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Case Studies and Q&A: Benzodiazepines and Opioid Maintenance Treatment

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Case #1: 50 year old female

- "My anxiety and panic have been out of control and I need to get back on my meds."
- History of polysubstance use disorder, on buprenorphine maintenance treatment
- Benzodiazepines have been prescribed for the past 30 years
  - Severe anxiety and panic attacks/agoraphobia: dizziness, flushing, SOB, fear of leaving house
  - Benzodiazepines helpful in reducing sx's – "the only thing that works"
- Was prescribed clonazepam 2 mg TID for about 10 years, then new provider tapered her to 1 mg TID about 8 years ago

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Case, cont.

- Has been prescribed both alprazolam and clonazepam in the past with doses up to clonazepam 1 mg TID
  - Taper took 2 years – patient was against the taper, had increase in anxiety and panic, several lapses to opioids and cocaine, taking benzodiazepines off street
  - Eventually, with help from therapist, stopped using drugs and street benzodiazepines
- Presents now after last psychiatrist left
  - New psychiatrist attempted further taper with aim of discontinuation
  - Pt reports constant crying, “I am terrified”, intense drug cravings

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Substance use history

- Stimulants – started using cocaine at age 12
  - Started using crack cocaine at age 14
  - Off and on for 30 years – quit completely 5 years ago
  - Was drug of choice
- Opioids – was prescribed Percocet, then Dilaudid after a fall that broke her jaw from alcohol intoxication at age 25
  - Was prescribed Dilaudid for 1 year and discontinued
  - Then started to use heroin IN, then progressed to IVDU
  - Started buprenorphine after a year and half of IV heroin use, has been on buprenorphine for 15 years
  - Last opioid use was 8 years ago

Substance use history, cont.

- Benzodiazepines – was given diazepam in her food by her mother's boyfriend at age 11 so that he could abuse her
  - Also was given alprazolam by mother as a teen
  - Started getting alprazolam prescribed at age 18 – was taking more than prescribed right away – "I was partying"
  - Was transitioned to clonazepam 2 mg TID at age 26 – "I took it responsibly"
- Alcohol – started drinking heavily at age 16 (6-pack of beer daily), accelerated to fifth of liquor daily at age 22, drinking off and on until she stopped completely drinking at age 35
  - Hx of withdrawal seizures/delirium tremens
  - Multiple inpatient detoxes
- Marijuana – uses occasionally, 2-3 times a month

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Mental health history

- Long history of childhood physical and sexual abuse – mother was 18 years old when she had patient, was addicted to heroin, would leave patient with different people (usually family but sometimes people she didn't know)
- "I was afraid a lot as a kid" – had a lot of generalized and social anxiety as a child
  - Panic attacks started at age 11
  - Pulled her hair as a child, started cutting at age 11 – self-harm calmed her
  - Benzodiazepines help with these sx's
- Long history of mood episodes
  - Clear depressive episodes starting as a child
  - Had manic episodes – increased energy, decreased need for sleep, very irritable
- Attempted suicide about 5 times, first was at age 8, most recent was over 20 year ago
- Has had 3 psychiatric hospitalizations – last was about 15 years ago

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Mental health history, cont.

- Medications
  - Aripiprazole 10 mg daily
  - Citalopram 40 mg daily
  - Bupropion SR 150 mg BID
  - Gabapentin 800 mg BID
  - Clonidine 0.2 mg qhs
  - Buprenorphine/naloxone 16/4 mg daily
- Engaged in psychotherapy for 10 years
  - Has been meeting several times a month with outside therapist for 5 years

Past medical history

- No significant past medical history

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Social history

- Living in own apartment with boyfriend of 9 years, daughter, and granddaughter
- One daughter – 30 years old, ran away at age 15 but moved back 4 years ago with a baby after patient showed she was not using drugs anymore
- Has GED, went to college for 1 year
- Has had several jobs – retail, restaurant, office work
  - Stopped working about 20 years ago
- Then started receiving disability for mental health problems

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Exam

- Appears stated age
- Crying, upset
- Anxious
- Tangential
- Gross cognition intact

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Discussion

- How should this patient be treated?

