Pharmaceutical Fentanyl's (PF) Role in Fentanyl- related Overdose Deaths

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Presenter Disclosures

Tammy L. Anderson, PhD.

(1) The following personal financial relationships with commercial interests relevant to this presentation existed during the past 12 months:

"No relationships to disclose"

Purpose of Study

To investigate the role of PF in drug overdose deaths

Learning Objectives include:

Describe the role of Pharmaceutical Fentanyl (PF) in fentanyl related overdose deaths.

Analyze patterns related to demographics, context, and drug types.

Target Audience:

Researchers; policy makers

MUSIC

Fentanyl: Drug That Killed Mac Miller, Prince and Tom Petty Has Long History of Abuse

Why Investigate Role of PF in Overdose Deaths?

1. US senators (Armstrong 2016) have recently called for limits on Rx fentanyl, worried PF is adding to the problem.

2. Recent case against INSYS pharmaceutical in expanding off-label SUBSYS prescribing (an Rx fentanyl formulation) outside of the cancer patient pool may justify their concerns (Armstrong 2016).

As opioid crisis raged, Insys pushed higher doses of addictive drug and pushed salespeople to 'own' doctors

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3. Third, there is mounting evidence that PF is diverted to the illegal market (Register- Herald 2016).
   - The DEA acknowledged "Pharmaceutical fentanyl is diverted in its transdermal patch, lozenge, and liquid forms. Pharmaceutical fentanyl is often diverted in personal use quantities" (DEA 2015).
   - And a recent study (reported in Vanderveen 2016) shows medical professionals in Colorado stole large quantities of the drug.

4. Basic neuroscience of addiction: opioid dependency requires higher dose opioids (tolerance, euphoria) making PF desirable, as evidenced by celebrity deaths and reports from addicted.

Current Narrative for Fentanyl Deaths

- CDC- published study (Peterson et al. 2016) findings suggest surges in fentanyl deaths in Florida and Ohio during 2013–2015 were closely related to increases in the IMF (*illegal fentanyl*) supply, as opposed to diverted PF (*pharmaceutical fentanyl*). Explanation:

    – 1) stability in prescribing and dispensing of PF

    – 2) the implication of illicitly produced fentanyl analogs in fentanyl deaths

    – 3) recent DEA reports linking most U.S. fentanyl deaths to IMF

    – 4) demographic characteristics of fentanyl decedents were similar to heroin decedents nationally

    – 5) interviews with persons using illicit drugs indicating that fentanyl appears to be mixed with or sold as heroin.

Methods

- The present study utilizes prescription drug (Rx) data from Delaware's Prescription Drug Monitoring Program (PDMP) and overdose death data from Delaware's Division of Forensic Science (DFS) for the period between _January 1, 2013 through March 31, 2015 (i.e., our study period)_.

- Overdose death data from DFS are compiled by medical examiners who investigate causes of death. Fentanyl deaths reported here were determined by MEs as a primary cause of death, while those classified as "all other deaths" featured another drug as a pinpointed as a primary cause of death by an ME.

- Note, deaths in either of these groups do not reflect the full toxicology results of the decedents.

- See Figure 1 for sample sizes.

