Increase in Drug Overdose Deaths Involving Fentanyl – Rhode Island, January 2012 – March 2014

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Abstract

Objective—This study identified socio-demographic, substance use, and multiple opioid prescriber and dispenser risk factors among drug overdose decedents in Rhode Island (RI), in response to an increase in overdose deaths (OD) involving fentanyl.

Methods—This cross-sectional investigation comprised all ODs reviewed by RI's Office of the State Medical Examiners (OSME) during January 2012–March 2014. Data for 536 decedents were abstracted from OSME's charts, death certificates, toxicology reports, and Prescription Monitoring Program (PMP) databases. Decedents whose cause of death involved illicit-fentanyl (N=69) were compared to decedents whose cause of deaths did not involve fentanyl (N=467).

Results—Illicit-fentanyl-decedents were younger than other-drug decedents (p=0.005). While more other-drug than illicit-fentanyl decedents had *postmortem* toxicological evidence of consuming heroin (31.9% vs. 19.8%; p<0.001) and various pharmaceutical substances (p=0.002–

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0.027), third-party reports indicated more recent heroin use among illicit-fentanyl decedents (62.3% v. 45.6%; p=0.002). Approximately 35% of decedents filled an opioid prescription within 90 days of death; of these, one-third had a mean daily dosage of >100 morphine milligram equivalents. Most decedents' opioid prescriptions were filled at 1–2 dispensers (83.9%), and written by 1–2 prescribers (75.8%). Notably, 29.2% of illicit-fentanyl and 10.5% of other-drug decedents filled prescriptions for buprenorphine, used to treat opioid use disorders.

Conclusions—Illicit-fentanyl deaths frequently involved other illicit drugs (e.g., cocaine, heroin). The proportion of all decedents acquiring >100 MME/day prescription dosages written and/or filled by few prescribers and dispensers is concerning. To protect patients, prescribers and dispensers should review PMP records and substance abuse history prior to providing opioids.

Table of Contents Summary

This study identified socio-demographic, substance use, and multiple opioid prescriber and dispenser risk factors among drug overdose decedents in Rhode Island, in response to an increase in overdose (OD) deaths involving fentanyl. While illicit-fentanyl deaths frequently involved other illicit drugs, about 35% of all decedents filled an opioid prescription within 90 days of death. The proportion of all decedents acquiring >100 MME/day prescription dosages written and/or filled by few prescribers and dispensers is concerning.

Keywords

Opioids; Fentanyl; Drug Overdose; Prescriptions; Heroin; Cocaine

Introduction

From 2009 to 2012, Rhode Island (RI) experienced a steady increase in drug overdose (OD) deaths. (1) Most involved non-prescription, illicit drugs (e.g., heroin, cocaine), which accounted for 53% of all ODs reported in 2012 (N=183). (1) In 2013, a small (n=14) temporary increase in ODs from acetyl fentanyl – an illegally produced opioid analog – was detected in northern RI. (2) Subsequently during January 2014, RI experienced twice as many ODs as in January of previous years. These deaths were mostly among people who inject drugs, and involved a different synthetic opioid – fentanyl.

First synthesized in the 1960s as a general anesthetic, (3) fentanyl is 50–100 times more potent than morphine and 30–50 times more potent than heroin (4). By 1990, and coinciding with physicians being encouraged to prescribe stronger analgesics (5), fentanyl was initially approved as an analgesic for cancer pain and then expanded to treat chronic pain. Between 1999 and 2002, the annual number of fentanyl prescriptions in the U.S. increased 150%, reaching 4.6 million. (6) Today, fentanyl is used for severe, chronic pain control.

As with other pharmaceutical opioids, fentanyl can be abused and has contributed to the national epidemic of drug poisoning deaths. (5) Additionally, illicitly manufactured fentanyl – produced by clandestine laboratories since the late 1970s and commonly consumed by heroin users – has been associated with ODs. (7) Between April 2005 and March 2007, over 1,000 ODs involving illicitly manufactured fentanyl were identified in New Jersey; Maryland; Chicago, Illinois; Detroit, Michigan; and Philadelphia, Pennsylvania. (8) The

desire for higher potency opioids in the face of heroin's declining purity led to the distribution of fentanyl and fentanyl-laced heroin, with a subsequent spike in illicit fentanyl ODs throughout the 2000s. (9, 10) Heroin abuse often occurs in the broader context of polysubstance use, especially prescription opioids and cocaine. (11)

Study Purpose

In February 2014, the Rhode Island Department of Health (RIDOH) requested the Centers for Disease Control and Prevention's (CDC) assistance in defining and characterizing a spike in ODs involving fentanyl. This study explored three types of risk factors for these ODs: a) socio-demographic characteristics; b) substance use and abuse, especially opioid abuse; and c) visiting multiple prescribers and dispensers to obtain opioid prescriptions (considered multiple provider episodes). Findings may help RIDOH target educational messages and review their OD prevention strategies. Based on expert advice from local and federal law enforcement, health care, public health, and drug rehabilitation and treatment professionals, it was hypothesized that OD deaths involving fentanyl were associated with illicit substance use.

Methods

This cross-sectional study was conducted as part of an epidemiological public health emergency investigation, in response to the increase in OD deaths involving fentanyl reported in RI between November 2013 and March 2014. As such, CDC's National Center for Injury Prevention and Control determined that human research regulations did not apply.

