# Is there still a role for benzodiazepines in general practice?

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*SUMMARY. Opinion on benzodiazepines has moved from optimism after their entry onto the market to disillusionment over their potential for dependence. Legal proceedings against manufacturers of benzodiazepines, health authorities and doctors will be taking place this year. Nonetheless, just over 18 million prescriptions for benzodiazepines were issued in 1990, most of which came from general practice. Is there any role left for this group of drugs? This review addresses the issues of dependence on an withdrawal from benzodiazepines and weighs up the evidence for their present vilification.*

*Keywords: benzodiazepines; literature reviews; drug long term use; drug dependence; drug withdrawal; GP role.*

## Introduction

BENZODIAZEPINES are unpopular drugs. The headline 'Britain's innocent addicts' in the *Observer* (20 March 1988, p.15), during its crusade against pharmaceutical companies and doctors, exemplifies public unease about tranquillizers in general and benzodiazepines in particular.[1] In a review of this subject in the *Journal* in 1985, it was concluded that benzodiazepines were the second line treatment in the management of anxiety and needed to be handled with care.[2] Do we have a different perspective now? Are benzodiazepines ever useful and should general practitioners be exhorting long term users of these drugs to abstain? What are the real dangers of the drugs when considered alongside widely available alternatives such as alcohol or over the counter hypnotics?[3]

## Prescribing

Benzodiazepine prescribing reached a peak in 1979 when almost 31 million prescriptions were dispensed in the United Kingdom.[4] Thereafter benzodiazepine prescribing declined in many industrialized countries.[5] Prescriptions for benzodiazepines in the UK fell by 16% between 1979 and 1985.[4] Prescribing has dropped again since 1985 with just over 18 million prescriptions dispensed in 1990 (Statistics Division, Department of Health). This change has occurred mainly because of a fall in new prescribing,[6] leaving a core of long term users who are principally treated in general practice. High rates of prescribing continue in France where it has been estimated that up to one in four general practice attenders in France leave the doctor's office with a prescription for a psychotropic drug, usually a benzodiazepine (Fuhrer R, paper presented at World Psychiatric Association meeting, Oslo, June 1991).

## Dependence

Although the possibility of dependence on benzodiazepines was detected soon after they were licensed in 1960[7] and warnings against overenthusiastic prescribing appeared throughout the 1970s,[8-9] it was not until the 1980s that considerable concern was expressed about their use.[10] In 1988 the Royal College of Psychiatrists issued a policy statement on benzodiazepines and dependence,[11] and in 1990 the American Psychiatric Association published the report of its task force.[12] However, by this time levels of prescribing had already declined.

Although few doubt the existence of a dependence syndrome which may include symptoms of shakiness, tremor, dizziness, insomnia, impaired concentration, nausea, dysphoria, headaches, incoordination, heightened sensory perception, lethargy, depersonalization, tiredness, blurred vision, feelings of hot or cold and muscle aching,[13] the incidence of the syndrome and the confounding influence of psychological and personality factors remain uncertain. The available evidence regarding illicit use of benzodiazepines demonstrates that they do not match the traditional drug abuse model. Although they are frequently used by people with histories of drug abuse, non-medical use in the general population is uncommon, and there is no evidence of the reinforcing effects leading to escalation of dosage which are typical of drugs of dependence such as the opiates.[14]

The percentage of people attempting to stop taking the drugs or reduce their dosage who report symptoms of benzodiazepine withdrawal varies between 30% and 100%, depending on the definition used.[15] The prevalence and severity of the syndrome depends on the length of time the drug has been taken, the dose taken, to some degree the half-life of the drug, personality factors, such as dependence and 'neuroticism', as well as greater baseline levels of anxiety and depression.[16-18] 'Pseudo-withdrawal' syndrome has occurred in at least two studies in which patients mistakenly believed they were being withdrawn from their drug.[19-21] The picture has been further complicated by claims that doctors' expectations of withdrawal symptoms may have a suggestive effect on patients.[22,23] It has also been suggested that reappearance of the original anxiety disorder which may persist after withdrawal could be labelled as continued withdrawal symptoms by patients eager to avoid being thought to have a weak character.[22] The level of public concern and media coverage of benzodiazepines as a 'social problem' may influence the rate of reported difficulties with them.[21] In Germany where there is considerably less media concern about benzodiazepines, only 2% of patients report difficulties with them.[24]

A 'post-withdrawal' syndrome has recently been suggested[25] to explain the sometimes long term and diffuse syndrome described by patients and reported in lay publications. Whether this syndrome, which continues long after the symptoms of acute withdrawal have subsided, is a result of the reappearance of psychological symptoms, a long-standing alteration in benzodiazepine receptors, or the suggestive effects of media attention, is unclear.

