Clinical Quicknotes
on Substance Use Disorders

Substance Use Disorders
Center of Excellence

Stimulants: Information and Intervention

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Quick Takes

- Stimulant use is a significant public health challenge, with 6.7 million people in the U.S. using illicit stimulants (methamphetamine and cocaine) and 3.9 million misusing prescription stimulants in 2024.
- The illicit stimulant supply is increasingly lethal—due to widespread fentanyl contamination, stimulants are now implicated in 30-40% of all Ohio overdose deaths.
- There are no current FDA-approved medications for the treatment of stimulant use disorders (StUDs), making evidence-based psychosocial treatments such as Contingency Management (CM) the cornerstone of clinical care.

Case History:

Jasmine is a 28-year-old woman who presents to an outpatient psychiatric clinic for worsening anxiety, insomnia, and "difficulty staying focused." She has a history of working in high-pressure service industry jobs, most recently as a barista. She reports occasionally using "a friend's Adderall" in the past and now has her own prescription (Adderall XR 20 mg QAM) prescribed by a telehealth provider she no longer sees.

Jasmine shows several red flags for stimulant misuse, including self-prescribing, poor continuity of care, diversion, and unresolved underlying anxiety and insomnia.

Think about what additional information you need to determine if Jasmine meets criteria for stimulant use disorder.

The Neurobiology and Epidemiology of Stimulant Use Disorder

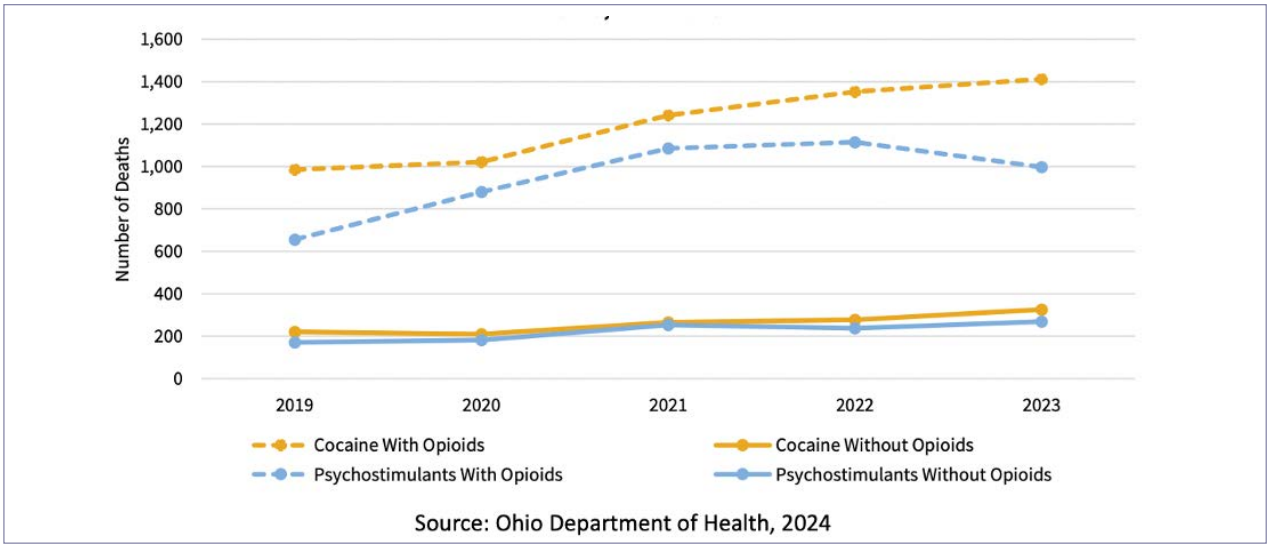
Like most substances implicated in substance use disorders (SUDs), central nervous system (CNS) stimulants have a strong impact on the brain's dopamine pathways. Specifically, they promote the release and/or prevent the reuptake of dopamine in the synapse. This causes dopamine to diffuse throughout various brain regions, most notably the mesolimbic pathway, which reinforces drug-seeking behavior by producing intense euphoria followed by intense cravings when the substance wears off.[1,2] Stimulant use disorder involves more than using the substance; it is defined as an inability to control use despite documented harms. Table 1 lists the diagnostic criteria for stimulant use disorder.[3]

