

**ECHO IDAHO**

Substance Use in Idaho

# Opioid and Benzodiazepine Tapering in Primary Care

3/12/26

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None of the planners or presenters for this educational activity have relevant financial relationship(s) to disclose with ineligible companies whose primary business is producing, marketing, selling, re-selling, or distributing healthcare products used by or on patients.



# Learning Objectives

- Review risks of chronic use of opioids and benzodiazepines
- Identify patients who may be appropriate for a taper
- Explore benefits and risks of tapering
- Review guidelines for tapering opioids and benzodiazepines
- Identify adjunctive management strategies when tapering – pharmacologic and non-pharmacologic

# Background

Many patients have been prescribed opioids or benzodiazepines for years or even decades – long-term use marketed as safe and beneficial



Image: NIH National Library of Medicine

**OxyContin<sup>®</sup> q12h**  
Controlled release oxycodone tablets

- Rapid onset of analgesia within 46 minutes**  
Comparable to immediate-release oxycodone<sup>1,2</sup>
- Full 12 hours of pain relief<sup>2,3</sup>**  
Provides uninterrupted sleep for an improved quality of life<sup>4</sup>
- No risk of acetaminophen or ASA toxicity<sup>5,6,7,8</sup>**  
No ceiling to analgesic efficacy<sup>9,10,11,12</sup>

**World Health Organization Pain Ladder (Adapted)<sup>13</sup>**

Increasing pain

- Step 1**  
• ASA  
• Acetaminophen  
• NSAIDs
- Step 2**  
• Oxycodone  
• Codeine
- Step 3**  
• Oxycodone  
• Morphine

**OxyContin<sup>®</sup> q12h** 10 mg 20 mg 40 mg 80 mg Small, colour-coded tablets

**One to Start and Stay With ...Easy to Dose, Easy to Titrate**

For prescribing information see page 432

For the relief of moderate to severe pain requiring the prolonged use of an opioid.

Side effects are similar to other opioid analgesics; the most frequently observed are constipation, nausea and somnolence.

Storage instructions may be present to reduce effects of drug theft. Please refer to prescribing information.

Warning: OxyContin should be prescribed and handled with the degree of caution appropriate to the use of a drug with abuse potential. Drug abuse is not a concern in patients with pain for whom the opioid is appropriately indicated.

\*Median time to onset of analgesia after single dose Day 1: 15 mg (30/1180) and OxyContin 20 mg (30/2018) use of tablets and 46 minutes, respectively. (Study 001) (N=100) in patients following administration of ground-up tablets. (N=100) (N=100)

<sup>1</sup>With adequate dosing, there is no intrinsic limit to the analgesic effect of oxycodone.

Product of  
Purdue Pharma Inc.  
Purdue Frederick  
Purdue Inc.

**You can't set her free. But you can help her feel less anxious.**

You know this woman. She's anxious, tense, irritable. She's fed this way for months. Bored by the seemingly insurmountable problems of raising a young family, and confined to the home most of the time, her symptoms reflect a sense of helplessness and isolation. Your reassurance and guidance may have helped some, but not enough. She's unconsciously changed her environment, of course. But it can't help. Her anxiety, tension, agitation and irritability, thus undermining her ability to cope with day-to-day problems. Eventually—no she regains confidence and composure—your doctor may be all she can rely on.

Indicated in anxiety, tension, agitation, irritability, and anxiety associated with depression.

May be used in a broad range of patients, generally with considerable dosage flexibility.

**Contraindications:** History of previous hypersensitivity to oxazepam. Oxazepam is not indicated in children.

**Precautions:** Hypersensitive reactions are rare, but use with caution where contraindications could develop from the use of these reactions, especially in the elderly. Use great care when the elderly are being treated with a certain increase in oxazepam concentration with a certain increase in oxazepam concentration. Use with caution in patients with a history of alcoholism, especially in patients with a history of alcoholism, because drug generally other prolonged excessive use may produce withdrawal symptoms, including tremor, rigidity, and hyperreflexia, and a history of alcoholism or alcohol abuse may increase the risk of withdrawal reactions in alcohol withdrawal. Safety for use in pregnancy has not been established. Not known in children, unless upon chronic therapy for 6 to 12 years old, not established.