## Adverse cognitive effects

As well as the possibility of dependence on benzodiazepines there exists the potential danger of adverse effects on cognitive function and behaviour. Laboratory findings of impaired psychomotor performance and short term memory are related to acute doses and have not been clearly replicated in behaviour outside the laboratory.[14] There also remains a lack of clear association between use of benzodiazepines and vehicle driving performance.[26] Although driving skills are not usually compromised by regular doses in the therapeutic range, they may be considerably impaired when the benzodiazepine is

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combined with alcohol.[27] Adverse cognitive effects occur most commonly in elderly patients, owing to reduced clearance from the body and higher plasma concentrations, and thus for these patients half the recommended adult dose is appropriate.[28]

## Legal issues

As at the end of March 1992 14 000 patients represented by more than 1800 firms of solicitors are bringing legal proceedings against the principal manufacturers of benzodiazepines (Balen P, Benzodiazepine Solicitors Group, personal communication). This case is the largest personal injury group action ever undertaken in the British courts.[29] The claim is one of failure by the companies to warn doctors of the risks of dependence and compensation will be sought for the damage resulting from dependence and the symptoms of withdrawal. In addition, 117 general practitioners and 50 health authorities are being sued (Balen P, personal communication).

The legal proceedings will be prolonged and complicated and while indecision persists, doctors will be uncertain whether or not to prescribe benzodiazepines. However, it should be made clear that these court proceedings are against doctors who are considered to have prescribed unwisely in the face of advice about the long term risks of benzodiazepines and it would seem unlikely that doctors are at any risk providing they keep within current prescribing guidelines. Maintenance of careful records is preferable to seeking signed consent from patients before prescribing the drug.

## Long term benzodiazepine users

There are between 800 000 and 1.6 million long term users of benzodiazepines in the UK.[4,30-32] In the mid-1980s, it was estimated that 10% of patients started on benzodiazepines in general practice were still taking the drug six months later.[33] Thus, it would seem that use can readily become long term. Most surveys report that long term users are more likely to be women, to have poor physical health and to suffer personality or psychological problems.[31,32,34,35] In addition, they are more likely than other patients to be taking other psychotropic drugs such as antidepressants.[34] People who take benzodiazepines in the long term for the purposes of sedation are usually elderly, again have a history of physical illness but are less likely to be psychologically distressed or to take other psychotropic drugs.[34,36]

In a study in the 1970s in which general practice consultations were observed directly, it was reported that in one in four consultations in which a psychotropic drug was prescribed, the patient's presenting symptoms were exclusively physical.[37] The link with physical disorder is complex. Benzodiazepines may be prescribed to alleviate the distress caused by a chronic physical disorder, physical disorder may provoke anxiety and hence a tranquillizer may be prescribed, or clustering of physical and psychological disorders, may occur in the same people.[34,38] There is also evidence that young people are prescribed benzodiazepines for minor muscle strains from sporting or similar injuries, despite lack of clear evidence of therapeutic efficacy.[39]

Is a general practitioner or a specialist more likely to initiate the prescription of benzodiazepines? The answer depends to some extent on who is asked; patients will more often cite the general practitioner.[31] However, it was reported in the 1970s that even among patients who were started on the drugs in hospitals or clinics, prescriptions may be continued by the general practitioner, without clear indications.[40] This is probably less likely to happen today.

Recent work on the attitudes of long term benzodiazepine users themselves indicates that they have mixed views about their drugs and do not conform to the media stereotype. Up to half would like to stop taking benzodiazepines, but most are uncertain how their family doctor regards their use of the drug.[41] A postal survey of long term benzodiazepine users reported that 79% of long term, daytime benzodiazepine users considered the tablets helpful and that data in their practice records provided no objective evidence of any ill effects.[35] Neither were patients likely to press for an escalation of the dose. The patients indicated some unease about the drugs and realized that the doctors in the practice were unhappy about long term tranquillizer use.

