

Stimulants 2023: Cocaine and Methamphetamine

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Welcome and Introductions

Presenter

Richard Rawson, Ph.D.

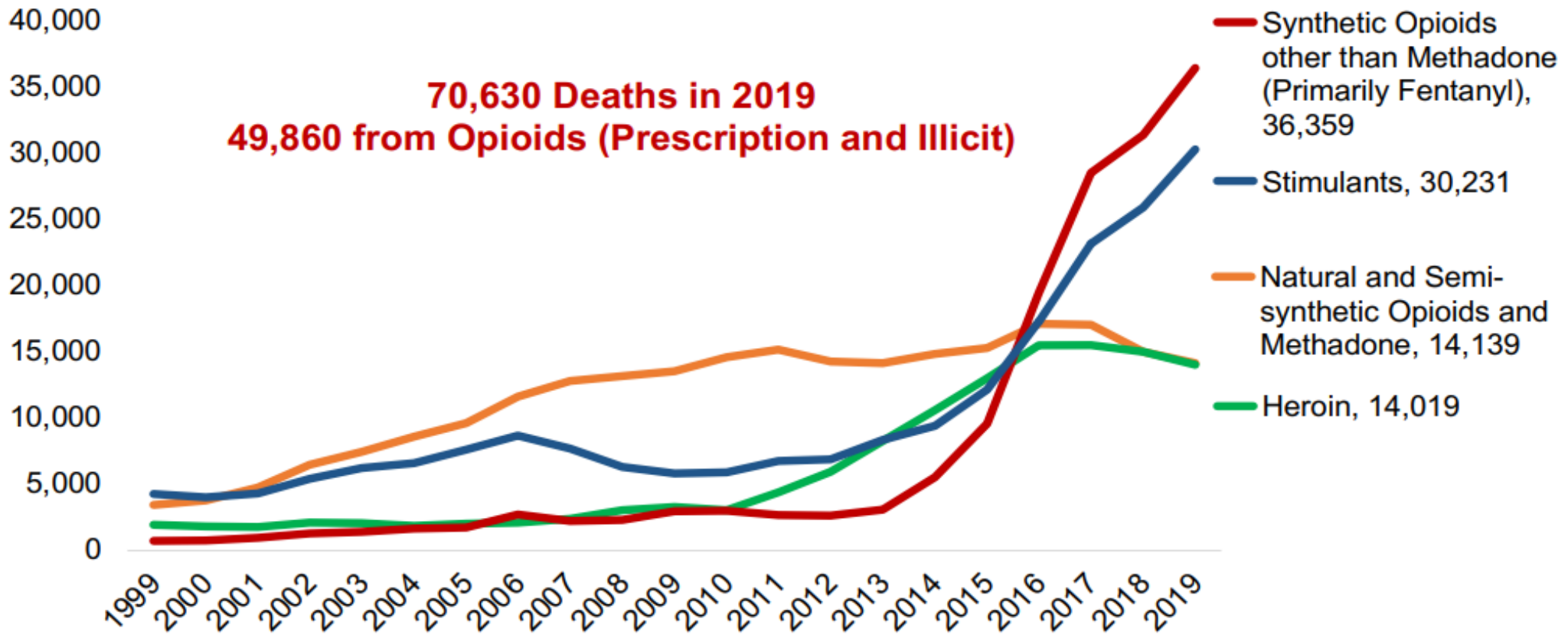
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University of Vermont, Burlington, Vermont
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University of California, Los Angeles, California

Objectives

- Interpret current stimulant use trends and overdose data.
- Describe impact of stimulant use on the brain.
- Discuss clinical challenges for stimulant use disorders.

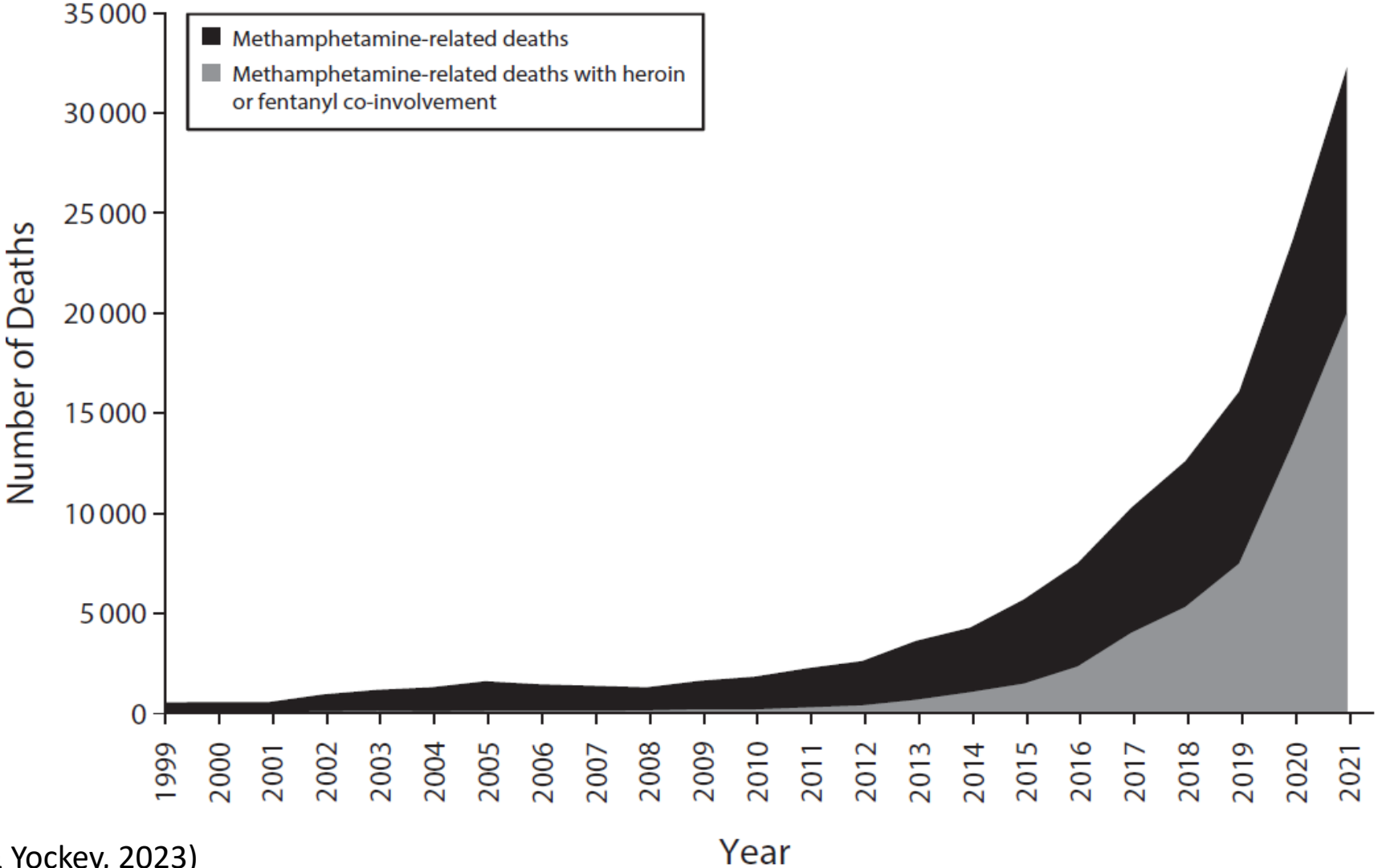
Evolution of Drivers of Overdose Deaths, All Ages

Analgesics → Heroin → Fentanyl → Stimulants



Source: The Multiple Cause of Death data are produced by the Division of Vital Statistics, National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), United States Department of Health and Human Services (US DHHS).

Deaths Involving Methamphetamine and Opioids



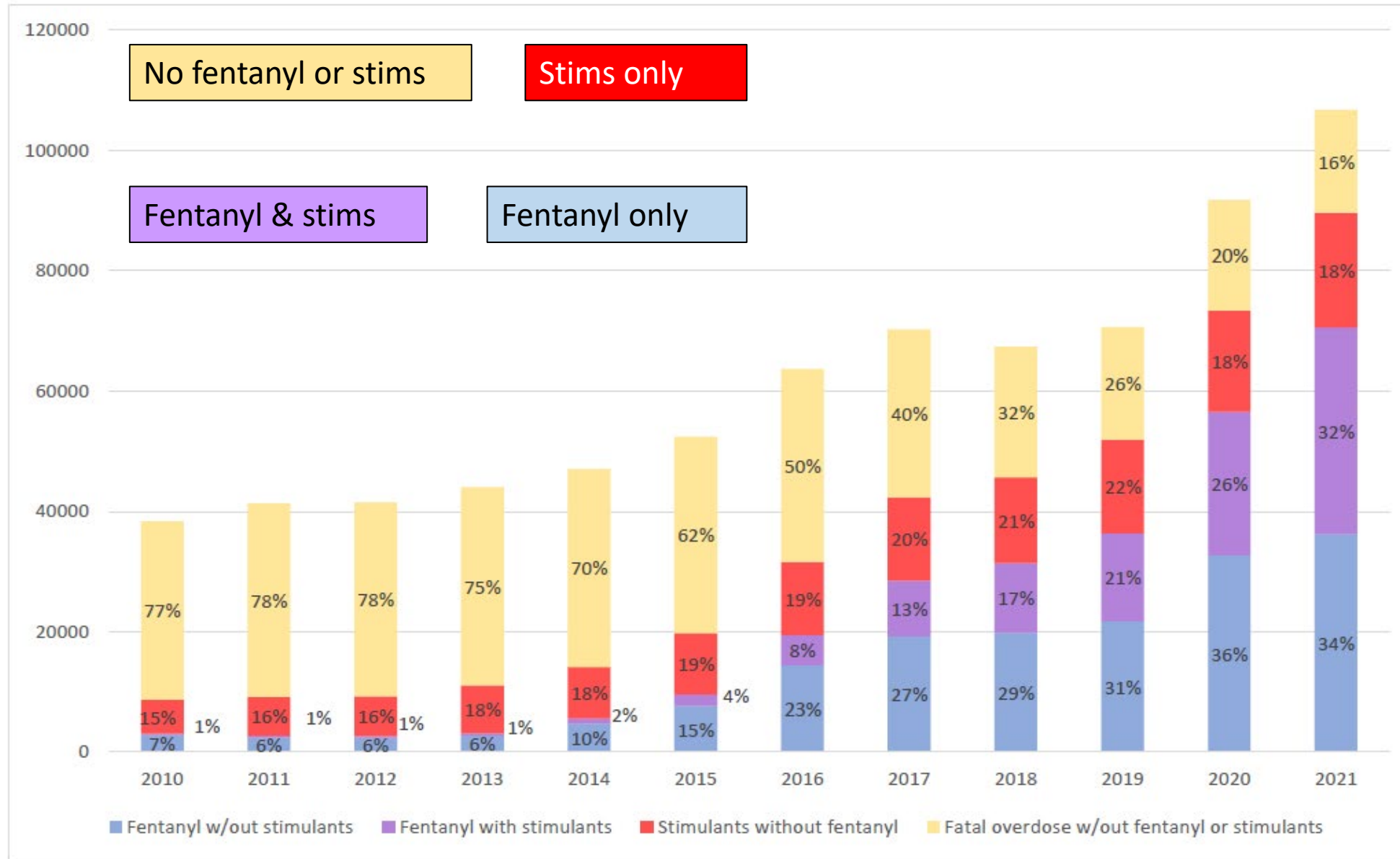
(Hoopsick & Yockey, 2023)

Methamphetamine Mortality

- Accelerated over the past 2 decades, peaking in 2021.
- Deaths co-involving heroin or fentanyl grown dramatically.
- Intentional co-use of stimulants and opioids has increased.
- Need to develop and implement harm reduction services, especially for polysubstance use.

(Hoopsick & Yockey, 2023)

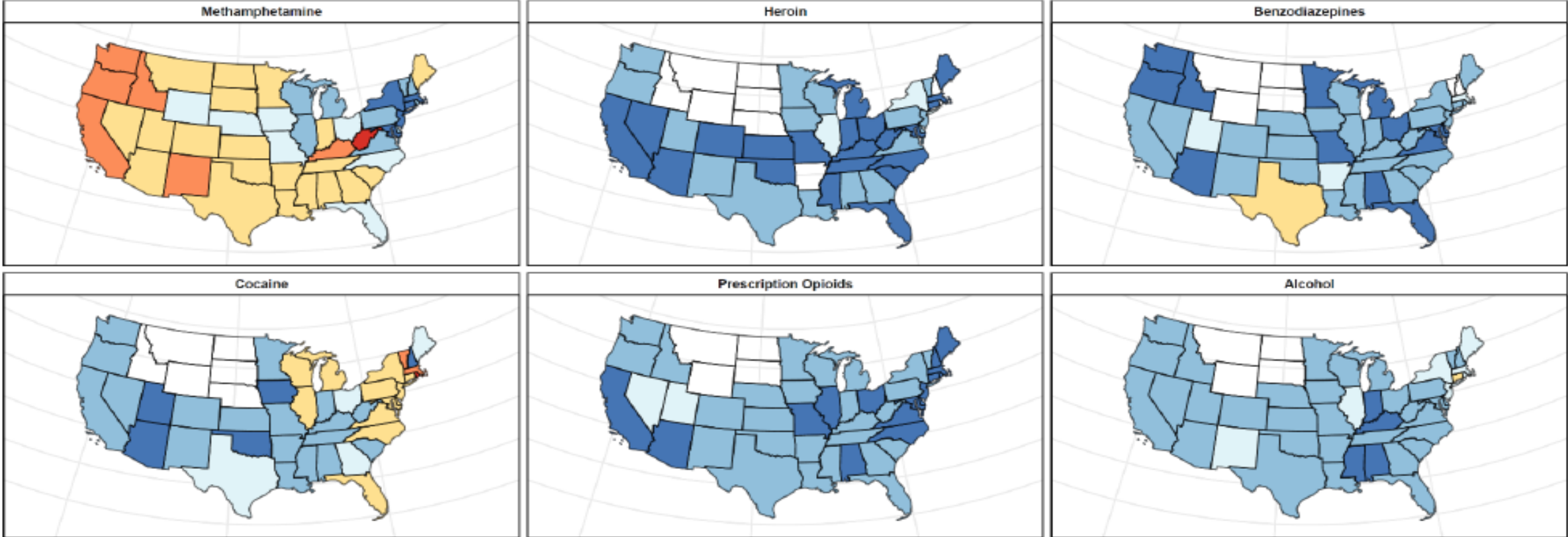
Overdose Deaths by Fentanyl and Stimulant Presence, 2010-2021



