

Methamphetamine 2020

New Risks, Current Treatments

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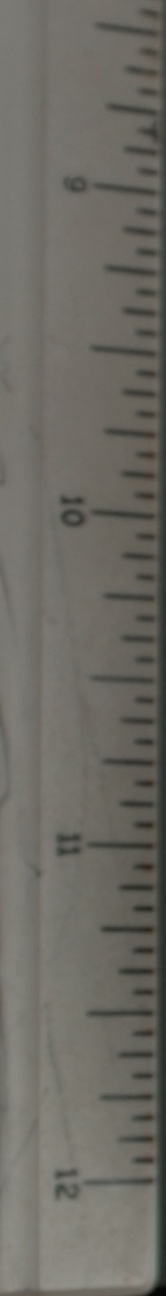
Professor Emeritus, UCLA Department of Psychiatry and Biobehavioral Sciences

2020

No Disclosures

Learning Objectives

- Participants will be able to explain the current epidemiology of cocaine and methamphetamine in the US
- Participants will be able to describe the most common clinical challenges in treatment people with stimulant use disorders.
- Participants will be able to review and discuss the current evidence-based practices for the treatment of individuals with stimulant use disorder.



ST

Methamphetamine

- In the 1990s and early 2000s, meth made from the decongestants, pseudoephedrine and ephedrine, poured out of domestic labs like those in the early seasons of “Breaking Bad.”
- Narcotics squads partially became hazmat teams.



Methamphetamine Availability Reduced

In 2005 Congress passed the Combat Methamphetamine Act, which put pseudoephedrine products behind the counter, limited amounts purchased, and tracked purchasers.

Although some meth makers tried “smurfing,” meth cases plummeted.

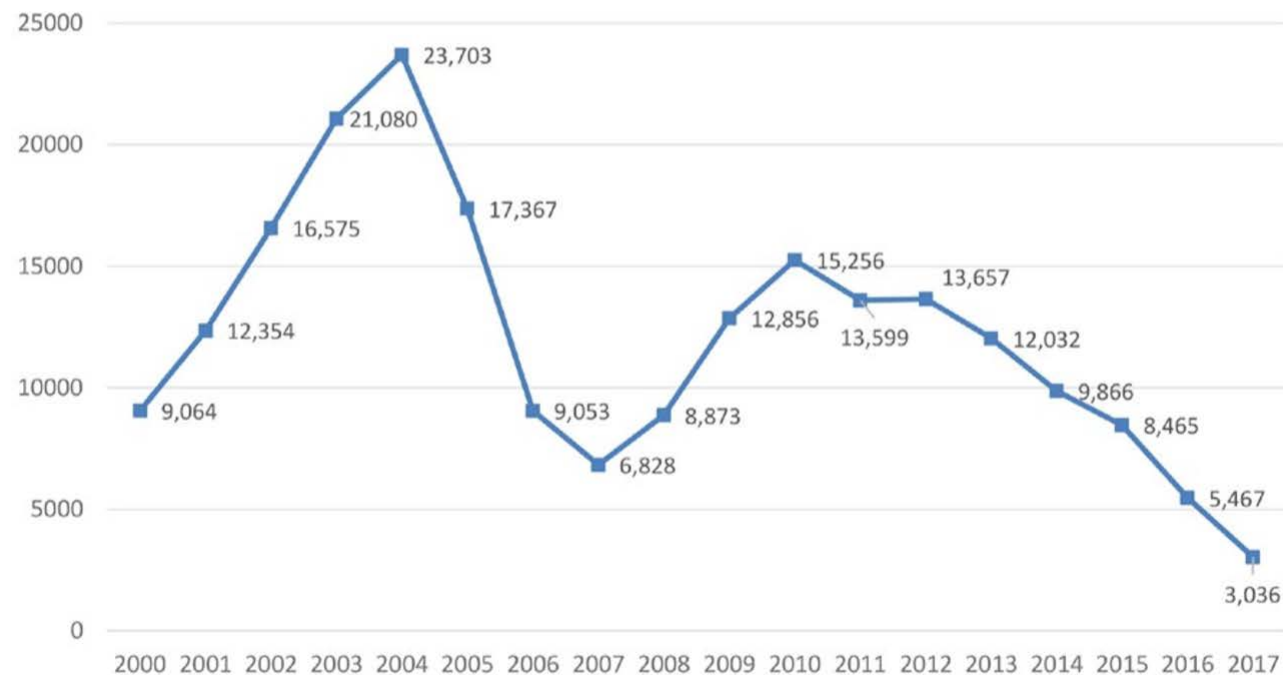
- With no more meth lab explosions on the nightly news, the public forgot about the drug.
- Mexican drug cartels stepped in improving production with higher potency and lower price (\$2,000 per pound; down from \$8,000)

Methamphetamine Lab Incidents

METHAMPHETAMINE

UNCLASSIFIED

Figure 76. Number of Methamphetamine Laboratory Incidents, 2000 – 2017.