Study Sample

The study population consisted of all ODs reviewed by the RI Office of the State Medical Examiners (OSME) between January 1, 2012 and March 31, 2014, and whose reported manner of death was accidental, pending determination or undetermined (N=630). This expanded time-frame allowed for the assessment of whether the increase in fentanyl-related deaths constituted an outbreak. Children ages 0–15 years (n=9), *in absentia* medical examiner reviews (n=15), pending cases that were *ad hoc* determined by the Chief Medical Examiner not to be ODs (n=40), and suicides (n=40) were excluded. The final sample size was 536 decedents (Figure 1).

Data Sources

This study comprised data from four RIDOH data sources: a) OSME's charts (electronic and hardcopy); b) RI Office of Vital Records' death certificates; c) RI State Health Laboratory toxicology reports; and d) RI's Prescription Monitoring Program (PMP) database.

OSME's charts contained socio-demographic, incident, autopsy, toxicology, and third party reports of drug use for each decedent. OSME compiled this information from medical examiners' (ME) reports, toxicology reports, emergency medical services and/or hospital reports, police reports, medical records, and other information provided to or requested by the ME to determine the cause of death. RI has a centralized ME system. All autopsy reports

are reviewed by the Chief ME, who certifies the cause of death based on the advice provided by the lead ME for each case.

Death certificates contained socio-demographic information on the decedent. Toxicology reports contained preliminary and confirmatory results of any toxicology tests performed on *postmortem* samples collected during autopsy or external inspection, and/or available *antemortem* samples collected during terminal hospitalizations, when the decedent was hospitalized for more than a few minutes.

RI's PMP database contained information on any prescriptions filled by the decedents at RI pharmacies or dispensers (i.e., product, strength, quantity, days, prescriber, pharmacy). All RI pharmacies and mail-order pharmacies licensed to do business in RI have been required to report Schedule II-IV prescription dispensing information (e.g., opioids) to the RI PMP system since July 1, 2013. Physicians are able to access this system to review their patients' prior prescriptions, as a tool to prevent overprescribing and drug diversion. (12, 13) Only prescriptions filled within 90 days of the decedent's date of death were considered for this study.

Definitions

Comparison groups—Illicit-fentanyl deaths included decedents for whom fentanyl was listed as an official cause of death or as a contributor on the final autopsy report provided by RI OSME, yet were not prescribed fentanyl. These decedents also included decedents for whom the cause of death was pending or non-specific, and preliminary toxicology reports identified fentanyl levels to be above the RI OSME working cutoff detection limit (i.e., enzyme-linked immunosorbent assay (ELISA) > 2 ng/ml), which also allows for the detection of fentanyl analogs (14). Consistent with the study's hypothesis and expert advice, decedents who filled at least one fentanyl prescription within 90 days of death were excluded from the fentanyl decedents group; only decedents whose deaths involved illicitly produced or acquired fentanyl remained in this group. **Other-drug deaths** included decedents for whom illicit fentanyl was not listed as an official cause of death or a contributor on the final autopsy report. These decedents also included those for whom the final cause of death was pending or non-specific, and fentanyl was not detected in toxicology analyses, as well as all decedents who filled fentanyl prescriptions within 90 days of death.

Prescription-related variables—Morphine milligram equivalents per day (MME/ day) refers to the average morphine milligram equivalents prescribed for daily use, based on all opioid prescriptions dispensed and reported to the PMP system within 90 days of a decedents' date of death. The MME/day for a given prescription is calculated by multiplying an MME conversion factor assigned to each opioid product's National Drug Code (15) by the strength of the product and the number of units prescribed per day (i.e., Strength*(Quantity/Days)*MME Conversion Factor). The number of units prescribed per day is found in the PMP; the MME conversion factors and strengths were obtained from a file compiled by CDC that lists opioids, benzodiazepines, muscle relaxants, and other drugs of interest to those studying prescription drug OD. Analyses included only the products

listed in the CDC MME file (16); elixirs and other cough/cold medications, injectables, and opioids infrequently used in outpatient settings were excluded. A decedent was considered to be at **increased risk for drug overdose** if his/her average MME/day was greater than 100, a frequently utilized cutoff for increased overdose risk (17, 18, 19, 20).

Prescriber refers to a physician or other health care worker licensed to prescribe opioid medications in the US, and who was identified in PMP records as having prescribed opioid prescriptions to at least one decedent within 90 days death. **Dispenser** refers to a pharmacy or other establishment authorized to store and dispense opioid prescriptions in the US, which was identified in PMP records as having dispensed at least one opioid prescription to decedents within 90 days of death. **Multiple provider episode** refers to a decedent filling opioid prescriptions provided by 3 or more prescribers, or 3 or more dispensers, within 90 days of death.

Toxicology variables—Preliminary (i.e., ELISA) and confirmatory toxicology test results identified **substances present in decedents' bodies** at the time of death or terminal admission to a hospital. This includes **illicit substances** (i.e., methamphetamine, cocaine, 6-Monoacetylmorphine (6MAM, a heroin metabolite), and heroin); **pharmaceutical substances**, which may have been used either illicitly or for legitimate medical purposes (i.e., acetaminophen, benzodiazepines, carisoprodol, codeine, methadone, morphine, oxycodone, tricyclic antidepressants, and zolpidem); **fentanyl-related substances** (i.e., acetyl fentanyl, fentanyl, 4-anilino-N-phenethyl-4-piperidine (ANPP, associated with illicit fentanyl manufacture)); and **opiates**, which includes both illicit and pharmaceutical products. Since there is no specific toxicology test for heroin, its presence was defined as *postmortem* toxicological evidence of morphine and at least one of the following requirements: *postmortem* toxicological evidence of codeine or 6MAM in decedent's body, presence of track marks in decedent's body, or presence of injection drug paraphernalia at the death scene. An aggregate **non-fentanyl-related illicit substance** variable was defined as a combined measure of the presence of any non-fentanyl illicit substances on the decedent's remains, excluding all pharmaceutical substances.

