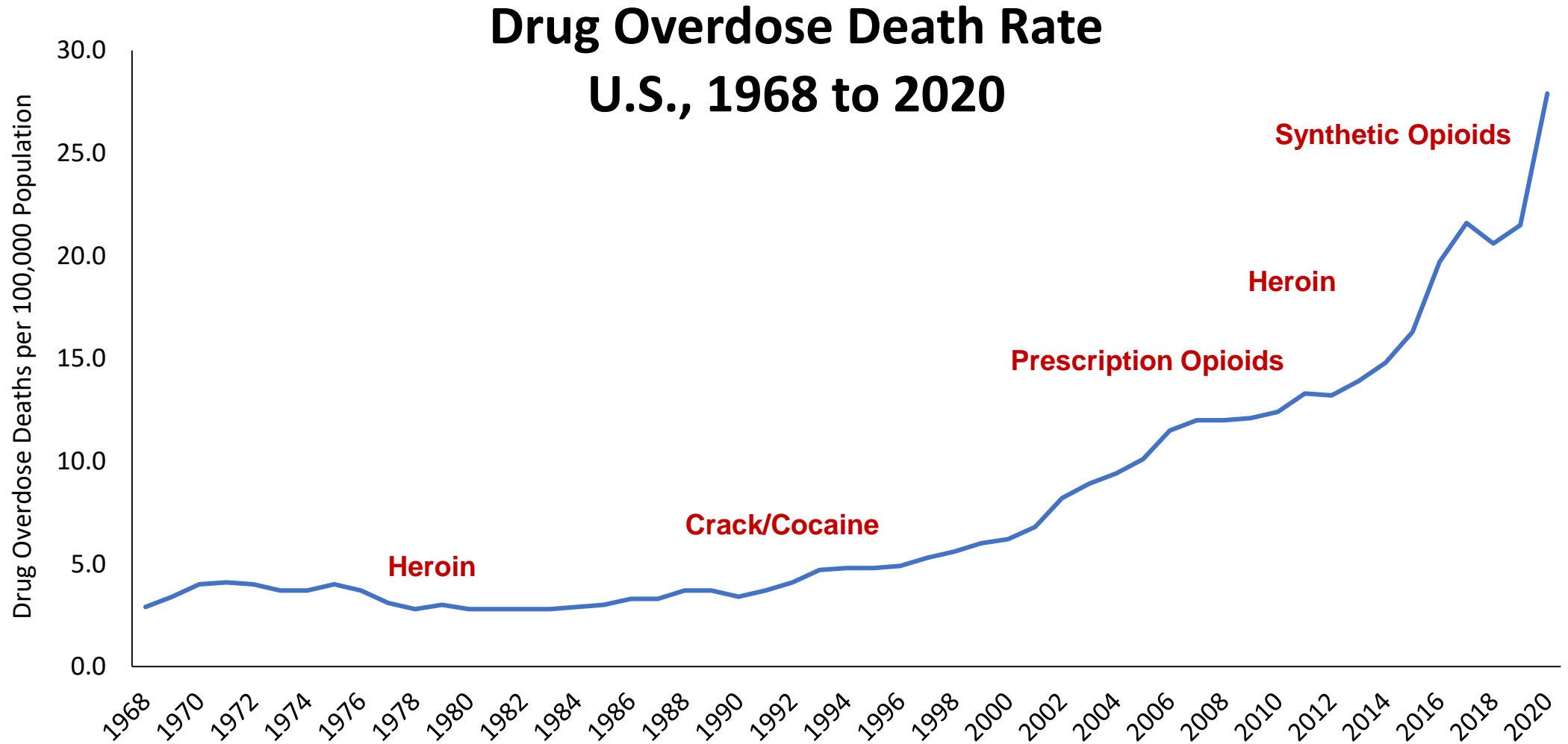


# Improving Addiction Treatment Practices

**Wilson Compton, Deputy Director  
National Institute on Drug Abuse**

# 40 Year Exponential Increases in U.S. Overdose Deaths



See: Jalal, et al. Science 2016, and Compton, Einstein, Jones. International Journal of Drug Policy. 2022.

# U.S. Drug Overdose Deaths

70,630 Deaths in 2019—49,860 from Opioids\*

93,398 Deaths in 2020—69,769 from Opioids\*

107,622<sup>^</sup> Deaths in 2021—80,816 from Opioids\*

<sup>^</sup>Provisional data (predicted values) released May 2022

\*Opioids include both illicit and prescription opioids

National Center for Health Statistics, National Vital Statistics System, mortality data

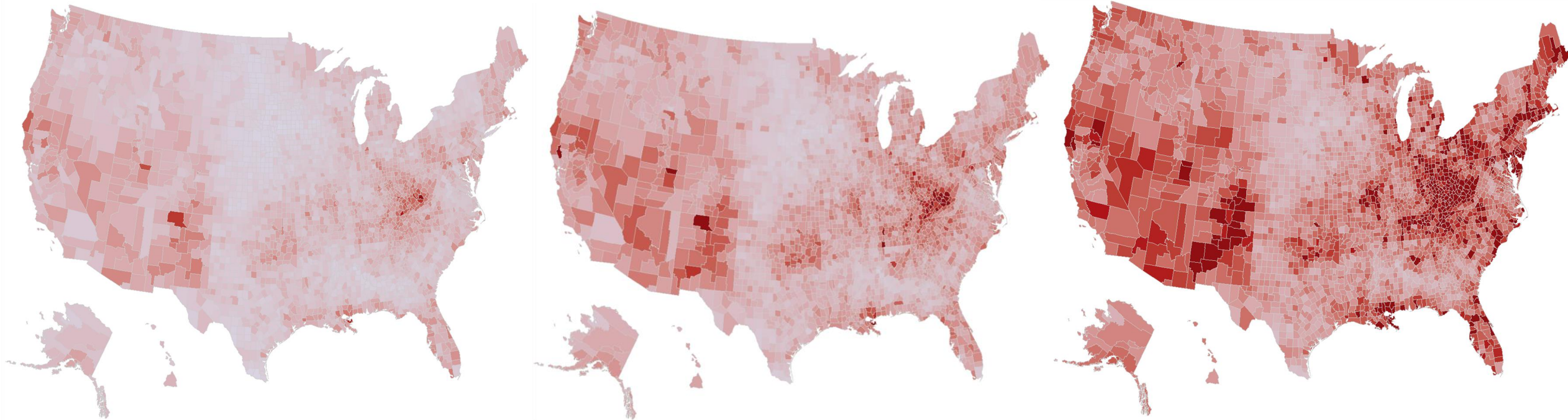
# Virtually All U.S. Regions Have Increased Drug Overdoses

