Drug and Alcohol Dependence 200 (2019) 59–63

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

journal homepage: www.elsevier.com/locate/drugalcdep

Short communication

Sociodemographic factors and social determinants associated with toxicology confirmed polysubstance opioid-related deaths

Joshua A. Barocas[a,b,*], Jianing Wang[a,b], Brandon D.L. Marshall[c], Marc R. LaRochelle[d], Amy Bettano[e], Dana Bernson[e], Curt G. Beckwith[f], Benjamin P. Linas[a,b], Alexander Y. Walley[d]

[a] Division of Infectious Diseases, Boston Medical Center (BMC), 801 Massachusetts Ave, 2nd Floor, Boston, MA 02118, USA
[b] Boston University School of Medicine, 801 Massachusetts Ave, 2nd Floor, Boston, MA 02118, USA
[c] Department of Epidemiology, Brown University School of Public Health, 121 South Main Street, Room 208 Box G-S121-2, Providence, RI 02912 USA
[d] Clinical Addiction Research and Education Unit, Section of General Internal Medicine, Department of Medicine, Boston University School of Medicine and Boston Medical Center, 801 Massachusetts Ave, 2nd Floor, Boston, MA 02118, USA
[e] Massachusetts Department of Public Health, 250 Washington Street, 6th Floor, Boston, MA 02108, USA
[f] Division of Infectious Diseases, Alpert Medical School of Brown University and the Miriam Hospital, 1125 N Main St, Providence, RI 02906, USA

ARTICLE INFO

Keywords:
Opioid-related overdose
Polysubstance use
Stimulants
Cocaine
Amphetamines

ABSTRACT

Background and aims: While prescribed and illicit opioid use are primary drivers of the national surges in overdose deaths, opioid overdose deaths in which stimulants are also present are increasing in the U.S. We determined the social determinants and sociodemographic factors associated with opioid-only versus polysubstance opioid overdose deaths in Massachusetts. Particular attention was focused on the role of stimulants in opioid overdose deaths.

Methods: We analyzed all opioid-related overdose deaths from 2014 to 2015 in an individually-linked population database in Massachusetts. We used linked postmortem toxicology data to identify drugs present at the time of death. We constructed a multinomial logistic regression model to identify factors associated with three mutually exclusive overdose death groups based on toxicological results: opioid-related deaths with (1) opioids only present, (2) opioids and other substances not including stimulants, and (3) opioids and stimulants with or without other substances.

Results: Between 2014 and 2015, there were 2,244 opioid-related overdose deaths in Massachusetts that had accompanying toxicology results. Toxicology reports indicated that 17% had opioids only, 36% had opioids plus stimulants, and 46% had opioids plus another non-stimulant substance. Persons older than 24 years, non-rural residents, those with comorbid mental illness, non-Hispanic black residents, and persons with recent homelessness were more likely than their counterparts to die with opioids and stimulants than opioids alone.

Conclusions: Polysubstance opioid overdose is increasingly common in the US. Addressing modifiable social determinants of health, including barriers to mental health services and homelessness, is important to reduce polysubstance use and overdose deaths.

1. Introduction

Drug overdose is the leading cause of accidental death in the U.S., with more

than 70,000 deaths in 2016 (Scholl et al., 2018). While opioids are present and likely causative in the majority of overdose deaths (Hedegaard et al., 2018; Scholl et al., 2018), it is crucial to gain a better understanding of which other drugs may also be involved and who is affected by polysubstance use. Studies have consistently demonstrated an increased risk of overdose death with concurrent opioid and benzodiazepine use (Hernandez et al., 2018; Sun et al., 2017). Concomitant use of stimulants—cocaine and methamphetamine—is rising and may also confer an additional risk of mortality (Al-Tayyib et al., 2017; Degenhardt et al., 2011; McCall Jones et al., 2017; Nechuta et al., 2018; Seth et al., 2018; Shiau et al., 2017; Turner et al., 2018). While other studies evaluated sociodemographic risk factors for drug overdose deaths broadly (Kandel et al., 2017; Nechuta et al., 2018), few have compared non-polysubstance opioid-related deaths with polysubstance opioid-related deaths, specifically with regard to stimulants. This knowledge gap may be fueling disparities in the public health response

