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Short communication

Methadone treatment and patient-directed hospital discharges among patients with opioid use disorder: Observations from general medicine services at an urban, safety-net hospital

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ABSTRACT

Introduction: People with opioid use disorder (OUD) have high rates of discharge against medical advice from the hospital. Interventions for addressing these patient-directed discharges (PDDs) are lacking. We sought to explore the impact of methadone treatment for OUD on PDD.

Methods: Using electronic record and billing data from an urban safety-net hospital, we retrospectively examined the first hospitalization on a general medicine service for adults with OUD from January 2016 through June 2018. Associations with PDD compared to planned discharge were examined using multivariable logistic regression. Administration patterns of maintenance therapy versus new in-hospital initiation of methadone were examined using bivariate tests.

Results: During the study time period, 1,195 patients with OUD were hospitalized. 60.6% of patients received medication for OUD, of which 92.8% was methadone. Patients who received no treatment for OUD had a 19.1% PDD rate while patients initiated on methadone in-hospital had a 20.5% PDD rate and patients on maintenance methadone during the hospitalization had a 8.6% PDD rate. In multivariable logistic regression, methadone maintenance was associated with lower odds of PDD compared to no treatment (aOR 0.53, 95% CI 0.34–0.81), while methadone initiation was not (aOR 0.89, 95% CI 0.56–1.39). About 60% of patients initiated on methadone received 30 mg or less per day.

Conclusions: In this study sample, maintenance methadone was associated with nearly a 50% reduction in the odds of PDD. More research is needed to assess the impact of higher hospital methadone initiation dosing on PDD and if there is an optimal protective dose.

1. Introduction

Discharge against medical advice (AMA) is a pressing hospital system quality and safety concern due to associations with higher rates of readmission, post-discharge mortality and healthcare costs (Choi et al., 2011; Yong et al., 2013; Glasgow et al., 2010). People who use drugs are more likely to discharge AMA (Choi et al., 2011; Merchant et al., 2020) and the rates of hospitalizations in this population have been increasing in the context of the current drug epidemic (Huhn et al., 2018; Ronan and Herzig, 2016; Weiss et al., 2016; Suen et al., 2021). The label "AMA discharge" can be stigmatizing, so here we use the terms patient-directed discharge (PDD) and self-discharge to describe the situation when a patient discharges from the hospital prior to the recommendation of the treating medical team (Eaton et al., 2020).

The hospital setting has been described as a "risk environment" for people who use drugs due to social-structural forces that enact negative biases in the provision of healthcare and leave patients vulnerable to undertreatment and harm (McNeil et al., 2014). People with opioid use disorder (OUD) who have self-discharged from the hospital have indicated that stigma from medical staff, inadequate treatment of pain and untreated opioid withdrawal symptoms were drivers for leaving (McNeil et al., 2014; Simon et al., 2019; Ling et al., 2021).

Some hospitals in the United States now offer inpatient addiction evaluation and treatment in order to address substance use disorders (SUD) in the hospital setting, provide SUD medication treatment, and link patients to ongoing care (Englander et al., 2019;

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Weimer et al., 2019). Inpatient initiation of medication for opioid use disorder (MOUD) has been shown to increase linkage to outpatient SUD care and, in some studies, reduce the rate of hospital readmission, but little is known about the relationship between hospital MOUD use and hospital discharge type (Barocas et al., 2020; Englander et al., 2019; Trowbridge et al., 2017).

The goal of this retrospective study was to assess associations with hospital methadone use and PDD. We hypothesized that patients who were maintained or initiated on methadone in-hospital would be less likely to self-discharge, compared to patients who received no MOUD, because opioid withdrawal symptoms and cravings would be better controlled.

2. Methods

2.1. Setting, study population, demographics and index admission measures

The setting, study population, identification of hospitalizations, demographic and index admission measures are described in a previous article based on the same dataset (Tierney et al., 2021). To summarize, the setting is an urban, academic county hospital prior to the implementation of an addiction consultation service. Details around provider training on MOUD are described elsewhere (Tierney et al., 2021). There were no formal inpatient protocols for methadone until the end of the study time period. There is a methadone clinic on the same campus as the hospital that provided rapid follow-up for discharged patients. Enrollment in an outpatient opioid treatment program was not required for initiation or titration of methadone in the hospital. In this community, heroin was more predominant than fentanyl for most of the study time period (Coffin and Rowe, 2020; Kral et al., 2021).

