Managing alcohol dependence *in practice*

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The impact on the patient

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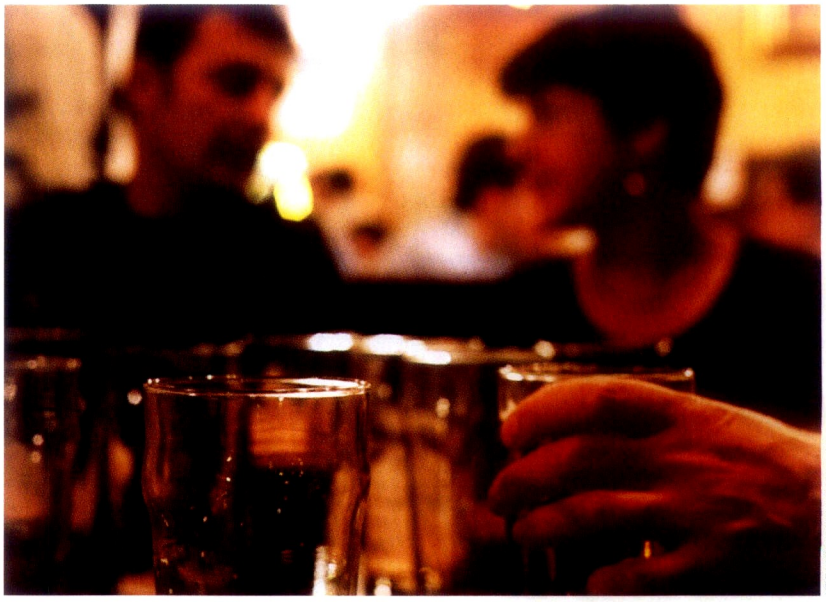
It is estimated from population surveys that around 5% of the UK population have problems with alcohol.[1] These problems can manifest themselves in many ways, both physical and psychological. This bulletin will explore the impact of alcohol dependence on the patient and how primary care physicians can assist patients in overcoming these problems.

There are approximately 33,000 alcohol-related deaths a year in Britain, and up to 14 million working days lost as a result of alcohol-related problems.[2] Alcohol is a factor in a substantial proportion of accidents and violent incidents, as well as being a common cause of hypertension and causing around 3% of cancers.[2] Most people with alcohol problems recover without any help, or with help from friends or organisations such as Alcoholics Anonymous (AA). Nevertheless, a large number of people will come to the attention of primary care specialists, and it is in primary care that the greatest impact can be made on addictions, and specifically on alcohol-related problems.

There is, however, also a positive side to alcohol consumption. It is increasingly clear that moderate consumption of alcohol is associated with increased lifespan. This is known as the 'J-shaped curve' (also referred to as a U-shaped curve), as mortality plotted against alcohol consumption looks like an elongated letter J (or U). The effect may be quite large – standardised mortality ratios as low as 0.5 for moderate drinkers have been found in one Danish study.[3] Consumption of no more than 21 units of alcohol per week for men and 14 for women is recommended by most medical bodies. Note that drinking ten pints on a Friday night does not have the desired effect, and that the effect is only significant in the over-50s.

The J-shaped curve probably goes part of the way to explaining the 'French paradox': the French on average smoke and drink heavily, as well as eating fatty foods, and yet their life expectancy is the same as ours.



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While moderate alcohol consumption can be beneficial, drinking ten pints on a Friday night is not a good idea

Spectrum of alcohol misuse disorders

The International Classification of Diseases (IDC-10)[4] recognises a number of ways in which alcohol can 'cost you more than the price on the bottle' (as AA defines alcoholism):

- Intoxication.
- Hazardous use – persistent patterns of use carrying high risk of future harm.
- Harmful use – persistent use already causing harm.
- Dependence. The 'dependence syndrome', first outlined by Edwards and Gross in 1976,[5] has the following features:

– **Subjective compulsion to use**

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Box 1. Withdrawal symptoms from alcohol