*Estimated Age-adjusted Death Rates per 100,000 for Drug Poisoning by County*

**2003**

**2013**

**2020**



Model-based Death Rate

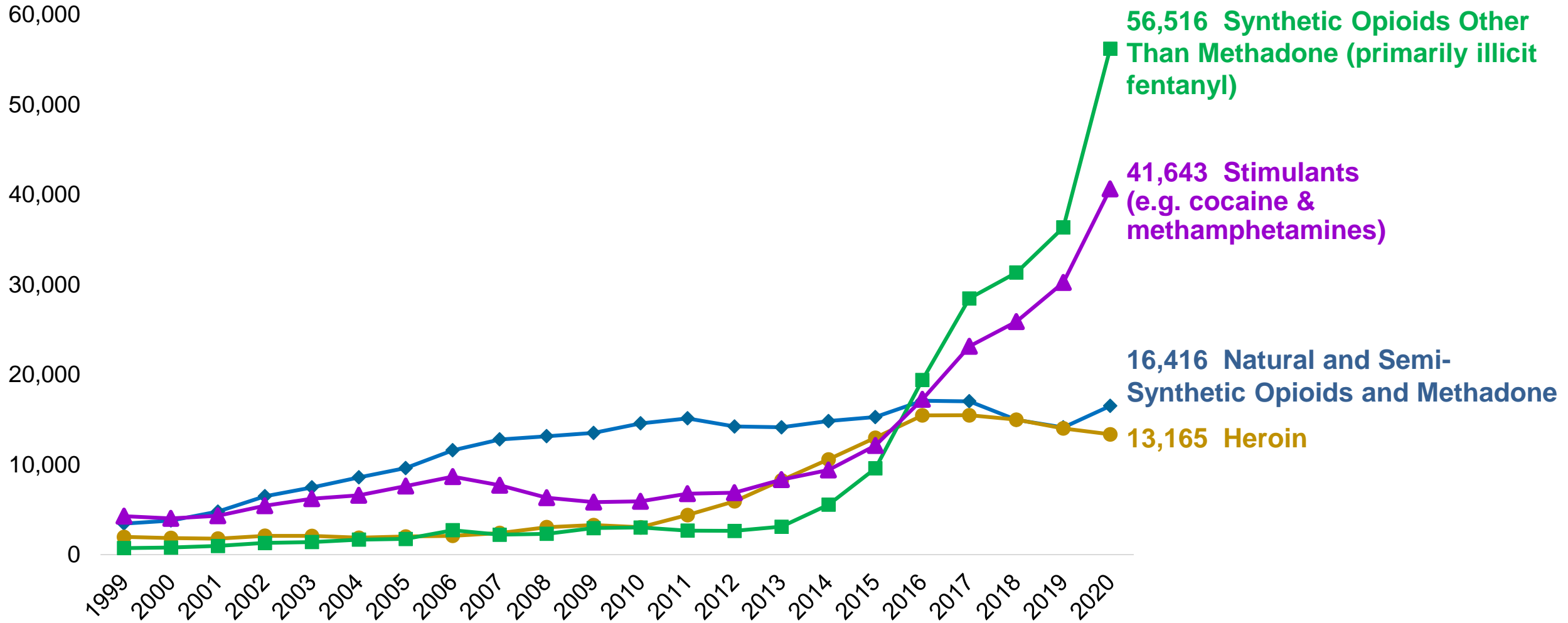
0.00



40.00

# Evolution of Drivers of Overdose Deaths:

*Analgesics* ➡ *Heroin* ➡ *“Fentanyl”* ➡ *Stimulants*



# Drug Overdose Deaths\* Increased in 2021

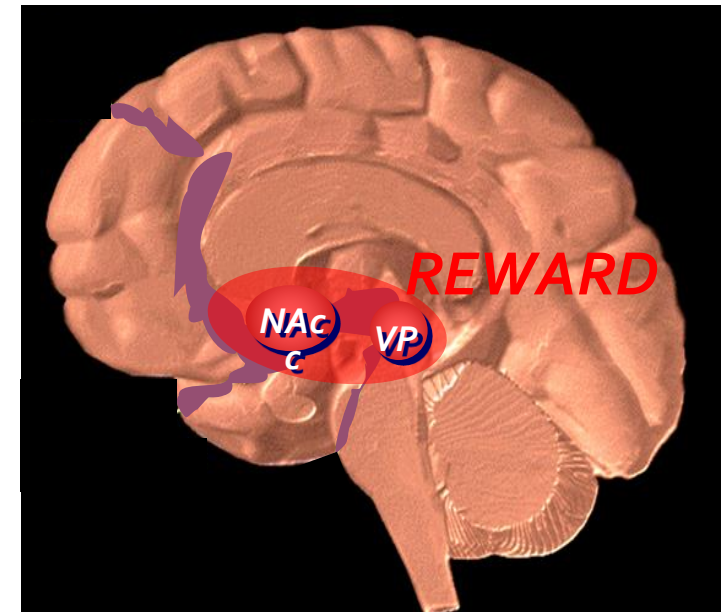
	ALL DRUGS	HEROIN	NAT & SEMI SYNTHETIC	METHADONE	SYNTHETIC OPIOIDS (mainly illicit fentanyl)	COCAINE	OTHER PSYCHO-STIMULANTS (mainly meth)
12/2020*	93,655	13,437	13,722	3,620	57,834	19,927	24,576
6/2021	101,850	11,157	13,928	3,770	65,453	21,469	29,576
12/2021*	107,622	9,137	13,503	3,612	71,238	24,538	32,856
Percent Change 12/20-12/21	<b>14.9%</b>	<b>-32.0%</b>	<b>-1.6%</b>	<b>-0.02%</b>	<b>23.2%</b>	<b>23.1%</b>	<b>33.7%</b>

\*NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months.  
<https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>





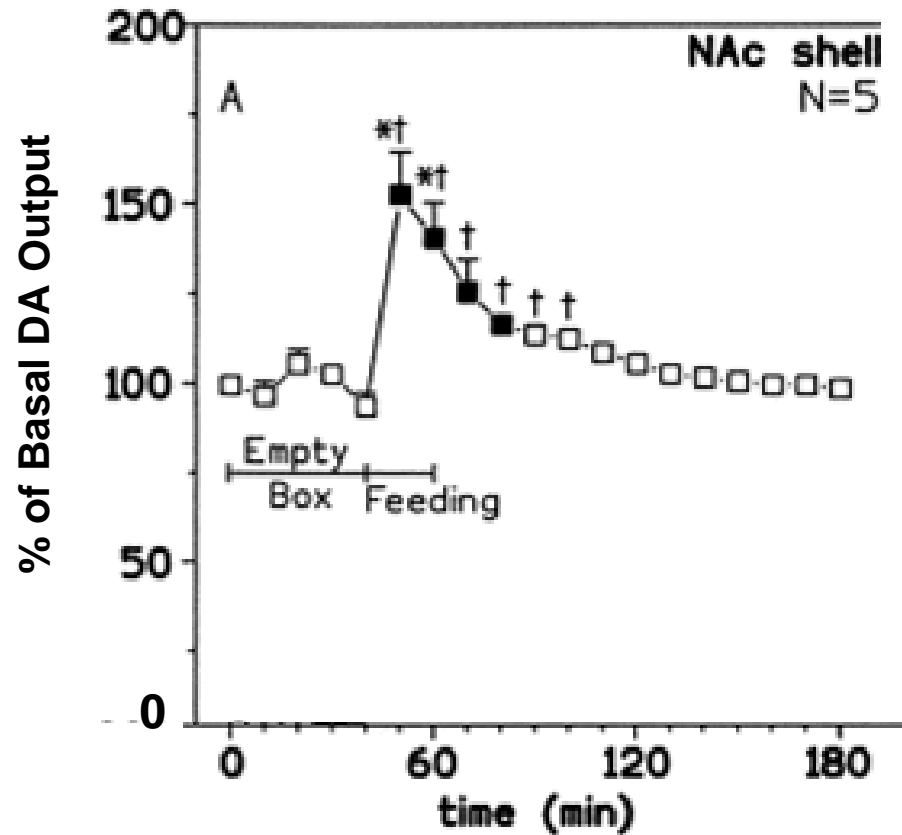
# Reward Circuit



**Drug use engages systems in the motivation pathways of the brain.**

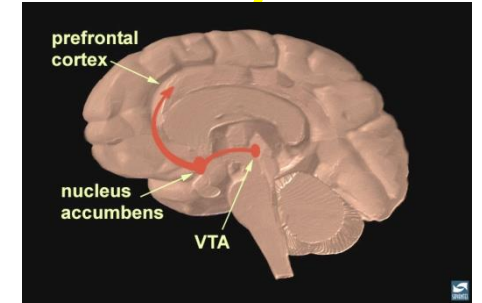
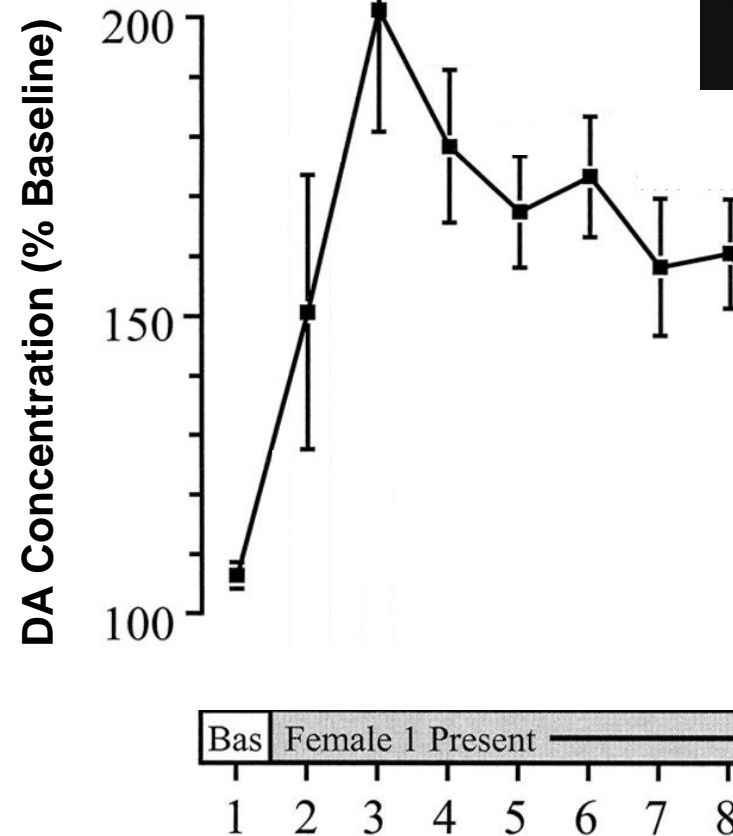
# Natural Rewards Elevate Dopamine Levels

