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Evidence-based Treatments for Stimulant Use Disorder:

The Impact of Stimulants on Brain, Body, and Behavior and Effective Treatment and Overdose Prevention Approaches

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April 7, 2026

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- PCSS-MOUD aims to increase the knowledge and skills of healthcare and counseling professionals about available evidence-based treatment approaches for substance use disorder (SUD) with a particular focus on opioid use disorder (OUD). PCSS-MOUD provides free training and mentoring to practitioners on the use of medications for OUD (MOUD) and the integration of these services into mainstream health care.

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All speakers have been advised that any recommendations involving clinical medicine must be based on evidence that is accepted within the profession of medicine as adequate justification for their indications and contraindications in patient care. All scientific research referred to, reported, or used in the presentation must conform to the generally accepted standards of experimental design, data collection, and analysis.

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Presenter

Thomas E. Freese, Ph.D.

Director

UCLA Integrated Substance Use and Addiction Programs

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Educational Objectives

At the conclusion of this activity participants should be able to:

1. Describe current trends in stimulant use and overdose in the U.S. and how this data informs clinical practice.
2. Identify evidence-based treatments for stimulant use disorder, including behavioral interventions.
3. Understand key administrative and clinical considerations for addressing stimulant use.

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Part 1

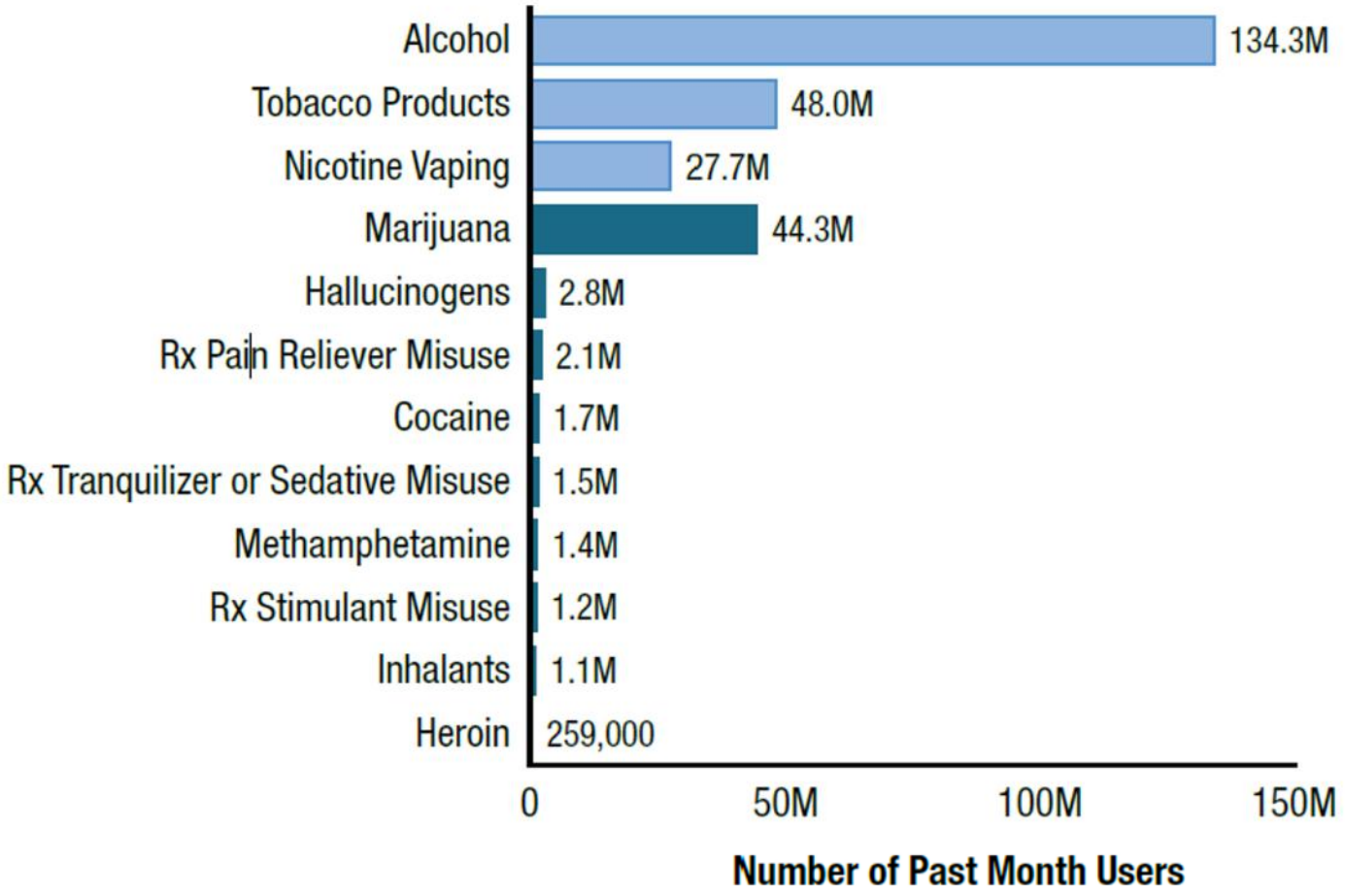
The Scope of Stimulant Use in the United States and Beyond

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 Southeast Asia
- Different precursors used in the manufacturing process

UNDOC, 2021

Numbers of People Reporting Past Month Substance Use among those Aged 12 or Older: 2022



SAMHSA, 2025

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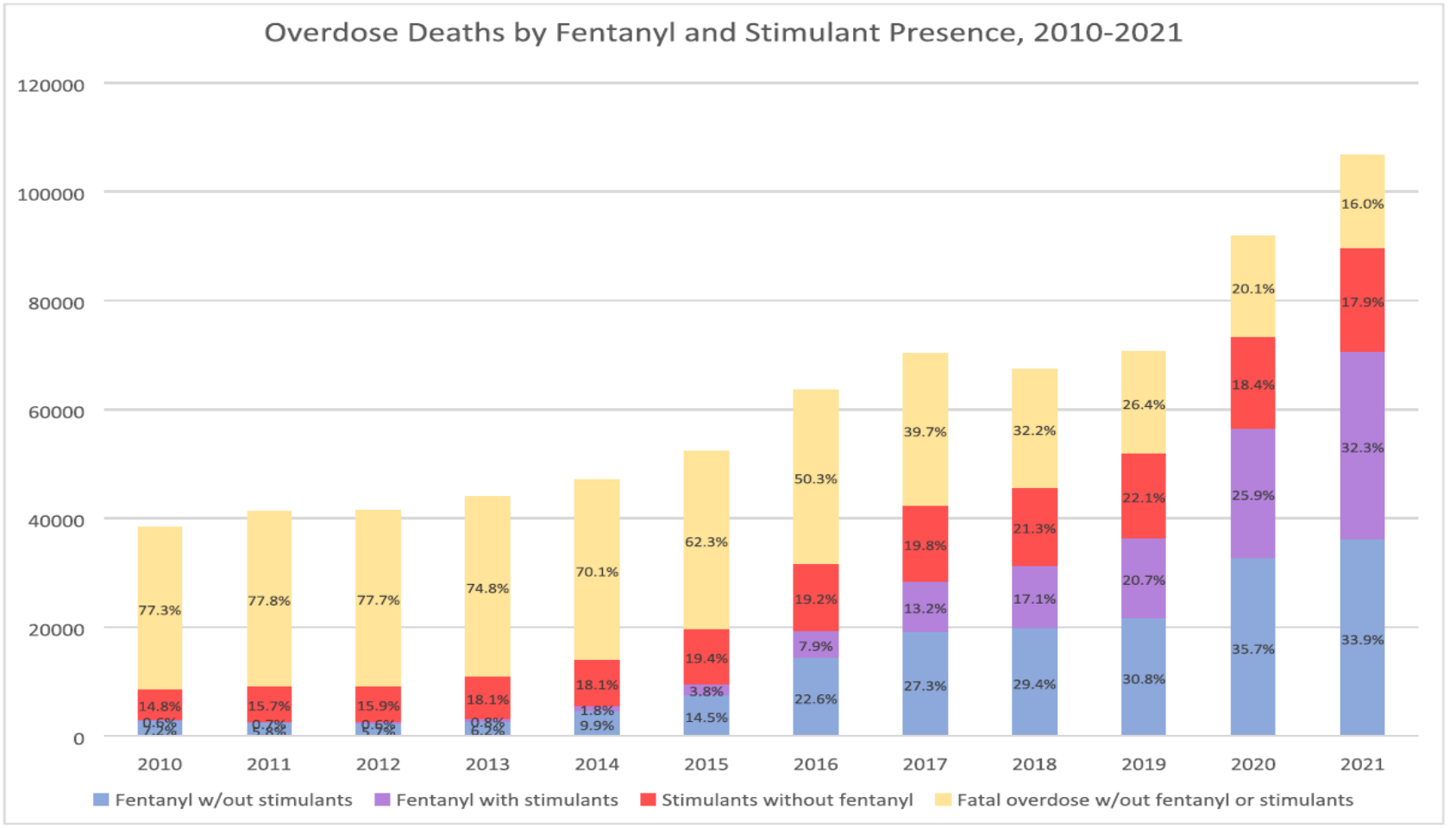
Another Way to Look at Overdose Deaths



SOURCE: Friedman & Shover, 2023

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Stimulants: What are We Talking About?

