



Fentanyl Overdose Deaths in Washington State

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May 5, 2017

Abstract

Background: Fentanyl-related drug overdose deaths have increased dramatically in some states. In 2016, the Washington State Toxicology Laboratory modified the testing protocol to detect fentanyl analogs and lower concentrations.

Objective: The objectives of this study were to determine if there was an increase in fentanyl-related overdose deaths from 2015 to 2016 in Washington State, and to describe the demographics of those who died from a fentanyl-related overdose in 2016.

Method: We reviewed the number of overdose deaths detected using the 2015 and 2016 fentanyl testing protocols at the State Toxicology Laboratory, linked state toxicology laboratory results to death certificates, and performed a descriptive analysis of the fentanyl-related overdose deaths.

Results: In the 2016 preliminary death certificate data, there were 70 lab-confirmed fentanyl-related overdose deaths compared to 28 in 2015. Using the 2015 testing protocol, 17 of the 2016 deaths would not have been detected and 53 would have been detected. These 53 cases represent an 86% increase in fentanyl-related overdose deaths from 2015, resulting in a rate ratio of 1.9 (95% confidence interval [CI], 1.6-3.1). A fentanyl analog was identified in 11 (15.7%) of the 70 fentanyl-related overdose deaths in 2016. In addition, 63 of the 70 fentanyl-related deaths tested positive for at least one other drug. Benzodiazepines (41%) were the most common other drug present, followed by other opioids (37%), antidepressants (26%), alcohol (21%) and non-benzodiazepine sedatives (17%). Of the 26 fentanyl-related deaths involving another opioid, the other opioid was heroin in 8 deaths (based on having heroin listed on the death certificate). Those who died from fentanyl-related overdose were mostly male (68%), had a median age of 38 years and their death was classified as unintentional (accidental) (84%).

Conclusions: In 2016, the number of fentanyl-related overdose deaths reported in Washington State increased from 2015, although the increase is not as sharp as observed in some eastern and mid-eastern states. The increase remained significant even when adjusting for the less sensitive 2015 test protocols. Use of the new protocols increased the number of fentanyl-related deaths detected by 32%. Unlike in the eastern U.S., where white

powder heroin is often mixed with fentanyl, the majority of the fentanyl-related overdose in Washington State in 2016 deaths did not involve heroin.

Background

Fentanyl, a synthetic opioid anesthetic, was introduced in the U.S. in the 1960s. It is a schedule II substance under the Controlled Substances Act ("*Accepted medical use, high potential for abuse, with use potentially leading to severe psychological or physical dependence*").

Fentanyl analogs are substances with a chemical structure similar to fentanyl. Fentanyl and its analogs have been abused and diverted from their medical indications, and produced from clandestine labs for the illicit drug market.

Many eastern states and British Columbia¹ have recently experienced a dramatic increase in overdose deaths due to fentanyl or its analogs. In the US from 2014 to 2015, the death rate from synthetic opioids other than methadone, which includes fentanyl, increased by 72% (Rudd et al., 2016).

Methods

Deaths were identified from death certificates from 2015 and 2016 obtained from the Washington State Department of Health (DOH) Center for Health Statistics. Deaths from 2016 were identified using the preliminary data available as of February 27, 2017.

Case Definitions

1. Preliminary fentanyl-related overdose death

Criteria 1: International Classification of Diseases, Tenth Revision (ICD-10) codes

A preliminary fentanyl-related overdose death was defined as a death with any of the following ICD-10 codes as the underlying cause of death:

- X40-X44: Accidental poisonings by drugs
- X60-X64: Intentional self-poisoning by drugs
- X85: Assault by drug poisoning
- Y10-Y14: Drug poisoning of undetermined intent

And, an ICD-10 contributing cause-of-death code of T40.4 (Synthetic opioids, other than methadone).

