

June 20, 2024



Defining Stimulant Use Disorder within Harm Reduction Framework

Emerging Prescription and Treatment Practices

Danielle Anderson, MD and Allison McBride, MPH

Visit www.vitalstrategies.org

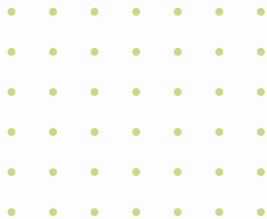
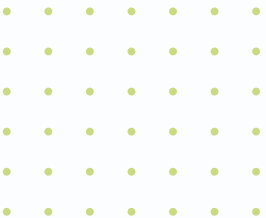
Agenda

- 1. Types of Stimulants, Effects, Chronic Use, and Complications**
- 2. National Trends**
- 3. Existing Treatment Recommendations and Emerging Practices**
- 4. Legal and Regulatory Landscape for Prescribing**
- 5. Promising Treatment Models and Outcomes**
- 6. Prescribing Barriers Among Providers**

Types of Stimulants, Effects, Chronic Use, and Complications

Stimulant Overview

- Drug class with action in the central and peripheral (sympathetic) nervous system
- Increase levels of **norepinephrine** and **dopamine** in the brain
- Plant-derived stimulants examples: cocaine (from *coca plant*), ephedrine (from *ephedra*), cathinone (from *khat*)
- Synthetic stimulants examples: methamphetamine



Stimulant Examples

Schedule I

- Khat
- MDMA (Ecstasy, Molly)
- Bath Salts (synthetic cathinones)

Schedule II

- Cocaine
- Methamphetamine
- Amphetamine Salts (Adderall[®], Dexedrine[®])
- Methylphenidate (Ritalin[®], Concerta[®])
- Lisdexamfetamine (Vyvanse[®])

Schedule III-IV

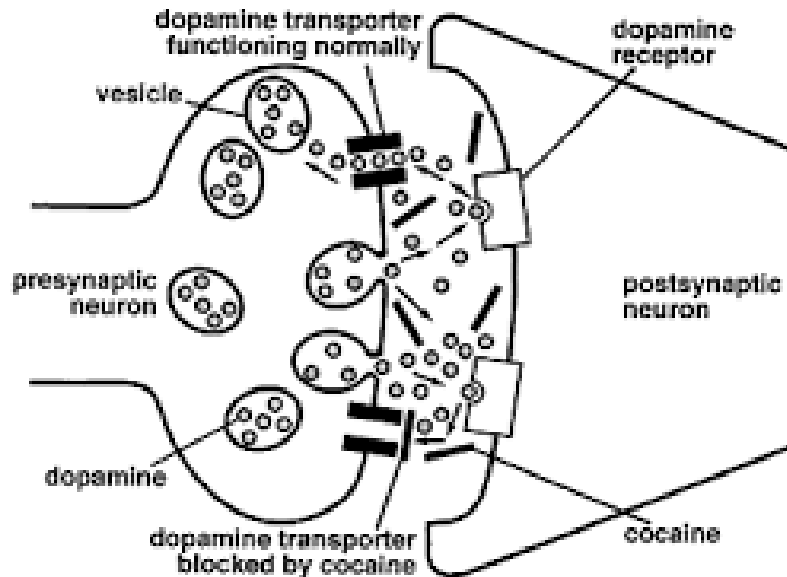
- Modafinal (Provigil[®])
- Phentermine (Adipex[®])
- Pseudoephedrine (Sudafed[®], Sine-aid[®]) (scheduling varies by state)

OTC

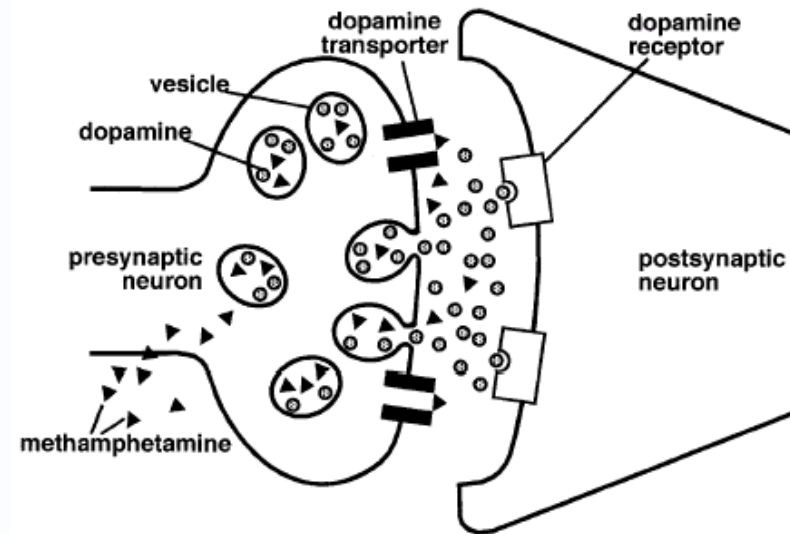
- Phenylephrine (Neo-synephrine[®])

