Stimulants and their Impact on Brain and Behavior: Best Practices and Approaches for Effective Treatment and Recovery

ATTC
Addiction Technology Transfer Center Network
Funded by Substance Abuse and Mental Health Services Administration

Grant Hovik, MA
ghovik@mednet.ucla.edu
Pacific Southwest Addiction Technology Transfer Center

Training Disclaimer

The UCLA Integrated Substance Use and Addiction Programs (ISAP) Training Department is funded by local, state, and federal agencies. The views expressed in written conference, training, and presentation materials or publications, and views expressed by staff or external consultants, trainers, speakers, and moderators do not necessarily reflect the official policies of UCLA ISAP's funders, nor does the mention of trade names, commercial practices, or organizations imply endorsement.

Educational Objectives

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

1. Identify three (3) specific national patterns and trends in stimulant use.
2. Recall at least three (3) short-term and three (3) long-term physical or psychological effects of stimulant use.
3. Apply at least two (2) specific behavioral treatment interventions that have been proven effective in treating people with a stimulant use disorder.

Language Matters

SOURCE: Mid-America ATTC, 2017

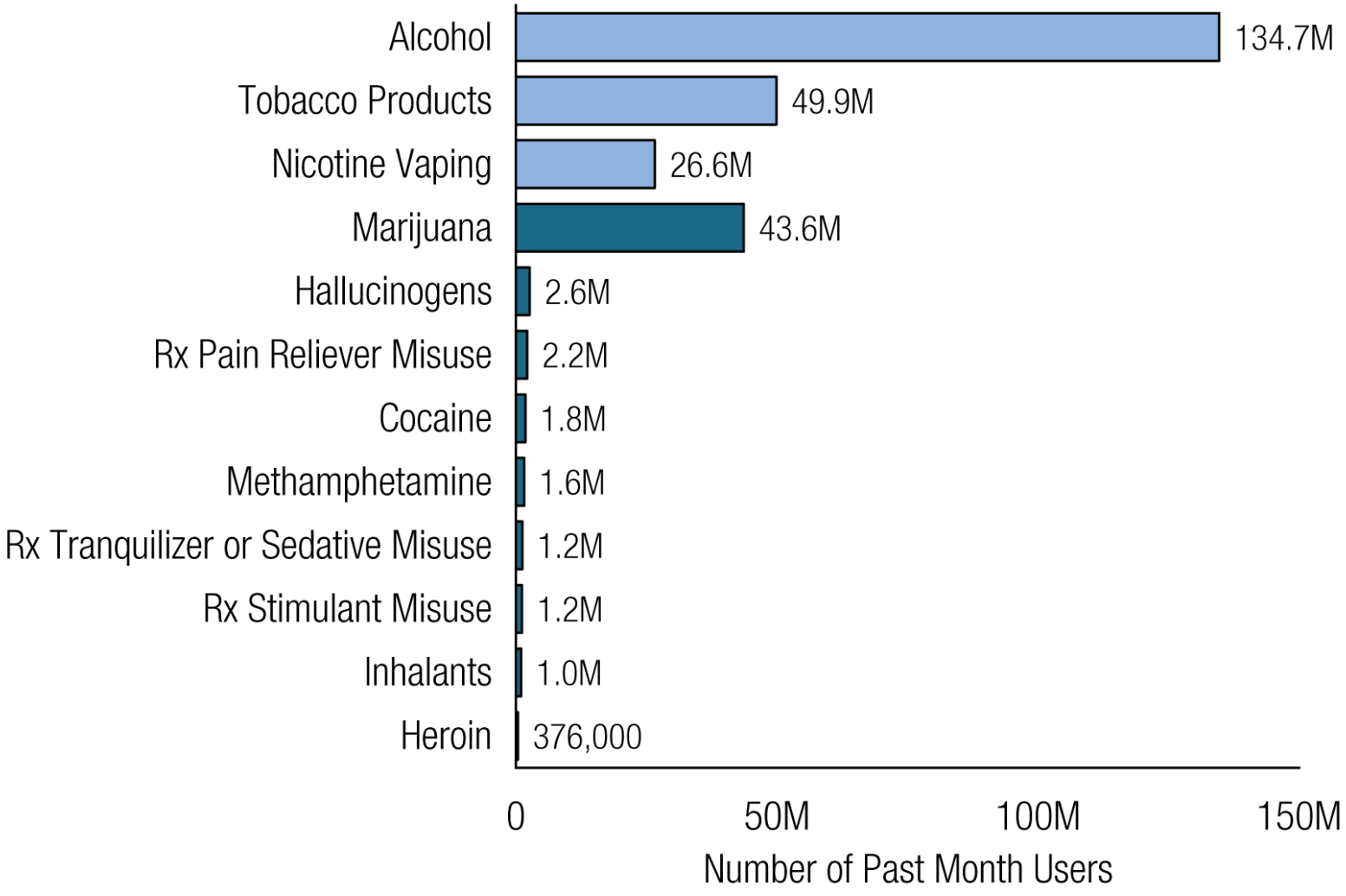
The Scope of Stimulant Use in the United States and Beyond

What we know…globally

- Amphetamine-type stimulants (ATS) constitute the 3rd most widely used illicit drug category in the world, following cannabis and opioids
- The type of ATS used varies by region
  - Amphetamines in Europe and the Middle East
  - Methamphetamine in the US, Australia, and SE Asia
- Different precursors used in the manufacturing process

SOURCE: UNODC, 2021

Past Month Substance Use: Among People Aged 12 or Older; 2023

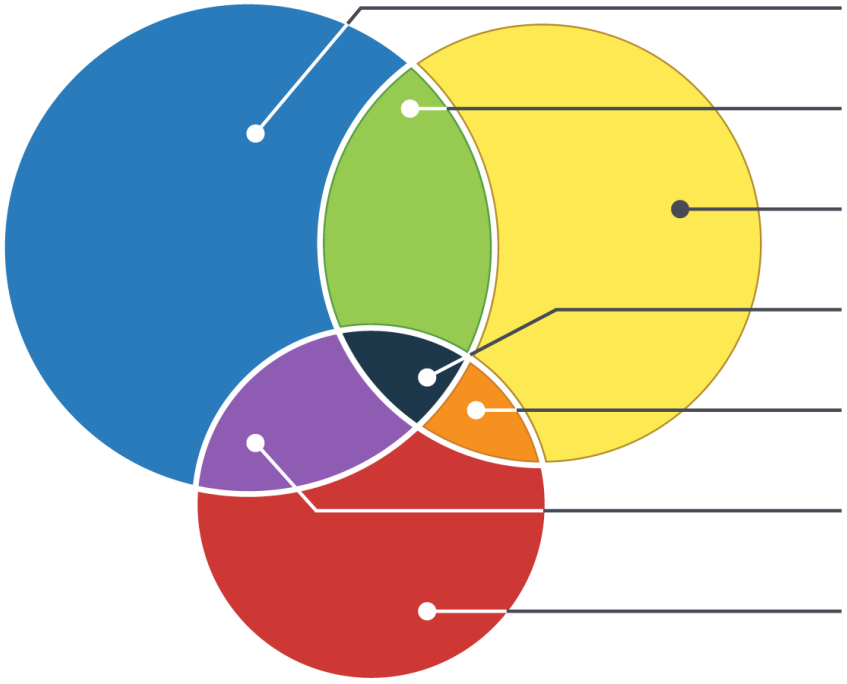


Rx = prescription.

Note: The estimated numbers of current users of different substances are not mutually exclusive because people could have used more than one type of substance in the past month.

SAMHSA
Substance Abuse and Mental Health Services Administration

Past Year Central Nervous System (CNS) Stimulant Misuse: Among People Aged 12 or Older; 2023



Cocaine Use Only (3.5 Million People)

Cocaine Use and Prescription Stimulant Misuse, but Not Methamphetamine Use (786,000 People)

Prescription Stimulant Misuse Only (2.8 Million People)

Cocaine and Methamphetamine Use and Prescription Stimulant Misuse (182,000 People)

Prescription Stimulant Misuse and Methamphetamine Use, but Not Cocaine Use (190,000 People)

Cocaine and Methamphetamine Use, but Not Prescription Stimulant Misuse (556,000 People)

Methamphetamine Use Only (1.7 Million People)

9.7 Million People Aged 12 or Older with Past Year CNS Stimulant Misuse

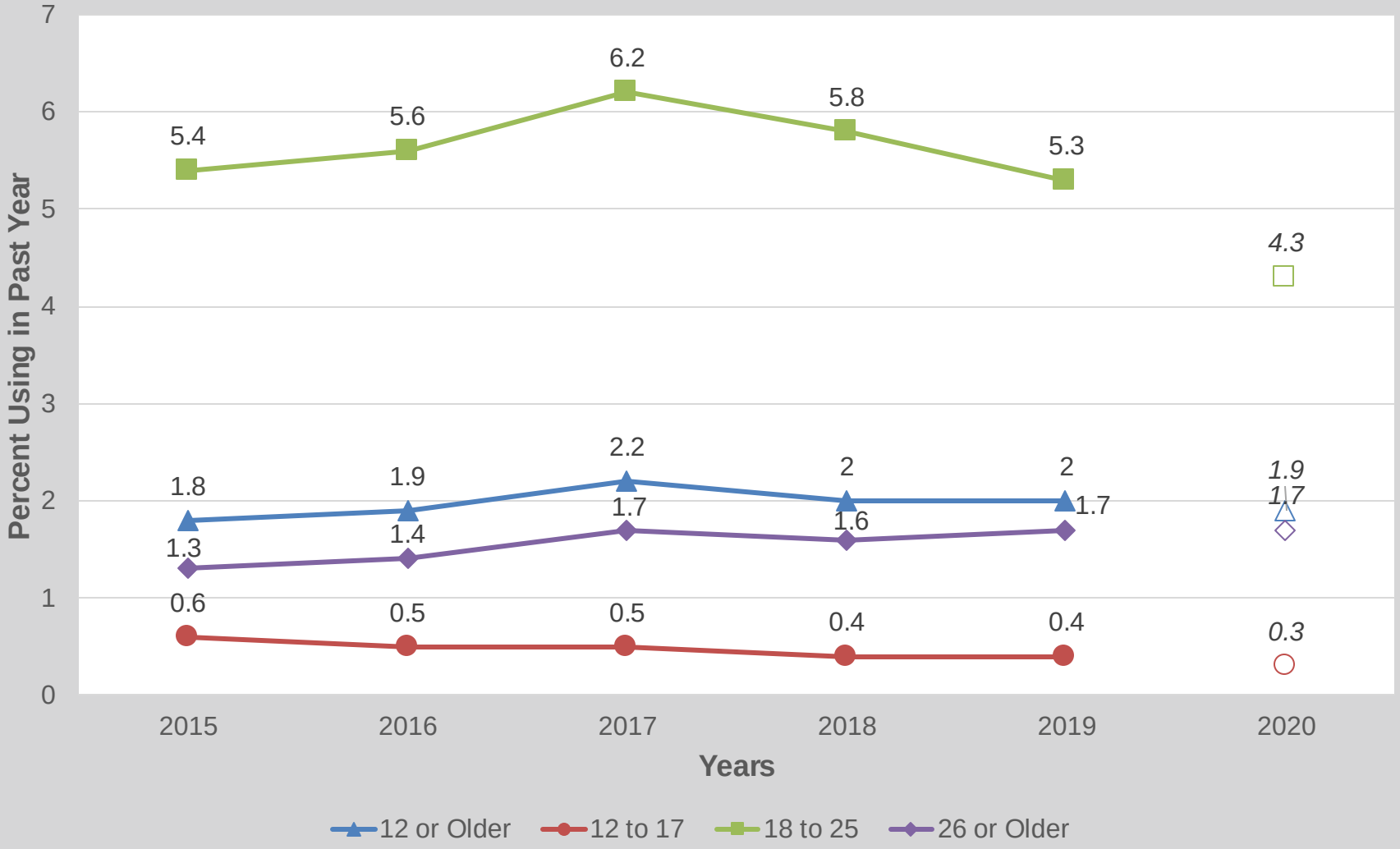
5.0 Million People Used Cocaine

3.9 Million People Misused Prescription Stimulants

2.6 Million People Used Methamphetamine

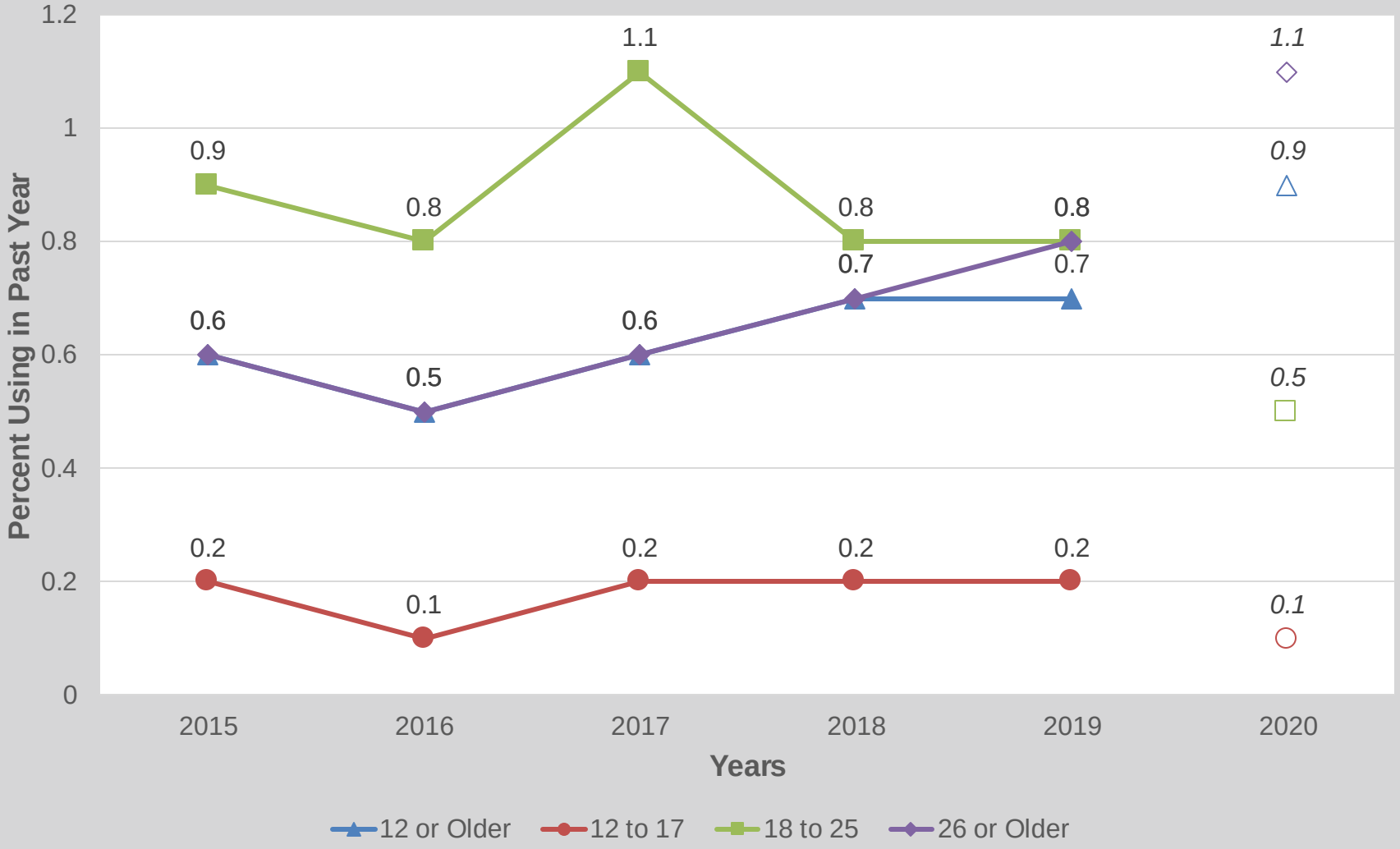
SAMHSA
Substance Abuse and Mental Health Services Administration

