Management of Other Substance Use Disorders:
Benzodiazepines
Cocaine and Other Stimulants
Cannabis

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Edward Nunes Disclosures

• Dr. Nunes has no relevant financial relationship(s) with ACCME defined commercial interests to disclose.

The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that is their responsibility to disclose this information.
Target Audience

• The overarching goal of PCSS-MAT is to make available the most effective medication-assisted treatments to serve patients in a variety of settings, including primary care, psychiatric care, and pain management settings.
Educational Objectives

• At the conclusion of this activity participants should be able to:
  ▪ Diagnose and formulate a treatment plan for misuse and use disorders of the following substances:
    – Benzodiazepines
    – Cocaine and other stimulants
    – Cannabis
The presentation will provide an overview of the evaluation and treatment of each of the following substance problems, particularly among patients with opioid use disorder

- Benzodiazepine use disorder
- Cocaine, methamphetamine, prescription stimulants
- Cannabis use disorder

Note: Alcohol use disorder is covered in detail in another SUD core curriculum presentation, but will be mentioned here to highlight common evaluation and treatment strategies across substance problems.
Co-morbidity of Opioid Use Disorder and Other Substance Use Disorders

• The presence of one substance use disorder increases the likelihood of other concurrent substance use and use disorders

• Thus, among individuals with opioid use disorder, other substance use and use disorders are common
  ▪ Especially benzodiazepines
  ▪ Also cocaine, and cannabis.

• When one substance is present, look for others
General Overview of Diagnosis and Treatment

- DSM-5 Criteria for Substance Use Disorder

- General principles of intervention
  - Screening
  - Brief Intervention
  - Treatment planning
    - Pharmacological interventions
    - Behavioral interventions
    - Levels of care
DSM-5 Substance Use Disorder: 11 Criteria or Symptoms

(American Psychiatric Association 2013)

- Loss of Control
  - 1. Uses more than intended
  - 2. Tries and fails to cut down or control use
  - 3. Spends a lot time using, recovering
  - 4. Craving

- Impairment due to substance use
  - 5. Failure to meet obligations
  - 6. Social or interpersonal problems
  - 7. Gives up important activities (social, work, etc.)
  - 8. Uses when physically hazardous
  - 9. Physical or psychological problems due to substance

- Tolerance/Withdrawal
  - 10. Tolerance: increased use, diminished effect over time
  - 11. Withdrawal: characteristic withdrawal symptoms or uses substance to avoid withdrawal
DSM-5 Substance Use Disorder:  
(American Psychiatric Association 2013)

• 2 or more symptoms/criteria yields a diagnosis of Substance Use Disorder

• Review DSM-5 for symptoms of intoxication and withdrawal of the various substances

• Severity
  ▪ **Mild**: 2 or 3 symptoms/criteria
  ▪ **Moderate**: 4 or 5 symptoms/criteria
  ▪ **Severe**: 6 or more symptoms/criteria
Screening: Asking about Substance Use

- **Ask about substance use**
  - Try to ascertain quantity, frequency, DSM-5 criteria (loss of control, impairment, tolerance/withdrawal)

- **Use Principles of Motivational Interviewing** *(Miller, Rollnick 2002)*
  - *Use the MI Spirit*
    - Collaborative
    - Evocative
    - Support the autonomy of the patient
  - Encourage patient to open up about substance use
  - Set goals around substance use and reducing/stopping substance use
Asking about Substance Use

Spirit of Motivational Interviewing (Miller, Rollnick 2002)

- **Collaborative**
  - Step out of the authoritative doctor role
  - Don’t tell the patient what to do (at least not right away)
  - Assume a more consultative stance

- **Evocative**
  - Draw out the patient’s point of view
    - Express curiosity
    - How the patient experiences substance use
    - What the patient values in life

- **Autonomy** (support the autonomy of the patient)
  - Put the patient in charge of his/her treatment plan
  - Encourage the patient to set goals
  - Support patient’s self-efficacy to change
Screening: Asking about Substance Use