(Friedman & Shover, 2022)

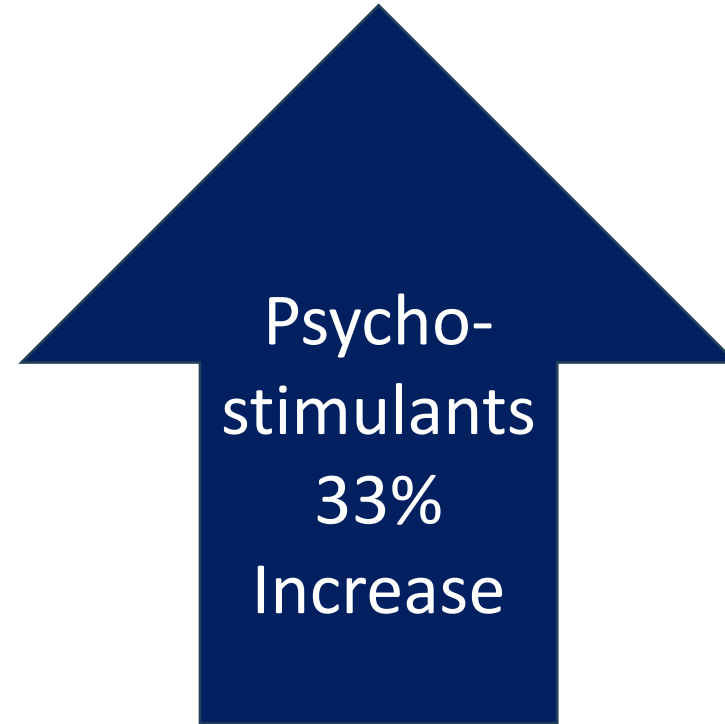
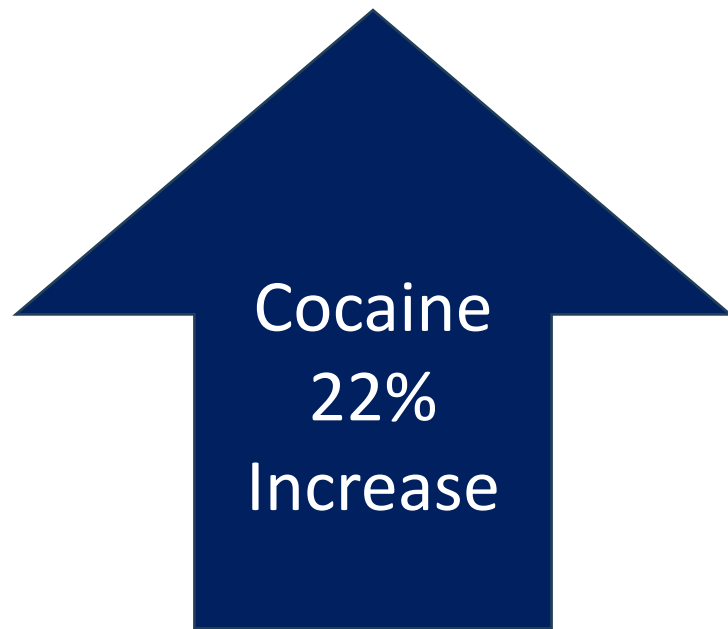
Percent of Fentanyl Overdose Deaths Containing Other Drug Classes by State, 2021

0-10% 10-20% 20-30% 30-40% 40-50% 50-60%



(Friedman & Shover, 2022)

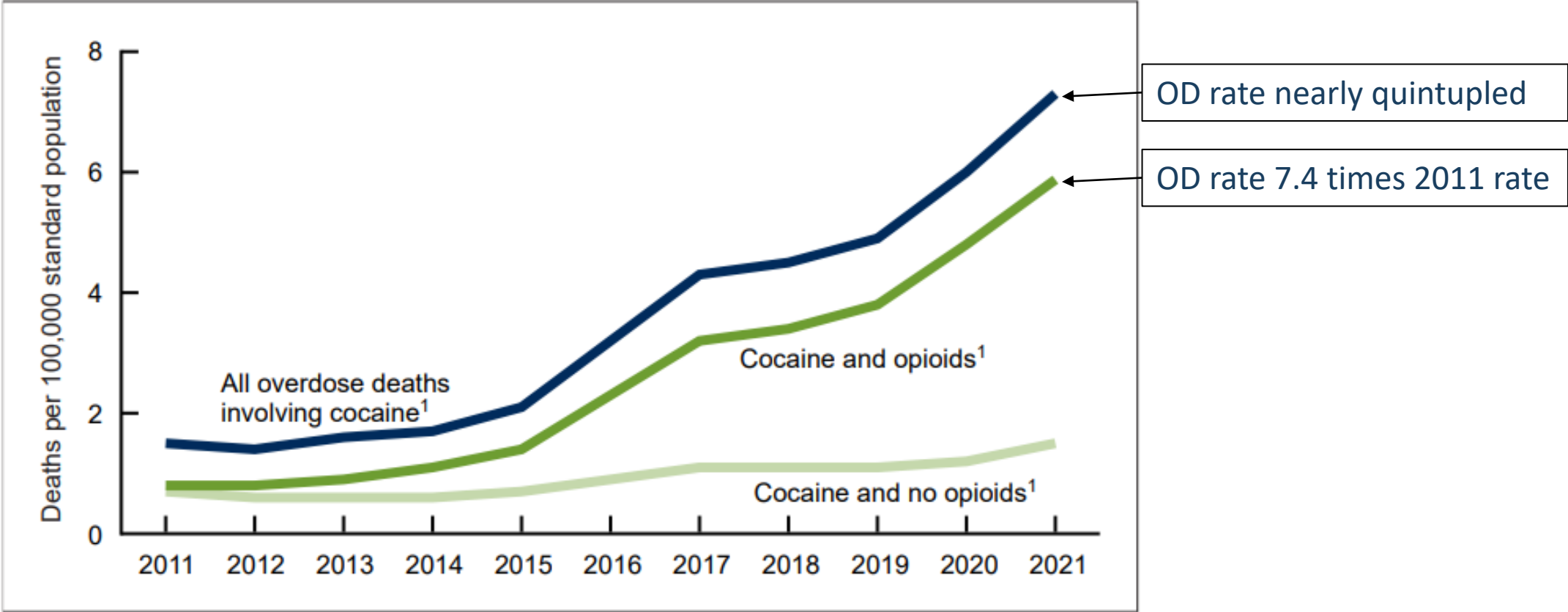
Drug Overdose Deaths



(Spencer, Miniño, & Garnett, 2023)

Rate of Drug Overdose Deaths Involving Cocaine and Opioids

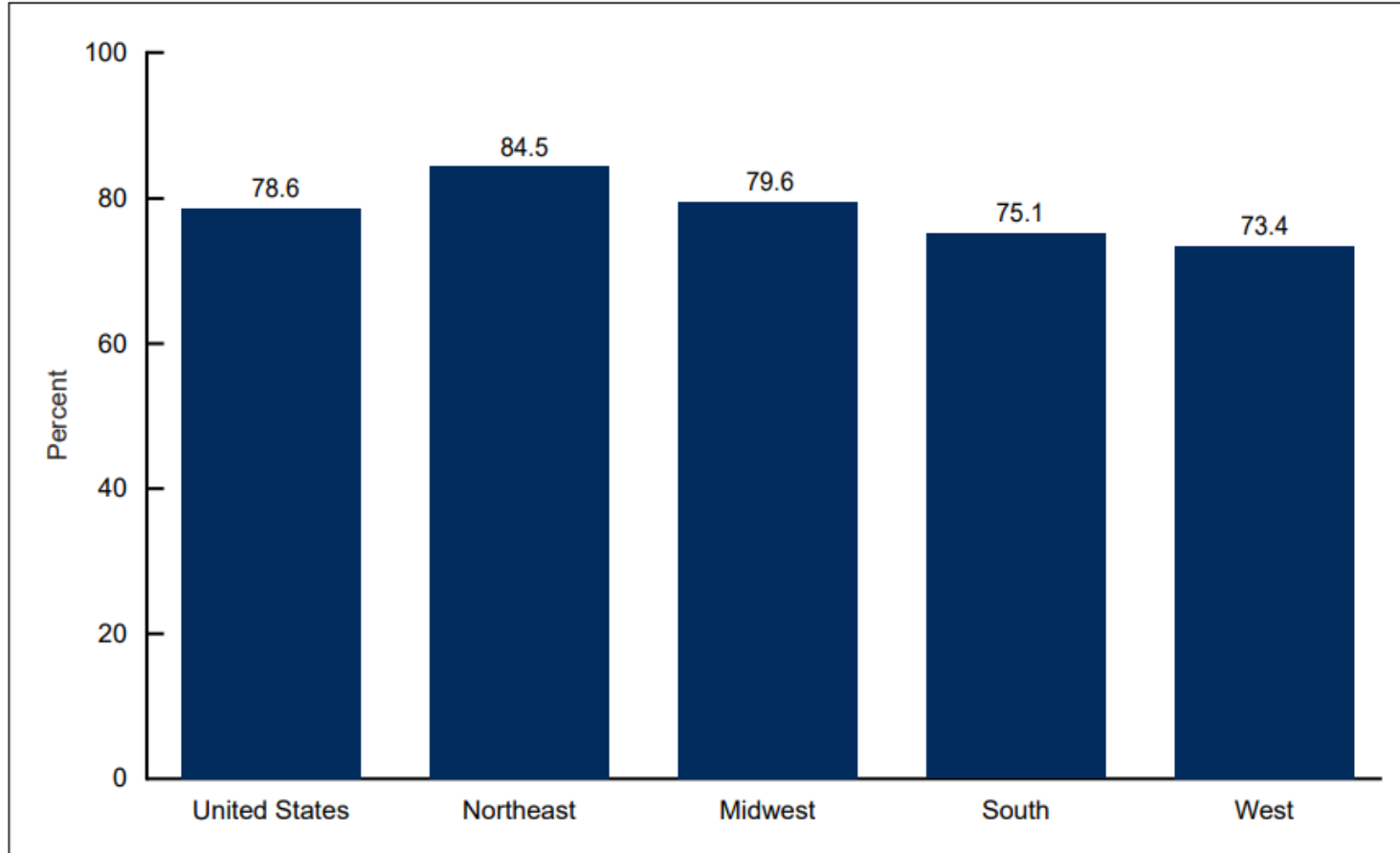
Figure 1. Age-adjusted rate of drug overdose deaths involving cocaine, by co-involvement of opioids: United States, 2011–2021



(Spencer, Miniño, & Garnett, 2023)

Percentage of Drug Overdose Deaths Involving Cocaine and Opioids by Region

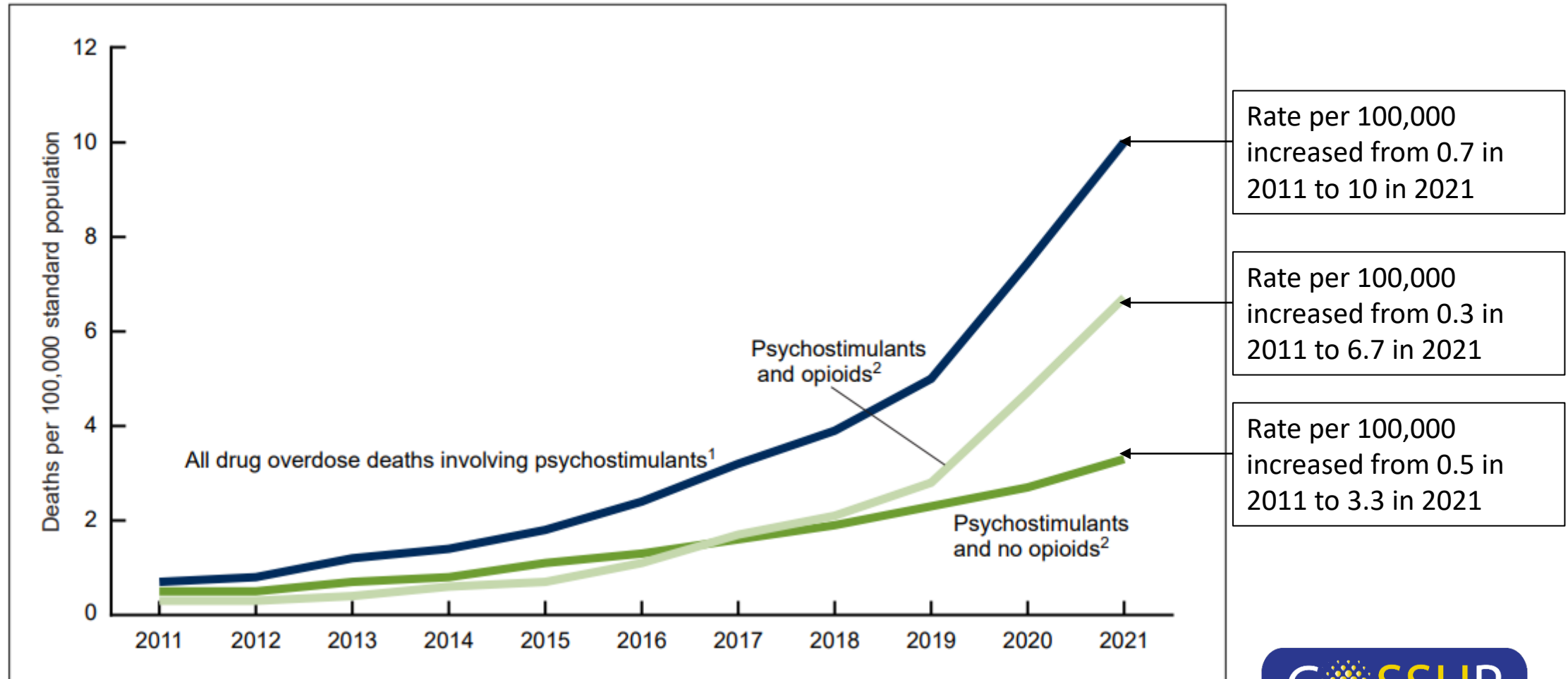
Figure 2. Percentage of drug overdose deaths involving cocaine with co-involvement of opioids, by Census region: United States, 2021



(Spencer, Miniño, & Garnett, 2023)