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Weighing risks and benefits

- <u>POTENTIAL RISKS:</u>
- Overdose death
  - Increased risk of mortality in opioid maintenance treatment
- Addiction to benzodiazepine

- <u>POTENTIAL BENEFITS:</u>
- Treats anxiety/distress, may prevent drug cravings
- Improves retention in opioid maintenance treatment

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Does this patient have benzodiazepine use disorder?

- DSM-5 diagnostic criteria
  - Problematic pattern of use leading to clinically significant impairment or distress manifested by at least 2 of the following in a 12-month period:
    - Taken in larger amounts or over longer period than intended
    - Persistent desire or unsuccessful efforts to cut down or control use
    - Great deal of time spent on obtaining substance
    - Craving
    - Recurrent use resulting in failure to fulfill major role obligations
    - Continued use despite recurrent social or interpersonal problems
    - Important social, occupational, recreational activities given up because of use
    - Recurrent use in situations in which it is physically hazardous
    - Continued use despite knowledge of having a recurrent problem caused by use
    - Tolerance (not considered when prescribed)
    - Withdrawal (not considered when prescribed)

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Benzodiazepine maintenance

- Tel Aviv methadone clinic
  - 66 patients with benzodiazepine use disorder
  - Offered clonazepam detoxification or clonazepam maintenance (not randomized)
  - Detox group – 8 week taper, maintenance group – started 2 mg TID and gradually tapered to individual maintenance dose
  - Medication was taken while observed (weekdays only)
  - Primary outcome – "failure" defined by evidence of excessive BZD use by patient self-report or clinician observation
  - At 12 months, 86% of detox group had "failure", 34.6% of maintenance group had failure

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Weizman et al., *Aust. N. Z. J. Psychiatry*, 2003

Benzodiazepine maintenance, cont.

- London methadone clinic
  - 278 patients: 80 never received benzodiazepine, 71 briefly/occasionally received benzodiazepine, 127 received benzodiazepine maintenance
  - Benzodiazepine maintenance: up to 30 mg/day diazepam or 8 mg/day clonazepam, observed daily dosing until illicit drug use stopped per urine drug screen, then take homes given
  - Maintenance group had higher incidence of alcohol use disorder, injection drug use, and psychiatric disorders
  - Maintenance group had better treatment retention compared to other groups and lower in-treatment mortality compared to never received benzodiazepine group
  - Mortality rate increased for all groups for those who dropped out of methadone
    - Mortality was much higher among those in the maintenance group after leaving treatment

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Bakker and Streel, *J Psychopharmacol*, 2017

Clinical course

- Dose of clonazepam was increased to 1 mg TID
- Patient stabilized
- Remains in treatment after a year post-dose change
- No evidence of illicit drug use

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Case #2: 33 year old male

- "Benzos are my drug of choice. I love benzos."
  - Uses to lessen chronic agitation, restlessness
  - Benzodiazepines lead him to lose things
  - Twice fired from work due to intoxication
- Left early from inpatient detox for benzodiazepines 1 month ago
  - Left after 5 days (of 7 day taper protocol) citing issues with staff
- Immediately restarted using benzos
  - Has been using since college
  - Uses "as much as I can get" - sometimes 5-10mg of alprazolam or clonazepam per day
  - Recently using ~4mg of alprazolam or clonazepam per day
  - Longest period of abstinence "a few months" while in jail
  - Abstains only in controlled environments
  - No seizures or hospitalizations
  - 1 blackout – considered an overdose

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Substance use history

- Opioids - started using prescription opioids in college, “I partied a lot”
  - Dropped out after 5 semesters
  - Age 22, began using IN heroin, slowly progressed to IVDU
  - Prior MOUD history: buprenorphine 6-7 years total, MMTP (in 2010) on max dose 105 mg daily
  - Last use of heroin/fentanyl was 2 months prior to presentation
  - Currently on maintenance buprenorphine (8-2mg BID)
- Stimulants – began using cocaine in college.
  - Used crack twice within the last month - "I don't use often”
  - Occasional use of street Adderall with last use 4 weeks ago
- Alcohol - denies
- Marijuana – daily use
- Tobacco – 1ppd