- Use tactics of Motivational Interviewing *(Miller, Rollnick 2002)*
  - Non-judgmental
  - Open questions
  - Listen and reflect
  - Try to get the patient talking about substance use and how it impacts his/her life
  - Listen for clues to DSM-5 criteria – indications of loss of control, impairment, tolerance/withdrawal
  - Try to get patient to set goals around substance use

- Screening instruments such as AUDIT or urine toxicology (office based dipsticks are handy) can be administered in advance and flag potential problem areas for inquiry
Treatment Planning

• Levels of care

• Behavioral Treatments

• Pharmacological Treatments

• Look for co-occurring psychiatric disorders
  ▪ Mood disorders (particularly depressive disorders), anxiety disorders, PTSD, ADHD
Levels of Care

• Levels corresponding to varying levels of severity
  ▪ Manage within primary care or other office-based setting (e.g. psychiatric outpatient setting)
  ▪ Outpatient, Intensive outpatient
  ▪ Residential, Medically supervised inpatient

• ASAM Criteria
  ▪ Algorithm for assigning an appropriate level of care, based on 6 dimensions of severity
    1. Acute intoxication or withdrawal potential
    2. Biomedical conditions/complications
    3. Emotional, behavioral, cognitive conditions
    4. Readiness to change
    5. Potential for relapse, continued use
    6. Recovery/living environment
Behavioral Treatments

- Medication Management (e.g. includes practical advice from provider)
- Motivational Interviewing
- 12-Step Facilitation
  - Encourages and guides participation in Alcoholics Anonymous, Narcotics Anonymous, etc.
- Cognitive Behavioral for Relapse Prevention
- Contingency Management
  - Rewards for a target behavior such as drug negative urine
- Network Therapy
  - Involving significant others to support the treatment plan
- Couples and family therapy
Pharmacological Treatments

• Medications for detoxification
  ▪ E.g. Anticonvulsants or benzodiazepine taper for alcohol or benzodiazepine/sedative use disorder

• Alcohol use disorder
  ▪ Naltrexone and extended-release injection naltrexone (Vivitrol®)
  ▪ Disulfiram
  ▪ Acamprosate

• Opioid use disorder
  ▪ Methadone
  ▪ Buprenorphine
  ▪ Extended-release injection naltrexone (Vivitrol®)
• Co-occurring psychiatric disorders are common among patients with opioid use and other substance use disorders, and have specific behavioral or pharmacological treatment indications
  ▪ Mood disorders such as Major Depression
  ▪ Trauma and Post-traumatic Stress Disorder (PTSD)
  ▪ Other anxiety disorders: social anxiety, agoraphobia
  ▪ Attention Deficit Hyperactivity Disorder (ADHD)

• When a patient is using substances this may signal the presence of psychiatric co-morbidity
  ▪ “Where there’s smoke, there’s fire”
A 35 year old man with opioid use disorder (prescription opioids which progressed to heroin) has initiated office-based treatment with buprenorphine, advanced to 16mg per day. He reports ceasing opioid use, and his urine toxicologies are consistently negative for all opioids but positive for buprenorphine.

However, his urines are intermittently positive for benzodiazepines, and he describes drinking alcohol two days per week, sometimes to intoxication.

What is the most appropriate next step in his treatment?

A. Increase buprenorphine to 24mg
B. Refer to methadone maintenance
C. Admit to inpatient detoxification
D. Start an outpatient long-acting benzodiazepine taper
E. Obtain more history
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

- **Answer:** E - Obtain more history

- **Explanation:**
  - There is no evidence that increasing buprenorphine dose or switching to methadone maintenance would be effective in addressing sedative or alcohol use, especially since the patient has stopped using illicit opioids, suggesting an adequate dose of buprenorphine has been reached.
  - More history is needed to determine the appropriate level of care and treatment plan.
    - Inpatient detoxification or outpatient benzodiazepine taper might or might not be appropriate, depending on the severity of other substance use and other relevant dimensions
    - Psychiatric comorbidity (e.g. anxiety or mood disorder) might be present and need specific treatment, such as with an antidepressant medication
Alcohol use disorder is the most common substance use disorder, along with nicotine.

