



Center on  
Rural Addiction  
UNIVERSITY OF VERMONT





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**This presentation is part of the  
Community Rounds Workshop Series**

These sessions are provided monthly thanks to the University of Vermont Center on Rural Addiction, the Vermont Center on Behavior and Health, and a grant from the Health Services and Resources Administration.

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# Treatment for Individuals who use Cocaine and Methamphetamine

Richard Rawson, PhD

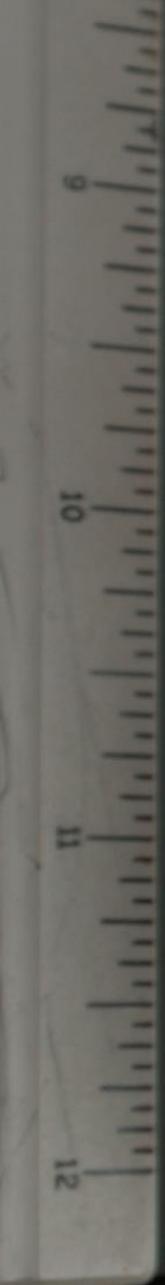
Research Professor, Vermont Center for Behavior and Health, University of Vermont, Burlington, VT  
Professor Emeritus, Department of Psychiatry and Biobehavioral Sciences, University of California, Los Angeles, CA

# No Disclosures

**Person-first language:** I am making a concerted effort to use person-first language to refer to individuals who use drugs/alcohol and/or are in treatment for substance use disorder (e.g. “Individuals who use cocaine or methamphetamine”), rather than more stigmatizing terms (e.g. “addict” or “cocaine/methamphetamine users”). Because old habits are difficult to change, I may inadvertently use the older and more stigmatizing terminology.  
I apologize in advance.

# 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 treating people with stimulant use disorder.
- Participants will be able to review and discuss the current evidence-based practices for the treatment of individuals with stimulant use disorder.



# 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 and dramatic increases in opioid overdose deaths, the public forgot about methamphetamine.

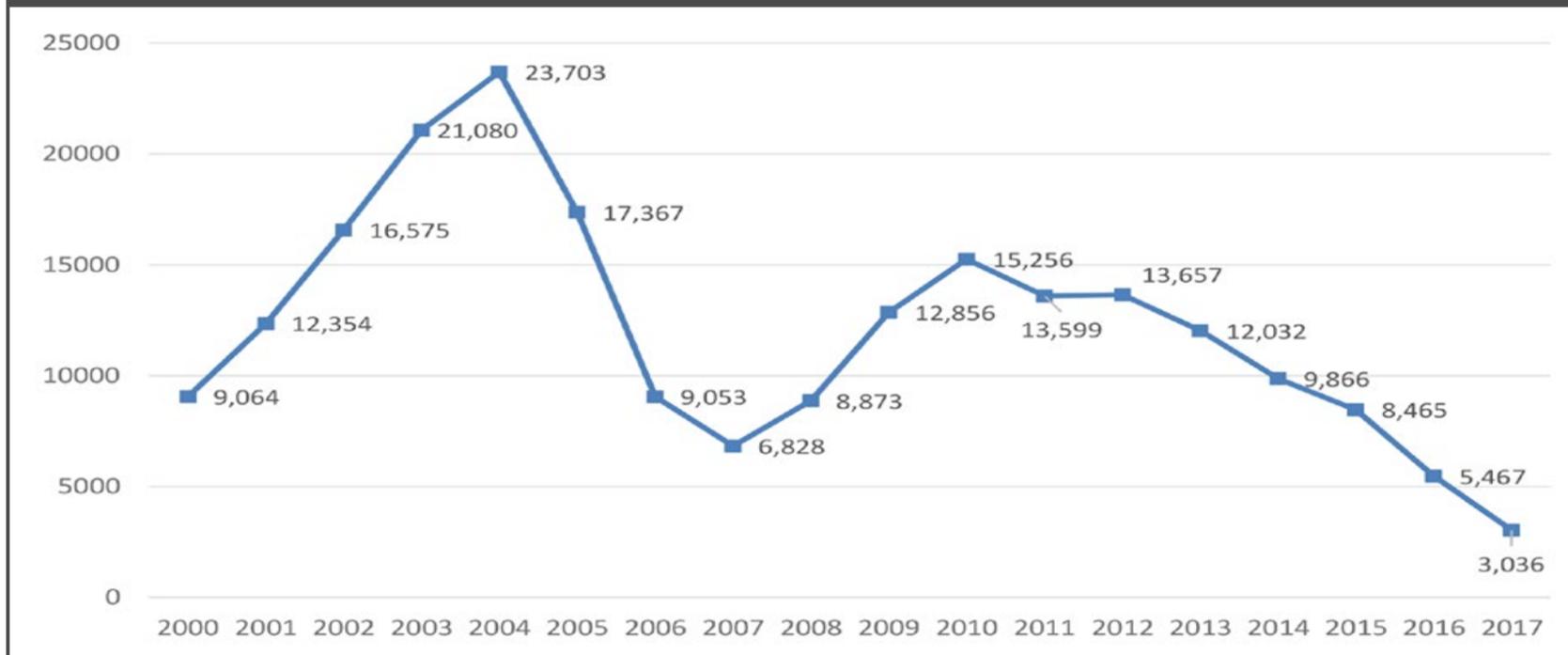
By 2010, Mexican drug cartels increased meth production with higher potency and lower price (\$2,000 per pound; down from \$8,000).

# 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 produced via P2P method is much more potent and potentially lethal.

