DRUG & ALCOHOL FINDINGS Research analysis

This entry is our analysis of a study added to the Effectiveness Bank. The original study was not published by Findings; click Title to order a copy. Free reprints may be available from the authors – click prepared e-mail. Links to other documents. Hover over for notes. Click to highlight passage referred to. Unfold extra text. The Summary conveys the findings and views expressed in the study. Below is a commentary from Drug and Alcohol Findings.

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Opioid treatment at release from jail using extended-release naltrexone: a pilot proof-of-concept randomized effectiveness trial.

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Addiction: 2015, 110(6), p. 1008–1014.

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Though few seemed willing to try this treatment, among those who did, opiate-blocking injections active for about a month helped formerly dependent prisoners in New York City's jail avoid relapse to regular opiate use after release.

SUMMARY For the first time in a typically short-stay municipal jail, the featured study assessed whether long-acting injectable naltrexone (an opioid 'antagonist' which blocks the effects of opiate-type drugs for about four weeks) can act as an anti-relapse bridge on release. In these jails opioid-dependent prisoners are usually detoxified from these drugs but do not start maintenance prescribing or relapse prevention programmes.

From January 2010 to July 2013 the study recruited 34 opioid-dependent men in New York City's jails who were not in and not planning to enter methadone or buprenorphine maintenance programmes, and who instead agreed to be allocated at random to a long-acting naltrexone injection versus no medication (the control group) in the week before their release. They were also scheduled for a repeat injection four weeks later. All the participants in the study received brief counselling and referral to treatment services they could apply to on release. Additional to medication, naltrexone patients also saw a doctor who supported and encouraged their retention in the naltrexone programme and promoted access to other community and 12-step recovery supports. Participants averaged in their 40s and were mostly unemployed. The trial was confined to men because most otherwise suitable female prisoners were already on pre-release methadone maintenance.

Naltrexone's effectiveness was primary judged by whether during the first four weeks of their release, the ex-prisoners had relapsed to opioid use, defined as having used these drugs on 10 or more days as revealed by their responses to questionnaires and by weekly urine tests in weeks two, three and four. Because before imprisonment all the prisoners had been using opioids (primarily heroin) daily, a positive or missing urine result was assumed to signify seven days of opioid use.

Key points
From summary and commentary

A US study recruited opioid-dependent prisoners who were not in and not planning to enter substitute prescribing programmes, and who agreed to be allocated at random long-acting naltrexone injections just before their release and again four weeks later.

In the eight weeks after release prisoners allocated to naltrexone were much less likely to lapse or relapse to use of opiate drugs but slightly more likely to inject.

Where substitute prescribing is available, few prisoners may opt for long-acting naltrexone, but whose who do will be helped to avoid re-addiction to opiate drugs, though not necessarily to improve other aspects of their lives or their substance use.

Main findings

All but two of the 17 prisoners allocated to naltrexone accepted the treatment and were injected with the drug, typically about five days before release. One of the injected patients was retained in prison, leaving 16 who could be assessed after release. Of these, 12 also accepted the second injection four weeks later. During the first four weeks after release, 15 of the 17 (88%) control offenders had 'relapsed' (defined by the study as having used opioids at least 10 times) compared to just six of 16 (38%) patients offered naltrexone, a large and statistically significant difference unlikely to have occurred by chance. Across the eight post-release weeks assessed by the study, over 90% of control patients had relapsed compared to half those offered naltrexone.

Confirming the impact of the injection, compared to controls, patients offered naltrexone were significantly more likely to submit urine tests free of opioids and to have sustained abstinence according to these tests and to their own accounts. This was the case not only in the first four weeks but also across the entire eight weeks after release, when eight of the 16 naltrexone patients remained abstinent but just one of the 17 controls.

There were, however, no significant differences on other measures including having injected drugs (6% of controls versus 25% offered naltrexone), used cocaine (47% versus 56%), or been re-imprisoned (41% versus 31%). There was also little difference in the small proportion who participated in other drug treatment programmes. There were no study-related serious adverse events, including no deaths and no accidental opioid overdoses.

The authors' conclusions

Compared with usual care and no medication, long-acting naltrexone is associated with significantly lower rates of relapse to regular use of opioid drugs among men in the United States following release from jail. The long-acting form of the medication was acceptable to a large proportion of participants, and half those offered it and who left jail did not use opioids in the eight weeks after their release. The results are comparable to those from initiating maintenance prescribing of methadone or buprenorphine shortly before release, demonstrating the feasibility and clear advantages of initiating pharmacotherapy in prison rather than just referring the prisoner to community services or offering treatment only after they leave prison.