Population prevalence (NESARC) of alcohol use disorder:
- 30% lifetime
- 8.5% current (past 12 months)

Prevalence of alcohol use or use disorder among those with opioid use disorder:
- Approximately 30%
Alcohol and Alcohol Use Disorder: Main Points

• Alcohol is a sedative on a broad continuum with benzodiazepines and other tranquilizers
• Alcohol use and use disorder commonly co-occur with other substance use and use disorders
• Alcohol use disorder extensively studied
  ▪ Risk factors: genetics, stress
  ▪ Behavioral Treatments: Motivational Interviewing; 12-Step Facilitation; Cognitive Behavioral approaches
• Alcohol will synergize with other sedatives (e.g. benzodiazepines) or opioids to produce increased intoxication and risk of respiratory depression, overdose and death
• Screen for alcohol use and use disorders and treat when appropriate, including consideration of medications
  ▪ FDA-approved: disulfiram, Acamprosate, naltrexone
  ▪ Others with evidence from clinical trials: Gabapentin, carbamazepine, topiramate, varenicline, antidepressants (if co-occurring depression), buspirone if co-occurring anxiety
Benzodiazepines and Other Sedatives

- Benzodiazepines are therapeutically useful medications, highly effective for acute treatment of anxiety and insomnia
- Act at GABA receptors, inhibitory effect on neurons
- Have abuse potential in vulnerable individuals
- Prevalence of benzodiazepine use disorder is low in the general population, but common among patients with opioid use disorder
  - Potentially dangerous because opioids and benzodiazepines synergize to increase intoxication, and risk of respiratory depression and overdose.
  - Overdose deaths often involve combination of opioids and benzodiazepines
Benzodiazepines among Patients on Methadone Maintenance (MMT)

• Prevalence 20% to 60% benzodiazepine use among patients on MMT

• Benzodiazepine use on MMT associated with
  ▪ Other drug use
  ▪ High risk behavior
  ▪ Depression, anxiety disorders
  ▪ Higher mortality
Why the Frequent Comorbidity of Benzodiazepine and Opioid Use Disorders?

- Benzodiazepines used to self-treat anxiety and insomnia associated with opioid withdrawal
- Co-occurring mood and anxiety disorders
  - PTSD, depression often involve anxiety and insomnia that respond to benzodiazepines
  - Self-treatment evolves into use disorder
  - Benzodiazepines prescribed then evolve into use disorder
  - Important to look for co-occurring disorders and institute more effective treatments (e.g. CBT, antidepressant medications)
Benzodiazepines: Spectrum of Use, Misuse, and Use Disorder

- Legitimate prescribed use
  - Low dose, no escalation of dose over time
  - Stable pattern, taken as prescribed
  - Good therapeutic response
- Even if use appears legitimate, monitor closely and seek non-addictive alternatives (e.g. an antidepressant medication for depression or anxiety disorder; a sedating antidepressant (e.g. trazodone) for sleep)
- Misuse (risky use)
  - Not as prescribed, or illicitly procured
  - Higher doses, taking more than prescribed
- Use Disorder
Red Flags for Misuse or Diversion

- Symptoms of intoxication or withdrawal
- Demands for a particular, usually fast acting, medication (alprazolam)
  - “Extended-release doesn’t work for me”
  - “Only Xanax works for me”
- Repeated lost prescriptions
- Discordant pill count
- Excessive preoccupation with securing medication supply
- Multiple prescribers
Benzodiazepine Abuse Potential Depends in Part on Pharmacokinetics

