Drug and Alcohol Dependence 204 (2019) 107473

Contents lists available at ScienceDirect

Drug and Alcohol Dependence

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

# Drug-related mortality after discharge from treatment: A record-linkage study of substance abuse clients in Texas, 2006–2012

Brandon C. Maughan[a,*], Emilie A. Becker[b]

[a] Department of Emergency Medicine, Oregon Health and Science University, Portland, OR, USA
[b] Texas Department of State Health Services, Austin, TX, USA

ARTICLE INFO

*Keywords:*
Drug-related death
Substance abuse treatment
Treatment discharge
Opioid overdose
Post-discharge mortality

ABSTRACT

*Background:* Patients have higher mortality immediately after substance abuse treatment discharge, but there are few data on post-discharge mortality differences across treatment modalities.

*Methods:* A retrospective cohort study examined individuals discharged from substance abuse treatment during 2006–2012 and probabilistically matched treatment records to death records. Logistic regression examined associations between drug-related death (DRD) and demographics; route, frequency, and classes of drugs abused; and treatment. Primary outcome was DRD during post-discharge days 0–28; secondary outcomes examined DRD during days 29–90 and 91–365.

*Results:* We examined 178,749 patients discharged from 254,814 treatment episodes. There were 97 DRD during days 0–28 (4.1/1000 person-years), 115 DRD during days 29–90 (2.6/1000 person-years; IRR 0.6 [95% CI 0.5–0.8]), and 293 DRD during days 91–365 (1.9/1000 person-years; IRR 0.5 [0.4–0.6]). Higher 28-day DRD was associated with abuse of opioids (aOR 2.5 [1.4–4.4]), depressants (aOR 2.0 [1.2–3.4]), or alcohol (aOR 1.7 [1.1–2.6]); and opioid injection (aOR 2.2 [1.3–3.7]). Lower DRD was associated with treatment completion (aOR 0.6 [0.4–0.9]), female sex (aOR 0.6 [0.4–0.8]), and employment (aOR 0.5 [0.3–0.9]). Among all patients, DRD rates were higher following residential (IRR 2.6, [1.6–4.2]) and detoxification (IRR 2.9, [1.7–4.9]) treatment compared to outpatient. Patients with prior opioid abuse had higher 28-day DRD after outpatient (6.7/1000 person-years; IRR 4.1 [1.8–9.1]), residential (13.6/1000 person-years; IRR 4.2 [2.2–8.2]), and detoxification (8.8/1000 person-years; IRR 3.2 [1.2, 8.5]) compared to those without.

*Conclusions:* Drug-related mortality is highest during days 0–28 after discharge, especially following residential and detoxification treatment. Opioid abuse is strongly associated with early post-discharge mortality.

## 1. Introduction

The increased mortality associated with active abuse of drugs and alcohol has been well documented, as multiple meta-analyses have shown significantly higher standardized mortality ratios for suicide, accidental death, and natural causes when compared to the general population (Degenhardt et al., 2011; Hulse et al., 1999; Laramée et al., 2015; Neeleman, 2001). Pharmacologic and psychosocial treatment for substance abuse can be effective at reducing the frequency and harms of substance use disorders (SUD) (Darker et al., 2015; Gates et al., 2016; Gossop et al., 2003; Klimas et al., 2014; McCarty et al., 2014; Nielsen et al., 2016; Reif et al., 2014), but evidence suggests that patients remain at elevated risk of mortality after treatment, especially in the first few weeks to months after discharge (Davoli et al., 2007; Degenhardt et al., 2009; Gossop et al., 2002; Merrall et al., 2013; Ravndal and Amundsen, 2010; White et al., 2015). For instance, among a cohort of nearly 70,000 drug users in Scotland, rates of drug-related death (DRD) in the first four weeks after discharge from any inpatient treatment were five times greater than the rates observed more than one year after discharge (Merrall et al., 2013). Similar trends have been observed among individuals with a history of substance use disorders who are released from prison (Merrall et al., 2010; Zlodre and Fazel, 2012). In both groups, reduced drug tolerance has been proposed as the mechanism responsible for the increased mortality upon resumption of drug use.

However, prior studies on post-discharge mortality have often focused on a single type of SUD treatment (e.g., inpatient treatment), and few have examined differences in drug related poisonings different treatment types during different post-discharge time intervals. There is also a little examination of this topic among North American

* Corresponding author at: OHSU Department of Emergency Medicine, Mail Code: CDW-EM, 3181 SW Sam Jackson Park Road, Portland, OR, 97239, USA.
*E-mail address:* maughabr@ohsu.edu (B.C. Maughan).

https://doi.org/10.1016/j.drugalcdep.2019.05.011
Received 29 October 2018; Received in revised form 23 February 2019; Accepted 6 May 2019
Available online 30 August 2019
0376-8716/ 

populations, which is an important deficit since there are substantial limitations in international extrapolations of drug-related mortality data (Fugelstad et al., 2017). The objectives of this study are to (a) identify the associations between different drug classes and rates of drug-related death following discharge from SUD treatment; (b) to identify temporal trends in DRD rates following discharge from SUD treatment; and (c) to measure differences in these DRD rates across treatment modalities.

## 2. Methods

### 2.1. Study design and population

We designed a retrospective record-linkage cohort study of adult patients who were admitted and discharged from at least one episode of substance abuse treatment delivered by contracted substance abuse providers for the Texas Department of State Health Services (DSHS) during 2006–2012. These patient records were linked to DSHS vital statistics death records during 2006–2013. The study received approval from the Texas DSHS Institutional Review Boards. Data were managed and analyzed using SAS 9.4 (SAS Institute; Cary, NC) and Stata 14 (StataCorp; College Station, TX).

