

Skeleton in the Cupboard

**BENZODIAZEPINES:
The Skeleton in the Cupboard
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Beat The Benzos Conference
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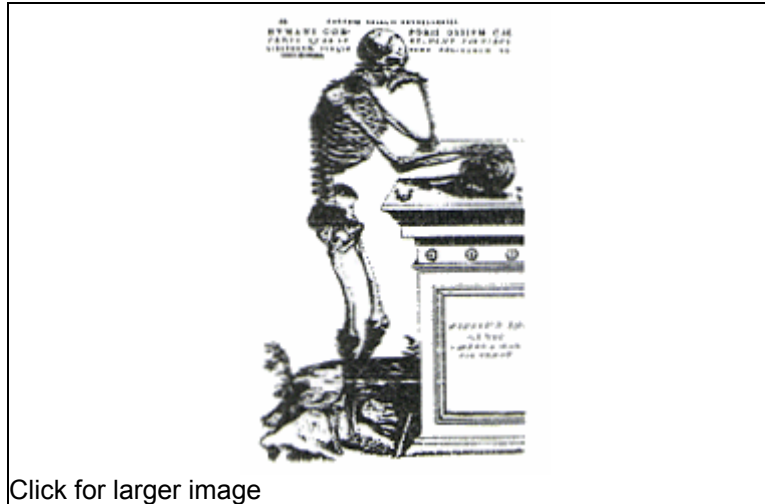
[TITLE SLIDE]

**BENZODIAZEPINES:
The Skeleton in the Cupboard**
Heather Ashton
Newcastle University

The benzodiazepine story goes on and on. For years benzodiazepines were the so-called wonder drugs, and prescriptions soared to 32 million a year in the UK in 1978. Then adverse effects were recognised (initially by the patients taking them) and doctors slowly responded by reducing prescriptions to the present 18 million or so. So by 2000 the problem was thought by some of the powers that be to have gone away.

But there are skeletons still lurking in the cupboard.

[SLIDE 2] SKELETON



And now some worms are crawling out of the woodwork. I will mention some of the latest twists in the story, and suggest some possible remedies including the management of withdrawal in long-term users.

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[SLIDE 3] THE CMO's LETTER

CMO's REMINDER 2004	
-	Benzos - short-term only (2-4 wks)
-	30% of GP prescriptions are for 56 tabs
-	12.7 million scripts in England in 2002-3: cost: £20.9 million

The latest twist is that in January this year the Chief Medical Officer (CMO) sent a statement to all doctors reminding them that benzodiazepines should only be prescribed for short-term treatment (2-4 weeks). This was a follow-up of similar advice from the Committee on Safety of Medicines in 1988. But the CMO pointed out that despite this advice many doctors were still prescribing the drugs long-term. 30% of the 12.7 million GP prescriptions were for 56 tablets at a cost of £20.9 million/year in England. He suggested that they should think about cutting down this use.

It was a great pity that the CMO gave little advice on the management of benzodiazepine withdrawal. He merely gave a web address to the British National Formulary (BNF). This gives excellent advice on withdrawal but it seems that many doctors don't read it or heed it.

The unfortunate consequence of the CMO's statement is that some health authorities have already cut their spending on benzodiazepines (e.g. South Tyneside) and some doctors have abruptly stopped or rapidly decreased their prescriptions.

Not surprisingly, this has caused great consternation among long-term prescribed benzodiazepine users. Benzodiazepine withdrawal is often not well managed and has gained the reputation among doctors and users alike of being a traumatic process involving much patient suffering and much doctors' time. This need not be the case if withdrawal is carefully managed. I give some evidence for this and describe some general principles of benzodiazepine withdrawal a bit later.

But first, why (apart from the cost) should patients withdraw from benzodiazepines?

As we all know, when used short-term, benzodiazepines are rapidly effective, efficient and relatively safe and have a number of valuable therapeutic uses.

[SLIDE 4] THERAPEUTIC USES

THERAPEUTIC ACTIONS OF BENZODIAZEPINES	
Actions	Clinical uses
Hypnotic	Short-term treatment of insomnia
Anxiolytic (tranquillising)	Short-term treatment of severe anxiety Short-term aid to alcohol withdrawal Acute treatment of violent psychotic states
Anticonvulsant	Epileptic and drug-induced convulsions
Amnesic	Predmedication before surgery
Muscle relaxant	Muscle spasms, dystonias

- Hypnotic
- Anxiolytic
- Anticonvulsant
- Amnesic
- Muscle relaxant

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However, like other drugs, benzodiazepines are not without adverse effects. These usually result from excessive dosage, interactions with other drugs, and particularly from long-term use. I will briefly mention some of these, although most will be familiar to you. Not everyone is aware of the extent of the damage that benzodiazepines can cause.

