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Co-occurring Opioid and Stimulant Use Disorders: Treatment and Management Approaches

Dr. J. Craig Allen, Medical Director, Rushford Center
Dr. Marc Fishman, Medical Director, Maryland Treatment Centers

March 21, 2023 from 2-3pm ET

Housekeeping

- You will be muted automatically upon entry. Please keep your phone line muted for the duration of the webinar.
- Webinar is being recorded and will be archived for future viewing at www.pcssNOW.org within 2 weeks.
- Submit questions in the Q&A box at the bottom of your screen.

Speakers

Craig Allen, MD
Medical Director of Rushford Center and Vice President of Addiction Services at Hartford HealthCare Behavioral Health Network

Marc Fishman, MD
Medical Director of Maryland Treatment Centers

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Disclosures
Craig Allen, MD

Craig Allen, MD, faculty for this educational activity, has no relevant financial relationship(s) with ineligible companies to disclose.

The content 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.

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Disclosures
Marc Fishman, MD

Marc Fishman, MD, faculty for this educational activity, has received a consulting fee from Alkermes, Indivior and Drug Delivery LLC. These relevant financial relationships have been mitigated.

The content 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 is to train healthcare professionals in evidence-based practices for the prevention and treatment of opioid use disorders, particularly in prescribing medications, as well for the prevention and treatment of substance use disorders.

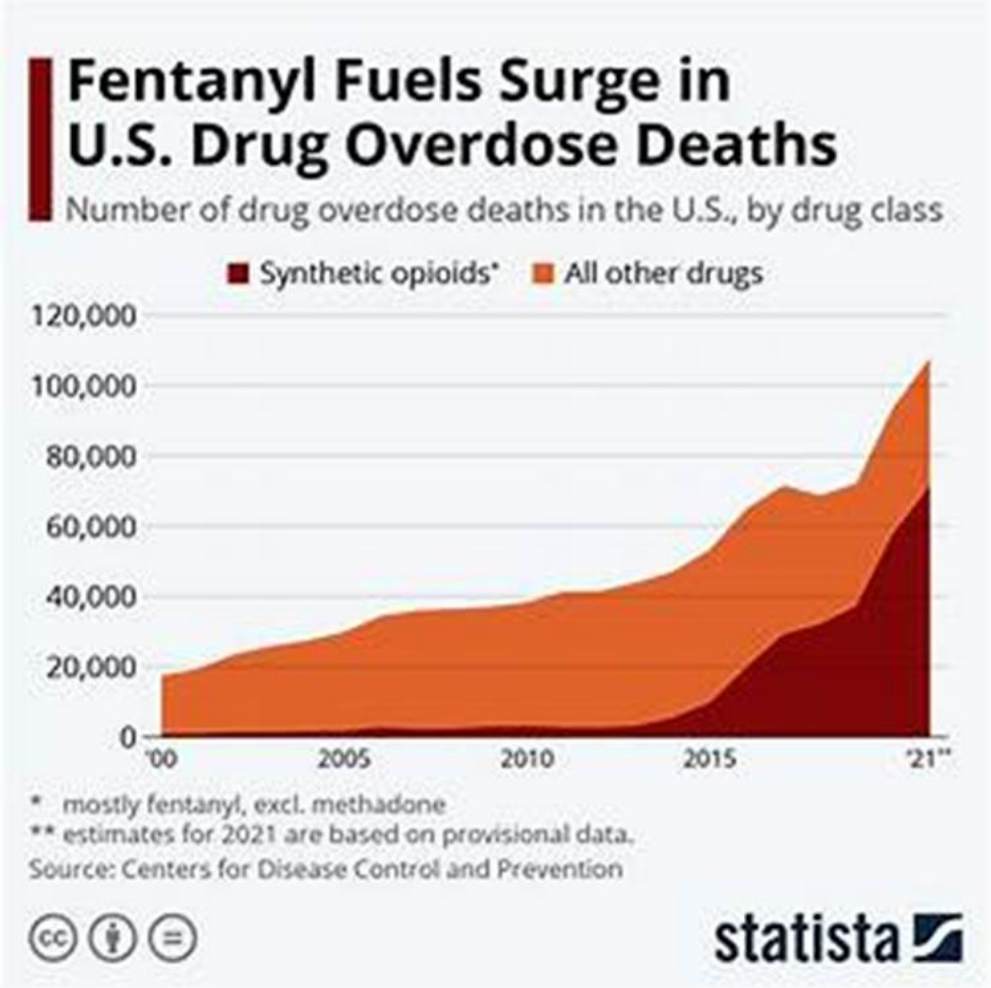
Educational Objectives

- At the conclusion of this activity participants should be able to:
  - Describe the broad context of co-occurring opioid and stimulant use and related overdose risk in the U.S.
  - Review evidence-based strategies for treating opioid use disorders and promising practices for treating stimulant use disorders
  - Identify evidence-based and promising strategies for treating co-occurring opioid and stimulant use disorders
  - Review psychiatric co-morbidities associated with opioid and stimulant use disorders