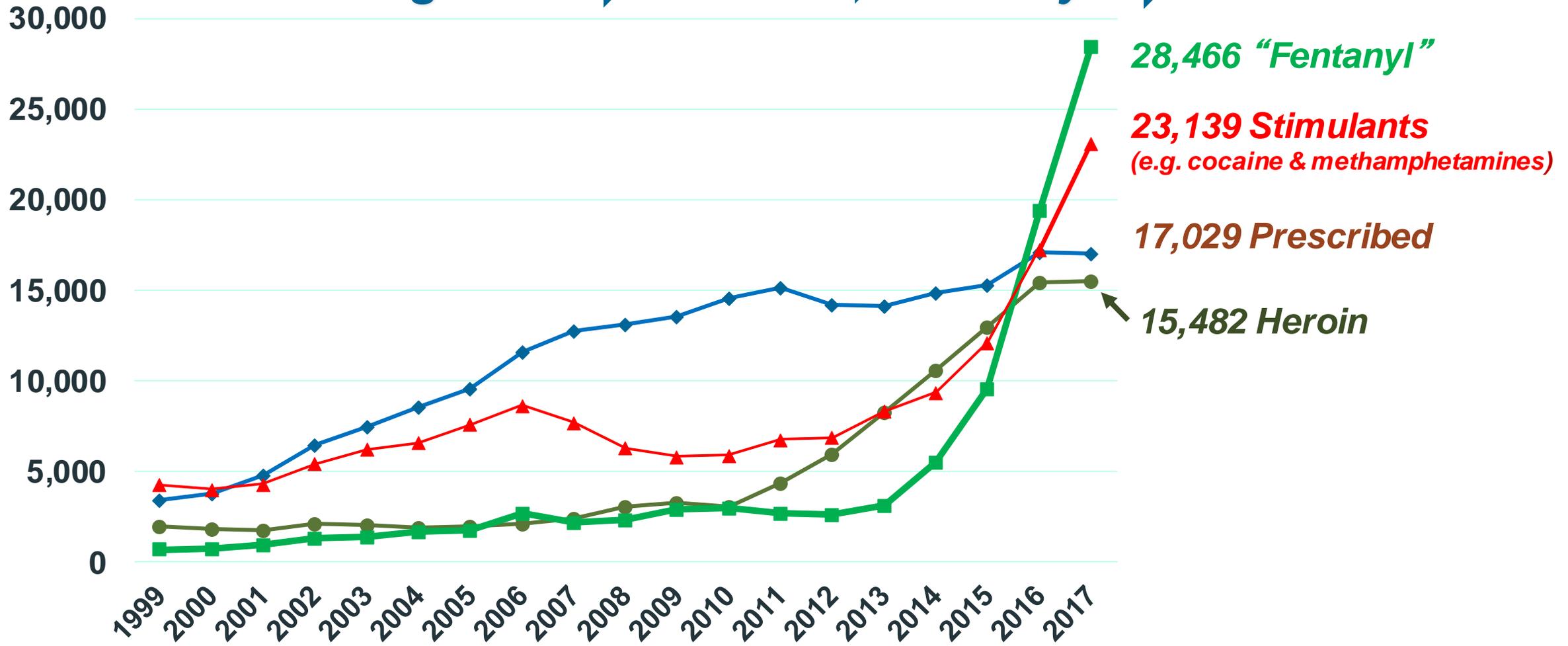
2018 - United States border agents seizing 10 to 20 times the amounts they did a decade ago.

2014-2020 Fentanyl-contaminated meth and cocaine became more prevalent. In many parts of the US, virtually all meth and cocaine have fentanyl included at the source.

June 2020. Isotonitazene—commonly referred to as "iso", a synthetic version of etonitazene is now found in individuals who overdose from cocaine in the Midwest.

# Evolution of Drivers of Overdose Deaths:

*Analgesics* → *Heroin* → *Fentanyl* → *Stimulants*



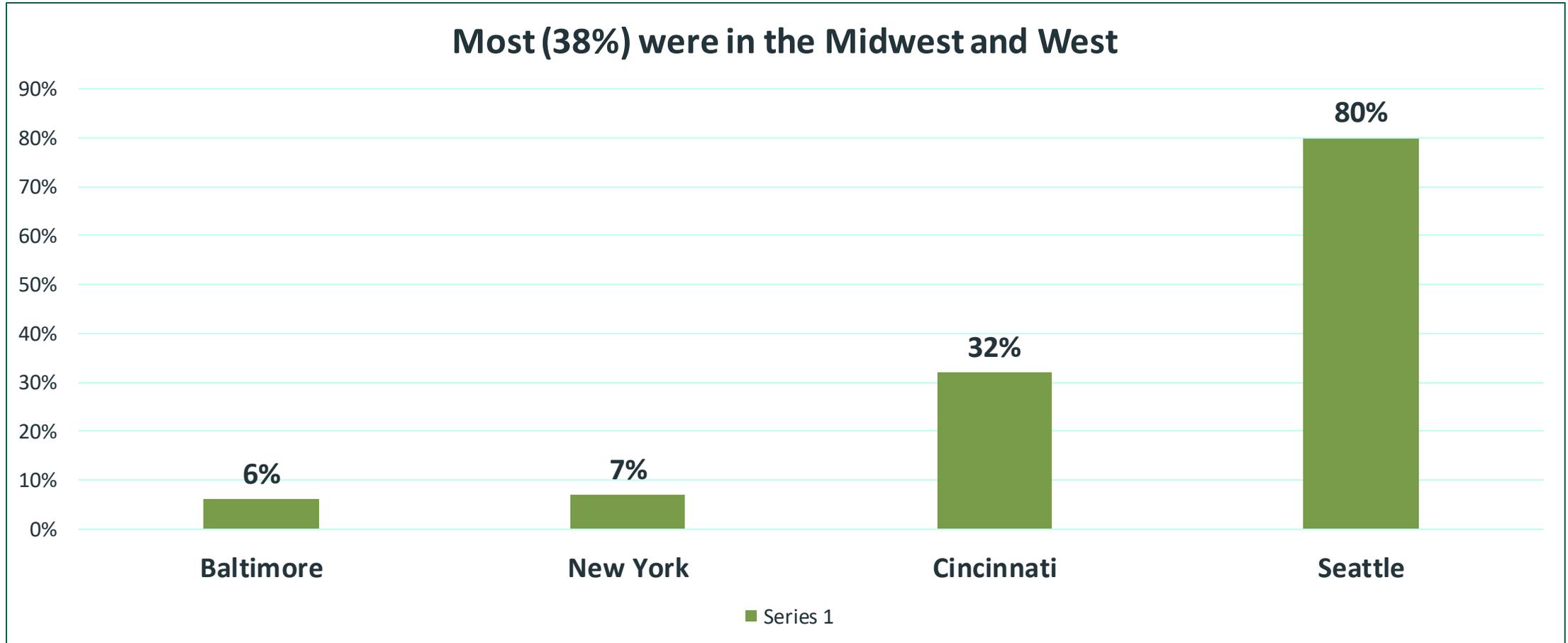
Compton WM & Jones CM, *Ann NY Acad Sci*, 2019; Data from CDC WONDER Database

# People who use Opioids who Test Positive for Stimulants at Emergency Departments

(Chawarski, 2020)

