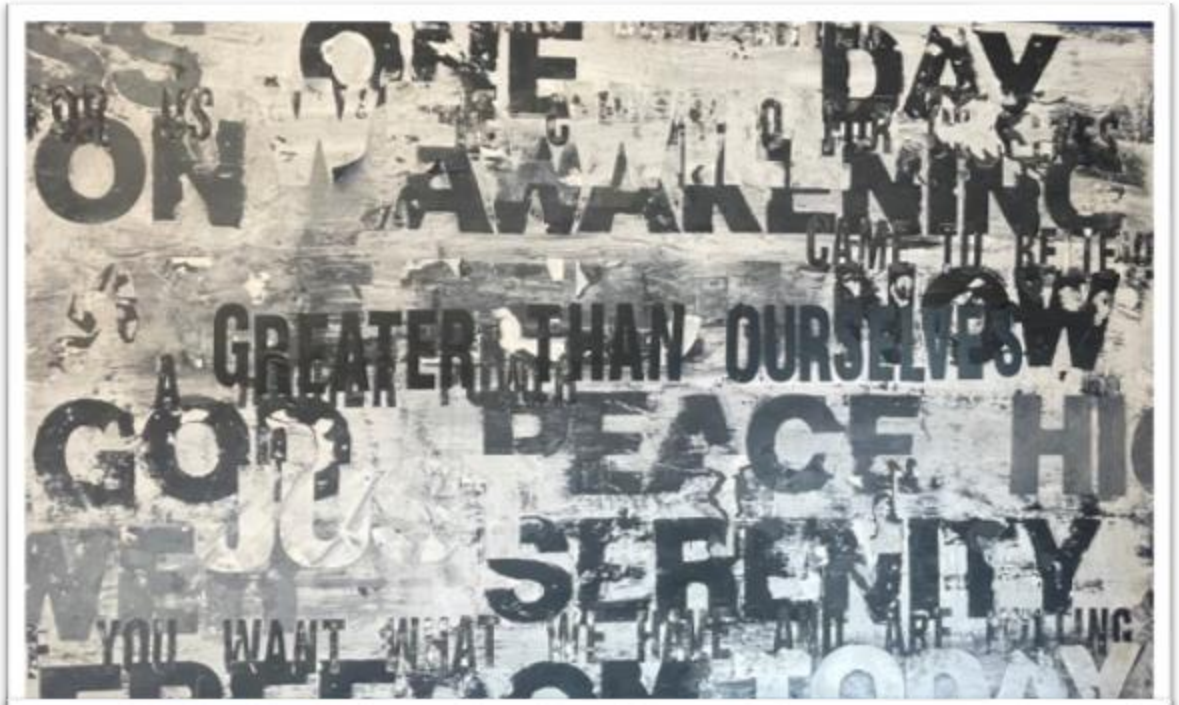


Stimulants: Cocaine & Methamphetamine

CRIT/FIT/CFS program – April 2024

Marielle Baldwin, MD, MPH

CARE Clinical Addiction Research and Education

Grayken Center for Addiction
Boston Medical Center

Disclosures

I have no financial or other perceived conflicts of interest to disclose in relation to this presentation

Learning Objectives

At the end of this session, participants will be able to:

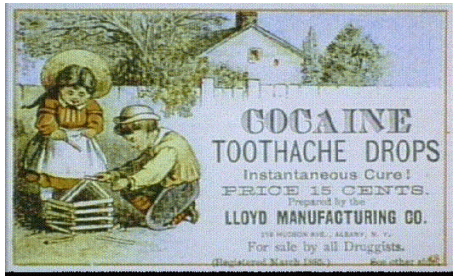
1. Understand how and why people use stimulants
2. Name the medical complications of stimulant use
3. Describe the current options for treatment of stimulant use disorders
4. Identify the characteristics of stimulant intoxication and techniques to manage overamping

Basics of Cocaine & Methamphetamine

Overview: Cocaine

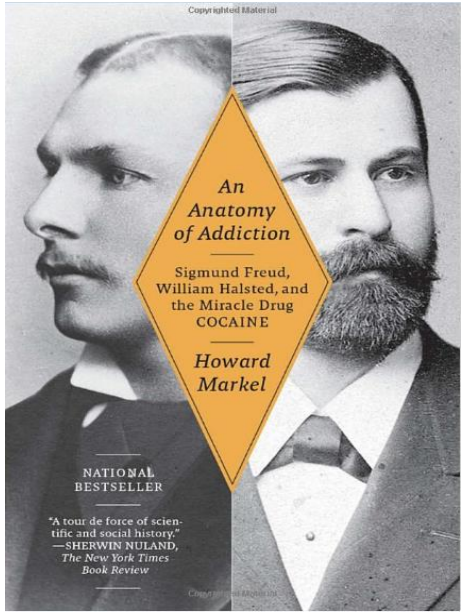
Derivative: erythroxylum coca leaves in Andes

History of Use:
Used in medicines and beverages until early 1900s



1885 Advertisement for Cocaine Toothache Drops

Street preparations 10-50% cocaine
Hydrochloride powder is sniffed or injected; *Blow, Snow, Powder*
Alkaline rocks (aka crack) are smoked; *Crack, Rock, Base*



Routes of Use: Intranasal, Intravenous, smoked/inhalation

Metabolized: Rapidly absorbed, metabolized (liver), and excreted in the urine.
Benzoylecgonine = metabolite

Prevents the reuptake of dopamine

Half-Life: IV 20-60 min, IN 60-90 min, smoked 5-15 min
IN slower onset and prolonged action v. IV or smoked.

Acute Medical Risks: myocardial infarction, arrhythmia, heart failure, hyperthermia, rhabdomyolysis, acute kidney injury, psychosis, death

Overview: (Meth)amphetamine

Derivative: lab derived from ephedrine components

Tina, Speed, Crystal, Crank, Ice, Meth

History of Use: 1893 methamphetamine first synthesized in Japan as decongestant

Route of Use: Inhalational, Intranasal, Intrarectal, Intravenous

Metabolized: Renal and hepatic clearance, highly bioavailable, slowly metabolized

Increases dopamine in synaptic terminal **AND prevents its reabsorption**

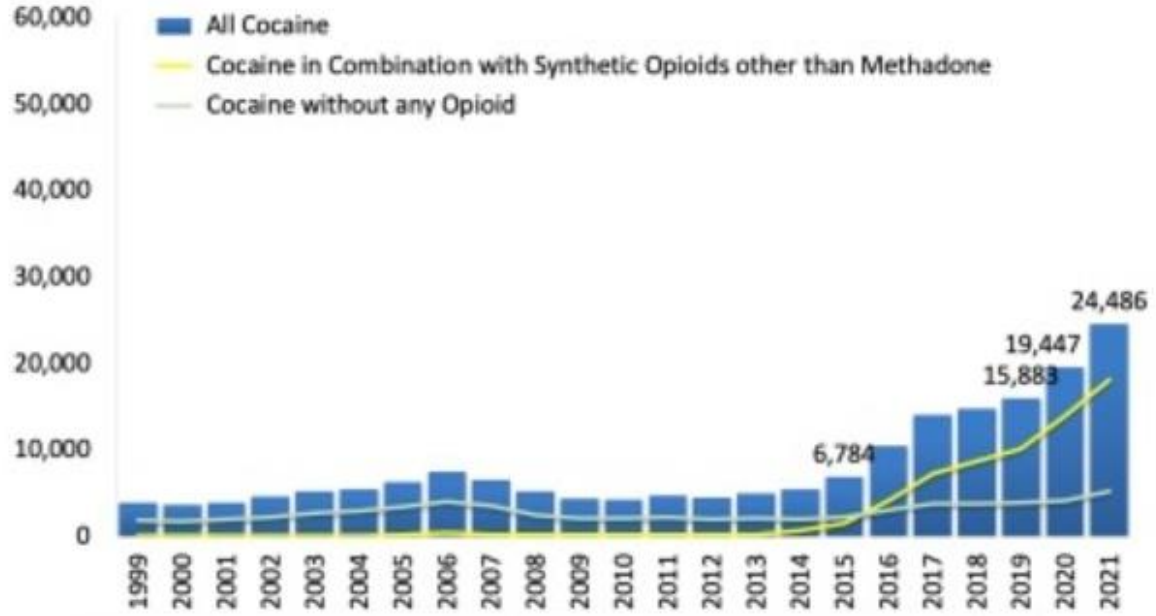
Half-Life: Peaks ~2-4 hours after use
Long ½ life, between 10-12 hours, independent of route of use