Figure 1. Study Design: Data Linkage Methods, Exclusions, and Sample Size
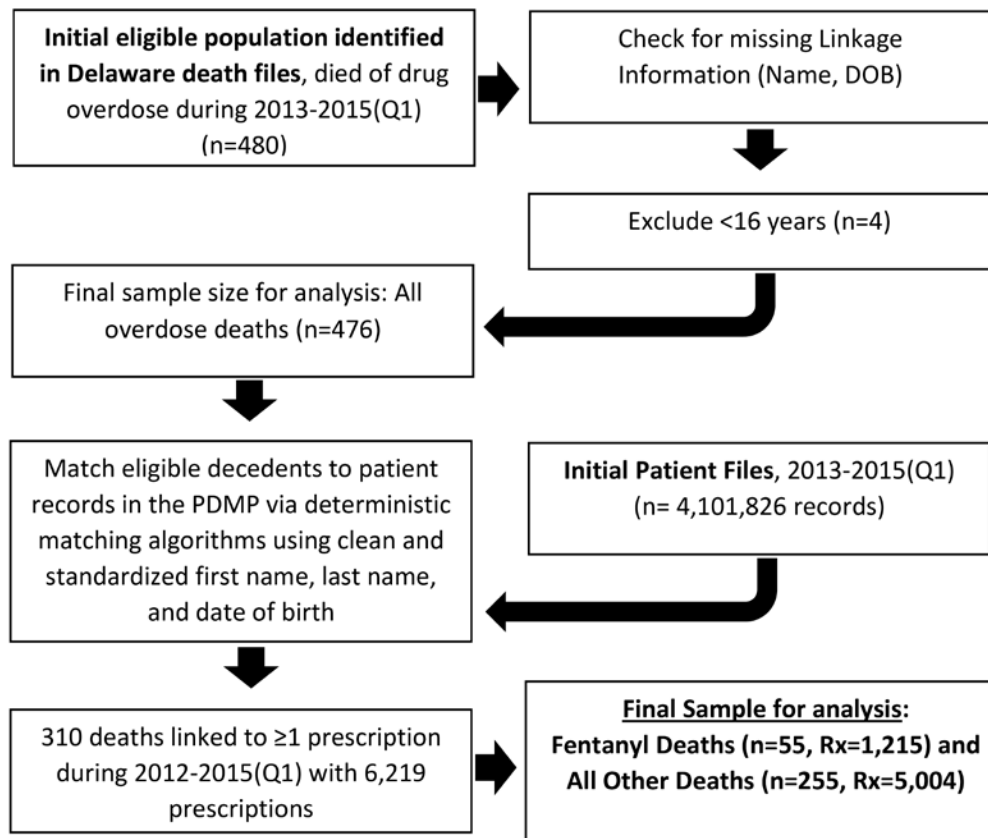
Table 1. Overdose Deaths by Time Period

	2013-2015Q1°	2016	2017
Total Deaths	476	305	345
Average Age	42.5	41.3	41.6
Male	298 (63%)	207 (68%)	238 (69%)
Fentanyl Deaths	68 (14%)	105 (34%)***	207 (60%)***
Average Age	41.0	38.5	39.4
Male	49 (72%)	90 (86%)*	145 (70%)*

°Q1=First Quarter 2015.

*p<.05, ***p<.001 indicates significant difference from previous year.

Table 2. Overdose Deaths 2013-2015Q1° by Matching Status

	Matched Decedents	Unmatched Decedents
Total Deaths (N=476)	310 (65%)	166 (35%)
Average Age	43.1	41.3
Male	184 (59%)*	114 (69%)
White	265 (85%)	134 (81%)
Fentanyl Deaths (N=68)	55 (81%)*	13 (19%)
Average Age	40.8	41.8
Male	39 (71%)*	10 (77%)
White	44 (80%)	12 (92%)
All Other Deaths (N=408)	255 (63%)	153 (37%)
Average Age	43.6	41.1
Male	145 (57%)	104 (68%)
White	221 (87%)	122 (80%)

°Q1=First Quarter 2015.

*$p<.05$; matched group has a higher share of females; decedents from fentanyl deaths were more likely to be matched (as were decedents from Rx Opioids in general); fentanyl decedents have a higher share of males compared to matched all other decedent group.