Hours–days	Few days
Sweating	Withdrawal seizures ('rum fits')
Tremulousness	Delirium tremens (confusion/clouding of consciousness,
Nausea/vomiting	severe tremor, vivid hallucinations
Agitation	(classically Lilliputian), terror)
Dysphoria	Wernicke's encephalopathy (ataxia, nystagmus,
	ophthalmoplegia (typically lateral rectus palsy), confusion)

('craving'). People feel that they must drink, and experience intense desires to do so when abstinent.
– Characteristic **withdrawal symptoms** (Box 1).
– **Loss of control** over onset, termination or levels of use. 'Subjective loss of control.'
– **Tolerance**, due to induction of liver alcohol dehydrogenase. May be lost if liver damage becomes extensive.
– **Progressive neglect of alternative pleasures or interests**. Severely dependent people do little other than drinking.
– **Persisting use despite evidence of harm**.
Other recognised features of addictions are:

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Problem drinkers are often depressed

- **Narrowing repertoire** (ie, people drink only one type of alcohol, often that providing the most 'bangs per buck').
- **Rapid reinstatement after abstinence**. It may take 15 years to build up to a bottle of spirits a day, but only a week or so after relapse to return to that level of consumption.

Addiction

Alcohol dependence is a specific example of addiction, which is a property of drugs that affect the central reward pathways of the brain. The problem when considering addiction is that the properties of a particular drug are not in themselves a sufficient explanation (the vast majority of people who use addictive substances such as alcohol, or even drugs such as heroin or cocaine, do not end up addicted to them). Drugs in use within society vary widely in their addictive potential irrespective of whether they are legal, prescription-only or illegal. For this reason, many people working in the field of addictions prefer to focus on the behaviours surrounding addiction, and emphasise the psychological and social aspects of drug use.

A general definition of addiction is 'any repetitive self-damaging behaviour'. This broad definition is useful, because it takes the focus away from the substance and puts it instead on the behaviour of the addicted person. Also, it generalises the concept so that it is something most of us can understand and have experienced. Most of us have engaged in behaviours damaging to ourselves or others around us, which we have found surprisingly difficult to change.

Aetiology

It is usual in the psychiatric world to think of causation in terms of biological, psychological and social factors. This is useful in addictions, where all three have important impacts on both the aetiology and treatment of addictive problems.

Biological factors

Effects of the substance. Alcohol has several effects on the brain. In common with almost all drugs of addiction, it stimulates the closely linked central reward systems mediated by endogenous opiates and dopamine. In addition, it antagonises glutamate, an important central excitatory chemical, acting at the N-methyl D-aspartate (NMDA) receptor, as well as having effects on gamma-aminobutyric acid (GABA) and calcium channels. These effects can explain both the acute actions of alcohol and withdrawal phenomena from alcohol.

Familial and genetic factors. It has long been known that alcohol dependence runs in families.[6] If anything, this is becoming more pronounced with time.[7] It is as though there are genetic risk factors triggered by environmental exposure. Over the past 50 years the general population's alcohol consumption has roughly doubled, so the influence of familial factors seems to have increased.

Adoption studies show that people end up with the level of risk of their biological (not adoptive) parents.

The major inherited risk factor is probably temperament. This consists of a number of inherited factors acting at a preconscious level to influence the way people learn from and react to situations. According to Cloninger,[8] type 1 or 'milieu-limited' alcoholics are people high in harm avoidance and low in novelty-seeking. They tend to be anxious and passive–dependent personalities, who drink for a sense of calm alertness. Their alcohol dependence develops late in life, in the context of many

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years of socially sanctioned heavy drinking. They tend to drink in binges, and feel guilty about this.

In contrast, type 2 or 'male-limited' alcohol dependence is found in people with very low harm avoidance and high novelty-seeking. They tend to drink very heavily from an early age, independent of environmental norms, and develop prominent physical symptoms of alcohol dependence.