[SLIDE 5] ACUTE TOXICITY

<p style="text-align: center;">ACUTE TOXICITY OF BENZODIAZEPINES</p> <p>1810 deaths attributed to benzodiazepines in UK 1990-1996</p> <p style="margin-left: 40px;">761 suicides 517 accidents 532 undetermined Home Office Statistics (1994 omitted)</p>
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Benzodiazepines have been regarded as remarkably non-toxic but they are not completely safe. Between 1990-1996 over 1800 deaths were attributed to benzodiazepine overdose in suicides, accidents and undetermined causes. In about two thirds of these cases, benzodiazepines were taken alone; in one third with alcohol or other drugs. Benzodiazepines are taken in 40% of self-poisonings. Temazepam, the commonest hypnotic used today, is the most toxic. The risk of a fatal outcome is greatly increased in the elderly and people with lung disease, and benzodiazepines increase the risk of fatality if taken with many other drugs that depress respiration. The combination of benzodiazepine with opiates causes about 100 deaths each year among drug abusers in Glasgow alone.

[SLIDE 6] OVERSEDATION

<p style="text-align: center;">OVERSEDATION WITH BENZODIAZEPINES</p> <ul style="list-style-type: none">- Drowsiness, poor concentration, mental confusion, muscle weakness, impaired balance, poor co-ordination- Most common with long-acting benzodiazepines- Elderly patients most vulnerable- Contributes to:<ul style="list-style-type: none">• falls and fractures in the elderly• traffic accidents• accidents at home and at work

Oversedation is a dose-related extension of the sedative/hypnotic effects of benzodiazepines. Symptoms include poor concentration, mental confusion, muscle weakness and impaired balance and co-ordination. They may persist as next-day hangover effects, especially with long-acting benzodiazepines such as nitrazepam and diazepam which can lead to accumulation with regular use. Elderly patients are the most vulnerable to oversedation but it can also occur in younger people and the effects are additive with other sedative drugs and alcohol.

These effects have been shown to contribute to falls and fractures in the elderly, traffic and other accidents. A recent study estimated that benzodiazepines cause 1600 traffic accidents and 110 driving-related deaths each year in the UK.

[SLIDE 7] MEMORY IMPAIRMENT

MEMORY IMPAIRMENT WITH BENZODIAZEPINES

- Impairment of learning and concentration
- Loss of memory for recent events
- Elderly patients most vulnerable - may lead to diagnosis of dementia
- Memory lapses, blackouts - may lead to shoplifting
- Impaired adjustment to bereavement

Benzodiazepines cause many cognitive impairments including impairment of memory. They make it difficult to learn new information and in particular cause amnesia for recent events. These effects are again most marked in the elderly and may falsely lead to a diagnosis of Alzheimer's disease. Yet many occupants of old people's homes and in the community are regularly prescribed benzodiazepines.

Benzodiazepines can also cause memory lapses - which can lead to charges of shoplifting, and may impair psychological adjustments to traumatic events such as bereavement.

[SLIDE 8] EMOTIONAL EFFECTS

EMOTIONAL EFFECTS OF BENZODIAZEPINES

- Paradoxical aggression, anger, violence associated with baby-battering, wife-beating, grandma bashing
- Depression, increased risk of suicide in depression
- Emotional anaesthesia

Benzodiazepines can occasionally cause paradoxical aggression and have been associated with baby battering, wife beating and grandma bashing. They can also cause depression and can precipitate suicide in depressed patients. They should not be used in depression although they are still commonly prescribed long term for depressed and anxious patients. They can also cause emotional blunting and apathy with inability to cope with the needs of children and family, an effect bitterly regretted by many long-term users.

[SLIDE 9] EFFECTS IN PREGNANCY

BENZODIAZEPINE EFFECTS IN PREGNANCY

- Floppy infant syndrome
Difficulties in breathing and suckling
- Withdrawal effects in neonates
Irritability, hyperexcitability, crying, feeding difficulties
- Developmental abnormalities ?? Contribute to cot deaths (SIDS), attention deficit disorders, autism spectrum

If taken regularly during pregnancy, benzodiazepines can cause adverse effects on the foetus and neonate and may possibly contribute to cot deaths since the neonate is unable to metabolise them

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efficiently. But they are still prescribed during pregnancy. (This problem will be discussed later by Susan Bibby.)