Table 3. Opioid Prescription History for Overdose Deaths 2013-2015Q1
(Decedents: n=310, Opioid Rx: n=3,167)

	Fentanyl Deaths (n=55 or 18%)	All Other Deaths (n=255 or 82%)
Total # of Opioid Prescriptions	730 (23%)	2,437 (77%)
Average # of Opioid Prescriptions per decedent	14.9 **	10.0
# Opioid Prescriptions per Decedent		
0	6 (11%)	38 (15%)
1-2	10 (18%)	72 (28%)
≥ 3	39 (70%)	145 (57%)
Opioid Prescriptions among Decedents 60 Days Before Death		
No	25 (45%)	133 (52%)
Yes	30 (55%)	122 (48%)

**p<.01

10

Table 4. Fentanyl Prescriptions prior to Overdose Death among Matched Cases

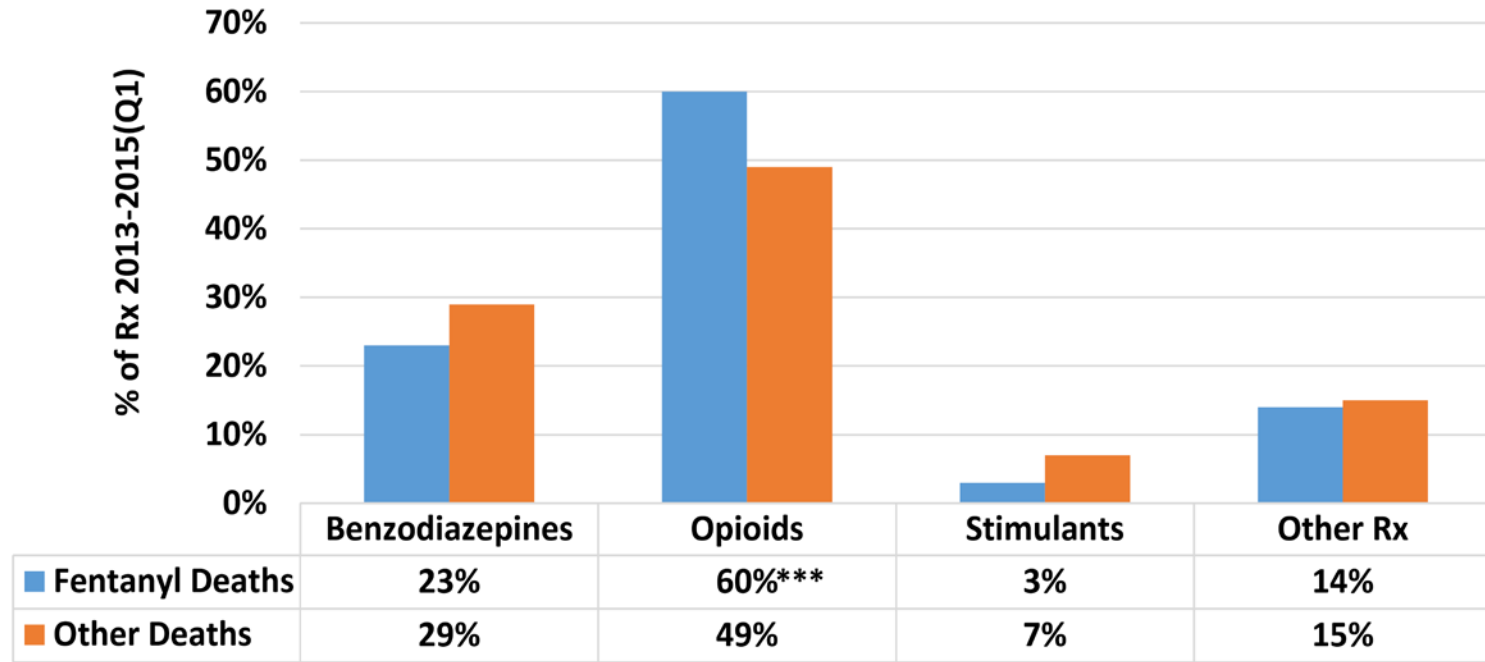|	Fentanyl Deaths (N=55)	All Other Deaths (N=255)
Ever Prescribed Fentanyl	24 (43%)***	13 (5%)
Prescribed Fentanyl within 60 Days of Overdose Death	20 (36%)***	2 (1%)