### 2.2. Data matching

Substance abuse treatment records and DSHS death records were linked using a probabilistic matching algorithm with five variables: first name, last name, birthdate, gender, and Social Security number (SSN). Records that matched all five variables were linked, and remaining records were examined for matches using three techniques. First, records were linked if they exactly matched four variables and the fifth variable differed by a minimal degree, measured as a generalized edit distance for numerical strings (birthday or SSN) or by soundex (a phonetic algorithm which encodes similar sounding portions of words) for names; both functions were performed using SAS (SAS Institute; Cary, NC). Second, records were linked if three variables matched exactly and the two remaining variables (both name variables or both numerical variables) had minimal difference by soundex or generalized edit distance. Third, due to a higher frequency of missing SSN data than for other variables, records were linked if patients lacked SSN data but matched exactly on all other variables. Many different databases using the SQL programming language have soundex or other string-matching algorithms that could be used to replicate this record linkage method.

### 2.3. Outcomes

We recorded the number of days from SUD treatment discharge until patients died, were readmitted to SUD treatment, or reached one year after discharge. Our primary outcome was drug-related mortality within 28 days of discharge from treatment, and secondary outcomes included drug-related mortality during days 29–90 and days 91–365 after discharge (Merrall et al., 2013; White et al., 2015). Drug-related deaths were defined in accordance with Jackson and Merrall (Jackson, 2001; Merrall et al., 2013) based on International Classification of Disease, 10th Edition (ICD-10) codes for primary cause of death: mental and behavioral disorders due to psychoactive substance misuse (ICD-10: F11–F16, F19), accidental poisoning (ICD-10: X40–X44), intentional self-poisoning (ICD-10: X60–X64), assault by drugs (ICD-10: X85), or poisoning of undetermined intent (ICD-10: Y10–Y14). We also calculated data on all-cause mortality during the same time intervals and reported these outcomes in Supplemental Table 1 for future reference.

### 2.4. Patient characteristics

Patient-level data included age at admission (< 25 years, 25–34 years, > 34 years), sex (female vs. male), race/ethnicity (non-Hispanic White vs. non-White or Hispanic), education (more than high school education vs. high school or less), and employment status at time of admission (yes vs. no).

### 2.5. Drug abuse and treatment characteristics

DSHS gathered data on patient-reported use of five drug classes: alcohol, depressants (e.g., benzodiazepines and barbiturates), marijuana, opioids, and stimulants (e.g., amphetamines or cocaine). Other variables relating to drug use and substance abuse treatment included frequency of drug use (at least once weekly vs. less often), use of opioids by injection (yes vs. no), and whether the patient had participated in prior DSHS SUD treatment during the study period. Patients were classified as not having completed treatment if they voluntarily discontinued program participation, were terminated by the facility (e.g., due to violation of program rules), were incarcerated, or were otherwise unable to continue treatment. Patients were excluded if they were transferred from DSHS-provided care to a private substance abuse treatment program since we were unable to assess treatment outcomes or post-discharge time at risk. Patients transferred from one type of DSHS-provided treatment to another (e.g., residential to outpatient) were retained in the data set and were considered to have a single continuous treatment episode.

Each patient treatment episode included at least one treatment service (outpatient, residential, detoxification, or opioid substitution therapy [OST]) but could include several concurrent or sequential treatments. Treatment types were classified according to the Treatment Episode Data Set (TEDS) minimum data set (MDS) field 18 (Center for Behavioral Health Statistics and Quality, 2018). Detoxification treatments included 24 -h programs at both hospitals and free-standing residential facilities (TEDS Service Categories 1–2). Residential programs included hospital-based, short-term non-hospital, and long-term non-hospital residential programs (TEDS Service Categories 3–5). Outpatient treatment encompassed intensive-outpatient, non-intensive-outpatient, and outpatient detoxification programs (TEDS Service Categories 6–8). Those clients with the use of medication-assisted opioid therapy (MAT), as indicated by MDS field 19, were classified as OST.

### 2.6. Model design and statistical analysis

Variables were selected for inclusion in a logistic regression model if they had a p-value less than 0.2 on univariate logistic regression for the primary outcome. The same variables were used in logistic regression models for subsequent time intervals. Clustering was used at the level of the patient to account for individuals with multiple separate treatment admissions during the study period. Adjusted odds ratios for predictive variables are shown with 95% confidence intervals (95% CI).

To describe differences in post-discharge mortality observed across treatments, we measured mortality rates per 1000 person-years (PY) for each treatment type. Incidence rate ratios (IRR) with 95% confidence intervals were calculated for residential, detoxification, and OST treatment programs relative to outpatient therapy. P-values for this comparison were calculated using Fisher's exact test with mid-p correction. Patients with multiple treatment types during a given episode of treatment were classified according to the treatment type that they finished last.

Due to the rapid rise in opioid-related overdoses in the United States over the last two decades, we examined the sensitivity of the above analysis by dichotomizing patients based on any reported history of opioid abuse. The association between treatment type and subsequent mortality rate was then separately calculated for both groups.

