National Addiction Centre

Institute of Psychiatry at The Maudsley

King's College London

Naloxone saves lives:
Understanding its Effectiveness

Professor Sir John Strang

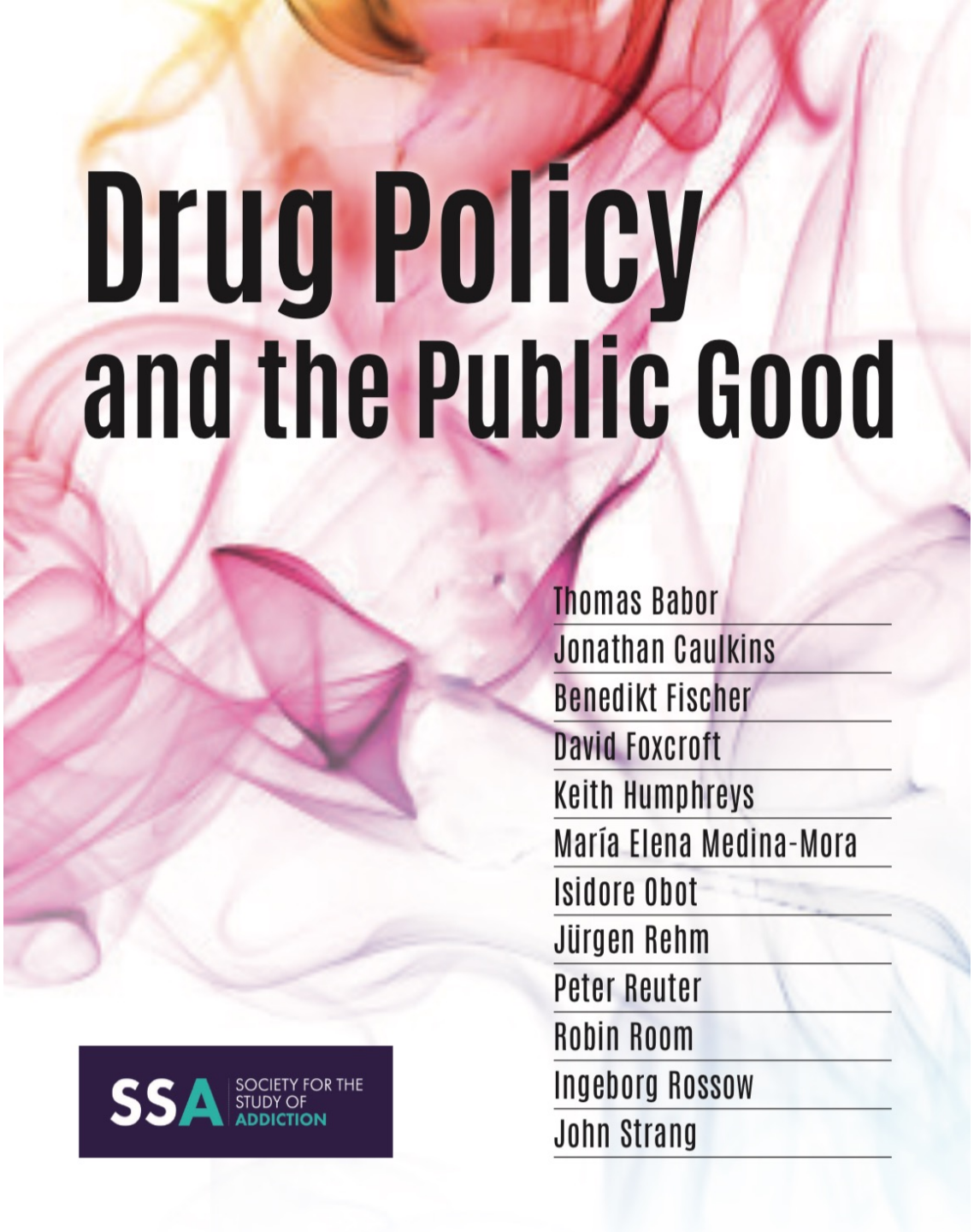
National Addiction Centre, King's College London, UK

KING'S HEALTH PARTNERS

Pioneering better health for all

Declaration (personal & institutional)

- NHS provider (community & in-patient); also Phoenix House, Lifeline, KCA.
- 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) Indivior, MundiPharma, Braeburn / Camurus, Accord/Molteni, dne and trial product supply from Camurus. (slides includes findings from work with Pharma).
- 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.
- The university (King's College London) registered intellectual property on a buccal naloxone formulation, and JS was named in a patent registration by a Pharma company as inventor of a novel concentrated naloxone nasal spray.


