The Opioid Crisis in America: *Trends, Progress and Challenges*

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Provisional* Drug Overdose Deaths 12-months Ending in Select Months

	ALL DRUGS	HEROIN	NAT & SEMI SYNTHETIC	METHADONE	SYNTHETIC OPIOIDS (mainly illicit fentanyl)	COCAINE	OTHER PSYCHO- STIMULANTS (mainly meth)
8/2021*	104,038	10,488	13,970	3,708	67,624	22,571	30,876
12/2021*	109,179	9,411	13,906	3,765	72,484	25,174	33,637
8/2022*	107,477	6,863	12,272	3,357	73,102	26,786	33,534
Percent Change 8/21-8/22	3.3%	-34.5%	-12.2%	-9.5%	8.1%	18.7%	8.6%

*NCHS Provisional drug-involved overdose death counts are <u>PREDICTED VALUES</u>, 12 months ending in select months. <u>https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm</u> MEDICATIONS FOR OPIOID USE DISORDER SAVE LIVES

SCIENCES · ENGINEERING · MEDICINE

FDA-Approved Medications



Reduced Risk of Overdose in Pregnant Women Given Medications for OUD



Jarlenski M et al., JAMA Network Open. 2022;5(4):e227964.

NIDA Clinical Trials Network



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



Testing integration of EB prevention and treatment interventions in 67 communities in 4 states

- **Optimizing Retention MOUD** ٠
- Subthreshold OUD Trial
- **ED-INNOVATION** •
- **ER Buprenorphine for OUD** ٠
- 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 ٠ OD deaths 40%
- OD education and naloxone distribution
- Increase access/utilization MOUD
- Decrease high-risk prescribing

Drug Overdose Deaths: 2019-2020



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

Synthetics Are Now Linked to Almost 90% of Opioid Overdose Deaths



Cocaine (T40.5)	Psychostimulants with abuse potential (T43.6)	Reported Value
Heroin (T40.1)	Synthetic opioids, excl. methadone (T40.4)	O Predicted Value
Methadone (T40.3)		O Tredicted Value
Natural & semi-synthetic opioids (T40.2)		
Opioids (T40.0-T40.4,T40.6)		

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)
- Fentanyls are 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

Automatic naloxone autoinjector



Neuromodulation Techniques



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 overdose death rate, overall

mon-fentanyl drug overdose death rate, overall

National Vital Statistics System multiple-cause-of-death 2015-2020 final and 2021 provisional data U.S. census monthly data. II: Joinpoints indicate significant changes in nonlinear trends using Bayesian Information Criterion. AQPC=average quarter percentage change during 2015 Q1-2022 Q2. ICD-10 cause of death code: synthetic opioids other than methadone (T40.4, primarily fentanyl and analogs).

Years of Life Lost (YLL) to Unintentional Drug Overdose Rapidly Rising in the Adolescent Population, 2016-2020





The number of adolescent 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



What Drives Vulnerability for Drug Use?

Social Determinants of Health



Adverse Childhood Experiences

Sexual



Divorce



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

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

Correlation Between Brain Volumes and Maternal Social Disadvantage Factor



A Cortical Volume Discovery Fl -log10(p) 3 95 R



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

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

Tomasi and Volkow, Mol Psychiatry 2021



- 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

PREVENTION: Pre-Addiction (SBI Renamed)

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.