Acute Effects of Stimulants in the Brain

Cocaine blocks dopamine reuptake



Methamphetamine causes dopamine release



Relative Dopamine Release

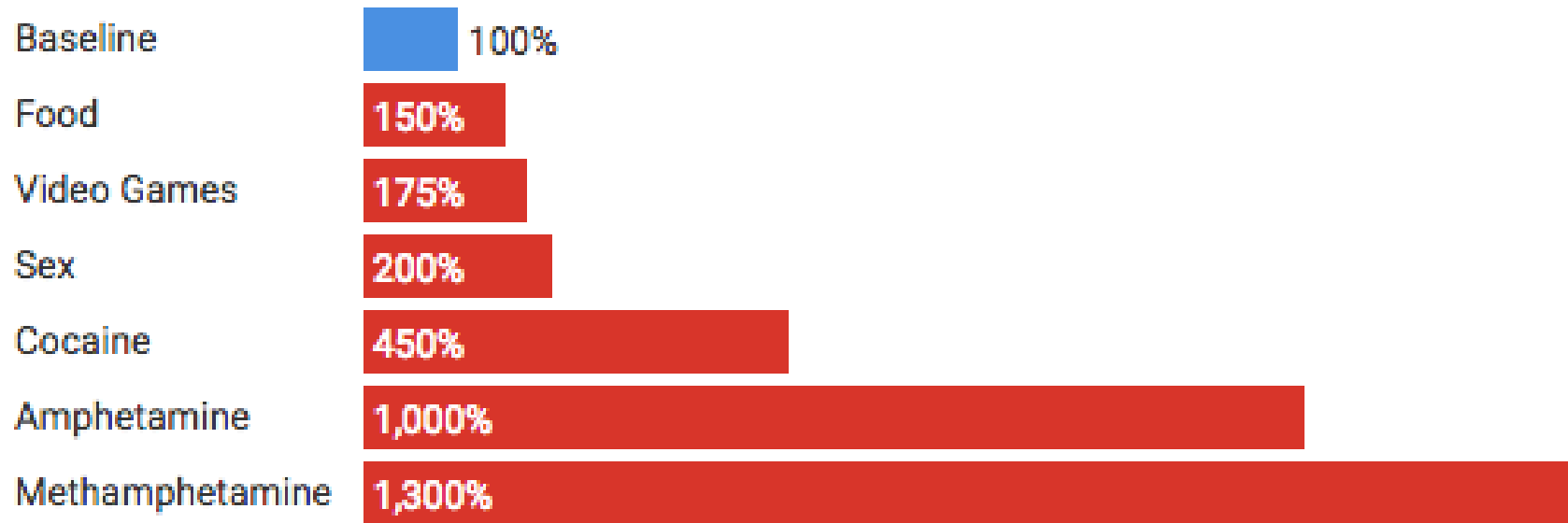
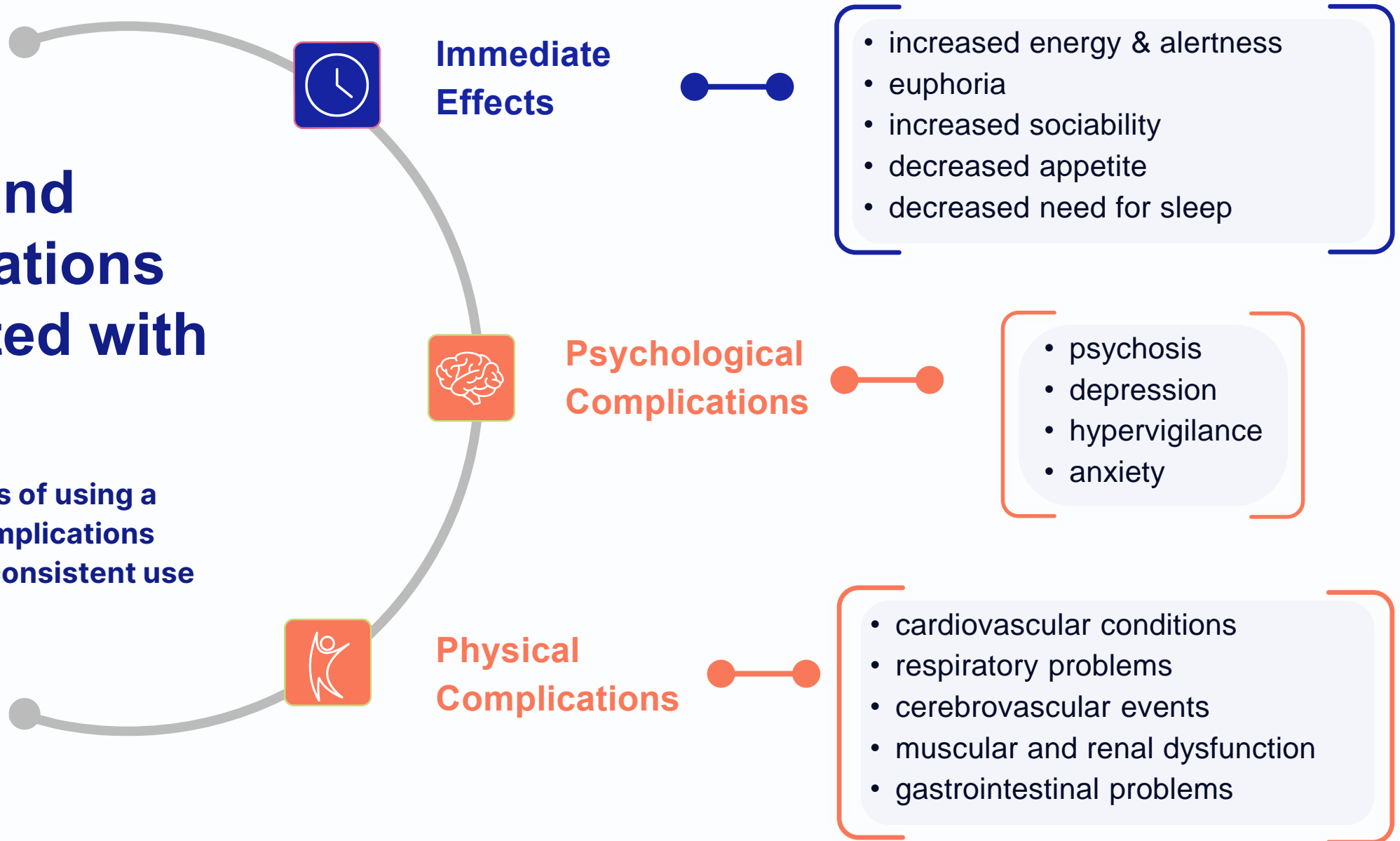


Chart: The Conversation, CC-BY-ND • Source: [National Institute on Drug Abuse](#) • [Get the data](#)

Effects and Complications Associated with of StUD

Immediate effects of using a stimulant and complications associated with consistent use of stimulants



Substance Use Disorder: DSM-5 (>2 Items in 12 Months)

- 1. Failure to fulfill responsibilities
- 2. Use in physically hazardous situations