Drug Policy
and the Public Good
Thomas Babor
Jonathan Caulkins
Benedikt Fischer
David Foxcroft
Keith Humphreys
María Elena Medina-Mora
Isidore Obot
Jürgen Rehm
Peter Reuter
Robin Room
Ingeborg Rossow
John Strang
SSA
SOCIETY FOR THE STUDY OF ADDICTION

(2018)

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
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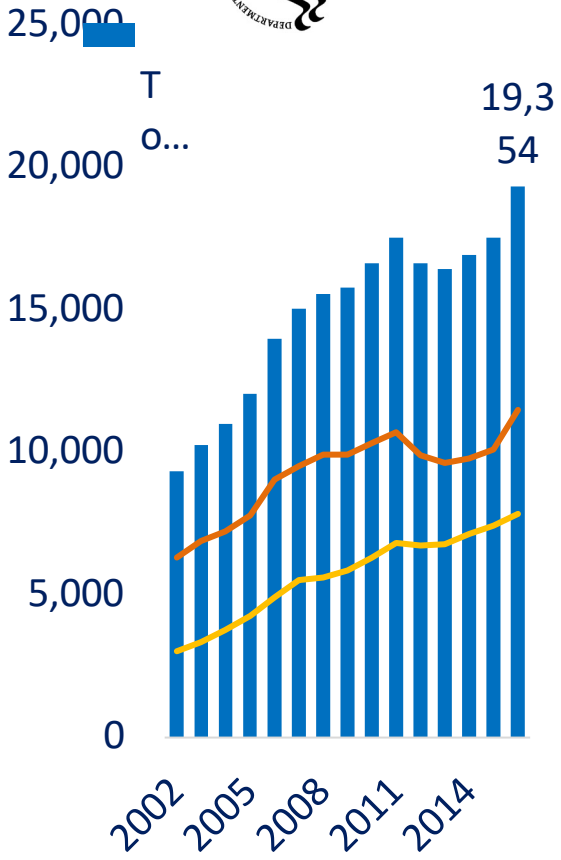
EMCDDA project group
Dagmar Hedrich and Roland Simon

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

National Institute on Drug Abuse

National Opioid Overdose Deaths, U.S.



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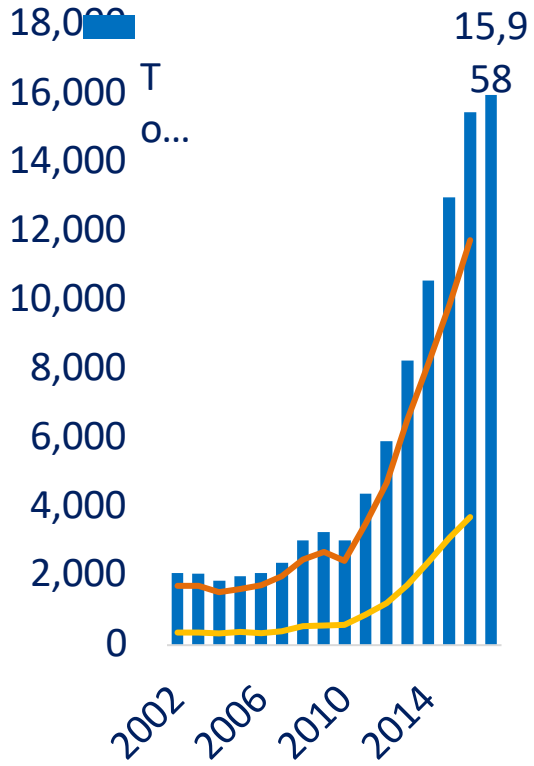
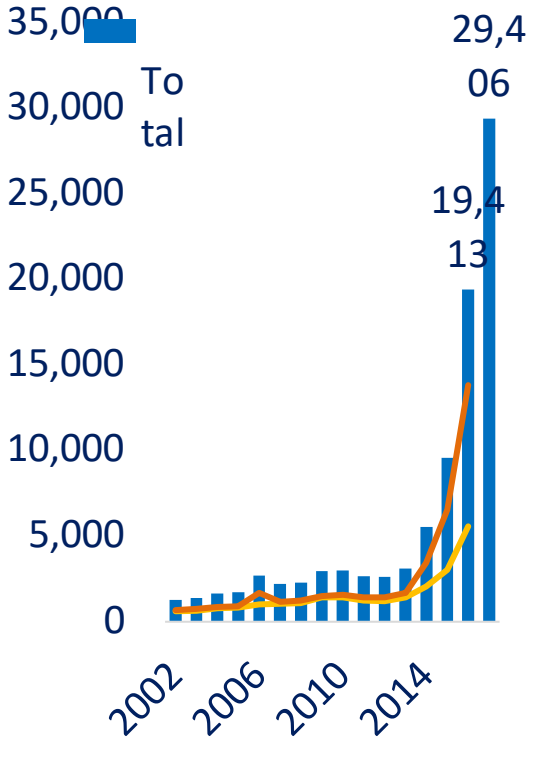