Trends in Past Year Use of Cocaine: 2015-2020



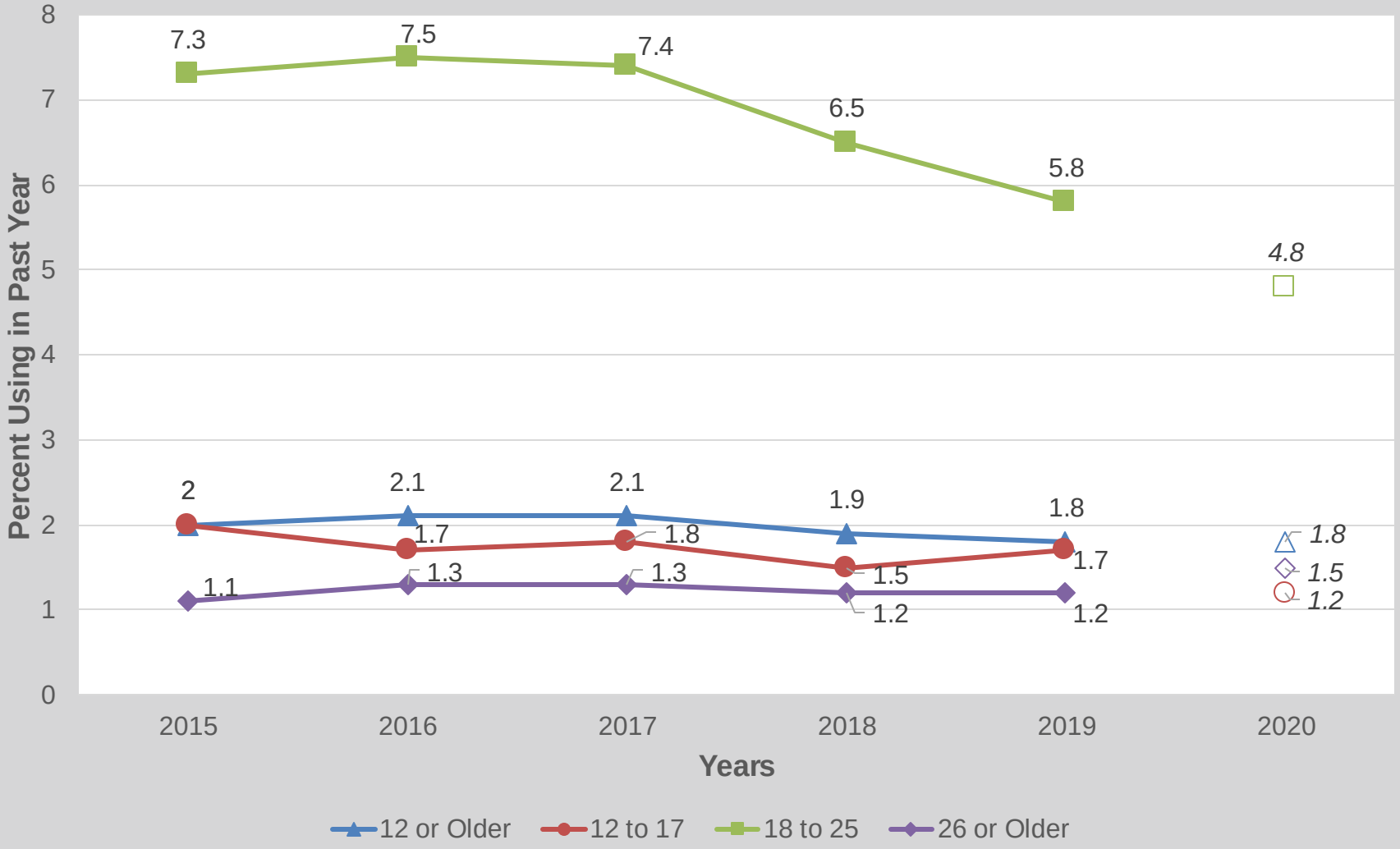
SOURCE: SAMHSA, 2021

Trends in Past Year Use of Methamphetamine: 2015-2020



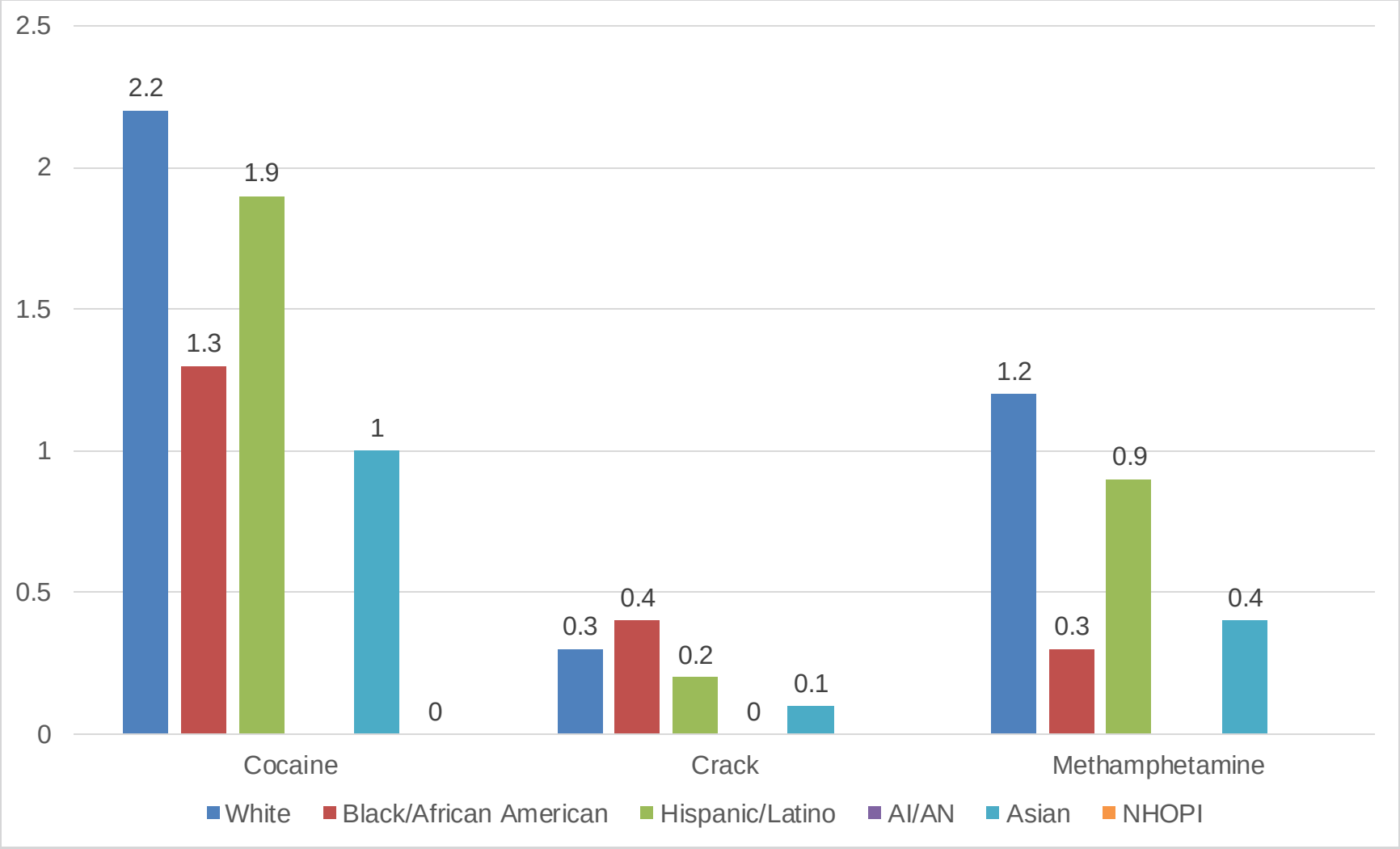
SOURCE: SAMHSA, 2021

Trends in Past Year Misuse of Prescription Stimulants: 2015-2020



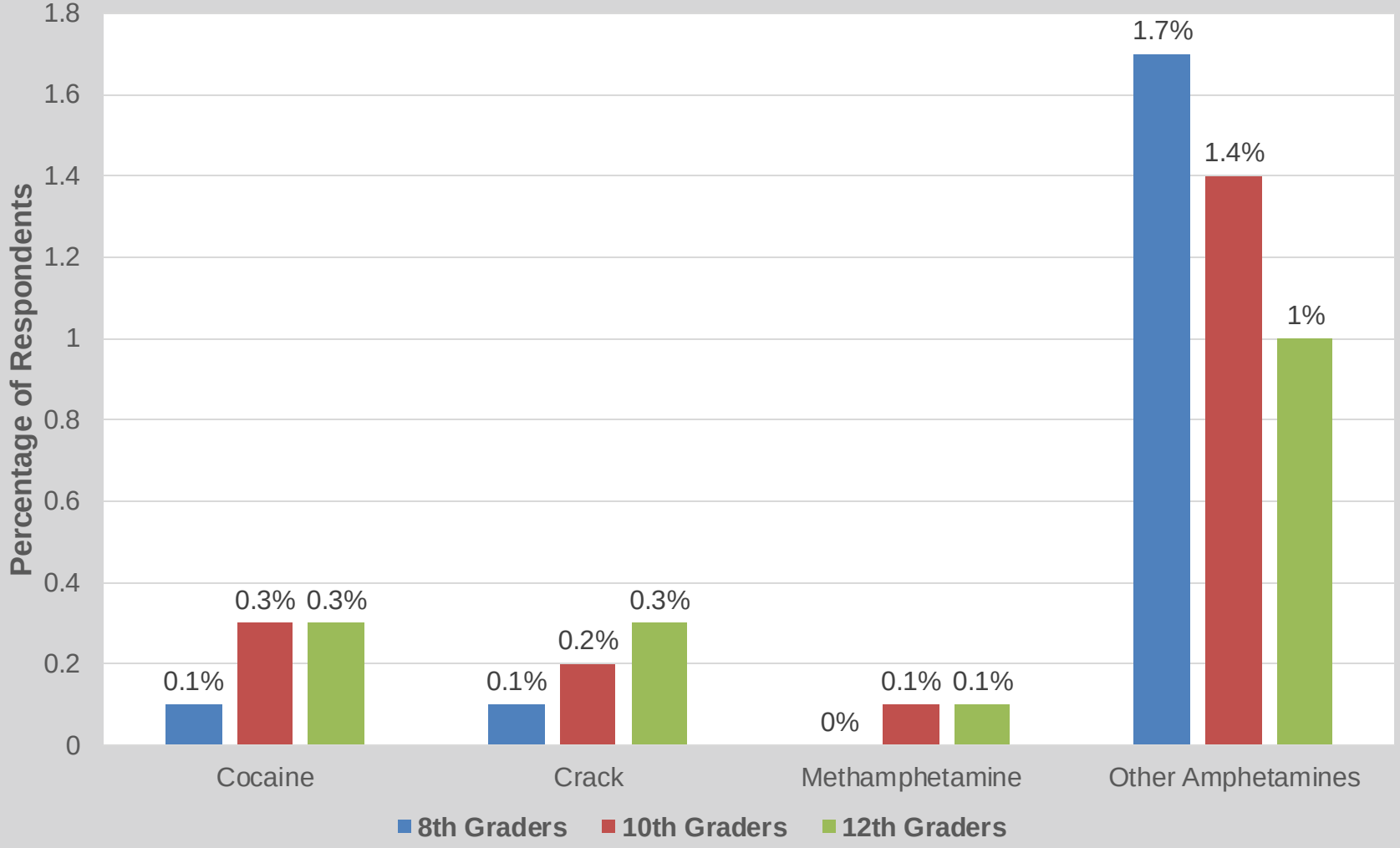
SOURCE: SAMHSA, 2021

Past Year Use (as Percentages) of Stimulants by Racial/Ethnic Group, 2020



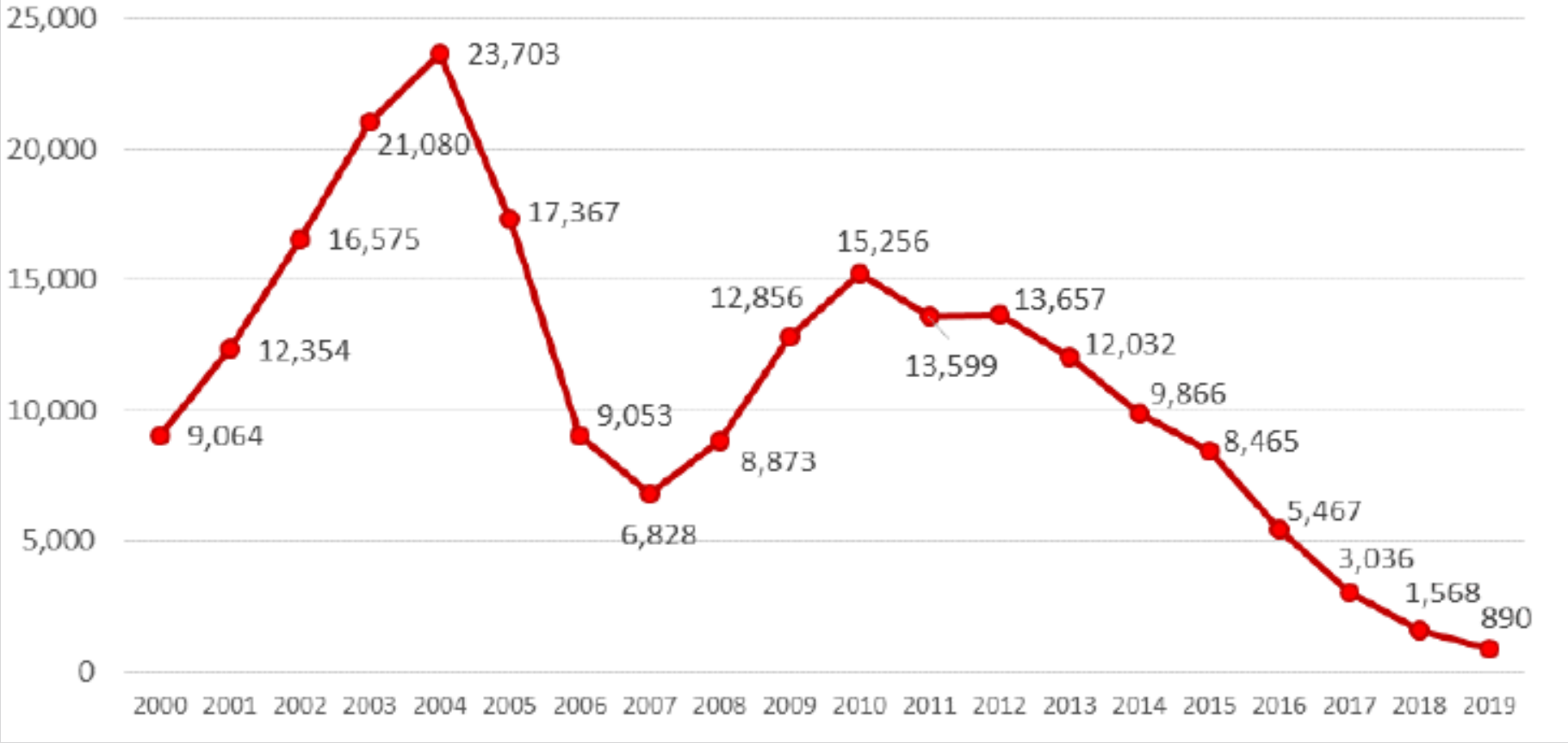
SOURCE: SAMHSA, 2020

Past Month Use of Stimulants among 8th, 10th, and 12th Graders: 2021



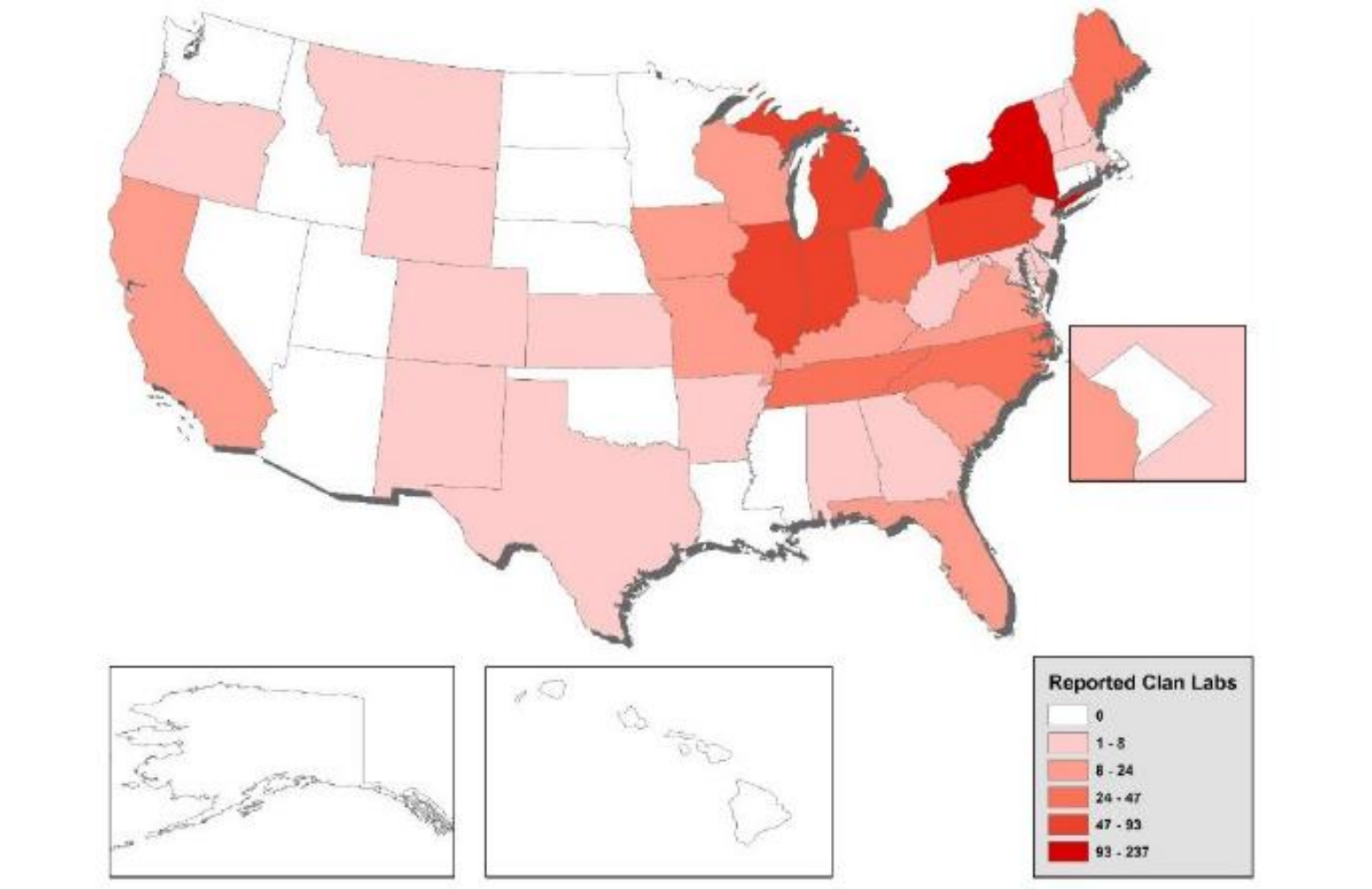
SOURCE: Johnson et al., 2022

Declines in the Domestic Production of Methamphetamine: 2000-2019



SOURCE: U.S. DOJ, DEA, 2021

U.S. Methamphetamine Lab Incidents: 2019



SOURCE: U.S. DOJ, DEA, 2021

Prevalence in Justice-Involved Populations

- 63-83% of arrestees test positive for at least one substance
- Methamphetamine use increased significantly in recent years
  - 31.7% of arrestees in western U.S. tested positive (2019)
- Racial and geographic disparities in enforcement and sentencing
- Gender differences: Women show higher rates of stimulant use disorders

The Cycle of Stimulant Use and Incarceration

- Reciprocal relationship between stimulant use and criminal behavior
- Primary pathways:
  - Economic-compulsive: crimes to support use
  - Systemic: violence within drug distribution networks
  - Pharmacological: behavior related to intoxication/withdrawal
- "Revolving door" phenomenon
- Post-release challenges: limited treatment access, housing barriers

Criminal Justice Policies and Stimulant Offenses

- Historical context: "War on Drugs" and stimulant sentencing
- Sentencing disparities: crack vs. powder cocaine
- Evolutions in policy approaches:
