ECHO IDAHO

Counseling Techniques for Substance Use Disorders

The Complications of Stimulant Medication During Substance Use Treatment

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Learning Objectives

- Review the association between ADHD and SUDs
- Review general risks associated with stimulant medication use in patients with SUD
- Discuss current recommendations and complications regarding stimulant medication prescription in patients with a history of StUD, OUD, and AUD

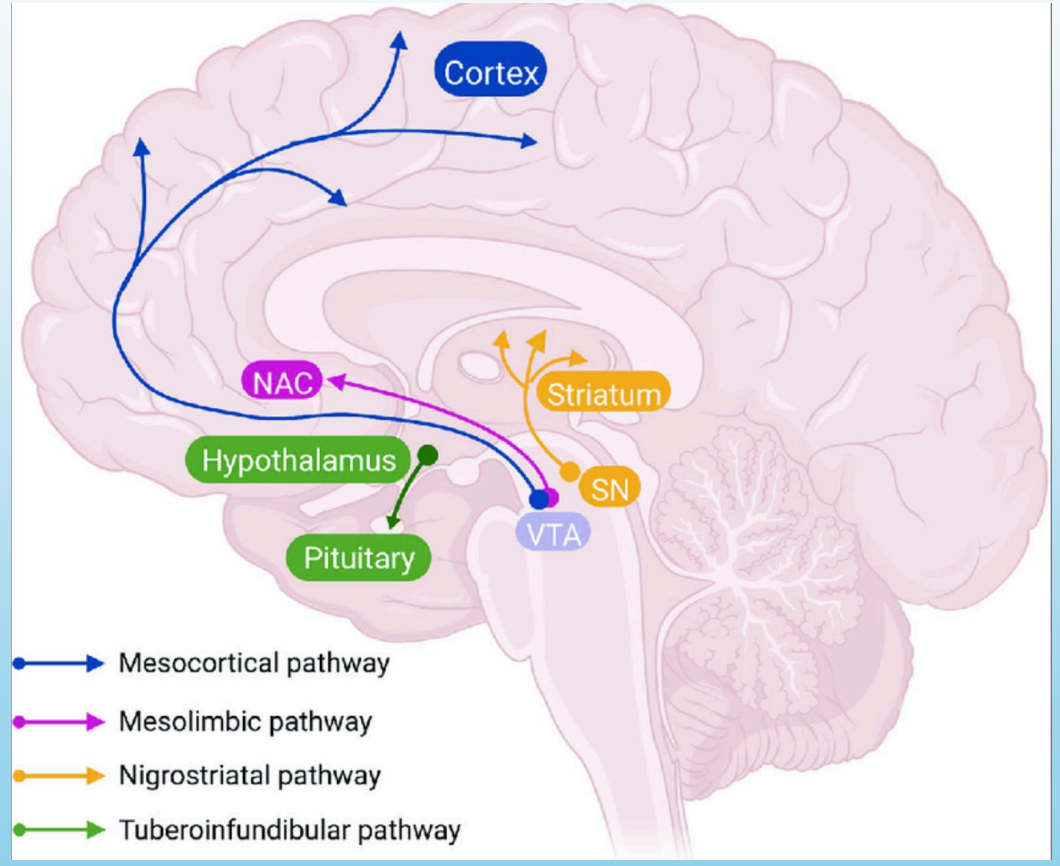
ADHD and SUDs Bidirectional Relationship

- **~20–25% of adults in addiction treatment meet ADHD criteria**
- **ADHD is an independent risk factor for SUD [(OR) 1.3–3.5]**

- **Comorbid ADHD–SUD is linked to:**
  - Earlier onset and faster addiction escalation
  - More severe addiction and higher rates of polysubstance use
  - Poorer treatment adherence and higher relapse rates
  - Greater psychosocial and functional impairment
  - More psychiatric comorbidities (e.g., mood disorders, ASPD)

ADHD/SUD: Possible shared etiology

- Abnormal functioning of the mesolimbic dopamine reward system
- Genetic polymorphisms in dopamine receptors, transports, and monoamine oxidase A



Caption

What are common risks associated with stimulant medication prescription in patients treated for SUD?

Misuse and Diversion Risks associated with Stimulant Medication Prescription in SUD

- **Individuals with SUD diagnosis have higher rates of:**
  - **Non-therapeutic use - 15–35% misuse** their prescribed stimulant at some point.
  - **Diversion -** Up to 22% report diverting their medication to others.
  - **Injection use -** particularly with short-acting formulations.