* Corresponding author at: Boston University Medical, Campus 801 Massachusetts Ave, 2ndFloor, Boston, MA, 02131, USA.
E-mail address: Joshua.Barocas@BMC.org (J.A. Barocas).

https://doi.org/10.1016/j.drugalcdep.2019.03.014
Received 2 January 2019; Received in revised form 12 March 2019; Accepted 14 March 2019
Available online 08 May 2019
0376-8716/

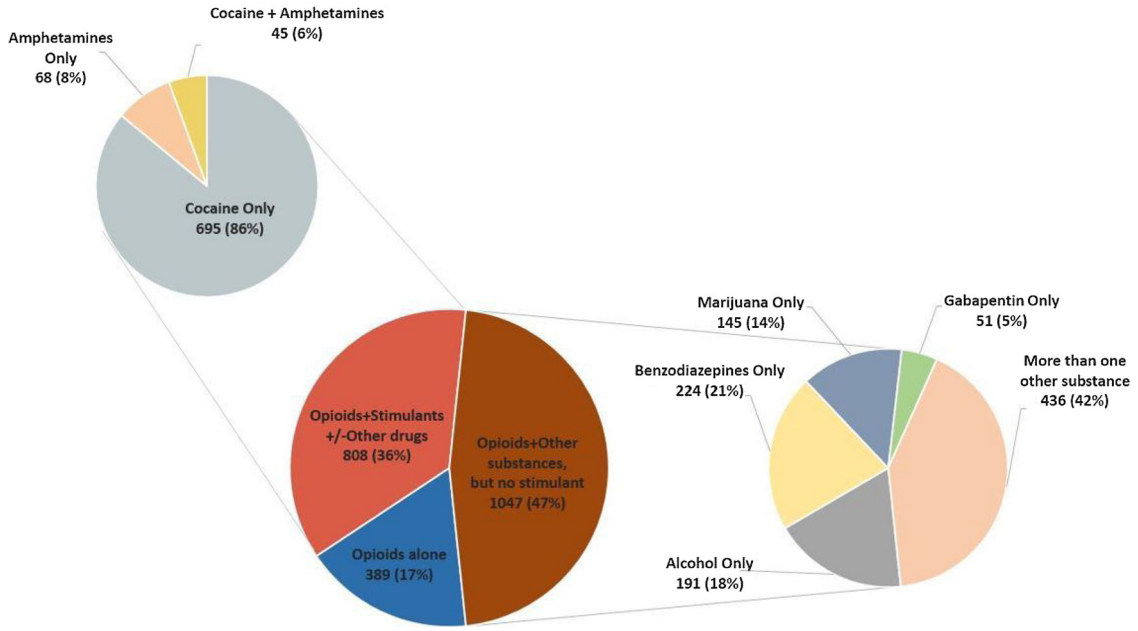

Fig. 1. Opioid-related overdose deaths with accompanying toxicology, 2014 and 2015, combined (n = 2,244).

to the overdose crisis and might overlook key social determinants of health that could help address the addiction crisis. We aimed to determine the factors associated with opioid-related polysubstance overdose death compared with opioid death alone.

2. Methods

We analyzed data from the Massachusetts Public Health Data Warehouse (PHD), previously described as the "Chapter 55″ database, a state-permitted, individually-linked database from several Massachusetts government agencies (Commonwealth of Massachusetts, 2017; The 190th General Court of the Commonwealth of Massachusetts, 2019). The PHD links claims-level data from the Massachusetts All-Payer Claims Database (APCD) to other state databases that include person-level demographics and data. Each record is de-identified and assigned a unique identification number that is consistent across all databases (Massachusetts Department of Public Health, 2017). We analyzed opioid overdose deaths among persons 11 years of age and older from January 1, 2014 through December 31, 2015. The creation of the PHD was mandated by law, and work within it is conducted by a public health authority.