## Food



[Di Chiara et al. \(1999\) Neuroscience.](#)

## Sex



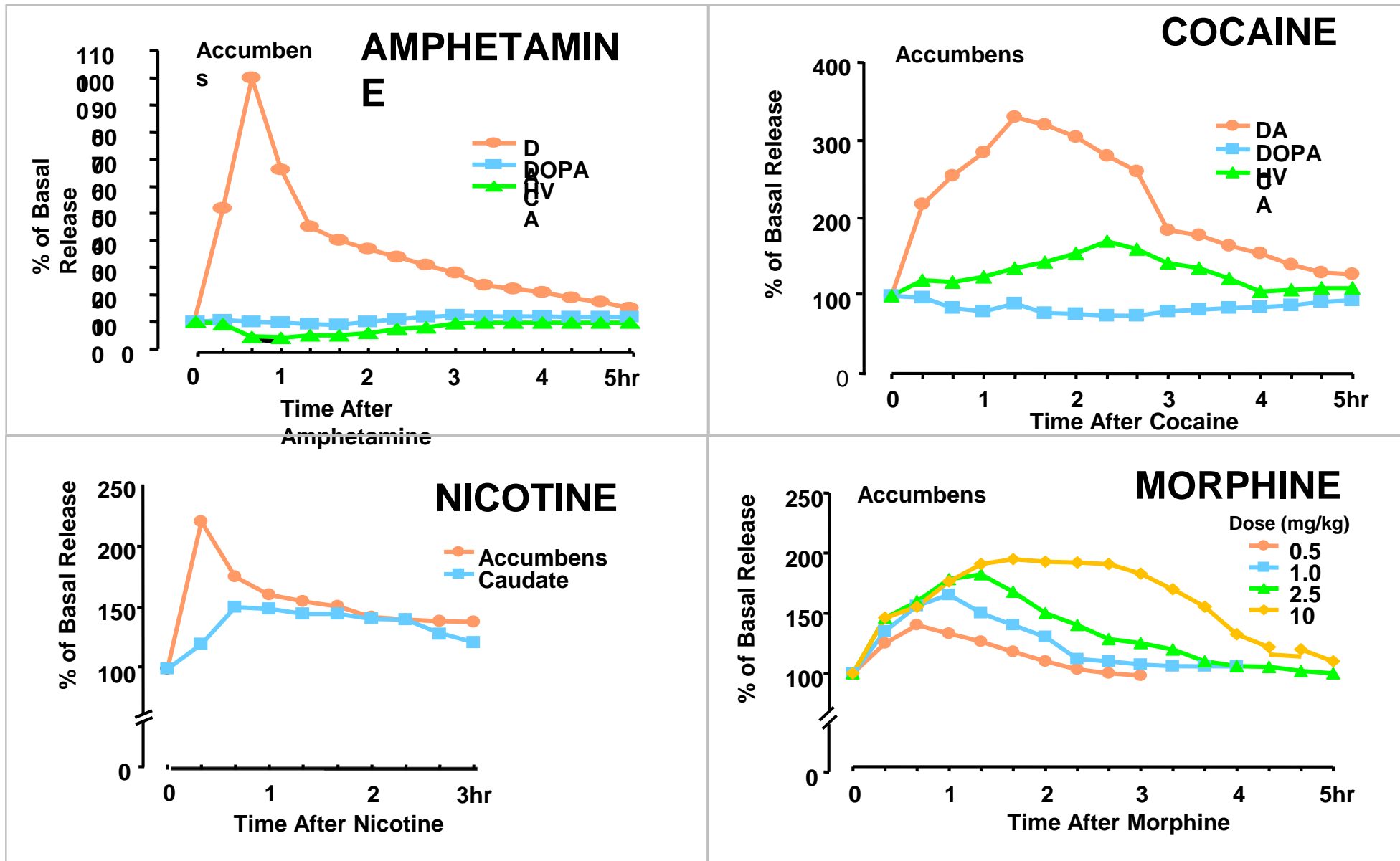
[Fiorino and Phillips. \(1997\) Neuroscience.](#)



# Current State of the Overdose Crisis

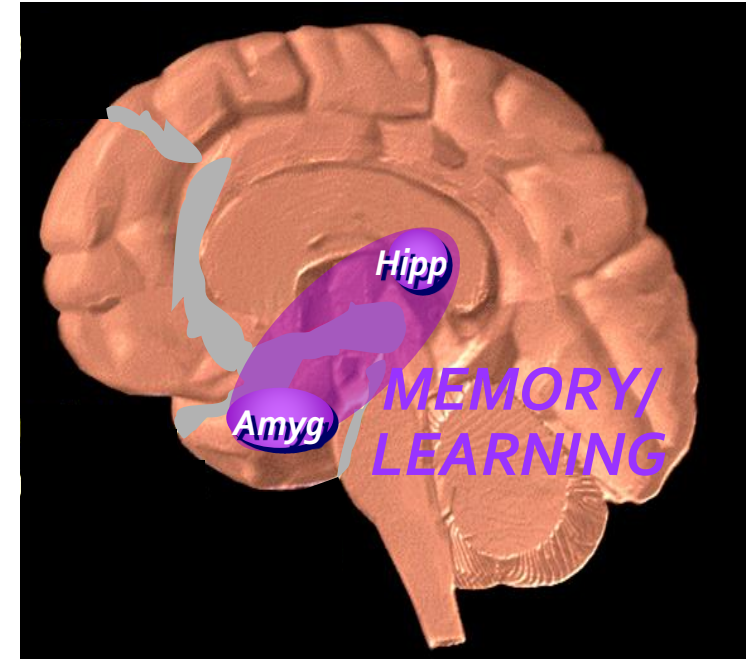
- Overdose crisis continues to be dominated by illicit synthetic opioids such as illicitly made fentanyl (IMF) and fentanyl analogs, but most overdose deaths also involve other drugs
- Patterns of substances used and how they are being used is changing, with rising stimulant use and co-use of opioids and stimulants, especially injection use
- Substance use and overdose patterns are tied to changes in supply:
  - Westward expansion of IMF and analogs
  - Eastward expansion of methamphetamine
  - Counterfeit pills containing IMF and analogs
- Proliferation of highly potent synthetic opioids into an unpredictable illicit drug supply increases overdose risk, especially among those using multiple substances and those unknowingly exposed
- Many missed opportunities for intervention and response