- **Risk factors include:**
  - Active substance use
  - Younger age
  - Inconsistent follow-up
  - Co-occurring mood or anxiety disorder
  - Immediate-Release (IR) Formulations have increase risk of misuse and diversion
  - Amphetamine derivatives > Methylphenidate

Behavioral Risks associated with Stimulant Medication Prescription in SUD

- **Masking of sedation/intoxication**
  - Increases the risk of overdose
  - May also lead to risky decisions due to the subjective feeling of being "in control" (ex. drinking and driving)
  - Fatigue masking and elevated mood can potentially lead to longer binge episodes
- **Increased risk taking**
  - Mixing stimulants with alcohol and other substances increases risky behavior
  - Physical altercations, unsafe sex, other substance use

Stimulant Medication Prescription in Patients Treated for StUD

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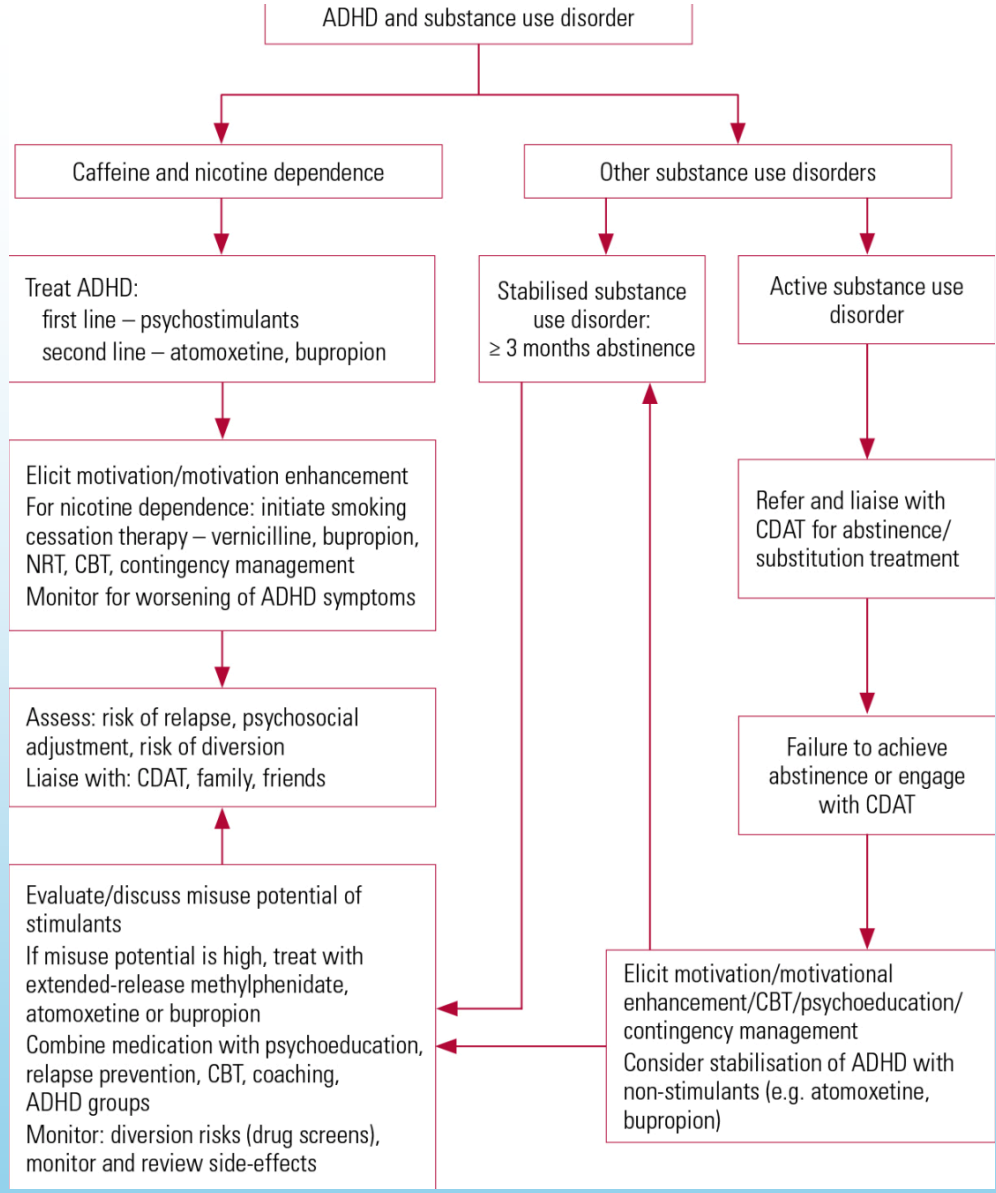
Treatment Pathway

