Evolving Role of Illicit Fentanyl in the Opioid Epidemic

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December 15, 2016

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.
Opioid Epidemic, United States 2000-2015

![Graph showing opioid-related deaths per 100,000 population from 2000 to 2015]

- Any Opioid
- Commonly Prescribed Opioids (Natural & Semi-Synthetic Opioids and Methadone)
- Heroin
- Other Synthetic Opioids (e.g., fentanyl, tramadol)

Prescription Fentanyl

- Synthetic opioid analgesic, not detected on standard urine screening tests
- 50X more potent than heroin
- Primary use is for managing surgical/postoperative pain, severe chronic pain, and breakthrough cancer pain*

*For more information on approved fentanyl products and their indications, see: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm?fuseaction=Search.SearchAction&SearchTerm=fentanyl&SearchType=BasicSearch
Illicitly-Manufactured Fentanyl (IMF)

- Includes fentanyl and fentanyl analogs
- Manufactured unlawfully in clandestine labs in China and Mexico
- Most recent increases in non-fatal and fatal fentanyl-involved overdoses linked to IMF
- Often mixed with heroin and/or sold as heroin, or as counterfeit pills

“While pharmaceutical fentanyl (from transdermal patches or lozenges) is diverted for abuse in the United States at small levels, this latest rash of overdose deaths is largely due to clandestinely-produced fentanyl, not diverted pharmaceutical fentanyl.”
Role of IMF vs Pharmaceutical Fentanyl

- Strong correlation between supply of illicit fentanyl and fentanyl-related deaths
- Similarity in demographics of heroin and fentanyl decedents
- Toxicology reports from field investigations show co-implication of other illicit drugs (heroin and/or cocaine)
- Qualitative data indicating illicit fentanyl often sold as heroin
- No change in pharmaceutical fentanyl prescribing rates in affected states
Change in rate of synthetic overdose deaths and reported fentanyl law enforcement seizures: 2013-2014

Trends in the number of synthetic opioid deaths, number of reported fentanyl law enforcement submissions, and rate of fentanyl prescriptions: 2010-2014

Law enforcement submissions (dark blue) and fentanyl-involved overdoses (light blue), Ohio, 2013-2014

Law enforcement submissions (dark blue) and fentanyl-involved overdoses (light blue), Florida, 2013-2014

## Similarities in Opioid OD Decedents
Ohio, 2014

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fentanyl (n=456)</th>
<th>Heroin (n=618)</th>
<th>Prescription Opioid (n=262)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>37.9 (SD 11.3)</td>
<td>39.9 (SD 11.7)</td>
<td>46.4 (SD 11.4)*</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>70.0%</td>
<td>72.8%</td>
<td>55.0%</td>
</tr>
<tr>
<td>Female</td>
<td>30.0%</td>
<td>27.2%</td>
<td>45.0%</td>
</tr>
<tr>
<td><strong>Race</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>89.3%</td>
<td>90.8%</td>
<td>90.5%</td>
</tr>
<tr>
<td>Black</td>
<td>9.4%</td>
<td>8.1%</td>
<td>8.4%</td>
</tr>
<tr>
<td><strong>Marital Status</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never Married/Single</td>
<td>54.0%</td>
<td>49.3%</td>
<td>31.2%</td>
</tr>
<tr>
<td>Divorced, separated, widowed</td>
<td>28.8%</td>
<td>34.8%</td>
<td>41.5%</td>
</tr>
<tr>
<td>Married</td>
<td>17.3%</td>
<td>16.0%</td>
<td>27.3%</td>
</tr>
</tbody>
</table>

Centers for Disease Control and Prevention. Morbidity and Mortality Weekly Report. Available from URL: [http://www.cdc.gov/mmwr/volumes/65/wr/mm6533a3.htm?s_cid=mm6533a3_e](http://www.cdc.gov/mmwr/volumes/65/wr/mm6533a3.htm?s_cid=mm6533a3_e), Accessed November 10, 2016.
Flow of Illicit Fentanyl from China