Outline

- Background – scope of the problem
- Medication treatments
- Psychiatric comorbidity
- Patient interview
- Summary recommendations
- Q&A

Scope of the problem



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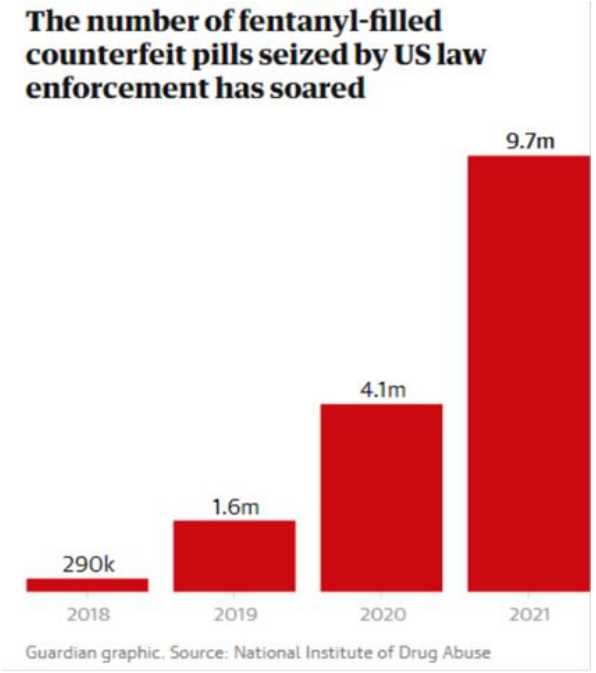
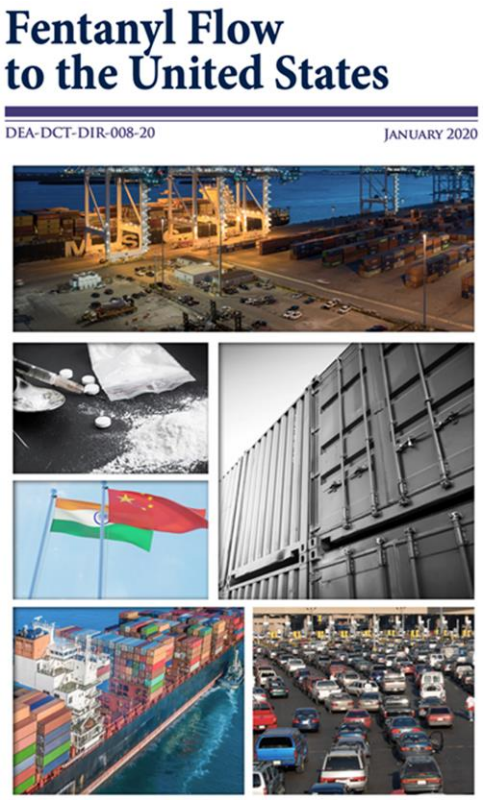
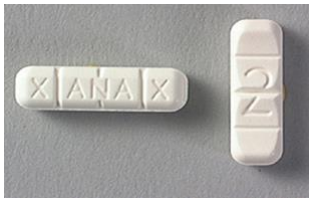
Scope of the problem

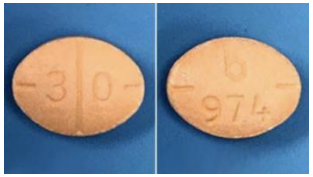




Illicitly Manufactured Fentanyl (IMF)

- Connecticut ranks 12th Nationally
- Blue M30
- White 2mg Xanax bars
- Adderall 30mg*





In 2022, DEA double fentanyl-laced, fake prescription pills seized in 2021. Also 131,000 pounds of methamphetamine, 4,300 pounds of heroin, and over 444,000 pounds of cocaine.