Acute Medical Risks: myocardial infarction, arrhythmia, heart failure, hyperthermia, rhabdomyolysis, acute kidney injury, psychosis (neurotoxicity), death

Epidemiology

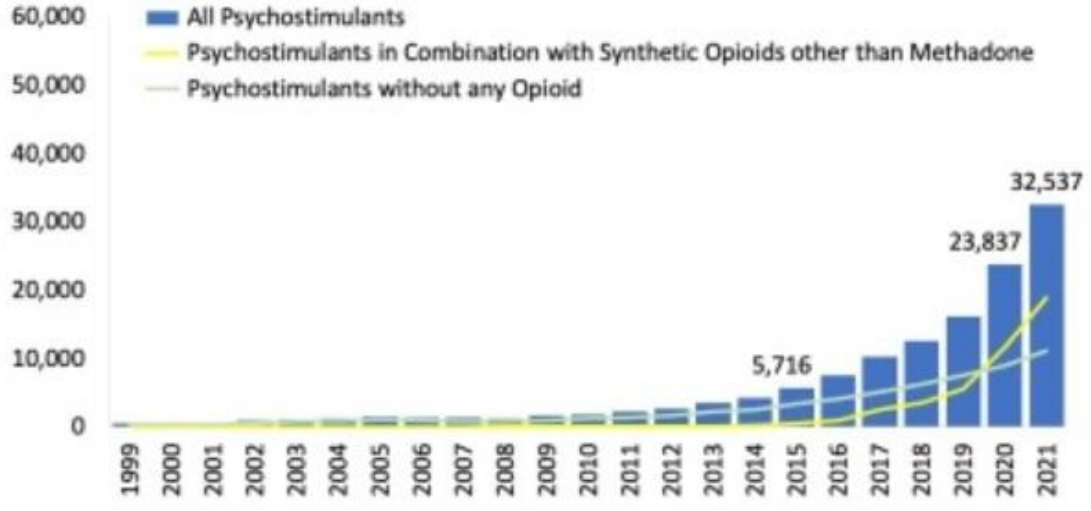
Stimulant-involved overdose deaths surging with opioids

Figure 8. National Drug Overdose Deaths Involving Cocaine*, by Opioid Involvement, Number Among All Ages, 1999-2021



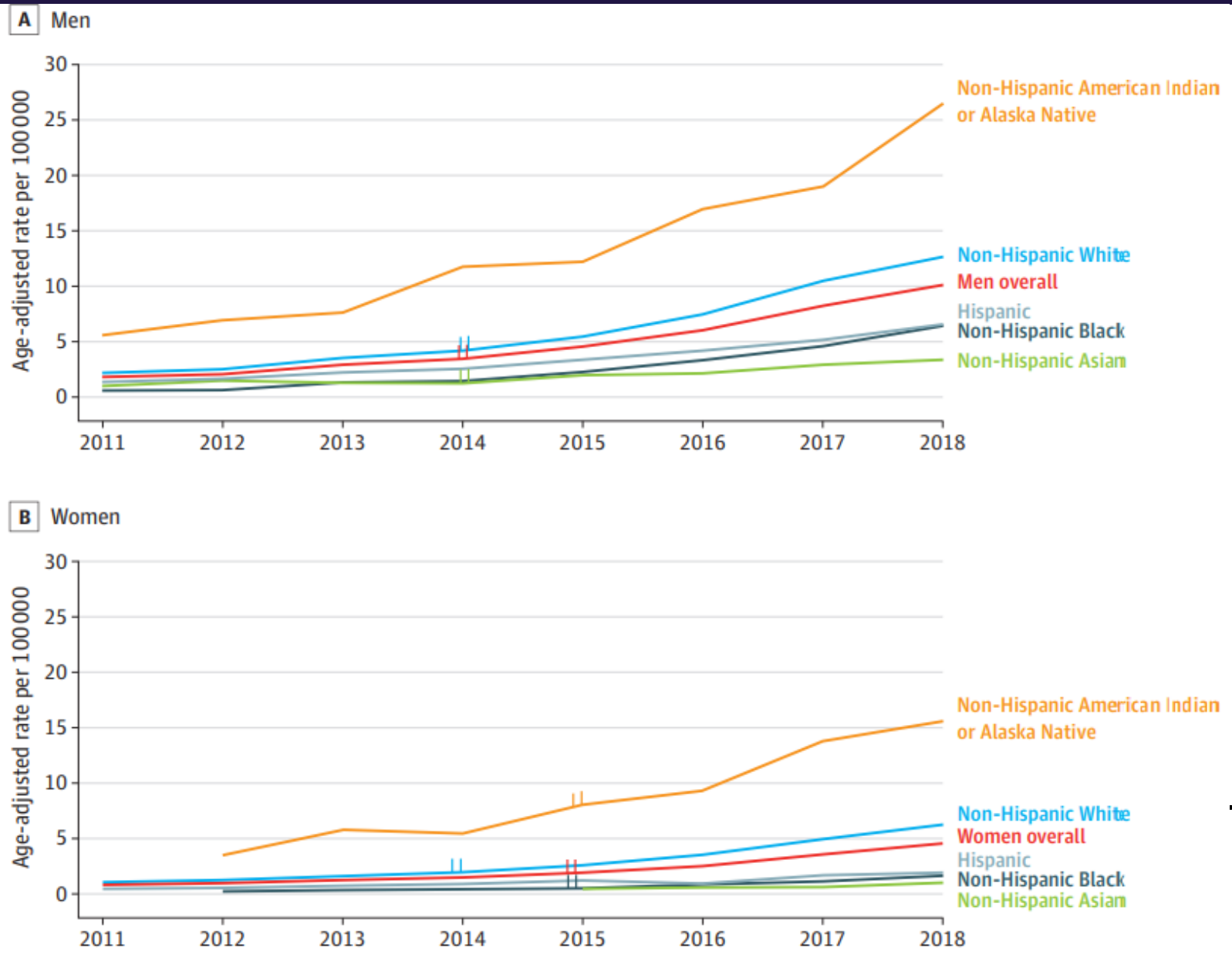
*Among deaths with drug overdose as the underlying cause, the cocaine category was determined by the T40.5 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2021 on CDC WONDER Online Database, released 1/2023.

Figure 7. National Overdose Deaths Involving Psychostimulants with Abuse Potential (Primarily Methamphetamine)*, by Opioid Involvement, Number Among All Ages, 1999-2021



*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 1999-2021 on CDC WONDER Online Database, released 1/2023.