First, we identified poisoning deaths in the Registry of Vital Records and Statistics mortality files using the International Classification of Disease (ICD-10) codes for underlying cause-of-death poisoning codes: X40–49 (unintentional) or Y10–Y19 (undetermined intent). For this study, we excluded X60–69 (intentional self-harm, suicide) and X85-X90 (assault or homicide). For overdoses, the death certificate lists drugs involved as immediate or contributory causes of death. These are included as ICD-10 "T-codes." Opioid involvement is indicated by the T-codes T40.0, T40.1, T40.2, T40.3, T40.4, and T40.6. We included only those opioid-related overdoses with toxicology data for opioids, stimulants, and selected other substances obtained from the Office of the Chief Medical Examiner (Supplementary Material).

Based on toxicology results, we divided the population into 3 mutually exclusive groups: (1) opioid-related deaths with opioids only on toxicology, (2) opioid-related deaths with opioids and an "other substance" (benzodiazepines, alcohol, marijuana, gabapentin, or clonidine) not including stimulants (cocaine or amphetamines) on toxicology, and (3) opioid-related deaths with opioids and stimulants with or without another substance on toxicology. We constructed a multinomial logistic regression model to compare these groups by certain variables (see Supplementary Table 1 for complete variable definitions and data sources). Hepatitis C virus (HCV) infection was not included in the primary analysis since it is incompletely classified in the PHD. A reference group was chosen for each independent variable. The comparison group among the three dependent variable categories of opioid-related death was chosen as only opioids present on toxicology (opioids alone). The model produced two sets of odds ratios and 95% confidence intervals (CIs) for each non-reference exposure variable group: 1) opioids and stimulants vs. opioids alone and 2) opioids and other substances, but no stimulants, present on toxicology vs. opioids alone.

To further examine whether characteristics were different among those who used opioids and stimulants only or opioids, stimulants, and other substances, we performed a secondary analysis in which we categorized the opioid-related deaths into 4 mutually exclusive toxicology groups: (1) opioids only on toxicology (comparison group), (2) opioids and stimulants only on toxicology, (3) opioids and other substances, but no stimulants, on toxicology, and (4) opioids, stimulants, and other substances on toxicology. The methods for this analysis were the same as for the primary analysis.

3. Results

Between 2014 and 2015, we identified 2,928 opioid-related overdoses in Massachusetts, and 2,244 (77%) had accompanying toxicology results (Supplementary Table 2). Of these opioid-related deaths with toxicology results, 72% involved fentanyl or heroin without prescription opioids; 9% involved prescription opioids without fentanyl or heroin; 19% involved both (Supplementary Table 3). Additionally, 83% of these opioid-related deaths involved another substance in addition to opioids. Specifically, 389 (17%) had opioids only; 1,047 (47%) had opioids and another substance that was neither cocaine nor amphetamines; 808 (36%) had opioids plus stimulants with or without another substance. The breakdown of other substances present on toxicology is outlined in Fig. 1.

The majority of opioid overdose deaths were among men (75%) and non-Hispanic white residents (86%), followed by non-Hispanic black residents (4.2%) (Table 1). Of the 808 deaths that involved stimulants, the proportion of residents who were non-Hispanic black was 6.2%. More than half (54%) of all overdoses occurred in people with

Table 1
Characteristics of opioid-related deaths with accompanying toxicology results in Massachusetts, 2014 and 2015 combined.