**Table 1**
Patient and Episode Characteristics.

| Patient Characteristics | Categories | Episodes | | Person-years | | Deaths | | |
|---|---|---|---|---|---|---|---|---|
| | | N | % | N | % | Total | DRD | DRD/1000 PY |
| All patients | | 2,54,814 | | 2,18,809 | | 1775 | 505 | 2.3 |
| Demographic factors | | | | | | | | |
| Age | Less than 25 years | 54,597 | 21% | 47,991 | 22% | 168 | 72 | 1.5 |
| | 25-34 years | 90,045 | 35% | 76,422 | 35% | 401 | 181 | 2.4 |
| | 35 years or greater | 1,10,172 | 43% | 94,396 | 43% | 1206 | 252 | 2.7 |
| Sex | Male | 1,45,675 | 57% | 1,27,124 | 58% | 1240 | 333 | 2.6 |
| | Female | 1,09,139 | 43% | 91,685 | 42% | 535 | 172 | 1.9 |
| Race | Nonwhite or hispanic | 1,27,669 | 50% | 1,11,076 | 51% | 682 | 159 | 1.4 |
| | White and non-hispanic | 1,27,145 | 50% | 1,07,733 | 49% | 1093 | 346 | 3.2 |
| Education | High school or less | 1,97,106 | 77% | 1,69,588 | 78% | 1292 | 357 | 2.1 |
| | More than HS education | 57,708 | 23% | 49,221 | 22% | 483 | 148 | 3.0 |
| Employed | No | 1,89,351 | 74% | 1,58,546 | 72% | 1514 | 441 | 2.8 |
| | Yes | 65,463 | 26% | 60,263 | 28% | 261 | 64 | 1.1 |
| Drugs abused | | | | | | | | |
| Alcohol | No | 1,28,108 | 50% | 1,07,927 | 49% | 738 | 288 | 2.7 |
| | Yes | 1,26,706 | 50% | 1,10,882 | 51% | 1037 | 217 | 2.0 |
| Depressants | No | 2,35,931 | 93% | 2,03,228 | 93% | 1615 | 420 | 2.1 |
| | Yes | 18,883 | 7% | 15,581 | 7% | 160 | 85 | 5.5 |
| Marijuana | No | 1,64,027 | 64% | 1,37,758 | 63% | 1392 | 392 | 2.8 |
| | Yes | 90,787 | 36% | 81,051 | 37% | 383 | 113 | 1.4 |
| Opioids | No | 1,90,121 | 75% | 1,68,555 | 77% | 1146 | 197 | 1.2 |
| | Yes | 64,693 | 25% | 50,254 | 23% | 629 | 308 | 6.1 |
| Stimulants | No | 1,26,832 | 50% | 1,08,065 | 49% | 1126 | 309 | 2.9 |
| | Yes | 1,27,982 | 50% | 1,10,744 | 51% | 649 | 196 | 1.8 |
| Drug use details | | | | | | | | |
| Injects opioids | No | 2,22,665 | 87% | 1,95,072 | 89% | 1403 | 304 | 1.6 |
| | Yes | 32,149 | 13% | 23,737 | 11% | 372 | 201 | 8.5 |
| Frequency of drug use | Not every week | 1,11,095 | 44% | 1,01,700 | 46% | 512 | 131 | 1.3 |
| | At least once weekly | 1,43,719 | 56% | 1,17,109 | 54% | 1263 | 374 | 3.2 |
| Treatment details | | | | | | | | |
| > 1 episode of SUD treatment | No | 1,76,389 | 69% | 1,57,001 | 72% | 1170 | 313 | 2.0 |
| | Yes | 78,425 | 31% | 61,809 | 28% | 605 | 192 | 3.1 |
| Completed SUD treatment | No | 1,12,301 | 44% | 94,796 | 43% | 907 | 271 | 2.9 |
| | Yes | 1,42,513 | 56% | 1,24,013 | 57% | 868 | 234 | 1.9 |
| Last Type of Treatment Received | Outpatient | 1,27,014 | 50% | 1,18,986 | 54% | 590 | 131 | 1.1 |
| | Residential | 71,878 | 28% | 58,913 | 27% | 582 | 179 | 3.0 |
| | Detoxification | 51,951 | 20% | 37,459 | 17% | 505 | 164 | 4.4 |
| | OST | 3,971 | 2% | 3,452 | 2% | 98 | 31 | 9.0 |

## 3. Results

### 3.1. Patient characteristics

The patient sample consisted of 178,749 individuals who were discharged from 254,814 treatment episodes and accrued a total of 218,809 person-years at risk within one year after discharge. Full sample characteristics are shown in Table 1. Fifty-seven percent of episodes were for male patients and 50% were for non-Hispanic white patients. Among all patients, the most frequently abuse drug classes were alcohol and simulants, both of which were reported by participants in 50% of episodes, followed by marijuana (36%), opioids (25%), and depressants (7%). Thirty-one percent of episodes were among participants with two or more treatment episodes during the study period. Patients in 56% of episodes were discharged following successful completion of treatment. The total number of DRD in the study cohort was 505, including 97 DRD during days 0–28, 115 DRD during days 29–90, and 293 DRD during days 91–365.

### 3.2. Factors associated with post-discharge mortality

Fourteen variables were selected for inclusion in our regression model. As shown in Table 2, demographic factors associated with the primary outcome included sex, education, and employment. Drug-related mortality was significantly associated with prior abuse of opioids (aOR 2.5, 95% CI [1.4, 4.4]), depressants (aOR 2.0 [1.2, 3.4], and alcohol (aOR 1.7 [1.1, 2.6). Use of opioids by injection was associated with additional risk of mortality (aOR 2.2 [1.3, 3.7]), and completion of substance abuse treatment was associated with lower mortality (aOR 0.6 [0.4, 0.9]).

Several of these non-demographic factors remained significantly associated with drug-related mortality during later time periods. Prior opioid abuse retained a statistically significant association with drug-related mortality at 29–90 days (aOR 2.0 [1.1, 3.5]) and 91–365 days (aOR 2.7 [1.9, 3.7]) after discharge. Depressant abuse was not significantly associated with drug-related mortality during 29–90 days after discharge but was significant during days 91–365 (aOR 2.7 [1.9, 3.7]). Injection opioid use remained a statistically significant factor associated with drug-related mortality at both 29–90 days (aOR 2.4 [1.4, 3.9] and 91–365 days (aOR 2.1 [1.5, 2.8]).

### 3.3. Temporal trends in post-discharge mortality

Table 3 shows the interval-specific mortality during the three post-discharge time periods. We observed drug-related mortality at a rate of 4.1/1000 PY (95% CI [3.3, 4.9]) during days 0–28 after discharge. The rate was significantly lower during days 29–90 (2.6/1000 PY [2.1, 3.1]; IRR 0.7 [0.5, 0.9]) and days 91–365 (1.9/1000 PY [1.6, 2.0]; IRR 0.5 [0.4, 0.6]). Individuals with prior opioid abuse had significantly higher DRD rates at 0–28 days (IRR 4.3 [2.9, 6.4]), 29–90 days (IRR 4.7 [3.3, 6.9]), and 91–365 days (IRR 5.7 [4.5, 7.2]) compared to individuals without this history.