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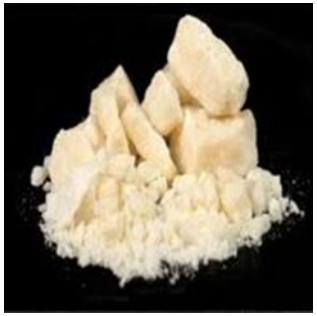
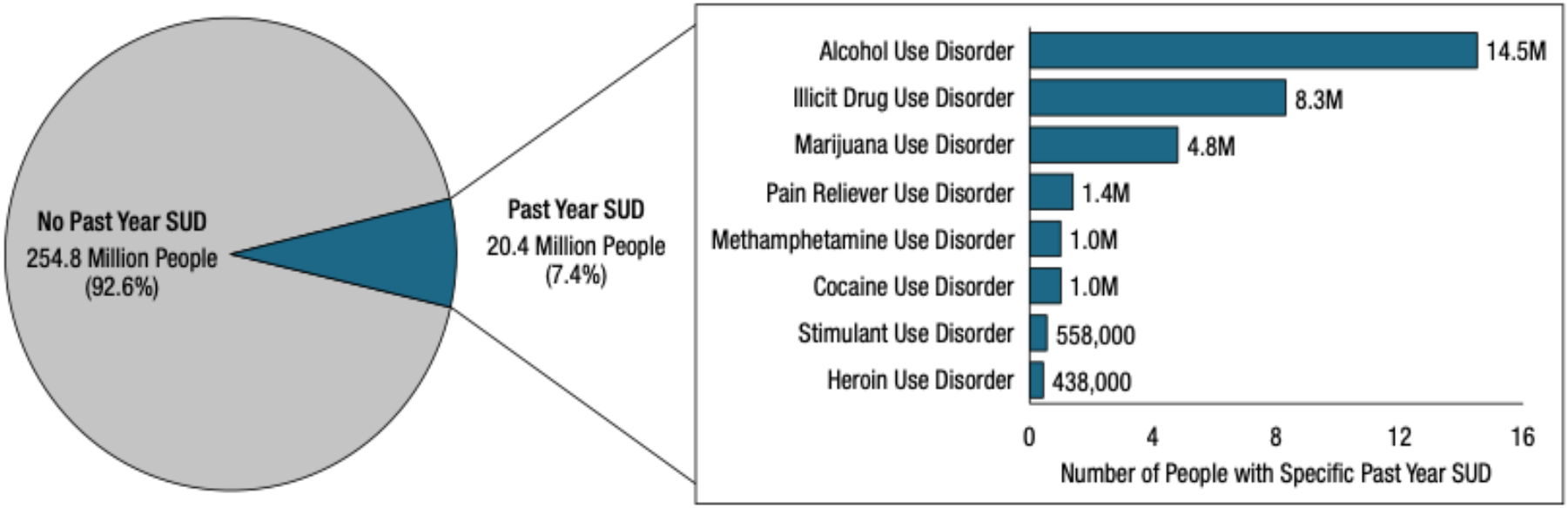
Scope of the problem



Cocaine –10-15% cocaine/crack supply contaminated with IMP

Prevalence

Figure 46. People Aged 12 or Older with a Past Year Substance Use Disorder (SUD): 2019



Note: The estimated numbers of people with substance use disorders are not mutually exclusive because people could have use disorders for more than one substance.

