naloxone to take away; 40 reported back, with 22 having given emergency naloxone (two on two occasions, one on three, and one on four).

The methods of administration were diverse.

Case 1 (Berlin)

"Three days ago, I was walking along the canal with a friend of mine. We saw a guy lying on the ground, with two people trying to help him—they were trying to help him breathe by mouth to mouth. When we ran over to them, we could tell it wasn't really working. The guy was blue in the face and hardly breathing any more. I could barely feel his pulse. Right away I gave him one ampoule of naloxone—I didn't think I could find a vein so I just shot it real slow into his upper arm. We tried to give him CPR and we called 911. Then the guy started to wake up and he started to breathe and shake a little bit. He was so thankful, he wanted to give me 50 Marks, but I wouldn't take it. When the medics came I told them I had given him the naloxone. The medics said 'Wow! So you guys have even got naloxone now?' But he thought it was great. He said we had probably just saved the guy's life." The ambulance staff then took the overdose victim to hospital for further observation.

The Jersey project

From October 1998 over the next 16 months naloxone (one minijet ready filled with 800 µg naloxone) was provided to 101 drug misusers in contact with local

BMJ
British Medical Journal

Emergency naloxone for heroin overdose

John Strang, Michael Kelleher, David Best, Soraya Mayet and Victoria Manning

BMJ 2006;333;614-615
doi:10.1136/bmj.333.7569.614

(2006)

Emergency naloxone for heroin overdose

Should it be available over the counter?

Naloxone saves lives. Timely injection of the opiate antagonist naloxone rapidly reverses the respiratory suppression of heroin overdose,[1 2] a major cause of death in young people.[3 4] Recent regulatory amendments increase significantly the extent to which naloxone can now be used to prevent opiate overdose deaths. In June 2005, in the Medicines for Human Use (Prescribing) (Miscellaneous Amendments) Order,[5] the United Kingdom added naloxone to the limited list of medicines that may be given by injection "by anyone for the purpose of saving life in an emergency" (alongside emergency adrenaline, glucagons, and snake antivenin). An emergency dose of naloxone may now be given to prevent death from heroin overdose without specific medical instruction. In August 2005, New York state passed legislation (bills A.7162-A (Dinowitz) and S.4869-A (Hannon)) establishing that physicians may lawfully prescribe naloxone explicitly for potential future opiate overdose, including the situation where it may be administered to someone else.

Many people who take overdoses of heroin die even though friends or family are present.[6] Peers often attempt to resuscitate,[7] sometimes incorrectly,[w1] and death may occur from respiratory arrest before

P+ *Summary of good practice with take-home naloxone and extra references w1-w7 are on bmj.com*

Addiction

RESEARCH REPORT

doi:10.1111/j.1360-0443.2008.02314.x

(2008)

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 Offor & Claudia Semmler

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

ABSTRACT

Aim To examine the impact of training in overdose management and naloxone provision on the knowledge and confidence of current opiate users; and to record subsequent management of overdoses that occur during a 3-month

Drugs: education, prevention and policy,
April 2008; 15(2): 211–218

informa
healthcare

(2008)

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 life-saving potential …

Strang, Manning, Mayet et al, (2008) Family carers and prevention of heroin overdose deaths: …… Drugs: Education, Prevention & Policy, 15: 211-218.

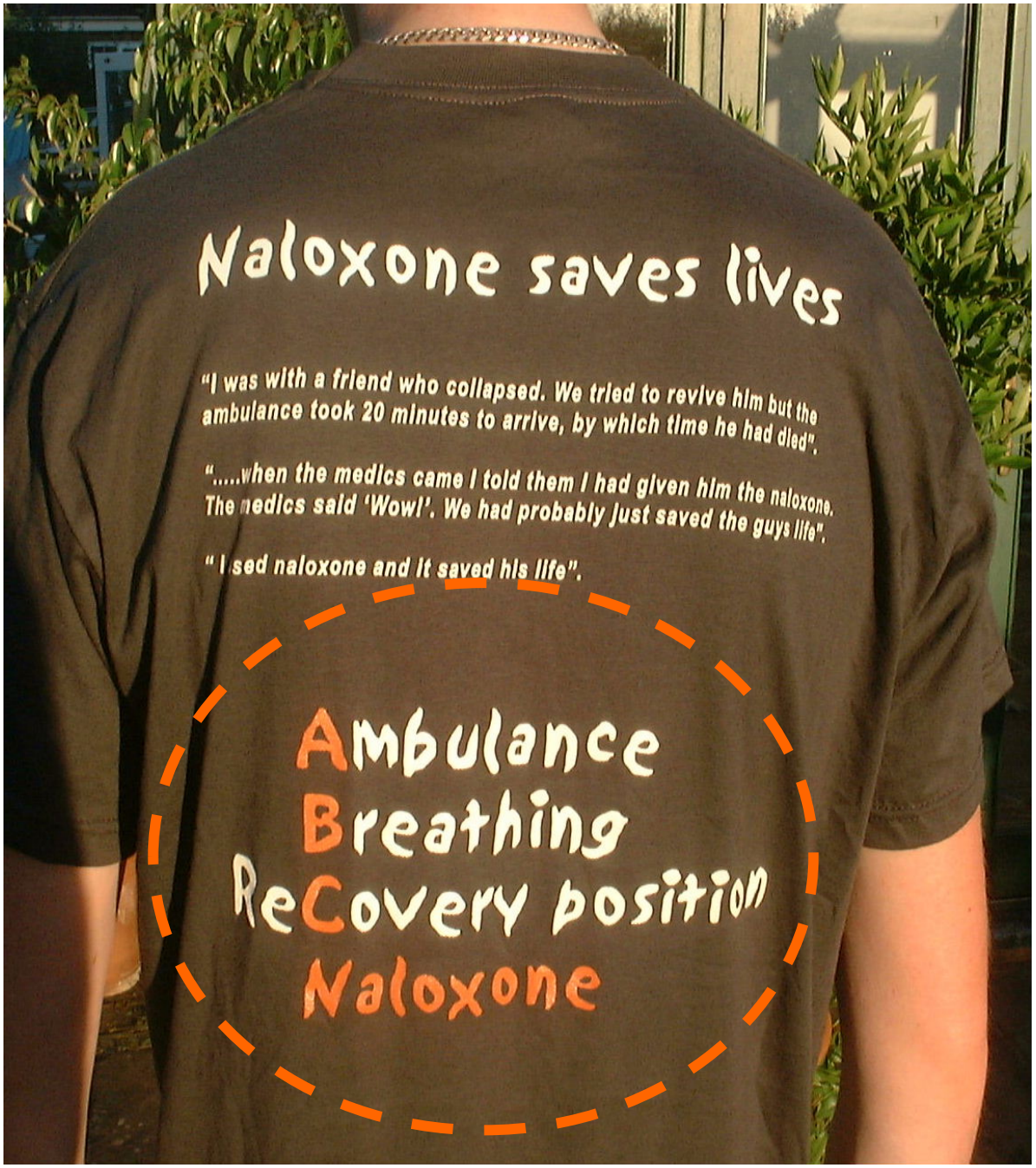
(2009-11)

"Pilot sites trained the carers and relations of opiate misusers to respond to overdoses and use the antidote naloxone. This appears to have helped save lives..."