[SLIDE 10] BENZODIAZEPINE DEPENDENCE

BENZODIAZEPINE DEPENDENCE

- Benzodiazepines are potentially addictive.
- Chronic use produces tolerance, dependence, withdrawal effects if stopped.
- There are 1 million chronic prescribed users in the UK.
- 50% or more of these are dependent on "therapeutic" doses.

But one of the greatest risks for the long-term prescribed benzodiazepine user is dependence. There is no doubt that benzodiazepines are potentially addictive. With regular use for only a few months or even weeks the body comes to depend on them both psychologically and physically for normal function. A degree of tolerance develops rapidly so that larger doses are needed to produce the initial effects, contrary to general belief, and many users escalate their dosage. In fact there is clear evidence showing that hypnotic effects are no longer effective after a few weeks, and anxiolytic effects after a few months. People continue taking them mainly to prevent withdrawal effects. If dosage is insufficient once tolerance has developed, or if the drug stopped, withdrawal symptoms develop. At present there are about 1 million long-term prescribed benzodiazepine users in the UK. Several studies, including our own in Newcastle, have shown from computerised prescribing records, that there are an average of over 180 such patients in every GP practice. Apparently there are over 5000 prescribed long-term users here in Oldham. Well over half of these are likely to be dependent.

Long-term users, even while continuing drug use, suffer both from the adverse effects I have already mentioned and also from apparent withdrawal effects - and long-term use is commonly accompanied by increasing illness.

[SLIDE 11] MORBIDITY IN FIFTY PATIENTS

MORBIDITY IN FIFTY LONG-TERM BENZODIAZEPINE USERS

After starting benzodiazepines:

- 20% took drug overdose requiring hospital admission
- 20% developed incapacitating agoraphobia
- 18% had GI investigations (irritable bowel)
- 10% had neurological investigations
(3 wrongly diagnosed as MS)
- 62% received other psychotropic drugs (antidepressants)
- 28% were taking 2 prescribed benzodiazepines

This slide shows the morbidity in the first 50 consecutive patients attending a benzodiazepine withdrawal clinic that I ran from 1982-1994. They had been on prescribed "therapeutic" doses of benzodiazepines for 5-20 years and wished to withdraw because they did not feel well while taking the drugs:

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- 20% - OD
- 20% - agoraphobia (+ many panic attacks)
- 18% - GI investigations
- 10% - neurological investigations (3 - "MS")
- 62% - other psychotropic drugs since starting Benzodiazepines (mainly antidepressants)
- 28% - 2 prescribed Benzodiazepines

These symptoms were not the cause for starting benzodiazepines, but developed during long-term use. In this series nearly 90% of the patients withdrew successfully and at a follow-up 3-5 years later there had been no more overdoses; the agoraphobia, panic attacks and neurological symptoms (including the MS) disappeared. These findings are a strong argument that the symptoms were caused by the benzodiazepines and that health improves after withdrawal.

[SLIDE 12] ILLICIT BENZODIAZEPINE ABUSE

ILLICIT BENZODIAZEPINE ABUSE

Over 140,00 illegal benzodiazepine abusers in the UK;
Numbers still rising here and worldwide

Benzodiazepines abused by:

90% of polydrug abusers (opiates, cocaine, amphetamines) to:

1. Increase "high"
2. Alleviate withdrawal effects
3. Act as "downers" to overcome "uppers"

50% of alcoholics attending for detoxification to:

1. Alleviate anxiety associated with alcohol use
2. Alcohol plus benzos gives a "buzz"

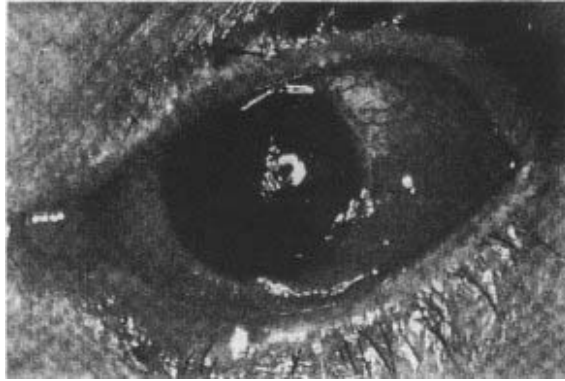
Some use benzodiazepines alone; high doses (oral, IV, snuff) to:

1. Give a kick
2. Provide relaxation and anxiety relief
3. Give confidence to engage in criminal activities

There is another problem that has arisen from benzodiazepine overprescribing - illicit abuse. There are probably at least 140,000 benzodiazepine abusers in the UK, and the number is still rising. Up to 90% of polydrug abusers worldwide also take benzodiazepines, and about 50% of alcoholics attending detox units obtain them illegally. In addition, some use high doses of benzodiazepines as their main recreational drug, taking it orally, as snuff or by IV injection. This latter practice carries all sorts of complications including not only AIDS and hepatitis but also abscesses, venous and arterial thrombosis and gangrene which may lead to amputation.

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[SLIDE 13] EYE COMPLICATION



A complication of temazepam injection. A man aged 40 who misused drugs and had had a leg amputated after ischaemic damage from intra-arterial injections presented with blindness of recent onset. He was blind in both eyes. The left eye was ophthalmoplegic, with corneal clouding and no pupillary reflexes. This was the result of his injecting gel temazepam into the inner canthus. This substance is known to cause vascular occlusion (with permission from Thompson *et al.* 1993).

This subject, a temazepam abuser, had thrombosed his arm veins, injected into the femoral artery and had a leg amputation because of gangrene. He then injected temazepam into his eye and became blind in both eyes as a result. (Surely evidence of a powerful addiction).

The tragedy of illicit benzodiazepine abuse is that it is iatrogenic (caused by doctors). The history is the same as barbiturates and amphetamines and others which originated as prescribed drugs but entered the illicit scene when they were commonly lying around in almost every household. The source of illicit benzodiazepines is mainly from pharmaceutical supplies and from GP prescriptions. Some GP patients sell their supplies; some children obtain them from their parent's prescriptions, and large amounts are stolen from chemists and pharmaceutical warehouses. Now illicit benzodiazepines are also coming in from Europe. Diazepam can be purchased on the Internet at a cost of £47 for 30x10mg tablets. Benzodiazepines are also becoming fashionable as "date rape" drugs.

[SLIDE 14] ADVERSE EFFECTS SUMMARY

ADVERSE EFFECTS OF BENZODIAZEPINES

1. Over-sedation

Depressed psychomotor performance, poor memory, ataxia contribute to car accidents, shoplifting. Most marked in the elderly, may produce mental confusion and contribute to falls and fractures

2. Additive effects with other CNS depressants

e.g. alcohol and drug overdose

3. Disinhibition

Aggression, contribute to baby battering, wife beating

4. Depression, emotional blunting

5. Adverse effects in pregnancy

Neonatal depression

6. Abuse

7. Tolerance, dependence, withdrawal effects

It is clear that there are a large number of reasons (including costs to individuals and to the community), summarised in this slide, **why** we should consider benzodiazepine withdrawal. As for **who** should withdraw, the risks are greatest as I have mentioned for long-term users and for elderly patients who together account for most benzodiazepine prescriptions. **When** should we do it? The answer of course, is now, but first we need to get across clear guidelines on **how** to do it. Here is where PCT workers - pharmacists, nurses, counsellors and others can be, and indeed already are, most helpful, and can give valuable advice to doctors.

[SLIDE 15] BENZODIAZEPINE WITHDRAWAL

BENZODIAZEPINE WITHDRAWAL BASIC PRINCIPLES

1. Gradual dosage reduction

- Individual withdrawal rate
- Adjuvant drugs

2. Psychological support

- Simple encouragement to psychological therapies
- long-term
- information
- motivation

Despite its reputation, a carefully managed withdrawal can often be pain-free and usually results in improvement in patients' physical and mental health and fewer visits to the doctor's surgery. The two cornerstones of successful withdrawal strategy are gradual dosage reduction and psychological support.

