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

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▶ Disulfiram treatment of alcoholism.

Chick J., Gough K., Falkowski W. et al.

British Journal of Psychiatry: 1992, 161, p. 84–89.
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Still relevant today, from the early 1990s this UK randomised trial of disulfiram in the treatment of alcohol dependence found that, given daily supervision to make sure patients took tablets they knew would cause unpleasant effects if they drank, the effect was to significantly reduce drinking.

SUMMARY By blocking the breakdown of alcohol in the body, disulfiram ('antabuse') produces unpleasant reactions in response to even low levels of drinking, so acts as an aversive deterrent. Specifically it inhibits the action of the liver enzyme aldehyde dehydrogenase, preventing the conversion of acetaldehyde to acetate. As a result, after drinking alcohol, acetaldehyde accumulates, causing flushing, throbbing headache, nausea, vomiting, and chest pain. Disulfiram is therefore indicated for patients who wish to remain abstinent.

In this the first UK controlled study of supervised disulfiram in the outpatient treatment of alcoholics, 126 patients who had relapsed after previous treatment were recruited at seven alcoholism treatment centres. They were randomly allocated to take disulfiram (200mg) or vitamin C tablets daily for six months under supervision usually at home by their spouses or partners or by clinic staff, who also monitored their drinking. Disulfiram patients were told about the drug's effects. Vitamin C patients were told that the tablets were only prescribed to offer a comparator for the disulfiram regimen. If they asked for more information, they were told vitamin C had been chosen because it would also remedy a possible alcohol-related vitamin deficiency. Patients were typically middle-aged, unemployed men. Counselling and other forms of psychosocial support were also provided. Nearly half the patients (but no more so on disulfiram) effectively rejected or dropped out of treatment; they were included in the outcome analyses.

Main findings

Based on interviews with the 8 in 10 followed up six months later and the reports of the people supervising consumption, over the six months of the intended treatment disulfiram patients reduced their drinking days and amounts drunk by significantly more. For example, based on their own accounts disulfiram patients had increased the number of days they had not drunk at all by 44 days more than control patients and reduced their average consumption by an extra 68 UK units per week.

By the final four weeks the reduction had evened out, and disulfiram patients had not drunk significantly less or lasted without drinking significantly longer than patients prescribed a vitamin, though they had drunk on just half the number of days – just under two days as opposed to just under four. Remission in symptoms of dependence and amelioration of alcohol-related problems were not significantly different. Patients, supervisors and clinicians – all of whom knew which medication the patient was taking – agreed that by the end of the six months disulfiram patients had gained greater control over their drinking than patients prescribed vitamins. In contrast, this was not the opinion of the interviewers who gathered follow-up data, who were meant to have been kept in the dark about which tablets had been taken. While two thirds of disulfiram patients wanted to continue their treatment, just a quarter prescribed the vitamin felt the same.

The authors' conclusions

Though by the end of the six months the impact may have waned, supervised disulfiram plus counselling improved drinking outcomes relative to an inactive nutritional supplement, and the treatment was popular with patients and the people associated with them. Supervision of dosing may be an important element as may making patients aware of the potential adverse consequences of drinking while taking disulfiram.

FINDINGS COMMENTARY In this study the comparator for disulfiram was relatively weak – tablets not intended to reduce drinking and which the patients were not led to expect would have impacts other than remedying possible vitamin C deficiency. Beyond the actual effects of the tablets, all the patients'

expectations presumably favoured disulfiram. It was also a test of disulfiram *during* its intended treatment span of six months, not whether those effects 'stick' once treatment ends. Indeed, there was evidence of waning in effect even during the six months, though with less drop-put and a larger sample, the final four weeks' halving in drinking days might have been statistically significant.

One theory-based response to concerns that disulfiram's effects may not 'stick' once the treatment ends is that (free source at time of writing) this would simply show the medication was effective, and that it is the role of longer term continuing care or aftercare to sustain the gains. In practice, a German study suggested that disulfiram's impact can last. It evaluated intensive two-year treatment of severe alcoholics using a similarly aversive medication followed by disulfiram. The result was high rates of long-term abstinence, outlasting the treatment period by seven years. In this study, joined by under half the patients who were asked and were eligible, administration was supervised by clinic staff, and few patients dropped out of treatment, perhaps spurred on by what were usually serious medical consequences of highly excessive drinking. The results highlighted disulfiram's psychological rather than pharmacological mechanisms of action, since on safety grounds a few patients prescribed inactive pills, but who were told they were a form of 'antabuse', fared at least as well as patients prescribed aversive medication. What these psychological mechanisms were has been speculated on by the study's authors: "patients learned to use disulfiram as a successful coping skill to prevent relapse and ... replaced the alcohol deterrent during psychotherapy by a broad spectrum of alternative behavior including participation in self-help groups and lifelong checkup sessions". However, with no randomly allocated comparison group offered all the therapy elements except aversive medication, this account is merely consistent with rather than proved by the findings.

For more on disulfiram see a discussion of key research and reviews in the Alcohol Treatment Matrix.

Thanks to research author Jonathan Chick for comments on the original draft entry. Commentators bear no responsibility for the text including the interpretations and any remaining errors.

Last revised 18 June 2020. First uploaded 31 May 2012

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