**Side Effects:** Therapy with oxazepam may cause drowsiness, dizziness, and headache, but these are usually mild and transient. Drowsiness, dizziness, and headache may also occur in patients with a history of alcoholism, especially in patients with a history of alcoholism. Other side effects include: blurred vision, dry mouth, and constipation. In patients with a history of alcoholism, especially in patients with a history of alcoholism, the following reactions have been reported during therapy: flushed face, tachycardia, and hypotension. These side effects have been reported during therapy. Patients should avoid alcohol and other drugs which may interact with oxazepam. Avoid alcohol, especially in patients with a history of alcoholism, especially in patients with a history of alcoholism. Avoid alcohol, especially in patients with a history of alcoholism.

To help you relieve anxiety and tension

**Serax<sup>®</sup> (oxazepam)**

With Laboratories  
Philadelphia, Pa.

**IN A WORLD WHERE CERTAINTIES ARE FEW...**

**Ativan<sup>®</sup>**  
lorazepam

NET WEIGHT 100 mg (3.527 g)  
LORAZEPAM



# Twin Epidemics

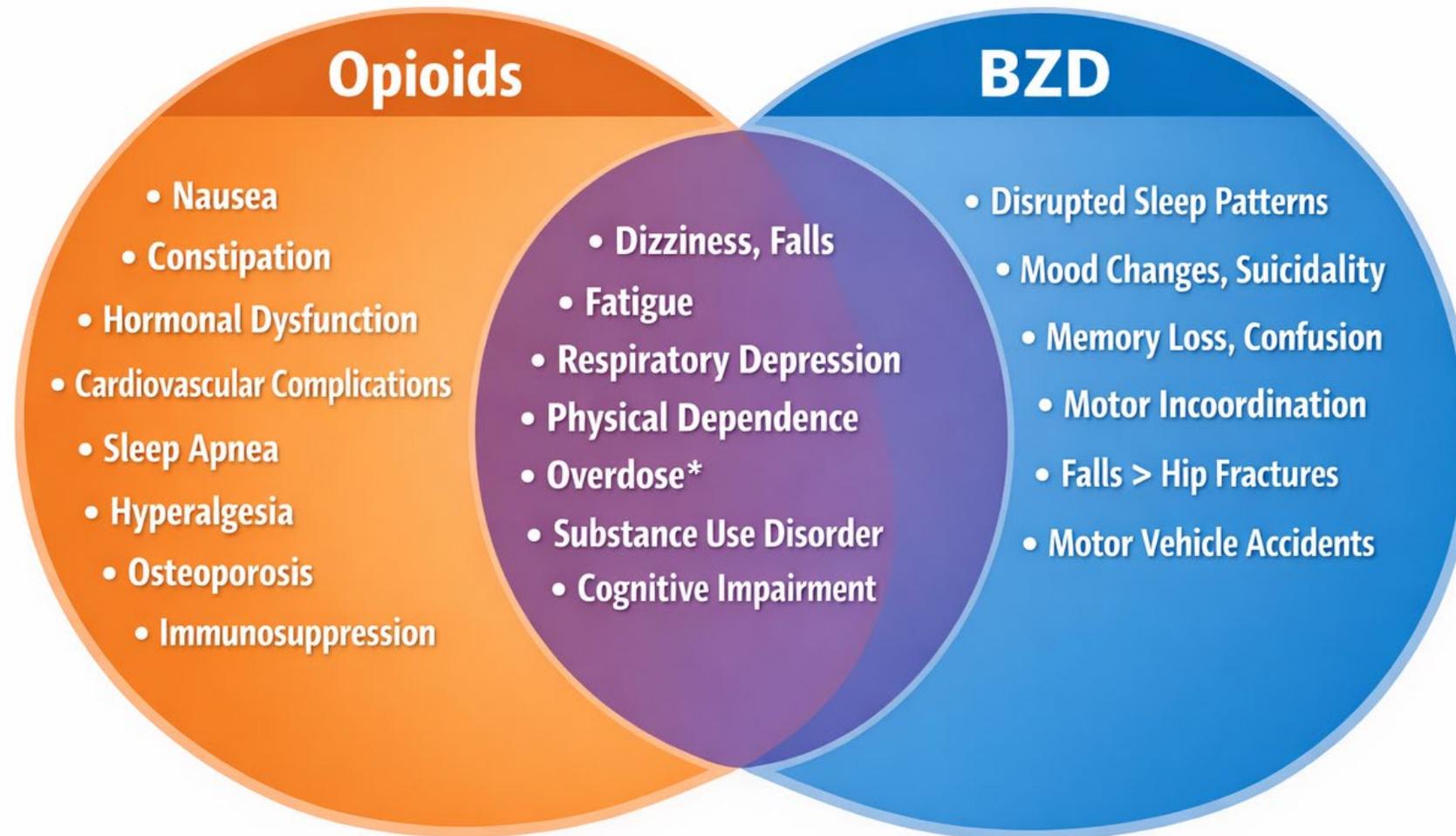
- Rx opioids quadrupled from 1999 to 2010
  - “Pain – the fifth vital sign”
- Rx BZD increased by 67% from 1996 to 2013, and quantity of BZD obtained more than tripled
  - Most commonly for anxiety, mood disorders, insomnia
- Concurrent increase in use disorders and overdose rates, among other issues