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Cocaine vs. Methamphetamine

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)

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

NIDA, 2019

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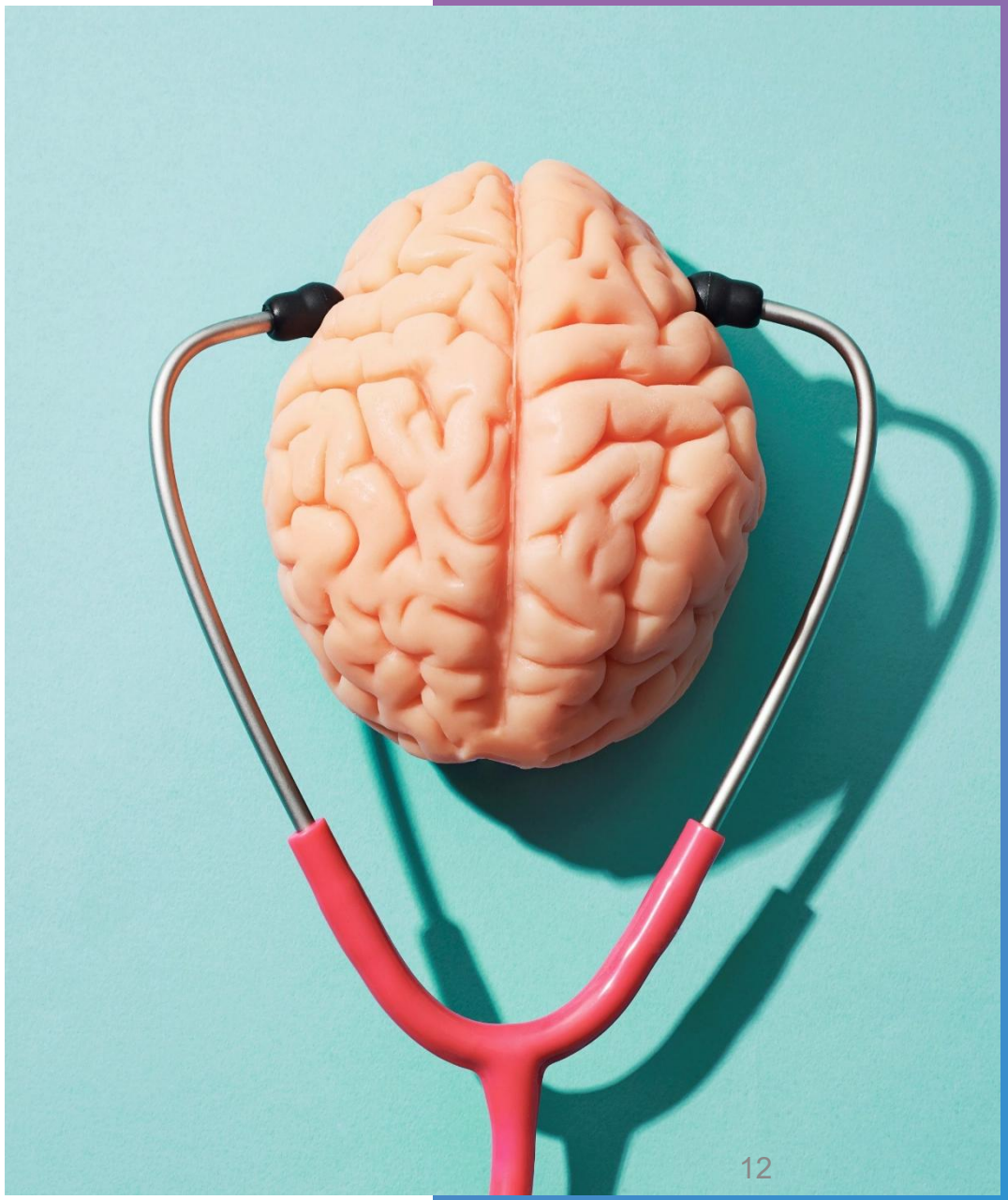
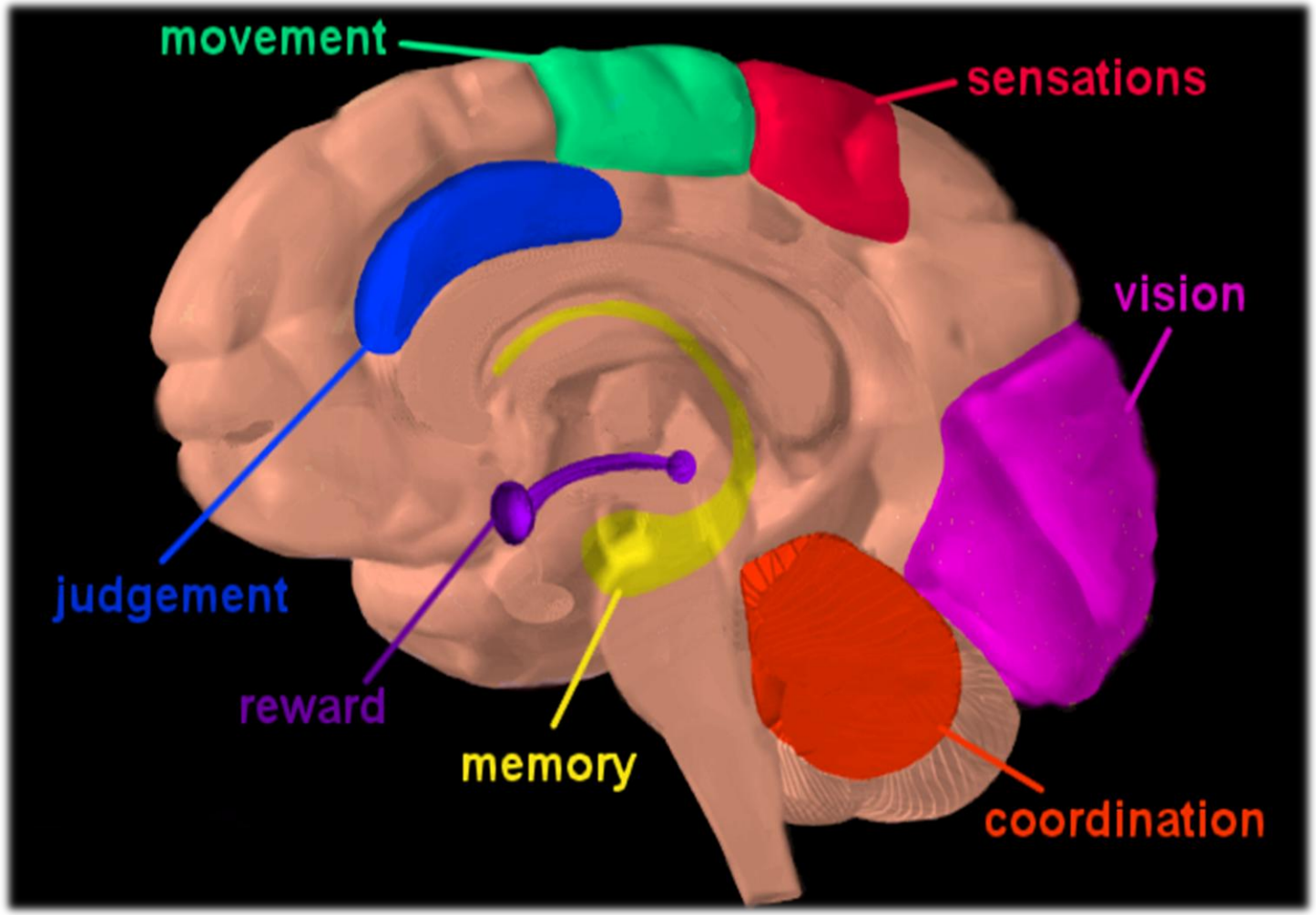
Part 2