National Center for Health Statistics, CDC



: National Center for Health Statistics, CD(

UNODC
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

Cochrane reviews and NICE Technology Appraisals about prescribing (esp OST)

e.g. Faggiano et al (2007) Cochrane review of significance of dose in OST

Retention rate - RCTs: High versus low doses at shorter follow-ups: RR=1.36 [1.13,1.63], and at longer ones: RR=1.62 [0.95,2.77].

Opioid use (self reported), times/w - RCTs: high versus low doses WMD= -2.00 [-4.77,0.77] high vs middle doses WMD= -1.89[-3.43, -0.35]

Opioid abstinence, (urine based) at >3-4w-RCTs: high versus low doses: RR=1.59 [1.16,2.18] high vs middle dosesRR=1.51[0.63,3.61]

Cocaine abstinence (urine based) at >3-4 w - RCTs: high versus low doses RR=1.81 [1.15,2.85]

Overdose mortality - CPSs: high-dose versus low-dose at 6 years follow-up RR=0.29 [0.02-5.34]; high-dose vs middle-dose at 6 years RR=0.38 [0.02-9.34]; middle-dose vs low-dose at 6 years RR=0.57 [0.06-5.06]

When in particular excess?

- During methadone early treatment
- Prison release
- Post-detox/rehab

RESEARCH REPORT

doi: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

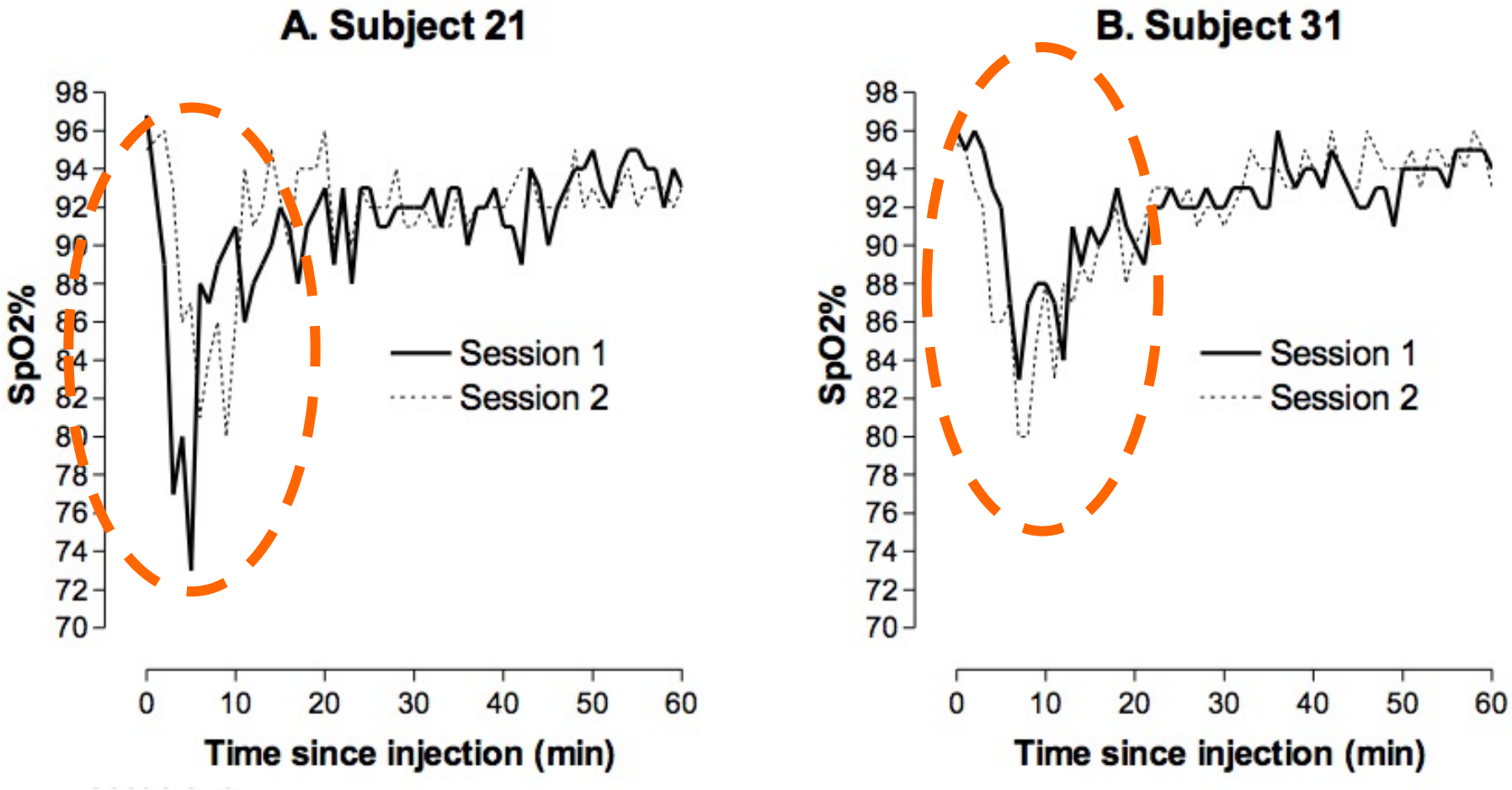
Aims To investigate drug-related deaths among newly released prisoners in England and Wales. **Design** Database linkage study. **Participants** National sample of 48 771 male and female sentenced prisoners released during 1998–2000 with all recorded deaths included to November 2003. **Findings** There 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

Why the special problem with heroin/opioids?

