

# WHAT TO DO ABOUT THOSE BENZOS!?!

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## Outline of Workshop

- The problem
- Why need guidance
- What's new in the evidence
- Your views & questions

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Who has Ever Had a Problem with  
Benzos?

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## Why are Benzos a Problem?

- Work
- Useful
- But:
  - Addictive
  - Severe withdrawal symptoms
  - Treat all people who use them as the same
  - Evidence is limited and changing

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## Why Do We Need New Guidelines

- New evidence:
  - Alcohol social drinking, effects on memory
- New understanding of old evidence:
  - Tolerance
- Thinking more sophisticated:
  - Time limits very arbitrary
  - Targeting of BDZ for longer term use
- Older guidelines problematic:
  - Simplistic
  - Not very evidence based

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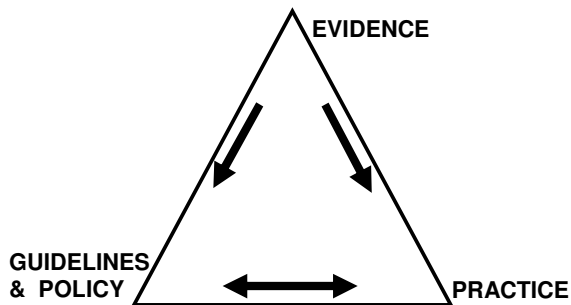
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## How Evidence Relates to Guidelines & Practice



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## Why are BDZ/Hypnotic Guidelines So Problematic?

- Opinion on use of BDZ varies widely
- Enormous divergence between BDZ guidelines, clinical practice & evidence
- BDZ guidelines have more to do with opinion & policy than evidence:
  - Drive to reduce 'inappropriate' prescribing of BDZ
  - Inappropriate defined as longer than 2-4 weeks
- Clinicians ignore guidelines:
  - Often understandable
  - Sometimes evidence based to do so

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## How “Addictive” are Benzos?

- Depends on population being considered
- Low risk: normal populations
  - Moderate drinkers > minimal drinkers
- Intermediate risk: psychiatric populations
  - One of safest drugs prescribed in mental health
- High risk: addict populations
  - Strong links with alcohol problems, opiate use and dependent personality disorder

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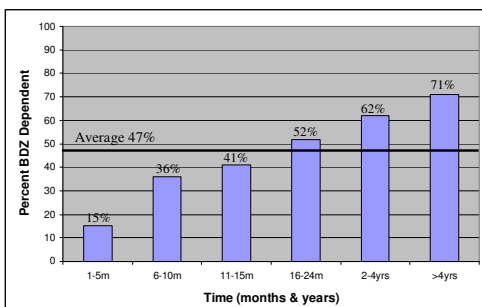
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## Rates of BDZ Dependence by Length of Use in Pts Using BDZ Daily in Primary Care

(De las Cuevas et al 2003, Canary Islands, N=1048)




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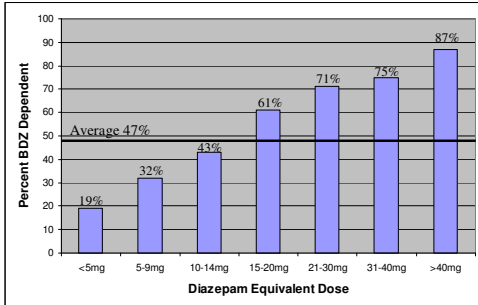
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**Rates of BDZ Dependence by Dose Used  
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**Tolerance to BDZ effects**

- Rapid tolerance to most unwanted effects & sedation, but may not be complete:
  - Buzz, rush, high, sedation
  - Amnesia, cognitive effects, ataxia, muscle relaxation
- Partial tolerance to antiepileptic effects
- Little tolerance to other therapeutic effects:
  - Anxiolytic, antipanic effects & amnesic effects post dose

Note: Different rates of development of tolerance indicates different mechanisms of action for the various effects

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**Effect of Tolerance on Behaviour**

- If rapid tolerance occurs (high, sedation):
  - Escalate dose
  - Use in binges
  - Inject rather than oral
  - Use in combination with other drugs
- If little tolerance occurs (anxiety):
  - No need to increase dose or increase speed of onset, binge or polydrug use

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## Who Escalates Their Use?

