The “NEW” Synthetic Opioid Epidemic

Every 16 minutes, a person in the United States dies from an opioid overdose

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Agenda

• The Issue

• Review of Opiates & Opioids

• Multi-faceted Solution

• What Does This Change
The Issue

Overdose Deaths Involving Opioids, United States, 2000-2015

The Issue - Ohio

• This is devastating our communities
  - 2007 - Unintentional drug poisoning became the leading cause of injury death in Ohio, surpassing motor vehicle crashes
  - From 1999-2014, Ohio’s death rate due to unintentional drug poisonings increased over 600 percent
  - Ohio’s death rate has grown faster than the national rate, with southern Ohio often being affected more than the rest of the state.
    • On average, nearly 6 people die each day in Ohio due to drug-related poisoning.

Number of Deaths and Death Rate per 100,000 from Unintentional Drug Overdose by Year, Ohio Residents, 1999-2014 - ODH
An opiate is a substance derived from the poppy plant (which contains opium). Opiates are sometimes called "natural" since the active ingredient molecules are made by nature, not manufactured by chemical synthesis.

Common opiates include:
- Morphine, Heroin, and Codeine

An opioid is a substance (molecule) that is synthetic or partly synthetic, meaning the active ingredients (molecules) are manufactured via chemical synthesis. Opioids often act just like opiates in the human body, because of the similar molecules.

Examples of opioids:
- Oxycodone, Fentanyl, Vicodin
Changes in the Opioid Epidemic

- The death rate of synthetic opioids, which includes drugs such as tramadol and fentanyl, increased significantly from 2014 to 2015.

- Recent state reports have indicated that increases in synthetic opioid-involved deaths have been associated with the number of drug products obtained by law enforcement testing positive for fentanyl.

- These reports indicate that increases in synthetic opioid-involved deaths are being driven by increases in fentanyl availability, likely due to illicitly-manufactured drugs.
Age-adjusted death rates for synthetic opioids are displayed by census region for 2014 to 2015.

- Death rates increased in all regions
  - 107.4% in the Northeast
  - 95% in the Midwest
  - 55.6% in the South
  - 12.5% in the West

- The synthetic opioid overdose death rate also increased in the United States overall—a statistically significant 72.2% increase from 2014 to 2015, with a total of 9,580 deaths in 2015.
Statistically significant changes in drug overdose death rates involving synthetic opioids by select states, United States, 2014 to 2015
What is Fentanyl?

• Fentanyl is a synthetic (man-made) opioid that is 50x more potent than heroin and 100x more potent than morphine. There are two types of fentanyl:

  – Pharmaceutical fentanyl, which is primarily prescribed to manage acute and chronic pain associated with advanced cancer.

  – Non-pharmaceutical fentanyl, which is illicitly manufactured, and is often mixed with heroin and/or cocaine—with or without the user’s knowledge—in order to increase the drug’s effect.

• The LD50 (lethal dose) for pure Fentanyl is estimated at 2 milligrams (mgs) for a typical adult.
Other High Potency Opioids

- There are many types of illicit fentanyl with varying strengths. There are 13 and counting analogues (substances with similar chemical make up with one or more molecules that are different) of Fentanyl all different strengths.

- Carfentanil, a large animal tranquilizer is one of them.
  - 10,000x’s stronger than Morphine

- Other analogues including:
  - butyrylfentanyl, furanyl fentanyl, ohmefentanyl, U-47700, etc.
Differences between Heroin & Fentanyl

• The difference in strength between heroin and fentanyl arises from differences in their chemical structures. The chemicals in both bind to the mu opioid receptor in the brain.

• Fentanyl gets there faster than morphine (the breakdown byproduct of heroin) because it more easily passes through the fat that is plentiful in the brain.

• Fentanyl has a very high affinity for the mu receptor so that a tiny amount is enough to start the molecular chain of events that instigates opioids’ effects on the body.
How do the patients know the difference?

- Simply… they do not.
- Despite the fact that some patients report being able to tell the difference, there is no actual evidence of that.
- In addition, many drug dealers are pressing the fentanyl (or its analogues) into pills that may be designed to look like prescription opioids.

Fentanyl pills made to look like oxycodone seized in Ohio (Cleveland)
Are fentanyl and other synthetic opioids more addictive than heroin?

- We don’t yet have much evidence that people are choosing these drugs rather than using them accidentally in pursuit of other opiates.

- Despite fentanyl and other synthetic opioid’s greater potency than heroin, this does not mean people prefer fentanyl, and actually, the opposite has been reported due to fear of overdose. (Strang et al, 2015)

- However, limited preliminary evidence suggests a possible preference for fentanyl in heroin-dependent individuals could occur. (Greenwald et al, 2004)
Where is it coming from?