Past Year Methamphetamine and Cocaine Use

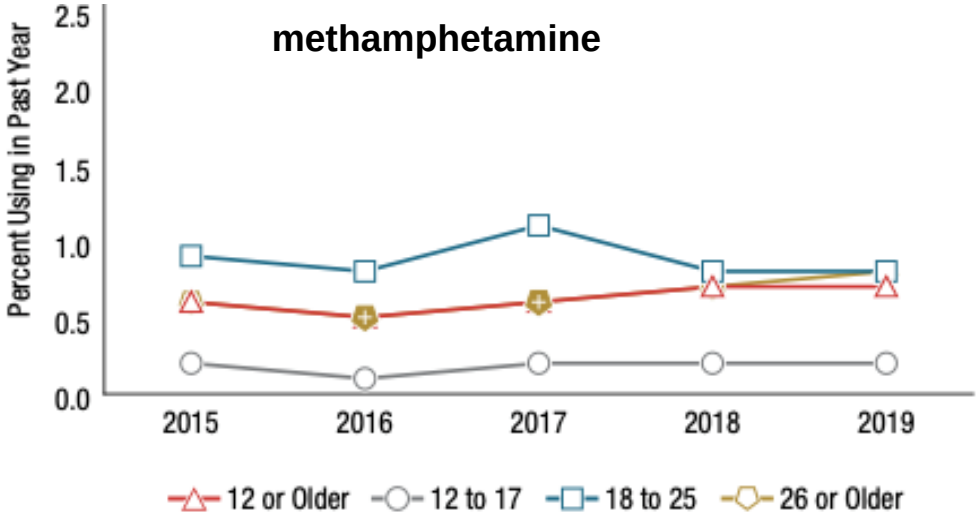
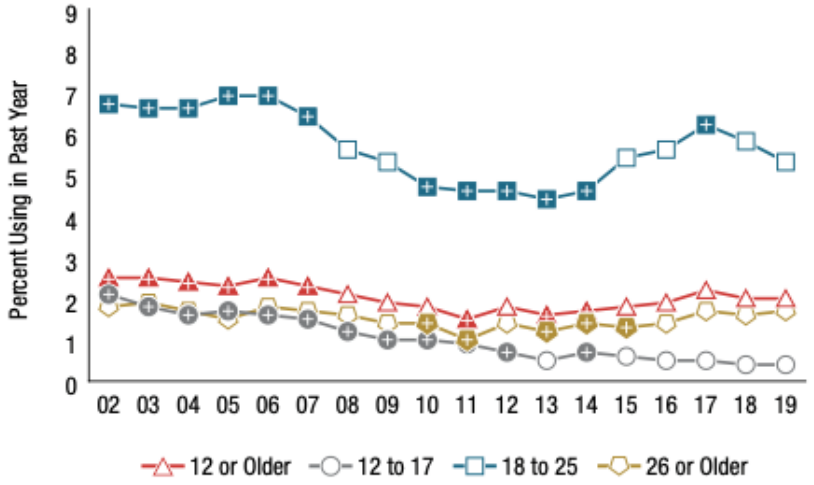


Figure 13. Past Year Cocaine Use among People Aged 12 or Older: 2002-2019



Source: NHSDUH

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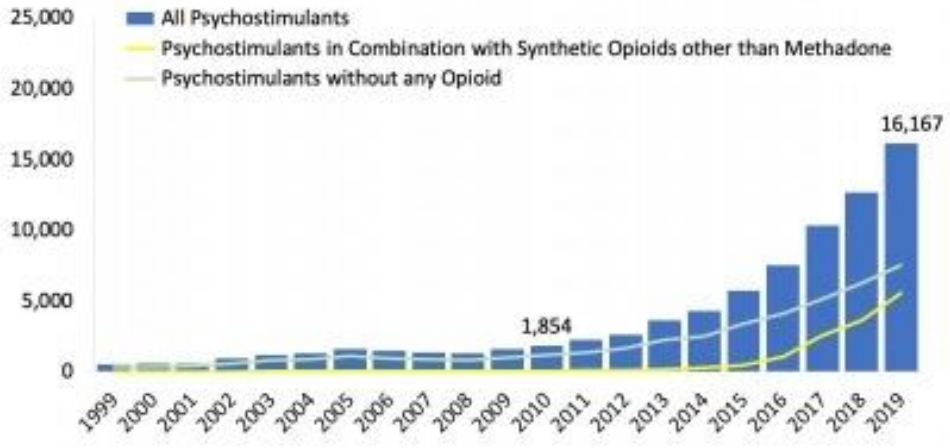
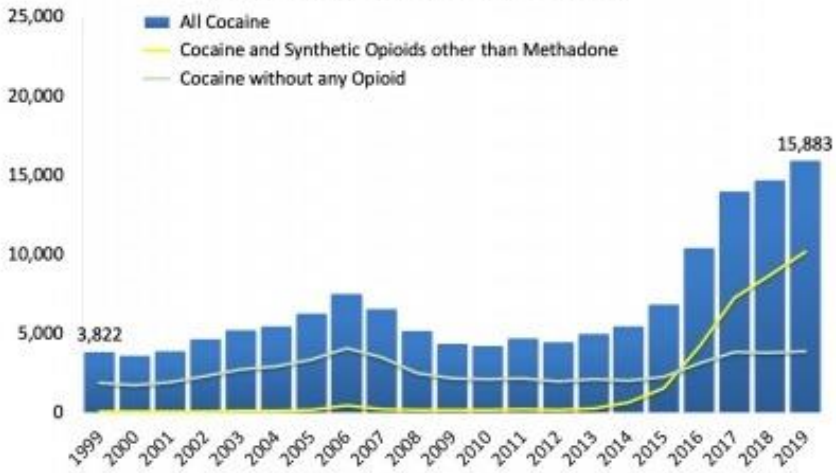
Overdose deaths
Methamphetamine, Cocaine alone and combined with Opioids

Figure 6. National Drug Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)*, by Opioid Involvement
Number Among All Ages, 1999-2019



*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 1999-2019 on CDC WONDER Online Database, released 12/2020.

