The Other Opioid Crisis: Heroin and Fentanyl

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Disclosures

- Nothing to disclose
Learning Objectives

- Describe the opioid overdose crisis in the United States today
- Discuss common beliefs and inconsistencies about the role of prescription opioids in the opioid crisis
- Identify the intersection of illicit drug use and clinical pain practice in today’s “opioid epidemic”
- Provide clinically relevant recommendations for navigating the current landscape without depriving pain care to patients in need

Is There More Than One Opioid Crisis?
The Facts: No Lack of Media Attention
The Facts

- People are dying...
- People are angry and reacting
- People are scared
- Overdoses from drugs (ALL drugs, legally prescribed or not) including opioids, hallucinogens, cocaine, etc.
  - ~ 64,000 deaths nationwide in 2016
  - ↑21% from 2015
  - More than 42,000 (66%) involved some type of opioid

Identifying drugs in overdose deaths

<table>
<thead>
<tr>
<th>State</th>
<th>All Deaths</th>
<th>Cases in Which No Drug Was Specified</th>
</tr>
</thead>
<tbody>
<tr>
<td>Louisiana</td>
<td>300</td>
<td>158</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>4,027</td>
<td>1,078</td>
</tr>
<tr>
<td>Alabama</td>
<td>798</td>
<td>620</td>
</tr>
<tr>
<td>Montana</td>
<td>118</td>
<td>64</td>
</tr>
<tr>
<td>Indiana</td>
<td>2,026</td>
<td>877</td>
</tr>
<tr>
<td>Delaware</td>
<td>392</td>
<td>329</td>
</tr>
<tr>
<td>Nevada</td>
<td>120</td>
<td>57</td>
</tr>
<tr>
<td>Kentucky</td>
<td>401</td>
<td>119</td>
</tr>
<tr>
<td>Florida</td>
<td>4,728</td>
<td>1,344</td>
</tr>
<tr>
<td>Utah</td>
<td>247</td>
<td>154</td>
</tr>
<tr>
<td>New Jersey</td>
<td>2,050</td>
<td>773</td>
</tr>
<tr>
<td>Mississippi</td>
<td>352</td>
<td>262</td>
</tr>
<tr>
<td>Wyoming</td>
<td>99</td>
<td>113</td>
</tr>
<tr>
<td>California</td>
<td>4,604</td>
<td>1,006</td>
</tr>
<tr>
<td>Arkansas</td>
<td>401</td>
<td>119</td>
</tr>
<tr>
<td>Idaho</td>
<td>198</td>
<td>123</td>
</tr>
<tr>
<td>North Carolina</td>
<td>27</td>
<td>17</td>
</tr>
<tr>
<td>Arizona</td>
<td>1,502</td>
<td>198</td>
</tr>
</tbody>
</table>

There is more than one opioid crisis. To better tackle the epidemic, Kentucky needed to know which drugs were causing lethal overdoses. By Kathryn Casteel. Published Jan. 17, 2018. https://fivethirtyeight.com/features/there-is-more-than-one-opioid-crisis/. Accessed January 18, 2018.

The Facts

- Drug(s) responsible may be unknown
  - Overdose is usually about RESPIRATORY DEPRESSION
- Sometimes causes are not reported
  - May depend on the state
  - Trends can be difficult to identify
- This may lead to a lack of focus
The Facts: Kentucky as an Example

The most common drugs found in Kentucky’s overdose victims
Based on an analysis of 1,471 drug overdose deaths in 2016

