Predictors for 30-Day and 90-Day Hospital Readmission Among Patients With Opioid Use Disorder

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Objectives: To identify the incidence, characteristics, and predictors for 30 and 90-day readmission among acutely hospitalized patients with opioid use disorder (OUD).

Methods: This retrospective, cohort study evaluated consecutive adults with OUD admitted to an academic medical center over a 5-year period (10/1/11 to 9/30/16). Multivariable logistic regression was used to determine independent predictors for 30 and 90-day readmissions based on pertinent admission, hospital, and discharge variables collected via chart review and found to be different (with a $P < 0.10$) on univariate analysis.

Results: Among the 470 adults (mean age 43.1 ± 12.8 years, past heroin use 77.9%; admission opioid agonist therapy use [buprenorphine 22.6%; methadone 27.0%]; medical [vs surgical] admission 75.3%, floor [vs ICU] admission 93.0%, in-hospital mortality 0.9%), 85 (18.2%) and 151 (32.1%) were readmitted within 30 and 90 days, respectively. Among the 90-day readmitted patients, median time to first readmission was 26 days. Buprenorphine use (vs no use) at index hospital admission was independently associated with reduced 30-day (odds ratio [OR] 0.47, 95% confidence interval [CI] 0.24–0.93) and 90-day (OR 0.57, 95% CI 0.34–0.96) readmission; prior heroin (vs prescription opioid) use was associated with reduced 90-day readmission (OR 0.59, 95% CI 0.37–0.94) and length of hospital stay was associated with both greater 30-day (OR 1.02, 95% CI 1.01–1.05) and 90-day (OR 1.04, 95% CI 1.01–1.06) readmission rates.

Conclusions: Among patients with OUD taking buprenorphine at the time of hospital admission, 30-day and 90-day hospital readmission was reduced by 53% and 43%, respectively.

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Opioid use disorder (OUD) is a chronic disease, characterized by the compulsive use of opioids, despite harmful consequences. More than 2 million Americans currently have OUD and deaths from opioid overdose have quintupled since 1999 (WONDER, 2017). Compared with patients without OUD, individuals with OUD are more likely to require hospitalization, emergency department evaluation, and urgent care services (Owens et al., 2014; Kirson et al., 2017).

Hospital readmission, particularly within 30 days of an acute care hospital discharge, is an outcome of great interest to clinicians, hospitals, and payers like the Centers for Medicare and Medicaid Services (CMS), given its association with quality of inpatient care and increased health care costs (Zuckerman et al., 2016; Centers for Medicare and Medicaid Services, 2018; Hatipoglu et al., 2018). Patients with OUD who undergo major surgery are 25% more likely to be readmitted to hospital within 30 days than patients without (Gupta et al., 2018).

Important questions regarding the prevalence, characteristics, and risk factors associated with hospital readmission among patients with OUD remain, particularly among patients hospitalized for a medical condition and those administered opioids during admission. The predictors for 30-day hospital readmission are unknown. Recognition of modifiable risk factors for readmission can help inform efforts focused on reducing readmission rates in patients with OUD. While the use of opioid agonist therapy (OAT), including methadone and buprenorphine, improves patient outcomes (Mattick et al., 2014; Weiss et al., 2015; Sordo et al., 2017), including mortality (Liebschutz et al., 2014), the association between OAT and hospital readmissions remains unclear. Lastly, the incidence, characteristics, and predictors of longer-term hospital readmission (ie, within 90 days) have not been evaluated.

The primary objective of our study was to determine the incidence of hospital readmission within 30 and 90 days for adults with OUD admitted to an acute care hospital for any reason and to identify predictors for these readmissions. We also sought to compare admission, hospital, and outcome characteristics, including use of OAT, between the index

hospitalization cohort, and those patients readmitted within 30 and 90 days.

METHODS

Study Design and Population

The study cohort included patients with OUD admitted to Massachusetts General Hospital (MGH)—a 999-bed academic medical center in Boston, MA, who received at least 24 hours of an opioid analgesic during admission. A priori, we hypothesized that patients with OUD exposed to non-OAT opioid analgesia during hospitalization would be at the greatest risk for hospital readmission and thus excluded patients who did not receive at least 24 hours of scheduled (or 4 doses of ''as-needed'') opioid analgesia during their hospitalization. Through author consensus, we assumed that this degree of opioid exposure would be significant enough to affect patient outcomes.