Psychological factors

Psychiatric. 'Dual diagnosis', another psychiatric diagnosis in addition to addiction, is found in up to half of addicted patients.[6] Common co-morbid diagnoses (with suggested treatment in brackets) include:

- Anxiety/panic disorders (selective serotonin reuptake inhibitors – SSRIs).
- Depression (antidepressants).
- Mania (neuroleptics/mood stabilisers).
- Schizophrenia (antipsychotics).
- Obsessive–compulsive disorders.
- 'Emotional or erratic' personality disorders, especially antisocial or borderline.

Classic/operant conditioning. Classic conditioning is where a previously neutral stimulus becomes associated with a reward (for example, Pavlov's dogs salivated when a bell was rung). An addicted person may experience craving for the substance when exposed to an environment or situation that has been associated with its use in the past. Operant conditioning refers to the fact that behaviours leading to a reward will tend to be repeated with increasing frequency (for example, rats will press levers to obtain sugar pellets). People addicted to alcohol will spend much of their time in drink-related behaviours, often to the exclusion of other important functions.

Ego defence/coping mechanism. 'I could murder a drink' is a phrase many of us use when we are considering alcohol as a coping mechanism. Alcohol is a euphoriant and relaxant in small doses, and this may reduce subjective tension. The use of larger amounts is unhelpful, because it is in effect a 'reality-denying' defence (the problems temporarily dissolve in alcohol, but remain unchanged the morning after, and the person is both poorer and hungover). People with addictions tend to overuse the substance as a coping mechanism, to the exclusion of all else, and their other skills tend to atrophy. Recovery consists partly in (re)learning skills to deal with life without the use of a substance as interlocutor.

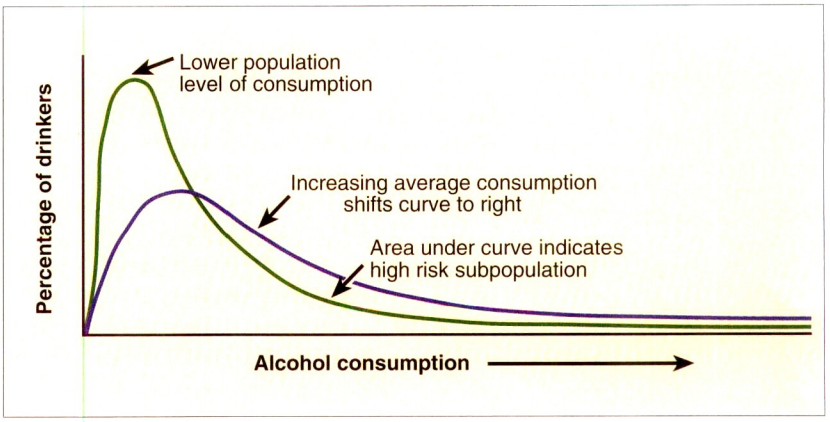

Figure 1. The Ledermann curve (adapted from Paton[11])

Social factors

Relative cost. This is by far the most significant determinant of population levels of consumption. The relative price of alcohol has more than halved over the past 40 years in the UK. In economic terms, alcohol and other addictive drugs are relatively 'inelastic' – ie, consumption is not very sensitive to price: increasing price by 14% only decreases consumption by about 4.5%.[9]

The Ledermann curve.[10] The distribution of consumption in a population follows a log normal curve (Figure 1)[11]; 10% of people in a population consume 50% of all alcohol. Increasing average consumption (reducing price) skews and shifts the curve to the right (heavy consumption) end.

Social mores/trends. Lifetime prevalence of alcohol dependence approximately doubled in both men and women between the 1925 and 1965 birth cohorts in the USA.[7]

Occupation. High-stress occupations, or ones in which there is easy access and constant exposure to alcohol, carry a high risk of dependence.[12]

Natural history

It is therefore apparent that various factors influence the tendency of individuals to become dependent on alcohol. However:

- Most people who use addictive drugs do not become addicted.
- Most people who do develop addictions recover, the vast majority without medical help.
- Vaillant's inner-city sample showed one-third of the total cohort developed problems by age 47, and around half of those recovered to controlled drinking or abstinence at the last count.[13]
- Those who are able to return to controlled drinking are those whose addictions never reach great severity.

