

History of Benzodiazepines: What the Textbooks May Not Tell You
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[SLIDE 1] Title slide

Early history of anxiolytic drugs

History has an inexorable way of repeating itself. It has always been a surprise to me that we have allowed history to repeat itself in medicine, when we could so easily learn from our mistakes. Here are some drugs which have been used medicinally to relieve anxiety and promote sleep throughout the ages:

[SLIDE 2] Anxiolytic drugs through the ages

Alcohol use goes back about 8000 years. The bible tells us that “Noah planted a vineyard – drank of the wine and was drunken”. Later alcohol was used medicinally as an anxiolytic though it was abused by some. In the Middle Ages, alchemists hailed alcohol as the long-sought elixir of life. But by the 18th century, with the introduction of cheap gin and the rise of gin palaces, the addictive properties of alcohol became widely recognised.

Opium also has a history extending over thousands of years and was taken to relieve anxiety. Sydenham in 1680 described it as the most universal and efficacious of all the “remedies which it has pleased Almighty God to give to men to relieve his sufferings”. But its addictive properties became apparent and in the 19th century De Quincy dubbed it the “dread agent of unimaginable pleasure and pain”.

Bromides were widely used as sedatives in the 1870s. They were also prescribed for epilepsy because they lessened sexual urges and epilepsy was thought to be a consequence of masturbation. But the dependence potential again became apparent.

Chloral hydrate and paraldehyde were synthesised around this time and introduced as sedatives, but both became associated with abuse and dependence.

Then came the barbiturates, introduced as hypnotics and sedatives between 1903 and 1912. The dependence-producing properties became increasingly apparent, together with alarm over the dangers of overdose. This led eventually in the 1970s to a campaign to replace them with benzodiazepines.

Meanwhile, other compounds with similar properties were introduced including ethylchlorvynol, carbromal, glutethimide, methyprylon and methaqualone, but their dependence potential and toxicity was soon recognised.

Benzodiazepines were discovered, more or less by chance, by Sternbach, working for Hoffman La Roche in New Jersey. In 1957 the original compound was found to have hypnotic, anxiolytic and muscle relaxant effects and the first benzodiazepine, chlordiazepoxide (Librium) was launched in the UK in 1960, followed by diazepam (Valium) in 1963. By 1983 there were 17 benzodiazepines on the market worth nearly \$3 billion worldwide. There are now 29 benzodiazepines available in Europe and the USA. I have already sketched the later history of benzodiazepines, yesterday, and the tardy realisation that they too, were dependence-producing and will say a bit more about it later today.

Now we are faced with the introduction of the Z drugs, zopiclone (introduced in 1998), zolpidem and zaleplon (in 2000) and now eszopiclone (in 2005). They act like benzodiazepines. Do we really think that they are free of dependence potential and abuse? I will return to this point later.

By the late 1970s benzodiazepines had become the most commonly prescribed of all drugs in the world. It was estimated that one in five of all women and one in ten of all men in Europe took them at some time each year. The drugs were prescribed long-term, often for many years, for complaints such as anxiety, depression, insomnia and ordinary life stresses.

But in the early 1980s in England long-term prescribed users themselves realised that the drugs tended to lose their efficacy over time and instead became associated with adverse effects. In particular, patients found it difficult to stop taking benzodiazepines because of withdrawal effects, and many complained that they had become 'addicted'. Throughout the 1980s there was a public outcry against benzodiazepines in the U.K. resulting in widespread media coverage in the press, radio and television and a burgeoning of self-help groups and withdrawal clinics.

History of my benzodiazepine withdrawal clinic

My own involvement with benzodiazepines started at this time. One day in 1981 a lady came hobbling on crutches into my general pharmacology clinic. She had been involved in a road traffic accident. She had two broken limbs in plaster and had been prescribed the benzodiazepine Ativan for muscle relaxation (1mg tds). She had noticed as she recovered that when the time for each dose of Ativan approached she experienced a strong craving for the next pill, along with anxiety, restlessness and muscle cramps. "I think I am addicted" she said, "Can you help me?" Naively I said "yes" although I had no experience in drug addiction at that time. She duly underwent a withdrawal process, during which she suffered many symptoms including anxiety, insomnia, hallucinations; tremor, muscle cramps and many other symptoms now (but not then) recognised as typical benzodiazepine withdrawal symptoms.