# Drug Use Causes a Release of Dopamine



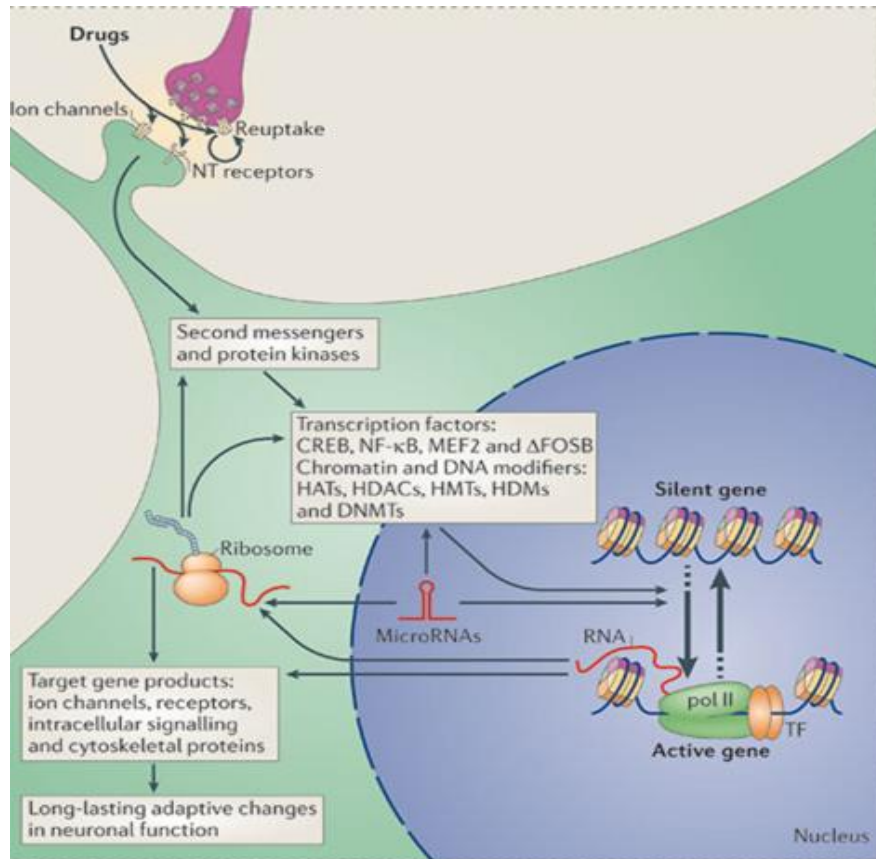
# Memory Circuit

***“People, Places  
and Things...”***



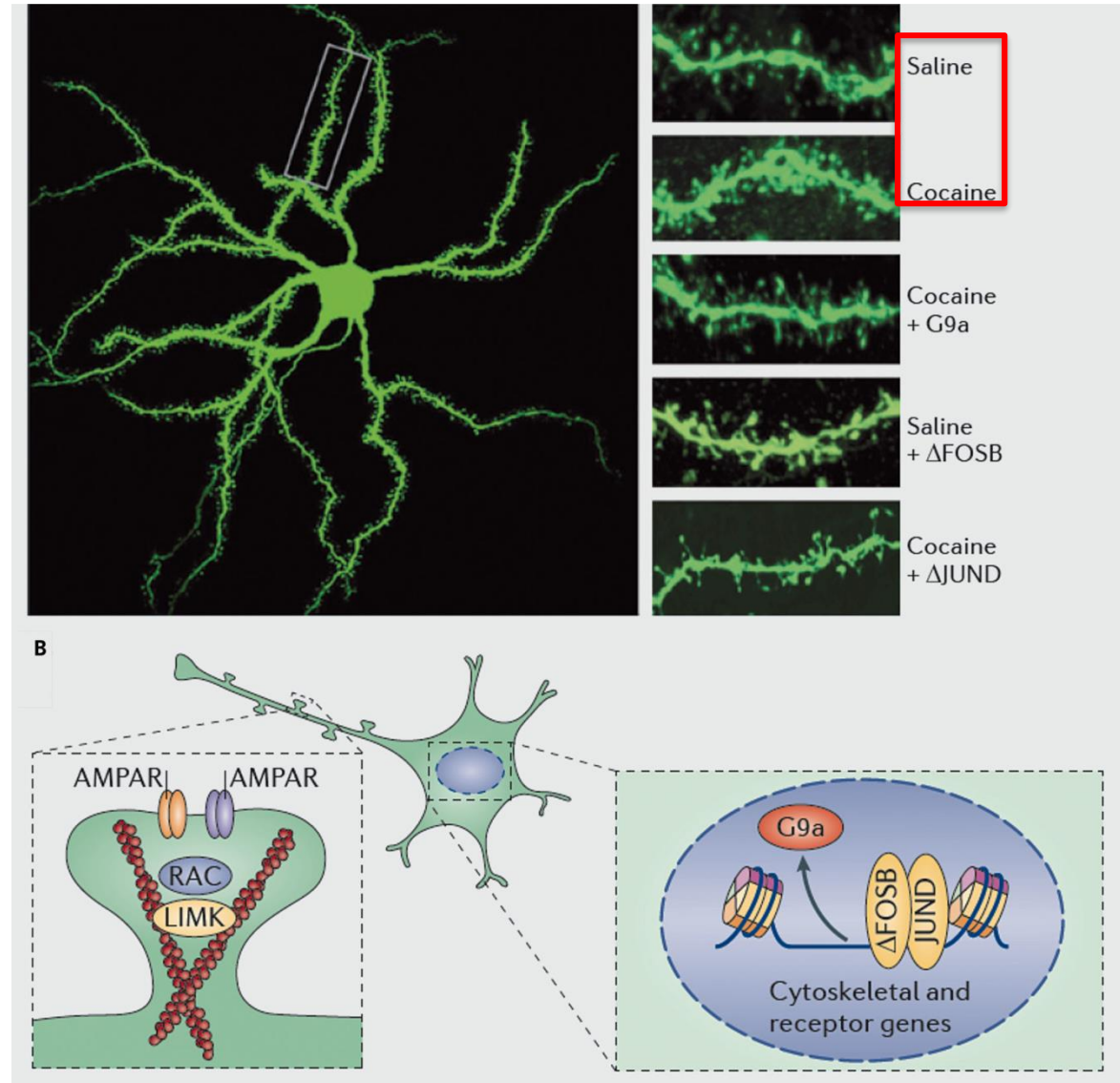
Memories Appear to Be A  
Critical Part of Addiction

# Drugs Trigger changes in Gene Expression that Either Strengthen or Weaken Synapses thus Creating a MEMORY



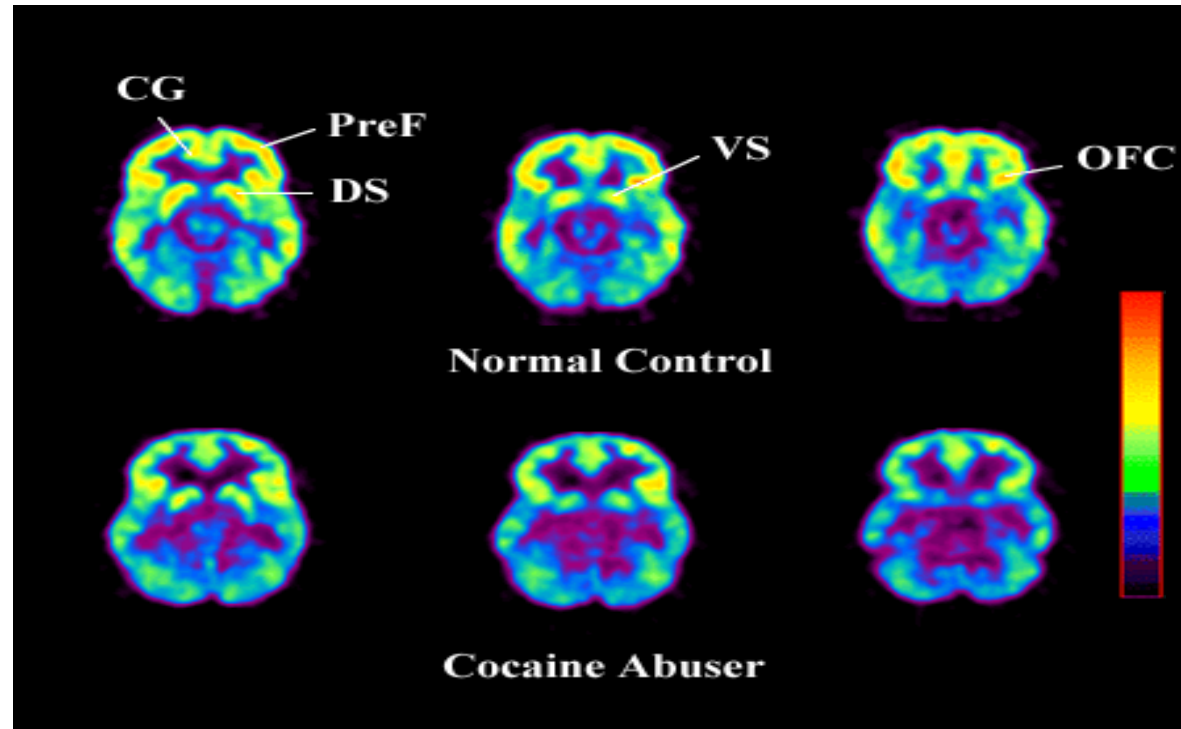
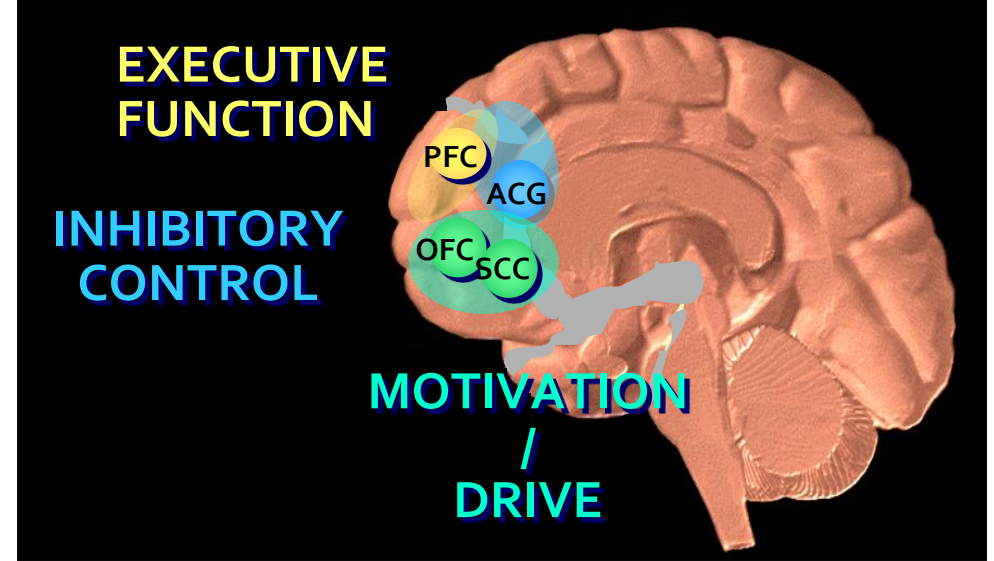
Nature Reviews | Neuroscience

Robison and Nestler. (2011) Nat Rev Neurosci.