The natural history of addiction is **recovery**. The people we see in addictions clinics are the extreme end of the spectrum of dependence. It is important to specify which population we are talking about when we give a prognosis. For example, the suicide rate for people with severe alcohol dependence seen in clinics is much higher than that for people with alcohol dependence in general.

Treatment: the changing of behaviour

Early prevention in primary care

The single most effective intervention in reducing harmful alcohol use (at an early stage, at

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Box 2. CAGE questionnaire[14]

- Have you ever thought you should **C**ut down?
- Have you ever had **A**rguments about your drinking?
- Have you ever felt **G**uilty about your drinking?
- Do you ever need an **E**yeopener?

Two positive answers is a level for concern; even one should at least provoke us into taking a short alcohol history (for example, 'How much did you have to drink yesterday/last week (the day/week before? and so on)').

least) is being told by a doctor to cut down. To treat patients effectively it is necessary to make a diagnosis. It is, therefore, essential to ask patients about their alcohol consumption – not only when a problem is suspected, but opportunistically (for example, at new patient interviews). The simplest questionnaire of all is CAGE (Box 2).[14]

Other possible signs that may alert the practitioner are:

- A smell of alcohol on the breath.
- Unexplained physical or psychological illness (alcohol replaces syphilis as the modern 'great mimic').
- Alcohol-related offences (for example, drink-driving, public order offences).
- Accidents.

Treatment of established addiction

Once addiction or any other behaviour pattern is established, treatment is aimed at facilitating the changes in behaviour necessary to overcome the problem. The essential principles of behaviour change comprise **cost–benefit analysis** and the **stages of change** (Box 3).[15]

Anyone will change their behaviour if the cost is greater than the benefit at that time. People are very adept at computing subjective cost–benefit analyses, including people with addictions. We need to try to understand and influence their cost–benefit analyses, not impose our own.

All treatments, in any modality, are aimed at facilitating some part of this process, and it is surprising how even very short interventions can have major long-term effects.

Categories of treatment

It is useful to think of treatments in terms of their objectives:

- Treatment of immediate symptoms of alcohol dependence.
- Treatment of 'dual diagnosis'.
- Long-term treatment.

It is also useful to distinguish between biological treatments and psychosocial treatments. Recovery from addiction is primarily a psychosocial process. It is about people changing their lives so that they no longer require the substance/behaviour. Drug treatments can be very valuable in relieving symptoms, but they do not 'cure' people.

Box 3. Stages of change and appropriate interventions[15]

- Pre-contemplation ('I don't have a problem'). Inform of risks.
- Contemplation ('I've got a problem, but I'm not ready to tackle it at the moment'). Help to consider options.
- Preparation (taking small steps – for example, reducing consumption). Encourage to continue, emphasise power to change.
- Action (stopping the behaviour). Encourage, emphasise positive benefits of changed behaviour.
- Maintenance (staying off alcohol). Continue to emphasise benefits.
- Relapse (may return to any previous stage – ie, the process is cyclical). Relapse is not an all-or-nothing phenomenon.

Treatment of the immediate symptoms of alcohol dependence

The vast majority of detoxifications are carried out in the community and, in general, these are as effective as inpatient ones and considerably less costly.

Detoxification is not offered to people who are grossly intoxicated, as commitments made under the influence have no validity when sober. The sort of people who are going to ask for detoxification when highly intoxicated are almost by definition not in the 'preparation' or 'action' stages of change.[15]

Neither is detoxification offered to people who threaten suicide when under the influence. It is well known in psychiatry that intoxication makes assessment of mental state unreliable. 'Manipulative' suicide threats should be seen for what they are: a maladaptive attempt to influence the way in which care is given. Care should be offered, calmly and appropriately, at the earliest opportunity.