Figure 7. National Drug Overdose Deaths Involving Cocaine*, by Opioid Involvement,
Number Among All Ages, 1999-2019



*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 1999-2019 on CDC WONDER Online Database, released 12/2020.

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Concurrent opioids + stimulants

- Very common
  - Past month use of methamphetamine doubled among treatment-seeking opioid users from 2011-2017 18.8 % to 34.2%
- Patient reported rationales --
  - Opioids take the edge off the stimulants, help come down
  - Stimulants improve functionality, energy, or wakefulness when using opioids.
  - Stimulants can be protective against opioid overdose ***Dangerous misperception***
- Unintentional fentanyl exposure also increasing with lacing of the street supply and fake prescription pills

Sources:
-Harrison, P et al., 2020, Drug Alcohol Rev. 39(7):914-23
-McNeil R, et al., 2020, Understanding concurrent stimulant use among people on methadone: A qualitative study. Drug Alcohol Rev. 39(3):209–15
-Lukac CD, et al., 2022, . Findings from the 2019 Harm Reduction Client Survey. Int J Drug Policy. 102:103602.
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-Blanken P, van den Brink W, Hendriks VM, et al., 2010, Eur Neuropsychopharmacology. 20(Suppl 2):S105–58

Biological hypothesis
We go together like…

- Chronic opioid exposure causes D2 hyperactivity and development of receptor super-sensitivity
- Opioid withdrawal as a state of exaggerated dopamine deficit
- Increased vulnerability to reinforcement by stimulants
- Reciprocally, stimulants may worsen opioid withdrawal, increasing opioid reinforcement

Strickland JC, Gipson CD and Dunn KE (2022) Dopamine Super sensitivity: A Novel Hypothesis of Opioid-Induced Neurobiological Mechanisms Underlying Opioid-Stimulant Co-use and Opioid Relapse. Front. Psychiatry 13:835816.

Medications for stimulant use disorder

- Enormous need
- Many attempts to find efficacy
- No home runs, nothing FDA-approved
- But some promising, and well worth trying

MOUD in Stimulant Use Disorder
Buprenorphine and XR-NTX Safe but Underutilized

Large (N=179K) multistate claims dataset over course of 1 yr

Findings:

- MOUD broadly safe and effective with other co-occurring SUDs including stimulants
- No difference in occurrence of OD or poisonings
  - Unfortunately,
    - other co-occurring SUDs reduce likelihood of MOUD compared to OUD alone (47% vs 30%; RR 0.66 for stimulants)
    - Lower adherence to treatment protocols by patients
    - Low tolerance of programs for with active co occurring stimulant use disorder

Xu et al. Comparative Effectiveness Associated With Buprenorphine and Naltrexone in Opioid Use Disorder and Cooccurring Polysubstance Use. JAMA Network Open. 2022;5(5):e2211363.

Stimulants
Methamphetamine vs Cocaine

- Both very high potency stimulants
- Overlapping clinical profiles and biology
- Regional and cultural differences in use patterns
- More similar than not
- More studies targeting cocaine than methamphetamine, expectation of dual coverage for medication treatments

Medications for stimulant use disorder
Agents that show promise

- Agonists
  - Mixed amphetamine salts (MAS), dextroamphetamine, methylphenidate, modafinil
- Topiramate
- Naltrexone
- Bupropion
- Topiramate + prescription stimulants
- Bupropion + Naltrexone
- Disulfiram
- Mirtazapine
- Buprenorphine (+ Naltrexone)

Prescription stimulants for stimulant use disorder
Possible implementation issues

- Attitudes
- Diversion and misuse
- Side effect profile and monitoring (mood, insomnia, BP)
- Duration of supply
- Medical staffing
- Direct administration (OTP-style?)

XR-Naltrexone for stimulant use disorder: Possible implementation issues

- Insurance coverage
- Q3 wk dosing
- Concern about co-use of opioids
- Medical staffing
- Patient acceptability
- What about adding bupropion?
- What about adding buprenorphine?

