

# What works in alcohol use disorders?

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**Abstract** Treatment of alcohol use disorders typically involves a combination of pharmacotherapy and psychosocial interventions. About one-quarter of people with alcohol dependence ('alcoholics') who seek treatment remain abstinent over 1 year. Research has consistently shown that less intensive, community treatment (particularly brief interventions) is just as effective as intense, residential treatment. Many psychosocial treatments are probably equally effective. Techniques for medically assisted detoxification are widespread and effective. More recent evidence provides some support for the use of drugs such as acamprosate to prevent relapse in the medium to long term.

There has been much recent debate and criticism of UK alcohol policy (Drummond, 2004; Hall, 2005). Over the past 20 years, per capita alcohol consumption in Britain has increased by 31%, leading to large increases in the prevalence of alcoholic cirrhosis, alcohol-related violence and heavy alcohol use. Alcohol misuse causes at least 22 000 premature deaths each year and costs the taxpayer an estimated £20 billion (Prime Minister's Strategy Unit, 2003). The key features of alcohol dependence and harmful use are listed in Box 1. About 5% of the UK population are dependent on alcohol (Farrell *et al*, 2001) and 8 million Britons drink more than recommended levels.

An excellent and authoritative review of alcohol treatment literature is provided by the Mesa Grande project (Miller *et al*, 2001). Updated on a regular basis, it includes a review of seven multicentre studies in the USA and Europe involving over 8000 treatment-seeking individuals. In the 2001 review, overall mortality at 1-year follow-up was about 1.5%. Clients reported an 87% reduction in alcohol consumption, with abstinence on 80% of days. Overall, 24% were abstinent for the entire year, and a similar proportion resumed controlled, problem-free drinking. These results were validated using confidants (often the client's spouse). Most relapses occurred within the first 3 months. These results are supported by other studies, including a recent review of alcohol treatment from the Scottish Executive (Ludbrook *et al*, 2005). By contrast, Vaillant (1983) estimated that 2–3% of alcohol-dependent individuals in the USA abstain spontaneously each year in the community.

Unfortunately there are many uncertainties in the evidence base for treatment of alcohol use disorders – not least of which is the cost-effectiveness of therapy. Many in-patient and residential alcohol services in the UK were downsized following the famous trials by Edwards (see below). Controversies also remain concerning the benefits of disulfiram and controlled drinking.

Ideally, trials of alcohol treatment should follow more than 70% of participants for 1 year and confirm alcohol consumption using relatives or other

## Box 1 Alcohol dependence and harmful use

Key features<sup>1</sup> of ICD–10 dependence include:

- Compulsion to drink
- Problems in controlling drinking
- Physiological withdrawal symptoms
- Escalating consumption, owing to tolerance
- Preoccupation with alcohol, to the exclusion of other pursuits
- Increasing time lost to hangovers
- Disregard of evidence that excessive drinking is harmful

### Harmful alcohol use

- Harmful use is diagnosed if there is evidence that alcohol is damaging an individual's mental or physical health, but criteria for dependence are not met

1. Full diagnostic criteria appear in ICD–10 (World Health Organization, 1992: pp. 75–76).

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confidants. Clients should be breathalysed at follow-up interviews. Appropriate outcome measures include time to first drink, time to relapse (more than five standard drinks in one day), biochemical markers (especially  $\gamma$ -glutamyl transferase and carbohydrate-deficient transferase) and functional outcome scales such as the Alcohol Problems Questionnaire. A number of the published trials fail to meet these ideals. Another common problem is an unusually high rate of adherence to medication regimens (often exceeding 70%) or conclusions based on very small samples.

## Home v. in-patient detoxification

Detoxification is a treatment designed to control both the medical and psychological complications that may occur temporarily after a period of heavy and sustained alcohol use. Clinical procedures for managing detoxification have been well described in an earlier article in *APT* (Raistrick, 2000). These usually involve chlordiazepoxide at diminishing doses over 7–10 days, with parenteral thiamine supplementation. Ideally the dose of medication should be titrated against withdrawal symptoms. The mean cell volume has been identified as the best predictor of withdrawal complications such as hallucinations or fits. These occur in 5–10% of patients and would indicate in-patient detoxification (Metcalf *et al*, 1995). Unfortunately a history of previous alcohol withdrawal seizures has little predictive value.

