



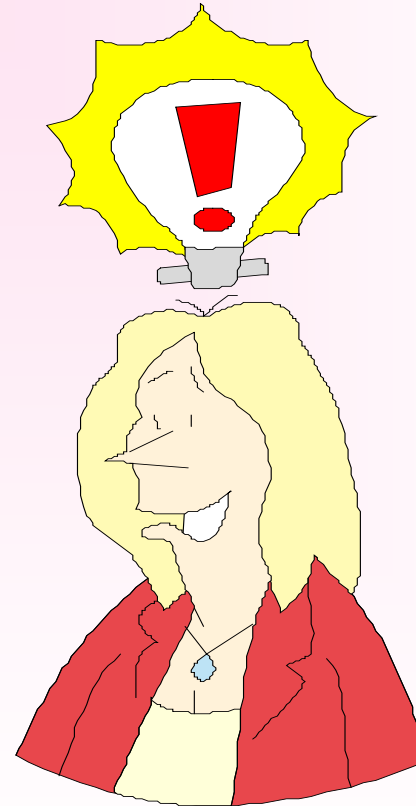
**Why are we still stuck around benzos
and how can guidance help us?!**

*Dr Chris Ford Clinical Director IDHDP
(International Doctors for Healthy Drug
Policies)*

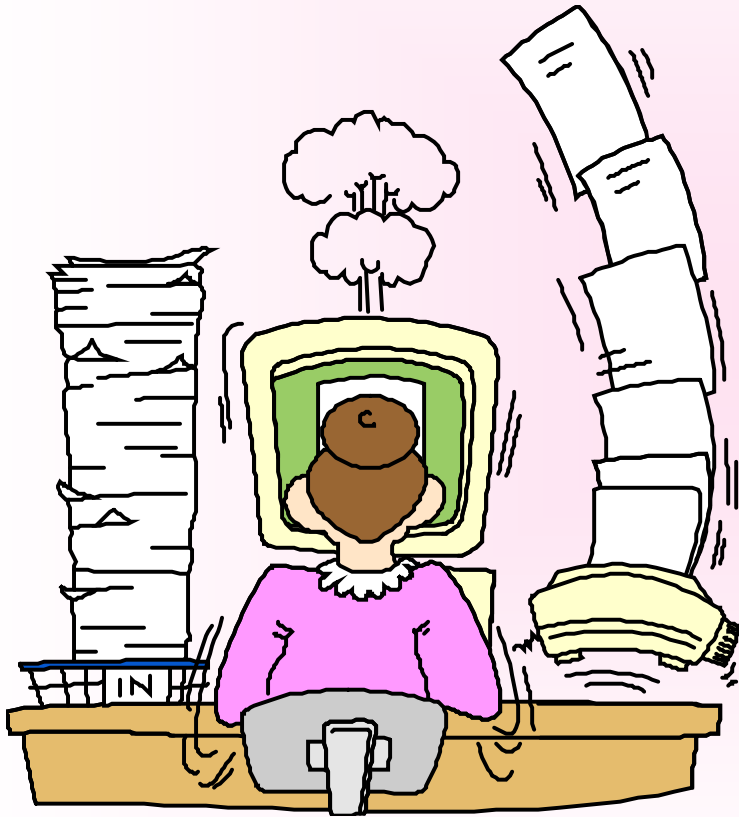
Thursday 16th May 2013

The Beginning

- Benzodiazepines always a problem
- Most loved Addiction
2004 *Jaffe et al*
- Not much help available