- It’s not a surprise

- Intravenous bolus
- Respiratory depressant
- Low therapeutic margin
- Uncertain dosing
- Aggravating other substances

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)

UNODC
United Nations Office on Drugs and Crime

World Health Organization

THE S-O-S-INITIATIVE

Stop Overdose Safely

UNODC-WHO Multi-site study on community management of opioid overdose, including emergency naloxone

AUTHORS: Gabriele Aiello (UNODC), Anja Busse (UNODC), Giovanna Campello (UNODC), Nicolas Clark (WHO), Christina Gamboa Riano (UNODC), Gilberto Gerra (UNODC), Wataru Kashino (UNODC), Dzmitry Krupchanka (WHO), Rebecca McDonald (King's College London), Vladimir Poznyak (WHO), Elizabeth Saenz (UNODC), John Strang (King's College London)

CONTACT: For further information on the S-O-S Initiative and for countries interested in joining the study with their own resources, please contact:

Vienna International Centre, P.O. Box 500, 1400 Vienna, Austria
Tel:+(43-1) 26060-0, Fax:+(43-1) 26060-5866, www.unodc.org,
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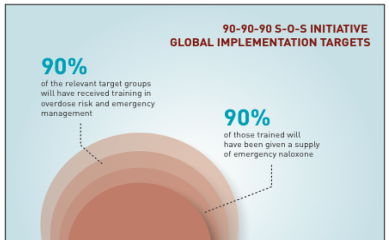
The S-O-S Initiative, promoting the expanded community management of opioid overdose, was launched by the United Nations Office on Drugs and Crime (UNODC) and the World Health Organization (WHO) at the Commission of Narcotic Drugs (CND) 2017.[1] In line with the WHO (2014) guidelines on "Community Management of Opioid Overdose", this initiative aims to save lives by promoting access to naloxone and training of potential first responders (including peers and family members) in overdose management.