The Partners Research Patient Data Registry (RPDR) was used to electronically identify consecutive adults over a 5-year period (10/1/2011 through 9/30/2016) having either an International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) or ICD-10-CM diagnostic code for OUD or an admission problem list denoting OUD who each received an opioid analgesic during their MGH admission (Heslin et al., 2017; Moore and Barrett, 2017). This single-center, retrospective cohort study was approved by the Massachusetts General Hospital (MGH) Institutional Review Board; patient consent was not required.

Of note, hospital policies and state-wide legislation were updated within the study period. A multidisciplinary addictions consult team was established at MGH in October, 2014. The team offered specialty consultation and encouraged evidence-based treatments for substance use disorders, including the initiation of OAT during hospitalization. Before this team was implemented, patients admitted to MGH with OUD would be seen by a psychiatry consult team who rarely initiated OAT during hospitalizations. In 2016, 2 months before the period of data collection ended, a new Massachusetts opioid law was implemented that reduced the maximum number of days opioids could be prescribed for outpatients with acute pain, mandated all opioid prescribers be part of the state prescription monitoring program, and established opioid stewardship programs (Office of Governor Charlie Baker, 2016).

Outcomes

A 30 or 90-day hospital readmission was defined to occur when a patient was readmitted to MGH (for any reason) within 30 or 90 days of discharge from their index hospitalization. Only the first readmission to MGH within the 30 or 90-day period was considered. A reliance on the MGH clinical information system for all study data precluded our ability to identify readmissions to non-MGH institutions, or healthcare delivery or deaths that occurred outside of MGH. Patients who died during the index hospitalization were excluded from all readmission analyses. For both the index and readmission hospitalizations, data were collected at the time of admission, during hospitalization, and at the time of hospital discharge. Data collected during the index hospitalization and first readmission (when it occurred) included pertinent demographic information, concomitant medical and psychiatric illnesses, opioid administration, OAT use, initiation or modification of OAT during hospitalization, the prescription of OAT and non-OAT opioid analgesia at the time of discharge, need for intensive care unit admission, mortality, length of stay, and patient disposition. The frequency of MGH ED visits (not requiring readmission) and all MGH readmissions (beyond the first readmission) over the 90-day evaluation period were also documented, but detailed data collection for these occurrences was not undertaken as they were outside of the scope of the study.

All data were collected by trained data extractors from the electronic medical record system at MGH (from October 1, 2011 to March 31, 2016 using the Longitudinal Medical Record [LMR] system [an in-house system developed at Partners Healthcare System]), and thereafter using Partners eCare (developed in conjunction with Epic (Verona, WI]). Research Electronic Data Capture (REDCap)—a secure, web-based application for validated data entry, transmission, and storage—was used to manage all extracted data.

Data Analysis

Through literature review and verbal author consensus, admission and hospital variables related to the index admission that could influence 30 and 90-day hospital readmissions were identified (Santora and Hutton, 2008; Holt et al., 2012; Stevens et al., 2017; Gupta et al., 2018). A logistic model was selected over a survival model given our focus on identifying predictors for readmission (rather than length of time to hospital readmission) and the lack of random censoring within the population (George et al., 2014). Continuous variables (eg, age, length of stay) were modeled as continuous independent predictors and categorical variables were modeled as indicator variables with the reference group indicated. Variables with a $P < 0.10$ during univariate analysis were entered into a multivariable logistic regression model using a forward (but not stepwise) selection process guided by Akaike Information Criteria to yield the final 30 and 90-day readmission prediction models, with the final model checked to ensure a parsimonious model with good fit (Greenland, 1989; Sharif et al., 2014; Strowd et al., 2015; Roberts et al., 2016; Karcutskie et al., 2017). As such, age and sex—variables that met inclusion criteria at the univariate stage—were not included in the final multivariate models. While older adults are more likely to be readmitted to hospital (Strowd et al., 2015; Hatipoglu et al., 2018), given that our cohort averaged 43 years old and there were no patients older than 65 years in it, we deemed age not relevant to consider. We deemed male sex alone not to be an important readmission predictor given that it likely served as a surrogate for other readmission predictors not easily captured (eg, males generally engage in riskier behavior than females [Mata et al., 2016]). Given that methadone and buprenorphine may have different effects on hospital readmission rate, we chose to evaluate them as distinct covariates and not as a combined variable. All statistical analyses were completed using SAS software version 9.4 for MS Windows (SAS, Cary, NC).

