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. The summary conveys the findings and views expressed in the study. Below is a commentary from Drug and Alcohol Findings.

Comparative effectiveness of different treatment pathways for opioid use disorder.

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How do different pathways for the treatment of problem opioid use compare under real-world conditions? For US patients with health insurance, opioid substitution therapy was associated with the greatest risk reduction. However, its protective effect may not be fully realised while federal and insurance plan restrictions continue to limit access to this treatment option.

SUMMARY Despite evidence that medication-based treatments for opioid use disorders improve survival and engagement with treatment, there is a lack of access to them in many parts of the United States, translating to an annual treatment gap of an estimated one million people with opioid use disorders.

The aim of the featured study was to determine the effectiveness of six different treatment pathways for opioid use disorders under real-world conditions, providing a greater understanding of the comparative effectiveness of treatments for policymakers, insurers, practitioners, and patients.

The six different treatment pathways were defined as:
- no treatment;
- inpatient withdrawal or residential services;
- intensive psychosocial therapy involving intensive outpatient treatment or hospitalisation for a short period of time;
- opioid substitution therapy with buprenorphine or methadone;
- treatment with naltrexone, which blocks the effects of opioids;
- non-intensive psychosocial therapy involving outpatient counselling.

Key points
From summary and commentary

This US study aimed to determine the effectiveness of six different treatment pathways for opioid use disorders under real-world conditions.

Methadone and buprenorphine maintenance were associated with the greatest reduction in risk. However, only a small proportion of patients (13%) accessed these treatment options.

The findings suggest a need to prioritise access to and retention in medication-based treatments for opioid use disorders.

The study used a large, nationally-representative sample of people whose healthcare costs were either met through private insurance or Medicare Advantage, a programme that provides federal health insurance benefits through private-sector health insurance. Data was taken from a database that included comprehensive information about medical, pharmacy, and psychosocial therapy claims to insurance companies.

All patients were at least 16 years old, with records indicating they had an opioid use disorder as defined by ICD-10 diagnostic criteria, and had been enrolled in their insurance scheme for at least three months before and after commencing treatment. For those not receiving treatment (one of the pathways identified), a proxy treatment start date was selected in order to provide a comparison.

The primary outcomes were (1) opioid-related overdose (fatal or non-fatal), and (2) acute care, defined as emergency department attendance or hospitalisation due to opioid use. These adverse clinical outcomes were selected as being indicative of a relapse to opioid use problems. However, they may underestimate the prevalence of relapse because they represent only *severe* consequences of ongoing use. A secondary outcome was admission for inpatient withdrawal or readmission for those who initiated treatment with inpatient withdrawal or residential services. All outcomes were followed up at three months and 12 months after starting treatment.

A total of 40,885 patients were included in the window of time between 1 January 2015 and 30 September 2017. Their average age was 48, just over half (54%) were male, and three-quarters (74%) were white. Over half (58%) were commercially insured and the remainder (42%) were enrolled in Medicare Advantage. Mental health problems were found in 45% of patients in the three months before the first treatment episode. Depression (24%) and anxiety (26%) were the most common mental health problems.

Main findings

The most common treatment pathway was outpatient counselling, followed by inpatient withdrawal or residential services, and buprenorphine or methadone; not receiving any treatment was more common than naltrexone or intensive psychosocial therapy:
- 24,258 received outpatient counselling;
- 6,455 received inpatient withdrawal or residential services;
- 5,123 received medical treatment with buprenorphine or methadone;
- 2,116 did not receive any treatment;
- 1,970 received intensive psychosocial therapy;

• 963 received medical treatment with naltrexone.

During the 12-month study period, the average duration of medical treatment was 150 days for buprenorphine and methadone, and 74 days for naltrexone.

Opioid overdose

By the three-month follow-up, 707 participants (2%) had experienced an overdose. Only treatment with buprenorphine or methadone was associated with a reduced risk of overdose at the three-month and 12-month follow-up. Compared to those receiving no treatment, there was a 76% reduction in the chance of an overdose occurring at three months and a 59% reduction in overdose at 12 months among patients receiving buprenorphine or methadone.

Furthermore, the longer the duration of treatment with buprenorphine or methadone, the lower the rate of overdose at the end of the 12-month follow-up period:
• 105 of those who received buprenorphine or methadone for 1–30 days had an overdose;
• 101 of those who received buprenorphine or methadone for 31–180 days had an overdose;
• 28 of those who received buprenorphine or methadone for more than 180 days had an overdose.

For comparison, 1,198 of those who received no medical treatment had an overdose.

Acute care

By the three-month follow-up, 773 (2%) patients had accessed acute care. Buprenorphine and methadone maintenance were associated with a reduced risk of needing acute care at the three-month and 12-month follow-up. Compared to those receiving no treatment, there was a 32% reduction in the chance of using acute care at three months and a 26% reduction at 12 months among patients receiving buprenorphine or methadone. Outpatient counselling was also associated with a reduction in acute care use (41% at three months, and 40% at 12 months) compared to no treatment.

Compared with buprenorphine or methadone, all treatment groups were more likely to have a post-treatment admission to inpatient withdrawal. Patients who initiated treatment with inpatient withdrawal or residential services were most likely to return. Treatment with naltrexone or intensive psychosocial therapy services was also associated with a higher risk of subsequent admission for supervised withdrawal during the three- and 12-month follow-up periods.

The authors' conclusions

To the authors' knowledge, this study featured the largest cohort of insured patients with opioid use disorders to date, providing a greater understanding of the comparative effectiveness of different treatments under real-world conditions in the United States.

