DRUG & ALCOHOL FINDINGS *Research analysis*

This entry is our analysis of a study considered particularly relevant to improving outcomes from drug or alcohol interventions in the UK. 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.

Defining dosing pattern characteristics of successful tapers following methadone maintenance treatment: results from a population-based retrospective cohort study.

Nosyk B., Sun H., Evans E. et al.

Addiction: 2012, 107(9), p. 1621–1629.

Based on detailed treatment records kept by the Canadian province of British Columbia, a slow taper liberally interspersed with stabilisation periods offers the best chance of sustainably withdrawing from methadone without severe relapse, but still very few manage to avoid this risk – an argument for careful consideration and informed consent before making the attempt.

SUMMARY Long-term substitution of illegal opioids with the opioid medication methadone (a treatment known as methadone maintenance) is the best established treatment for preventing harm from dependence on heroin and allied drugs, but successfully terminating the treatment has proved difficult.

Reviews have found that while withdrawal severity can be ameliorated, very few patients complete the process of tapering (gradual dose reduction) methadone preparatory to treatment exit, and relapse is common among those who do complete. Nevertheless, methadone detoxification and dose-tapering among maintained patients remain common. Patients may choose to detoxify due to what usually prove unrealistic expectations for recovery, pressure from family or others, the stigma associated with methadone, programme-related factors, financial or travel difficulties, or to see whether they can cope without treatment. Their doctors may taper them for disciplinary reasons or, in some jurisdictions, due to funding constraints or regulations governing the treatment.

Key points
From summary and commentary

The detailed dispensing database kept by British Columbia in Canada enabled an analysis of the factors associated with sustained remission from opioid dependence after being withdrawn from methadone maintenance.

A slow taper of a year or more liberally interspersed with stabilisation periods seemed to offer the best chance of avoiding relapse over the next 18 months.

Even then the great majority of taper attempts were followed by relapse, and overall fewer than 1 in 20 tapers ended in treatment exit and sustained remission.

Despite extensive clinical experience, research evidence is sparse, and important questions remain regarding dose-tapering strategies. Are the commonly recommended weekly dose reductions of 5–10% optimal? Should dose reduce steadily without a break? Does it matter how long the patient had been in treatment before tapering starts?

A detailed medication dispensing database covering the entire province of British Columbia in Canada, including its many methadone-maintained patients, offered an opportunity to move towards answering these questions. This data was drawn on to establish to what degree and under what circumstances detoxifying from methadone was followed by sustained remission

from opioid dependence. [As generally in the UK], in British Columbia methadone is recommended to be delivered with a maintenance-oriented philosophy, provided by general practitioners or specialised centres offering additional psychosocial care, and dispensed and consumed under supervision at community pharmacies.

Over the 11 years from 1996 to 2006, records were sifted to identify all complete episodes (ie, they started and ended during this period) of methadone maintenance lasting unbroken for at least 31 days. Of these 25,545 episodes, in 14,602 after at least 12 weeks of treatment the dose was reduced, and remained reduced or was reduced further for at least four weeks, indicating a tapering process rather than a dose adjustment or some other reason for a fluctuating dose. However, many of these tapers were quickly reversed, so the sample was sifted further to the 4,917 episodes which terminated before July 2005 with a detoxification lasting at least four weeks – defined as episodes where during the final four weeks of treatment the dose was still falling and/or had decreased below 5 mg a day. The July 2005 cut-off meant every patient could be tracked for 18 months after treatment ended, a period which it was known would include the majority of relapses signalled by a return to treatment.

The study aimed to assess the degree to which these tapers were followed by sustained remission. No direct measure of sustained remission was available, but a proxy was constructed from the province's records on hospital admissions and deaths. The criteria were that the patient had tapered to 5 mg or less a day of methadone in the final week of treatment and survived the following 18 months without re-entering treatment or having to be admitted to hospital for reasons related to their opioid use. Primarily at issue was what proportion of the 4,917 treatment episodes which ended with a taper were followed by this indictor of sustained remission, and what features of the prior treatment appeared to make this most likely. The features tested were:

- how long the patient had been in treatment before the taper started;
- how long the taper lasted from its start to the end of the treatment episode;
- how rapidly across the taper the dose typically decreased in proportional terms;
- as above, but how rapidly in *absolute* terms (ie, mg per week) the dose decreased; and
- how (dis)continuously the dose decreased during the taper – the degree to which the taper was interrupted by weeks when the dose was held steady, measured as the number of weeks which included a dose decrease in proportion to the duration of the taper in weeks.
- how steeply the dose decreased during the weeks when it fell.