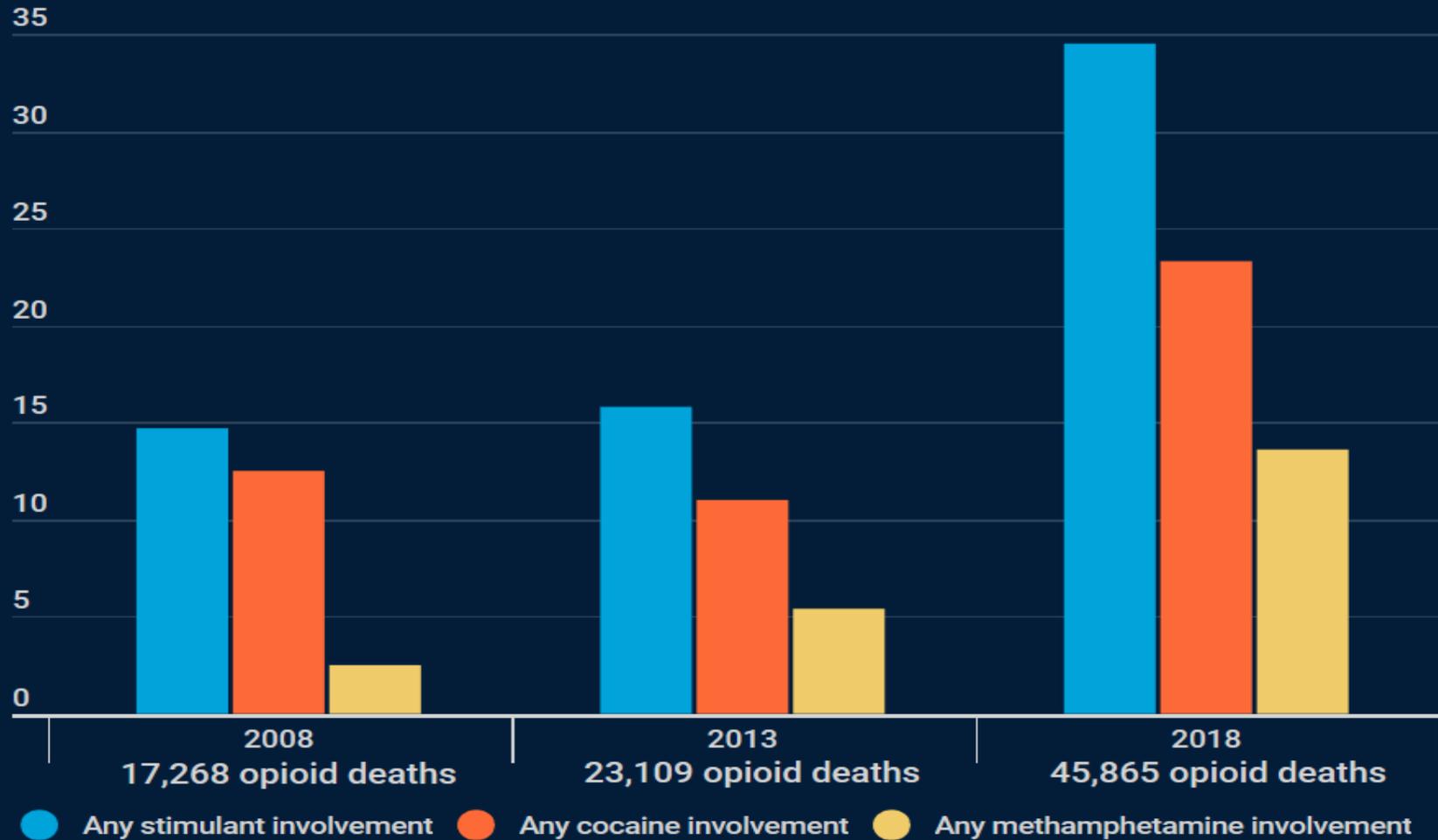
- Emergency department (ED) patients with untreated opioid use disorder (N=396) and enrolled between February 2017 and January 2019 in Baltimore, Cincinnati, NYC, and Seattle
- 38% of 396 people who use opioids tested positive for stimulants at emergency departments
- Characteristics of people who use both opioids and stimulants.
  - Younger; white (69%); higher rates of incarceration
  - Higher rates of injection (79% vs 47%)
  - Higher rates of HCV
  - More had overdosed (23% vs 13%)
  - Unstable housing (67% vs 49%)