# Motivation & Executive Control Circuits

Dopamine is also associated with motivation and executive function via regulation of frontal activity.





The fine balance in connections that normally exists between brain areas active in **reward**, **motivation**, learning and memory, and **inhibitory control**

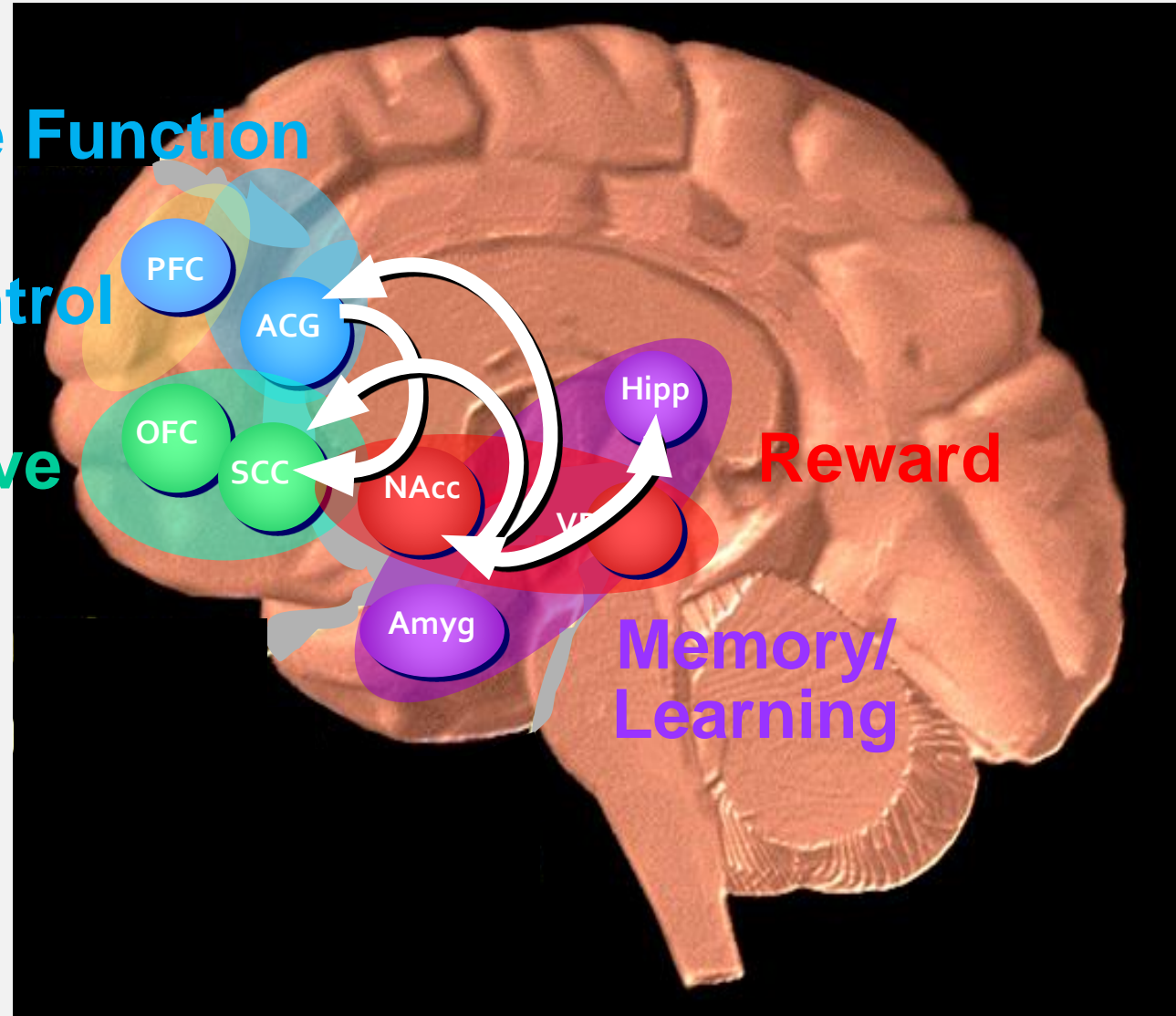
Executive Function

Inhibitory Control

Motivation/Drive

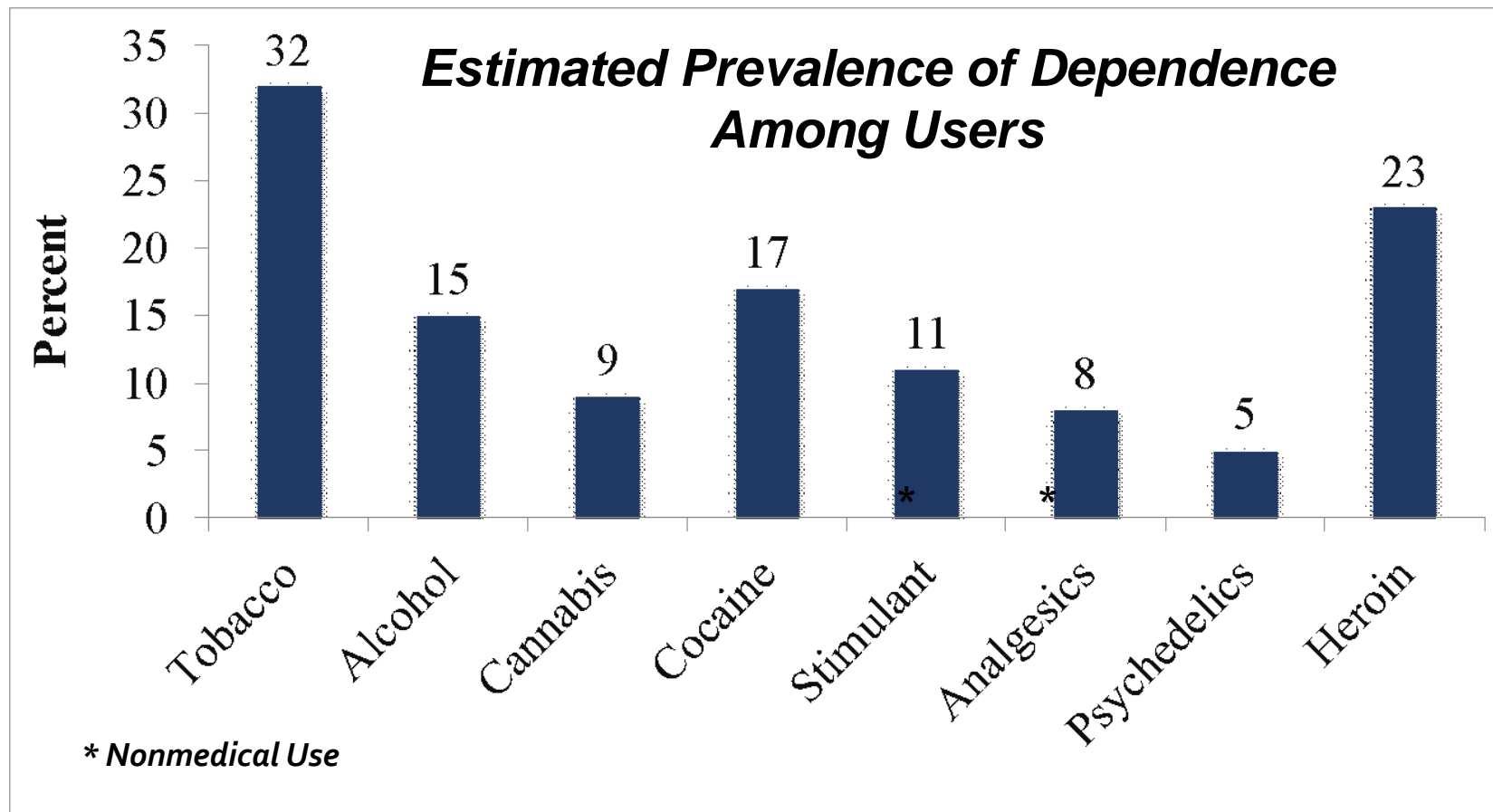
becomes severely disrupted in **ADDICTION**

