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.

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▶ Emergency department-initiated buprenorphine/naloxone treatment for opioid dependence: a randomized clinical trial.

D'Onofrio G., O'Connor P.G., Pantalon M.V. et al.

JAMA: 2015, 313(16), p. 1636–1644.

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Unique trial tests what emergency doctors should do when screening identifies opioid dependence. More effective at promoting treatment and curbing opioid use than referral and brief advice was, it seems, actually initiating treatment in the form of buprenorphine maintenance.

SUMMARY Patients dependent on prescription opioids and heroin have an increased risk of health problems, and often seek medical care in the emergency department, offering an opportunity to identify them and engage them in treatment.

This clinical trial tested the relative efficacy of three types of interventions for people with opioid dependence, initiated in the emergency department of an urban teaching hospital in the USA between 2009 and 2013. 71,742 patients were screened for opioid use by research staff, and of these 329 were identified as dependent on opioids (prescription or illegally produced), eligible for the study, and willing to participate. Patients already in formal addiction treatment were excluded, though 70% had at some time been in treatment for drug use problems. The 329 were randomly assigned to one of three progressively more extensive interventions intended to promote engagement with treatment for their dependence, the non-medical elements of which were delivered not by emergency department clinicians, but by research staff:

Key points
From summary and commentary

This study tested the relative efficacy of three different emergency department-initiated interventions for patients dependent on prescription opioids or heroin.

Treatment with buprenorphine resulted in a greater percentage of patients engaged in treatment and fewer days of self-reported illicit opioid use than referral or brief advice.

Based on these findings, and those of other studies, starting buprenorphine treatment in the emergency department could be a feasible response to what is a chronic and relapsing condition.

Referral group: After being identified, these patients received a handout providing names, locations, and telephone numbers of addiction treatment services in the area and telephone access to call a clinician or facility of their choice. This was delivered by a researcher *not* involved in the patients' medical care and trained *not* to use any motivating statements.

Brief intervention group: Patients received a 10–15 minute manualised, audiotaped brief negotiation interview. This involved a researcher raising the subject of opioid dependence, providing feedback on the patient's substance use, enhancing motivation, negotiating, and advising. Interventionists were required to implement 27 'critical actions', such as asking the patient's permission to discuss opioid use. Using the same procedures as for the referral group,

the researcher also facilitated treatment entry, but additionally directly linked the patient with their chosen service, reviewing the patient's eligibility for services and arranging transportation.

Buprenorphine treatment group: Patients were offered a similar brief negotiation interview to that offered the brief intervention group, but were additionally offered an immediate start to treatment with buprenorphine–naloxone, an opioid medication which by substituting for the opioid the patient has been using can decrease withdrawal, craving, and non-medical use of opioids. This treatment was initiated in the emergency department for patients exhibiting moderate to severe opioid withdrawal, or given as a take-home dose to patients not exhibiting opioid withdrawal. For patients with moderate to severe opioid withdrawal, sufficient take-home daily doses were provided to ensure patients had adequate medication until a scheduled appointment in the hospital's primary care centre within 72 hours. Doses were 8 mg on day 1 and 16 mg on days 2 and 3. For all patients, buprenorphine treatment was provided at a surgery separate from the emergency department for 10 weeks using established procedures with visits ranging from weekly to twice-monthly. After 10 weeks, patients were transferred for ongoing opioid maintenance treatment or offered withdrawal from the medication over a two-week period based on their stability, insurance, and preference. Patients in the referral and brief intervention groups did not receive treatment for withdrawal symptoms as part of the study; this was at the discretion of their emergency department doctor.

Outcomes were measured 30 days after patients were assigned to their intervention group. The primary outcome was engagement in formal addiction treatment, including opioid prescribing, inpatient or residential treatment, intensive outpatient programmes, or treatment at non-specialist medical services such as primary care practices.

Secondary outcomes included self-reported number of days of illicit opioid use in the past seven days, urine toxicology results for illicit opioid use, HIV risk-taking behaviour using an 11-item validated scale for drug use and sexual behaviour, and receipt of different types of addiction treatment services.

Most patients (66%) had been identified through screening, a third (34%) when they sought treatment for opioid dependence, and 9% after admission due to an overdose. Around half of the total sample (53%) reported intravenous drug use, and a quarter (25%) prescription opioid use. Smoking was common among patients (88%), and, to a lesser extent, so was the use of cocaine (55%), cannabis (53%) and sedatives (47%), as well as heavy drinking (34%). Nearly three-quarters (73%) reported a lifetime history of prior drug treatment and 14% prior alcohol treatment. Mental health problems were prevalent with more than half of patients (51%) reporting prior psychiatric treatment, and 23% requiring a psychiatric evaluation at their first visit.