- Rapid absorption = more rapid onset, more “high”
  - Alprazolam (Xanax™) and diazepam (Valium™) are rapidly absorbed orally
  - Clonazepam (Klonopin™), lorazepam (Ativan™), chlordiazepoxide (Librium™), oxazepam (Serax™) more slowly absorbed
- Rapid absorption also = more rapid onset of anxiolysis, which can be beneficial therapeutically
- Shorter half-life = greater risk of withdrawal effects
  - Benzodiazepine withdrawal resembles alcohol withdrawal, including risk of seizures and delirium
  - Withdrawal also drives drug seeking and use disorder
- Alprazolam (rapid absorption, short half life) is the most popular illicit or abused benzodiazepine
Benzodiazepine-like Sleep Medications

• “Z drugs”: Zolpidem (Ambien®), etc.
• Supposedly less abuse potential due to subunit selectivity at GABA receptors
• But, in practice more similar to benzodiazepines than different
  ▪ Rapid absorption, short half-life
  ▪ Rebound insomnia and sleep-walking are common,
  ▪ Withdrawal effects
• Use with caution in patients with opioid use disorder
• Also implicated in overdose deaths
Alternatives to Benzodiazepines for Sleep

- Sleep hygiene and CBT for sleep
- Treat the underlying causes of sleep disturbance
  - Mood or anxiety disorders
  - Opioid withdrawal, stimulant intoxication, other substance effects
- Sedating antidepressants
  - E.g. trazodone (but beware of priapism in men), mirtazapine (Remeron®), tricyclic antidepressants at low doses (e.g. doxepin, amitriptyline) or antihistamines
- Melatonin and melatonin agonists (Ramelteon™)
- Orexin antagonist (Suvorexant™)
Evaluation for Benzodiazepine Use Disorder

- Quantity, pattern and type (high abuse potential, e.g. alprazolam)
- Evaluate DSM-5 criteria
  - Patients may tend to deny excessive use or impairment
  - Useful to obtain collateral information from reliable significant others
    - Is the patient observed to be intoxicated, sedated, uncoordinated?
- Check prescription monitoring program for multiple prescribers
Evaluation of Benzodiazepine Use: Urine Toxicology

- Standard immunoassays are not sensitive to all benzodiazepines
  - Standard assays test for nordiazepam and oxazepam, main metabolites of many benzodiazepines including older medications (diazepam, chlordiazepoxide)
  
- Some newer, higher potency benzodiazepines (e.g. alprazolam, clonazepam) have different structures and metabolic end products to which the assays less sensitive
  - May be question of lower concentration
  - Maybe related to structural differences
  - Request lower threshold for detection, or more sensitive assay
Benzodiazepine Use Disorder: Treatment

- Evidence on treatment is limited
- Advise to quit or cut down, using Motivational Interviewing
- CBT may be helpful (Morin, 2004; Otto, 2010)
- Taper or “detoxification” (see next slide)
- Evaluate mood or anxiety disorders and substitute alternative medications (SSRI/SNRI, buspirone, carbamazepine, valproate, gabapentin, pregabalin, quetiapine)
- Level of care
  - Consider inpatient treatment if high dose benzo use, severe use disorder, substantial intoxication, overdose risk (especially in conjunction with opioids)
Benzodiazepine Discontinuation: Substitution and Taper Strategy

- Substitute a benzodiazepine with lower abuse potential and long half life (e.g. clonazepam or chlordiazepoxide) or phenobarbital
- Choose equivalent starting dose (see Table on next slide)
- Taper dose slowly over period of weeks to months
- Oxazepam is a good choice if there is substantial liver impairment
- Anticonvulsants (e.g. carbamazepine, pregabalin) may be useful as adjuncts to benzodiazepine taper
# Benzodiazepine Equivalency Table
*(adapted from Medscape 2018)*

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax™)</td>
<td>0.5 - 1</td>
</tr>
<tr>
<td>Chlordiazepoxide (Librium™)</td>
<td>10-25</td>
</tr>
<tr>
<td>Clonazepam (Klonopin™)</td>
<td>0.25-0.5</td>
</tr>
<tr>
<td>Diazepam (Valium™)</td>
<td>5-10</td>
</tr>
<tr>
<td>Lorazepam (Ativan™)</td>
<td>1-2</td>
</tr>
<tr>
<td>Oxazepam (Serax™)</td>
<td>15-30</td>
</tr>
</tbody>
</table>

• 35 year old man with opioid use disorder, on buprenorphine 16mg per day, illicit opioid abstinent, urines intermittently positive for benzodiazepines, and describes drinking alcohol twice per week.