THE NTA OVERDOSE AND NALOXONE TRAINING PROGRAMME FOR FAMILIES AND CARERS

NHS
National Treatment Agency
for Substance Misuse


National
Addiction
Centre


Naloxone saves lives
"I was with a friend who collapsed. We tried to revive him but the ambulance took 20 minutes to arrive, by which time he had died".
".....when the medics came I told them I had given him the naloxone. The medics said 'Wow!'. We had probably just saved the guys life".
" I sed naloxone and it saved his life".
Ambulance
Breathing
ReCovery position
Naloxone

Addiction

RESEARCH REPORT

doi:10.1111/j.1360-0443.2009.02724.x

Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose

(2009)

Debra Kerr[1,2], Anne-Maree Kelly[2,3], Paul Dietze[4,5], Damien Jolley[5] & Bill Barger[6]

Victoria University, School of Nursing and Midwifery, St Albans, Victoria, Australia,[1] University of Melbourne, Parkville, Victoria, Australia,[2] Joseph Epstein Centre for Emergency Medicine Research, Sunshine Hospital, St Albans, Victoria, Australia,[3] The Macfarlane Burnet Institute for Medical Research and Public Health, Melbourne, Victoria, Australia,[4] Monash Institute of Health Services Research, Clayton, Victoria, Australia[5] and Ambulance Victoria, Doncaster, Victoria, Australia[6]

ABSTRACT

Aims Traditionally, the opiate antagonist naloxone has been administered parenterally; however, intranasal (i.n.) administration has the potential to reduce the risk of needlestick injury. This is important when working with populations known to have a high prevalence of blood-borne viruses. Preliminary research suggests that i.n. administration might be effective, but suboptimal naloxone solutions were used. This study compared the effectiveness of concentrated (2 mg/ml) i.n. naloxone to intramuscular (i.m.) naloxone for suspected opiate overdose. **Methods** This randomized controlled trial included patients treated for suspected opiate overdose in the pre-hospital setting. Patients received 2 mg of either i.n. or i.m. naloxone. The primary outcome was the proportion of patients who responded within 10 minutes of naloxone treatment. Secondary outcomes included time to adequate response and requirement for supplementary naloxone. Data were analysed using multivariate statistical techniques. **Results** A total of 172 patients were enrolled into the study. Median age was 29 years and 74% were male. Rates of response within 10 minutes were similar: i.n.

Journal of Urban Health: Bulletin of the New York Academy of Medicine
doi:10.1007/s11524-013-9803-1

(2013)

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*

PLOS | ONE

(2015)

RESEARCH ARTICLE

Understanding Heroin Overdose: A Study of the Acute Respiratory Depressant Effects of Injected Pharmaceutical Heroin

Caroline J. Jolley[1‡*], James Bell[2,3‡], Gerrard F. Rafferty[1], John Moxham[1], John Strang[2,3]

1 Division of Asthma, Allergy and Lung Biology, Faculty of Life Sciences and Medicine, King's College London, King's Health Partners, Denmark Hill, London, United Kingdom, **2** National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, King's Health Partners, Denmark Hill, London, United Kingdom, **3** Addictions Services, South London & Maudsley NHS Foundation Trust, King's Health Partners, Denmark Hill, London, United Kingdom

‡ CJJ and JB are joint first authors on this work.
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OPEN ACCESS

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Abstract

Opioids are respiratory depressants and heroin/opioid overdose is a major contributor to the excess mortality of heroin addicts. The individual and situational variability of respiratory depression caused by intravenous heroin is poorly understood. This study used advanced respiratory monitoring to follow the time course and severity of acute opioid-induced respiratory depression. 10 patients (9/10 with chronic airflow obstruction) undergoing supervised injectable opioid treatment for heroin addiction received their usual prescribed dose of injectable opioid (diamorphine or methadone) (IOT), and their usual prescribed dose of oral opioid (methadone or sustained release oral morphine) after 30 minutes. The main outcome measures were pulse oximetry (SpO_2%), end-tidal CO_2% ($ETCO_2$%) and neural respiratory drive (NRD) (quantified using parasternal intercostal muscle electromyography). Significant respiratory depression was defined as absence of inspiratory airflow >10s, SpO_2% < 90% for >10s and $ETCO_2$% per breath >6.5%. Increases in $ETCO_2$% indicated significant respi-

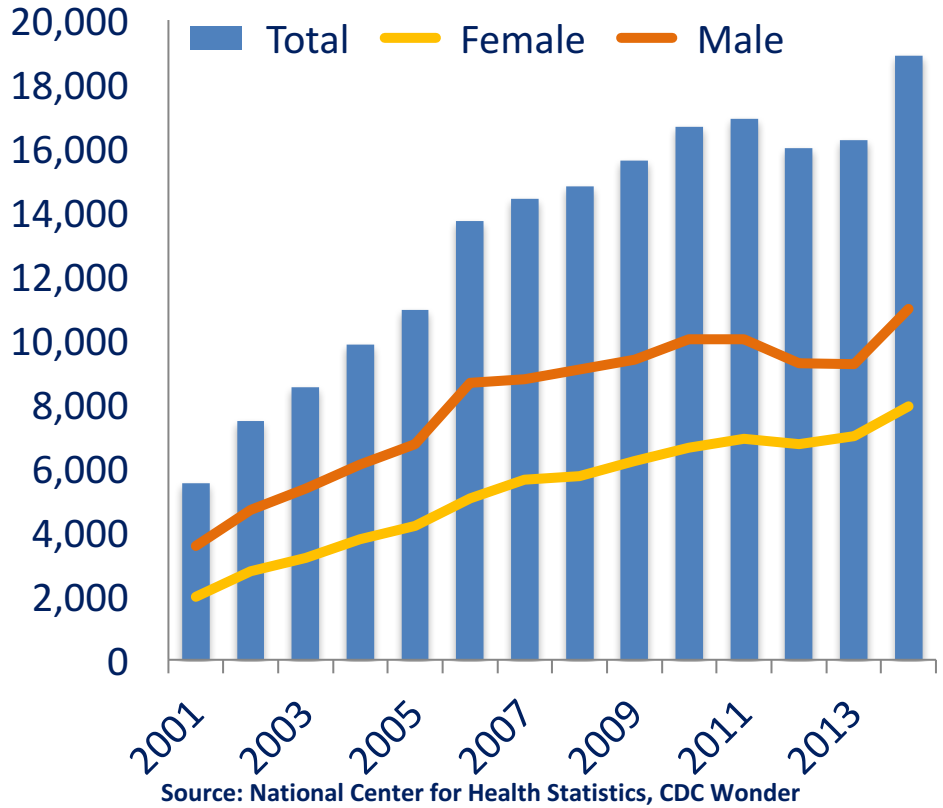
Structure of lecture

1. **Drug deaths: where are they concentrated?**
2. Understanding heroin/opioid overdose
3. Treatment as prevention
4. Mobilising civilian emergency response
5. Improving the approach for the future

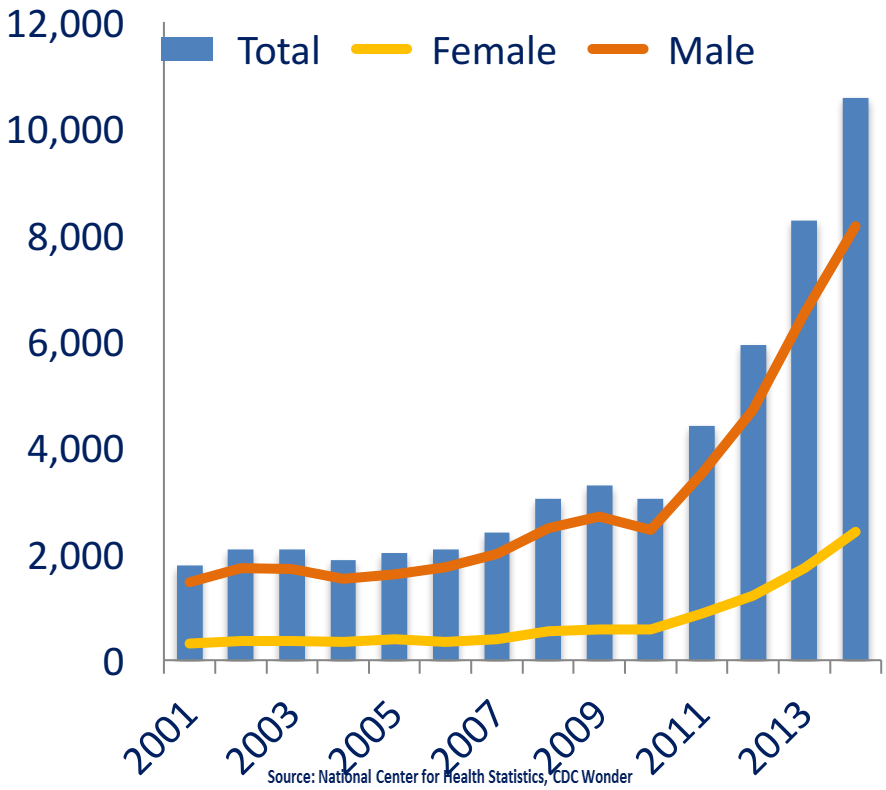
National Institute on Drug Abuse

National Overdose Deaths

Number of Deaths from Heroin & Prescription Opioids



Source: National Center for Health Statistics, CDC Wonder



Source: National Center for Health Statistics, CDC Wonder

When in particular?