**Table 2**
Logistic regression for drug-related death during 0–28 days, 29–90 days, and 91–365 days after discharge.

| Patient Characteristics | Analytical Groups | 0-28 days aOR (95% CI) | 29-90 days aOR (95% CI) | 91-365 days aOR (95% CI) |
|---|---|---|---|---|
| Demographic factors | | | | |
| Age | Less than 25 years | (ref) | | |
| | 25-34 years | 1.4 (0.7, 2.2) | 1.8 (0.9, 3.5) | 1.3 (0.9, 1.8) |
| | 35 years or greater | 1.1 (0.6, 2.0) | 2.5 (1.3, 4.7)** | 2.0 (1.4, 2.8)** |
| Sex | Male | (ref) | | |
| | Female | 0.6 (0.4, 0.8)** | 0.6 (0.4, 0.9)** | 0.8 (0.6, 0.96)* |
| Race/Ethnicity | Nonwhite or Hispanic | (ref) | | |
| | Non-Hispanic white | 1.5 (0.96, 2.2) | 2.0 (1.3, 3.0)** | 1.9 (1.5, 2.5)** |
| Education | High school or less | (ref) | | |
| | More than HS education | 1.6 (1.04, 2.4)* | 1.3 (0.9, 1.9) | 1.2 (0.9, 1.5) |
| Employed | No | (ref) | | |
| | Yes | 0.5 (0.3, 0.9)* | 0.8 (0.5, 1.3) | 0.5 (0.4, 0.8)** |
| Drugs abused | | | | |
| Alcohol | No | (ref) | | |
| | Yes | 1.7 (1.1, 2.6)* | 1.2 (0.8, 1.8) | 1.2 (0.9, 1.5) |
| Depressants | No | (ref) | | |
| | Yes | 2.0 (1.2, 3.4)** | 1.2 (0.7, 2.2) | 2.0 (1.5, 2.6)** |
| Marijuana | No | (ref) | | |
| | Yes | 0.8 (0.5, 1.4) | 0.9 (0.6, 1.5) | 1.0 (0.7, 1.3) |
| Opioids | No | (ref) | | |
| | Yes | 2.5 (1.4, 4.4)** | 2.0 (1.1, 3.5)* | 2.7 (1.9, 3.7)** |
| Stimulants | No | (ref) | | |
| | Yes | 1.0 (0.7, 1.6) | 0.6 (0.4, 0.9)* | 1.0 (0.8, 1.2) |
| Drug use details | | | | |
| Injects opioids | No | (ref) | | |
| | Yes | 2.2 (1.3, 3.7)** | 2.4 (1.4, 3.9)** | 2.1 (1.5, 2.8)** |
| Frequency of drug use | Not every week | (ref) | | |
| | At least once weekly | 1.1 (0.7, 1.8) | 1.3 (0.8, 1.0) | 1.1 (0.8, 1.4) |
| Treatment details | | | | |
| > 1 episode of SUD treatment | No | (ref) | | |
| | Yes | 0.9 (0.6, 1.4) | 1.0 (0.7, 1.6) | 0.9 (0.7, 1.1) |
| Completed SUD treatment | No | (ref) | | |
| | Yes | 0.6 (0.4, 0.9)* | 0.8 (0.5, 1.1) | 0.8 (0.6, 0.98)* |

* < 0.05.
** < 0.01.

### 3.4. Mortality differences by treatment type

When comparing different treatment programs, we observed substantial differences in mortality rates both within and across time intervals. Among the full cohort, patients discharged from outpatient treatment had a DRD rate of 2.2/1000 PY during days 0–28, which was substantially lower than the mortality rates observed for patients discharged from residential (5.6/1000 PY; IRR 2.6 [1.6, 4.2]), detoxification (6.3/1000 PY; IRR 2.9 [1.7, 4.9]), or OST treatment programs (13.1/1000 PY; IRR 6.0 [2.3, 15.6]) (Table 4). Similar differences between treatment programs were observed at 29–90 and 91–365 days. Among the subset of patients with prior opioid abuse, rates of post-discharge DRD were 3.2–6.5 times higher than in patients without such a history. For instance, patients with prior opioid abuse had a DRD rate of 13.6/1000 PY in the first 28 days after discharge from residential treatment, whereas other patients in the cohort had a DRD rate of only 3.2/1000 PY during the same time and setting.

## 4. Discussion

This study examined drug-related mortality among 178,749 individuals during 218,809 person-years following discharge from substance abuse treatment provided by contracted providers to the Texas Department of Health Services during 2006–2012. This study has three major findings.

### 4.1. Risk factors for post-discharge mortality

First, we identified that drug-related mortality in the immediate post-discharge period (i.e., within 28 days) was significantly associated with prior abuse of alcohol, depressants, or opioids, and we observed that use of injection opioids was associated with additional risk above opioid abuse in general. Completion of SUD treatment was associated with lower mortality.

The largest prior studies to examine similar outcomes as our investigation were by Merrall et al. (Merrall et al., 2013) and White et al. (White et al., 2015), both of which examined patients in the Scottish Drugs Misuse Database (SDMD). Their studies used similar record-linkage approaches as ours, used the same definition of drug-related death, and had sufficiently large samples to achieve high statistical power (e.g., 1383 DRDs in Merrall et al. and 2523 DRDs in White et al.). These analyses found similar results as ours, including significantly higher rates of drug-related deaths among individuals with history of injection drug use and alcohol abuse. In regard to injection drug use, direct comparisons are difficult due to differences in the categories used; we examined the risk of injection drug use relative to no prior such behavior, while Merrall and White both examined the risk of present drug injection (within 1 month) relative to a reference category of patients with prior (but not current) injection drug use. However, if one compared the odds of mortality among present drug injectors to those who reported no prior injection, the odds ratios for mortality among present injectors would be approximately 2.1 in the Merrall cohort and 2.2 in the White cohort, which are very similar to the odds ratios we observed (range 2.1–2.4) during all three post-discharge intervals. In regard to alcohol abuse, we observed a statistically significant association with mortality during days 0–28 (aOR 1.7) but not during subsequent time periods. In contrast, Merrall and White observed statistically significant but slightly lower odds ratios (1.54 and 1.48, respectively) for mortality during averages of 5 and 2 years of follow-up (Merrall et al., 2013; White et al., 2015). Pierce et al. also