Source: El Paso Intelligence Center National Seizure System as of June 12, 2018

Methamphetamine Today

- Methamphetamine, experts say, has never been purer, cheaper or more lethal.
- 2014-2018 fentanyl-contaminated meth and cocaine became more prevalent
- 2018 - United States border agents seizing 10 to 20 times the amounts they did a decade ago.
- Methamphetamine, experts say, has never been purer, cheaper or more lethal

Potential Lethal Dose Heroin, Fentanyl and Carfentanil



Comparing the size of lethal doses of heroin, fentanyl, and carfentanil. The vials here contain an artificial sweetener for illustration. (New Hampshire State Police Forensic Laboratory)

Two Milligrams of Fentanyl – A Potential Lethal Dose



Source: Network Environmental Systems (NES)

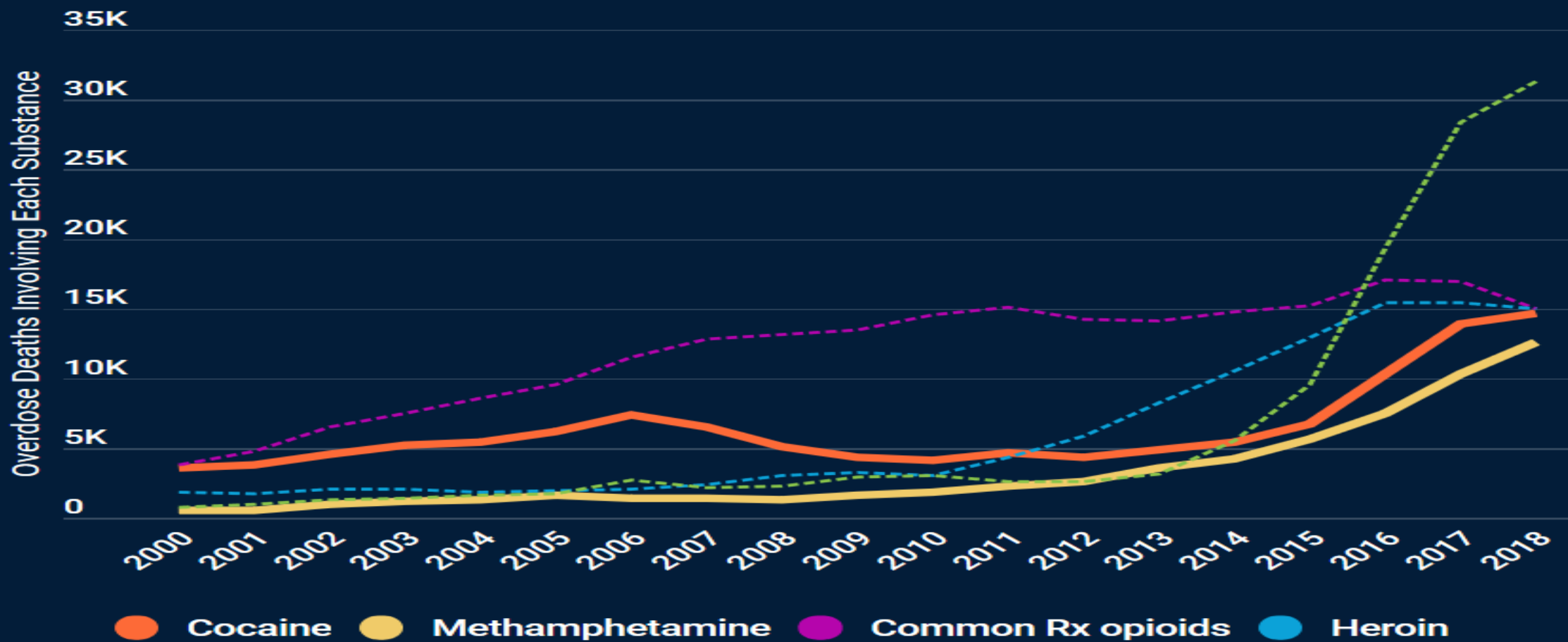
**A Kilo of:
Heroin nets
\$60 k
Fentanyl
nets \$1.2 mil**

A lethal dose of carfentanil 1/100th of the amount shown next to the penny.