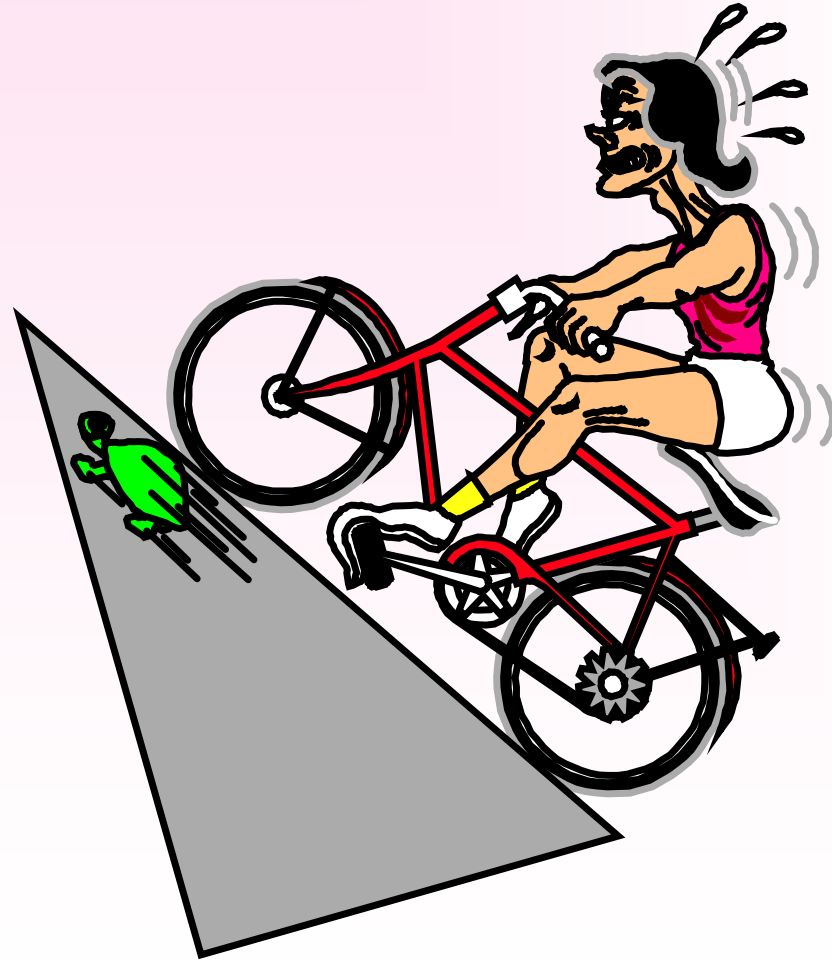
Needed help



- Second most common drug
- Unsure what to do
- Wrote BZ guidance for use in people who use drugs
- Problem wider
- Wide divergence between published guidelines and clinical practice
- Guidance not in reality