¹ The BC Public Health Opioid Overdose Emergency - March 2017 Update, <http://www2.gov.bc.ca/assets/gov/health/about-bc-s-health-care-system/office-of-the-provincial-health-officer/overdose-response-progress-update-march2017.pdf>

Criteria 2: Death certificate text

In addition to criteria 1, the death was considered to be fentanyl-related if "fentanyl" was listed as a contributing cause of death on the death certificate.

2. Confirmed fentanyl-related overdose death

A confirmed fentanyl-related overdose death was a death where fentanyl or a fentanyl analog was detected by the toxicology lab. While most cases were first identified from death certificates, a few were first identified by the laboratory and then verified on the death certificate.

Fentanyl deaths among Washington State residents that occurred out-of-state couldn't be confirmed. Statistical analyses were limited to persons whose death occurred in Washington State.

Toxicology Testing

Fentanyl and fentanyl analogs were screened by the state toxicology lab:

1. The testing for fentanyl analogs started in July 2016. The screening test can detect the analogs listed in Table 1 at a concentration as low as 0.1-0.2 ng/ml.
2. In August 2016, the state toxicology lab began using a method that could detect fentanyl at levels as low as 0.5 ng/ml (from a threshold of 2.5 ng/ml previously).

Table 1. Fentanyl Analogs Screened

Fentanyl Analogs
3-methyl fentanyl
4-ANPP
4-methoxy butyryl fentanyl
Acetyl fentanyl
Acetyl norfentanyl
Beta-hydroxy thio fentanyl
Butyryl fentanyl
Furanyl fentanyl
Iso butyryl fentanyl
Para-fluoro butyryl fentanyl
Para-fluoro fentanyl
Valeryl fentanyl
U-47700 (synthetic opioid)
Carfentanil (new addition)

U-47700 is a selective μ -opioid receptor agonist, but not technically a fentanyl analog but it was included in the analysis (Mohr et al., 2016).

In addition to the fentanyl and fentanyl analogs, the state toxicology lab provided the data on other drugs detected.

Statistical Analysis

Descriptive analysis included fentanyl-related overdose deaths by month, other drugs present, county, intent, sex, age, race, and ethnicity. In this report, the county is the county where the death occurred. The significance of the change in fentanyl-related overdose death rates were ascertained by a rate ratio, with exact confidence intervals assuming a Poisson distribution (Fay, 2010). The 95% confidence intervals for crude rates were calculated using the exact method for incidence rate from the R package “epiR”.² The Wilson's method for binomial proportion was applied to the percentage confidence intervals. The confidence intervals for median age was estimated by bootstrap.

When looking at polysubstance overdose deaths, other drugs were identified based on toxicology findings. Heroin was identified based on being listed as a contributing cause on the death certificate. For the trend analysis comparing all opioid, heroin and fentanyl overdose deaths, heroin and fentanyl deaths were identified based on those drugs being listed as a contributing cause of death on the death certificate, while overall opioid overdose deaths were tabulated using ICD-10 codes.

Results

Fentanyl and Fentanyl Analog Overdose Deaths and Rates

In 2016 in Washington State, 70 drug overdose deaths related to fentanyl or a fentanyl analog were confirmed (Table 2). The crude rate was 1.0 per 100,000 (95% confidence interval [CI], 0.8-1.2). In 2015, 28 fentanyl-related drug overdose deaths were confirmed. The crude rate was 0.4 per 100,000 (95% CI, 0.3-0.6).

To better compare the 2015 and 2016 deaths, the 2016 deaths were adjusted to the less sensitive testing protocols used in 2015. Using this adjustment, 53 of the 70 2016 deaths would have been detected, for a crude rate of 0.7 per 100,000 (95% CI, 0.6-1.0). The 53 deaths in 2016 adjusted for the 2015 testing protocol represents an 86% increase from 2015. The 2015 to 2016 rate ratio was 1.9 (95% CI, 1.2-3.1). Adjusting the 2016 deaths to 53 using the 2015 protocol, excludes 8 deaths with a fentanyl concentration below 2.5 ng/mL and 9 deaths involving analogs (Table 3).