• Further history: He has been under financial stress and may be depressed. He buys alprazolam (2mg “sticks”) from his former heroin dealer) and takes a half (1mg) at night to sleep. He drinks 2 to 4 beers to “relax” and acknowledges feeling high. His wife, who does not drink or take drugs and seems reliable, says she is aware of his alprazolam use for sleep, is worried about his alcohol use, but has not witnessed severe intoxication or loss of consciousness while drinking. He is holding down a job with no lateness or absences. He wants to stop drinking and buying drugs from the dealer, but says he has tried and been unable to stop either alcohol or alprazolam.

• Which medication treatment would be the most appropriate first choice to help him stop drinking?
  A. Naltrexone
  B. Disulfiram
  C. Acamprosate
  D. Gabapentin
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

- **Answer:** B - Disulfiram

- **Explanation:**
  - Disulfiram prevents drinking in most patients who adhere to daily doses. However, its effectiveness depends on adherence. A good strategy is to have a significant other witness the daily ingestion of the disulfiram. It sounds like this patient’s wife could do this, and the patient seems motivated to cooperate. The patient should be educated about the disulfiram reaction and to initiate disulfiram on a day when he has not been drinking.
  - Naltrexone would be contraindicated, because it would precipitate opioid withdrawal in a patient maintained on buprenorphine.
  - Acamprosate has been shown to be modestly effective in reducing relapse to drinking after a detoxification. It has not been shown effective among outpatients actively drinking.
  - Gabapentin, though not FDA approved for treatment of Alcohol or Benzodiazepine Use Disorder, is a good thought: Low abuse potential (though there have been reports of misuse); may help with anxiety and sleep; one clinical trial has shown it helpful among outpatients with alcohol use disorder; probably not as powerful an effect as disulfiram (assuming adherence).
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

• What would be the most appropriate next step in managing his benzodiazepine use?
  A. Admit for inpatient benzodiazepine detoxification
  B. Prescribe alprazolam, 1 mg at bedtime with a taper schedule
  C. Prescribe clonazepam, 1 mg at bedtime, and continue until cause of insomnia better understood
  D. Prescribe low dose (10 to 25 mg) doxepin and tapering doses of clonazepam
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

- **Answer:** D - Prescribe low dose (10 to 25 mg) doxepin and tapering doses of clonazepam

- **Explanation:**
  - You want to get the patient off benzodiazepines, particularly alprazolam, because of the abuse potential. Doxepin at low doses is non-addictive, relatively safe, and may help with sleep. Ideally engage his wife to supervise the clonazepam taper.
  - Inpatient detoxification is probably an over-reaction. He is using a relatively low dose of alprazolam, is unlikely to experience substantial withdrawal, and has a good chance of success with outpatient management and clonazepam taper.
  - Alprazolam taper might work, but more advisable to prescribe a benzodiazepine with lower abuse potential, and longer half life for a taper.
  - Clonazepam has less abuse potential than alprazolam, due to slower absorption and elimination, but again, ideally you want to get him off benzodiazepines. His sleep may be treatable with a safer non-benzodiazepine (like doxepin), while doing more work to understand the cause of the sleep problem.
Cocaine, Methamphetamine, Prescription Stimulants

- Cocaine and amphetamines are indirect acting sympathomimetics promoting release of dopamine, norepinephrine, and serotonin from their respective neurons
  - Cocaine blocks reuptake pump on cell surface and is also a local anesthetic
  - Amphetamines promote release of catecholamines, in part by blocking uptake into storage vesicles
- Rewarding effects ("high") and addictive potential stem mainly from release of dopamine in ventral striatum (brain reward system)
Milder Stimulants with Lower Abuse Potential