Rate of Overdose Deaths Involving Psychostimulants with Opioids

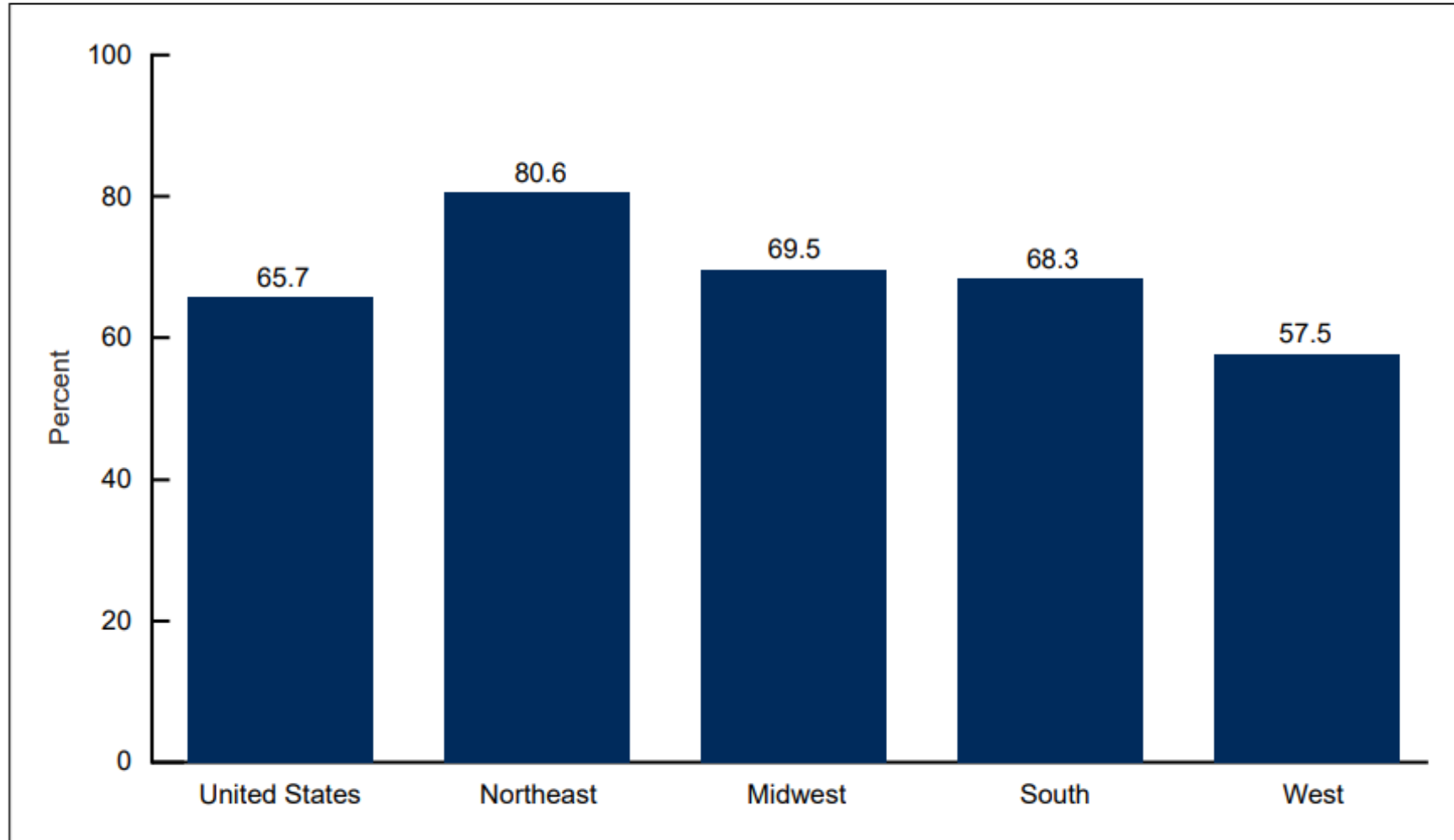
Figure 3. Age-adjusted rate of drug overdose deaths involving psychostimulants, by co-involvement of opioids: United States, 2011–2021



(Spencer, Miniño, & Garnett, 2023)

Percentage of Overdose Deaths Involving Psychostimulants by Region

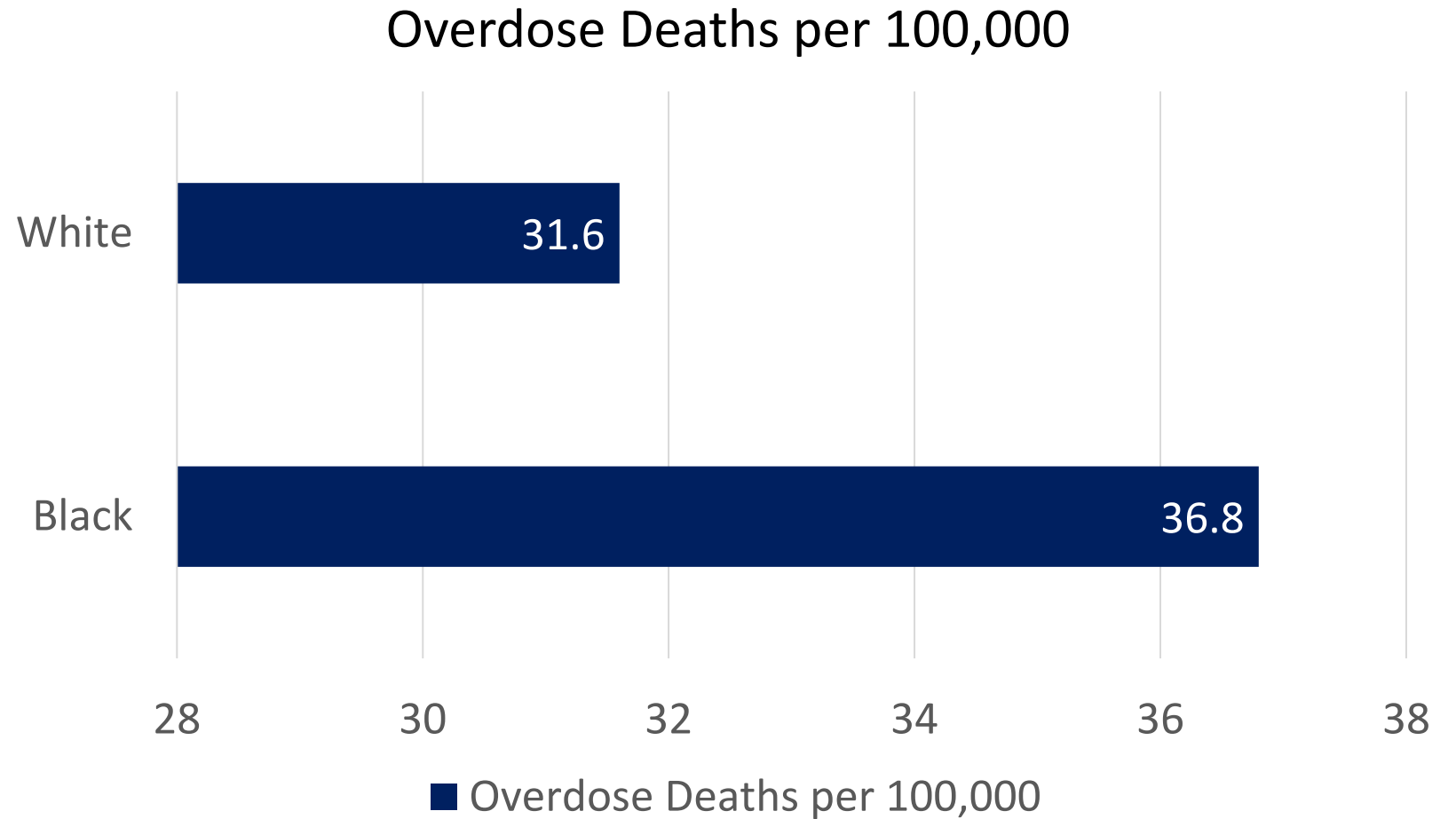
Figure 4. Percentage of drug overdose deaths involving psychostimulants with co-involvement of opioids, by Census region: United States, 2021



(Spencer, Miniño, & Garnett, 2023)

Overdose Rates

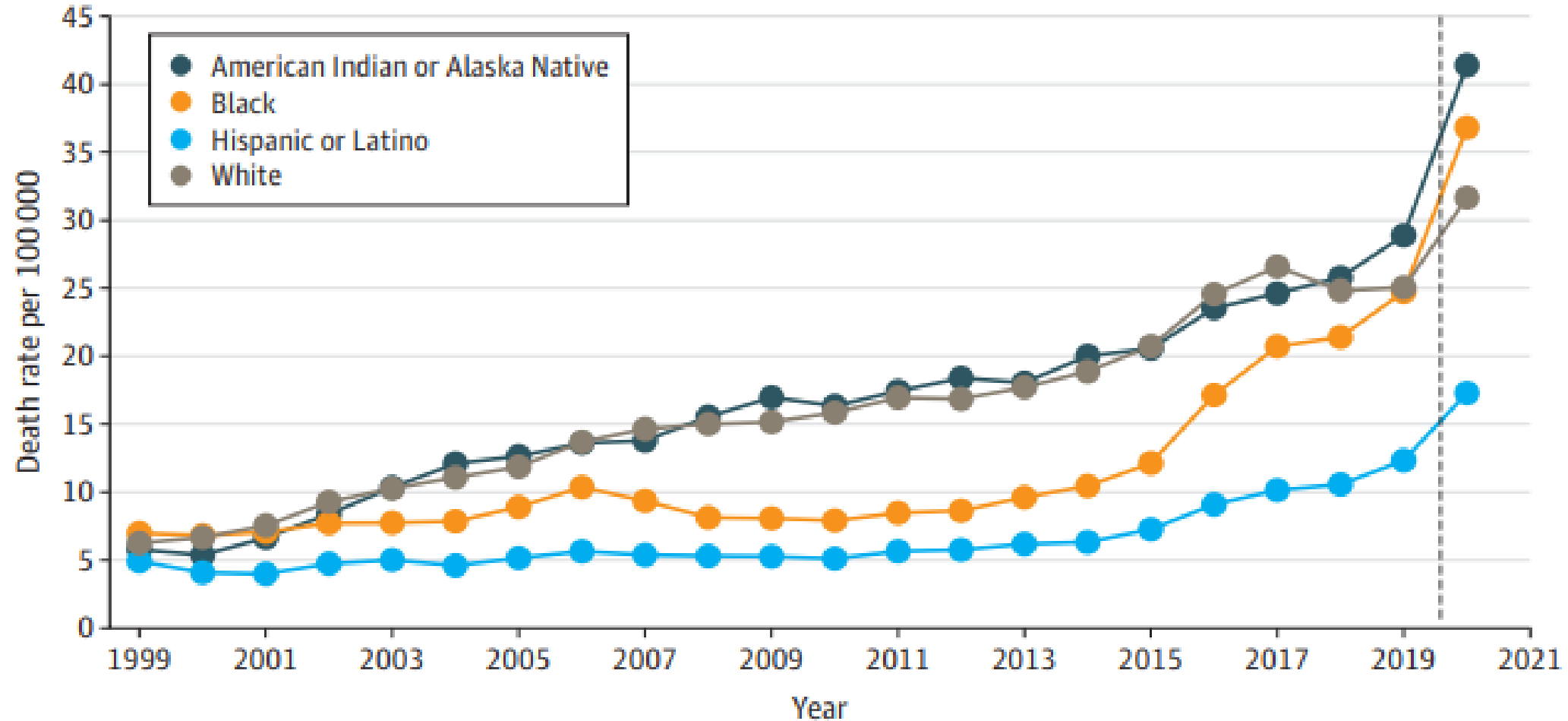
In 2020, overdose rate among Blacks higher than whites for first time since 1999.



(Friedman & Hansen, 2022)

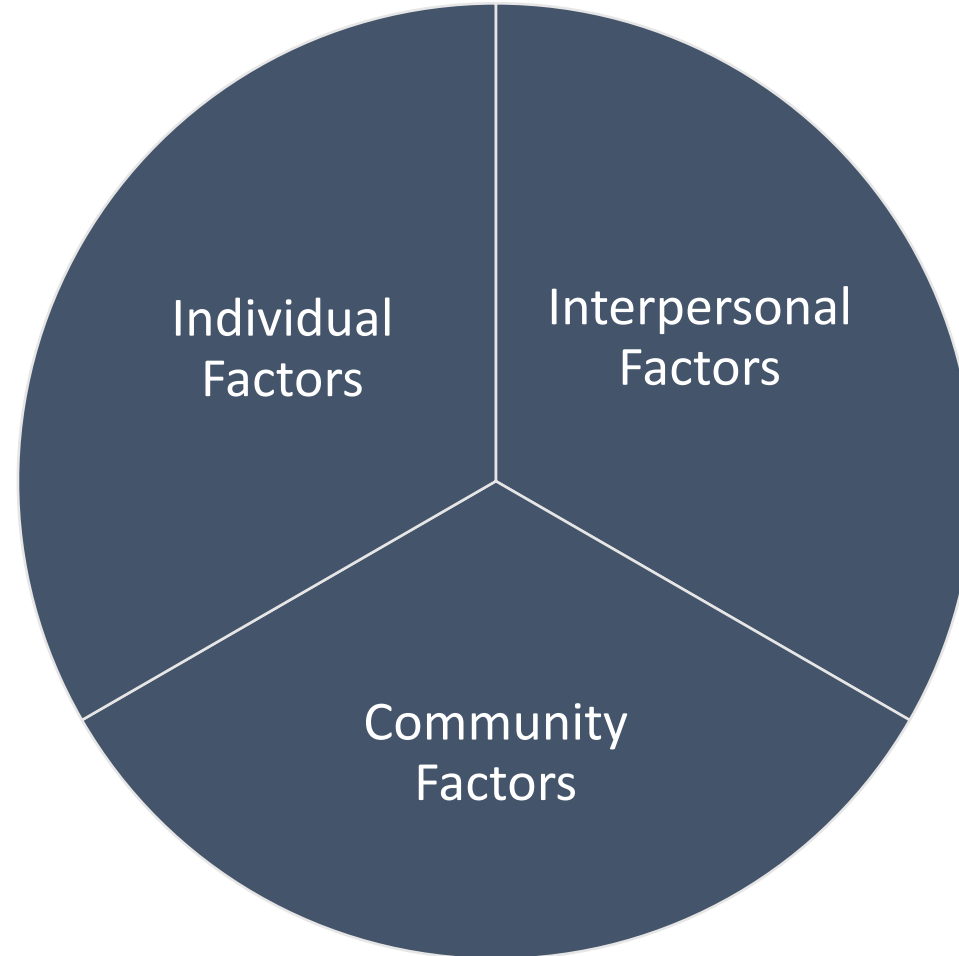
Drug Overdose Mortality per 100,000 Population

B Rate per 100 000 population



(Friedman & Hansen, 2022)

Contributing Factors



(Hansen, Carvalho, McDonald, & Havens, 2021)

Individual Factors

- Found methamphetamine (MA) high attractive (energy, focus, confidence).
 - “...gave me the confidence and courage to do things I normally didn’t wanna do.”
- Used MA to treat health concerns, including attention difficulties, mood disorders, emotional trauma.

