Drug Overdose Crisis in America

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40 Year Exponential Increases in U.S. Overdose Deaths

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

Evolution of Drivers of Overdose Deaths:

- **Stimulants** (e.g. cocaine & methamphetamines)
- **Heroin**
- **Synthetic Opioids Other Than Methadone (primarily illicit fentanyl)**
- **Natural and Semi-Synthetic Opioids and Methadone**
- **Fentanyl**

Virtually All U.S. Regions Have Increased Drug Overdoses

*But Rates Vary*

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

2003 2013 2020

### Drug Overdose Deaths* Continue to Increase

<table>
<thead>
<tr>
<th>Date</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>3/2021*</td>
<td>99,567</td>
<td>12,733</td>
<td>14,061</td>
<td>3,893</td>
<td>63,389</td>
<td>20,780</td>
<td>27,435</td>
</tr>
<tr>
<td>9/2021</td>
<td>105,654</td>
<td>10,227</td>
<td>14,023</td>
<td>3,733</td>
<td>68,880</td>
<td>23,127</td>
<td>31,647</td>
</tr>
<tr>
<td>3/2022*</td>
<td>109,247</td>
<td>8,328</td>
<td>13,376</td>
<td>3,527</td>
<td>73,473</td>
<td>25,959</td>
<td>33,994</td>
</tr>
<tr>
<td>Percent Change 3/21-3/22</td>
<td>9.7%</td>
<td>-34.6%</td>
<td>-4.9%</td>
<td>-9.4%</td>
<td>15.9%</td>
<td>24.9%</td>
<td>23.9%</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/vsrr/drug-overdose-data.htm](https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm)
Overdoses Before and During the COVID-19 Pandemic

Men aged 15-34

Rate per 100,000 population

Women aged 15-34

Rate per 100,000 population

Men aged 35-64

Rate per 100,000 population

Women aged 35-64

Rate per 100,000 population


Han et al., unpublished
Fentanyl-involved and Non-fentanyl Overdose Death Rates In US Youth Aged 15-19 Prior To and During The COVID Pandemic

Number of Pills Containing Fentanyl Seized by Law Enforcement in the United States, 2018 – 2021

Estimates based on data reported by the Office of National Drug Control Policy’s High Intensity Drug Trafficking Areas program

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.
Current strategy broadly focuses on drug overdose and specifically considers increase in methamphetamine harms.
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. R Spoth et al. (2013) American Journal of Public Health
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.
FDA-Approved Medications

Medications for Opioid Use Disorder Save Lives

Reduced Risk Overdose in Pregnant Women Given Medications for OUD

<table>
<thead>
<tr>
<th>Weeks of MOUD</th>
<th>Reduced Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>10</td>
<td>57%</td>
</tr>
<tr>
<td>20</td>
<td>82%</td>
</tr>
<tr>
<td>30</td>
<td>92%</td>
</tr>
<tr>
<td>40</td>
<td>97%</td>
</tr>
</tbody>
</table>

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**

![Bar graph showing relapse-free survival](image)

**Relapse-free survival**

- XR-NTX: 80%
- No Medication: 20%

**ED-initiated Buprenorphine Increased TX Engagement**

- Buprenorphine: 78%
- Referral: 37%
**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.
NIDA Research Pivots to Address Overdose Trends
Treating Overdose, Advancing Research on Fentanyl

• How do we reverse fentanyl overdose?
  ▪ Should naloxone doses be higher?
  ▪ Are long-acting formulations of naloxone needed?
  ▪ Are there other medications or medication combinations that would be more effective?

• What are appropriate detoxification strategies?

• How do we treat fentanyl addiction?
  ▪ In pregnancy and postpartum?

• How do we treat fentanyl involved neonatal abstinence syndrome?
Addressing Overdose Deaths in 2022

• Providing effective treatment to pain patients including the appropriate use of opioids when needed is necessary but not sufficient
• Treatment of Opioid Use Disorders is CRUCIAL but not sufficient
• Treatment of Substance Use Disorders in addition to OUD is now necessary to prevent overdose deaths
• Prevention of drug use including illicit prescription drug use is necessary to prevent overdoses