Institution: King's College London

Unit of Assessment: UoA4 – Psychology, Psychiatry & Neuroscience

Title of case study: 14: Preventing heroin overdose deaths with take-home emergency naloxone

1. Summary of the impact

King's College London (KCL) researchers discovered that heroin overdose is a common and accidental occurrence which is usually witnessed. Risk of fatal overdose on prison release is exceptionally high with 1 in 200 dying of an overdose within four weeks. KCL researchers proposed and tested the acceptability of prior provision of take-home emergency supplies of the heroin antidote naloxone. KCL research created the stimulus for a national training project for families and carers to administer naloxone and as a result, lives are now being saved. KCL research had a substantial impact on national and international policy and service delivery with take-home naloxone programs introduced around the world. KCL researchers lead the first trial to assess the effectiveness of naloxone for prisoners on release.

2. Underpinning research

Naloxone is an antidote injection used by A&E doctors and ambulance crews to reverse heroin overdose and thereby prevent overdose death. Research at Institute of Psychiatry, KCL provided the original conception and articulation of the life-saving potential of provision of take-home naloxone (1). It was proposed as a novel harm reduction technology transfer that takes an existing proven technology (emergency naloxone) and places it with the individuals (family or peers) actually present at the overdose crisis. Research at KCL on naloxone has been led by Prof John Strang (1995-present, Professor of Addictions), Prof John Marsden (1999-present, Professor of Addictions Psychology), Prof Michael Gossop (1993-2010, Honorary Professor of Addictions), Prof Michael Farrell (1993-2011, Professor of Addictions Psychiatry), Dr Soroya Mayet (2005-08, Research worker) and Dr Victoria Manning (1997-2009, Research worker).

KCL research defined the problem and the acceptability of a potential solution

Initial KCL work in 1999 focused on estimating the extent and nature of overdose. Interviews with 312 current injecting drug users in London found overdose to be a common occurrence (38%) and being a witness to an overdose even more likely (54%). Of those who had overdosed (n=117), 81% were with someone else at the time but only 27% received emergency medical help. The majority of overdoses were accidental, only 10% were with suicidal intent (2). This evidence spurred KCL researchers to lead the first study testing the acceptability and feasibility of distributing naloxone to drug users for use in emergency situations. Surveys of 142 within-treatment and 312 out-of-treatment injecting drug users found that 70% considered naloxone distribution to be a good proposal and 89% of those who had witnessed a fatal overdose would have administered it if it had been available. The research estimated that at least two thirds of overdose fatalities could be prevented by administration of home-based supplies of naloxone (3).

KCL researchers developed the tools for implementation

KCL researchers developed and delivered training projects and studied the impact on knowledge, attitudes and behaviour of drug users, staff and carers. A KCL study in 2008 involved training 239 opiate users in naloxone administration and provided them with take-home emergency supplies. Of the 186 interviewed at 3-month follow-up, six overdoses occurred with no use of naloxone, with one death. But no deaths occurred in the 12 occasions where naloxone was used (4). KCL researchers also looked at others who may need training, particularly clinicians and families. A study of training involving 219 addiction services clinicians found that training increased the proportion willing to use naloxone in an opioid overdose from 77% to 99% (5). A KCL-led survey of 147 carers (mainly parents) identified them as another population with a huge unmet need for training in overdose management. While only 26% had received any such training, 88% indicated they would like it, especially with a naloxone administration component (6). Following this, in 2013, KCL researchers led a randomised trial of 187 carers with half receiving take-home naloxone training, half receiving basic information. At 3-month follow-up, 35% and 54% in the training group increased their knowledge and attitudes respectively, compared to 11% and 30% in the control group (7).

KCL research to decrease death in prison populations

Prison populations are at particular high risk of heroin use. KCL researchers examined the mortality rates of 48,771 prisoners released during 1998-2000. In the first four weeks post-discharge, KCL

work identified there was an 8-fold increased mortality rate (over and above the already-recognised excess mortality of heroin users) (8), with 1 in 200 being dead within four weeks of release from prison (9). Armed with these data KCL researchers recommended an overdose prevention programme in the community for this population, utilising resuscitation techniques and take-home naloxone. In 2009, the first large randomised trial (N-ALIVE) was designed by KCL researchers to investigate whether heroin overdose deaths post-prison release can be prevented by provision of take-home emergency naloxone and in 2012 it began. It involves 5,600 prisoners on release and will give a definitive conclusion on lives saved in a real-world application (9).