  - Mandatory minimums → sentencing reform
  - Drug courts and diversion programs
  - Harm reduction initiatives
- State-level policy variations and outcomes

Methamphetamine and Opioid Co-Ingestion – What are the Issues?

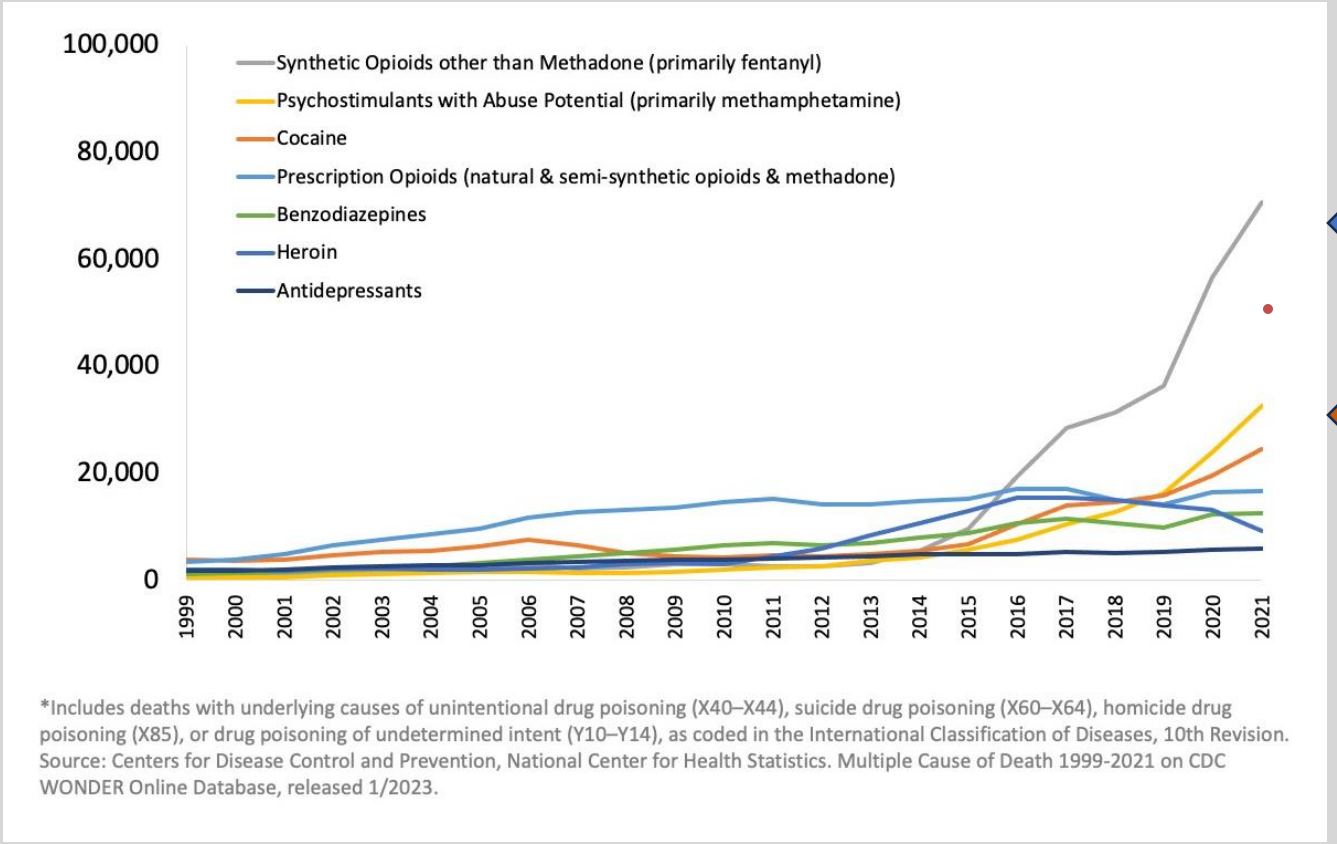
- A synergistic effect occurs when using meth and an opioid together (i.e., the result of using both is greater than either alone)
- The stimulant effect counterbalances the depressant effect, thus increasing overdose risk (respiratory depression AND cardiac arrest)
- The most potent effect seems to be in the first 90 minutes of co-ingestion

SOURCES: Ellis et al., 2018; Tian et al., 2017; Meacham et al;, 2016; Trujillo et al., 2011

What are Some Treatment Implications for Methamphetamine and Opioid Co-Ingestion?

- Make sure you have sufficient naloxone kits available for overdoses
  - Because of the interaction effect, it may require more than one dose to counteract the effects of meth and heroin
- Combine medication-assisted treatment for heroin with contingency management for meth
  - It may be better to use buprenorphine rather than methadone, since methadone and meth would still have a potent interaction (for people who relapse on meth during treatment)
- Exercise may help to reduce methamphetamine use and reduce depression and anxiety symptoms

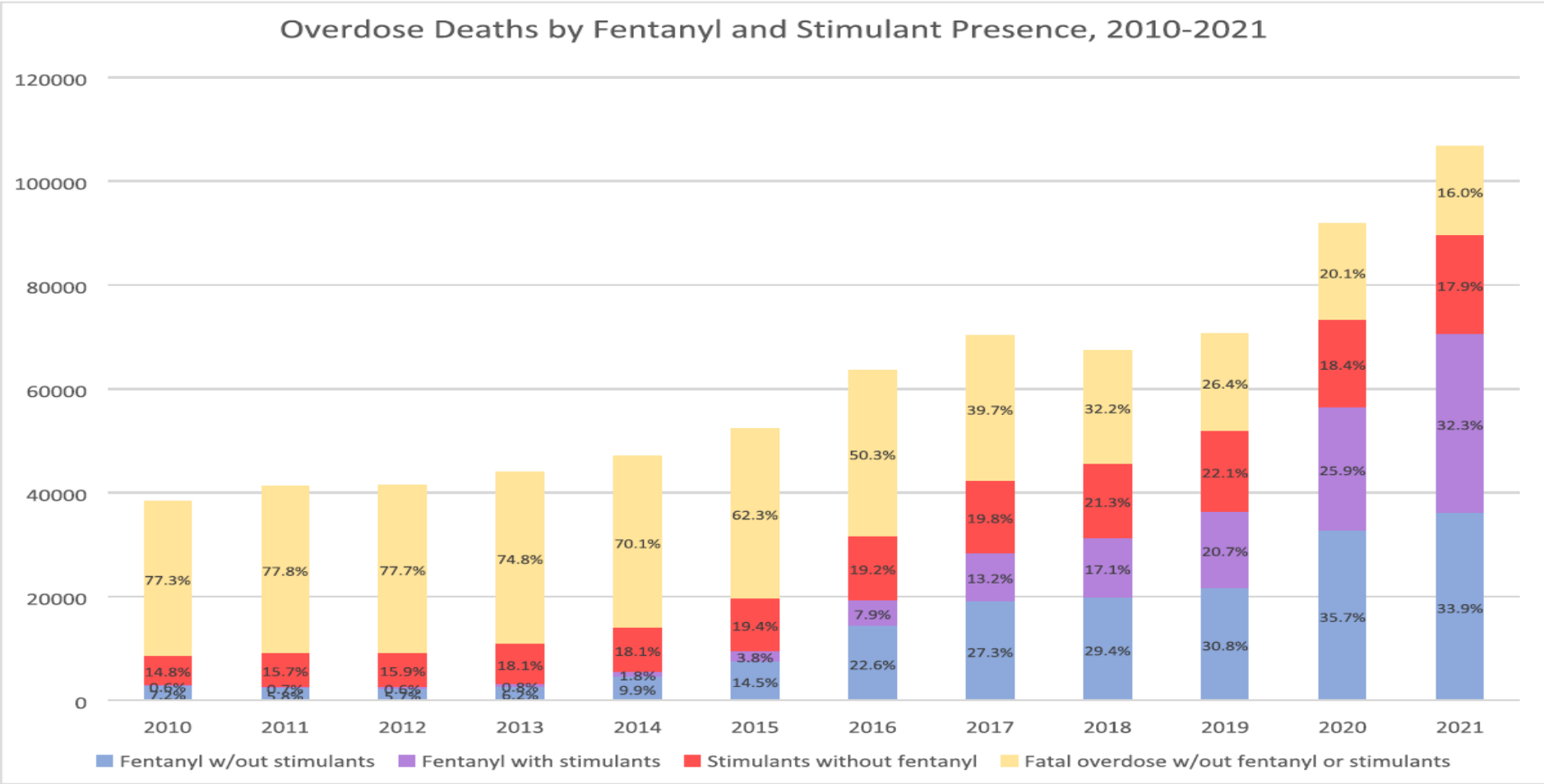
Drivers of Drug Poisoning Deaths Evolve from Opioids to Stimulants



*Includes deaths with underlying causes of unintentional drug poisoning (X40–X44), suicide drug poisoning (X60–X64), homicide drug poisoning (X85), or drug poisoning of undetermined intent (Y10–Y14), as coded in the International Classification of Diseases, 10th Revision. 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.