Sent on journey

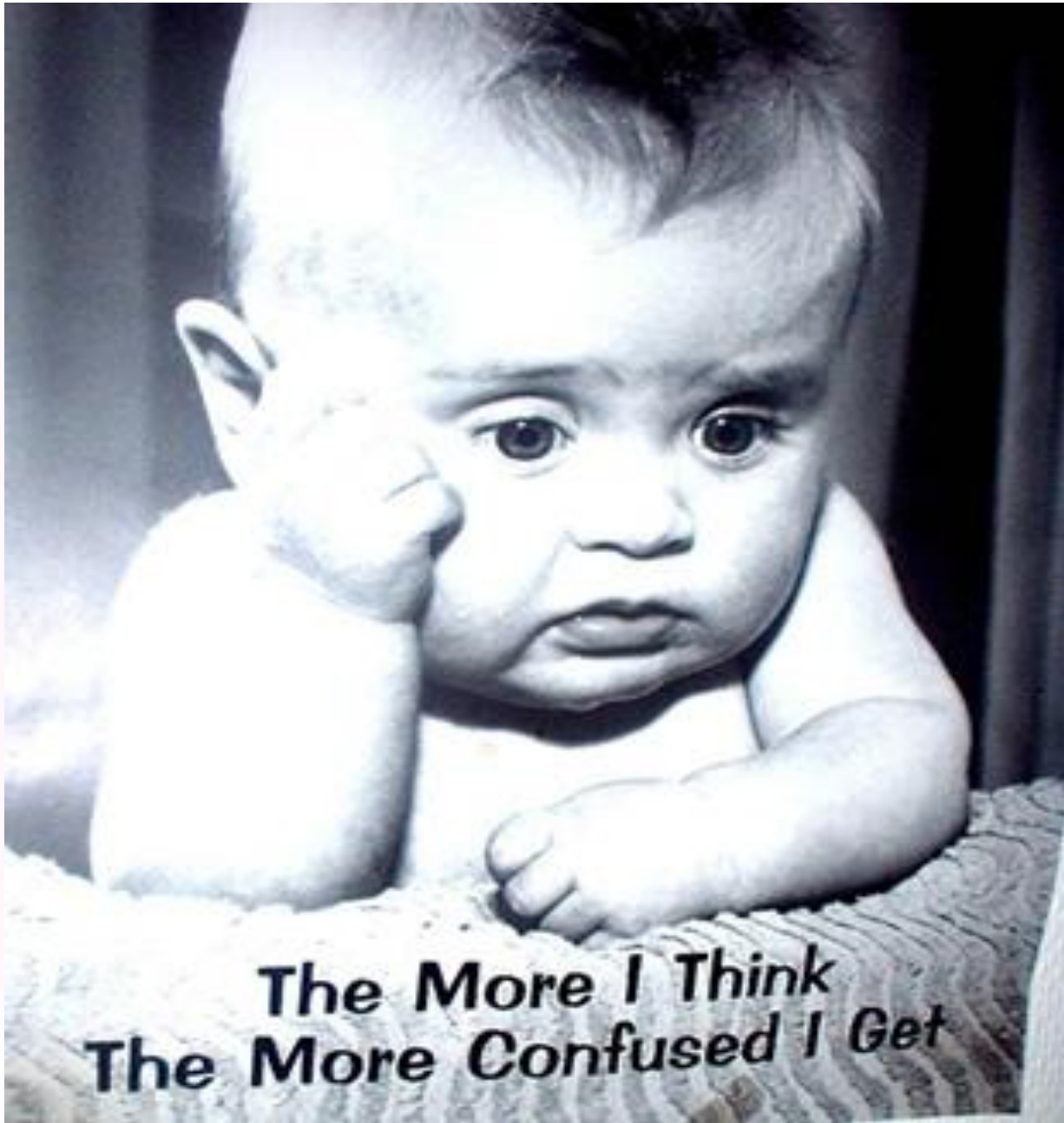
- Difficult
- Maverick



Wide variation in practice

- Why such wide variation in practice?
 - BZ sometimes given as quick fix in general practice
 - Sometimes BZ given rather than opioid
 - Questionnaire to Drug Services: 75% detox, 35% maintenance
 - (Williams 2005)





**The More I Think
The More Confused I Get**

Introduction

- Benzodiazepines are widely prescribed
 - Short-term for a variety of conditions
 - Efficacy well established
- Combination of effectiveness and risks of long-term use
 - Reason why benzodiazepines cause us such a headache in clinical practice

IN A WORLD
WHERE CERTAINTIES
ARE FEW...



NO WONDER
Ativan[®]
(lorazepam) 
IS PRESCRIBED BY SO MANY
CARING CLINICIANS.

Please see additional page for full summary of prescribing information.

Introduction

- Should only be prescribed for maximum of 2-4 weeks
 - Many people are prescribed for much longer
- Numbers taking prescribed benzodiazepines worldwide is enormous
 - Over 1 million people in the UK are on long-term
- Up to half of long-term users have difficulties in stopping benzodiazepines because of withdrawal symptoms



It is more difficult to withdraw people from benzodiazepines than it is from heroin.

Professor Malcolm H Lader
Institute of Psychiatry London 1999



The benzodiazepines are probably the most addictive drugs ever created and the vast army of enthusiastic doctors who prescribed these drugs by the tonne have created the world's largest drug addiction problem.

- DR VERNON COLEMAN, 1992

Current prescribing

- we are still doing it!



