Wilson M. Compton, M.D., M.P.E.
Deputy Director
National Institute on Drug Abuse
Increased Drug **Overdose** Death Rates
Estimated Age-adjusted Death Rates per 100,000 for Drug Poisoning by County.

67,367 Deaths in 2018
46,802 from Opioids (Prescription and Illicit)
Evolution of Drivers of Overdose Deaths:

Evolution of Drivers of Overdose Deaths:

**Analgesics**

Evolution of Drivers of Overdose Deaths:

Analgesics ➔ Heroin

See: Compton WM & Jones CM, Ann NY Acad Sci, 2019;
Updated for 2018 from WONDER Database and Hedegaard et al. NCHS Data Brief, no 356. January, 2020
Evolution of Drivers of Overdose Deaths:

Analgesics ➔ Heroin ➔ “Fentanyl”

**Direct and Indirect Pathways** from Prescriptions to Misuse

- People misusing analgesics **Directly & Indirectly** obtain them by prescription

**Source where pain relievers obtained for most recent misuse**

- Prescription: 87%
- Friend/Relative: 54%
- Other: 10%

Source: Han, Compton, et al. Annals of Internal Medicine 2017
ECONOMICS: Heroin Increases Due to Lower Price

"Retail" Price Per Pure Gram

ECONOMICS: Heroin Increases Due to Lower Price and Greater Availability

**ECONOMICS:**

Cheap Fentanyl Precursor Chemicals

Criminal Chemistry
Traffickers manufacturing fentanyl often purchase the key ingredient from China, which doesn't regulate its sale. Here's how the chemical building blocks become a highly profitable street drug.

The key ingredient is NPP, 25 grams of which can be bought from China for about $87.

NPP can be combined with about $720 of other chemicals to produce fentanyl.

The resulting 25 grams of fentanyl cost about $810 to produce... and are equivalent to up to $800,000 of pills on the black market.

*Average current price from Chinese suppliers

†Prices from U.S. suppliers

Sources: NES Inc.; Drug Enforcement Administration; Calgary Police

THE WALL STREET JOURNAL.
Methamphetamine (and other stimulants): An Emerging Issue

Heroin and Methamphetamine Treatment Admissions in the U.S.

Jones, Underwood, Compton Addiction 2019
Evolution of Drivers of Overdose Deaths:

Analgesics → Heroin → “Fentanyl” → Stimulants

OVERDOSE DEATHS BY DRUG (CDC, August 2020)

12 MONTH-ENDING PROVISIONAL NUMBER OF DRUG OVERDOSE DEATHS BY DRUG OR DRUG CLASS, UNITED STATES

- National provisional estimates include deaths occurring within the 50 states and the District of Columbia
- All 50 states reported and of year final data through 2019.
<table>
<thead>
<tr>
<th></th>
<th>ALL DRUGS</th>
<th>HEROIN</th>
<th>NAT &amp; SEMI – SYNTHETIC</th>
<th>METHADONE</th>
<th>SYNTHETIC OPIOIDS</th>
<th>COCAINE</th>
<th>OTHER PSYCHO-STIMULANTS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>JANUARY 2019</strong> *</td>
<td>68,211</td>
<td>15,205</td>
<td>12,566</td>
<td>3,058</td>
<td>31,961</td>
<td>14,876</td>
<td>13,323</td>
</tr>
<tr>
<td><strong>JANUARY 2020</strong> *</td>
<td>72,707</td>
<td>14,144</td>
<td>12,075</td>
<td>2,789</td>
<td>38,015</td>
<td>16,496</td>
<td>16,854</td>
</tr>
<tr>
<td><strong>Change</strong></td>
<td><strong>6.59%</strong></td>
<td><strong>-6.98%</strong></td>
<td><strong>-3.91%</strong></td>
<td><strong>-8.80%</strong></td>
<td><strong>18.94%</strong></td>
<td><strong>10.89%</strong></td>
<td><strong>20.95%</strong></td>
</tr>
</tbody>
</table>
COVID-19 AND OVERDOSE ANALYSIS: ODMAP

- 61% of ODMAP participating counties reported an increase in overdoses after stay-at-home orders issued.
- There was a 17.59% total increase in that timeframe.