- 3. Social/interpersonal problems
- 4. Cravings

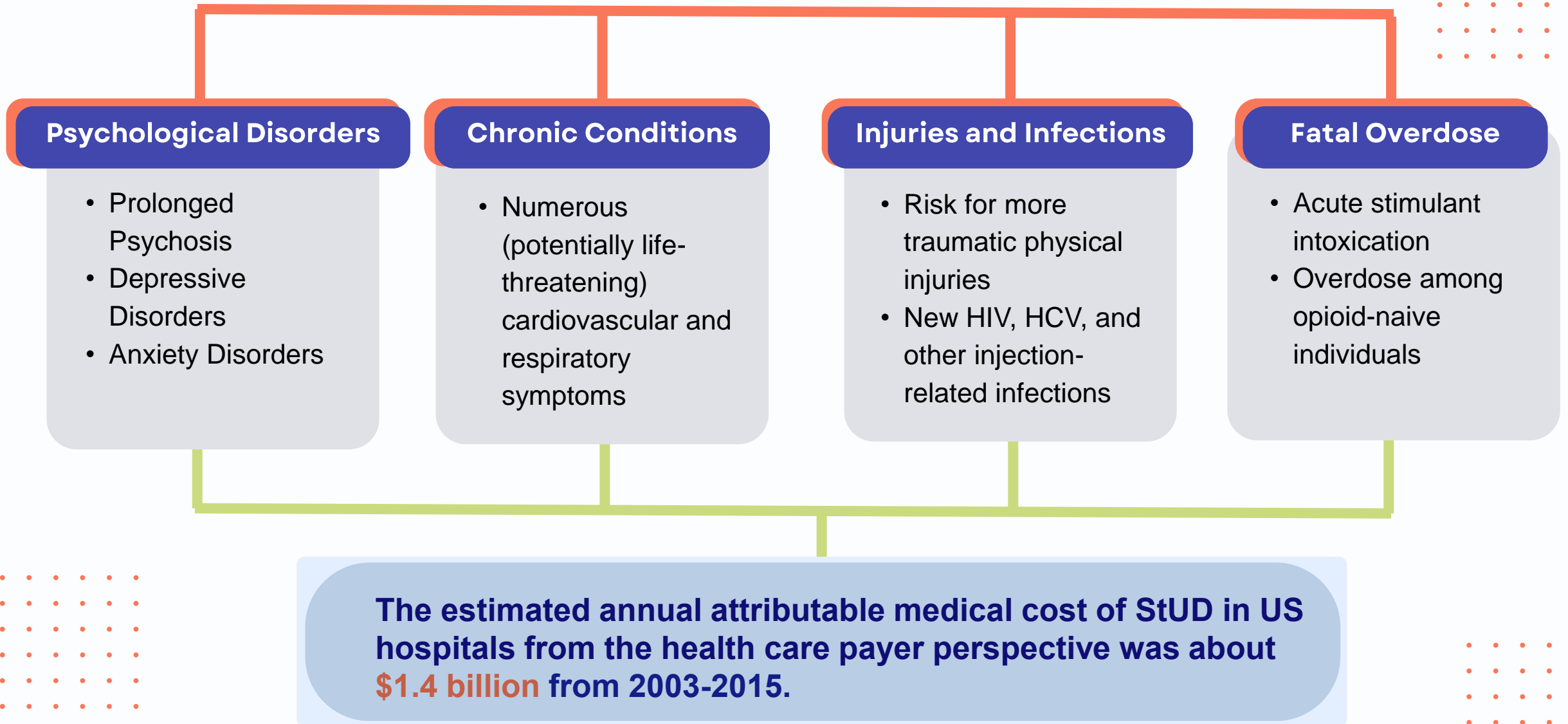
- 5. Use larger amounts or longer than intended
- 6. Cannot cut down
- 7. ↑ time spent to get, use, and recover
- 8. Give up or ↓ other important parts of life
- 9. Ongoing use despite problems
- 10. Tolerance
- 11. Withdrawal

Mild= 2-3

Mod= 4-5

Severe= 6+

Risks Associated with Chronic StUD



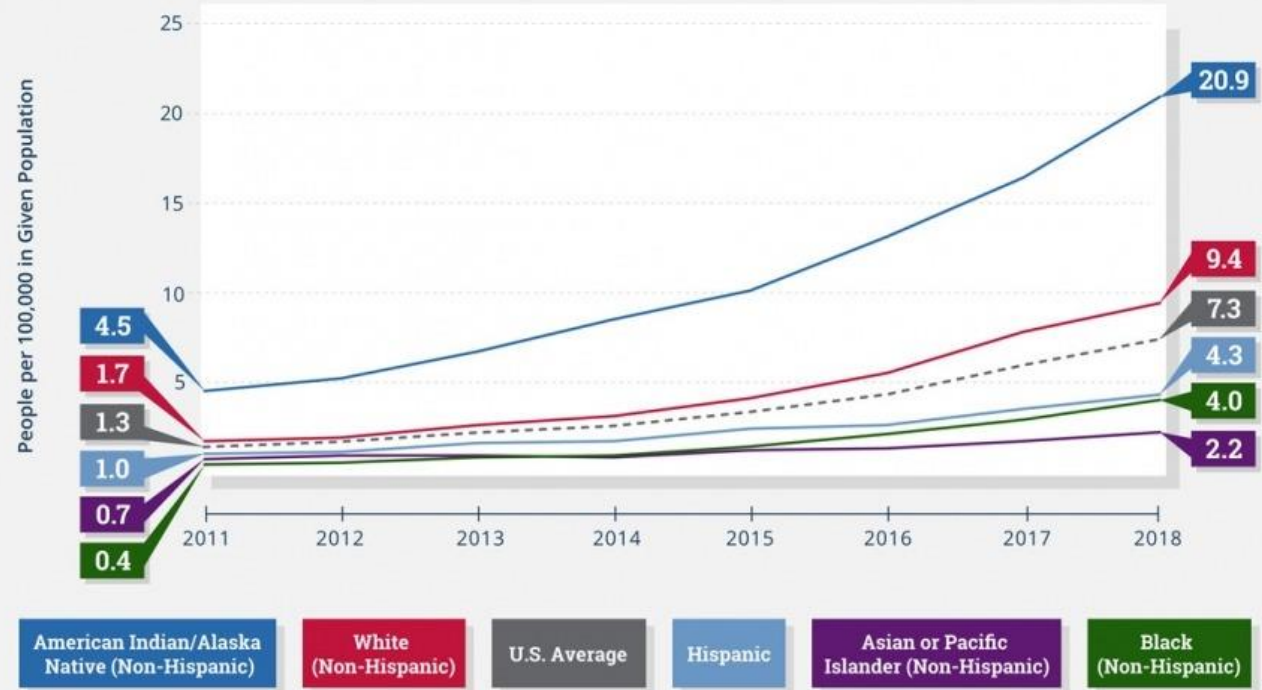
National Trends

Stimulant Use Trends

- In 2020, **2.5 million** people ages 12 and over reported methamphetamine use
- **53 percent** met criteria for Stimulant Use Disorder
- Less than 1 out of 3 received treatment
- **32,537 people died in 2021 from an overdose** involving stimulants other than cocaine. (primarily methamphetamine)

- “Binge and Crash” pattern of use is popular
- Concurrent use of methamphetamine or cocaine plus opioids = “**speedball**”
- **Overdose deaths involving stimulants on the rise** – often methamphetamines with other substances, especially opioids like fentanyl

