

The background is a dense, abstract painting featuring numerous faces in various colors and expressions, rendered in a style reminiscent of Vincent van Gogh's 'Olympia' or similar expressionist works. The colors are vibrant and varied, including blues, greens, yellows, and reds, set against a darker, textured background.

# MENTAL HEALTH IMPACTS OF METHAMPHETAMINE

Eleasa Sokolski, MD

3/14/25

9<sup>th</sup> Annual Adult Mental Health Update





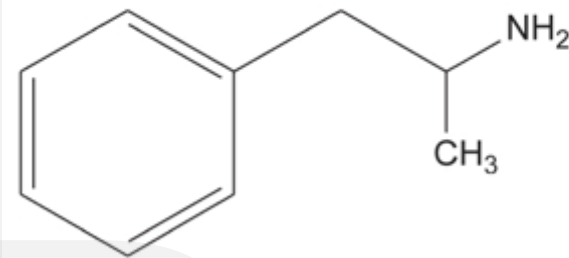
## DISCLOSURES

- I have no financial disclosures.
- I will be discussing off-label use of medications to treat stimulant use disorder.

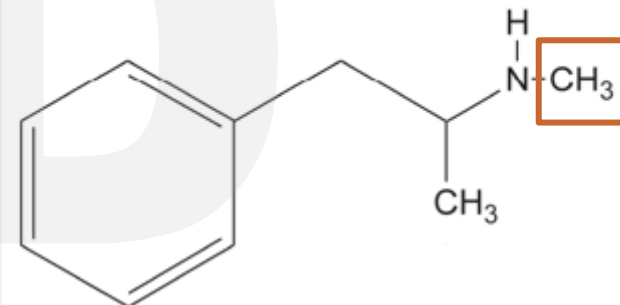
## WHAT IS METHAMPHETAMINE?

- An amphetamine derivative used worldwide
- The methyl group makes the molecule more **lipophilic**, allowing it to better penetrate the blood-brain barrier compared to other amphetamines

Amphetamine



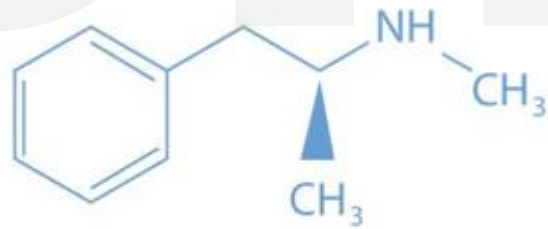
Methamphetamine



Powerful central nervous system stimulant



2 Enantiomeric Forms of Methamphetamine



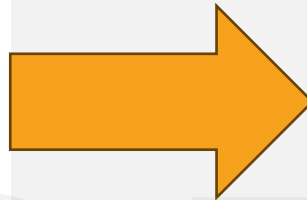
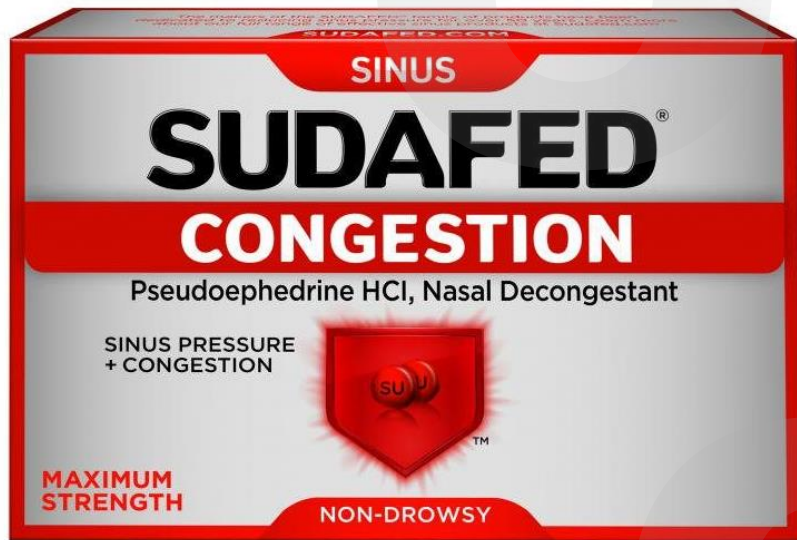
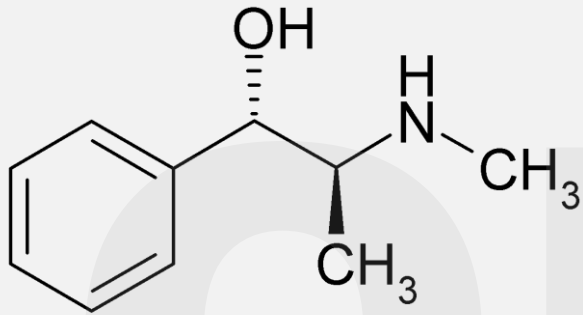
D-Methamphetamine  
(dextro-Methamphetamine)



L-Methamphetamine  
(levo-Methamphetamine)



Nasal decongestant  
Found in some formulations  
of Vicks Vapor Inhaler



<https://www.bbc.com/news/world-latin-america-48531849>

Problem of increased worldwide **production/supply**, increased **purity** of (d)-methamphetamine, and **decreased cost**



A resident of Skid Row, in Los Angeles, holding crystal methamphetamine, in August 2021 (Rachel Bujalski for The Atlantic)

SCIENCE

## 'I DON'T KNOW THAT I WOULD EVEN CALL IT METH ANYMORE'

Different chemically than it was a decade ago, the drug is creating a wave of severe mental illness and worsening America's homelessness problem.