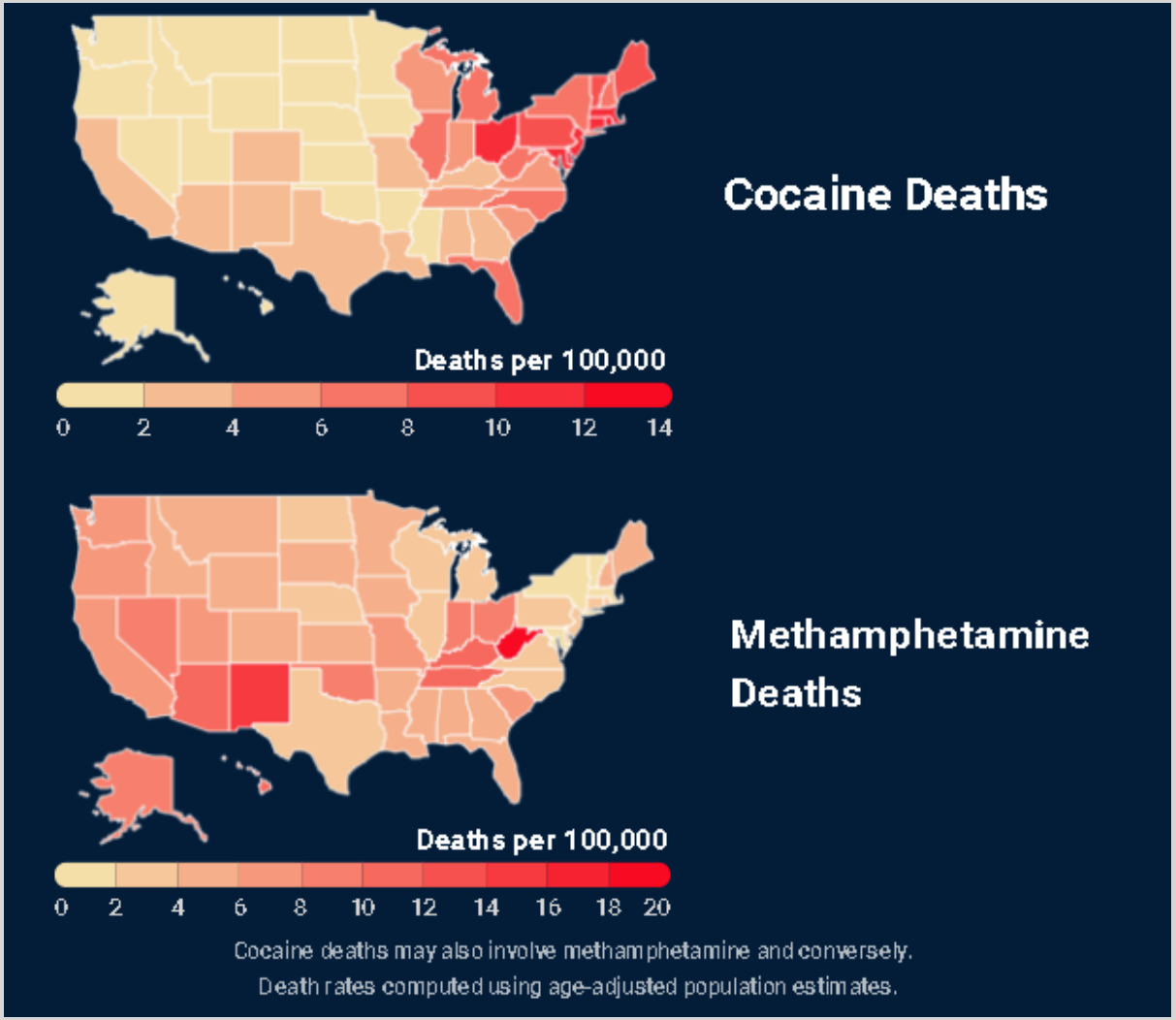
SOURCE: CDC, 2023

OVERDOSE DEATHS



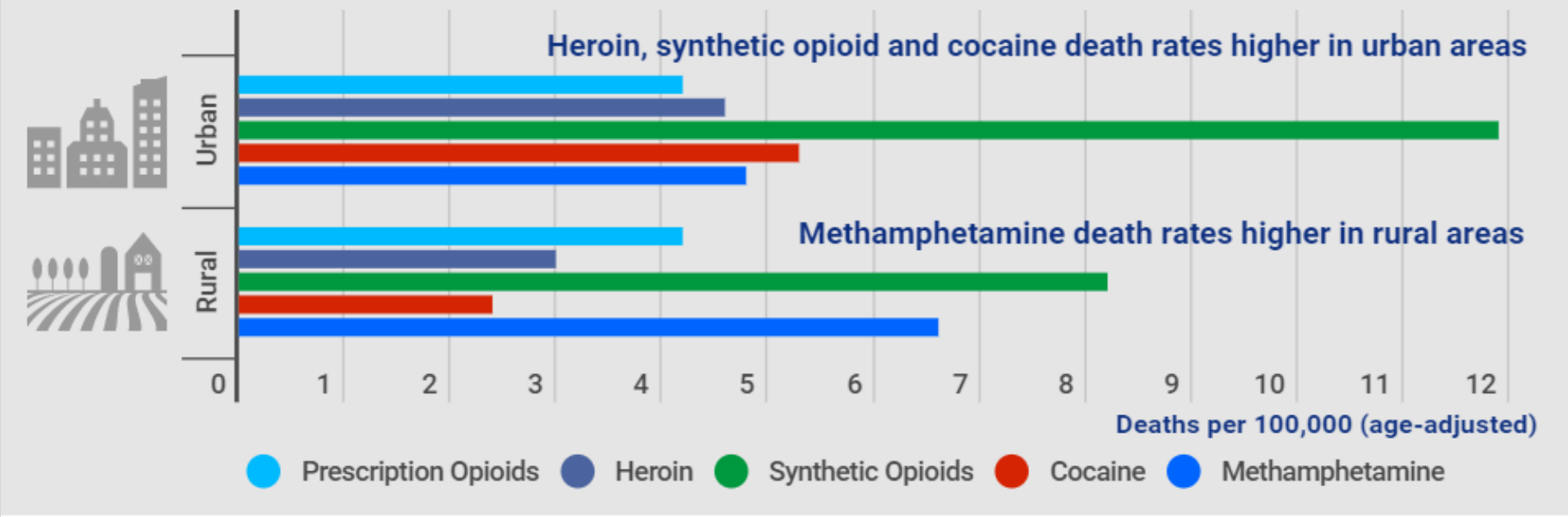
Friedman J, Shover CL. Addiction. 2023 Sep 13. **DOI: 10.1111/add.16318**

Geographic Differences in Stimulant-Related Deaths, 2019



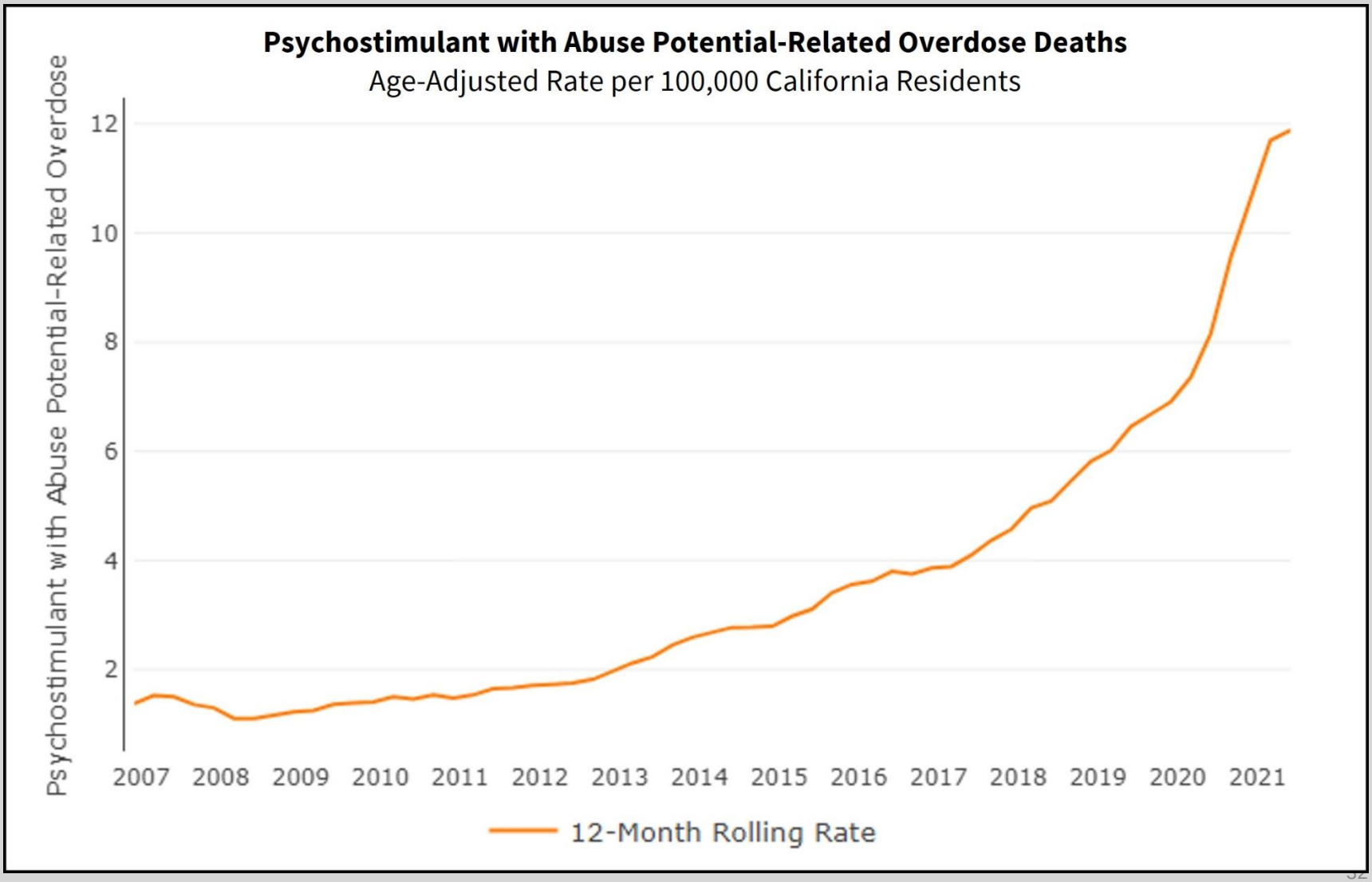
SOURCE: NIHCM Foundation, 2021

Differential Drug-Related Death Rates in Rural vs. Urban Areas



SOURCE: NIHCM Foundation, 2021

Stimulant Overdose Deaths in California



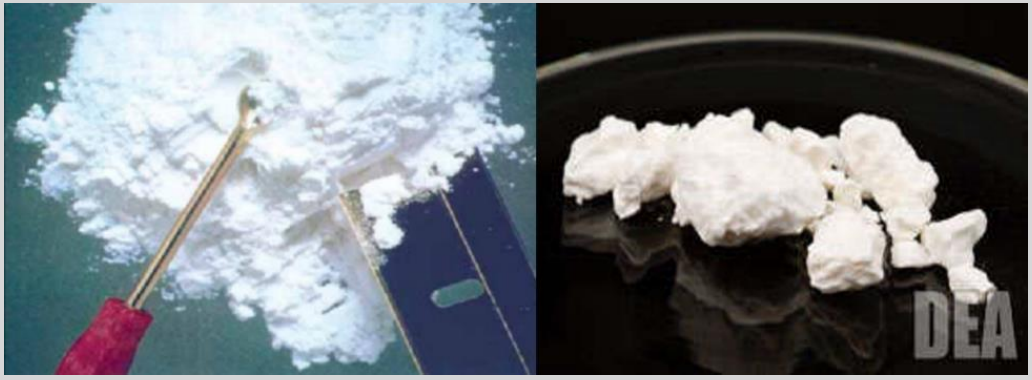
California Overdose Surveillance Dashboard

Stimulants:
What are We Talking About?

The Broader Classification: Stimulants

Methamphetamine

Powder and Crack Cocaine



Forms of Cocaine

- Powder cocaine (Hydrochloride salt)
- Smokable cocaine (Crack, rock, freebase)
- Cocaine half-life: ~1-2 hours

SOURCE: NIDA, 2018

Methamphetamine

Methamphetamine Powder

Description: Beige/yellowy/ off-white powder

Base / Paste Methamphetamine

Description: 'Oily', 'gunky', 'gluggy' gel, moist, waxy

Crystalline Methamphetamine

Description: White/clear crystals/rocks; 'crushed glass' / 'rock salt'

SOURCE: NIDA, 2019

Cocaine vs. Methamphetamine

Methamphetamine

- Stimulant
- Man-made
- Smoking produces a long-lasting high
- 50% of drug is removed from body in 12 hours
- Increases dopamine release and blocks dopamine re-uptake
- Limited medical use

Cocaine

- Stimulant and local anesthetic
- Plant-derived
- Smoking produces a brief high
- 50% of drug is removed from body in 1 hour
- Blocks dopamine re-uptake
- Limited use as a local anesthetic (surgical)

SOURCE: NIDA, 2019

The Impact of Stimulants on the Brain and Body

Substance Use Disorder is a Brain Disease

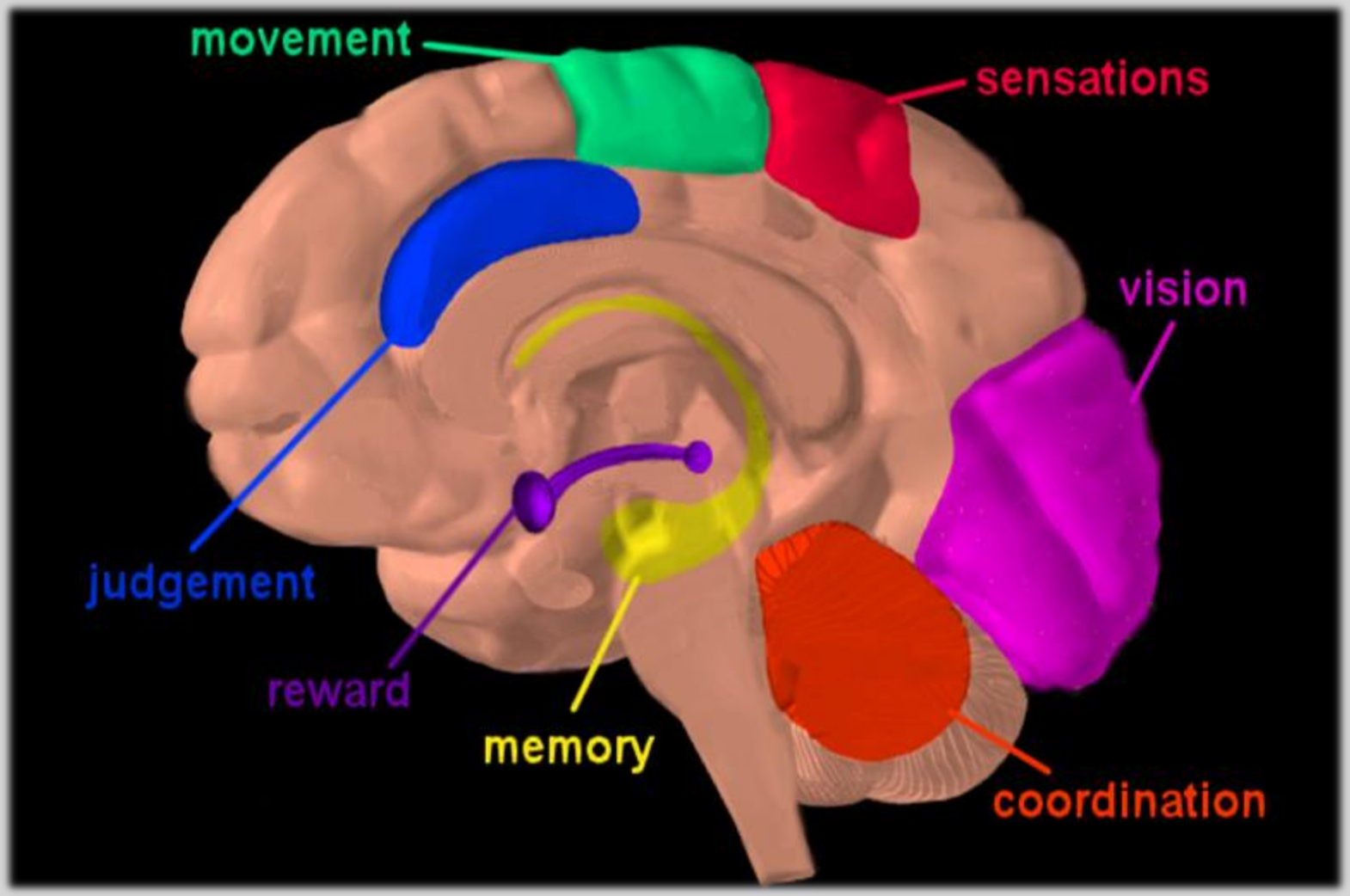
- “Addiction is a brain disease”

  Alan Leshner, Ph.D.