Chlordiazepoxide detoxification

The recommended agent for detoxification is chlordiazepoxide. Because of the risks in overdose, chlormethiazole is no longer recommended for detoxification. In addition, it seems that chlordiazepoxide has a lower addictive potential.

Outpatient detoxification with chlordiazepoxide usually needs supervision by a spouse or friend. Daily prescription is sometimes advisable if supervision is inadequate. The starting dose is 20–30 mg *qds*. As a rule of thumb, this will be enough for people drinking 15–30 units per day. If this is inadequate, it can be increased to 30–40 mg *qds*. The dose is then tapered – for example, 30 mg *qds* x 1/7, 20 mg *qds* x 1/7, 10 mg *qds* x 1/7, 5 mg *qds* x 1/7, 5 mg *bd* x 1/7. It is then stopped.

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Additional treatment is strongly recommended, it consists of thiamine 200 mg *bd* and two multivitamin tablets daily. Parenterovite IM, or even IV, is coming back into vogue in severe cases – the risk of anaphylaxis is much lower than the risk of Wernicke–Korsakoff syndrome.

What is a successful detoxification?

The doctrine of harm minimisation implies that we should accept limited success, and the 'stages of change' cycle[15] implies that success is rarely immediate or total. There are some patients for whom detoxification every three months, followed by six weeks of abstinence, then relapse, is a very good result. At least their liver and nervous system (and their lives) have had six weeks to recover, and if they accumulate enough time abstinent, even in short stretches, psychosocial recovery may begin.

Treating 'dual diagnosis'

Up to 50% of people with addictions also have another psychiatric diagnosis,[6] and in most cases this is primary (ie, the other diagnosis precedes the addiction). Common dual diagnoses found in the Epidemiological Catchment Area study in the USA (10,000 people interviewed in three cities) were schizophrenia, affective disorders and anxiety disorder.[1]

Other clinical pictures which may present with alcohol problems include mood instability/borderline personality (carbamazepine/valproate) and obsessive–compulsive disorder (SSRIs; high dose, long term).

It is necessary to treat both the addiction and the primary diagnosis (see Case study 1). There are two fallacies of addictions work. The 'counselling fallacy' is that if we find the cause of the addiction and fix that, the addiction will stop. This is wrong – addiction, once established, behaves as a second primary diagnosis. The 'medical fallacy' is that only the addiction needs treating. This is also wrong. If somebody has, for example, been using alcohol as an anxiolytic, then leaving them with their anxiety disorder untreated is worse than useless.

Note that generic counselling has not been proven effective: it needs to be focused on specific areas where the patient is experiencing problems.

Long-term treatment

It is a truism that giving up a drug or behaviour is easy, and that staying off it is the difficult part. A number of exciting recent developments in both medical and psychosocial fields have improved success rates in the maintenance of abstinence.

We know from behavioural work that incentives are much more effective if they are immediate, and that behaviour only changes if the costs of the behaviour outweigh the benefits. Relapse would be expected to be common in addictions, because the cost–benefit analysis of drinking will change over time. When someone is in a dire physical state, and homeless, the costs of drinking are salient and obvious; when they have recovered, the cost of the first few drinks is not high, and the immediate benefit (tension reduction, cessation of craving) may be very high indeed.

So, in order to improve success rates in the treatment of addiction, we need to: increase the cost and reduce the benefit of drinking; or increase the benefits and reduce the costs of abstinence; and increase the immediacy of impact of costs and benefits.

One long-standing medical treatment (disulfiram) and one new one (acamprosate) help us to do this. Another drug, the opiate antagonist naltrexone, has also been shown to be useful although it is not currently licensed for the treatment of alcohol dependence in the UK. It should probably only be used with specialist guidance.