² epiR: Incidence rate confidence intervals

Table 2. Comparing 2015 and 2016 Fentanyl and Fentanyl Analog Overdose Deaths Adjusting for the Change in Testing Protocols, Washington State

Year	Death Count	Population	Crude Rate*	Lower 95% CI Crude	Upper 95% CI Crude
2016	70	7183700	1.0	0.8	1.2
2016 (adjusted for 2015 testing protocol)	53	7183700	0.7	0.6	1.0
2015	28	7061410	0.4	0.3	0.6

*Rate per 100,000

Table 3. Fentanyl-related Overdose Deaths by Testing Protocol, 2016, Washington State

		No Fentanyl	Fentanyl <2.5 ng/mL	Fentanyl >=2.5 ng/mL	Total
Analog present	No	0	7	52	59
	Yes	9	1	1	11
Total		9	8	53	70

Figure 1 shows the confirmed fentanyl-related overdose deaths by month of occurrence. The fewer number of deaths in the last quarter of 2016 may reflect the lag in the confirmation and reporting of drug overdose deaths to DOH Center for Health Statistics.

Figure 1. 2016 Confirmed Fentanyl or Fentanyl Analog Overdose Deaths by Month, Washington State

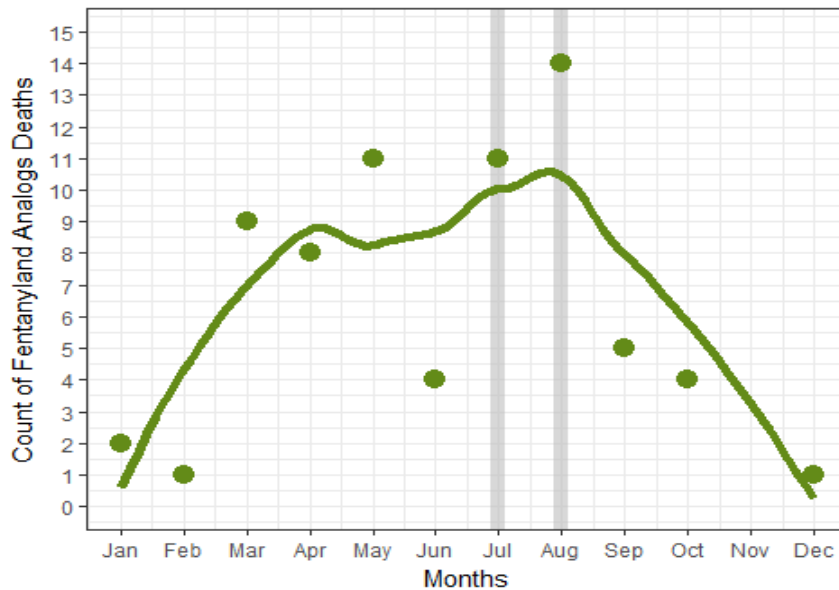


Figure 2. Fentanyl-related, Opioid and Heroin Overdose Deaths, 2006-2016, Washington State