  Former Director, National Institute on Drug Abuse
- This statement in the late 1990’s began to change the way drug abuse/dependence were viewed, at least by the medical and scientific communities
- Unfortunately, much stigma remains among general public as well as among healthcare providers

SOURCE: Leschner, 1997

Brain Areas Affected by Psychoactive Substances

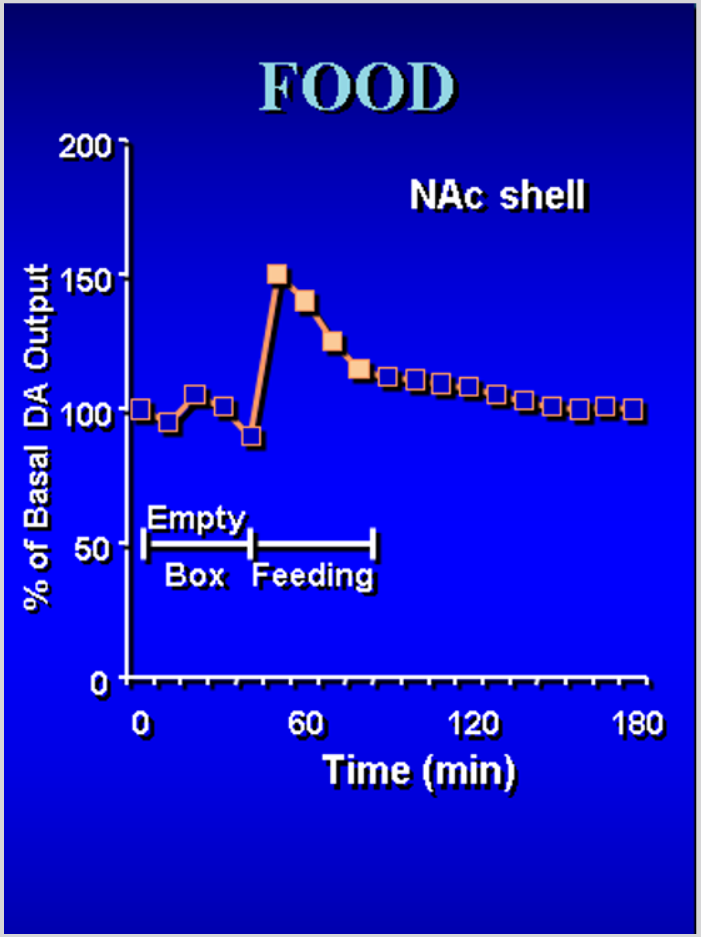


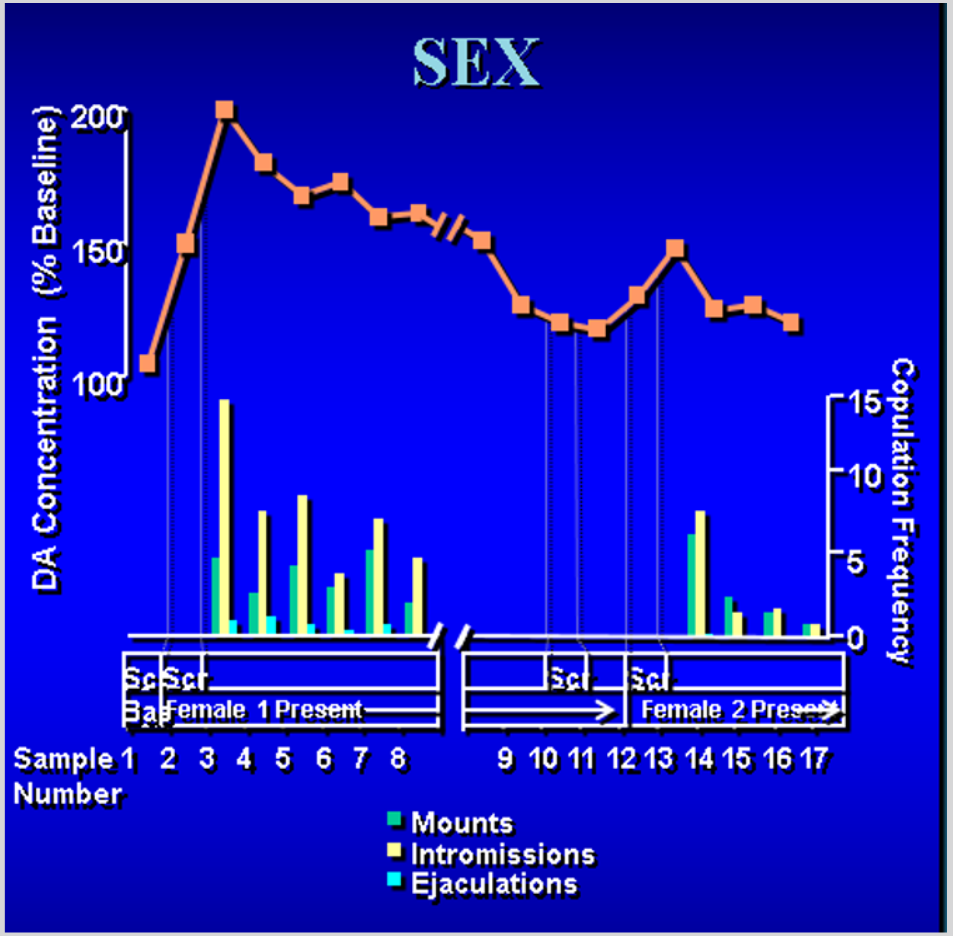
SOURCE: NIDA, 2019

Let's First Take a Look at Normal Dopamine Functioning

SOURCE: Meyers, 2008

Natural Rewards Elevate Dopamine Levels



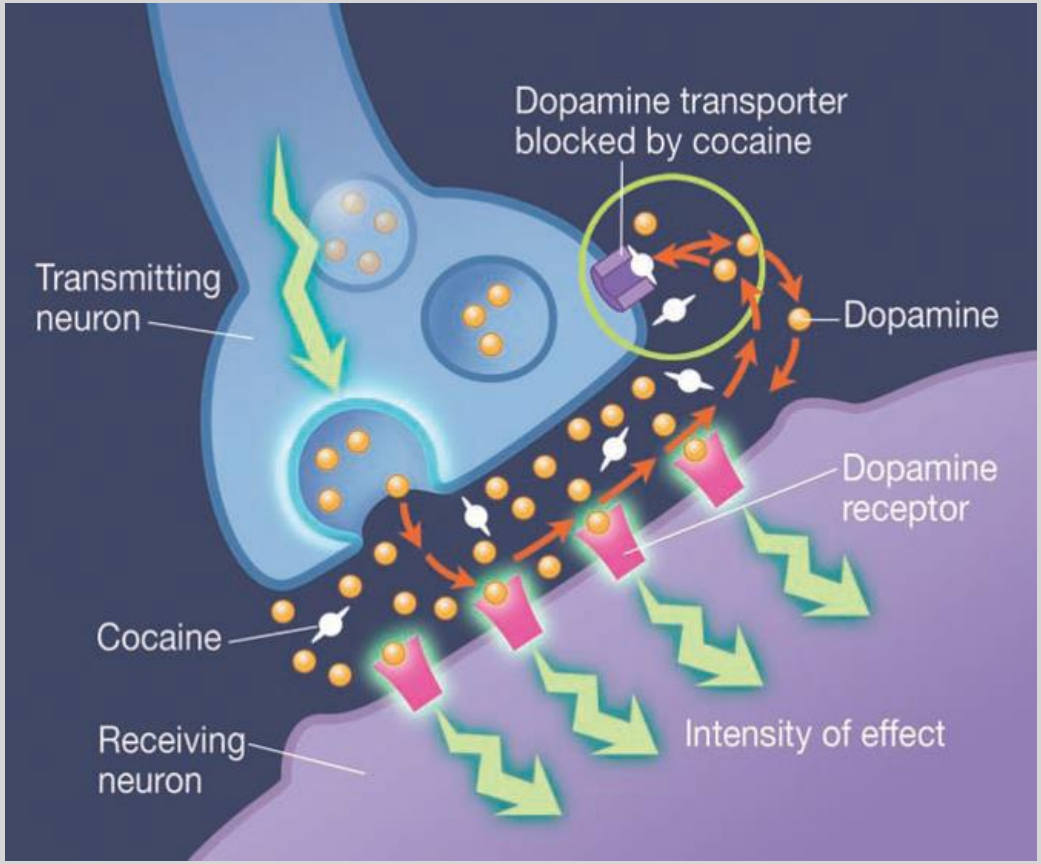


SOURCES: Bassareo & DiChiara, 1999;
Fiorino & Phillips, 1997

How the Brain Responds to Methamphetamine

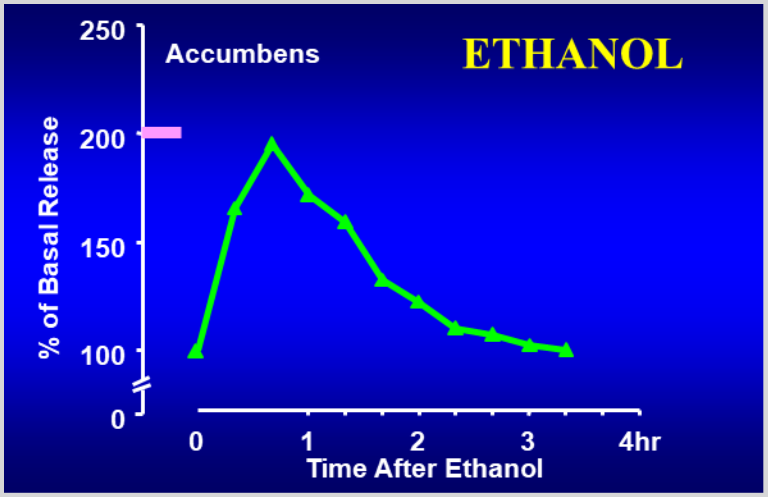
SOURCE: Meyers, 2008

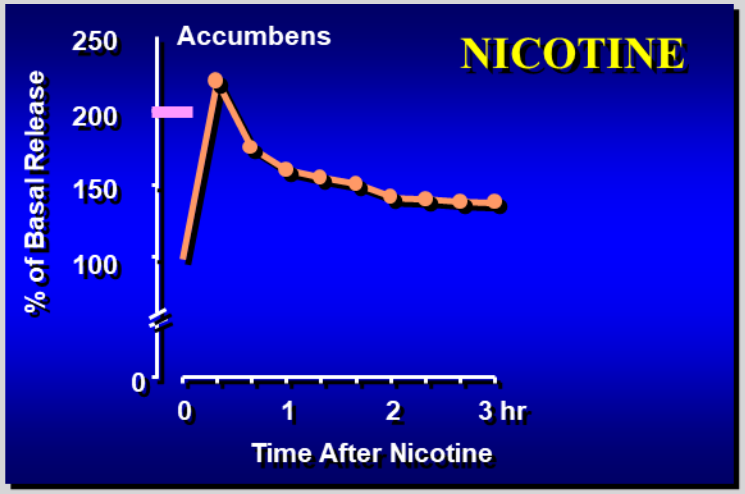
How Does Cocaine Produce its Effects?