- **Treatment concern**
  - Stimulant prescriptions may worsen misuse or trigger relapse
- **Emerging evidence supports:**
  - Properly managed ADHD treatment (including stimulants) may improve outcomes
- **No evidence based treatment guidelines exist for prescribing stimulant medications in patients with SUD**
- Risk stratified approach
  - Low risk - Permanently abstinent
  - Moderate/High Risk
    - Current use, no dependence
    - Active SUD



Caption

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Stimulant Medication Prescription for ADHD in StUD patients

- **Psychosocial treatment is the primary treatment for StUD**

- **If medication is used for ADHD:**
  - Consider non-stimulants (atomoxetine, bupropion)
  - Consider long-acting methylphenidate over amphetamine
  - **Consider using higher doses (discussed on next two slides)**

- **Close monitoring essential**:
  - Drug screen monitoring
  - Small prescriptions/pill counts

- **Re-evaluate if relapse occurs**
  - Adjust/discontinue meds
  - Intensify psychosocial SUD treatment

Treatment Outcomes - High Dose Stimulant Medication for ADHD in StUD patients

- A 24-week randomized, double-blind, placebo-controlled trial in Sweden involving 54 incarcerated men (mean age ~42 yrs) diagnosed with ADHD and amphetamine dependence.
  - Treatment with high-dose OROS methylphenidate (up to 180 mg/day) began two weeks before prison release and continued in outpatient care, alongside twice-weekly visits and weekly cognitive-behavioral therapy
- **Results:**
  - Significant reduction in self-reported ADHD scores in the methylphenidate group
  - Significantly lowered risk of relapse to substance use (including amphetamine)
    - Abstinence rates: 10 out of 27 participants (37%)
    - Placebo group: 4 out of 27 participants (15%)
  - Improved retention in treatment

Treatment Outcomes - Stimulant Medication Prescription for ADHD in StUD patients

- "Extended-Release Mixed Amphetamine Salts vs Placebo for Comorbid Adult ADHD and Cocaine Use Disorder"
  - A 13-week randomized, double-blind, three-arm, placebo-controlled clinical trial in the U.S., involving 126 adults meeting DSM-IV-TR criteria for both ADHD and cocaine use disorder.
  - Participants were randomized to receive extended-release mixed amphetamine salts (MAS-ER) at either 60 mg or 80 mg daily, or placebo, along with weekly individual cognitive-behavioral therapy
- Results
  - **Improved ADHD symptom reduction (≥30%)**
  - **Improved continuous abstinence**
    - 80 mg: 30.2% abstinent
    - Placebo: 7.0% abstinent

Stimulant Medication Prescription in Patients Treated for OUD

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Complications of Stimulant Medication during Opioid Use Disorder Treatment

ADHD and OUD: Epidemiology & Comorbidity

- ADHD is present in ~18–23% of individuals with opioid use disorder (OUD). (versus 2.5-4% in adults in general)

- **Comorbid ADHD is associated with more severe OUD**
  - Earlier substance use onset
  - Higher relapse and hospitalization rates
  - More psychiatric comorbidities
  - Greater addiction severity and social dysfunction

- **Comorbid ADHD is associated with worse OUD treatment outcomes:**
  - Lower retention in opioid agonist therapy (e.g., methadone, buprenorphine)
  - Higher dropout, impulsivity, and overdose risk
  - Poorer treatment compliance

- **Stimulant treatment for ADHD *may* help symptoms but must be used cautiously**
- **Effects on OUD outcomes are unclear and may vary depending on which MOUD is used.**

Stimulant Medication Prescription for ADHD with **Buprenorphine** MOUD

- **Significantly increases MOUD treatment retention**
- **Improved ADHD symptom control**
- **Possible benefit with regard to OUD cravings/use**
  - A systematic review of 18 studies concluded that ADHD treatment in OUD populations is generally associated with reduced illicit substance use, better retention, and improvement in ADHD severity
- **Decreased *overall* risk of overdose**
  - One study found that a stimulant prescription was associated with a 19% increased odds of drug overdose, but this was offset by a 36% lower risk of attrition
  - In British Columbia cohorts, stimulant prescriptions paired with buprenorphine were linked to a **53% reduction in overdose risk**
- **No significant pharmacological interactions reported**