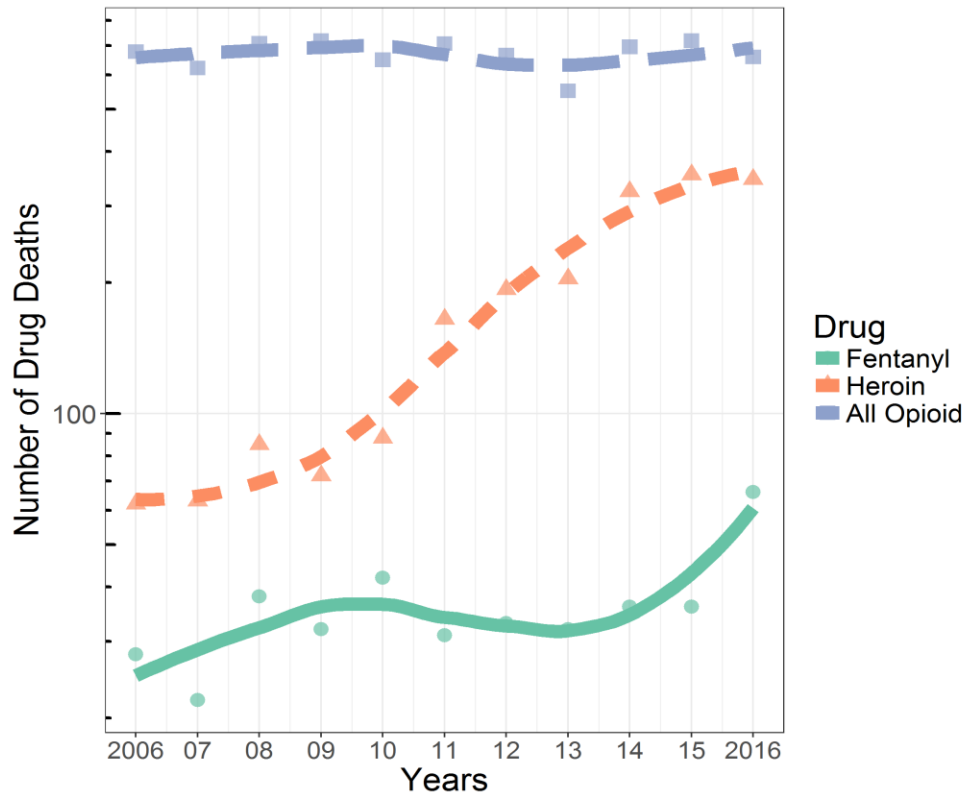


Figure 2 displays the trends in fentanyl-related, heroin and all opioid overdose deaths from 2006-2016 in Washington State. While overall opioid overdose deaths in Washington State have remained stable during this time period, heroin overdose deaths increased starting in 2010, and fentanyl-related overdose deaths increased starting in 2016.

Fentanyl Analog Types

In 11 of the 70 (15.7%) fentanyl-related overdose deaths in 2016, at least one fentanyl analog or a novel synthetic opioid agonist was detected (Table 4). In 9 of these 11 deaths, no fentanyl was detected. In 6 of the 11 deaths, more than one fentanyl analog was detected.

Table 4. Fentanyl Analog Overdose Deaths, 2016, Washington State

Decedent	4-ANPP	Acetyl fentanyl	Furanyl fentanyl	Para-fluoro butyryl fentanyl	Para-fluoro fentanyl	U-47700	Total
1	1	0	1	0	0	1	3
2	1	0	1	0	0	1	3
3	1	0	1	0	0	1	3
4	1	0	1	0	0	0	2

5	0	0	0	1	1	0	2
6	1	0	1	0	0	0	2
7	0	0	0	0	0	1	1
8	0	1	0	0	0	0	1
9	0	1	0	0	0	0	1
10	1	0	0	0	0	0	1
11	0	0	0	0	0	1	1
Total	6	2	5	1	1	5	20