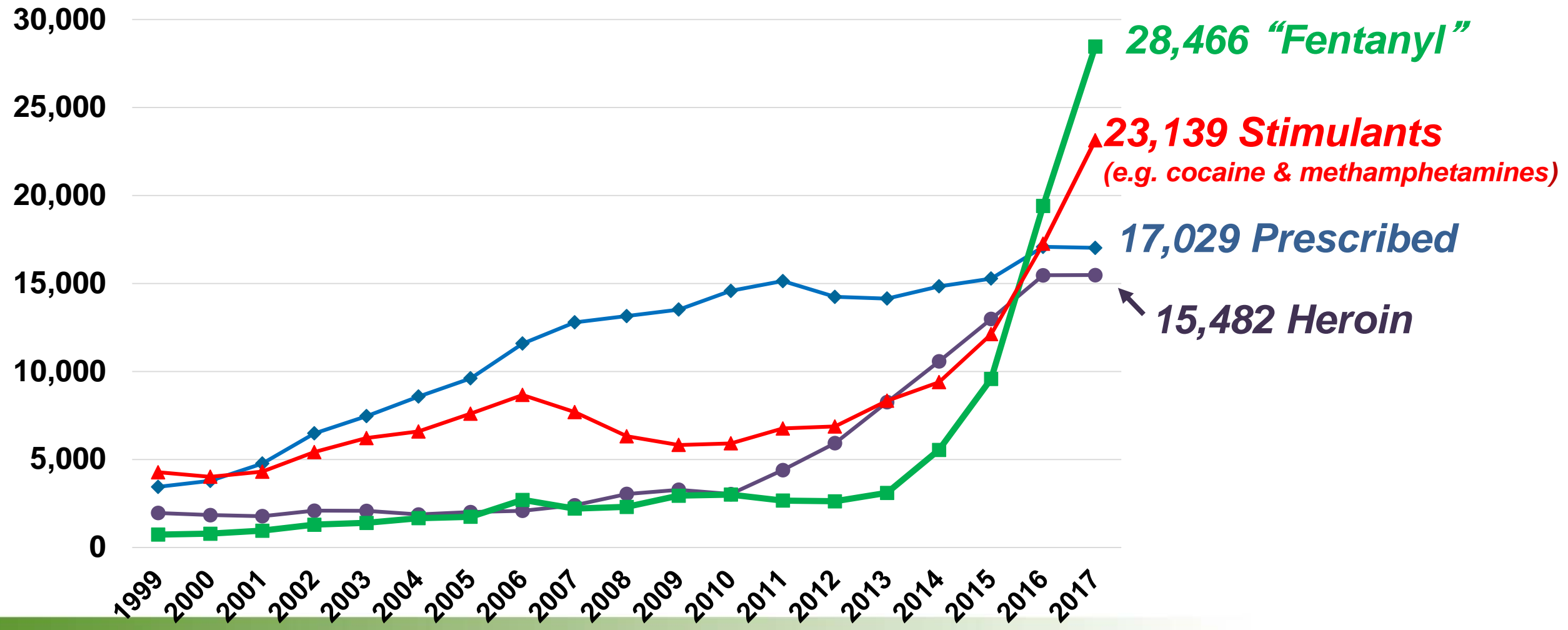
Beyond Opioids:

Rapid increase in drug deaths involving stimulants



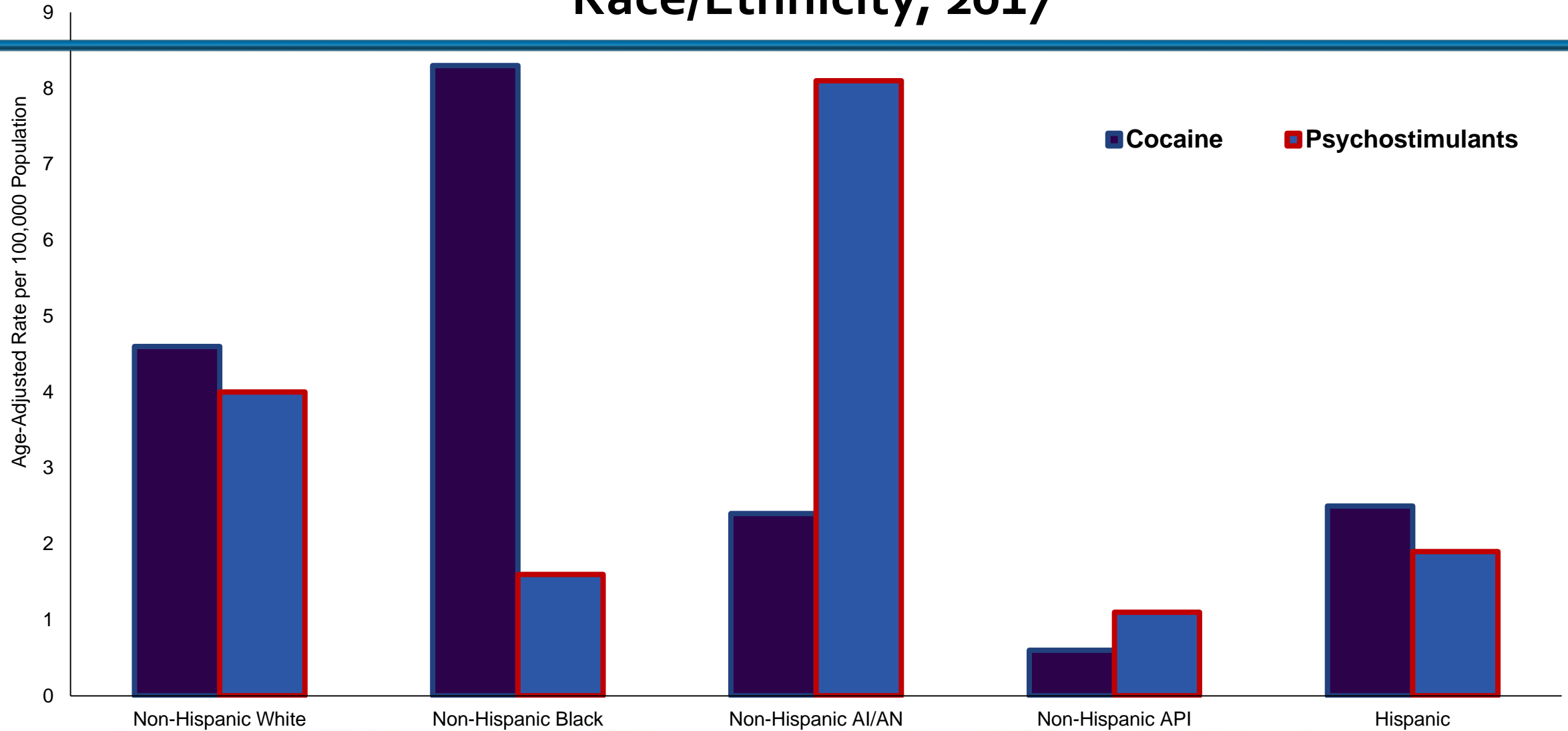
Evolution of Drivers of Overdose Deaths:

Analgesics ➡ *Heroin* ➡ *Fentanyl* ➡ *Stimulants*



See: Compton WM & Jones CM, *Ann NY Acad Sci*, 2019; Data from CDC WONDER Database

Cocaine and Psychostimulant Overdose Deaths by Race/Ethnicity, 2017



**Kariisa M, et al. *MMWR Morb Mortal Wkly*
Rep. 2019;68(17):388-395**

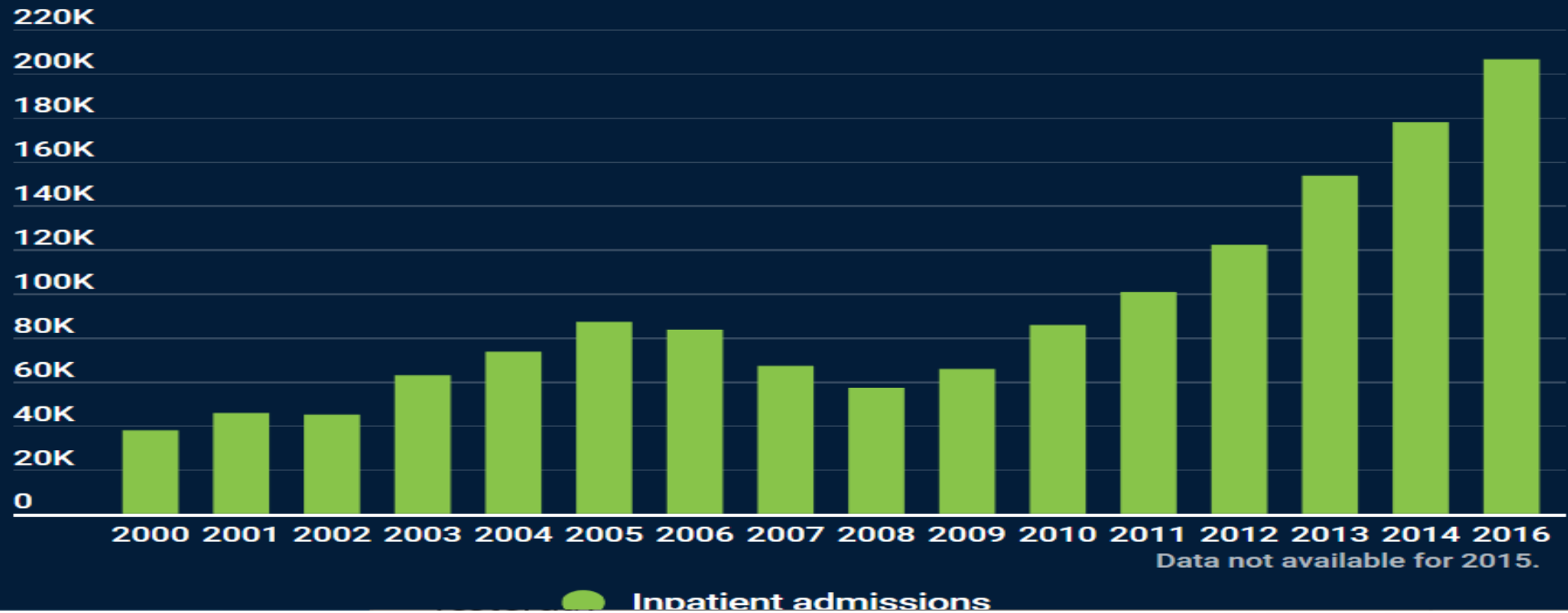




Methamphetamine is placing a rapidly increasing burden on the hospital system

Inpatient Admissions

Emergency Department Visits



**Association between methamphetamine use
and retention among patients
with opioid use disorders treated with
buprenorphine**

