Prevalence and correlates of non-fatal overdose among people who use drugs: findings from rapid assessments in Massachusetts, 2017–2019

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Abstract

Background: People who experience non-fatal overdose (NFOD) are at high risk of subsequent overdose. With unprecedented increases in fentanyl in the US drug supply, many Massachusetts (MA) communities have seen a surge in opioid-related overdoses. The objective of this study was to determine factors associated with lifetime and past year NFOD in at-risk MA communities.

Methods: We conducted multiple rapid assessments among people who use drugs (PWUD) in eight MA communities using non-probability sampling (purposive, chain referral, respondent-driven) methods. We collected sociodemographic, substance use, overdose history, substance use treatment, and harm reduction services utilization data. We examined the prevalence of NFOD (lifetime and past year) and identified factors associated with NFOD through multivariable logistic regression analyses in a subset of 469 study participants between 2017 and 2019.

Results: The prevalence of lifetime and last year non-fatal opioid overdose was 62.5% and 36.9%, respectively. Many of the study participants reported heroin (64%) and fentanyl (45%) use during the 30 days preceding the survey. Nonprescription buprenorphine and fentanyl use were independently associated with higher odds of lifetime NFOD, while marijuana use was associated with lower odds of lifetime NFOD ($p < 0.05$). Injection as the route of administration, benzodiazepine, nonprescription buprenorphine, heroin, and fentanyl use were independently associated with higher odds, while methadone use was associated with lower odds of past year NFOD ($p < 0.05$).

Conclusion: We documented a high prevalence of past year and lifetime NFOD among PWUD in MA. Our findings provide indicators that can help inform interventions to prevent overdoses among PWUD, including overdose prevention, medication treatment, and naloxone distribution.

Keywords: Non-fatal opioid overdose, People who use drugs, Rapid assessment, Massachusetts, Fentanyl

Introduction

In the USA, the opioid overdose epidemic has exacted an immense cost of human life, with over 400,000 lives lost over the last two decades [1]. The epidemic has also had a significant economic impact, with estimated costs totaling $631 billion between 2015 and 2018 alone [2]. Increase in the prescription of prescription opioids and
subsequent increase in opioid overdose deaths marked the first wave of the opioid overdose epidemic [3, 4]. It was followed by second wave of the opioid overdose epidemic, characterized by the rise in heroin use and heroin-related overdose deaths in the early to mid-2010s [4, 5]. The third wave of the opioid overdose epidemic began with the surge in illicit fentanyl-related overdose in recent years [4, 6]. Non-fatal overdoses (NFOD) represent a significant and ever-growing problem among individuals with substance use disorder. Moreover, people who experience NFOD are at a very high risk of subsequent overdose [7–10], and are also at risk of other comorbidities [11, 12]. Furthermore, accurate surveillance of NFOD is a challenge as these events are often only reported when a patient receives documented medical services such as emergency department visits and hospitalization [13, 14]. Understanding the prevalence and factors associated with overdose events is critical to guide future interventions.

In Massachusetts (MA), opioid-related fatal overdoses have steeply increased over the past 20 years, from 375 in 2000 to an estimated 2,104 in 2020. In 2019, fentanyl was detected in toxicology screens in 92% of fatal opioid overdoses [15]. Expanded access to and utilization of the overdose reversal drug, naloxone (brand name Narcan), is necessary to prevent fatal overdoses and research suggests that the rates of NFOD have also been climbing, with the number of emergency medical services (EMS)-administered naloxone rescues reaching approximately 15,000 in 2019 [16]. The risk of one-year mortality in people who experienced NFOD and received treatment at an emergency department is approximately 5% in MA [17]. While positive changes in state health policy have been introduced in recent years, including a 7-day limit to first opioid analgesic prescription, implementation of a prescription drug monitoring program, initiation of new syringe services programs, and development of statewide overdose education and naloxone distribution program, high rates of opioid-related overdoses have persisted in MA and present a substantial public health challenge, meriting further research. In the recent years, the success of these safe injection sites in other nations [18, 19] has prompted increased interest in establishment of safe injection sites in the USA. A recent letter to the editor published in NEJM describes the effectiveness of an unsanctioned injection site in the USA [20, 21], and in July 2021, Rhode Island passed legislation to plan and pilot safe consumption spaces.

Existing studies examining factors associated with opioid use and overdose indicate that young adults, men, non-Hispanic (NH) white people, individuals with less than a high school education, and homeless people are at increased risk of illicit opioid use and adverse opioid-related health outcomes, including overdose [4, 22–25]. However, detailed assessment substance use patterns and experiences in people who use drug is necessary given the high rates of opioid-related overdoses in MA. To that end, the goal of the current study was to estimate the prevalence of NFOD and determine factors associated with lifetime and past year NFOD in high-risk MA communities to better understand which groups may be at greatest risk for NFOD as well as to inform targeted interventions to combat the opioid overdose epidemic.

**Methods**

**Study population and recruitment**

Between August 2017 and November 2019, we conducted mixed-methods rapid assessments with people who use drugs (PWUD) in MA [26, 27]. Individuals were eligible for the study if they were 18 years of age or older, a resident of MA, and reported using an illicit drug in the past 30 days. Individuals who used marijuana alone were not eligible, as marijuana has been legal in the state of MA since 2016. In this paper, we present the findings from the quantitative data collected during the study.

We selected geographic regions of MA in which surveillance data showed a rising trend in fatal overdoses between 2016 and 2017 [28]. These regions included: Lowell, Lawrence, Quincy, Upper Cape Cod (Barnstable, Mashpee, Yarmouth, Falmouth), Springfield, Chicopee, the North Shore (Lynn, Salem, Beverly, Peabody), and New Bedford. In preparation for recruitment, we conducted environmental scans comprised of a review of publicly available public health and surveillance data, community walk-throughs, and meetings with community partners to identify locations for participant recruitment. We partnered with local organizations (e.g., syringe services programs (SSPs), homeless shelters, health centers) to facilitate the recruitment of potential participants. The detailed methodology used for the recruitment of study participants is described elsewhere [29]. The study design was adapted from World Health Organization Rapid Assessment and Response guide [30]. Briefly, we used a combination of non-probability sampling methods (primarily purposive, chain referral, and respondent-driven) to recruit participants. Potential participants were screened for eligibility by phone or in person. We obtained verbal informed consent from all participants before initiating study procedures. All participants completed a one-time, interviewer-administered survey on an electronic tablet or on paper. The survey assessed sociodemographic variables, information on substance use in the last 30 days, route of substance use, history of overdose experiences and overdose response, and knowledge and experiences about substance use treatment and harm reduction services. The survey was administered in English and Spanish and took approximately 45 min. Each
participant received a $20 gift card upon completion of the survey and up to $15 ($5 each) for referring up to three other eligible participants. The study was approved by the Institutional Review Boards of the Boston University Medical Campus and the Massachusetts Department of Public Health.