Unfortunately, little is known of the views of general practitioners concerning the usefulness or otherwise of benzodiazepines. Although it is believed that doctors disapprove of their use, there appears to have been little systematic enquiry into doctors' attitudes.

## Can general practitioners help long term users to withdraw?

Although the prescribing habits of general practitioners have been studied,[40,42] and the physical and psychiatric profile of long term users in general practice described,[31,35,36,43] there has been less examination of the ability of general practitioners to help their chronic users withdraw from benzodiazepines. Withdrawal of long term users may be most appropriately carried out in general practice where the majority of these drugs are prescribed.

Hopkins and colleagues[44] used a carefully structured programme in an attempt to help patients who had been taking the drug for three months or more to withdraw — 58% of patients attempting withdrawal were successful and a further 17% reduced their dose. In a study to assess the effectiveness of psychological management of anxiety, Cormack and Sinnott found that a letter advising patients taking benzodiazepines for at least a year to cut down on their dose of the drug was as effective as a treatment group run by a psychologist.[45] However, a low response rate to the study, together with a high percentage of drop outs from the group programme, prevented any definite conclusion. In a study of 71 long term users, minimal intervention by the general practitioner by interview or letter was compared with a control non-intervention strategy — 16 patients in the intervention group but none of the patients in the control group stopped taking their tablets entirely.[46]

There have been at least two studies of withdrawal among elderly people. In the first, 20 elderly volunteers who were long term users of benzodiazepines for sedation were randomized to a treatment or control group, treatment consisting of four sessions by a psychologist, each of an hour, in the patient's home.[47] Eight of the 10 patients in the control group resumed nightly consumption of benzodiazepines compared with only two of the 10 patients in the treatment group. In the second study, a large controlled trial of withdrawal among elderly long term users of benzodiazepines in a general practice setting, a practice nurse provided support, counselling and relaxation therapy to patients in the intervention group agreeing to attempt to withdraw from their drugs.[48] After nine months 10% of patients in the control group had stopped medication and 10% had reduced it. However, among the 46% of patients in the intervention group who agreed to attempt reduction 41% had stopped taking their benzodiazepine completely and 43% were able to reduce their dosage.

## Outlook following benzodiazepine withdrawal

Studies of the long term outcome for patients who have managed to stop taking benzodiazepines have not covered those people who have withdrawn in general practice. Nevertheless, evidence from outpatient studies has demonstrated that at least half manage to abstain from the drugs for at least five years, despite

occasional periods of re-use.[49-51] Those who fail to abstain are no more likely to have social, psychological or withdrawal problems that those who succeed, nor is the half-life of the benzodiazepine which was being taken a significant predictor of success. Women, however, are significantly more likely than men to abstain from benzodiazepines in the long term,[49] as are younger patients.[51]

Although longer duration of benzodiazepine use is associated with failure to maintain abstinence, this may reflect a greater chronicity of illness and thus a continued need for symptomatic treatment. In a recent follow up of long term users who had been withdrawn for two to five years, moderate to marked anxiety was found in 25% of patients who remained abstinent and in 35% of those who did not.[51] Some long term users may be taking benzodiazepines because of chronic or recurrent anxiety or depression rather than physical dependence.

## Should general practitioners help users to withdraw?

Five years ago the response to this question would have been less equivocal. Many patients withdrawing from benzodiazepines were attending clinics or hospital outpatient departments and research in general practice was demonstrating that although success rates were not spectacular, simple intervention was possible and was reasonably successful for those patients willing to attempt it. In the 1990s there are fewer long term users and less new prescribing is taking place. Studies of new prescribing, in London at least, have proved impossible because of a lack of subjects and studies of withdrawal in general practice are hampered by a lack of patients whom general practitioners consider might benefit from stopping the drugs.

While many patients may indeed be physiologically dependent on benzodiazepines, such dependence does not justify the judgement that they are abusing the drugs.[14] Patients who remain as long term users may not all benefit from withdrawal and if pressured to withdraw may simply resort to other psychotropic substances, legal or illegal, some of which are more damaging to physical and psychological health.