RESULTS

Baseline characteristics, OAT use, and hospital outcomes for the 470 patients in the index hospitalization cohort are described in Table 1. In brief, this was a predominately white, male, middle-aged group of patients insured by Medicaid, admitted through the emergency department from home, and having a wide variety of acute medical and surgical conditions. Many patients had 1 or more additional psychiatric and/or substance use disorders. Patients very rarely required admission to the ICU; only 4 (0.9%) died in the hospital. Notably, the number of patients taking OAT at the time of index admission, during index hospitalization, and at index hospitalization discharge varied (46 of 232 [19.8%] patients taking OAT at the time of index hospital admission were not discharged on it; 44 of 364 [12.1%] patients not taking an OAT at index hospital admission were discharged on it).

In all, 85 of 470 (18.2%) patients were readmitted to MGH at least once within 30 days and 151 of 470 (32.1%) were readmitted at least once within 90 days after index hospitalization discharge. The daily risk for hospital readmission from the time of discharge is present in Fig. 1. Among patients readmitted within 90 days, median time to first readmission was 26 days. In all, 58 (12.3%) patients were readmitted to MGH at least twice within 90 days. An additional 68 (14.6%) patients presented to the MGH emergency department at least once within 90 days, but were not readmitted. The characteristics and hospital outcomes for the patients readmitted during both the 30 and 90-day posthospitalization periods are also presented in Table 1.

Factors deemed, a priori, to have the greatest potential likelihood of influencing hospital readmission are compared between the 30-day readmitted and non-readmitted patients in Table 2, and between the 90-day readmitted and non-readmitted patients in Table 3. For the 30-day readmission group, admission buprenorphine use (vs no use) and length of hospital stay were found to be different between readmitted and non-readmitted patients at a $P < 0.10$ in the univariate analysis and therefore included in the regression analysis. The multivariable analysis revealed that patients taking buprenorphine at the time of their index admission were 53% less likely to be readmitted to hospital within 30 days. The analysis also revealed that the longer a patient stayed in the hospital during their index hospitalization, the more likely they were to be readmitted within 30 days, with each additional day spent hospitalized increasing the odds of readmission by 2%.

For the 90-day readmission group, prior heroin (vs prescription opioid) use, buprenorphine use (vs no use) at the time of index hospitalization, admission to a medical (vs surgical) service, and length of hospital stay were each found to be different at $P < 0.10$ between the readmitted and non-readmitted groups in the univariate analyses and were therefore included in the multivariable regression analysis. This multivariable analysis found that patients using heroin (rather than prescription opioids) in the period before the index hospitalization were 41% less likely to be readmitted at 90 days; patients taking buprenorphine (vs a prescription opioid) at the time of index hospitalization were 43% less likely to be readmitted within 90 days; patients admitted to a medical service (versus a surgical service) were nearly twice as likely to be readmitted during this period; and the longer a patient stayed in the hospital during their index hospitalization, the more likely they were to be readmitted within 90 days, with each additional day increasing the odds of readmission by 4%.

DISCUSSION

Our study is the first to examine the characteristics, incidence, and factors associated with hospital readmission for a mixed medical–surgical population of patients with OUD admitted to an academic medical center. Nearly 1 out of 5 patients was readmitted within 30 days, and approximately 1 out of 3 patients was readmitted within 90 days. Importantly, patients treated with buprenorphine at the time of index hospitalization were approximately half as likely to be readmitted within 30 days and 43% less likely to be readmitted within 90 days. With only 21% of the study patients taking buprenorphine at the time of index hospitalization, future controlled research needs to evaluate whether failure to initiate buprenorphine before hospital discharge may represent an important modifiable risk factor for hospital readmissions in patients with OUD.