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Dosage reduction

Benzodiazepine dosage should be tapered gradually since abrupt or over-rapid withdrawal, especially from high doses, can precipitate convulsions, acute psychotic or confusional states, anxiety, panic attacks and other symptoms. The rate of tapering should be individually adjusted according to the patient's needs. It should take into account factors such as the dose and type of benzodiazepine, duration of use, reasons for prescription, lifestyle, personality, environmental stresses and amount of available support. Various authors suggest optimal times of between 6-8 weeks to a few months for the duration of withdrawal, but some patients may need a year or more, a view endorsed by the BNF and my own experience with patients. It is not worth hurrying the process especially when benzodiazepines have been taken for years. Patients should be empowered to control their own rate of reduction at whatever pace they find tolerable. For those on therapeutic doses, withdrawal is best carried out as an outpatient, allowing time for pharmacological and psychological adjustments to a benzodiazepine-free lifestyle in their own environment. High dose abusers may need to start in hospital.

There are advantages to conducting the withdrawal from diazepam because of its long elimination half-life (up to 200 hrs for active metabolite), allowing a smooth, gradual fall in blood concentrations, and its availability in low dosage forms (2mg tablets that can be halved), permitting small dosage reductions. There is evidence that withdrawal is often more difficult from short-acting, potent benzodiazepines such as lorazepam. Conversion from other benzodiazepines to diazepam should be conducted in stages, allowing for equivalent potencies between different benzodiazepines.

[SLIDE 16] EQUIVALENT POTENCIES

Indications and characteristics of benzodiazepines		
Drug	t _{1/2} (h) [metabolite]	Approx. equivalent oral dosages (mg)
Hypnotics		
Loprazolam	6-12	1
Lormetazepam	10-12	1
Nitrazepam	15-38	10
Temazepam	8-15	20
Triazolam	2-5	0.5
Anxiolytics		
Alprazolam	6-12	0.5
Chlordiazepoxide	5-30 [36-200]	25
Diazepam	20-100 [36-200]	10
Lorazepam	10-18	1
Oxazepam	4-15	20

This slide shows the half-lives and approximately equivalent potencies for different benzodiazepines. For example, lorazepam (Ativan) is about 10 times as potent as diazepam and has a much shorter half-life and the smallest tablet strength is 1 mg - equivalent to 10mg diazepam.

Once converted to diazepam, I have found that reductions of 1mg every 1-2 weeks are generally well tolerated from diazepam 20mg, but when 5mg is reached decrements of 0.5mg at a time may be preferred.

If switching to diazepam, which should be done gradually and stepwise, proves really difficult, liquid preparations of some benzodiazepines (diazepam, temazepam and nitrazepam) are available and some obliging pharmacists will make up oral solutions or capsules to order.

It is helpful to draw up a formal withdrawal schedule with the agreement of the patient. Here are some examples:

[SLIDE 17] WITHDRAWAL SCHEDULE FROM NITRAZEPAM AND TEMAZEPAM

Withdrawal from nitrazepam 10mg or temazepam 20mg with diazepam substitution		
Starting dose	nitrazepam 10mg	temazepam 20mg
Stage 1 (1 week)	nitrazepam 5mg diazepam 5mg	temazepam 10mg diazepam 5mg
Stage 2 (1 week)	Stop nitrazepam diazepam 10mg	Stop temazepam diazepam 10mg
Stage 3 (1-2 weeks)	diazepam 9mg	diazepam 9mg
Stage 4 (1-2 weeks)	diazepam 8mg	diazepam 8mg
Continue reducing diazepam by 1mg every 1-2 weeks or more slowly if necessary		

Many other detailed examples of withdrawal schedules from different benzodiazepines are given in this booklet, which can be obtained free on the web, and Barry (Haslam) has a few copies here.

[SLIDE 18] MANUAL

**BENZODIAZEPINES:
How they work and
how to withdraw**

Protocol for the treatment of
benzodiazepine withdrawal

Available free at:
<http://www.benzo.org.uk/manual/index.htm>

There is no need to draw up a schedule right up to the end. The schedule should be flexible and may need review and adjustment after the first few weeks according to clinical progress. It may be necessary to stand still at a certain stage if circumstances change, for instance if there is a family crisis. However, going backwards or taking extra tablets in times of stress should generally be avoided.

[SLIDE 19] ADJUVANT DRUGS

ADJUVANT DRUGS

Sometimes indicated:
Antidepressants - depression, agoraphobia, sedation
Beta-blockers - tremor, palpitations
Sedative antihistamines

Not helpful:
buspirone, clonidine, Z-drugs
flumazenil(?), gabapentin(?)

Various drugs have been tested for their ability to ease the withdrawal process. Mostly they are not helpful, except in individual cases. I will not go into details here but both antidepressants and beta-blockers can themselves cause withdrawal effects. And in particular the Z-drugs (zopiclone, zolpidem and

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zaleplon) which are increasingly used by some doctors, should not be used in withdrawal since they act in the same way and have all the same adverse effects as benzodiazepines including dependence and abuse.