“It was, you know, the best to me, the best thing ever. I got PTSD from my childhood, and when I sleep, I have nightmares. So, meth kept me awake, and I didn’t have them nightmares, and I was better. I thought I was better. I was numbing my pain.”

Individual Factors (contd.)

- Was way to treat chronic pain.
 - A 39-year-old male laborer with a history of chronic back pain said, “When we’ve got a big day at work, I’ll take me a couple hits that morning, work all day, daylight to dark or whatever we have to do.”
- Helped suppress withdrawal symptoms and opioid cravings.

“Meth will stop withdrawal; did you know that? For anything. It stops it for any kind of drugs—Xanax, Neurontin, pain pills, Suboxone. So, a lot of people have used meth to get off Suboxone.”

Interpersonal Factors

- Initiation of MA often facilitated by members of participant's drug network.
- Many given MA without knowing what it was.

“I was 15 when I first tried meth. I saw one of my friends that I had not seen in a while, and she tells me that she had ‘ice cream.’ I didn't know what it was. And my person that I got weed off was out, so I gave her \$20. I was looking for weed, but as soon as I took my first hit of meth I was like, ‘Oh my god’ because I fell in love.”

- MA increasingly available everywhere.

(Hansen, Carvalho, McDonald, & Havens, 2021)

Community Factors

- MA now easiest illicit substance to acquire.
 - “Meth already took over. Meth is on every corner, every street, every straight stretch you see.”
 - “You don’t even hear about selling Lorcets or Percocets anymore. Opioids are gone except for people who actually take them for real pain.”
- Ubiquity made MA affordable.

(Hansen, Carvalho, McDonald, & Havens, 2021)

Stimulants



Stimulants

- **Description:** A group of synthetic and plant-derived drugs that increase alertness and arousal by stimulating the central nervous system. Although MDMA (ecstasy) has some hallucinogenic properties, it is often classified as a stimulant.
- **Medical uses:** Short-term treatment of obesity, narcolepsy, and hyperactivity in children.
- **Method of use:** Intravenous, intranasal, oral, smoking.

Methamphetamine vs. Cocaine

Cocaine	Methamphetamine
Half-life: 2 hours	Half-life: 10 hours
Paranoia: 4-8 hours following drug cessation	Paranoia: 7-14 days

- MA psychosis may require medication/hospitalization and may not be reversible.
- Neurotoxicity appears to be more profound with amphetamine-like substances.

Methamphetamine



Perris, California: Largest Domestic Methamphetamine Seizure (2,200 lbs.) on October 2, 2020



Potency and Purity

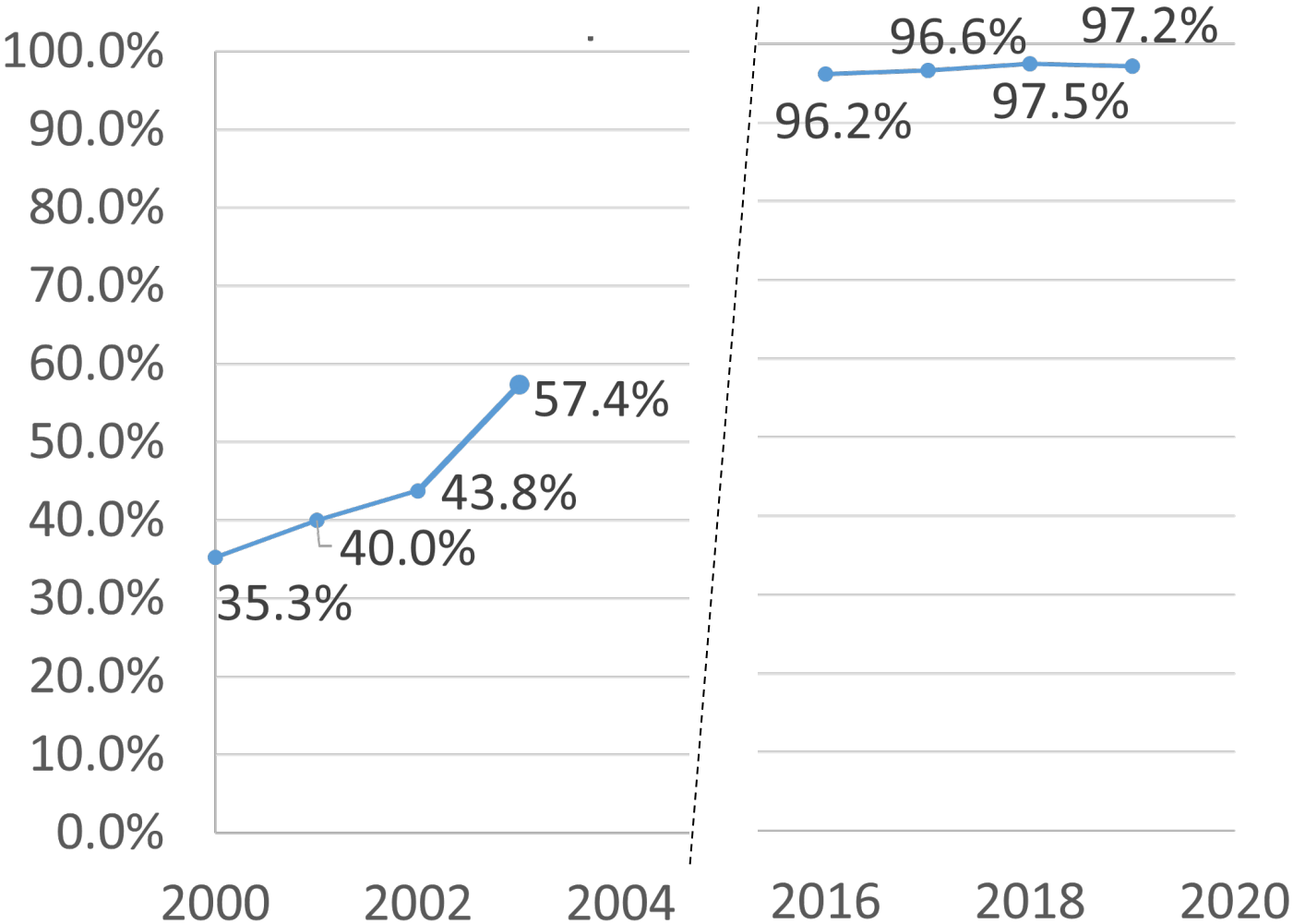
Potency

How much of drug is needed to produce effect

Purity

How much MA present compared to other inert substances

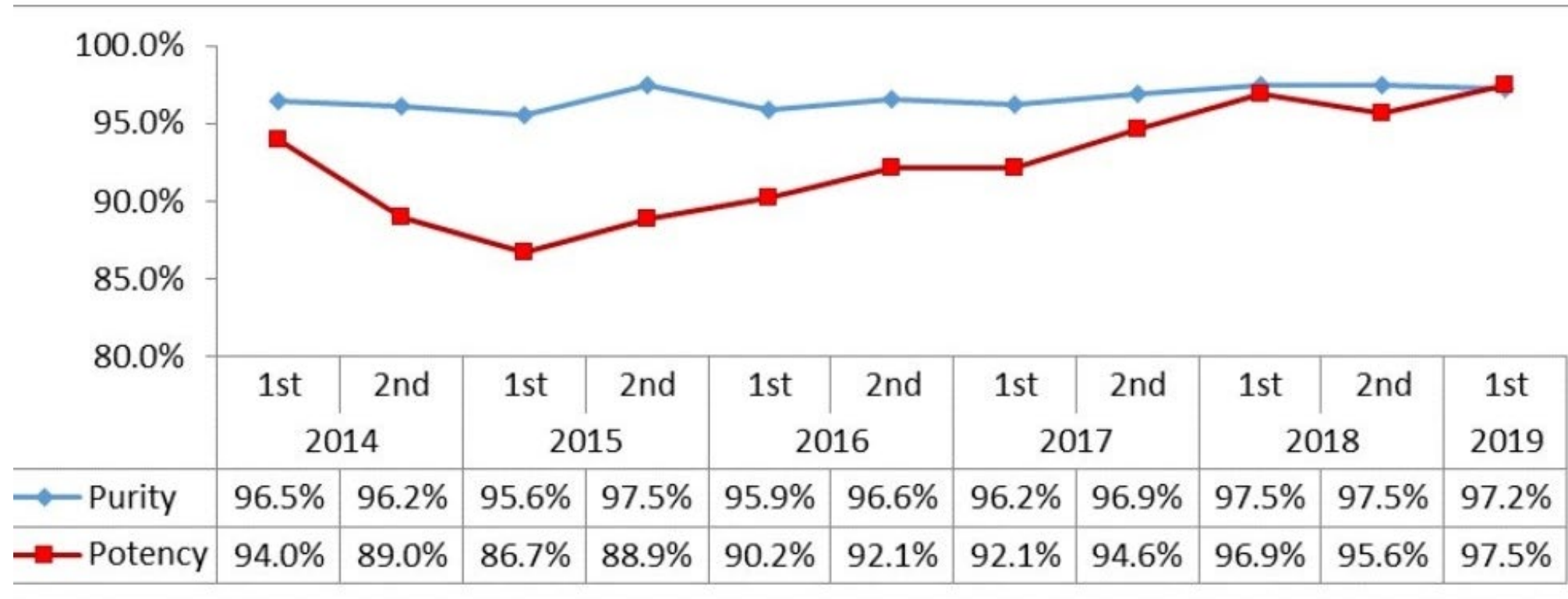
Methamphetamine Purity 2000-2003 & 2016-2019



(U.S. Department of Justice National Drug Intelligence Center, 2005; U.S. Department of Justice Drug Enforcement Administration, 2021)



Methamphetamine Purity and Potency



(U.S. Department of Justice Drug Enforcement Administration, 2021)

Methamphetamine Overdose

Assume a person who overdoses on MA is also experiencing a fentanyl overdose, typically evidenced by decreased respiration (stopped breathing).

- Treat with naloxone, using protocols for fentanyl.

Methamphetamine Overdose (contd.)

- With a MA overdose without fentanyl, death can occur from:
 - Hyperthermia or very high body temperature.
 - Stroke.
 - Cardiac events.
- An individual may have a combined overdose from fentanyl and MA, requiring treatment for both drugs.

Stimulant Effects

Stimulants: Acute Effects

- Euphoria.
- Increased talkativeness.
- Hyperactivity.
- Erratic changes in mood.
- Increased blood pressure.
- **Elevated body temp.**
- Rapid heart and breathing rates.
- Reduced fatigue.
- Reduced hunger.
- Increased energy.
- Increased sexual drive.
- Increased self-confidence.

Stimulants: Chronic Effects

- Psychosis.
- Paranoia.
- Symptoms of anxiety and depression.
- Social withdrawal.
- Emotional volatility.
- Violence.

Stimulants: Psychiatric Consequences

- Paranoia.
- Protracted memory impairment.
- Depressive/dysthymic reactions.
- Hallucinations.
- Psychosis.
- Panic disorders.
- Rapid addiction.

Psychostimulant Withdrawal

Crash (Days 1–3)	Peak symptoms (Days 2–10)	Residual symptoms (from 1–8 weeks)
<ul style="list-style-type: none">• Exhaustion• Depression• Oversleeping• No cravings	<ul style="list-style-type: none">• Dysphoria (unease)• Lack of energy• Increased appetite• Generalized aches and pains• Re-emergence of mild psychotic features, including:<ul style="list-style-type: none">▪ Misperceptions▪ Paranoid ideation▪ Hallucinations▪ Anxiety• Sleeplessness• High craving	<ul style="list-style-type: none">• Episodic craving• Insomnia <p>Fluctuating:</p> <ul style="list-style-type: none">• Irritability• Agitation• Restlessness• Dysphoria• Lethargy• Amotivation

(Adapted from Pead, Lintzeris & Churchill, 1996)

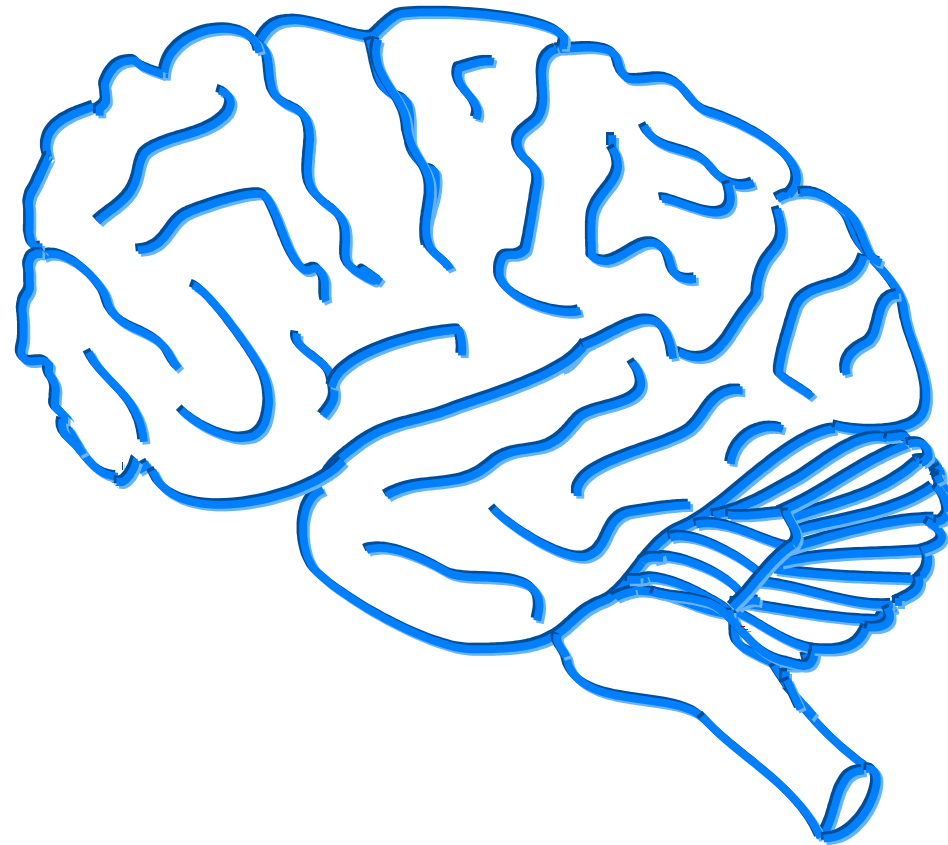
Factors Associated with Methamphetamine Withdrawal