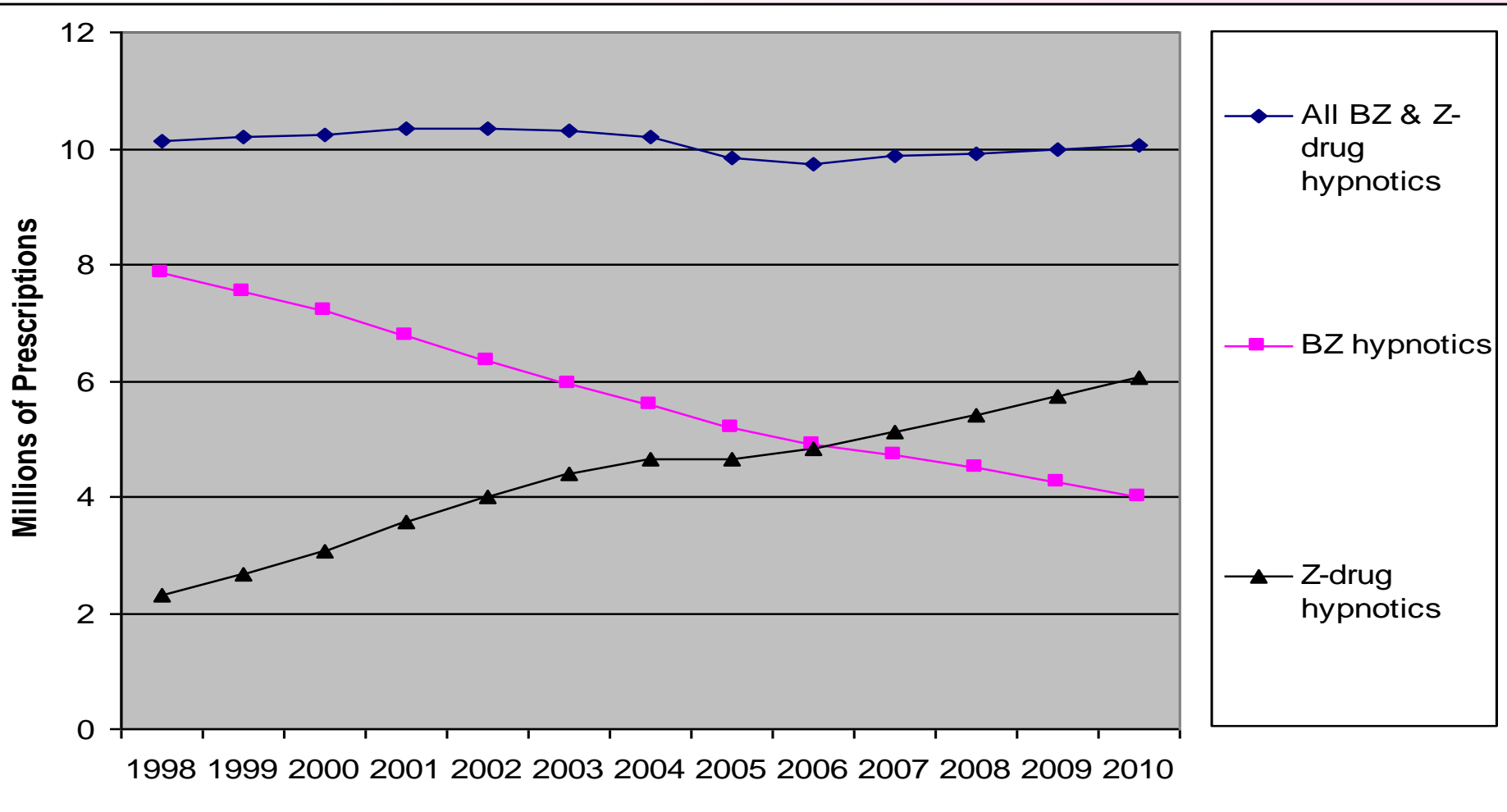
Prescribing

- Over the last decade:
 - Level of combined BZ & Z-drug prescribing has remained stable
 - BZ for anxiety has steadily risen
 - Also Z drugs risen



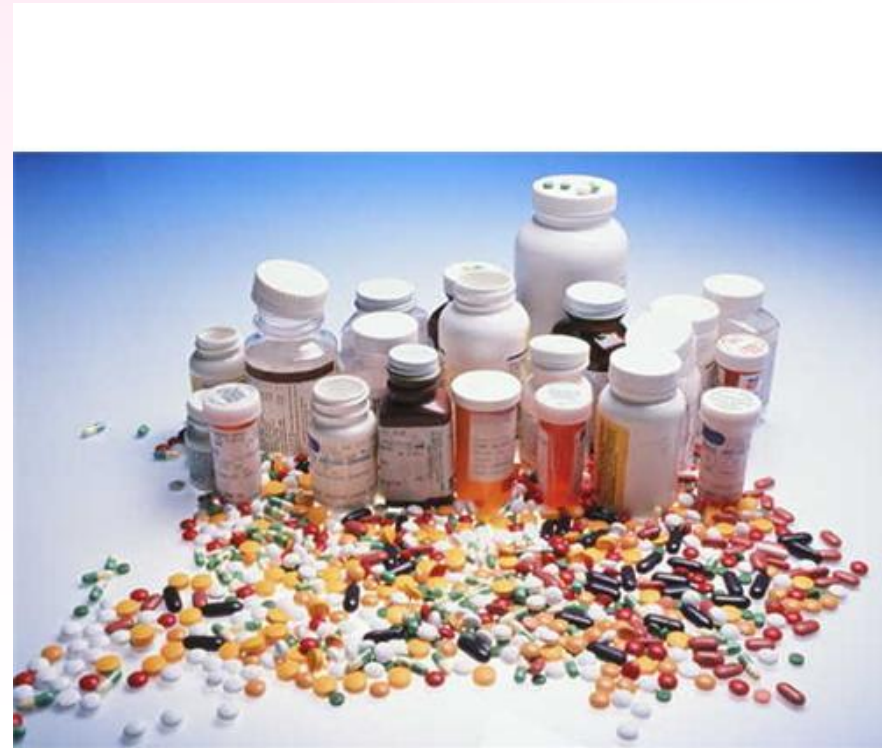
BZ and Z-Drug Hypnotics in the Community by BNF Category