- **Bupropion:**
  - Antidepressant
  - Acts mainly on norepinephrine, also modest dopamine release
  - Mildly energizing but little euphoria, rarely abused

- **Modafinil** (Provigil™) and r-modafinil (Nuvigil®)
  - FDA approved to combat daytime sleepiness in sleep apnea, narcolepsy or shift work
  - Also used off label for ADHD, chronic fatigue and depression
Prescription Stimulants

- Dexedrine, mixed (d and l) amphetamine salts (Adderall™)
- Methylphenidate (like cocaine it blocks dopamine reuptake)
- Effective treatments for ADHD, and as adjunctive medications in treatment resistant depression
- Extended release formulations (e.g. Adderall XR™, Concerta® (extended release methylphenidate), Vyvanse® (pro-drug of amphetamine))
  - Slower absorption
  - Less “high” and less abuse potential
Methamphetamine

- Variation on amphetamine
  - Readily synthesized in illicit laboratories
- Prevalence varies by region, subculture
  - More common in west, Midwest
  - Associated with risky sex, because of sexual stimulating effects
- Oral, smoked or injected
- Neurotoxicity
  - More so than other stimulants
  - Multiple potential physical and psychological adverse effects
Stimulants and Opioid Use Disorder

• Cocaine use commonly co-occurs with opioid use disorder
  ▪ Casual, occasional use
  ▪ Use together with opioids to enhance the high (“speed-balling”)
  ▪ Full use disorder
• Stimulant use may also be observed among patients with opioid use disorder
  ▪ Sometimes prescribed for putative ADHD, diagnosis not always clearly established
Prescribed Stimulants: Red Flags

- Similar to prescribed benzodiazepines, certain “red flags” are suggestive of misuse or use disorder
  - Symptoms of intoxication or withdrawal
  - Demands for a particular medication, usually immediate release (vs. extended-release)
    - “Extended-release doesn’t work for me”
    - “Only regular (immediate release) Adderall works for me”
  - Repeated lost prescriptions
  - Discordant pill count
  - Preoccupation with securing medication supply
  - Multiple prescribers
Cocaine or Other Stimulant Use Disorder: Evaluation

- Cocaine may be intranasal, intravenous, or smoked ("free-base", "crack")
- Methamphetamine may be oral, intranasal, smoked, or intravenous
- Difficult to quantify the dose
  - Query days per week
  - Route (smoked and intravenous more severe)
  - Hours per day using
  - DSM-5 use disorder symptoms (loss of control, impairment, tolerance/withdrawal)
  - Dollars spent, or amount consumed in dollar value
    - Drugs may be obtained in exchange for services (e.g. delivering, dealing, sex for drugs)
- Cocaine/stimulant withdrawal consists of fatigue, depression (may be severe, suicidal ideation), insomnia then hypersomnia, and may impair functioning for several days
Cocaine Use Disorder: Treatment

• Behavioral treatment is the mainstay
  ▪ Advice, Motivational Interviewing
  ▪ Contingency Management (Higgins, Petry)
  ▪ CBT for Relapse Prevention (Carroll, Rawson)
  ▪ 12-Step Facilitation (Donovan, Daley)

• Medications
  ▪ Many have been tested, some hints of effectiveness, none clearly effective or FDA approved
    - Examples: Noradrenergic antidepressants (tricyclics, bupropion); disulfiram; topiramate
Attention deficit hyperactivity disorder (ADHD) is common among patients with substance use disorders (approx. 20% prevalence)

Diagnosis depends on careful lifetime history to establish ADHD diagnosis during childhood

Extended release mixed amphetamine salts (Adderall XR™) increased cocaine abstinence compared to placebo among outpatients with cocaine use disorder (Levin et al., 2015)

Among patients receiving methadone with opioid use disorder, extended-release methylphenidate treatment was safe, and not associated with misuse. However, no beneficial effect was observed on cocaine use outcome compared to placebo (Levin et al., 2007)
Amphetamine/Methamphetamine Use Disorder: Treatment