TABLE 1. DIAGNOSTIC CRITERIA FOR STIMULANT USE DISORDER

Diagnostic Criteria for Stimulant Use Disorder	
• Inability to control use • Unsuccessful attempts to cut down or quit • Preoccupation with the drug(s) • Cravings and urges to use the substance • Missing important role obligations due to substance use • Continuing to use even if it causes relationship problems	• Giving up important social, occupational, or recreational activities • Repeated use even if it puts you in danger • Continuing to use even if it causes/makes worse physical or psychological problems • Tolerance • Withdrawal
Diagnosis requires at least two of these symptoms during a 12-month period	

These substances represent a significant public health challenge—national statistics indicate 6.7 million people aged 12 or older used illicit stimulants (methamphetamine and cocaine) and 3.9 million misused prescription stimulants in 2024.[4] Figure 1 gives a look at trends of overdose deaths associated with psychostimulants both with and without opioids in Ohio between 2019 and 2023. Fentanyl contamination of the stimulant supply is well documented, which likely reflects both deliberate adulteration and unintentional cross-contamination during processing and packaging.[5,6] The strong association with powder forms rather than crystalline forms suggests shared supply chains and handling as a major driver.[5,6] Shared equipment (e.g., scales, grinders, pill presses, or containers) used to handle both fentanyl and stimulants can leave trace amounts of fentanyl in stimulant supplies. Additionally, counterfeit pills may contain fentanyl instead of the expected drug. Because fentanyl is extremely potent, even small amounts can cause fatal overdose, especially in users with no opioid tolerance. This underscores the importance of naloxone availability and other overdose prevention and health risk reduction tools like fentanyl test strips, even for stimulant users.

FIGURE 1: NUMBER OF UNINTENTIONAL OVERDOSE DEATHS INVOLVING STIMULANTS IN OHIO, 2019-2023[7]



Source: Ohio Department of Health, 2024

Three months later, Jasmine presents to the ED agitated and complaining that people have been following her. She is certain they are going to harm her because she hears them talking about her outside her house, and worse yet, she hears them in the hall of the ED. She admits to using methamphetamine to supplement her Adderall, and urine drug screen (UDS) is positive for both methamphetamine and fentanyl. Your words of reassurance don't help, and you decide that some medication might. You prescribe olanzapine.

The Clinical Spectrum: Intoxication, Withdrawal, and Long-Term Effects.

Stimulant use disorder (StUD) is driven by the cycle of intoxication and withdrawal—recall of the initial euphoria leads the patient to desire to use again when the withdrawal symptoms (or "crash") set in. Symptoms of intoxication include euphoria, agitation, anorexia, tachycardia, hypertension, pupil dilation, paranoia, hallucinations, hyperthermia; and in severe cases, seizure, stroke, cardiac arrhythmias and myocardial infarction (MI). Withdrawal causes largely opposite symptoms: dysphoria, lethargy, hypersomnia, hyperphagia, bradycardia, intense craving, and depression.[3] Withdrawal is not considered medically life-threatening, but patients can be at higher risk of suicide, and psychotic symptoms can persist long after the active drug clears the patient's system.