- Prison release
- Post-detox/rehab
- During methadone induction

BMJ
British Medical Journal

(1998)

Mortality from overdose among injecting drug users recently released from prison: database linkage study

S R Seaman, R P Brettle, S M Gore

Abstract

Objective: To assess whether injecting drug users have a higher than usual risk of death from overdose in the 2 weeks after release from prison.
Design: Soundex coding of surnames and information on date of birth were used to link entry and release dates from the local prison between 1983 and 1994 with clinical data from Edinburgh City Hospital's cohort of male injecting drug users who are infected with HIV.
Setting: Edinburgh City Hospital and Edinburgh Prison.
Subjects: 316/332 male injecting drug users infected with HIV in the City Hospital HIV cohort; 16 were excluded because they were enrolled after developing AIDS or because their precise date of death was not available.
Main outcome measure: Relative risk of dying from overdose before developing AIDS and relative risk of dying of all causes before developing AIDS during the 2 weeks after release from prison: this was compared and 0.029/1000 days during other times of liberty. The relative risk of death from overdose became 7.7 (1.5 to 39.1) after temporal matching (when the comparison was limited to the first 2 weeks after release *v* the next 10 weeks). The crude relative risk in an analysis combining stratified prison term and the 2 weeks after release was 4.5 (1.7 to 11.7) for death from overdose. After temporal matching these risks became 1.8 (0.4 to 9.2).
Conclusion: Prisons should evaluate interventions to reduce the risk of death from overdose after release.

Introduction

The risk of death from overdose may be greater in injecting drug users who resume drug use after a period of abstinence during which their tolerance may have declined.[1] Imprisonment is an enforced period of abstinence from, or may lead to a radical reduction in, drug use.[2] We investigated the risk of death from overdose among male injecting drug users in the Edinburgh City Hospital HIV cohort[3] in the 2 weeks

RESEARCH REPORT

dot:10.1111/j.1360-0443.2007.02081.x

Acute risk of drug-related death among newly released prisoners in England and Wales

(2008)

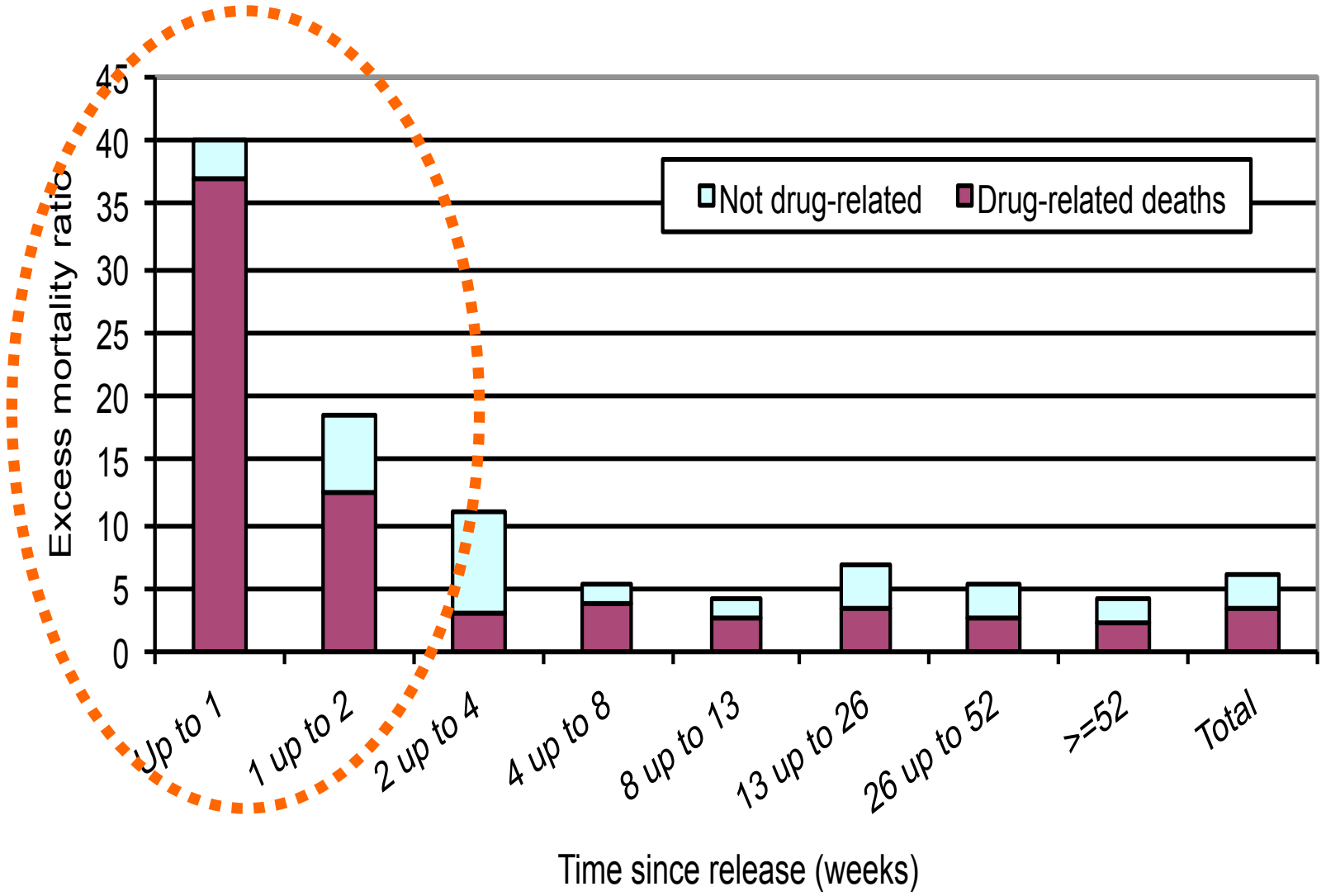
Michael Farrell & John Marsden

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

When? Clustering in time and space



Singleton et al, 2002

Structure of lecture

1. Drug deaths: where are they concentrated?
2. **Understanding heroin/opioid overdose**
3. Treatment as prevention
4. Mobilising civilian emergency response
5. Improving the approach for the future

PLOS | ONE

(2015)

RESEARCH ARTICLE

Understanding Heroin Overdose: A Study of the Acute Respiratory Depressant Effects of Injected Pharmaceutical Heroin

Caroline J. Jolley[1‡*], James Bell[2,3‡], Gerrard F. Rafferty[1], John Moxham[1], John Strang[2,3]

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OPEN ACCESS

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Published: October 23, 2015

Abstract

Opioids are respiratory depressants and heroin/opioid overdose is a major contributor to the excess mortality of heroin addicts. The individual and situational variability of respiratory depression caused by intravenous heroin is poorly understood. This study used advanced respiratory monitoring to follow the time course and severity of acute opioid-induced respiratory depression. 10 patients (9/10 with chronic airflow obstruction) undergoing supervised injectable opioid treatment for heroin addiction received their usual prescribed dose of injectable opioid (diamorphine or methadone) (IOT), and their usual prescribed dose of oral opioid (methadone or sustained release oral morphine) after 30 minutes. The main outcome measures were pulse oximetry (SpO_2%), end-tidal CO_2% ($ETCO_2$%) and neural respiratory drive (NRD) (quantified using parasternal intercostal muscle electromyography). Significant respiratory depression was defined as absence of inspiratory airflow >10s, SpO_2% < 90% for >10s and $ETCO_2$% per breath >6.5%. Increases in $ETCO_2$% indicated significant respi-