U.S. Overdose Deaths Involving Methamphetamine in People Ages 25 – 54*



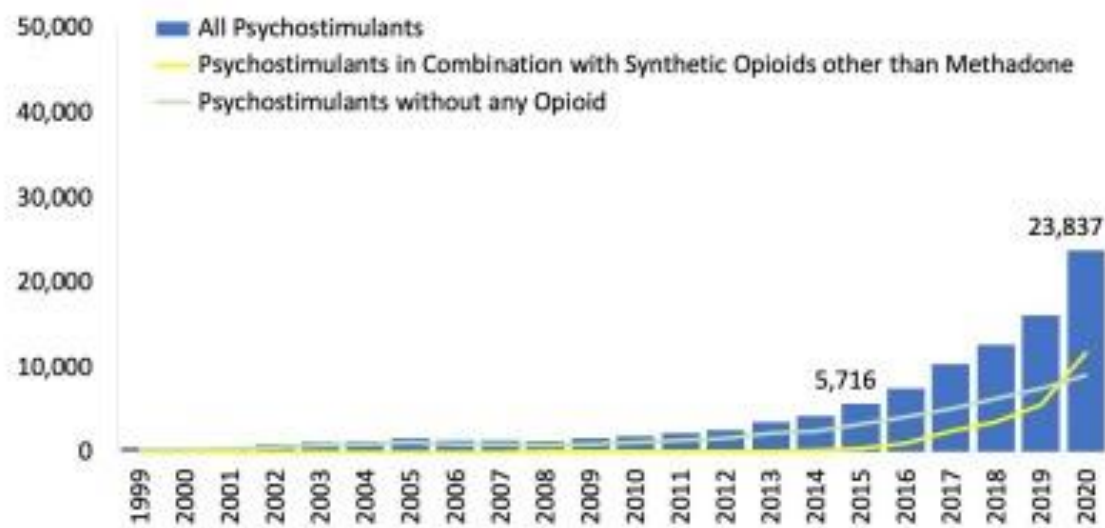
*Recent national data show that most people who use methamphetamine are between 25 and 54 years old, so investigators limited analysis to this age group.

Concurrent Opioid and Stimulant Use: A Growing Problem

- Methamphetamine use among those seeking treatment for primary heroin use increased from **2.1%** in 2008 to **12.4%** in 2017 (1).
- Number of overdose deaths involving stimulants and opioids is rising:
- In 2017, close to 75% of ***cocaine-involved deaths*** and roughly half of other ***psychostimulant involved deaths*** involved at least one opioid (2).

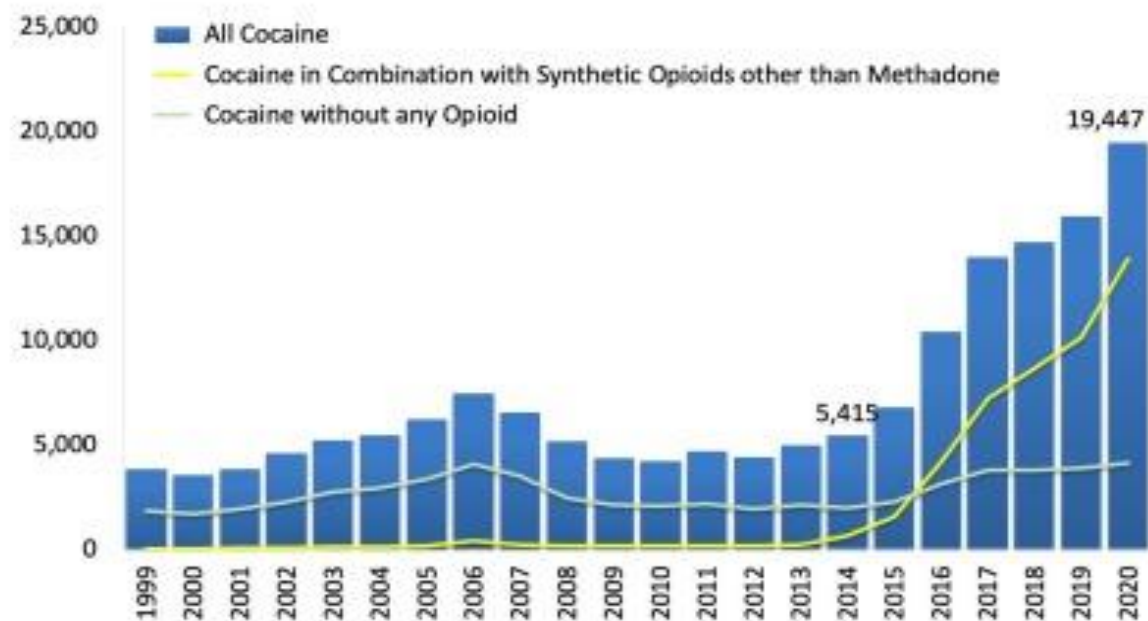
1. Jones CM, Underwood N, Compton WM. Increases in methamphetamine use among heroin treatment admissions in the United States, 2008–17. *Addiction* 2020;115:347–53. 2. MMWR. 2019; 68(17);388-395

**Figure 6. National Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)*, by Opioid Involvement
Number Among All Ages, 1999-2020**



*Among deaths with drug overdose as the underlying cause, the psychostimulants with abuse potential (primarily methamphetamine) category was determined by the T43.6 ICD-10 multiple cause-of-death code. Abbreviated to psychostimulants in the bar chart above. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

Figure 7. National Drug Overdose Deaths Involving Cocaine*, by Opioid Involvement, Number Among All Ages, 1999-2020



*Among deaths with drug overdose as the underlying cause, the cocaine category was determined by the T40.5 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

Kentucky Trends

- In 2022, there were 2,135 overdose deaths in Kentucky

Substances Found in Drug Overdose Decedent Toxicology Testing

Table 7: Counts of Substances Identified Through Toxicology Testing of Kentucky Resident Drug Overdose Decedents, 2022

Substance	Frequency
Fentanyl	1,548
4-ANPP	1,227
Methamphetamine	1,069
Amphetamine	882
Acetylfentanyl	453
Gabapentin	448
THC	416
Cocaine	335

Data are provisional and subject to change. Produced by the Kentucky Injury Prevention and Research Center, as bona fide agent for the Kentucky Department for Public Health. May 2023. Data source: Drug Overdose Fatality Surveillance System