Following this lady's appearance at my clinic there was a trickle of others which soon grew to a stream and finally a flood of patients referred by their doctors because they wished to stop their benzodiazepines. As a result, I had to start a dedicated benzodiazepine withdrawal clinic. I continued this clinic single handedly for 12 years at two sessions every week until 1994 when I had to retire (you have to retire at 65 from clinical work under the National Health Service). Strangely, none of my medical colleagues wished to become involved in this clinic or to take it over in 1994, so the clinic closed down. I think that the current medical training did not equip most doctors for listening to anxious patients with many complaints, patients who were time-consuming and required repeated consultations. I myself spent most of the time simply listening to the patients and learning from them how to come off benzodiazepines.

Adverse effects of long-term benzodiazepine use

Over 300 patients passed through this clinic and over 90% successfully withdrew.

[SLIDE 3] Morbidity in 50 patients

This slide shows some of the symptoms in the first 50 patients attending the clinic. They had been on prescribed, so-called “therapeutic” doses of benzodiazepines for 1-22 years (mean, 10years) and wished to withdraw. They ranged from 20 to 72 years of age, (mean age 46yrs); 40 were females.

- 20% had taken drug overdoses requiring hospital admission in suicide attempts
(illustrating that benzodiazepines cause or exacerbate depression)
- 20% had developed incapacitating agoraphobia
(in addition to the majority who had panic attacks)
- 18% had undergone GI investigations (irritable bowel)
(a condition closely linked to anxiety)
- 10% had undergone neurological investigations
(3 wrongly diagnosed with ms on the basis of muscle weakness and tremor, blurred vision and patches of numbness – signs often associated with anxiety states)
- 62% had been prescribed other psychotropic drugs, mainly antidepressants, since starting benzodiazepines
- 28% were taking a combination of two benzodiazepines, the second added after the first become insufficient. This illustrates the development of tolerance and dosage escalation with benzodiazepines.

These symptoms were not the original cause for starting benzodiazepines but developed during the course of prolonged use. It seems clear that long-term benzodiazepines actually aggravate or cause further anxiety and depression. In the 90% of patients in this series who successfully withdrew, and I followed for 10 years, there were no more overdoses; the agoraphobia, panic attacks, depression and neurological symptoms, including the alleged MS, disappeared. The fact that patients improve after withdrawal is a strong argument that symptoms are related to the benzodiazepines and are not due to some underlying psychiatric disorder, as many psychiatrists have claimed.

Some of these patients developed withdrawal symptoms while coming off benzodiazepines. Between 1980 and 1985 a number of controlled trials by Lader, Tyrer and others showed that withdrawal symptoms from regular therapeutic doses of benzodiazepines were real and that they indicated dependence on these drugs.

Benzodiazepine withdrawal symptoms

[SLIDE 4] Benzodiazepine withdrawal symptoms

These have since been described by many authors and include a range of symptoms common to all anxiety disorders (such as panic attacks, agoraphobia, insomnia, nightmares, tremors and muscle tension) and some relatively specific to benzodiazepines (such as perceptual distortions, hallucinations, sensory hypersensitivity and sometimes psychotic symptoms). However, these symptoms are not obligatory if withdrawal is carried out slowly and carefully – as I shall describe later. They nearly always improve after some weeks although in a small proportion the symptoms may be protracted.

[SLIDE 5] Protracted withdrawal symptoms

Anxiety, depression and gastrointestinal symptoms may persist for many months, though gradually declining. A number of neurological symptoms including tinnitus, motor

and sensory symptoms and global cognitive impairment may be very long-lasting and raise the question of whether benzodiazepines may cause permanent neurological damage.

The publicity surrounding benzodiazepines in the 1980s resulted in a reduction of benzodiazepine prescribing levels in the UK from its height of 32 million in 1976 (for a population of 50 million) down to about 18 million in 2000. And by 2000 the benzodiazepine problem was largely perceived to have gone away. National Health withdrawal clinics had shut down, the media no longer found benzodiazepines newsworthy and self-help groups closed down because of lack of public financial support.

Skeleton in the closet: costs of inappropriate prescribing

But the problem has not gone away.

[SLIDE 6] Skeleton surveying skull

The skeletons were merely shut in the closet and now some worms are beginning to crawl out of the coffin.

For example, there are still nearly one million long-term benzodiazepine users in the UK and four million or more in the US. There is a growing problem of benzodiazepine abuse – benzodiazepines are taken by over 90% of alcohol and illicit drug abusers and sometimes in their own right. Benzodiazepines are inappropriately prescribed at all stages of life – from the elderly who take them chronically as sleeping pills or are given them to keep them quiet in retirement homes and psychiatric units; to discharged psychiatric patients still taking benzodiazepines prescribed in hospital; to women still being prescribed them in pregnancy, and to their developing foetuses and newborn infants.