*Treatment aims to restore this balance*

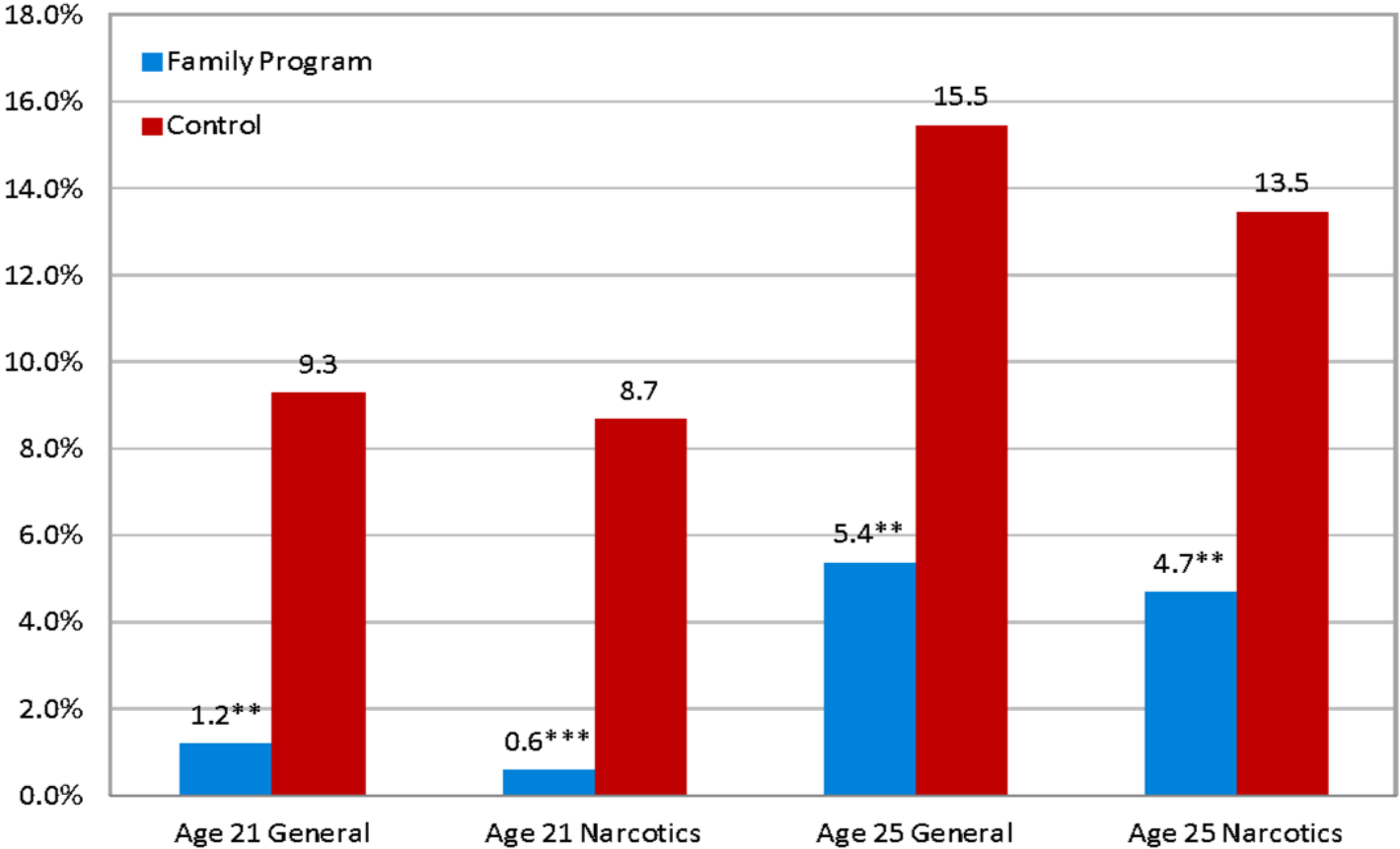


# Key Question: *Is Addiction Inevitable?*

**NO—Use is NOT the same as addiction, but heavy use and adolescent initiation increases risk.**



# Universal Substance Use Prevention May Reduce Later Misuse of Opioids



**Targeting Youth to Prevent Later Substance Use Disorder: An Underutilized Response to the US Opioid Crisis**

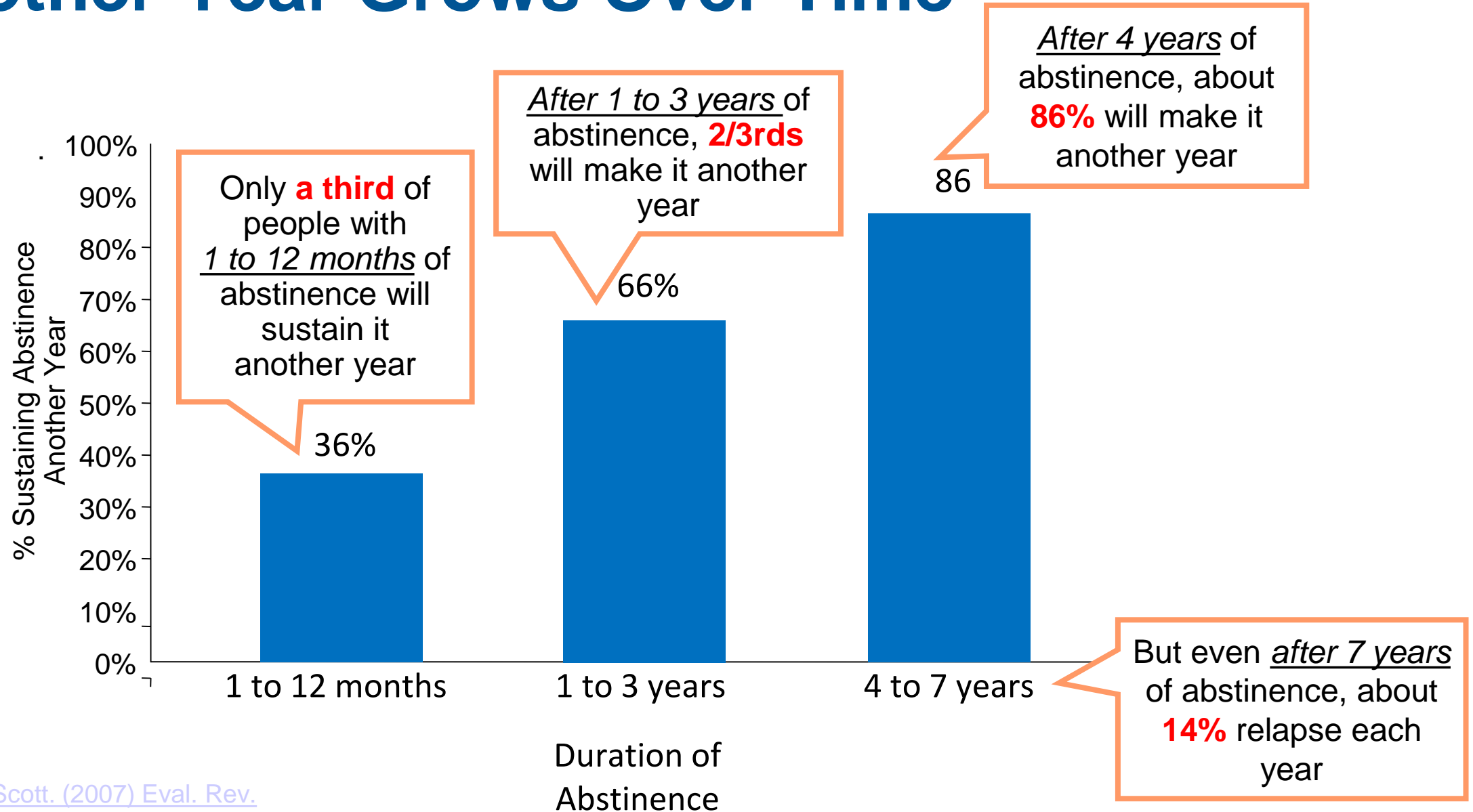
WM Compton, CM Jones, GT Baldwin, et al.  
*AJPH.* 2019;109:2185-S189.