Disparities in Methamphetamine-Involved Overdose Deaths



- Native American/ Indigenous communities have the highest rates of methamphetamine related overdose death
- Overdose rate for AI/AN men: 26.4/100,000
- Overdose rate for AI/AN women: 15.6/100,000

Han et al, JAMA Psych, 2021

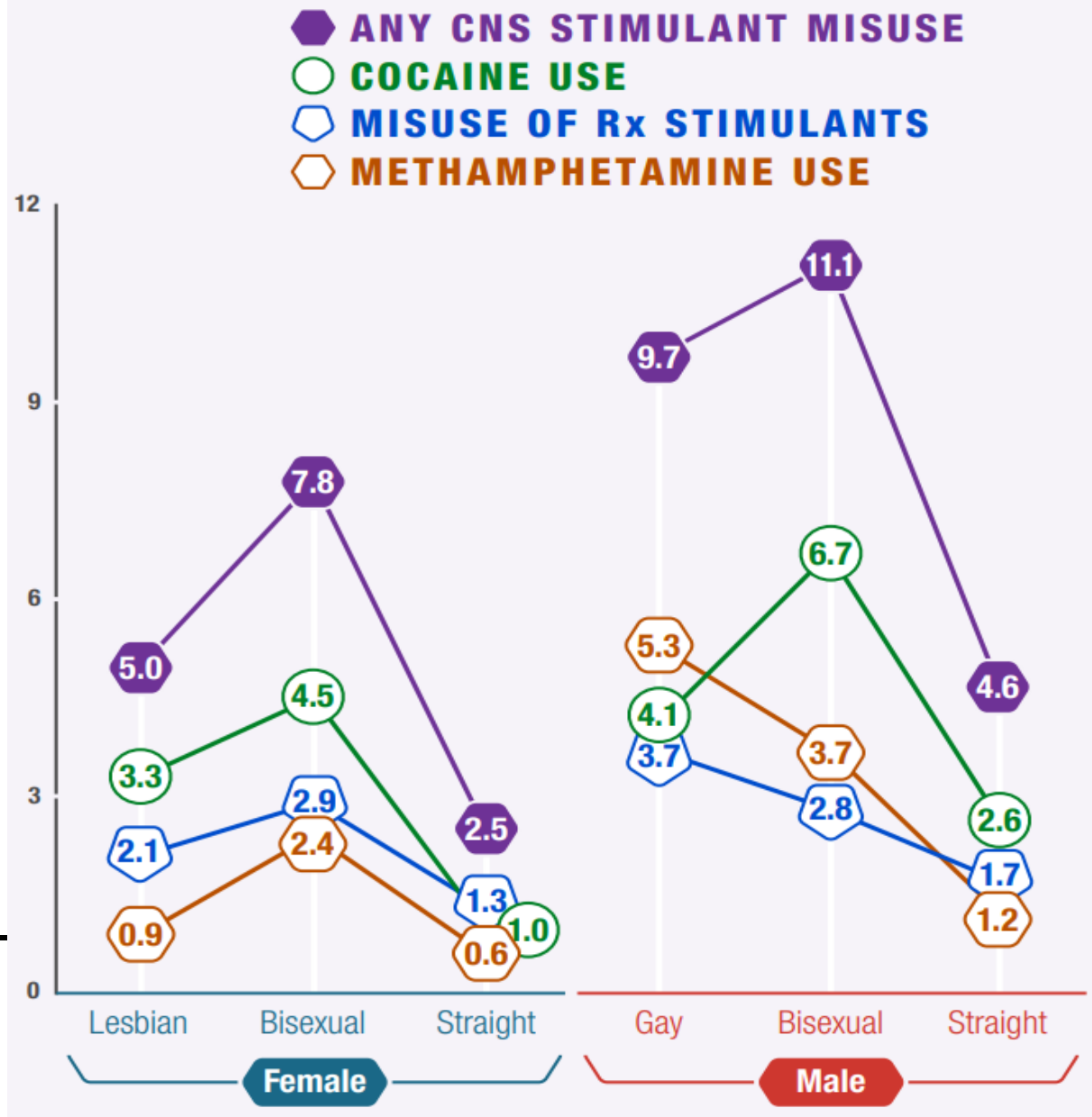
CARE Clinical Addiction Research and Education

Grayken Center for Addiction
Boston Medical Center

Stimulant Use and Sexuality

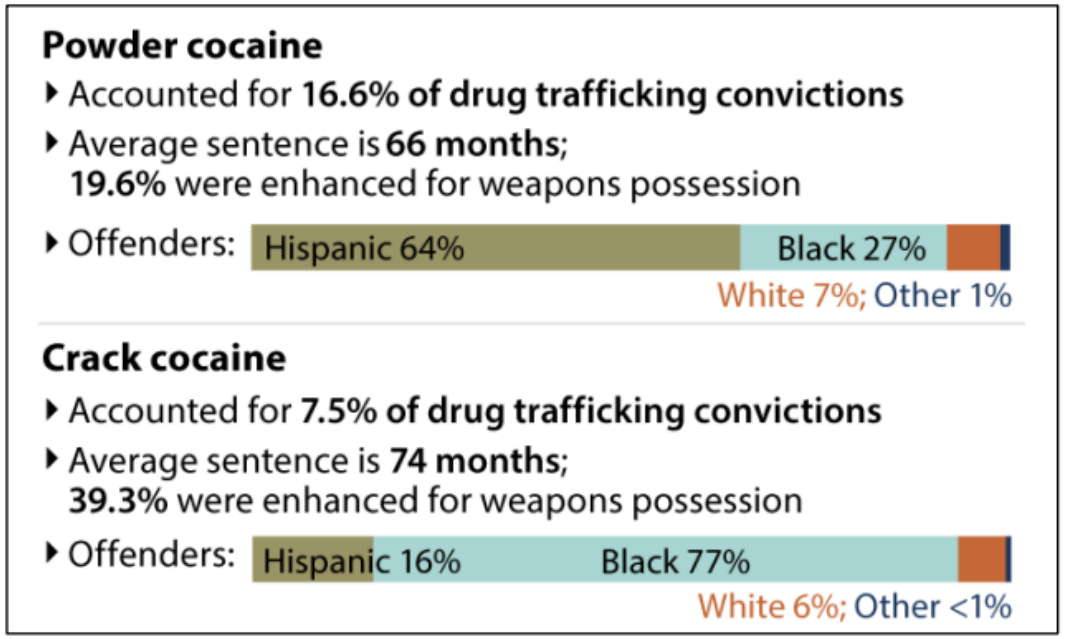
- Sexuality diverse patients are twice as likely as heteronormative counterparts to have any type of stimulant use disorder
- Highest rates of methamphetamine use are among gay identifying men
- Highest rates of cocaine use among bisexual men and women

SAMHSA, 2023



Legacy of Structural Racism

Figure 1. Federal Cocaine Trafficking Convictions, FY2020



Source: CRS presentation of data from U.S. Sentencing Commission, *Quick Facts: Powder Cocaine Trafficking Offenses*, June 2021; and U.S. Sentencing Commission, *Quick Facts: Crack Cocaine Trafficking Offenses*, June 2021.

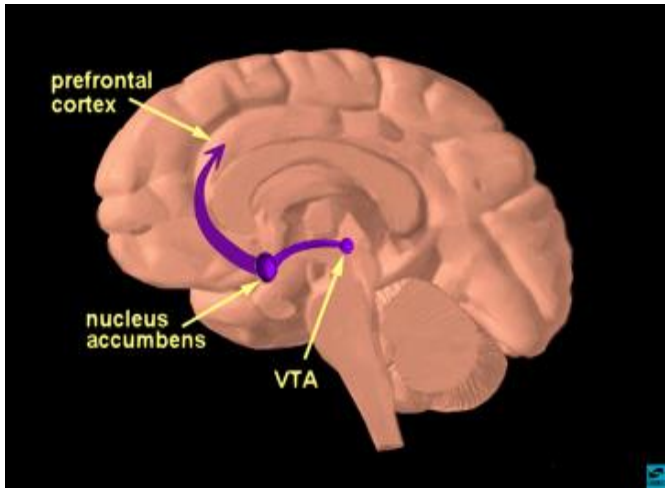
- **1972 Controlled Substances Act**: did not distinguish powder from crack cocaine
- **1986 Anti Drug Abuse Act:** mandatory min sentencing for trafficking (100:1 ratio - 5 yrs for 5g crack vs 500g of powder)
- **1988 Anti-Drug Abuse Act**: 5 year min for simple possession of crack
- **2010 Fair Sentencing Act:** reduced sentencing disparity to 18:1 ratio crack:powder cocaine
- **2018 First Step Act:** applied the 2010 rules retroactively and allowed for resentencing