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Psychiatric history

- Endorsed sx's of generalized anxiety disorder
  - Denies panic attacks
  - Denies trauma history
  - Denies social anxiety
- Reports past diagnosis of ADHD and has been treated with stimulants in the past
- Has had sx's of depressive disorder in the past but not currently
- Denies manic sx's
- Denies hx of suicide attempts or psychiatric hospitalizations

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Past medical history/medications

- No significant past medical history
- No current medications

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Social history

- HS grad, dropped out after 2.5 years, first year did well but did worse as he started using more drugs
- Jobs in food delivery, sales, factory work
- Most recently worked at an auto parts store, but was fired due to intoxication
  - Subsequently lost housing and became homeless
  - Sleeping in mother's backyard (not allowed in house)
- Recently broke up with GF
  - Has newborn baby
  - Last saw 1 month prior, being cared for by ex-GF

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Initial exam

- Easily distracted, cooperative
- Slurred speech
- Tangential
- Forgets things quickly
- Requires frequent redirection

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Assessment

- Severe benzo use disorder (primary use disorder)
  - No history of complicated withdrawal
  - Has overdosed in the past
  - Currently intoxicated on benzodiazepines
  - Unable to complete recent inpatient detox program
- Moderate OUD in early remission
  - On buprenorphine
- Seeking outpatient withdrawal management benzodiazepines

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Discussion

- Is this patient a candidate for outpatient benzodiazepine detoxification?
- How should he be treated?

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Approaches to benzodiazepine withdrawal management

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Taper rate

- Little data on best taper rate
- Gradual reduction
  - 25-50% every 1-2 weeks over 6-10 weeks
  - Taper rate can be modified based on patient's ability to tolerate withdrawal sx's
- Withdrawal sx's during taper
  - Typically worse with longer duration of benzodiazepine use
  - Subjective sx's can worsen as dose nears zero
    - Can slow taper towards end of taper

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Choice of benzodiazepine

- No clinical trials comparing benzodiazepines for taper
- If patient is largely taking short-acting benzodiazepines, can switch to long-acting
- Short-acting benzodiazepines associated with:
  - Higher dropout rates in benzodiazepine discontinuation trials
  - Worse rebound anxiety
  - More severe withdrawal sx's

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Frequency of monitoring

- Weekly visits are preferred over longer time between visits
- Daily monitoring is ideal but often not feasible
- Taper rate should correspond to withdrawal sx's

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Adjunctive therapies

- Multiple meta-analyses of benzodiazepine discontinuation trials
  - Little evidence of effectiveness for adjunctive medications
  - Number of trials is limited and study populations are heterogenous
- Psychosocial interventions
  - CBT is best-studied and effective
  - Other effective options: relaxation therapy, psychoeducation

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Agreed to outpatient benzodiazepine taper

- We agreed to almost daily clinic attendance (M-Sa)
- Daily benzodiazepine prescription
- Bi-weekly urine drug screens
- Agreed to abstinence from opioids, street benzodiazepines, alcohol, or other sedative-hypnotics
- He acknowledged that he would continue cannabis use
- Buprenorphine-naloxone 8-2mg BID prescribed

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Proposed taper

- Currently taking approximately 50 mg of diazepam daily
- 5-week taper with diazepam proposed
  - 40 mg daily for 1 week
  - 30 mg daily for 1 week
  - 20 mg daily for 1 week
  - 10 mg daily for 1 week
  - 5 mg daily for 1 week

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Clinical course

- Adherence to taper was good overall
- Used illicit clonazepam twice, cocaine twice, and Adderall twice
- Was homeless, staying in shelter or street throughout
- Taper was lengthened by approximately a week at various time points due to withdrawal sx's
- Completed taper on day 40

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Follow-up

- 2 years post-detox, patient remains abstinent from benzodiazepines and other drugs
- Anxiety is adequately treated with SSRI
- Receiving stimulant for ADHD
- Employed, back together with GF and helping to raise child

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Questions?

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