Oxygen saturation: IV versus IM

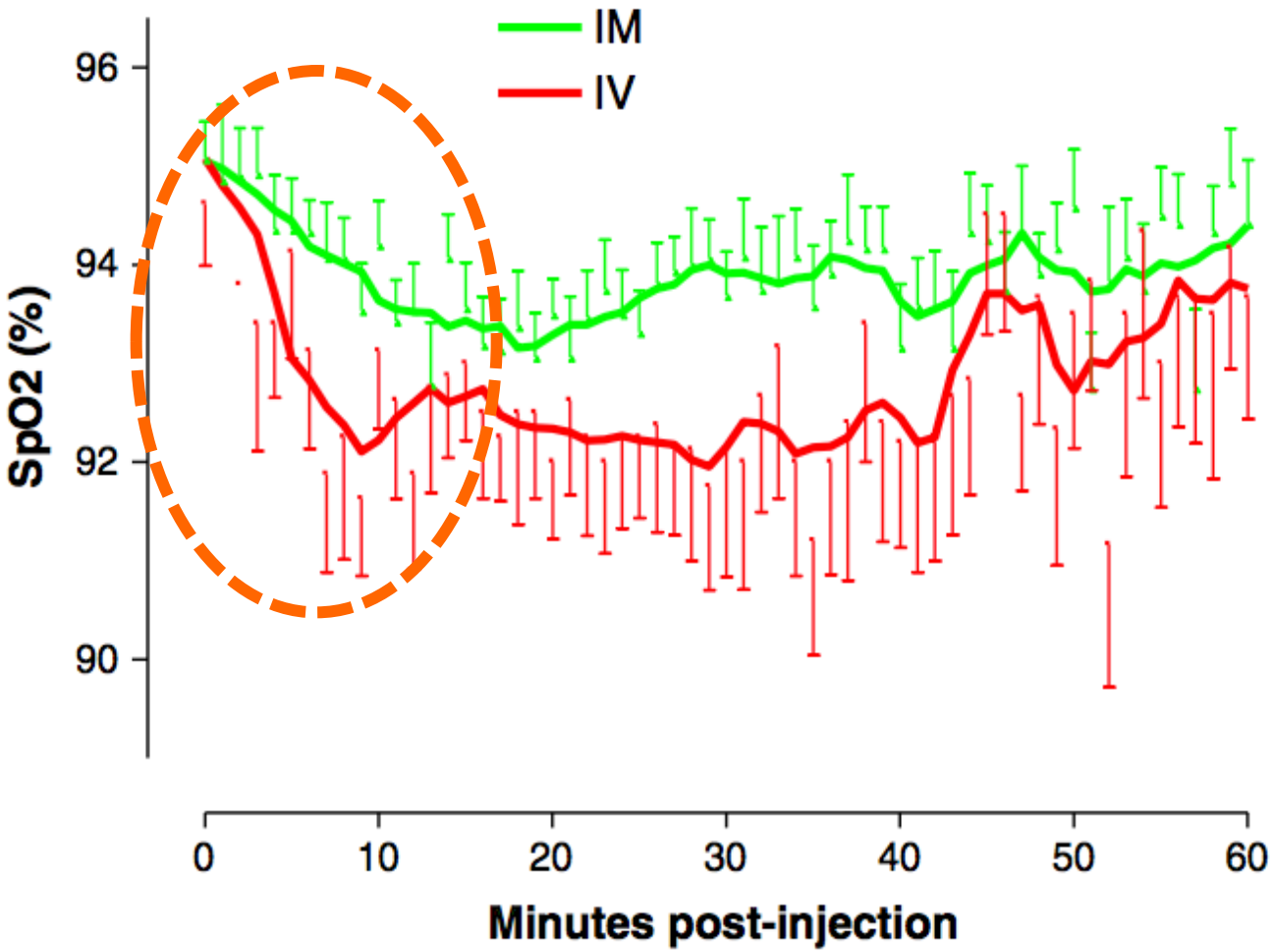
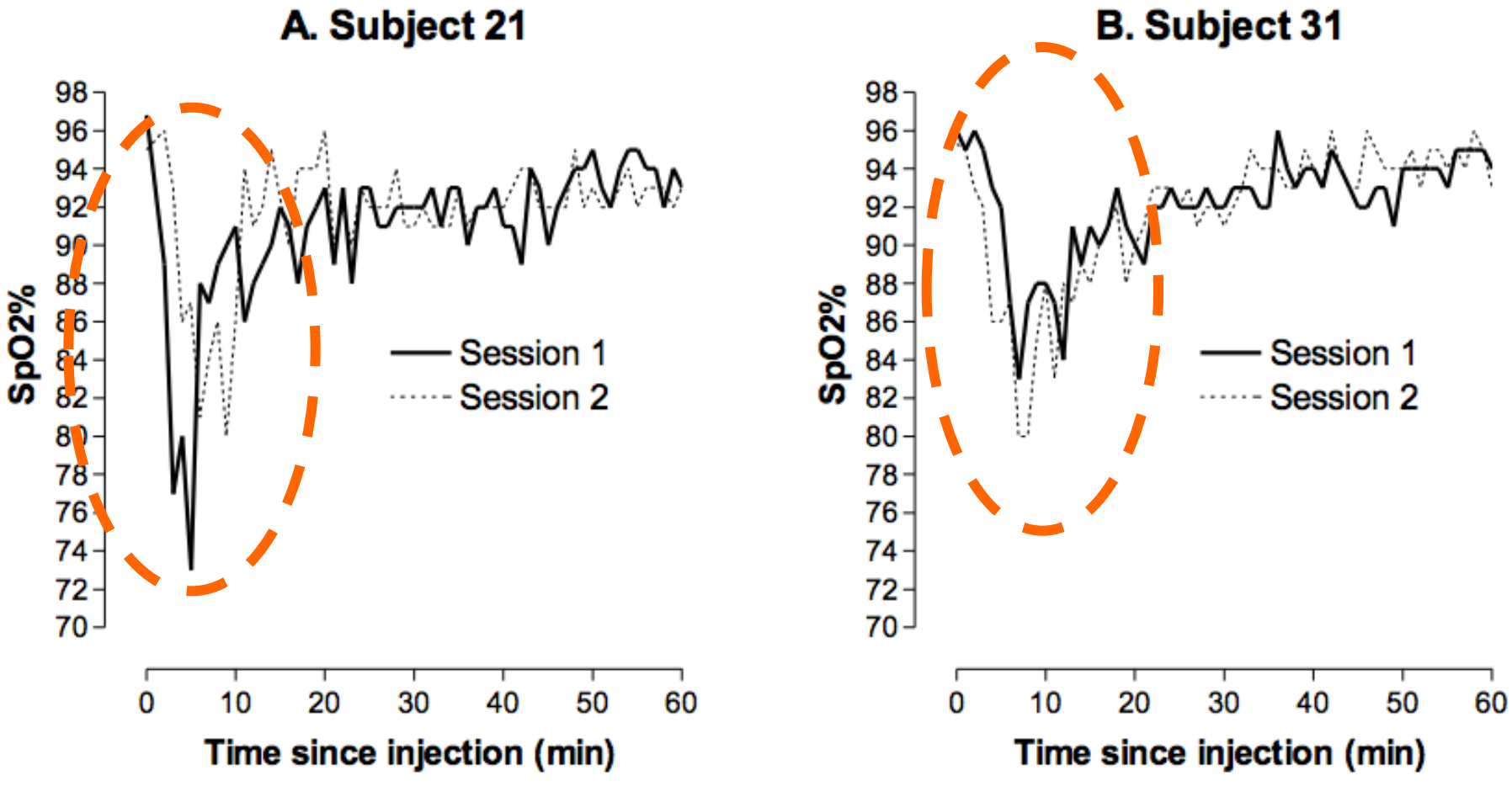


Figure 1 Oxygen saturation after intravenous (IV) and intramuscular (IM) injection of heroin

Oxygen saturation: case study



Subject 21 (41 year old male) injected 180mg heroin intravenously on both occasions.