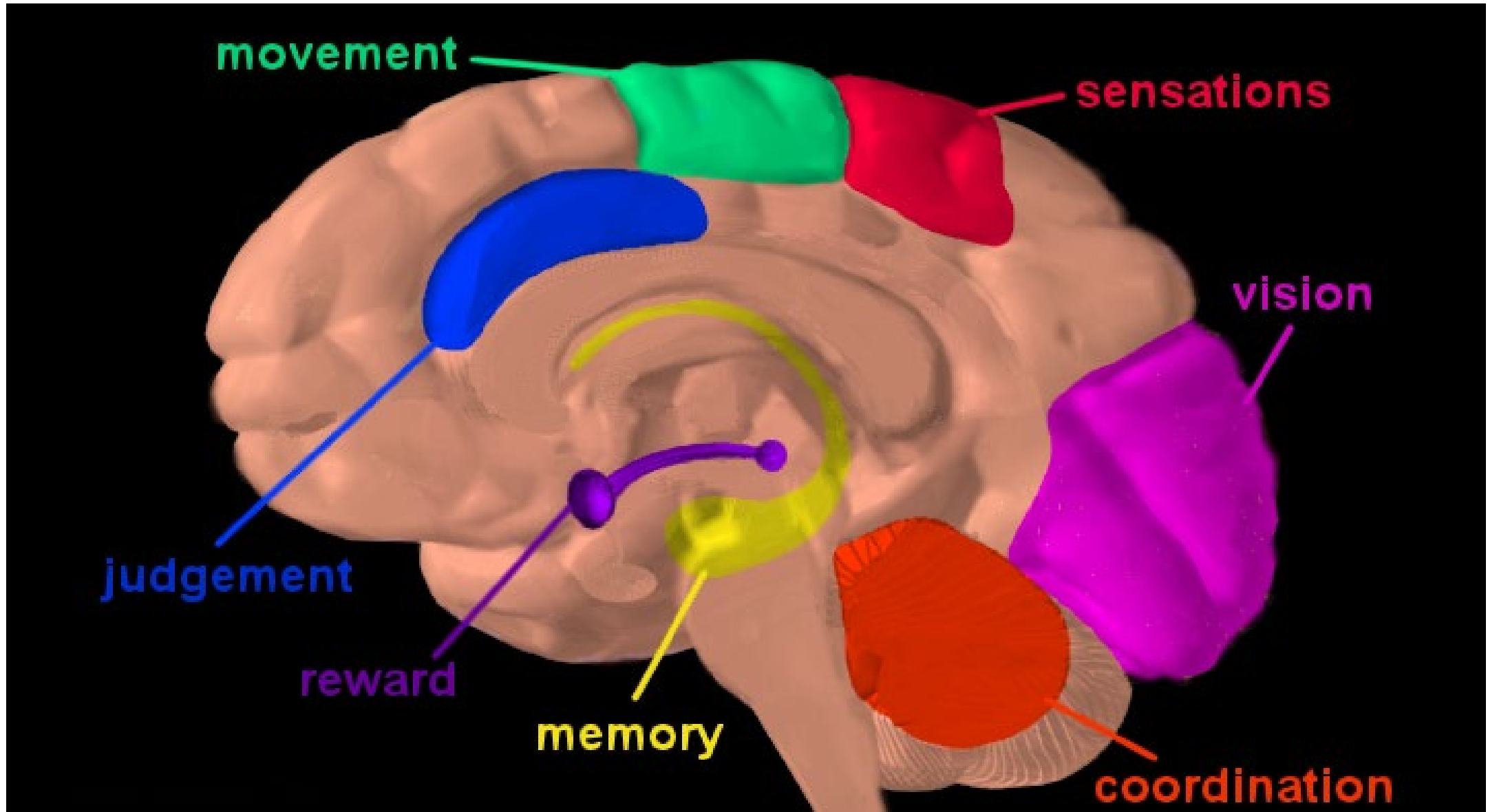
- Tranquilizer use associated with MA withdrawal may be reflective of self-medication of anxiety and sleeplessness in withdrawal.
- MA withdrawal symptoms common among people who inject drugs and associated with receptive syringe sharing.
- Receptive syringe sharing associated with rushed injecting in public settings with increased risk of overdose and other adverse outcomes.
- Safe supply and syringe services programs targeting people who inject MA are indicated.

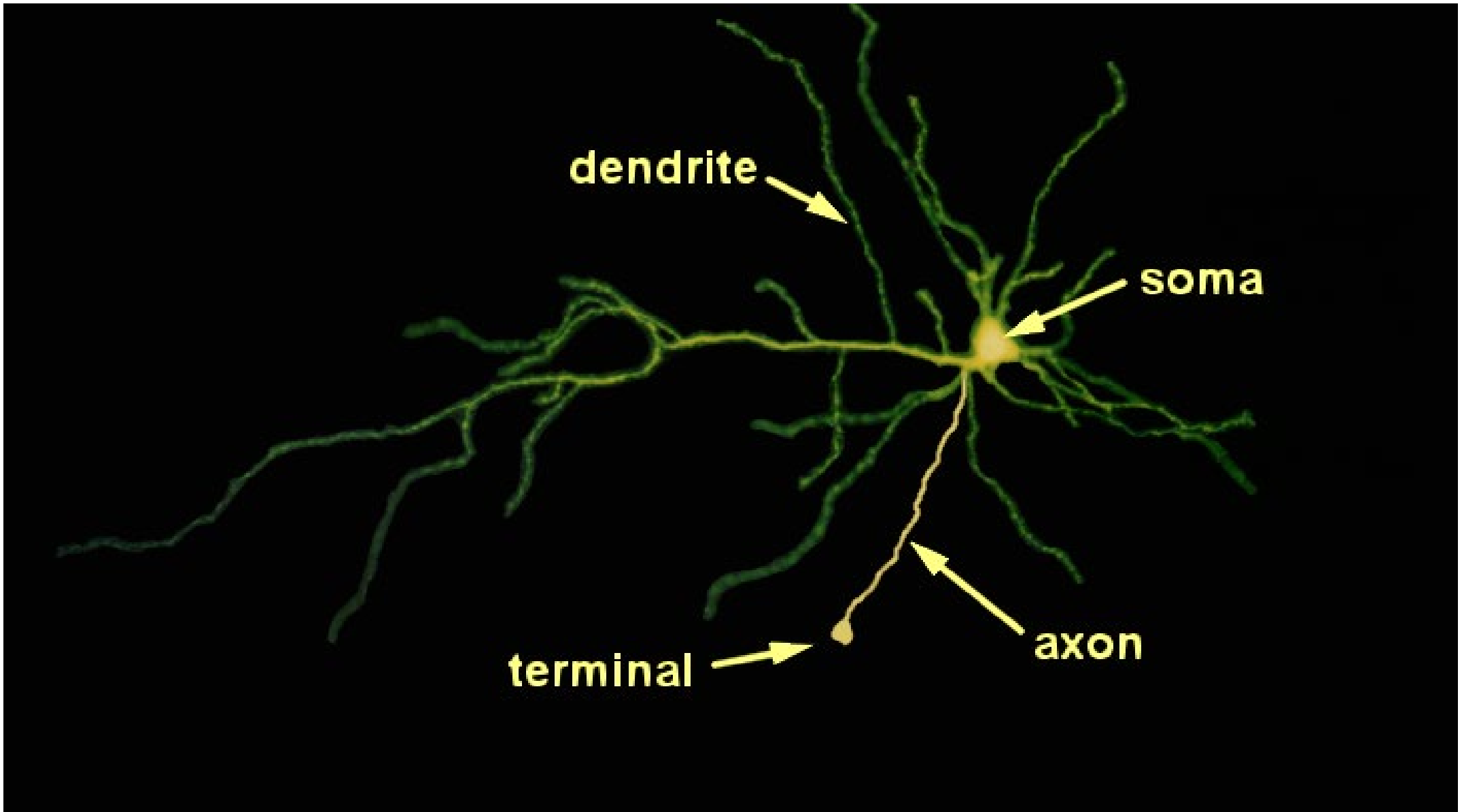
(Zhao, Kral, Simpson, Ceasar, Wenger, Kirkpatrick, & Bluthenthal, 2021)

