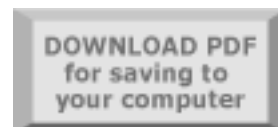


## DRUG ALCOHOL FINDINGS **Your selected document**

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### ► [Comparison of methadone and buprenorphine for opiate detoxification \(LEEDS trial\): a randomised controlled trial.](#)



**Wright N.M.J., Sheard L., Adams C.E. et al.**

**British Journal of General Practice: December 2011.**

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*Three English prisons hosted the first randomised trial of tapering doses of buprenorphine versus methadone to ease the withdrawal of opiate users entering prison. As outside prison, there was little difference in their effectiveness, and three months later just a fifth of the (former) prisoners were assessed as no longer using illegal opiates.*

**Summary** Subject to clinician discretion, in English prisons [sublingual](#) buprenorphine or oral methadone are recommended first-line medications to help ease the process when new prisoners ask to be withdrawn from the opiate-type drugs they had been taking before admission. Outside prison, these options have been found roughly equivalent in enabling patients to complete the process and achieve abstinence from opiate-type drugs. The featured study was the first to test whether this remained the case in prison.

Study treatments were offered between 2006 and 2008 at the healthcare departments of three remand prisons (two for men, one for women) in the north of England. In the medical reception areas researchers asked newly admitted prisoners aged 21–65 to join the study if urine tests had indicated use of illicit opiates, they said they wanted to detoxify and remain abstinent, and they were expected to stay in custody for at least another 28 days. Of the 439 who could have joined the study, 289 agreed and started one of the two treatments. Typically they were around 31 years of age and had used opiates for 10 years, just over half injecting and most of the rest smoking the drugs.

These 289 patients were randomly allocated either to a methadone or a buprenorphine detoxification programme overseen by general medical staff. No attempt was made to 'blind' patients or clinicians to the allocation. Detoxification was typically conducted over 20 days, tapering down from a five-day stabilisation dose of 30mg methadone or 8mg

buprenorphine daily.

The primary outcome was whether patients were abstinent from illicit opiates **eight days** after completing detoxification, confirmed by urine test if they were still in the original prisons or by their own accounts or clinical notes if they had left. By these means it could be ascertained whether 213 of the 289 patients had used opiates after completing their detoxifications. Similar procedures were followed one, three and six months after detoxification, when 159, 94 and 60 patients (the latter considered too few for analysis) could be reassessed.

## Main findings

At no point in the follow-up period were patients prescribed one of the medications significantly more likely to be opiate-free than those prescribed the other. This was the case whether all patients were included in the analyses (the assumption being that missing cases were not abstinent) or only those who could be reassessed. Eight days after the programmes ended, just over 50% of both sets of patients were assessed as abstinent (around 70% of those who could be reassessed), a figure which fell to 20% (62% of those who could be reassessed) three months after the programmes ended.

There remained no statistically significant differences between abstinence rates after other variables had been taken in to account, of which initially the most important was whether the prisoner was still in prison. If they were, abstinence was 18 times more likely at eight days and 13 times at one month. By three months when just 17% of patients could be urine tested [Editor's note; indicative that most had left their initial prisons], whether the patient had tested abstinent two months before was the dominant factor. In contrast, whether they had tested abstinent at the eight-day point was unrelated to abstinence at three months. Age and variables reflecting treatment and opiate use history were unrelated to abstinence.

## The authors' conclusions

In a prison general practice setting, methadone and buprenorphine were equally effective in helping patients become abstinent eight days after their detoxifications ended. Being abstinent at this point was a strong predictor of being abstinent one month after the programmes ended; remaining in prison also strongly predicted abstinence. These findings suggest that on effectiveness grounds, either methadone or buprenorphine should be offered as a first-line treatment, taking into account patient preferences. However, sublingual buprenorphine is more vulnerable to being 'diverted' to the illicit market in drugs in prison, so where this is a problem, methadone is preferable.

Shortly after release there is a high risk of detoxified former prisoners relapsing and dying from drug-related causes. To minimise the risk of relapse, it would be prudent to offer detoxification only to patients who have made a planned decision to undergo it and whose care can be handed over to community primary care services on release.

