Improving Addiction Treatment Practices

Wilson Compton, Deputy Director
National Institute on Drug Abuse
40 Year Exponential Increases in U.S. Overdose Deaths

Drug Overdose Death Rate
U.S., 1968 to 2020

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^ Deaths in 2021—80,816 from Opioids*

^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

Evolution of Drivers of Overdose Deaths:

**Analgesics** → **Heroin** → **“Fentanyl”** → **Stimulants**

- **56,516** Synthetic Opioids Other Than Methadone (primarily illicit fentanyl)
- **41,643** Stimulants (e.g. cocaine & methamphetamines)
- **16,416** Natural and Semi-Synthetic Opioids and Methadone
- **13,165** Heroin

## Drug Overdose Deaths* Increased in 2021

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

*NCHS Provisional drug-involved overdose death counts are PREDICTED VALUES, 12 months ending in select months. [https://www.cdc.gov/nchs_nvss_vsrdrdrug_overdose_data.htm](https://www.cdc.gov/nchs_nvss_vsrdrdrug_overdose_data.htm)
Drug use engages systems in the motivation pathways of the brain.
Natural Rewards Elevate Dopamine Levels


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

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 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.

*Nonmedical Use*

**Estimated Prevalence of Dependence Among Users**

- Tobacco: 32%
- Alcohol: 15%
- Cannabis: 9%
- Cocaine: 17%
- Stimulant: 11%
- Analgesics: 8%
- Psychedelics: 5%
- Heroin: 23%

*Anthony et al. (1994) Experimental and Clinical Psycho Pharmacolog*
Universal Substance Use Prevention May Reduce Later Misuse of Opioids

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

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

Opioid addiction is a chronic relapsing condition.
The Likelihood of Sustaining Abstinence
Another Year Grows Over Time

After 1 to 3 years of abstinence, 2/3rds will make it another year.

After 4 years of abstinence, about 86% will make it another year.

Only a third of people with 1 to 12 months of abstinence will sustain it another year.

But even after 7 years of abstinence, about 14% relapse each year.

• Methadone
  ▪ MOR agonist

• Buprenorphine
  ▪ MOR partial agonist, KOR/DOR antagonist

• Naloxone
  ▪ MOR antagonist

• Naltrexone
  ▪ MOR antagonist

• Lofexidine
  ▪ α2 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**

**Relapse-free survival**

**ED-initiated Buprenorphine Increased TX Engagement**

Lee JD, et al. (2015) *Addiction*
Lee JD, et al. (2016) *NEJM*
Lee JD et al., (2018) *Lancet*
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
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 (t1/2 1.3–2.4 h) than fentanyl (t1/2 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.

Beetham, et al. (2021) Health Affairs
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
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.
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.