**Table 3**
Temporal Trends in Drug-Related Deaths after Discharge.

| Days Since Discharge | All Patients | | | | Prior Opioid Abuse | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Yes | | | | No | | | | IRR (Yes vs. No) |
| | DRD | PY | DRD/1000 PY | IRR (vs. 0-28) | DRD | PY | DRD/1000 PY | IRR (vs. 0-28) | DRD | PY | DRD/1000 PY | IRR (vs. 0-28) | |
| 0-28 | 97 | 23,796 | 4.1 (3.3, 4.9) | (ref) | 57 | 5,930 | 9.6 (7.1, 12.1) | (ref) | 40 | 17,866 | 2.2 (1.5, 2.9) | (ref) | 4.3 (2.9, 6.4)** |
| 29-90 | 115 | 44,141 | 2.6 (2.1, 3.1) | 0.6 (0.5, 0.8)** | 69 | 10,616 | 6.5 (5, 8) | 0.7 (0.5, 0.9)* | 46 | 33,525 | 1.4 (1, 1.8) | 0.6 (0.4, 0.9)* | 4.7 (3.3, 6.9)** |
| 91-365 | 293 | ####### | 1.9 (1.7, 2.2) | 0.5 (0.4, 0.6)** | 182 | 33,707 | 5.4 (4.6, 6.2) | 0.6 (0.4, 0.7)** | 111 | ####### | 0.9 (0.8, 1.1) | 0.4 (0.3, 0.6)** | 5.7 (4.5, 7.2)** |

* < 0.05.
** < 0.01.

**Table 4**
Treatment-Associated Trends in Drug-Related Deaths after Discharge.

| Treatment Type | Days Since Discharge | All Patients | | | | Prior Opioid Abuse | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Yes | | | | No | | | | IRR (Yes vs. No) |
| | | DRD | PY | DRD/1000 PY | IRR (vs Outpatient) | DRD | PY | DRD/1000 PY | IRR (vs Outpatient) | DRD | PY | DRD/1000 PY | IRR (vs Outpatient) | |
| Outpatient | 0-28 | 27 | 12,381 | 2.2 (1.4, 3) | (ref) | 9 | 1,348 | 6.7 (2.3, 11) | (ref) | 18 | 11,033 | 1.6 (0.9, 2.4) | (ref) | 4.1 (1.8, 9.1)* |
| | 29-90 | 35 | 23,527 | 1.5 (1, 2) | (ref) | 12 | 2,501 | 4.8 (2.1, 7.5) | (ref) | 23 | 21,026 | 1.1 (0.6, 1.5) | (ref) | 4.4 (2.2, 8.8)* |
| | 91-365 | 69 | 83,077 | 0.8 (0.6, 1) | (ref) | 29 | 8,326 | 3.5 (2.2, 4.7) | (ref) | 40 | 74,751 | 0.5 (0.4, 0.7) | (ref) | 6.5 (4, 10.5)** |
| Residential | 0-28 | 36 | 6,452 | 5.6 (3.8, 7.4) | 2.6 (1.6, 4.2)* | 20 | 1,468 | 13.6 (7.7, 19.6) | 2.0 (1.1, 3.7)* | 16 | 4,983 | 3.2 (1.6, 4.8) | 2.0 (0.7, 5.4) | 4.2 (2.2, 8.2)* |
| | 29-90 | 35 | 11,914 | 2.9 (2, 3.9) | 2.0 (1.3, 3.1)* | 19 | 2,685 | 7.1 (3.9, 10.2) | 1.5 (0.8, 2.6) | 16 | 9,229 | 1.7 (0.9, 2.6) | 1.6 (0.7, 3.9) | 4.1 (2.1, 7.9)* |
| | 91-365 | 108 | 40,547 | 2.7 (2.2, 3.2) | 3.2 (2.4, 4.2)** | 56 | 8,793 | 6.4 (4.7, 8) | 1.8 (1.3, 2.6)* | 52 | 31,754 | 1.6 (1.2, 2.1) | 3.1 (1.8, 5.2)* | 3.9 (2.7, 5.7)** |
| Detox | 0-28 | 29 | 4,583 | 6.3 (4, 8.6) | 2.9 (1.8, 4.7)* | 24 | 2,735 | 8.8 (5.3, 12.3) | 1.3 (0.7, 2.4) | 5 | 1,847 | 2.7 (0.3, 5.1) | 1.7 (0.6, 4.5) | 3.2 (1.2, 8.5)* |
| | 29-90 | 41 | 7,990 | 5.1 (3.6, 6.7) | 3.4 (2.2, 5.4)** | 34 | 4,726 | 7.2 (4.8, 9.6) | 1.5 (0.9, 2.6) | 7 | 3,264 | 2.1 (0.6, 3.7) | 2.0 (0.8, 4.8) | 3.4 (1.5, 7.6)* |
| | 91-365 | 94 | 24,886 | 3.8 (3, 4.5) | 4.5 (3.4, 6.0)** | 76 | 14,247 | 5.3 (4.1, 6.5) | 1.5 (1.1, 2.2)* | 18 | 10,639 | 1.7 (0.9, 2.5) | 3.2 (1.8, 5.4)* | 3.2 (1.9, 5.3)* |
| OST | | | | | | 5 | 381 | 13.1 (1.7, 24.5) | 2.0 (1.1, 3.6)* | | | | | |
| | | | | | | 4 | 710 | 5.6 (0.1, 11.1) | 1.2 (0.7, 2.1) | | | | | |
| | | | | | | 22 | 2,361 | 9.3 (5.4, 13.2) | 2.7 (1.9, 3.8)** | | | | | |