The high readmission rates we report are similar to those experienced by patients discharged from the hospital after chronic obstructive pulmonary disease or congestive heart failure exacerbations—populations of patients far older and with much greater comorbidity than the OUD cohort we evaluated (Alford et al., 2006; Sharif et al., 2014; Roberts et al., 2016). Strategies that have been shown to reduce 30-day readmission rates in patients without OUD should be evaluated in the OUD population. These might include pharmacist-led medication reconciliation and counseling, clear communication of discharge instructions, adequate use of interpreters for patients with limited English proficiency, 7-day clinician phone follow-ups, participation in a readmission-focused collaborative or a readmission reduction incentive program with insurers (Walker et al., 2009; Pandor et al., 2013; Linden and Butterworth, 2014; Chambers et al., 2016; Ziaeian and Fonarow, 2016). Increasing state and national attention to the opioid overdose crisis is expected to expand initiatives focused on addressing OUD. Greater access to OAT within healthcare systems and increased use of well-proven programs like inpatient addiction consult teams are important areas for expansion (Wakeman et al., 2017). Despite the strong evidence that OAT improves clinical outcomes for patients with OUD (Liebschutz et al., 2014; Mattick et al., 2014; Weiss et al., 2015; Sordo et al., 2017; Larochelle et al., 2018) and practice guidelines advocating its use (Dematteis et al., 2017), only a small proportion of patients are treated with it (Andrews et al., 2014). Buprenorphine has been shown to improve rates of abstinence from illicit opioids, increase treatment retention, reduce incidence of hepatitis C infection, and reduce mortality (Liebschutz et al., 2014; Tsui et al., 2014; Weiss et al., 2015; Larochelle et al., 2018). In healthcare settings, including hospitals and emergency departments, buprenorphine has been shown to increase treatment retention after discharge (D'Onofrio et al., 2015; Sordo et al., 2017). Additionally, buprenorphine treatment has been shown to reduce overall inpatient admissions and total healthcare costs

TABLE 1. Baseline, Hospital and Discharge Characteristics Between the Index Hospitalization and the 30-day and 90-day Readmission Cohorts

