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Short Report

Epidemiology of fentanyl-involved drug overdose deaths: A geospatial retrospective study in Rhode Island, USA

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Introduction

Since late 2013, the North American opioid overdose epidemic has been exacerbated by deaths involving prescription and illicitly manufactured fentanyl, a synthetic opioid analgesic (Gladden, Martinez, & Seth, 2016; US Drug Enforcement Administration, 2015). More recently, Australia has also reported a sharp increase in fentanyl overdoses among people who inject drugs (Latimer, Ling, Flaherty, Jauncey, & Salmon, 2016). The high potency of fentanyl means that only a miniscule amount (less than 2 mg, the equivalent of two grains of salt) can lead to overdose and death (Hess, Stiebler, & Herz, 1972). Difficult to distinguish from other drugs, illicitly manufactured fentanyl is an increasingly common adulterant in heroin and other illicit substances (US Drug Enforcement Administration, 2016). Sharp increases in fentanyl contamination in counterfeit prescription pills have also been observed (Centers for Disease and Control Prevention, 2016), increasing the risk of fentanyl overdose among persons seeking medications on the illicit market—representing a large and geographically widespread population. Consequently, fentanyl overdose risk now extends well beyond those regions previously impacted by heroin.

States in the US, including Maryland, Massachusetts, Ohio, and Florida, have all reported dramatic increases in fentanyl-related deaths (Peterson et al., 2016). Among six states that publish data on fentanyl fatalities, the number of fentanyl-involved deaths increased by over 350% between 2013 and 2014, from 392 to over 1400 (Gladden et al., 2016). In British Columbia, Canada, the number of drug overdose deaths involving fentanyl has sharply increased from 13 in 2012 to over 330 in just the first nine months of 2016 (British Columbia Coroners Service, 2016). A recent study involving clients of the Sydney Medically Supervised Injecting Centre in Australia found injection of fentanyl increased more than any other drug between 2013–2015, and the overall risk for fentanyl-related overdose was nearly 4.5 times higher than risk for overdose with other opioids (Latimer et al., 2016).

Despite the recent surge in fentanyl-related overdose deaths, there is a paucity of data regarding the characteristics, circumstances, and toxicology of fentanyl overdose decedents. Moreover, few studies have examined whether the geospatial distribution of fentanyl-related overdose deaths differs from that of non-fentanyl deaths. To inform more targeted and improved overdose prevention efforts, we conducted a detailed epidemiological and geospatial investigation of fentanyl-associated overdose deaths in Rhode Island, a state with the fifth highest rate of overdose mortality in 2015 (Rudd, Seth, David, & Scholl, 2016).

Methods

We conducted a retrospective review of accidental drug overdose deaths occurring in Rhode Island between January 1, 2014 and September 30, 2016. In accordance with state policy (Rhode Island Department of Health, 2015), cases were considered confirmed accidental drug-related overdose fatalities if: (i) the death was pronounced in Rhode Island; (ii) the final manner of death was deemed an accident by the medical examiner, and (iii) a drug is listed on the death certificate as the primary cause of death or a significant contributing factor. Each case was reviewed independently by a minimum of two trained research assistants; discrepancies were resolved by consensus. The study was exempt from IRB review as the analysis was conducted on behalf of public health and did not involve living subjects.

Data regarding sociodemographic characteristics of the decedent, toxicological analyses, and circumstances of the overdose were abstracted from medical examiner files. For each case, a medical examiner had previously determined the drug type (i.e.,

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illicit drug, prescription drug, or combined) based on a number of factors, including the results of toxicological analyses, death scene investigation, autopsy, and prior history of illegal drug use. The Office of the Chief Medical Examiner also provided data on the type and number of drugs seemed contributory to the cause of death. Our research team then extracted additional data regarding the setting of each overdose and the suspected route of administration, based on a detailed review of medical examiner reports (e.g., recent track marks), police reports (e.g., drug paraphernalia), as well as death scene investigation photos. Toxicological reports confirmed drug presence and provided quantification of fentanyl and metabolites. Exact locations corresponding to the address at which each overdose occurred were mapped using ArcGIS software (version 10.4), and were categorized as urban, suburban, or rural based on standard US census definitions.

We compared fentanyl-associated with non-fentanyl-associated deaths using chi-square tests and Wilcoxon rank sum tests. We also examined changes in selected overdose characteristics over time using the Mantel–Haenszel test for trend. Log-binomial regression was used to estimate risk ratios and 95% confidence intervals. To determine factors independently associated with fentanyl overdose, variables significant at $P < 0.05$ were included in a multivariable model. Heroin as a contributing cause of death, overdose drug type, and oral route of administration was removed from the final model due to collinearity with other variables. Finally, we conducted a hot spot analysis and calculated Getis-Ord Gi* statistics to identify clusters of fentanyl and non-fentanyl attributable overdoses, respectively.

Results

A total of 778 accidental drug overdose deaths in Rhode Island were observed during the study period. In total, 358 (46.0%) were attributable to acute fentanyl intoxication, increasing from 84 (35.0%) in 2014 to 138 (55.6%) during the first nine months of 2016 ($P < 0.001$). The total number and proportion of deaths attributable to acute fentanyl intoxication by month is shown in Fig. 1. We did not observe significant changes over time in the proportion of deaths involving injection drug use or multiple drugs; however, the proportion of deaths that were illicit drug-related increased from 50.4% in 2014 to 62.9% in 2016 ($P = 0.011$).