Polysubstance

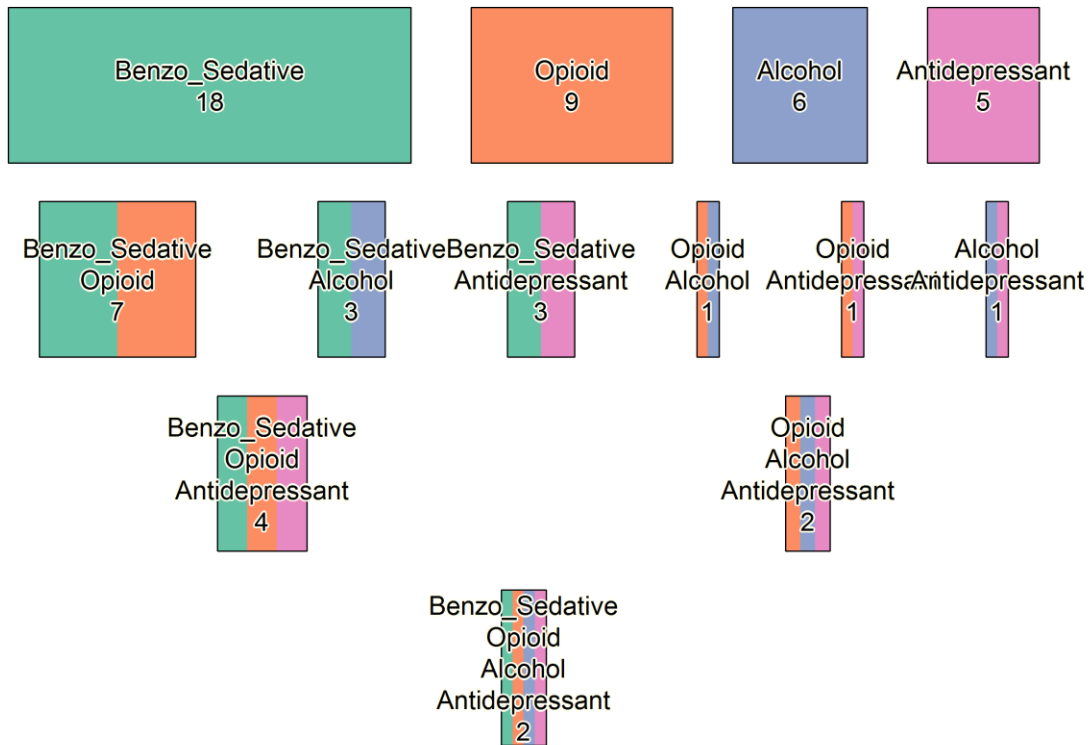
Sixty-three (63) of the 70 fentanyl-related overdose deaths had at least one other drug identified in the toxicology testing. Table 5 displays the most common drug classes identified. Among the 70 deaths, 29 or 41.4% (95% CI, 30.6-53.1%) had benzodiazepines identified, and 12 or 17.1% (95% CI, 10.1-27.6%) had a non-benzodiazepine sedative identified. Together 37 or 53% of the deaths had a benzodiazepine or non-benzodiazepine sedative identified. Other opioids were present in 26 or 37% (95% CI, 26.8-48.9%) of the fentanyl-related deaths. Antidepressants were found in 18 or 25.7% (95% CI, 16.9-37.0%) of the 70 deaths. Table 11 in the Appendix has a complete list of all the drug classes identified, and Table 12 shows the antidepressants by class.

Table 5. Top Five Drug Classes Identified by Toxicology Testing Among the Fentanyl-related Overdose Deaths, 2016, Washington State

Class	Death Count	Percent	Lower 95% CI Percent	Upper 95% CI Percent
Benzodiazepine	29	41.4	30.6	53.1
Other Opioid	26	37.1	26.8	48.9
Antidepressant	18	25.7	16.9	37.0
Alcohol	15	21.4	13.4	32.4
Non-benzodiazepine Sedative	12	17.1	10.1	27.6

Figure 3 shows the number of deaths by drug class, and combinations of drug classes identified among the fentanyl-related overdose deaths. The different rows of the graph displays the drug combinations. The graph is limited to the top five classes after combining benzodiazepine and sedative. As shown in Table 11, there are other drug classes present in the 63 deaths with additional drug other than fentanyl.

Figure 3. Combinations of the Top Five Drug Classes Identified Among the Fentanyl-related Overdose Deaths, 2016, Washington State



Counties

The distribution of the 70 fentanyl-related overdose deaths in 2016 by the county where the death occurred is shown in Table 6 and Figure 4.