Patients experiencing stimulant intoxication should be approached with a calm and reassuring demeanor. Clinicians should determine medical and psychiatric stability (MI, stroke, seizures, suicidal ideation, homicidal ideation, psychosis) and consider whether other substance use disorders (SUDs) are present as they prepare to admit the patients to the appropriate treatment setting. There is no specific pharmacological treatment for stimulant intoxication, but symptoms can be managed. Agitation or severe anxiety may respond to benzodiazepines. Psychosis may respond to antipsychotics. Olanzapine is a strong choice for managing acute stimulant-induced psychosis, as it effectively reduces agitation and hallucinations with a relatively rapid onset and low risk of extrapyramidal side effects, and is available in oral disintegrating tablet and intramuscular forms providing flexibility in administration.

Hyperadrenergic symptoms (tachycardia, hypertension, diaphoresis, mydriasis, tremors, insomnia, hyperthermia, nausea and vomiting, palpitations) may respond to benzodiazepines, with beta blockers or calcium channel blockers considered for more refractory symptoms and aggressive treatment of hypertension when needed. For seizures, consider benzodiazepines first, followed by phenobarbital and propofol if needed.[8]

Stimulant use disorders, if untreated, can have long-lasting effects including cognitive impairment, increased risk of Parkinson's syndrome, depression, and infectious diseases.[9] It is essential that patients be given evidence-based treatment.

Jasmine's presentation confirms she meets criteria for StUD, specifically: inability to control use, tolerance, and continuing to use despite psychological problems. She continued on olanzapine, finding relief from symptoms. Jasmine agrees to outpatient follow-up. She expresses some insight into the dangers of her use and asks for help "cutting back" but resists full abstinence. She also has a history of PTSD and is open to trauma-informed therapy. She wants to keep working but worries she'll "fall apart without something to help her focus."

Psychosocial Interventions and Safety Measures

According to the most recent research, over 90% of patients with substance use disorders do not feel they need any form of treatment.[4] It is vital to provide education regarding the modern evidence-based treatment methods. ASAM and AAAP identify Contingency Management (CM) as the standard of care along with useful adjunctive treatments including Community Reinforcement Approach (CRA), and cognitive behavior therapy (CBT). Other useful modalities include motivational interviewing (MI), case management and coordinated care, physical exercise, mindfulness meditation, and Twelve Step Facilitation (TSF).[8] Because of the high levels of fentanyl in the illicit psychostimulant supply, clinicians should

also provide other life-saving measures, such as educating patients to never use alone, always using fentanyl testing strips on any drug, and carrying naloxone and knowing how to use it. Patients should also be educated on health risk reduction services, oral health, and nutrition.[8]

> *Jasmine enrolls in an intensive outpatient program (IOP). Utilizing a Motivational Interviewing (MI) approach, her counselor helps her explore her ambivalence, eventually guiding her toward a goal of complete abstinence from illicit stimulants. She engages in Contingency Management (CM), earning small voucher rewards for providing negative urine drug screens, which reinforces her early recovery. Concurrently, she begins Prolonged Exposure therapy, a trauma-informed modality to address her underlying PTSD. Initially, processing her trauma triggers intense cravings for methamphetamine. However, the combination of CM incentives and the coping skills developed in her CBT groups allows her to navigate these triggers without returning to use. After two months, she notes a significant decrease in her PTSD-related hypervigilance and nightmares.*

Pharmacological Considerations

There are no FDA-approved medications for the maintenance treatment of stimulant use disorders. Most published studies have methodological issues (small number of subjects, uncontrolled, etc.). Contradictory conclusions are present in various studies. SAMHSA and NIDA are actively investigating potential medications to treat stimulant use disorders.

Many individuals with StUD (and other SUDs) have co-occurring mental health or substance use disorders, and when considering pharmacological treatment for StUD, the presence of a co-occurring mental health or substance use disorder may help guide decisions about medication treatment options.

- Clinicians should ask the following questions when considering medication treatment for stimulant use disorder:
- Are there co-morbid addiction(s) that have established pharmacological treatment?
- Are there co-morbid psychiatric disorders that have established treatments?
- Should you use controlled drugs?

  a. Stimulants for ADHD? (Possibly.)

  b. BZDS for anxiety? (Generally, no.)
- Might patients benefit from medication for StUD even with sparse data?