There are large and uncounted socioeconomic costs associated with benzodiazepines, as shown here (enumerate).

[SLIDE 7] Socioeconomic costs of inappropriate benzodiazepine prescribing (enumerate)

[VIDEO] Heather Jones

This video illustrates the typical sequence of events in a long-term benzodiazepine user who was one of the early patients at my clinic. It was made over 10 years ago but is sadly still typical of many patients today and illustrates many of the points I have mentioned. (Incidentally, though the subject refers to me, I had nothing to do with the making of this video).

Reasons for inappropriate benzodiazepine prescribing

Why are benzodiazepines still so commonly prescribed inappropriately? One factor is that doctors have failed to follow guidelines limiting them to short-term usage. In the short-term, that is 2-4 weeks only or intermittent use, benzodiazepines have many excellent therapeutic, even life-saving properties, illustrated here (enumerate).

[SLIDE 8] Therapeutic actions of benzodiazepines (short-term) (enumerate)

Used long-term, however, they can produce many adverse effects that I have no time to describe in detail. They include: (enumerate)

[SLIDE 9] Adverse effects of benzodiazepines (long-term)

Doctors have been slow to give up the idea that benzodiazepines are so benign that they can be continued for life.

Secondly, doctors and drug companies have been slow to recognise the difference between different benzodiazepines, both in rates of elimination and in relative potency. This slide shows equivalent potencies and elimination rates of some anxiolytics.

Equivalent potencies of different benzodiazepines

[SLIDE 10] Half-lives and equivalent potencies of benzodiazepine anxiolytics

Explain slide (elimination half-lives and approximate clinical potency of some benzodiazepines compared to diazepam). The three most potent in this group of anxiolytics are alprazolam, clonazepam and lorazepam which are 10-20 times more potent than diazepam. This difference is often disregarded and the drugs prescribed in excessive dosage. For example, I have recently seen patients prescribed alprazolam in daily doses of 4-6mg – equivalent to 80-120mg of diazepam. Alprazolam is no longer prescribed under the NHS in the UK though it can be prescribed privately. I have also recently seen lorazepam prescribed in 6, 10, and over 12mg daily doses – again in equivalence up to 120mg diazepam. Both these drugs are fairly short-acting and have to be taken 3-4 times a day. Patients often suffer mini-withdrawal symptoms between doses. Clonazepam is also very potent, 10-20 times the strength of diazepam. In the UK it is only officially indicated as an anticonvulsant for epilepsy but it is popular in the US and British doctors are following suit and prescribing it for anxiety.

All these three drugs are highly addictive; dependence develops rapidly and they are particularly hard to withdraw from. This difficulty is partly due to the relatively excessive dosage used, partly I suspect from their potency which probably means that they bind particularly avidly to GABA/BZ receptors, partly because equivalent potencies are not adhered to when switching patients to other benzodiazepines such as Valium or Librium in attempts at withdrawal, and partly because they are not available in small enough dosage strengths to allow for gradual dosage reduction. In the UK Ativan is only available in 2.5mg or 1mg tablets. The 1mg tablet is equivalent to 10mg diazepam. Even if you halve it you are withdrawing by decrements of 5mg in diazepam equivalents, which can be a big drop for some people. Strangely, 0.5mg Ativan tablets are available in the US and Canada, but all attempts to get the drug company (Wyeth) to supply this in the UK have failed.

Many physicians in the US switch patients on alprazolam or lorazepam onto clonazepam for withdrawal in the belief that its longer half-life will make withdrawal easier. However, clinical experience shows that clonazepam is also difficult to withdraw from, and patients do much better switching onto diazepam which has a much longer half-life including active metabolites for up to 200 hours, allowing a smoother and slower fall in blood concentration. Also diazepam comes in 1mg tablets which can be halved allowing very small dosage decrements. Yet for some reason I have found that American doctors are very reluctant to prescribe diazepam.

