



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



The Facts: No Lack of Media Attention



**OPIOID
EPIDEMIC**



**HEROIN
EPIDEMIC**



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
- ******Now there are questions about accuracy regarding CDC data and opioid analgesics******



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There Is More Than One Opioid Crisis. To better tackle the epidemic, Kentucky needed to know which drugs were causing fatal overdoses. By Kathryn Casper
 Published Jan. 17, 2018. <https://thehill.com/pain/week/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

Identifying drugs in overdose deaths

In each state, 2016

State	No. Deaths	Total	Share
Kentucky	888	478	47.8%
West Virginia	4,637	2,375	49.9%
Alabama	758	588	43.7%
North Carolina	228	48	38.7%
Virginia	2,588	6,67	39.8%
Delaware	282	88	31.1%
Nebraska	138	37	30.8%
Arkansas	482	1,13	28.7%
Florida	4,788	1,544	24.2%
Ohio	842	53	18.9%
New Jersey	2,898	481	22.4%
Mississippi	782	38	22.2%
Wyoming	88	31	21.2%
California	4,894	888	20.1%
Alaska	312	62	19.8%
Colorado	842	178	19.7%
Kentucky	888	478	18.8%
Illinois	1,212	188	15.5%
North Dakota	72	22	14.5%
Arizona	1,382	188	14.2%

There Is More Than One Opioid Crisis. To better tackle the epidemic, Kentucky needed to know which drugs were causing fatal overdoses. By Kathryn Casper. Published Jan. 17, 2018.

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The Facts: Kentucky as an Example

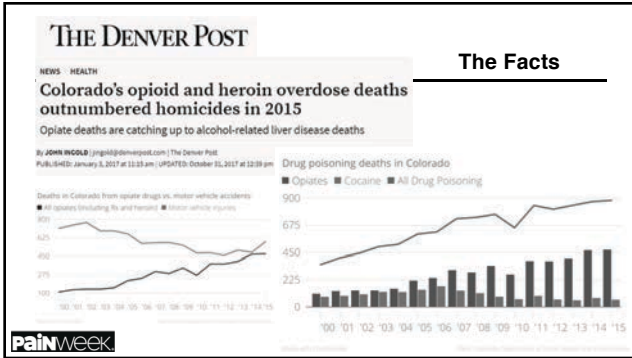
The most common drugs found in Kentucky's overdose victims

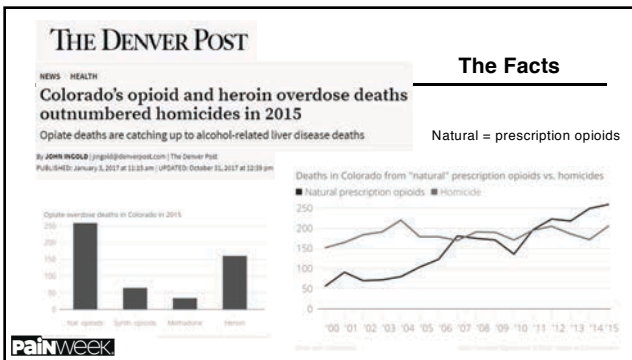
Based on an analysis of 1,478 drug overdose deaths in 2016

Individual drugs		Two-drug combinations		Three-drug combinations	
DRUG	SHARE	DRUGS	SHARE	DRUGS	SHARE
Morphine	45.1%	Heroin, morphine	24.3%	Heroin, morphine, codeine	18.5%
Fentanyl	27.6%	Fentanyl, morphine	23.7%	Heroin, morphine, fentanyl	11.6%
Gabapentin	22.6%	Codeine, morphine	20.8%	Morphine, codeine, fentanyl	8.3%
Alprazolam	23.3%	Heroin, codeine	18.8%	Heroin, morphine, THC-COOH	7.8%
THC-COOH	24.6%	Gabapentin, morphine	14.2%	Heroin, codeine, fentanyl	7.8%
Heroin	24.7%	Morphine, THC-COOH	12.8%	Fentanyl, morphine, THC-COOH	7.3%
Codeine	26.7%	Alprazolam, morphine	12.6%	Alprazolam, heroin, morphine	7.3%
Ethanol	18.4%	Methamphetamine, amphetamine	12.0%	Gabapentin, heroin, morphine	7.1%
Oxycodone	13.2%	Heroin, fentanyl	11.7%	Gabapentin, fentanyl, morphine	6.8%
Methylphenidate	17.1%	Oxycodone, morphine	11.5%	Alprazolam, codeine, morphine	6.8%

