



**Ministry of
JUSTICE**

National Offender
Management Service



*Department
of Health*

Offender Health

Wellington House
133-155 Waterloo Road
London
SE1 8UG
Tel: 0207 972 2000
Fax: 0207 972 4881/1389

To: Prison Governing Governors
PCT Chief Executives (via 'the week')
PCT Offender Health Leads

CC: Integrated Drug Treatment System Regional Development Managers

21st February 2011

DH External Gateway Reference: 14394

Dear Colleagues,

RE: Randomised Trial of the Effectiveness of Naloxone

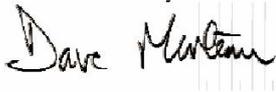
You will be aware of the high risk of fatal drug overdose for injecting drug users in the first weeks after release from prison custody.

The Medical Research Council has approved a randomised pilot trial in UK prisons into the potential for the heroin antidote Naloxone to reduce drug-related deaths when issued at the point of release to individuals with a history of injecting drug use. The N-ALIVE Trial will specifically study the number of lives that might be saved by this approach.

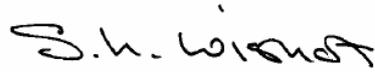
Resources will be provided in prisons to support the trial, which has been designed to fit with prison regimes. The trial has national ethical approval as well as both Research Quality Assurance and National Research Committee approvals from the Ministry of Justice.

We have attached details of the study to this letter. The N-ALIVE Trial Management Group will aim to contact suitable prisons in the near future to discuss the trial and the staffing support that comes with it. In the meantime, for any further information or questions regarding the Pilot N-ALIVE Trial, please contact the Trial Manager, Dr. Nicola Muirhead, by email: ncm@ctu.mrc.ac.uk or phone 0207 670 4636.

Yours sincerely,



David Marteau
Section Head: Substance Misuse
Offender Health



Dr Susan Wishart
Chair, National Research
Committee

Chief Investigator, Professor John Strang,
Institute of Psychiatry, Kings College London,



Principal Investigator, Professor Sheila Bird,
Biostatistics Unit, Medical Research Council,



Principal Investigator, Professor Max Parmar,
Clinical Trials Unit, Medical Research Council



**PILOT N-ALIVE
NALoxone InVEstigation**

**Prison-based Naloxone-on-release pilot randomised controlled
prevention trial
Summary V1.4, 1.2.11**



N-ALIVE Trial wallet containing the Naloxone, overdose management information and authorisation to carry card.

Summary of N-ALIVE Pilot and Main Randomised Controlled Trials

Heroin-related deaths account for around 8% of all UK deaths in individuals aged 15-44. For UK prisoners, the risk of a drugs-related death is 7.5 times higher in the first fortnight after their release than at comparable other times at liberty. Indeed, one in 200 released prisoners, with a history of heroin injection, dies from a drugs-related death within 4 weeks of leaving prison. Nearly all these overdose deaths are potentially preventable. However, existing prevention approaches have not adequately resolved the high risk of overdose death soon after release from prison or other settings where drug tolerance may be reduced. In Scotland, for example, drugs-related deaths occurring within four weeks of release from prison remained at around 13% between 2002 and 2005, despite Scottish Prison Service's adoption of methadone maintenance.

The N-ALIVE project (**NAL**oxone **InVE**stigation) has two stages: the Pilot randomized trial and the Main randomised trial. Ultimately, a total of 56,000 participants are planned to be recruited in total. The Main N-ALIVE Trial is a large prison-based randomized controlled trial, designed to test the effectiveness of giving naloxone-on-release to prisoners with history of heroin use to prevent fatal opiate overdoses. Naloxone is an opiate antagonist commonly used to reverse the effects of a heroin overdose.

The Pilot N-ALIVE Trial is aimed to demonstrate feasibility by recruiting the first 10% of participants (5,600 participants). The Main N-ALIVE Trial will assess the number of lives that could be saved by routine provision of Naloxone-on-release to adult prisoners aged 18-44 years with a history of heroin injection who are released after 7 or more days in prison (whether post-detoxification, on maintenance treatment, or otherwise). The Pilot Trial includes an ancillary study in which the participants who give their additional consent will be contacted once by phone. This sub-study will allow collection of additional qualitative information on opiate use, overdoses, and Naloxone use soon after release.