In the 1960s in-patient psychotherapy over several weeks was the preferred method of therapy for alcohol dependence. However, published reports have consistently failed to find any difference in outcome between long and short in-patient detoxification programmes (Miller & Hester, 1986). For example Foster *et al* (2000) report a study of 64 alcohol-dependent patients admitted for either 7 or 28 days. About 60% relapsed (drank more than the recommended weekly intake) over the 3-month follow-up period.

Edwards & Guthrie (1967) reported a classic trial of 40 alcohol-dependent men who were randomly assigned to in-patient or 'intensive' out-patient treatment. Treatment duration for both groups was 7–9 weeks. Participants were followed up each month for 1 year. Social worker support and medication were used to provide assistance where necessary, for example by encouraging return to work. There was no significant difference in outcome between the groups when assessed by independent raters.

Edwards & Guthrie's influential paper encouraged the development of home detoxification

procedures that have become the preferred method of treatment for most people dependent on alcohol. Clients can usually complete home detoxification in 5–9 days. In ideal circumstances they are visited twice daily for the first 3 days and medication is supervised by a relative. Clients are breathalysed and medication withheld if they have consumed significant amounts of alcohol.

Hayashida *et al* (1989) reported a randomised trial of in-patient (77) and out-patient (87) detoxification using oxazepam with daily clinic visits. In-patient detoxification was significantly shorter than out-patient detoxification (6.5 v. 9.2 days). Fewer out-patients completed the procedure (72 v. 95%). There were no serious medical complications in either group. Both groups had improved at 6 months, with no significant differences; nearly half the participants were completely abstinent. In-patient detoxification cost 9–20 times more than out-patient detoxification. Hayashida *et al* noted that the Veterans Administration Medical Centre in Philadelphia had reported the out-patient detoxification of more than 6000 individuals with no serious adverse consequences. Many of these people had no supportive friends or relatives. Home detoxification can also be conducted by a nurse or general practitioner without recourse to a specialist. Other trials have shown no difference in outcome between in-patient and home detoxification (Irvin *et al*, 1999).

## Treatment intensity

Research has consistently shown that less intensive treatments are as effective as the more intensive options (Chick *et al*, 1988). For example, Edwards *et al* (1977) reported another classic trial of 100 alcohol-dependent men randomised to a treatment group and an advice-only group. The treatment group received a 12-month programme involving introduction to Alcoholics Anonymous (AA), calcium cyanamide, drugs to cover withdrawal, regular contact with a psychiatrist, advice on abstinence strategies and interpersonal problems, and regular support for the patient's wife from a social worker. If out-patient management failed, participants were offered in-patient detoxification for around 6 weeks. Participants in the advice-only group were offered just a sympathetic explanation that the responsibility for improvement lay with them and they were advised to abstain from alcohol completely. There was no difference between the two groups on outcome measures, including alcohol consumption. For example, 50–60% of each group still had significant drinking problems at 12 months.

These results have been confirmed in other populations. For example, Chapman & Huygens (1988) reported a study of 113 alcohol-dependent men in New Zealand randomised to a single confrontational interview or a 12-week programme involving 6 weeks' in-patient treatment. There was no difference between groups, with about one-third of participants abstinent after 18 months.

In the USA, Project MATCH (see below) showed very similar outcomes between the three forms of psychotherapy under study (Project MATCH Research Group, 1997). The four-session motivational enhancement therapy was just as effective as the 12-session treatments (twelve-step facilitation therapy or cognitive-behavioural therapy). Furthermore UKATT, the UK Alcohol Treatment Trial (2005), which is also discussed below, found that three-session motivational enhancement therapy was 48% cheaper but equally as effective as an eight-session social behaviour/network therapy.

## Brief interventions

Brief interventions are short, focused discussions (often of less than 15 min) that can reduce alcohol consumption in some individuals with hazardous drinking (Wallace *et al*, 1988; Fleming *et al*, 1997). Brief interventions are designed to promote awareness of the negative effects of drinking and to motivate change. Most share a set of common components such as feedback about the adverse effects of alcohol, comparison of the individual's consumption with drinking norms and discussion of the adverse effects of drinking. They are often based on motivational interviewing (see below).