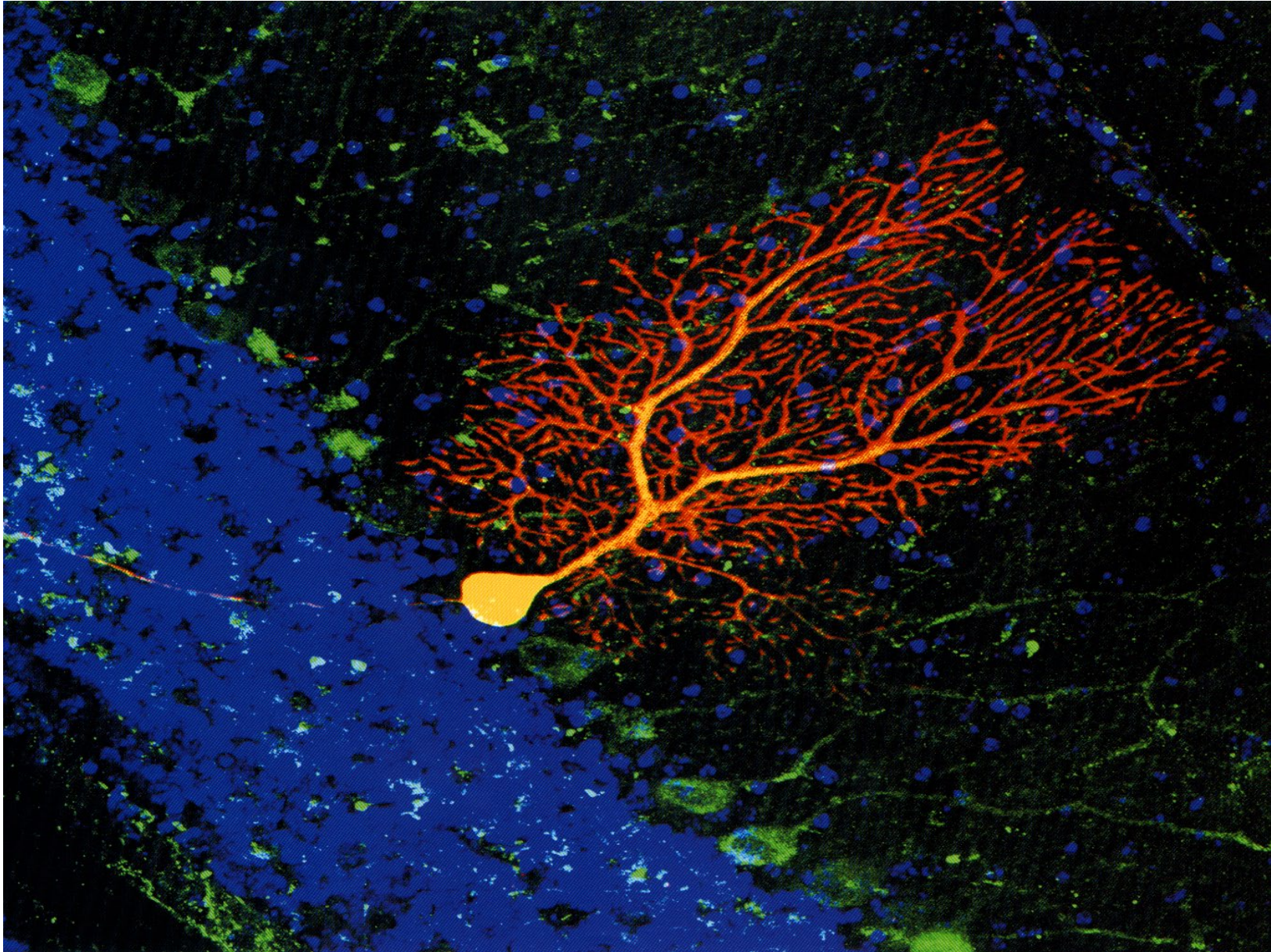
Stimulants and the Brain

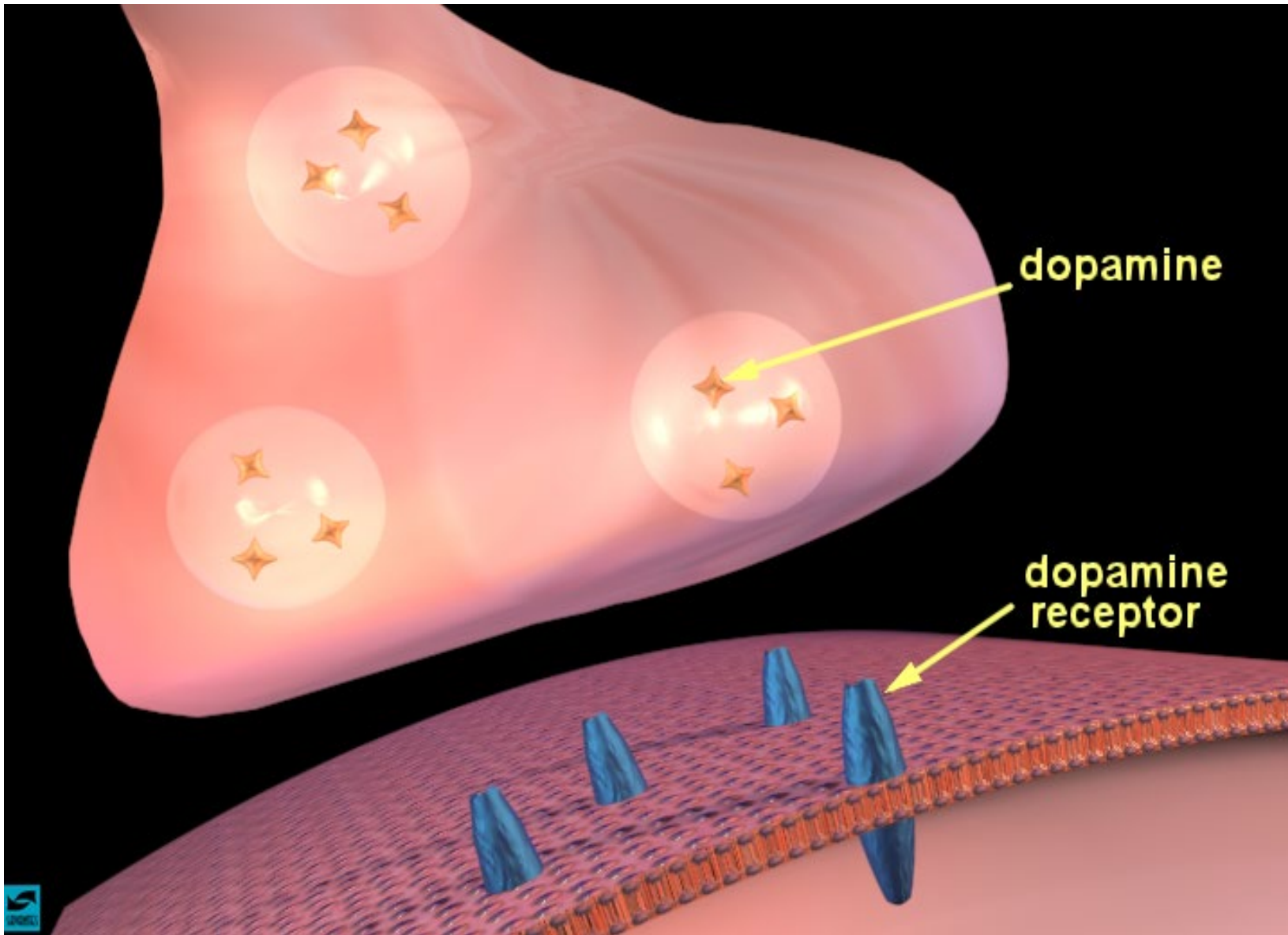
A major reason people take stimulants is that they like what it *does to their brains*.

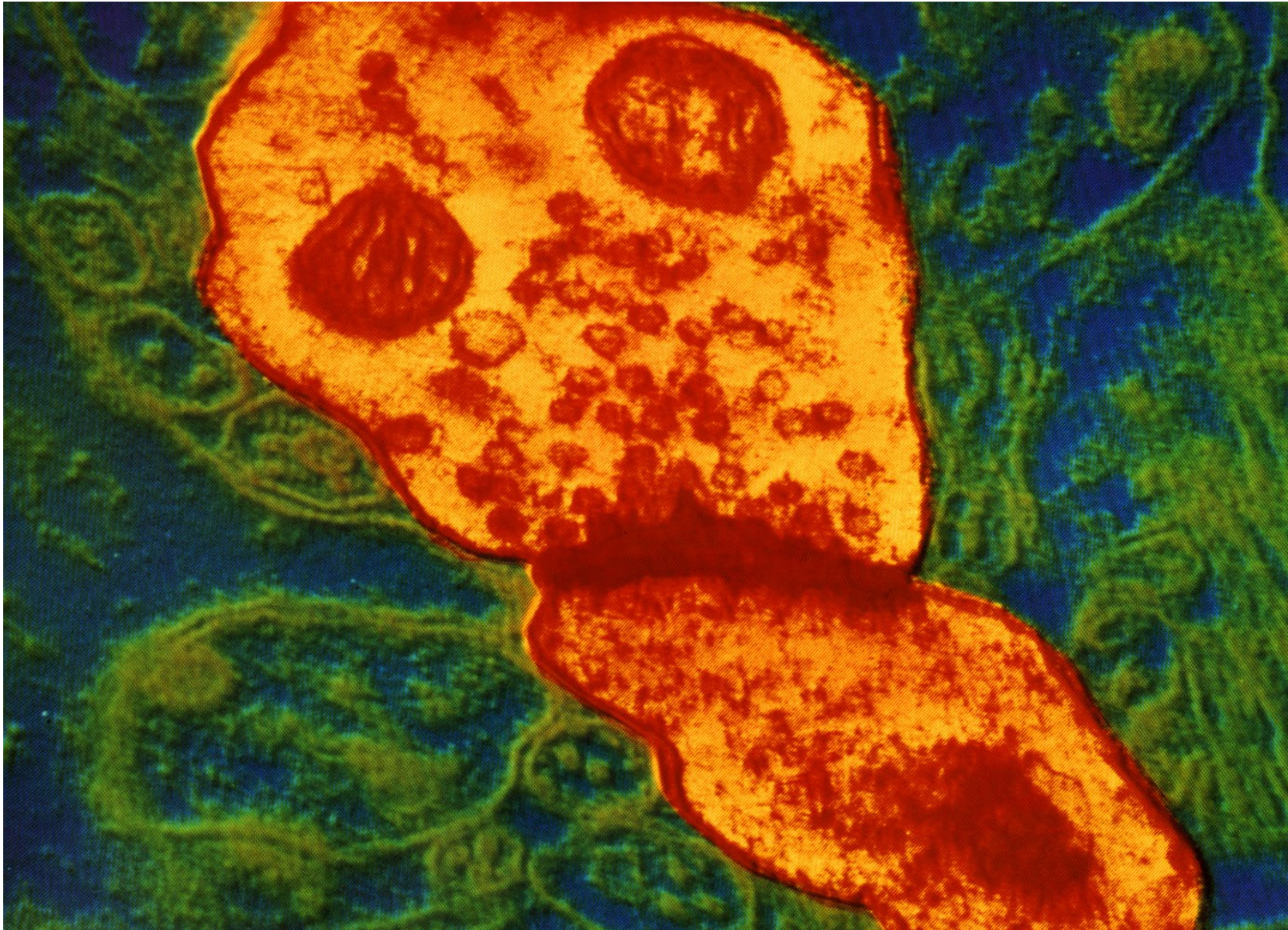


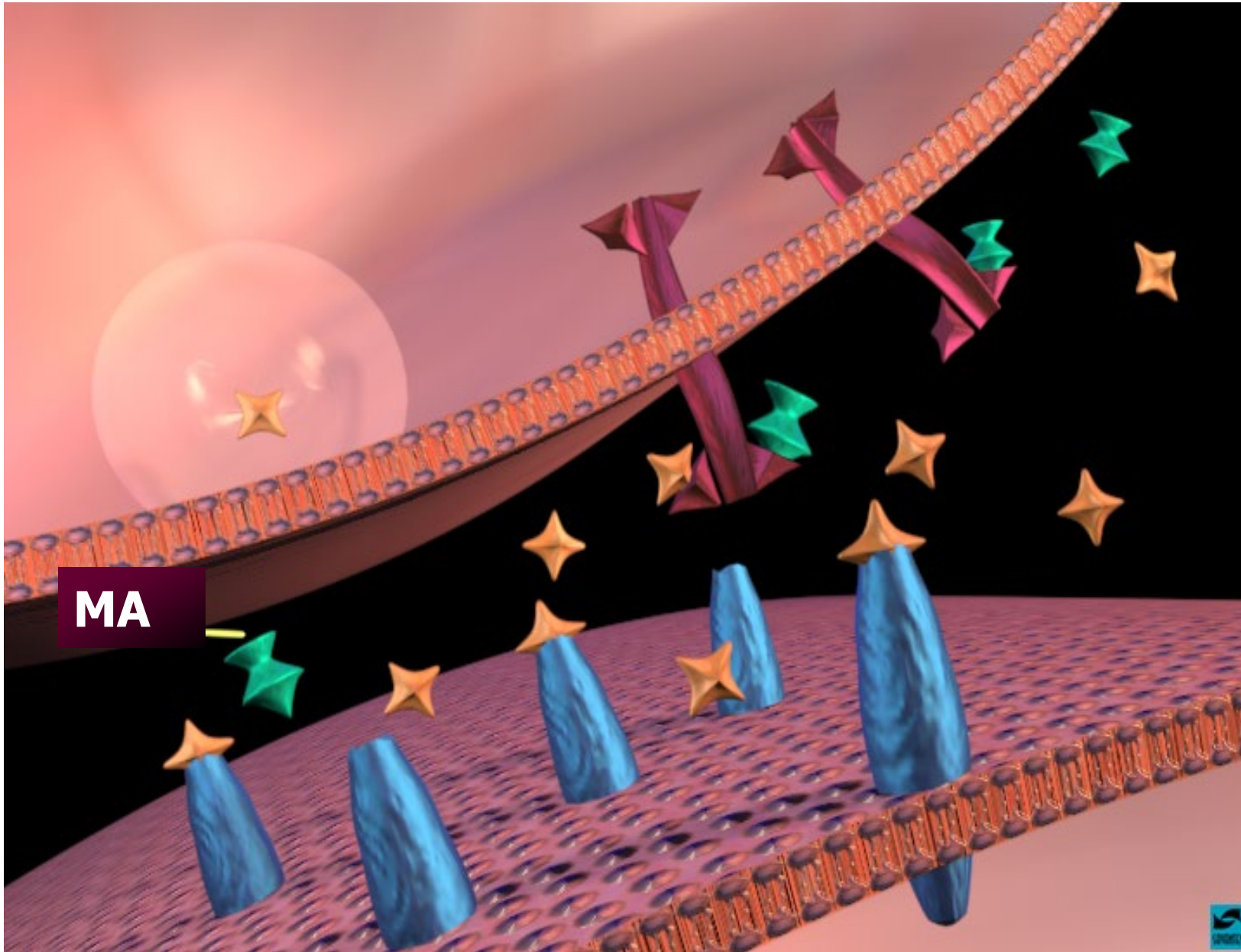






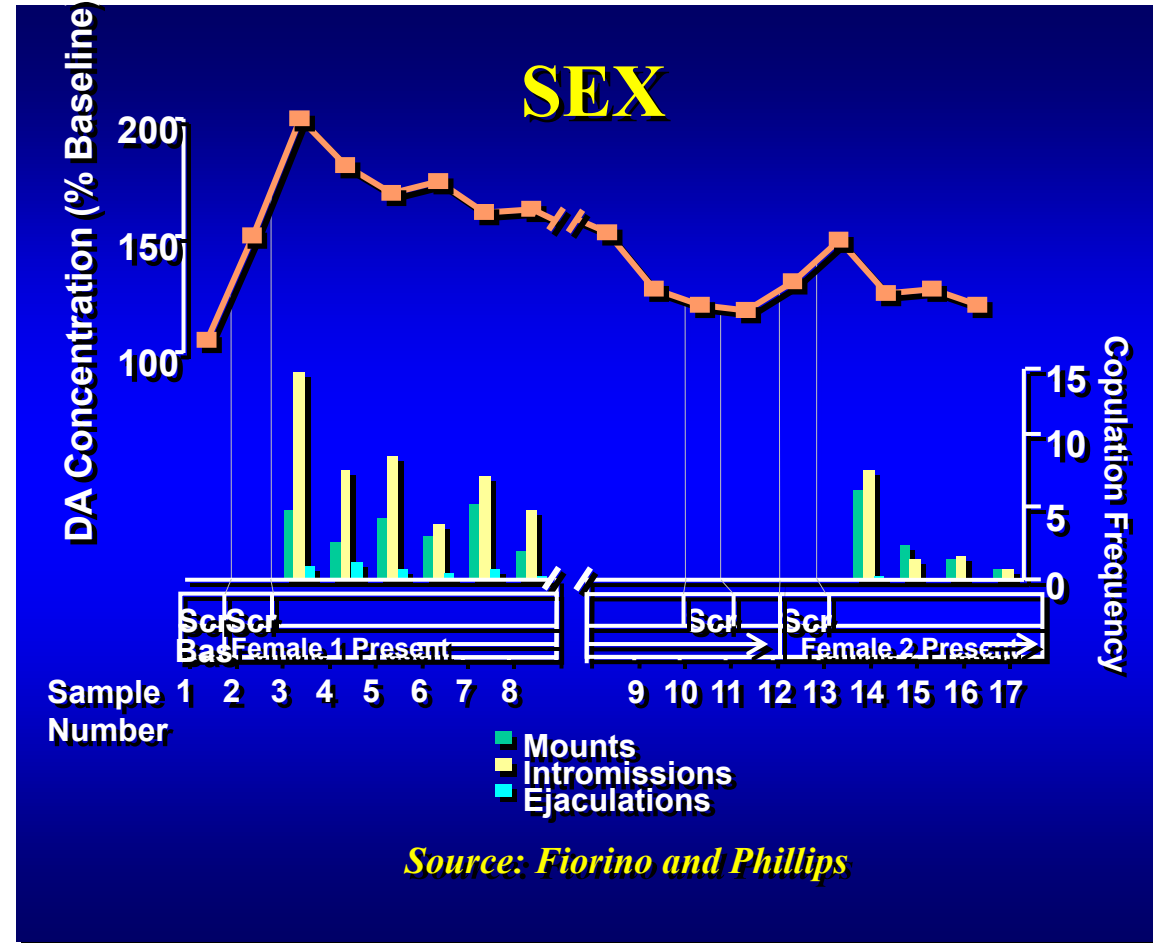
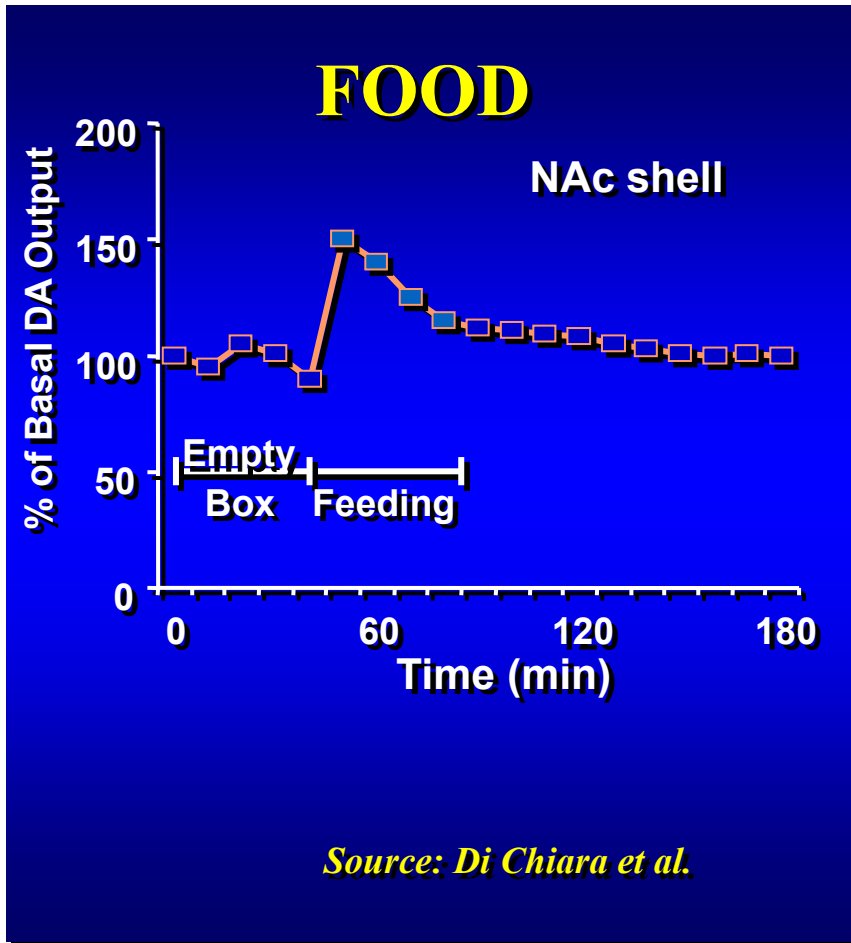