* < 0.05.
** < 0.01.

found that rates of DRD in the first 28 days after discharge were twice as high among patients discharged from residential treatment compared to those discharged from OST (18.8 DRD/ 1000 PY vs. 9.3 DRD/1000 PY) (Pierce et al., 2016). In contrast, we found similar rates of DRD during days 0–28 between patients discharged from residential treatment (13.6/1000 PY) and those discharged from OST (13.1/1000 PY). In the Pierce study, DRD rates in both of these groups were substantially higher than those observed among patients treated with psychological services alone (3.9 DRD/1000 PY); this latter group may be somewhat similar to the outpatient treatment cohort in our study, although our corresponding DRD rate was notably higher (6.7 DRD/1000 PY).

However, not all prior research has reached similar findings. Ravndal et al. prospectively followed 276 patients in inpatient substance abuse treatment programs in Norway during 1998–2006 and assessed risk factors associated with overdose deaths during the first four weeks after discharge (Ravndal and Amundsen, 2010). Unlike our study, their results found no significant association between overdose death and alcohol abuse, use of heroin, or use of injection drugs; however, their study had a small number of deaths (36) during the observed time period and may have been underpowered to detect these associations.

Our study identified a significant association between post-discharge mortality and prior abuse of benzodiazepines or other non-alcohol depressants. Prior findings on the association between benzodiazepine abuse and drug-related death have been mixed. Gossop et al. identified that prior benzodiazepine abuse was significantly associated with overdose death (OR 3.3 [95% CI 1.6, 7.0]) in a prospective cohort study of 1075 drug misusers during four years of follow-up after they began substance abuse treatment (Gossop et al., 2002); however, nearly 20% of deaths in that study (9/53) occurred while patients were still in treatment, which limits the comparison to our study. Sedative abuse was not significantly associated with post-discharge mortality in analyses by Merrall and White of the SDMD dataset during 1996–2006 (Merrall et al., 2013; White et al., 2015), but analysis of the SDMD data during 2006–2010 found a statistically significant association between prior benzodiazepine abuse and drug-related death (HR 1.28 [95% CI 1.13, 1.46]) after treatment discharge (White et al., 2015). Significant differences in patient characteristics may partially explain these discordant findings; only 7% of patients in our study reported prior depressant abuse, in contrast to 30% and 37% of patients in the Merrall and Gossop studies, respectively (Gossop et al., 2002; Merrall et al., 2013). This method of record linkage could be adapted to examine other drugs identified by epidemiological reports such as the National Drug Early Warning System (NDEWS) to understand the mortality risks of local drug patterns.

### 4.2. Temporal trends in post-discharge mortality

Our second major conclusion affirms in a North American population that post-discharge mortality is significantly associated with the type(s) of drugs previously abused and the time since discharge. We observed the highest DRD rates in the immediate post-discharge period (i.e., first 28 days) and saw significant declines in subsequent time periods.

Residential treatment has been examined in several prior studies of post-discharge mortality. Among patients in our cohort who were most recently in residential treatment, we observed significantly lower DRD rates than Merrall during post-discharge days 0–28 (22/1000 PY vs. 5.6/1000 PY), days 29–90 (11/1000 PY vs. 2.9/1000 PY), and days 91–365 (11/1000 PY vs. 2.7/1000 PY)(Merrall et al., 2013). These discordant results could reflect underlying difference in our populations as the Merrall cohort included a substantially greater proportions of patients with prior opioid abuse (65% vs. 25%). Among the subset of patients in our study prior opioid abuse, the rate remained lower than those reported by Merrall at 0–28 days (22/1000 PY vs. 13.6/1000 PY), 29–90 days (11/1000 PY vs. 7.1/1000 PY), and 91–365 days (11/1000 PY vs. 6.4/1000 PY). One possible confounder is that the population examined by Merrall had a much higher rate of injection drug use (48% vs. 13%) than in our study. Rates of mortality after residential treatment in the 2006–2010 SDMD cohort by White (White et al., 2015) were similar to those reported by Merrall.

Davoli et al. prospectively followed 10,258 patients who abused heroin and were admitted for SUD treatment (including residential, semi-residential, or OST with methadone) in Italy during 1998–2001 (Davoli et al., 2007). The observed mortality rate in the first 30 days after discharge was 23.2 DRD/1000 PY, although this mortality rate was unfortunately not stratified by treatment type. Among patients in our cohort with prior opioid abuse, we found a lower drug-related death rate of 13.6/1000 PY in days 0–28 after residential treatment discharge and 13.1 DRD/1000 PY in days 0–28 after OST discharge. Again, the difference in mortality could potentially be explained by route of drug use; opioid injection is associated with higher mortality rates and other worse health outcomes (Black et al., 2013; Lake and Kennedy, 2016) compared to oral opioid use, and 72% of patients in the Davoli study reported injection drug use while only 13% of our sample did so.

In regard to post-discharge mortality after OST, we compared our results to a comprehensive systematic review and meta-analysis by Sordo et al. which examined overdose-related mortality after cessation of either methadone- or buprenorphine-based OST in 19 study cohorts comprising over 122,000 patients (Sordo et al., 2017). Our point estimate for drug-related mortality rates in the first 28 days after discharge (13.1/1000 PY) was somewhat higher than those reported by that study for methadone treatment (4.2/1000 PY) or buprenorphine treatment (10.8/1000 PY), but they are not statistically significantly different due to the relatively small number of OST patients in our data set.

Several additional factors could explain the observed differences in mortality rates between our study and others. First, there may be international differences in medical examiners' practices regarding classification of deaths as drug-related. Authors have suggested that differences in forensic practices may make limit the value of international comparisons of drug-related death mortality (Fugelstad et al., 2017). Furthermore, our cohort had a substantially lower proportion of patients with a history of opioid use, and particularly a lower proportion of patients with injection drug use, than other study cohorts. This difference could be partially responsible for the lower rates of mortality observed in our cohort.