[SLIDE 20] BENZODIAZEPINE WITHDRAWAL

**BENZODIAZEPINE WITHDRAWAL
BASIC PRINCIPLES**

1. Gradual dosage reduction

- Individual withdrawal rate
- Adjuvant drugs

2. Psychological support

- Simple encouragement to psychological therapies
- long-term
- information
- motivation

The second cornerstone of benzodiazepine withdrawal is psychological support. The degree of support required is variable. For many patients, particularly elderly patients on long-term hypnotics, the need is minimal. A randomised controlled trial of 191 elderly GP patients on long-term hypnotics in Newcastle found that a simple letter from the GP suggesting that they try cutting the dose by half a tablet a month, or a single 12 minute GP consultation giving similar advice, resulted in 34% of them stopping completely or reducing dosage by over 25%. At 6 month follow-up, these patients showed improvement in mental and physical health, no withdrawal or sleep problems and fewer visits to their doctor compared with a control group who stayed on their hypnotics.

[SLIDE 21] RESOURCES NEEDED NOW

RESOURCES NEEDED NOW

- Primary care teams
- Benzo support organisations
- Dedicated NHS benzo withdrawal clinics
- Research into long-term effects
- Support for patients

However, a considerable number of the million long-term benzodiazepine users need more help than this. Some need repeated encouragement and information about withdrawal symptoms - which are often largely due to fear.

Visits to GP surgeries by primary care teams such as community pharmacists, nurses and counsellors have been shown to be very valuable here. They can work with GPs, suggesting and supervising withdrawal schedules and supporting patients throughout withdrawal - thus saving GP time. Resources from Health Authorities are needed to deploy and train more PCT workers.

Access for patients to support organisations, such as [Barry Haslam's here in Oldham](#), can also be of great benefit. There are far too few benzodiazepine support groups in the UK and resources are badly needed to support existing groups and to set up and train a countrywide network for people to turn to for information, advice and support. (I have a list of some presently available helplines for patients here for anyone interested.)

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Some patients - particularly those on long-term so-called anxiolytic benzodiazepines and patients with psychiatric disorders - need expert advice and formal cognitive, behavioural and other therapies directed towards anxiety management. These services are very hard to come by. There are no longer any dedicated benzodiazepine withdrawal clinics. The waiting list for a clinical psychologist (despite assurances from the Department of Health) is currently 2-6 months, and most of these are not experienced in benzodiazepine withdrawal.

Dedicated benzodiazepine clinics and more clinical psychologists are needed, and these will also require appropriate training about benzodiazepines. Hard drugs detox units are not suitable for prescribed benzodiazepine users.

Such types of support need to be available not only during dosage reduction but also for a long period afterwards since patients remain vulnerable to stress after withdrawal and need time to develop drug-free stress-coping skills which they have never been able to learn while on benzodiazepines.

Research is also needed on long-term effects of benzodiazepines and also support for patients who end up with irreversible damage due to benzodiazepines (I will mention some protracted effects in a minute).

What about patients who do not want to withdraw? First of all, they should never be forced, but their motivation may be increased by explanation of the risks of staying on - such as falls and fractures, driving accidents and intellectual impairment. Secondly, they may be encouraged to try a small reduction in dosage on their own initiative. They may be surprised to find it is easier than they think. But clearly no responsible doctor should compel a patient into withdrawal or to undergo rapid dose reduction. Such attempts usually fail and may drive the patient to seek illicit supplies.

Withdrawal Symptoms

With a gradual withdrawal at the patient's own pace, withdrawal symptoms can be minimal.

[SLIDE 22] WITHDRAWAL SYMPTOMS

BENZODIAZEPINE WITHDRAWAL SYMPTOMS Symptoms common to all anxiety states	Relatively specific to benzodiazepine withdrawal
Anxiety, panic attacks, agoraphobia	Perceptual disturbances, sense of movement
Insomnia, nightmares	Depersonalisation, derealisation
Depression, dysphoria	Hallucinations (visual, auditory), misperceptions
Excitability, jumpiness, restlessness	Distortion of body image
Poor memory and concentration	Tingling, numbness, altered sensation
Dizziness, light-headedness	Formication
Weakness, "jelly legs"	Sensory hypersensitivity (light, sound, taste, smell)
Tremor	Muscle twitches, jerks, fasciculation
Muscle pain, stiffness (limbs, back, neck, jaw, head)	Tinnitus
Sweating, night sweats	*Confusion, delirium
Palpitations	*Fits
	*Psychotic symptoms
*Usually confined to rapid withdrawal from high doses of benzodiazepines	