The Impact of Stimulants on the Brain and Body



Brain Areas Affected by Psychoactive Substances



NIDA, 2019

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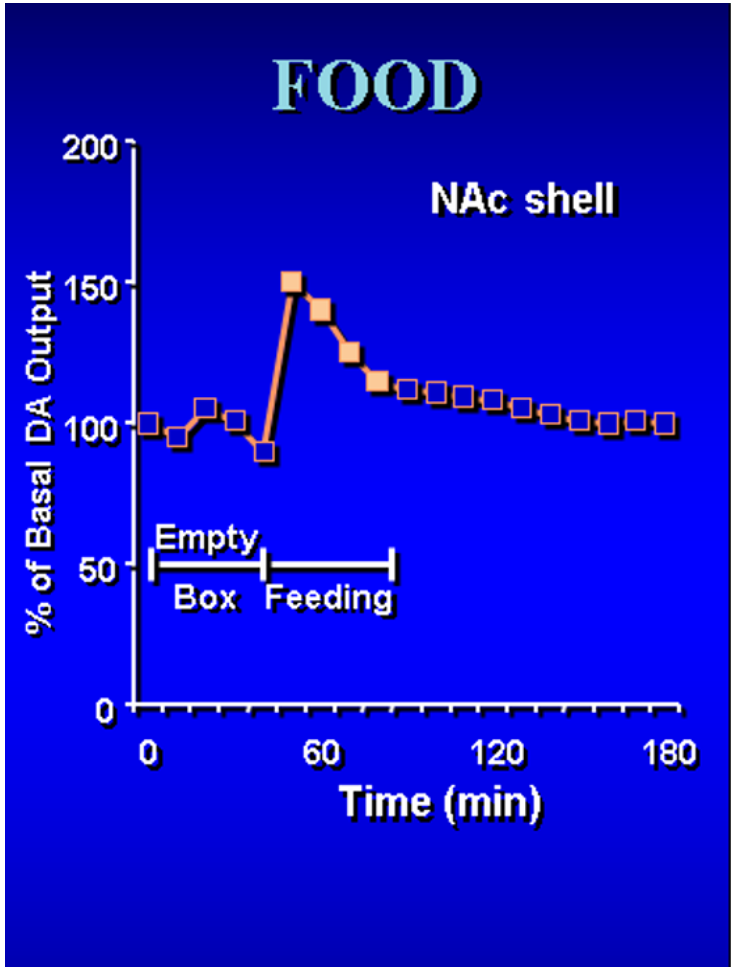
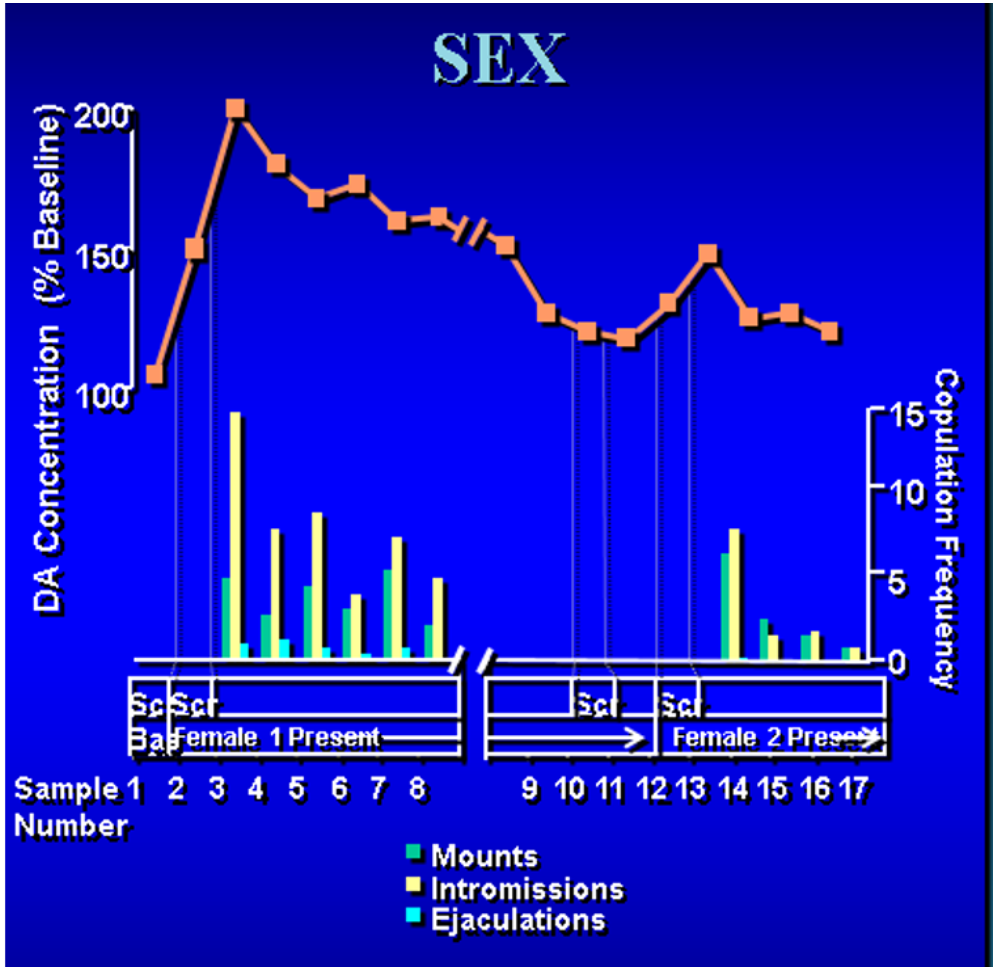
Let's First Take a Look at Normal Dopamine Functioning

https://vimeo.com/418131516

Natural Rewards Elevate Dopamine Levels





Source: Blum et al., 2012

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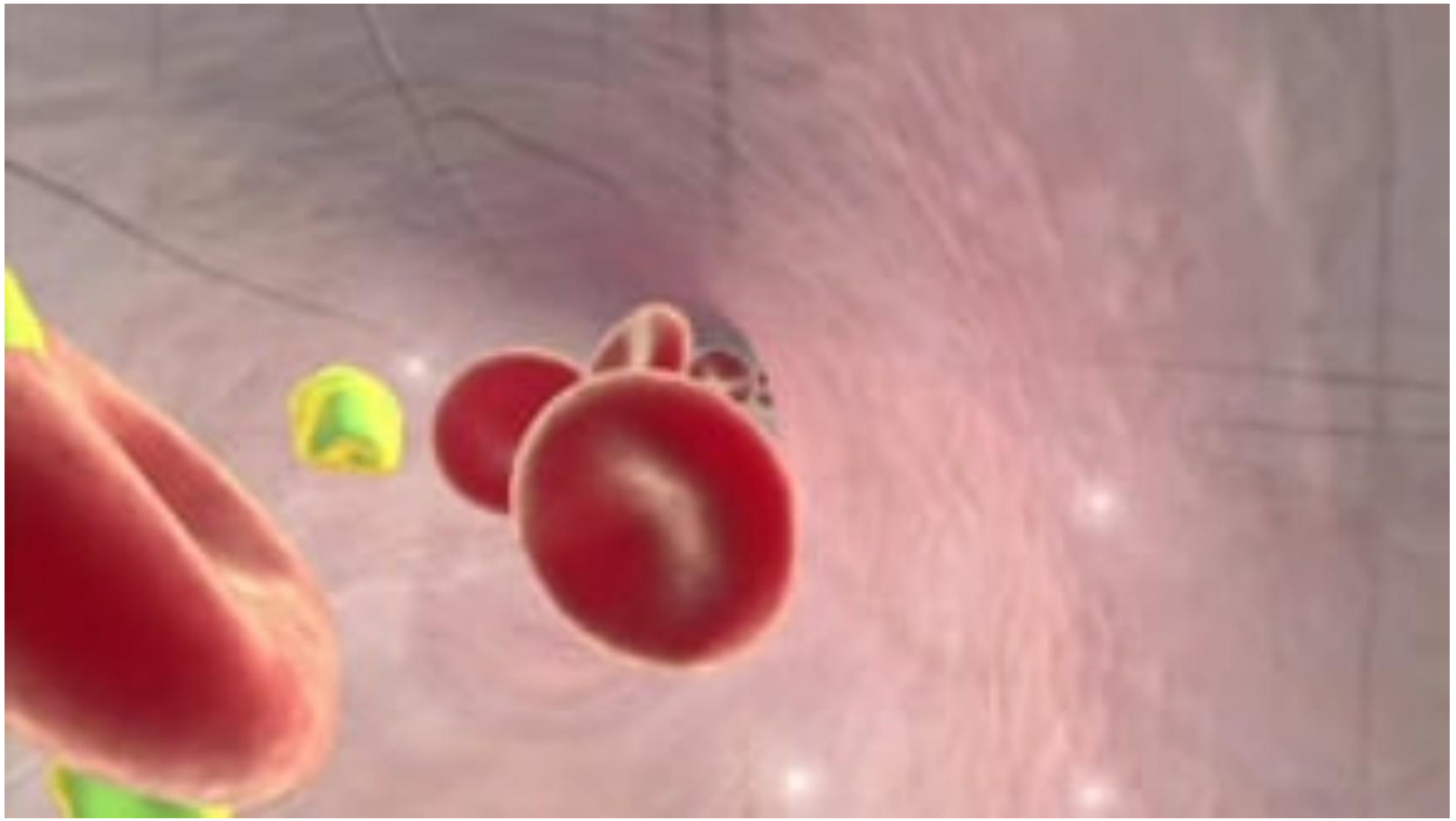
How the Brain Responds to Methamphetamine