United Nations Member States and other stakeholders are encouraged to work towards universal coverage of opioid overdose management strategies including naloxone, as outlined in the following three targets:



The initiative was developed within the framework of the UNODC-WHO Programme on Drug Dependence Treatment and Care (UNODC project GLOK32), which aims to promote and support, with a particular focus on low- and middle-income countries, evidence-based and ethical treatment policies, strategies and interventions to reduce the health and social burden caused by drug use and dependence.

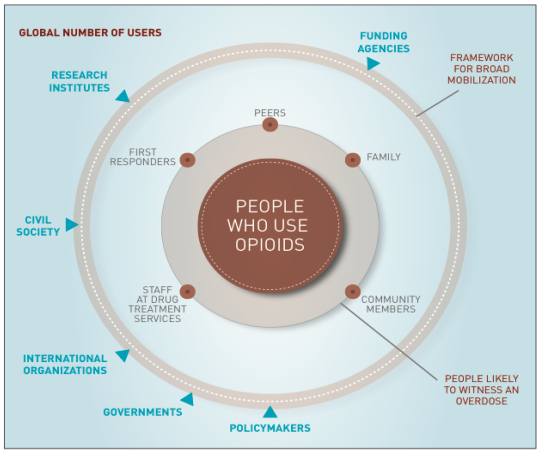
A number of high-level, international policy documents provide the global policy framework for this initiative:

- The Sustainable Development Goal (SDG) 3, Target 3.5: "Strengthen the prevention and treatment of substance abuse"
- Outcome Document of the 2016 United Nations General Assembly Special Session on the World Drug Problem (2016)
- Commission on Narcotic Drugs (CND) resolution 55/7 on "Promoting measures to prevent drug overdose, in particular opioid overdose" (2012)

The technical foundation for this initiative is defined by the following UNODC and WHO documents:

- WHO Guideline Community management of opioid overdose (2014)
- UNODC-WHO discussion paper "Opioid Overdose: Preventing and Reducing Opioid Overdose Mortality" (2013)
- UNODC-WHO International Standards for the Treatment of Drug Use Disorders (2016)
- WHO Guidelines for the Psychosocially Assisted Pharmacological Treatment of Opioid Dependence (2009)

Under the umbrella of the UNODC-WHO Programme on Drug Dependence Treatment and Care and the S-O-S initiative, a UNODC-WHO Multi-site study on community management of opioid overdose, including emergency naloxone, is currently being developed and key elements of the study protocol are presented here.



This initiative aims to support Member States in their efforts to develop policy and legal frameworks for the community management of overdose approach. Moreover, it encourages broad partnerships between national governments, regional organizations, research institutes, civil society, interested funding agencies and other entities to work towards the 90-90-90 targets.

A further aim of this initiative is to mobilize and support people likely to witness an overdose in the community, with particular focus on people who use drugs, peers, as well as family members. The ultimate goal is to contribute towards reducing deaths due to preventable opioid overdose.

THE FACTS

Drug use and drug use disorders are a public health, developmental and security problem both in industrialized and developing countries. Drug disorders are associated with health problems, poverty, violence, criminal behaviour and social exclusion. Prevention and treatment of drug use disorders are essential demand reduction strategies of significant public health importance. Opioid use disorders and drug-related deaths, often from opioid overdose, are of concern in many parts of the world.

! With an estimated 207,400 drug-related deaths in 2014, corresponding to 43.5 deaths per million people aged 15-64, the number of drug-related deaths worldwide is unacceptably high, yet has remained relatively stable, although with significant variations in some jurisdictions.

