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▶ Adjunctive counseling during brief and extended buprenorphine-naloxone treatment for prescription opioid dependence.

Weiss R.D., Potter J.S., Fiellin D.A. et al.

Archives of General Psychiatry: 2011, 68(12), p. 1238–1246.

From the USA, the first large study to randomly allocate patients dependent on prescription opioids to different treatments found that despite wanting to detoxify, all but a few relapsed after withdrawal from substitute medication; more intensive and specialist counselling did not help.

Summary Editor's introduction: In this study treatment was based on prescribing buprenorphine-naloxone tablets. Buprenorphine is the main alternative to methadone for substitute prescribing treatments for opiate addiction. Like methadone it offers the opiate-type effects patients have become dependent on in a way which enables them to get on with their lives rather than dominating them. It can be taken daily or once every two or three days and fatal overdose is much less likely than with either heroin or methadone, making it particularly suitable for non-specialist settings such as primary care. Adding the opiate blocking drug naloxone to buprenorphine (the combination marketed as Suboxone) is intended to reduce the risk of the tablets being crushed and injected rather than absorbed under the tongue as intended. When injected but not when absorbed under the tongue, naloxone blocks the opiate-type effects of buprenorphine, reducing the incentive to inject. For this reason the combined medication is considered particularly suitable for non-specialist settings and where supervising consumption is not possible or desirable.

In the USA many patients dependent on opiate-type drugs use not illegal drugs like heroin but opioid painkillers produced for medical use. How these patients will react to more or less provision of counselling in opiate substitute prescribing programmes is unclear, as is whether their generally better prognosis means they can more quickly be withdrawn from substitute medications. The featured study addressed these questions at outpatient substance abuse treatment clinics prescribing buprenorphine-naloxone (Suboxone) as a substitute medication. It planned to stabilise patients on the medication and then withdraw them over a short period, offering more extended stabilisation and withdrawal to those who did not succeed at the first attempt. The aim was to test the kind of 'stepped' treatment strategy which might be applied in routine practice, and at the same time to test whether offering additional specialist substance misuse counselling would improve on the kind of counselling/medical care available in primary care settings.

At the ten clinics 653 adult patients dependent on prescription opioids joined the study. They had to

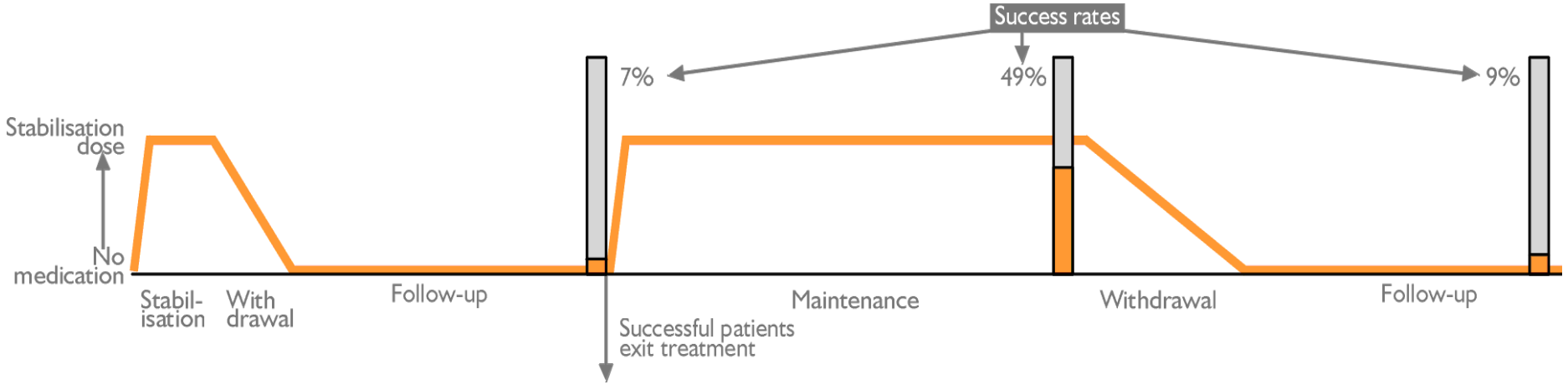
be willing to be detoxified and have clearance from their doctor if the prescription was for pain. People with an appreciable history of heroin use or dependence, who had injected the drug, or were dependent on other drugs, could not join the study. Nine in 10 of the patients were white and nearly two thirds were employed full time. On average they had taken opioid analgesics nearly every day in the last month and had used these drugs for five years. A third had previously been treated for their opioid dependence. Very few were using cocaine. Four in ten reported chronic pain.

Initial detoxification treatment consisted of induction on to buprenorphine-naloxone, two weeks of stabilisation, then two weeks over which doses were reduced to zero. Patients were then followed up for eight weeks. Medication was dispensed weekly to be taken daily. Patients who completed this entire programme successfully with minimal continuing opioid use simply ended their treatment. But as soon as this became apparent, patients who were not going to complete successfully were offered more extended treatment consisting of 12 weeks (rather than two) stabilisation on buprenorphine-naloxone and reduction to zero over four (rather than two) weeks. As before, they were then followed up for another eight weeks. To be considered to have responded well to this extended treatment, patients had to have not used opioids during their final week of stabilisation and in at least two of the previous three weeks. Additionally, these patients were assessed against a similar yardstick at the end of the eight-week follow-up.

During each phase patients were randomly allocated to (usually brief) weekly sessions of primary care-style counselling/care from their doctors, or to this plus longer sessions of specialist substance misuse counselling initially twice a week. These sessions were offered while substitute medication was being prescribed and at the start of the initial eight-week follow-up period. Using a skills-based format with interactive exercises and take-home assignments, the more specialist counselling covered a wider range of relapse prevention issues in greater depth, including coping with high-risk situations, managing emotions, and dealing with relationships. Both approaches were based on manuals from an earlier study of buprenorphine-naloxone treatment in primary care.