(based on ePACT data in England 1998 to 2010)



Properties and clinical actions

- Many BZs, all similar properties, potency varies
- Rapidly & fully absorbed orally, leading to peak effects within $\frac{1}{2}$ to 2 hours of ingestion
- Fat-soluble
- Enter CNS rapidly
- Faster increased abuse
- Long half-lives are more likely to produce residual effects such as sedation falls the next day



Classification of BZ

Rapid Onset

Intermediate Onset

Slow Onset

Ultra short half-life (< 8 hours)

midazolam

zopiclone^s

zolpidem^s

zaleplon^s

Short half-life (8-24 hours)

flunitrazepam^s

lormetazepam^s

oxazepam^a

temazepam^s (oral
solution or caps)

lorazepam^{a,s}

loprazolam^s

temazepam^s (tabs)

Long half-life (\geq 24 hours)

diazepam^{a,s}

alprazolam^a

chlordiazepoxide^a

nitrazepam^s

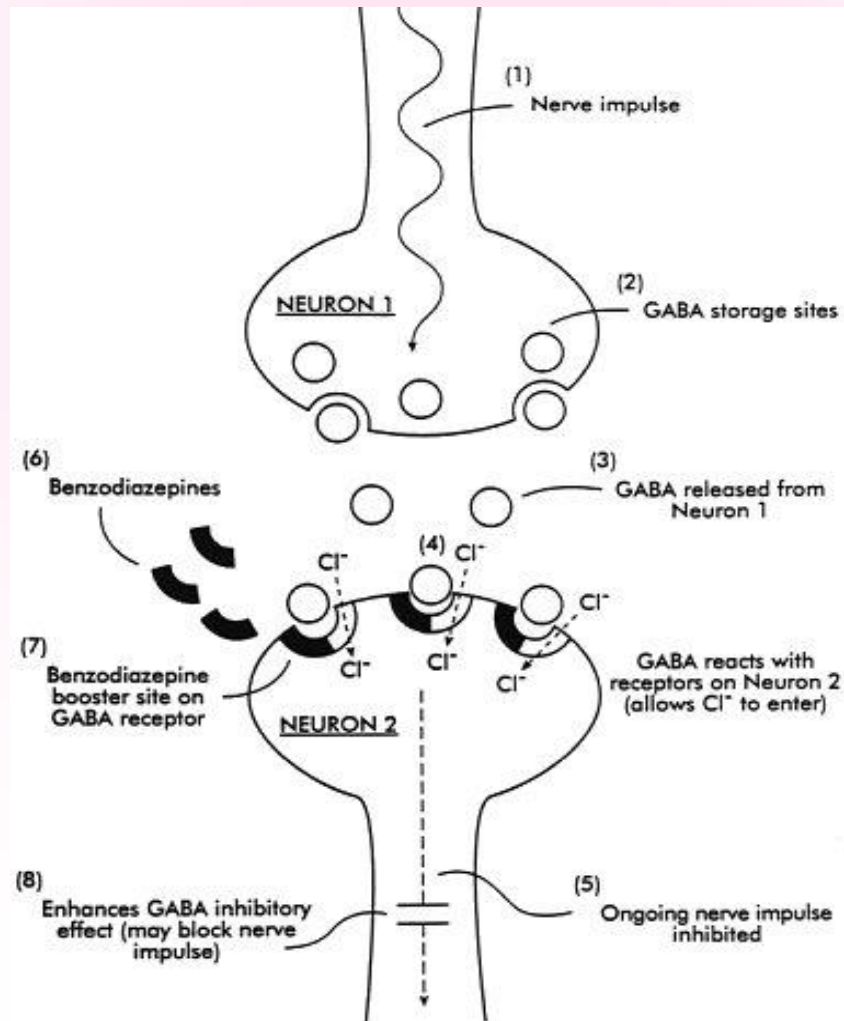
clonazepam^e

flurazepam^s

clobazam^{a,e}

a = anxiolytic, s = hypnotic, e = antiepileptic

BZ enhance GABA activity (inhibitory neurotransmitter)



Further properties and clinical actions

- Tolerance: physiological reaction
 - original dose of the drug has progressively less effect
 - higher dose is required to obtain same effect
- Rate of development of tolerance may vary for different drug effects
 - such as relief of anxiety, sedation and pleasure
 - can develop at different speeds
 - vary between individuals

Who uses BZ?

- Many different people
 - All ages
 - Both genders
 - But about half population don't find effects positive or reinforcing
- Spectrum of people ranging from therapeutic users to pleasure-seekers
 - But there is commonality



Treatment of insomnia & anxiety

- Start with addressing underlying problems
- Then using: talking therapies, CBT & self-help
- Drug treatment - not first line - can include:
 - Benzodiazepines, Z-drugs, SSRIs, melatonin
- Benzodiazepines / Z-drugs used lowest dose & shortest time
 - Maximum 2-4 weeks
- Not for the long-term treatment of anxiety or insomnia or treat short-term mild anxiety
- Primarily relieve and suppress symptoms, rather than being curative for any disorder

Harder to stop than start

- Caution with any patient
- More if a current or past:
 - drugs or alcohol
 - personality disorder
- Must have a plan for using 2 - 4 weeks or use very intermittently