! Preventable overdose deaths contribute to between roughly a third to a half of all drug-related deaths, which are attributable in most cases to opioids, even though it is known that treatment of opioid dependence especially with long acting opioid agonists reduces the risk of

BMJ
British Medical Journal

(1996)

Heroin overdose: the case for take-home naloxone

Home based supplies of naloxone would save lives

Non-fatal overdose is an occupational risk of heroin misuse[1] and fatal overdose is a common cause of premature death in heroin users.[2-4] One of the major contributors to a fatal outcome is the inadequacy of heroin users' responses to the overdoses of their peers. They may delay calling an ambulance for fear of the police arriving, and their efforts to revive comatose users are often ineffective. The distribution of naloxone to opiate users was first mooted in 1992[5] as an intervention that would be life saving in such situations.[6] With a rising toll of deaths from heroin overdose it is time to take the suggestion seriously.

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

Naloxone has a long established use in emergency resuscitation of patients with opiate overdose.[9] Such a tried and tested

even greater risk if further opiates have been used in the interim).[15] A black market in naloxone might develop if opiate misusers wanted to protect themselves from overdoses: in such a case, however, the drug would be used for its intended purpose, and the black market would simply circumvent inequalities in access to the drug.

If naloxone were to be provided to opiate misusers for emergency resuscitation it would need some modification. The onset of many overdoses is too sudden to allow time for the victim to open an ampoule, draw up the contents, and inject himself or herself. The drug might be better provided in a dis-
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the shelf lif
emergencies—
still be life sav

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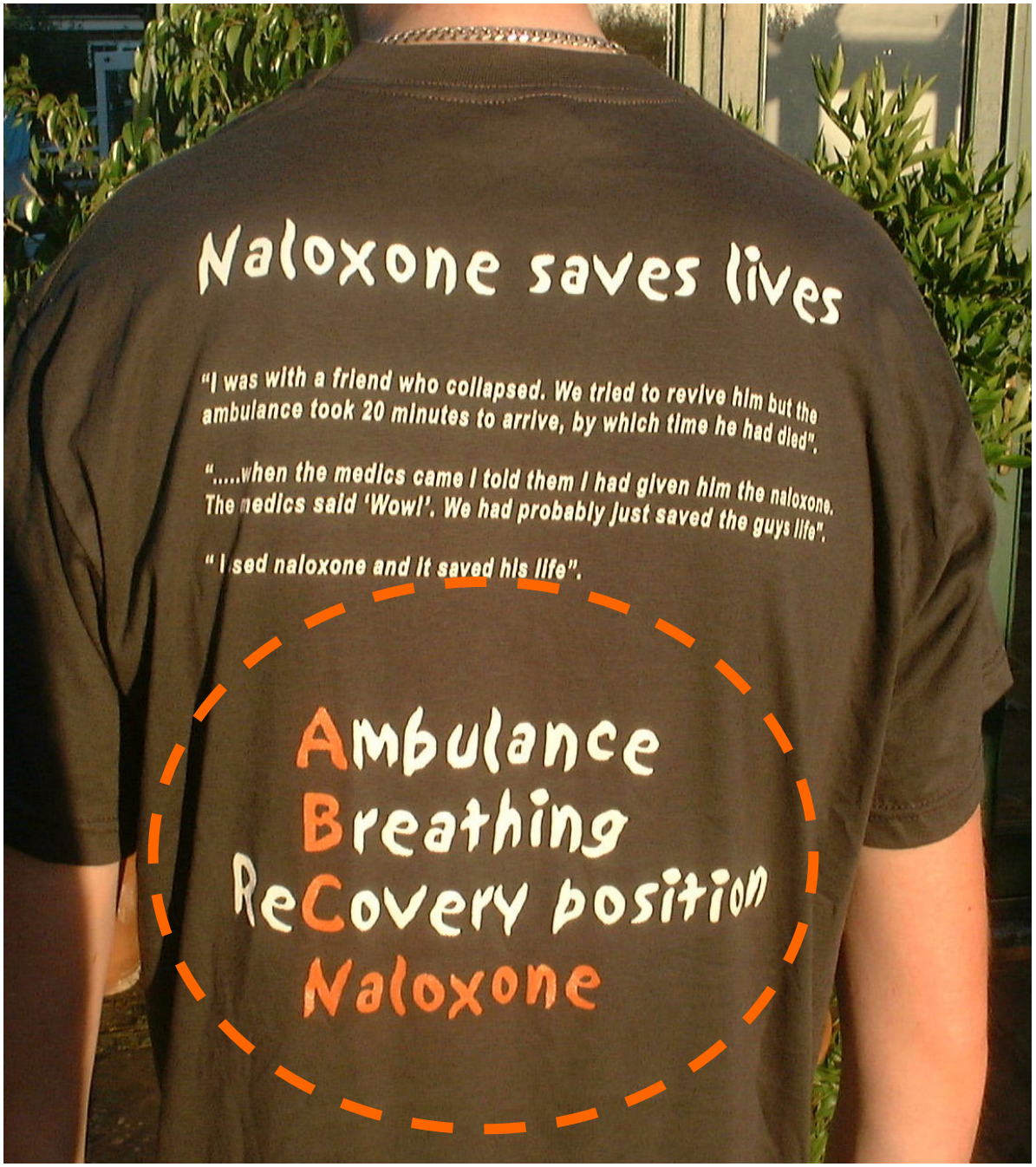
Naloxone saves lives
"I was with a friend who collapsed. We tried to revive him but the ambulance took 20 minutes to arrive, by which time he had died".
".....when the medics came I told them I had given him the naloxone. The medics said 'Wow!'. We had probably just saved the guys life".
" I sed naloxone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