By Sam Quinones

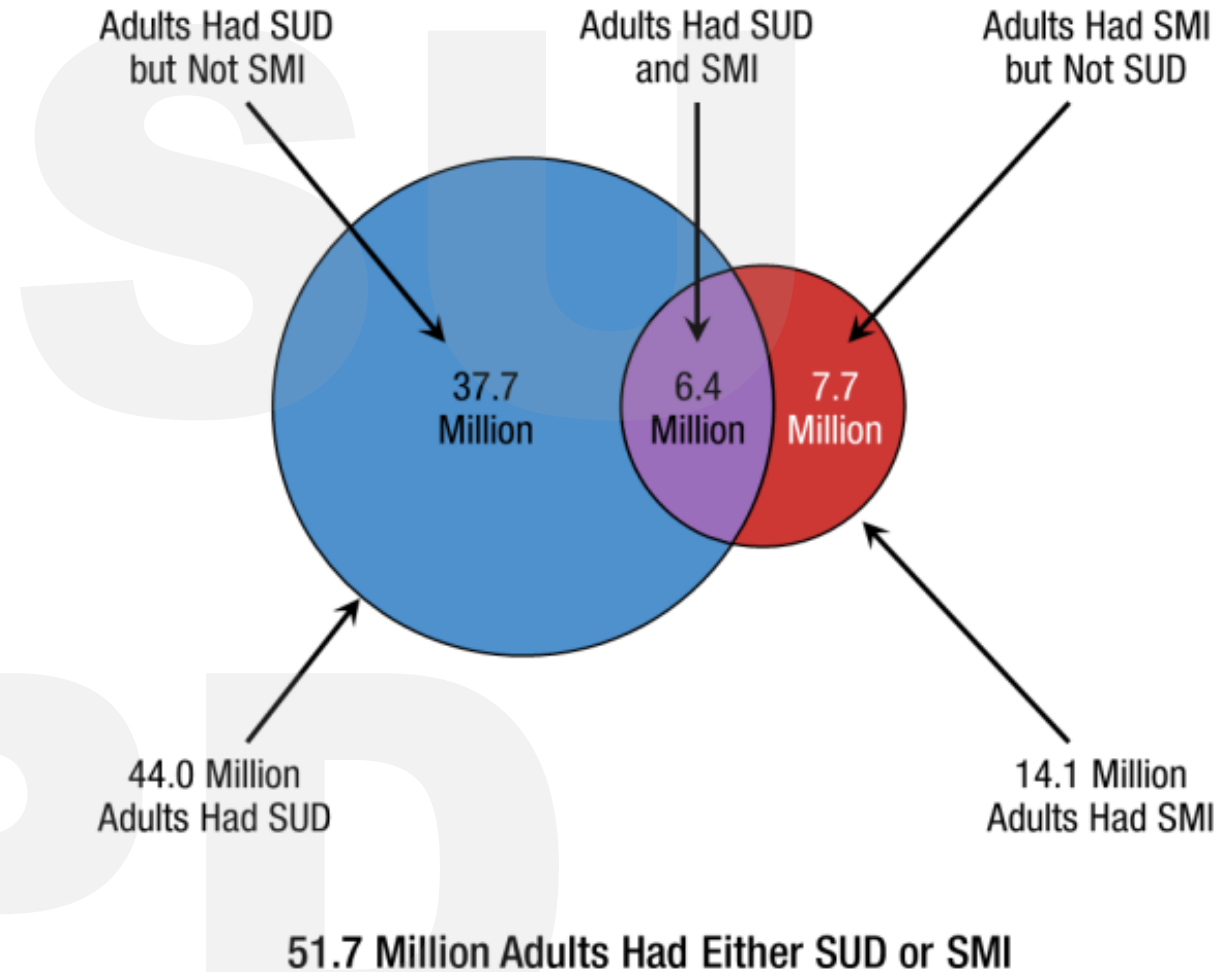
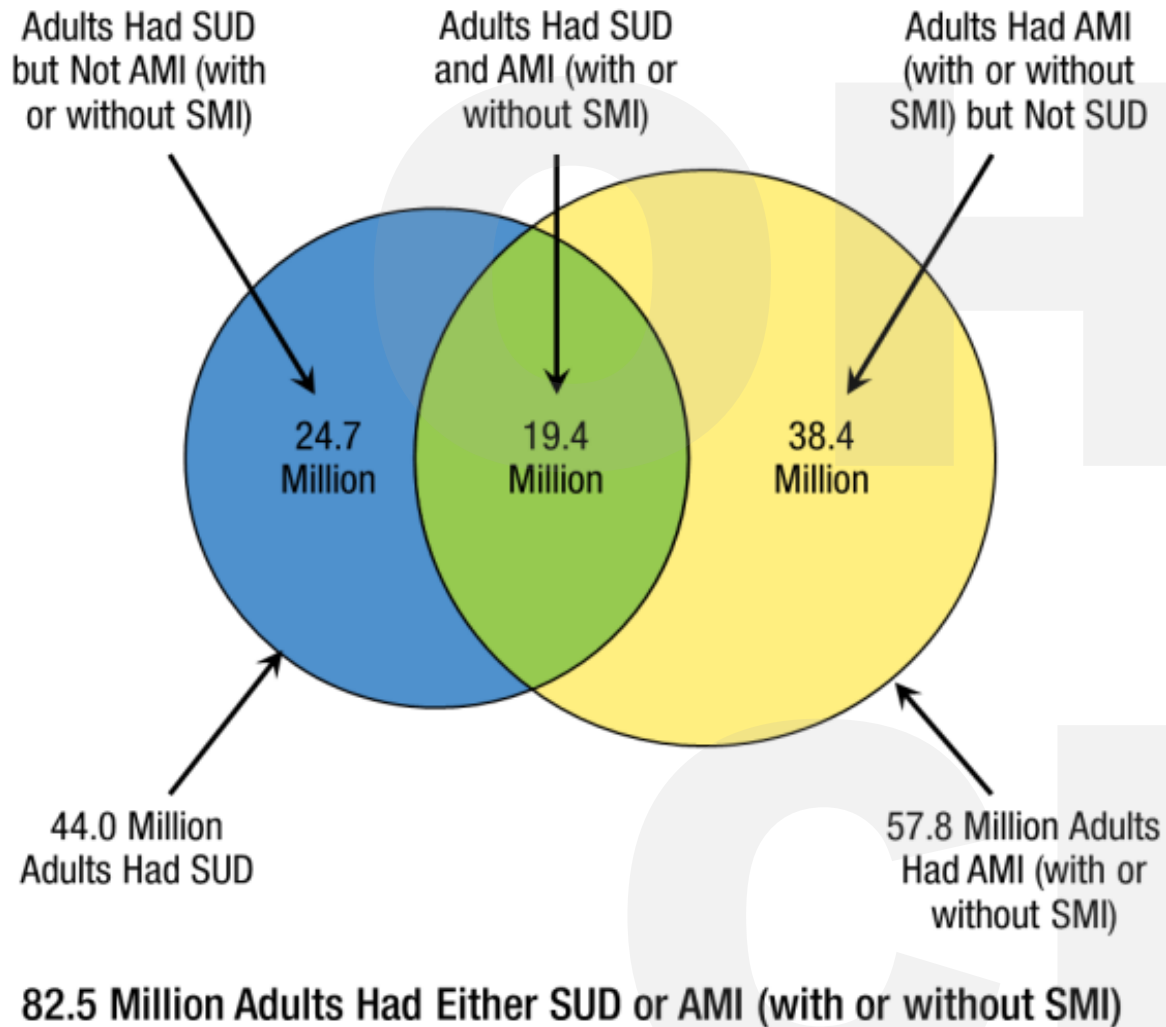
## EPIDEMIOLOGY