Study measures

1. Outcome variables (non-fatal overdose)

We obtained data to assess lifetime and past year experiences with NFOD by first asking study participants whether they had ever experienced a drug-related overdose. If participants answered in the affirmative, we asked for the month and year when they experienced their most recent overdose. We then calculated the time between the survey date and the date of the participant’s last overdose to determine whether the NFOD had occurred during the past year. For this study, we used lifetime NFOD and last year NFOD as outcome measures. We also collected information on the details regarding the most recent NFOD such as substance used during the most recent NFOD and whether the participant was taken to a hospital after the overdose.

2. Sociodemographic variables

We operationalized age into three categories: less than 30 years (young adults), 30–45 years, and more than 45 years of age based on the data distribution. We combined race and ethnicity into four independent categories: NH white, Hispanic, NH Black, and NH other. We categorized educational attainment into two groups: less than high school and high school graduate or higher. We also evaluated other sociodemographic indicators: housing status (binary: housed vs. unhoused), unemployment status (binary: yes/no), insurance type (categorized as public vs. other), history of arrest (yes/no), history of incarceration (binary: yes/no), and involvement in the sex trade (binary: yes/no).

3. Substance use variables

We examined substance use in the last 30 days, including use of crack, cocaine, methadone (prescribed), buprenorphine (obtained through one’s own prescription), buprenorphine (not obtained by one’s own prescription), amphetamine, benzodiazepine, pain medication (which included non-opioid pain medications), fentanyl, heroin, and marijuana. Based on the route of administration of the substances, we also created four dummy variables that indicated how these substances were taken: orally, snorted, smoked, and injected. The dummy variables were non-exclusive (i.e., an individual could have used substances by several routes) and non-specific (i.e., the route of administration was not specific to a type of drug or substance).

4. Naloxone knowledge and access

We asked the study participants whether they knew about naloxone (yes/no). Based on their response to the naloxone knowledge questions (i.e., if answered “yes”), the study participants were also asked whether they currently had naloxone on them (yes/no), had been trained for naloxone administration (yes/no), knew where to get naloxone (yes/no), and to rate the difficulty of obtaining naloxone (categorized into binary variables: easy/ extremely easy vs. neutral/difficult/extremely difficult). In our analysis, for individuals who did not know about naloxone, we imputed the values for naloxone branching logic questions with a missing response as “no.”

Data analysis

We excluded participants who did not have a history of opioid use to reduce the risk of combining opioid overdoses with stimulant overdose. We calculated descriptive statistics for all study variables of interest. Using Chi-squared and Fisher exact tests, we examined global differences in sociodemographic variables, substance use, and naloxone knowledge items by the history of NFOD (ever and last year). We used logistic regression models to identify sociodemographic, substance use, and harm reduction knowledge factors that were associated with past year and lifetime NFOD. Through bivariate analyses, we identified covariates that were significant at \( p < 0.20 \) for consideration in multivariable models. We assessed potential multicollinearity between covariates by estimating the variance inflation factor (VIF); variables with a VIF of 10 or more were removed from the final models. We finally eliminated duplicative variables and those not conceptually distinct. We also used site random effects to account for the differences in recruitment sites, recruitment methods, and recruitment time. We conducted all analyses in SAS 9.4 (Cary, North Carolina).

Results

We recruited 494 PWUDs between 2017 and 2019. After excluding non-opioid users, we retained 469 participants. Most study participants were male (61.9%), NH white (59.7%), and between the ages of 30–45 years (50.8%). More than one in four participants (28.4%) did not complete high school, and 60.0% were unemployed. Approximately 88.3% of the participants had a history
of past arrest and 62.2% had a history of incarceration. The prevalence of lifetime NFOD was 62.5%, and 36.9% of the sample reported experiencing NFOD within one year of the survey (Table 1). Sixty-four percent of the participants reported using heroin, and 45% reported using fentanyl in the last 30 days. Participants also commonly reported the use of buprenorphine (nonprescription: 10.7%) and marijuana (43.1%). Only 15% of the participants reported using pain medications. The most frequently mentioned route of administration was injection (59.5%). More than eight in ten participants reported ever receiving formal drug treatment. Additionally, 97.2% reported that they knew about naloxone. A substantial proportion (62.7%) had naloxone with them at the time of the survey, and 89.8% knew where to get naloxone in the community.

At the time of the most recent NFOD (in the last year), a majority of the participants reported using heroin (120/170) or fentanyl (97/170 [information not shown in table]). Polysubstance use at last NFOD was common, with 109 participants reporting having used two or more drugs during the overdose episode. Ninety-four participants reported that they were transported to the hospital for their most recent NFOD, and of those, only 37.2% rated their experience there as positive (vs. 26.6% neutral, 36.2% negative).

In our bivariate analyses, drug use and harm reduction service use were significantly associated with lifetime and past year history of NFOD (Table 2). The use of prescription buprenorphine, nonprescription buprenorphine, benzodiazepines, fentanyl, and heroin was all significantly and positively associated with history of lifetime NFOD (p < 0.05). Marijuana use was negatively associated with history of lifetime NFOD (p < 0.05). The use of nonprescription buprenorphine, benzodiazepines, fentanyl, and heroin was significantly associated with last year NFOD (p < 0.05). Injection as the route of administration was significantly associated with increased odds of both any and last year NFODs, whereas snorting was associated with decreased odds of any NFOD (both last year and lifetime), and oral substance use was associated with decreased odds of last year fatal overdose (p < 0.05). Additionally, we observed that having naloxone on hand, being trained for naloxone use, knowing where to get naloxone, and perceived difficulty in getting naloxone in the community were all significantly associated with higher odds of having a history of lifetime NFOD (p < 0.05).

In the multivariable models, after adjusting for sociodemographic variables, random effects of site, and other factors, we found that nonprescription buprenorphine use (adjusted odds ratio [aOR]: 1.9, 95% [confidence interval] CI: 1.2–3.0) and fentanyl use (aOR: 2.4, 95% CI: 1.6–3.8) were significantly and independently associated with higher odds of a history lifetime NFOD, while marijuana use (aOR: 0.6, 95% CI: 0.3–0.98) was negatively and independently associated with a NFOD history (Table 3). Benzodiazepine (aOR: 1.6, 95% CI: 1.1–2.4), nonprescription buprenorphine (aOR: 2.1, 95% CI: 1.2–3.6), heroin (aOR: 1.9, 95% CI: 1.1–3.5), and fentanyl (aOR: 1.6, 95% CI: 1.1–2.2) use along with injection as the route of administration (aOR: 2.6, 95% CI: 1.6–4.4) were all positively associated with last year NFOD, holding all else constant. Only current methadone use (aOR: 0.4, 95% CI: 0.3–0.6) was significantly and independently associated with lower odds of past year NFOD (Table 4). Among the sociodemographic variables considered when compared to NH Whites, only Hispanic (aOR: 0.6, 95% CI: 0.4–0.99) and NH Black race (aOR: 0.6, 95% CI: 0.4–0.9) were associated with lower odds of lifetime NFOD. For the past year NFOD experience, only people who identified as Hispanic (vs. NH White people) were at lower risk (aOR: 0.5, 95% CI: 0.3–0.9). The odds of experiencing past year non-fatal overdose for people who use drugs identifying as NH Black were not significantly different from people who use drugs who identified as NH White.