Polydrug Use is Common: Other Substance Use Among Past Year Opioid Misusers Aged 18+ (NSDUH, 2018)

Among Adults Aged 18+ in the Past Year

Among Past Year Opioid Misusers Aged 18+

- Opioids: 3.8%
- Heavy Alcohol (PM): 16.9%
- Cigarettes: 52.1%
- Marijuana: 49.4%
- Cocaine: 16.7%
- Methamphetamine: 3.3%
National Drug Overdose Deaths Involving Prescription Opioids, Number Among All Ages, 1999-2018

- Prescription Opioids
- Prescription Opioids Without Other Synthetic Narcotics
- Prescription Opioids and Other Synthetic Narcotics

Graph showing the increase in national drug overdose deaths involving prescription opioids from 1999 to 2018.
Percent of Synthetic Opioid-Related Overdose Deaths Involving Illicit or Psychotherapeutic Drugs or Alcohol, United States, 2016

- Other drug or alcohol (n=15,472)
- Other opioids (n=9,299)
- Heroin (n=5,781)
- Cocaine (n=4,184)
- Prescription opioids (n=4,055)
- Benzodiazepines (n=3,308)
- Alcohol (n=2,150)
- Psychostimulants (n=1,042)
- Antidepressants (n=1,002)
- Antipsychotics (n=385)
- Other illicit drugs (n=144)
- Barbiturates (n=88)

Source: CM Jones, EB Einstein, WM Compton *JAMA* 2018;319(17):1819-1821.
### Benzodiazepine Use Among U.S. Adults: Correlates with Opioids

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Adults with Benzodiazepine Use Weighted % (SE)</th>
<th>Adults without Benzodiazepine Use Weighted % (SE)</th>
<th>Benzodiazepine Use vs. No Use OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Rx opioid</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PY use disorders</td>
<td>60.4 (2.27)</td>
<td>39.6 (2.27)</td>
<td><em>27.7</em></td>
</tr>
<tr>
<td>PY misuse only</td>
<td>36.1 (0.99)</td>
<td>63.9 (0.99)</td>
<td><em>10.2</em></td>
</tr>
<tr>
<td>PY use, lifetime misuse</td>
<td>30.6 (1.25)</td>
<td>69.4 (1.25)</td>
<td><em>8.0</em></td>
</tr>
<tr>
<td>PY use, no lifetime misuse</td>
<td>18.9 (0.34)</td>
<td>81.1 (0.34)</td>
<td><em>4.2</em></td>
</tr>
<tr>
<td>LT use, no PY use</td>
<td>9.0 (0.25)</td>
<td>91.0 (0.25)</td>
<td><em>1.8</em></td>
</tr>
<tr>
<td>Never use+</td>
<td>5.2 (0.17)</td>
<td>94.8 (0.17)</td>
<td><em>1.0</em></td>
</tr>
<tr>
<td><strong>Heroin</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PY heroin use or disorders</td>
<td>60.5 (3.21)</td>
<td>39.5 (3.21)</td>
<td><em>11.2</em></td>
</tr>
<tr>
<td>LT use, no PY use</td>
<td>28.9 (1.67)</td>
<td>71.1 (1.67)</td>
<td><em>3.0</em></td>
</tr>
<tr>
<td>Never heroin use+</td>
<td>12.0 (0.15)</td>
<td>88.0 (0.15)</td>
<td><em>1.0</em></td>
</tr>
</tbody>
</table>

Prescribed Benzodiazepines, OD Deaths and Buprenorphine Discontinuation among People Receiving Buprenorphine Treatment

a. Fatal opioid overdose**

b. Non-fatal opioid overdose**

c. All-cause mortality**

d. Buprenorphine discontinuation

*Adjusted for sex, age, race, Medicaid receipt, diagnosis of depressive disorder, anxiety disorder, bipolar/psychotic disorder, SSRI receipt, time-varying buprenorphine dose, and recent hospital-based mental health encounter (Supplement Table 2 shows full model results).

**Note truncated y-axis for fatal overdose, non-fatal opioid overdose, and all-cause mortality.

***Denotes number of buprenorphine treatment episodes
17% of pregnant women are prescribed an opioid during pregnancy.

Rising rates of HCV

Acute Cases of HCV in USA
Zibbell et al.
*Am J Public Health* 2018;108:175-181

HIV (and Hepatitis C) Outbreak Linked to Oxymorphone Injection Use in Indiana, 2015
Peters et al.

Counties Deemed Highly Vulnerable to Rapid Dissemination of HCV or HIV

Source: Van Handel et al, JAIDS 2016
Injection of Rx opioids (and attendant crushing, cooking, and injection practices) are associated with:

– Scarring
– Abscesses and cutaneous infections
– Endocarditis
– Thrombotic microangiopathies

HHS Five-Point Opioid Strategy

1. Better addiction prevention, treatment, and recovery services
2. Better data
3. Better pain management
4. Better targeting of overdose reversing drugs
5. Better research
Doctors Continue to Prescribe Opioids for Ninety-one Percent of Overdose Patients

In a 2-year follow-up of 2848 commercially insured patients who had a nonfatal opioid overdose during long-term opioid therapy:

- 63% of high-dose opioid pts still on high dose 31-90 days after OD
- 17% of high-dose patients overdosed again within two years
- 33-39% of those with active opioid prescriptions during follow-up also were prescribed benzodiazepines.