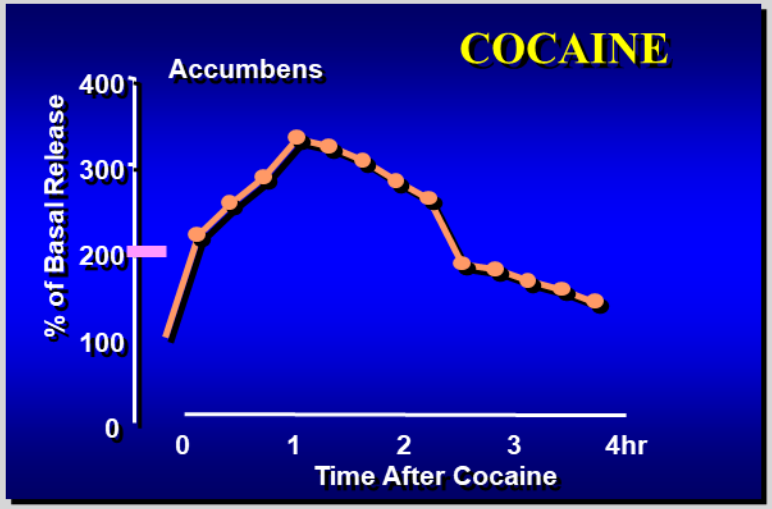


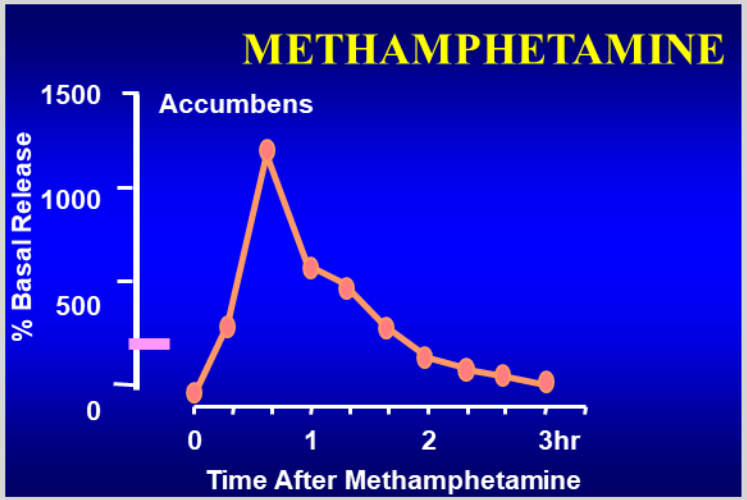
SOURCE: NIDA, 2016

Effects of Drugs on Dopamine Release



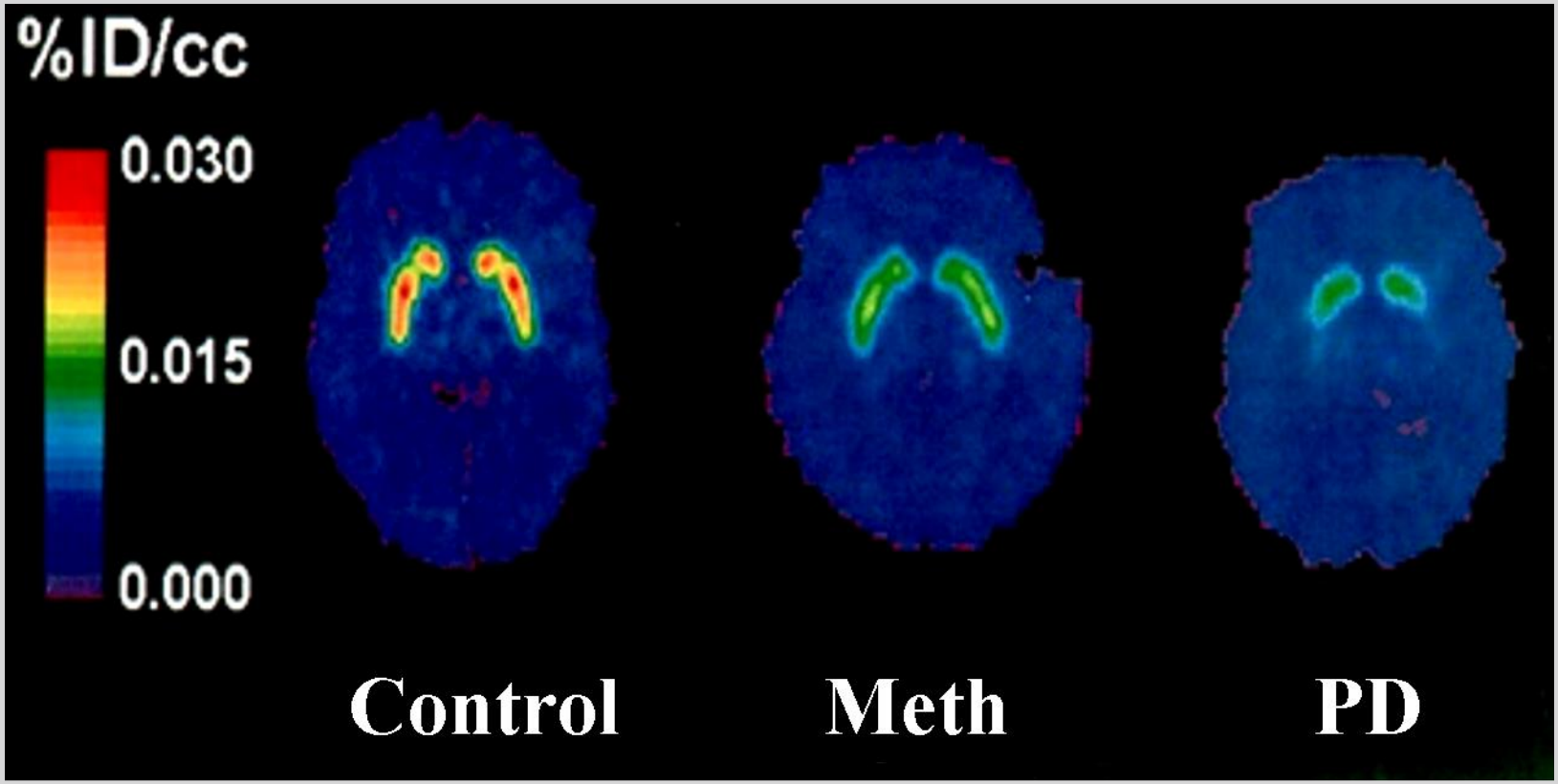






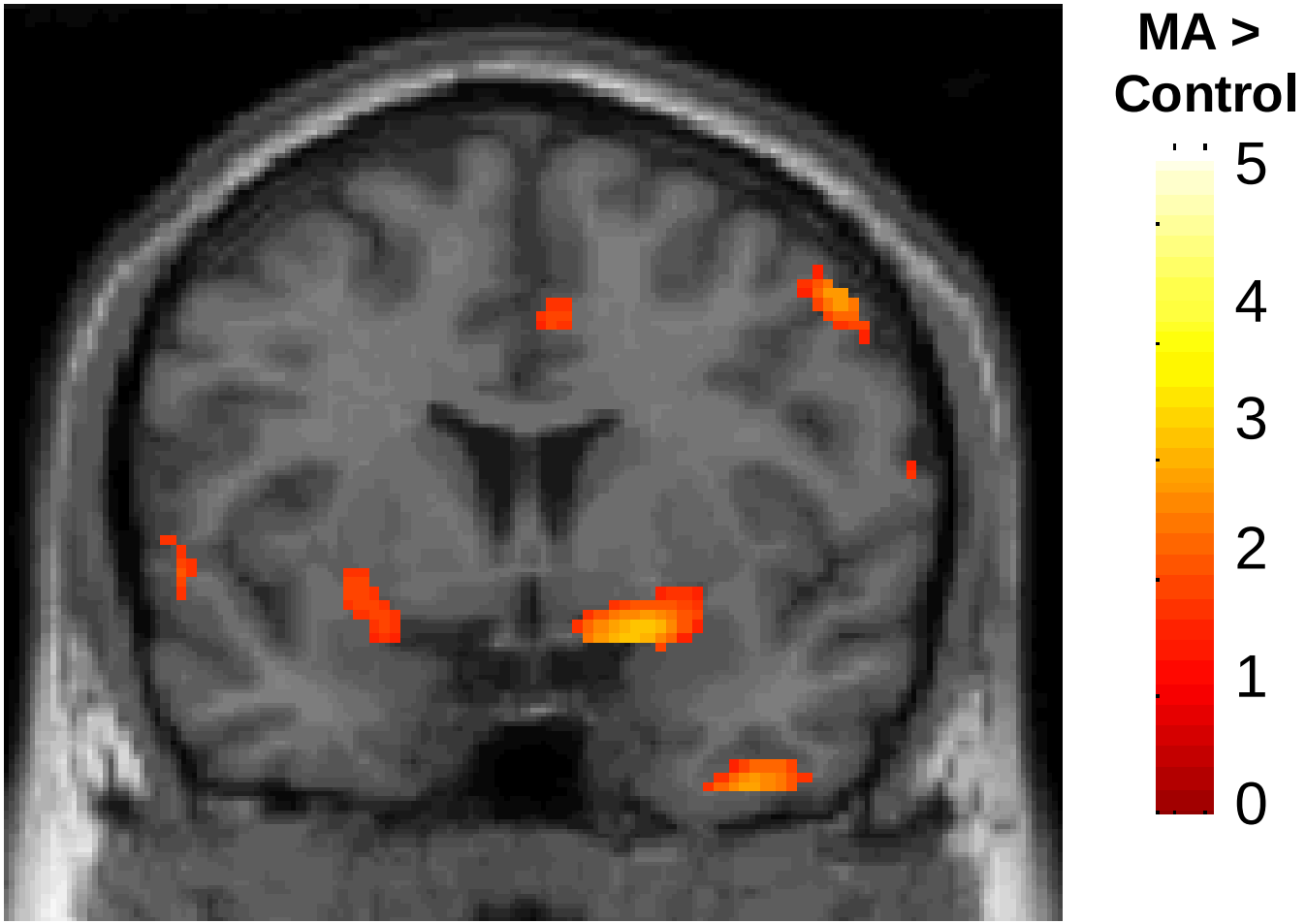
SOURCES: Shoblock et al., 2003;
DiChiara & Imperato, 1988

Decreased Dopamine Transporter Binding: Use of Meth and Parkinson's Disease

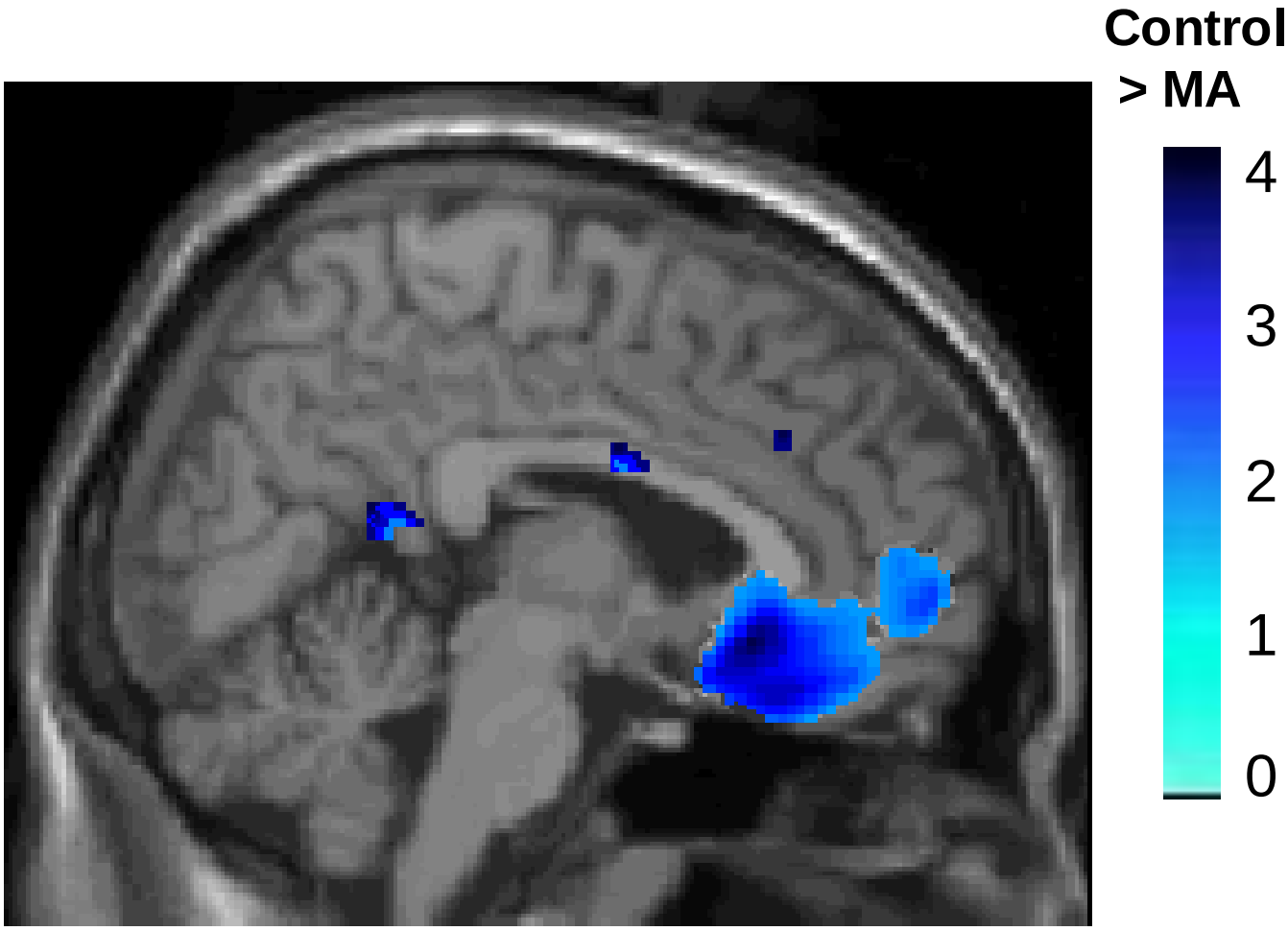


SOURCE: McCann et al., 1998

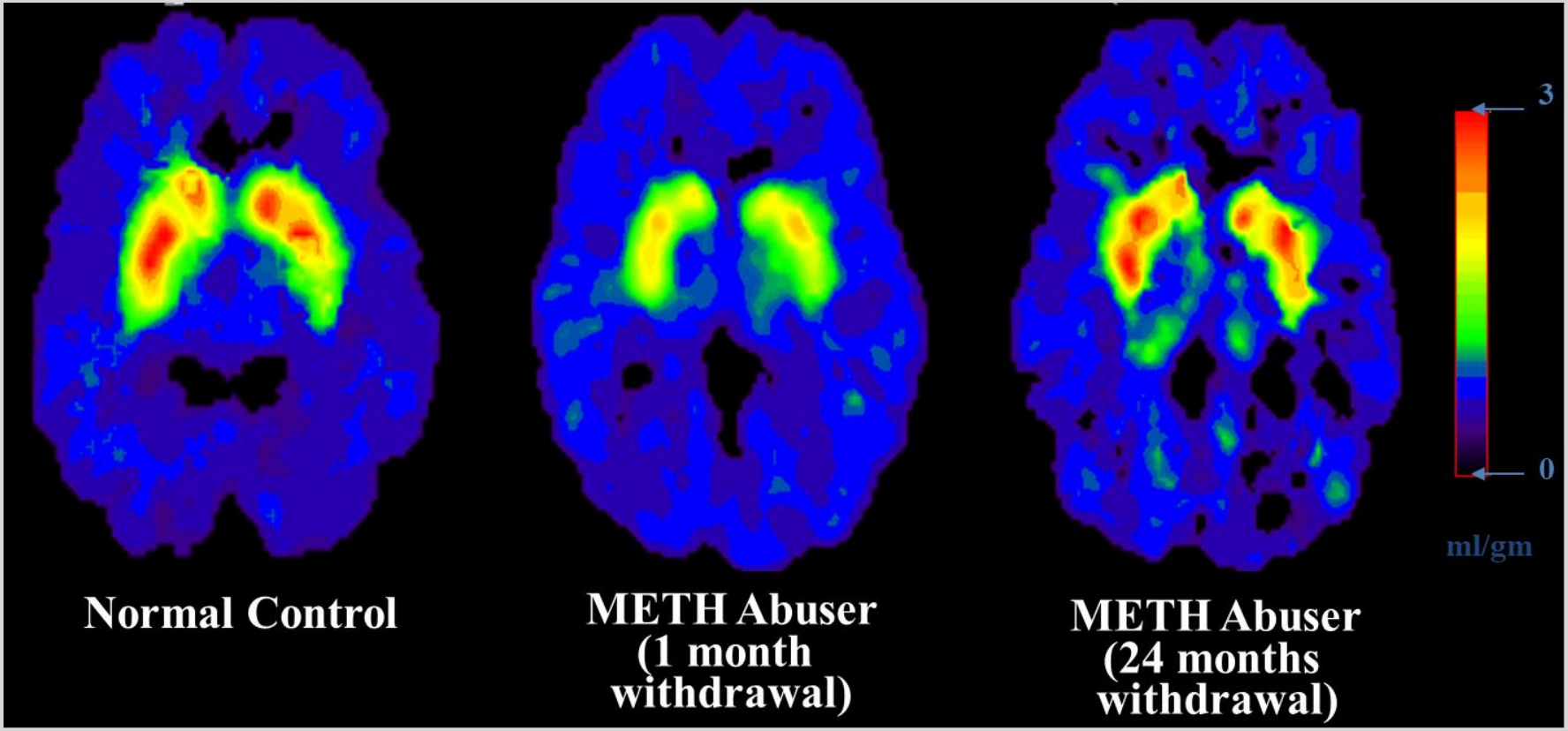
“Old Brain” is Overactive



“New Brain” is Underactive



Partial Recovery of Brain Dopamine Transporters Following Protracted Abstinence



SOURCE: Volkow et al., 2001

Acute and Chronic Effects of Stimulants

Acute Physical Effects of Stimulants

Increases

- Heart rate
- Blood pressure
- Pupil size
- Respiration
- Sensory acuity
- Energy