Data were collected from an electronic medical record using ICD-10 codes, with a subset of records reviewed manually to confirm an OUD diagnosis. We examined the first hospitalization with an OUD-related diagnosis from January 1st, 2016 to June 30th, 2018 for all non-pregnant, adult patients admitted to the family medicine and internal medicine inpatient services for any primary medical problem. Demographic and clinical data such as MOUD use, discharge diagnosis, and length of stay were captured for this index hospital encounter. Since the number of patients who received buprenorphine was small, and methadone and buprenorphine have unique clinical considerations in their use (e.g. duration of titration to therapeutic dose), we excluded patients who received buprenorphine and focused the analysis on methadone only. A severity of illness score was assigned to each hospitalization at our institution for billing purposes. The score is on a scale of 1 to 4, with 4 being the most severe (Horn et al., 1984), and was determined by examining the medical record after discharge.

The discharge types in our electronic medical record were organized into the following categories: regular outpatient, AMA, absent without leave (AWOL), transferred to another facility or service, death in the hospital, and forensic facility. PDD included patients with AMA and AWOL discharges. Planned discharges were all other discharge types excluding death and forensic facility. All patients who died in the hospital, or who were incarcerated during their hospitalization were excluded because these patient groups did not have the same ability as others to self-discharge or to be followed to the discharge outcome.

2.2. Methadone treatment measures

Maintenance methadone versus in-hospital methadone initiation was classified using pharmacy records and manual chart review when pharmacy records were missing or unclear. Last methadone dose was confirmed with the opioid treatment program by the treating team. In this study, a patient was considered newly initiated if they had been off treatment for at least 7-days prior to their hospitalization. This time frame was chosen based on clinical experience in the hospital and confirmed with a chart review of a subset of records that found patients who were off methadone beyond the 7-day time frame were commonly re-initiated at starting doses and titrated back up to therapeutic doses. Methadone dosing for each hospital day was captured so that maximal dose reached during hospital stay, time to first dose, and percentage of hospital days on methadone could be assessed.

2.3. Analysis

Associations between baseline demographic and clinical descriptors and the odds of PDD were examined using univariate and multivariable logistic regression models. Covariates were selected based on previously published associations with PDD (Yong et al., 2013; Franks et al., 2006; Ling et al., 2018; Pytell and Rastegar, 2018; Tawk and Dutton, 2015). Descriptive statistics and Wilcoxon rank sum tests were used to compare methadone-related measures between those on maintenance versus hospital initiated methadone. Logistic regression was also used to assess the association between methadone dose and PDD among patients initiated in-hospital, adjusting for length of stay. Maximal methadone dose was treated as a continuous variable with 5 mg dose increments. Statistics were performed using RStudio version 1.4.1717.

2.4. Ethics statement

Approval was granted by the University of California, San Francisco Institutional Review Board (IRB #18–25,148). Patient consent was not required.

3. Results

Our sample included 1195 unique patient hospitalizations involving an OUD diagnosis who met inclusion criteria based on age, pregnancy status, incarceration, and in-hospital death. After excluding 52 patients who received buprenorphine there were 1143 patients in the sample, of whom 15% had a PDD (Supplemental Figure 1). Demographic and clinical measures are reported in Table 1. Patients in the study sample were predominantly male, English speaking, and had Medicaid insurance; the majority had a co-occurring cocaine or stimulant use disorder. The most common primary discharge diagnoses were skin and soft tissue infections (22.0%), sepsis and bacteremia (13.5%), pulmonary disease (7.5%), and opioid-related (4.5%).

About three-fifths (58.8%) of patients received methadone while inpatient; 30.5% were initiated during the admission and the remainder were continued on outpatient maintenance therapy. One fifth (19.1%) of patients who did not receive MOUD had a PDD, 20.5% of patients who were initiated on methadone had a PDD, and 8.6% of patients maintained on outpatient methadone treatment during the hospitalization had a PDD (p <0.001).