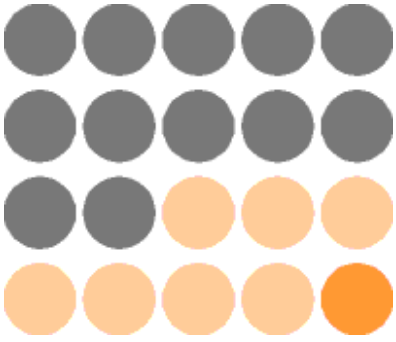
The results were adjusted for other possible influences on the chances of sustained remission, including maximum weekly dose during treatment and treatment 'adherence' – the proportion of their intended doses actually taken by the patient.

Main findings

Of the 4,917 treatments which ended with a detoxification, around a quarter – 1305 – ended with a daily methadone dose of 5 mg or less. Of these effectively completed detoxifications, about half (646) resulted in apparently sustained remission, representing just over 1 in 8 of the 4,917 treatments which ended with detoxification, under 1 in 20 of the 14,602 in which a taper was attempted at some time (▸ chart), and 1 in 40 of all 25,545 episodes completed during the study period.

In the following 18 months the 'unsuccessful' half of completed detoxifications were usually followed by treatment re-entry (458 of 659 episodes) or opioid-related hospitalisations (319 episodes). Another 29 patients died, the equivalent of about 1.5 deaths per 100 patients over a year.

The analysis then identified treatment factors related to the success of the 4,917 treatments which ended with detoxification, adjusting for other influences in the attempt to isolate what may be cause and effect relationships. Because they overlapped so much, factors characterising in different ways the rapidity of detoxification had to be analysed separately, meaning their independent contributions to securing lasting remission could not readily be teased out.



Treatment episodes in which detoxification was attempted. Orange dots are completed detoxifications. Final dot represents the fewer than 1 in 20 lastingly successful methadone

tapers.

Variations in the success rate of treatment episodes ending in a detoxification were best accounted for by factoring in how long the taper lasted. Adjusting for other influences, the longer the taper (only tapers lasting at least four weeks were assessed) the greater the chances of sustained remission. Relative to tapers of under 12 weeks, those lasting 12 weeks to a year were 3.6 times more likely to be followed by sustained remission, those lasting over a year, 6.7 times. As well as duration, the rapidity of the decrease in dose was also related to the chances of sustained remission. A relatively steep weekly decrease across the entire taper of over 4% a week was nearly 27% less likely to be followed by sustained remission than more gradual tapers.

The most complex analysis combined the continuity of the taper (proportion of weeks when the dose reduced) with the rapidity of the dose decrease during the weeks when the dose did reduce. Holding doses steady on between half to three-quarters of the weeks of the taper (the most common pattern) was followed by the highest remission rate. Both proportionately more and proportionately fewer steady-state weeks were associated with a lower chance of lasting remission. Unlike the dose change over the *whole* taper, a relatively steep step down during the weeks when the dose fell was associated with a higher chance of sustained remission. Steps down between 5% and 15% were associated with twice the chance of lasting remission of the more typical step down of under 5%; further steepening the step was not associated with further increases in lasting remission.

Once other factors were adjusted for, how long (after 12 weeks) the patient had been in treatment before tapering was unrelated to the chances of it being followed by sustained remission. In contrast, how 'compliant' the patient had been with taking their methadone during the entire treatment episode was consistently related to a higher chance of sustained remission. Additionally, treatment episodes during which daily doses had reached or exceeded 60 mg were less likely to see an end-of-treatment taper being followed by sustained remission than when the dose had remained lower.

Being young (under 25), male, and in some analyses relatively healthy in the run-up to treatment, were also associated with greater chances of sustained remission after ending treatment with detoxification.

Even when the withdrawal process was relatively optimal, the chances of a lastingly successful end to opioid use problems were small. Tapers lasting over a year still failed to stick in 78% of cases and as did 87% when the taper rate was typically under 4%. Leavening the taper with a half to three-quarters of weeks when dose remained stable was still followed by an 83% 'failure' rate in the 18 months after treatment ended.

The authors' conclusions

Analyses adjusted for other influences suggest that regardless of how early in treatment they are initiated, longer and more gradual tapers with dose decreased in only a quarter to half of the weeks have a substantially higher chance of success than other tapering schedules.

The overall rate of success was just 13% among the 4,917 treatment episodes selected for the study, 4.4% among all episodes during which a taper was started, and 2.5% among all completed episodes – poor outcomes consistent with previous findings. Methadone maintenance patients have a variety of reasons for seeking to achieve a drug-free state, but need to be informed of the high risks of relapse and adverse health outcomes. Such are the risks that regulatory bodies should consider mandating informed consent before tapering can be started.