Many have been described. Most of these are common to all anxiety states - anxiety, insomnia etc. - and many of these are actually due to fear of withdrawal symptoms. Some symptoms seem to be relatively specific to benzodiazepine withdrawal - such as perceptual distortions, hallucinations, sensory hypersensitivity, muscle twitches, etc. Most of these occur only if the withdrawal is too rapid or if the

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patient has been switched to another benzodiazepine at the wrong equivalent dose. A recent trial in elderly patients on long-term benzodiazepine hypnotics whose dosage was tapered with placebo over 8-9 weeks found that the symptom scores of patients who withdrew were no different from those who stayed on the hypnotics. 80% of the patients on the tapering regime stopped their medication completely by six months and showed significant improvements in cognitive function and experienced no adverse effects on sleep or increase in anxiety (Curran *et al.* 2003).

[SLIDE 23] PROTRACTED SYMPTOMS

SOME PROTRACTED BENZODIAZEPINE WITHDRAWAL SYMPTOMS

Anxiety
Insomnia
Depression
Gastrointestinal symptoms
Neurological:
 tinnitus
 paraesthesiae - tingling, numbness,
 pain usually in limbs, extremities
Motor symptoms:
 muscle pain, weakness,
 tension, painful tremor, shaking attacks, jerks,
 blepharospasm
Cognitive impairment

Occasionally patients, usually those who have undergone a too rapid, traumatic withdrawal, are left with protracted symptoms. Anxiety and depression and GI symptoms may take a year or more to subside and a number of neurological symptoms may be long-lasting - such as tinnitus, numbness, motor symptoms and muscle pain - and are occasionally irreversible. Traumatic withdrawal experiences, may lead to PTSD which may persist. There is also evidence that cognitive impairment due to benzodiazepines does not always recover completely although it improves after withdrawal. It has been suggested that long-term benzodiazepine use may add to age-related cognitive decline. A few CT scan studies have shown cortical shrinkage in chronic benzodiazepine users although the evidence is equivocal. More research is needed e.g. MRI. People with protracted and irreversible symptoms may be unable to work and earn an income. They need suitable financial support.

Outcome of withdrawal

With carefully managed withdrawal in motivated patients the outcome is good. The success rate for stopping is around 80-90% and the relapse rate after five years is low - less than 20% - and patients can always have a second or third go at withdrawal (they say it takes 7-8 attempts to be successful in stopping cigarette smoking). The final success of benzodiazepine withdrawal is not affected by duration of use, type or dosage of benzodiazepine severity of symptoms, psychiatric history, or the presence of personality disorder. Mental and physical health improves after withdrawal in most long-term users, and there is no evidence of increased alcohol use or psychiatric morbidity.

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Prevention

[SLIDE 24] PREVENTION

PREVENTION OF BENZODIAZEPINE DEPENDENCE

1. Short-term (2-4 weeks) or intermittent brief courses only
2. Minimal effective dosage
3. Avoid potent benzodiazepines (e.g. lorazepam)
4. Selection of patients
5. Education in withdrawal management
6. Eductaion about dependence risks of new drugs (zopiclone, zolpidem, zaleplon)

Clearly the way forward now is prevention. This requires doctors to stick to short-term or intermittent brief courses of benzodiazepines in new patients; to use minimal doses, and to avoid potent benzodiazepines such as lorazepam where possible. They should avoid prescribing benzodiazepines for those with a previous history of alcohol or drug dependence. And more education is needed for doctors and health care workers about the management of benzodiazepine withdrawal in long-term users. Education is also needed about the dependence risks of new drugs such as the Z-drugs. Prescriptions for these drugs have now reached nearly 5 million/year in the UK, but they have all the properties of benzodiazepines. SSRIs such as paroxetine also cause withdrawal effects. The drug companies no doubt have more drugs up their sleeves.

We must not allow history to go on repeating itself with generation after generation of drugs that cause dependence and withdrawal, and lead to illicit abuse. Overprescribing of benzodiazepines is a world-wide problem - even worse in Europe and North America than in the UK. But with proper action this country could lead the way towards a solution.