In the multivariable regression analysis, older age (aOR 0.98, 95% CI 0.96–0.99; one year increase), higher severity of illness score (aOR 0.79, 95% CI 0.64–0.98; one point increase on 1–4 scale) and the presence of an anxiety disorder (aOR 0.57, 95% CI 0.37–0.88) were associated with a decreased odds of PDD. White non-Hispanic identity was associated with an increased odds of PDD compared to other racial groups. Patients on maintenance methadone had a decreased odds of PDD compared to those who received no treatment in the hospital (aOR 0.53, 95% CI 0.34–0.81) while patients initiated on methadone did not (aOR 0.89, 95% CI 0.56–1.39) (Table 1).

Methadone administration patterns are described in Table 2. Patients initiated on methadone received medication on a slightly smaller portion of hospital days compared to patients on maintenance methadone (74.2% vs. 79.2%, $p = 0.049$). Mean maximal doses of methadone were lower among patients newly started on methadone compared to maintenance therapy (32.9 mg vs. 80.5 mg, p<0.001). In logistic regression analysis of patients initiated on methadone, there were decreased odds of PDD with higher maximal methadone doses (aOR 0.91, 95% CI 0.80–

Table 1
Patient characteristics and hospitalization measures associated with patient-directed discharge.

Variable	Total Sample (n = 1143)	PDD Discharge (n = 172)	Planned discharge (n = 971)	Univariable Logistic Regression OR (95% CI)	Multivariable Logistic Regression aOR (95% CI)
Age, mean (SD), years*	48.6 (13.2)	42.6 (12.7)	49.6 (13.0)	0.96 (0.95–0.97)	0.98 (0.96–0.99)
Male sex	801 (70.1)	128 (74.4)	673 (69.3)	1.29 (0.90–1.88)	1.13 (0.77–1.70)
Race / Ethnicity					
White, non-Hispanic	561 (49.1)	107 (62.2)	454 (46.8)	REF	REF
Black, non-Hispanic	362 (31.7)	41 (23.8)	321 (33.1)	0.54 (0.37–0.79)	0.61 (0.39–0.94)
Hispanic	140 (12.2)	17 (9.9)	123 (12.7)	0.59 (0.33–0.99)	0.58 (0.32–1.02)
Other / Unknown	80 (7.0)	7 (4.1)	73 (7.5)	0.41 (0.17–0.85)	0.44 (0.18–0.96)
English as primary language**	1101 (96.3)	167 (97.1)	934 (96.2)	1.32 (0.56–3.89)	–
Insurance type					
Medicaid	863 (75.5)	141 (82.0)	722 (74.4)	REF	REF
Medicare	224 (19.6)	15 (8.7)	209 (21.5)	0.37 (0.20–0.62)	0.56 (0.29–1.02)
Other	56 (4.9)	16 (9.3)	40 (4.1)	2.05 (1.09–3.69)	1.37 (0.69–2.60)
Homelessness, n = 1135***	538 (47.4)	92 (53.8)	446 (46.3)	1.35 (0.98–1.88)	0.98 (0.68–1.42)
Co-occurring disorders					
Cocaine or other stimulant use	735 (64.3)	122 (71.0)	613 (63.1)	1.42 (1.01–2.04)	1.15 (0.79–1.71)
Alcohol use	392 (34.3)	50 (29.1)	342 (35.2)	0.75 (0.53–1.07)	0.91 (0.61–1.34)
Psychotic disorder	214 (18.7)	32 (18.6)	182 (18.7)	0.99 (0.64–1.49)	1.26 (0.78–1.99)
Anxiety disorder	412 (36.0)	44 (25.6)	368 (37.9)	0.56 (0.39–0.81)	0.57 (0.37–0.88)
Mood disorder	487 (42.6)	59 (34.3)	428 (44.1)	0.66 (0.47–0.93)	0.91 (0.61–1.36)
Severity of Illness Score, mean (SD), scale 1–4*, n = 1123***	2.4 (0.8)	2.1 (0.8)	2.4 (0.8)	0.65 (0.53–0.80)	0.79 (0.64–0.98)
OUD Treatment Status					
No MOUD	471 (41.2)	90 (52.3)	381 (39.2)	REF	REF
Methadone maintenance	467 (40.9)	40 (23.3)	427 (44.0)	0.40 (0.26–0.59)	0.53 (0.34–0.81)
New methadone initiation	205 (17.9)	42 (24.4)	163 (16.8)	1.09 (0.72–1.63)	0.89 (0.56–1.39)
Length of hospital stay, median (IQR), days**	4 (3-7)	3 (2-4)	4 (3-8)	0.89 (0.84–0.93)	-

