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Tapering Patients off of Benzodiazepines

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General Disclosures

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Speaker Disclosures

- I have no disclosures to report

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Objectives

1. Be able to identify patients that would benefit from tapering off of benzodiazepines
2. Become familiar with ways to engage patients in a benzodiazepine taper
3. Become familiar with effective outpatient benzodiazepine taper strategies

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Benzodiazepines - Background

- Commonly prescribed for anxiety and insomnia
- Current clinical guidelines suggest short term duration of use
- Despite guidelines long-term use is common

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Benzodiazepines by the Numbers

Table 1. Prevalence of Any Benzodiazepine Use, Long-term Benzodiazepine Use, and Use of Long-Acting Benzodiazepines by Sex and Age Group in the United States in 2008[a]

Variable	Mean age, y, %			
	18-35	36-50	51-64	65-80
US Population				
With any benzodiazepine use, y	2.6	5.4	7.4	8.7
Among men	1.7	3.7	5.3	6.1
Among women	3.6	7.1	9.2	10.8
Among Persons With Any Benzodiazepine Use				
With long-term benzodiazepine use[b]	14.7	22.4	28.0	31.4
Among men	15.6	22.8	28.4	28.8
Among women	14.2	22.2	27.8	32.6
With any long-acting benzodiazepine use, y	24.1	25.4	25.4	23.8
Among men	26.9	29.5	29.4	27.1
Among women	22.7	23.3	23.4	22.4

JAMA Psychiatry. 2015 Feb;72(2):136-42. doi: 10.1001/jamapsychiatry.2014.1763.

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Identification - Case

- A 26 year-old female presents to your office to establish care. She has a history of generalized anxiety disorder and denies other active medical complaints aside from a broken ankle that she recently went to an ER for. She reports that "most" medications give her brain-zaps and that her current medications are the only ones that she will take. Her current medication list includes clonazepam 1mg po BID, alprazolam 0.5mg po TID prn anxiety, and valium 5mg po QHS. You verify the above prescriptions with the prescriber monitoring program and she has gotten the above medications for > 1 year from multiple prescribers and also recently has received oxycodone from her recent ER visit.

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Cues to Taper

- Multiple prescribers for controlled substances
- Use of opiates with benzodiazepines
- Pregnancy
- Length of benzodiazepine prescription
- Multiple benzodiazepine agents
- Unwillingness to try other interventions
- Early refills / escalating use
- Older age
- Worsening medical conditions
- Primary diagnosis is PTSD
- Alcohol abuse

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Engagement - Case

- A 26 year-old female comes to your clinic to establish care. She has a history of GAD and has been on Sertraline 100mg po daily, alprazolam 1mg BID, and clonazepam 1mg po qhs for the last year. Her GAD7 is 1 (low anxiety score) and overall she feels that her anxiety is well treated aside from some afternoons. She has had some complaints about her performance at work which worries her as she is planning to have a child some time in the upcoming year.

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Engaging the Patient

- Evaluate clinical need for use
- Evaluate for common side-effects: impaired memory, sedation, psychomotor effects
- Increased risk of accidents and injuries (especially in elderly)
- May increase risk for dementia
- May be exacerbating symptoms
- Pregnancy - cleft palate and neonatal withdrawal

Lader, M. (2011), Benzodiazepines revisited—will we ever learn?. Addiction, 106: 2086-2109.

doi:10.1111/j.1360-0443.2011.03563.x

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Not Engaging is a Common Pitfall!

- Benzodiazepines are often started and not revisited for several months
- Providers can be reluctant to discuss tapering for multiple reasons
- Brief interventions do work - information pamphlets in Britain sent to patients taking benzodiazepines > 1 year had a 4x higher likelihood of ceasing benzodiazepine use
- Education in nursing homes is also effective!

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Taper Agent Guidelines

- Substitution of agents rather than gradual dose reduction of a benzodiazepine has worse outcomes
- Goal is to achieve a predictable decline in blood levels
  - Consolidate to one agent
  - Scheduled rather than as needed
  - Convert to long-acting if able
- Dosage forms are important (Valium has a liquid form with 1mg/ml)