Recent substance-use variables—Reports of decedents' recent substance use was categorized as **prescription drug use** (i.e., antidepressant, benzodiazepines, antipsychotics, anticonvulsants, sedative, other) or **illicit drug use**; the latter is further categorized as **any type** (i.e., heroin, cocaine, marijuana, methamphetamines, injection drug use, prescription drugs for non-medical purposes, other) or specifically **heroin**. This information is based on third-party reports (e.g., family, friends, medical records) recorded in decedent's OSME charts.

Socio-demographic variables—Decedents were also described in terms of their **age group** (i.e., 17–20, 21–25, 26–35, 36–45, 46–55, 56–65, over 65 years), **sex** (i.e., female, male, unknown), **race and ethnicity** (i.e., non-Hispanic black, non-Hispanic white, Hispanic, other), **marital status** (i.e., divorced/widowed, married, single, unknown), and **veteran status** (i.e., no, yes, unknown).

Data Collection and Analyses

To reduce data entry errors, an electronic data abstraction form to collect data from OSME charts was developed utilizing Epi Info 7 software. (21) Individual PMP data files were downloaded for each decedent from the PMP online system. All data sources were linked based on the unique identifying number assigned to each individual. Data were de-identified for analyses.

Descriptive analyses were conducted for all deaths. Frequencies and proportions were calculated for all socio-demographic, substance use/abuse, and multiple provider episode variables. Bivariate comparisons between potential risk factors and illicit-fentanyl and other-drug decedents were examined using chi-square or Fisher's Exact Tests, and T-tests assessed significant statistical differences (i.e., $p < 0.05$) in proportions and means, respectively. The trend of all deaths, highlighting those involving illicit-fentanyl, was assessed by week across the study period. All data analyses were conducted using SAS v. 9.3. (22)

Results

In total, 12.9% (n=69) of the 536 OD deaths involved illicit-fentanyl and 87.1% (n=467) involved other drugs. Illicit-fentanyl deaths included those whose primary (n=51) or contributing (n=1) cause of death involved illicit fentanyl, and those with a pending/non-specific cause of death for whom fentanyl was detected via toxicology tests (n=23). Decedents that filled fentanyl prescriptions within 90 days of their death (n=6) were considered part of the other-drug group (Figure 1).

While illicit-fentanyl deaths were reported throughout the study period, two notable increases were identified in March – April 2013 (weeks 61–74) and November 2013 – March 2014 (weeks 98–115) (Figure 2). These correspond to a previously reported outbreak of OD deaths involving acetyl fentanyl in northeast RI (1) and the increase in ODs involving fentanyl that resulted in this public health response. (23)

Socio-demographic Characteristics

Decedents' ages ranged between 17 and 86 years, with a median age of 45 years. Most decedents were male (68.1%), non-Hispanic white (87.1%), and single (49.3%). Nearly 7% of decedents were known to be military veterans. No statistically significant differences in sex, race and ethnicity, marital or veteran status were found between decedents whose deaths involved illicit-fentanyl vs. other-drugs. However, illicit-fentanyl decedents were significantly younger than other-drug decedents ($p=0.005$); a third of illicit-fentanyl decedents were between 26 and 35 years old (34.8%, n=24) (Table 1).

Toxicological Evidence of Substance Use

At the time of death, 63% (n=336) of all decedents had at least one non-fentanyl-related illicit substance present in their bodies; illicit-fentanyl (58.0%) and other-drug deaths (63.4%) did not differ in whether they had non-fentanyl-related illicit substances in their toxicology report. *Postmortem* toxicological evidence of illicit substance use among all decedents was highest for illicit substances that are frequently injected, such as cocaine and

heroin. The difference in toxicological evidence of cocaine among illicit-fentanyl (39.1%) and other-drug (30.4%) deaths was not statistically significant. However, significantly more other-drug (31.9%) than illicit-fentanyl (18.8%) deaths had toxicological evidence of heroin consumption (p=0.000). Additionally, significantly higher proportions of other-drug than illicit-fentanyl deaths had toxicological evidence of consuming pharmaceutical opioids (i.e., codeine, methadone, morphine, oxycodone) (Table 2).

Reported Recent Substance Abuse

Third-party reports (e.g., family, friends, medical records) showed that nearly half of all decedents had a recent history of alcohol (48.3%), tobacco (44.6%) or any type of illicit drug use (47.8%). Significantly more illicit-fentanyl than other-drug decedents were reported to be recent users of any type of illicit drugs (62.3% v. 45.6%, p=0.002) and, specifically, heroin (49.3% v. 28.3%, p=0.000). Over 13% of all decedents had reports of prior OD, and 18.1% were reported to have undergone any type of drug treatment or rehabilitation at least once (Table 2).

Recent Opioid Prescription History

Of the 536 decedents in this study, 186 (34.7%) had at least one opioid prescription filled within 90 days of death – accounting for a nearly identical proportion among illicit-fentanyl and other-drug deaths (Table 2). Nearly a third (32.8%) of all decedents with opioid prescriptions were prescribed more than 100 MME/day, placing them at increased risk for OD (Table 3). Among 26–35 year olds, only 24.8% (n=27) filled at least one opioid prescription within 90 days of death, yet 70.4% (n=19) in this age group were prescribed more than 100 MME/day (mean, 108.7 MME/day) (data not shown).