SAMHSA, 2020; NSDUH, 2015

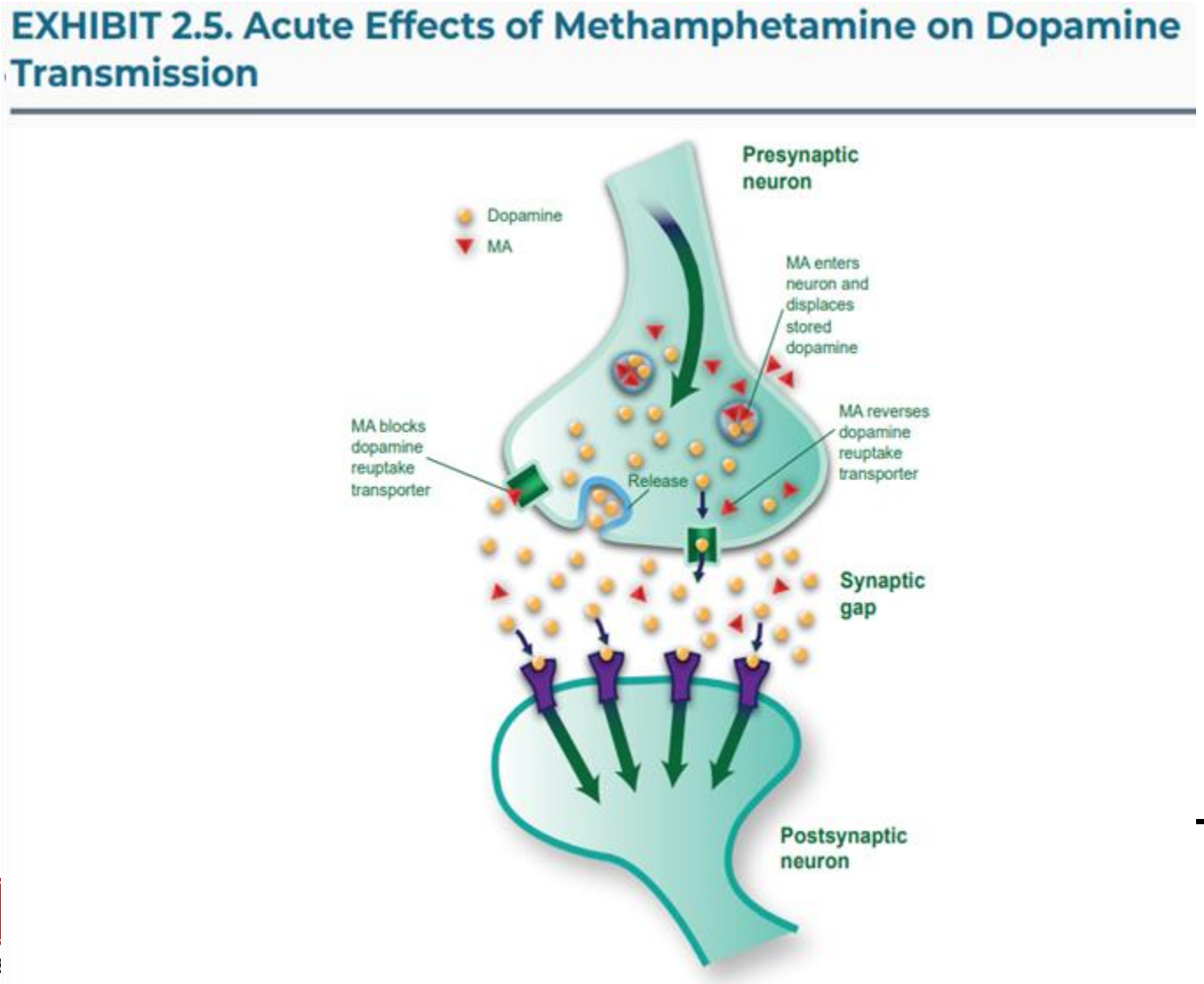
Stimulants: Why & How

Why do people use stimulants?

- Euphoria / rush
  - Onset and intensity depends on delivery method
- Increased energy, attention/focus
- Increased vigilance (survival)
- Diminished social inhibition
- Sexual enhancement (libido)
- Decreased appetite
- To counteract the sedative effect of opioids



Neurochemical Impact



- Cocaine prevents the reuptake of dopamine from the synapse.
- Methamphetamine both increases dopamine in the synaptic terminal **AND** prevents its reabsorption.
- **Excessive dopamine with stimulant use is responsible for many of the motor and mood symptoms**
- Alternatively, a dopamine deficit with abstinence contributes to the typical acute and post-acute withdrawal symptoms

(Paulus & Stewart, 2020)

PK: Cocaine

	IV	Smoked	Snorted
Time to effect	10-60sec	3-5sec	1-5min
Peak concent.	3-5min	1-3min	15-20min
Half-life	20-60min	5-15min	60-90min

Lange, R. A. and L. D. Hillis (2001). "Cardiovascular complications of cocaine use." N Engl J Med **345**(5): 351-8.

PK: Methamphetamine

	IV	Smoked	Snorted	Ingested
Time to effect	15-30 sec	Immediate	3-5 min	15-20 min
Peak concent.	2-4 h	2-4 h	2-4 h	2-4 h
Half-life	10-12 h	10-12 h	10-12 h	10-12 h

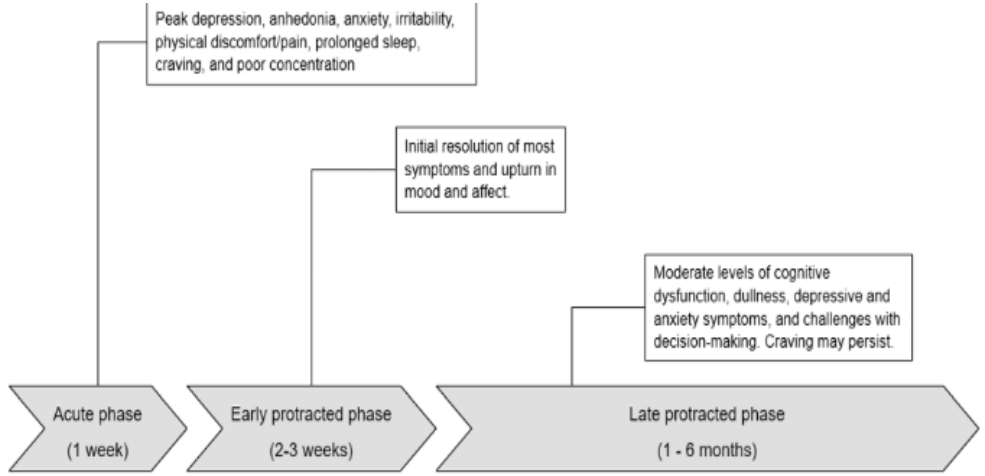
Lineberry 2006

Binge Patterns of Use

- Binge patterns may include using sporadically or may occur multiple days in a row and may be common with early use.
- During a binge, initial substance use increases the desire to use more.
- Decreased desire to use varies based on stimulant:
  - Cocaine – 46 hours
  - Methamphetamines – day 4-5
- Binge use patterns may result in more severe side effects and adverse events at the end of a binge episode.