I will describe withdrawal methods in more detail later, First you may ask how these equivalents were arrived at. Most were determined by direct clinical titration. In about 1983 Professor Michael Rawlins and I in Newcastle titrated the dose of diazepam required to substitute, in terms of anxiety symptoms, in 20 anxious patients on various doses of lorazepam. The mean came to an equivalence of 9.8mg diazepam for 1mg lorazepam. This is close to the equivalence of 1:10mg now officially accepted in most texts. Similar clinical tests were conducted for other benzodiazepine such as alprazolam though some equivalents are based on clinical experience during withdrawal of patients on various benzodiazepines who were switched to diazepam. Some equivalents were derived from animal work and human trials by drug companies. There is now a general consensus, at least in the UK, about equivalent potencies for both anxiolytic and hypnotic benzodiazepines. They are quoted in the British National Formulary produced by the British Medical Association and the Royal Pharmaceutical Society circulated to all doctors and in many published papers. Unfortunately, not all doctors read or heed this advice!

[SLIDE 11] Half-lives and equivalent potencies of some benzodiazepine hypnotics

This slide shows the equivalences and half lives of some benzodiazepine hypnotics. Triazolam is very potent, again 20 times the strength of diazepam and very short acting. It can give rise to withdrawal symptoms the next day, and it was removed from the UK formulary in 1995. Flunitrazepam is also potent but long-acting. It gained general popularity as a “date-rape” drug, because of the prolonged amnesia it induces. Nitrazepam, temazepam and flurazepam are less potent and have a medium duration of action but can cause a hangover the next day.

All these equivalencies are of course approximate. There is considerable individual variation in how people react to benzodiazepines. In addition, there are subtle differences in the pharmacological profiles of different drugs, and the equivalences do not always work at higher doses. For example, in my clinical experience diazepam is rather more sedative than lorazepam (Ativan) which is more anxiolytic. So if you abruptly change someone on say 6mg Ativan to 60mg of diazepam, he is likely to become very sleepy but may still be anxious. However, you can accomplish a changeover if you do it gradually and stepwise, dose by dose, titrating each dose to the clinical response. People also have differences in the speed at which they metabolise drugs, but on the whole the equivalences apply generally, except possibly in the case of benzodiazepines which have active metabolites such as diazepam where the half-lives of these can vary from 36-200hrs.

Patients at special risk from benzodiazepines

Individual differences apply more to the third reason why benzodiazepines are prescribed inappropriately, which is when they are given in the wrong dose to the wrong people.

[SLIDE 12] Vulnerable patients

The elderly are especially susceptible to the sedative effects of benzodiazepines which may cause mental confusion, cognitive impairment suggesting dementia and ataxia leading to falls and fractures. This is partly because of reduced metabolism, especially oxidation and partly because of increased central nervous system vulnerability. Benzodiazepine dosage for elderly patients should always be half of the adult dose, and benzodiazepines which are not

oxidised but conjugated, such as oxazepam and temazepam are preferred. Patients with chronic respiratory or liver disease are at increased risk of respiratory depression, which can be fatal, and oversedation and benzodiazepines are relatively contraindicated in these cases. Benzodiazepines should be avoided in patients with depression which they may aggravate and increase the risk of suicide. Additive effects may occur with patients taking other depressant drugs such as alcohol or sedative antidepressants. In pregnancy there is a risk of adverse effects on the foetus, neonatal depression (floppy baby syndrome) and neonatal withdrawal effects. Patients with a history of alcohol or drug abuse or those with personality disorder may be more likely to become dependent. There are also genetic differences in drug metabolism. Slow metabolism of benzodiazepines, and also of alcohol, is common in orientals, and the recommended dose of benzodiazepines in Hong Kong, for example, is half that recommended in Europe and North America. On the other hand, some drugs such as barbiturates and nicotine in smoking induce liver enzymes, increasing the rate of metabolism. Benzodiazepines are not enzyme inducers but the rate of metabolism may be affected by other drugs which induce or inhibit liver enzymes (ketoconazole). Finally tolerance to previous benzodiazepine use, alcohol or barbiturates may reduce sensitivity to benzodiazepines.

With all these caveats for benzodiazepines, what about the more recently introduced “Z drugs” – zopiclone, zolpidem, zaleplon and now the introduction of eszopiclone (Lunesta)?

The Z drugs

[SLIDE 13] The Z drugs

These are not chemically benzodiazepines but they bind to GABA receptor complexes which are close to or actually coupled with benzodiazepine receptors. They are said to be more selective, binding mainly to the α_1 GABA receptor subtype which mediates the hypnotic effects of benzodiazepines. In practice they are not all that selective and have much the same actions as benzodiazepines. In the UK, the National Institute for Clinical Excellence (NICE), which advises the Health Service on optimum drug use, recommended that Z drugs should be used for short-term treatment only (2-4 weeks) and then only as second line treatments after benzodiazepines. They concluded that the Z drugs produced the same therapeutic and adverse effects as benzodiazepine hypnotics, including tolerance, dependence and abuse, and were also more expensive.