The key findings was that opioid substitution therapies were associated with a considerable reduction in the risk of overdose and need for emergency or inpatient medical care up to 12 months later, suggesting a need for treatment models to prioritise access to and retention in medication-based treatments for opioid use disorders, and health insurance programmes to reduce restrictions on use of medications for treating opioid use disorders.

Despite the known benefit of opioid substitution therapies with buprenorphine or methadone, only 13% patients initiated them. Most patients in the cohort accessed psychosocial services or inpatient withdrawal, both of which are less effective than the medication-based treatments above. It is possible that people accessed public sector treatments that were not captured in the data, particularly for methadone, which was not covered through the federal health insurance plan and may not have been covered without the patient 'topping up' the money paid through their commercial insurance plan in order to meet the full costs. Low rates of medication-based treatment among this insured population highlight the need for strategies to improve access to and coverage for medical treatments of opioid use disorders.

The results also demonstrated the importance of retaining patients in medical treatment. People who received methadone or buprenorphine for longer than six months experienced fewer overdose events and serious opioid-related acute care use compared with those who received shorter durations of treatment or no treatment. These findings are consistent with prior research (1 2 3 4 5) demonstrating high rates of recurrent opioid use if medication is discontinued prematurely.

FINDINGS COMMENTARY Some of the takeaways from the featured study are specific to the US context, but there are also some more generalisable conclusions to the United Kingdom and elsewhere about the protective effect of being prescribed and then remaining in opioid substitution therapies.

Internationally the evidence is strong that being in treatment – and especially for opiate users, being in a substitute prescribing programme – helps prevent overdose deaths. This means that apart from specific harm reduction initiatives, lives can be saved by simply extending the reach and duration of treatments associated with a reduced death rate. The featured study affirmed these findings, showing a reduced risk of adverse events among patients in opioid substitution therapy compared to no treatment at all, and a correlation between duration of treatment and risk of overdose, with only 28 of those in receipt of buprenorphine and methadone for more than 180 days having an overdose compared with 105 of those in treatment for under 30 days, and 1,198 of those who received no medical treatment at all.

The study examined the real-world effectiveness of different treatment pathways for opioid use disorders using a very large sample of patients, and found that methadone and buprenorphine maintenance were associated with the greatest reduction in the risk of an overdose or need for acute inpatient care – yet, only a small proportion of patients (13%) had access to opioid substitution therapy. Due to the way the study was designed, it is possible that patients on different treatment pathways had different characteristics that were associated with the outcomes. However, in the case of opioid substitution therapy, the findings do reflect the

wider evidence base about the protective effect of being and staying in treatment, and conversely the risk of not being in treatment or having the duration of that treatment curtailed.

The potential under-utilisation of opioid substitution therapies in the US, suggested by the study, could be attributed to a range of factors. Guidelines for clinicians in the country support the use of opioid substitution therapies (for example, see the comprehensive recommendations from the American Society of Addiction Medicine). However, what is supported on paper may not always be possible or easy in practice. The following are just some examples of the structural barriers to providing methadone within the US healthcare system:

- There are strict federal regulations around the administration of methadone. For a facility to offer methadone in the US it must meet specific requirements and obtain approval from the state, the Substance Abuse and Mental Health Services Administration, and the Drug Enforcement Administration. Other medications for treating opioid use disorders such as buprenorphine and naltrexone do not require the same level of oversight.
- Methadone is one of the most frequently excluded, or not explicitly covered, treatments in medical insurance for people with substance use problems.
- In some cases, insurance that covers methadone requires prior authorisation to ensure the treatment is medically necessary before it is approved, which can delay access to the first dose, in some cases risking relapse or death.

The US versus UK healthcare system

The US healthcare system is organised very differently to the UK. The former is a patchwork of publicly- and privately-funded health insurance, and the latter is publicly-funded through general taxation and is free at the point of delivery.

Public health insurance in the US covered only 34% of the population in 2018, while private health insurance covered 67% of the population, and a further 27.5 million people (9%) were left uninsured. In this context the under-utilisation of particular treatments or therapies, such as methadone and buprenorphine for opioid use disorders, is only part of the story. For some people who fall through the gaps there may be no access at all.

There may also be cultural and social factors affecting the way different treatment pathways are perceived and 'rated' by patients and clinicians. The US opioid crisis is driven in large part by an epidemic of prescription opioid dependence. The featured study did not distinguish between patients primarily or initially dependent on prescription or illicit opioids – different routes into dependence and potentially different identity positions which may have a bearing on the acceptability of the various treatment pathways to patients.

Interviews with 18 patients in the US who were in receipt of methadone maintenance therapy revealed that stigma surrounding the treatment itself was a "prevalent and serious concern" for the majority. One of the common stereotypes about methadone was that all people on methadone were introduced to opioids through illegal 'street drugs' such as heroin, despite this not tending to be their experience. Most had been introduced to opioids through prescription drugs – 50% through physicians' prescriptions, and 44% through friends/family. One of the consequences of this stigma was a reluctance to initiate, access, or continue methadone at least in part because of negative beliefs internalised about 'the kind of people' who need methadone.

Estimates of people dependent on opioids who are in treatment show far higher treatment penetration in England than in North America. The European average for the proportion of opioid users in treatment is around 50%, while Canada and the US are approximately 28%. France reports the highest rate at 76%, and England falls at about 60%.

An Effectiveness Bank hot topic examines the crisis of (and response to) overdose deaths in the UK.

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