Therapy for Stimulant Use Disorder

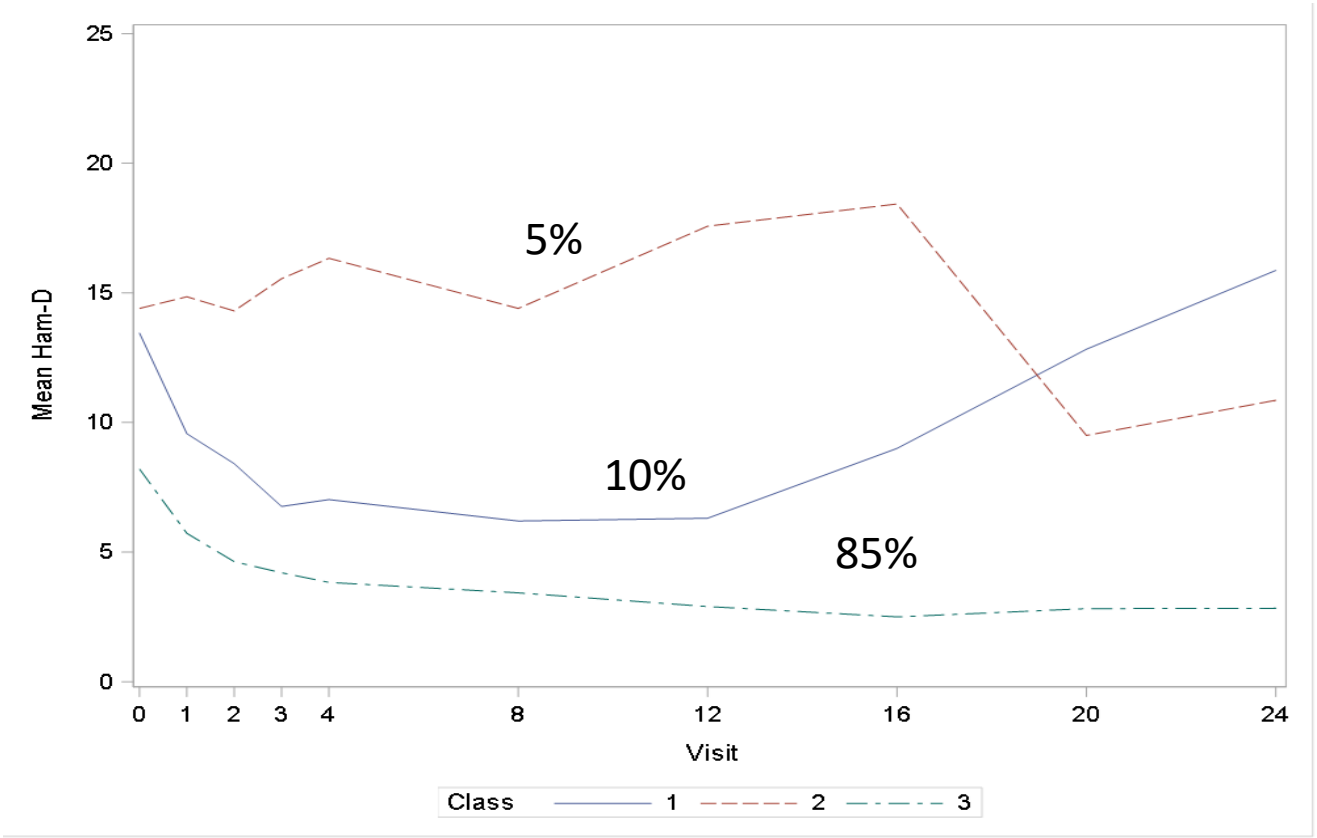
- Cognitive-behavioral and contingency management interventions.
  - Ex. the Matrix Model—a 16-week treatment approach that combines behavioral therapy, family education, individual counseling, 12-step support, drug testing, and encouragement for non-drug-related activities.
- Contingency management interventions, tangible incentives in exchange for engaging in treatment and maintaining abstinence.
  - Ex. Motivational Incentives for Enhancing Drug Abuse Recovery (MIEDAR), incentive-based method promoting cocaine and methamphetamine abstinence, NIDA's National Drug Abuse Clinical Trials Network.

Psychiatric co-morbidity

Depression in OUD

Depression improves with MOUD in **most, but not all** OUD patients

HAM-D scores across time in XBOT MOUD study



Vest N, Wenzel K, Choo T-H, Pavlicova M, Rotrosen J, Nunes E, Lee JD, Fishman M. Trajectories of depression among patients in treatment for opioid use disorder: a growth mixture model secondary analysis of the XBOT trial. *Am J Addict*. 2023; 1- 10.