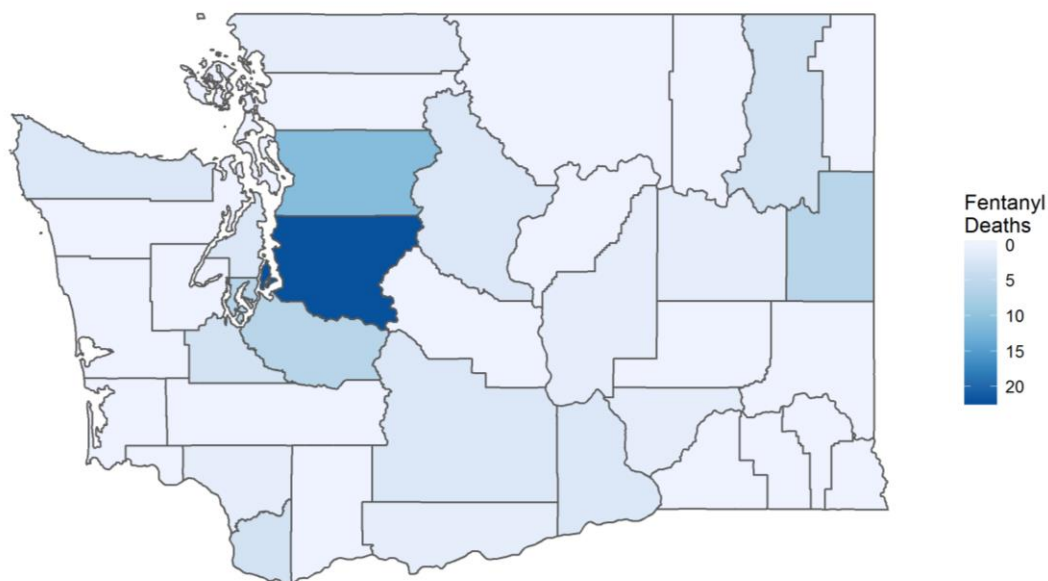
Table 6. Fentanyl-related Overdose Deaths by County of Overdose, 2016, Washington State

Year	Death Count	Population	Crude Rate*	Lower 95% CI Crude	Upper 95% CI Crude
Benton	2	190505	1.0	0.3	3.8
Chelan	2	75916	2.6	0.8	9.5
Clallam	2	73408	2.7	0.8	9.8
Clark	3	461019	0.7	0.2	1.9
Cowlitz	1	104846	1.0	0.2	5.3
Franklin	1	88664	1.1	0.3	6.3
Grant	1	94605	1.1	0.3	5.9
King	22	2105101	1.0	0.7	1.6

Kitsap	2	262590	0.8	0.2	2.8
Klickitat	1	21273	4.7	1.1	26.2
Lincoln	1	10640	9.4	2.3	52.4
Pierce	6	844494	0.7	0.3	1.5
Snohomish	11	772855	1.4	0.8	2.5
Spokane	6	492527	1.2	0.6	2.7
Stevens	3	44101	6.8	2.5	19.9
Thurston	3	272685	1.1	0.4	3.2
Whatcom	1	212536	0.5	0.1	2.6
Yakima	2	250907	0.8	0.2	2.9
WA State	70	7183700	1.0	0.8	1.2

**per 100,000*

Figure 4. Fentanyl-related Overdose Deaths by County of Overdose, 2016, Washington State



Intent: Intentional or Unintentional Deaths

Of the 70 fentanyl-related overdose deaths in 2016, the majority (84.3%, 95% CI 74.0-91.0%) were classified as unintentional (Table 7).

Table 7. Fentanyl-related Overdose Deaths by Intent, 2016, Washington State

Intent	Death Count	Percent	Lower 95% CI Percent	Upper 95% CI Percent
Suicide	3	4.3	1.5	11.9
Undetermined	2	2.9	0.8	9.8

Unintentional	59	84.3	74.0	91.0
Pending/missing	6	8.6	4.0	17.5

Sex

Of the 70 fentanyl-related overdose deaths in 2016, 48 (68.6%, 95% CI 57.0-78.2%) were males (Table 8). Males constituted 8 out of the 11 deaths involving fentanyl analogs (73%).