On average, decedents who filled at least one opioid prescription within 90 days of death filled 7.3 (s.e.=0.2) opioid prescriptions, with a median 85.1 MME/day (mean ($\bar{x}$)=45.1, s.e.=4.9) during that period. Decedents whose deaths involved other-drugs filled significantly more opioid prescriptions ($\bar{x} \pm$ s.e.= 7.5 ± 0.2 v. 6.0 ± 0.4; p=0.001) with higher MME/per day ($\bar{x} \pm$ s.e.= 148.5 ± 5.3 v. 114.2 ± 9.9; p=0.039) than those whose deaths involved illicit-fentanyl (Table 3). Illicit-fentanyl decedents (29.2%) filled significantly more prescriptions for buprenorphine – an opioid partial antagonist utilized in medication assisted treatments (MAT) for drug addiction – than other-drug decedents (10.5%; p=0.019) (Table 4). This includes 37.5% of all 26–35 year old illicit-fentanyl decedents. Over half of 26–35 year olds also filled oxycodone (59.3%; n=16) and hydrocodone (51.9%; n=14) prescriptions within 90 days of death (data not shown). Differences in other opioid prescriptions filled by decedents were not statistically significant (Table 4).

Multiple Provider Episodes

Most decedents did not have multiple provider episodes (3 prescribers or dispensers). Over 75% of all decedents who filled opioid prescriptions within 90 days of death (75.8%) obtained these from 1–2 prescribers; only 24.2% filled opioids provided by 3 or more prescribers. On average, decedents whose deaths involved other drugs filled prescriptions from more prescribers than illicit-fentanyl decedents ($\bar{x} \pm$ s.e.= 2.6 ± 0.1 v. 1.9 ± 0.2;

p=0.000) (Table 3). Young adults ages 26–35 years filled opioid prescriptions provided mostly by 1–2 prescribers (85.2%, n=23) (data not shown).

The majority of decedents who filled opioid prescriptions within 90 days of death (83.9%) did so at 1–2 dispensers (e.g., pharmacies); 16.1% filled them at 3 or more dispensers. On average, decedents whose deaths involved other drugs obtained these at more dispensers than illicit-fentanyl decedents ($\bar{x} \pm$ s.e.= 2.0 ± 0.0 v. 1.5 ± 0.1; p=0.000) (Table 3). Young adults ages 26–35 years filled these opioid prescriptions at 1–2 dispensers (81.5%, n=22) (data not shown).

Discussion

Illicit-fentanyl deaths were often associated with other illicit drugs that are frequently injected (i.e., heroin, cocaine). Significantly more other-drug than illicit-fentanyl deaths had toxicological evidence of heroin and various pharmaceutical substances. Yet, third-party reports of decedents' recent substance abuse found that significantly more decedents whose deaths involved illicit-fentanyl than other-drug decedents were recent users of any type of illicit substance, and specifically heroin. Furthermore, the proportion of all decedents who filled opioid prescriptions at levels considered high risk for overdose (>100 MME/day) within 90 days of death is concerning.

Apart from illicit-fentanyl decedents being significantly younger than other-drug decedents, no other socio-demographic differences were identified. Overall, decedents' socio-demographic characteristics were consistent with the literature; most were non-Hispanic white and male. (11) On average, other-drug decedents obtained opioid prescriptions from significantly more prescribers and/or dispensers than illicit-fentanyl decedents; multiple provider episodes were not a significant risk factor for illicit-fentanyl ODs. This suggests that perhaps illicit-fentanyl decedents were further along in the opioid abuse trajectory – relying less on prescription opioids and more on illicit drugs – and at a younger age, compared to other-drug decedents.

Significantly more decedents whose deaths involved illicit-fentanyl had third-party reports of recent illicit drug use – especially of heroin – than other-drug decedents. In fact, nearly 20% of illicit-fentanyl deaths had *postmortem* toxicological evidence of heroin and over a third had evidence of cocaine in their bodies. Yet significantly more other-drug (31.9%) than illicit-fentanyl (18.8%) deaths had toxicological evidence of heroin consumption. Limitations in the study's heroin case definition and data sources could have resulted in illicit-fentanyl deaths that tested positive for morphine not being classified as heroin positive by the time the study's data was collected (i.e., 3 out of 16 total morphine positive illicit-fentanyl deaths).

Illicit-fentanyl deaths were not solely associated with consuming one particular type of non-fentanyl illicit substance. This is consistent with findings from law enforcement investigations, which suggest illicit-fentanyl deaths were mostly associated with illicit injection drug use, with the illicit fentanyl or fentanyl analog being used alone, in place of, at the same time as, or mixed with heroin (e.g., fentanyl-tainted heroin).

It is notable that among all decedents with opioid prescriptions, approximately one-third received >100 MME/day within 90 days of death. It is especially concerning that among young decedents (26–35 years) with opioid prescriptions, over 70% were prescribed >100 MME/day. Furthermore, these prescriptions were mostly provided to each decedent by a single prescriber and dispenser, not multiple providers. Additionally, over half of 26–35 year old decedents with opioid prescriptions had been prescribed buprenorphine within the same time period; they were likely receiving MAT for opioid use disorders. Prescriptions for opioids to treat pain should be closely monitored since the combination of buprenorphine with other opioids, whether illicit or prescription, could raise the MME to levels associated with increased risk of overdose. Considering this and the fact that over 34% of illicit-fentanyl decedents were 26–35 years old at the time of death, this study's findings disturbingly suggest these young decedents started the opioid abuse trajectory (i.e., prescription opioids to illicit drugs) at a younger age and with a fast-approaching fatal outcome.

Study Limitations

This study was subject to at least four limitations. First, analyses are limited to the data that were abstracted while in the field during this public health emergency response investigation, which occurred while the outbreak was ongoing; some decedents' primary and contributing causes of death were still pending or under review. The study's case definition considers this limitation, and allows for illicit-fentanyl and other-drug decedents to be classified based on preliminary toxicology findings.

