12.1 'Real-world' studies show that medications do suppress heavy drinking

Findings Three trials have found that drugs commonly used to treat alcohol dependence improve outcomes for an appreciable minority of patients even under conditions close to normal practice. To enhance their real-world relevance, relatively few patients were excluded from the trials and then mainly for medical rather than research reasons.

Set in France, study ❶ of acamprosate involved 149 family doctors who recruited 422 patients seeking or already in treatment for alcohol dependence. All received the doctor's normal treatment (generally detoxification followed by longer term therapy) and for a year a randomly selected half were also prescribed acamprosate. Most patients were married and working and over 80% remained in treatment for the year. Even without acamprosate, about half the patients achieved a successful outcome (ie, no alcohol-related problems) and doctors thought about the same proportion had at least moderately improved. But with the drug, around 1 in 7 more patients met these criteria: nearly two-thirds no longer reported alcohol-related problems compared to half those not prescribed acamprosate, their quality of life had improved more, and they abstained from alcohol more often (81% versus 67% of days).

Study ❷ tested naltrexone (an alternative to acamprosate) as a supplement to the normal therapy offered by a typical, frontline US substance abuse centre. For 12 weeks, 145 new patients were randomly allocated to therapy alone, plus placebo pills, or plus naltrexone. In contrast to the French study, about half the patients were unemployed, most were single, and therapy was usually a demanding outpatient regime with inpatient admission for continuing drinkers. Perhaps partly for these reasons, compliance was poorer than in France. Though most patients had been ordered into treatment by the courts, about 4 in 10 stopped taking the pills and over a quarter dropped out of treatment altogether. Overall, neither the dummy nor the real pills improved outcomes. However, naltrexone did significantly and substantially help the 40% of patients still drinking when they started the trial. Without naltrexone, they drank far more than those who had started treatment sober; with naltrexone, they reduced their drinking to about the same level.

The importance of family support was evident in study ❸ in India which compared naltrexone with disulfiram (Antabuse). After detoxification, 100 patients attending a private psychiatric hospital were randomly but openly (they knew which drug they were being given and its effects) assigned to the two drugs. While disulfiram is being taken, unpleasant reactions after drinking act as an effective deterrent, but unless a relative or clinician supervises its administration, patients typically discontinue the drug and resume drinking. The 105 patients selected for the trial all had a stable home environment usually featuring an extended family, one of whom had agreed to take the lead in supervising their medication, and most were working. In these circumstances, virtually all the patients completed the year of the study. On disulfiram 86% avoided relapse to heavy drinking compared to 44% on naltrexone and twice as many remained abstinent throughout. Though patients on naltrexone typically resumed drinking, they did substantially reduce their consumption.

In context In the French acamprosate study (❶), the placebo effect cannot be excluded and is likely to have contributed to the outcomes, but this would also be the case in normal practice. Perhaps more serious is the fact that the doctors were barred from prescribing not just acamprosate but also naltrexone to the control patients. They may have felt unable to give them optimal care. Communicated to the patient, this might have adversely affected outcomes, boosting the apparent advantage of acamprosate. Excellent retention is thought to have been largely due to treatment being provided by the patient's family doctor rather than a special clinic, but would also (as in India) have been influenced by mainly intact family and working lives.

These props to sticking with treatment were largely lacking in the US naltrexone study (❷) where, even though it lasted just three months, more patients discontinued treatment than in the other trials. Nevertheless, patients who (because they were drinking at the time) had a chance to sample the way naltrexone dampens the desired effects of drinking reacted by cutting their consumption. This finding confirms previous work indicating that naltrexone's strength is less in sustaining abstinence than in helping patients who resume drinking avoid a return to heavy drinking.

In India (study ❸) all the patients started treatment after completing detoxification and were presumably alcohol-free, perhaps one reason why disulfiram proved more effective than naltrexone. Another may have been that naltrexone was not paired with anti-relapse skills training designed to help avoid lapses becoming relapses, but with relatively unstructured, abstinence-oriented therapy.

Practice implications All these medications are best seen as helping to sustain an intoxication-free space during which patients can be helped to find other ways to cope and to construct lives incompatible with heavy drinking. Each has its own strengths and limitations.

Patients committed to abstinence who have strong home-based or clinical support, especially in the form of someone to supervise consumption, can sustain disulfiram therapy and remain abstinent as a result, though some will not be suitable due to medical contraindications. In other circumstances, pharmacotherapies like naltrexone and acamprosate which do not demand total abstinence are more likely to be adhered to and can cut consumption. Even with these drugs, compliance is a key issue and can be improved by counselling designed to motivate compliance and to minimise side effects such as fatigue and nausea, and by engaging family members or other associates to monitor consumption of the pills. Naltrexone may be the better option for people who are not aiming for or find it hard to stop drinking altogether, and for those with a strong desire to drink in order to achieve what they experience as a pleasurable state of intoxication. However, side effects are more common and more severe (though only rarely such that patients have to stop taking the drug) than with acamprosate and the drug is contraindicated in patients with certain liver problems or who are also dependent on opiates. There is also the complication that in a medical emergency, patients who have recently taken naltrexone will find that opiates fail to control pain, one reason why some prefer not to take the drug.

Featured studies ❶ Kiritze-Topor P. *et al*. "A pragmatic trial of acamprosate in the treatment of alcohol dependence in primary care." *Alcohol & Alcoholism*: 2004, 39(6), p. 520-527. AC ❷ Killeen T.K. *et al*. "Effectiveness of naltrexone in a community treatment program." *Alcoholism: Clinical and Experimental Research*: 2004, 28(11), p. 1710-1717. AC ❸ De Sousa A. *et al*. "A one-year pragmatic trial of naltrexone vs disulfiram in the treatment of alcohol dependence." *Alcohol & Alcoholism*: 2004, 39(6), p. 528-531. AC

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