**1.6 million U.S.  
adults reported use  
of methamphetamine  
in the past year**

**Highest rates among  
men age 35-49**

**27.3% of those who  
used reported using  
200+ days that year**

**406,000 reported past-  
year serious mental  
illness**



AMI = Any Mental Illness  
SMI = Serious Mental Illness

## “TWIN EPIDEMICS”

- Among patients with opioid use disorder, past-month use of methamphetamine increased from 19% in 2011 to **34% in 2017**.
- Concurrent use of opioids and methamphetamine **increases overdose risk**.
- Methamphetamine may be used to balance the sedating effects of opioids or to decrease symptoms of opioid withdrawal.

# 12 Month-Ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class

Based on data available for analysis on: September 1, 2024

After opening the **drug class dropdown**, click the top of the dropdown menu again to make the checkboxes disappear.



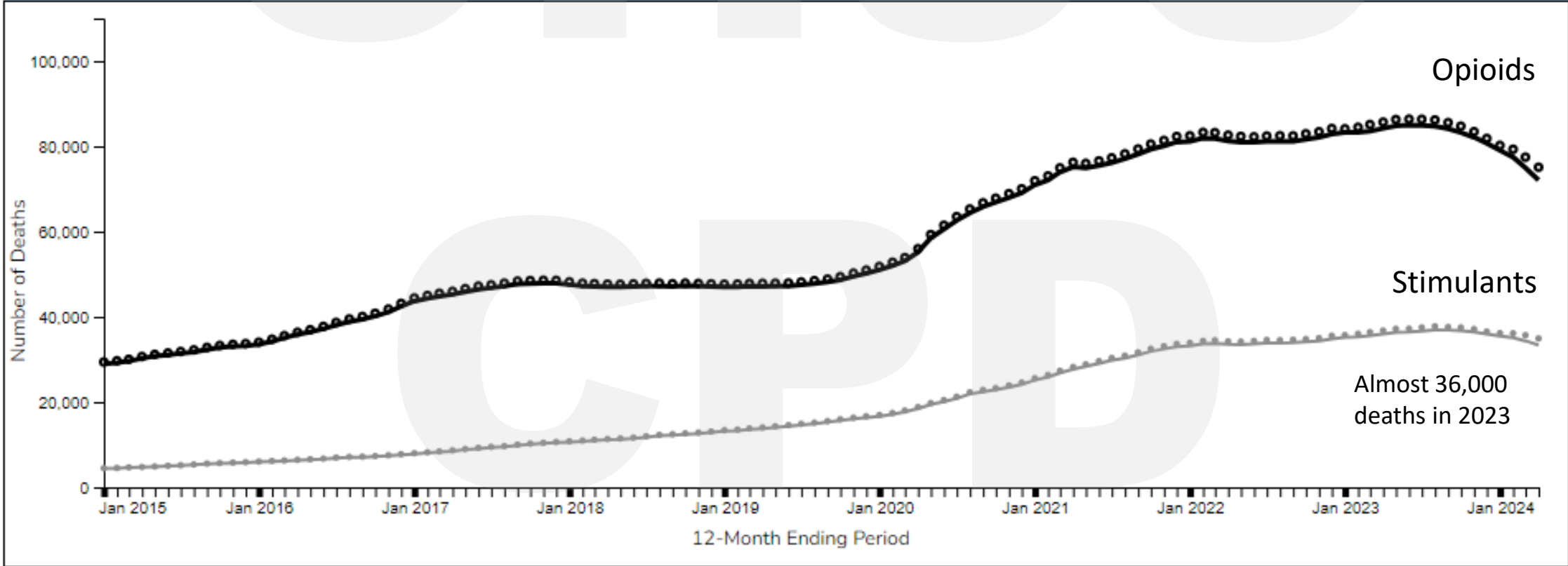
Select Jurisdiction

United States

Select specific drugs or drug classes

Select drug class

Figure 2. 12 Month-Ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class: United States