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 Published Jan. 17, 2018. <https://thehill.com/pain/week/there-is-more-than-one-opioid-crisis/>. Accessed January 18, 2018.



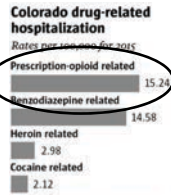




THE DENVER POST

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"



Source: Colorado Dept. of Public Health and Environment
The Denver Post

By JIMMY FRANK (jfrank@denverpost.com) The Denver Post
Published November 5, 2017 at 12:01 pm; Updated November 6, 2017 at 11:02 am

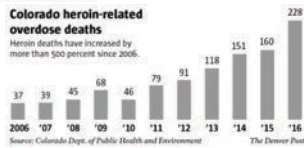
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THE DENVER POST

The Facts

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.



Source: Colorado Dept. of Public Health and Environment
The Denver Post

By JIMMY FRANK (jfrank@denverpost.com) The Denver Post
Published November 5, 2017 at 12:01 pm; Updated November 6, 2017 at 11:02 am

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THE DENVER POST

Doctors will soon get opioid prescription "report cards."

To educate doctors about the dangers of overprescribing opioids, Colorado is testing a relatively new idea that is showing early results — prescriber report cards.

The reports, also known as scorecards, will give clinicians a summary of their prescriber history and how they rank with their peers in the same specialty in terms of dosage, duration and type of drug.



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"

By JIMMY FRANK (jfrank@denverpost.com) The Denver Post
Published November 5, 2017 at 12:01 pm; Updated November 6, 2017 at 11:02 am

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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?

*Bill of Rights for
People with Chronic Pain*

The right to have your report of pain taken seriously and to be treated with dignity and respect by doctors, nurses, pharmacists and other healthcare professionals.

The right to have your pain thoroughly assessed and promptly treated.

The right to be informed by your doctor about what may be causing your pain, possible treatments, and the benefits, risks and costs of each.

The right to participate actively in decisions about how to manage your pain.

The right to have your pain re-assessed regularly and your treatment adjusted if your pain has not been eased.

The right to be referred to a pain specialist or other healthcare provider if your pain persists.

The right to get clear and prompt answers to your questions, take time to make decisions, and refuse a particular type of treatment if you choose.

THE DENVER POST

NEWS HEALTH

Chronic pain patients say they are hurt by Colorado's opioid prescription guidelines

Some Colorado doctors are refusing to prescribe opioids to chronic pain sufferers.



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 Clinical Implications

Centers for Disease Control and Prevention
CDC 24/7 Saving Lives. Protecting People™

Understanding the Epidemic

The Facts

Record Overdose Deaths Heroin Use Preventing Overdose Deaths

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

- The majority of drug overdose deaths involve an opioid¹
- Since 1999 the # of overdose deaths quadrupled²
 - Prescription opioids
 - Heroin
- 91 Americans die every day from an opioid overdose

1. Rudd RA, Seth P, David F, Scholl L. Increases in Drug and Opioid-Involved Overdose Deaths — United States, 2010–2015. MMWR Morbidity and Mortality Weekly Report. 2016;65(24):635–642. DOI: 10.15585/mmwr.mm6524a1
2. CDC. Rising drug overdose deaths: a public health research (NCHS). Atlanta, GA: CDC, National Center for Health Statistics; 2016. Available at: <http://www.cdc.gov>

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Understanding the Epidemic

The Facts

Record Overdose Deaths **Heroin Use** Preventing Overdose Deaths

Heroin use is trending up:

- From 2002-2013, past month/year heroin use and addiction have all increased among 18-25 year olds¹
- Among new heroin users, 75% report abusing prescription opioids prior to using heroin²
- Heroin-related deaths more than tripled from 2010-2015
 - The largest increase was for those heroin-related deaths involving synthetic opioids - FENTANYL

1. Centers for Disease Control and Prevention. Demographic and Substance Use Trends Among Heroin Users — United States, 2002–2013. MMWR 2015; 64(24):719–725
2. Mahon PK, Ottner JC, Davies C. Associations of nonmedical pain reliever use and initiation of heroin use in the United States. CBHQ Data Review. 2013.