Main findings

Treatment with buprenorphine significantly increased engagement in addiction treatment, reduced self-reported illicit opioid use, and decreased use of inpatient addiction treatment services, compared with brief interventions and referral. However, it did not significantly decrease the rate of urine samples testing 'positive' for opioids, or HIV risk-taking behaviours.

Primary outcome

At 30 days after being allocated to their respective interventions, records available for nearly all the patients showed that engagement in treatment was significantly more common in the buprenorphine group (78%) than the brief intervention (45%) and referral (37%) groups.

Secondary outcomes

Based on interviews with three-quarters of the patients, the number of days of self-reported illicit opioid use in the buprenorphine group reduced significantly from 5.4 days per week to 0.9 days, compared with a reduction from 5.6 days to 2.4 days in the brief intervention group, and from 5.4 days to 2.3 days in the referral group.

Among the two-thirds of patients (220 of 329) submitting urine samples, there was no significant difference between the groups for percentages testing 'negative' for opioid use – 58% of the buprenorphine group, 43% of the brief intervention group, and 54% of the referral group.

Over the 30 days of the follow-up period, significantly fewer buprenorphine patients used inpatient addiction treatment services than patients in the brief intervention group and the referral group (11%, 35%, and 37% respectively). There was no difference in the average number of outpatient visits or in the use of emergency department-based addiction treatment.

There were significant reductions in HIV risk-taking behaviour in all three groups. However, there were no statistically significant differences between groups.

The authors' conclusions

Buprenorphine treatment resulted in a greater percentage of patients engaged in treatment, fewer days of self-reported illicit opioid use, and fewer patients using inpatient addiction treatment services than referral or brief advice. Based on these and other findings (1 2 3), emergency department-initiated buprenorphine could be a feasible response to what is a chronic and relapsing condition.

The American College of Emergency Physicians should consider broadening the scope of its position statement (which acknowledges that emergency physicians "are positioned and qualified to mitigate the consequences of alcohol abuse through screening programs, brief intervention, and referral to treatment") to include opioid use disorders.

FINDINGS COMMENTARY This paper highlighted the tendency for people dependent on opioids to access medical care in the emergency department, which for the patient can indicate a lack of access to preventative primary health care, and a greater susceptibility to acute illnesses that necessitate urgent secondary care.

Emergency medicine runs the gamut from major trauma and medical emergencies to minor injuries and illness. The British Medical Association describes the working environment as "often hectic and unpredictable … fast-paced, challenging and heavily multidisciplinary". A number of initiatives have been rolled out in primary care aimed at "reducing unscheduled care needs" and alleviating the strain on hospitals, including incentivising general practitioners to improve chronic disease management, crisis intervention teams for mental health problems, drug and alcohol services, rapid response teams, community matrons and schemes such as home care respiratory teams (4 5). However, there remains a vulnerable patient population, referred to as "frequent attenders", who disproportionately rely on the emergency department to meet their healthcare needs.

Based on the greater percentage of patients engaged in addiction treatment, fewer days of self-reported illicit opioid use, and fewer patients using inpatient addiction treatment services, the authors of this study suggested that facilitating buprenorphine treatment within the emergency department (with a view to continuing treatment in primary care) could be a feasible and efficacious option for patients identified as opioid dependent through screening. Furthermore, despite fewer patients being in treatment at 30 days, resort to inpatient treatment was more common among patients *not* offered buprenorphine, suggesting that buprenorphine treatment helped prevent crises and/or the need for detoxification.

The advantage gained by initiating buprenorphine-based treatment was arguably all the more impressive since both sets of comparison patients were offered treatment-promoting interventions which went beyond the current standard of emergency department care: the referral group received detailed referral information about community services categorised by insurance coverage, and the brief intervention group received a psychosocial intervention with a facilitated referral. As the authors noted, the level of intervention in the referral group may have diminished the ability of the study to detect a difference between the referral and brief intervention groups. This feature of the study also meant that while it shows the *extra* difference made by initiating buprenorphine-based treatment compared to the other interventions, we cannot know how much better any of these were than doing nothing at all, or only what is usual in emergency departments.