**Discussion**

We examined the prevalence and correlates of NFOD among PWUD across MA between 2017 and 2019. We observed a high prevalence of lifetime (62.5%) and past year (37%) overdose in the study population. Nonprescription buprenorphine use and fentanyl were significantly, positively, and independently associated with higher odds of NFOD, whereas marijuana and methadone use were associated with lower odds of NFOD.

The estimates of NFOD prevalence observed in our study are significantly higher than recently published estimates of the history of lifetime NFOD in PWUD, which range from 15 to 58% [8, 31–34]. The rise of fentanyl in the illicit drug supply across the USA has resulted in a high prevalence of NFOD and a sharp rise in fatal OD [35–37]. Forty-five percent of our study participants also reported using fentanyl and among those 76% reported any overdose. Our findings are consistent with previous studies in MA, which have linked 75% to 94% of opioid-related overdoses to fentanyl [35, 38]. Findings from our multivariable regression models also strongly support the association between specific substance use (e.g., heroin use, fentanyl) and use patterns (i.e., injection drug use) with NFOD. These findings are consistent with prior research linking overdose risk to heroin and injection drug use [34, 39]. Criminalization of illicit substances can create an environment where people who use drugs opt toward high-risk behavior such as sharing and reusing needles. Previous studies indicate that such practices...
| Variables                  | Category          | Total responses (N) | Percentage who had any overdose % (n) | p-value (2 sided) | Percentage who had last year overdose % (n) | p-value (2 sided) |
|---------------------------|-------------------|---------------------|---------------------------------------|-------------------|-------------------------------------------|-------------------|
| Gender                    | Female            | 177                 | 38.3 (111)                            | 0.904             | 38.6 (66)                                 | 0.857             |
|                           | Male              | 288                 | 61.7 (179)                            |                   | 61.5 (105)                               |                   |
| Race                      | NH\textsuperscript{a} white | 280          | 64.0 (188)                            | 0.049             | 61.3 (106)                               | 0.85              |
|                           | Hispanic          | 125                 | 23.8 (70)                             |                   | 24.9 (43)                                |                   |
|                           | NH Black          | 35                  | 5.8 (17)                              |                   | 6.9 (12)                                 |                   |
|                           | NH other          | 29                  | 6.5 (19)                              |                   | 6.9 (12)                                 |                   |
| Age                       | < 30 years        | 117                 | 23.8 (70)                             | 0.588             | 21.4 (37)                                | 0.369             |
|                           | 30–45 years       | 238                 | 50.7 (149)                            |                   | 52.6 (91)                                |                   |
|                           | > 45 years        | 113                 | 25.5 (75)                             |                   | 26.0 (45)                                |                   |
| Education                 | High School or more | 335           | 71.7 (210)                            | 0.955             | 69.4 (120)                               | 0.416             |
|                           | Less than HS      | 133                 | 28.3 (83)                             |                   | 30.6 (53)                                |                   |
| Employment status         | Unemployed        | 281                 | 59.2 (174)                            | 0.622             | 58.4 (101)                               | 0.574             |
|                           | Employed          | 187                 | 40.8 (120)                            |                   | 41.6 (72)                                |                   |
| Housing status            | Housed            | 151                 | 33.3 (98)                             | 0.521             | 36.4 (63)                                | 0.141             |
|                           | Not Housed        | 317                 | 66.7 (196)                            |                   | 63.6 (110)                               |                   |
| Insurance type            | Other             | 28                  | 4.4 (13)                              | 0.059             | 4.1 (7)                                  | 0.166             |
|                           | Public            | 436                 | 96.6 (280)                            |                   | 95.9 (166)                               |                   |
| Traded sex for money*     | Yes               | 118                 | 38.7 (82)                             | 0.027             | 39.7 (50)                                | 0.104             |
|                           | No                | 227                 | 61.3 (130)                            |                   | 60.3 (76)                                |                   |
| History of incarceration  | Yes               | 291                 | 69.6 (204)                            | <0.001            | 68.0 (117)                               | 0.047             |
|                           | No                | 177                 | 30.4 (87)                             |                   | 32.0 (45)                                |                   |
| Substance use in the last 30 days |                |                     |                                       |                   |                                          |                   |
| Crack                     | Yes               | 276                 | 64.9 (179)                            | 0.246             | 39.5 (109)                               | 0.162             |
| Cocaine                   | Yes               | 303                 | 63.0 (191)                            | 0.832             | 39.3 (119)                               | 0.148             |
| Methadone                 | Yes               | 109                 | 67.9 (74)                             | 0.2               | 30.3 (33)                                | 0.103             |
| Buprenorphine \(\text{Rx}\) | Yes             | 128                 | 71.1 (91)                             | 0.021             | 43.0 (55)                                | 0.094             |
| Buprenorphine (non-Rx)    | Yes               | 50                  | 76.0 (38)                             | 0.04              | 52.0 (26)                                | 0.019             |
| Amphetamine               | Yes               | 38                  | 76.3 (29)                             | 0.07              | 47.4 (18)                                | 0.162             |
| Benzodiazepine            | Yes               | 127                 | 72.4 (92)                             | 0.008             | 44.9 (57)                                | 0.162             |
| Fentanyl                  | Yes               | 211                 | 76.3 (161)                            | <0.001            | 47.4 (100)                               | <0.001            |
| Heroin                    | Yes               | 301                 | 69.8 (210)                            | <0.001            | 44.9 (135)                               | <0.001            |
| Marijuana                 | Yes               | 202                 | 55.9 (113)                            | 0.009             | 33.2 (67)                                | 0.1466            |
| Pain medication           | Yes               | 71                  | 13.6 (294)                            | 0.230             | 24 (13.9)                                | 0.599             |
| Route of administration of substance use |                |                     |                                       |                   |                                          |                   |
| Oral                      | Yes               | 150                 | 66.7 (100)                            | 0.223             | 46 (69)                                  | 0.005             |
| Smoke                     | Yes               | 280                 | 63.2 (177)                            | 0.774             | 39.3 (110)                               | 0.19              |
| Snort                     | Yes               | 208                 | 54.8 (114)                            | 0.002             | 32.7 (68)                                | 0.093             |
| Inject                    | Yes               | 279                 | 77.8 (217)                            | <0.001            | 47.3 (132)                               | <0.001            |
| Snort or inject           | Yes               | 407                 | 66.1 (269)                            | <0.001            | 39.6 (161)                               | 0.002             |
| Naloxone knowledge        | Do you know what naloxone is? | Yes | 456                 | 63.2 (288)                            | 0.211             | 37.3 (170)                               | 0.295             |
|                           | Do you currently have naloxone? | Yes | 294                 | 68.4 (201)                            | 0.001             | 39.8 (117)                               | 0.091             |
|                           | Have you ever been trained to use naloxone? | Yes | 350                 | 66.6 (233)                            | 0.003             | 38.3 (134)                               | 0.282             |
can also predispose individuals to the risk of transmitting infectious diseases such as HIV and HCV [12, 40, 41]. In light of these risks and the current HIV outbreak in the state, findings from the present study underscore the urgency of efforts to address the health of people using heroin and fentanyl in MA.

