The Opioid Crisis in America: Trends, Progress and Challenges

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Director, National Institute on Drug Abuse
## Provisional Drug Overdose Deaths 12-months Ending in Select Months

<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><strong>8/2021</strong>*</td>
<td>104,038</td>
<td>10,488</td>
<td>13,970</td>
<td>3,708</td>
<td>67,624</td>
<td>22,571</td>
<td>30,876</td>
</tr>
<tr>
<td><strong>12/2021</strong>*</td>
<td>109,179</td>
<td>9,411</td>
<td>13,906</td>
<td>3,765</td>
<td>72,484</td>
<td>25,174</td>
<td>33,637</td>
</tr>
<tr>
<td><strong>8/2022</strong>*</td>
<td>107,477</td>
<td>6,863</td>
<td>12,272</td>
<td>3,357</td>
<td>73,102</td>
<td>26,786</td>
<td>33,534</td>
</tr>
<tr>
<td><strong>Percent Change</strong></td>
<td><strong>3.3%</strong></td>
<td><strong>-34.5%</strong></td>
<td><strong>-12.2%</strong></td>
<td><strong>-9.5%</strong></td>
<td><strong>8.1%</strong></td>
<td><strong>18.7%</strong></td>
<td><strong>8.6%</strong></td>
</tr>
<tr>
<td><strong>8/21-8/22</strong></td>
<td></td>
<td></td>
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</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)
Reduced Risk of Overdose in Pregnant Women Given Medications for OUD

Reduced Risk of Overdose

<table>
<thead>
<tr>
<th>10 weeks of MOUD</th>
<th>20 weeks of MOUD</th>
<th>30 weeks of MOUD</th>
<th>40 weeks of MOUD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>92</td>
<td>97</td>
</tr>
<tr>
<td></td>
<td></td>
<td>57</td>
<td></td>
</tr>
</tbody>
</table>

Jarlensti M et al., JAMA Network Open. 2022;5(4):e227964.
Drug Overdose Deaths: 2019–2020

Kariisa M et al., MMWR Morb Mortal Wkly Rep. 2022

NIDA Clinical Trials Network

Conducts rigorous, multisite clinical trials to determine effectiveness of treatment strategies in diverse clinical settings and populations

- Optimizing Retention MOUD
- Subthreshold OUD Trial
- ED-INNOVATION
- ER Buprenorphine for OUD
- Polysubstance Use Disorder
- Rural Initiative
- Telehealth for SUD

- 66 approved research protocols
- 12 multisite clinical trials: including MOUD trials
- National surveys: stigma, SUD services, state/local policies
- Simulation, predictive & geospatial modeling
- Pilot studies on emerging service delivery
- Diversity supplements

- Goal: Reduce opioid-related OD deaths 40%
- OD education and naloxone distribution
- Increase access/utilization MOUD
- Decrease high-risk prescribing

HEAL INITIATIVE
Build Evidence for OUD treatment in justice populations

Testing integration of EB prevention and treatment interventions in 67 communities in 4 states
Synthetics Are Now Linked to Almost 90% of Opioid Overdose Deaths

Ahmad FB, Rossen LM, Sutton P. Provisional drug overdose death counts. National Center for Health Statistics. 2022a
**Why are FENTANYL and analogues so dangerous?**

- **Potency:** fentanyl is ~50x more potent (mg/kg basis) than heroin; 2mg can be lethal.
- **Lack of pharmaceutical standards:** fentanyl doses used to lace other drugs vary (i.e., for counterfeit pills DEA reports that doses can range from .02 to 5.1 mg).
- **Fentanyl is more lipophilic than heroin; rapid brain penetration → faster onset** [reduced time for naloxone rescue].
- **Overdose reversals from fentanyl require higher and multiple naloxone doses.**
- **Physical dependence from fentanyl is stronger than for heroin making treatment initiation with medications for OUD more challenging.**
Therapeutic Developments to Address Overdose Crisis

- **Therapeutics for Overdoses**
  - Drug Sequestrants
  - Automatic reversals
  - Novel opioid antagonist
  - Respiration stimulators
  - Reversal polysubstance overdoses

- **Medications for OUD**
  - New formulations
  - Novel targets
  - Alternative outcomes: craving, sleep, SUD severity

- **Immunotherapies**
  - Vaccines
  - Antibodies

- **Neuromodulation**

- **Digital Therapeutics**

- **Combined Treatments**
  - Treatment of other substance use disorders, polysubstance UD, co-morbidities
Why have fentanyls supplanted other opioids and used to contaminate other drugs?