Two separate levels of naloxone advocacy

- **The activist movement, civilian action, and assertion of legitimacy of take-home naloxone**
- **The adoption and incorporation by policymakers and health professionals of take-home naloxone as permitted and required action**
- *Different decisions on way forward ??*

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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.

ADDICTION

(2017)

RESEARCH REPORT

doi:10.1111/add.14033

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

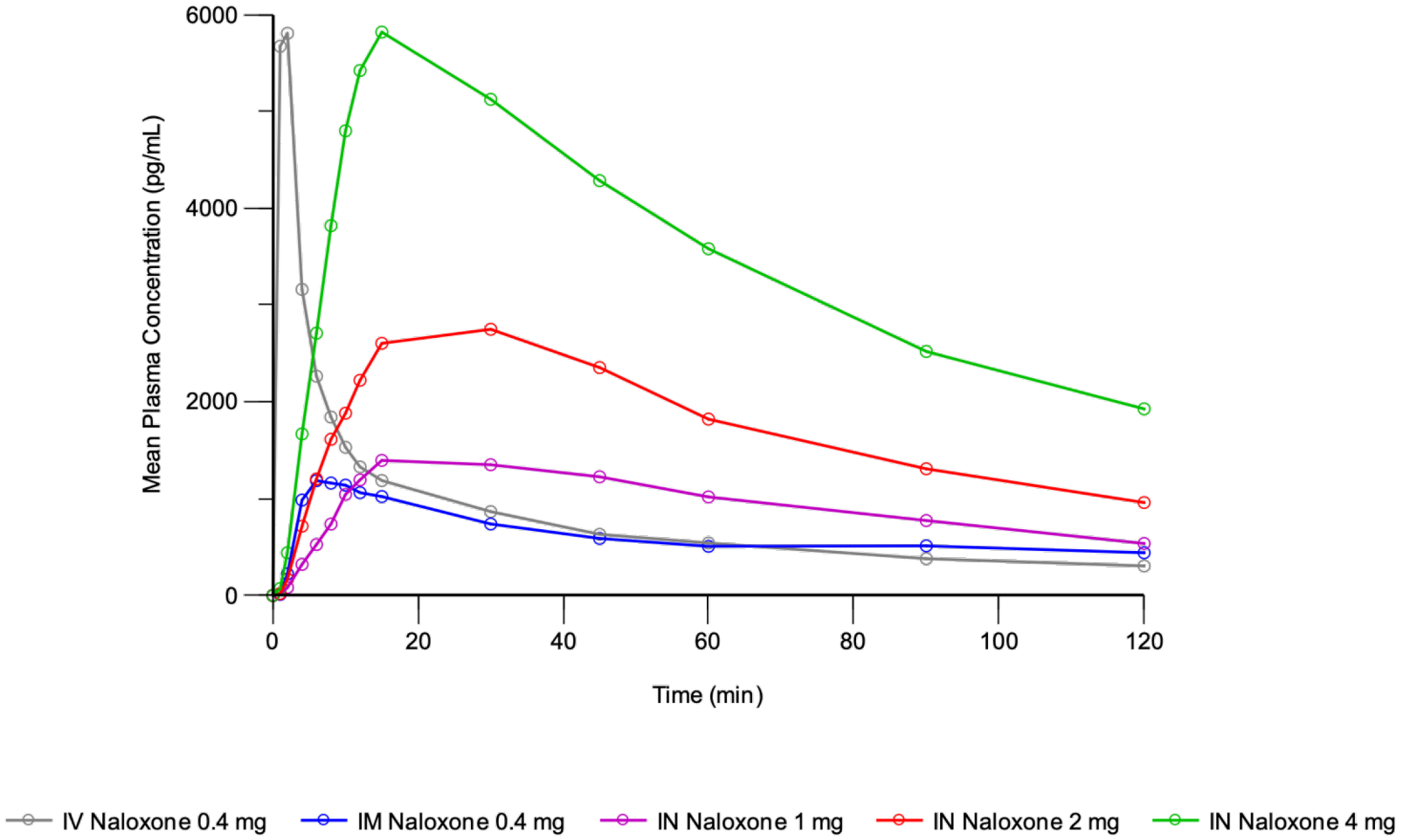
Rebecca McDonald[1], Ulrike Lorch[2], Jo Woodward[3], Björn Bosse[4], Helen Dooner[3], Gill Mundin[3], Kevin Smith[3] & John Strang[1]