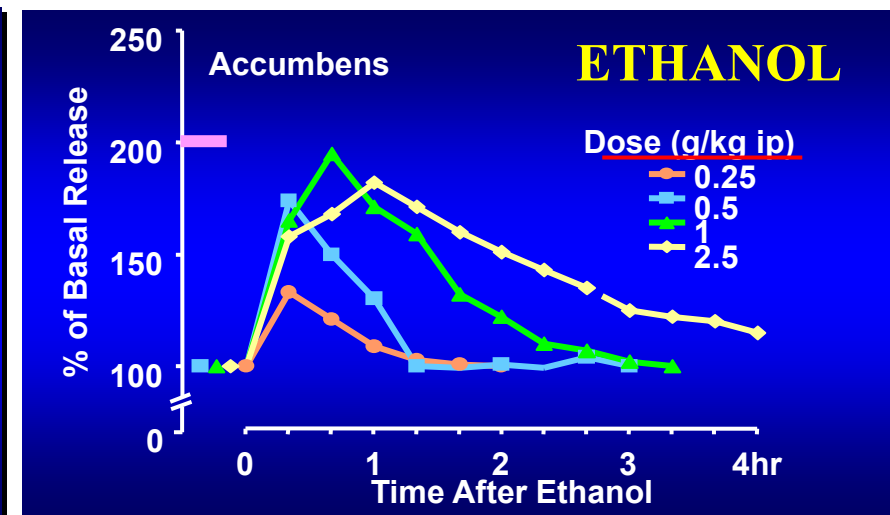
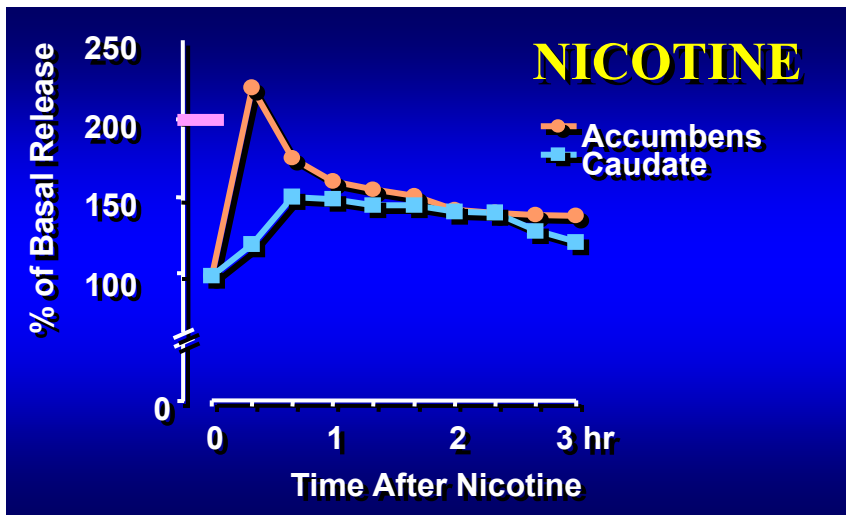
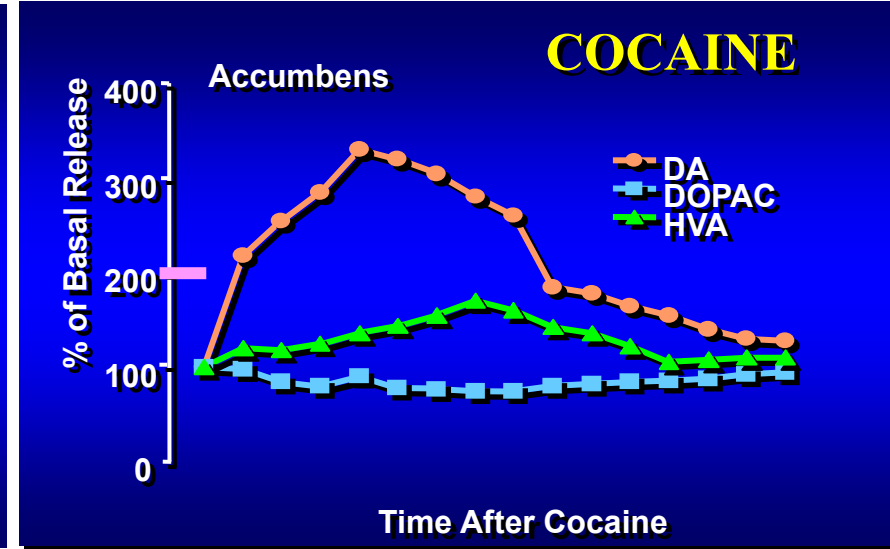
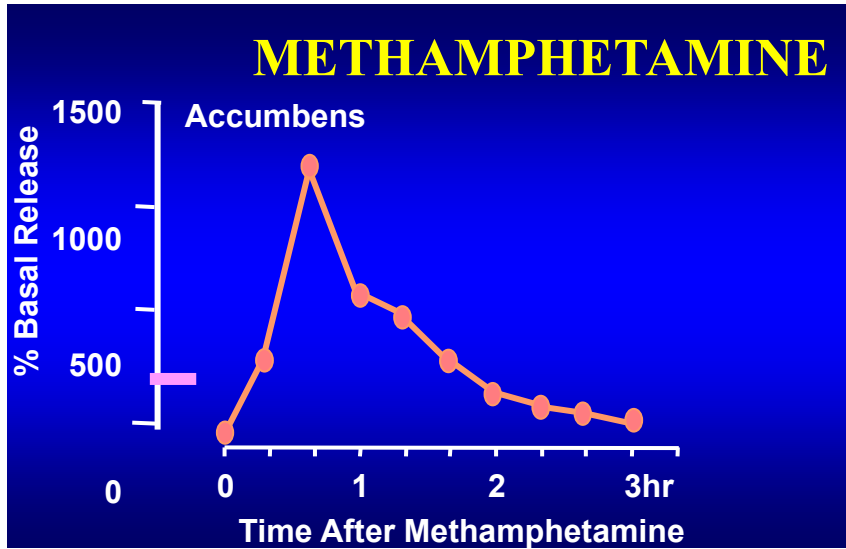
MA

Natural Rewards Elevate Dopamine Levels



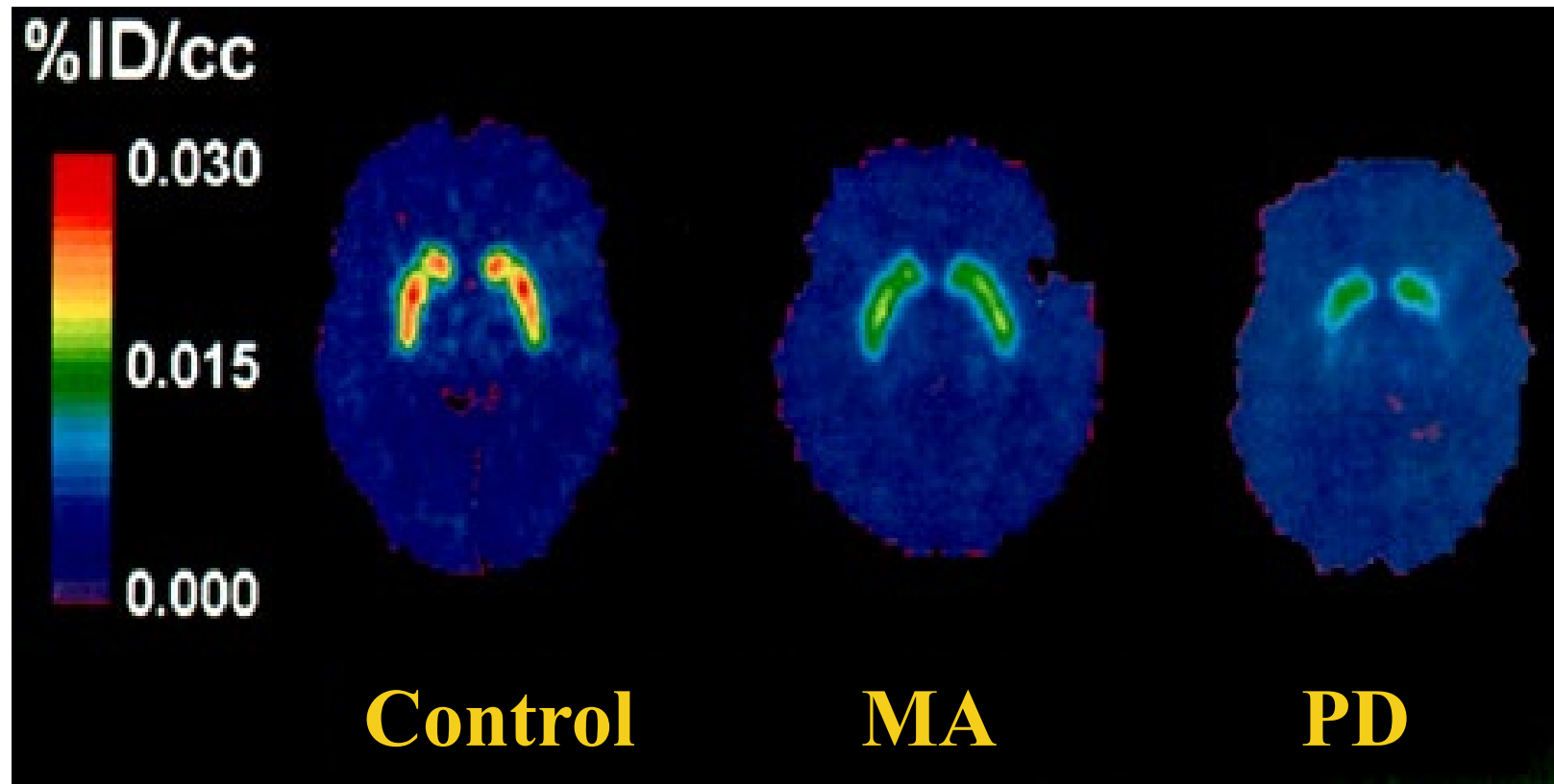
(Di Chiara, et al.,1996; Fiorino and Phillips, 1999)

Effects of Drugs on Dopamine Release



(Shoblock & Sullivan, 2002; Di Chiara & Imperato, 1988)

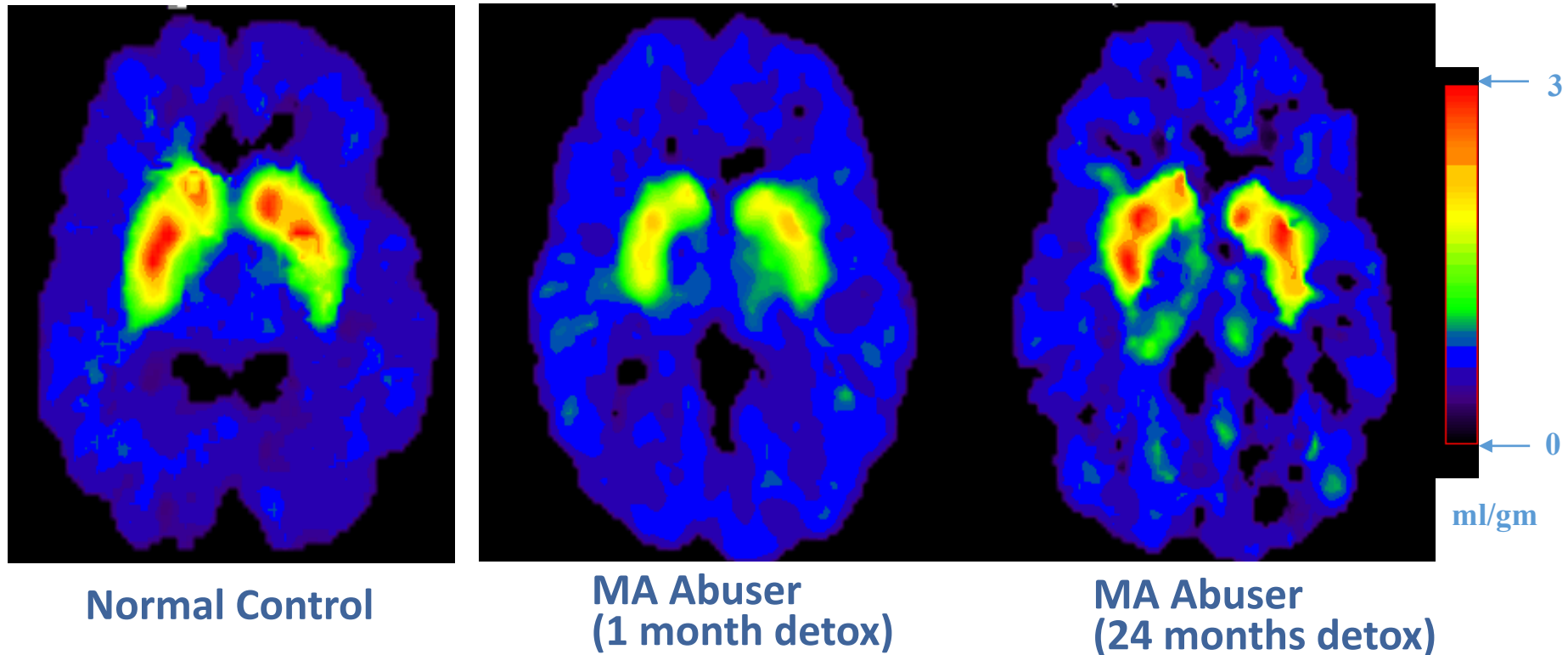
Decreased Dopamine Transporter Binding in Methamphetamine Users Resembling Parkinson's Disease