# People who use Opioids who Test Positive for Stimulants at Emergency Departments (Chawarski, 2020)

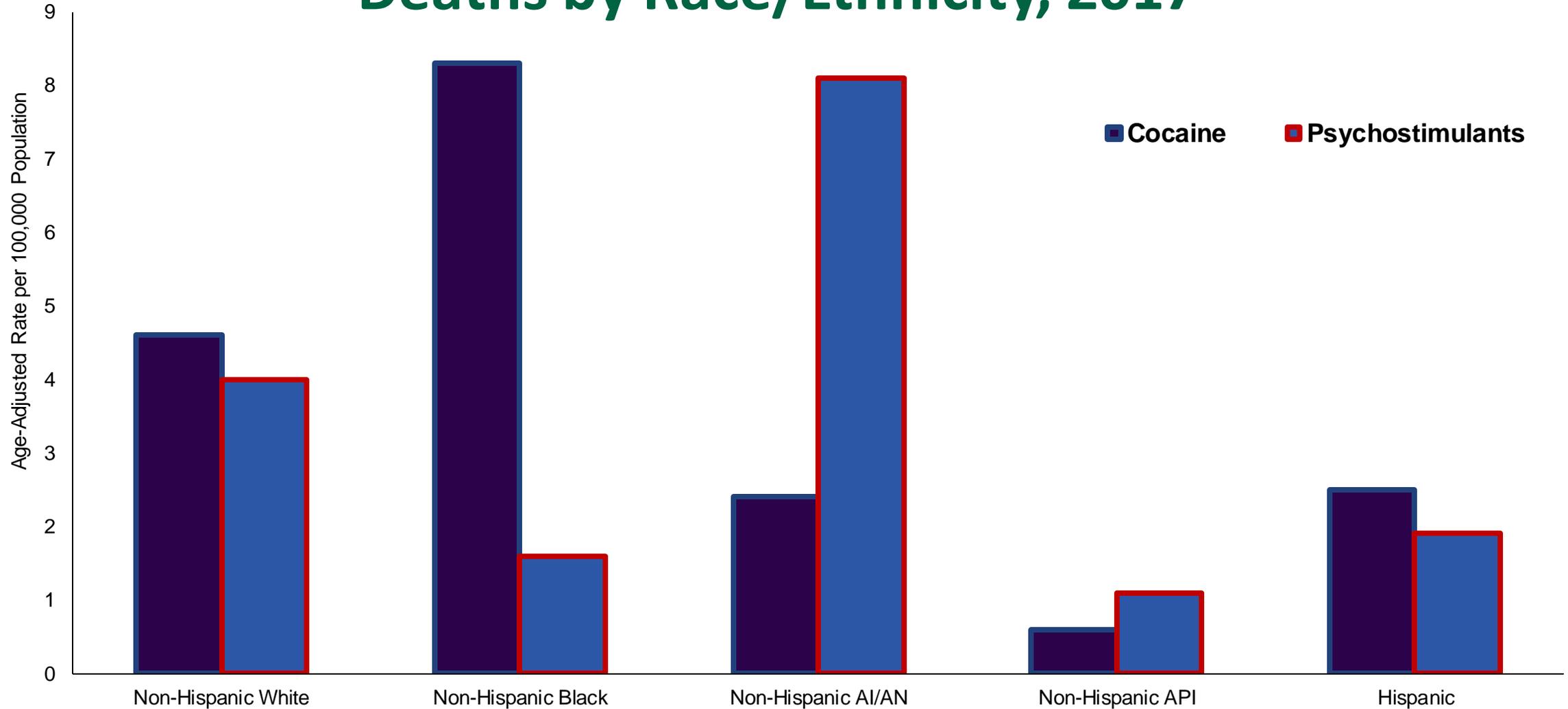




## Of all opioid overdose deaths, a growing proportion also involve stimulants



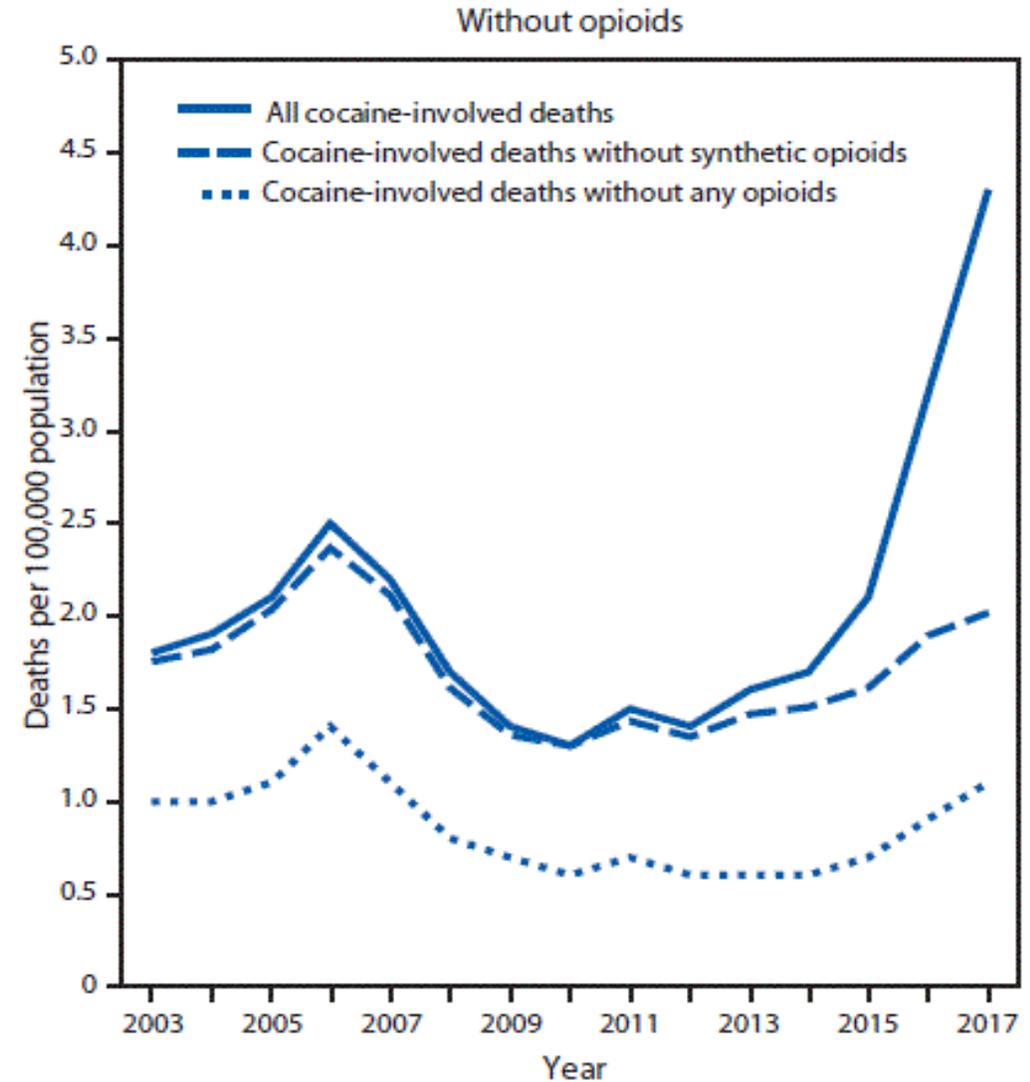
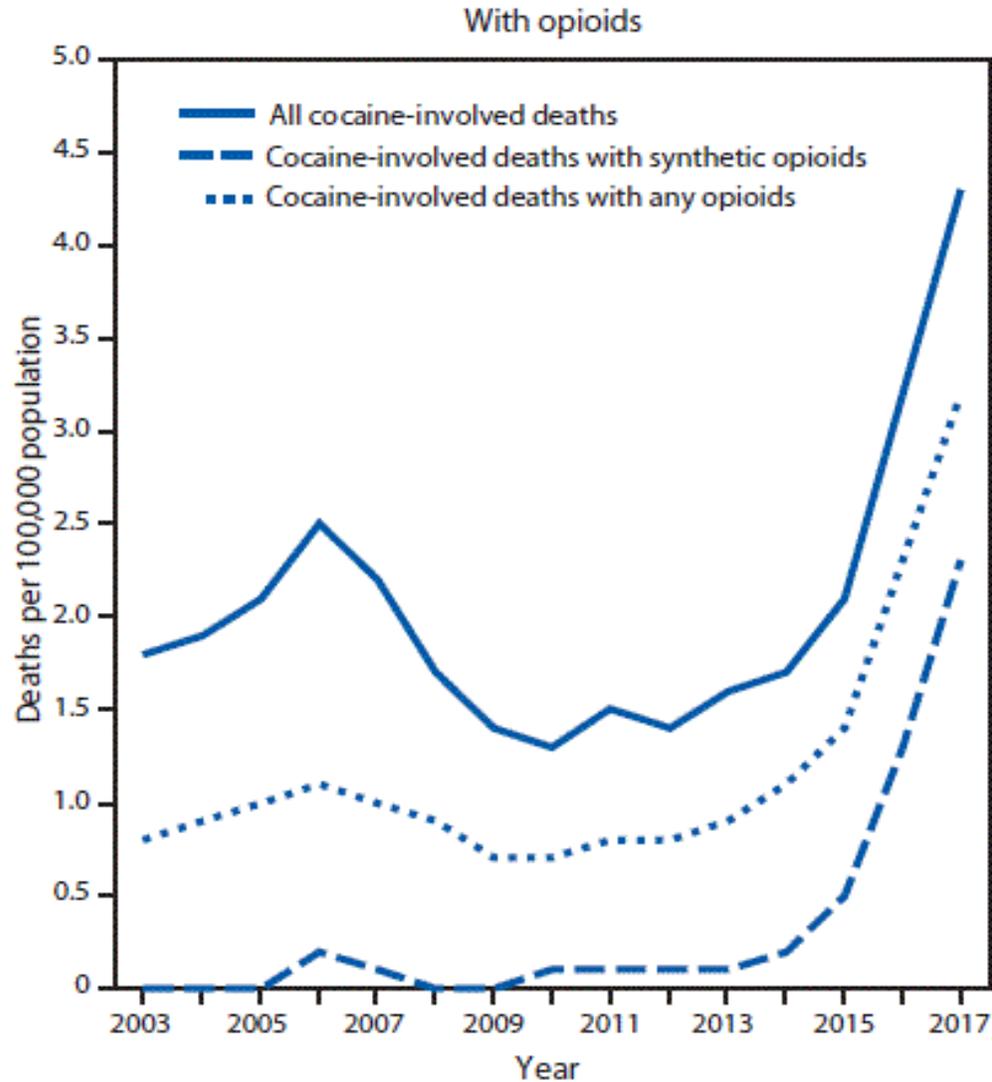
# Cocaine and Psychostimulant Overdose Deaths by Race/Ethnicity, 2017