Journal of Substance Abuse Treatment

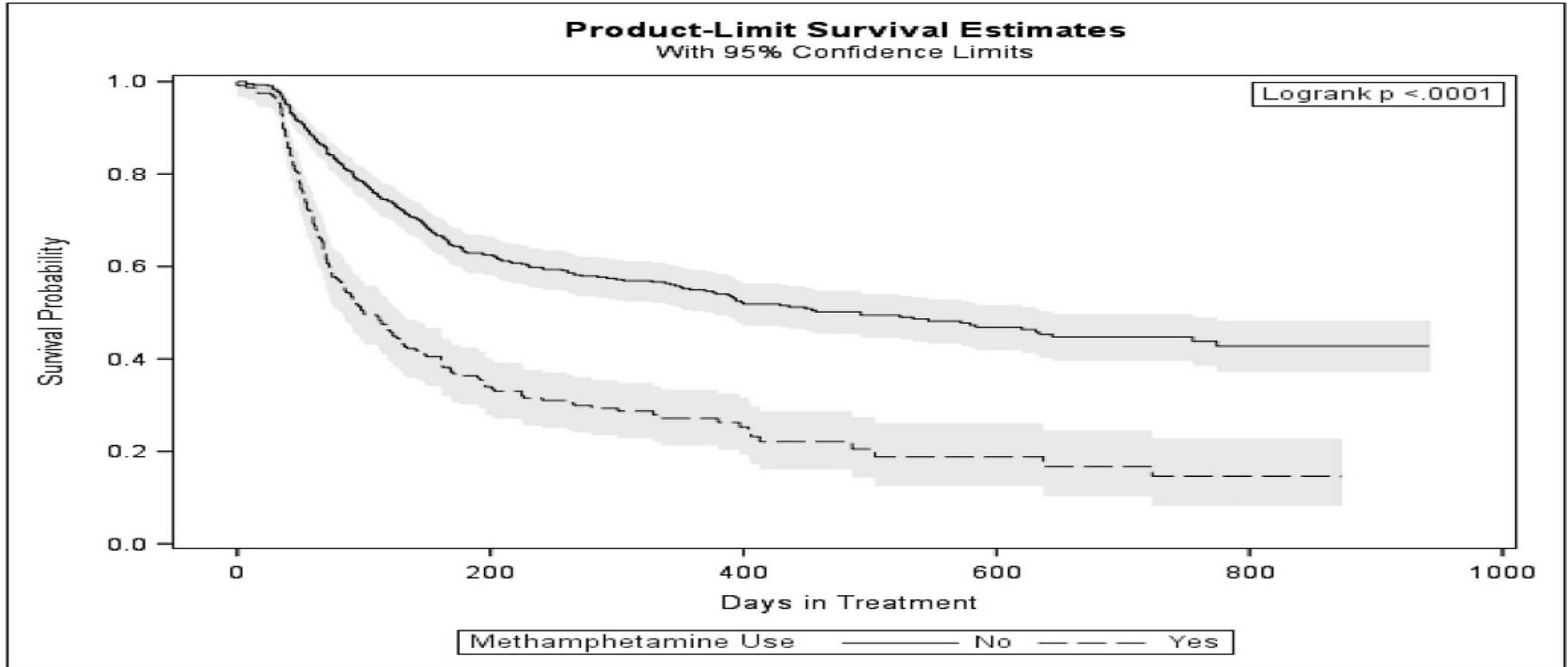
109 (2020) 80–85

Judith I. Tsui, et al.

Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine

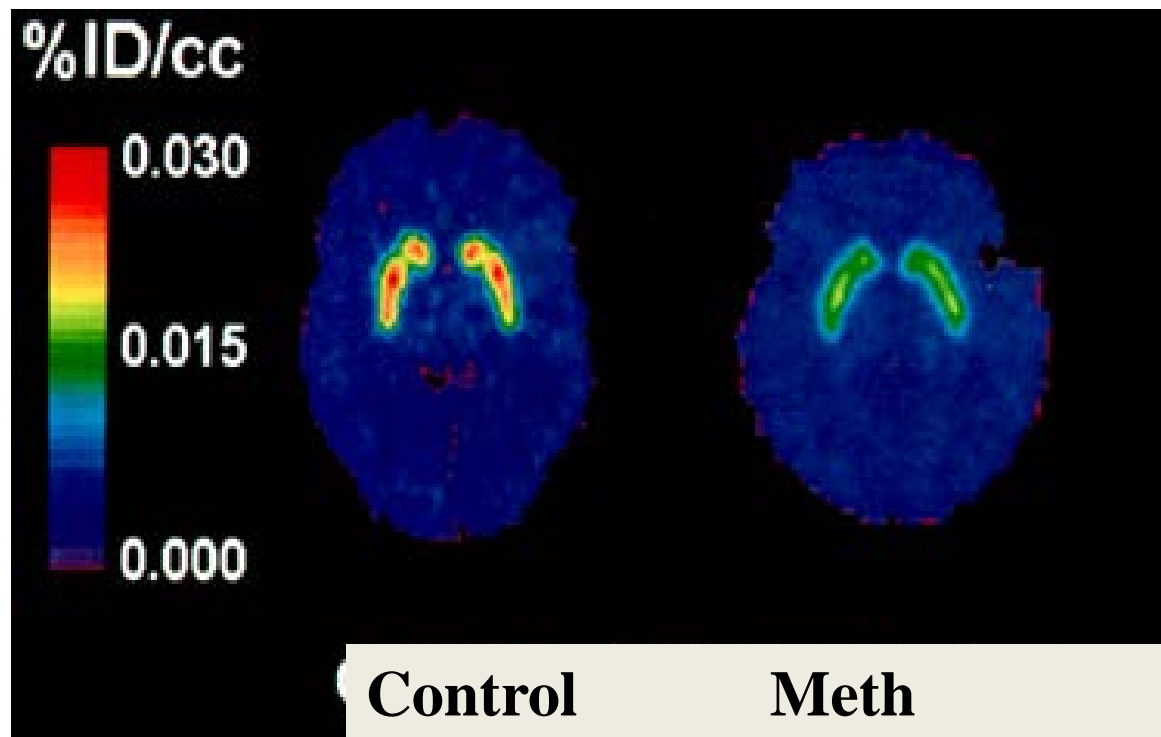
- The study utilized data on adult patients receiving buprenorphine from Washington State Medication Assisted Treatment-Prescription Drug and Opioid Addiction program clinics between November 1, 2015 and April 31, 2018 (N=799) Past 30-day substance use data were collected at baseline and 6-months, as well as date of program discharge.
- 30% (n=237) individuals reported meth use at admission. Baseline methamphetamine use was associated with more than twice the relative hazards for discharge in adjusted models (aHR=2.39; 95% CI: 1.94–2.93).

Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine



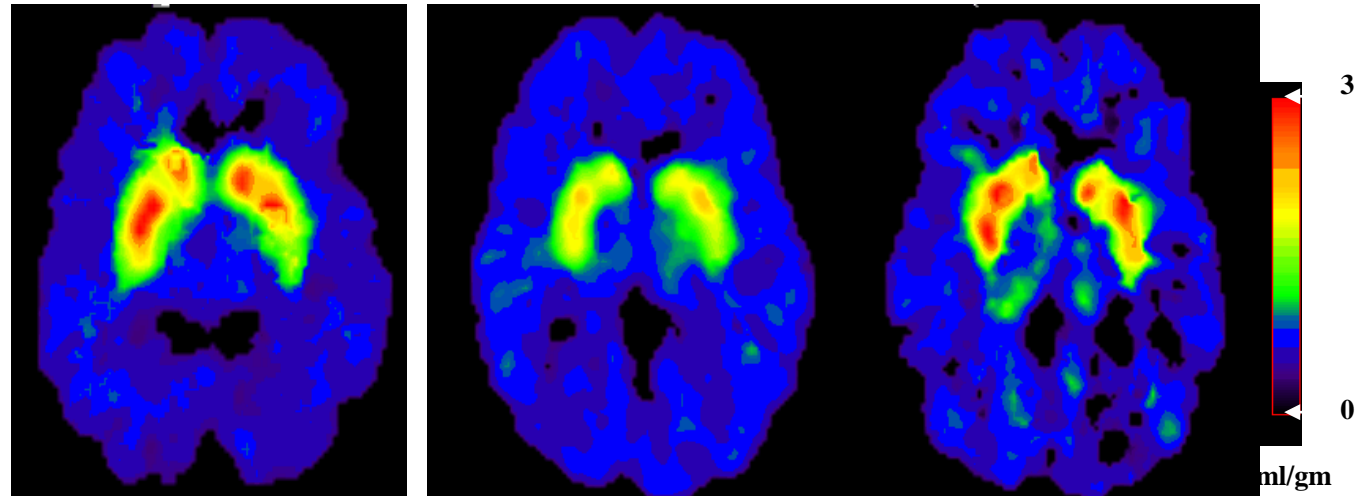
Chronic Methamphetamine Causes Changes in the Brain

Decreased Dopamine Transporter Binding In People Who Use Methamphetamine Resembles That In Parkinson's Disease Patients



Source: McCann U.D.. et al., *Journal of Neuroscience*, 18, pp. 8417-8422, October 15, 1998.

Partial Recovery of Brain from Methamphetamine After Abstinence



Normal Control

Using meth
(1 month abstinent)

Using meth
(14 months abstinent)

Source: Volkow, ND et al., *Journal of Neuroscience* 21, 9414-9418, 2001.

Dopamine improvements after 1 year

UCLA

Medical Issues Related to Methamphetamine Use

Neurobiology, Clinical Presentation, and Treatment of Methamphetamine
Use Disorder

Paulus and Stewart, JAMA Psychiatry, 2020

Neurotoxicity

- Excessive dopamine results in damaged cell structures
- Cell death
- Activation of dopamine D3 receptors resulting in hyperthermia
- Disruption of the blood-brain barrier
- Overall the altered brain state is consistent with degenerative central nervous system diseases.