Factors driving emergence of Fentanyl

- **High profit potential at low volume of product**
  - Thousands of dollars of fentanyl $\rightarrow$ millions of dollars of fentanyl laced heroin or counterfeit Rx pills

- **High portability and ability to ship in low quantities that avoid inspection thresholds**

- **Ease of concealing into white powder heroin**
  - Similar color/consistency to white powder heroin
  - Similarity of its high to heroin
Increases in Fentanyl Drug Confiscations and Fentanyl-related Overdose Fatalities

This is an official
CDC HEALTH ADVISORY

October 26, 2015

Table 1: Top 10 states by total Fentanyl Seizures, 2014, unpublished NFLIS data

<table>
<thead>
<tr>
<th>Rank</th>
<th>State</th>
<th>Number of Fentanyl seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ohio</td>
<td>1245</td>
</tr>
<tr>
<td>2</td>
<td>Massachusetts</td>
<td>630</td>
</tr>
<tr>
<td>3</td>
<td>Pennsylvania</td>
<td>419</td>
</tr>
<tr>
<td>4</td>
<td>Maryland</td>
<td>311</td>
</tr>
<tr>
<td>5</td>
<td>New Jersey</td>
<td>238</td>
</tr>
<tr>
<td>6</td>
<td>Kentucky</td>
<td>232</td>
</tr>
<tr>
<td>7</td>
<td>Virginia</td>
<td>222</td>
</tr>
<tr>
<td>8</td>
<td>Florida</td>
<td>163</td>
</tr>
<tr>
<td>9</td>
<td>New Hampshire</td>
<td>177</td>
</tr>
<tr>
<td>10</td>
<td>Indiana</td>
<td>133</td>
</tr>
</tbody>
</table>

Centers for Disease Control and Prevention Health Advisory. Available from URL: https://emergency.cdc.gov/han/han00384.asp
Dramatic Increase in Fentanyl-related Overdose Deaths, Ohio, 2012-15

Dramatic rise in proportion of Fentanyl OD deaths, Ohio, 2010-2015

* Prescription Opioids not including fentanyl.
** No specific drug was identified. In about 6 percent of the cases, no specific drug is identified in the death certificate data. As such, reported drugs are likely under-estimates of their true contribution to the burden of fatal drug overdoses in Ohio.


Kentucky: Fentanyl-Related Overdose Deaths

- 24% of overdose deaths in 2015 involved fentanyl
- Fentanyl deaths rapidly increased two straight years in a row.
  - 39 to 128 from 2013-2014
  - 128 to 230 from 2014-2015

[Map and data chart showing overdose deaths by county in Kentucky involving fentanyl, 2014-2015 combined]

Pennsylvania: Fentanyl-Related Overdose Deaths

- 27% of overdose deaths in 2015 involved fentanyl or around 913 deaths*

*Estimated by multiplying total overdose deaths reported 3,383 by 27.0%
Maine OD Deaths in 2015

- 32% of overdose deaths in 2015 involved fentanyl
Maryland OD Deaths

28% of OD deaths in 2015 attributed to Fentanyl

Report from Maryland Dept. of Health and Mental Hygiene, available at:
New Hampshire Overdose Deaths

- Nearly 2/3 of overdose deaths in 2015 involved fentanyl

*Figure 1: New Hampshire Overdose Deaths, by Drug and Year, 2010–2015*

NDEWS New Hampshire HotSpot Report, available at
Massachusetts Opioid-Related Overdose Deaths

- 74% of opioid overdose deaths in 2015 with toxicology data tested positive for fentanyl

NYC Advisory on Fentanyl
October, 2016

- Nearly 50% of all OD deaths in first half of 2016 involved fentanyl
- Fentanyl had been involved in 16% of OD deaths in 2015