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Benzodiazepine Comparisons

Oral benzodiazepines: Indications, onset, half-life, and equivalent doses

Drug	FDA-approved indication(s)	Onset of action	Approximate half-life (hours) in healthy adults	Approximate equivalent dose (mg)[a]
Alprazolam	Anxiety disorders, panic disorder	Intermediate	6.3 to 26.9 (IR), 10.7 to 15.8 (XR)	0.5
Chlordiazepoxide	Anxiety disorders, acute alcohol withdrawal, preoperative apprehension and anxiety	Intermediate	24 to 48	10
Clonazepam	Seizure disorders, panic disorder	Intermediate	18 to 50	0.25 to 0.5
Clorazepate	Anxiety, seizures, acute alcohol withdrawal	Fast	40 to 50	7.5
Diazepam	Anxiety disorders, acute alcohol withdrawal, muscle spasms, convulsive disorders	Very fast	20 to 100	5
Estazolam	Insomnia	Intermediate	10 to 24	0.3 to 2
Flurazepam	Insomnia	Intermediate	47 to 100	30
Lorazepam	Anxiety	Intermediate	10 to 20	1
Oxazepam	Anxiety, acute alcohol withdrawal	Slow to intermediate	5 to 20	30
Quazepam	Insomnia	Intermediate	39 to 73	5 to 15
Temazepam	Insomnia	Intermediate	3.5 to 18.4	30
Triazolam	Insomnia	Fast	1.5 to 5.5	0.25

IR: immediate release; XR: extended release

[a]Interpret with caution, conflicting data exist

Bostwick JR, Casher MI, Yasugi S. Benzodiazepines: a versatile clinical tool. Current Psychiatry 2012;11(4):55-64.

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Taper Schedules

- Gradual dose reduction (10-25% increments) has been proven superior to abrupt cessation
- No consensus on rate - in general most tapers occur over 8-12 weeks and are tailored to the patient
- Dose changes often must be smaller later in the taper to avoid withdrawal
- Flexibility in dosing schedule is necessary to combat withdrawal symptoms

Addiction. 2009 Jan;104(1):13-24. doi: 10.1111/j.1360-0443.2008.02364.x. Epub 2008 Oct

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Taper Timeline Examples

Recommendations for tapering benzodiazepines

Duration of use	Recommended taper length	Comments
<6 to 8 weeks	Taper may not be required	Depending on clinical judgment and patient stability/preference, consider implementing a taper, particularly if using a high-dose benzodiazepine or an agent with a short or intermediate half-life, such as alprazolam or triazolam
8 weeks to 6 months	Slowly over 2 to 3 weeks	Go slower during latter half of taper. Tapering will reduce, not eliminate, withdrawal symptoms. Patients should avoid alcohol and stimulants during benzodiazepine withdrawal
6 months to 1 year	Slowly over 4 to 8 weeks	
>1 year	Slowly over 2 to 4 months	

Bostwick JR, Casher MI, Yasugi S. Benzodiazepines: a versatile clinical tool. Current Psychiatry 2012;11(4):55-64.

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Benzodiazepine Withdrawal

- Can cause seizures and be fatal if done abruptly
- Symptoms appear after 1-2 days for shorter acting agents and up to 8 days for longer acting agents
- Roughly 15-30% of patients will develop withdrawal symptoms after only 4-6 weeks of use

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Withdrawal Symptoms

Table 3 Common withdrawal symptoms [120,125].

Psychological symptoms	
Anxiety, possible terror and panic attacks	Agitation and restlessness
Mood swings	Paranoia
Impaired concentration	Impaired memory
Indecision	Dysphoria
Nightmares	Insomnia
Bodily symptoms	
Perspiration	Increased urinary frequency
Hot and cold flushes	Headache
Muscular spasms, twitches cramps	Stiffness
Aches and pains	Fatigue and weakness
Numbness and tingling	Electric shock sensations
Blurred vision	Dizziness
Loss of appetite and weight loss	Nausea and vomiting
Tachycardia	Postural hypotension
Dry mouth	Chest pain
Flu like symptoms	Gastrointestinal problems
Perceptual symptoms	
Increased sensitivity to touch	Increased sensitivity to sound (hyperacusis)
Tinnitus	Objects moving
Metallic taste in mouth	Taste and smell disturbances
Increased sensitivity to light	Photophobia
Derealization (feelings of unreality)	Depersonalization

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Additional Notes

- CBT in addition to gradual dose reduction has some modest benefit
- Overall evidence for pharmacotherapy is quite weak
  - Last Cochrane review in 2006 - withdrawn in 2013 given that it is out of date
    - Had mild support for carbamazepine for benzodiazepine cessation but evidence is weak and other studies have not showed statistical significance
  - Buspar largely found to be ineffective
  - Some evidence for and against SSRI's - again small effect sizes
  - Some evidence for melatonin withdrawal symptoms in patients with sleep disturbance

Cochrane Database Syst Rev. 2006 Jul 19;(3):CD005194.

Addiction. 2009 Jan;104(1):13-24

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Take Home Points

- Talk to your patients on long-term benzodiazepines about continued use - don’t wait for “red flags”
- Spend ample time to engage the patient about potential downsides of benzodiazepine use
- Gradual dose reductions of a single benzodiazepine tailored to the patient are the most effective way to achieve benzodiazepine cessation

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