Many reviews have shown the effectiveness of brief interventions (e.g. Wilk *et al*, 1997; Hall, 2005). Moyer *et al* (2002) report a meta-analysis of 34 controlled trials comparing brief interventions (fewer than five sessions) offered to treatment-seeking and non-treatment-seeking people with alcohol misuse. Brief interventions were shown to be moderately effective in the non-treatment-seeking groups, especially for those with less severe alcohol problems (effect sizes of 0.14–0.67 were reported). However, this analysis found no similar evidence for people from the treatment-seeking populations. Other reviewers estimated that brief interventions reduce alcohol consumption by around 24% compared with control conditions (Effective Health Care Team, 1993). Many of these trials included people with severe alcohol problems.

A UK trial involving 909 men and women with excessive alcohol consumption randomly assigned to brief interventions or usual care showed that mean alcohol consumption in men was reduced by

18 drinks per week compared with 8 for the control group (Wallace *et al*, 1988). Project TrEAT (Trial for Early Alcohol Treatment) involved 723 people with problem drinking randomly assigned to brief interventions or no treatment. At 12 months the mean number of drinks per week had fallen from 19 at baseline to 11 in the intervention group and to 15.5 in controls (Fleming *et al*, 1997).

## The great debate: abstinence v. controlled drinking

The controversial idea that some people recovering from alcohol dependence ('recovering alcoholics') can resume drinking was suggested by Davis (1962). This followed a study at London's Maudsley Hospital of 93 alcohol-dependent individuals, of whom seven had become 'normal' drinkers. The goal of controlled (moderate or non-problem) drinking usually includes some limit on alcohol consumption (e.g. 4 units per day) provided that drinking does not lead to signs of dependence, intoxication or social, legal or health problems. This runs contrary to the abstinence-based philosophy of Alcoholics Anonymous.

Controlled drinking may be an option for young, socially stable drinkers with short, less severe drinking histories (e.g. alcohol consumption of less than 4 units per day with normal liver function tests). An individual's belief that controlled drinking is an achievable goal is also a good prognostic factor. Most authors agree that controlled drinking should not be recommended for people with heavy dependence or those with protracted alcohol problems (Rosenberg, 1993). Controlled drinking is an attractive option for public health strategies aimed at non-dependent problem drinking.

The majority of studies of controlled drinking involve very different treatment interventions, as well as different goals. Hence it has been difficult to distinguish the effect of the advice (controlled drinking or abstinence) from other aspects of treatment. However, Sanchez-Craig *et al* (1984) reported one of the few randomised controlled trials. A sample of 70 people with early-stage problem drinking received six sessions of weekly cognitive-behavioural therapy and were randomised to groups with either a controlled drinking or an abstinence goal. There was no difference in outcomes at 2 years. In both groups at 6 months, drinking had been reduced from 51 to 13 drinks per week and 40–50% of participants had relapsed. These results were similar to those of a randomised controlled study by Foy *et al* (1984). Whereas the debate between controlled drinking and abstinence is unresolved, the trials indicate that clients

themselves decide which of these goals to follow and that they are often uninfluenced by the agenda set by the therapists.

## Alcoholics Anonymous

Alcoholics Anonymous is a worldwide organisation that has provided mutual aid for alcoholics for over 60 years. It uses the twelve-step approach (a disease or Minnesota model). Box 2 shows these steps, as they are unfamiliar to many clinicians. They involve the recognition that alcoholism is a relapsing illness that requires complete abstinence. Clients are required to acknowledge their alcoholism and also

### Box 2 The twelve steps of Alcoholics Anonymous

- 1 We admitted we were powerless over alcohol – that our lives had become unmanageable.
- 2 Came to believe that a Power greater than ourselves could restore us to sanity.
- 3 Made a decision to turn our will and our lives over to the care of God as we understood Him.
- 4 Made a searching and fearless moral inventory of ourselves.
- 5 Admitted to God, to ourselves and to another human being the exact nature of our wrongs.
- 6 Were entirely ready to have God remove all these defects of character.
- 7 Humbly asked Him to remove our shortcomings.
- 8 Made a list of all persons we had harmed, and became willing to make amends to them all.
- 9 Made direct amends to such people wherever possible, except when to do so would injure them or others.
- 10 Continued to take personal inventory and when we were wrong promptly admitted it.
- 11 Sought through prayer and meditation to improve our conscious contact with God as we understood Him, praying only for knowledge of His will for us and the power to carry that out.
- 12 Having had a spiritual awakening as the result of these steps, we tried to carry this message to alcoholics and to practice these principles in all our affairs.