Prior research attributes fatal overdose rates to the high prevalence of fentanyl in the drug market [6, 35, 42]. Access to medication for opioid use disorders (MOUD) and harm reduction services—two evidence-based overdose prevention measures [43–45], have been shown to reduce fatal overdoses in many regions of the USA [9, 43, 46]. In examining access to harm reduction services among PWUD in MA, we found that a high proportion of participants reported carrying naloxone (62.7%) compared to estimates (17%-48%) from studies in other locations [34, 37, 47]. This higher prevalence of naloxone access among participants in our sample is likely due to the fact that MA has been at the forefront of public health responses to the opioid overdose epidemic [46, 48, 49]. Since 2006, MA has provided access to health insurance for all residents. Additionally, MA has implemented state-funded harm reduction services such as overdose education and naloxone distribution since 2005, with additional access to naloxone through pharmacies since 2018 [46, 48–50]. The observation that difficulty in accessing naloxone was associated with NFOD experience suggests there is still much room for improvement in community naloxone provision and equity in who can easily access this lifesaving medication. Further, the state’s well-established 9-1-1 Good Samaritan Law, which provides limited immunity for drug-related charges when responding to a suspected overdose emergency, may have contributed to increased overdose rescues and thus improved survival in at-risk individuals, thereby leading to a higher prevalence of having experienced NFOD [46, 48, 49, 51, 52]. However, it is important to note that our study did not specifically examine the details surrounding the participants overdose to conclusively estimate the effect of GSL on the number of overdose rescues.

Participants who reported using non-prescribed buprenorphine in the 30 days before the study interview had approximately twofold increased odds of having experienced NFOD during the past year and in their lifetime, whereas current use of prescribed buprenorphine was not associated with NFOD. Buprenorphine is a key medication for the effective treatment of OUD [53]. But like all medication treatments for chronic conditions, it is most effective with prolonged and consistent therapeutic use. It is generally understood that the use of nonprescription buprenorphine is an attempt to self-treat withdrawal symptoms associated with opioid dependence, which is facilitated by buprenorphine’s low risk of adverse events, a safety profile as a partial agonist, and greater availability [54–57]. Prior studies have reported a lower risk of NFOD with non-prescribed buprenorphine use [34, 56], though neither were conducted in places where or during periods when fentanyl was the dominant opioid being consumed. As we are unable to establish temporality due to the cross-sectional nature of the study design, it is difficult to disentangle whether the withdrawal symptoms may have played in mediating NFOD risk. It is possible that individuals who have had prior overdoses may be motivated to utilize non-prescribed buprenorphine as a means to reduce their risk of overdose and also serve as the first step to initiation of formal treatment [54–56]. The utilization of nonprescription of buprenorphine represents a complex dynamic of interaction between people with OUD and their substance use behaviors, substance use treatment providers, substance use treatment policy, and rurality. In states where prescribed buprenorphine access is limited due to stricter regulation of MOUD treatment, the presence of higher substance use-related stigma, or rurality, use of nonprescription buprenorphine may confer added protection to an individual with OUD [58]. In MA,
where MOUD is more easily accessible, the use of non-prescription buprenorphine could also be indicative of higher risk-taking behavior and or mistrust of substance use treatment providers [59]. The findings highlight the importance of ensuring access to buprenorphine as a harm reduction measure, decriminalization of buprenorphine diversion, and improved availability through pharmacies [60, 61].

| Variables                  | Comparison                      | Ever experienced non-fatal opioid overdose | p-value | Last year non-fatal opioid overdose | p-value |
|---------------------------|---------------------------------|------------------------------------------|---------|------------------------------------|---------|
| Gender                    | Female vs male                  | 1.02 (0.70–1.51)                         | 0.904   | 1.04 (0.70–1.53)                   | 0.857   |
| Race                      | Hispanic vs NH other            | 0.67 (0.29–1.56)                         | 0.448   | 0.74 (0.33–1.7)                    | 0.569   |
|                           | NH black vs NH other            | 0.50 (0.18–1.37)                         | 0.111   | 0.74 (0.27–2.04)                   | 0.689   |
|                           | NH white vs NH other            | 1.08 (0.48–2.41)                         | 0.048   | 0.86 (0.40–1.88)                   | 0.813   |
| Age                       | 30–45 years vs >45 years        | 0.85 (0.53–1.36)                         | 0.588   | 0.94 (0.59–1.48)                   | 0.371   |
|                           | Less than 30 years vs >45 years | 0.76 (0.44–1.29)                         | 0.041   | 0.70 (0.41–1.20)                   | 0.416   |
| Education                 | High school or more vs less than high school | 1.01 (0.67–1.53)                         | 0.955   | 0.84 (0.56–1.27)                   | 0.416   |
| Employment                | Employed vs unemployed          | 1.10 (0.75–1.62)                         | 0.622   | 1.12 (0.76–1.64)                   | 0.574   |
| Housing                   | Housed vs not housed             | 1.14 (0.76–1.71)                         | 0.521   | 1.35 (0.91–2.01)                   | 0.142   |
| Insurance                 | Public vs other                 | 2.07 (0.96–4.46)                         | 0.063   | 1.84 (0.77–4.43)                   | 0.172   |
| Traded sex for money*     | Yes vs no                       | 1.70 (1.06–2.72)                         | 0.028   | 1.46 (0.93–2.31)                   | 0.104   |
| Substance use in the last 30 days |                          | | | | |
| Crack                     | Yes vs no                       | 1.25 (0.86–1.83)                         | 0.246   | 1.32 (0.90–1.93)                   | 0.162   |
| Cocaine                   | Yes vs no                       | 1.04 (0.71–1.54)                         | 0.832   | 1.34 (0.90–2.00)                   | 0.148   |
| Methadone                 | Yes vs no                       | 1.35 (0.85–2.12)                         | 0.201   | 0.68 (0.43–1.08)                   | 0.104   |
| Buprenorphine (Rx²)       | Yes vs no                       | 1.67 (1.08–2.59)                         | 0.022   | 1.42 (0.94–2.16)                   | 0.095   |
| Buprenorphine (non-Rx)    | Yes vs no                       | 2.02 (1.02–3.97)                         | 0.043   | 2.00 (1.11–3.62)                   | 0.021   |
| Amphetamines              | Yes vs no                       | 2.02 (0.93–4.37)                         | 0.075   | 1.60 (0.82–3.12)                   | 0.165   |
| Benzodiazepine            | Yes vs no                       | 1.82 (1.17–2.84)                         | 0.008   | 1.59 (1.05–2.40)                   | 0.029   |
| Fentanyl                  | Yes vs no                       | 3.03 (2.03–4.52)                         | < 0.001 | 2.28 (1.56–3.35)                   | < 0.001 |
| Heroin                    | Yes vs no                       | 2.31 (1.56–3.41)                         | < 0.001 | 2.78 (1.82–4.26)                   | < 0.001 |
| Marijuana                 | Yes vs no                       | 0.60 (0.41–0.88)                         | 0.009   | 0.75 (0.51–1.10)                   | 0.147   |
| Pain medication           | Yes vs no                       | 0.73 (0.44–1.22)                         | 0.231   | 0.85 (0.50–1.45)                   | 0.559   |
| Route of substance use    |                                  | | | | |
| Oral                      | Yes vs no                       | 1.29 (0.86–1.94)                         | 0.222   | 1.76 (1.18–2.62)                   | 0.005   |
| Smoke                     | Yes vs no                       | 1.06 (0.72–1.55)                         | 0.773   | 1.29 (0.88–1.90)                   | 0.190   |
| Snort                     | Yes vs no                       | 0.55 (0.37–0.80)                         | 0.002   | 0.72 (0.49–1.06)                   | 0.093   |
| Inject                    | Yes vs no                       | 5.14 (3.43–7.70)                         | < 0.001 | 3.26 (2.15–4.96)                   | < 0.001 |
| Snort or inject           | Yes vs no                       | 2.88 (1.67–4.99)                         | < 0.001 | 2.73 (1.41–5.28)                   | 0.003   |
| Naloxone knowledge and access |                                  | | | | |
| Do you know what naloxone/Narcan is? | Yes vs no                 | 2.00 (0.66–6.05)                         | 0.22    | 1.98 (0.54–7.3)                    | 0.304   |
| Do you currently have naloxone/Narcan kit with you? | Yes vs no            | 1.91 (1.30–2.80)                         | 0.001   | 1.41 (0.95–2.08)                   | 0.091   |
| Have you ever been trained to use naloxone/Narcan? | Yes vs no          | 1.89 (1.24–2.89)                         | 0.003   | 1.27 (0.82–1.97)                   | 0.282   |
| Do you know where to get naloxone/Narcan? | Yes vs no              | 2.87 (1.56–5.30)                         | 0.001   | 1.65 (0.85–3.21)                   | 0.141   |
| Around here, how easy would you say it is to get naloxone/Narcan to take home with you? | Easy/extremely easy vs neutral/difficult/extremely difficult | 0.58 (0.34–1.00)                         | 0.048   | 1.23 (0.72–2.10)                   | 0.445   |