Where the general practitioner decides that withdrawal is warranted, it should always be gradual and the patient should be left feeling they have some control. Simultaneous treatment with propanolol or a cyclic antidepressant may ameliorate some of the withdrawal symptoms.[52] The role of additional psychological treatment is less clear,[53] although some form of adjunct therapy usually of a relaxation or problem solving nature may be helpful.[23,52] Withdrawal may sometimes be a slow and difficult process,[23] although brief advice may be as effective as more complicated regimens in certain cases.[45]

## Should general practitioners prescribe benzodiazepines?

To address this question we must first consider current indications for benzodiazepines in general practice and secondly, what general practitioners are currently doing for patients who in former times would have been prescribed a benzodiazepine tranquillizer.

In considering the first issue, it is important to avoid polarized views of tranquillizers as a form of social control or as merely a symptomatic amelioration of emotional problems. No matter how much doctors may desire, and work towards changes in society which would remove much psychological suffering, they are meanwhile called upon to deal with this distress in their surgeries.

There remain clear indications for what are a useful group of drugs. The role of benzodiazepines in the treatment of epilepsy, major muscle spasticity and the psychoses will continue. Despite views to the contrary,[52] judicious use of benzodiazepines to ameliorate the enormous emotional strain of unexpected bereavement, divorce or assault may be necessary and is humane. Furthermore, occasional use of a benzodiazepine for sedation is justified in cases of acute insomnia caused by emotional distress, a change in sleeping environment or jet lag,[54] and is arguably safer than freely available alternatives such as alcohol.[3] The evidence that their anxiolytic and sedative effects are short lived has not been substantiated.[14,55] Drury has suggested that explanation and simple advice about the use of hot drinks, reading or the radio are sufficient to counteract chronic insomnia.[2] However, many doctors and their patients feel helpless when these home remedies fail, as they so often do, and there are no obvious reasons for the lack of sleep such as psychological distress, pain or other physical discomfort. A recent review of the use of benzodiazepines as a sedative in the United States of America concluded that despite evidence of misuse and overuse, 85% of people with severe insomnia remain untreated and would benefit from proper diagnosis and care, which in some cases would include the use of a benzodiazepine.[56]

It should be remembered that many patients are aware of the potential of benzodiazepines for dependence and can take them for a short period only. It would seem sensible, nevertheless, to avoid issuing prescriptions which last for more than 14 days at a time, and to take particular care when prescribing for people who were formerly dependent on benzodiazepines. Those patients with major psychological difficulties may be better served by a psychiatric opinion. Perhaps the strongest contraindication for the prescription of a benzodiazepine is in patients suffering major personality difficulties in whom dependence or abuse appears to be much more likely. Use of benzodiazepines for long term sedation in elderly people should also be avoided, where possible, because of the potential for memory impairment and confusion. In addition, the prescribing doctor must always keep in mind the street value of benzodiazepines as a drug of abuse and endeavour where possible to ensure that indications for the drug are genuine.

It is more difficult to address the issue of what general practitioners are currently doing in place of prescribing a benzodiazepine. Brief psychotherapy, often of a cognitive behavioural or reflective counselling type, has been shown to be as effective as the prescription of a minor tranquillizer[57,58] and as cost effective in terms of time. In contrast, other work has indicated that the most productive approach, at least for anxiety disorders presenting in general practice, is a combination of cognitive behavioural therapy and a benzodiazepine.[59] Intuitively it is difficult to believe, however, that doctors are counselling substantial numbers of their distressed patients, or that they necessarily have the appropriate skills to do so.[60] Even for practices that have access to counselling or psychotherapy services, the sheer load of psychological distress that general practitioners see every day is overwhelming.

It is likely that many general practitioners now make use of antidepressants for minor psychiatric morbidity. In fact several of the newer compounds, such as fluoxetine, have been marketed with general practitioners in mind, as useful for brief periods of 'low mood'. However, these drugs are potentially toxic in overdose or accidental poisoning and little is known about their long term complications.

## Conclusion

The chairperson of the American Psychiatric Association task force on benzodiazepine dependence, toxicity and abuse stated that at standard therapeutic doses, short term treatment with a benzodiazepine is usually without substantial toxicity or the development of dependence.[28] Short term prescribing of benzodiazepines in general practice for those patients who do not have major psychiatric, personality or dependence problems would seem to be perfectly justifiable. Doctors must, however,

point out to patients the possible risks of dependence which could occur with long term use.

There is growing interest in psychiatric treatments in general practice[61] and counselling is increasingly becoming available to patients, either by the general practitioner or by other members of the primary health care team such as attached counsellors. Nonetheless, thoughtful use of benzodiazepines is arguably better practice than prescribing the newer antidepressants.

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