Subject 31 (42 year old female) injected 150mg intramuscular heroin in session 1 and 160mg heroin in session 2. (unpublished)

Structure of lecture

1. Drug deaths: where are they concentrated?
2. Understanding heroin/opioid overdose
3. **Treatment as prevention**
4. Mobilising civilian emergency response
5. Improving the approach for the future

BMJ (2010) RESEARCH

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,[1,3] Matt Hickman, professor in public health and epidemiology[1]

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[2]National Addiction Centre, Institute of Psychiatry, King's College London, London, UK
[3]London School of Hygiene and

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.

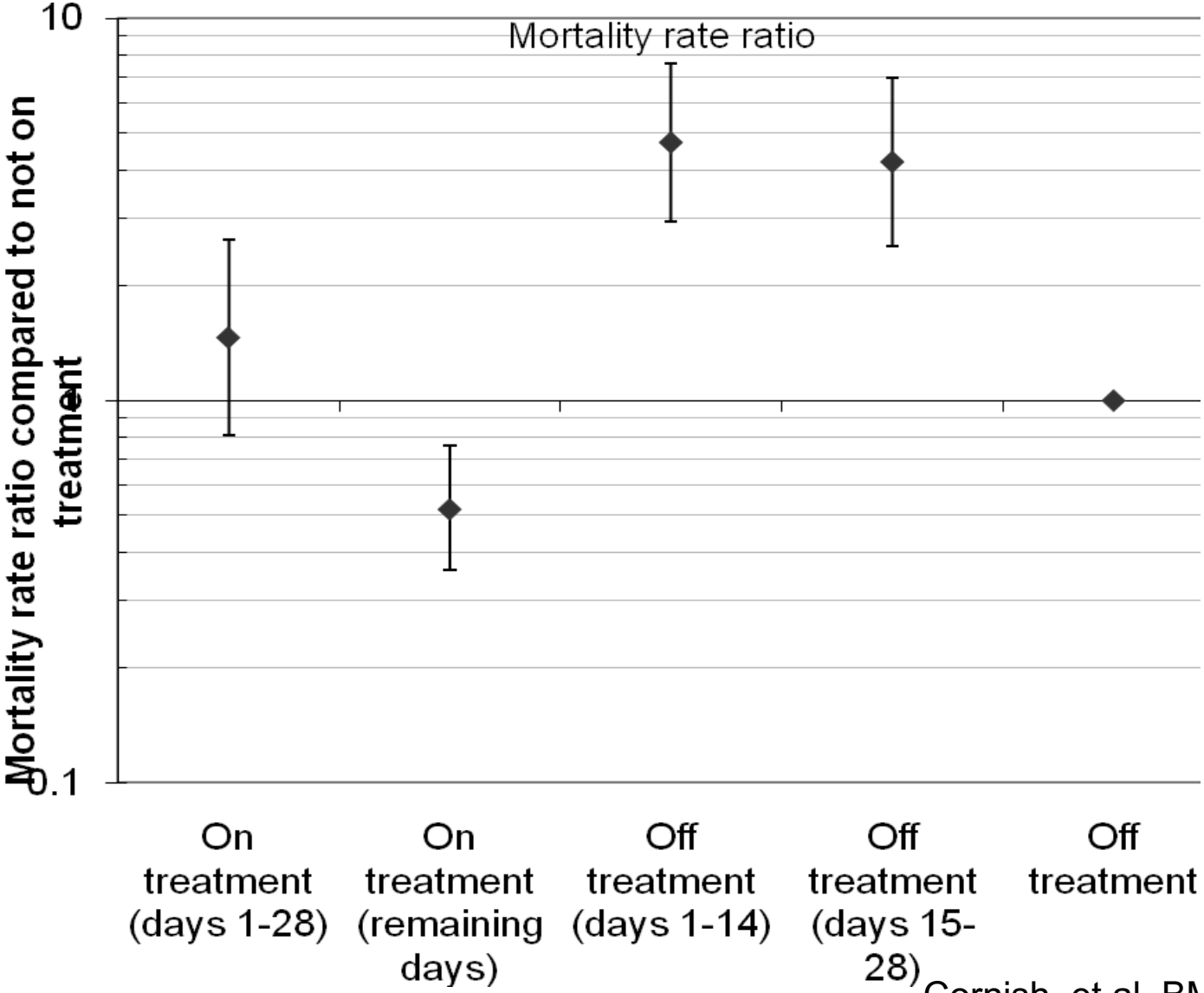
Setting UK General Practice Research Database

treatment. Further research is needed to investigate the effect of average duration of opiate substitution treatment on drug related mortality.

INTRODUCTION

Opiate users have a high risk of death and contribute

Risk of death during and after OST treatment



Cornish, et al. BMJ. 2010; 341:c547

Addiction

RESEARCH REPORT

doi:10.1111/add.12536

The impact of opioid substitution therapy on mortality post-release from prison: retrospective data linkage study

(2014)

Louisa Degenhardt[1,2,3,4], Sarah Larney[1,5], Jo Kimber[1,6], Natasa Gisev[1], Michael Farrell[1], Timothy Dobbins[7], Don J. Weatherburn[8], Amy Gibson[9], Richard Mattick[1], Tony Butler[10] & Lucy Burns[1]

National Drug and Alcohol Research Centre, University of New South Wales, Sydney, NSW, Australia,[1] School of Population and Global Health, University of Melbourne, Melbourne, Vic., Australia,[2] Murdoch Children's Research Institute, Melbourne, Vic., Australia,[3] Department of Global Health, School of Public Health, University of Washington, Seattle, WA, USA,[4] Alpert Medical School, Brown University, Providence, RI, USA,[5] Centre for Research on Drugs and Health Behaviour, London School of Hygiene and Tropical Medicine, London, UK,[6] National Centre for Epidemiology and Population Health, Research School of Population Health, ANU College of Medicine, Biology and Environment, Australian National University, Canberra, ACT, Australia,[7] New South Wales Bureau of Crime Statistics and Research (BOCSAR), Sydney, NSW, Australia,[8] University of Western Sydney, Sydney, NSW, Australia[9] and Kirby Institute, University of New South Wales, Sydney, NSW, Australia[10]

ABSTRACT

Aims Release from prison is a high-risk period for mortality. We examined the impact of opioid substitution therapy (OST), for opioid dependence during and after incarceration, upon mortality post-release. **Design** A cohort was formed of all opioid-dependent people who entered OST between 1985 and 2010 and who, following first OST entry, were released from prison at least once between 2000 and 2012. We linked data on OST history, court and prison records and deaths. **Setting** New South Wales (NSW), Australia. **Participants** A total of 16 453 people released

Addiction

(2017)

SSA SOCIETY FOR THE STUDY OF ADDICTION

RESEARCH REPORT

doi:10.1111/add.13779

Does exposure to opioid substitution treatment in prison reduce the risk of death after release? A national prospective observational study in England

John Marsden[1], Garry Stillwell[1], Hayley Jones[2], Alisha Cooper[3], Brian Eastwood[3], Michael Farrell[4], Tim Lowden[3], Nino Maddalena[3], Chris Metcalfe[2], Jenny Shaw[5] & Matthew Hickman[2]

Addictions Department, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK,[1] School of Social and Community Medicine, Faculty of Health Sciences, University of Bristol, Bristol, UK,[2] Alcohol, Drug and Tobacco Division, Health and Wellbeing Directorate, Public Health England, London, UK,[3] National Drug and Alcohol Research Centre, University of New South Wales, New South Wales, Australia[4] and Institute of Brain, Behaviour and Mental Health, University of Manchester, Manchester, UK[5]

ABSTRACT

Background and Aims People with opioid use disorder (OUD) in prison face an acute risk of death after release. We estimated whether prison-based opioid substitution treatment (OST) reduces this risk. **Design** Prospective observational cohort study using prison health care, national community drug misuse treatment and deaths registers. **Setting** Recruitment at 39 adult prisons in England (32 male; seven female) accounting for 95% of OST treatment in

Structure of lecture

1. Drug deaths: where are they concentrated?
2. Understanding heroin/opioid overdose
3. Treatment as prevention
4. **Mobilising civilian emergency response**
5. Improving the approach for the future

Structure of lecture

1. Drug deaths: where are they concentrated?
2. Understanding heroin/opioid overdose
3. Treatment as prevention
4. Mobilising civilian emergency response
5. **Improving the approach for the future**

Three challenges:

1) Can it be non-injectable?