* Variable not assessed in first site (Lowell) hence not included in multivariable analyses

OR: odds ratio

CI: confidence interval

NH: non-Hispanic

Rx: prescription
We also observed that the odds of lifetime NFOD were lower in Hispanic and NH Black people compared to NH white people. However, a different pattern of past year NFOD emerged, suggesting similarities with respect to risk, which is in congruence with previously reported findings [10, 62]. The opioid overdose epidemic primarily affected NH white people in the early and mid-2000s owing to the disparities in opioid prescribing [4]. However, as the epidemic evolved, a much broader population is being impacted. A recently published study indicated that the greatest increase in opioid-related mortality was seen in NH Black men, indicating the need to provide focused interventions for a minority population that was previously thought to have lower risks [15, 63]. The odds of past year NFOD were no different between NH white and Blacks; thus, our sample corroborates the recent and concerning fatal overdose trends nationally by race and, for the first time in the literature, suggests that the alarming increase appears to extend to NFOD events as well.

The findings from our study also indicate that methadone and marijuana use is associated lower odds of having a history of NFOD, even while using other illicit drugs in the past month. Methadone is commonly used in the treatment of OUD. Given that methadone maintenance reduces opioid cravings and that there is relatively limited diversion risk, the association between methadone and lower odds of past year NFOD suggests that methadone has been effective in reducing behaviors (e.g., fentanyl use, injection of drugs) and circumstances (e.g., incarceration, loss of tolerance) that increase the risk for fatal overdose. More research, however, is needed to understand the motivation for taking methadone among those with and without a history of NFOD (both lifetime and last year). Additionally, we found a strong inverse association between marijuana use and lifetime NFOD (aOR: 0.6). The legalization of medical marijuana has been shown to reduce the use of prescription drugs in Medicare part D and Medicaid enrollees in some studies [64, 65]. Segura et al. showed no effect of marijuana laws on the non-medical use of opioids [66], while other studies have found that marijuana use is related to an increased risk of having OUD [67–69]. Additional studies show the reduced use of illicit opioids in people who used marijuana frequently [70–73]. The association between marijuana and reduced odds of NFOD could be channeled through several pathways. Marijuana could possibly be used to manage underlying pain, stave off drug cravings, or intentionally limit the use of opioids by active users. Recent legal access to marijuana, for recreational or medical purposes, may encourage reduced use of illicit substances by creating safer, more consistent channels to a mind-altering substance. It is also likely that we observed

| Variable                        | Comparison                        | aORa | 95% CIb | p-value |
|---------------------------------|-----------------------------------|------|--------|---------|
| Gender                          | Female vs male (ref)              | 0.82 | 0.51–1.31 | 0.400 |
| Race                            | Hispanic vs NHc white (ref)       | 0.63 | 0.4–0.99 | 0.045 |
|                                | NH other vs NH white (ref)        | 1.11 | 0.42–2.92 | 0.828 |
|                                | NH black vs NH white (ref)        | 0.60 | 0.40–0.91 | 0.016 |
| Age                             | Less than 30 years vs more than 45 years (ref) | 0.64 | 0.4–1.00 | 0.051 |
|                                | 30–45 years vs more than 45 years (ref) | 0.74 | 0.49–1.13 | 0.165 |
| Education                       | High school or more vs less than HS (ref) | 0.94 | 0.62–1.45 | 0.793 |
| Have naloxone/Narcan            | Yes vs no (ref)                   | 1.49 | 0.85–2.60 | 0.168 |
| Drug use route: snort or inject  | Yes vs no (ref)                   | 1.72 | 0.98–3.02 | 0.058 |
| Substance use in the last 30-days|                                   |     |        |         |
| Alcohol                         | Yes vs no (ref)                   | 0.94 | 0.62–1.43 | 0.781 |
| RxB Buprenorphine               | Yes vs no (ref)                   | 1.36 | 0.91–2.04 | 0.129 |
| Non-Rx Buprenorphine            | Yes vs no (ref)                   | 1.94 | 1.24–3.02 | 0.004 |
| Amphetamine                     | Yes vs no (ref)                   | 1.42 | 0.69–2.89 | 0.338 |
| Benzodiazepine                  | Yes vs no (ref)                   | 1.49 | 1.00–2.23 | 0.052 |
| Fentanyl                        | Yes vs no (ref)                   | 2.44 | 1.58–3.77 | < .0001 |
| Heroin                          | Yes vs no (ref)                   | 1.40 | 0.88–2.21 | 0.153 |
| Marijuana                       | Yes vs no (ref)                   | 0.57 | 0.33–0.98 | 0.042 |

*a aOR adjusted odds ratio  
*b CI confidence interval  
*c NH non-Hispanic  
*d Rx prescription
these associations (reduced risk) because marijuana is more frequently being used by people who do not intentionally use opioids and, therefore, would be at low risk of NFOD.