Kentucky Overdose Deaths-Two Drug Combination 2022

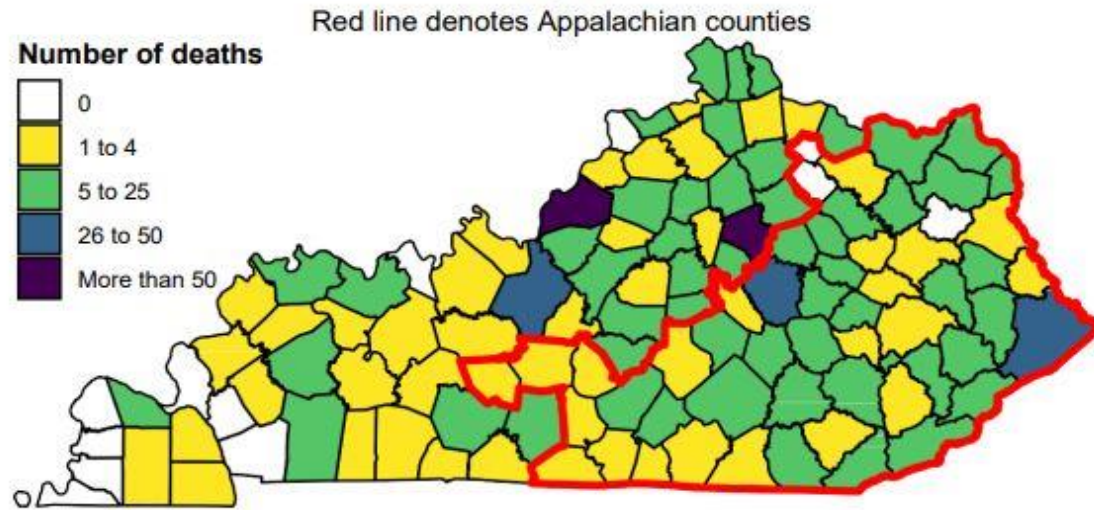
Drug Combinations Identified Through Toxicology

Table 8: Most Common Two-Drug Combinations Identified Through Toxicology for Drug Overdose Deaths Among Kentucky Residents, 2022

Drug Combination	Number of Deaths
4-ANPP, Fentanyl	1,327
Amphetamine, Methamphetamine	924
Fentanyl, Methamphetamine	863
Amphetamine, Fentanyl	717
4-ANPP, Methamphetamine	681
4-ANPP, Amphetamine	577

Data are provisional and subject to change. Produced by the Kentucky Injury Prevention and Research Center, as bona fide agent for the Kentucky Department for Public Health. May 2023. Data source: Drug Overdose Fatality Surveillance System

Figure 3: Number of Drug Overdose Deaths for which Methamphetamine Was Identified through Toxicology by Kentucky County of Residence, 2022



Produced by the Kentucky Injury Prevention and Research Center, as bona fide agent for the Kentucky Department for Public Health. May 2023.

Data source: Kentucky Death Certificate Database, Kentucky Office of Vital Statistics, Cabinet for Health and Family Services.

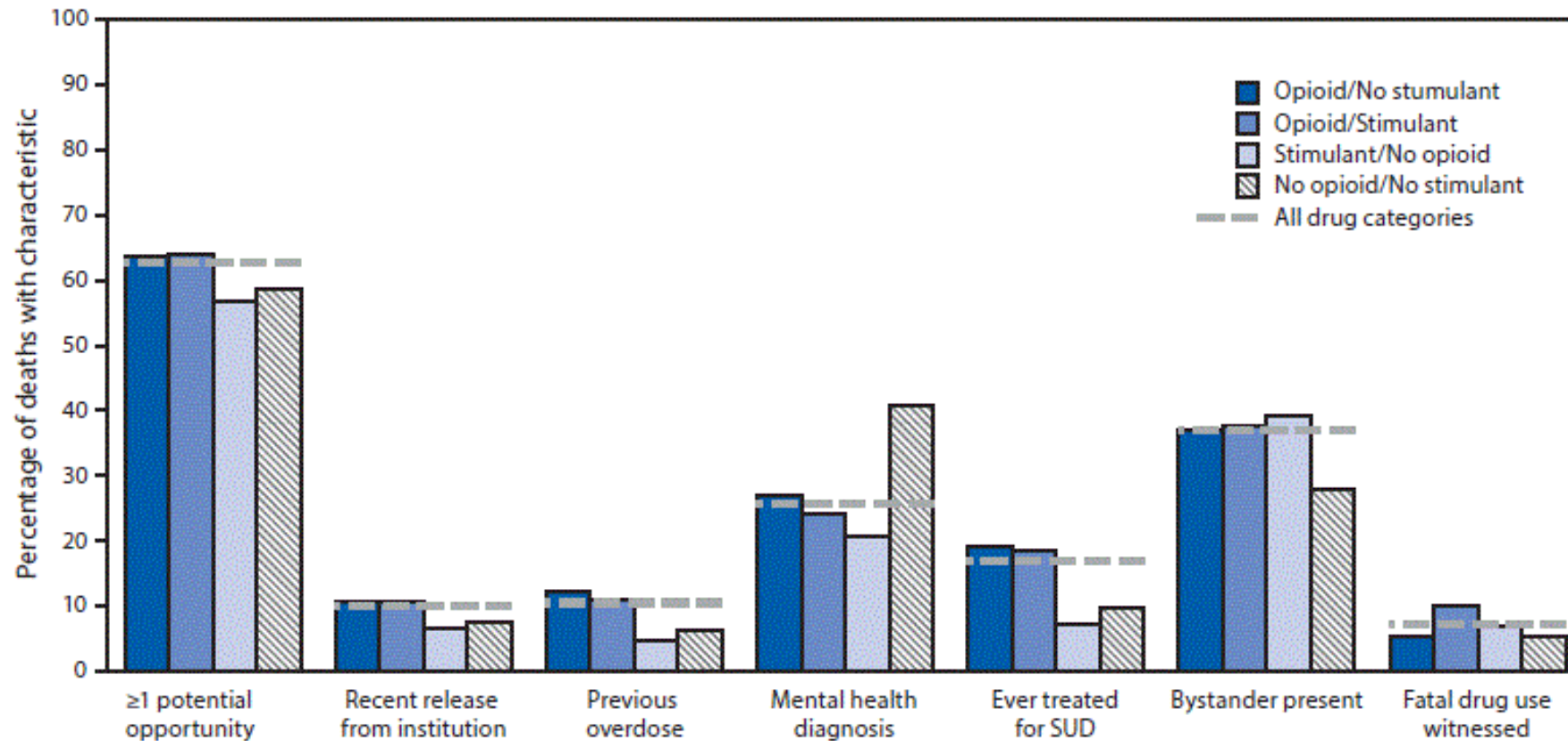
Twin Epidemics: Opioids and Methamphetamine

Two different mechanisms of action, so why are persons with OUD also using methamphetamine?