• Easier to produce than heroin (*no opium poppy cultivation*) – supply chain issues largely absent

• Synthesis is not complex (3-4 steps)

• More easily transported: 40 g fentanyl powder (Altoids tin) is equivalent to ~ 1 kg of heroin

• Fentanyl’s high potency makes allows drug dealers to mix with other illicit drugs (*heroin, cocaine and methamphetamine*), diluting them an increasing profits

• Profits much larger than for other illicit drugs including illicitly manufactured prescription pills (*Oxycontin, Vicodin, Aderall, benzodiazepines*) such that fentanyl
Fentanyl-involved and Non-fentanyl Overdose Death Rates In US Youth Aged 15-19 Prior To and During the COVID Pandemic

AQPC=10.7 (95% CI=9.3,12.1), $P<.0001$

AQPC=-2.7 (95% CI=-6.2, 0.8), $P=.13$

The number of adolescent years of life lost (YLL) to unintentional drug overdose in the US more than doubled from 2019 to 2020 after remaining relatively stable between 2016 and 2019.

Hermans, SP et al., J Adolescent Health 2022.
Evidence Based Prevention Strategies:

Target Reducing Risk and Increasing Protective Factors

**RISK**
- Early Aggressive Behavior
- Poor Social Skills
- Lack of Parental Supervision
- Substance Use
- Drug Availability
- Poverty

**PROTECTION**
- Self Control
- Parental Monitoring & Support
- Positive Relationships
- Academic Competence
- Anti-Drug Use Policies
- Strong Neighborhood

Individual
Family
Peer
School
Community
What Drives Vulnerability for Drug Use?

Social Determinants of Health

Adverse Childhood Experiences

<table>
<thead>
<tr>
<th>ABUSE</th>
<th>NEGLECT</th>
<th>HOUSEHOLD DYSFUNCTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>Physical</td>
<td>Mental Illness</td>
</tr>
<tr>
<td>Emotional</td>
<td>Emotional</td>
<td>Incarcerated Relative</td>
</tr>
<tr>
<td>Sexual</td>
<td></td>
<td>Mother treated violently</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Substance Abuse</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Divorce</td>
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</tbody>
</table>

ACE Score
N=8603

ACE account for one half to two third of serious problems with drug use

PEDIATRICS 111: 564-572, 2003
Brain Development and the Effects of ACE and Genetics

HEALthy Brain and Child Development (HBCD) Study

Longitudinal study to understand normative neurodevelopment from birth to 9-10 years and assess impact of in utero exposures to drugs and harmful environments.

Adolescent Brain Cognitive Development (ABCD) Study

Longitudinal study of about 10,000 children from ages 9-10 through early adulthood to assess factors that influence individual brain development trajectories and functional outcomes.

Correlation Between Brain Volumes and Maternal Social Disadvantage Factor

Effects of family income (FI) on cortical volume and cognitive performance.

JAMA Netw Open. 2022;5(4):e227045.

Tomasi and Volkow, Mol Psychiatry 2021
No opioid misuse → Opioid Misuse → Opioid Use Disorder → Received Treatment for OUD

9,500,000 2,500,000 278,000

Data Source: National Survey on Drug Use and Health

- social determinants of health, health equity, and policy,
- interventions that expand on scientific and technological advances
- implementation, scale-up and sustainment of prevention services

INFRASTRUCTURE NEEDED TO DEPLOY AND SUSTAIN PREVENTION
Multifaceted Approach is Needed to Address Overdose Deaths

- Addressing the needs of patients suffering pain
- Expanding the treatment of OUD 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 occasional illicit prescription drug use is now **necessary** to prevent overdoses.
- Need of **timely access to data** on drug overdoses and on emerging new drugs and drug mixtures (xylazine) at the regional level.
- Need to develop **antidotes from overdoses** including drug combinations
THANK YOU!
Major Barriers/Gaps

- Addressing **STIGMA**
- Need for **closing the treatment gap**
- Need for **prevention infrastructure**
- Need for **training of providers** to treat SUD
- **Inadequate reimbursement** for SUD treatment
- Persisting challenges for **medication development**
- Addressing **continuity of care** for SUD
- Addressing **justice setting populations**
Measures to define and detect Pre-Addiction

• This is a research need

• Meanwhile, DSM 5 diagnoses are reliable and easy to implement. Criteria for “Mild to Moderate” SUD are reasonable starting points for defining “pre-addiction”

Effective interventions for Pre-Addiction

• Treatments designed for severe SUD are usually inappropriate for mild cases.

• Payers support screening and 1-4 motivational counseling sessions, which are effective in reducing alcohol misuse. However, less data exists for other SUD. Also, more intensive interventions are likely needed for more severe symptoms.

• Need to develop pre-addiction interventions and test their effectiveness.

McLellan, Koob and Volkow (in press)