Characteristic	Index Hospitalization (n = 470)	Readmission Within 30 d (n = 85)	Readmission Within 90 d (n = 151)
Baseline			
Age, mean ± SD	43.1 ± 12.8	44.9 ± 11.9	44.8 ± 12.8
Male, n (%)	293 (62.3)	59 (69.4)	104 (69.0)
White, n (%)	420 (89.4)	79 (92.9)	138 (91.4)
Medicaid insurance, n (%)	393 (83.6)	69 (81.2)	123 (81.5)
Primary reason for admission, n (%)			
Infectious	135 (28.7)	31 (36.5)	64 (42.3)
Gastrointestinal/hepatic/renal	84 (17.9)	11 (12.9)	16 (10.6)
Neurologic/psychiatric	48 (10.2)	11 (12.9)	20 (13.4)
Toxic ingestion/overdose	39 (8.3)	10 (11.8)	16 (10.6)
Respiratory	34 (7.2)	1 (1.2)	3 (2.0)
Trauma/burns	33 (7.0)	4 (4.7)	6 (4.2)
Obstetrical/gynecological	30 (6.4)	2 (2.4)	3 (2.0)
Cardiac	29 (6.2)	5 (5.9)	10 (6.6)
Other	34 (7.3)	10 (11.8)	13 (8.6)
Admitted through ED, n (%)	422 (89.8)	75 (88.2)	135 (89.4)
Location before hospitalization, n (%)			
Home	367 (78.1)	53 (62.4)	100 (66.2)
Unstably housed	47 (10.0)	15 (17.6)	28 (18.5)
Inpatient psychiatric/addiction facility	46 (9.8)	2 (2.4)	3 (2.0)
Other	5 (2.1)	13 (15.3)	45 (29.6)
Psychiatric comorbidities, n (%)			
Depression	214 (45.5)	42 (49.4)	74 (48.7)
Other substance use disorder	177 (37.7)	30 (35.3)	52 (34.2)
Anxiety	168 (35.7)	30 (35.3)	55 (36.2)
Bipolar disorder	67 (14.3)	13 (15.3)	24 (15.8)
Post-traumatic stress disorder	58 (12.3)	12 (14.1)	21 (13.8)
Personality disorder	45 (9.6)	1 (1.2)	2 (1.3)
Primary opioid used			
Heroin, n (%)	366 (77.9)	66 (77.6)	110 (72.8)
Prescription opioids, n (%)	104 (22.1)	19 (22.4)	41 (27.2)
Other substance(s) used, n (%)			
No	263 (56.0)	50 (58.8)	88 (58.3)
Yes	207 (44.0)	35 (41.2)	63 (41.7)
Marijuana	85 (18.1)	18 (21.2)	27 (17.9)
Cocaine	130 (27.7)	19 (22.4)	41 (27.2)
Non-prescribed stimulant	10 (2.1)	2 (2.4)	3 (2.0)
Non-prescribed benzodiazepine	64 (13.6)	9 (10.6)	16 (10.6)
Alcohol use, n (%)			
Never	240 (51.1)	50 (58.8)	86 (57.0)
Active use	112 (23.8)	20 (23.5)	31 (20.5)
No history available	118 (25.1)	15 (17.6)	34 (22.5)
Non-OAT prescription opioid use, n (%)	94 (20.0)	32 (37.6)	51 (33.8)
As needed use	47 (10.0)	28 (32.9)	45 (29.8)
Scheduled use	47 (10.0)	4 (4.7)	6 (4.0)
Daily use of 50—99 mg ME*	19 (4.0)	9 (10.6)	13 (8.6)
Daily use ≥ 100 mg ME*	39 (8.3)	17 (20.0)	26 (17.2)
OAT prescription opioid use, n (%)			
Buprenorphine	106 (22.6)	21 (24.7)	35 (23.2)
Methadone	127 (27.0)	24 (28.2)	45 (29.8)
During hospitalization			
Initial admission unit, n (%)			
Floor	437 (93.0)	79 (92.9)	142 (94.0)
Medical	329 (75.3)	61 (77.2)	115 (81.0)
Surgical	108 (24.7)	18 (22.8)	27 (19.0)
ICU	33 (7.0)	6 (7.1)	9 (6.0)
Medical	25 (75.8)	4 (66.7)	6 (66.7)
Surgical	8 (24.2)	2 (33.3)	3 (33.3)
Daily ME administered*	33 (167)	45 (175)	132 (201)
Proportion of hospital days opioid administered (%)	100 (15.1)	100 (9)	100 (9)
Hospital discharge			
Discharged on non-OAT opioid, n (%)	396 (84.3)	37 (43.5)	79 (52.1)
Length of stay*	6 (6)	5 (3)	5 (5)
Ever admitted to an ICU, n (%)	62 (13.2)	10 (11.8)	14 (9.3)
In hospital mortality, n (%)	4 (0.9)	2 (2.4)	2 (1.3)
Hospital disposition, n (%)			
Home/	284 (60.9)	54 (65.1)	93 (63.2)
Unstably housed	28 (6.0)	9 (10.8)	19 (12.9)
Left against medical advice	20 (4.3)	5 (6.0)	8 (5.4)
Inpatient psychiatric hospital	16 (3.4)	2 (2.4)	4 (2.7)
Another acute care hospital	10 (2.1)	0 (0)	0 (0)
Medical rehabilitation	7 (1.5)	0 (0)	1 (0.7)
Residential addiction program	2 (0.4)	0 (0)	0 (0)
LTACH	0 (0)	11 (13.3)	21 (14.1)
Other	38 (8.1)	2 (2.4)	3 (2.0)
Missing	65 (13.8)	0 (0)	0 (0)

ED, emergency department; ICU, intensive care unit; LTACH, long-term acute care hospital; ME, morphine equivalents; OAT, opioid agonist therapy.
*Median (interquartile range).