Short Answers to Hard Questions About the Opioid Crisis

The Facts: Times are Changing

- Characteristics of Opioid Drug Overdoses:
 - Fast
 - Deadly
 - Scary
 - Socioeconomic status – neutral
 - Abuse-history – neutral
 - Increasing exponentially

Drug overdose deaths involving ...

20,000 deaths per year

15,000

10,000

5,000

0

00 02 04 06 08 10 12 14

Heroin and Synthetic

Common prescription opioids

Source: National Center for Health Statistics, Data by Census Bureau and Population

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 Understanding the Epidemic

The Clinical Implications

Record Overdose Deaths
 Preventing Overdose Deaths

- 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

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 Understanding the Epidemic

The Facts

Statistically significant drug overdose death rate increase from 2015 to 2016, US states

Statistically significant increase
 Yes No
Statistically significant increase from 2015 to 2016

SOURCE: CDC/NCHS National Vital Statistics System, Mortality
https://www.cdc.gov/drugoverdose/data/statedeaths.html. Accessed January 20, 2018.

- 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



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<https://www.drugabuse.gov/publications/heroin-facts> Accessed January 22, 2018.

CDC Centers for Disease Control and Prevention
CDC 24/7 Saving Lives. Protecting People.SM
Understanding the Epidemic

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

Heroin Use Has INCREASED Among Most Demographic Groups

	2002-2007	2008-2012	% increase
SEX			
Male	2.4	3.6	50%
Female	0.2	1.6	100%
AGE YEARS			
12-17	1.8	1.6	—
18-24	2.5	2.2	100%
25 or older	1.2	1.9	58%
RACE/ETHNICITY			
Non-Hispanic white	1.4	3.1	114%
Other	2	1.7	—
ANNUAL HOUSEHOLD INCOME			
Less than \$24,999	2.4	3.5	46%
\$25,000-\$49,999	1.3	2.3	77%
\$50,000 or more	1	1.6	60%
HEALTH INSURANCE COVERAGE			
None	4.2	4.7	12%
Medicaid	4.2	4.2	0%
Private or other	0.8	1.3	63%

¹Annual average rate of heroin use (per 1000 people in each group)

¹ Centers for Disease Control and Prevention. Vital Signs: Today's Heroin Epidemic: — More People at Risk, Multiple Drugs Abused. MMWR 2015.
Compton W.W., Jones C.M., and Baldwin G.T. Understanding the Relationship between Prescription Opioid and Heroin Abuse. NEJM.

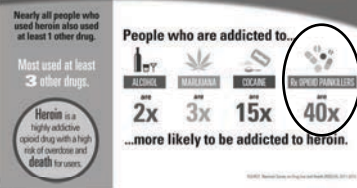
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CDC Centers for Disease Control and Prevention
CDC 24/7 Saving Lives. Protecting People.SM
CDC Vital Signs July 2015

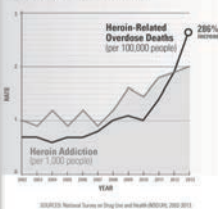
The Facts

- The Heroin Epidemic


Heroin use is part of a larger substance abuse problem.



Heroin Addiction and Overdose Deaths are Climbing




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National Institute
on Drug Abuse

Research Report Series

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



1. <https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/introduction>. Accessed January 30, 2018.
2. https://d4fmgmeflla.cloudfront.net/sites/default/files/tech_and_heroin_rr_layout_final.pdf. Accessed January 30, 2018.