National Addiction Centre, Institute of Psychiatry, Psychology and Neuroscience, King's College London, London, UK,[1] Richmond Pharmacology Ltd, Croydon University Hospital (Woodcroft Wing), Croydon, UK,[2] Mundipharma Research Ltd, Cambridge Science Park, Cambridgeshire, UK[3] and Mundipharma Research GmbH and Co. KG, Limburg, Germany[4]

ABSTRACT

Background and Aims Take-home naloxone can prevent death from heroin/opioid overdose, but pre-provision is difficult because naloxone is usually given by injection. Non-injectable alternatives, including naloxone nasal sprays, are currently being developed. To be effective, the intranasal (i.n.) spray dose must be adequate but not excessive, and early absorption must be comparable to intramuscular (i.m.) injection. We report on the pharmacokinetics (PK) of a specially produced concentrated novel nasal spray. The specific aims were to: (1) estimate PK profiles of i.n. naloxone, (2) compare early systemic exposure with i.n. versus i.m. naloxone and (3) estimate i.n. bioavailability. **Design** Open-label, randomized, five-way cross-over PK study. **Setting** Clinical trials facility (Croydon, UK). **Participants** Thirty-eight healthy volunteers (age 20–54 years; 11 female). **Intervention and comparator** Three doses of i.n. (1 mg/0.1 ml, 2 mg/0.1 ml,

Key findings: Naloxone mean PK profile



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

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.

Achievements

- Acceptability and feasibility of mobilising (a) peer group, (b) family members, (c) other personnel such as hostel staff and police
- Successful training of peers, family, staff
- Local and national schemes for pre-supply of naloxone – being done, and appear successful
- UN and WHO recognition and guidance
- Addition of concentrated naloxone nasal spray

Conclusion: naloxone next steps

- **The training** – (a) risk awareness, (b) crisis detection, (c) interim emergency care, (d) continued care
- **The intervention workforce** – peers, family, treatment/care staff, other first-responders
- **The products** – training (+/- cardio; peer/family; face2face or online; naloxone (IM/nasal; dose titration); portability
- **The science** – implementation studies; product developments & testing
- **Public policy-making and public commitment** – challenge stigma and inertia (self & others; opt-out vs opt-in)

Overall message

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

Thank you