NYC Health Advisory Report, available at:
Influx of Fentanyl-laced Counterfeit Pills and Toxic Fentanyl-related Compounds Further Increases Risk of Fentanyl-related Overdose and Fatalities

Distributed via the CDC Health Alert Network
August 25, 2016, 15:15 ET (3:15 PM ET)
CDCHAN-00395
Main points from HAN Update

- Sharp increase in the availability of counterfeit pills containing fentanyl
  - Oxycodone, Xanax, Norco
  - “Hundreds of thousands of counterfeit pills” have entered U.S. market since 2014
  - Counterfeit pills often closely resemble the authentic medications they were designed to mimic, and the presence of fentanyl is only detected upon laboratory analysis.
Main points from HAN Update

- Widening risk profile for exposure to Fentanyl-related compounds
  - Now including those who misuse oral prescription medications
  - Broader geographic impact is possible, beyond areas impacted by IMF.
Main points from HAN Update

- Continued increases in the supply and distribution of illicitly-manufactured fentanyl (IMF)
  - Drug submissions testing positive for illicitly manufactured fentanyl doubling from 2014 to 2015 (from 5,343 to 13,882).
  - Number of states reporting more than 100 fentanyl submissions increased from 11 to 15
Number of Reported Law Enforcement Submissions Testing Positive for Fentanyl by State: 2013

Number of Reported Law Enforcement Submissions Testing Positive for Fentanyl by State: 2015

Main points from HAN Update

Widening array of fentanyl analogs being mixed with heroin or sold as heroin

- **Acetyl Fentanyl**: number of drug submissions testing positive for acetyl fentanyl increased from 463 in 2014 to 1,870 in 2015
- **Furanyl Fentanyl**: in 2016, 244 drug submissions tested positive for furanyl fentanyl by July
- **Carfentanil**: confirmed or suspected cases in as many as 9 states, mostly in Midwest and South regions.
DEA Emerging Threat Report – Mid Year 2016

**OPIOIDS/ANALGESICS**

FENTANYL ACCOUNTED FOR APPROXIMATELY 70% OF THE OPIOID IDENTIFICATIONS. OF THE 268 FENTANYL IDENTIFICATIONS, FENTANYL WAS FOUND AS THE ONLY CONTROLLED SUBSTANCE IN APPROXIMATELY 50% OF THE IDENTIFICATIONS AND WAS FOUND IN COMBINATION WITH HEROIN IN 33% OF THE IDENTIFICATIONS. ACETYLEFENTANYL WAS THE NEXT MOST PROMINENT OPIOID ACCOUNTING FOR 13% OF THE IDENTIFICATIONS.

- Valeryl fentanyl: 4
- Butyryl fentanyl: 5
- U-47700: 12
- ANPP: 17
- Furanyl fentanyl: 25
- Acetylfentanyl: 50
- Fentanyl: 268

The number of furanyl fentanyl identifications increased significantly over the course of the first half of 2016, from 1 identification in the first quarter to 25 identifications by the end of the first half of the year.

RECOMMENDATIONS
Improved Detection of IMF

Public Health Departments
- Explore various methods for rapidly identifying drug overdose outbreaks (e.g., Emergency Dept. syndromic surveillance)
- Track and monitor fentanyl/heroin submission trends
- Track decedent demographics and risk factors (e.g., drug type and route of administration) and geographic concentrations of drug supply and drug use to inform prevention efforts
- Collaborate with law enforcement

Law Enforcement
- Rapid testing of evidence from drug overdose scenes
- Collaborate with public health
- Protection of first responders when handling suspected IMF, white powders and unknown substances
CDC/NIOSH Recommendations on Occupational Exposure to Fentanyl

- N100 level of respiratory protection
- Coveralls with tight-fitting sleeves
- Gloves
- Eye Protection

Available at http://www.cdc.gov/niosh/topics/fentanyl/risk.html; last accessed Dec. 9, 2016
Improve Detection: Medical Examiners/Coroners