Source: CDC NVSS, 2019

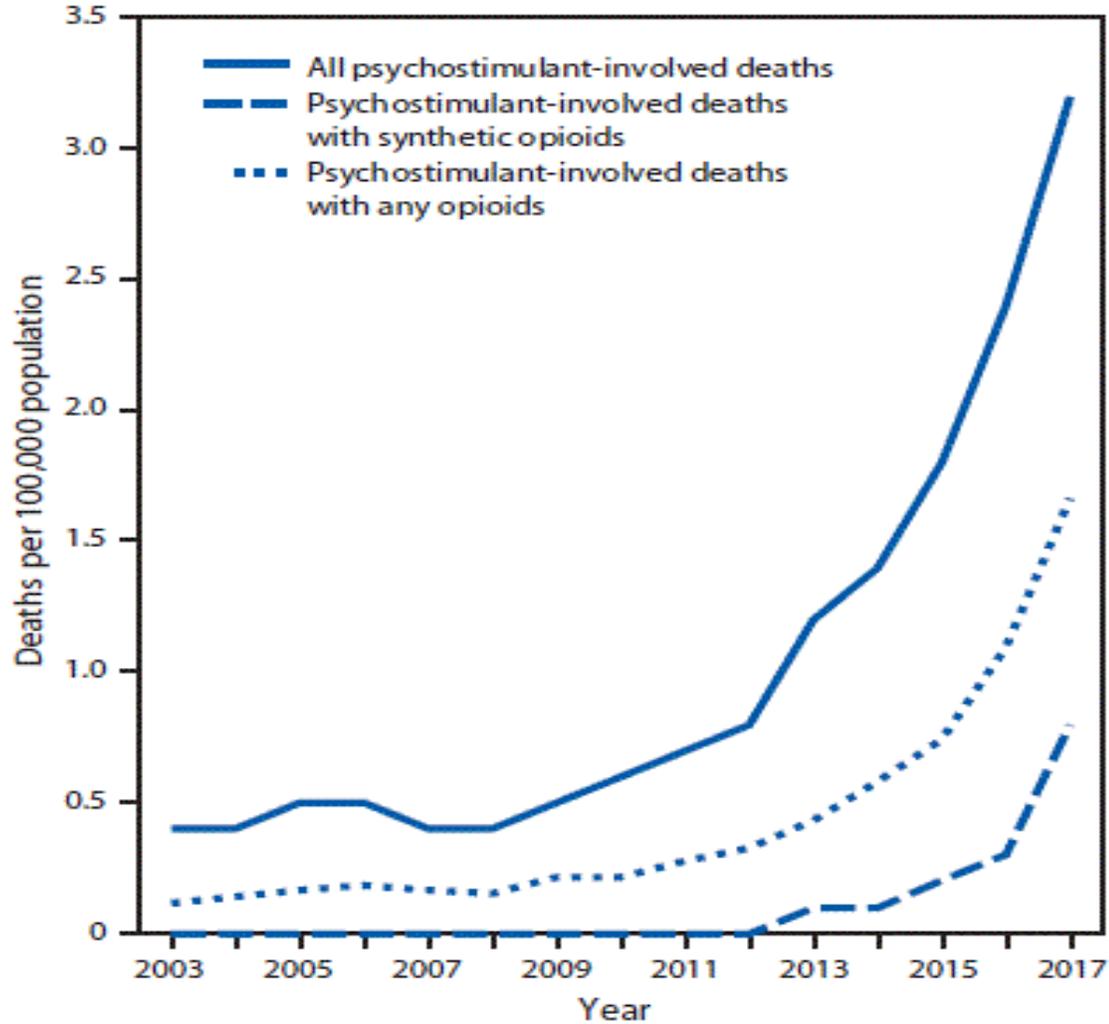
**Kariisa M, et al. MMWR Morb Mortal Wkly  
Rep. 2019;68(17):388-395**