3. References to the research

1. Strang, J., Darke, S., Hall, W., Farrell, M., Ali, R. Heroin overdose: the case for take-home naloxone. British Medical Journal 1996;312: 1435 (62 Scopus citations).
2. Powis, B., Strang, J., Griffiths, P., Taylor, C., Williamson, S., Fountain, J., Gossop, M. Self-reported overdose among injecting drug users in London: Extent and nature of the problem. Addiction 1999;94: 471-478 (90 Scopus citations).
3. Strang, J., Powis, B, Best, D., Vingoe, L., Griffiths, P., Taylor, C., Welch, S, Gossop, M. Preventing opiate overdose fatalities with take-home naloxone: pre-launch study of possible impact and acceptability. Addiction 1999; 94: 199-204 (83 Scopus citations).
4. Strang, J., Manning, V., Mayet, S., Best, D., Titherington, E., Santana, L., Offor, E., Semmler, C. Overdose training and take-home naloxone for opiate users: prospective cohort study of impact on knowledge and attitudes and subsequent management of overdoses. Addiction 2008;103:1648-1657. Doi:10.1111/j.1360-0443.2008.02314.x (34 Scopus citations).
5. Mayet, S, Manning, V, Williams, AV, Loaring, J and Strang, J. Impact of training for healthcare professionals on how to manage an opioid overdose with naloxone: effective, but dissemination is challenging. International Journal of Drug Policy 2011;22: 9-15 Doi:10.1016/j.drugpo.2010.09.008 (3 Scopus citations).
6. Strang, J., Manning, V., Mayet, S., Titherington, E., Offor, E., Semmler, C., and Williams, A. Family carers and the prevention of heroin overdose deaths: unmet training need and overlooked intervention opportunity of resuscitation training and supply of naloxone. Drugs: Education, Prevention and Policy 2008;15:2, 211-218. Doi:10.1080/09687630701731205 (11 Scopus citations).
7. Williams, A., Marsden, J. & Strang, J. Training family members to manage heroin overdose and administer naloxone: randomised trial of effects on knowledge and attitudes. Addiction 2013. Doi:10.1111/add.12360
8. Farrell M, Marsden J. Acute risk of drug-related death among newly released prisoners in England and Wales. Addiction 2008;103:251-5. Doi:10.1111/j.1360-0443.2007.02081.x (76 Scopus citations).
9. Strang, J, Bird, S and Parmar, M. Take-home emergency naloxone to prevent heroin overdose deaths after prison release: rationale and practicalities for the N-ALIVE randomised trial. Journal of Urban Health 2013;90(5):983-996. Doi:10.1007/s11524-013-9803-1

Grants

- 2006/07 National Treatment Agency circa £120,000 to develop, deliver and evaluate naloxone training (PI: Prof Strang)
- 2010 Medical Research Council circa £1,000,000 to run N-ALIVE pilot trial (PI: John Strang, Max Parmer, Sheila Bird)
- 2009-12 Department of Health circa £700,000: drug-related deaths on release from prison and impact of provision of treatments (PIs: Farrell and Marsden)

4. Details of the impact

As a result of KCL research, take-home naloxone is now part of regular treatment provision in several parts of the world. Lives are being saved when previously death occurred in the interval between initial discovery of heroin overdose and the eventual arrival of ambulance or medical staff.

KCL research impacts on services: KCL research has had an especially substantial impact in Scotland (1a). Following meetings of KCL experts with the Scottish Minister and the Scottish Health Department, the pre-provision of emergency naloxone (alongside training in overdose management) has been introduced as part of regular clinical care for those at risk. In 2011/12 3, 445 'take home' naloxone kits were issued in Scotland through the National Naloxone Programme (2,730 issued in the community; 715 by prisons). Of these, 90% were supplied to people at risk of

opioid overdose and the remainder to consenting family members and friends. Around 10% have been used for actual overdose resuscitation (1b).Take-home naloxone programs have also been established in Wales from 2011 (1c).

Beyond the UK, from 2012 such programs have also been introduced in the Australian Capital Territory (ACT) in Australia (1d) where KCL research (including Strang 2008) is cited in the case for naloxone (1e). Provision of take-home naloxone is now in the health strategy of the state of Victoria and its provision is currently being planned from 2013 onwards (1f).

KCL research impacts on national and international policy: The Government's Advisory Council on the Misuse of Drugs (ACMD) in 2012, concluded that "naloxone provision is an evidence-based intervention which can save lives," and recommended wider provision of take home naloxone. KCL research, and evidence provided by Prof Strang, were central contributions to this report, both in its discussion surrounding community use of naloxone (Strang 1999, Strang 2008b) and in the increased risk following imprisonment (Farrell 2008 and the N-ALIVE trial) (2a).

KCL research has also had an impact at the international level. For example, as a result of a presentation by Prof Strang, the Danish government identified the need to develop plans for provision of take-home naloxone to prevent heroin overdose deaths (2b). In March 2012, a new United Nations resolution was passed as part of the work of the Commission on Narcotic Drugs to 'promote measures to prevent drug overdose, in particular opioid overdose' and a commitment 'to collect and circulate available best practices on the prevention and treatment of and emergency response to drug overdose, in particular opioid overdose, including on the use and availability of opioid receptor antagonists such as naloxone and other measures based on scientific evidence' (2c).

There has been much interest expressed in the outcomes of the N-ALIVE trial by the ACMD (2a) and organisations including the World Health Organization & United Nations Office on Drugs and Crime which cite the trial in discussions on preventing and reducing opioid overdose mortality (2d). Wider provision has recently been recommended by the UK Government's Advisory Council on the Misuse of Drugs (2012).