Table 2 outlines what is known about pharmacological treatments for various stimulant use disorders along with the level of certainty and the symptoms of each which may respond to these treatments. It should be noted that the use of psychostimulants for StUD, including cocaine use disorder (CUD) and methamphetamine use disorder (MUD), is controversial. Early studies of psychostimulants for CUD and MUD showed only low-quality, inconsistent evidence of benefit, with no clear improvement in treatment retention.[10,11] More recent studies challenge this assumption and suggest that in a subset of patients they may be of value, with meta-analyses suggesting higher doses of prescription psychostimulants may decrease cravings and improve abstinence rates, though effect sizes remain limited.[12,13] Further study is needed, particularly regarding how alternative outcome measures like “reduced use” might capture clinically meaningful treatment signals that traditional abstinence endpoints miss.[14] The authors of this QuickNote suggest that psychostimulants for CUD or MUD should only be prescribed by physicians who are board-certified in addiction medicine or addiction psychiatry or have similar training. Additionally, it is recommended that long-acting preparations be used preferentially, and that close monitoring is utilized by checking pill counts, the state prescription drug monitoring program (or PDMP, which in Ohio is OARRS) and obtaining urine drug screens.

TABLE 2: ASAM AND AAAP PHARMACOLOGICAL RECOMMENDATIONS FOR TREATMENT OF STUDS

Pharmacological Treatment	Cocaine Use Disorder	Methamphetamine Use Disorder
Bupropion	• May promote abstinence from cocaine* • Other considerations: ◦ Patients with co-occurring tobacco use disorder (TUD) ◦ Patients with co-occurring depressive disorders ◦ Contraindicated with anorexia and seizure history	• May promote abstinence from methamphetamine* • Other considerations: ◦ Patients with co-occurring tobacco use disorder (TUD) ◦ Patients with co-occurring depressive disorders ◦ Contraindicated with anorexia and seizure history
Bupropion plus naltrexone	No evidence of efficacy	• Moderate certainty of benefit** • Other considerations: ◦ Represents the strongest overall pharmacotherapy signal for methamphetamine based on major clinical trials (e.g., ADAPT-2). Requires combination of XR injectable naltrexone plus oral XR bupropion. ◦ Patients with AUD* ◦ Patients with TUD* ◦ Patients with depressive disorders*
Topiramate	• May promote reduced use of cocaine* • Other considerations: ◦ Patients with co-occurring alcohol use disorder (AUD)	• May promote reduced use of methamphetamine* • Other considerations: ◦ Patients with co-occurring alcohol use disorder (AUD)
Mirtazapine	No evidence of efficacy	• May promote reduced use of methamphetamine* • Other considerations: ◦ May be beneficial for patients with co-occurring depressive disorders

Modafinil	• May promote reduced use of cocaine in those without AUD*	No evidence of efficacy
Topiramate plus XR mixed amphetamine salts (e.g., Adderall XR)	• May promote reduced use of cocaine and decrease cravings** • Other considerations: ◦ Patients with co-occurring ADHD or AUD**	No evidence of efficacy
Methylphenidate (e.g., Concerta)	• May promote cocaine abstinence* • Other considerations: ◦ Patients with co-occurring ADHD ◦ Can consider higher doses of LA formulations	• May promote methamphetamine abstinence* • Other considerations: ◦ Patients with co-occurring ADHD ◦ Can consider higher doses of LA formulations
*Low certainty of benefit **Moderate Certainty of benefit Information gathered from ASAM and AAAP.[8]		

Despite her initial progress with CM, CBT, and trauma-informed therapy, Jasmine experiences a brief return to methamphetamine use after a particularly challenging week at work. She quickly re-engages with her treatment team, expressing frustration. While her PTSD symptoms have improved, she reports that her profound "inability to focus" is severely hindering her job performance and driving her cravings to use stimulants again.