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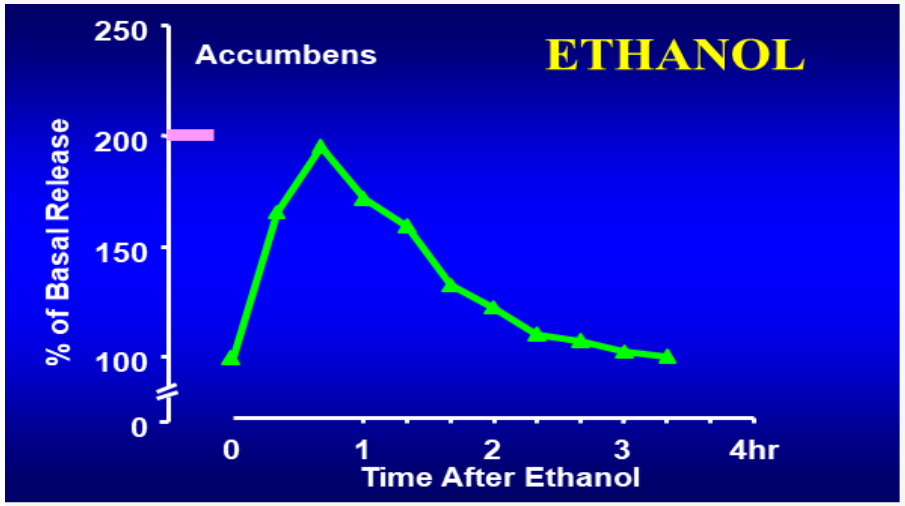
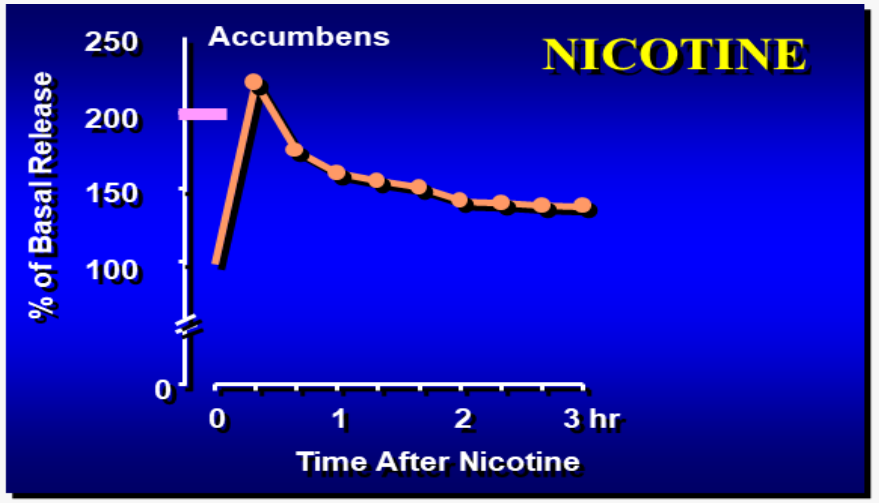
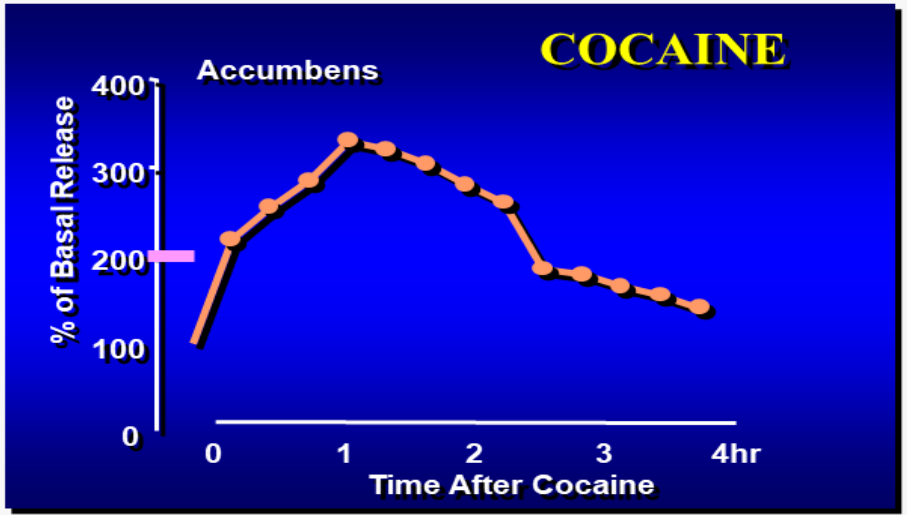
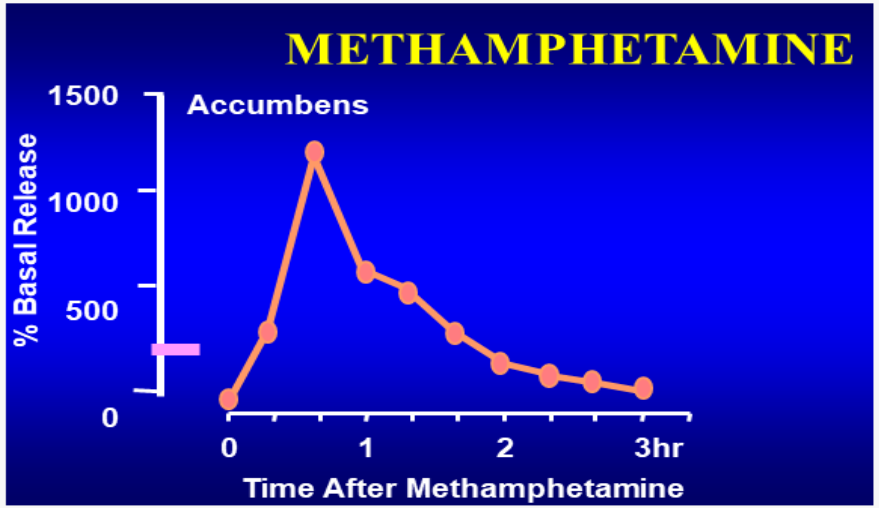
Effects of Drugs on Dopamine Release