# Cocaine-related deaths 2003-2017

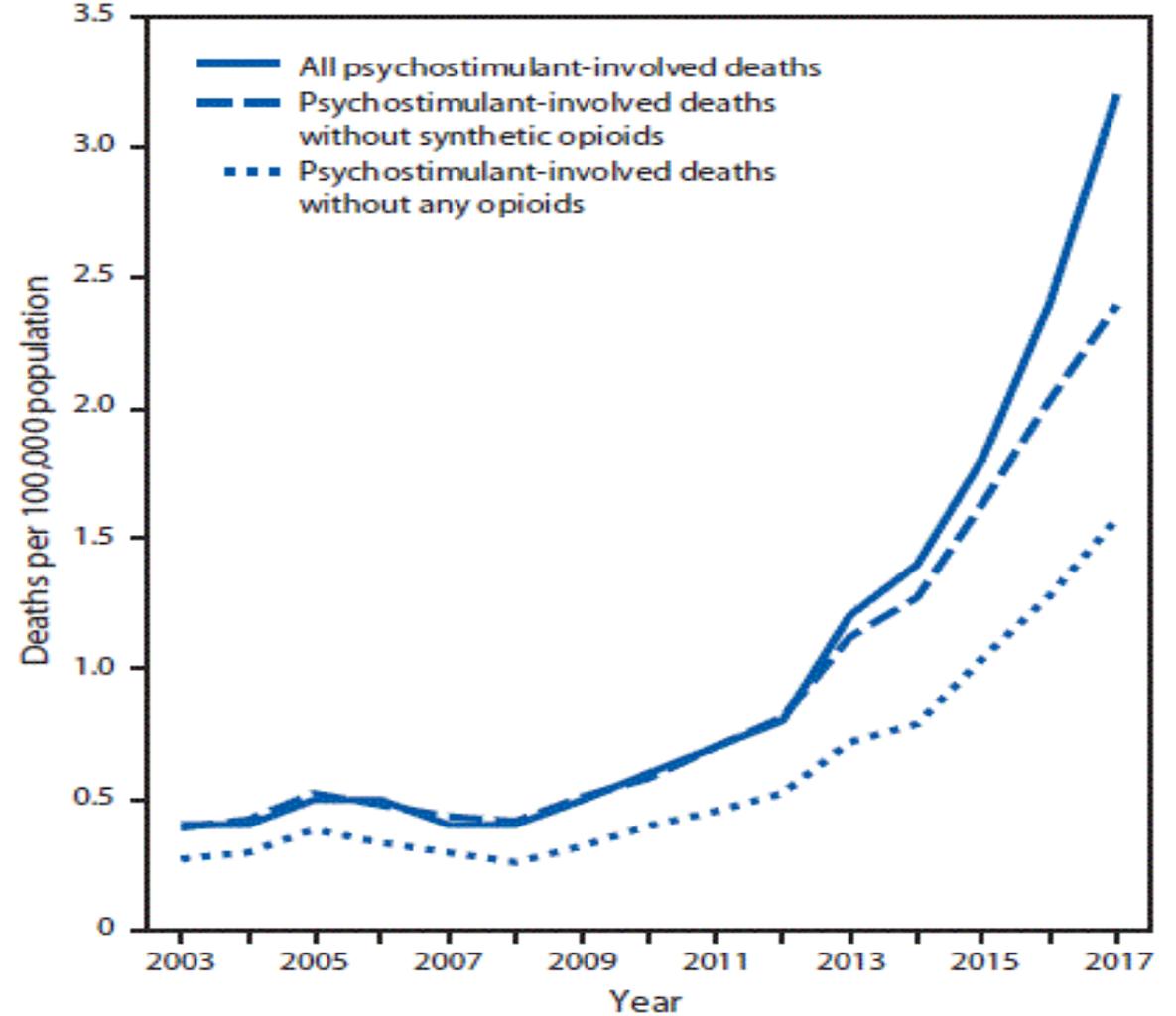


# ATS-related deaths 2003-2017

With opioids



Without opioids

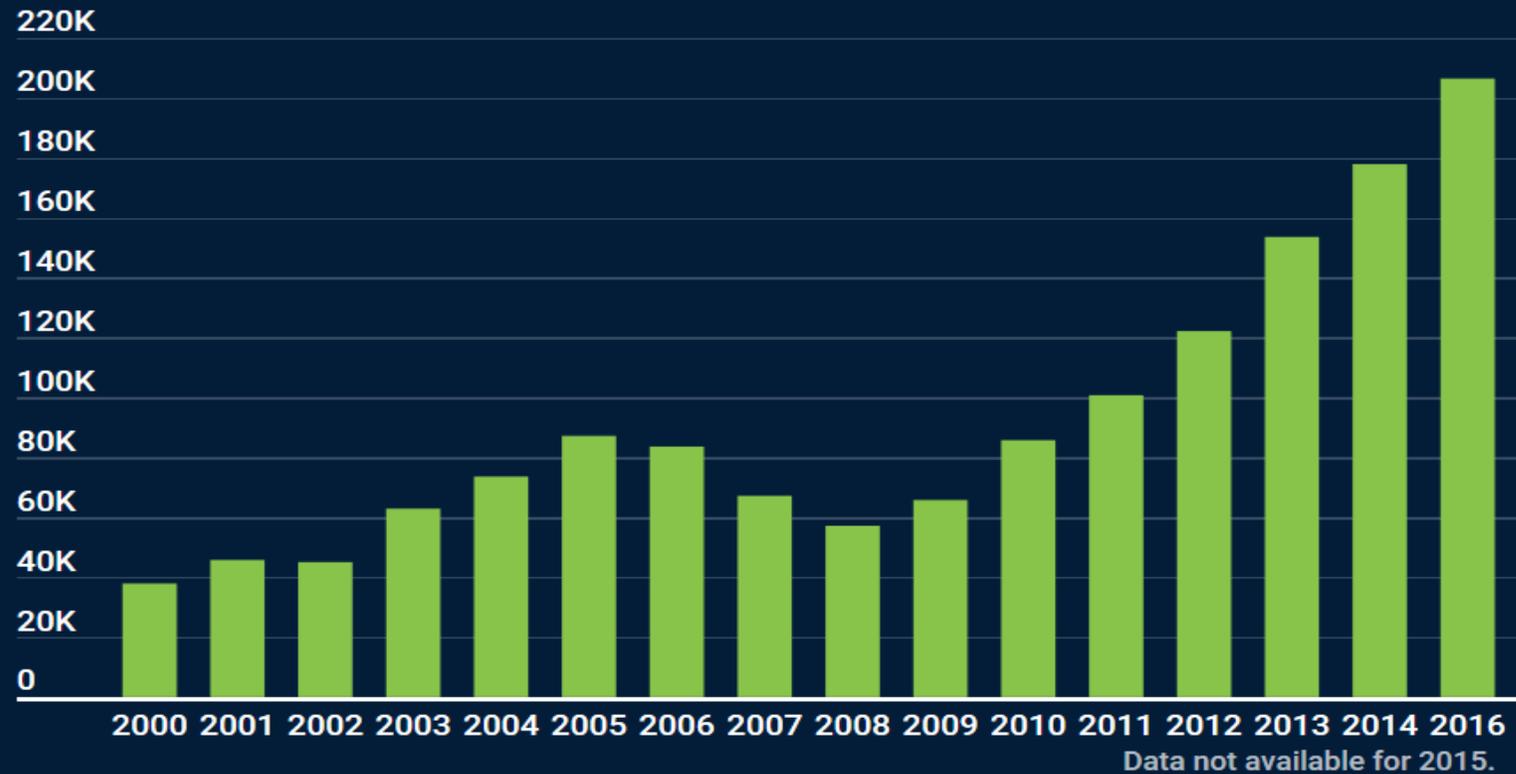




## Methamphetamine is placing a rapidly increasing burden on the hospital system

Inpatient Admissions

Emergency Department Visits



 Inpatient admissions



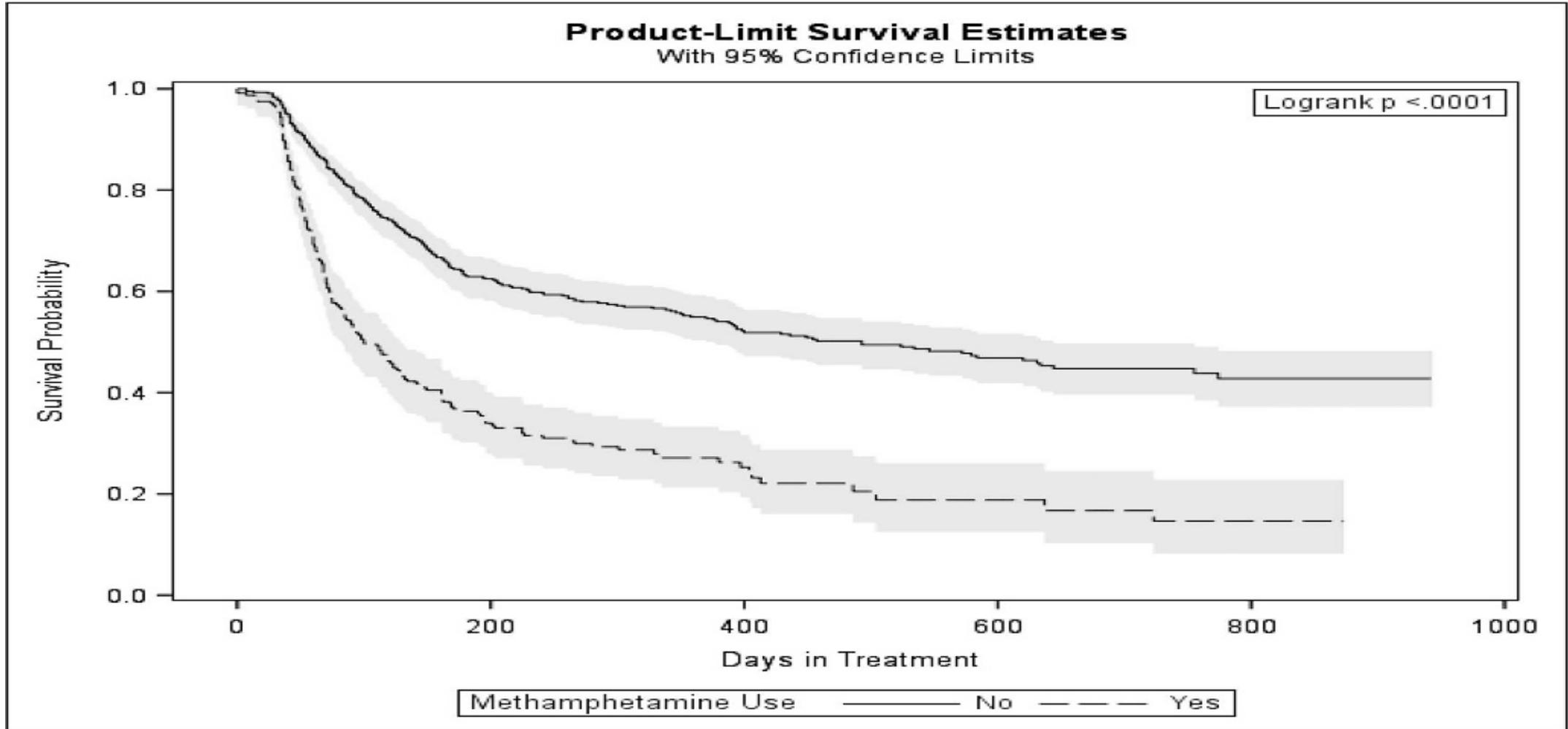
# **Association between methamphetamine use and retention among patients with opioid use disorders treated with buprenorphine**

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



# Impacts of Methamphetamine Use

# Medical Issues Related to Methamphetamine Use

Neurobiology, Clinical Presentation, and Treatment of  
Methamphetamine Use Disorder  
(Paulus and Stewart, JAMA Psychiatry, 2020)

- Neurotoxicity, cognitive effects
- Cardiovascular and cerebrovascular symptoms
- Need for pharmacologic interventions

# 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

- Soon after cessation of methamphetamine use:
  - Poor performance on motor and processing tasks
  - Poor performance on verbal fluency and attention
- Even after prolonged abstinence:
  - Poor learning efficiency and comprehension
  - Poor visual-spatial processing
  - Slow processing and psychomotor speed

# 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, route of administration (injection more severe) 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.

# 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

# Stroke and Methamphetamine use in Young Adults: a Review (Lappin et al., 2017)

- 7 articles reviewed reporting stroke in young adult (<45) methamphetamine users.
- 81 hemorrhagic, 17 ischemic strokes reported.
- Hemorrhagic associated with oral or injection route of administration.
- Ischemic associated with inhalation.
- Following hemorrhagic stroke, 1/3 died.
- Following ischemic stroke, 1/5 died.

# Stroke and Methamphetamine use in Young Adults: a Review (Lappin et al., 2017)

- Treatment providers should be aware of the heightened risk of stroke in young methamphetamine users.
- Be aware of early signs and symptoms:
  - Numbness
  - Headache
  - Speech and language difficulty
  - Vision problems
  - Dizziness

# **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)

- Women are disproportionately vulnerable to stimulant use and abuse.
- Vulnerability is related to hormones and reinforcement of gender constructs.
- Women progress faster from first exposure to addiction.
- Prenatal stimulant use is more common than opioid use.