Because of her history of methamphetamine use and previous diversion of prescription Adderall, her provider decides against prescribing a controlled psychostimulant. Instead, they initiate a trial of bupropion. Bupropion is selected because it may promote abstinence from methamphetamine (as outlined in Table 2), and because some evidence suggests it may be a useful off-label option for managing symptoms of ADHD in adults.[15] Over the next three months, Jasmine reports that her focus and energy levels have stabilized. With her attentional issues addressed, her cravings diminish, and she successfully returns to providing methamphetamine-negative urine drug screens.

When treating patients with co-occurring disorders like Jasmine, it is recommended to treat the patient holistically and in an integrated manner—the mental health disorder should be treated simultaneously with the substance use disorder. Controlled substances should be avoided if possible. Psychosis, mania, depression, anxiety, and insomnia should be managed as usual. If there is high suspicion that symptoms were induced by substances, clinicians may consider slowly tapering psychotropic medications after an extended period of psychiatric stability and be vigilant for return of symptoms. Stimulant intoxication and withdrawal can mimic or mask other psychiatric conditions, including mania, depression, anxiety, and attentional problems. Clinicians should consider whether symptoms predated substance use or persist through a period of abstinence before establishing a co-occurring diagnosis.

> *Six months later, Jasmine's clinical picture has significantly improved. Following her brief return to use and the successful initiation of bupropion, she has maintained complete abstinence from illicit methamphetamine. With sustained abstinence from stimulants, she was also successfully tapered off olanzapine without recurrence of psychotic symptoms. She continues to engage consistently in trauma-informed therapy for her underlying PTSD and the Contingency Management (CM) program. While she still experiences occasional cravings, her stabilized focus and developed coping skills allow her to navigate them effectively. She continues to carry naloxone as a safety measure, is thriving at work, and reports feeling grounded and in control of her life.*

Stimulant use is a pervasive public health issue, implicated in 30–40% of all overdose deaths in Ohio in 2023.[7] Because illicit stimulants are frequently—and often unknowingly—combined with highly potent substances like fentanyl, providing naloxone and other risk reduction resources to all stimulant users is a critical intervention. While the treatment for stimulant withdrawal remains largely supportive, long-term management requires a nuanced approach. For patients ambivalent about changing their use, Motivational Interviewing (MI) is highly recommended; for those motivated to engage, evidence-based practices such as Contingency Management (CM) serve as the standard of care. Although medication-assisted treatment for stimulant use disorders is still in its infancy, pharmacological interventions can be carefully considered as part of an integrated, holistic care plan.

For Additional Information on This Topic

- ASAM/AAAP Clinical Practice Guideline on the Management of Stimulant Use Disorder: https://pubmed.ncbi.nlm.nih.gov/38669101/
- SAMHSA Evidence-Based Resource Guide Series: Treatment of Stimulant Use Disorders: https://library.samhsa.gov/product/treatment-stimulant-use-disorders/pep20-06-01-001
- National Institute on Drug Abuse (NIDA) – Stimulant Reports: https://nida.nih.gov/
- Project DAWN (Deaths Avoided With Naloxone) – Ohio Department of Health: https://odh.ohio.gov/know-our-programs/project-dawn

Upcoming and Current Trainings on Substance Use Disorders

- Ohio Substance Use Disorders Center of Excellence
- American Academy of Addiction Psychiatry
- American Society of Addiction Medicine
- The Providers Clinical Support System-Medications for Opioid Use Disorders (PCSS-MOUD)

At the SUD COE, we are committed to bringing you resources and trainings that meet your needs in providing care to patients with substance use disorders. Please let us know what suggestions you have for improving Clinical QuickNotes, or topics that you would like addressed by clicking here: QuickNotes Feedback Survey.

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This QuickNote is an overview only and is not intended to be the sole resource for addressing stimulant use. The reader is encouraged to seek more information from sources listed in "For Additional Information on This Topic."

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