### Fun Seeking

- Assoc abuse of BDZ
- Seeking positive effects
- Often escalate BDZ dose
- Lower doses not enough
- Typically take BDZ as single dose in day
- Includes bingers & those who use to potentiate drug effects

### Self-Medicating

- Not assoc BDZ abuse
- Seek relief from distress
- Rarely escalate BDZ dose
- Lower doses effective
- Typically take BDZ 3-4 times a day
- Includes regular BDZ users & illicit use to help with problems

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## BDZ EVIDENCE - What's New

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## Reassessing the Risk-Benefit Profile of BDZ

- Memory problems:
  - More of an acute & chronic issue than previously thought
- Emotional & coping problems :
  - More of an issue long-term than previously thought
- Liking (& predisposition to addiction):
  - More prevalent than previously thought
- Pharmacology:
  - No reversal of underlying neurotransmitter abnormalities
  - Tolerance: Develops more slowly for therapeutic indications than previously thought
- Long-term use:
  - May be appropriate where tolerance is unlikely to occur

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### Memory Problems Associated with Therapeutic BDZ Use

- Memory problems routinely occur in people who take BDZ
- Incomplete tolerance occurs to memory even after long term use
- Difficulty acquiring new information at therapeutic doses of BDZ:
  - Occurs with every dose taken
  - A specific deficit in remembering recent events
  - Also interferes with concentration & attention
  - In longer term, reduced confidence in memory ability leads to poorer social functioning e.g. difficulty remembering names of new people

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### Transient Global Amnesia with High Dose BDZ Use

- Loss of memory for previous day's events, although behaving normally at the time:
  - Feel 'floaty', warm & comfortable with no worries
  - Feel invincible & invisible ('Rambo syndrome'), so may commit crimes but not remember
  - Pt may decide to stop BDZ use because of it
  - Flunitrazepam (Rohypnol) used in date rape
- Similarly with high dose zopiclone (30mg+)
- ? Similar to 'alcoholic blackouts'
- Loss of memory for unpleasant events is utilised for premedication & anaesthesia

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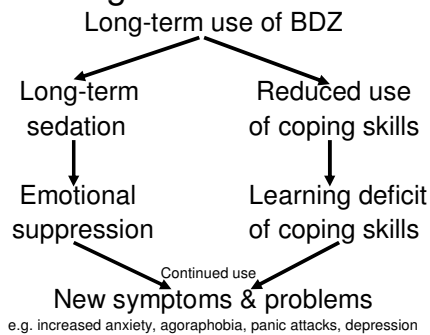
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### Effect on Emotions & Coping of Long-Term BDZ Use




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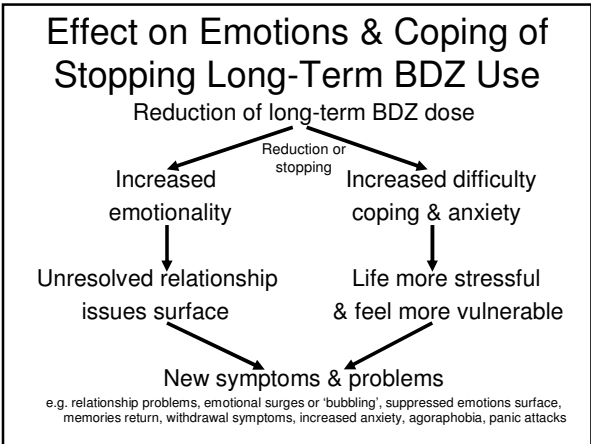
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### BDZ Pharmacology: BDZ as Symptomatic Tx Only

Work merely by suppressing symptoms, rather than reversing underlying neurotransmitter abnormalities:

- BDZ useful for self-limiting problems e.g. insomnia, anxiety:
  - Once self-limiting problem resolved, can be stopped
- If underlying problems exist that are not self-limiting:
  - Underlying problems must also be tackled, as the BDZ will not resolve them e.g. psychological issues
  - If underlying problems not resolved, problems continue so risk of prescribing long term
- So primarily prescribe BDZ for self-limiting problems or problems that will resolve i.e. shorter-term use only
  - If prescribe BDZ for other types of problems, may end up prescribing long term

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### Only Give BDZ Longer Term if ...