Second, inconsistencies in the documentation or availability of information for each decedent could have affected the study's findings, especially decedents' history of substance abuse. This information was gathered by the OSME *postmortem*, based on third-party interviews and/or findings from death scene investigations. As such, our study likely underestimates substance abuse across all decedents.

Third, prescription data were obtained by searching for each decedent by name and date of birth, via RI's PMP secure query system. This produced records with multiple residential addresses for most decedents. It was not possible to confirm whether these decedents had changed residence, or if prescription data for multiple individuals with the same name and date of birth was being produced by RI's PMP query system. Also, it is not possible to know if all opioid prescriptions filled by decedents were consumed by them, nor if they obtained opioid prescriptions through illicit means (e.g., black market).

Finally, toxicological analyses are unable to distinguish between pharmaceutical and illicitly manufactured fentanyl. Therefore, it was not possible to determine if illicit-fentanyl decedents consumed illicitly manufactured fentanyl – a suspected contributor to recent increases in heroin-related deaths (24) –, or illicitly acquired pharmaceutical fentanyl.

Conclusions

In 2012, Rhode Island ranked 19th in prescribing opioid pain relievers (89.6 opioid prescriptions per 100 persons) and 17th in prescribing high-dose opioid pain relievers (5.2

per 100). (25) However, this study's fentanyl-related deaths were associated with the use of illicit fentanyl and other drugs that are frequently injected (e.g., heroin, cocaine). Yet, the high overdose risk levels of MME/day prescribed within 90 days of death is concerning; the risk is even greater when heroin or illicit fentanyl is used simultaneously with prescription opioids. This outbreak occurred within the context of the current heroin epidemic in the US, driven by the increase in prescription opioid use for non-medical purposes (11), and heroin's higher availability, lower cost and increased purity. (10, 11)

Collaborations between law enforcement, public health, health care, and recovery/treatment sectors are needed to reduce access to illicit drugs (e.g., heroin, cocaine), including illicitly manufactured or obtained fentanyl, and help those in need to recover from substance use disorders. Medication assisted treatment (MAT) is recommended for patients struggling with substance abuse, including abuse of illicit and prescription opioids; people who abuse prescription opioids are 40 times more likely to also abuse heroin. (11) Reviewing patient's prescription and illicit substance abuse history prior to starting MAT is advised; subsequently, monitoring PMP data and routine urine drug testing for specific substances (e.g., buprenorphine, heroin, prescription opioids, cocaine, benzodiazepines) is recommended. (26, 27) Increasing first-responder, family member, and opioid user access to opioid antagonists (e.g., naloxone) can also reduce overdoses and improve opioid safety. (11, 28)

Addressing pain is an important part of clinical care; it is estimated that 11.2% of people in the US suffer from chronic pain. (29) While diverse non-opioid treatment options for acute and chronic pain exist (e.g., physical therapy, non-steroidal anti-inflammatory drugs) and should be considered prior to starting an opioid treatment regimen, the benefits of opioid medications may occasionally outweigh the risks. Given the strong association between prescription opioid abuse and abuse of illicit drugs such as heroin, it is imperative that prescribers and dispensers ensure patients' safety when utilizing opioid medications.

Providers should assess patients' substance abuse history and risk for abuse prior to prescribing opioids and start with the lowest effective dose (30, 31, 32), during a pre-determined timeframe 30, 32). Prescribers should monitor the patients' pain intensity (30, 31), level of functioning (30, 31, 32), and evidence of aberrant behaviors or adverse effects (30, 31). It is important for prescribers to ensure patients receive appropriate pain treatment, while preventing or reducing their risk for adverse outcomes. Illicit, non-prescription opioids are not always sought for recreational purposes; sometimes they are sought as an alternate mechanism for pain control.

Additionally, it is recommended that prescribers and dispensers verify patients' prescription drug history prior to dispensing opioids. PMPs are a useful tool for this task. Given the relationship between heroin and prescription opioid abuse, (33, 34) these actions – in conjunction with following guidelines for opioid prescribing–might reduce both heroin and prescription opioid abuse and overdoses. Utilizing PMP data to identify prescribers and dispensers associated with opioid overdose deaths and patients with high MME/day is also recommended.