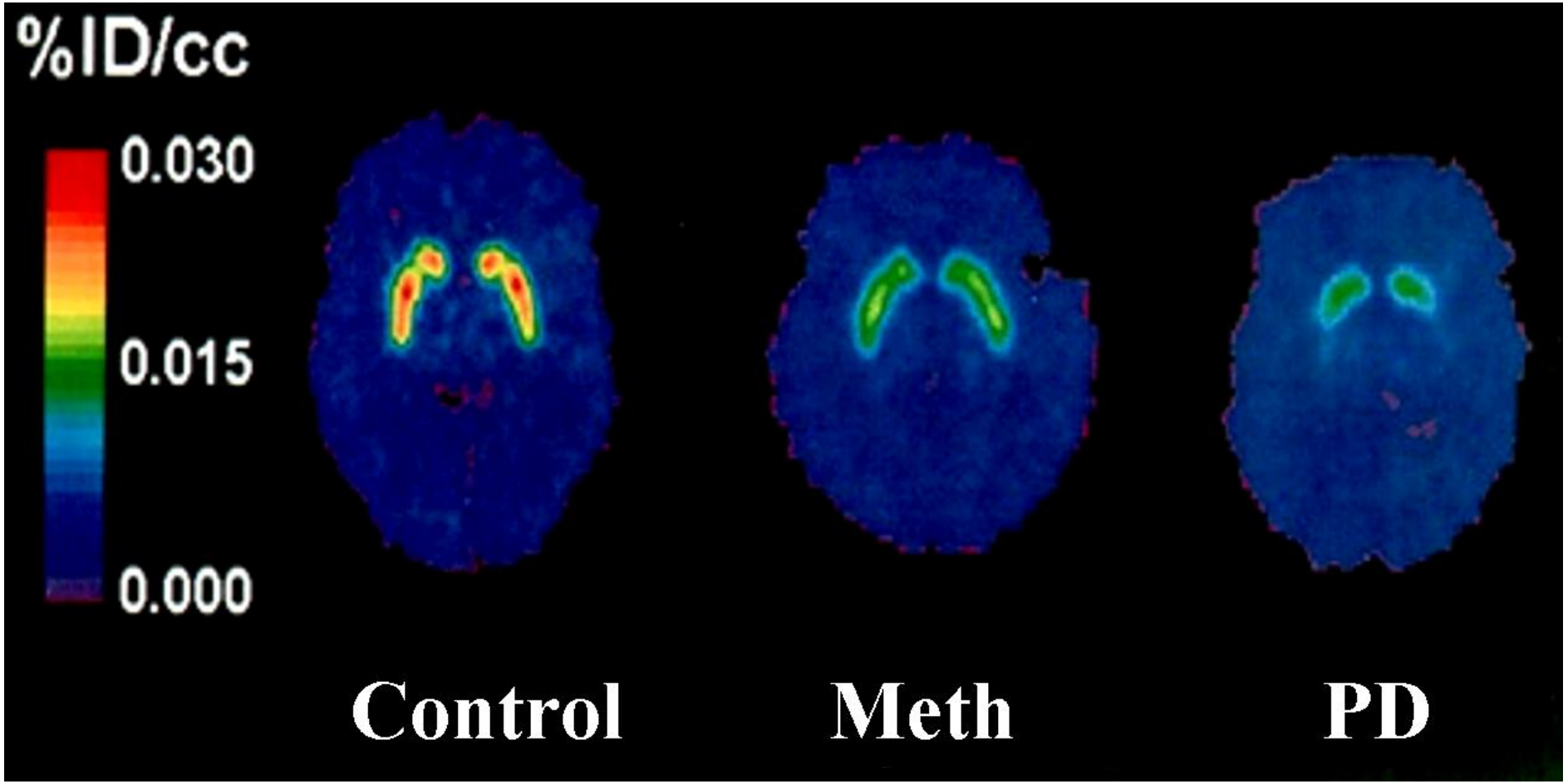






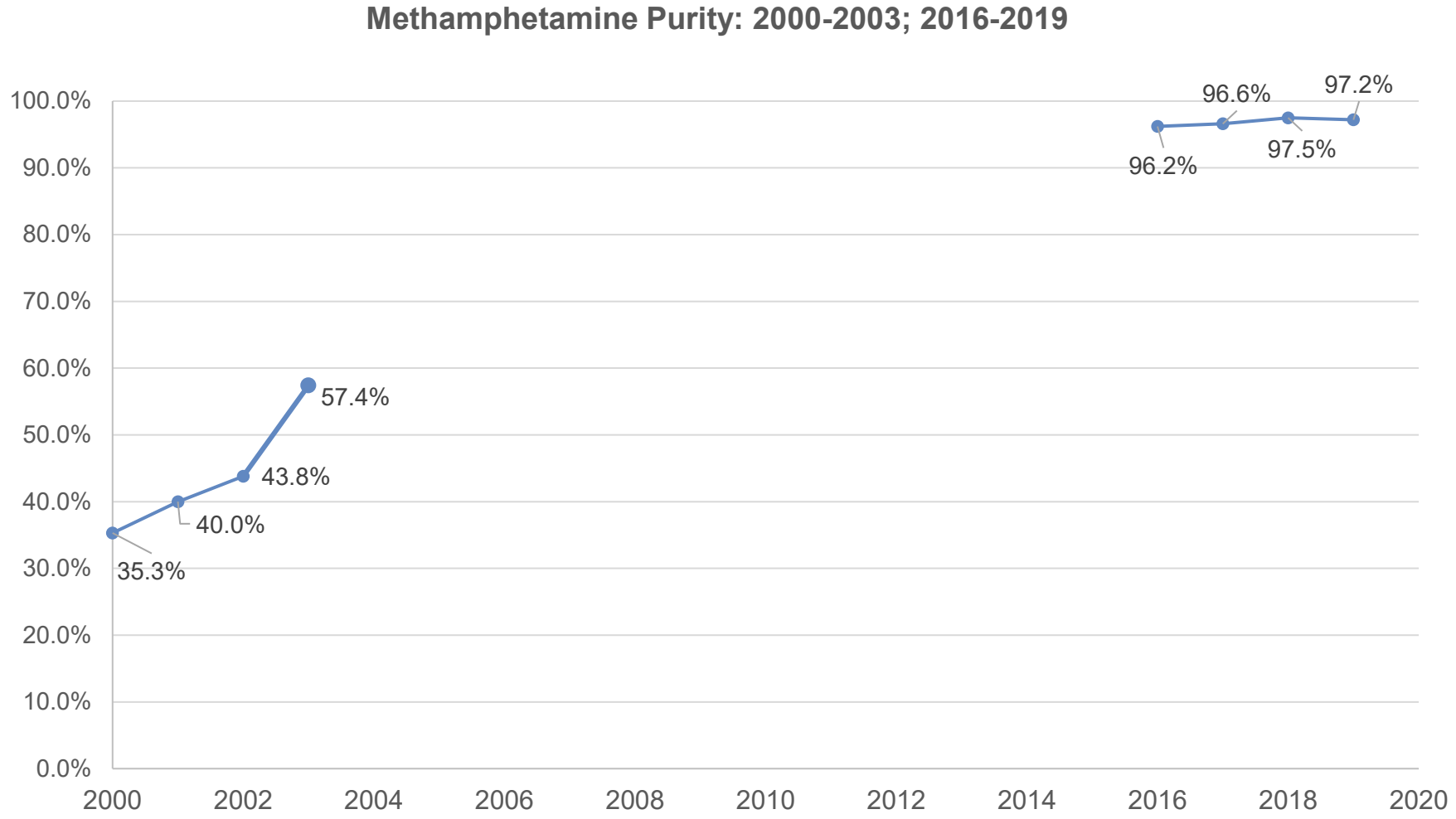
Shoblock et al., 2003; DiChiara & Imperato, 1988; Blum et al., 2012

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



McCann et al, 1998; Lappin & Dark, 2021; Poisson, Engel & Saunders, 2021; olfaghari & Shafiee-Kandjani, 2024

Methamphetamine Purity: 2000-2003 vs. 2016-2019



Drug Enforcement Administration, 2021

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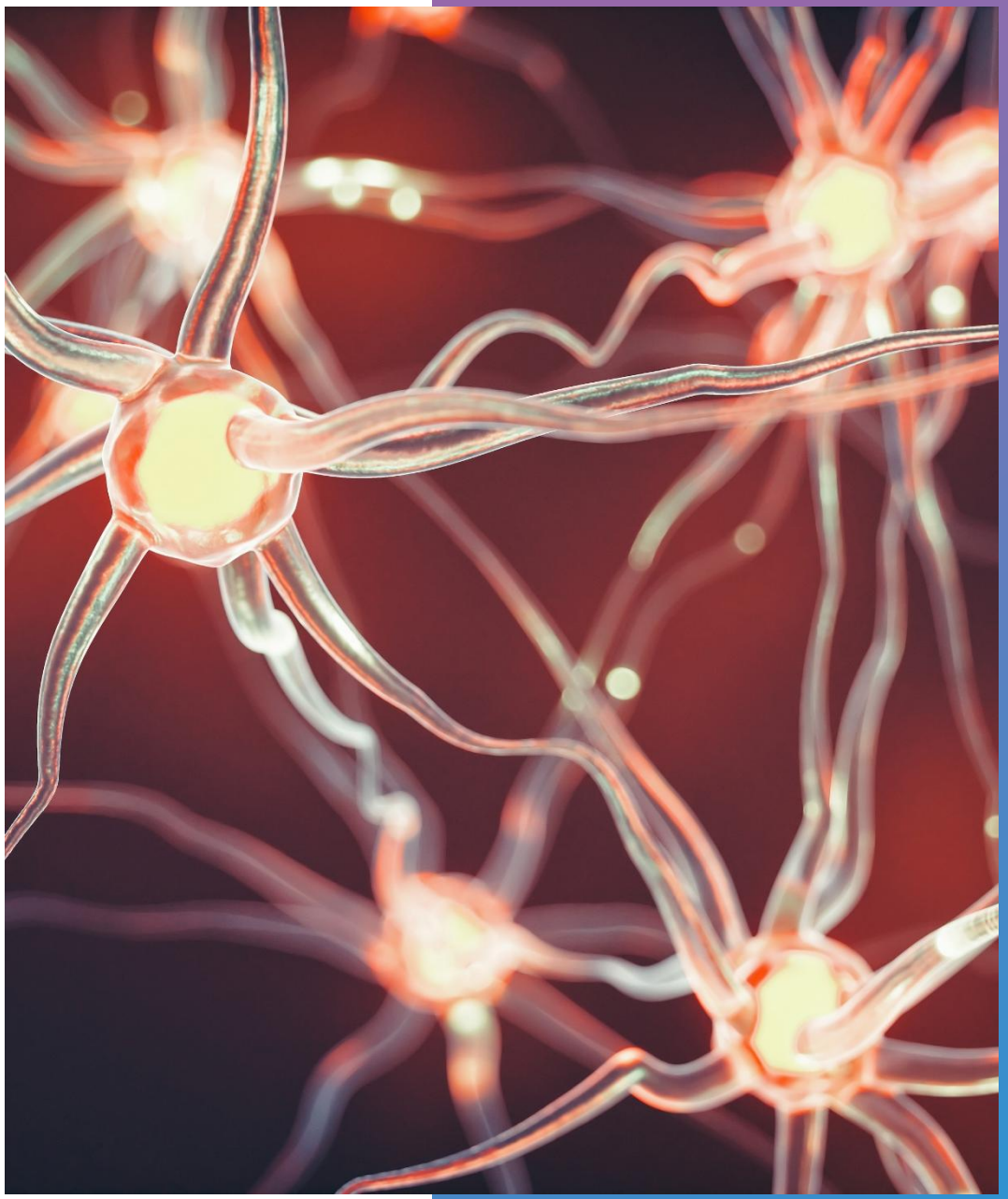
Acute and Chronic Effects of Stimulants



Acute Stimulant Overdose

- Severe hyperthermia
- Convulsions
- Severe dehydration
- Anxiety/panic
- Paranoia
- Delirium
- Rhabdomyolysis → acute renal failure
- Stroke
- Myocardial infarction

NIDA, 2019

Physical and Psychological Effects of Chronic Stimulant Use

- 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)