As a clinical example, a psychiatrist recently asked my advice about the nursing sister he was helping to withdraw from lorazepam (Ativan). She developed quite severe withdrawal symptoms as the dosage was lowered and had trouble sleeping. To help her, the psychiatrist prescribed zopiclone (Zimovane) to take at night. She found that this drug completely relieved her withdrawal symptoms. In fact, it was so successful that she started taking zopiclone in the daytime as well. She ended up taking zopiclone six times a day as well as at night, ending up with a total dose of over 40mg/day (the recommended dose is 7.5mg at night). The psychiatrist was chagrined to find that he had merely replaced one form of addiction with another.

There are a number of cases in the literature of such escalation of dosage with zopiclone, followed by dependence and withdrawal symptoms on stopping. There are also an increasing number of cases reported of misuse and abuse of high doses of zolpidem (Ambien).

This can result in hallucinations and psychosis and is reminiscent of the adverse effects of triazolam (Halcion), the short-acting benzodiazepine hypnotic now banned in the UK.

Now eszopiclone is being promoted for long-term use and the manufacturers report trials lasting two weeks to six months of its hypnotic effects. They report little tolerance or loss of efficacy over these periods and a low incidence of rebound insomnia or anxiety (3.7%) on stopping. Euphoria was noted in high doses, suggesting an abuse potential. I remain sceptical of these results which involved relatively small numbers of subjects with various types of insomnia. I am not convinced that eszopiclone is all that different from zopiclone, apart from its potency, and I think it would be prudent to limit it to short-term use until proved otherwise.

There is a basic pharmacological principle that any drug which acts on intrinsic body receptors will cause adaptive changes in these receptors if used chronically. This is because the body is programmed to restore homeostasis if its internal environment is disturbed. For every drug action in the body there is an equal (as far as possible) reaction which tends to restore the *status quo*. This mechanism underlies the development of drug tolerance and dependence and also of withdrawal reactions if the drug is stopped. It applies not only to benzodiazepines but also to non-psychotropic drugs like β blockers. For example, β blockers such as propranolol are used to slow the heart and lower the blood pressure. If these are suddenly stopped there is a rebound of increased heart rate and raised blood pressure. We accept that tolerance and withdrawal reactions occur with benzodiazepines, barbiturates and all the hypnotic and sedative drugs that have gone before. We even understand much about the molecular mechanisms involved – which I won't go into here. There seems no reason to believe that these reactions will not apply to Z-drugs.

I suspect that the Z-drugs will undergo the fate of many newly introduced drugs – a fate that is becoming all too familiar.

[SLIDE 14] Historical evolution of new drugs
Management of benzodiazepine withdrawal

So how should we withdraw benzodiazepines in people who have become dependent through long-term use? I have already described this in some detail elsewhere. I make no claims that this is the last word in benzodiazepine withdrawal, but the methods are based on experience in my withdrawal clinic and on many other patients I have been in contact with since then.

[SLIDE 15] Benzodiazepine withdrawal

The basic principles for people withdrawing from therapeutic doses of benzodiazepines are simple: gradual dosage reduction and anxiety management if needed. It is generally agreed that dosage should be tapered gradually. Abrupt withdrawal, especially from high doses, can precipitate convulsions, acute psychotic or confusional states and panic reactions. The rate of tapering should be tailored to the patient's individual needs, taking into account lifestyle, personality, environmental stresses, reasons for taking benzodiazepines, amount of support available and other personal factors. Various authors suggest optimal times of 6-8 weeks to a few months for the duration of withdrawal, but some patients may take a year or more. The best results are achieved if the patient himself (not the doctor) is in control of the rate of withdrawal and proceeds at whatever rate he or she finds tolerable. The

doctor and patient together can devise a mutually agreed withdrawal schedule, but this may require readjustments from time to time according to progress. If problems arise, either in the form of increased symptoms or extra environmental stresses, it may be necessary to stabilise the dosage for a few weeks or to reduce the rate of withdrawal. But it is important always to go forwards, avoiding a backward step of increasing the dosage again.

The size of each dosage reduction depends on the starting dose. Patients on higher doses can usually tolerate larger dose decrements than those on lower doses. For patients taking less than 20mg diazepam or equivalent, reductions of 1mg every 1-2 weeks are generally tolerated. When dosage is down to 4-5mg diazepam or equivalent, decrements of 0.5mg may be preferred. On the other hand, initial dosage reductions of 2mg every 1-2 weeks may be appropriate for patients starting on 40mg diazepam or equivalent.