- Most of the attention has focused on Mexican cartels that are adding the drug to heroin smuggled into the United States.
- But Chinese suppliers are providing both raw fentanyl and the machinery necessary for the assembly-line production of the drug.
- “We have seen an influx of fentanyl directly from China,” said Carole Rendon, the acting US attorney for the northern district of Ohio in Cleveland. “It’s being shipped by carrier.”
- Chemists are also synthesizing fentanyl and its analogues here in the US (lab, one pot, etc.)
Why would they do this?

- Basic economics:
  - Unlike heroin, which requires careful cultivation of poppy fields, synthetic opioids can be manufactured on an industrial scale.

- It costs $3,000 to $4,000 to produce a kilo of fentanyl = the same cost as to produce a kilo of heroin
  - One kilo of heroin sells has a street value of $300,000-600,000 dollars

- But fentanyl's extreme potency means it can be cut and split into many more kilos, increasing a dealer's profits.
  - One kilo of fentanyl can produce profits of $1.3 million

- There also other driving factors such as transport
What are we going to do??

Just because today is not easy doesn’t mean you should give up. It only means you have to fight harder.

- Anon
Continue the Multi-Faceted Solution

- Prevention: Preventing youth drug use before it starts
- Treatment: Creating better pathways to treatment and recovery
- Law enforcement: cracking down on drug trafficking
- Appropriate Prescribing: encouraging appropriate use and availability of pain medication
- Harm Reduction: Saving lives by expanding access to naloxone, etc.
What Does This Change?

• Significantly Increased Mortality

• Safety for First Responders

• Need for Naloxone Expansion

• Must Expand Evidence-Based Treatment
  – Including MAT
Significant increase in morality associated with increase in fentanyl presence.

On the left, a lethal dose of heroin; on the right, a lethal dose of fentanyl.

[Image of vials labeled 'HEROIN' and 'FENTANYL']

[Graph showing overdose deaths for Heroin and Other Synthetic Opioids (e.g., fentanyl, tramadol) from 2008 to 2015]
First Responder Safety

• Fentanyl and its analogs pose a potential hazard to first responders who could unknowingly come into contact with these drugs in their different forms (including police working dogs).
• While dermal (skin) absorption of fentanyl commonly occurs through prescribed use of the drug, inhalation of powder is the most dangerous exposure route for illicitly-manufactured fentanyl (either may be deadly).
• The DEA recommends that officers do not field test drugs if fentanyl is suspected. The substance should be carefully collected and sent to a laboratory.
• This highlights the need for first responders to wear personal protective equipment (PPE) to effectively manage risks that may cause an exposure.
Naloxone (Narcan) Expansion

• Naloxone must be readily available for both patients and first responders

• The highest FDA-approved doses should be carried by both (Narcan, Evzio)
  – Especially by the public – ease of use

• Time = Brain (Anoxic brain injury at 4 min.)
  – IF not readily available and effective, overdose mortality and morbidity both increase
Expand Evidence-Based Treatment

- **Medical** - including MAT
  - Comprehensive assessment & intake – SAME DAY or NEXT DAY
  - Outpatient withdrawal management (and ongoing pharmacological management)
  - Care coordination and monitoring

- **Psychological**
  - Clinical assessment (ASAM PLACEMENT CRITERIA)
  - Therapy (individual, group, and family, etc.)

- **Social**
  - Case management
    - Can include all of the following: crisis support, family services, legal services, vocational services, transportation, housing, etc.
  - Involving social support networks – AA, NA, etc.
Are There Changes in Treatment?

- It is more important than ever to expand evidence based models that are proven to reduce mortality – MAT
  - Induction onto MAT is sometimes more challenging
- Longer acting injectables may prove to be superior in the long run
- Detoxification alone is deadly
- Toxicology testing has gotten more complicated
Summary

• The Opioid Epidemic is Devastating
  – It is Evolving and Worsening

• The Solution is Multi-faceted – There is HOPE
  – Prevention
    • Don’t get started
  – Treatment
    • MAT works; and there are new medications on the horizon
  – Law enforcement
    • Need appropriate resources to combat the evolving problem
  – Appropriate Prescribing
    • Continue to reduce new exposures and limit those that must be prescribed
  – Harm Reduction
    • Naloxone must be expanded
References

- [www.cdc.gov](http://www.cdc.gov)
- [www.drugpolicy.org](http://www.drugpolicy.org)
- ASAM - American Society Of Addiction Medicine
- COPE - Coalition On Physician Education In Substance Use Disorders
- SAMHSA – Substance Abuse And Mental Health Services Administration
- NIDA – National Institute On Drug Abuse
- Surgeon Generals Report on Alcohol, Drugs, and Health
- VA Clinical practice guideline on Substance Use Disorder treatment