<table>
<thead>
<tr>
<th>Individual drugs</th>
<th>Two-drug combinations</th>
<th>Three-drug combinations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug</td>
<td>Share</td>
<td>Drug</td>
</tr>
<tr>
<td>Morphine</td>
<td>45.4%</td>
<td>Heroin, morphine</td>
</tr>
<tr>
<td>Fentanyl</td>
<td>31.0%</td>
<td>Feentany, morphine</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>32.8%</td>
<td>Codeine, morphine</td>
</tr>
<tr>
<td>Alprazolam</td>
<td>25.5%</td>
<td>Heroin, codeine</td>
</tr>
<tr>
<td>THCCOOH</td>
<td>24.9%</td>
<td>Morphine, THCCOOH</td>
</tr>
<tr>
<td>Heroin</td>
<td>24.7%</td>
<td>Alprazolam, morphine</td>
</tr>
<tr>
<td>Codeine</td>
<td>26.7%</td>
<td>Methamphetamine, amphetamine</td>
</tr>
<tr>
<td>Ethanol</td>
<td>18.4%</td>
<td>Heroin, fentanyl</td>
</tr>
<tr>
<td>Oxycodone</td>
<td>17.2%</td>
<td>Oxycodone, oxymorphone</td>
</tr>
<tr>
<td>Methamphetamine</td>
<td>17.1%</td>
<td></td>
</tr>
</tbody>
</table>

In cases in which multiple drugs are detected, every individual drug — as well as every two- and three-drug combination — is counted separately.

Pain Week

There is More Than One Opioid Crisis. To better tackle the epidemic, Kentucky needed to know which drugs were causing lethal overdoses. By Kathryn Casteel

The Denver Post

Colorado's opioid and heroin overdose deaths outnumbered homicides in 2015
Opiate deaths are catching up to alcohol-related liver disease deaths

By JOHN INGOLD | jingold@denverpost.com | The Denver Post
PUBLISHED: January 3, 2017 at 11:15 am | UPDATED: October 21, 2017 at 12:39 pm

Drug poisoning deaths in Colorado
Opiates | Cocaine | All Drug Poisoning

Deaths in Colorado from opiate drugs vs. motor vehicle accidents
- All opiates (including fentanyl and heroin)
- Motor vehicle injuries

Data: Colorado Department of Public Health and Environment
The Facts

Colorado’s opioid and heroin overdose deaths outnumbered homicides in 2015

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The Facts

Natural = prescription opioids

Deaths in Colorado from "natural" prescription opioids vs. homicides

- Natural prescription opioids
- Homicide

Made with Chartbuilder
Data: Colorado Department of Public Health and Environment

The Denver Post
POLITICS	COLORADO POLITICS
Here’s how Colorado is combating the prescription opioid and heroin epidemic

Colorado is exploring opioid prescription limits, prescriber report cards and new treatment options.

By JOHN FRANK | jfrank@denverpost.com | The Denver Post
PUBLISHED: November 5, 2017 at 12:01 am | UPDATED: November 6, 2017 at 11:02 am

The nation’s drug epidemic kills someone in Colorado about every 9 hours and 36 minutes, a fact that rings like a siren for state leaders who are combating the leading driver: prescription and illicit opioids.

The most alarming trend is the rate of heroin deaths. The number of overdoses caused by heroin, an opioid, continues to skyrocket, contributing to 228 deaths last year, compared with just 79 five years earlier, according to state figures.
**The Facts**

- "The state tracks opioid prescriptions, but doctors aren't required to check the database"
- "The vast majority of states require clinicians to check the Prescription Drug Monitoring Program (PDMP) database before writing most opioid prescriptions"

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A crackdown on overprescribing isn't enough — drug treatment options remain a challenge.

According to policymakers, Colorado's initial efforts to restrict opioid prescriptions may have an unintended effect: pushing addicts to opioids such as heroin or fentanyl. The trend is spotlighting the limited treatment options for drug users who want help.

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The Facts

- “The idea is that prescribers might be prescribing more than average for their particular specialty”
- “They’ll say ‘Oh, I better look at things more closely!’”
- “What we are hoping to see is a change in prescriber behavior”