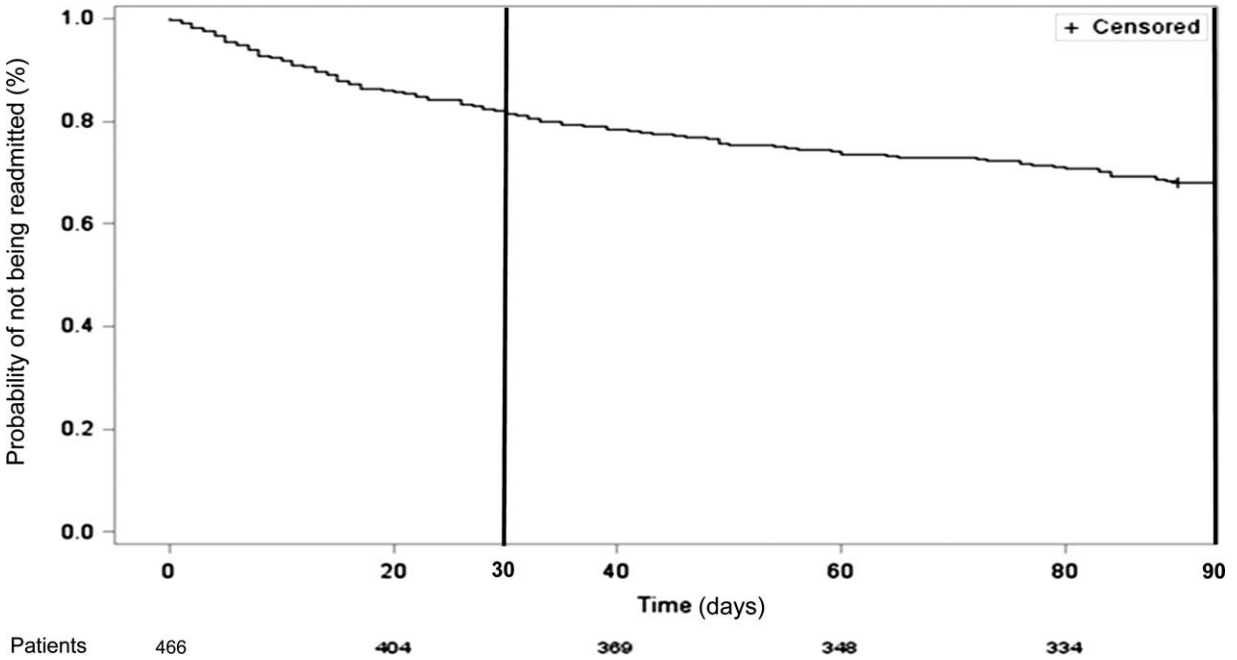

FIGURE 1. Probability for hospital readmission over the course of the 90 day postindex hospitalization period. The solid vertical lines indicate the 30-day and 90-day readmission periods. For patients having 2 or more readmissions in 90 days, only the first readmission is plotted in this figure.

(Tkacz et al., 2014). While the retrospective nature of our study limits our ability to assign causality, our results provide additional support that buprenorphine may reduce healthcare utilization. Importantly, the acquisition cost for a buprenorphine prescription after hospital discharge would be expected to be far less than the costs associated with hospital readmission, particularly at an academic medical center like the one where this study was conducted.

Compared with buprenorphine, it remains unclear why the proportion of patients taking methadone at the time of index hospitalization was nearly identical between the readmitted and non-readmitted patients at both 30 and 90 days

TABLE 2. Comparison of Index Hospitalization Factors Between Patients Readmitted Within 30 Days and Those Not Readmitted Within 30 Days, and Factors Independently Associated With Readmission Within 30 Days

Index Hospitalization	Readmission Within 30 d (n = 85)	No Readmission Within 30 d (n = 381)	Univariate Logistic Regression		Multivariable Logistic Regression	
			OR (95% CI)	*P*	aOR (95% CI)	*P*
Admission						
Age (yrs), mean ± SD	44.9 ± 11.9	42.5 ± 12.9	1.02 (0.996, 1.03)	0.12		
Male (vs female), n (%)	59 (69.4)	231 (60.6)	1.47 (0.89, 2.44)	0.13		
White (vs other) race, n (%)	79 (92.9)	338 (88.7)	1.68 (0.69, 4.07)	0.26		
Medicaid (vs private) insurance, n (%)	69 (81.2)	320 (84.0)	1.37 (0.74, 2.54)	0.31		
Heroin (vs prescription opioid) use, n (%)	66 (77.7)	298 (78.2)	0.97 (0.55, 1.70)	0.91		
Benzodiazepine use (vs no use), n (%)	9 (10.6)	55 (14.4)	0.70 (0.33, 1.48)	0.35		
Cocaine use (vs no use), n (%)	19 (22.4)	109 (28.6)	0.72 (0.41, 1.25)	0.24		
Buprenorphine use (vs no OAT use), n (%)	11 (12.9)	95 (24.9)	0.45 (0.23, 0.88)	0.02*	0.47 (0.24, 0.93)	0.03
Methadone use (vs no OAT use), n (%)	23 (27.1)	103 (27.0)	1.00 (0.59, 1.70)	0.97		
During hospitalisation						
Admission to ICU, n (%)	8 (9.4)	50 (13.1)	0.69 (0.31, 1.51)	0.35		
Medical admission, n (%)	69 (81.2)	281 (73.8)	1.54 (0.85, 2.77)	0.16		
Buprenorphine use (vs no OAT use), n (%)	12 (14.1)	79 (20.7)	0.63 (0.33, 1.21)	0.17		
Methadone use (vs no OAT use), n (%)	36 (42.4)	155 (40.7)	1.07 (0.67, 1.73)	0.78		
Discharge						
Length of stay, median (IQR)	8.0 (6.0–13.0)	6.0 (4.0–10.0)	1.03 (1.003, 1.05)	0.03*	1.02 (1.01, 1.05)	0.05
Prescribed opioid (vs not), n (%)	47 (55.3)	192 (50.4)	1.22 (0.76, 1.95)	0.41		
Buprenorphine use (vs no OAT use), n (%)	13 (15.3)	83 (21.8)	0.65 (0.34, 1.23)	0.18		
Methadone use (vs no OAT use), n (%)	24 (28.2)	113 (29.7)	0.93 (0.55, 1.57)	0.80		