- Discuss fully before issuing short-term that it is one-off, the risks of driving etc, and explain long-term risks



Established dependence

Prescribing for patients with established benzodiazepine dependence, is more controversial

But not addressing it and / or abrupt withdrawal of benzodiazepines carries significant risks



Different groups who are dependent

1. Therapeutic dose dependence
 - sometimes called 'involuntary addicts'
 - started for reason and continued
2. High dose dependence
 - may have started as prescription and then escalated dose often from illicit sources
 - no other drug or alcohol problems
3. Recreational high dose
 - Used by people who use other, often illicit drugs, OTC/POM and/or alcohol

Adverse effects & problems with long-term use

- BZ & related drugs:
 - Usually effective at first
 - Nearly all problems come from long-term use **SO AVOID**
- Long-term use of BZ associated with considerable physical, mental and social health problems & death:
 - long-term cognitive effects, memory impairment, emotional blunting, weakening of coping skills, depression, increased anxiety, insomnia, irritability and amnesia, paradoxical excitement

Success of reduction

- Withdrawal is possible in most patients who are dependent
 - But need to address problems related to prolonged use
 - Long-term effects disappear in most people 6-12 months after stopping
- With slow reduction and psychological support
 - Most patients lose their anxiety, panics, agoraphobia etc.
 - Relapse low with benzodiazepines

Withdrawal symptoms

- Long-term use can cause withdrawal symptoms in many people - between 30 and 45%
- Risk increases with:
 - longer use, higher doses & high-potency benzodiazepines
 - patients with chronic psychiatric and personality problems
 - those with chronic physical health problems
 - History of current or past alcohol or other dependence
- Withdrawal symptoms can take almost any psychological and / or somatic falling into 3 groups:
 - anxiety symptoms, such as anxiety and agitation
 - distorted perceptions such as abnormal body sensation
 - major incidents such as fits, which are all rare

Symptoms of BZ Withdrawal Syndrome

(Based on Humphreys & Hallström 1995, Ashton 1991)