Psychostimulant Withdrawal

- 53-97% of people experience withdrawal with abstinence after prolonged use
- Dopamine stores may take 12-18 months to recover, if at all, after chronic methamphetamine use
- Withdrawal symptoms may last *weeks to months*:
  - **Acute (1-7 days):** (severe) depression, anhedonia with suicidal ideation, anxiety, fatigue with hypersomnia or insomnia, intense cravings, poor concentration, irritability, physical discomfort (myalgias), psychomotor retardation or agitation
  - **Post-acute (early protracted, 2-4 wks):** vivid/unpleasant dreams, intermittent cravings w/nighttime awakenings
  - **Late protracted (> 4 weeks):** mild cognitive dysfunction, ”cognitive dullness”, impairments in memory and executive functioning, moderate depression/anxiety intermittent cravings



Li, M; Shoptaw, S; Addiction, 2022

FIGURE 1 Summary of stimulant withdrawal symptoms across different phases (with time-frame following abstinence)

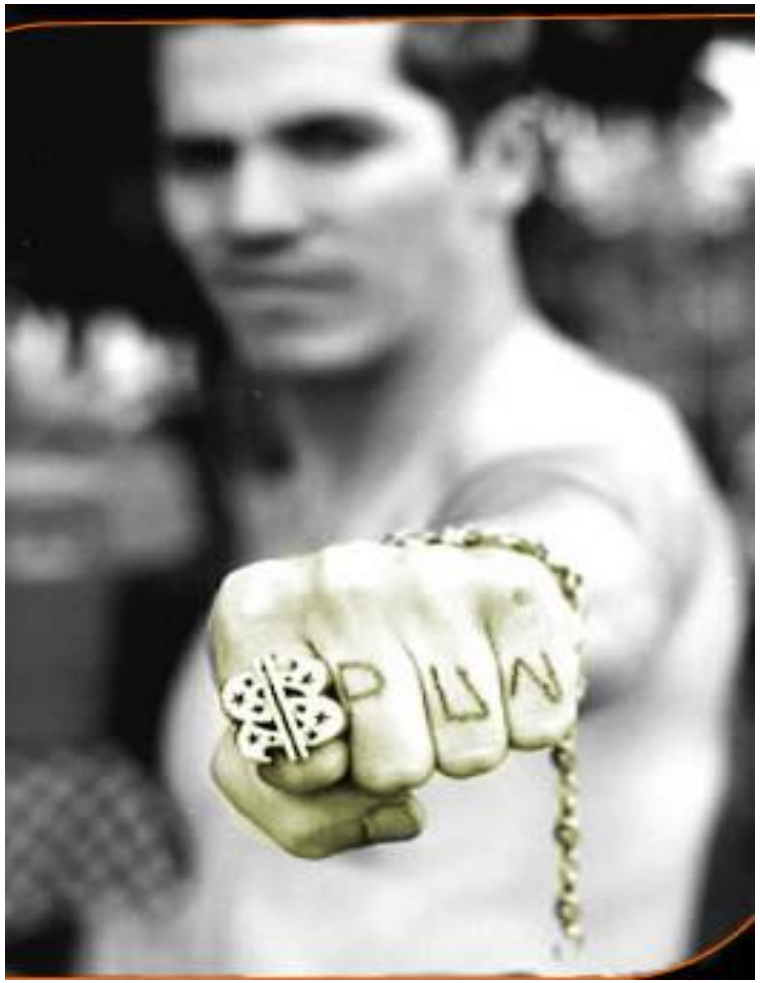
Health Consequences of Chronic Stimulant Use

Dental
- Darkened teeth
- Periodontal disease

Pulmonary
- Acute pulmonary edema
- Pulmonary HTN
- Inhalation injury

Cardiovascular
- Hypertension
- Arrhythmias
- Cardiomyopathy
- Acute Coronary Syndrome
- Aneurysm/dissection
- Erectile dysfunction

Infectious
- HIV/AIDS
- HCV/HBV
- STIs
- SSTIs



Neuro-psychiatric
- Stroke
- Seizure
- Depression
- Anxiety
- Mania
- Psychosis (paranoia, AH/VH/TH)

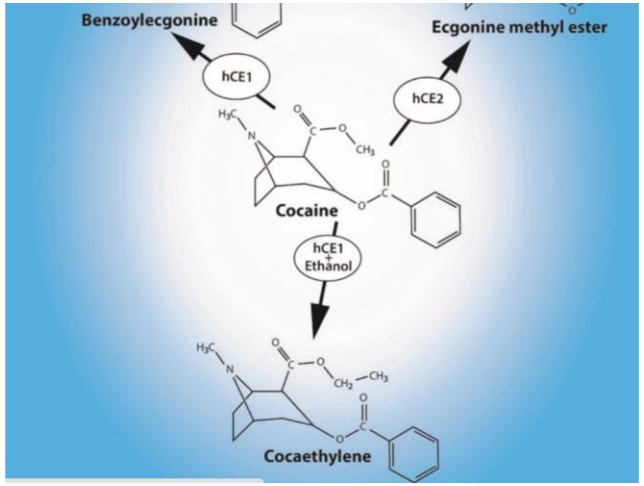
Liver
- Drug-induced hepatitis
- Cirrhosis or liver failure

Renal/Metabolic
- Rhabdomyolysis
- AKI/CKD
- Hyperthermia

Skin
- Superficial/deep tissue wounds/infections
- Excoriations
- Chemical burns

Cocaethylene Toxicity

- **Cocaethylene** = psychoactive substance produced when cocaine is used in presence of alcohol
  - Alcohol interferes with metabolism of cocaine
- Longer ½ life, more potent, larger volume of distribution
- 60-90% of people who use cocaine also use alcohol
  - Alcohol as a "landing gear" from cocaine
  - Prolongs and/or potentiates effects of cocaine
- Estimated to be 10x more cardiotoxic than cocaine alone
- Increased likelihood of liver injury, neurologic effects (seizures), death



Treatment of Stimulant Use Disorders

Pharmacologic Management

- No FDA approved medications for stimulant use disorders
- Preliminary research **with promise** for:
  - IM naltrexone + bupropion (methUD)
  - mirtazapine (methUD)
  - mixed amphetamine salts (CUD + ADHD, meth withdrawal)
  - topiramate (CUD)
  - topiramate + mixed amphetamine salts (CUD)
  - modafinil (post-acute stimulant withdrawal)

(S3 Practice Guidelines, 2016)

Promising medications for Cocaine Use Disorder

Cocaine Use Disorder	Comparison	Population	Outcomes	Dropout
Nuijten M et al. Lancet. 2016; 387:2226-34.	**Dexamphetamine** 60mg QD vs. placebo	73 Dutch patients with cocaine UD with OUD on MOUD (methadone)	At 12 weeks Fewer days of cocaine use More cocaine-neg tox tests No differences in craving, use of other substances, or criminality	11% dropout
Levin FR et al. JAMA Psychiatry. 2015 1;72:593-602.	**Mixed amphetamines** (MAS-ER) 60-80mg QD vs. placebo	126 US patients with adult-ADHD and cocaine UD	At 13 weeks Reduced ADHD symptoms: 60-75% vs 40% 3-wk abstinence: 30-17% vs. 7%	26% dropout
Dakwar E et al. Am J Psychiatry. 2019 176(11):923-930.	40 min infusion of **ketamine** at 0.5mg/kg vs. midazolam + All 5-wks counseling	55 inpatients with cocaine UD	At 5 weeks Abstinence: 48% vs. 11% Cravings: Ketamine 58% lower	dropout: 26% ketamine; 57% midazolam
Levin FR et al. DAD 2020 206:107700.	**MAS-ER** at 60mg QD + **topiramate** 100 BID vs. plaebo	127 adults with CUD using at least 9 days in the prior month	At 3 weeks Abstinence: 14% vs. 0%	20% discontinued for elevated HR/BP