# 12 Month-Ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class

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Select Jurisdiction

▼

Select specific drugs or drug classes

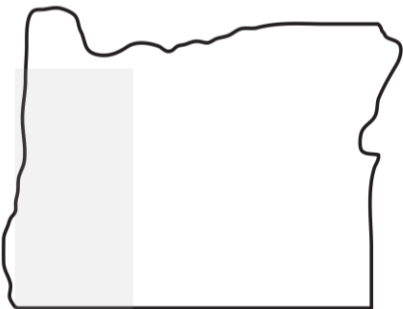
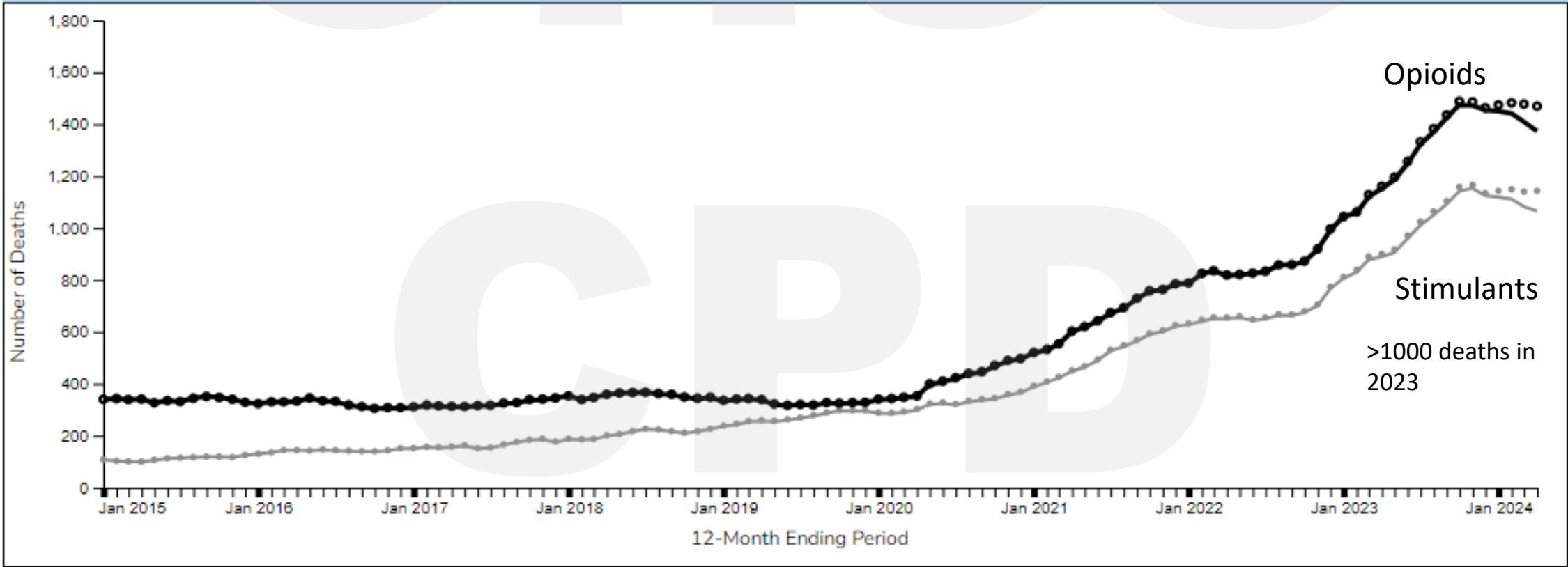
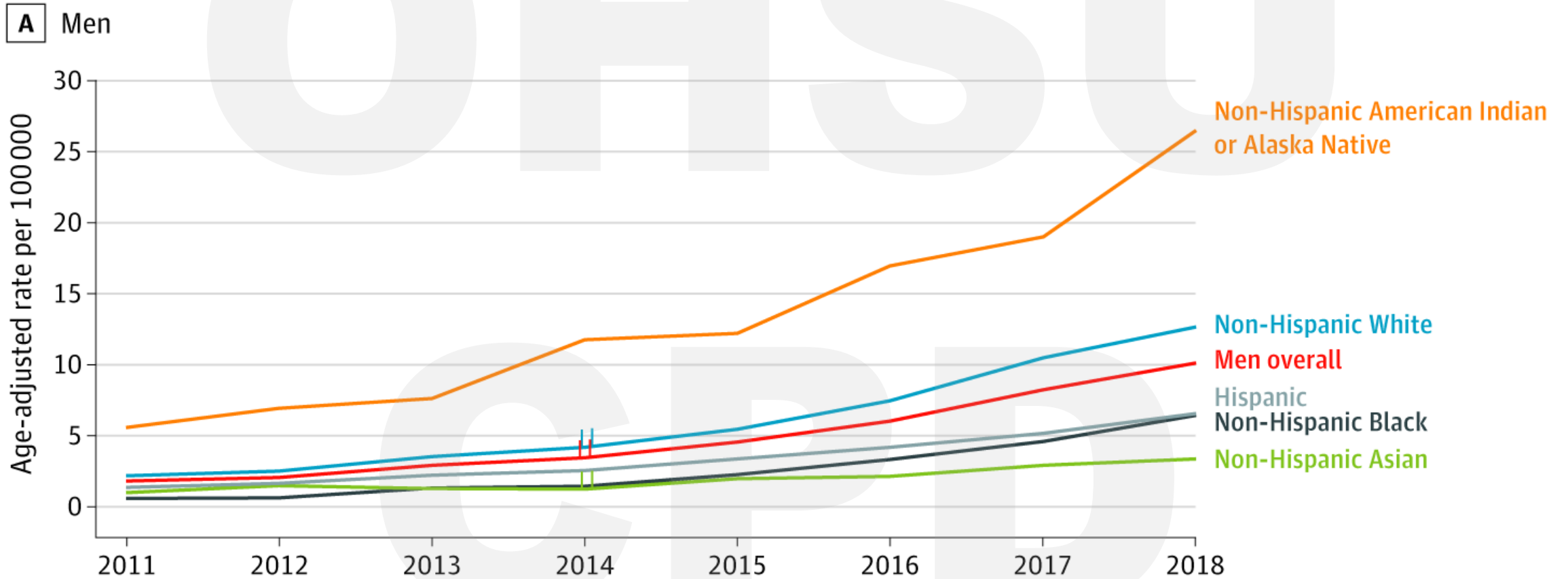