Our findings should be considered in light of several limitations. We focused on high-overdose-risk communities in MA; hence, our results may not be generalizable to other regions of the state. Additionally, the data we collected were based on self-report, which is prone to recall and reporting bias. The lack of substance use testing can also affect the reported rates of heroin and fentanyl use as many participants could have unknowingly used heroin contaminated with fentanyl. The high rate of naloxone possession observed in our study could also have been due to the oversampling of participants from substance use treatment and harm reduction centers. To protect the confidentiality of participants and encourage participation, exact dates of care and health events were not obtained for this rapid assessment. Month and year of events were self-reported by participants, however, and allowed broadly for exploring the order of exposure if not the precise timing of exposure, which may be better achieved in a different study design. Furthermore, we carried out the rapid assessments over an extended period between August 2017 and November 2019, during which time substance use patterns could have changed. Notably, however, we used a random effects model to account for any variability associated with recruitment location, method, and time. The study also lacked an assessment of mental health issues in the population, which could have a significant association with a history of both lifetime and recent NFOD. Future research with this population could explore behavioral health considerations more broadly as well as motivations for using prescribed, non-prescribed, and illicit substances in relation to overdose risk.

### Conclusion

Our study provides strong evidence indicating that NFOD is a significant issue in MA, driven primarily by factors associated with specific drugs—fentanyl, heroin—and their use by injection. Expected and unexpected fentanyl use continues to pose a considerable challenge to public health efforts to save lives, as

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### Table 4
Factors independently associated with past year overdose among RACK study participants, Massachusetts, 2017–2019

| Variable                                      | aOR  | 95% CI  | p-value |
|-----------------------------------------------|------|---------|---------|
| Gender                                        | Female vs male (ref) | 1.01 | 0.74–1.37 | 0.955 |
| Race                                          | Hispanic vs NH
| white (ref) | 0.54 | 0.31–0.92 | 0.024 |
| NH other vs NH white (ref) | 0.79 | 0.47–1.34 | 0.378 |
| NH black vs NH white (ref) | 1.07 | 0.90–1.28 | 0.460 |
| Age                                           | Less than 30 years vs more than 45 years (ref) | 1.31 | 0.67–2.55 | 0.435 |
| 30–45 years vs more than 45 years (ref) | 1.01 | 0.48–2.13 | 0.974 |
| Education                                     | High school or more vs less than HS (ref) | 0.88 | 0.45–1.72 | 0.701 |
| Housed                                        | Yes vs no (ref) | 0.98 | 0.68–1.41 | 0.903 |
| Have naloxone/Narcan                           | Yes vs no (ref) | 0.93 | 0.63–1.37 | 0.710 |
| Drug use route: inject                        | Yes vs no (ref) | 2.63 | 1.57–4.4 | <0.0001 |
| Substance use in the last 30-days             | | | |
| Crack                                         | Yes vs no (ref) | 1.17 | 0.84–1.63 | 0.356 |
| Cocaine                                       | Yes vs no (ref) | 1.06 | 0.63–1.76 | 0.83 |
| Methadone                                     | Yes vs no (ref) | 0.42 | 0.30–0.59 | <0.0001 |
| Rx
| Buprenorphine                                 | Yes vs no (ref) | 1.13 | 0.78–1.64 | 0.515 |
| Non-Rx Buprenorphine                          | Yes vs no (ref) | 2.10 | 1.23–3.56 | 0.006 |
| Amphetamine                                   | Yes vs no (ref) | 1.18 | 0.62–2.22 | 0.619 |
| Benzodiazepine                                | Yes vs no (ref) | 1.64 | 1.14–2.37 | 0.008 |
| Fentanyl                                      | Yes vs no (ref) | 1.55 | 1.08–2.22 | 0.018 |
| Heroin                                        | Yes vs no (ref) | 1.91 | 1.05–3.46 | 0.033 |
| Marijuana                                     | Yes vs no (ref) | 0.73 | 0.39–1.37 | 0.323 |

**Notes:**

- aOR adjusted odds ratio
- CI confidence interval
- NH non-Hispanic
- Rx prescription
is evident even in places like MA, where there are high levels of awareness and use of naloxone. Given the high risk of fatal overdose among people with a history of NFOD [7–10], our findings highlight the need for interventions that promote uptake of MOUD and improved access to naloxone across all PWUDs. Ongoing efforts to ensure equity and access to treatment and harm reduction supplies are needed to effectively address the opioid overdose epidemic and reduce the incidence of NFOD and fatal overdose among PWUDs.

Acknowledgements
We are grateful to Sarah Ruiz, Abigail Tapper, and Aubri Esters for their support in carrying out these rapid assessments. The project team is greatly indebted to the participants who gave of their time and shared their experiences to inform the study findings.

Authors’ contributions
TG, WP, and PC conceptualized and implemented the initial study design for the RACK Study. All authors contributed to the conceptualization of the current analyses. SS drafted the initial version of the paper. SS and TG finalized the statistical analyses. All authors assisted with the interpretation of the findings. All authors contributed to the revision of the manuscript. All authors have read and approved the final manuscript.

Funding
Funding from the Centers for Disease Control and Prevention (NU17CE002724 (PI: Alawad), NU17CE002724 (PI: Ruiz)) to the Massachusetts Department of Public Health, Bureau of Substance Addiction Services, supported this research. The funder had no role in the design of the study and collection, analysis, and interpretation of data or in writing the manuscript.

Availability of data and materials
The datasets collected and analyzed for the current study are not publicly available due to privacy concerns but are available from the corresponding author on reasonable request and pending the approval of the state of Massachusetts Department of Public Health.

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Review Boards of the Boston University Medical Campus and the Massachusetts Department of Public Health.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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Received: 3 July 2021 Accepted: 16 August 2021
Published online: 30 August 2021