(McCann, Wong, Yokoi, Villemagne, Dannals, & Ricaurte, 1998)

**Prolonged drug use changes
the brain in fundamental and
long-lasting ways.**

Partial Recovery of Brain Dopamine Transporters in Methamphetamine Abuser After Protracted Abstinence



(Volkow, et al., 2001)

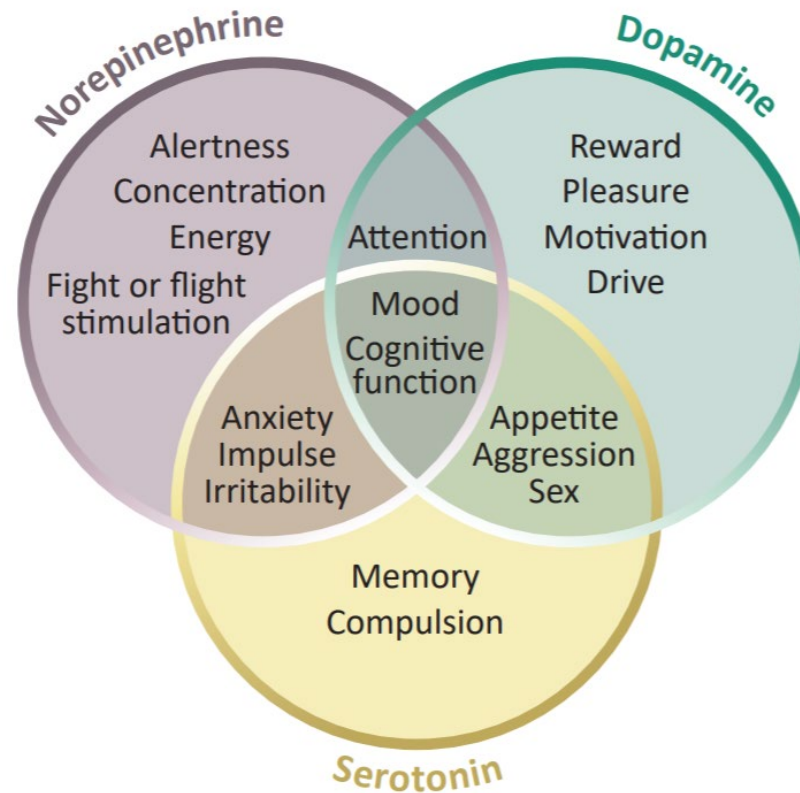
Methamphetamine Neurotoxicity

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

(Paulus & Stewart, 2020)

Behavioral Effects of Neurotransmitters

FIG. 1 Behavioural effects mediated by the three main neurotransmitters



(Paulus & Stewart, 2020)

Cognitive Effects

Soon after cessation of MA use:

- Poor performance on motor and processing tasks.
- Poor performance on verbal fluency and attention.

After prolonged abstinence:

- Poor learning efficiency and comprehension.
- Poor visual-spatial processing.
- Slow processing and psychomotor speed.

(Rawson, 2023)

Cognitive Effects (contd.)

- More than 2/3 of those with MA use disorder show cognitive impairment.
- Impairment is associated with older age, longer duration of use, injection route of administration, and greater frequency of use.
- Impairment may limit ability to follow through with treatment, comprehend advice and direction in treatment, and generally achieve good treatment outcomes.

(Rawson, 2023)

Cerebrovascular and Cardiovascular Disease

Leading causes of death with MA use disorder:

- Strokes on rise, most often with young men.
- Strokes primarily hemorrhagic.

Cardiovascular disease associated with MA use:

- Pulmonary hypertension.
- Cardiac arrhythmia.
- Cardiomyopathy.

Stimulant Use in Pregnancy

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

(Smid, Metz, & Gordon, 2019)

Stimulant Use in Pregnancy (contd.)

- A study compared MA-exposed maternal-child pairs and unexposed pairs (Derauf et al., 2007) to look at long-term effects.
 - At 1 month, 33% MA-exposed mothers did not have custody compared to 2% of unexposed.
 - At age 3 years, heavy prenatal MA use was associated with anxiety/depression and attention problems.
 - At age 7.5 years, MA-exposed children had poorer cognitive function.
- Another study of 4- to 5-year-old children found impoverished vocabulary and poorer fluency with language among MA-exposed children.

Dental Effects

- Rampant caries and tooth fracture most common (Shaner, 2002; 2006).
- Periodontal disease.
- Mechanisms:
 - Poor oral hygiene.
 - Dry mouth inhibiting saliva.
 - Dehydration from appetite suppression and increased psychomotor activity.
 - Soft drink consumption.
 - Grinding/clenching of teeth.
 - Smoking.

(Rawson, 2023)

Dermatological Effects

- Itching.
- Ulcers and skin picking (formication, “meth bugs”).
- Abscesses (“skin popping” confers greatest risk).
- Cellulitis.
- Burn injuries.
- Ulcers associated with co-use of xylazine.

(Rawson, 2023)

Methamphetamine Presentations in ER

- Clinical effects:
 - Behavioral disturbance, 78%.
 - Tachycardia, 56%.
 - Hypertension, 42%.
 - Hyperthermia, 5%.

(Isoardi, Ayles, Harris, Finch, & Page, 2019)

Case of Hyperthermia Treatment in ER

- Indiana School of Medicine.
- 21-year-old unresponsive after ingesting MA.
- Temperature: 107.9°F.
- Cooling blankets and bags of ice applied. Temperature still 104.7°F after 46 minutes.
- Patient put in a body bag filled with an ice slurry. Temperature dropped to 97.7°F.

(Wang, Lupov, & Sloan, 2019)

Clinical Challenges:

Treating Individuals with Stimulant Use Disorder

- Overdose death/lethality of currently available MA.
- Limited understanding of stimulant use disorder.
- Ambivalence about need to stop use.
- Impulsivity/poor judgement.
- Cognitive impairment and poor memory.
- Anhedonia (loss of ability to feel pleasure).

(Rawson, 2023)

Treating Individuals with Stimulant Use Disorder (cont'd.)

- Hypersexuality/hyposexuality.
- Violence and psychosis.
- Powerful Pavlovian trigger-craving response.
- Elevated rates of psychiatric co-morbidity.
- **Very difficult to engage in treatment.**
- **Very poor retention in outpatient treatment.**

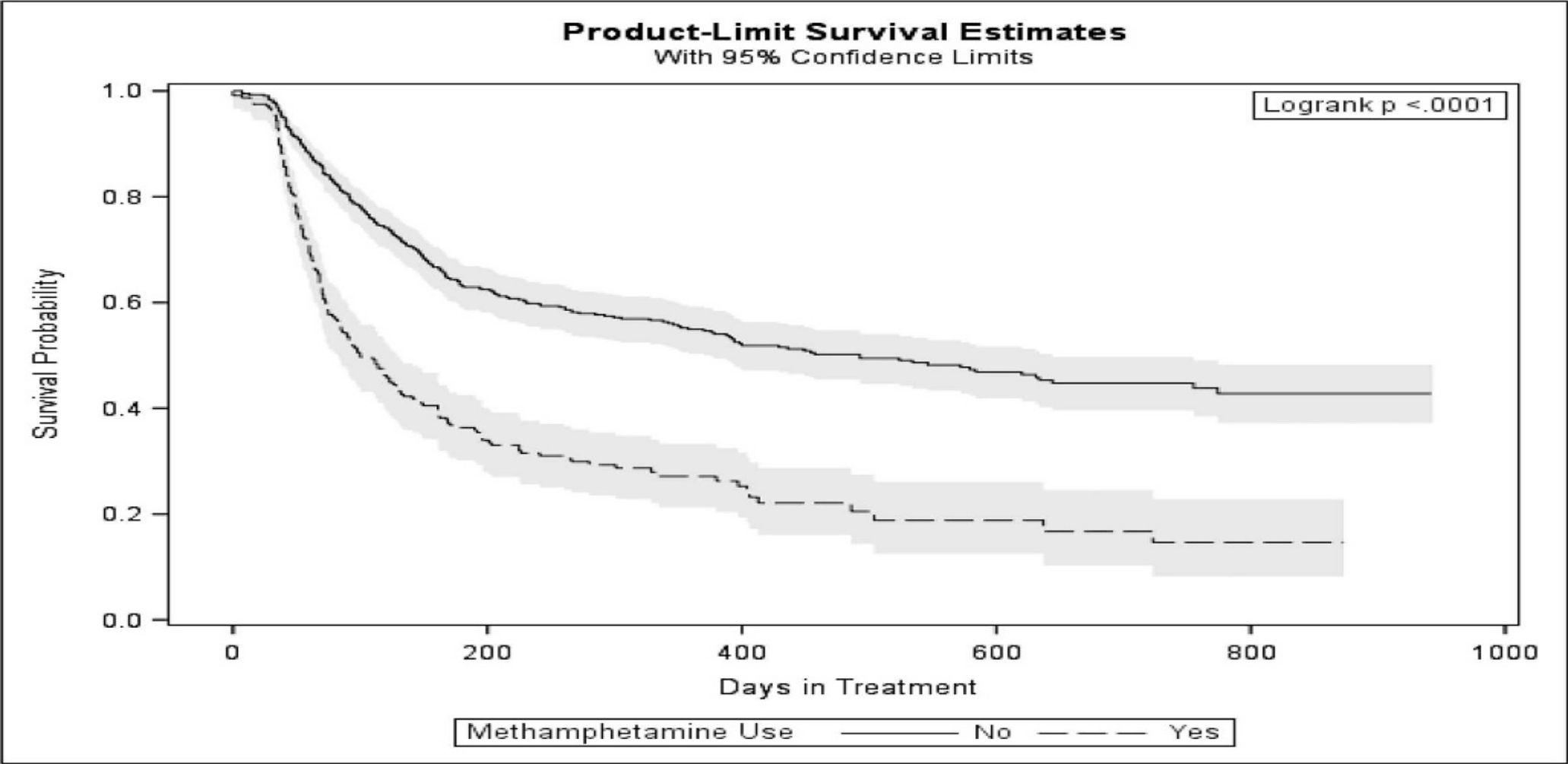
(Rawson, 2023)

Special Treatment Considerations

- People who use injectable drugs.
- People who use stimulants daily or in very high doses.
- Women (high rates of physical/sexual abuse).
- Individuals who are experiencing homelessness, chronically mentally ill, and/or have high levels of psychiatric symptoms at admission.
- Men who have sex with men.
- People who use stimulants and under the age of 21.
- **Individuals in medication treatment for opioid use disorder.**

(Rawson, 2023)

Association Between Methamphetamine Use and Retention



(Tsui, et al., 2020)

Interest in Reducing MA and Opioid Use

46%

Of individuals who use methamphetamine as their main drug who expressed interest in reducing/ stopping their meth use

82%

Of individuals who use opioids as their main drug who expressed interest in reducing/ stopping their opioid use

(McMahan, et al., 2020)

Treatment Retention

- Meta-analysis of in-person psychosocial stimulant use disorder treatment looking at dropout rates in the first 90 days of treatment.
- Results yielded overall average dropout rates and predictors of dropout.
- Nearly one-third drop out of psychosocial stimulant use disorder treatments.

(Lappan, et al., 2020)

Substance Targeted and Treatment Dropout Rate

Treatment Target	Dropout Rate
Heroin	25.1%
Tobacco	25.5%
Alcohol	26.1%
Cocaine	48.7%
Methamphetamine	53.5%

(Rawson, 2023)

Harm Reduction Strategies

- Information about medical and psychiatric effects of MA.
- Overdose education (fentanyl).
- Syringe exchanges.
- Naloxone (for opioid overdose).
- Not using drugs without anyone else present.
- Injection “testing.”
- Injection “taking turns.”
- Quiet rooms and wash-up/shower rooms.
- Condoms/safe-sex education.
- Topical antibiotic creams and ointments for injection sites.

Current Status of Treatment Approaches for Methamphetamine Use Disorder

- **Contingency management.**
- Cognitive Behavioral Therapy (CBT) and Community Reinforcement Approach (CRA).
- Motivational Interviewing (MI).
- Physical exercise.

Contingency Management

- A technique employing the **systematic delivery of positive reinforcement for desired behaviors**.
 - In the treatment of MA use disorder, vouchers or prizes can be “earned” for submission of MA-free urine samples or attendance at treatment sessions.

Effectiveness of Contingency Management

- Review of 27 studies that included contingency management intervention for MA users.
- Found:
 - Reduced MA use in 26 of 27 studies.
 - Longer retention in treatment.
 - More therapy sessions attended; higher use of other services and medical services.
 - Reductions in risky sexual behavior.
 - Increases in positive affect and decreases in negative affect.

(Brown and DeFulio, 2020)

Exercise

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

(Mooney, Larissa, et al. 2014)

Medications

Medications for Cocaine Use Disorder

- Medications with positive studies and under consideration:
 - Topiramate.
 - Modafinil.
 - Bupropion.
 - Amphetamine salts.
 - Disulfiram (mixed, worse retention).
 - Propranolol (WD).
 - Buprenorphine + naltrexone.

Medications for Methamphetamine Use Disorder

- Medications with positive studies and under consideration:
 - Bupropion/naltrexone.
 - Mirtazapine.
 - Bupropion.
 - Naltrexone.
 - Methylphenidate.
 - D-amphetamine.
 - Topiramate.

Provider Quick Tips

- [Clinical Provider Quick Tips](#)

Questions



Contact Information

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References

- Brown, Haley, and Anthony DeFulio. 2020. “[Contingency Management for the Treatment of Methamphetamine Use Disorder: A Systematic Review.](https://doi.org/10.1016/j.drugalcdep.2020.108307)” *Drug and Alcohol Dependence* 216: 108307. Retrieved October 6, 2023 from <https://doi.org/10.1016/j.drugalcdep.2020.108307>.
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