- Anxiety symptoms:
 - Anxiety, dysphoria, muscle pains, tremor/shaking, fatigue, visual & sleep disturbance, headache, sweating, nausea/anorexia/weight loss
- Distorted perceptions (may be useful as new symptoms to help distinguish from recurrence of anxiety):
 - Hypersensitivity to stimuli (sound, light, touch, taste, smell)
 - Abnormal body sensations (distortion of body image, formication muscle twitching, tinnitus, burning sensations)
 - Abnormal sensation of movement (floor undulating, walls tilting)
 - Depersonalisation, derealisation, paraesthesia, dysphoria
- Major incidents (1-2% esp if high dose, stopping abruptly):
 - Epileptiform seizures, visual hallucinations, delirium, psychosis

Protracted withdrawal syndrome

- Occurs in up to 15% of patients
- Most have taken benzodiazepines for many years - over 20 years
- Most symptoms go within 1 year

Symptom	Usual course
• Anxiety	• Gradually diminishes over 1 year
• Insomnia	• Gradually diminishes over 6–12 months
• Depression	• May last a few months. May respond to antidepressants
• Cognitive impairment	• Gradually improves but may last for >1 year
• Perceptual symptoms: tinnitus, paraesthesia, pain (usually in limbs)	• Gradually recede but may last for at least 1 year
• Motor symptoms: muscle pain, weakness, tension, painful tremor, jerks	• Gradually recede but may last for at least 1 year and rarely persist for longer
• Gastrointestinal symptoms	• Gradually recede

Before starting a detox

- Consideration when and how to detoxify
 - Extra help and services needed
- Remember to ask about alcohol
 - Easy to substitute alcohol for BZ
- Before starting a reduction
 - Tackle any underlying problems
 - Ensure any physical or psychiatric health problems treated
 - Give information about the problems of long-term benzodiazepine use and explain the process of withdrawal and possible effects

The detox

- Tailor the dose reduction to the individual
- Taper it & don't be in a hurry
- Monitor frequently
 - Assess the need for additional support & therapies
 - Enquire about general progress & withdrawal & rebound symptoms
- If patients experience difficulties with a dose reduction, encourage them to persevere
 - Suggest delaying the next step down
 - Do not revert to a higher dosage
- Consider substitution of short or medium acting BZ by long-acting compounds (diazepam)

Examples of Hypnotic Reduction Protocols to Support Withdrawal

(number of tablets per day)

Stage of detox	Nitrazepam	Temazepam	Lormetazepam	Zopicline	Zolpidem & Zaleplon
(tablet size)	5mg	10mg	0.5mg	3.75mg	5mg
8	4	4	6	7	3½
7	3	3	5	6	3
6	2½	2½	4	5	2½
5	2	2	3	4	2
4	1½	1½	2	3	1½
3	1	1	1	2	1
2	½	½	½	1	½
1	½ alt nights	½ alt nights	½ alt nights	1 alt nights	½ alt nights
0	stop	stop	stop	stop	stop



Dealing with BZ detox problems

1. Rebound anxiety/insomnia:
 - Reassure (and prepare at start of treatment)
2. Continuing anxiety/depression:
 - Treat psychiatric problems more effectively
3. Difficulty coping with stress:
 - Increase psychosocial support
4. Difficulty sleeping:
 - Reassure/sleep hygiene / zopiclone / melatonin (short)
5. Difficulty coping with BZ withdrawal symptoms
 - Use longer half-life e.g. diazepam
6. Liking BZ too much to reduce it:
 - use slow onset
7. Using different amounts each day or binging:
 - Increase frequency of pickup, even to daily

Medication to help detox

- No substitute drugs for BZ
- Generally best avoided
- Rarely:
 - Antidepressants
 - Beta-blockers
 - Mood stabilizers
 - Melatonin
- May help some symptoms



BAP recommendations BZ using patients

British Association for Psychopharmacology

(Lingford-Hughes, Welch, Peters & Nutt 2012)

- Depends on severity of dependence:
 - Early/mild dependence: minimal interventions e.g. info, GP advice & letters (A)
 - Established dependence: graded reduction (A)
- Effectiveness of graded reduction:
 - Increased with additional psychological therapies (B) esp. panic disorder, insomnia (but not for depression, addiction)
 - Not increased with additional pharmacological therapies - consider antidepressants, melatonin, valproate, flumazenil on individual basis (C)
- Switching from short to long half-life BZ:
 - Do only if having problematic withdrawal symptoms on reduction (D)
- Evidence poor for illicit users - maintenance not supported (D)