References
1. Hedegaard H, Warner M, Minino AM. Drug overdose deaths in the United States, 1999–2015. NCHS Data Brief. 2017;273:1–8.
2. Davenport S, Weaver A, Caverly M. Economic Impact of Non-Medical Opioid Use in the United States Annual Estimates and Projections for 2015 through 2019. Society of Actuaries Available online: https://www.soa.org/globalassets/assets/files/resources/research-report/2019/econ-impact-non-medical-opioid-use.pdf (accessed on 25 September 2019). 2019.
3. Paulozzi LJ, Jones CM, Mack KA, Rudd RA. Vital signs: overdoses of prescription opioid pain relievers—United States, 1999–2008. MMWR Morb Mortal Wkly Rep. 2011;60(43):1487–92.
4. Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. The changing face of heroin use in the United States: a retrospective analysis of the past 50 years. JAMA Psychiatry. 2014;71(7):821–6.
5. Rudd RA, Paulozzi LJ, Bauer MJ, et al. Increases in heroin overdose deaths—28 States, 2010 to 2012. MMWR Morb Mortal Wkly Rep. 2014;63(39):849–54.
6. O’Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths involving fentanyl, fentanyl analogs, and U-47700—10 States, July–December 2016. MMWR Morb Mortal Wkly Rep. 2017;66(43):1197–202.
7. Stoove MA, Dietze PM, Jolley D. Overdose deaths following previous non-fatal heroin overdose: record linkage of ambulance attendance and death registry data. Drug Alcohol Rev. 2009;28(4):347–52.
8. Kinner SA, Milloy MJ, Wood E, Qi J, Zhang R, Kerr T. Incidence and risk factors for non-fatal overdose among a cohort of recently incarcerated illicit drug users. Addict Behav. 2012;37(6):691–6.
9. Larochelle MR, Bernson D, Land T, et al. Medication for opioid use disorder after nonfatal opioid overdose and association with mortality: a cohort study. Ann Intern Med. 2018;169(3):137–45.
10. Ofson M, Wall M, Wang S, Crystal S, Bianco C. Risks of fatal opioid overdose during the first year following nonfatal overdose. Drug Alcohol Depend. 2018;190:112–9.
11. Amari E, Rehm J, Goldner E, Fischer B. Nonmedical prescription opioid use and mental health and pain comorbidities: a narrative review. Can J Psychiatry. 2011;56(8):495–502.
12. Deegenhardt L, Peacock A, Colledge S, et al. Global prevalence of injecting drug use and sociodemographic characteristics and prevalence of HIV, HBV, and HCV in people who inject drugs: a multistage systematic review. Lancet Glob Health. 2017;5(12):e1192–207.
13. Liu S, Scholl L, Hoots B, Seth P. Nonfatal drug and polydrug overdoses treated in emergency departments—29 States, 2018–2019. MMWR Morb Mortal Wkly Rep. 2020;69(34):1149–55.
14. Knowitlton A, Weir BW, Hazzard F, et al. EMS runs for suspected opioid overdose: implications for surveillance and prevention. Prehosp Emerg Care. 2013;17(3):317–29.
15. Massachusetts Department of Public Health. Data Brief: Opioid-Related Overdose Deaths among Massachusetts Residents. 2021.
16. Massachusetts Department of Public Health. MA Opioid-Related EMS Incidents 2013–2019. Massachusetts Department of Public Health 2020.
17. Weiner SG, Baker O, Bernson D, Schuur JD. One-year mortality of patients after emergency department treatment for nonfatal opioid overdose. Ann Emerg Med. 2020;75(1):13–7.
18. Salomon AM, van Beek I, Amin J, Kaldor J, Maher L. The impact of a supervised injecting facility on ambulance call-outs in Sydney. Australia Addict. 2010;105(4):676–83.
19. Marshall BD, Milloy MJ, Wood E, Montaner JS, Kerr T. Reduction in overdose mortality after the opening of North America’s first medically supervised safer injecting facility: a retrospective population-based study. Lancet. 2011;377(9775):1429–37.
20. Kräi AH, Davidson PJ. Addressing the nation’s opioid epidemic: lessons from an unsanctioned supervised injection site in the US. Am J Prev Med. 2017;53(6):919–22.
21. Kräi AH, Lambdin BH, Wenger LD, Davidson PJ. Evaluation of an unsanctioned safe consumption site in the United States. N Engl J Med. 2020;383(6):589–90.
22. Schepis TS, Teter CJ, McCabe SE. Prescription drug use, misuse and related substance use disorder symptoms vary by educational status and attainment in U.S. adolescents and young adults. Drug Alcohol Depend. 2018;189:172–7.
23. Martins SS, Kim JH, Chen LY, et al. Nonmedical prescription drug use among US young adults by educational attainment. Soc Psychiatry Psychiatr Epidemiol. 2015;50(5):713–24.

24. Wu LT, Zhu H, Swartz MS. Treatment utilization among persons with opioid use disorder in the United States. Drug Alcohol Depend. 2016;169:117–27.

25. Chatterjee A, Yu EJ, Tishberg L. Exploring opioid use disorder, its impact, and treatment among individuals experiencing homelessness as part of a family. Drug Alcohol Depend. 2018;188:161–8.

26. Harris K, Jerome N, Fawcett S. Rapid assessment procedures: a review and critique. Hum Organ. 1997;56(3):375–8.

27. Finch C, Stimson GV, Rhodes T. Poznyak V. Rapid assessment: an international review of diffusion, practice and outcomes in the substance use field. Soc Sci Med. 2004;59(9):1819–30.

28. Massachusetts Department of Public Health. Number of opioid-related overdose deaths, All Intents by City/Town 2013–2017. Massachusetts Department of Public Health 2018.

29. Hughto JM, Gordon L, Stoppa TJ, et al. Understanding opioid overdose risk and response preparedness among people who use cocaine and other drugs: mixed-methods findings from a large, multi-city study. J Subst Abuse. In Press. 2021.

30. Stimson GV, Finch C, Rhodes T. The rapid assessment and response guide on injecting drug use (IDU-RAR). Geneva: WHO; 1998.

31. Coffin PO, Tracy M, Bucchiarelli A, Ompad D, Vlahov D, Galea S. Identifying injection drug users at risk of nonfatal overdose: Acad Emerg Med. 2007;14(7):616–23.

32. Liebling EJ, Green TC,Hadland SE, Marshall BDL. Injection drug use and overdose among young adults who use prescription opioids non-medi-cally. Addict Behav. 2018;76:20–6.

33. Milloy MJ, Kerr T, Mathias R, et al. Non-fatal overdose among a cohort of active injection drug users recruited from a supervised injection facility. Am J Drug Abuse. 2008;34(4):499–509.

34. Otachi JK, Vundl N, Surratt HL. Examining factors associated with non-fatal overdose among people who inject drugs in rural Appalachia. Subst Use Misuse. 2020;55(5):1935–42.

35. Somerville NJ, O’Donnell J, Gladden RM, et al. Characteristics of fentanyl overdose—Massachusetts, 2014–2016. MMWR Morb Mortal Wkly Rep. 2017;66(14):382–6.

36. Marshall BDL, Krieger MS, Yedinak JL, et al. Epidemiology of fentanyl-involved drug overdose deaths: age/gender retrospective study in Rhode Island, USA. Int J Drug Policy. 2017;46:130–5.

37. Latkin CA, Dayton L,Davey-Rothwell MA, Tobin KE. Fentanyl and Drug Overdose: Perceptions Of Fentanyl Risk, Overdose Risk Behaviors, And Opportunities For Intervention Among People Who Use Opioids in Baltimore, USA. Subst Use Misuse. 2019;54(6):988–1006.

38. Massachusetts Department of Public Health. Data brief: opioid-related overdose deaths among Massachusetts residents. Boston: Department of Public Health; 2020.

39. Compton WM, Jones CM,Baldwin GT. Relationship between non-medical prescription-opioid use and heroin use. N Engl J Med. 2016;374(2):154–63.

40. Alpern C, Dawson EL, John B, et al. Opioid use fueling HIV transmission in an urban setting: an outbreak of HIV infection among people who inject drugs—Massachusetts, 2015–2018. Am J Public Health. 2020;110(1):37–44.