# Benzodiazepines (BZD)

- Controlled substance in the sedative-hypnotic, anxiolytic class
- GABA-A receptor agonist > CNS depressant
  - ↔ • Short-acting: midazolam, triazolam
  - ↔ • Intermediate acting: alprazolam, lorazepam, oxazepam, and temazepam
  - ↔ • Long-acting: diazepam, clonazepam, chlordiazepoxide
- Prescribed for: Panic disorder, insomnia, anxiety, seizures, alcohol withdrawal, amnesia, agitation
  - **Short-term use recommended (<4 weeks)** unless indication for long-term use (severe treatment-resistant GAD or bipolar, complex seizure disorders, spasticity, sleep disorders w/ abnormal movements, end-of-life care)

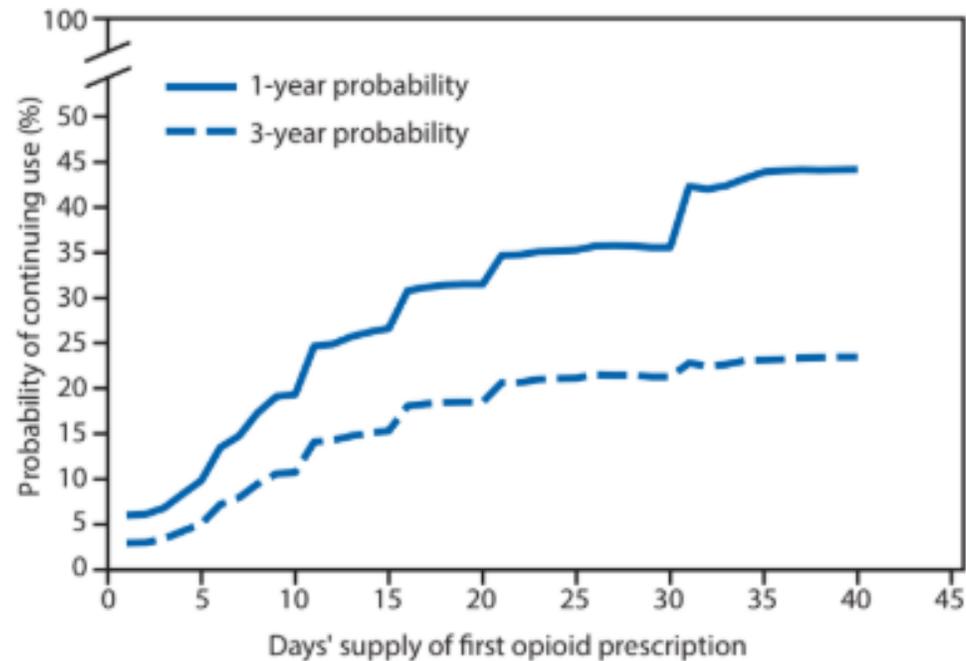
# Risks of chronic opioid and BZD use



*\* Overdose can be fatal*

# Risk for continued use, dependence, SUD

FIGURE 1. One- and 3-year probabilities of continued opioid use among opioid-naïve patients, by number of days' supply\* of the first opioid prescription — United States, 2006–2015