Stopping the last few milligrams is often seen by patients as particularly difficult, because of fears of how they will cope without any drug at all. However, the final parting is often surprisingly easy, especially as confidence increases during withdrawal, and patients are encouraged by their new sense of drug-free freedom.

For most patients on therapeutic doses of benzodiazepines withdrawal is best carried out as an outpatient. Rapid withdrawal in detoxification clinics, even with phenobarbitone substitution, is inappropriate because the patient has no time to build up alternative living skills, which may take many months. Detoxification in drug and alcohol clinics is utterly inappropriate and traumatic for people involuntarily addicted to benzodiazepines by doctors' prescriptions.

The general aim of the dosage tapering strategy is to achieve a smooth, slow, steady fall in blood concentration of benzodiazepine, allowing time for the body to adjust to the change. This slow, smooth decline is not possible with rapidly eliminated benzodiazepines like lorazepam, (Ativan) or alprazolam (Xanax) with which blood concentrations fluctuate with peaks and troughs between each dose. It is therefore often advisable for those taking these drugs to switch to diazepam. When doing so, it is important to keep in mind the equivalent potencies that I have mentioned, and also to make the changeover gradually in a stepwise fashion, replacing each dose, or even half dose, one at a time over perhaps weekly intervals. Withdrawal can then proceed as for diazepam with small decrements of 0.5-1mg at a time, decrements that are not easily achievable with other benzodiazepines. The same technique can be used for Klonopin. I know that some patients report that they find this difficult, but I suspect it is because the changeover is not carried out carefully enough, with due regard to potencies and individual differences.

I should add that some benzodiazepines are available in liquid form and it is possible to withdraw from these directly, reducing dosage millilitre by millilitre or drop by drop.

What about adjuvant drugs? Are there any drugs that help to cushion the withdrawal process? The short answer is no: any drug that substitutes for benzodiazepines is benzodiazepine-like itself. However, several drugs have been tried, though none have proved generally useful.

[SLIDE 16] Adjuvant drugs in benzodiazepine withdrawal

Antidepressant drugs may be indicated if depression is severe, and anyone already on an antidepressant should continue it until after the benzodiazepine has been withdrawn. Antidepressants, including SSRIs, have been shown to have anxiolytic effects and may be indicated as longer-term treatment for chronic anxiety disorders. Small doses of sedative antidepressants can be helpful for insomnia. But all antidepressants, as I mentioned yesterday, also produce withdrawal effects when stopped.

β blockers may help tremor and palpitations as a temporary measure. Carbamazepine and other anticonvulsants prevent fits during withdrawal from high doses of benzodiazepines. Sedative antihistamines such as Phenergan may help with sleep but should not be used long-term.

Bispirone, clonidine, and nifedipine have all been shown to be unhelpful. Gabapentin has been claimed to be beneficial but there are no controlled trials. The benzodiazepine receptor antagonist flumazenil (Romazicon) was effective in some trials but has to be given intravenously and repeatedly and it can actually precipitate reactions.

None of these drugs (except possibly antidepressants) should be necessary for people on therapeutic doses withdrawing slowly enough.

[SLIDE 15 again]

What about psychological support? Many people require little more than simple and repeated encouragement and proper information. Self-support groups can be a great help for many. Some may need more formal psychological therapies including anxiety management, stress-coping strategies and cognitive behavioural therapy. Support when needed should be available both during and after withdrawal. Some patients may remain vulnerable to stress for some months.

In general practice settings, even minimal information can be effective. In one general practice study of elderly patients on long-term hypnotics, a single letter advising them to try reducing by half a tablet every few weeks resulted in significant dose reduction or complete withdrawal within six months, with improvement in mental and physical health and no withdrawal symptoms or sleep problems. Another general practice study of withdrawal in elderly hypnotic users using placebo tablets found that 80% had withdrawn in six months with no sleep or withdrawal problems and significant improvement in cognitive performance.

Of course patients have to be motivated to withdraw – it is no use forcing withdrawal on reluctant patients. But a single medical consultation explaining the risks of long-term benzodiazepine use, or even media publicity can help to motivate people.

Finally, what can we do to halt overprescription of benzodiazepines in the future and to prevent yet more people getting caught in the so-called tranquilliser trap?

Steps needed to reduce benzodiazepine overprescribing

[SLIDE 17] Some steps needed to reduce benzodiazepine overprescribing

(Enumerate)