Eligible prisoners who give informed consent will be randomized to receive, on release from custody, either a pack containing a single 'rescue' injection of Naloxone or a control pack containing no Naloxone. The trial is 'double-blind' prior to the participant's release so that neither the participant nor prison staff will know the allocation until the participant opens his/her assigned pack after release.

What are the principal questions to be addressed?

Pilot Trial: What happens to the Naloxone and the participants, in terms of heroin use and overdoses (witnessed or experienced) within 4 and 12 weeks after release? Do 75% of prisoners assigned to Naloxone carry it with them in the first 4 weeks after release? Do prisons and prisoners participate in the numbers expected and required for the Main Trial? Do the N-ALIVE procedures work well logistically in the National Offender Management

Service, or will they need to be changed for the Main Trial? If changes are necessary, what needs to be done?

Main Trial: Does giving Naloxone on release to prisoners with a history of heroin injection reduce heroin overdose deaths by 28% in the first 12 weeks after release?

Why do the Pilot and Main Trials need to be randomized?

N-ALIVE's intervention has been specifically designed to fit in with prison procedures and to disseminate information about emergency Naloxone to prisoner-peers (whether randomized or not). It needs prison-based staff specifically for N-ALIVE – as per any well-delivered intervention for prisoners (e.g. hepatitis B immunization; methadone maintenance).

The N-ALIVE Pilot and Main Trials have to be randomized for the following reasons. First, Take-home Naloxone is not currently routinely issued by English prisons, nor by any prison system outside of the UK. Scotland's policy on take home Naloxone has, however, changed in 2011. Second, the risks for ex-prisoners are unknown (even by them). We cannot anticipate how availability of Naloxone-on-release might alter the riskiness of their heroin use behaviour and thus there is the possibility that providing Naloxone in this way may do more harm than good. We shall only be able to clearly assess this through a randomized trial. Third, there is also the possibility that providing Naloxone in this way has no effect because either the individual does not carry the Naloxone with them or, when needed, the Naloxone is not used or not appropriately used. Fourth, the N-ALIVE awareness/information video is a prison-wide backdrop, which aims to reach all prisoners attending the prison's induction session on drug awareness – not only to inform them about N-ALIVE but so that, as peers, they know about, and how to use, emergency Naloxone, and also understand why it is necessary to randomize. Fifth, prisoners realise better than anyone that, for prisons to improve (health) services to prisoners, effectiveness has to be beyond question for the public to be persuaded – and that requires randomization. Sixth, we are dealing with a 'captive population', and thus prison-based research must cleave to the highest ethical and scientific standards, which means randomization of individuals and the need for prevention policies to demonstrate cost-effectiveness. Finally, for context on costs, less than £1.60 per day is spent on a prisoner's food. Thus, UK prisons are hard-pressed but they can, *and have*, delivered unimpeachable high-quality research evidence using now-internationally recognised 'inside methodologies', because they were properly supported to do so.

Where will the N-ALIVE Pilot and Main Trials be conducted?

Both the N-ALIVE Pilot and Main Trials will be conducted in prisons in England, under the National Offender Management Service.

How will the results of the trials be used?

The N-ALIVE Trials will inform health policy for prisons and other drug treatment agencies. Public health policy importance is recognized by the Department of Health, the Scottish Executive, the Ministry of Justice and the

Home Office. The reduction of drugs-related deaths has been a key target of UK Governments' Drugs Strategy, which at the last report was being failed. If the Main N-ALIVE Trial demonstrates that Naloxone-on-release delivers a cost-effective 28% reduction in prisoners' drugs-related deaths in the first 12 weeks after release, then the prison services need only remove the randomization step to implement the intervention. All other procedures would operate as during the trial. It is estimated that, if implemented, the methods used in the N-ALIVE Trial could save in the order of 200 lives a year in the UK.

The results of both the Pilot and the Main randomised controlled trials are also likely to generate considerable international interest.

Current situation

The Pilot N-ALIVE Trial has been funded by the Medical Research Council. The trial was initiated in spring 2010 and participant recruitment via prisons is scheduled to begin in early 2011.

Contact information For more information, please contact the N-ALIVE team: n-alive@ctu.mrc.ac.uk or Nicola Muirhead on 0207 670 4636