In interpreting these findings, it is important to recognise that outcomes in any study which tracks real-world processes may not be caused by the factors highlighted by the study, but by others which these research designs are unable to fully eliminate or adjust for. For example, it could be that steeper tapers were disciplinary in nature[, the implication being that they were applied to 'difficult' patients and/or during treatments which do not follow clinical guidelines – factors which (rather than the steepness of the taper) may have accounted for poorer outcomes]. Conversely, episodes with more gradual tapering may be indicative of

individualised care, with doses titrated and tapered according to individual needs in suppressing withdrawal symptoms. [In this scenario, individualised care may be the salient factor, and though expressed more often in gradual tapering, might in other cases result in a steeper decline if that suits the individual best.]

Another example of how the results need to be carefully interpreted may be the unexpected relationship between maximum dose during treatment and the chances of sustained remission after a treatment-end detoxification. Doses of at least 60 mg are recommended and help retain patients in treatment, yet the featured analysis found these associated with a lower chance of sustained remission. The explanation could be that an individualised approach to treatment results in more severely dependent patients being prescribed higher doses. In this scenario, maximum maintenance dose is not a causal factor, but merely a marker of the severity which impedes sustained remission after leaving treatment.

It should also be acknowledged that the criteria for successful detoxification used by the study are more directly indicative of medical safety and patient stability following treatment than of relapse, which may occur without hospitalisation, treatment re-entry, or death. Also, the findings emerged from British Columbia, where treatment is heavily subsidised and characterised by a maintenance philosophy, and licensed doctors can provide treatment outside the context of specialised centres.

FINDINGS COMMENTARY In a UK-like treatment policy and practice context, the finding that fewer than 1 in 20 treatment episodes featuring a methadone taper ended with detoxification and no subsequent return to treatment, hospitalisation, or death, is likely to over-estimate the relapse-free success rate after terminating methadone. Many other patients will have relapsed without notching up these indicators. These kinds of findings should temper the recent enthusiasm in UK government circles (one embodied in treatment success indicators) for promoting more rapid and widespread exit from methadone maintenance and allied treatments.

The year after the featured study was published the literature comparing methadone-based detoxification with alternatives was reviewed according to the rigorous protocols of the Cochrane Collaboration. Reviewers concluded that “slow tapering with temporary substitution of long-acting opioids, could reduce withdrawal severity. Nevertheless, the majority of patients relapsed to heroin use.”

In line with these findings, UK studies (1 2) have implied that “to save the lives of patients dependent on heroin or similar drugs, they should be engaged and retained in substitute prescribing programmes like methadone maintenance until there is little risk of their relapsing after leaving”. However, how to establish there is little risk of relapse remains unclear. The featured study contributes significantly to making this clearer, suggesting that though remaining low, the success rate is improved when methadone is tapered over a long period – a year or more – liberally interspersed with periods of stabilisation, with the dose reducing overall at less than 5% a week. UK clinical guidelines are not entirely in line with these findings. They suggest that “Following stabilisation on methadone the dose can be reduced at a rate which will result in zero in around 12 weeks. This is usually a reduction of around 5 mg every one or two weeks” – briefer and possible also steeper than the featured study found most effective.

The finding that the chances of success were not significantly lower among patients longer in treatment counters fears that prolonged treatment is both a sign of and a contributor to patients being ‘stuck’ on methadone.

Adjusting the methadone taper is not the only way to attempt to ease the transition out of substitute prescribing treatment. Other strategies include transition first to buprenorphine, an opioid medication which can substitute for illegal opioids but seems easier to withdraw from than methadone (1 2 3).

Patients who have chosen rather than been forced to detoxify, who do so after a period of stability, and who are considered suitable by staff, also have the greatest chance of staying free of opioid drugs.

The authors of the featured article stressed their findings may be dependent on the British Columbian context. Part of that context is the availability of services which can boost what has become known as 'recovery capital' – resources which raise the chances of sustainably ending dependent substance use, the implications of which were recognised in 1926 in a report generally recognised as the foundation for opioid maintenance in Britain. Its authors speculated that had there been sufficient support available (they were thinking of residential recovery centres) and enough leverage to get addicts to use it, maintenance might no longer be needed. Similarly, today it can reasonably be speculated that in British Columbia as in the UK, failure to provide (among other services) high quality relapse-preventing housing, employment, family reconciliation services, and mental health care, is one reason why terminating methadone and allied treatments is so often followed by relapse and the risks entailed in a return to regular illicit opioid use. However, those resources would need to be substantial (1 2) to match the power of continuing substitute prescribing. Short of an ideal set of wrap-around support services, retention in substitute prescribing programmes is internationally recognised as the best way to safeguard both the patients and the communities they live in.

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