- Behavioral treatment is the mainstay
  - Contingency Management (Petry)
  - CBT for Relapse Prevention (Carroll, Rawson)
  - 12-Step Facilitation (Donovan and Daley)

- Medications
  - None clearly effective or FDA approved
  - Hints of effectiveness from some trials: e.g. naltrexone, bupropion, mirtazapine (one study)
Cocaine and Other Stimulant Use Disorder: Levels of Care

- Limited evidence regarding cocaine or other stimulant use disorder can be managed on an outpatient basis, but studies demonstrate limited positive outcomes.
- Withdrawal does not usually require intensive medical supervision, unless patient becomes severely depressed or suicidal during withdrawal.
- Level of care depends mainly on level of psychosocial impairment:
  - More severe impairment or disorganization:
    - Intensive outpatient
    - Inpatient/residential to enforce abstinence and try to put in place a long term plan.
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

- 35 year old man with opioid use disorder, on buprenorphine 16mg per day, illicit opioid abstinent, urines intermittently positive for benzodiazepines, and describes drinking alcohol twice per week. He continues to drink 2 to 4 beers at night and to take alprazolam before bed, he says to help him sleep.

- The patient now begins to produce cocaine positive urines. He says he takes cocaine in the morning to combat fatigue and get to work on time. He also says his work is often tedious and the cocaine helps him stay focused. He denies all symptoms of a cocaine use disorder. He asks for a prescription for Adderall (immediate release), mentioning that several years ago a doctor diagnosed him with ADHD and treated him with Adderall. Childhood history yields no indication of problems with performance or behavior at school.
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

• What would be the most appropriate next step in his treatment?
  A. Institute Contingency Management, where cocaine positive urines trigger reductions in buprenorphine dose
  B. Prescribe Adderall, immediate release
  C. Prescribe Adderall, extended release
  D. Counsel that ongoing alprazolam and alcohol use may contribute to his fatigue
  E. Obtain collateral history from his mother about his childhood years
Case Vignette: Patient on Buprenorphine with Benzodiazepine and Alcohol Use (cont.)

• **Answers:**
  - D. Counsel that ongoing alprazolam and alcohol use may contribute to his fatigue, **and**
  - E. Obtain collateral history from his mother about his childhood years

• **Explanation:**
  - Alcohol may disrupt sleep, and alprazolam may combine with buprenorphine to produce fatigue. Reducing or eliminating alcohol and benzodiazepines may improve fatigue and reduce the need for cocaine.
  - A diagnosis of ADHD should not be dismissed, as the diagnosis can be difficult in adults. Collateral history from a parent regarding the childhood history can be valuable in establishing whether ADHD was likely present in childhood, which is required for diagnosis of ADHD in an adult.
  - Without a clear childhood history consistent with ADHD, one would hesitate to make the diagnosis and prescribe a stimulant. If prescribing a stimulant, an extended release formulation preferred over immediate release due to greater abuse potential of immediate release.
  - Contingency Management is effective for treating cocaine use disorder, but of the type where a cocaine negative urine earns a reward (e.g. a voucher worth money or gift). Reduction of buprenorphine is a punishment (not effective) and would undermine treatment of the opioid use disorder.
Cannabis Use and Use Disorder

• Cannabis contains multiple potentially active compounds
  ▪ THC
    – Cannabinoid receptor partial agonist
    – Mainly responsible for psychoactive effects
    – Promotes dopamine release
  ▪ Cannabidiol
    – Does not release dopamine and does not, in itself, appear to have abuse potential
    – Potential anticonvulsant, analgesic effects
  ▪ Different strains contain different concentrations
  ▪ Contemporary strains can be highly potent
    – Severe intoxication
    – Greater risk of use disorder
    – Cognitive impairment, “amotivational syndrome”
Cannabis and Opioid Use Disorder