2) Does dose matter?

3) Making provision universal


2 mg
1 mg / mL
NALOXONE HYDROCHLORIDE
INJECTION, USP

Narcan rescue kit[18]

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

FOR DEBATE

doi:10.1111/add.13209

Clinical provision of improvised nasal naloxone without experimental testing and without regulatory approval: imaginative shortcut or dangerous bypass of essential safety procedures?

John Strang*, Rebecca McDonald*, Basak Tas & Ed Day

National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

*Joint first authors

Population Pharmacokinetics of Intravenous, Intramuscular, and Intranasal Naloxone in Human Volunteers

Jonathonm Dowling, Geoffrey K. Isbister,†‡¶ Carl M. J. Kirkpatrick,‡ Daya Naidoo,§ and Andis Graudins*‖*

Abstract: To investigate the pharmacokinetics of naloxone in healthy volunteers, we undertook an open-label crossover study in which six male volunteers received naloxone on five occasions: intravenous (0.8 mg), intramuscular (0.8 mg), intranasal (0.8 mg), intravenous (2 mg), and intranasal (2 mg). Samples were collected for 4 hours after administration for 128 samples in total. A population pharmacokinetic analysis was undertaken using NONMEM. The data were best described by a three-compartment model with first-order absorption for intramuscular and intranasal administration, between-subject variability on clearance and central volume, lean body weight on clearance, and weight on central volume. Relative bioavailability of intramuscular and intranasal naloxone was 36% and 4%, respectively. The final parameter estimates were clearance, 91 L/hr; central volume, 2.87 L; first peripheral compartment volume, 1.49 L, second peripheral compartment volume, 33.6 L; first intercompartmental clearance, 5.66

with opioid poisoning requiring naloxone therapy are often difficult to cannulate as a result of previous intravenous substance abuse. This may delay the administration of antidote therapy. Intravenous drug abusers are also at increased risk of carrying bloodborne infections that could be transmitted to healthcare workers through needlestick injuries.[1] The half-life of naloxone is significantly shorter than most of the opioid agents, so its duration of action is shorter than that of most opioid agents. Patients may awaken from opioid toxicity and want to remove themselves from medical care when there is the risk of recurrence of opioid toxicity after the effects of naloxone wear off. This is a particular concern with long-acting opioids such as methadone and has prompted the use of a combination of intravenous and intramuscular naloxone in the field to prolong its duration of action. However, this approach is not evidence-based or based on an understanding

Addiction
RESEARCH REPORT

(in press, 2017)

Pharmacokinetics of concentrated naloxone nasal spray for opioid overdose reversal: Phase-I healthy volunteer study

Rebecca McDonald[1], Ulrike Lorch[2], Jo Woodward[3], Björn Bosse[4], Helen Johnson[3], Gill Mundin[3], Kevin Smith[3], & John Strang[1]

Pharmacokinetics study in healthy volunteers: concentrated naloxone nasal spray

Rationale:

- Naloxone has no pharmacological effect in healthy volunteers
- Clinical standard: 0.4mg intramuscular (IM) reference (Hertz, 2012)
- *Aim 1:* Assess IN naloxone pharmacokinetics, incl bioavailability
- *Aim 2:* Compare early exposure: IN vs. IM

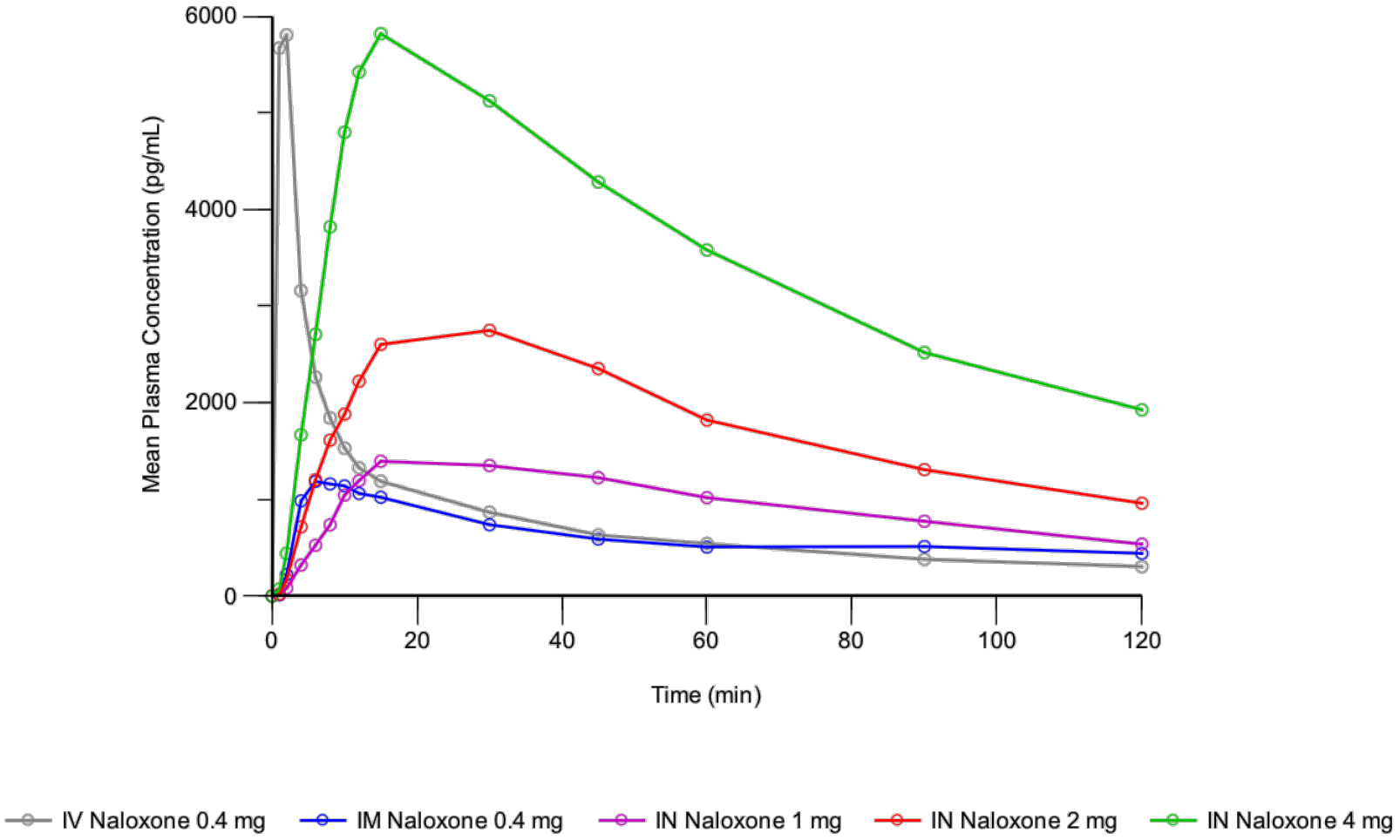
Design:

- Open-label, randomized 5-way crossover (n=38)
- Three intranasal (IN) vs. two parenteral doses
  - **IN 1mg/0.1mL vs.**
  - **IN 2mg/0.1mL vs.**
  - **IN 4mg/0.2mL vs.**
  - IV 0.4mg/mL vs.
  - IM 0.4mg/mL (reference)