aOR, adjusted odds ratio; CI, confidence interval; ICU, intensive care unit; IQR, interquartile range; OAT, opioid agonist therapy; OR, odds ratio; SD, standard deviation.
*$P < 0.10$ and variable included in multivariate model.

TABLE 3. Comparison of Index Hospitalization Factors Between Patients Readmitted Within 90 Days and Those Not Readmitted Within 90 Days, and Factors Independently Associated With Readmission Within 90 Days

Index Hospitalization	Readmission Within 90 d (n = 151)	No Readmission Within 90 d (n = 315)	Univariate Logistic Regression		Multivariable Logistic Regression	
			OR (95% CI)	*P*	aOR (95% CI)	*P*
Admission						
Age (yrs), mean ± SD	44.8 ± 12.3	42.1 ± 12.9	1.02 (1.00, 1.03)	0.03	—	—
Male (vs female), n (%)	104 (68.9)	186 (59.0)	1.54 (1.02, 2.32)	0.04	—	—
White (vs other) race, n (%)	138 (91.4)	279 (88.6)	0.73 (0.38, 1.42)	0.36		
Medicaid (vs private) insurance, n (%)	123 (81.5)	266 (84.4)	1.24 (0.74, 2.06)	0.42		
Heroin (vs prescription opioid) use, n (%)	110 (72.8)	254 (80.6)	0.64 (0.41, 1.02)	0.06*	0.59 (0.37, 0.94)	0.03
Benzodiazepine use (vs no use), n (%)	16 (10.6)	48 (15.2)	0.66 (0.36, 1.20)	0.18		
Cocaine use (vs no use), n (%)	41 (27.2)	87 (27.6)	0.98 (0.63, 1.51)	0.92		
Buprenorphine use (vs no OAT use), n (%)	24 (15.9)	82 (26.0)	0.54 (0.33, 0.89)	0.02*	0.57 (0.34, 0.96)	0.03
Methadone use (vs no OAT use), n (%)	40 (26.5)	87 (27.6)	0.96 (0.62, 1.49)	0.85		
During hospitalization						
Admission to ICU, n (%)	15 (9.9)	43 (13.7)	1.43 (0.77, 2.67)	0.26		
Medical admission, n (%)	125 (82.8)	225 (71.4)	1.92 (1.18, 3.13)	0.009*	1.97 (1.20, 3.25)	0.007
Buprenorphine use (vs no OAT use), n (%)	32 (21.2)	60 (19.0)	0.91 (0.56, 1.49)	0.71		
Methadone use (vs no OAT use), n (%)	61 (40.4)	131 (41.6)	1.00 (0.68, 1.49)	0.98		
Discharge						
Length of stay, median (IQR)	8.0 (5.0–13.0)	5.0 (4.0–9.0)	1.03 (1.01, 1.06)	0.005*	1.04 (1.01, 1.06)	0.003
Prescribed opioid (vs no opioid), n (%)	84 (55.6)	155 (49.2)	1.30 (0.88, 1.91)	0.95		
Buprenorphine use (vs no OAT use), n (%)	28 (18.5)	68 (31.6)	0.83 (0.51, 1.35)	0.45		
Methadone use (vs no OAT use), n (%)	44 (29.1)	93 (29.5)	0.98 (0.64, 1.91)	0.92		

aOR, adjusted odds ratio; ICU, intensive care unit; IQR, interquartile range; OAT, opioid agonist therapy; OR, odds ratio; SD, standard deviation.
*$P < 0.10$ and variable included in multivariate model.