Total No. (%)	Opioids alone[a] No. (%)	Opioids + Other substances[b], without stimulants[c] No. (%)	Opioids +/- Other substances with stimulants No. (%)	
Total	2244	389 (17)	1047 (47)	808 (36)
Age				
11-24	224 (10)	53 (14)	110 (10)	61 (8)
25-44	1279 (57)	220 (56)	565 (54)	494 (61)
45+	741 (33)	116 (30)	372 (36)	253 (31)
Sex				
Male	1674 (75)	303 (78)	791 (76)	580 (72)
Female	570 (25)	86 (22)	256 (24)	228 (28)
Race/Ethnicity				
White, non-Hispanic	1934 (87)	334 (87)	943 (91)	657 (82)
Black, non-Hispanic	94 (4)	13 (3)	31 (3)	50 (6)
Hispanic	186 (8)	34 (9)	59 (6)	93 (11)
Other	21 (1)	§	§	§
Residence				
Non-Rural Rural	2088 (93)	351 (90)	968 (92)	769 (95)
	156 (7)	38 (10)	79 (8)	39 (5)
HIV status				
Yes	24 (1)	§	§	§
Homeless[d]				
Yes	338 (15)	47 (14)	143 (42)	148 (44)
Mental health comorbidity[e]				
Yes	1220 (54)	165 (42)	599 (57)	456 (56)
Incarceration in past 12 months[f]				
Yes	149 (7)	28 (19)	51 (34)	70 (47)
MOUD in the past 12 months[g]				
Yes	536 (24)	88 (16)	231 (44)	217 (40)

[a]Opioids include opiates, fentanyl, tramadol, designer fentanyl, heroin, hydrocodone, morphine, oxycodone, codeine, hydromorphone, oxymorphone, or prescription opioids not otherwise classified) on toxicology.
[b]Other substances include marijuana, alcohol, gabapentin, benzodiazepines, or clonidine on toxicology.
[c]Stimulants include cocaine and amphetamines on toxicology.
[d]Homelessness during any period of time.from 2011 to 2015.
[e]Includes depression, bipolar disorder, schizophrenia.
[f]Any release from prison or jail in Massachusetts in the 12 months that preceded the fatal overdose.
[g]Medication for opioid use disorder; includes naltrexone, methadone, or buprenorphine in the 12 months that preceded the fatal overdose.
[§]Cells with 1–10 observations were suppressed.

comorbid mental health disease.

Results of the multinomial regression are outlined in Supplementary Table 4. Persons in both of the older age groupings (25–44 and 45 and older) were more likely than the youngest age group (ages 11–24) to overdose with stimulants present than with opioids alone (ages 25-44: odds ratio (OR): 1.84, 95% confidence interval (CI): 1.23–2.76; ages 45 and older: OR: 1.7, 95% CI: 1.10–2.64). The majority of all overdose deaths occurred among those living in non-rural areas (93%). Residents of rural areas were less likely than residents of non-rural areas to overdose with opioids and stimulants on toxicology than with opioids alone (OR: 0.52, 95% CI: 0.33 − 0.84), whereas the opposite was true for persons with other mental illness compared to those without mental illness (OR: 1.56, 95% CI: 1.20–2.03). Finally, persons with recent incarceration were less likely than those without recent incarceration to die of opioids with non-stimulant substances than with opioids alone (OR: 0.53, 95% CI: 0.36 − 0.79).

There were also statistically significant and clinically notable findings in the secondary analysis in which the population with stimulants was subcategorized into those with and without other substances (Supplementary Table 5). In this analysis, non-Hispanic black residents were more likely than non-Hispanic white residents to die with stimulants and opioids than with opioids alone (OR: 2.18, 95% CI: 1.01–4.70). Persons with current or recent homelessness were more likely than persons without to die with stimulants and opioids than with opioids alone (OR: 1.85, 95% CI:1.15 − 2.98).

4. Discussion

This study demonstrates that among Massachusetts residents who die from an opioid-related overdose, five out of six (83%) involve another substance in addition to an opioid, and 19% of all deaths involve both heroin or fentanyl and prescription opioids. Using multiple substances, in addition to opioids, is the rule rather than the exception for opioid-related deaths.