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the harm they are causing themselves and others. New participants are encouraged to attend '90 meetings in 90 days'. Participants may engage the support of a sponsor who is an AA member who has been sober for at least 1 year. Overall, around half of new AA participants continue for at least 3 months, and about two-thirds of all members have been sober for over 1 year (Chappel, 1997).

Alcoholics Anonymous groups are widely available, inexpensive and popular, but it has been difficult to demonstrate their effectiveness. Randomised controlled trials have not found AA groups or the twelve-step approach to be superior to alternative treatments (Nowinski *et al*, 1992; McCrady *et al*, 1996). The evidence suggests that the twelve-step approach is at least as effective as most structured psychotherapies. A meta-analysis by Tonigan (1996) of 74 studies demonstrated a modest improvement in overall drinking patterns in AA members. However, participants are often involved in other forms of treatment, and studies are typically small and rarely randomised.

## Project MATCH

Project MATCH (Matching Alcohol Treatments to Client Heterogeneity) was a multicentre US trial involving two groups of participants (Project MATCH Research Group, 1997). One group, of 774 individuals (the after-care group) was recruited from patients receiving care after in-patient treatment for alcoholism. The other, of 952 individuals (the out-patient-only group), was recruited from people about to receive out-patient treatment for alcoholism. Participants in each group were randomly assigned to three forms of manualised psychotherapy: four sessions of motivational enhancement therapy, 12 sessions of twelve-step facilitation or 12 sessions of cognitive-behavioural therapy. There was no control group. Stringent efforts were made to ensure that the treatment manuals were followed, including tape-recording each consultation. Follow-up was at 1 and 3 years. Rigorous entry criteria were applied, which led to high treatment adherence but might also have resulted in a degree of favourable patient selection. Participants receiving each of the three treatments showed significant improvements, although there was no significant difference between the three treatment modalities. At 1 year, 35% of the after-care clients (who had undergone in-patient detoxification) had remained completely abstinent, compared with 20% of the out-patient-only sample. Project MATCH was hugely expensive and is the largest trial of any form of psychotherapy in history.

## UKATT

The United Kingdom Alcohol Treatment Trial (UKATT) involved 742 people seeking treatment for alcoholism at seven sites around the UK. Participants were randomised to social behaviour and network therapy or to motivational enhancement therapy, with follow-up at 3 and 12 months. Both groups reported similar, substantial reductions in alcohol consumption and alcohol-related problems, better mental health and improved quality of life based on a variety of measures (UK Alcohol Treatment Trial, 2005). For example the number of days abstinent from alcohol increased from 30% at baseline to 46% at 1 year, whereas average alcohol consumption per drinking day fell from 27 units to 19. Much like Project MATCH, only 23% of the 3241 treatment-seeking clients ultimately completed the trial. This may have produced a degree of favourable patient selection.

## Psychological therapies

### Motivational enhancement therapy

Motivational enhancement therapy (also called motivational interviewing) was developed by William Miller (Miller & Rollnick, 2000). It is based on theories of cognitive dissonance and attempts to promote a favourable attitude to change. Briefly, instructing people dependent on alcohol of the problems of drinking and the advantages of abstinence tends to encourage them to present contradictory arguments. This may reinforce their entrenched attitudes and encourage continued drinking. In motivational interviewing, the clients themselves give reasons why they should be abstinent and draw up a list of problems caused by their alcoholism. Box 3 gives the FRAMES formulation that encompasses the principles of motivational interviewing.