Main findings

As defined by the study, just 43 of the 653 patients − about 7% − successfully completed initial stabilisation/detoxification ▶ *chart*. These outcomes were assessed eight weeks after buprenorphine-naloxone had been withdrawn. In contrast, while still being prescribed maintenance doses of the drug, and even though they had 'failed' the initial treatment, half (49.2%) the 360 patients who took up the offer of further treatment were successful, meaning they used virtually no other opioid drugs. But these patients too generally responded poorly after their substitute medication was withdrawn; just 31 or about 9% could be shown to have virtually avoided opioid use eight weeks later, a statistically significant difference from when they were still being prescribed maintenance doses. At none of these measurement points had those offered extended and specialist counselling done better than those just offered primary care consultations with their doctors.



Similar results were found when 'success' was defined as complete abstinence from opioid use in the previous four weeks. Among patients offered extended treatment, over the last four weeks after being withdrawn from buprenorphine-naloxone, and virtually regardless of the counselling option, just 6–7% had been abstinent, significantly fewer than the 36% over the last four weeks week of being prescribed maintenance doses. Urine tests corroborated these results.

Chronic pain at the start of the study made no difference to outcomes or the impact of the counselling options, and nor in the first phase did a history of heroin use. However, in the extended treatment phase patients who had ever used heroin were less likely to be more or less opioid-free (37% v. 54%) while maintained on buprenorphine-naloxone.

Nearly all the medication doses were taken and most counselling sessions of whatever kind were attended, ranging from nearly 82% of primary care visits in the first phase to 64% of drug counselling sessions in the second. Most patients experienced some adverse effects possibly related to the medication, but very few left treatment as a result. Psychiatric symptoms were the most common serious adverse events, particularly (in five cases) depression leading to hospitalisation, all soon after completion of medication withdrawal.

The authors' conclusions

While maintained on full doses of substitute buprenorphine-naloxone many patients stopped using other opioids, but even after 12 weeks of stabilisation, over 90% continued or resumed opioid use after the medication had been withdrawn. Consistent with an earlier study of heroin users prescribed buprenorphine-naloxone in primary care, offering even (compared to that study) fairly intensive drug counselling in addition to medical visits did not help. This high rate of unsuccessful detoxification is notable given the promising nature of the caseload: largely employed, well educated, with relatively brief opioid use histories, and little other current substance use. The contrast with the maintenance phase substantiates research which has consistently demonstrated the benefit of longer-term opioid substitute treatment.

On the positive side, the study shows that primary care doctors can successfully treat many patients dependent on prescription opioids, with or without chronic pain, by prescribing buprenorphine-naloxone on a maintenance basis plus relatively brief weekly medical management visits; half the patients who started this treatment did well while it lasted. However, when tapered off this medication, relapse to opioid use or treatment drop-out was overwhelmingly the most likely result. Though serious incidents were few, physicians should monitor psychiatric symptoms when

tapering such patients from opioids.

Though chronic pain did not affect opioid use outcomes, it was of relatively moderate intensity overall; patients whose doctors deemed their pain severe enough to require ongoing opioid therapy were excluded from the study. It is not known whether these findings can be generalised to patients with severe pain or those seeking treatment for pain rather than for opioid dependence. For reasons yet to be clarified, patients with even minimal lifetime heroin use more often used other opioids while maintained on buprenorphine-naloxone.

FINDINGS For a relatively unresearched caseload dependent on pharmaceutical opioids, and despite their relatively high stock of 'recovery capital' and willingness to try detoxification, these findings confirm the verdict of World Health Organization guidelines that compared to maintenance treatment, opioid withdrawal results in poor outcomes in the long term.

In retrospect, the attempt at rapid detoxification at the start of the study appears to have created a discontinuity in treatment which contributed to the fact that 250 of the 653 patients were lost touch with, while gaining just 43 successful detoxification completions. This attrition in turn meant that though half the patients who resumed maintenance treatment then substantially reduced their use of other opioids, they constituted just 27% of the patients who started the study. If virtual cessation of non-medical opioid use is the yardstick of success, it seems likely that many more patients would have attained this if from the start they had been prescribed maintenance doses rather than rapidly transitioned to detoxification.

From another perspective, the study illustrates the well-known high failure rate of outpatient detoxification, and the high relapse rate after any form of detoxification when not immediately and seamlessly followed by residential care. But since most of the sample were employed full time, it could be that only a minority would have been able to spend months in residential detoxification and rehabilitation. Offering instead fairly intensive outpatient drug counselling seemed largely futile, as most appointments were missed.

Lack of impact of extra counselling is also a general finding across studies of adding psychosocial therapy to opiate substitute prescribing – a testament to the power of routine methadone and buprenorphine maintenance.

While the rationale for substituting pharmaceutical opioids for illegal heroin seems clear – including preventing crime and injecting-related damage and infection, and making sure pure drugs are taken – the rational for substituting one pharmaceutical opioid for others is less clear, especially since the criminal activity involved is less worrying to the general public. One answer is the dramatic increase in US overdose deaths related to the non-medical use of opioid painkillers, deaths which in the USA now outnumber those due to heroin and cocaine combined, and which substantially contribute to overdose deaths from prescription drugs which by 2008 had approached the number of deaths from motor vehicle crashes (1 2). For patients dependent on painkillers, substituting methadone might be seen as a counterproductive escalation in the intensity of the opiate-type effects they experience. Buprenorphine is generally felt to leave patients less sedated and more able to function normally, and to be easier to withdraw from.

Guidance is available for UK general practitioners on the treatment of opioid dependence.

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