Acknowledgments

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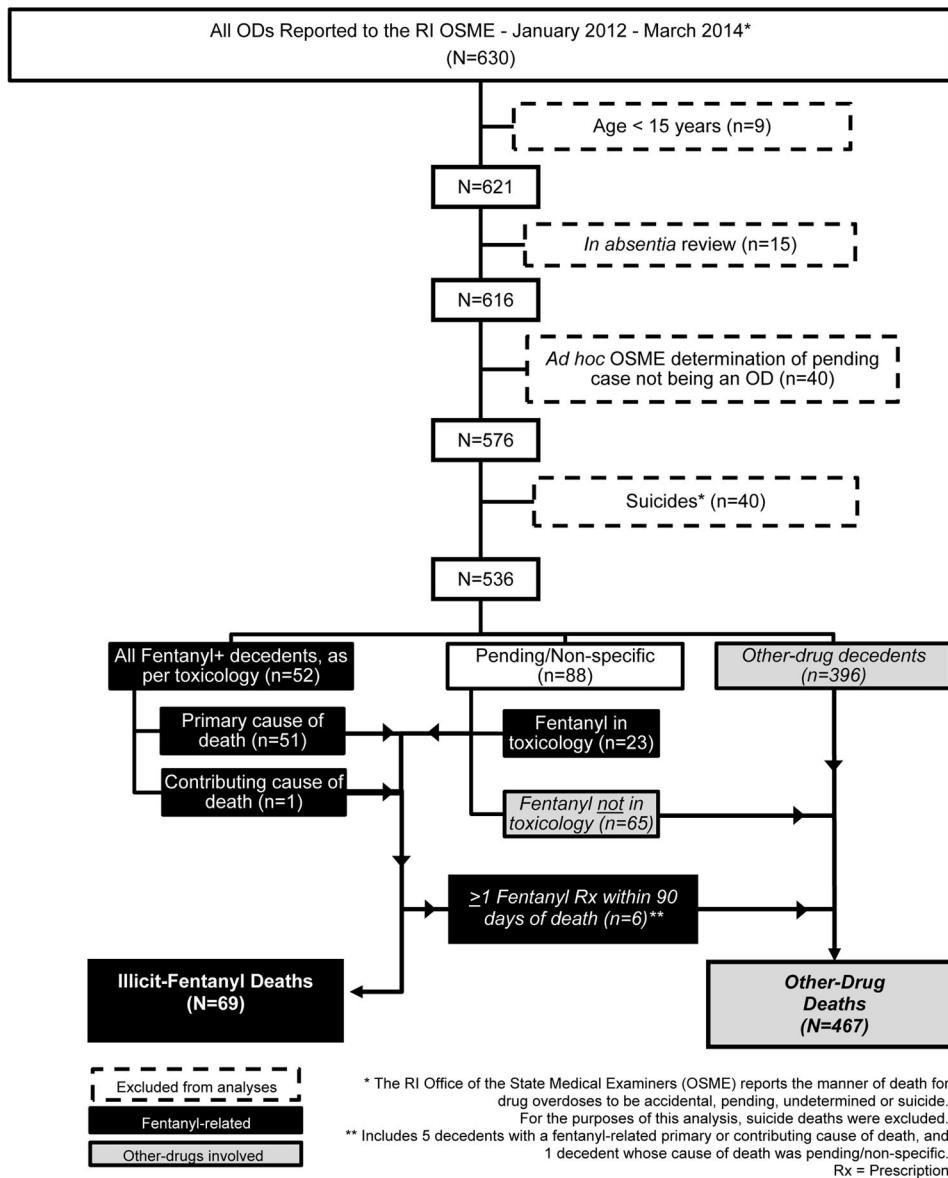**Fig. 1.**
Study Population: Drug Overdose (OD) Deaths in Rhode Island (RI), January 2012 – March 2014.
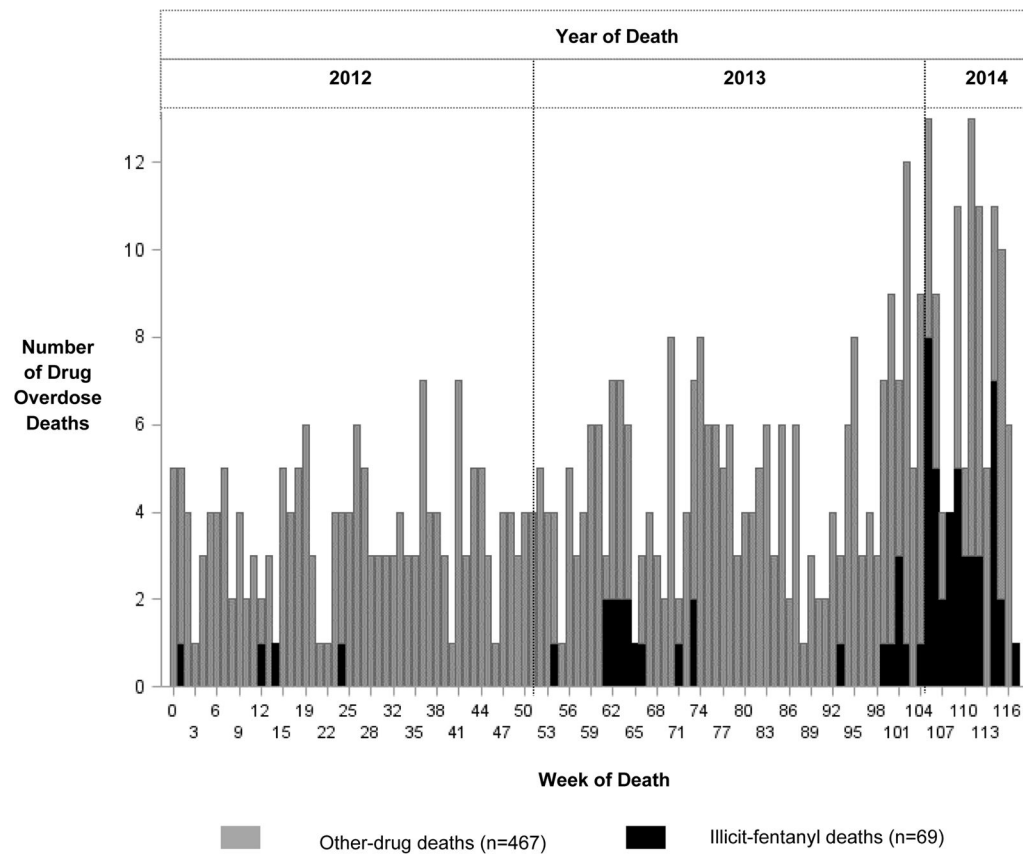
Fig. 2.
Number of Drug Overdose Deaths, by Week of Death – Rhode Island, January 2012 – March 2014 (N=536).