Figure 2. 12 Month-Ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class: Oregon



From: **Methamphetamine Overdose Deaths in the US by Sex and Race and Ethnicity**

JAMA Psychiatry. 2021;78(5):564-567. doi:10.1001/jamapsychiatry.2020.4321

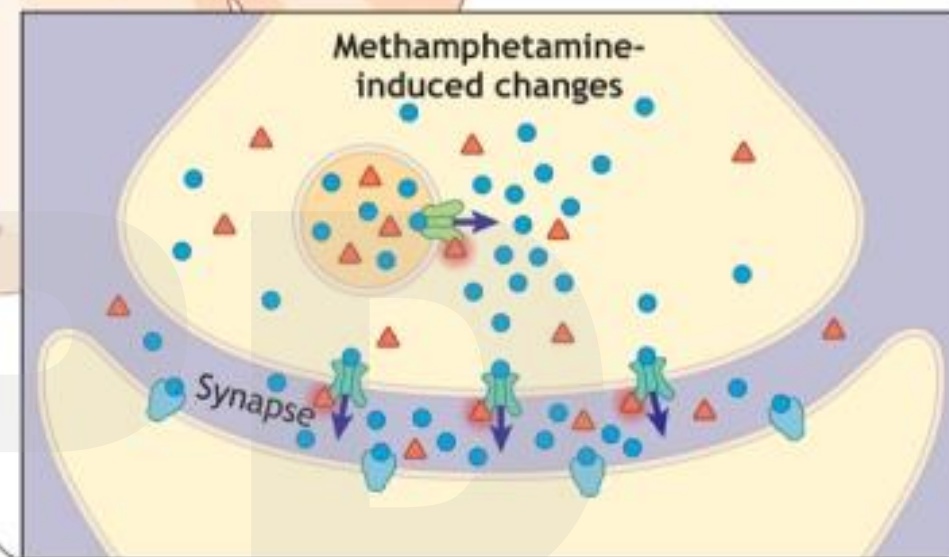
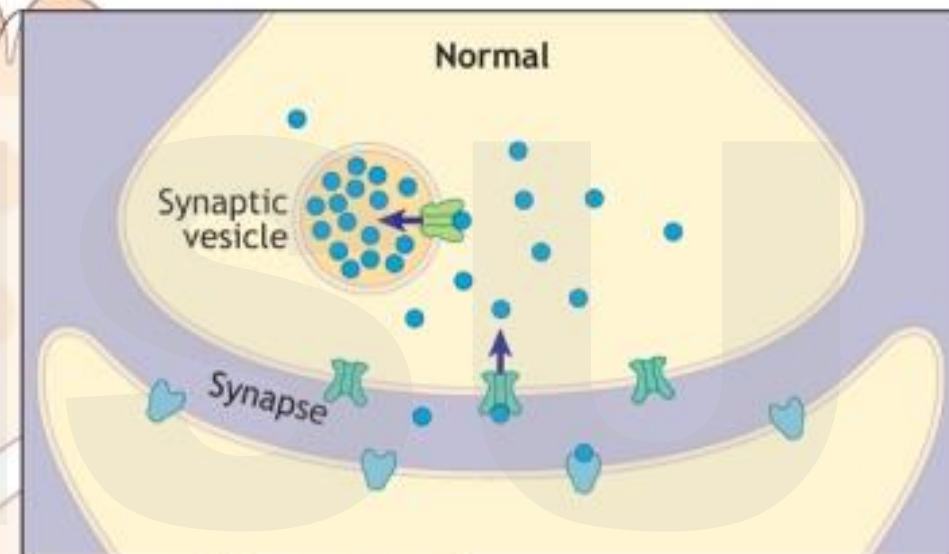




# CLINICAL PRESENTATION



Caudate  
Internal capsule  
Putamen  
External globus pallidus  
Anterior commissure  
Ventral striatum



▲ Methamphetamine  
● Dopamine  
Y Dopamine transporter  
Y Vesicular monoamine transporter 2  
Y Dopamine receptor



# METHAMPHETAMINE INTOXICATION

- Anxiety/irritability, panic
- Paranoia, psychosis
- Tactile hallucinations -i.e. "bugs crawling on skin"
- Repetitive behaviors (skin picking)
- Restlessness, agitation, tremor
- Increased heart rate, pupil dilation, sweating, nausea
- Chest pain

# METHAMPHETAMINE INTOXICATION

- Seizures
- Stroke
- Acute myocardial infarction
- Arrhythmias



# METHAMPHETAMINE-INDUCED PSYCHOSIS

- **#1 – paranoid delusions**
  - May be associated with violence
- Internal preoccupation – “locked inside my head”
- Disorganized behaviors, stereotyped movements

## RISK FACTORS FOR PSYCHOSIS

- **Dose-dependent increase in psychotic symptoms.**
- Higher risk with concurrent use of cannabis and alcohol.
- Route of administration- ***smoking does not appear to be protective!***
- Additional risk factors:
  - Sleep deprivation
  - Genetic vulnerability
  - Family history of psychiatric illness
  - Personal history of a primary psychotic disorder, affective disorders, personality disorders (schizotypal, antisocial)