***p<.0001

Table 5. Top 10 Most Often Prescribed Drugs to Overdose Decedents between 2013 – 2015Q1
(Total # Prescriptions = 6,219)

Fentanyl Decedents (55 decedents with 1,215 prescriptions)

Rank	Drug	%
1	Oxycodone 5, 10, 15, 20, 30 MG Tablet	16.5
2	Fentanyl 12, 25 ,50, 75, 100 MCG/HR Patch, Citrate OTFC 200 MCG	14.1
3	Alprazolam, .25, .5, 1, 2, 3 MG Tablet	10.7
4	Oxycodone-Acetaminophen 5-325, 10-325, 10-650, 7.5-325, 7.5-500	7.8
5	Clonazepam .5, 1, 2 MG Tablet, 2MG ODT, 1MG DIS Tablet	6.0
6	Hydrocodone-Acetaminophen 5-300, 5-325, 5-500, 7.5-300, 7.5-325, 7.5-500, 7.5-750, 10-325, 10-500, 10-660, 10-750	5.5
7	Zolpidem 5, 10, 12.5 MG Tablet	5.5
8	Suboxone 8 MG-2 MG, 4 MGG-1MG, 2MG-.5MG, 12MG-3MG SL Film, 8MG-2MG TAB	4.1
9	Carisoprodol 250, 350 MG Tablet	4.0
10	Lyrica 50, 75, 100, 150, 200, 300 MG Capsule	4.0
Total % of all Prescriptions		**78.2**

All Other Decedents (255 with 5,004 prescriptions)

Rank	Drug	%
1	Alprazolam, .25, .5, 1, 2, 3 MG Tablet	16.0
2	Oxycodone 5, 10, 15, 20, 30 MG Tablet	11.0
3	Oxycodone-Acetaminophen 5-325, 10-325, 10-650, 7.5-325, 7.5-500	8.3
4	Clonazepam .5, 1, 2 MG Tablet, 2MG ODT, 1MG DIS Tablet	7.2
5	Suboxone 8 MG-2 MG, 4 MGG-1MG, 2MG-.5MG, 12MG-3MG SL Film, 8MG-2MG TAB	6.8
6	Zolpidem 5, 10, 12.5 MG Tablet	6.2
7	Morphine Sulfate ER 15, 30, 60, 100, 200 MG TAB, IR 15, 30 MG TAB 100MG/5MG SOLN, 50MG/ML VIAL	5.2
8	Hydrocodone-Acetaminophen 5-300, 5-325, 5-500, 7.5-300, 7.5-325, 7.5-500, 7.5-750, 10-325, 10-500, 10-660, 10-750	5.0
9	Amphetamine Salts 5, 10, 15, 20, 30 MG Tablet	3.0
10	Lyrica 50, 75, 100, 150, 200, 300 MG Capsule	3.0
Total % of all Prescriptions		**71.7**

Figure 2: Distribution of Prescriptions by Drug Types and Overdose Death Type

***p<.0001

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Delaware Opioid Metric Intelligence Project

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The Delaware Opioid Metric Intelligence Project (DOMIP) – provides community surveillance capabilities in Delaware to help reduce its prescription and illicit drug problems. DOMIP achieves this by integrating data on overdose deaths, crime, population characteristics and community resources into a user-friendly web application called the *DOMIP Mapping app*. The mapping app contains six-years (2013–2018) of integrated data that will allow for unprecedented community surveillance, statistical analysis and mapping of a wide range of opiate and crime-related metrics, at the US census tract, zip code, Delaware House District and county levels. Users can also select layers to view where overdose deaths are concentrated and plot treatment resources therein. Such information will inform best practices that assist efforts to reduce the negative impact of the opioid problem on all Delawareans.

Please see our *tutorial* to help navigate the map

Dr. Tammy Anderson discussed the Opioid Crisis in Delaware in Science Cafe. **Listen to the podcast**

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This project has also received support from the Delaware Criminal Justice Information System and the State of Delaware Division of Forensic Science.

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