**In this study, for 100 young adults in general population starting Rx abuse, only 35 young adults from an intervention community started.**

Notes: General=Misuse of opioids or CNS depressants or stimulants. Source: R Spoth et al. American Journal of Public Health 2013

**Opioid addiction is a  
chronic relapsing  
condition.**

# The Likelihood of Sustaining Abstinence Another Year Grows Over Time





**MEDICATIONS**  
**FOR**  
**OPIOID**  
**USE**  
**DISORDER**  
**SAVE**  
**LIVES**

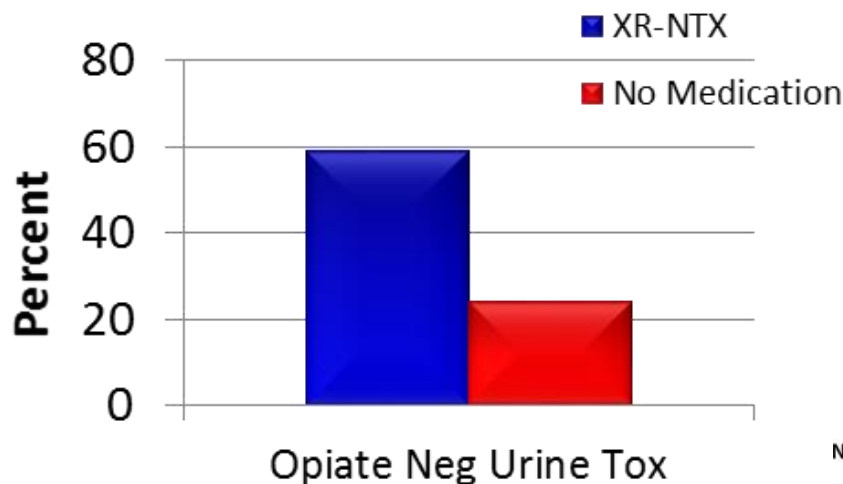
March 20, 2019

- **Methadone**
  - MOR agonist
- **Buprenorphine**
  - MOR partial agonist, KOR/DOR antagonist
- **Naloxone**
  - MOR antagonist
- **Naltrexone**
  - MOR antagonist
- **Lofexidine**
  - $\alpha$ 2 adrenergic receptor agonist

# Science = Solutions: Improving Addiction Treatment

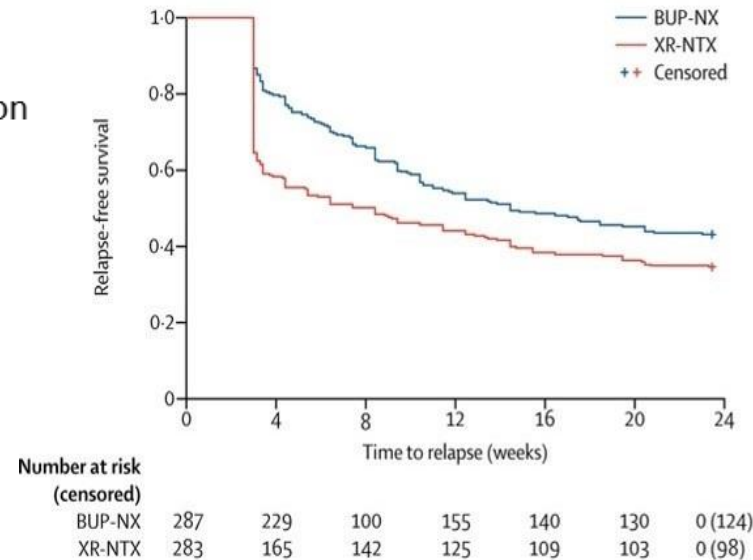
- Initiating buprenorphine treatment in the **emergency department** improves treatment engagement and reduces illicit opioid use
- Extended-release naltrexone initiated in **criminal justice** settings lowers relapse rates and overdoses
- **BUP-Nx** more effective than **XR-Naltrexone** overall but appear equally safe and effective after induction

## Post Prison-Release Outcomes



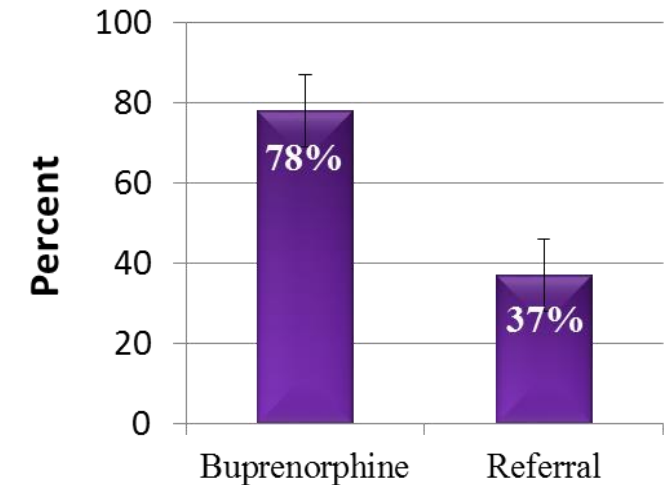
[Lee JD, et al. \(2015\) \*Addiction\*](#)  
[Lee JD, et al. \(2016\) \*NEJM\*](#)

## Relapse-free survival



[Lee JD et al., \(2018\) \*Lancet\*](#)

## ED-initiated Buprenorphine Increased TX Engagement



*D'Onofrio JAMA. 2015.*

# Treating Stimulant Use Disorder

## ADAPT-2 Trial Results Deliver a Breakthrough in Long Search for Methamphetamine Use Disorder Medication

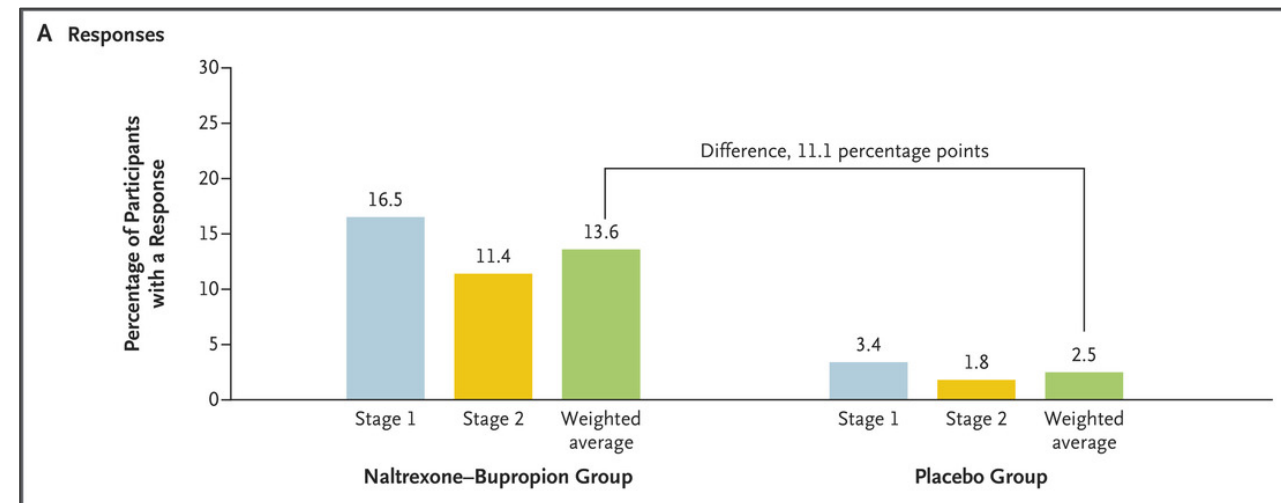
- No FDA approved medications for stimulant use disorder or overdose
- Contingency management is the most effective treatment but is challenging to implement and underutilized
- NIDA prioritizing investment in development of medications to treat stimulant use disorders

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

### Bupropion and Naltrexone in Methamphetamine Use Disorder

M.H. Trivedi, R. Walker, W. Ling, A. dela Cruz, G. Sharma, T. Carmody, U.E. Ghitza, A. Wahle, M. Kim, K. Shores-Wilson, S. Sparenborg, P. Coffin, J. Schmitz, K. Wiest, G. Bart, S.C. Sonne, S. Wakhlu, A.J. Rush, E.V. Nunes, and S. Shoptaw



# Treating Fentanyl OUD and Overdoses

- Limited data on efficacy of medication to treat fentanyl OUD
- Methadone is effective in fentanyl OUD.
  - Methadone protected against death, but relapse rates were high ([Stone, et al., 2018](#), [Stone, et al. 2020](#)).
- Buprenorphine is effective in fentanyl OUD ([Wakeman, et al., 2019](#)).
  - Harder to initiate patients on buprenorphine
- Naltrexone no published data
- Deaths from fentanyl are increasing in spite of naloxone ([Torralva and Janowsky, 2019](#)).
- OD from fentanyl require multiple naloxone doses ([Schumann et al., 2007](#), [Somerville et al., 2017](#))
  - Shorter duration of naloxone (t<sub>1/2</sub> 1.3–2.4 h) than fentanyl (t<sub>1/2</sub> 7-8 h)
  - Slower clearance of fentanyl in frequent users
- Chest wall rigidity induced by fentanyl, which might reflect noradrenergic and cholinergic effects.