NIDA, 2019

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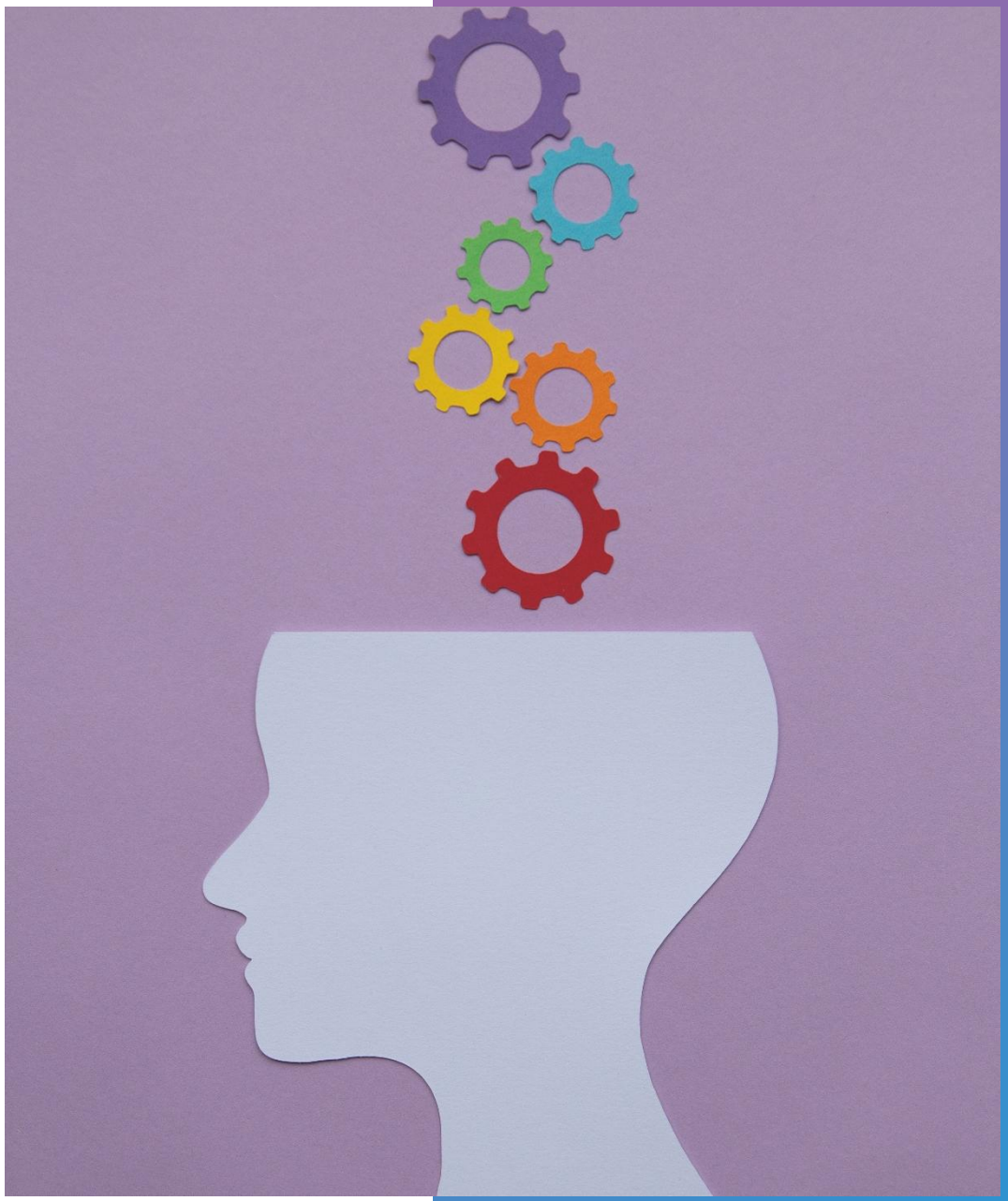
Cognitive and Memory Effects of Stimulant Use



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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.

Fitzpatrick et al., 2020

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Treatments for Stimulant Use Disorders – Medications

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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

Skolnick, 2015

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Medication Treatments

- Pharmacotherapies, including psychostimulant medications, may be utilized off-label to treat StUD
- When prescribing controlled medications, clinicians should closely monitor patients and perform regular ongoing assessments of risks and benefits for each patient
- Psychostimulant medications should only be prescribed to treat StUD by:
  - *Physician specialists who are board certified in addiction medicine or addiction psychiatry; and*
  - *Physicians with commensurate training, competencies, and capacity for close patient monitoring.*

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Methamphetamine Use Disorder Pharmacotherapy

Headline:

There are no FDA Approved Medicines for Stimulant Use Disorder

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Medications for Methamphetamine Use Disorder (MUD)*

- **Bupropion (signal for lower frequency MA use)**
  - Additional consideration for tobacco use d/o, depression
- **XR-Naltrexone injection + high dose bupropion XL**
- **Mirtazapine (two small studies)**
  - Additional consideration for depression
- **Topiramate (low-level MA use)**
  - Additional consideration for AUD
- **Methylphenidate-ER (higher frequency MA use)**
  - Additional consideration for ADHD

ASAM/AAAP, 2024

*There are no FDA Approved Medicines for Stimulant Use Disorder

XR-Naltrexone Injection Plus Bupropion XL

- Medications: XR-NTX 380mg via intramuscular injection every three weeks in combination with bupropion XL titrated to 450mg daily
- 12-week, 2 stage trial (N= 403 Stage 1, N= 225 Stage 2)
- Response defined as at least three MA-negative urine samples out of four during the final two weeks; urine collected twice weekly
- Weighted avg response 13.6% with XR-NTX–bupropion vs 2.5% with placebo
- Treatment effect: between-group difference in overall weighted response (11.1%)

Trivedi et al., 2021

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Cocaine Use Disorder Pharmacotherapy

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Medications for Cocaine Use Disorder (CUD)*

- Modafinil (without co-occurring AUD)
- Topiramate (lower frequency cocaine use)
- Additional consideration for AUD
- Mixed Amphetamine Salts-ER + Topiramate
- Additional consideration for AUD, ADHD
- Mixed Amphetamine Salts-ER
- Bupropion (best when combined with CM)

*There are no FDA Approved Medicines for Stimulant Use Disorder

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Cocaine vs Reward

People who use drugs will choose relatively small rewards over drugs

Higgins et al., 1994

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Contingency Management (CM)

Contingency Management for Stimulant Use Disorder

A behavioral technique employing the systematic delivery of positive reinforcement for desired behaviors that are incompatible with stimulant use. In the treatment of stimulant use disorder, tangible items (e.g., gift cards) can be “earned” for submission of stimulant-free urine samples or for completion of other selected behaviors.

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Contingency Management for Stimulants: Research Summary (1)

- CM is the **most effective** way to help people stop using stimulant drugs.
- 18 studies demonstrate that CM works to **reduce stimulant use** for people who are receiving MOUD treatment.
- CM has a **higher retention rate** than other stimulant use disorder treatments.

AshaRani et al., 2020; Bentzley, et al., 2021; Bolívar et al., 2021; Higgins et al., 1994

Contingency Management for Stimulants: Research Summary (2)

- The effects of CM can last for **up to one year after the intervention ends.**
- CM that targets stimulant abstinence leads to **reduced alcohol use**, **cigarette smoking**, **depressive symptoms**, and **psychiatric hospitalizations.**
- CM is **cost-effective.**

Ginley et al., 2021; Miguel et al., 2017; McDonell et al., 2021b; Olmstead & Petry, 2009

Contingency Management for Stimulants: Research Summary (3)

- Cultural factors
  - CM has demonstrated efficacy in the U.S., Brazil, China, and other countries
  - CM has been adapted, tested, and found to be effective in partnership with Native American and Alaska Native communities
- Other Populations
  - CM is associated with reductions in substance use in populations with co-occurring serious mental illness

Hser et al., 2011; Miguel et al., 2022; McDonell et al., 2021a; McDonell et al., 2021b)

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Funding CM

- Medicaid 1115 Waiver
- SOR/TOR Grant
- Opioid Settlement Funds
- Grants
- Local/Agency/Community Funding

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Recovery Incentives Program

https://vimeo.com/1092526189

The Four Essential "Ingredients" of Contingency Management

- Clearly define a single behavior.
- Frequently measure behavior.
- Provide tangible incentives soon after behavior is observed.
- Withhold incentive when behavior is not observed while maintaining supportive attitude.

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Use a Positive Approach

- Reframe the use of UDTs (rewards vs punishment).
- Stay encouraging by focusing on next opportunity to earn a recovery incentive.
- Emphasize the lack of punishment/ negative consequences.
- Gets clients excited about treatment – they have something to look forward to.
- Helps build the therapeutic alliance.

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Urine Testing in Contingency Management

Flip the Script!