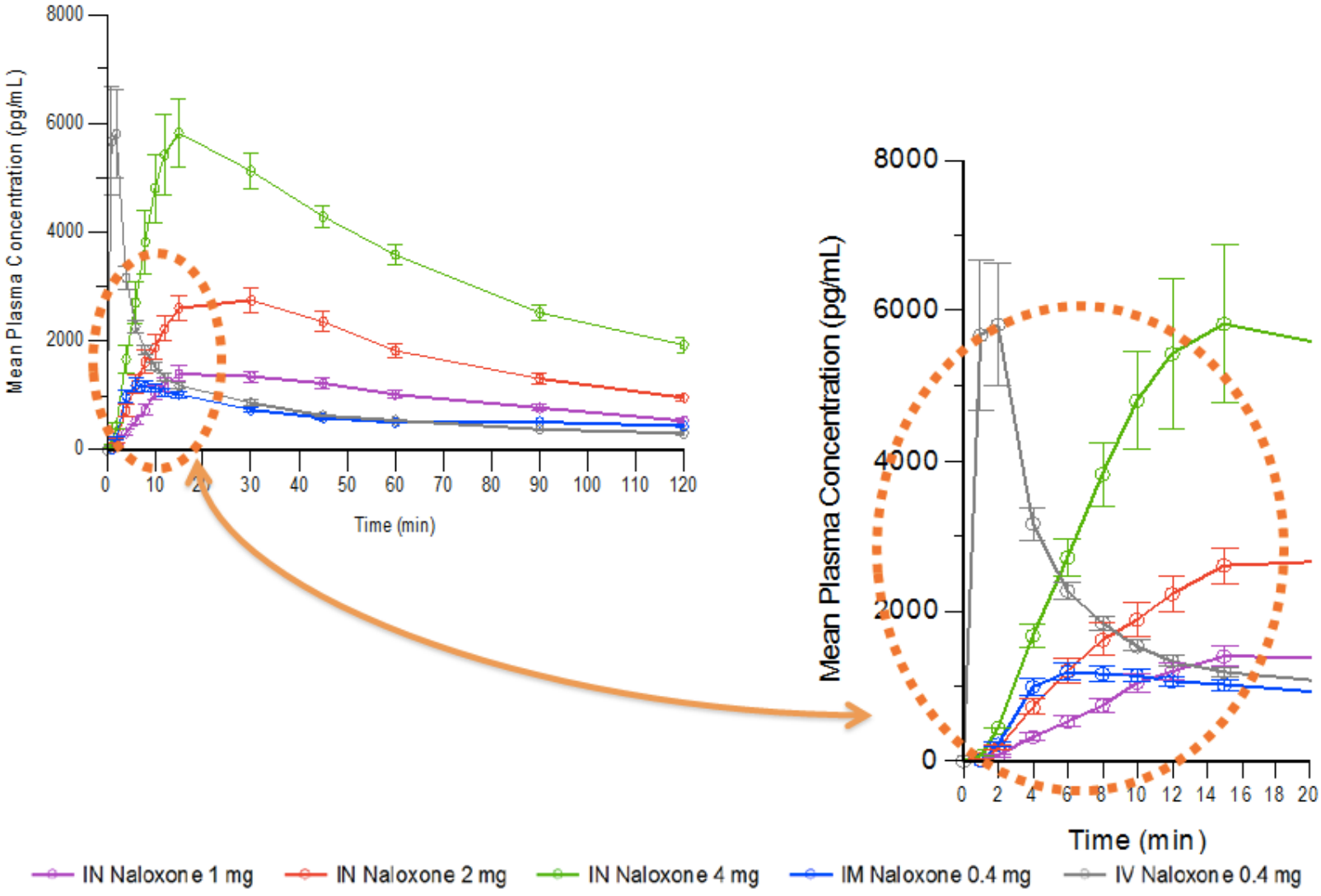
Methods:

- IN spray as 0.1ml from Aptar device
- Intense early blood sampling 0-15 min (+1, 2, 3, 4, 6, 8, 10, 12.5, 15 min)

Key findings: Naloxone mean PK profile



Key findings: Early naloxone exposure (AUCp)



Key findings: Bioavailability

	Ratio (%) 90% CI (lower, upper)		
	IN 1 mg	IN 2 mg	IN 4 mg
Absolute Bioavailability IN : IV*	50 (44.6, 56.6)	47 (41.7, 52.6)	48 (43.3, 53.5)
Relative Bioavailability IN : IM**	51 (45.2, 57.1)	47 (41.7, 53.5)	48 (43.2, 54.1)

*IV 0.4 mg used as the reference treatment for the comparison
**IM 0.4 mg used as the reference treatment for the comparison

Injection-free Alternatives (cont'd)

molecular pharmaceutics

(2016)

Article

pubs.acs.org/molecularpharmaceutics

Amorphous Formulation and *in Vitro* Performance Testing of Instantly Disintegrating Buccal Tablets for the Emergency Delivery of Naloxone

Abdulmalik Alqurshi,[†] Zahrae Kumar,[†] Rebecca McDonald,[‡] John Strang,[‡] Asma Buanz,[§] Shagufta Ahmed,[∥] Elizabeth Allen,[∥] Peter Cameron,[⊥] James A. Rickard,[⊥] Verity Sandhu,[⊥] Chris Holt,[⊥] Rebecca Stansfield,[⊥] David Taylor,[†] Ben Forbes,[†] and Paul G. Royall*[,†]

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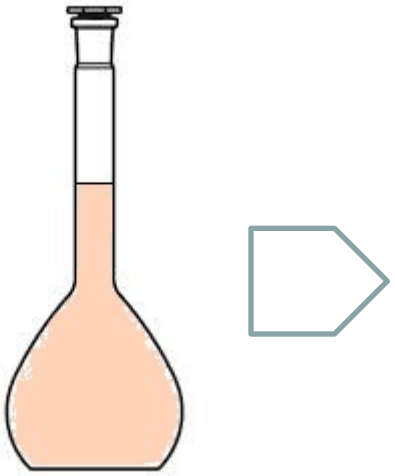
[§]UCL School of Pharmacy, University College London, 29-39 Brunswick Square, London, U.K., WC1N 1AX

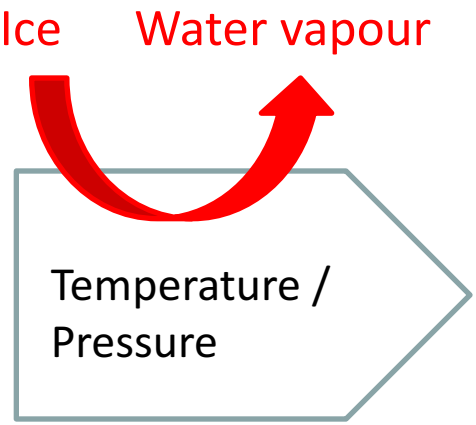
[∥]Quintiles Ltd, Quintiles Drug Research Unit at Guy's Hospital, 6 Newcomen Street London, U.K., SE1 1YR

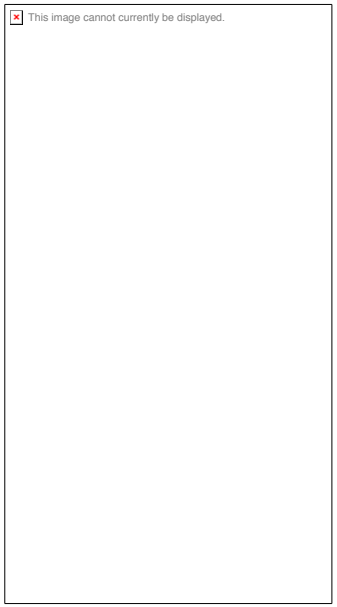
[⊥]Guy's and St Thomas' NHS Foundation Trust Pharmacy Manufacturing Unit, Guy's Hospital, Great Maze Pond, London, U.K., SE1 9RT

3 | Naloxone Instant Melt Tablet Development

SOLUTION → FREEZE → DRY → TABLET







Stock solution
Naloxone and pharmaceutical grade excipients in water for injection

Solution pipetted into blister wells (top) and frozen (bottom) ready for lyophilisation

Frozen tablets lyophilised using tailored temperature and pressure cycle

Instant melt tablet

Three challenges:

1) Can it be non-injectable?