# 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 (> 3days per week) was associated with anxiety/depression and attention problems.
- At age 7.5 years methamphetamine exposed children had poorer cognitive function.

# Symptoms Preceding Death from Toxic Methamphetamine Effects

- Collapse
- Breathing difficulty
- Hyperthermia
- Seizures
- Individuals 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

# 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.
- **Isolation, stress, anxiety, and depression can lead to more substance use and more fatal overdoses.**

# Clinical Challenges

# Clinical Challenges Treating Individuals with Stimulant Use Disorder

- Overdose death
- Limited understanding of stimulant addiction
- Ambivalence about need to stop use
- Impulsivity/Poor judgement
- Cognitive impairment and poor memory

# Clinical Challenges Treating Individuals with Stimulant Use Disorder (continued)

- Anhedonia
- Hypersexuality
- Violence and psychosis
- Powerful Pavlovian trigger-craving response
- Elevated rates of psychiatric co-morbidity
- Very poor retention in outpatient treatment

## Special Treatment Consideration Should Be Made for the Following Groups

- People who use injectable 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 who use stimulants who are under the age of 21.
- Individuals in medication treatment for OUD.

# Clinical Interventions

# Harm Reduction Strategies for Individuals who use Stimulants

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

# Naloxone for Individuals who use Stimulants?

- With increasing rates of fentanyl mixed into samples of methamphetamine (and cocaine), individuals who use stimulants are at much higher risk for overdose death due to their lack of tolerance for opioids.
- Individuals 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.

# Clinical Management of Individuals who use Stimulants: Acute Psychosis

- Symptoms of acute psychosis: Auditory hallucinations, and visual (flashing lights, peripheral artifacts), olfactory, and tactile sensations. In addition, powerful paranoia and persecutory delusions are extremely common.
- Stimulant-induced psychosis is generally transient and may require use of either a benzodiazepine or an antipsychotic, both of which should be discontinued when acute symptoms have resolved.
- Risperidone and olanzapine are less likely to cause extrapyramidal symptoms and their sedative properties may ameliorate psychomotor agitation.
- Monitor for hyperthermia and dehydration when antipsychotics are used in patients with acute stimulant intoxication.