Colorado opioid-related deaths

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 to 19 years</td>
<td>Male: 11.3</td>
</tr>
<tr>
<td></td>
<td>Female: 6.3</td>
</tr>
<tr>
<td>20 to 24 years</td>
<td>Male: 12.0</td>
</tr>
<tr>
<td></td>
<td>Female: 12.5</td>
</tr>
<tr>
<td>25 to 34 years</td>
<td>Male: 16.3</td>
</tr>
<tr>
<td></td>
<td>Female: 15.2</td>
</tr>
<tr>
<td>35 to 44 years</td>
<td>Male: 15.5</td>
</tr>
<tr>
<td></td>
<td>Female: 15.1</td>
</tr>
<tr>
<td>45 to 64 years</td>
<td>Male: 12.6</td>
</tr>
<tr>
<td></td>
<td>Female: 12.5</td>
</tr>
<tr>
<td>65+ years</td>
<td>Male: 9.6</td>
</tr>
<tr>
<td></td>
<td>Female: 9.2</td>
</tr>
</tbody>
</table>

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IMPORTANT SOCIETAL QUESTIONS
Is the Current Climate Living up to Promises Made in the Past?
Does the chronic pain patient still have rights?

Is this a problem about chronic pain patients abusing prescription pain medications?

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The Clinical Implications

Now, across Colorado and the rest of the nation, these policies intended to address opioid abuse have unexpectedly harmed patients who depend on the drugs to treat chronic conditions, pain specialists and patient advocates say. The policies are supposed to offer guidance — helpful advice to doctors to be cautious in prescribing more than a certain amount of opioids to any one patient.

Officials at the Colorado Department of Regulatory Agencies are looking at revising the guidelines. The Colorado Consortium for Prescription Drug Abuse Prevention, a group of medical and drug experts, is also working on ideas to protect pain patients while cracking down on opioid abuse.
The Facts

Drug overdose deaths in the United States continue to increase in 2015

- The majority of drug overdose deaths involve an opioid
- Since 1999 the # of overdose deaths quadrupled
  - Prescription opioids
  - Heroin
- 91 Americans die every day from an opioid overdose

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Heroin use is trending up

- From 2002-2013, past month/year heroin use and addiction have all increased among 18-25 year olds
- Among new heroin users, 75% report abusing prescription opioids prior to using heroin
- Heroin-related deaths more than tripled from 2010-2015
  - The largest increase was for those heroin-related deaths involving synthetic opioids: FENTANYL

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The Facts: Times are Changing

- Characteristics of opioid drug overdoses:
  - Fast
  - Deadly
  - Scary
  - Socioeconomic status – neutral
  - Abuse-history – neutral
  - Increasing exponentially

The Clinical Implications

- Improved opioid prescribing
- Expanded access to substance abuse treatment
- Naloxone
- Prescription Drug Monitoring Programs (PDMPs)
- State-level strategies to prevent high risk prescribing and opioid overdoses
- Improved detection of illegal opioid use by law enforcement
The Facts

- Opioids (prescription and illicit) are main drivers
- 5 highest states:
  - West Virginia
  - Ohio
  - New Hampshire
  - Pennsylvania
  - Kentucky

The “Other” Epidemic
Heroin

- Highly addictive
- It is an opioid
- Made from morphine
  - ~3 times more potent
- A natural substance
  - Extracted from the opium poppy plant
    - Asia
    - Mexico
    - Colombia

The Facts

- Heroin use has been increasing¹
  - Men
  - Women
  - Most age groups
  - All income levels
- Past misuse/abuse of prescription opioids is the strongest risk factor for starting heroin²

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² Compton WM, Jones CM, and Baldwin GT. Understanding the Relationship between Prescription Opioid and Heroin Abuse. NEJM

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The Heroin Epidemic

Heroin use is part of a larger substance abuse problem.

Nearly all people who used heroin also used at least 1 other drug.

Most used at least 3 other drugs.

Heroin is a highly addictive opioid drug with a high risk of overdose and death for users.

People who are addicted to...

- Alcohol
- Marijuana
- Cocaine
- RX Opioid Painkillers

are

2x
3x
15x
40x

...more likely to be addicted to heroin.