Disulfiram

Disulfiram (Antabuse; Dumex Limited, UK) is the only drug we ever prescribe hoping that the patient will not feel the pharmacological effect. It is in fact a behavioural treatment: the patient takes the tablet in the morning, and says to him/herself: 'I can't drink today'. It costs about £20 per month.[16]

Disulfiram inhibits acetaldehyde dehydrogenase. A build-up of acetaldehyde causes flushing, palpitations, severe nausea and vomiting. There are immediate aversive consequences on relapse.

A disadvantage of disulfiram is that it may cause death if alcohol is consumed. Side-effects include a smell of garlic on the breath, and some gastrointestinal upsets. There can be problems with accidental consumption of alcohol (for example, in trifle), or use of alcohol-containing products such as perfumes (may cause rashes).

Disulfiram has only been shown in randomised controlled trials to be effective if supervised – ie, given and monitored by someone else.

Clinical tip: Disulfiram is very useful for those who tend to relapse on impulse, and may be even more effective if combined with anticraving medications (see below).

Craving: an important stimulus to relapse

Craving can be defined as a persistent desire to consume a substance, or carry out a behaviour, and is one of the cardinal symptoms of addiction.

Case study 1: Treatment of 'dual diagnosis'

A 28-year-old man, who tended to drink in binges, was referred to me by his alcohol counsellor for assessment of his mental state, after repeated short spells of abstinence (of no longer than two to three weeks) ending in serious relapses. At interview, he reported his relapses to be precipitated by severe anxiety, beginning when he stopped drinking, and (unlike withdrawal-related anxiety) worsening with the length of time he was abstinent. He reported that he had always used alcohol to help him cope with severe generalised anxiety, which he had suffered from since his teens.

He was treated with nefazodone 50 mg *bd* and pindolol 2.5 mg *tds*, a powerful and rapidly-acting anxiolytic combination. At review two weeks later, he was abstinent and reported that anxiety was no longer a problem for him. When last seen, he was three months abstinent and in full-time employment.

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Counselling in a group situation can be helpful in alcohol dependence

It can be highly debilitating, causing preoccupation with the substance when it is not being consumed, and has been shown to predict relapse.[17] Recent discoveries allow cravings to be treated medically, improving outcome in terms of both abstinence rates and frequency or severity of relapse.

The only product licensed in the UK for the treatment of craving is acamprosate.

Acamprosate

Acamprosate (Campral EC; Merck Pharmaceuticals, UK) has been on the market in France since 1990, and there is a great deal of evidence, from both clinical trials and clinical experience, that it is effective.

Its major advantage in practice is that it is very well tolerated, and the side-effect profile is such that patients sometimes need assuring that they are not taking a placebo. The cost is about £50 per month.[16]

Acamprosate is a GABA analogue which antagonises glutamate and normalises NMDA-receptor functioning. It has shown a dose-related effect on withdrawal symptoms and alcohol consumption in animal studies.[17]

Acamprosate reduces craving and there seems to be no reduction of effect with time. It may be particularly effective against conditioned withdrawal. It more than doubles long-term (>1 year) abstinence rates and reduces both frequency and severity of relapse.[18] The usual dose is 666 mg *tds*, or 666 mg as a first dose and 333 mg *bd* if <60 kg.

The main side-effect is diarrhoea, though this is uncommon. Doses may sometimes need to be adjusted to take account of side-effects or partial therapeutic effects. Psychosocial interventions are also important, as in Case study 2.

Clinical tip: Acamprosate may be most valuable in patients for whom the cost of drinking is already high (see Case study 2). These are often those with late-onset alcohol dependence (Cloninger's type 1: anxious, passive–dependent personalities; binge drinking associated with guilt).

Who benefits from anticraving or aversive treatment?

The objective of this treatment is to promote abstinence for long enough to allow psychosocial recovery to take place.

In practical terms, the people most likely to benefit are those for whom craving, or the subjective compulsion to drink, is a feature of the abstinent state. Patients reporting craving should be given a three-month initial trial with acamprosate (which can be used in combination with disulfiram), and then reviewed at six and 12 months.