Urine testing in standard SUD treatment

- Focused on the consequences of positive test results
- Often requires abstinence from all substances
- Lab-based testing often required
- Infrequent testing (e.g., monthly)
- May have external implications (e.g., legal, child custody)

Urine testing in Stimulant-focused CM

- Focused on celebrating negative test results
- CM incentives are based on stimulant UDT results only!
- Point of Care tests preferred
- Twice-weekly for 12 weeks, once/week for another 12 weeks
- Urine tests meant for therapeutic intervention, not legal record

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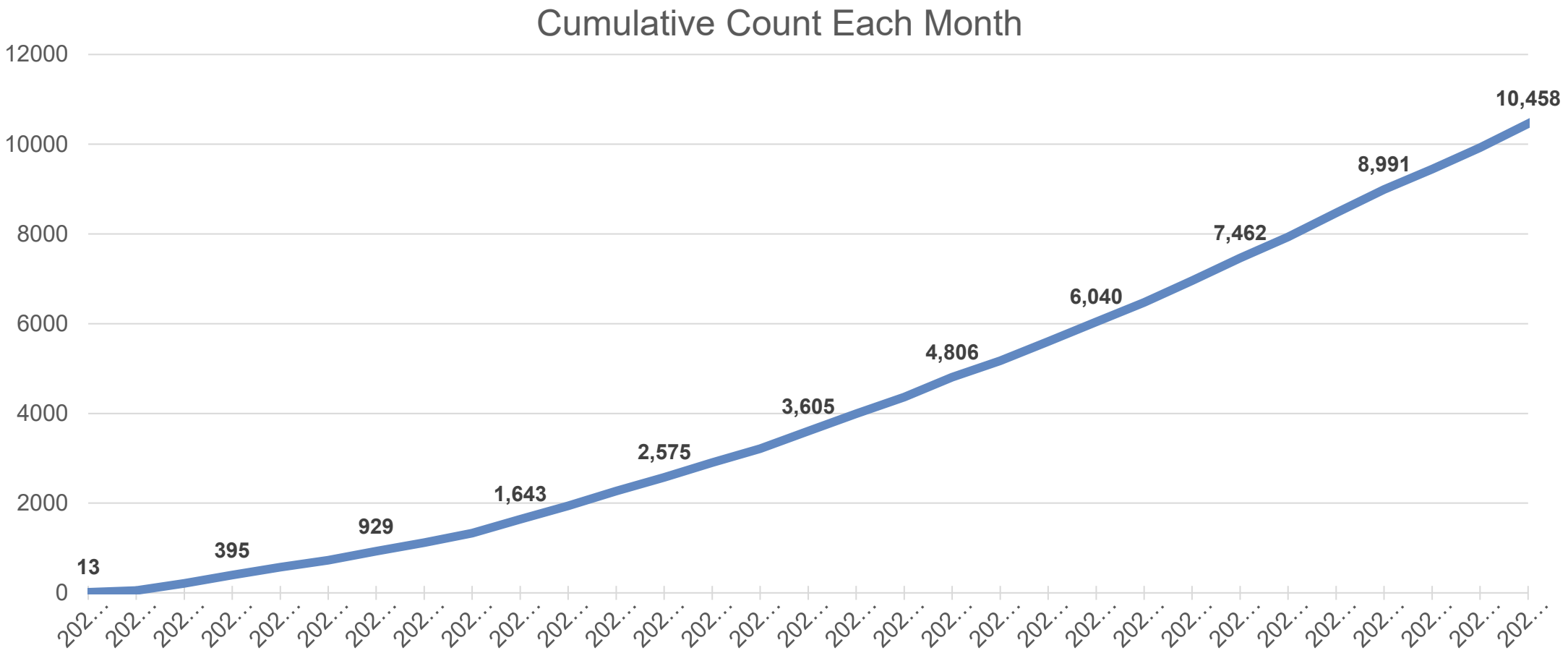
Monthly Enrollment April 2023 through October 2025



Unpublished data from CA Recovery Incentives Program

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UDT Results by Retention

RETENTION			UDT RESULTS	
Definition	N	%	% negative	% negative counting unexcused absences as positive
Completed the full program (168 days or 24 weeks)	1,654	33.0%	96.9%	88.9%
84 days but less than 168 days (>12 weeks but < 24 weeks)	1,354	27.0%	96.6%	78.5%
30 days but less than 84 days (> 1 month but < 12 weeks)	1,034	20.6%	93.1%	59.6%
1 day but less than 30 days (< 1 month)	968	19.3%	84.9%	50.3%
TOTAL	5,010	100%	96.1%	80.2%

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Recovery Incentive Services Provided

April 2023 – October 2025

- Over 200,000 documented CM Tx Services provided
  - More than 192K Stimulant Negative UDTs (96% of UDTs)
  - Just over 8K Stimulant Pos UDTs
- $3,000,000 in incentives earned for Stimulant Negative UDTs
  - $2.7M in actual gift card rewards delivered to members through the Portal.
  - $300K banked by clients for later distribution

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Recovery Incentives Program Success Stories

- A member shared that last year, he was stealing Christmas gifts, and this year, he was buying them.
- Another member went from jail, to residential treatment, to outpatient treatment and the Recovery Incentives Program, to getting a job at the site he was receiving CM services from as a maintenance worker.
- One member involved his sons in his treatment plan. He had each son pick a vendor from the IM Portal. One son picked GameStop, and the other Walmart. Every time he came home from a CM visit, his kids would ask, ***"How much did we get today?"*** The member did not want to disappoint his kids, so that keeps him motivated to continue to test negative and bring home earned incentives.
- Upon completion of the Program, a member received a certificate of completion. He said it was the first time he's ever completed anything in his entire life.

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Common Challenges of Implementing CM (1)

- Resistance to the idea of incentives, i.e., “Why do clients need extrinsic motivation?”
  - *Overcome with education and testimony from clients*
- Working twice-weekly visits into clinic workflow
  - *CM visits only take 10-15 mins*

Common Challenges of Implementing CM (2)

- Challenges of tracking incentive escalation, reset, recovery, and recovery incentive distribution
- Office of the Inspector General (OIG) prohibits the use of incentives to pay clients for billable encounters (anti-kickback regulations)
  - *Most contingency management programs must comply with OIG-defined Safe Harbor requirements. It is critically important to follow a defined protocol to avoid potential for fraud or the appearance of kickbacks*

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Audience Q&A | Discussion

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Want to Read More about the Program?

- Urada, D., Padwa, H., Antonini, V. Tsoi, C., Gregorio, L., Freese, T., Rutkowski, B., Rawson, R., Lee, A. N., Bass, B., Khurana, D., Loya, C., Cooper, M., Gilbert, M., & Zakher, E. (2025). **Evaluation of the recovery incentives program: California's contingency management benefit.** *Drug and Alcohol Dependence,* 267(S). https://doi.org/j.drugalcdep.2024.112298
- Freese, T. E., Rutkowski, B. A., Peck, J. A., Padwa, H., Thompson, C., Datrice, A., Simmons, J., Cooper, M., Loya, C., Trupiano, D., & Rawson, R. A. (2024). **California's Recovery Incentives Program: Implementation strategies.** *Journal of Substance Use and Addiction Treatment*, 167, 209513. https://doi.org/j.josat.2024.209513
- Freese, T. E., Rutkowski, B. A., Peck, J. A., Urada, D., Clark, H. W., Nigusse Bland, A., Friedman, J., & Rawson, R. A. (2023). **Recovery incentives program: California's contingency management benefit.** *Preventive Medicine*, 176, 107703. https://doi.org/10.1016/j.ypmed.2023.107703

- More to come!

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Encourage Success — Stimulant-Negative UDT

UDT is Negative for Stimulants – Respond with ***JOY***

J oin	them in celebration!
O ffer	encouragement to keep up the good work
Y ield	positivity by reminding them that they can earn even more with continued stimulant-negative test results

Santamaria, 2023a

(Remember, the incentive is doing the heavy lifting!)

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Encourage Success — Stimulant-Positive UDT

UDT is Positive for Stimulants – Respond with ***EASE***

E ncourage	by using a non-judgmental and matter-of-fact approach
A pplaud	their efforts for coming to the visit
S pecify	that their next opportunity is very soon (provide details for next visit
E mpower	by asking if there's anything you can do to support them (if you have the capacity to do so)