- Cannabis use is common among patients with opioid use disorder, including those being treated with methadone, buprenorphine, or naltrexone.
- Shared neuropharmacological mechanisms:
  - Cannabis withdrawal and opioid withdrawal syndromes share features, including irritability, insomnia, anxiety.
- Cannabis may have analgesic properties.
- Patients report taking cannabis to help with sleep or anxiety.
Cannabis Use Disorder: Evaluation

- **Quantify**
  - Days using
  - Pattern of use
  - “joints”, “blunts” (1 “blunt” ~ 3 joints)
  - Quantitation difficult because of variations in potency

- Elicit DSM-5 use disorder symptoms (loss of control, impairment, tolerance/withdrawal)

- Patients often deny impairment
  - Get collateral report from significant others
  - Failure to perform to potential in school, career
  - Use Motivational Interviewing approach
Cannabis Use Disorder: Treatment

- Behavioral treatment is mainstay
  - Advice to cut down, Motivational Interviewing
  - CBT for Relapse Prevention
  - Contingency management

- Medications
  - Various medications tested; None have proven effective in clinical trials

- Levels of care
  - Most cannabis use disorder can be managed in office or other outpatient setting
  - Inpatient rarely necessary for safety reasons, but may be valuable to initiate abstinence when other efforts have failed
Co-occurring Opioid and Other Substance Use: Conclusions

• Co-occurring substance use is common among patients with opioid use disorder
  ▪ Alcohol, benzodiazepines, cocaine and other stimulants, cannabis

• First step is evaluation
  ▪ Ask, applying principles of MI
  ▪ Quantity and frequency of use
  ▪ Seek collateral report from reliable significant others
  ▪ Evaluate per DSM-5 use disorder criteria
    - Classify as mild, moderate, severe
    - Consider safety concerns, especially overdose risk
Co-occurring Opioid and Other Substance Use: Conclusions

• Look for other co-occurring disorders
  ▪ Depression, anxiety, PTSD
  ▪ ADHD
  ▪ Sleep
  ▪ Pain

• Consider behavioral or pharmacological treatments for other substance use disorders

• Much co-occurring substance use is mild to moderate severity, can be managed in office or outpatient setting
  ▪ Indications for intensive outpatient or inpatient care
    – Serious risks such as overdose or gross intoxication
    – Severe psychosocial impairment
    – Failure to improve at lower level of care
References

  ▪ Chapter 47: Medications for Use in Alcohol Rehabilitation. Myrick H, Kranzler HR, Ciraulo DA, Saxon AJ, Jaffe JH. p.713
References


- Textbook of Substance Abuse Treatment by the American Psychiatric Publishing. Editors Galanter and Kleber (please format as appropriate).
PCSS Mentor Program

• PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.

• PCSS mentors are a national network of providers with expertise in addictions, pain, evidence-based treatment including medication-assisted treatment.

• 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.

• No cost.

For more information visit: pcssNOW.org/mentoring
Have a clinical question?

Ask a Colleague

A simple and direct way to receive an answer related to medication-assisted treatment. Designed to provide a prompt response to simple practice-related questions.

Ask Now
PCSS-MAT is a collaborative effort led by the American Academy of Addiction Psychiatry (AAAP) in partnership with the: Addiction Technology Transfer Center (ATTC); American Academy of Family Physicians (AAFP); American Academy of Neurology (AAN); American Academy of Pain Medicine (AAPM); American Academy of Pediatrics (AAP); American College of Emergency Physicians (ACEP); American College of Physicians (ACP); American Dental Association (ADA); American Medical Association (AMA); American Osteopathic Academy of Addiction Medicine (AOAAM); American Psychiatric Association (APA); American Psychiatric Nurses Association (APNA); American Society of Addiction Medicine (ASAM); American Society for Pain Management Nursing (ASPMN); Association for Medical Education and Research in Substance Abuse (AMERSA); International Nurses Society on Addictions (IntNSA); National Association of Community Health Centers (NACHC); National Association of Drug Court Professionals (NADCP), and the Southeast Consortium for Substance Abuse Training (SECSAT).

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