The 'survival curves' (Figure 2) indicate that after 12 months, abstinence is relatively well established and the drug can be withdrawn with little risk of relapse.[19] If in doubt, ask the patient. Craving is a subjective psychological state, and patients can tell us how a treatment is affecting them. Stopping or continuing acamprosate (or disulfiram) should always be a collaborative experiment, with the patient as the judge of effectiveness.

Case study 2: Acamprosate

A Scottish man was referred after being made redundant from the civil service in a 'reorganisation'. He was depressed, had insomnia and was not coping; this was treated with fluoxetine 20 mg *mane* and trazodone 50 mg *nocte*. He also reported that for 25 years he had been drinking six cans of beer every night, but that this was 'not a problem'. Over subsequent months, it became clear, especially from talking to his wife, that his alcohol use caused him to become abusive and argumentative, and was putting a severe strain on their marriage. He had serious problems even contemplating stopping drinking, but admitted that he was not able to control the amount he drank.

He was given acamprosate, which helped him to reduce the number of drinking days. He still experienced powerful urges to drink in the evening (conditioned withdrawal), so the afternoon dose of acamprosate was increased to 999 mg, which completely abolished this problem. Occasional relapses after arguments stopped altogether when a family intervention was used. This involved regular family meetings, at which his wife and son specifically praised him for remaining abstinent (rather than just criticising his drinking) and said how proud of him they were.

At the last follow-up, he had been entirely abstinent for eight months on high-dose acamprosate, his self-esteem was high and he was back in work. He needed to be reassured that he could continue on acamprosate for as long as was necessary, as he was already becoming nervous about the idea of stopping it after a year.

Psychosocial treatment

Vaillant and Milofsky's four factors leading to recovery in alcoholics were derived from a 35-year follow-up study of 'normal' men, from an inner-city sample.[13] At the latest count, approximately one-third had had alcohol problems at some point, and half of those had recovered. The four factors are:

1. **Behaviour modification** (drinking results in immediate negative consequences):
   - Medical consequences.
   - Compulsory supervision or sustained confrontation.
2. **Substitute dependence** (drug or behaviour).
3. **New love relationship**.
4. **Hope/self-esteem**:
   - Religious involvement.
   - AA involvement.

Vaillant and Milofsky note that AA provides all four of these factors in one form or another.[13]

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Again, the lesson is that medical intervention may provide breathing space for people to work to change their lives; it will not of itself produce those changes. Hence the necessity for multidisciplinary working in the treatment of severe alcohol disorders. In Vaillant and Milofsky's study[13] (and in real life), much of the psychosocial 'treatment' came from non-statutory agencies. In general practice, simple advice plus medical treatment may be all that is needed.

Conclusion

General practice can provide a framework to identify and assist alcohol dependent patients through community reinforcement. This comprises a collection of techniques, all of which have been demonstrated in trials to be effective in helping people with alcohol problems. As we have seen in this bulletin, patients need to be given significant social pressure to change, and rewarded for becoming and remaining abstinent. Key components are:

- Brief intervention – problem/solution-focused interventions.
- Medication (disulfiram/ acamprosate).
- Behavioural/marital therapy.
- Social skills training.
- Relapse prevention. Relapse is a multi-step process (the patient has to get the money, go to the shop, buy the alcohol and pour it out), and at each stage alternatives can be generated, which divert them from drinking, or drinking more.