Our study supports the notion that there are sociodemographic risk factors that are associated with overdose deaths that involve other substances—particularly stimulants—along with opioids. This analysis demonstrated that non-Hispanic blacks are twice as likely to die with opioids and stimulants than with opioids alone compared with non-Hispanic whites. A recent national study demonstrated that cocaine-related overdose death rates in non-Hispanic blacks were nearly equal to opioid-related overdose death rates in non-Hispanic whites (Shiels et al., 2018). It appears non-Hispanic blacks are at increased risk for death from opioid and stimulant use than their non-Hispanic white counterparts, which may be the result, in part, of a cocaine supply that is contaminated with illicitly produced fentanyl (Khatri et al., 2018; Tomassoni et al., 2017). It is crucial to recognize this risk in an already marginalized population such that education efforts address the increasing risk of unintentional exposure to opioids in this population.

Our study is unique in that it highlights important modifiable risk factors associated with different types of overdoses. For example, persons with comorbid mental illness accounted for more than half of all overdoses and were more likely to die with other substances—with or without stimulants—than opioids alone. Current or recent homelessness was a risk factor for overdose with opioids and stimulants, whereas recent incarceration was a risk factor for overdose with opioids alone as opposed to polysubstance overdose. Taken together, these findings provide two key lessons. First, to adequately address the drug overdose

epidemic, modifiable risk factors— social determinants of health such as access to mental health services, homelessness, and incarceration—must be addressed on a systemic level. Second, interventions aimed at decreasing overdose mortality need to account for the context of polysubstance use. For instance, overdose with opioids alone among persons recently released from incarceration may reflect the lack of opioid use disorder treatment availability in the penal system. Polysubstance opioid-related overdose may reflect inadvertent exposure to opioids, which might be the case among those recently on medications for opioid use disorder, or it may reflect the increased risk of relapse among those with co-occurring substance use disorders and mental health disorders (Brands et al., 2008; Maremmani et al., 2007; White et al., 2014). It may also reflect that the combined use of stimulants and opioids (e.g., "speedballs") may lead a person to use increased amounts of opioids or at increased frequency, leading to greater risk of overdose (Glick et al., 2018). Also, people intending to use cocaine, but who were opioid naïve, may unwittingly be exposed to fentanyl mixed into cocaine, which may cause an opioid overdose (Khatri et al., 2018; Tomassoni et al., 2017). Our study draws attention to the heterogeneity of the problem at hand and that there is not a one-size-fits-all approach to addressing the overdose epidemic, which is increasingly driven by polysubstance use. The type of opioid, the presence of polysubstance use, and the social context all influence the type of education and prevention approaches that are needed.

Some limitations to this study merit attention. First, we report only opioid-related overdose deaths and did not examine overdose deaths that did not include opioids as the cause of death based on ICD codes. The original intent of the legislation that mandated the establishment of the PHD was to study and respond to opioid-related overdoses (The 190th General Court of the Commonwealth of Massachusetts, 2019). As a result, the toxicology results for non-opioid related deaths were not initially included in the linked datasets. Also, the lack of comprehensive toxicology on all decedents may limit the generalizability of the study. Second, the two-year time period for this study was dictated by data availability (i.e., toxicology reports only available for 2014 and 2015) rather than a hypothesis-based justification. Future studies should assess overdose trends over longer time horizons to corroborate or refute these findings. Third, while the PHD individually links multiple datasets, in most cases these datasets are comprised of administrative data that may be incomplete, such as the APCD that forms the backbone of the database. Thus, certain characteristics (e.g., HCV status) are incompletely classified and were not included in the analysis. Fourth, the variable we used for rurality dichotomized rural and non-rural communities, so we were not able to investigate differences in urban and suburban locations. Finally, we did not include all possible drugs found on toxicology; rather, we chose the ones most likely to be involved in opioid overdoses. Future studies could consider additional drugs that act on the central nervous system but were not included in this analysis.