- **Opioids:** Risk of developing OUD 2-3x higher for 7-30 day Rx vs <7 days, and 5.5x higher for >90 MME
- **BZD:** 58%-100% of those prescribed BZDs for >1 mo become physically dependent
  - 1.5% will develop BZD use disorder

# When to consider a taper

- Taking opioids or benzodiazepines regularly
- When risks > benefits
  - High-risk comorbidities, i.e. pulmonary disease, OSA, kidney/liver disease, prolonged QTc, bipolar disorder, SI w/ hx of OD, PTSD (BZD)
  - Concurrent use of opioids + benzos, alcohol, other CNS depressants
  - Age >65
  - Overdose or risky behaviors, non-adherence to treatment plan
- Adverse effects > particularly falls, cognitive impairment
- Concern for SUD
  - If OUD, consider agonist therapy
- No reduction in pain (opioids) or improvement in function

# Patient-centered approach: **BRAVO** protocol

- **B**roaching the subject
  - Involve the patient, take time, acknowledge fear
- **R**isk-benefit calculation
  - Of medication and taper
- **A**ddiction assessment
  - 4 C's
- **V**elocity and **v**alidation
  - Go slow, adjust as needed, validate experiences
- **O**ther strategies
  - Adjunctive medications, behavioral interventions





# Addiction assessment

- 4 C's
  - Compulsive behavior of using substance
  - Continued use despite negative consequences
  - Loss of control
  - Cravings
- Concerning behaviors with medication
- *Cannot* use tolerance and withdrawal as criteria for SUD with prescribed medications – physical dependence expected
- If SUD suspected, consider concurrent behavioral interventions, agonist therapies if OUD (buprenorphine, methadone), addiction medicine consult



# Tapering opioids – Mr. O

- Mr. O is a 71 yo M with sleep apnea, depression, and chronic low back pain for which he has been prescribed Oxycodone for 7 years, currently taking 15mg 6x daily (135 MME). He reports worsening pain control (7-8/10 most days) and chronic fatigue
- Voices frustration with his life revolving around his medication, but fears going without it
- Also takes Tylenol, Lisinopril, Gabapentin
- Drinks 2-4 beers per week



# Tapering opioids – Mr. O

B

- Taper previously mentioned, appointment today for follow-up to discuss
  - Time set aside, reflect on experiences, acknowledge anxiety

R

- Risk/benefit calculation
  - Reported benefits of opioids: Small, temporary improvement in pain
  - Risks of opioids: Side effects, hyperalgesia, other CNS depressants, dependence, sleep apnea
  - Benefits of tapering: often improved pain control and other opioid-related problems, freedom from “living by the pill”, improved QOL
  - Risks of tapering: Worsening of pain, withdrawal symptoms, psychological distress including SI\*, risk of overdose\*
    - Most commonly due to tapering too quickly

# Tapering opioids and risk of adverse events

- CDC 2016 Guidelines > fear and rapid tapers > patient harm
- 2020 observational study: increased risk of death from **overdose** or **suicide** after stopping long-term opioid treatment
  - Longer on opioids before stopping, higher risk
  - Highest risk in the first 3 months after tapering
  - Did not examine taper protocols or context in which opioid stopped
- 2019 study found 7% risk reduction in opioid-related ED visits or hospitalizations with each additional week of tapering time prior to opioid discontinuation



# CDC 2022 Guidelines



Shared  
decision-making



Avoid abrupt  
discontinuation



Individualized plan,  
adjust as needed



Reduce risks with  
opioid use

- When opioids are needed, prescribe at lowest effective dose and duration
- Non-opioid therapies at least as effective as opioids for many common types of acute pain
- Guidelines intended for situations other than cancer-related pain, sickle cell disease, palliative care, and end-of-life care



# Tapering opioids – Mr. O

A

- Low concern for OUD > follows dosing schedule, denies cravings, few negative consequences, wants to stop