# Clinical Management of Individuals who use Stimulants: Intoxication

- Symptoms include: Euphoria, hyperexcitability, hypersexuality, increased locomotor activity, agitation, and psychotic symptoms, including paranoia and hallucinations.
- Objective findings of hypertension, tachycardia, and arrhythmias that present on EKGs of users reflect sympathetic overdrive.
- Acute agitation from MA intoxication is most often the condition that leads users to seek medical attention, and “talking down” the patient in a calm environment is the first course of action.
- Benzodiazepines may be effective in acute management of agitation and distress and may reduce seizure potential.

# Clinical Management Individuals who use Stimulants: Withdrawal

- Stimulant withdrawal symptoms consist of severe fatigue, cognitive impairment, feelings of depression and anxiety, anergia, confusion, and paranoia.
- For the majority of patients experiencing acute withdrawal/early-phase abstinence, most symptoms resolve within 2 to 10 days.
- Rest, exercise, and a healthy diet may be the best management approach for most people in withdrawal.
- Those with heightened agitation and sleep disturbance may respond to benzodiazepines, but acute depression and anhedonia associated with early abstinence generally resolve without intervention.

# Treatment for Individuals with Stimulant Use Disorder

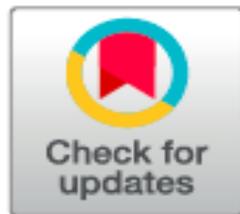
# Systematic Reviews and Meta-Analyses

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 <sup>1,2,3</sup>, Marco Ciabattini <sup>4</sup>, Gian Loreto D'Alò <sup>4</sup>, Riccardo De Giorgi <sup>1,2</sup>, Cinzia Del Giovane<sup>5</sup>, Carolina Cassar<sup>6</sup>, Luigi Janiri<sup>3</sup>, Nicolas Clark <sup>7</sup>, Michael Joshua Ostacher <sup>8,9</sup>, Andrea Cipriani <sup>1,2\*</sup>

**1** Department of Psychiatry, University of Oxford, Oxford, United Kingdom, **2** Oxford Health NHS Foundation Trust, Warneford Hospital, Oxford, United Kingdom, **3** Institute of Psychiatry and Clinical Psychology, Catholic University of the Sacred Heart, Rome, Italy, **4** School of Hygiene and Preventive Medicine, University of Rome Tor Vergata, Rome, Italy, **5** Institute of Primary Health Care (BIHAM), University of Bern, Bern, Switzerland, **6** Department of Dynamic and Clinical Psychology, Sapienza University of Rome, Rome, Italy, **7** Mental Health and Substance Abuse, World Health Organization, Geneva, Switzerland, **8** Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California, United States of America, **9** Department of Psychiatry, VA Palo Alto Health Care System, Palo Alto, California, United States of America



# 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 favoring the outcomes assessed, tailored CBT alone or with CM was also effective in the target population.

*The American Journal on Addictions*, 23: 205–210, 2014

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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**

**Nancy M. Petry, PhD,<sup>1</sup> Dominick DePhilippis, PhD,<sup>2</sup> Carla J. Rash, PhD,<sup>1</sup>  
Michelle Drapkin, PhD,<sup>2</sup> James R. McKay, PhD<sup>2</sup>**

<sup>1</sup>University of Connecticut School of Medicine, Farmington, Connecticut

<sup>2</sup>Dept of Veterans Affairs and University of Pennsylvania, Philadelphia, Pennsylvania

# Contingency Management Apps

**DynamiCare Health** is a platform for families and individuals that reinforces a person's recovery from addiction and rewards healthy behavior.

- Random breath and saliva tests verified by selfie video.
- GPS verified treatment attendance.
- A supportive recovery coach.
- Monetary rewards on a smart debit card for treatment achievements.
- [www.dynamicarehealth.com](http://www.dynamicarehealth.com).

# The three major challenges to using CM

- Medicaid regulations that restrict the amount of incentives that can be given to patients to \$75 per patient per year.
- Where does the funding for incentives come from?
- Staff resistance to the idea of incentives
  - Patients should not have to be “paid” or “bribed”; recovery is the reward
  - Motivation needs to come from within, etc.....

# Current Status of Treatment Approaches for Methamphetamine Use Disorder

- Contingency management unanimously (5 systematic reviews and meta-analyses) found to have the most robust evidence of effectiveness.
- Other approaches with lesser but 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 individuals with methamphetamine use disorder: Physical Exercise (PE). (e.g. Rawson et al, 2015)

# Exercise Summary

- For individuals in the first 100 days of meth recovery, exercise:
  - Improves physical conditioning
  - Reduces weight gain
  - Improves cardiovascular functioning (increases heart rate variability)
  - Reduces symptoms of anxiety and depression
  - Reduces craving for methamphetamine
  - Enhances recovery of dopamine system (D2/D3 receptors)
  - Reduces relapse to methamphetamine post discharge (except in very heavy users)

# Medications

# Medications for Methamphetamine Use Disorder

Medications with positive studies and under consideration

- bupropion
- mirtazapine \*\*\*\*\*
- naltrexone
- methylphenidate
- d-amphetamine
- topiramate

# Risks for Rural Communities from Increasing Methamphetamine Availability and Use

Rural areas of the US were home to much of the meth production in the 1990-2005 period of escalated meth use. Consequently, there are established markets and trafficking networks and the availability and use of meth have escalated very rapidly.

The current more potent meth and meth mixed with fentanyl, create severe medical and psychiatric and social service (e.g. child welfare) consequences that overwhelm the limited health, mental health and social service systems in the rural US.

Because of big distances between population centers, response times for first responders are longer than in urban areas. This creates much greater risk for individuals who overdose from meth.

# Challenges in Providing Treatment for Individuals with Stimulant Use Disorder in Rural Areas

- Medical and psychiatric services with knowledge of stimulant use disorder- related knowledge are limited.
- Limited number of specialty treatment providers.
- Shortage of trained workforce.
- Distances for treatment-seeking individuals to travel to attend clinical services reduce access to care.
- Use of telemedicine can be limited by poor internet availability.
- Training and technical assistance opportunities are less available in rural areas.

## Summary/takeaways

- The methamphetamine being used in 2020 is more lethal than in earlier years due to more potent formula and addition of fentanyl.
- New research has provided a better understanding of the medical and psychiatric consequences of methamphetamine use.
- Behavioral treatments, particularly contingency management, have evidence of efficacy.
- There are no medications with FDA approval for the treatment of individuals with methamphetamine use disorder.



Questions?

[RRAWSON@UVM.EDU](mailto:RRAWSON@UVM.EDU)



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**Thank you for participating in this  
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**Our next session will be held on September 30, 2020 from 12-1pm:  
*Suicide and Substance Use Disorders, Sanchit Maruti, MD***

For additional information:

Contact us by e-mail at [CORA@uvm.edu](mailto:CORA@uvm.edu)

Center on Rural Addiction: <https://uvmcora.org/>

Vermont Center on Behavior and Health: <http://www.med.uvm.edu/behaviorandhealth/>



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