- Ellis et al studied motivations for co-occurring use of meth and opioids and found:
 - High seeking: 51%
 - Balance of effect: 38%
 - Available as an opioid substitute: 15.2%
 - Escape from life/numbness: 9.7%
 - Addiction: 9.0%
 - Social Setting: 6.2%

Potential Opportunities for Intervention by Opioid/Stimulant Involvement

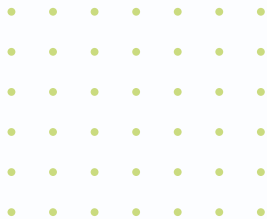
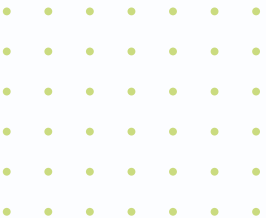
State Unintentional Drug Overdose Reporting System (SUDORS), 25 Jurisdictions, Jan-July 2019



Existing Treatment Recommendations and Emerging Practices

Treatment of Stimulant Use Disorders (StUD)

- To date there are **no effective FDA-approved medications** to treat stimulant use disorder
- Treatment is individualized and requires a comprehensive assessment. *Patient specific* treatment plans may include:
 - Off-label use of prescription medications
 - Psychosocial, counseling and behavioral interventions
 - Harm reduction/overdose prevention



Behavioral Treatments for StUDs

- Meta-analysis: 50 RCTs, 12 psychosocial interventions in 6,942 participants
- Contingency Management (CM) plus Community Reinforcement (CR) most effective for:
 - Abstinence (OR 2.8 $p=0.013$)
 - Retention (OR 3.9, $p<0.001$)
- **CM plus CR more effective than CBT**

Evidence Based Interventions for StUDs

Practice	Motivational Interviewing	Contingency Management	Community Reinforcement Approach	Cognitive Behavioral Therapy
Review rating	Strong Evidence	Strong Evidence	Strong Evidence	Strong Evidence
Focus of the practice	Resolving clients' ambivalent feelings and insecurities and enhancing the internal motivation needed to change their behavior	Positively reinforcing desired behaviors	Identifying behaviors that reinforce stimulant use and making a substance-free lifestyle more rewarding than one that includes substances	Helping clients improve the quality of their lives not by changing their circumstances, but altering their perceptions of those circumstances
Can be used in outpatient and inpatient healthcare settings	✓	✓	✓	✓
Specific Training Available	✓		✓	✓
Can be practiced by peers	✓	--	--	--
Has been used successfully with males and females	✓	✓	✓	✓
Special populations with whom the practice has been successfully implemented	Men who have sex with men	Men who have sex with men; Co-occurring opioid use disorder; Severe mental disorders	Adolescents	--
Intensity and Duration of Treatment	No prescribed intensity and duration	No prescribed intensity and duration; typically 12 weeks	No prescribed intensity and duration; recommended for 24 weeks	No prescribed intensity and duration; typical range of 5 to 10 months

Medications: Current Studies

ASAM/AAP Clinical Practice Guideline on Management of Stimulant Use Disorder provides review of evidence for medications that have been shown to have some benefit to help with stimulant use disorder

Medications Commonly Used for StUDs

Drug Class	Drug
Antidepressants	Mirtazapine, Bupropion
Prescription Stimulants	Mixed Amphetamine Salts, Modafinil
Anticonvulsants	Topiramate
Opioid Antagonists	Naltrexone (+bupropion)

Legal and Regulatory Landscape for Prescribing

Federal and State Laws: Prescribing CS for StUD



Federal

- Federal law does not explicitly restrict the dispensing (and prescribing) of controlled substances to treat SUD.
- General rule: the prescription must be issued for a legitimate medical purpose by a practitioner acting in the usual course of their professional practice.
- An alternative, more risk averse approach: pursuing an FDA investigational new drug application (INDA), to study already approved medications for new indications or in new patient populations.

VS

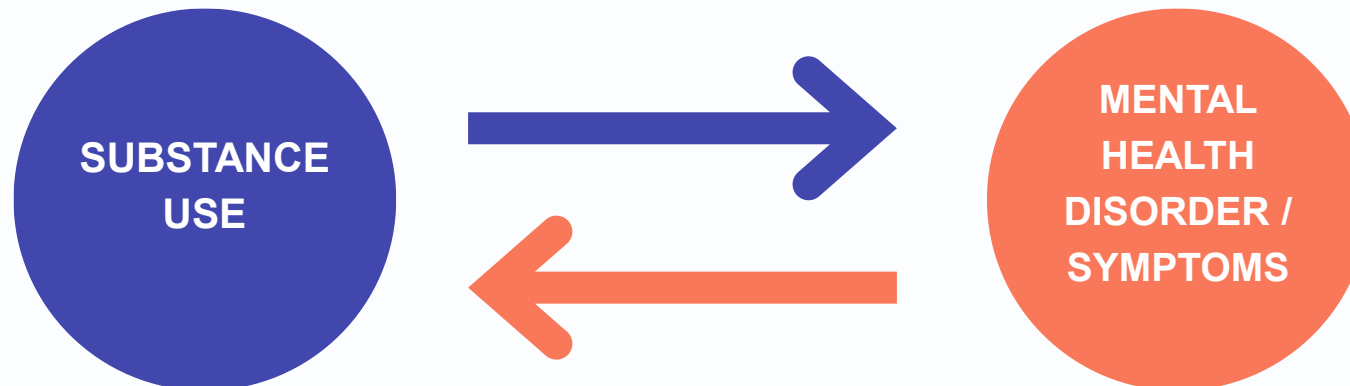


State

- States are the primary regulators of medical practice of prescribing.
- Kentucky's state laws (1) allow a licensee to apply for a waiver "for a legitimate medical purpose", (2) require stating the diagnosis to justify treatment with a controlled substance, and (3) include additional assessment requirements for prescribing
- Prescribing indicators under KY law with controlled stimulants include
 - Narcolepsy;
 - Attention deficit/hyperactive disorder;
 - Resistant depressive disorder;
 - Moderate or severe binge-eating disorder (adult);
 - Drug-induced brain dysfunction;

Types of Prescribing Practices and Medicaid Coverage

- **Prescribing Under Another Diagnosis The Patient Has**
 - Definition: When a provider prescribes for the treatment of another mental disorder or condition that may have benefits for StUD as well.
 - Examples include prescribing:
 - Stimulants: Attention deficient disorder (ADD aka ADHD) or narcolepsy diagnosis
 - Anti-depressants: Major depressive disorder or anxiety disorder diagnosis
 - Naltrexone or other drugs: Alcohol use disorder or another SUD
 - There are many other examples as well
 - This approach is more likely to be covered by Medicaid and other insurance providers, as what they are prescribing is FDA-approved for the patient's co-occurring diagnosis.