# WITHDRAWAL

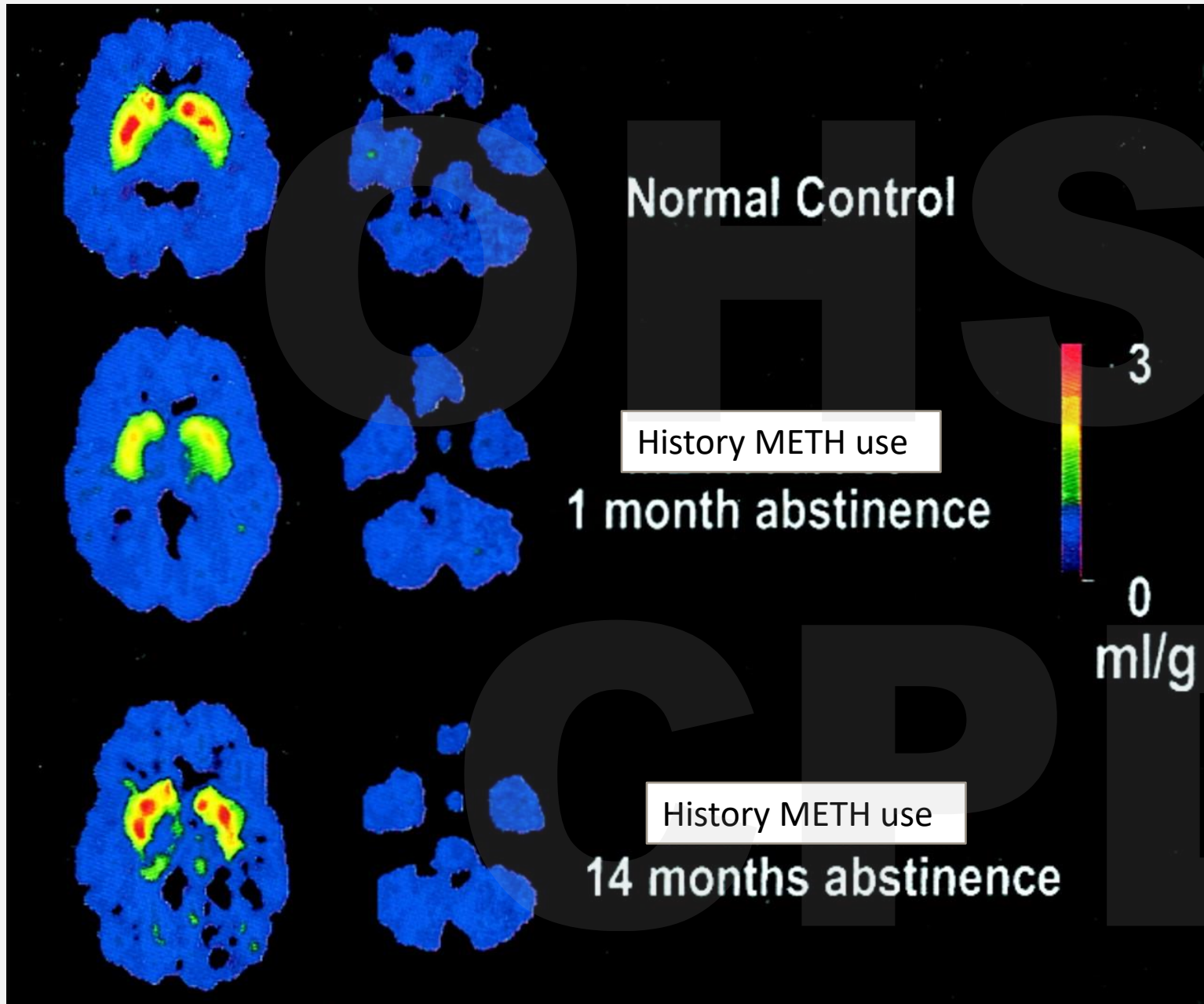
- Depression
- Fatigue
- Low motivation
- Trouble concentrating
- Increased sleep duration (but poor quality)
- Increased appetite



## CHRONIC USE: NEUROLOGIC EFFECTS



- **Structural changes in the brain**
  - Decreased levels of dopamine receptors and transporters
  - Decreased cerebral blood flow in the prefrontal cortex
- Multiple direct **neurotoxic** effects in the brain – oxidative stress, mitochondrial injury, neuronal cell death, nerve terminal degeneration, and breakdown of the blood brain barrier.
- Dysregulation of the immune system leads to a pro-inflammatory state.



Loss of dopamine transporters

Recovery of dopamine transporters

## CHRONIC USE: NEUROLOGIC EFFECTS

- Like schizophrenia, chronic methamphetamine use can cause cognitive impairments and **executive dysfunction**, including deficits in verbal and working memory.
- Studies have documented similarities between methamphetamine-induced neurotoxicity and **traumatic brain injury**.
- There is also an increased risk for **hemorrhagic stroke** among those who use methamphetamine.

## CHRONIC USE: DEPRESSION

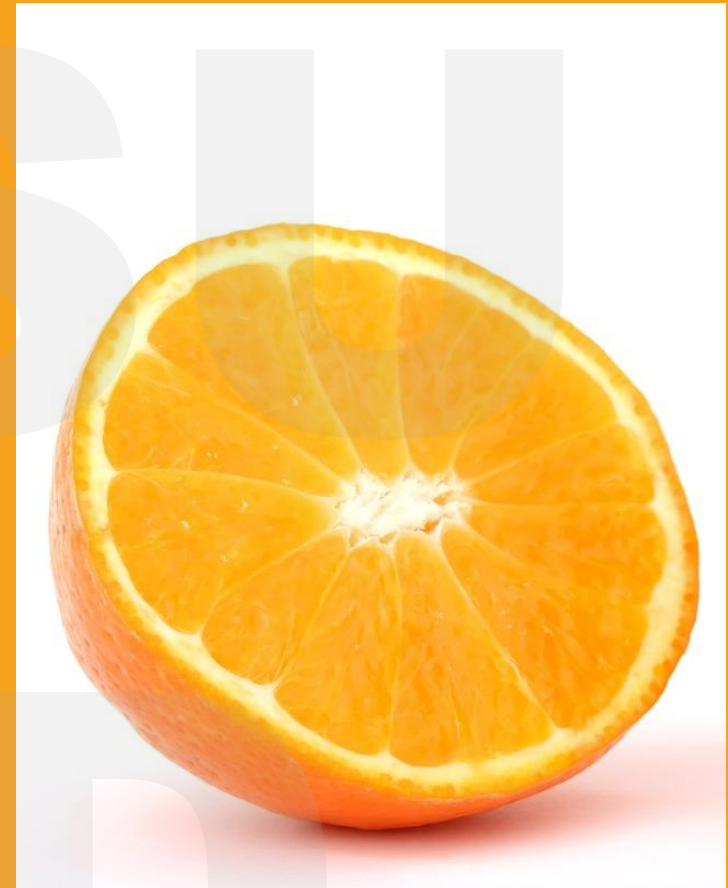
- Chronic use of methamphetamine is associated with higher rates of depression.
- **Anhedonia** is a common symptoms of methamphetamine withdrawal.
- Treatment for methamphetamine use disorder with structured psychosocial interventions can reduce depression over time.