V

- You discuss options for pace of taper with Mr. O
- Patients on daily opioids >1 year, reduce by 5-10% of original dose every month or slower
  - If on daily opioids <1 year, could reduce by 10-20% q2-4 weeks
  - Faster if safety concern or patient preference
  - On long + short acting? Individualized approach
- Mr. O prefers to start tapering by ~10% every month



# Tapering opioids – Mr. O

- Other pain management strategies to discuss with our patient:
  - Non-opioid medications (NSAIDs, Tylenol, lidocaine patches)
  - Physical therapy
  - Massage, acupuncture, yoga
  - Psychotherapy, mindfulness, opposite action skills
  - Involve support of family/friends
- Mr. O agrees to schedule Tylenol and practice mindfulness

# Tapering opioids – Mr. O

- Starting Rx: Oxycodone 15mg 6x/day (135 MME)
  - Month 1: 15mg 5x/day + 7.5mg 1x/day (124 MME, ~8% reduction)
    - F/u: Having some increased pain, but overall doing well
  - Month 2: 15mg 5x/day (112 MME, ~8% reduction)
    - F/u: Reports increased pain, runny nose, and sweating
- You validate Mr. O's symptoms, provide education on withdrawal symptoms, discuss taper adjustments and other strategies
  - Keep same dose cadence as able (BID, TID), involve patient in which to wean first
  - Slow down/pause as needed, but don't go backwards
  - Set expectations > symptoms often worsen before they improve



# Tapering opioids

- Monitor for symptoms of opioid withdrawal – uncomfortable, but rarely dangerous
  - Increased pain\*, muscle aches, anxiety, nausea, runny nose, sweating, diarrhea, anxiety, insomnia, dysphoria, irritability, dilated pupils, goose bumps

TABLE 1

## Medications to Relieve Opioid Withdrawal

Medications	Symptoms
Antidepressants (e.g., trazodone)	Irritability, pain, sleep disturbance
Antidiarrheal agents	Diarrhea
Antiepileptics	Neuropathic pain
Clonidine	Autonomic symptoms, such as rhinorrhea, diarrhea, sweating, tachycardia, hypertension
Hydroxyzine	Insomnia, anxiety
Nonsteroidal anti-inflammatory drugs (e.g., ibuprofen)	Myalgia

**Note:** Avoid prescribing benzodiazepines for opioid withdrawal because they can also lead to dependence and addiction.



# Tapering opioids – Mr. O

- Mr. O wants to continue with taper
  - Month 1: 15mg 5x/day + 7.5mg 1x/day (124 MME, ~8% reduction)
    - F/u: Having some increased pain, but overall doing well
  - Month 2: 15mg 5x/day (112 MME, ~8% reduction)
    - F/u: Reports increased pain, runny nose, and sweating
  - Month 3: 15mg 4x/day + 10mg 1x/day (105 MME, ~5% reduction)
  - Add lidocaine patches, clonidine 0.1mg 2-3x daily PRN, and refer to PT
    - F/u: Doing better with smaller dose reduction and co-interventions
  - Month 4-6: Continue 5% reductions monthly
    - F/u: Going on a trip with his brother, asks to pause the taper for this month