Heroin Addiction and Overdose Deaths are Climbing

286% Increase

Heroin-Related Overdose Deaths (per 100,000 people)

Year

2002
2004
2006
2008
2010
2012
2013

Rate

0
1
2
3

National Institute on Drug Abuse

Research Report Series

"The relationship between prescription opioid abuse and increases in heroin use in the US is under scrutiny. These substances are all part of the same opioid drug category and overlap in important ways"

The Facts

- “Current” ~ 2013-2015 research regarding prescription opioids and heroin shows:
  - Prescription opioid abuse is a risk factor for heroin use
  - Heroin use is rare in prescription drug abusers (<4% start within 5 years)
  - Although similar effects, risk factors are different
  - A subset of people who abuse prescription opioids may progress to heroin use
  - Availability of drug(s) is associated with increased use and overdose
  - Heroin use is driven by cost advantage and availability
  - Emphasis is needed on prevention and treatment


And...

- “Analyses suggest that those who transition to heroin use tend to be frequent users of multiple substances (polydrug users)”

A + B ≠ C

Recommendations that impact us:
- Screen and identify high-risk individuals
- Treat people with substance abuse disorders
- Naloxone

The Clinical Implications

Responding to the Heroin Epidemic

- **PREVENT** People From Starting Heroin
  - Reduce prescription opioid painkiller abuse.
  - Improve opioid painkiller prescribing practices and identify high-risk individuals early.

- **REDUCE** Heroin Addiction
  - Ensure access to Medication-Assisted Treatment (MAT).
  - Treat people addicted to heroin or prescription opioid painkillers with MAT which combines the use of medications (methadone, buprenorphine, or naltrexone) with counseling and behavioral therapies.

- **REVERSE** Heroin Overdose
  - Expand the use of naloxone. Naloxone is a life-saving drug that can reverse the effects of an opioid overdose when administered at home.

The Facts – The “F” Word

- **Fentanyl**
  - Originally developed as an anesthetic
  - One of the safest opioids
  - High LD50/ED50 ratio
  - More potent than morphine
    - 100 times more potent
  - More potent than heroin
    - 20-50 times more potent
  - NOT NEW

Fentanyl is a synthetic opioid approved for treating severe pain, such as advanced cancer pain. Illicitly manufactured fentanyl is the main driver of recent increases in synthetic opioid deaths.
Case 1

- 42-year-old Hispanic male
  - Addicted to heroin
  - Comes to the same street corner every day to buy heroin
    - First dose usually free
  - He’s actually buying heroin laced with fentanyl
  - “It’s a new epidemic” he says
  - “If you catch a bag of pure fentanyl, that Narcan ain’t bringing you back”
  - “I just watched my friend die from fentanyl”

Heroin and Fentanyl: A “Perfect” Pair

- The overwhelming majority of the time fentanyl is paired with heroin
- To get a better “high”
- “Better” economic profile
Fentanyl

- Drug seizures involving fentanyl are going up dramatically

**The Facts**

Drug seizures containing fentanyl

![Graph showing drug seizures involving fentanyl]

Source: DEA, National Forensic Laboratory Information System


Defined geographic distribution

**The Facts**

Figure 2 NFLIS regional trends in fentanyl reported per 100,000 persons aged 15 or older, January 2001–December 2015

Note: U.S. census 2015 population data by age were not available for this publication. Population data for 2015 were imputed. A dashed trend line indicates that estimates did not meet the criteria for precision or reliability, including the 2002 estimate in the West and the 2001 estimate in the Northeast.
The Chinese Connection Fueling America’s Fentanyl Crisis

A vast network beginning in China feeds fentanyl, a deadly synthetic opioid, to the U.S., Mexico and Canada.

By JEANNE WHALEN and BRIAN SPEEGLE
Updated June 23, 2016 1:44 a.m. ET

Criminal Chemistry
Traffic cops 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 $570.

NPP can be combined with about 570 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.