#### Box 3 Principles of motivational interviewing: the FRAMES formulation

- F Provide Feedback on behaviour
- R Reinforce the patient's Responsibility for changing behaviour
- A State your Advice about changing behaviour
- M Discuss a Menu of options to change behaviour
- E Express Empathy for the patient
- S Support the patient's Self-efficacy

After Miller & Rollnick (2000)

Project MATCH showed motivational enhancement therapy to be effective, although only four sessions were used, compared with 12 sessions of the other treatments. Motivational interviewing is an ideal brief therapy for patients with problem drinking in primary care.

Motivational enhancement therapy in UKATT comprised three sessions, each of 50 min, over 8–12 weeks. It combined counselling in the motivational style with objective feedback. Significant others were generally excluded from the sessions, in contrast to Project MATCH. Motivational enhancement therapy costs around £129 per patient.

### Twelve-step facilitation

Twelve-step facilitation is a form of structured intervention to enhance engagement with AA (Nowinski *et al*, 1992). In Project MATCH it was delivered individually rather than at conventional AA groups. However, the objectives included encouraging participants to become members of AA groups and to accept the AA philosophy.

### Cognitive-behavioural therapy

Cognitive-behavioural therapy (cognitive-behavioural coping skills) for alcoholism is based on the work of Marlatt & Gordon (1985). This assumes that alcoholism is a maladaptive habit rather than purely physiological responses to alcohol. Drinking becomes a means of coping with difficult situations, unpleasant moods and peer pressure. Consequently coping skills are taught to deal with these high-risk situations (Carroll & Schottenfeld, 1997).

Cognitive-behavioural therapy involves several techniques, many of which have been studied in isolation. The terminology is confusing and varied. In general, cognitive-behavioural therapy for alcoholism includes techniques such as relapse prevention, behavioural marital therapy, social skills training and community reinforcement approaches. Many of these techniques are also subsumed under the heading of behavioural skills training. Exhaustive reviews by Miller & Wilbourne (2001) and Finney & Monahan (1996) identified variations of these techniques as some of the most effective treatments for alcoholism.

Many forms of relapse prevention treatment are based on cognitive-behavioural therapy. Irvin *et al* (1999) reported a meta-analysis that included ten randomised controlled trials of relapse prevention treatment in alcoholism. The overall effect size was 0.37, conventionally regarded as medium to large.

Follow-up periods varied from 6 months to 1 year. Significantly, there was a greater effect on psychosocial function than on drinking behaviour.

### **Social skills training**

Social skills training is a component of cognitive-behavioural therapy. The method assumes that a larger repertoire of coping skills will reduce the stress of high-risk situations and provide alternatives to alcohol use. Techniques involve assertiveness training, modelling and role-playing of skills such as refusal of alcohol and dealing with interpersonal problems.

At least 25 controlled trials of social skills training have been published. One of these was a randomised trial of eight weekly 90-min sessions of social skills training or group discussion (Ericksen *et al*, 1986). Over 1 year clients in the social skills training group drank one-third less than those in the discussion group, had twice as many sober days (77 v. 32%) and remained abstinent for six times as long after discharge.

### **Community reinforcement approach**

The community reinforcement approach was developed in North America (Sisson & Azrin, 1986) and is a form of behavioural marital and family therapy. According to the original programme, a friend or family member, usually the spouse, uses the provision or removal of agreed reinforcers to reward periods of sobriety and punish drinking. Reinforcers include access to radio, television, newspapers, telephone or driving licence. The spouse may also be shown how to identify and take advantage of moments when the drinker is most motivated to enter treatment, reinforce attendance at relapse prevention groups (usually AA) and supervise disulfiram. The prescribing of disulfiram, early access to a counsellor in the event of relapse and the involvement of neighbours and friends were introduced to enhance the programme's effectiveness. These programmes typically require 30 h of the client's time.

Many of the randomised studies by enthusiasts of the community reinforcement approach report >90% abstinent days compared with 10–45% for individual counselling (Edwards & Steinglass, 1995). Dramatic reductions in alcohol consumption were observed even while the spouse was undergoing training before the partner began treatment. UKATT provides some information on the use of a variation of community reinforcement and cognitive-behavioural therapy in the UK, although it is impossible to determine the effectiveness of each component. The effectiveness of the

#### **Box 4 Principle components of contingency management**

- The clinician arranges the environment such that alcohol use is readily detectable
- Reinforcers are arranged to reward abstinence
- Incentives are withheld following alcohol use
- Reinforcement from alternative sources (employment, family or social) is increased to compete with that from alcohol

community reinforcement approach itself has not been confirmed in the UK.