Compared to non-fentanyl overdoses, fentanyl overdose decedents were significantly younger (median = 38 [IQR: 29–49] vs. 46 [IQR: 34–55], $P < 0.001$). More than one in four (28.2%) of fentanyl overdoses occurred among individuals aged 18–29. Fentanyl overdoses were also more likely to: be an illicit drug or a combined illicit drug & prescription drug death; have evidence of injection drug use; and have multiple drugs contribute to the cause of death (Table 1). Compared to non-fentanyl overdoses, fentanyl overdoses were significantly less likely to be attributed to an oral route of drug administration, and have heroin, oxycodone, methadone, or other prescriptions deemed contributory to the cause of death (see Table 1). In the final multivariable model, fentanyl overdoses were independently more likely to: occur in 2015 (adjusted risk ratio [ARR] = 1.41, 95%CI: 1.18–1.70) and 2016 (ARR = 1.47, 95%CI: 1.23–1.75) compared to 2014, respectively; occur among persons aged 18–29 (ARR = 1.41, 95%CI: 1.13–1.75); involve injection drug use (ARR = 1.36, 95%CI: 1.18–1.54); involve multiple drugs (ARR = 1.74, 95%CI: 1.44–2.09); and were less likely to have oxycodone (ARR = 0.67, 95%CI: 0.48–0.94) or methadone (ARR = 0.51, 95%CI: 0.33–0.80) deemed contributory to the cause of death.

Detailed fentanyl toxicological results were available from 345 (96.4%) cases. The majority (n = 301, 87.2%) was obtained from femoral blood samples. Of these, the median fentanyl concentration was 11.0 ng/ml (range: 0.3–110.0 ng/ml). Norfentanyl was

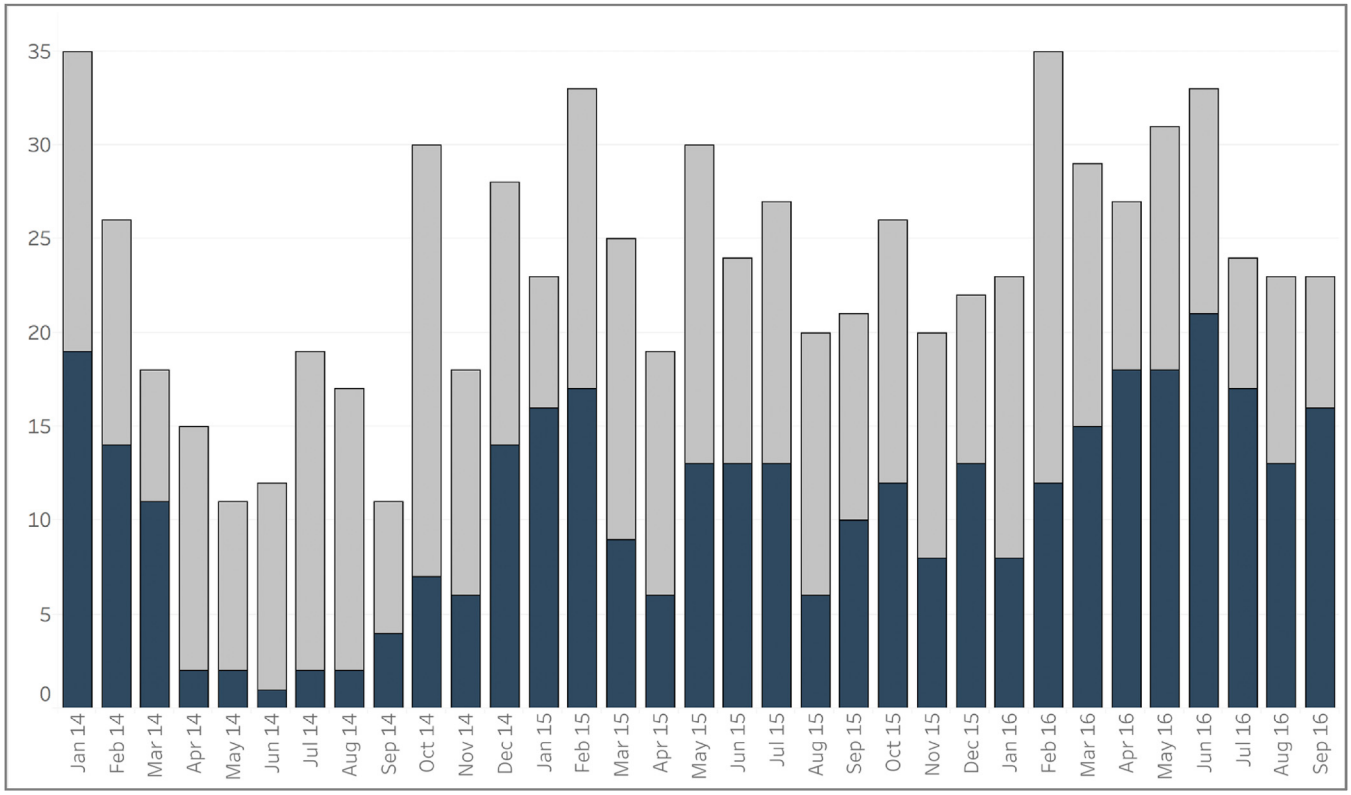

Fig. 1. Total number of overdose deaths by month (grey bars) and number attributable to acute fentanyl intoxication (blue bars) in Rhode Island, Jan 2014–Sep 2016 (for interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).