### 4.3. Differences in post-discharge mortality associated with treatment modality

Across the full patient sample, we observed a difference in mortality rates associated with discharge from controlled environments (residential and detoxification) versus uncontrolled environments (outpatient) with controlled environments having higher rates than outpatient; the differences in mortality rates were smaller and less consistently significant when the cohort was stratified by prior opioid abuse. Loss of physiological tolerance may be more likely in controlled treatment settings, which could contribute to unintentional overdose deaths if patients resume their prior substance abuse. However, we also found OST treatment was associated with a higher post-discharge mortality rate than outpatient treatment, and OST patients receive opiates on a daily basis, so they are less likely to lose their tolerance. This difference could potentially be due to confounders (e.g. route of administration; medical or psychiatric comorbidities; available psychosocial supports) that our data set cannot fully address.

### 4.4. Limitations

This study has several limitations. First, patients' drug histories are self-reported, and it is possible that patients could withhold relevant information about prior drug abuse. Second, although our linkage

method was could account for numeric transpositions and different spellings of names, clients with multiple missing or changing linking variables across time (e.g., a patient without an SSN who changed names between discharge and death) might not be matched to our death records. Third, our data set lacks certain clinical variables (e.g., medical comorbidities) and treatment variables (e.g., medications used for OST) that may confound some results. Fourth, our data are limited to patients discharged from a single (albeit large) provider of substance abuse treatment services in a single state, and our results may not be generalizable to patient populations with private insurance or in other geographic locations. Fifth, because this study only examined patients who were discharged from treatment, mortality trends are not generalizable to individuals who remain successfully in treatment; this is especially true for individuals in OST, whose duration of treatment may extend appropriately for many years. A reasonable estimate based on working knowledge of the program is that this data set contains about 60% of OST clients. Sixth, Texas has a county-based mix of medical examiners and coroners, so there is variability in the policies and procedures used to assign causes of death throughout the state. It is likely that at least some drug-related causes of death were either not reported or incorrectly reported in our data set. However, under-reporting seems a more likely problem than over-reporting. Seventh, near the end of this study's time period, DSHS imposed a time limit of several years on OST treatment length after which clients would have to move to self-pay but some waivers were provided, and this policy was discontinued. Finally, our results on treatment-associated post-discharge mortality are meant to be descriptive rather than to imply causation. We anticipate that physicians and other treatment providers triage patients into treatment programs of differing intensity based on many factors such as perceived severity of the patient's substance use disorder, their available resources, and psychiatric comorbidities. In this regard, the results are meant to illustrate the variability in post-discharge mortality rates and to provide more discrete outcomes data for different patient sub-populations rather than to suggest that the different treatment types are causally associated with these outcomes.

## 5. Conclusions

Our study affirms in a large cohort of patients receiving publicly-funded SUD treatment in the United States that drug-related mortality is highest in the first four weeks after treatment discharge. Mortality rates drop by more than 50% beyond the first 90 days after discharge. Individuals who previously abused alcohol, depressants, or opioids have a risk of post-discharge mortality that is 3–4 times higher than those who did not, and prior use of opioids by injection further increases this risk. Patients discharged from outpatient treatment programs have substantially lower rates of post-discharge mortality compared to those discharged from residential, detoxification, or OST programs. This information may help treatment providers counsel patients more appropriately, such providing education on the availability of naloxone without prescription in most states, and to more closely monitor high-risk patients after treatment discharge to improve their health outcomes.

## Contributors

EAB conceptualized the study design with assistance from BCM. EAB obtained IRB approval. Primary data analysis was performed by BCM. BCM drafted the initial manuscript with critical revision for important intellectual content by EAB. EAB supervised the overall study. Both authors reviewed and approved the final manuscript.

## Role of funding source

Dr. Maughan was supported in part by the National Heart, Lung, and Blood Institute through the Oregon Emergency Care Research Multidisciplinary Training Program (5K12HL133115). The funding source had no role in the study.

## Declaration of Competing Interest

The authors declare no competing interests. The opinions expressed in this paper are those of the authors and do not represent the official view or policy of any government agency or business.

## 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.2019.05.011.

## References

Black, R.A., Trudeau, K.J., Cassidy, T.A., Budman, S.H., Butler, S.F., 2013. Associations between public health indicators and injecting prescription opioids by prescription opioid abusers in substance abuse treatment. J. Opioid Manag. 9, 5–17. https://doi.org/10.5055/jom.2013.0142.

Center for Behavioral Health Statistics and Quality, 2018. Combined Substance Use and Mental Health Treatment Episode Data Set (TEDS) State Instruction Manual. (Accessed 10 September 2018). https://wwwdasis.samhsa.gov/dasis2/manuals/combined_su_mh_teds_manual_ver_4.3.pdf.

Darker, C.D., Sweeney, B.P., Barry, J.M., Farrell, M.F., Donnelly-Swift, E., 2015. Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. Cochrane Database Syst. Rev. CD009652. https://doi.org/10.1002/14651858.CD009652.pub2.

Davoli, M., Bargagli, A.M., Perucci, C.A., Schifano, P., Belleudi, V., Hickman, M., Salamina, G., Diecidue, R., Vigna-Taglianti, F., Faggiano, F., VEdeTTE Study Group, 2007. Risk of fatal overdose during and after specialist drug treatment: the VEdeTTE study, a national multi-site prospective cohort study. Addiction 102, 1954–1959. https://doi.org/10.1111/j.1360-0443.2007.02025.x.

Degenhardt, L., Bucello, C., Mathers, B., Briegleb, C., Ali, H., Hickman, M., McLaren, J., 2011. Mortality among regular or dependent users of heroin and other opioids: a systematic review and meta-analysis of cohort studies. Addiction 106, 32–51. https://doi.org/10.1111/j.1360-0443.2010.03140.x.