All values are reported as n (%) unless otherwise indicated.
* The odds ratio is associated with a one unit increase in the variable. For severity of illness, a score of 1 is least severe and 4 is most severe.
**Language was omitted from the multivariable model since majority spoke English. Length of stay was not entered into the model because it is in part determined by the outcome of interest.
*** There was missing data for housing status and the severity of illness score. Sample size for these measures are indicated in table.
Abbreviations: PDD = patient directed discharge; IQR = interquartile range; SD = standard deviation; OUD = opioid use disorder; MOUD = medication for opioid use disorder.

Table 2
Patterns of inpatient methadone administration for opioid use disorder by engagement status.

	Total	In-Hospital Initiation	Maintenance	Bivariate P-Value
Methadone, n	672	205	467	–
PDD, n (%)	82 (12.2)	42 (20.5)	40 (8.6)	<0.001*
Time to first dose, mean (SD), days	2.0 (1.7)	2.2 (2.5)	1.9 (1.1)	0.945
Percent of hospital days methadone was received, mean% (SD)	77.7 (21.6)	74.2 (24.5)	79.2 (20.1)	0.049
Dose, mean (SD), mg	66.0 (43.2)	32.9 (17.1)	80.5 (43.1)	<0.001
Maximal daily dose while hospitalized**				
30 mg or less, n (%)	187 (27.8)	125 (61.0)	62 (13.3)	–
31–60 mg, n (%)	189 (28.1)	68 (33.2)	121 (25.9)	–
61–90 mg, n (%)	131 (19.5)	12 (5.9)	119 (25.5)	–
91 mg or more, n (%)	165 (24.6)	0 (0.0)	165 (35.3)	–

Abbreviations: PDD = patient directed discharge; SD = standard deviation.
*Statistical test for this comparison was a chi-square test while other comparisons in this table were assessed with a Wilcoxon Rank Sum Test.
**The medication dose used for comparisons in this table was the highest dose reached on any one day during the hospitalization.

1.03; 5 mg dose increments), after adjusting for length of stay, but this did not reach statistical significance.

4. Discussion

This study contributes to the existing literature by analyzing a large cohort of patients with OUD admitted to general medicine services in a safety-net hospital, with high rates of PDD and methadone use. In this single-site study, fifteen percent of patient hospitalizations with an OUD diagnosis had a PDD, similar to previously reported rates of PDD among patients with OUD (Merchant et al., 2020; Santos et al., 2020; Stranges et al., 2009; Ti and Ti, 2015). Approximately sixty percent of patients received methadone in-hospital and those who were initiated in-hospital primarily received low doses. Our hypothesis that in-hospital methadone would reduce PDDs compared to no MOUD treatment was true only for patients on maintenance methadone.

Maintenance methadone was associated with a decreased odds of PDD while starting methadone in-hospital was not, consistent with two studies of hospitalized patients with infective endocarditis or osteomyelitis who received MOUD (Suzuki et al., 2020; Jo et al., 2021). Two other studies, one of hospitalized patients with serious infections (Nolan et al., 2020) and another of patients admitted to an HIV ward (Chan et al., 2004), found reduced odds of PDD with in-hospital MOUD use, but neither study distinguished between maintenance and hospital initiation of MOUD.

The patient group on maintenance methadone may not have experienced withdrawal symptoms or cravings because they received a therapeutic dose of medication and therefore were less likely to have a PDD. This group has also already engaged in ongoing medical care, which may have contributed to their ability to navigate inpatient medical care and increased the likelihood they would remain hospitalized for treatment. Previous studies have shown that hospitalizations are a "reachable moment" to start MOUD and connect patients to ongoing care (Englander et al., 2019; Trowbridge et al., 2017; Velez et al., 2017). More research is needed to determine if this practice could reduce PDD in subsequent hospitalizations among patients who are not on MOUD at the time of admission.