NIH
National Institute
on Drug Abuse

Research Report Series


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

1. <https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/introduction>. Accessed January 30, 2018.
2. https://d4fmgmeflla.cloudfront.net/sites/default/files/tech_and_heroin_rr_layout_final.pdf. Accessed January 30, 2018.

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NIH
National Institute
on Drug Abuse

Research Report Series


The Facts

■ And...

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

– Jones CM. Heroin use and heroin use risk behaviors among nonmedical users of prescription opioid pain relievers – United States, 2002-2004 and 2008-2010. *Drug Alcohol Depend.* 2013;132(1-2):95-100.

A + B ≠ C



1. <https://www.drugabuse.gov/publications/research-reports/relationship-between-prescription-drug-abuse-heroin-use/introduction>. Accessed January 30, 2018.
2. https://d4fmgmeflla.cloudfront.net/sites/default/files/tech_and_heroin_rr_layout_final.pdf. Accessed January 30, 2018.

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CDC Centers for Disease Control and Prevention
CDC 360° Strategic Planning Framework

CDC Vital Signs July 2015

The Clinical Implications

■ Recommendations that impact us:

- Screen and identify high-risk individuals
- Treat people with substance abuse disorders
- Naloxone

Responding to the Heroin Epidemic

PREVENT
People From Starting Heroin

Reduce prescription opioid painkiller abuse.
Promote 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.
Use naloxone, a life-saving drug that can reverse the effects of an opioid overdose when administered in time.

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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: Overdoses On The Rise

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.

50-100x MORE POTENT THAN MORPHINE

196% increase in deaths from 2012 to 2015

SYNTHETIC OPIOID DEATHS: ACROSS THE U.S.

73% increase in deaths from 2012 to 2015

264% increase in deaths from 2012 to 2015

ILICITLY MANUFACTURED FENTANYL

Although prescription sales have fallen, legitimate recreational and medical use have increased significantly, contributing to a sharp spike in synthetic opioid deaths.


100 TIMES MORE HEROIN DEATHS SINCE 2010

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Case 1

■ 42 year-old Hispanic male

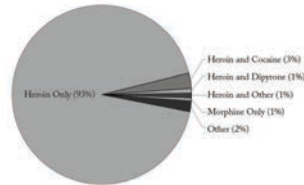
- Addicted to heroin
- Comes to the same street corner every day to buy heroin
 - First dose usually free
- He's actually buying heroin laced with fentanyl
- "It's a new epidemic" he says
- "If you catch a bag of pure fentanyl, that Narcan ain't bringing you back"
- "I just watched my friend die from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



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Heroin and Fentanyl: A “Perfect” Pair The Facts

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



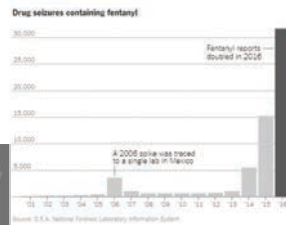
Note: Percentages may not sum to total because of rounding.

U.S. DEPARTMENT OF JUSTICE
OFFICE OF DIVERSION CONTROL
NFLIS
NATIONAL FORENSIC
LABORATORY
INFORMATION SYSTEM
Special Report: Opiates and Related Drugs
Reported in NFLIS, 2009–2014

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Fentanyl The Facts

- Drug seizures involving fentanyl are going up dramatically



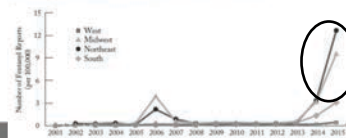
U.S. DEPARTMENT OF JUSTICE • OFFICE OF DIVERSION CONTROL
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LABORATORY
INFORMATION SYSTEM
NFLIS Brief: Fentanyl, 2001–2015

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Fentanyl The Facts

- Defined geographic distribution

Figure 2 NFLIS regional trends in fentanyl reported per 100,000 persons aged 15 or older, January 2001–December 2015¹



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.

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NFLIS Brief: Fentanyl, 2001–2015

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The Facts

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.

Criminal Chemistry
Fentanyl manufacturers 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 29 grams of which can be bought from China for about \$67.

NPP can be combined with about \$700 of other chemicals to produce fentanyl.