## CHRONIC USE: PERSISTENT PSYCHOSIS

- Among recreational amphetamine users, **>75% experience transient psychotic symptoms.**
- **36% of people who misuse methamphetamine** will go on to develop psychosis lasting beyond the period of intoxication.
- The average recovery period is within one week.
- In a subset of patients (16-26%) symptoms will become chronic and persist >1 month despite abstinence from methamphetamine.



Schizophrenia



Chronic Methamphetamine  
Psychosis

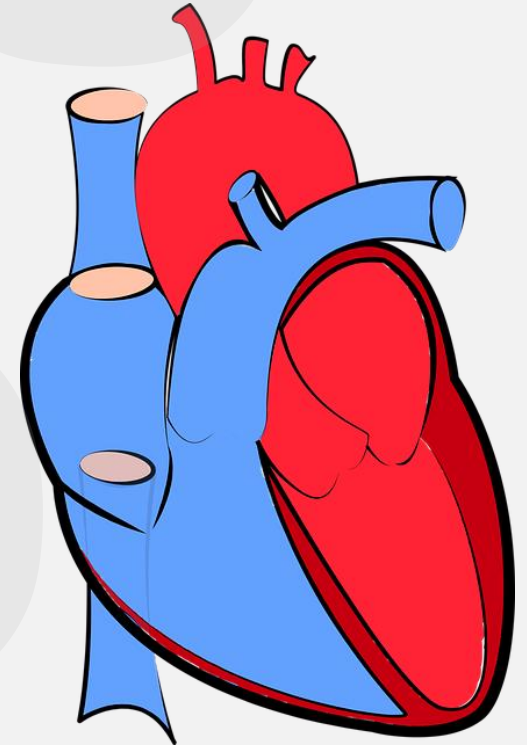
- Some patients experience prolonged psychotic symptoms (months to years).
- High rates of returning to use of methamphetamine.
- Recent evidence that cognitive impairment can **improve with abstinence**.

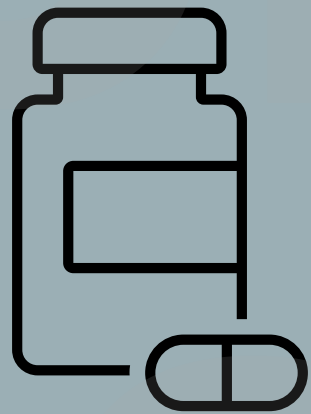


Brecht and Herbeck, 2014  
Wang, 2021  
Nie, 2020

## CHRONIC USE: PHYSICAL HEALTH EFFECTS

- Hypertension
- Dilated cardiomyopathy
- Arrhythmias
- Aortic dissection
- Pulmonary disease (direct toxicity, pulmonary HTN)
- Intestinal ischemia
- Infection risk with IV use (HIV, Hepatitis C)





TREATMENT

## GENERAL CONSIDERATIONS

- Use a non-judgmental approach and avoid stigmatizing language
- Explore the patient's goals-
  - Reduce amount? Discontinue? Continue to use but more safely?
- Understand perceived benefits and risk of harm with use