5. Conclusions

In sum, we identified social determinants and sociodemographic factors that are associated with opioid overdose deaths involving multiple substances. There is an urgent need to develop and implement tailored programs that address polysubstance use among people who use opioids, especially for populations that are marginalized by and from the healthcare system. This is a crucially important step to addressing the crisis of drug-related harms and associated health disparities in the U.S.

Contributors

All authors made substantial contributions to this manuscript. Dr. Barocas designed the study and directed its implementation, including quality assurance and control. Ms. Wang, Ms. Bernson, and Drs. Marshall, Beckwith, LaRochelle, Linas and Walley helped design the analytic strategy and provided content expertise. Ms. Bettano and Ms. Bernson helped with data analysis and data quality assurance and control. All authors were involved in manuscript preparation and review, and all authors approve the final manuscript.

Role of funding source

This work was supported by a 2018 supplemental grant from the Providence/Boston Center for AIDS Research [P30AI042853 to J.A.B, B.M, C.G.B, B.P.L, A.Y.W]; the Charles A. King Trust Fellowship [to J.A.B]; the University of Baltimore and the Office of National Drug Control Policy [G1799ONDCP06B to M.R.L, B.P.L and A.Y.W]; the National Institute on Drug Abuse at the National Institutes of Health [P30DA040500 to B.P.L, and A.Y.W; R25DA037190 to J.A.B and C.G.B; K23DA042168 to M.R.L]; and the National Institute of General Medical Sciences [P20GM125507 to B.D.L.M].

Conflict of interest

No conflict declared.

Acknowledgments

We would like to acknowledge the Massachusetts Department of Public Health for creating the unique, cross-sector database used for this project and for providing technical support for the analysis. The Massachusetts Department of Public Health was not engaged in human subjects research, and no IRB review was required. This project was determined by the Boston Medical University Campus Institutional Review Board to be non-human subjects research.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2019.03.014.

References

Al-Tayyib, A., Koester, S., Langegger, S., Raville, L., 2017. Heroin and methamphetamine injection: an emerging drug use pattern. Subst. Use Misuse 52, 1051–1058.
Brands, B., Blake, J., Marsh, D.C., Sproule, B., Jeyapalan, R., Li, S., 2008. The impact of benzodiazepine use on methadone maintenance treatment outcomes. J. Addict. Dis. 27, 37–48.
Commonwealth of Massachusetts, 2017. FY2018 Budget Summary, 2017. Commonwealth of Massachusetts, Boston, MA. https://www.mass.gov/how-to/fiscal-year-2018-budget.
Degenhardt, L., Singleton, J., Calabria, B., McLaren, J., Kerr, T., Mehta, S., Kirk, G., Hall, W.D., 2011. Mortality among cocaine users: a systematic review of cohort studies. Drug Alcohol Depend. 113, 88–95.
Glick, S.N., Burt, R., Kummer, K., Tinsley, J., Banta-Green, C.J., Golden, M.R., 2018. Increasing methamphetamine injection among non-MSM who inject drugs in King County, Washington. Drug Alcohol Depend. 182, 86–92.
Hedegaard, H., Miniño, A.M., Warner, M., 2018. Drug overdose deaths in the United States, 1999-2017. NCHS Data Brief, no 329. National Center for Health Statistics, Hyattsville, MD.
Hernandez, I., He, M., Brooks, M.M., Zhang, Y., 2018. Exposure-response association between concurrent opioid and benzodiazepine use and risk of opioid-related overdose in Medicare part D beneficiaries. JAMA Netw. Open 1, e180919.
Kandel, D.B., Hu, M.C., Griesler, P., Wall, M., 2017. Increases from 2002 to 2015 in prescription opioid overdose deaths in combination with other substances. Drug Alcohol Depend. 178, 501–511.
Khatri, U.G., Viner, K., Perrone, J., 2018. Lethal fentanyl and cocaine intoxication. N. Engl. J. Med. 379, 1782.
Maremmani, I., Pani, P.P., Mellini, A., Pacini, M., Marini, G., Lovrecic, M., Perugi, G., Shinderman, M., 2007. Alcohol and cocaine use and abuse among opioid addicts engaged in a methadone maintenance treatment program. J. Addict. Dis. 26, 61–70.
Massachusetts Department of Public Health, 2017. An Assessment of Fatal and Nonfatal Opioid Overdoses in Massachusetts. Massachusetts Department of Public Health, Boston, MA, pp. 2011–2015. https://www.mass.gov/files/documents/2017/08/31/data-brief-chapter-55-aug-2017.pdf.
McCall Jones, C., Baldwin, G.T., Compton, W.M., 2017. Recent increases in cocaine-related overdose deaths and the role of opioids. Am. J. Public Health 107, 430–432.
Nechuta, S.J., Tyndall, B.D., Mukhopadhyay, S., McPheeters, M.L., 2018.