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Psychiatric co-morbidity
Stimulants

- Depression , ADHD, Psychosis, Anxiety, insomnia, ***bipolar disorder***

- Presents questions for treatment
  - Acute presentation
  - Longer term

- Management of acute intoxication/withdrawal
    - benzodiazepines, beta-blockers, antiarrhythmic agents, and antihypertensive medications
  - Agitation
  - Psychosis
  - Sleep disturbance

Co-occurring disorders diagnostic approaches: Sensitivity vs specificity

Take a stance

- Wait for the possibility of spontaneous resolution
  - Better diagnostic precision
  - Less possibility of unnecessary treatment
  - Less opportunity for early and effective treatment

- Move ahead with a presumptive diagnosis
  - Less diagnostic precision
  - Possibility of over-aggressive treatment
  - Better opportunity for earlier and more effective treatment

Approaches to treatment
Co-occurring psychiatric disorders

ADHD

- History of rapid spontaneous sx resolution probably predictive
- Pre-existing versus precipitated attentional issues
- Psychiatric Rx can be an engagement tool

Psychosis, depression, insomnia, bipolar (mania, depression, irritability, lability)

- History of rapid spontaneous sx resolution probably predictive
- But lingering sxs productive target for treatment

Insomnia

- low hanging fruit for relief

Depression

- Are mirtazapine or bupropion preferred anti-depresants?

Persistent psychosis and depression poor prognosis, but treat aggressively

Psychosis and Stimulants

- Common presentation in acute intoxication
- >50% develop psychotic sxs

- 80% resolution with 30d abstinence, but 10-15% persistence

- Common vulnerability: schizophrenia incidence 5x greater in relatives of those with meth-induced psychosis

Approaches to treatment for all Substance Use Disorders

ENGAGEMENT is KEY

- + PEERS/Recovery Support Specialists

- Harm reduction strategies. Eg. nPEP or PrEP, screen for infections, education on “overamping”, plan for treatment while lowering the barriers to access when someone is ready

- Naloxone for everyone
  - Naloxone saturation in a community saves lives

Patient interview

patient interview recording

Stimulant use disorder medications: Summary conclusions

- Maybe not home runs, but very solid doubles, esp in the absence of anything better
- Are these ready for prime time? YES
- Does effect for one stimulant generalize to the other? Probable overlap
- What about real world conditions
  - Patients, logistics, attrition, adherence, monitoring and support, insurance coverage

Case

- 48 M longstanding smoked cocaine, injection heroin, multiple treatment dropouts
- Stabilized on buprenorphine with opioid abstinence, but continues cocaine
- Topiramate titration to 300 mg/d, subjective reduction in craving, use reduced but persistent
- Side effects leading to topiramate dose reduction
- Addition of Mixed Amphetamine Salts - extended release (MAS-ER), titration to 50 mg/d, gradual improvement, best retention to date, intermittent HTN

Case

- 36 M chronic methamphetamine, hospitalized following suicidal depression with paranoid delusions, treated with SSRI and aripiprazole
- Intermittent relapse to MA but retained in OP treatment
- Switch SSRI to bupropion, switch to more sedating antipsychotic and titrate with waxing/waning psychosis and insomnia
- Add naltrexone, add topiramate

Overall
Conclusions, questions and next steps

- Very exciting to see our tool chest expanding! (although we can anticipate adoption will lag)
- MOUD-forward approaches, no reason to shy away because of concurrent stimulants
- Shouldn’t we aspire to a standard in which every patient offered full menu of options including these? What will it take?
- What about possible augmentation effects of more intensive counseling? CM?
- What about patient selection and treatment matching strategies? Sequencing?
- More shall be revealed – stay tuned for further research and real world experience

Never give up

- Therapeutic optimism is itself a very powerful intervention
- Persistent engagement despite struggles
  - Treatment should not require already being cured
  - Treatment should be offered for co occurring medical, psychiatric and SUDs
  - Harm reduction strategies should be employed
- Re-engagement after drop-out and relapse
  - Discussion and plan can help facilitate return
- Higher levels of care as available

Take home messages

- Try any and all of these
- Increasing treatment effectiveness even a little would be worthwhile. Any engagement in treatment for longer retention would be worthwhile.
- Prescription stimulants maybe most promising (but potential adoption barriers)
- Naltrexone (+/- bupropion), topiramate, disulfiram
- If able to retain, consider combos and serial trials
- **Therapeutic optimism remains our best tool!**

There will not be a quiz!
(…but maybe Q&A)