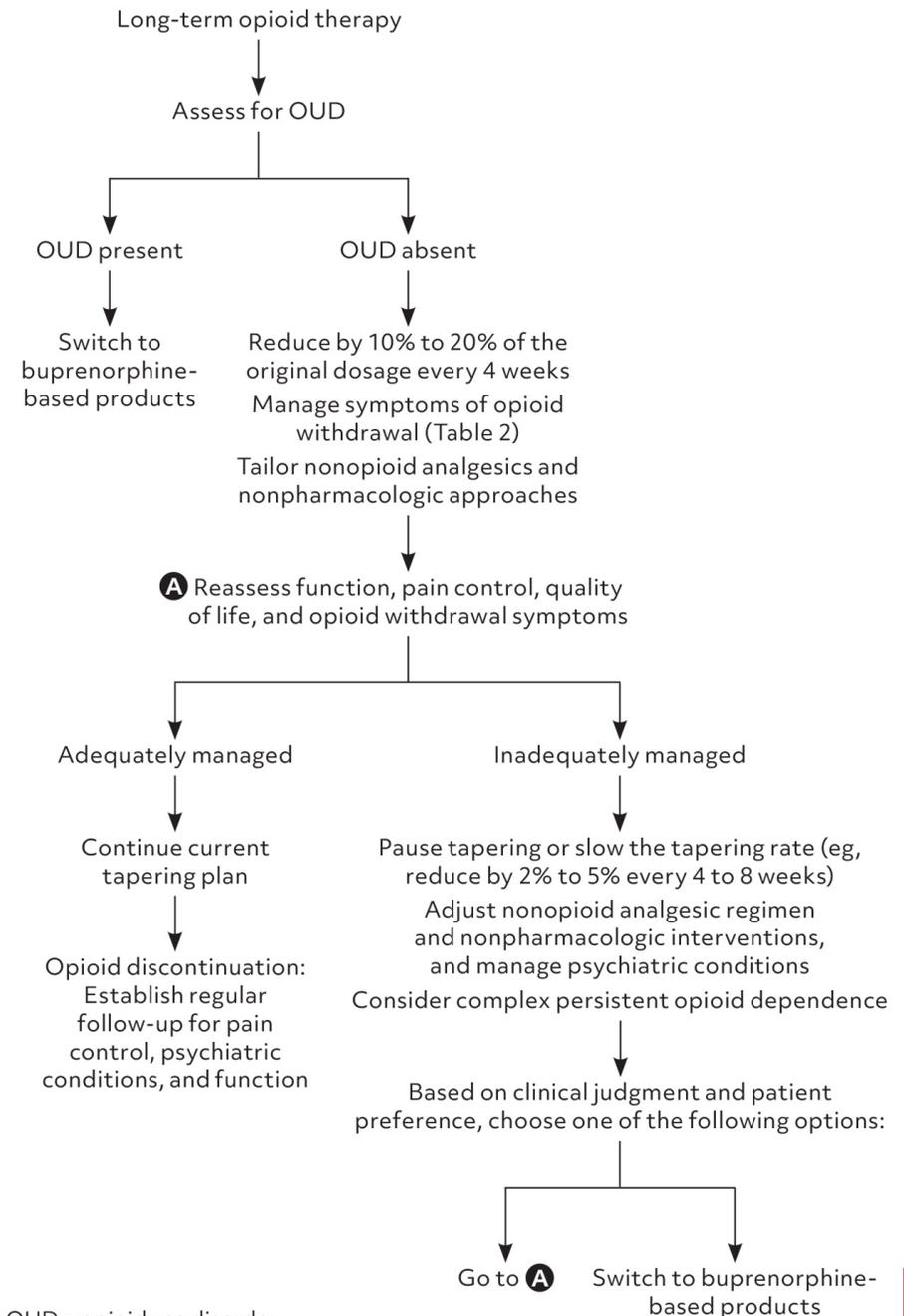


# Tapering opioids – Mr. O

- Month 7: Taper paused and you see Mr. O for f/u. He admits he supplemented his Oxycodone with some of his brother's Hydrocodone prescription and has been doing so for the past few months. He knows he shouldn't be doing this and has tried to stop, but pain has been severe. He's started to crave more medication, and has stopped attending PT
- Now concern for OUD > discuss treatment
  - Transition to buprenorphine (ask for help if needed!)
  - Continue multimodal pain control and behavioral interventions

# Resources for tapering opioids

- VA Pain Management Opioid Taper Decision Tool
- HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics



OUD = opioid use disorder.