Table 1

Socio-demographic Characteristics of Drug Overdose Decedents – Rhode Island, January 2012 – March 2014 (N=536)

	Total N (%)	Drug Overdose Decedents N (%)		Chi-Square Test (p-value)
		Illicit-Fentanyl *(N=69)*	Other-Drug *(N=467)*	
Age, in Years (median=45, min=17, max=86)				
17–20 years	9 (1.7)	4 (5.8)	5 (1.1)	
21–25 years	31 (5.8)	4 (5.8)	27 (5.8)	
26–35 years	109 (20.3)	24 (34.8)	85 (18.2)	
36–45 years	123 (23.0)	13 (18.8)	110 (23.5)	**0.005**[*]
46–55 years	171 (31.9)	15 (21.7)	156 (33.4)	
56–65 years	82 (15.3)	9 (13.0)	73 (15.6)	
Over 65 years	11 (2.1)	0	11 (2.4)	
Sex				
Female	150 (28.0)	21 (30.4)	129 (27.6)	
Male	365 (68.1)	42 (60.9)	323 (69.2)	0.061
Unknown	21 (3.9)	6 (8.7)	15 (3.2)	
Race and Ethnicity				
Non-Hispanic Black	25 (4.7)	3 (4.4)	22 (4.7)	
Non-Hispanic White	467 (87.1)	61 (88.4)	406 (86.9)	0.941[*]
Hispanic	38 (7.1)	4 (5.8)	34 (7.3)	
Other	6 (1.1)	1 (1.5)	5 (1.1)	
Marital Status				
Divorced or Widowed	146 (27.2)	14 (20.3)	132 (28.3)	
Married	98 (18.3)	9 (13.0)	89 (19.1)	0.130
Single	264 (49.3)	40 (58.0)	224 (48.0)	
Unknown	28 (5.2)	6 (8.7)	22 (4.7)	
Veteran Status				
No	475 (88.6)	60 (87.0)	415 (88.9)	
Yes	37 (6.9)	3 (4.4)	34 (7.3)	0.164[*]
Unknown	24 (4.5)	6 (8.7)	18 (3.9)	

Notes: Percentages refer to the proportion of decedents represented within illicit-fentanyl and other-drug overdose deaths (i.e., column percentages). **Bold** indicates that differences between illicit-fentanyl and other-drug decedents are statistically significant.

[*] Denotes Fisher Exact test, due to small expected cell counts.

Table 2

Drug Overdose Decedents' Toxicology Reports and Substance Use History – Rhode Island, January 2012 – March 2014 (N=536)

	Total N (%)	Drug Overdose Deaths N (%)		Chi-Square Test (p-value)
		Illicit-Fentanyl (*N=69*)	Other-Drug (*N=467*)	
Toxicological Reports of Substances Present in Decedent's Body				
Illicit substances				
Cocaine (P)	169 (31.5)	27 (39.1)	142 (30.4)	0.146
Heroin *	162 (30.2)	13 (18.8)	149 (31.9)	**0.000**
6MAM (C)	48 (9.0)	3 (4.4)	45 (9.6)	0.151
Non-fentanyl-related illicit substance **	336 (62.7)	40 (58.0)	296 (63.4)	0.386
Fentanyl-related substances				
Acetyl fentanyl (C)	15 (2.8)	14 (20.3)	1 (0.2)	**<0.000**
ANPP (C)	10 (1.9)	9 (13.0)	1 (0.2)	**<0.000**
Fentanyl (C)	42 (7.8)	35 (50.7)	7 (1.5)	**<0.000**
Fentanyl (P)	79 (14.7)	68 (98.6)	11 (2.4)	**<0.000**
Opiates (P)	269 (37.7)	26 (37.7)	243 (52.0)	**0.026**
Pharmaceutical substances				
Acetaminophen (P)	28 (5.2)	0 (0.0)	28 (6.0)	0.38 ***
Benzodiazepines (C)	204 (38.1)	24 (34.8)	180 (38.5)	0.548
Carisoprodol (P)	14 (2.6)	0 (0.0)	14 (3.0)	0.234 ***
Codeine (C)	75 (14.0)	3 (4.4)	72 (15.4)	**0.013**
Methadone (P)	71 (13.3)	3 (4.4)	68 (14.6)	**0.020**
Morphine (C)	188 (35.1)	16 (23.2)	172 (36.8)	**0.027**
Oxycodone (P)	81 (15.1)	2 (2.9)	79 (16.9)	**0.002**
Tricyclic antidepressants (P)	66 (12.3)	4 (5.8)	62 (13.3)	0.078
Zolpidem (P)	16 (3.0)	2 (2.9)	14 (3.0)	0.964
Reported Recent Substance Use				
Alcohol	259 (48.3)	26 (37.7)	233 (49.9)	0.058
Tobacco	239 (44.6)	36 (52.2)	203 (43.5)	0.175
Illicit drug use				

	Total N (%)	Drug Overdose Deaths N (%)		Chi-Square Test (p-value)
		Illicit-Fentanyl (N=69)	Other-Drug (N=467)	
Any type	256 (47.8)	43 (62.3)	213 (45.6)	**0.002**
Heroin	166 (31.0)	34 (49.3)	132 (28.3)	**0.000**
Reported Prior Drug Overdose	73 (13.6)	9 (13.0)	64 (13.7)	1.000 ***
Reported Past Drug Addiction Treatment	97 (18.1)	16 (23.2)	81 (17.3)	0.411 ***
Filled 1 Opioid Prescription² *(within 90 days of death)*				
No	350 (65.3)	45 (65.2)	305 (65.3)	0.988
Yes	186 (34.7)	24 (34.8)	162 (34.7)	

Notes: Percentages refer to the proportion of decedents represented within illicit-fentanyl and other-drug overdose deaths (i.e., column percentages). Information on recent substance use, prior overdose and past drug treatment or rehabilitation was obtained by reviewing each decedent's medical examiner chart, which was based on 3rd party reports (e.g., family members, friends, medical records). **Bold** indicates that differences between illicit-fentanyl and other-drug deaths are statistically significant.