### **Social behaviour and network therapy**

Social behaviour and network therapy is based on the principle that people with serious drinking problems need to develop a social network that supports change. It uses techniques adapted from cognitive-behavioural therapy and the community reinforcement approach to help clients build these networks. The therapy was developed for UKATT, where it involved eight 50-min sessions over 8–12 weeks (Copello *et al*, 2002). Social behaviour and network therapy costs around £221 per patient.

### **Contingency management**

Contingency management is particularly useful when there is no significant other to provide forms of community reinforcement. The four principle components of contingency management are shown in Box 4.

Petry *et al* (2000) described a study of a contingency management technique whereby abstinence (a negative breathalyser test) or the completion of various steps towards treatment goals earned participants the right to draw vouchers from a bowl and win prizes ranging from \$1 to \$100 in value (from a \$1 meal voucher to a hand-held television). No negative consequences resulted from self-reported alcohol use. Forty-two alcohol-dependent people were randomised to receive standard treatment plus contingency management or to standard treatment alone. Standard treatment involved attending 5 days per week for 5 h each day for the first 4 weeks, with follow-up sessions varying from 1 to 3 per week for a further 4 weeks. After 8 weeks each participant in the contingency management group had earned an average of \$200. Eighty-four per cent of the contingency management group completed the treatment course v. 22%

of the controls. Furthermore, 69% were abstinent v. 39% of controls.

Although contingency management is an effective addition to many forms of treatment, it creates an ethical controversy by 'paying' alcoholics not to drink. Furthermore, there is a tendency to relapse when the reinforcing regime is ended. This may explain the reluctance of many services to introduce contingency management.

### Cue exposure

When someone who has been dependent on alcohol encounters cues previously paired with drinking, such as a bottle or the smell of alcohol, they may experience responses such as craving and withdrawal-like symptoms which can motivate them to drink. Cue exposure involves repeated exposure to such stimuli in an attempt to extinguish the cravings and other undesirable responses. Although results for this approach have been variable, there is now some evidence of the benefit of cue exposure from the Mesa Grande project (Drummond & Glautier, 1994; Miller *et al.*, 2001; Ludbrook *et al.*, 2005). In one trial, 100 alcohol-dependent patients were randomised to ten sessions of cue exposure plus coping skills training or to a meditation and relaxation control condition (Rohsenow *et al.*, 2001). At 12-month follow-up individuals in the experimental group who had lapsed reported fewer heavy drinking days than those in the meditation and relaxation group (12 v. 25% were heavy drinking days). They also made greater utilisation of coping skills techniques.

### Therapeutic communities and residential rehabilitation

Therapeutic communities ('rehab') typically require prolonged residence (often 12–18 months). Clients are closely involved in running the programmes, including selecting and discharging residents. Abstinence is usually a prerequisite. Despite the long tradition of this approach and its continued popularity, very little critical research has been performed into its effectiveness. Although therapeutic communities are extremely expensive, of the 361 controlled studies of in-patient treatment for alcohol dependence, involving 72 000 clients, reviewed by Miller & Wilbourne (2002) only one involved treatment in a therapeutic community. This showed no benefit over the control treatment.

Most studies of therapeutic communities are conducted without control groups and the lack of randomisation probably leads to selection bias in favour of more motivated patients. One such,

reported by Van de Velde *et al.* (1998), involved 881 participants, three-quarters of whom had alcohol dependence, residing in Dutch therapeutic community providing a 1-year programme. Forty-five per cent of the participants remained in the therapeutic community for at least 5 months. At 2.5 years the proportion drinking heavily (more than 4 units per day) had fallen from 77% to 20%. Almost half of those who had been dependent on alcohol were abstinent after 4.5 years.