# Tapering BZD – Ms. B

- Ms. B is a 42 yo F with PTSD who is transitioning to you as her PCP. She was initially prescribed alprazolam a little over 3 years ago for panic attacks after losing her job and getting a divorce. She takes 1mg alprazolam three times daily
- She notes feeling more depressed recently. She doesn't go out as much because loud, crowded environments are often triggering for her PTSD
- She's had trouble concentrating for years now, and wonders if she has ADHD



# Tapering BZD – Ms. B

B

- You gently express concern that this dose is fairly high and educate on risks with long-term use; express empathy

R

- Ms. B risk/benefit calculation
  - Reported benefits of BZD: Helps with sleep, anxiety
  - Risks of BZD: Trouble concentrating, worsening PTSD and depression, decreased efficacy of trauma-focused psychotherapy
  - Benefits of tapering: Improved cognition, possible improvements in anxiety and sleep, improved quality of life
  - Risks of tapering: Withdrawal, insomnia, destabilization of psychiatric conditions, SI\*, ?mortality\*



# Tapering BZD – Ms. B

- She is initially hesitant to taper, has experienced intolerable anxiety in the past when she’s run out, even experiences some between doses
  - You educate on withdrawal symptoms and reassure her that you will work with her to minimize these. She denies history of complicated withdrawal
- A**
- No current signs of BZD use disorder

**TABLE 4**

## **Benzodiazepine Withdrawal Symptoms**

Common rebound symptoms that occur within one to four days for short-acting benzodiazepines (e.g., alprazolam, lorazepam) and four to 10 days for long-acting benzodiazepines (e.g., diazepam, chlordiazepoxide): anxiety, insomnia, and restlessness

Subsequent common withdrawal symptoms (usually mild to moderate):

Agitation or irritability	Loss of appetite
Difficulty concentrating	Myalgias
Dizziness	Nausea
Headache	Sleep disturbances

Rare withdrawal symptoms (a concern with abrupt discontinuation at high dosages [more than 10 mg of diazepam equivalent daily]):

Diaphoresis	Psychosis
Palpitations	Seizure
Panic attacks	Tremors

*Information from references 26, 28, 33, and 34.*

# Tapering BZD – determining withdrawal risk

**Table 3. Risk for Clinically Significant BZD Withdrawal\***

<b>Duration of BZD Use</b>	<b>Frequency of BZD Use</b>	<b>Total Daily BZD Dose</b>	<b>Risk for Clinically Significant Withdrawal<sup>†</sup></b>
Any	≤3 days per week	Any	Rare
<1 month	≥4 days per week	Any	Lower risk, but possible
1–3 months	≥4 days per week	Low <sup>‡</sup>	Lower risk, but possible
1–3 months	≥4 days per week	Moderate <sup>§</sup> to high <sup>**</sup>	Yes, with greater risk with increasing dose and duration
≥3 months	≥4 days per week	Any	Yes, with greater risk with increasing dose and duration

- <sup>†</sup> Many factors influence the risk of physical dependence and BZD withdrawal syndrome, including but not limited to age, co-occurring physical and mental health conditions, other substance use, and prior history of withdrawal.
- <sup>\*\*</sup> Half-lives are unknown for some novel synthetic benzodiazepines available in the illicit market.
- <sup>‡</sup> A low daily dose is estimated as 10 mg diazepam equivalents or less (eg, ≤0.5mg clonazepam, ≤2 mg lorazepam, ≤1 mg alprazolam). See Appendix H for BZD dose equivalents.
- <sup>§</sup> A moderate daily dose is estimated as 10–15 mg diazepam equivalents (eg, 0.5–1.5 mg clonazepam, 2–3 mg lorazepam, 1–2 mg alprazolam). See Appendix H for BZD dose equivalents.
- <sup>\*\*</sup> A high daily dose is estimated as more than 15 mg diazepam equivalents (eg, >1.5 mg clonazepam, >3 mg lorazepam, >2 mg alprazolam). See Appendix H for BZD dose equivalents

# Tapering BZD – Ms. B



- Recognizing that tapering can worsen existing PTSD symptoms, you consult with Ms. B's psychiatrist and together with the patient develop a tapering strategy
- Decrease dose by 5-10% every 2-4 weeks
  - Should not exceed 25% every 2 weeks
  - Lower doses for less time may tolerate a more rapid taper (i.e. <3 months)
  - If short acting benzo, consider cross-taper to long-acting clonazepam or diazepam (beware in older adults and liver disease)
- You discuss with Ms. B the recommendation to first transition to clonazepam, and she agrees