Decreases

- Appetite
- Sleep
- Reaction Time

SOURCE: NIDA, 2019

Acute Psychological Effects of Stimulants

Increases

- Confidence
- Alertness
- Mood/Euphoria
- Sex drive
- Energy
- Talkativeness

Decreases

- Boredom
- Loneliness
- Timidity

SOURCE: NIDA, 2019

Chronic Physical Effects of Stimulants

- Tremor
- Weakness
- Dry mouth
- Weight loss
- Cough
- Sinus infection
- Dental Problems
- Sweating
- Burned lips; sore nose
- Oily skin/complexion
- Headaches
- Diarrhea
- Anorexia

SOURCE: NIDA, 2019

Chronic Psychological Effects of Stimulants

- Confusion
- Concentration
- Hallucinations
- Fatigue
- Memory loss
- Insomnia
- Irritability
- Paranoia
- Panic reactions
- Depression
- Anger
- Psychosis

SOURCE: NIDA, 2019

Chronic Stimulant Use (1)

Acute overdose:

- Severe hyperthermia
- Convulsions
- Severe dehydration
- Rhabdomyolysis (too much myoglobin being filtered by the kidneys) → acute renal failure
- Stroke
- Myocardial infarction

SOURCE: NIDA, 2019

Chronic Stimulant Use (2)

Organ system damage

- Respiratory (pulmonary hypertension, difficulty breathing, pleuritic chest pain, decreased capacity)
- Neurological (stroke, seizure, hemorrhage, cerebral vasculitis)
- Renal failure (resulting from rhabdomyolysis)
- Hepatic failure (resulting from rhabdomyolysis)
- Cardiac (tachycardia, arrhythmia, reduced heart rate variability, myocardial infarction, heart failure)

Psychological effects

- Psychosis (hallucinations, delusions)
- Affective (depression, suicidal ideation, mania)

SOURCE: NIDA, 2019

Other Chronic Methamphetamine Problems

- Eye ulcers
- Over-heating
- Obstetric complications
- Anorexia / weight loss
- Tooth wear, cavities
- “Speed bumps”

SOURCE: NIDA, 2019

Use of Methamphetamine Leads to Severe Tooth Decay

- Methamphetamine-related dental issues are characterized by severe tooth decay and gum disease
- Teeth often break or fall out

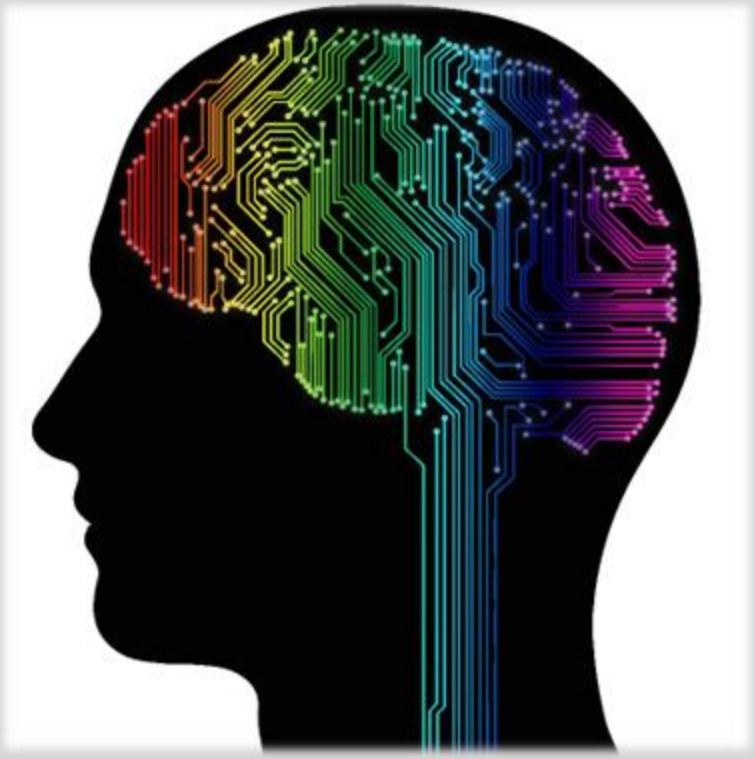
SOURCE: American Dental Association, 2017

Effects of Stimulant Use During Pregnancy

- Maternal migraines and seizures
- Premature membrane rupture
- Separation of placental lining from uterus prior to delivery
- High blood pressure
- Edema and seizures
- Spontaneous miscarriage
- Preterm labor
- Difficult delivery

SOURCES: Smid et al., 2019; NIDA, 2016; Cain et al., 2013; Volkow, 2005

Cognitive and Memory Effects of Stimulant Use



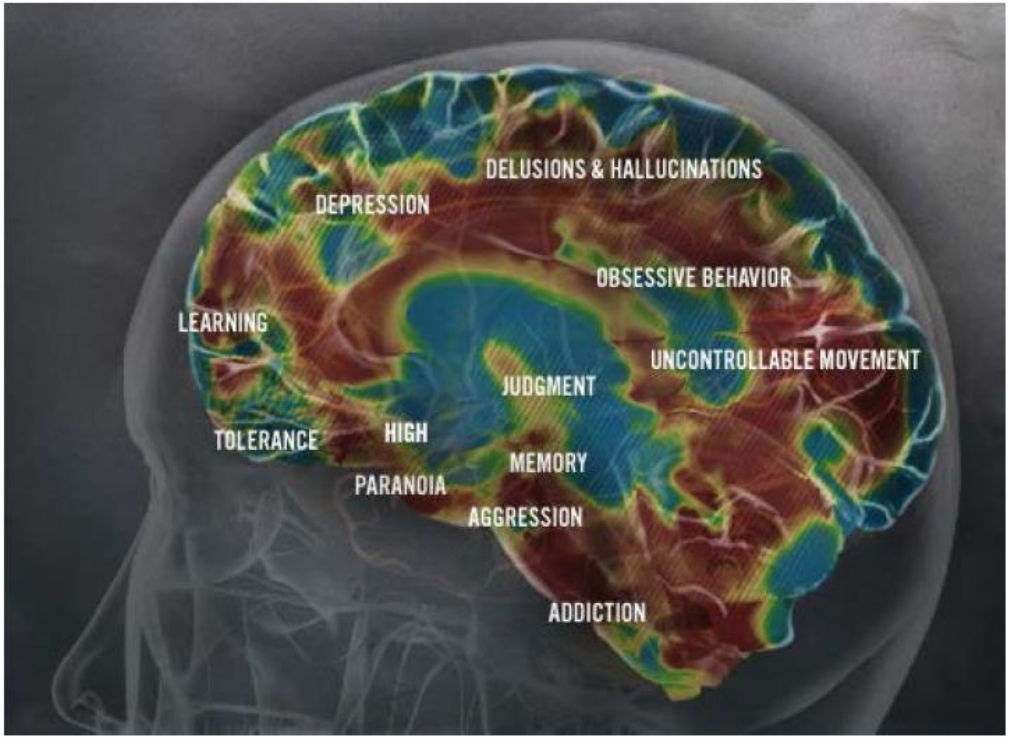
Cognitive Deficits in Methamphetamine Use Disorder

- Compared 108 methamphetamine treatment seekers and 50 matched controls.
- Methamphetamine use was associated with impulsive decision making and disinhibition.
- Greater disinhibition associated with longer durations of methamphetamine use.

SOURCE: Fitzpatrick et al., 2020

Cognitive Effects of Chronic Substance Use and Dependence

- In general, meta-analyses conclude there are medium to large persistent effects for most substances of abuse.
- The risk for cognitive impairment increases with:
  - Earlier onset of abuse
  - Greater amount of use
  - Longer duration of use and abuse



- **Almost all data is based on cross-sectional data.**
- **Longitudinal studies are needed to rule out pre-existing cognitive impairments, and to characterize course of impairments across recovery.**

http://www.methproject.org/answers/what-does-meth-do-to-your-brain.html#Brain-Damage

Cognitive Effects of Chronic Substance Use

- General effects of most substances:
  - Episodic memory
  - Emotional processing
  - Executive functions (e.g., planning and decision making)
- Specific effects:
  - Alcohol and Psychostimulants: impulsive action and cognitive flexibility
  - Alcohol and MDMA: spatial processing, perceptual speed, and selective attention
  - Cannabis and Methamphetamine: prospective memory
  - Cannabis and MDMA: processing speed and complex planning.

Strategies for Cognitive Impairment

- *Reducing* substance use may be more acceptable than total abstinence
  - Any reduction in use is progress
  - Affirm early successes to enhance self-efficacy

- When beginning tx & during early recovery, clients often feel worse before they feel better
  - Educate client to anticipate changes in mood, symptoms, lifestyle, and peer relations

(Carey et al., 1996)

Strategies for Cognitive Impairments

MODIFY TREATMENT PROTOCOLS

- **Decrease** length of sessions (attention, memory)
- Take **structured breaks** (attention, focus, memory)

- **Increase** session frequency (practice)
- **Repeat** presentations of therapeutic information (detox, 2 weeks, 4 weeks, 1 month, 3 months, etc.)
- **Multi-modal presentations**—audio, visual, experiential, verbal, hot/cold situations, etc.

- **How could you do this at your agency?**

Bates, et al., 2013; Huckans, et al., 2013

Grohman, K. & Fals-Stewart, W., 2003, 2012; Medalia, A. & Revheim, N., 2003; & Aharonovich, E., et al., 2003, 2005, 2011

Strategies for Cognitive Impairments

- Use **memory aids—** calendars, planners, phone apps, diagrams
- Teach **stress management, breathing, relaxation, and mindfulness meditation** skills
- Provide **immediate feedback** and corrective experiences
- Repeat instructions, **put things in writing,** provide short/direct instructions

Methamphetamine Use and Violence

- Compared to no use, amphetamines use was associated with a 2-fold increase in the odds of hostility or violence
- Frequent use increases the risk of violent behavior

- Other risk factors included: psychotic symptoms, alcohol or other drug use, psychosocial problems, and impulsivity
- People who use methamphetamine are also more likely to be victims of abuse or violent acts
- Women who used methamphetamine are significantly more likely to experience partner abuse/violence

SOURCES: Foulds et al., 2020; Cohen et al., 2003

Treatment Considerations for People Who Use Stimulants

Stigma and Its Impact on Recovery

- Multiple layers of stigma:
  - Substance use stigma ("addict," "junkie")
  - Criminal record stigma ("ex-con," "felon")
  - Stimulant-specific stigma (methamphetamine, crack)
- Impacts:
  - Reduced treatment-seeking (42% less likely)
  - Barriers to employment (15-30% callback reduction)
  - Housing discrimination (up to 70% rejection rate)
  - Internalized shame and reduced self-efficacy
- Disproportionate effects on marginalized communities

Justice-Based Interventions for Stimulant Use

- Pre-arrest diversion programs (e.g. LEAD model)
  - 58% reduction in recidivism
- Drug courts: specialized dockets for SUD offenders
- Prison-based therapeutic communities
- Medication continuation during incarceration
- Reentry programs with integrated services
  - Housing, employment, healthcare coordination

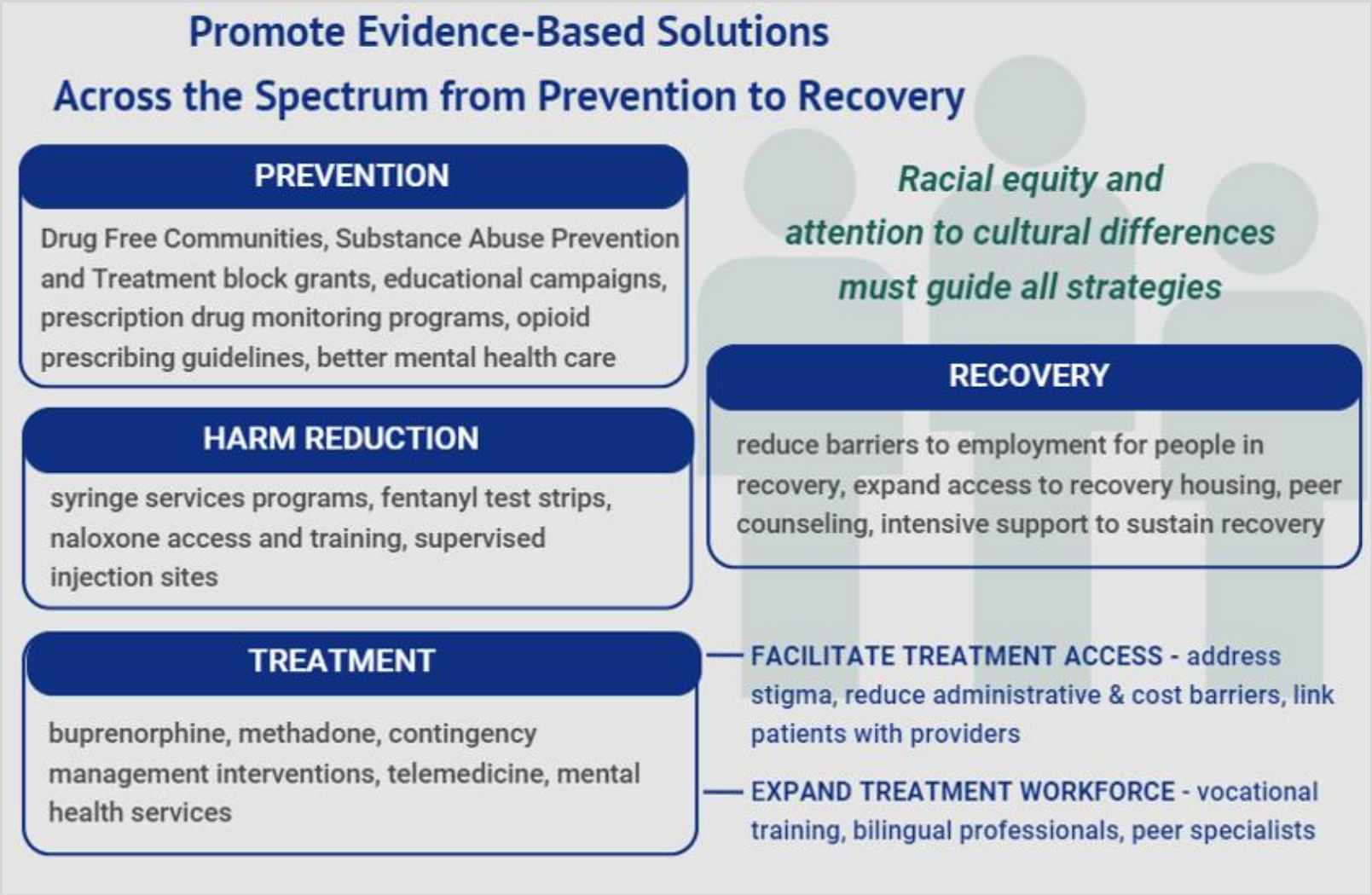
Case : Michael 34 years old

Michael is a 34-year-old man who began using methamphetamine at age 19 to cope with untreated depression and the stress of working multiple jobs. His use escalated from occasional to daily over the past five years, coinciding with housing instability following a relationship breakdown. Michael has been arrested three times for possession and once for theft (stealing electronics to sell for drug money). He is currently on probation after serving eight months in county jail for his latest offense.