41. Ganster K, Alpern C, John B, et al. Notes from the field: HIV diagnoses among persons who inject drugs—Northeastern Massachusetts, 2015–2018. MMWR Morb Mortal Wkly Rep. 2019;68(10):253–4.

42. Wilson N, Karissa M, Seth P, Smith HT, Davis NL. Drug and opioid-involved overdose deaths—United States, 2017–2018. MMWR Morb Mortal Wkly Rep. 2020;69(1):290–297.

43. National Academies of Sciences E, Medicine. Medications for opioid use disorder save lives. National Academies Press, 2019.

44. Amato L, Davoli M, Minozzi S, Ferroni E, Ali R, Ferrari M. Methadone at tapered doses for the management of opioid withdrawal. Cochrane Database Syst Rev. 2013;2013(2):CD003409.

45. Brugal MT, Domingo-Salvany A, Puig R, Barrio G, García de Olalla P, de la Fuente L. Evaluating the impact of methadone maintenance programs on mortality due to overdose and aids in a cohort of heroin users in Spain. Addiction. 2005;100(7):981–989.

46. Walley AY, Xuan Z, Hackman HH, et al. Opioid overdose rates and imple-mentation of overdose education and nasal naloxone distribution in Massachusetts: interrupted time series analysis. BMJ. 2013;346:f1714.

47. Allen T, White RH, O’Rourke A, Groib SM, Kirkley ME, Sherman SG. Take-home naloxone possession among people who inject drugs in rural West Virginia. Drug Alcohol Depend. 2019;204:107581.

48. Bagley SM, Forman LS, Ruiz S, Cranston K, Walley AY. Expanding access to naloxone for family members: the Massachusetts experience. Drug Alcohol Rev. 2018;37(4):480–6.

49. Davis CS, Ruiz S, Glynn P, Picarello G, Walley AY. Expanded access to naloxone among firefighters, police officers, and emergency medical technicians in Massachusetts. Am J Public Health. 2014;104(8):e7–9.

50. The Commonwealth of Massachusetts. Policy No. 2018–04: Naloxone Dispensing via Standing Order. In: Executive Office of Health and Human Services DoPH, ed.2018.

51. Stopka TJ, Donahue A, Hutcherson M, Green TC. Nonprescription naloxone and syringe sales in the midst of opioid overdose and hepatitis C. virus epidemics: Massachusetts, 2015. J Am Pharm Assoc (2003). 2017;57(2):534–544.

52. Doonan MT, Tull KR. Health care reform in Massachusetts: implementa-tion of coverage expansions and a health insurance mandate. Milbank Q. 2010;88(1):54–80.

53. Mattick RP, Breen C, Kimber J, Davoli M. Buprenorphine maintenance versus placebo or methadone maintenance for opioid dependence. Cochrane Database Syst Rev. 2014(2):CD002207.

54. Silverstein SM, Danuielatyte R, Miller SC, Martins SS, Carlson RG. On my own terms: Motivations for self-treating opioid-use disorder with non-prescribed buprenorphine. Drug Alcohol Depend. 2020;210:107668.

55. Danuielatyte R, Nahhas RW, Silverstein S, et al. Patterns of non-prescribed buprenorphine and other opioid use among individuals with opioid use disorder: a latent class analysis. Drug Alcohol Depend. 2019;204:107574.

56. Carlson RG, Danuielatyte R, Silverstein SM, Nahhas RW, Martins SS. Unintentional drug overdose: Is more frequent use of non-prescribed buprenorphine associated with lower risk of overdose? Int J Drug Policy. 2020;79:102722.

57. Bazaari AR, Yokell M, Fu JJ, Rich JD, Zaller ND. Illicit use of buprenorphine/naloxone among injecting and noninjecting opioid users. J Addict Med. 2011;5(3):175–80.

58. Loewoll MR, Havens JR. Inability to access buprenorphine treatment as a risk factor for using diverted buprenorphine. Drug Alcohol Depend. 2012;126(3):379–83.

59. Allen B, Harocopos A. Non-prescribed buprenorphine in New York City: motivations for use, practices of diversion, and experiences of stigma. J Subst Abuse Treat. 2016;70:61–7.

60. Green TC, Bratberg J, Finnell DS. Opioid use disorder and the COVID 19 pandemic: a call to suspend regulatory easements and further expand access to treatment. Subst Abus. 2020;41(2):147–9.

61. Pozo BD, Krasner LS, George SF. Decriminalization of diverted buprenor-phine in Burlington, Vermont and Philadelphia: an intervention to reduce opioid overdose deaths. J Law Med Ethics. 2020;48(2):373–375.

62. Park JN, Weir BW, Allen ST, Chaulk P, Sherman SG. Fentanyl-contaminated drugs and non-fatal overdose among people who inject drugs in Balti-more, MD. Harm Reduction J. 2018;15(1):34.

63. Althoff KN, Leifheit KM, Park JN, Chandran A, Sherman SG. Opioid-related overdose mortality in the era of fentanyl monitoring: a shifting epidemic by person, place, and time. Drug Alcohol Depend. 2020;216:108321.

64. Wen H, Hockenberry JM. Association of medical and adult-use Marijuana laws with opioid prescribing for medicare enrollees. JAMA Intern Med. 2018;178(5):673–9.

65. Bradford AC, Bradford WD. Medical Marijuana laws reduce prescrip-tion medication use in medicare part D. Health Aff (Millwood). 2016;35(7):1230–6.

66. Secura LE, Mauro CM, Levy NS, et al. Association of US Medical Marijuana Laws with nonmedical prescription opioid use and prescription opioid use disorder. JAMA Netw Open. 2019;2(7):e192716–e192716.

67. Olsson M, Wall MM, Liu SM, Blanco C. Cannabis use and risk of pre-scription opioid use disorder in the United States. Am J Psychiatry. 2018;175(1):47–53.

68. Liang D, Wallace MS, Shi Y. Medical and non-medical cannabis use and risk of prescription opioid use disorder: Findings from propensity score matching. Drug Alcohol Rev. 2019;38(6):597–605.
69. Caputi TL, Humphreys K. Medical Marijuana users are more likely to use prescription drugs medically and nonmedically. J Addict Med. 2018;12(4):295–9.

70. Lake S, Walsh Z, Kerr T, et al. Frequency of cannabis and illicit opioid use among people who use drugs and report chronic pain: a longitudinal analysis. PLoS Med. 2019;16(11):e1002967.

71. Reddon H, DeBeck K, Socias ME, et al. Frequent Cannabis use and cessation of injection of opioids, Vancouver, Canada, 2005–2018. Am J Public Health. 2020;110(10):1553–60.

72. Kral AH, Wenger L, Novak SP, et al. Is cannabis use associated with less opioid use among people who inject drugs? Drug Alcohol Depend. 2015;153:236–41.

73. Bergeria CL, Huhn AS, Dunn KE. The impact of naturalistic cannabis use on self-reported opioid withdrawal. J Subst Abuse Treat. 2020;113:108005.

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