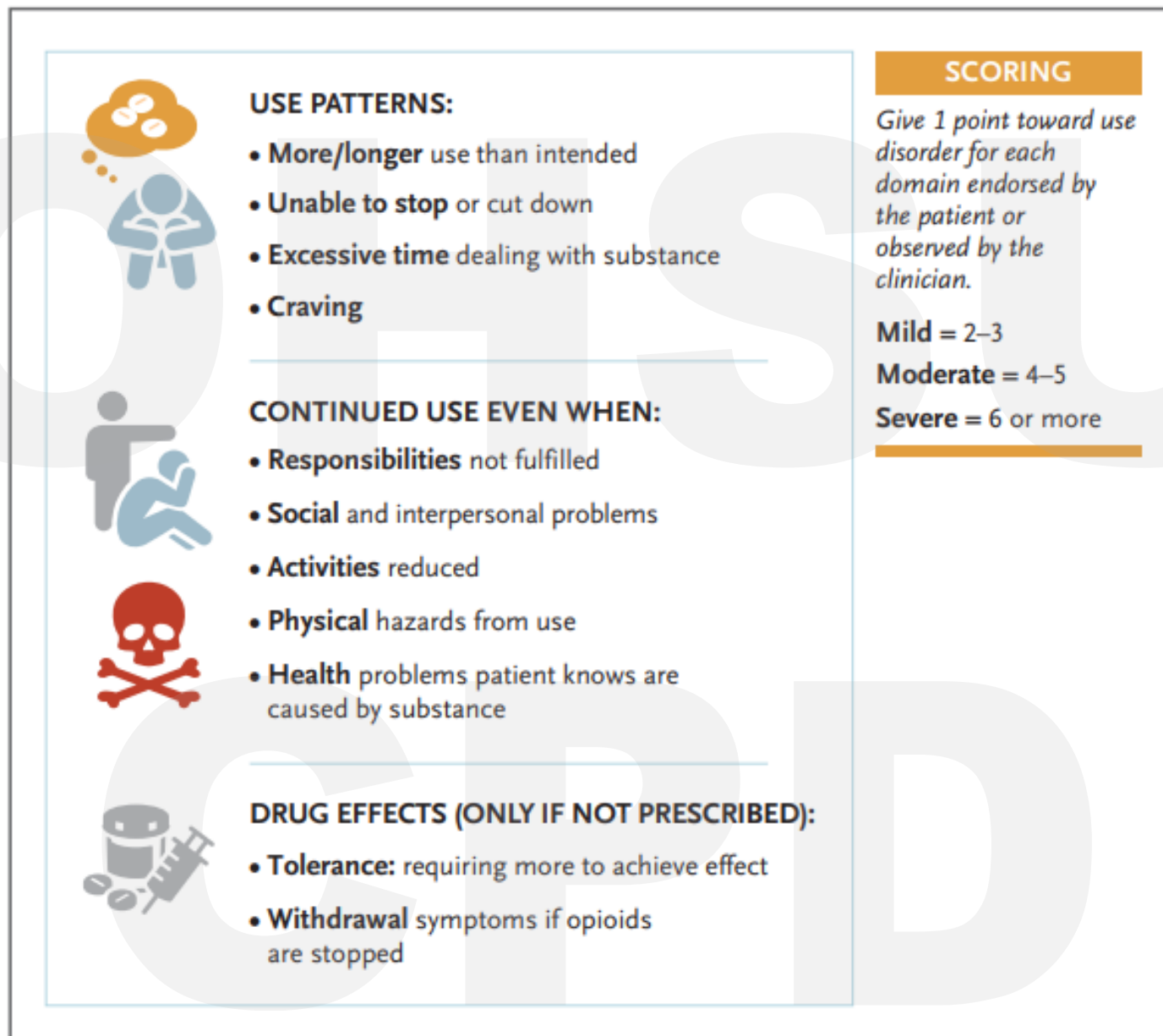


Figure 3. Adapted DSM-5 Criteria for Substance Use Disorder.

## TREATMENT OF METHAMPHETAMINE USE DISORDER

- No FDA-approved medications
  - Some off-label options
- Behavioral therapy is the cornerstone of treatment!
  - **Contingency management**
  - Cognitive behavioral therapy
  - Matrix Model
  - Residential treatment

## CONTINGENCY MANAGEMENT (CM)

- Both **voucher-based reinforcement** and **prize incentives** CM have been shown to be effective behavioral treatments for stimulant use disorder.
- Studies have demonstrated that CM can reduce stimulant use even among participants with serious mental illness



## HOW DOES CM WORK?

Desired  
behavior  
is chosen

- Treatment and/or counseling engagement
- Substance abstinence

Behavior  
confirmed

- Attendance confirmed
- Drug test negative

Reward  
provided

- Prizes are given immediately
- Celebrate!

## CM IS EFFECTIVE

A review of 27 studies on CM (including 15 RCTs) showed:

- Increased abstinence from methamphetamine
- Increased treatment retention, attendance, and engagement
- Reductions in risky sexual behavior and number of sexual partners

## THERE'S AN APP FOR THAT

- Smartphone based CM provides financial incentives (via gift-cards or debit cards) for attending appointments, counseling sessions, doing CBT-based readings and answering comprehension questions, and/or providing negative drug screens.
- Initial studies show promise for reducing stimulant use in patients enrolled in outpatient buprenorphine maintenance treatment.



<https://www.affecttherapeutics.com/>

## PHARMACOTHERAPY

- No FDA-approved medications
- Some off-label options include:
  - Bupropion XL 450mg +/- XR-naltrexone 380mg q3 weeks (ADAPT-2 Trial)
  - Mirtazapine 15mg -> 30mg QHS
  - N-acetyl cystine (NAC) 2400mg daily

Consider oral naltrexone  
if XR not available!

## ADDRESS TOXICITIES

- Cardiovascular
  - Smoking cessation
  - Treat chronic hypertension, heart failure
- Neuropsychiatric
  - Good sleep
  - Consider antipsychotics for persistent psychosis

## TREATMENT OF PERSISTENT PSYCHOSIS

- Antipsychotic medications may help alleviate psychotic symptoms.
  - Second > First generation antipsychotics
  - Assess risks vs benefits if using long term
- Benefit less clear for patients who continue to use methamphetamine frequently.

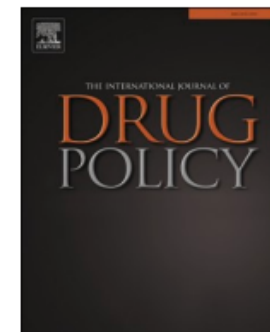




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## International Journal of Drug Policy

journal homepage: [www.elsevier.com/locate/drugpo](http://www.elsevier.com/locate/drugpo)



### Short Report

# Evaluation of methamphetamine assist packs: As-needed antipsychotics for self-management of methamphetamine-associated psychiatric toxicity

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# PREVENTION

- Screen for infections and chronic illnesses
  - HIV, Hep B, Hep C, TB, STIs
- Provide vaccinations
- Harm reduction measures
  - Clean needles and/or pipes
  - Naloxone
  - Fentanyl test strips
- Support for basic needs (housing food)



# ENGAGEMENT



Peer Support!



## TAKE HOME POINTS

1. Use of methamphetamine can cause an acute sympathomimetic toxidrome with symptoms of tachycardia, hypertension, anxiety/agitation, and psychosis.
2. Chronic use of methamphetamine is neurotoxic and leads to structural brain changes that can cause chronic psychosis and cognitive impairment.
3. There are no FDA-approved medications for methamphetamine use disorder. There is very good evidence for contingency management and several medications can be considered off-label.
4. Antipsychotics have a role for treating persistent symptoms of psychosis after disruption of methamphetamine use but need to balance risks vs benefits.

QUESTIONS?

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