Since his release three weeks ago, Michael has been staying at a local shelter but struggles to maintain employment due to withdrawal symptoms, ongoing cravings, and difficulty concentrating. He reports wanting to "get sober" but has attempted recovery twice before, each time relapsing within months when facing triggers in his environment or employment stress. Michael has inconsistent access to transportation and has lost contact with family members who might otherwise provide support. His probation requirements include weekly drug testing, but he has already missed one appointment due to confusion about the schedule.

- What strengths can we identify in Michael's case that might support recovery?
- What barriers might Michael face?
- What services should we prioritize given limited resources?

The Importance of Evidence-Based Solutions When Working with People Who Use Stimulants



SOURCE: NIHCM Foundation, 2021

Are there Medications for the Treatment of Stimulant Use Disorder?

- The short answer is NO
- A few medicines have had positive results in clinical trials
- To date, these medicines have not demonstrated reproducible results
- Much more research is needed to determine the overall efficacy of these medicines

SOURCE: Skolnick, 2015

What Do the Results from the Latest Methamphetamine Medication Trial Tell Us?

- Multi-site, double-blind, two-stage, placebo controlled trial to evaluate the efficacy and safety of extended-release injectable naltrexone plus oral extended-release bupropion
- 403 participants enrolled in stage 1; 225 participants enrolled in stage 2
  - Stage 1: 18 of 109 participants (16.5%) in the naltrexone-bupropion group and 10 of 294 (3.4%) in the placebo group had a response
  - Stage 2: 13 of 114 (11.4%) in naltrexone-bupropion group and 2 or 111 (1.8%) in the placebo group had a response

SOURCE: Trivedi et al., 2021

Medications Considered for Methamphetamine Use Disorder

A 2019 meta analysis of medication trials found no strong/consistent evidence for MA abstinence, reducing use, or improving treatment retention.

Some evidence found to support

- Methylphenidate
- Topiramate (better if abstinent at treatment entry)
- Bupropion (better in low severity users)
- Mirtazapine
- Naltrexone

SOURCES: Chan, et al., 2019; Chan, et al., 2018

Medications Considered for Cocaine Use Disorder

A 2018 meta analysis of medication trials found no strong/consistent evidence for cocaine abstinence, reducing use, or improving treatment retention. Strongest evidence for **bupropion**, **psychostimulants**, **topiramate** for abstinence and **antipsychotics** for retention.

Other research has found some evidence for:

- Modafinil (dopamine agonist)
- Disulfiram
- Propranolol
- Buprenorphine+naltrexone

SOURCES: Chan et al., 2018; Kampman, 2019; Shorter & Kosten, 2011; Poling et al., 2006

Behavioral Treatments

- Contingency Management
- Community Reinforcement Approach
- Cognitive Behavioral Therapy/Relapse Prevention
- Motivational Interviewing
- Matrix Model
- Exercise
- Mindfulness

Psychosocial Interventions for Individuals with Cocaine and Amphetamine Use Disorder

- Meta-analysis of 50 clinical studies (6,943 participants) on 12 different psychosocial interventions for cocaine and/or amphetamine addiction.
- The **combination of contingency management and community reinforcement approach**, was the most efficacious and most acceptable treatment both in the short and long term.

SOURCE: De Crescenzo et al., 2018

More (Recent) Evidence for Contingency Management as a Response to Stimulant Use (1)

- A 2020 systemic review of 27 studies found that contingency management has broad benefits in:
  - Greater drug adherence
  - Higher utilization of other treatments and medical services
  - Reductions in risky sexual behavior
- Recommendation: Outpatient programs that offer treatment to people with a methamphetamine use disorder should **prioritize adoption and implementation of contingency management**

SOURCE: Brown & DeFulio, 2020

More (Recent) Evidence for Contingency Management as a Response to Stimulant Use (2)

Results A total of 157 studies comprising 402 treatment groups and 15 842 participants were included.

Only contingency management programs were significantly associated with an increased likelihood of having a negative test result for the presence of cocaine (OR, 2.13; 95%)

Conclusions In this meta-analysis, contingency management programs were associated with reductions in cocaine use among adults.

SOURCE: Bentzley et al., 2021

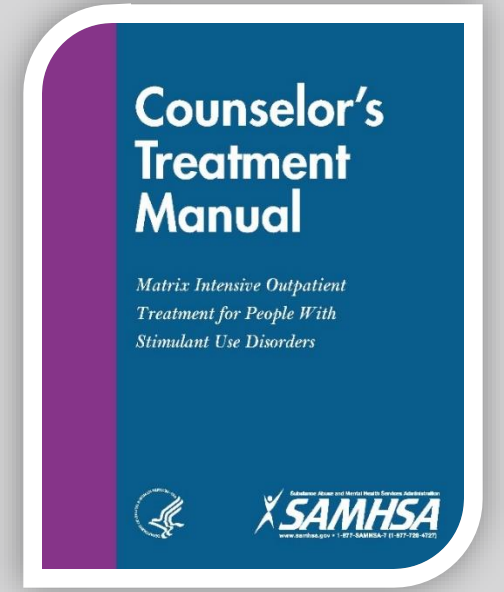
Responding to Global Stimulant Use: Challenges and Opportunities

- Psychosocial interventions **other than contingency management** have weak and non-specific effects on stimulant problems
- No effective pharmacotherapies have been approved
- Substantial research investment is needed to develop more effective, innovative, and impactful prevention and treatment

SOURCE: Farrell et al., 2019

Behavioral Approach: Matrix Model

- 16-week intensive outpatient treatment was modestly better treatment as usual to improve retention and reduce methamphetamine use
- Therapist functions as teacher and coach
- Incorporates a variety of approaches
  - CBT
  - CM
  - MI
  - 12-Step Facilitation
  - Family Involvement
  - Person-centered therapy



SOURCES: CSAT, 2006; Rawson, et al., 2004

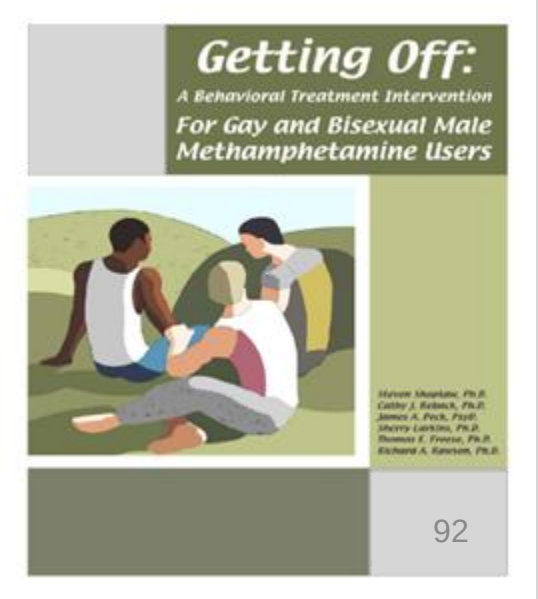
Getting Off: A Behavioral Treatment Intervention for Gay and Bisexual Men Who Use Methamphetamine

Contingency Management (CM):

- Provide increasingly valuable reinforcers for urine samples documenting drug abstinence

Gay-specific Cognitive Behavioral Therapy (GCBT):

- Cognitive Behavioral strategies for instilling abstinence and preventing relapse in a gay-specific HIV risk reduction intervention



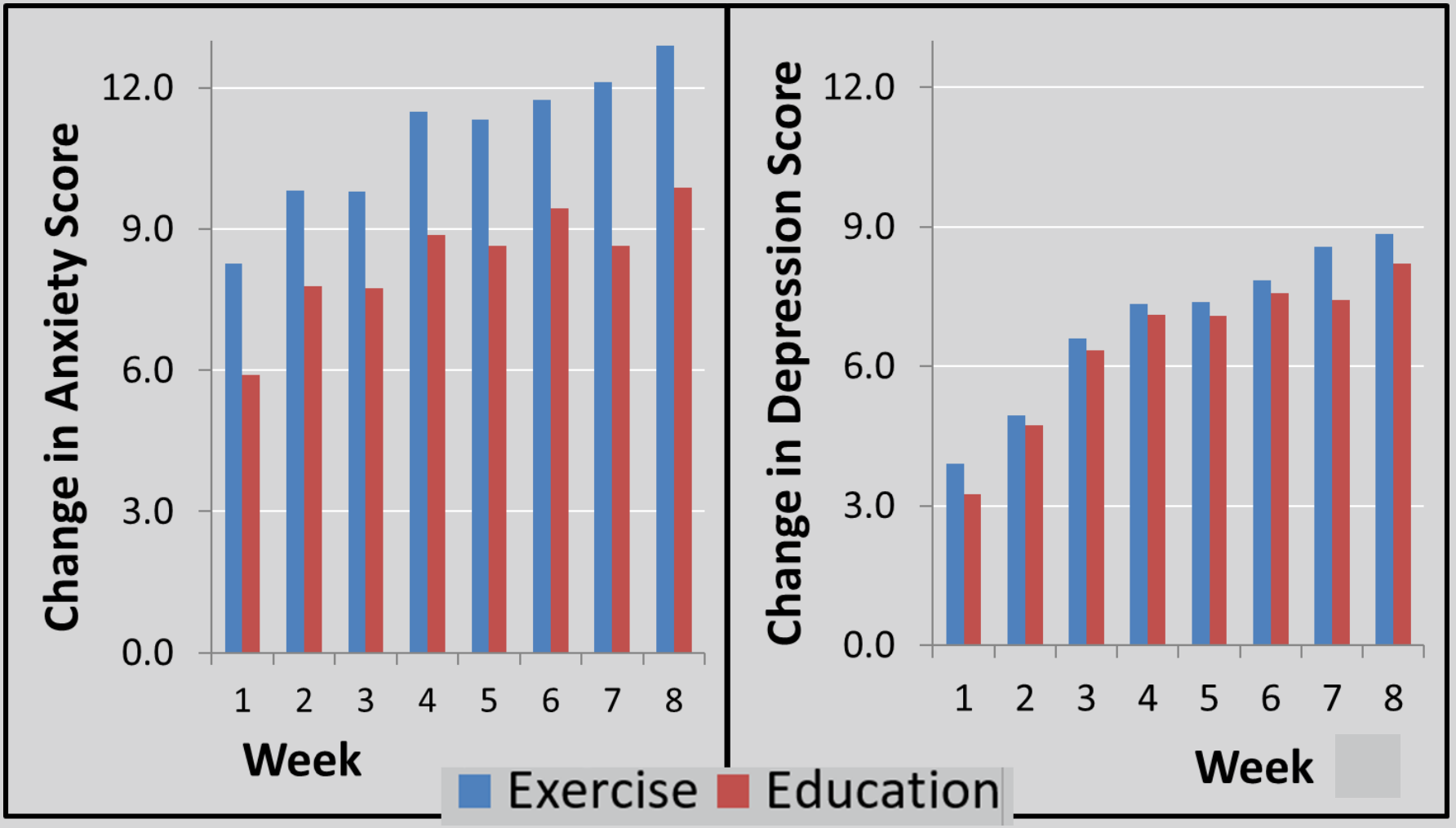
SOURCES: Reback et al., 2014; Shoptaw et al., 2005

Does Exercise Improve Outcomes Post-Treatment?

- Yes!
- Fewer exercise participants returned to meth use compared to the education participants at 1-, 3-, and 6-months post-discharge (not statistically significant)
- Significant interaction found for self-reported meth use and meth urine drug test results – lower severity users in the exercise group reported using meth significantly fewer days at the three post-discharge time points than lower severity users in the education group
- Lower severity users in the exercise group also had a lower percentage of positive urine results at the three time points than the lower severity users in the education group (relationships not seen in higher severity groups)

SOURCE: Rawson et al., 2015

The Impact of Exercise on Depression and Anxiety Symptoms



SOURCE: Rawson et al., 2015

SAMHSA's Guiding Principles of Recovery

SOURCE: US DHHS, SAMHSA, 2012

Responding to the Impact of Long-Term Stimulant Use

- Awareness of the challenges of early recovery
  - Overloading people with paperwork or complex tasks
- Patience with the healing process for each individual
  - From themselves
  - From behavioral health community
  - From family and friends

SOURCE: Tennessee Works, 2020

Recommendations for Evidence-Based Practice

- Universal screening for stimulant use at justice entry points
- Ensuring treatment continuity across transitions
- Expanding contingency management availability
- Cross-training for justice and treatment professionals
- Integrating peer support throughout justice continuum
- Addressing social determinants: housing, employment
- Implementing coordinated data systems

Concluding Thoughts

- The availability and use of cocaine and methamphetamine is widespread across the U.S. and beyond
- Central nervous system stimulants effect multiple organ systems, including the brain, heart, lungs, kidneys, liver, and skin
- The brain does have the ability to heal from use of stimulants, it just takes time
- A variety of behavioral interventions have been shown to be effective
- No FDA-approved medications exist (yet)
- Recovery is possible

Resources for Continued Learning

- ATTC Network's *Focus on Stimulant Misuse* Web Page: https://attcnetwork.org/centers/global-attc/focus-stimulant-misuse
- *Evidence-Based Resource Guide Series: Treatment of Stimulant Use Disorders*: https://store.samhsa.gov/product/Treatment-of-Stimulant-Use-Disorder/PEP20-06-01-001
- Northwest ATTC's *Contingency Management for Healthcare Settings Self-Paced Online Course*: https://healtheknowledge.org/course/search.php?search=Contingency+Management
- *Treatment for Stimulant Use Disorders* (TIP 33 Update): https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP21-02-01-004.pdf

Stimulant 101 National Curriculum

- Core Daylong Curriculum
- Condensed Three-Hour Live Virtual Overview
- Conference Keynote Presentation
- Supplemental Modules
  - Child welfare issues, gender differences, stimulant use in the context of polysubstance use, rural vs. urban differences, meth use and HIV among MSM, stimulants and HIV, and recovery approaches
- Culture Modules
  - African American, American Indian/Alaska Native, and Latinx Populations

Thank You For Your Time

- For questions, please contact Grant at ghovik@mednet.ucla.edu
- The various components of the ATTC Stimulant 101 curriculum are posted at: https://attcnetwork.org/centers/global-attc/focus-stimulant-misuse
- For additional information regarding SUD treatment-related Training/TA, please visit: http://www.attcnetwork.org
- For additional information regarding HIV/AIDS-related Training/TA, please visit: https://aidsetc.org/