**Table H.1. Benzodiazepine Approximate Dose Equivalents to 10 mg Oral Diazepam<sup>†</sup>**

<b>Benzodiazepine</b>	<b>ATC Therapeutic Class</b>	<b>VA/DoD SUD CPG (2021)<sup>1</sup></b>	<b>Ashton Manual (2002)<sup>2‡</sup></b>
Alprazolam	Anxiolytic	1	0.5
Chlordiazepoxide	Anxiolytic	25	25
Clonazepam	Antiepileptic	1	0.5
Clorazepate	Anxiolytic	15	15
Diazepam	Anxiolytic	10	10
Estazolam	Sedative–Hypnotic	1	1-2
Flurazepam	Sedative–Hypnotic	15	15-30
Lorazepam	Anxiolytic	2	1
Oxazepam	Anxiolytic	30	20
Quazepam	Sedative–Hypnotic	10	20
Temazepam	Sedative–Hypnotic	15	20
Triazolam	Sedative–Hypnotic	0.25	0.5

# Tapering BZD – Ms. B

- • Psychosocial interventions - Ms. B chooses to engage in counseling and downloads the CBT-I app to help with her insomnia
  - Also discuss healthy activity and food choices, foster social connections
- Adjunctive medication options
  - Set expectations! Nothing benzos like a benzo
  - Anxiety – SSRIs, SNRIs, buspirone, clonidine, hydroxyzine, gabapentin, propranolol
  - Insomnia – Trazodone, mirtazapine, melatonin, ramelteon, doxepin, doxylamine

# Tapering BZD – Ms. B

- Starting Rx: Alprazolam 1mg TID
  - Week 1: Continue alprazolam 1mg BID, start clonazepam 1mg daily
  - Week 2: Continue alprazolam 1mg daily, increase clonazepam to 1mg BID
    - F/u: Pt doing well, has not noticed much of a difference with the changes
  - Week 3: STOP alprazolam, increase clonazepam to 1mg TID
  - Week 4: Continue clonazepam 1mg TID
    - F/u: Doing well, feeling very anxious about decreasing the dose but agrees to try
  - Week 5-6: 1mg BID + 0.75mg daily (8% reduction)
    - F/u: Increased anxiety, difficulty sleeping
    - Has f/u with her psychiatrist who starts sertraline and hydroxyzine. Increases her frequency of counseling
  - Week 7-10: Taper paused, continue 1mg BID + 0.75mg daily



# Tapering BZD – Ms. B

- Patient is gradually tapered off clonazepam, down 0.25mg every 2-4 weeks with pauses as needed until she is down to 0.5mg TID (takes about 8 months)
- Taper is slowed to decrease by 0.125mg every 4-6 weeks
- You follow up frequently, especially after a dose decrease, to monitor symptoms
- Ms. B has made several behavioral changes to manage her anxiety and improve sleep. PTSD symptoms are improving and she is going out more with friends
- After nearly 2 years, able to stop clonazepam completely! Stable on sertraline and hydroxyzine prn, regular therapy

# Tapering BZD – additional considerations

- Could consider blind taper with patient's consent
- Consider inpatient management if...
  - History of complicated withdrawal (seizures, DTs) from BZD or alcohol
  - Previous unsuccessful attempts in tapering
  - Significant harm related to continued use of BZD, rapid taper indicated
  - History of near-fatal overdose
  - Active psychiatric instability
  - Lack of psychosocial support
  - Pregnancy



# Pregnancy & Lactation

- Important to weigh risks and benefits of the medications *and* of a taper as they apply to the maternal/fetal dyad
  - Both opioids and BZD carry risks of fetal harm
  - Withdrawal, untreated pain, anxiety, and sleep disorders also pose a risk to the fetus
- Esp if concern for OUD, supervised opioid withdrawal NOT recommended for most women
  - Consideration of buprenorphine or methadone IS recommended
- If decision made to taper, do so VERY slowly
- Coordinate with OB/pediatrician
- Consider higher level of care and close follow-up
- Breastfeeding encouraged



# Key Points

- Opioids and benzodiazepines have many risks with chronic use
- Recommend gradual and flexible approach to tapering – often takes months to years and everyone is different
- Utilize psychosocial interventions and adjunctive medications
- Regularly follow-up and re-visit goals; if cannot taper fully off, lower still better

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