Solutions toward **Responsible Prescribing**: Guidance

**Opioid Prescribing Guidelines** March 2016

- Intended for primary care providers
- Applies to patients >18 years old in chronic pain outside of end-of-life care
- **Focuses on:**
  - Determining when to initiate or continue opioids for chronic pain
  - Opioid selection, dosage, duration, follow-up and discontinuation
  - Assessing risk and addressing harms of opioid use

---

**JAMA**

Dowell, Compton, Giroir.
2019;322(19):1855–1856

**Patient-Centered Reduction or Discontinuation of Long-term Opioid Analgesics:**

**The HHS Guide for Clinicians**

**Focuses on:**

1. Criteria for reducing or discontinuing opioid therapy
2. Considerations prior to deciding to taper opioids
3. Ensuring patient safety prior to initiating taper
4. Shared decision-making with patients
5. Rate of opioid taper
6. Opioid withdrawal management
7. Behavioral health support
8. Challenges to tapering

*Dosage changes, particularly rapid reductions in dose, can harm patients or put them at risk if not made in a thoughtful, deliberative, collaborative, and measured manner.*
State Policy, Practice and Legal Changes Appear to Help: FL and WA Examples of State Efforts to Address Opioid Analgesic Overdose

Florida Prescription-Related OD Deaths 2003-2012

Washington Prescription Opioids OD Deaths and Hospitalizations 1995-2012


Franklin et al. AJPH 2015;105(3):463-469
Universal Drug Use Prevention:
Three studies suggest impact of universal prevention on Rx drug misuse

In this study, for 100 young adults in general population starting Rx misuse, 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
Universal Drug Use Prevention:
Three studies suggest impact of universal prevention on Rx drug misuse

Targeting Youth to Prevent Later Substance Use Disorder: An Underutilized Response to the US Opioid Crisis
Compton WM, Jones CM, Baldwin GT, Harding FM, Blanco C, Wargo EM

In this study, for 100 young adults in general population starting Rx misuse, 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
Naloxone Distribution

Direct intervention to save lives:
Nasal spray and Auto-injector formulations

April 5, 2018
Surgeon General’s Advisory on Naloxone and Opioid Overdose

I, Surgeon General of the United States Public Health Service, VADM Jerome Adams, am emphasizing the importance of the overdose-reversing drug naloxone. For patients currently taking high doses of opioids as prescribed for pain, individuals misusing prescription opioids, individuals using illicit opioids such as heroin or fentanyl, health care practitioners, family and friends of people who have an opioid use disorder, and community members who come into contact with people at risk for opioid overdose, knowing how to use naloxone and keeping it within reach can save a life.

BE PREPARED. GET NALOXONE. SAVE A LIFE.
Medication Assisted Treatment (MAT)

- **DECREASES:**
  - Opioid use
  - Opioid-related overdose deaths
  - Criminal activity
  - Infectious disease transmission

- **INCREASES**
  - Social functioning
  - Retention in treatment
Medication Assisted Treatment (MAT)

Opioid Treatment “Cascade of Care”

- **DECREASES:**
  - Opioid use
  - Opioid-related overdose deaths
  - Criminal activity
  - Infectious disease transmission

- **INCREASES**
  - Social functioning
  - Retention in treatment

But MAT is highly underutilized!
Relapse rates are very high!

Williams, Nunes, Bisaga, Levin  *Am J Drug Alcohol Abuse* 2019
Medication Assisted Treatment (MAT) (Opioid Effect)

- **Full Agonist**
  - Methadone: Daily Dosing

- **Partial Agonist**
  - Buprenorphine: 3-4X week

- **Antagonist**
  - Naltrexone: ER 1 month

**Log Dose**

- **DECREASES:**
  - Opioid use
  - Opioid-related overdose deaths
  - Criminal activity
  - Infectious disease transmission

- **INCREASES**
  - Social functioning
  - Retention in treatment

**But MAT is highly underutilized!**

**Relapse rates are very high!**
Enhancing Pain Management

- Advance Effective Treatments for Pain Through Clinical Research
- Accelerate Discovery and Development of Pain Treatments
- Expand Therapeutic Options
- Enhance Treatments for Infants with NAS/NOWS
- Develop New and Improved Prevention & Treatment Strategies
- Optimize Effective Treatments
1. Biology and Chemistry of Pain and Opioid Addiction
2. Non-Biological Contributors to Opioid Addiction
3. Pain Management
4. Prevention of Opioid Addiction
5. Treatment of Opioid Addiction and Sustaining Recovery
6. Overdose Prevention and Reversal
7. Community Consequences of Opioid Addiction
8. Opportunities for Enhanced Coordination

Summary:

- The opioid crisis remains driven by illicit fentanyl, as stimulant overdose deaths are also rising
- Evidence-based prescribing practices and mitigation of co-occurring conditions are required to reduce harms
- Prevention interventions, naloxone distribution, and medication treatment are key to addressing the opioid crisis
- **Ongoing research will build future solutions**

[www.drugabuse.gov](http://www.drugabuse.gov)


*Science = Solutions*