2) Does dose matter?

3) Making provision universal

Addiction
SSA SOCIETY FOR THE STUDY OF ADDICTION
RESEARCH REPORT
doi:10.1111/add.13027

Naloxone—does over-antagonism matter? Evidence of iatrogenic harm after emergency treatment of heroin/opioid overdose

(2015)

Joanne Neale[1] & John Strang[2]

Reader in Qualitative and Mixed Methods Research, National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK[1] and Professor of the Addictions, National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK[2]

ABSTRACT

Aim To analyse drug users' views and experiences of naloxone during emergency resuscitation after illicit opiate overdose to identify (i) any evidence of harm caused by excessive naloxone dosing ('over-antagonism'); and (ii) implications for the medical administration of naloxone within contemporary emergency settings. **Design** Re-analysis of a large qualitative data set comprising 70 face-to-face interviews conducted within a few hours of heroin/opioid overdose occurring, observations from hospital settings and a further 130 interviews with illicit opiate users. Data were generated between 1997 and 1999. **Setting** Emergency departments, drug services and pharmacies in two Scottish cities. **Participants** Two hundred illicit opiate users: 131 males and 69 females. **Findings** Participants had limited knowledge of naloxone and its pharmacology, yet described it routinely in negative terms and were critical of its medical administration. In particular, they complained that naloxone induced acute withdrawal symptoms, causing patients to refuse treatment, become aggressive, discharge themselves from hospital and take additional street drugs to counter the naloxone effects. Participants believed that hospital staff should administer naloxone selectively and cautiously, and prescribe counter-naloxone medication if dosing precipitated withdrawals. In contrast, observational data indicated that participants did not always know that they had received naloxone and hospital doctors did not necessarily administer it incautiously. **Conclusions** Opiate users in urban Scotland repeatedly report harm caused by naloxone over-antagonism, although this is not evident in observational data. The concept of contemporary legend (a form of folklore that can be based on fact and provides a means of communicating and negotiating anxiety) helps to explain why naloxone has such a feared reputation among opiate users.

Types of toxicity?

a) Pharmacological toxicity

b) Behavioral toxicity

c) Reputational toxicity

Three challenges:

1) Can it be non-injectable?

2) Does dose matter?

3) Making provision universal

ADDICTION

SSA SOCIETY FOR THE STUDY OF ADDICTION

REVIEW

doi:10.1111/add.13326

Are take-home naloxone programmes effective? Systematic review utilizing application of the Bradford Hill criteria

Rebecca McDonald & John Strang

National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK

ABSTRACT

Background and Aims Fatal outcome of opioid overdose, once detected, is preventable through timely administration of the antidote naloxone. Take-home naloxone provision directly to opioid users for emergency use has been implemented recently in more than 15 countries worldwide, albeit mainly as pilot schemes and without formal evaluation. This systematic review assesses the effectiveness of take-home naloxone, with two specific aims: (1) to study the impact of take-home naloxone distribution on overdose-related mortality; and (2) to assess the safety of take-home naloxone in terms of adverse events. **Methods** PubMed, MEDLINE and PsychINFO were searched for English-language peer-reviewed publications (randomized or observational trials) using the Boolean search query: (opioid OR opiate) AND overdose AND prevention. Evidence was evaluated using the nine Bradford Hill criteria for causation, devised to assess a potential causal relationship between public health interventions and clinical outcomes when only observational data are available. **Results** A total of 1397 records (1164 after removal of duplicates) were retrieved, with 22 observational studies meeting eligibility criteria. Due to variability in size and quality of the included studies, meta-analysis was dismissed in favour of narrative synthesis. From eligible studies, we found take-home naloxone met all nine Bradford Hill criteria. The additional five World Health Organization criteria were all either met partially (two) or fully (three). Even with take-home naloxone administration, fatal outcome was reported in one in 123 overdose cases (0.8%; 95% confidence interval = 0.4, 1.2). **Conclusions** Take-home naloxone programmes are found to reduce overdose mortality among programme participants and in the community and have a low rate of adverse events.

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Naloxone kits issued across Scotland

31/07/2012

The Scottish Government today welcomed figures that show naloxone is being distributed the length and breadth of Scotland and is being made available to those at risk of opiate overdose.

Scotland was the first country in the world to announce a national naloxone programme, in November 2010. The programme is centrally coordinated and funded by the Scottish Government, empowering individuals, families, friends and communities to reverse an opiate overdose. Naloxone provides more time for an ambulance to arrive and further treatment to be given to those in opiate overdose situations.

Figures published today show that 3,445 naloxone kits were issued in Scotland in 2011/12 through this national programme. Scottish Government investment in the programme funds a national coordinator based at the Scottish Drugs Forum and support to Alcohol and Drugs Partnerships and Health Boards to enable them to deliver naloxone training and supply naloxone kits to people at risk.

UNODC (2013)

United Nations Office on Drugs and Crime

World Health Organization

DISCUSSION PAPER
UNODC/WHO 2013

Opioid overdose: preventing and reducing opioid overdose mortality

(2014)

Community management of opioid overdose

Recommendation

People likely to witness an opioid overdose should have access to naloxone and be instructed in its administration to enable them to use it for the emergency management of suspected opioid overdose.

World Health Organization

thebmj

BMJ 2014;349:g6580 doi: 10.1136/bmj.g6580

EDITORIALS

(2014)

Take-home emergency naloxone to prevent deaths from heroin overdose

Now enough experience to justify it

John Strang *professor*[1], Sheila M Bird *professor*[2], Paul Dietze *professor*[3], Gilberto Gerra *chief*[4], A Thomas McLellan *chief executive officer*[5]

[1]National Addiction Centre (Institute of Psychiatry and The Maudsley), King's College London, London SE5 8AF, UK; [2]Biostatistics Unit, Cambridge CB2 0SR, UK ; [3]Burnet Institute, Melbourne, Australia; [4]UNODC Drug Prevention and Health Branch Division, United Nations Office on Drugs and Crime, Vienna, Austria; [5]Treatment Research Institute, Philadelphia, PA 19106, USA

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

In 2012, a United Nations resolution identified the need for more effective prevention of drug overdose, including the use of naloxone.[6] The same year, the first large scale randomised

Naloxone Monograph from EMCDDA (European Monitoring Centre on Drugs and Drug Addiction) (2016)

European Monitoring Centre for Drugs and Drug Addiction

INSIGHTS EN 20

264

Preventing opioid overdose deaths with take-home naloxone

(2016)

Editors
John Strang and Rebecca McDonald
National Addiction Centre, Addictions Department, Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom

EMCDDA project group
Dagmar Hedrich and Roland Simon

http://www.emcdda.europa.eu/news/2016/1/preventing-opioid-overdose-naloxone

- Clinical guidelines across the EU should be adapted to **establish take-home naloxone provision as a care standard (e.g. on an opt-out basis)**, where (former) opioid users are routinely offered a take-home naloxone kit.

- In the UK, hepatitis-B vaccination already exists on an opt-out basis in prisons (NICE, 2012), and this could serve as model for future prison-based take-home naloxone-on-release schemes.

Conclusion: preventing heroin/opioid overdose deaths

- Particularly at-risk populations (heroin; IV>chasing; co-drug; ♂>♀)
- Times of intense risk (prison release; post-hospital; post-rehab)
- Protective effect of evidence-based treatments (esp OST)
- Pre-prepare family, peers & practitioners for emergency intervention
- Recognise responsibility (standard of care; presumption of provision)

Overall message

- Proud of what we have achieved
- Humble about how much more we need to do

Thank you