Sociodemographic factors, prescription history and opioid overdose deaths: a statewide analysis using linked PDMP and mortality data. Drug Alcohol Depend. 190, 62–71.
Scholl, L., Seth, P., Kariisa, M., Wilson, N., Baldwin, G., 2018. Drug and opioid-involved overdose deaths - United States, 2013-2017. MMWR Morb. Mortal. Wkly. Rep. 67, 1419–1427.
Seth, P., Scholl, L., Rudd, R.A., Bacon, S., 2018. Overdose deaths involving opioids, cocaine, and psychostimulants - United States, 2015-2016. MMWR Morb. Mortal. Wkly. Rep. 67, 349–358.
Shiau, S., Arpadi, S.M., Yin, M.T., Martins, S.S., 2017. Patterns of drug use and HIV infection among adults in a nationally representative sample. Addict. Behav. 68, 39–44.
Shiels, M.S., Freedman, N.D., Thomas, D., Berrington de Gonzalez, A., 2018. Trends in U.S. drug overdose deaths in non-Hispanic black, Hispanic, and non-Hispanic white persons, 2000-2015. Ann. Intern. Med. 168, 453–455.
Sun, E.C., Dixit, A., Humphreys, K., Darnall, B.D., Baker, L.C., Mackey, S., 2017. Association between concurrent use of prescription opioids and benzodiazepines and overdose: retrospective analysis. BMJ 356, j760.
The 190th General Court of the Commonwealth of Massachusetts, 2019. Chapter 55 of the acts of 2015. An Act Requiring Certain Reports for Opiate Overdoses. The 190th General Court of the Commonwealth of Massachusetts, Boston, MA. https://malegislature.gov/Laws/SessionLaws/Acts/2015/Chapter55.
Tomassoni, A.J., Hawk, K.F., Jubanyik, K., Nogee, D.P., Durant, T., Lynch, K.L., Patel, R., Dinh, D., Ulrich, A., D'Onofrio, G., 2017. Multiple fentanyl overdoses— new Haven, Connecticut, June 23, 2016. MMWR Morb. Mortal. Wkly. Rep. 66, 107–111.
Turner, C., Chandrakumar, D., Rowe, C., Santos, G.M., Riley, E.D., Coffin, P.O., 2018. Cross-sectional cause of death comparisons for stimulant and opioid mortality in San Francisco, 2005-2015. Drug Alcohol Depend. 185, 305–312.
White, W.L., Campbell, M.D., Spencer, R.D., Hoffman, H.A., Crissman, B., DuPont, R.L., 2014. Patterns of abstinence or continued drug use among methadone maintenance patients and their relation to treatment retention. J. Psychoactive Drugs 46, 114–122.