Stimulant Medication Prescription for ADHD with **Methadone** MOUD

- **Overdose Risk**
  - In British Columbia cohorts, stimulant prescriptions paired with methadone were linked to a **51% increased risk of overdose** (fatal or non-fatal)

- **No Evidence of Improved MOUD Treatment Outcomes**
  - No observational or randomized trials in methadone-maintained patients demonstrate improved treatment retention, reduced opioid use, or reduced craving with stimulant treatment.
  - The single RCT comparing methylphenidate, bupropion, and placebo showed no significant benefit on retention or illicit use and high placebo response (~46%)

- **Pharmacologic Safety**
  - There were **no studies reporting significant drug–drug interactions**
    - **Theoretical increase in CV adverse effects if prolonged QTc**
  - The observed **elevated overdose risk** likely stems from stimulant-driven masking of sedative effects with increased opioid consumption

Stimulant Medication Prescription for ADHD with **Methadone** MOUD

- **Unclear ADHD Treatment Outcomes**
  - Levin et al. (2006) conducted the only methadone-based RCT using sustained-release methylphenidate 20–40 mg BID (i.e., up to ≈80 mg/day)—which is at the upper end of typical therapeutic dosing in adults
    - All groups (methylphenidate, bupropion, placebo) showed significant ADHD symptom improvement, but no statistically significant difference between arms
  - A 2023 review of ADHD in subjects with substance use disorder—including stimulant misuse—notes that **high-dose stimulant regimens** may yield moderate ADHD symptom relief.

Stimulant Medication Prescription for ADHD with **Naltrexone** MOUD

- **Limited direct evidence on MOUD outcomes**
  - No studies specifically examine ADHD treatment with stimulants in patients stabilized on naltrexone MOUD (oral or injectable).
  - A systematic review of 18 studies (including methadone, buprenorphine, and naltrexone patients) found that ADHD treatment generally improved retention and reduced illicit substance use, though specific naltrexone data was sparse

- **Attenuation of stimulant-induced euphoria**
  - In adults with ADHD, adding naltrexone (50 mg) to long-acting methylphenidate reduced subjective "likeability" during titration, suggesting naltrexone may lower stimulant abuse potential

- **No known safety signal regarding masking intoxication or overdose**
  - There are no documented complications of stimulant use masking effects of naltrexone or leading to overdose—but data remain limited.

Do stimulant prescriptions increase the risk of developing OUD in patients on LTOT?

- **Scherrer et al. (2022) "Prescription stimulant use during long-term opioid therapy and risk for opioid use disorder"**
  - In a cohort of ~5,700 adults receiving ≥90 days of opioid therapy, 2.8% had overlapping stimulant prescriptions.
  - Unadjusted analysis showed higher OUD risk among dual users (HR 1.75; 95% CI: 1.17–2.61).
  - After adjusting for confounders, the association was no longer significant (adjusted HR 0.89; 95% CI: 0.47–1.71)—indicating no increased risk of OUD with stimulant co-prescribing

- **Wei et al. (2018) – "Prevalence of and Factors Associated With Long-term Concurrent Use of Stimulants and Opioids Among Adults With Attention-Deficit/Hyperactivity Disorder"**
  - Among adults with ADHD, long-term concurrent use of stimulants and opioids was present in ~5.4%.
  - Long-term opioid use was more prevalent in patients who received stimulants (16.5%) versus those who did not (13.0%).
  - This suggests that ADHD patients treated with stimulants may be more likely to begin LTOT, but does not establish increased OUD risk directly due to stimulants

Stimulant Medication Prescription in Patients Treated for AUD

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Prevalence of ADHD and AUD

- **Prevalence of AUD is higher in patients with ADHD**
  - ~43% versus 29%
- **Prevalence of ADHD is higher in patients with AUD**
  - ~20% of adults with AUD exhibit comorbid ADHD, compared to 2-6% in the general adult population
- **Comorbid ADHD is associated with worse AUD outcomes**
  - Greater severity of alcohol-related problems
  - Higher relapse rates