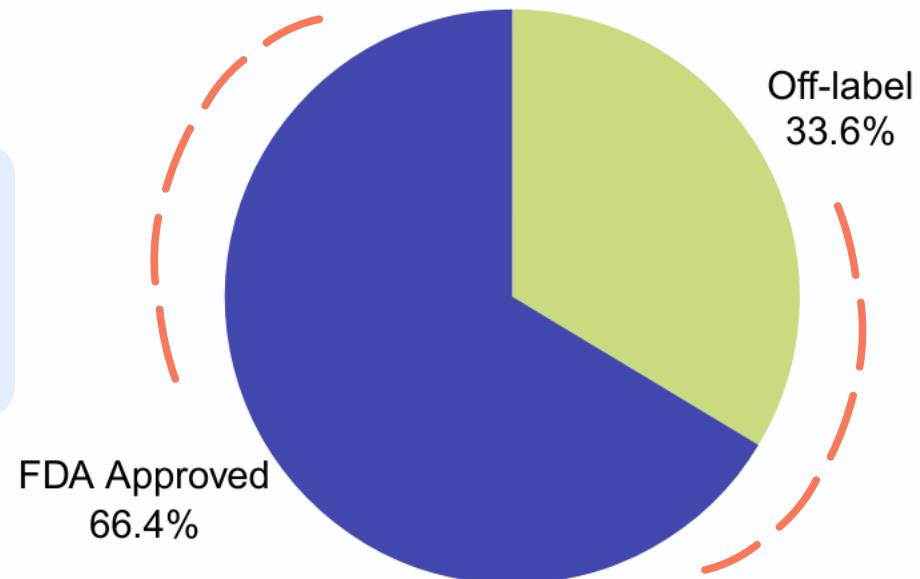


Types of Prescribing Practices and Medicaid Coverage

- **Prescribing as Off-Label**

- Definition: When a provider explicitly prescribes a drug for a condition that is different from the condition that the FDA has approved it for.
- Considered a standard medical practice with variations.
- Off-labeling prescribing comes with insurance barriers.
 - There is variable coverage under Medicaid and most other insurance providers (even for non-stimulants pharmaceuticals) due to the lack of FDA-approved indications for treating StUD.

One third of all total prescriptions in the US are prescribed as off-label, making the practice of prescribing off-label for StUD not an unusual practice.



Movement from ASAM and FDA

- **ASAM Clinical Guidelines for Prescribers**

- Released first national clinical guidelines addressing pharmacological treatment options for StUD in November 2023.
- Guidelines include: treatment recommendations, managing stimulant intoxication and withdrawal, and secondary and tertiary prevention (including harm reduction)
- Experts have said its release serves as a starting point but will require further details and strategic dissemination to facilitate translation into daily clinical practice and existing workflows.

QUALITY CARE

Stimulant Use Disorder

Developed by ASAM and AAAP, this guideline focuses on the identification, diagnosis, treatment, and promotion of recovery for patients with stimulant use disorder, stimulant intoxication, and stimulant withdrawal.

[DOWNLOAD GUIDELINE →](#) [READ ANNOUNCEMENT →](#)



Movement from ASAM and FDA

- **FDA Guidance for Drug Manufacturers**

- Issued draft guidance outlining steps drug manufacturers to develop new pharmacological treatments for StUD to be quickly approved (as in years).
- Guidance around developing new treatments for StUD include:
 - Targeting the underlying biology of StUD
 - Addressing the co-occurring mental health disorders that often accompany StUD
 - Improving treatment adherence and retention
- The FDA states they are open to new endpoints for clinical trials (except for a general reduction in use), such as measuring the number of days a person does not use drugs instead of complete abstinence – signaling that prescribing does not need to result in abstinence.

GUIDANCE DOCUMENT

Stimulant Use Disorders: Developing Drugs for Treatment

OCTOBER 2023

[Download the Draft Guidance Document](#) [Read the Federal Register Notice](#)

Draft **Level 1 Guidance**

Not for implementation. Contains non-binding recommendations.

[f Share](#) [X Post](#) [in LinkedIn](#) [✉ Email](#) [🖨 Print](#)

Docket Number: [FDA-2023-D-1848](#)
Issued by: Center for Drug Evaluation and Research

Promising Treatment Models and Outcomes Involving Prescriptions

Research Background and Data Collection

- **Initial Community Interest from Harm Reduction Twitter**

- In February 2022, I asked harm reduction Twitter (X) their thoughts surrounding the concept of an MOUD-like option for stimulant use. The tweet received over 450 likes and 100 responses.

Has anyone ever looked into using adderall as medication therapy for meth use? I'm really annoying all my addiction medicine folks in my life with this one and I can't let it go after an old client said it would be the only way for them to stop using meth.

- **Qualitative Interviews**



Dates

January - July
2023



Interviewees

Clinicians &
researchers
(10)



Locations

US & Canada



Focus

Prescribing
practices for
StUD



Outreach

Cold emails &
consent forms

Prescribing Requires a Harm Reduction Framework

- **Individual Differences Determine Prescribing and Care Decisions**
 - Providers are finding that one prescribed medication does not work across the board for all patients, like it appears for most MOUD options.
 - Interviewees described how finding the best fit medication for a StUD patient is a lot like trial-and-error testing that is associated with stabilizing a patient's blood pressure.
 - They also found that valuing patient perspectives and their lived experiences fosters improved customized care and outcomes.
- **Moving Beyond Equating Successful Treatment with Abstinence**
 - Interviewees' emerging overall objective for prescribing is (1) mitigate harm by substituting consumption of unregulated drugs, (2) encourage reduced stimulant use, and (3) promote improved quality of life.
 - This way of thinking looks very different from how we typically define and promote "recovery", in which someone has to be completely abstinent from the substance they are being treated for.

Using less amounts is success, right? Using less days is a success. And abstinence is not the only pathway. Celebrating those other smaller successes, it's improving their quality of life.

Any improvement is improvement and for some folks that is trending towards abstinence and for other folks it's really just maintaining successes in other aspects of their lives.

Multifaceted Integrated Treatment Strategies Work

- **Combining Treatments**

- Multifaceted treatment plans may be more effective than relying on a singular prescription(s).
- Example: medications + psychotherapy techniques + contingency management.