### Drug treatments

#### Disulfiram

Disulfiram prevents the breakdown of alcohol by acetaldehyde dehydrogenase. This leads to accumulation of acetaldehyde, causing headache, flushing, palpitations, nausea and vomiting. Disulfiram was extremely popular in the 1950s and 1960s and was hailed as a 'cure' for alcoholism. This enthusiasm has waned with the results of more recent trials. Hughes & Cook (1997) reviewed 24 outcome studies for oral disulfiram and 14 using implants from 1967 to 1995. Most studies were flawed and reported no significant benefits for disulfiram. There was no good evidence in favour of implanting disulfiram tablets. In the largest trial 605 men were randomly assigned to three groups, including oral disulfiram v. placebo over 1 year. There was no overall difference in drinking outcome (Fuller *et al.*, 1986). For example, the proportion continuously abstinent was 19% in the disulfiram group v. 16% in the control group. However, disulfiram did lead to a reduction in the number of drinking days (49 v. 86). Only 20% of participants had acceptable adherence with the medication regimens.

Chick *et al.* (1992) report one placebo-controlled trial involving 126 alcohol-dependent individuals randomised to receive supervised disulfiram or placebo. Over the 6-month follow-up period, the average increase in the number of abstinent days was 100 for the disulfiram group and 69 for the placebo group. Alcohol use was reduced by 70–80% in the disulfiram group compared with 50% in placebo group. Fifty-five per cent of participants adhered to the protocol. Although the trial was randomised, participants were not masked to treatment. This trial was really a composite of disulfiram and community reinforcement. Nevertheless, this is one of the few convincing trials to show significant benefits of disulfiram.

Disulfiram causes potentially fatal acute hepatotoxicity in about 1 in 25 000 patients. This has led several authors to recommend either frequent (every 2 weeks) liver function tests or avoidance

of disulfiram in those with abnormal liver function (Fuller & Gordis, 2004). It must be remembered that alcoholism itself is often fatal. However, disulfiram remains unproven after over 50 years of use.

### **Naltrexone**

Naltrexone is an orally active opiate receptor antagonist that is thought to reduce the pleasurable effects of drinking. At least 10 controlled trials, involving 1500 participants, have been published (Kiefer *et al.*, 2003). Two early randomised controlled trials compared naltrexone with placebo in people with alcohol dependence (O'Malley *et al.*, 1995). Overall, 54% of patients remained abstinent at 12 weeks in the naltrexone group compared with 31% in the placebo group. However, the difference became less dramatic after 6 months (O'Malley *et al.*, 1996).

Chick *et al.* (2000a) reported a double-blind randomised controlled trial involving 169 patients assigned to naltrexone or placebo after medical detoxification. Fewer than half completed the 12-week trial. Intention-to-treat analysis revealed no significant difference in drinking outcomes between the groups (complete abstinence occurred in about 20%). However, the quantity of alcohol consumed and the number of non-abstinent days were halved in the 70 participants in the naltrexone group who took 80% of the tablets given to them.

Volpicelli *et al.* (1997) reported a study of 97 alcohol-dependent patients. The relapse rate at 12 weeks was 53% in controls and 35% in patients receiving naltrexone. The proportion of drinking days was 11% in controls and 6% in those receiving naltrexone. However, adherence to treatment was exceptionally good, with 73% reporting that they had taken over 90% of the prescribed tablets. Overall these studies report a medium to large effect size of 0.3–0.6 (Kiefer *et al.*, 2003).

By comparison, the largest double-blind randomised controlled trial of naltrexone involved 627 participants. At 1 year there was no difference between groups (Krystal *et al.*, 2001). For example, the proportion of drinking days was 15–19% in the two groups receiving naltrexone and 18% in the placebo group, while the mean time to relapse was 72 days in those receiving naltrexone and 62 days in those taking the placebo. (Relapse is conventionally defined as consuming more than five standard drinks on 1 day.) Adherence to the medication regimen was 44% over the year.

Although recent meta-analyses indicate that naltrexone may be as effective as acamprosate, naltrexone does not have a licence for treatment of alcohol dependence in the UK. Furthermore, research has shown less evidence of efficacy in

European trials than in the USA (Soyka & Chick, 2003).