Stimulant Medication Prescription during Alcohol Use Disorder Treatment

- **Limited evidence**
  - No published clinical trials that directly assess the impact of treating ADHD with stimulant medication specifically in patients with comorbid Alcohol Use Disorder
  - A 3-month double-blind, placebo-controlled trial of atomoxetine in adults with ADHD and comorbid AUD found:
    - Clinically significant ADHD symptom improvement.
    - Inconsistent or limited effects on alcohol consumption or relapse risk
- **Current evidence suggests:**
  - Stimulant medications can improve ADHD symptoms in patients with AUD
  - No demonstrated, consistent benefit in improving AUD-outcomes

Stimulant Medications with MAUD Treatment

- **Naltrexone + stimulant (safe)**
  - No drug-drug interactions
  - Blunts stimulant euphoric effect
  - No masking of alcohol intoxication

- **Acamprosate + stimulant (safe)**
  - No drug-drug interactions

- **Disulfiram + stimulant (caution)**
  - Disulfiram inhibits dopamine β-hydroxylase, raising dopamine levels.
  - Combining this with stimulants may **increase dopaminergic tone**, possibly leading to:
    - Agitation, anxiety, insomnia
    - Risk of precipitating mania or psychosis in vulnerable individuals.

Negative AUD Outcomes Associated with Stimulant Medications

Mixing stimulants with alcohol is well-known to be dangerous.

- The stimulant can mask the sedative effects of alcohol, causing individuals to feel less intoxicated than they truly are.
- This often leads to drinking more alcohol than usual.
  - Studies have shown that when people take prescribed methylphenidate with alcohol, they end up consuming **significantly more alcohol** than they would otherwise.
  - This combination increases risk of alcohol overdose (since warning signs like drowsiness are delayed) and risky behaviors like drunk driving.

Medical Complications of Stimulant Medication during Alcohol Use Disorder Treatment

Cardiovascular risks

- Stimulants increase blood pressure and heart rate, which can compound alcohol's cardiovascular effects (e.g., arrhythmia, hypertension, cardiomyopathy).
- In patients with alcohol-related cardiac disease, stimulants may exacerbate underlying conditions (e.g., QTc prolongation, atrial fibrillation).

Liver disease

- While stimulants are primarily metabolized hepatically, they rarely cause hepatotoxicity on their own.
- In advanced alcohol-related liver disease, altered metabolism could increase stimulant levels, although data are limited. Potentially exacerbate hepatic encephalopathy.
- Risk increases if the patient is also taking disulfiram or other hepatotoxic medications.

Seizure threshold

- Both alcohol withdrawal and stimulant medications can lower seizure threshold, especially in early recovery.
- Caution is warranted if the patient has a history of alcohol withdrawal seizures or is on medications that affect seizure risk.

Psychiatric Complications of Stimulant Medication during Alcohol Use Disorder Treatment

Insomnia

- Common in early AUD recovery and exacerbated by stimulants.
- Sleep disruption can increase relapse risk, worsen mood, and impair executive function.

Anxiety and agitation

- Stimulants can worsen generalized anxiety, panic, and irritability, which are frequently present in AUD recovery.
- Can also mimic alcohol withdrawal symptoms (e.g., restlessness, tremor).

Mood destabilization

- Risk of mania, hypomania, or mood swings, especially in patients with comorbid bipolar disorder (often underdiagnosed in AUD).
- Mixed or manic presentations can be precipitated by dopaminergic stimulation.

Psychosis

- Alcohol use and withdrawal can cause alcohol-induced psychosis; stimulants may worsen or precipitate psychotic symptoms in vulnerable individuals.
- Especially risky if there is a history of delirium tremens, hallucinations, or paranoid ideation.

Key Points

- ADHD and SUDs have a bidirectional relationship, but the presence of SUD does not preclude treatment of ADHD with a stimulant medication.
- Stimulant prescription in patients with a history of StUD
  - Stimulant mediation is not recommended with active use
  - Higher than average doses may be beneficial in patients who are abstinent.
- Stimulants with Opioids
  - Stimulants are effective at treating ADHD symptoms, may improve OUD outcomes, and are safe with buprenorphine.
  - With NTX, there is less euphoria associated with stimulant use.
  - Risk/benefits are less favorable with methadone.
- Stimulants with AUD
  - Improve ADHD symptoms, but no clear improvement on AUD
  - Caution with disulfiram
- Stimulant use is associated with “masking” of intoxication and risky behavior with sedatives

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