Promising medications for Methamphetamine Use Disorder

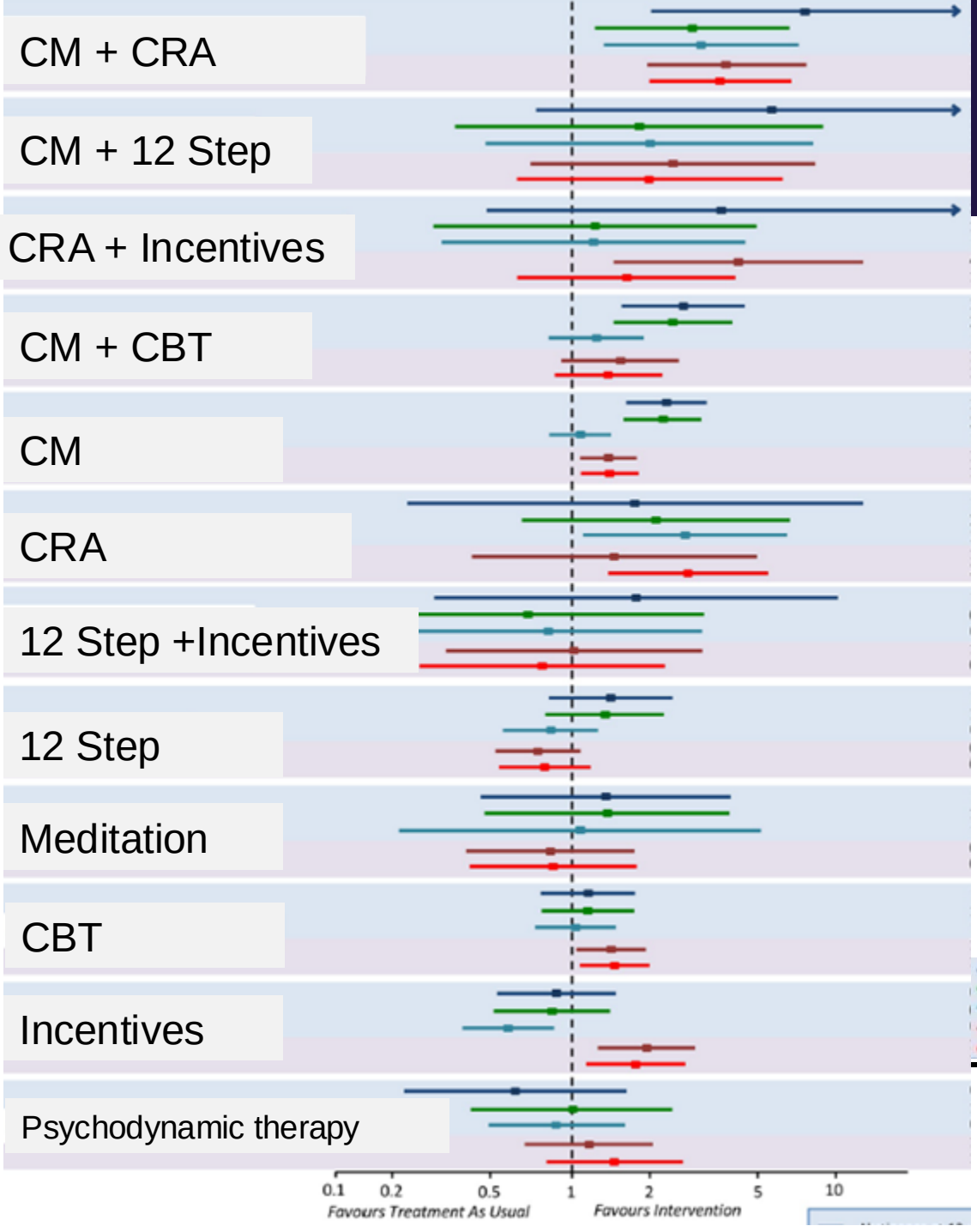
MA Use Disorder	Comparison	Population	Outcomes	Limitations
Coffin PO et al. JAMA Psychiatry 2020 77(3):246-255	**Mirtazapine** 30mg vs. placebo once daily + counseling	120 men who have sex with men who use methamphetamine	At 24 weeks RR of 0.75 for MA use RR <0.52 for multiple sex partners, condomless anal sex Improved depressive symptoms and insomnia severity	Medication adherence was almost 40%
Trivedi MH et al. N Engl J Med. 2021 384(2):140-153	**IM-NTX** 380mg Q3wks +**Bupropion** 450mg vs. placebo	403 with MA UD in stage 1 and 225 with MA UD in stage 2	At 12 weeks BPP+NTX 13.6% vs. Placebo 2.5% (3 of 4 MA negative urine tox)	Adherence to medication was 75-86%, Adverse events: Nausea, vomiting, dizziness

Non-pharmacologic Management

Behavioral Interventions for StUD

Evidence-Based Treatments	Description of Treatment	References
Contingency Management	Provides reinforcers ($, gift cards, motivational encouragement, etc) for treatment adherence.	(Bach et al., 2020; Brown & DeFulio, 2020; Lake et al., 2020; Minozzi et al., 2016; Okafor et al., 2020)
Community Reinforcement Approach	Using therapeutic modalities, job training, education, behavioral skills training, social training, relapse prevention and relationship counseling.	(Meyers et al., 2011; Riccardo De Giorgi et al., 2018; Stitzer et al., 2011)
Matrix Model	An 8-16-week structured intensive outpatient group utilizing group therapy, connection to self-help, and exploration of underlying causes of disease. Regular UDS screening.	(Huber et al., 1997; Rawson et al., 1995, 2002)
Exercise Supported Recovery	Varying exercise programs have been described, but those with a combination of daily aerobic and anaerobic exercise are associated with long term recovery.	(Huang et al., 2020; Killeen et al., 2020; Liu et al., 2021; Zhou et al., 2021)
Trauma-Informed Care Seeking Safety	A therapeutic model for the treatment of co-occurring PTSD and SUD that emphasizes the need to be safe in order to explore and cope with trauma.	(Lange-Altman et al., 2017; Lenz et al., 2016; Morley et al., 2016; Murphy et al., 2019; Najavits & Anderson, n.d.; Sperlich et al., 2021; Takahashi et al., 2020)

Comparing Behavioral Health Approaches



Research indicates that a combination of behavioral health approaches are most effective in producing abstinence at 12 weeks

Contingency management combined with any additional behavioral health approach improves outcomes

DeCrescenzo, et al, 2018

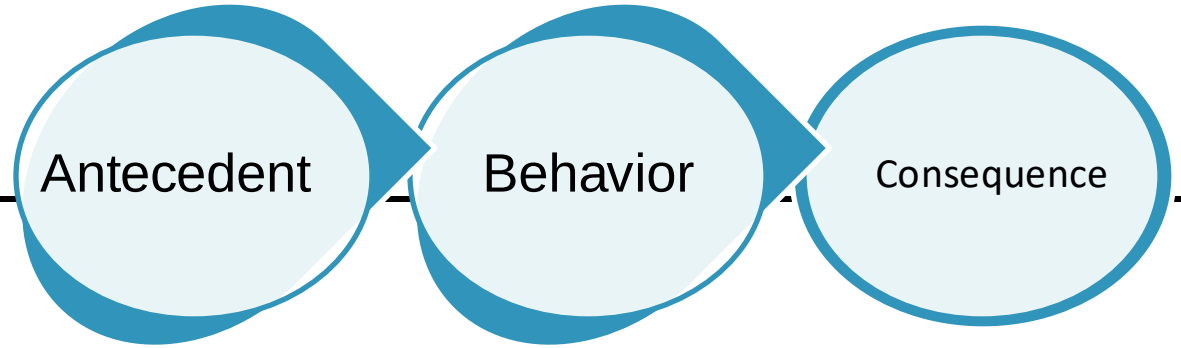
Key: CRA=Community Reinforcement Approach, CM=Contingency Management, CBT=Cognitive Behavioral Therapy

CARE Clinical Addiction Research and Education

Grayken Center for Addiction
Boston Medical Center

Basics of Contingency Management

- CM is a behavioral health intervention based in operant conditioning principles that provides tangible reinforcers for evidence of behavior change
- Essential theory behind CM: “A behavior that is reinforced in close temporal proximity to its occurrence will increase in frequency” (ex. engagement in care is reinforced with cash given to patient at the visit/point of engagement)
- In CM programs that focus on abstinence, the magnitude of reinforcement provided should increase with sustained periods of abstinence