### **Acamprosate**

Early studies suggested that acamprosate (an analogue of the inhibitory neurotransmitter  $\gamma$ -aminobutyric acid) approximately doubled the chances of achieving continuous abstinence following detoxification and increased the number of abstinence days by 30–40% (e.g. Sass *et al.*, 1996). At least 14 controlled trials, involving 4000 participants, have been published (Kiefer *et al.*, 2003). However, Chick *et al.* (2000b) reported the largest single study of acamprosate: the United Kingdom Multicentre Acamprosate Study. This involved 581 patients (one-third of whom were episodic drinkers, the rest dependent) randomly assigned to acamprosate or placebo under double-blind conditions. Overall adherence to treatment was poor (35%) and there was no significant difference in drinking outcomes between groups at 6 months. The mean total number of abstinent days was 77 v. 81 days (acamprosate v. placebo), and complete abstinence was achieved in 12% and 11% respectively. Since this time, several other trials have reported more encouraging results, to the extent that the number needed to treat for acamprosate has been estimated at 8.15 (Soyka & Chick, 2003). Another review, based on data from Belgium and Germany, has calculated that acamprosate prescription may result in a healthcare cost saving of £600 per patient (Ludbrook *et al.*, 2005).

Kiefer *et al.* (2003) reported a randomised double-blind placebo-controlled study of 160 alcohol-dependent in-patients receiving naltrexone, acamprosate, a combination of naltrexone and acamprosate, or placebo. The relapse rate was about 50% in the placebo group and 30% for those receiving active medication. The relapse rate in the combination group was 25%. However, 80% adhered to the medication protocol and 90% attended follow-up appointments. Although 782 in-patients were informed about the study, only 160 chose to take part. These facts suggest a bias in favour of more highly motivated patients.

### **Conclusions**

Research has consistently shown that less intensive, community-based treatment for alcoholism is just as effective as prolonged in-patient care. Large trials such as Project MATCH and UKATT show no significant difference between the various forms of psychosocial treatment. The dramatic improvements suggested by early trials of pharmacotherapy



in relapse prevention have seldom been supported by later studies. There remains concern about trials of relatively expensive drugs (such as acamprosate and naltrexone) that report unusually high treatment adherence rates. Nevertheless more recent evidence provides some encouragement for the use of these agents. It is salient to note that some of the most effective means of reducing alcohol consumption, such as increasing taxation and restricting access, are being abandoned by governments 'bent on deregulation' (Hall, 2005). Government policy is likely to be influenced by the facts that the alcohol industry generates over £13 billion each year for the UK exchequer and employs well over 1.4 million people (Raistrick, 2005).

## Declaration of interest

None.

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## MCQs

- 1 The following are diagnostic features of alcohol dependence:**
- compulsion to take alcohol
  - escalation of amount used
  - withdrawal syndrome
  - visual hallucinations.

**2 Concerning effectiveness:**

- home detoxification is less effective than residential detoxification
- intensive treatment is more effective than brief interventions
- Alcoholics Anonymous is probably as effective as newer psychotherapies
- randomised trials have shown that controlled-drinking techniques are as effective as abstinence-based techniques in problem drinkers.

**3 Project MATCH showed the following:**

- motivational interviewing was more effective than twelve-step facilitation
- overall there was no significant difference between the three treatment modalities
- about 20% of the out-patient sample abstained for 1 year
- disulfiram was more effective than acamprostate.

**4 The following techniques are correctly described:**

- motivational interviewing in alcoholism attempts to promote a favourable attitude change towards abstinence or reduced drinking
- cognitive-behavioural coping skills treatment involves learning how to identify and deal with high-risk situations for relapse
- the community reinforcement approach involves a friend or family member providing reinforcement for periods of sobriety and negative consequences for drinking
- contingency management involves prolonged residence in a therapeutic community.

**5 The following drugs are correctly described:**

- disulfiram inhibits the breakdown of alcohol
- acamprostate is a potent anticonvulsant
- naltrexone blocks the effects of endogenous opioids
- chlormethiazole is the treatment of choice for medically assisted detoxification.

### MCQ answers

1	2	3	4	5
a T	a F	a F	a T	a T
b T	b F	b T	b T	b F
c T	c T	c T	c T	c T
d F	d F	d F	d F	d F