**FINDINGS** In a prison setting this study confirms the rough equivalence of methadone and buprenorphine as detoxification medications. Along with other studies, the conclusion is that, as outside prison, these are the first-choice agents in terms of completing detoxification from illegal opiate use and the comfort of patients. The usual criterion of completion of detoxification is less relevant in prison where simply leaving the setting is

not an option, non-completion is often for reasons (such as release or transfer) outside the control of both patients and medical staff, and patients who do opt to end the treatment may still be forced to complete detoxification unaided due to the difficulty of obtaining illegal drugs. However, 'difficulty' is not 'impossibility', as exemplified by urine test results from the 152 patients tested in prison eight days after the end of their detoxification programmes, of whom 33 tested positive for illegal opiates. It also seems from the study and from others that abstinence from illicit opiates achieved in the controlled environment of a prison is no indication of lasting abstinence. By three months after programme end, patients assessed as abstinent at eight days were non-significantly less likely still to be assessed as abstinent.

### Other UK trials

Some of the same authors had previously conducted a [similar trial](#) in a remand prison in Leeds, but this time among men only and comparing buprenorphine with an alternative opioid drug, dihydrocodeine. Results favoured buprenorphine. Five days after completing the programmes, significantly more buprenorphine patients tested negative for opiates (57% v. 35%). However, this advantage did not translate in to longer-term gains from one to six months after programme end. At three months, 28% of all the patients were assessed as abstinent and 52% of those who could be assessed, similar to the featured study's tally of 20% and 62%.

Given that prison enforces an end to dependent use if not to use altogether, a more relevant criterion on which to judge detoxification methods may be the comfort of the patients. This was the one of main criteria in a [randomised trial](#) of detoxification from opiates in a prison in southern England, which pitted methadone against the non-opioid drug [lofexidine](#). It found the two medications offered equivalent amelioration of withdrawal symptoms, and that of those patients able to complete the process, 88% of methadone patients did so compared to 70% in the lofexidine group – not a statistically significant difference, but suggestive of an advantage for methadone of the kind seen outside prison.

### Reviews and guidance

A [review published in 2010](#) applied a new methodology to combine results from comparisons of the main medications used to help opiate-dependent patients complete withdrawal. It enabled the analysis to include *indirect* comparisons between two medications which, even though they may not have not been compared head-to-head, have been compared to the same third medication. The criterion of effectiveness was [completing](#) the detoxification programme. Taking all the data in to account, it was estimated that for every 100 people who completed a methadone detoxification, 164 would complete if prescribed buprenorphine, but in the three head-to-head comparisons the medications seemed roughly equivalent. From 1.6 to nearly four times as many people completed procedures based on the two opiate-type medications (buprenorphine and methadone) than those based on either of the non-opioid medications (lofexidine and clonidine). It was concluded that both opiate-type medications were probably more effective than clonidine and lofexidine and that buprenorphine seemed the most effective of all at promoting completion. These were also the findings of another [major review](#) which used a different methodology to combine findings.

As the authors comment, the prison setting imposes special limitations on patient choice, for any individual patient there may be overriding contraindications, and everywhere cost is an issue, as is the extra time involved in supervising buprenorphine administration set against its greater safety in overdose. But on effectiveness grounds alone, in general choice of medication in can largely be based on the individual's informed preferences, based partly on the implications of the research cited above. British studies ([1 2](#); details in [background notes](#) to an earlier Findings analysis) have found that patients who choose one of the least effective medications (lofexidine) do as well as those who choose the most effective (methadone or buprenorphine), possibly because the least dependent and perhaps most motivated patients opt to do without opiate-type drugs.

British guidance ([1 2](#); details in [background notes](#) to an earlier Findings analysis) adds that patients already being prescribed methadone or buprenorphine on a maintenance basis or to stabilise them prior to detoxification should normally continue with the same medication. Though this should not override patient preference, guidance sees clonidine and lofexidine as most suitable for patients with low levels of dependence or who may not be dependent at all.

Completion is the main criterion for the success of detoxification, but it is a success which comes with risks. The guidance cited above warns that the loss of tolerance (the ability to tolerate higher doses after becoming used to regularly taking a drug) following detoxification heightens the risk of overdose and death if patients return to opiate-type drugs, especially if at the same time they drink or take benzodiazepines. This risk is greatest among patients who complete the detoxification phase of the programme ([1 2 3](#)), highlighting the need to carefully select and prepare detoxification candidates and to invest in aftercare. Patients who complete withdrawal in protected environments without having chosen to stop using opiates may be particularly ill-equipped to sustain an opiate-free life when they leave. Ironically, outpatient programmes which test the patient's resolve in real-world conditions may be safer because relapse is more likely to occur before tolerance is eliminated. See fuller discussion in [background notes](#) to an earlier Findings analysis.

*Thanks for their comments on this entry in draft to Nat M.J. Wright of HMP Leeds in England. Commentators bear no responsibility for the text including the interpretations and any remaining errors.*

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