Success rates in RCTs for BZ detox

(Meta-analyses: Oude Voshaar et al 2006, Parr et al 2008)

- Primary care patients:
 - Routine care : 5-10% successfully detox
 - RC vs minimal interventions: an additional 15% detox
 - Abstinence largely sustained at FU
- Secondary care patients:
 - Routine care: 15-20% successfully detox
 - RC vs graded redn: an additional 20-35% detox
 - GR vs abrupt substitution with drug: 20% less complete
 - Abstinence largely sustained at FU

Longer term prescribing

- Decision to prescribe longer-term should be rare and made with care
 - Risk of all the negative effects including cognitive impairment etc.
 - Unfortunately, most often results from inadvertent continuation of short-term prescriptions
 - Failed detox



Self-Help for Tranquilliser Withdrawal

- Ashton self-help manual for benzodiazepine withdrawal
www.benzo.org.uk/manual
- The Council for Information on Tranquillisers & Antidepressants (CITA)
www.citawithdrawal.org.uk
- Battle Against Tranquillisers (BAT)
www.bataid.org

Illicit drug use

- Complex why people who use illicit drugs, use BZ:
 - And big problem with 90% people in one year in Px report use and half report illicit use in last 3 months
 - May be simply as "self-medication" to make them feel normal or to be able to cope
 - May be for anxiety, insomnia, to enhance opiate effect, help mood, improving confidence and/or to reduce voices
 - May enjoy effects and use in binges
 - Help come down from amphetamines, ecstasy, crack and cocaine and / or to combat opiate withdrawal symptoms

Prescribing to BZ & Opiate Users

Provide opiate prescribing only initially



Optimise opiate treatment

counselling & psycho-social interventions, self-help



Reassess whether need for BZ still exists



Consider BZ - initial stabilisation & reduction

over 6 wks to 6 mths

Should we prescribe BZ to people who use drugs and / or alcohol?

- Polarise practitioners into
 - 'purists' and 'realists'
- Most people who use drugs and / or alcohol have used BZ
- Most of us have found ourselves in a position having to judge whether to continue BZ prescription
- How to decide?

Do the guidelines help?

Drug misuse
and dependence
UK guidelines on
clinical management



“The task of the Recovery Orientated Drug Treatment Expert Group has been to describe how to meet the ambition of the Drug Strategy 2010 to help more heroin users to recover and break free of dependence...”

**MEDICATIONS IN
RECOVERY
RE-ORIENTATING
DRUG DEPENDENCE
TREATMENT**

BAP key uncertainties for illicit BZ users

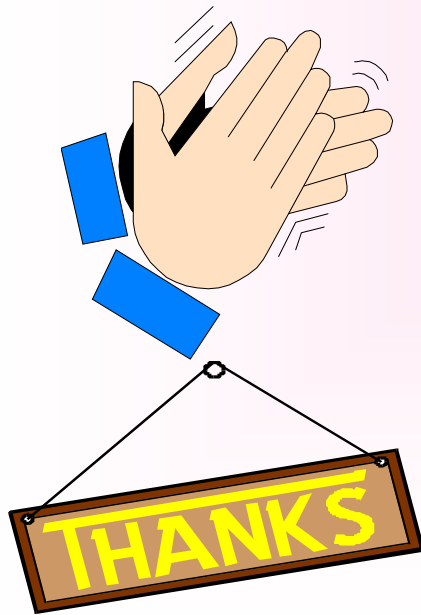
- What is the optimal speed or duration of gradual dose reduction?
- Is a stepped model of simpler to more complex interventions for detox helpful?
- Is there a role for BZ agonist maintenance therapy?
- Do modified detox strategies for high-dose users (e.g. partial redn & stabilisation at therapeutic dose before completing redn) work?

BZ: Key messages

- BZ is not 1st line treatment for insomnia & anxiety
- BZ suppress symptoms, don't cure, risk dependence
- If use drugs (including BZ) short-term only - better not to start
- Multiple long-term adverse effects
- If people present been on long-term: explain, support and mainly detox, individual plan and don't be in hurry
- Success of detoxification good
- Longer-term only if: treat each person as an individual, risks understand & stopping worse than continuing



Why are we still stuck around benzos and how can guidance help us?!



Chris Ford

chrishelen.ford@virgin.net