Cognition

- It is estimated the more than 2/3 of those with methamphetamine use disorder show cognitive impairment.
- Impairment is associated with older age, longer duration of use, and greater frequency of use.
- May limit ability to follow through with treatment, comprehend advice and direction in treatment, and generally achieve good treatment outcomes.

Cognitive Deficits in Methamphetamine Use Disorder

Fitzpatrick et al., 2020

- 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.

Methamphetamine and Violence

Foulds et al., 2020

- Review of 28 studies.
- 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.

Cerebrovascular and Cardiovascular Disease

- Leading causes of death with methamphetamine use disorder
- Strokes are increasing most often with young men
- Strokes are primarily hemorrhagic

- Associated with methamphetamine use:
 - Pulmonary hypertension
 - Cardiac arrhythmia
 - Cardiomyopathy

Smid, M., Metz and Gorden (2019) Stimulant Use in
Pregnancy – an under-recognized epidemic among
pregnant women Clin Obstet Gynecol . 2019 March ;
62(1): 168–184

Stimulant Use in Pregnancy

Smid et al., 2019

- Meta-analysis of 31 studies found cocaine use during pregnancy increased risk of pre-term delivery, low birth weight, small for gestational age, earlier gestational age at delivery, and reduced birth weight (Gouin, 2011).
- Meta-analysis of 8 studies found methamphetamine use during pregnancy was associated with earlier gestational age at delivery, lower birth weight, and smaller head circumference (Kalaitzopoulos, 2018).
- Infants with prenatal exposure to methamphetamine exhibit jitteriness, drowsiness, and respiratory distress suggesting withdrawal.
- Cocaine and methamphetamine are excreted in breastmilk and contraindicate breastfeeding.

Stimulant Use in Pregnancy

Smid et al., 2019

- Long-term follow-up of 204 methamphetamine exposed maternal-child pairs and 208 unexposed (Derauf et al., 2007).
- At one month 33% methamphetamine-exposed mothers did not have custody compared to 2% of unexposed.
- At age 3 years heavy prenatal methamphetamine use (≥ 3 days per week) was associated with anxiety/depression and attention problems in children.
- At age 7.5 years methamphetamine-exposed children had poorer cognitive function.

Symptoms Preceding Death from Toxic Methamphetamine Effects

- Collapse
- Breathing difficulty
- Hyperthermia

- People who use Methamphetamine presenting with acute intoxication may be at risk for fatality with symptoms:
 - Labored breathing,
 - Angina, palpitations
 - Cough
 - Coughing up blood
- Should be closely monitored

“Double-Jeopardy: Methamphetamine use and HIV as Risk Factors for COVID-19” Carrico et al., 2020

- Damage to the immune system by HIV plus immune system damage from methamphetamine increases risk for COVID-19
- Methamphetamine use is associated with sexual risk behavior among MSM. Suggests poor adherence to social distancing guidelines
- Men who seek out partners for substance use and sex could cause COVID-19 clusters (has happened in Miami).
- COVID-19 related stress and psychiatric disorders leads to increased substance use and poorer SA treatment outcomes.
- Authors suggest more use of telehealth approaches.

Collision of the COVID-19 and the Addiction Epidemics

Volkow, 2020

- Chinese Center for Disease Control report fatality rate of 6.3% for people with chronic respiratory diseases compared to 2.3% overall.
- People who smoke, vape, use opioids or have an SUD are vulnerable.
- Opioid use causes hypoxemia.
- Methamphetamine use causes pulmonary damage.
- Social distancing increases risk of overdose with fewer people available to administer naloxone.
- Limited access to support for those in recovery.
- Isolation, stress, anxiety, and depression can lead to more substance use.

Clinical Challenges

Clinical Challenges with Stimulant Dependent Individuals

- Overdose death
- Limited understanding of stimulant addiction
- Ambivalence about need to stop use
- Impulsivity/Poor judgement
- Cognitive impairment and poor memory
- Anhedonia
- Hypersexuality
- Violence and psychosis
- Powerful Pavlovian trigger-craving response
- Very poor retention in outpatient treatment
- Elevated rates of psychiatric co-morbidity

Special Treatment Consideration Should Be Made for the Following Groups

- People who inject drugs
- People who use stimulants daily or in very high doses.
- Women (high rates of physical/sexual abuse)
- Homeless, chronically mentally ill and/or individuals with high levels of psychiatric symptoms at admission.
- Men who have sex with men (MSM)
- People under the age of 21.
- Individuals in medication treatment for OUD

Clinical Interventions

Harm Reduction Strategies for People Who Use Stimulants

- Information about medical and psychiatric effects of meth
- Overdose Education (fentanyl)
- Syringe Exchanges
- Naloxone (for opioid overdose)
- Quiet rooms and washup/shower rooms
- Condoms/safe sex education
- Topical antibiotic creams and ointments for injection sites
- Water (dehydration)
- Tooth paste/tooth brush

Naloxone for People Who Use Stimulants?