References

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- Trivedi et al. Bupropion and Naltrexone in Methamphetamine Use Disorder N Engl J Med 2021;384:140-53**.**
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PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder.
- PCSS Mentors are a national network of providers with expertise in **addictions, pain, evidence-based treatment including medications for opioid use disorder (MOUD)**.
- 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:

https://pcssNOW.org/mentoring/

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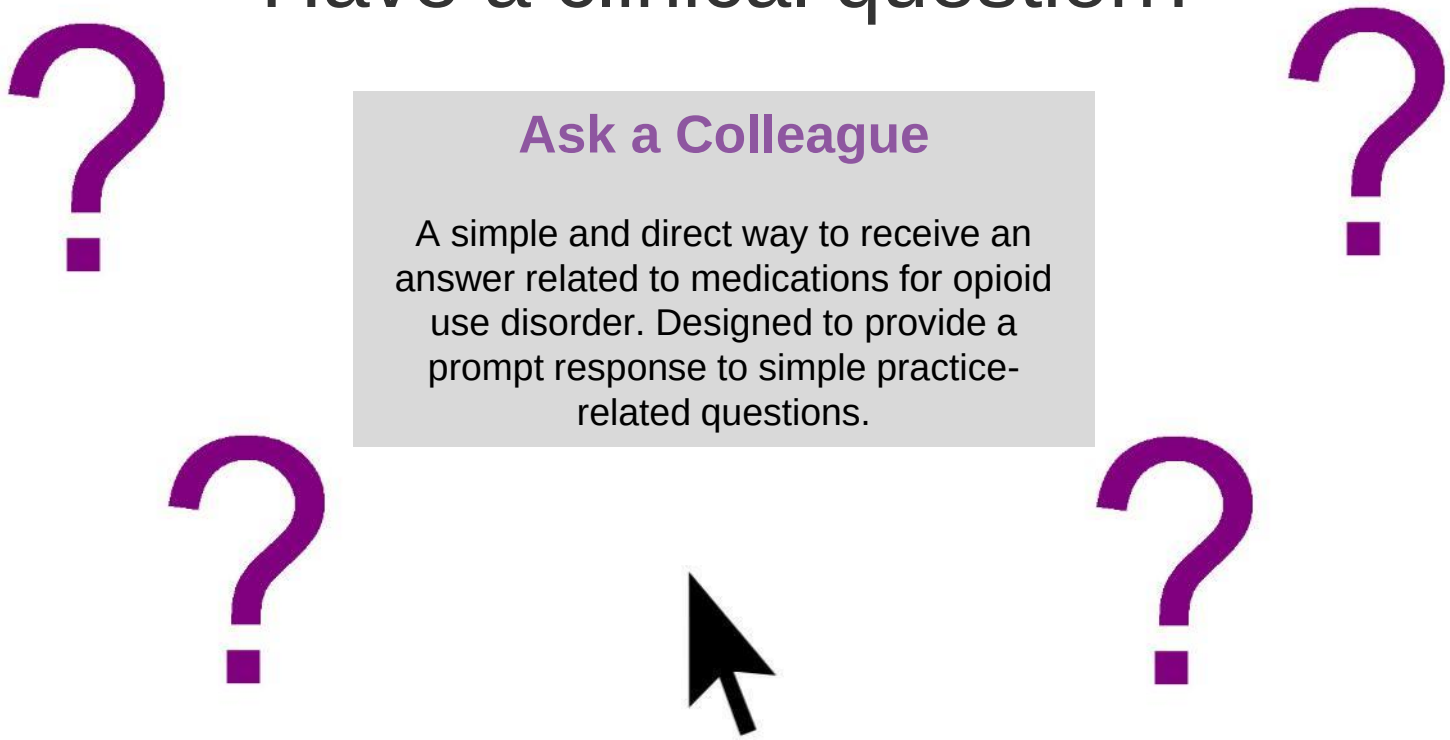
PCSS Discussion Forum

Have a clinical question?



Ask a Colleague

A simple and direct way to receive an answer related to medications for opioid use disorder. Designed to provide a prompt response to simple practice-related questions.

http://pcss.invisionzone.com/register

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American Academy of Pain Medicine	Association for Multidisciplinary Education and Research in Substance use and Addiction
American Academy of Pediatrics	Council on Social Work Education
American Pharmacists Association	International Nurses Society on Addictions
American College of Emergency Physicians	National Association for Community Health Centers
American Dental Association	National Association of Social Workers
American Medical Association	National Council for Mental Wellbeing
American Osteopathic Academy of Addiction Medicine	The National Judicial College
American Psychiatric Association	Physician Assistant Education Association
American Psychiatric Nurses Association	Society for Academic Emergency Medicine

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