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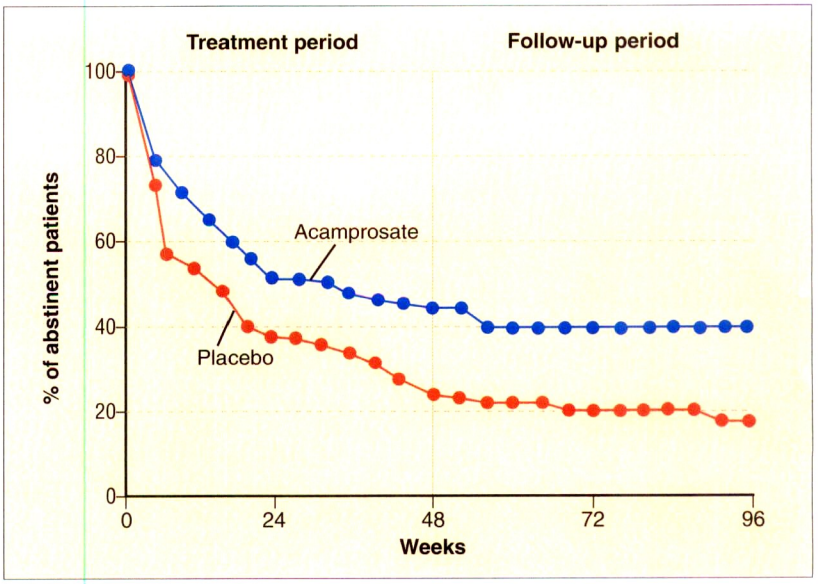

Figure 2. Survival curves[19]

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PRESCRIBING INFORMATION (UK)
Campral EC acamprosate
Presentation: Off-white round enteric-coated tablets, containing 333mg acamprosate calcium. Printed on one side with 333. **Properties:** Acamprosate may act by stimulating GABAergic inhibitory neurotransmission and antagonising excitatory amino acids, particularly glutamic acid. **Uses:** Maintenance of abstinence in alcohol-dependent patients. It should be combined with counselling. **Dosage and Administration:** *Adults ≥ 60kg:* 6 tablets per day (2 tablets taken three times daily with meals). *Adults < 60kg:* 4 tablets per day (2 tablets in the morning, 1 at noon and 1 at night with meals). Recommended treatment period one year, starting as soon as possible after the withdrawal period. Treatment should be maintained if the patient relapses. *Elderly:* Not recommended. *Children:* Not recommended. **Contraindications:** Known hypersensitivity to the drug, renal insufficiency (serum creatinine > 120 micromol/L), severe hepatic failure (Childs-Pugh classification C), pregnancy, lactation. **Precautions and Warnings:** Campral EC does not constitute treatment during the withdrawal period. **Interactions:** None observed in studies with diazepam, disulfiram or imipramine. The concomitant intake of alcohol and acamprosate does not affect the pharmacokinetics of either alcohol or acamprosate. **Side Effects:** Diarrhoea, and less frequently nausea, vomiting and abdominal pain; pruritus. These are usually mild and transient. An occasional maculopapular rash and rare cases of bullous skin reactions have been reported. Fluctuations in libido have been reported. Should not impair the patient's ability to drive or operate machinery. **Overdose:** Gastric lavage; should hypercalcaemia occur, treat patient for acute hypercalcaemia. **Legal Category:** POM. **Pharmaceutical Precautions:** None. **Package Quantities and Basic NHS Price:** 84 blister packed tablets £24.95. **Marketing Authorisation Number/Holder:** 13466/0001, Lipha SA, Lyon, France. **Date of Preparation:** 15 January 1998. Further information is available on request from Lipha Pharmaceuticals Ltd, Harrier House, High Street, West Drayton, Middx, UB7 7QG. Tel: 01895 452200.

SPECIAL COMMENDATION
AWARDED 1998
PRIX GALIEN AWARD
FOR INNOVATIVE
PHARMACEUTICAL PRODUCTS

BRAIN BIOCHEMISTRY ADAPTS TO LIFE WITH ALCOHOL

CAMPRAL EC HELPS PATIENTS ADAPT TO LIFE WITHOUT ALCOHOL

Non-aversive **Campral EC** can help reduce the craving in patients who are adapting to a life without alcohol.

Campral EC
acamprosate

SUPPRESSES CRAVING, REDUCES RELAPSE AND MAINTAINS ABSTINENCE IN THE ALCOHOL-DEPENDENT PATIENT

Date of preparation: October 1999

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