The resulting 29 grams of fentanyl cost about \$100 to produce.

and are equivalent to up to \$800,000 of pills on the black market.

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

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

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A Fentanyl Crisis

The Washington Post

Fentanyl linked to thousands of urban overdose deaths

In the nation's largest cities, fentanyl is becoming a major part of the national opioid crisis.

By: JAMES J. HOGAN, JAMES J. HOGAN, and JAMES J. HOGAN

Aug. 15, 2017

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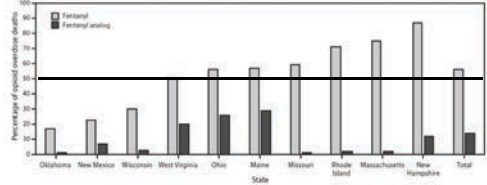
The Implications

In 24 of the nation's largest cities fatal fentanyl-related overdoses increased 600% from 2014-2016

Increasing Fentanyl Overdoses

The Facts

FIGURE. Percentage of opioid overdose deaths testing positive for fentanyl and fentanyl analogs, by state — 10 states, July–December 2016



Morbidity and Mortality Weekly Report, November 3, 2017 / Vol. 66 / No. 43 US Department of Health and Human Services/Centers for Disease Control and Prevention

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Different Types of Fentanyl and Presentations

▪ Different formulations and varying potencies:

– Fentanyl

– Analogs

- Acetyl Fentanyl
- Ocfentanil
- Carfentanyl
- Remifentanyl
- Alfentanil
- Sufentanil
- Furanylfentanyl



▪ Presentations

- Powder
- Counterfeit pills
- Etc.

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Carfentanyl

The Facts

- 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



Elephant tranquilizer is the latest lethal addition to the heroin epidemic. By Leah Rial and Peter Hermann. October 10, 2017. Washington Post. The article reports on the use of carfentanyl, a powerful synthetic opioid, in the heroin epidemic. It mentions that carfentanyl is 10,000 times more potent than morphine and is often used in counterfeit pills. The article also mentions that carfentanyl is used as an elephant tranquilizer and that it has been found in the blood of people who have died from heroin overdoses.

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The Facts

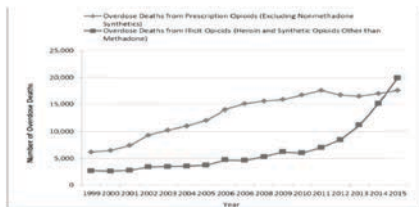
- Fentanyl in the wrong hands is deadly
- Potentially contributing significantly to overdose/fatal overdose risk
- Analogs not often tested for in routine toxicology testing
- Naloxone is a bridge to survival but not a final solution
 - Re-narcotization from fentanyl is common
 - CO₂ will persist
 -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

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SUMMARY

The Co-existing Opioid Crises

The Facts



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PAIN MANAGEMENT AND THE OPIOID EPIDEMIC
 BALANCING MEDICAL AND PAIN-RELATED BENEFITS
 AND RISKS OF PAIN-RELATED OPIOID USE
 Prepared for the U.S. Food & Drug Administration
 by the Center for Communications Programs
 at the University of Michigan

We didn't Start the Fire...Or did We?

- 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



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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"



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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



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However...

The Facts

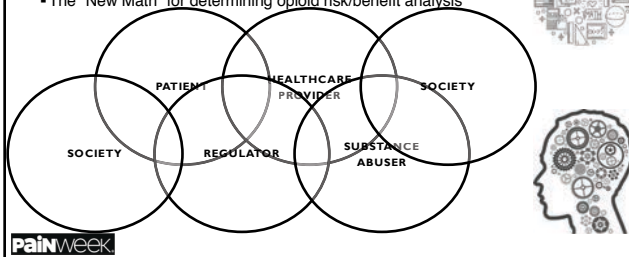
Drug-related deaths remain highest in the U.S.



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Clinical Considerations and Implications

- The "New Math" for determining opioid risk/benefit analysis



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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 the other crisis





"Cure sometimes, treat often, comfort always."
— Hippocrates

Questions?