Table 8. Fentanyl-related Overdose Deaths by Sex, 2016, Washington State

Sex	Death Count	Percent	Lower 95% CI Percent	Upper 95% CI Percent
Female	22	31.4	21.8	43.0
Male	48	68.6	57.0	78.2

Age

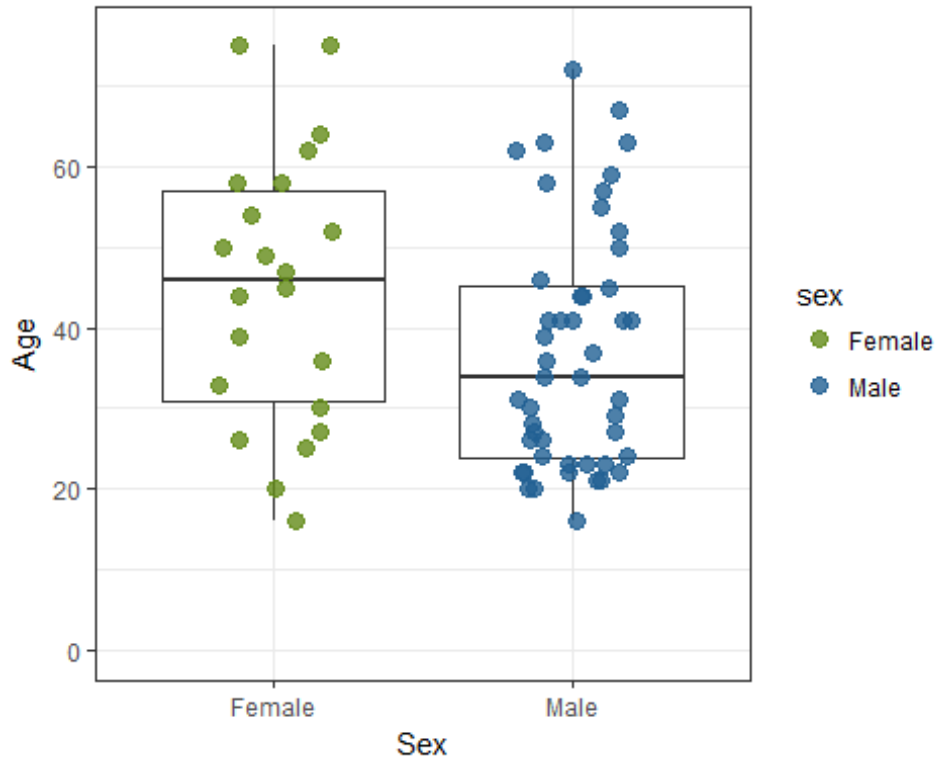
The median age of the 70 fentanyl-related deaths was 38 years old (95% CI, 25-53 years), with a range of 16-75 years. In the 11 deaths involving fentanyl analogs alone, the median age was 34 years old (95% CI, 22-44 years).

Table 9. Fentanyl-related Overdose Deaths by Age and Sex, 2016, Washington State

Sex	Min	25%	50%	75%	Max	Mean	Total
Male	16	30.7	46	57	75	44.8	22
Female	16	23.7	34	45.2	72	37.1	48
Total	16	26	38	51.5	75	39.5	70

The age distribution of the fentanyl-related overdose deaths is shown in table 9 and figure 5, the median age among males was 34 years old (95% CI, 23.5 -49.0 years) and 46 years old among females (95% CI, 29.5-58.0 years).

Figure 5. Boxplots of Age Among the 70 Fentanyl-related Overdose Deaths by Sex, 2016, Washington State



Race and Ethnicity

Of the 70 fentanyl-related overdose deaths in 2016, 81.4% (95% CI, 70.8-88.8%) were white (Table 10).