- **Integrated Treatment Models and Retention**

- StUDs often coincide with other mental health and substance use disorders, but do not receive sufficient treatment for both simultaneously.
- The integrated treatment model delivers combined treatment for co-occurring disorders at the same time, rather than as siloed or sequential treatment.
- Several studies support this model by demonstrating that treating StUD with a prescribed amphetamine, improved patients' adherence to buprenorphine treatment.
- Interviewees expressed hope that with the expansion of integrated treatment, combined billing under Medicaid will follow suit.



The big carrot is the take home, right? You [don't] want to be required to come into the clinic every day and you've got to give up your meth use to get there.



Addressing StUD amidst Housing Instability

- **Context of Housing Instability and Challenges to Recovery**
 - Individuals unhoused may have a very high prevalence of StUD, as housing instability can
 - (1) increase chaotic stimulant use
 - (2) threaten one's safety, thus leading one to engage in survival-based stimulant use
 - Achieving full recovery among this population is difficult given substantial barriers to accessing integrated, tailored medical and behavioral treatment and safe and stable housing.
- **Strategies for Engagement**
 - Harm reduction approaches that build trust and engagement by meeting basic needs for food, shelter, and safety before insisting on immediate treatment has been successful.
 - Conducting active outreach to encampments and shelters and not waiting for individuals to come to clinics removes logistical barriers for individuals.
 - Integrating housing and wraparound programs and support can facilitate further engagement with medical and behavioral treatments.

When we were interviewing people [-], young women were describing how they do meth all night to stay awake because it was too dangerous to sleep during the night when they can't access proper shelters. It's a very dangerous city with a long history of violence towards women [-] So they're doing meth all night as a form of survival.

Patient Outcomes with Successful Treatment

- **Clinically Defining Treatment Success**

- Sustained treatment engagement and adherence was an important metric of success, regardless of reduction in use.
- Several interviewees highlighted the need for individualized goals and flexible definitions of success - what constitutes a "win" is dependent on each patient's circumstances and priorities.
- Overall, interviewees agreed that complete abstinence from the patient's drug of choice was unrealistic and that an improvement in the patient's quality of life better defined one's total success.



Prescribing Barriers Among Providers

Concerns about Safety, Efficacy, and Benefits vs Risks of Prescribing High Dose Stimulants

- **Little Data and Knowledge on Safety and Efficacy**
 - Some interviewees found that high doses of stimulants tend to produce near and sometimes more stabilizing effects in comparison to unregulated stimulants.
 - Many providers lack nuanced pharmacological knowledge and maintained discomfort around proper dosing, particularly with off-label and higher doses of prescription stimulants.
 - A consistent concern among providers was the risk and management of adverse cardiovascular side effects, such as an increase for hypertension, tachycardia, and arrhythmia.
 - Interviewees also communicated concerns around how prescribing high dose stimulants can have the potential to induce psychosis in a patient, which then can subsequently create a higher chance for a patient to put themselves in physical danger or having more run-ins with law enforcement.
 - Several interviewees interested in or actively prescribing stimulants for StUD, wonder if the benefits of prescribing outweigh the risks with current limited data and guidance.



Are we improving their quality of life? Or are we further harming them?"



Provider Liability and Monitoring Concerns

- **Cautious Prescribing Due to Liability and Monitoring Concerns**
 - A consistent question from the interviews: If a patient was to have a fatal or non-fatal event linked to an off-label controlled stimulant they were prescribed, will they, as a provider, be legally liable and/or sued?
 - Prescriptions for StUD do not have the same controls as MOUD, particularly buprenorphine, has for OUD.
 - Worries also emerged around the potential for investigations by licensing boards, the DEA, and that Medicaid may not approve off-label prescribing or caution against deviations from standards of care.
- **Clear Guidance on Regulations Would Enable Measured Innovation**
 - DEA restrictions on controlled substances and state laws create uncertainty about what prescribing practices are legally permissible or prohibited.
 - Guidance spelling out the regulations, legal boundaries, and parameters would provide reassurance to prescriber to cautiously explore measured innovations in treating StUD.

“
As of now, providers that are
doing stimulant replacement
are doing it either
underground or case by case.
”

“
There's been a lot of effort in
[the state] and I imagine
beyond to monitor providers
prescribing of scheduled meds.
”

Stigma and Misconceptions Among Providers

- **Stigma and Misconceptions around StUD**

- Providers can be hesitant or avoid treating patients and refer them out, due to perceptions that patients with StUD are difficult, chaotic, and aggressive.
- Patients often sense provider stigma and judgment when seeking help for stimulant use.
- Some providers mistakenly generalize treatment approaches from cocaine to methamphetamine despite distinct neurological effects, reflecting a lack of nuanced understanding and an overarching stigma in viewing all stimulant use as equally uncontrollable.
- Harm reduction approaches also may be seen as "enabling."
- More provider training and exposure, centered around harm reduction principles, is likely needed to reduce stigma and encourage compassionate care.

I think calling it what it is - it's fear based. It's from fear mongering from websites and videos and all these things. If we can address that head on, I think once people see others get better, it all changes.

Insufficient Expertise, Knowledge Sharing, and Philosophies

- **Scarcity of Accessible Addiction Specialists**
 - Most care often occurs in general medical settings by non-specialists, that do not feel equipped to treat StUD, especially in rural areas with even more limited access to specialists.
 - Integrated care models and Telehealth models can bridge existing gaps in expertise.
- **Philosophy of Treatment Programs and Accreditation**
 - Interviewees commented on how organizational cultures may cling to historical abstinence-only philosophies and that medical leadership may be resistant to new harm reduction approaches.
 - Interviewees also mentioned accreditation standards and metrics reinforce status quo of existing treatment protocols for StUD.
- **Lack of Best Practice Sharing**
 - Some interviewees felt professionally isolate, unaware of occurring innovative approaches and in need of a space to share experiences.
 - There is hope that the combination of pilots and emerging ASAM guidelines will influence the wider community to further discuss innovative prescribing and complimenting practices.

Key Take Aways

1. **StUDs are difficult to treat and involve off-label use of current prescription medications, behavioral interventions, and harm reduction.**
2. **With the rise in hospitalizations and overdoses involving stimulants, it is imperative that CRA and CM are incorporated into more treatment programs**
3. **Medications can be an important part of the treatment for StUD, but more research is needed to understand the benefits of existing medications.**
4. **Guidance for treating StUD is slowly developing at the national level, but not quickly enough in response to the growing need.**
5. **Providers are actively treating people with StUD, but they didn't begin without internal and external advocacy**

Questions?