Santamaria, 2023b

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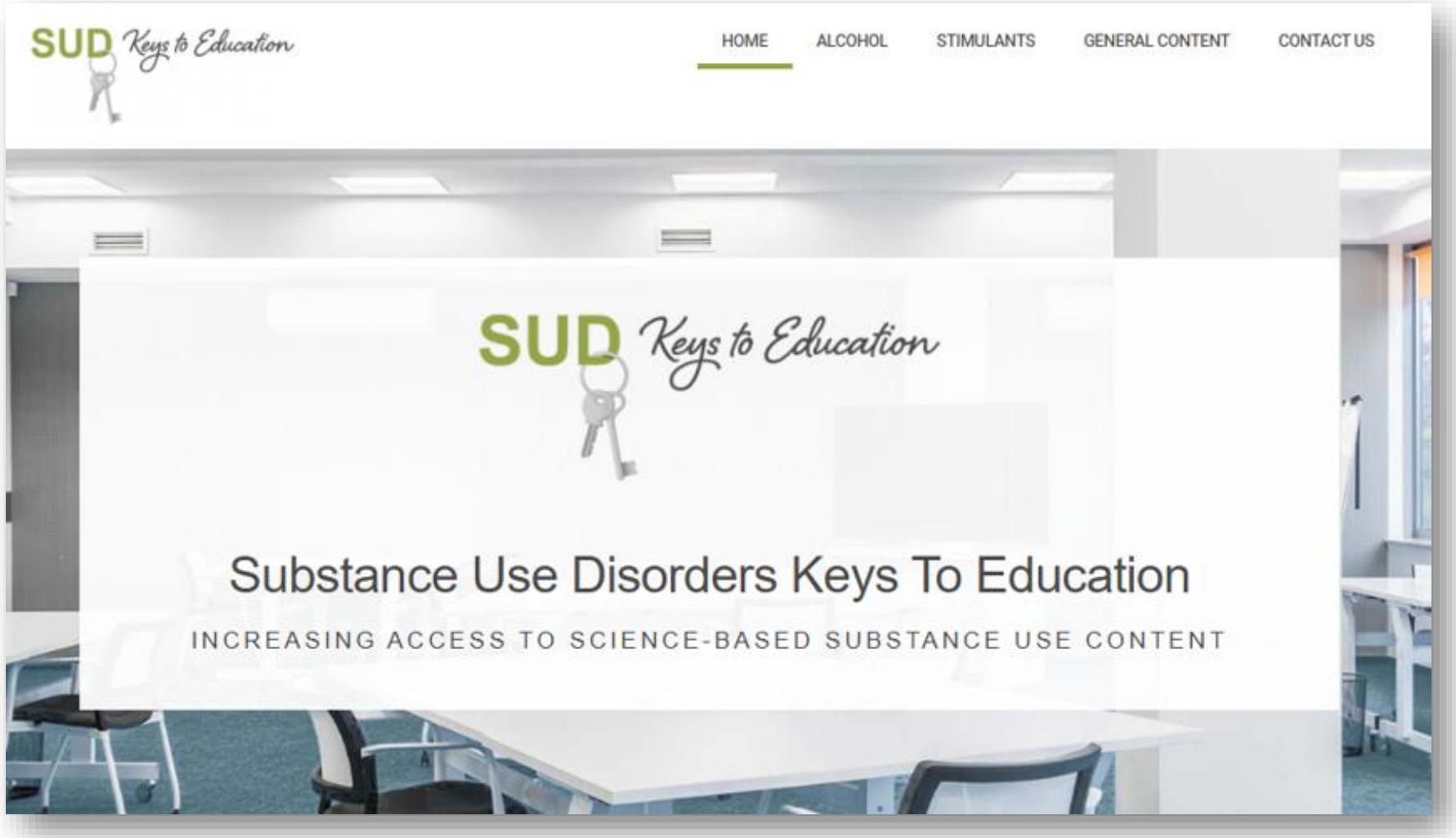
A new resource…



SUD Keys to Education - MPATTC Learning

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References

1. American Society of Addiction Medicine (ASAM) & American Academy of Addiction Psychiatry (AAAP). (2023). *The ASAM/AAAP clinical practice guideline on the management of stimulant use disorder.* https://www.asam.org/quality-care/clinical-guidelines/stimulant-use-disorders

2. American Society of Addiction Medicine (ASAM) & American Academy of Addiction Psychiatry (AAAP). (2024). *Treating stimulant use: Methamphetamine use disorder pharmacotherapy* [Presentation slides]. View presentation

3. Bassareo, V., & Di Chiara, G. (1999). Differential responsiveness of dopamine transmission to food-stimuli in nucleus accumbens shell/core compartments. *Neuroscience, 89*(3), 637–641.

4. Blum, K., Simpatico, T., Femino, J., Waite, R. L., Downs, B. W., Madigan, M., Giordano, J., Braverman, E. R., & Oscar-Berman, M. (2012). Neurogenetic impairments of brain reward circuitry link to reward deficiency syndrome (RDS): Potential nutrigenomic induced dopaminergic activation. *Journal of Genetic Syndromes & Gene Therapy, 3*(4), e115. https://doi.org/10.4172/2157-7412.1000e115

5. Di Chiara, G., & Imperato, A. (1988). Drugs abused by humans preferentially increase synaptic dopamine concentrations in the mesolimbic system of freely moving rats. *Proceedings of the National Academy of Sciences of the United States of America, 85*(14), 5274–5278.

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PCSS-MOUD Steering Committee

- PCSS-MOUD is led by the American Academy of Addiction Psychiatry (AAAP), in collaboration with a coalition of national professional and healthcare organizations.

Learn more about the Steering Committee and its partner organizations: **https://pcssnow.org/about/steering-committee/**

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PCSS-MOUD Mentoring Program

- Designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid use disorder (MOUD).
- Supported by a national network of providers with expertise in addictions, pain, and evidence-based treatment, including MOUD.
- Three mentoring options are available to meet your needs.
- No cost to participate.

For more information visit:
https://pcssNOW.org/mentoring/

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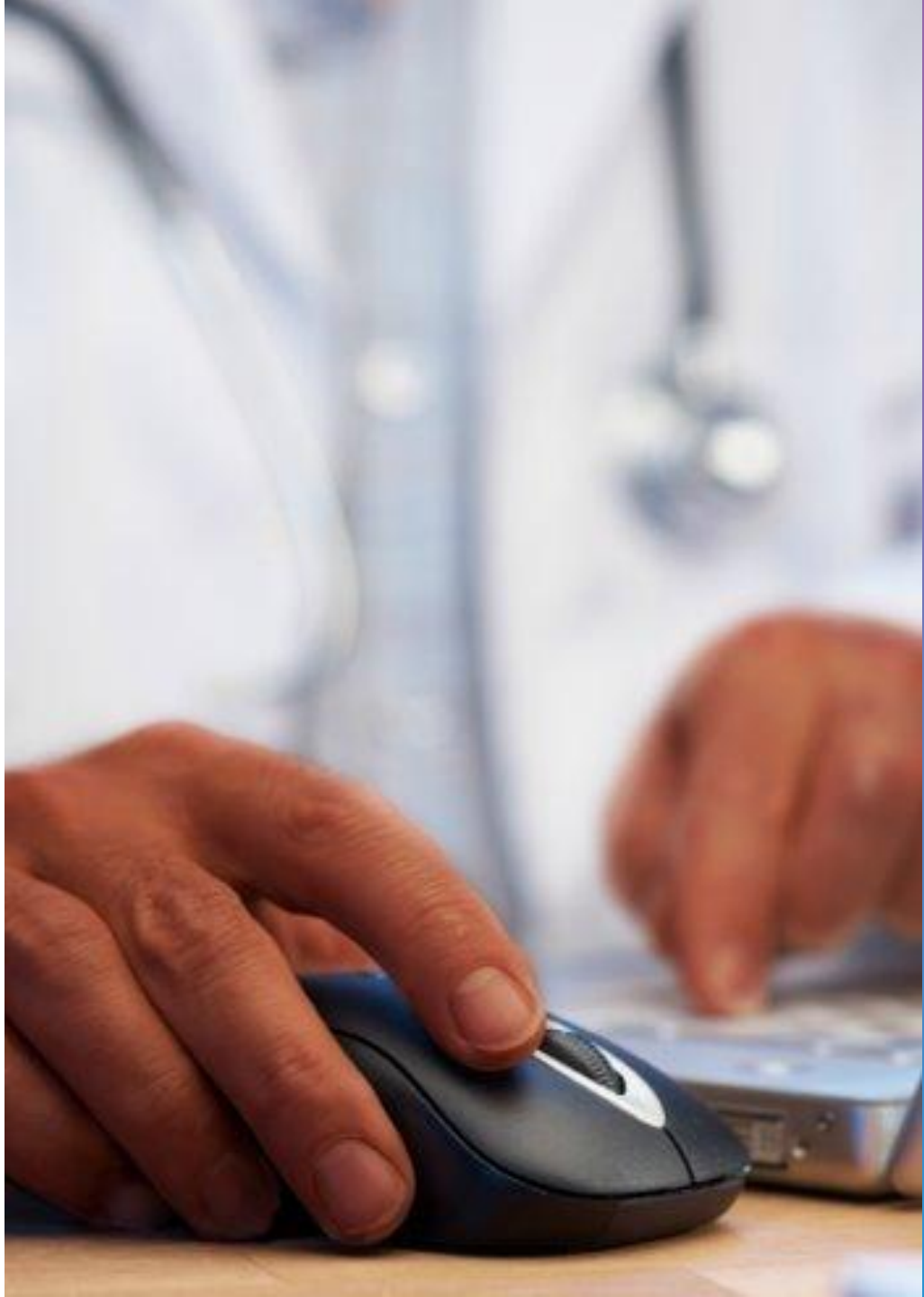
1: Discussion Forum

- An online discussion forum moderated by addiction specialists where health professionals can post questions and receive answers from clinical experts and other colleagues.

Register here at no cost!

For more information visit:
https://pcssNOW.org/mentoring/



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2: Ask a Clinical Question

- A simple and direct way to receive an answer related to Substance Use Disorder, Opioid Use Disorder, and other related topics. Designed to provide a prompt response to clinical questions via email.

Submit your clinical question

For more information visit:
https://pcssNOW.org/mentoring/

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3: One-on-One Mentoring

- Provides individualized, one-on-one guidance via email, phone, or in-person (if feasible), to discuss specific clinical issues. Members are “matched up” with one of our mentors in their region. This is the most in-depth of the three PCSS-MOUD mentoring tools. Please contact **pcssmentoring@aaap.org** to receive a mentor request form.

Browse our Mentors

For more information visit:
https://pcssNOW.org/mentoring/

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