Petry et al, 2011

Neuroscience of Reward

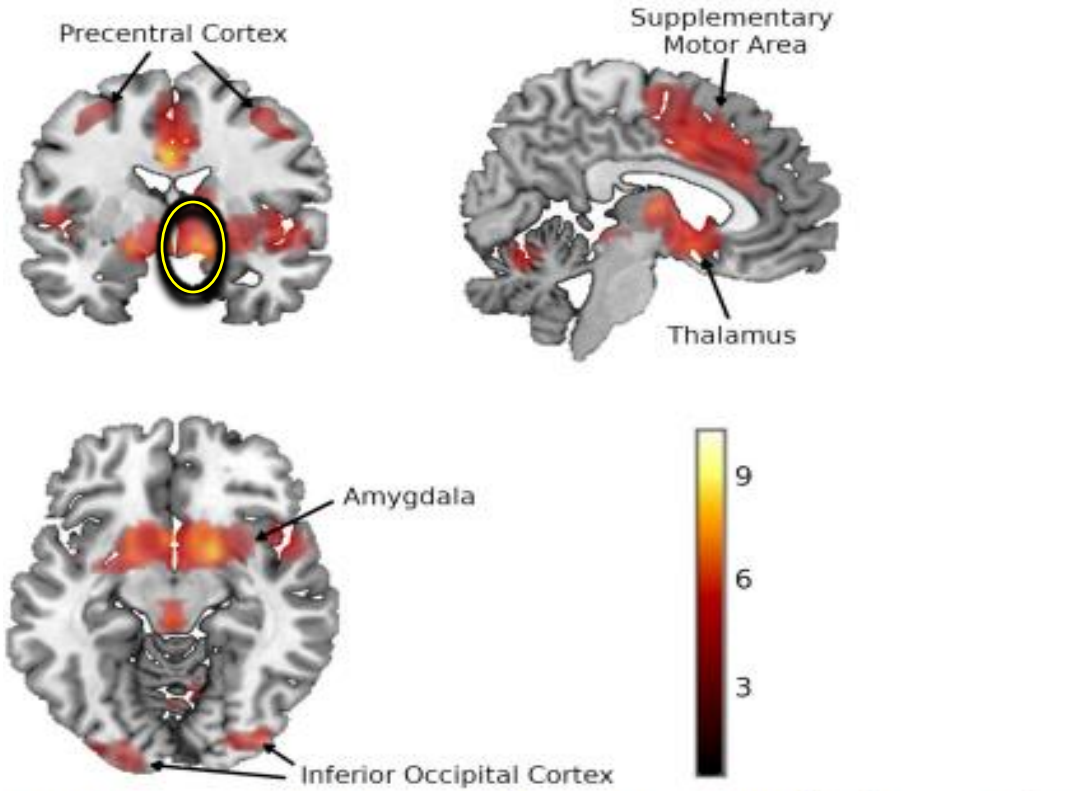


Fig 2. Activations associated with monetary reward anticipation in 45 studies. Depth of colour is proportional to the Z-value.

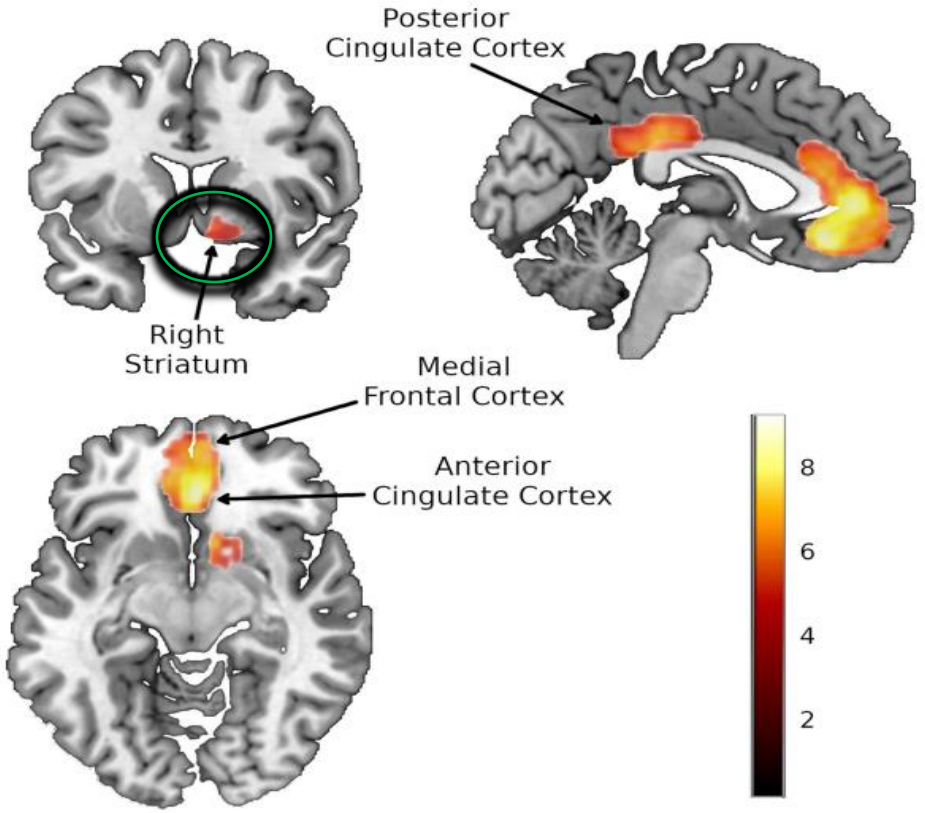


Fig 3. Activations associated with monetary reward delivery in 28 studies. Depth of colour is proportional to Z-value.