after index hospitalization discharge. Unfortunately, the reason for methadone use (ie, as OAT versus analgesia) before index hospitalization was rarely reported in the medical record. However, the fact that the proportion of patients taking methadone (n = 127) at the time of index hospitalization at a twice-daily frequency or more (a frequency associated with analgesia vs OAT use) was low (25/127, 19.8%), and similar between the 90-day readmitted (6.0%) and non-readmitted (5.0%) patients, suggests use of methadone for pain (vs as OAT) in our cohort was uncommon. Moreover, the daily (median [interquartile range] mg) reported methadone dose at the time of index hospitalization admission was relatively high (85 [55, 110] mg), also suggesting most methadone use was for OAT (and not chronic pain) (Alford et al., 2006). With practice models for methadone and buprenorphine administration being different, the patients who were administered methadone may have underlying risks for readmission that could not be accounted for in a retrospective study such as ours (Pinto et al., 2010).

We found that heroin use was inversely related to 90-day readmission rate, which may be due to the barriers to healthcare access for this patient population. Patients who use heroin may be less likely to seek treatment, which may include buprenorphine initiation, due to the greater stigma associated with heroin compared with prescription opioid addiction. Additionally, because the emergence of fentanyl and even more potent opioids, patients who use heroin are at higher risk of overdose death than those who use prescription opioids (Sordo et al., 2017). Given that patients who died outside of the MGH system were not captured in our analysis, it is possible that the lower readmission rates found for patients with a history of heroin use is due to greater out of hospital mortality.

Our analysis has additional potential limitations. There may be variables associated with hospital readmission that we did not consider. Readmission rates and predictors for readmission may be different among patients with OUD who are hospitalized and never receive an opioid, patients admitted to a community hospital, patients from different regions in the USA, or patients with characteristics different from those in our cohort. All data were collected retrospectively, thereby limiting our ability to attribute causal relationships between the identified predictors, particularly admission buprenorphine use, and hospital readmissions. There may also be reasons for hospital readmission which were not documented in the medical record. We were not able to collect data on what happened to patients between hospital discharge and readmission other than what was documented in the hospital readmission record. While we considered several clinically relevant factors with the potential to affect hospital readmission, others may have gone unmeasured. This was particularly evident in our inability to capture readmissions to outside hospitals. Had this been possible, we suspect readmission rates would have been higher. Index hospitalization opioid dose and/or potency used may have also influenced readmission rates; however, this analysis was outside of the scope of the present study and should be considered during future research efforts.

Opioid policy changes during the course of the study may have resulted in increased screening and modified treatment of patients with OUD. Although patients had to have an OUD diagnosis for more than 6 months to be included, the retrospective nature of the study precluded prospective screening of subjects to determine that OUD remained an active condition. As discussed, we were unable to completely discern whether methadone was being used to treat pain (vs

OUD), thus limiting our ability to make any interpretations about the similar readmission rates between patients receiving methadone at discharge versus those who did not. Finally, we did not evaluate OAT dose as a variable that could impact readmission rate.

Additional research areas include cost analyses of outcomes of this study, the relationship between admitting service and readmission rates, the association between in-hospital non-OAT opioid usage and hospital length of stay, predictors for emergency department visits, the readmission predictors for patients with OUD admitted due to an OUD-related condition (eg, overdose) versus a non-OUD-related medical or surgical cause, and the evolution of prescribing patterns within the rapidly changing landscape of pain and OUD treatment.

In summary, 30-day and 90-day readmission rates for patients with OUD are high and comparable with those observed in populations that are older, sicker, and have more chronic conditions. Use of buprenorphine appears to be associated with a reduction in hospital readmission in patients with OUD, yet nearly 80% of the patients in our cohort were not administered this therapy. While the epidemic of opioid addiction and overdose continues to cause devastating outcomes throughout the country, only a minority of patients suffering from OUD have adequate access to effective OAT. Future prospective, controlled research is required to characterize the impact of initiating buprenorphine treatment before hospital discharge on hospital readmission among patients with OUD.

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