*
Toxicological heroin evidence was defined as the presence of morphine and at least one of the following requirements: codeine or 6MAM identified in toxicology, presence of track marks in decedent's body, or presence of intravenous drug paraphernalia on the death scene.

**
Includes the following illicit substances: amphetamine, cannabinoids, cocaine, methamphetamine, 6MAM and heroin; and opiates. Excludes other licit prescription substances presented on the table (e.g., codeine, morphine) which may or may not have been consumed by decedents for legitimate medical purposes.

***
Fisher's Exact Test (p-value) is presented due to small expected cell counts.

(P) = Preliminary toxicology results (i.e., ELISA)

(C) = Confirmatory toxicology results

ANPP = 4-anilino-N-phenethyl-4-piperidine

6MAM = 6-Monoacetylmorphine

Table 3

Opioid Use Among Decedents Filling at Least One Opioid Prescription within 90 Days of Death – Rhode Island, January 2012 – March 2014 (N=186)

	Total N (%)	Drug Overdose Decedents N (%)		Chi-Square Test (p-value)	T-Test (p-value)
		Illicit-Fentanyl (*N=24*)	Other-Drug (*N=162*)		
Opioid Prescriptions Filled					
$\bar{x}$ ± s.e. *(median, min – max)*	7.3 ± 0.2 (6, 1–23)	6.0 ± 0.4 (5, 1–14)	7.5 ± 0.2 (6, 1–23)	N/A	**0.001**
1–2 prescriptions	53 (28.5)	12 (50.0)	41 (25.3)	**0.006**	N/A
3 prescriptions	133 (71.5)	12 (50.0)	121 (74.7)		
Average MME Prescribed per Day					
$\bar{x}$ ± s.e. *(median, min–max)*	145.1 ± 4.9 (85.1, 7.5–779.6)	114.2 ± 9.9 (94.4, 7.7–342.1)	148.5 ± 5.3 (85.1, 7.5–779.6)	N/A	**0.039**
100 MME/day	125 (67.2)	17 (70.8)	108 (66.7)	0.343	N/A
>100 MME/day	61 (32.8)	7 (29.2)	54 (33.3)		
Prescribers Associated with Filled Opioid Prescriptions					
$\bar{x}$ ± s.e. *(median, min – max)*	2.5 ± 0.1 (2, 1–8)	1.9 ± 0.2 (1, 1–6)	2.6 ± 0.1 (2, 1–8)	N/A	**0.000**
1–2 providers	141 (75.8)	20 (83.3)	121 (74.7)	0.178	N/A
3 providers	45 (24.2)	4 (16.7)	41 (25.3)		
Dispensers that Filled Opioid Prescriptions					
$\bar{x}$ ± s.e. *(min – max)*	2.0 ± 0.0 (2, 1–5)	1.5 ± 0.1 (1, 1–4)	2.0 ± 0.0 (2, 1–5)	N/A	**0.000**
1–2 dispensers	156 (83.9)	23 (95.8)	133 (82.1)	0.069 *	N/A
3 dispensers	30 (16.1)	1 (4.2)	29 (17.9)		

Notes: Only drug overdose decedents that filled opioid prescriptions within 90 days of death (N=186), and the prescribers and dispensers associated to those opioid prescriptions are shown in this table. Percentages refer to the proportion of decedents represented within illicit-fentanyl and other-drug overdose deaths (i.e., column percentages). **Bold** indicates that differences between illicit-fentanyl and other-drug decedents are statistically significant.

*
Fisher's Exact Test (p-value) is presented due to small expected cell counts.

$\bar{x}$ ± s.e. = mean ± standard error

N/A = Not applicable

Table 4

Opioid Products Filled by Drug Overdose Decedents within 90 Days of Death – Rhode Island, January 2012 – March 2014 (N=186)

		Number of Decedents Who Filled Opioid Prescriptions			
		Drug Overdose Decedents N (%)		Chi-Square Test (p-value)	Fisher's Exact Test (p-value)
	Total N (%)	Illicit-Fentanyl (N=24)	Other-Drug (N=162)		
Buprenorphine	24 (12.9)	7 (29.2)	17 (10.5)	N/A	**0.019**
Codeine	10 (5.4)	3 (12.5)	7 (4.3)	N/A	0.123
Fentanyl	6 (3.2)	0 (0.0)	6 (3.7)	N/A	0.863
Hydrocodone	82 (44.1)	8 (33.3)	74 (45.7)	0.128	N/A
Hydromorphone	6 (3.2)	0 (0.0)	6 (3.7)	N/A	0.863
Methadone	11 (5.9)	0 (0.0)	11 (6.8)	N/A	0.418
Morphine	12 (6.5)	0 (0.0)	12 (7.4)	N/A	0.361
Oxycodone	112 (60.2)	13 (54.2)	99 (61.1)	0.258	N/A
Oxymorphone	1 (0.5)	0 (0.0)	1 (0.6)	N/A	>0.999

Notes: Only drug overdose decedents that filled opioid prescriptions within 90 days of death (N=186) are considered in this table. Percentages refer to the proportion of decedents represented within illicit-fentanyl and other-drug overdose deaths (i.e., column percentages). **Bold** indicates that differences between illicit-fentanyl and other-decedents are statistically significant.

N/A = Not applicable