# Buprenorphine Access in Pharmacies

- Providers, patients, and staff report patient difficulty accessing buprenorphine in pharmacies ([Jones et al., 2021](#), [Ostrach et al., 2022](#), [Textor et al., 2022](#)).
- Many traditional retail pharmacies do not consistently stock buprenorphine ([Hill et al., 2022](#), [Kazerouni et al., 2021](#)).
- There are disparities in access to buprenorphine.
  - Pharmacies in New York neighborhoods with low rates of health insurance were significantly less likely to have buprenorphine in stock ([Marotta et al., 2021](#)).
- Potential causes of concern from pharmacists about buprenorphine “caps” and lack of communication between physicians prescribing buprenorphine and pharmacists ([Cooper et al., 2020](#), [Carpenter et al., 2022](#), [Ventricelli et al., 2020](#)).
- Pharmacists express varying willingness to dispense buprenorphine under different conditions ([Trull et al., 2021](#), [Textor et al., 2022](#)).
- Some hospitals do not have buprenorphine on their inpatient formulary ([Pham et al., 2022](#)).



# Access to Naloxone

- Naloxone nasal spray was available in 69.5% of community pharmacies across 11 U.S. states from May 2020-April 2021 (n=4,984) ([Hill et al., 2022](#)).
  - In MA, findings suggest increased dispensing of naloxone, in part by naloxone standing orders ([Chatterjee, et al., 2022](#)).
  - Limited availability of naloxone at independent community pharmacies in GA even after the standing order was issued ([Gilbert, et al., 2021](#)).
  - Most pharmacies in TX do not appear to be willing and able to dispense prescribed buprenorphine/naloxone films and naloxone nasal spray to patients with OUD in a timely manner ([Hill, et al., 2021](#)).
- No municipal-level racial/ethnic inequities in naloxone distribution in RI nor MA ([Nolen, et al., 2022](#)), but there are few studies focused on inequity particularly among vulnerable populations (those with physical disabilities or unstable housing) ([Martignetti & Sun, 2022](#)).
- Pharmacists express support of dispensing naloxone in rural and urban pharmacies in NY ([Tofighi, et al., 2021](#)). Still, research findings indicate underutilization of pharmacists with a specific need of programs and training to support their naloxone dispensing.

# Residential Addiction Treatment: High Costs and Misleading Recruitment Practices

- Non-representative survey of n=368 programs
- One-third of callers were offered admission before clinical evaluation
- Most programs required up-front payments, with for-profit programs charging more than twice as much (\$17,434) as nonprofits (\$5,712).
- Recruitment techniques (for example, offering paid transportation & “luxury” amenities) were used frequently by for-profit, but not nonprofit, programs.
- Practices including admission offers during the call, high upfront payments, and recruitment techniques were common even among programs with third-party accreditation and state licenses.

# How Do We Address the Failure to Implement Evidence Based Treatments?

- Sustainable models of care (e.g. use of pharmacies)
- Economic research
  - Costs of not intervening; cost of relapse; averted cost with extended-release formulations
- Integrated healthcare interventions
- Telehealth

# Implementation Science: CTN, JCOIN, HCS, Prevention



NIH  
**HEAL**  
INITIATIVE

**JCOIN**  
JUSTICE COMMUNITY OPIOID INNOVATION NETWORK

NIH  
**HEAL**  
INITIATIVE

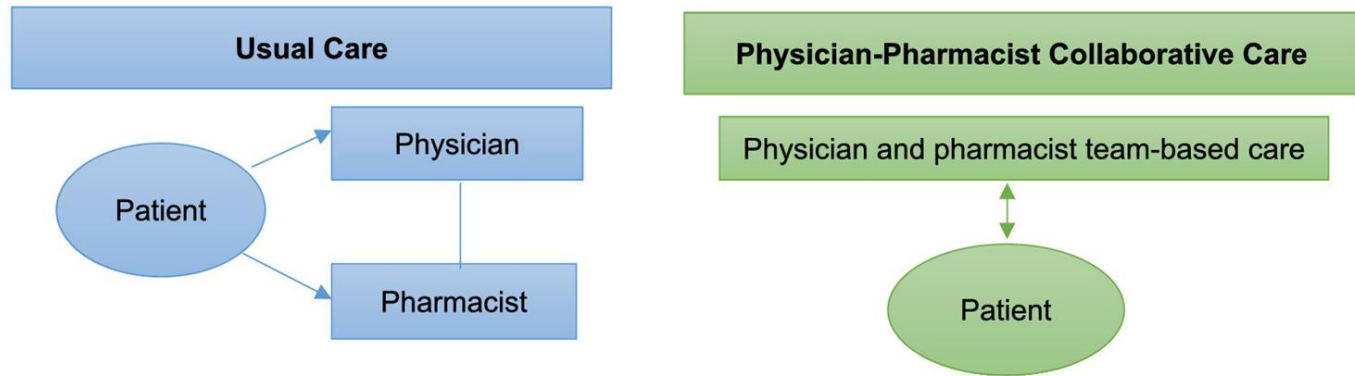
HEALing  
Communities  
Study

[Enhancing the National Drug Abuse Treatment Clinical Trials Network to Address Opioids](#) Expand research conducted by NIDA CTN to address emergent needs presented by the opioid crisis.

[Justice Community Opioid Innovation Network](#) Study quality care for OUD in justice populations. Help create partnerships between local and state justice systems and community-based treatment providers.

[HEALing Communities Study](#) is investigating coordinated approaches for deploying evidence-based strategies to prevent and treat OUD in 67 communities in 4 states.

# Buprenorphine Physician–Pharmacist Collaboration In The Management Of Patients With Opioid Use Disorder (OUD): Results From A Multisite Study Of The National Drug Abuse Treatment Clinical Trials Network



<ul style="list-style-type: none"> <li>▪ <i>Role:</i> Physician evaluates patient, prescribes buprenorphine, determines dosage, and monitors drug use and treatment safety. Pharmacist checks PDMP* and dispenses buprenorphine.</li> <li>▪ <i>Visit:</i> Patient sees physician monthly and as needed. Patient sees pharmacist for prescription refill.</li> <li>▪ <i>Communication:</i> Physician and pharmacist communicate about the prescription as needed.</li> </ul>	<ul style="list-style-type: none"> <li>▪ <i>Role:</i> Physician and pharmacist collaborate on patient’s care. Physician provides clinical guidance and/or coaching to pharmacist. Physician prescribes buprenorphine and determines dosage. Pharmacist conducts dose reconciliation and patient education, and monitors drug use, treatment safety and adverse events. Pharmacist checks PDMP* and dispenses buprenorphine. Pharmacist provides feedback to physician.</li> <li>• <i>Visit:</i> Patient sees pharmacist monthly and as needed. Patient sees physician as needed.</li> <li>▪ <i>Communication:</i> Physician and pharmacist communicate monthly or more frequently about patient’s progress.</li> </ul>
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\*PDMP: Prescription Drug Monitoring Program

A collaborative care model for people with OUD that involves buprenorphine-waivered physicians and community pharmacists appears to be feasible to operate in the U.S. and have high acceptability to patients.



# Research and Identify Best Practices for Recovery Support Services and Strategies to Sustain These Services

- Research Networks for the Study of Recovery Support Services for Persons Treated with Medications for Opioid Use Disorder
- NIDA supports a portfolio of research on infrastructure support to advance the development of efficacy and/or effectiveness research on recovery support services for people with opioid use disorder.

# Summary

- The overdose epidemic continues to evolve - increases in polysubstance use and opioid co-involvement with other drugs.
- Neuroscience has illuminated changes in brain networks and molecules that underlie addiction and serve as treatment targets.
- Opioid addiction is a chronic relapsing condition—but recovery is possible.
- Treatment systems need to address long-term needs.
- Science offers solutions – both shorter term and longer.