Several factors may contribute to the unchanged rates of PDD among patients who were initiated on methadone compared to those who received no MOUD. There could be unmeasured confounding, such as OUD severity, that changes the association we found. Dosing may also play a role. Methadone doses must be started low and slowly titrated to avoid oversedation; therefore, it can take weeks to reach therapeutic doses (Baxter et al., 2013). In this sample, most patients initiated on methadone received low doses, raising concern about undertreatment as a driver of PDD. Higher methadone dosing did not have a statistically significant association with lower odds of PDD, but a prior study found both lower doses and fewer administrations of methadone were associated with PDD (Santos et al., 2020), suggesting that adequate dosing could be an important factor in preventing PDD. Higher doses of methadone have been shown to improve retention in the outpatient setting, but the dose needed to help improve retention in the hospital setting remains unknown. Future studies should consider examining the potential benefits of rapid titration of methadone and use of buprenorphine rather than methadone because it can be titrated to a therapeutic dose over a short period of time (Noska et al., 2015; Hemmons et al., 2019). These approaches may be of particular importance today given that many patients have higher tolerances due to the current predominance of fentanyl in the drug supply.

Methadone treatment does not address many other drivers of PDD such as childcare responsibilities, making outpatient appointments, financial concerns, hospital restrictions, mistreatment, and undertreatment of other conditions (Ling et al., 2021; Summers et al., 2018). Understanding factors associated with PDD may help hospitals and providers better align care with patient goals and facilitate the use of shared decision making to avoid labeling discharges as "against medical advice" to begin with (Alfandre et al., 2017). Additional interventions, including stigma reduction, harm reduction strategies (Dong et al., 2020; Sharma et al., 2017; Ti et al., 2015) and inpatient addiction medicine specialty care, may be required to reduce PDD, especially among patients not on MOUD in the community.

Similar to the findings of previous studies, we found that younger age was associated with higher odds of PDD (Yong et al., 2013; Pytell and Rastegar, 2018; Alfandre, 2009). However, contrary to previous studies, we did not find male sex, being a member of a racial or ethnic minority group, or psychiatric disorders, with the exception of anxiety disorder, to be associated with PDD (Yong et al., 2013; Franks et al., 2006; Ling et al., 2018; Pytell and Rastegar, 2018; Tawk and Dutton, 2015). Our findings are not intended to flag certain patient characteristics as potential drivers of PDD, but instead to help us reflect on how hospital care may not be best serving individuals with certain identities, conditions, or social circumstances.

4.1. Limitations

This was a single site study in an urban, safety-net hospital with no addiction consultation service at the time; the results may not be generalizable to other hospitals. The study was not designed to assess for a causal relationship between MOUD and discharge type. Therefore, the described relationships represent associations and not true cause-and-effect. Patients in the MOUD treatment groups likely have unmeasured, underlying differences making the comparison groups not exchangeable. We did not capture patient reasons for PDD, pain, or Clinical Opioid Withdrawal Scale assessments, OUD severity or stability; nor did we capture the use of other opioids used during the hospital stay, which could have relevance for MOUD dosing and discharge type. This sample of patients was identified using ICD-10 billing codes, which are intended for administrative purposes and do not capture all clinical data (Lagisetty et al., 2021; Rowe et al., 2021). As a result, the number of the patients with OUD in our sample could be inaccurate, especially for those who did not receive MOUD or had mild use disorder. We were unable to distinguish between patients who received methadone for detox purposes only and those who had intention of continuing maintenance therapy post-discharge.

4.2. Conclusions

In this sample of hospitalized patients with OUD, PDD was common. Patients on maintenance methadone were less likely to have a PDD than those not on MOUD. We did not find an association between low-dose methadone initiation in-hospital and PDD, highlighting a need for additional research and more nuanced strategies for addressing PDD.

Contributions

Conception or design of the work: Tierney, Rowe, Coffa, Coffin, Snyder.

Data collection: Tierney, Rowe.

Data analysis: Sarnaik.

Data interpretation: Tierney, Rowe, Sarnaik, Coffa, Coffin, Snyder.

Drafting the article: Tierney.

Editing and critical revision of the article: Tierney, Rowe, Sarnaik, Coffa, Coffin, Snyder.

Final approval of the version to be published: Tierney, Rowe, Sarnaik, Coffa, Coffin, Snyder.

Project supervision: Snyder.

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Declaration of Competing Interest

No conflicts declared.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.dadr.2022.100066.

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