KCL work triggers naloxone training initiatives: KCL research (Strang et al, 2008) created the stimulus for the National Treatment Agency (NTA) to set up a network of training projects for families and carers. In 2009-10, the NTA expanded the training programme originally conceived by KCL and selected 16 pilot sites in England where 495 carers were trained to respond to an overdose. In 15 sites participants were also trained to administer naloxone. The results of the pilot, reported in 2011 by the NTA, showed 18 overdoses where carers used naloxone and two where carers applied basic life support. All the drug users survived the overdose (3a). The methodology explicitly cites KCL research (Strang 2008b) identifying the unmet training needs of carers when detailing the rationale for the programme (3b).

The impact of KCL research on overdose training and naloxone provision to develop improved methods of preventing heroin overdose deaths is stated in a letter from the National Treatment Agency, dated June 2012 (3c):

"*The NTA recognises the significant impact that research by Professor Strang and colleagues has had on the area of substance misuse treatment and, more specifically in this instance, to training in overdose management and provision of take-home naloxone. […] He was the first researcher in the UK to investigate the possibility of providing naloxone as a take-home medication to service users and their carers […] Preventing drug-related deaths is a key outcome of the government's Drug Strategy 2010. The NTA therefore looks forward to the forthcoming results of the current N-ALIVE randomised controlled trial of naloxone on-release to prisoners at risk of opioid overdose."*

KCL research also led the development of training materials for non-governmental organisations including the British Red Cross. For example, by 2012, Red Cross staff and services users from the Service User Support Team and South Gloucestershire Drug and Alcohol Service had delivered

naloxone training to 249 people locally. A video (3d), to which Prof Strang contributed, and supporting booklets, are distributed to Operations Directors throughout the UK to set up local training programmes.

Dissemination of research: KCL researchers have communicated the rationale behind the provision of take home naloxone to public and professional audiences in the UK. This includes an article in The Guardian (4a) and an interview on Film Exchange on Alcohol and Drugs (FEAD), a public engagement initiative of the Lifeline Project, a charity delivering a range of drug addiction services in the UK aimed at services users, the workforce and the wider community (4b).

5. Sources to corroborate the impact

1) Impact on Services

a. The Scottish National Naloxone Programme: what is it and how did we get there? Presentation by Andrew McAuley, Public Health Adviser NHS Scotland (Naloxone Saves Lives Conference, Swansea, November 2011) http://www.naloxonesaveslives.co.uk/presentations/andrew-mcauley.ppt
b. NHS National Services Scotland - National Naloxone Programme Scotland Monitoring Report: naloxone kits issued in 2011/12 (July 2012) http://www.isdscotland.org/Health-Topics/Drugs-and-Alcohol-Misuse/Publications/2012-07-31/2012-07-31-naloxone-monitoring-report.pdf?68803042174
c. Introduction in Wales: Provision of take-home naloxone (May 2011) http://wales.gov.uk/newsroom/socialjustice/2011/110519naxolone/?lang=en
d. Australian Capital Territory (ACT) - Expanding Naloxone Availability in the ACT (Dec 2011) http://www.atoda.org.au/policy/naloxone/
Letter from Alcohol and Other Drug Policy Unit, Australia Capital Territory available on request (2013)
e. Document prepared for the ACT: The case for the wider distribution of naloxone in Australia http://www.atoda.org.au/wp-content/uploads/The_heroin_reversal_drug_naloxone_FIN2.pdf
f. Naloxone announcement Victoria, Australia (Aug 2013) http://www.premier.vic.gov.au/media-centre/media-releases/7729-life-saving-treatment-to-reduce-overdose-deaths.html

2) Impact on National and international Policy

a. ACMD – Consideration of Naloxone (May 2012) https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/119120/consideration-of-naloxone.pdf
b. Statement of gratitude and acknowledgement from Minister of Health, Denmark; and from Adviser, Ministry of Health, Denmark (2012) available on request.
c. United Nations Commission on Narcotic Drugs Resolution 55/7 (March 2012) http://www.unodc.org/documents/commissions/CND-Res-2011to2019/CND-Res-2012/Resolution_55_7.pdf
d. World Health Organisation (2013) Opioid overdose: preventing and reducing opioid overdose mortality: https://www.unodc.org/docs/treatment/overdose.pdf

3) Training programmes

a. National Treatment Agency - NTA overdose and naloxone training programme for families and carers (Aug 2011) http://www.nta.nhs.uk/uploads/naloxonereport2011.pdf
b. Methodology - Appendices http://www.nta.nhs.uk/uploads/appendices-final.pdf
c. Letter from Chief Executive, National Treatment Agency (2012) available on request
d. British Red Cross - Community Based First Aid Film featuring Prof Strang (2012) http://www.omni-productions.co.uk/our-work/british-red-cross/

4) Dissemination of research

a. The Guardian (05 June 2009) families to receive antidote to help drug users who overdose http://www.theguardian.com/society/2009/jun/25/drug-overdose-antidote-naloxone-families
b. FEAD (Film Exchange on Alcohol & Drugs) (Oct 2010) http://www.fead.org.uk/video/video.php?videoid=294&adminPreview=true#sthash.gmx2Hwpw.dpuf