- Treatment remains effective:
  - Reduces core symptoms of disorder and effect worthwhile
  - Tolerance is incomplete, helped by using PRN
- If better than other Tx on risk vs benefit profile:
  - Lower adverse effects
  - Lower risks of misuse or diversion
  - Better than other medications that reverse underlying neurotransmitter abnormalities
- But don't give BDZ if:
  - BDZ no longer effective or worse than other Tx

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## Risks & Benefits

- Clinicians need to maintain an overview of benefits and adverse effects, with the associated risks:
  - Rebound and memory problems effects with every dose, on both short & long term use
  - Adverse effects at initiation only, such as sedation, and most cognitive & motor effects (on short term use only)
  - Adverse effects which develop or accumulate over time, such as tolerance, emotional suppression, coping responses and dependence (on longer term use only)
  - Associated risks such as misuse (overuse/underuse), diversion and overdose

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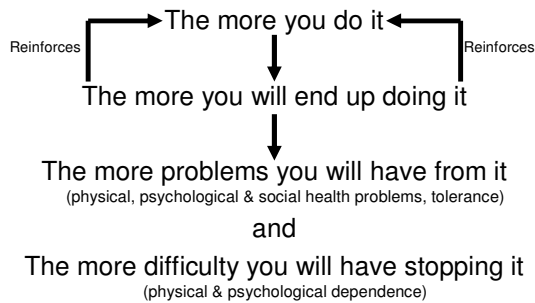
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## BDZ Pharmacology - Addictiveness



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## The Slippery Slope to Psychological Addiction & Harm

- At the top:
  - Pt can easily stop themselves going down
  - Relatively little harm
- In the middle:
  - Pt can't easily stop themselves going down
  - Harm accumulating
- At the bottom:
  - Maximum harm & psychological addiction



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### “Benzo Trap” to Long-Term Use

- Start BDZ:
  - Short term use for a clear indication
- Slippery slope & extension of prescribing occurs:
  - Pressure from patient & indication becomes less clear (e.g. to help cope)
- BDZ script becomes difficult to stop:
  - Patient clearly ‘likes’ BDZ and reports continuing efficacy
  - Underlying problems not resolved

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### Avoiding the ‘Benzo Trap’

- Keep indications for use clear & appropriate
- Don’t give for chronic poor coping/general stress
- Try to manage the patient’s expectations
- If extension of BDZ script requested:
  - Assess reasons why carefully, including reassessing diagnosis
  - Assess recent efficacy, adverse effects & associated risks
- If BDZ liking may be present:
  - Reassess & monitor even more carefully, esp. if a high risk of misuse

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### Degree of Psychological Reinforcement from Taking BDZ

- Speed of onset of positive effects:
  - Rapid onset drugs assoc. with most abuse:
    - Whether longer half-life (e.g. diazepam) or shorter half-life (e.g. flunitrazepam)
  - Slow onset drugs assoc. with least abuse
    - e.g. oxazepam is BDZ of choice if misusing BDZ (unless pregnant)
- Also related to dose of BDZ:
  - Higher dose gives bigger positive effect (‘buzz’)

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## What Does this Mean in Practice?

### Old Guidelines:

1. Use lowest dose for briefest time, max 2-4 weeks
2. Use only one BDZ. If need hypnotic & already on long-half life BDZ anxiolytic, give same at night
3. Dose used should be in therapeutic range
4. Reduce gradually after both short term & long term use
5. Only use in acute self-limiting situations or conditions
6. Only use for severe symptoms
7. Do not use in those with a history of addiction

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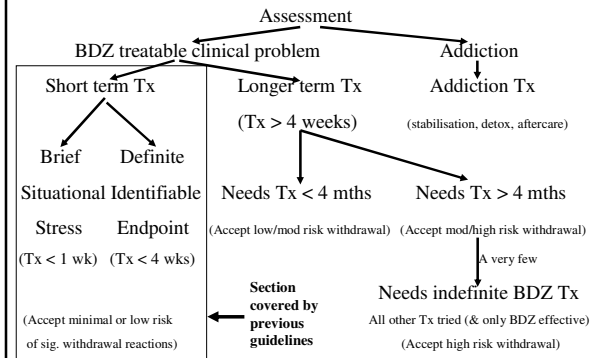
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## Categories of BDZ Prescribing




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## Problems with Old Guidelines

- Minimise risk, but no balance of risk & benefit
- Excludes the longer term conditions where BDZ most useful e.g. anxiety disorders
- Need to reduce BDZ dose as soon as the therapeutic dose is reached or even before!
- No guidance on treatment of:
  - Moderate symptoms
  - Treatment resistance to non-BDZ drugs
  - Treatment in drug/alcohol users
- The evidence base for the 2-4 week time limits doesn't stand up to scrutiny

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## So How Can we Improve on This?