Terminology

- A very small amount of fentanyl is potentially fatal
- This applies to licit or illicit fentanyl
  - Illicitly manufactured fentanyl is likely no more dangerous than legally manufactured fentanyl
- Fentanyl label:
  - FENTANYL CITRATE SHOULD BE ADMINISTERED ONLY BY PERSONS SPECIFICALLY TRAINED IN THE USE OF INTRAVENOUS ANESTHETICS AND MANAGEMENT OF THE RESPIRATORY EFFECTS OF POTENT OPIOIDS
  - AN OPIOID ANTAGONIST, RESUSCITATIVE AND INTUBATION EQUIPMENT AND OXYGEN SHOULD BE READILY AVAILABLE
  - Fentanyl may cause muscle rigidity, particularly involving the muscles of respiration
  - DIMINISHED SENSITIVITY TO CO2 STIMULATION MAY PERSIST LONGER THAN DEPRESSION OF RESPIRATORY RATE

The Facts

- Fentanyl can be manufactured anywhere
  - Synthetic
- N-Phenethyl-4-piperidinone is NPP
  - Intermediate precursor to fentanyl
- It is cheap
- It is not going anywhere
A Fentanyl Crisis

In 24 of the nation’s largest cities, fatal fentanyl-related overdoses increased 600% from 2014-2016.
Different Types of Fentanyl and Presentations

- Different formulations and varying potencies:
  - Fentanyl
  - Analogs
    - Acetyl fentanyl
    - Ocfentanil
    - Carfentanyl
    - Remifentanil
    - Alfentanyl
    - Sufentanyl
    - Furanylfentanyl

- Presentations
  - Powder
  - Counterfeit pills
  - Etc.

Carfentanyl

- Synthetic
- Large animal anesthetic
- 100 times more potent than fentanyl
- 10,000 times more potent than morphine
- Airborne/skin exposure often fatal
  - 2012 Moscow Theater Hostage Crisis

The Facts

The Washington Post

Elephant tranquilizer is the latest lethal addition to the heroin epidemic

By Lynh Bui and Peter Hermann

April 26, 2017

Members of the Royal Canadian Mounted Police go through a decommissioning procedure of carfentanyl. (The Canadian Press)
The Facts

- Fentanyl in the wrong hands is deadly
- Potentially contributing significantly to overdose/fatal overdose risk
- Analogs not often tested for in routine toxicology testing
- Naloxone is a bridge to survival but not a final solution
  - Re-narcotization from fentanyl is common
  - CO₂ will persist
  - Diminished hypoxic drive may persist

SUMMARY
The Co-Existing Opioid Crises

The Facts

- Significant controversy exists to the relationship between prescription opioids and the heroin/fentanyl epidemic
  - Tracking back to prescribers
    - The 1990s when opioid prescribing increased
    - Pain being designated as the “fifth vital sign” in 2000
    - Pain Bill of Rights
    - Evolution of “pill mills”
  - Related to cost and availability
    - Heroin and fentanyl are cheaper and stronger
Case 2

• 26-year-old white female
  – Has 2 children ages 4 & 7 who live with their godmother
  – Became addicted to opioids after being prescribed oxycodone post C-section
  – Addiction to oxycodone, transitioned to heroin
  – Addiction to heroin, transitioned to heroin/fentanyl
  – “If there’s no fentanyl in it, I don’t want it at all”
  – Tried 14-day rehab without success
    • “This is all I know anymore...It’s all I know”

Who and What is Our Responsibility?

We Are Involved Like it or Not
Does the United States Own the Problem??

- We are not alone
- This is a global issue
- In 2015, approximately ¼ billion people abused/misused drugs
  - ~ 29.5 million (0.6% of global adult population) engaged in problematic use/suffered from substance use disorder
- 70% of the global burden of disease caused by drug use disorders attributable to opioid use

However...

Drug-related deaths remain highest in the US
Clinical Considerations and Implications

- The “New Math” for determining opioid risk/benefit analysis

Final Thoughts

- We must consider the parallel “opioid” crises that exist today
  - Our role in these problems
- Heroin and fentanyl are not going anywhere
- Remember the “New Math”
- Naloxone is likely something to keep top of mind
- Avoidance of “risky” situations is critical
- Strongly consider and document appropriate candidates for fentanyl-based therapies
- Everyone is looking at us as an integral part of solving this “other” opioid crisis
- Everyone is looking to us to be a part of the solution
Final Thoughts

But… Let’s not make patients “pay” for these crises

“Cure sometimes, treat often, comfort always.”
— Hippocrates
Questions?