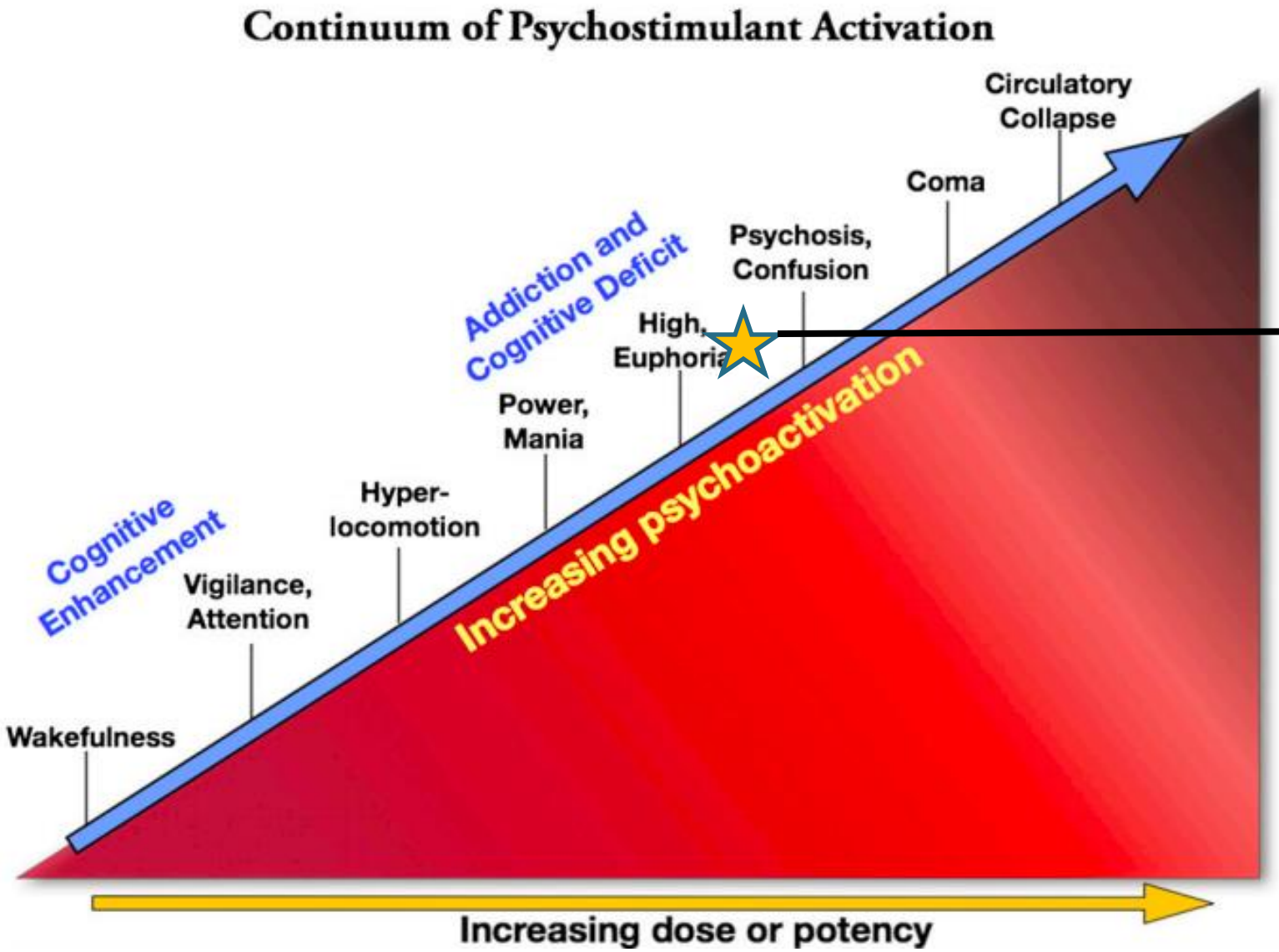
Monetary Reward Anticipation

Monetary Reward Delivery

Jauhar et al., PLOS 2021

Addressing Stimulant Intoxication

Overamping



- Begins with extended period of euphoria
- After dose exceeding the level of desired euphoria
- Exacerbated by sleep deprivation, dehydration
- May experience: altered mental status, psychosis (VH/AH/TH, paranoia) as result
- Patients may experience acute medical complications

Wood et al., 2014

Signs of Overamping

Physical	Psychological
Headache	Paranoia
Jaw grinding	Altered perceptions of reality
Spasticity/dyskinesia	Persecutory delusions
Xerostomia (dry mouth)	Auditory hallucinations
Chest pain	Visual hallucinations
Seizure	Tactile hallucinations/disturbances
Hyperthermia	
Hypertension	Protective behaviors: hypervigilance, fear, anxiety, panic, agitation, increased sensory awareness
Syncope	

De-escalation

A	G	R	O	+
Assess	Gauge	Respond	Observe	Positive Reinforcement
Using a patient-centered focus, asses the cause of the patient's agitation. CALMLY engage the patient in conversation.	How are you feeling? Be mindful of the feelings that you may be projecting that may escalate or de-escalate the patient.	Be calm yet firm in your interactions. Use open ended questions and empathetic listening to respond to the patient's concerns.	Observe verbal and non-verbal cues. Is this working?	As the patient starts to de-escalate offer them something. A place to sit, a glass of water, a snack.

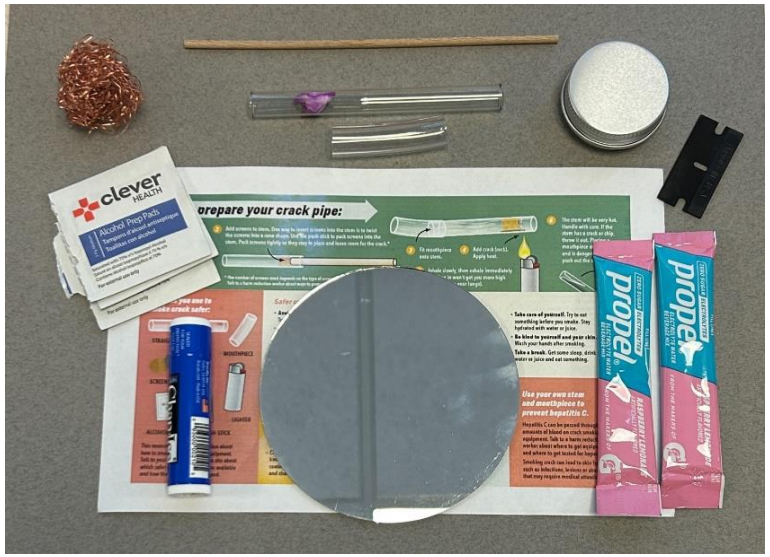
Interventions

- **Cool down space to reduce stimuli:**
  - Quiet, low light setting; white noise machine
  - Eye mask or sunglasses & earplugs
  - Place to lie down/rest (cot or exam room table or floor mat)
- **Address appetite/hydration**
  - Offer snacks
  - Offer water, gum for dry mouth; chapstick
- **Pharmacologic Interventions:**
  - Benzos for anxiety
  - Neuroleptics (eg. olanzapine) for agitation
  - For increased BP+HR, use vasodilators and CCB or non-selective beta-blockers
  - Treat hyperthermia (external cooling)

Harm Reduction Practices

Overdose Prevention

- Patient education on contaminated drug supply
- Distributing fentanyl test strips
- Naloxone education and **on site** distribution
- Safer supply distribution (booty bumping kits, safer smoking kits for meth/cocaine, safer injection equipment)
- For people repeatedly testing positive for fentanyl, consider starting MOUD

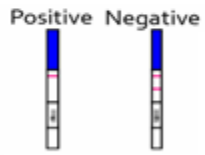


Fentanyl Test Strips

1. Add sterile water to your **empty** baggie or the **cooker you just prepped** – mix well!
   **Load your shot FIRST! Only test your rinse water!
2. **Dip the test strip** in the water, in up to the first line & **hold for 15 seconds**
3. **Place test strip** on sterile surface or across top of cooker.

One line POSITIVE

Two lines NEGATIVE



ter

r

STI and Infectious Disease Screening & Treatment

- Screening for STIs and infectious diseases, including HIV, HBV, HCV at frequency based on risk or on a schedule for at risk patients.
  - Increased risk for HIV with rectal stimulant use associated with sex (chemsex), though less risk than IVDU
- Screening for TB
- Screening for syphilis (high prevalence in MSM/chemsex)
- Screening for GC/CT at *all* sites of contact (pharyngeal, genital, rectal)
- Safer sex supplies (condoms, lube, booty bumping kits)
- Education/Rx for nPEP and PrEP with low threshold for initiation
  - Consider injectable cabotegravir (apretude) if available
- Immunize for HAV, HBV, Mpox, HPV, Tdap, influenza, COVID

Self Care Planning

- Discuss plan for binge use:
  - Eat, stay hydrated, and have appropriate supplies including first aid kit and condoms/lubricant
- Wash your hands
- Take breaks if possible
- Identify safe space to crash/sleep
- Agitation, depression and anxiety are common post stimulant use
  - connect patient with a BH provider or local services

Resources

START Resources

STIMULANT
TREATMENT
AND
RECOVERY
TEAM

CLINICAL GUIDELINES

A COLLABORATIVE
CARE APPROACH

Grayken Center for Addiction
Training & Technical Assistance
Boston Medical Center

BOSTON MEDICAL CENTER START Stimulant Treatment and Recovery Team

Medical Group Plan

BOSTON MEDICAL CENTER START Stimulant Treatment and Recovery Team

Behavioral Health Group Plan

BU
Boston University School of Medicine

CARE Clinical Addiction Research and Education

Grayken Center for Addiction
Boston Medical Center

Stimulant Trainings

Stimulants 101

- Introduction to stimulant treatment in the outpatient setting
- 1 hour - CME offered

Essentials of Stimulant Use Disorder

- Overview of evidence-based interventions for StUD
- 3 hour - CME offered

Register Here

Free education with continuing education credits and support funded and supported by:

MA Department of Public Health BSAS Prevent • Treat • Recover • For Life www.mass.gov/dph/bsas

Opioid Response Network

BU Boston University School of Medicine

CARE Clinical Addiction Research and Education

Grayken Center for Addiction Boston Medical Center

TIP 33

TIP 33- SAMHSA

CARE Clinical Addiction Research and Education

Grayken Center for Addiction
Boston Medical Center