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### a) Different Populations

- Be aware different people use for different reasons:
  - Fun use & self-medication
- Be aware of different level of risk for different populations:
  - Anxiety & insomnia
  - Poor copers and chronic stress
  - Drinkers, including social drinkers
  - Drug users, especially opiate and BDZ users

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### b) Only Prescribe BDZ when ALL 5 Criteria been Met

1. Clear indication for which BDZ use is appropriate
2. Define & agree the short term goals with the patient
3. Have treated underlying causes (e.g. anxiety, insomnia) with other means first
4. Weigh up the risks & benefits of initiating BDZ (or not initiating them):
  - Discuss with patient memory & other cognitive effects, driving, rebound, dependence
  - If unsure benefits outweigh risks, do not prescribe
5. If short term use, symptoms must be self-limiting or if longer term use, only where tolerance is unlikely & if better than other non-BDZ treatment (or when recommended by specialists)

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### c) Reducing Inappropriate Prescribing of BDZ

Don't prescribe outside evidence based guidelines:

- For longer than is advisable
- In larger amounts than is advisable
- Regular use, when PRN would be better
- In situations where BDZ are not advisable:
  - Not the most appropriate treatment option
  - Not warranted for the diagnosis
  - Contraindicated

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### Reducing Inappropriate Prescribing of BDZ (cont)

Do terminate the prescription when BDZ should no longer be prescribed:

- No longer clear evidence of benefit
- Adverse effects significant e.g. memory
- Associated risks increasing:
  - Slippage down the slippery slope is occurring
  - When using illicit BDZ, diverting, overusing or 'loosing' scripts
  - When drinking alcohol when taking BDZ

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### d) Avoiding Inadvertent Long-Term BDZ Use

- If risk of long-term use on initiating script, treat as any other addiction medication:
  - Agree goals/aims
  - Specify length of script & when you will review it
  - Issue short term scripts only (initially)
  - Use BDZ PRN (intermittently) as standard
- Review regularly:
  - Assess progress towards goals, efficacy, adverse effects & associated risks
  - No automatic renewals (initially)
- Ensure continuity of prescriber

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### e) Long-Term Use Defensible when all 5 Criteria been Met

1. Treatment resistant: alternatives failed
2. Benefits outweigh risks
3. Decision taken in conjunction with patient including discussing risk of dependence
4. Treatment is strictly individualised
5. Need for treatment reviewed periodically

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### f) Illicit BDZ Users Need to Meet Five Additional Criteria Before Prescribing

1. You have a least 2 BDZ positive urine screens
2. No BDZ negative urine screens in the last 4 months
3. Evidence from the history & symptoms that the Pt is physically dependent on BDZ or has the BDZ dependency syndrome
4. You believe that the benefits of treatment will outweigh the risks (diversion, overdose etc)
5. You are happy to do so

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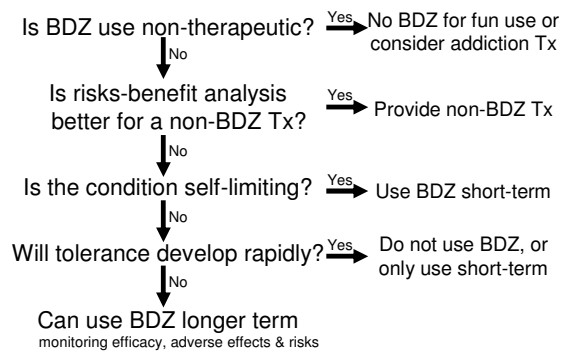
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### Summarising How to Prescribe BDZ



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## Summary

- BDZ prescribing is complex but knowledge increasing, so risk-benefit balance has changed
- BDZ suppress symptoms & don't treat the cause
- Follow the RULES OF FIVE for prescribing
- Short term use ok for self-limiting conditions
- Longer term use ok if no tolerance
- In illicit drug users, prescribe as for addiction
- Avoid slipping into longer prescribing:
  - Avoid use for general stress & poor coping
  - Be more active when initiating & reviewing

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## Any Questions?

- Adverse effects:
  - Memory problems
  - Emotional problems, coping
- Risk-benefit analysis:
  - Short and longer term use
  - Use in illicit drug users, drinkers

Thank you  
Chris Ford and Fergus Law

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