In this study, a considerable proportion (a third) of patients were recruited when they sought treatment for opioid dependence at the hospital, and just under half of all patients (45%) reported that they either usually accessed health care at the emergency department or did not access it at all. These figures, derived from a teaching hospital in the United States, may not be reflective of the use or non-use of healthcare in other countries. The UK, for example, ensures free healthcare at the point of use, which removes one of the barriers to accessing treatment, whereas the US has a more fragmented insurance-based healthcare system, which in 2017 according to a Gallup poll left 12% of people without healthcare insurance.

In this case, emergency department-initiated buprenorphine treatment and 10-week follow-up support was provided regardless of insurance. While this presented the possibility that participation in the study afforded patients in the buprenorphine group access to 10 weeks of treatment which they might otherwise have been unable to afford or ineligible for under their insurance – and therefore the possibility that it might have affected their motivation to participate and 'do well' – the authors noted that 80% of study patients had health insurance.

To evaluate the longer-term outcomes of emergency department intervention, the authors followed up a cohort of the original sample (who completed at least one additional assessment) at two, six, and 12 months. They found again that buprenorphine was associated with significant increases in engagement with addiction treatment and reductions in illicit opioid use two months later, but not at the other time points. This was perhaps unsurprising as the 10-week primary care support that went along with the buprenorphine treatment would still have been in place at the two-month follow-up. As the authors said, this means that in the US context, arranging and offering buprenorphine-based treatment in the emergency department is effective at promoting treatment engagement and reducing opioid use only so long as the initial treatment lasts. When, following this, patients have to make their own arrangements, other factors determine treatment uptake. There was no lasting affiliation to or preference for treatment due to the experience initiated in the department, and according to the featured paper, most participants (70% of the sample) had been in treatment before, so presumably many could have started treatment even without a specific intervention.

Compared with referral to community-based treatment or combined brief intervention and referral, the same group of researchers found that emergency department-initiated buprenorphine was more cost-effective, providing high value as an intervention for opioid dependence in the emergency department.

Pregnant women were excluded from the featured study – something not uncommon in clinical trials, and arguably necessary in this case due to contraindications (6 7) around the combined medication buprenorphine–naloxone. However, this was not one of the exclusion criteria in the original research plan, and its addition was not explained in the paper. While this may simply reflect the widespread presumption against including pregnant women, it does have implications for the evidence base of treatment options for opioid dependence, and the question, 'for whom are these treatments feasible and effective?'

Last published in 2017, there is no more important document for UK clinicians involved in treating problem drug use than the so-called 'Orange guidelines' (synthesised in the Effectiveness Bank). The text stresses the importance of having follow-on treatment organised and working in conjunction with treatment services outside the hospital. Context-specific elements are discussed, including the assessment of opioid dependent patients within general hospital settings (turn to page 212 of the full document):

> *"While hospitalisation can offer an excellent opportunity to engage a patient in starting specialist treatment of dependence, hospital doctors are strongly encouraged only to initiate [opioid substitution therapy] as part of, or with clear advice and support from, a specialist drug treatment team (either through any liaison service available or by contacting the relevant community drug service)…"*
>
> *"However, it is still vital for the hospital doctor to be able to treat opioid withdrawal states for all patients:*
> *• Those confirmed as already in receipt of [opioid substitution therapy] can be promptly and carefully initiated back onto [opioid substitution therapy], taking account of opioid tolerance confirmed to be present.*
> *• Those not already on [opioid substitution therapy] can have any acute opioid withdrawals treated in a timely fashion, consistent with safe prescribing. There should be attempts to seek specialist advice so that plans for further assessment or later transfer for ongoing drug treatment can be discussed."*

Both buprenorphine and methadone are recognised by the World Health Organization as 'essential medicines', but of the available opiate-type medications, methadone is the dominant choice worldwide and in the UK.

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DOCUMENT 2011 Buprenorphine/naloxone for opioid dependence: clinical practice guideline

STUDY 2010 Home- versus office-based buprenorphine inductions for opioid-dependent patients

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STUDY 2018 The impact of buprenorphine and methadone on mortality: a primary care cohort study in the United Kingdom

STUDY 2008 Screening, brief interventions, referral to treatment (SBIRT) for illicit drug and alcohol use at multiple healthcare sites: comparison at intake and 6 months later

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STUDY 2014 Primary care-based buprenorphine taper vs maintenance therapy for prescription opioid dependence: a randomized clinical trial