- With increasing rates of fentanyl mixed into samples of methamphetamine (and cocaine), people who use stimulants are at much higher risk for overdose death due to their lack of tolerance for opioids.
- People who use stimulants should be educated about the dangers of fentanyl and offered naloxone (Narcan) in case of opioid overdose.
- Note, fentanyl has greater affinity for the opioid receptor than naloxone= more difficult to reverse overdose.

Treatment for Individuals with Stimulant Use Disorders

Systematic Reviews and Meta-analyses

RESEARCH ARTICLE

Comparative efficacy and acceptability of psychosocial interventions for individuals with cocaine and amphetamine addiction: A systematic review and network meta-analysis

Franco De Crescenzo ^{1,2,3}, Marco Ciabattini ⁴, Gian Loreto D'Alò ⁴, Riccardo De Giorgi ^{1,2}, Cinzia Del Giovane⁵, Carolina Cassar⁶, Luigi Janiri³, Nicolas Clark ⁷, Michael Joshua Ostacher ^{8,9}, Andrea Cipriani ^{1,2*}

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Meta-Analysis Findings

Network meta-analysis was used to analyze 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.

Psychosocial Interventions for Cocaine and Psychostimulant Amphetamines Related Disorders.

Werner Paulo Knapp, Bernardo Soares, Michael Farrell, Maurício Silva deLima. (2009)

The Cochrane Collaboration.

Twenty-seven randomized controlled studies (3663 participants) fulfilled inclusion criteria and had data that could be used for at least one of the main comparisons.

- **The comparisons between different type of behavioral interventions showed results in favor of treatments with some form of contingency management in respect to both reducing dropouts and lowering cocaine use.**

Responding to global stimulant use: Challenges and opportunities

Lancet (Farrell et al, 2019)

Psychosocial interventions other than contingency management have weak and non-specific effects on stimulant problems and there are no effective pharmacotherapies. Substantial research investment is needed to develop more effective, innovative, and impactful prevention and treatment.

Non-pharmacological interventions for methamphetamine use disorder: a systematic review Drug and Alcohol Dependence, AshaRani, PV, et al. 2020

- 44 Studies reviewed.
- Conclusions: While Contingency Management (CM) interventions showed the strongest evidence favouring the outcomes assessed, tailored CBT alone or with CM was also effective in the target population.

Current status of Treatment Approaches for Methamphetamine Use Disorder

- Contingency management unanimously (5 systematic reviews and meta-analyses) found to have best evidence of effectiveness.
- Other approaches with lesser but clear evidence of support: Cognitive Behavioral Therapy (CBT) and Community Reinforcement Approach (CRA)
- Approach with evidence for treatment of a broad variety of SUD: Motivational Interviewing (MI).
- Approach with recent studies showing benefit to people who use methamphetamine: Physical Exercise (PE). (eg. Rawson et al, 2015)

**Do People Who Use Methamphetamine
Respond Differently to Behavioral Treatments
than People Who Use Cocaine?**

Implementation

The American Journal on Addictions, 23: 205–210, 2014
Copyright © American Academy of Addiction Psychiatry
ISSN: 1055-0496 print / 1521-0391 online
DOI: 10.1111/j.1521-0391.2014.12092.x

Nationwide Dissemination of Contingency Management: The Veterans Administration Initiative

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Medications

Medications for Methamphetamine Use Disorder

- Medications with positive studies and under consideration

bupropion

mirtazapine *****

naltrexone

methylphenidate

d-amphetamine

topiramate

Medication

- Many clinical trials
- No medication has been FDA-approved for stimulants
- Most promising are bupropion (Wellbutryn) and mirtazapine (Remeron)
- Challenges of medication compliance and recruiting participants

TRUST: Treatment of Uusers of Stimulants:
TRUST

An Integrated Behavioral Model

TRUST: The Components

TRUST is an integrated, evidence-based, multi-component program for the treatment of individuals with stimulant use disorders. The contents of this program will include strategies including:

1. motivational incentives (based on contingency management research),
2. elements of cognitive behavioral therapy
3. elements of community reinforcement approach,
4. motivational interviewing skills,
5. physical exercise
6. Self-help (12-Step; Moderation management) program participation encouraged.

In addition, an appendix will include a set of other EBPs to augment the core program at the discretion of each organization.

TRUST: The Priorities

- 1. Establish a positive, compassionate, respectful, non-judgemental relationship with individuals who use stimulants to promote their engagement and retention in treatment. Individuals in treatment die from overdose and other causes at lower rates than those who are not in treatment
- 2. Provide incentives to promote participation (retention) in treatment. Retention is the single most important measure of treatment benefit. All treatment benefits (eg reduced drug use and criminal involvement, improved employment and other measures of functioning) are directly associated with treatment retention
- 3. Provide respectful evidence-based guidance/information/support to stimulant-using individuals that can help them make changes in their lives that will promote a reduction/discontinuation of methamphetamine/cocaine use.

Thank you

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