However, the trial did not compare naltrexone to an inactive but otherwise identical placebo, and patients and researchers both knew whether a prisoner had been allocated to naltrexone versus to the control group, meaning the results might to some extent be due to the expectations of the participants rather than the effects of the medication

results might to some extent be due to the expectations of the participants rather than the effects of the medication. Generally already on methadone, no women were included in the trial, an indication of the challenge of attracting prisoners to opiate-blocking treatment when opioid medications are also available. Further, the results did not reflect what might happen if this treatment were widely implemented by a large urban jail. Follow-up trials at two US sites are intended to recruit a much larger sample and to include women.

COMMENTARY In the UK, neither implants nor long-acting injections of naltrexone have been licensed for medical use. They can still be and have been prescribed, but patient and doctor have to accept the added responsibility of using a product which has not yet been shown to meet the safety and efficacy requirements involved in licensing. Until a product licence has been issued for these medications for the treatment of opioid dependence, their role in the UK will probably be minor or experimental or largely confined to private practice, and use in prisons is unlikely.

The featured study showed that among (formerly) opiate-dependent prisoners prepared to accept this treatment, and for whom maintenance prescribing is unwanted or unavailable, long-acting naltrexone is greatly superior to usual care in preventing return to regular opioid use in the weeks immediately after release. The same ability to help avoid relapse after withdrawal has been found for non-prisoner patients in Norway and in a trial in Russia in which comparison patients were injected with an identical but inactive placebo. However, with such a small and probably atypical sample, it is unsafe to assume that the featured study's results would apply to opiate-addicted prisoners in general, and an eight-week trial does not give sufficient time for the treatment to demonstrate (or fail to do so) its ability to help overcome addiction on a longer term basis. Additional recovery support was offered to the naltrexone patients before their release which may also have partly accounted for their doing better on release.

A worrying finding in the featured trial was that many more former prisoners offered naltrexone injected drugs after release from prison – 25% versus 6% of controls. Also, slightly more had used cocaine (56% versus 47%) and only slightly fewer had been returned to prison (31% v. 41%). Given the small size of the sample, none of these differences were statistically significant, but they do seem to suggest that while they restrict use of heroin or other illegal opioids, naltrexone injections did not control other forms of drug use and did little to stabilise other aspects of the patients' lives.

Though for randomised trials seen as a flaw, the lack of a placebo mimicking naltrexone among control patients means the study's results are closer to reflecting real-world conditions, when patients would know whether they had been injected with naltrexone, and this knowledge and associated expectations would affect how they reacted.

That it took over three years to find the 34 prisoners in New York City's jails who joined the featured study, and that no women could be included, seems to indicate that among prisoners the demand for long-acting naltrexone is small. In any treatment which does not offer substitute drugs, once patients do start, drop-out is typically substantial, apparent in the featured study in the inability to re-contact six of the 16 naltrexone patients and nine of the 17 no-medication patients for eight-week follow-up interviews. Unless incentivised in some way – for example, by offering early release – it seems likely that naltrexone injections will be accepted only by prisoners who, though dependent on opiate-type drugs before their sentence, are prepared to commit to a month without being able to experience the effects of these drugs, yet are not confident they can resist re-addiction on leaving prison – an unusual combination. An often false confidence in their determination and ability to build on prison by starting an opioid-free life on release leads many patients to reject medication of any kind.

The featured trial tested naltrexone injections against no medication rather than against what may be considered the 'gold standard' approach of offering methadone or buprenorphine maintenance in prison and seamlessly continuing it on release. However, a Norwegian study did make this comparison, randomly allocating prisoners dependent on opiates before their sentences either to methadone maintenance or to a six-month naltrexone implant in the month before their release date. Of the 111 inmates who qualified for the trial, just 11 started methadone treatment in prison and 16 were implanted with naltrexone. Among the 44 patients in the trial, compared to before their imprisonment, on average in the six months after release use of heroin and illicit benzodiazepines had fallen substantially, but not by significantly more among those allocated to methadone versus to naltrexone. Even if long-acting naltrexone and methadone are of equivalent effectiveness among those prepared to be randomised to either treatment, methadone may be more acceptable to greater range of prisoners.

Long-acting naltrexone also has a role among offenders under criminal justice supervision outside prison. In a US study, among offenders who chose or agreed to this treatment, it helped support an improvement in rates of abstinence from alcohol and other drugs over three times that for psychosocial treatment only, over four times that for oral naltrexone, and over 10 times that for buprenorphine maintenance.

More broadly, an Effectiveness Bank hot topic concluded that the clearest candidates for naltrexone implants and injections are patients who are motivated to return to a life without opiate-type drugs, and who have the resources, stability and support to sustain this, are unlikely simply to use other drugs instead, but who when free to experience opiates, cannot resist using them. Long-acting formulations may also be considered for unstable patients at very high risk of overdose, but who will not accept or do poorly in substitute prescribing programmes. Other candidates might include those unwilling or unable to accept daily supervised consumption if this is a requirement of being prescribed substitute medications.

Thanks for their comments on this entry in draft to David Marteau of the University of East London, formerly of the Offender Health section at the UK Department of Health. Commentators bear no responsibility for the text including the interpretations and any remaining errors.

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