Degenhardt, L., Randall, D., Hall, W., Law, M., Butler, T., Burns, L., 2009. Mortality among clients of a state-wide opioid pharmacotherapy program over 20 years: risk factors and lives saved. Drug Alcohol Depend. 105, 9–15. https://doi.org/10.1016/j.drugalcdep.2009.05.021.

Fugelstad, A., Ramstedt, M., Thiblin, I., Johansson, L.A., 2017. Drug-related deaths: statistics based on death certificates miss one-third of cases. Scand. J. Public Health. https://doi.org/10.1177/1403494817745187.. Online First (https://journals.sagepub.com/toc/sjpc/0/0).

Gates, P.J., Sabioni, P., Copeland, J., Le Foll, B., Gowing, L., 2016. Psychosocial interventions for cannabis use disorder. Cochrane Database Syst. Rev. CD005336. https://doi.org/10.1002/14651858.CD005336.pub4.

Gossop, M., Marsden, J., Stewart, D., Kidd, T., 2003. The national treatment outcome research study (NTORS): 4-5 year follow-up results. Addiction 98, 291–303.

Gossop, M., Stewart, D., Treacy, S., Marsden, J., 2002. A prospective study of mortality among drug misusers during a 4-year period after seeking treatment. Addiction 97, 39–47.

Hulse, G.K., English, D.R., Milne, E., Holman, C.D., 1999. The quantification of mortality resulting from the regular use of illicit opiates. Addiction 94, 221–229.

Jackson, G., 2001. Drug-related Deaths in Scotland in 2000. Occas. Pap. No. 5. (Accessed 10 January 2018). http://www.webcitation.org/6BPJuZF1X.

Klimas, J., Tobin, H., Field, C.-A., O'Gorman, C.S., Glynn, L.G., Keenan, E., Saunders, J., Bury, G., Dunne, C., Cullen, W., 2014. Psychosocial interventions to reduce alcohol consumption in concurrent problem alcohol and illicit drug users. Cochrane Database Syst. Rev. CD009269. https://doi.org/10.1002/14651858.CD009269.pub3.

Lake, S., Kennedy, M.C., 2016. Health outcomes associated with illicit prescription opioid injection: a systematic review. J. Addict. Dis. 35, 73–91. https://doi.org/10.1080/10550887.2015.1127712.

Laramée, P., Leonard, S., Buchanan-Hughes, A., Warnakula, S., Daeppen, J.-B., Rehm, J., 2015. Risk of all-cause mortality in alcohol-dependent individuals: a systematic literature review and meta-analysis. EBioMedicine 2, 1394–1404. https://doi.org/10.1016/j.ebiom.2015.08.040.

McCarty, D., Braude, L., Lyman, D.R., Dougherty, R.H., Daniels, A.S., Ghose, S.S., Delphin-Rittmon, M.E., 2014. Substance abuse intensive outpatient programs: assessing the evidence. Psychiatr. Serv. 65, 718–726. https://doi.org/10.1176/appi.ps.201300249.

Merrall, E.L.C., Bird, S.M., Hutchinson, S.J., 2013. A record-linkage study of drug-related death and suicide after hospital discharge among drug-treatment clients in Scotland, 1996-2006. Addiction 108, 377–384. https://doi.org/10.1111/j.1360-0443.2012.04066.x.

Merrall, E.L.C., Kariminia, A., Binswanger, I.A., Hobbs, M.S., Farrell, M., Marsden, J., Hutchinson, S.J., Bird, S.M., 2010. Meta-analysis of drug-related deaths soon after release from prison. Addiction 105, 1545–1554. https://doi.org/10.1111/j.1360-

0443.2010.02990.x.
Neeleman, J., 2001. A continuum of premature death. Meta-analysis of competing mortality in the psychosocially vulnerable. Int. J. Epidemiol. 30, 154–162.
Nielsen, S., Larance, B., Degenhardt, L., Gowing, L., Kehler, C., Lintzeris, N., 2016. Opioid agonist treatment for pharmaceutical opioid dependent people. Cochrane Database Syst. Rev. CD011117. https://doi.org/10.1002/14651858.CD011117.pub2.
Pierce, M., Bird, S.M., Hickman, M., Marsden, J., Dunn, G., Jones, A., Millar, T., 2016. Impact of treatment for opioid dependence on fatal drug-related poisoning: a national cohort study in England. Addiction 111, 298–308. https://doi.org/10.1111/add.13193.
Ravndal, E., Amundsen, E.J., 2010. Mortality among drug users after discharge from inpatient treatment: an 8-year prospective study. Drug Alcohol Depend. 108, 65–69. https://doi.org/10.1016/j.drugalcdep.2009.11.008.
Reif, S., George, P., Braude, L., Dougherty, R.H., Daniels, A.S., Ghose, S.S., Delphin-Rittmon, M.E., 2014. Residential treatment for individuals with substance use disorders: assessing the evidence. Psychiatr. Serv. 65, 301–312. https://doi.org/10.1176/appi.ps.201300242.
Sordo, L., Barrio, G., Bravo, M.J., Indave, B.I., Degenhardt, L., Wiessing, L., Ferri, M., Pastor-Barriuso, R., 2017. Mortality risk during and after opioid substitution treatment: systematic review and meta-analysis of cohort studies. BMJ 357, j1550. https://doi.org/10.1136/bmj.j1550.
White, S.R., Bird, S.M., Merrall, E.L.C., Hutchinson, S.J., 2015. Drugs-related death soon after hospital-discharge among drug treatment clients in Scotland: record linkage, validation, and investigation of risk-factors. PLoS One 10, e0141073. https://doi.org/10.1371/journal.pone.0141073.
Zlodre, J., Fazel, S., 2012. All-cause and external mortality in released prisoners: systematic review and meta-analysis. Am. J. Public Health 102, e67–75. https://doi.org/10.2105/AJPH.2012.300764.