Screen for fentanyl in suspected opioid overdose

- Increase in fentanyl submissions
- Increase in opioid-involved overdose fatalities, especially unusually large spikes in heroin or unspecified drug overdose fatalities

Screen specimens using an ELISA test that can detect fentanyl

- If positive, GC/MS to detect possible analogs

Standardized methods for determining cause and reporting the death

- SAMHSA consensus definitions
Overdose Response with Naloxone

- Naloxone administration by injecting partners/bystanders is saving lives
  - Situation would be much worse without community access
  - Need to get bystanders to call 911, especially given the fentanyl’s rapid onset
  - Good Samaritan Laws are key for ensuring bystanders call 911
  - Rescue breathing and CPR are critical for responding to fentanyl-induced overdose

- Naloxone administration by first responders and EMS is a critical component

- Diminished effectiveness associated with fentanyl
  - Multiple (nasal) doses required to reverse fentanyl overdose
  - Respondents aware of naloxone’s reduced affect on fentanyl ODs
  - Co-use of opioids and benzodiazepines highly prevalent and may play a role

- Diversify naloxone strength and formulations and increase supply in community
  - Nasal (IMS-limited, FDA approved) 1ml/mg per nostril for total of 2mg of drug
  - Nasal (ADAPT, not FDA approved) single dose is 4mg
  - IM (Abbot) single dose is 0.4mg/ml
  - Multiple doses per overdose will drain already limited resources for purchasing drug
FDA Advisory Committee Meeting

- FDA Joint Committee convened on October 5, 2016 to discuss
  - naloxone products intended for use in the community
  - the most appropriate dose or doses of naloxone to reverse the effects of life-threatening opioid overdose in all ages
  - the role of having multiple doses available in this setting
- Voted 15-13 for a raised dose, but did not specify the precise dose
- FDA will consider whether to accept recommendation from the Advisory Committee
Opioid Use Disorder & Evidence-based Drug Treatment

- **Promote safer opioid prescribing practices and leverage opportunities for drug treatment**
  - Explore opportunities to assist physicians in identifying patients misusing/abusing opioids and help facilitate treatment referrals.
  - Reduce co-use and co-prescribing of opioids and benzodiazepines
  - Expand and improve use of Prescription Drug Monitoring Programs (PDMP)
  - Expand access to medication-assisted treatment (buprenorphine/methadone/naltrexone)
    - In combination with counseling and behavioral therapies for substance use disorders

- **Public health messaging to raise awareness and reduce stigmatization**
  - Education on addiction as a chronic illness—not a flaw in moral character
  - Educate safety and effectiveness of medicated assisted treatment (e.g. Suboxone©)
  - Practice harm reduction: meet PWUD “where they’re at”
  - Encourage “safer” opioid misuse among persons unwilling or unable to stop using
    - Don’t use alone
    - Make sure peers/friends have naloxone on hand
    - Reduce co-use of sedatives and opioids
Public Health Messaging

WATCH OUT:
FENTANYL IS IN NYC
Fentanyl is a dangerous opioid that's showing up in heroin, cocaine and pills marked as Xanax®

IF YOU KNOW SOMEONE USING DRUGS, TELL THEM TO:

USE WITH SOMEONE ELSE: If you overdose, you want someone around to help.
TAKE TURNS: Don’t use at the same time, and be prepared with naloxone. Have a phone on hand in case you need to call 911.
TEST YOUR DRUGS: Use a small amount first to see how strong your drugs are. Even a tiny amount of fentanyl can cause an overdose.
CARRY NALOXONE: More than one dose of naloxone may be needed to reverse a fentanyl overdose.
AVOID MIXING DRUGS: Mixing drugs—including alcohol—increases your risk of overdose.

Acknowledgements

- Thanks to the following CDC scientists, whose slides were utilized for portions of this presentation:
  - Grant Baldwin
  - Rita Noonan
  - Matthew Gladden
  - Jon Zibbell
  - Noah Aleshire
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