Table 10. Fentanyl-related Overdose Deaths by Non- Hispanic Race and Hispanic, 2016 Washington State

Race	Death Count	Percent	Lower 95% CI Percent	Upper 95% CI Percent
American Indian/Alaska Native, non-Hispanic	1	1.4	0.3	7.7
Asian, non-Hispanic	3	4.3	1.5	11.9
Black, non-Hispanic	3	4.3	1.5	11.9
Hispanic	4	5.7	2.2	13.8
Multi-race, non-Hispanic	1	1.4	0.3	7.7
Native Hawaiian and Other Pacific Islander, non-Hispanic	1	1.4	0.3	7.7
White, non-Hispanic	57	81.4	70.8	88.8

Discussion and Conclusions

In 2016, the number of fentanyl-related overdose deaths reported in Washington State increased from 2015, although the increase is not as sharp as observed in some eastern and mid-eastern states. The increase remained significant even when adjusting for the less sensitive 2015 test protocols. Use of the new protocols introduced in 2016 increased the number of fentanyl-related deaths by 32%. Unlike in the eastern U.S., where white powder heroin is often mixed with fentanyl, the majority of the fentanyl-related overdose deaths in Washington State in 2016 did not involve heroin.

The findings in this report have several limitations. The 2016 death data were preliminary at the time of the analysis. There are likely more deaths that hadn't been reported to DOH Center for Health Statistics, especially those that occurred in the last quarter of 2016. Although most drug overdose deaths in this report are unintentional, the report included all intents. The medicolegal classification of manner or intent may underestimate suicides (Rockett et al., 2014). Procedures used in death investigations including tests performed to determine which drugs may have been present vary by jurisdiction and over time. Drug overdose death certificates do not always include all of the specific type of drugs involved in the death, and this also varies by jurisdiction. Neither death certificates nor toxicology testing identify between prescription and illicitly-made fentanyl, except for the analogs. Heroin involved fentanyl-related overdose deaths were identified by using those deaths that had heroin listed on the death certificate. However because heroin and morphine are metabolized similarly (Davis et al., 2016), some heroin deaths may have had morphine listed on the death certificate, resulting in an underreporting of heroin deaths and the combination of fentanyl and heroin overdose deaths. There were 12 deaths that listed morphine on the death certificate.

The sedative effects and intrinsic risks of consuming alcohol, benzodiazepines, antidepressants, anticonvulsants and many other drugs along with opioids, make attributing deaths to a specific drug or combination of drugs challenging (Fudin et al., 2014).

It is critical to continue to track fentanyl-related drug overdose trends in Washington State so that we can monitor the impact and target prevention messages and strategies.

Appendix

Table 11. All Drug Classes Identified among the Fentanyl-related Overdose Deaths, 2016, Washington State

Drug Class	Death Count	Percent	Lower 95% CI Percent	Upper 95% CI Percent
Benzodiazepine	29	41.4	30.6	53.1
Other opioid	26	37.1	26.8	48.9
Antidepressant	18	25.7	16.9	37.0
Alcohol	15	21.4	13.4	32.4
Sedative	12	17.1	10.1	27.6
Psychostimulant	9	12.9	6.9	22.7
Cocaine	8	11.4	5.9	21.0
Gabapentin	6	8.6	4.0	17.5
Antitussive	3	4.3	1.5	11.9
Anticonvulsant	2	2.9	0.8	9.8
Cannabis	2	2.9	0.8	9.8
Antiarrhythmic	1	1.4	0.3	7.7
Antihistamine	1	1.4	0.3	7.7
Antihypertensive	1	1.4	0.3	7.7
Antipsychotic	1	1.4	0.3	7.7
Phenobarbital	1	1.4	0.3	7.7

Table 12. Antidepressants Identified Among the Fentanyl-related Overdose Deaths, by Class, 2016, Washington State

Antidepressant Class	Death Count
SSRI-antidepressant	18
Tricyclic-antidepressant	8
Heterocyclic-antidepressant	4
SNRI-antidepressant	1

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