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Sociodemographic and prescribing characteristics that impact long-term retention in buprenorphine treatment for opioid use disorder among a statewide population

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Abstract

Background and Aims: Partial opioid agonist medications for opioid use disorder reduce mortality and morbidity, however long-term retention in treatment is challenging. The objective of this study was to identify patient and prescription characteristics associated with long-term buprenorphine treatment retention.

Methods: We used data from the Rhode Island prescription drug monitoring program to identify residents who initiated buprenorphine treatment and determine if they were retained in long-term buprenorphine treatment 12-months after treatment initiation. Multivariable logistic regression models were used to identify sociodemographic and prescription characteristics associated with long-term buprenorphine retention.

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CRediT authorship contribution statement

Authors contributed to the manuscript (MS) in the following manner. Study concept: BDH, LCC, EAS, FLB, JM, CO. Study design: BDH, LCC, EAS, FLB. Data analysis: BDH. Interpretation of results: BDH, LCC, EAS, FLB. Drafting of the MS: BDH, LCC, EAS, FLB. Critical revision of the MS: BDH, LCC, EAS, JB, JM, AN, CO, FLB.

Conflicts of interest

All authors declare that they have no conflicts of interest.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.drugalcdep.2022.109680.

Findings: During the study period 4898 unique Rhode Island residents initiated buprenorphine treatment, of whom 37.8 % were retained in treatment at 12-months. Demographic factors associated with a higher odds of long-term buprenorphine retention included older age, female sex, Medicaid insurance (vs private), and living closer to the pharmacy where the prescription was filled. Individuals who were prescribed the tablet formulation (aOR: 0.82 [95 % CI 0.72, 0.93]) or received a non-buprenorphine opioid during the follow-up window (aOR: 37 [95 % CI 0.31, 0.44]) had lower odds of long-term treatment at 12-months. Individuals who received at least one day of overlapping benzodiazepine and buprenorphine prescriptions (aOR: 2.00 [95 % CI 1.70, 2.34]) and those given a longer days supply (aOR: 1.26 [95 % CI 1.01, 1.56]) had higher odds of long-term treatment at 12-months. Findings were similar for treatment retention at 6-months in sensitivity analyses.

Conclusions: These findings highlight several modifiable prescribing practices associated with long-term buprenorphine retention, suggesting that clinicians and public health practitioners can help remove barriers to long-term retention.

Keywords

Buprenorphine; Opioid use disorder; Opioid; Retention; Healthcare; Prescription drug monitoring

1. Introduction

In 2020, an estimated 2.7 million individuals in the United States were living with opioid use disorder (OUD); however, only 278,000 (10%) had received medications for opioid use disorder (MOUD) in the prior 12 months (Center for Behavioral Health Statistics and Quality, 2021). MOUD reduces the risk of fatal and non-fatal drug overdose, helps individuals abstain from or reduce their illicit opioid use, and lowers healthcare utilization and costs. These benefits are often greatest when individuals are retained in long-term treatment (Sordo et al., 2017; Ronquest et al., 2018; Ruetsch et al., 2017; Biondi et al., 2022; Shcherbakova et al., 2018; Chang et al., 2019; Kinsky et al., 2019).

Long-term retention in treatment is challenging, and discontinuation of MOUD is common. Discontinuation of buprenorphine treatment can exceed 50% within weeks to months of initiation (Biondi et al., 2022; Shcherbakova et al., 2018; Hser et al., 2014; Morgan et al., 2018; Saloner et al., 2017; Pizzicato et al., 2020). Numerous factors may contribute to treatment discontinuation, including co-morbidities, copays, prior authorization requirements, prescriber characteristics, and other social and structural barriers (Ronquest et al., 2018; Saloner et al., 2017; Pizzicato et al., 2020).

As opioid overdose fatalities continue to rise, a nuanced understanding of the factors that impact treatment retention could inform interventions to improve long-term treatment retention and subsequent health outcomes. While prior studies have evaluated factors associated with long-term buprenorphine retention, these analyses were generally limited to specific sub-populations (e.g., Medicaid population) or occurred in the pre-fentanyl era (Pizzicato et al., 2020). The objective of this study was to identify patient and prescription characteristics associated with long-term buprenorphine retention among a

statewide population using the most up-to-date Prescription Drug Monitoring Program (PDMP) data available.

2. Methods

2.1. Data sources and study design

We conducted a retrospective cohort study of Rhode Island (RI) residents who initiated buprenorphine treatment between July 1, 2017, and June 30, 2020 utilizing buprenorphine prescription data from the RI-PDMP between July 1, 2016 and June 30, 2021. The RI-PDMP receives data on all controlled prescriptions dispensed by community pharmacies in RI, as well as all controlled prescriptions dispensed to RI residents in surrounding states (34 of 50 states currently report to RI).

Initiation was defined as the date an individual first filled a buprenorphine prescription after a period of ≥ 12 months without filling any buprenorphine prescriptions. Due to the focus on buprenorphine treatment for OUD, buprenorphine products primarily used for pain management were excluded including name brand and generic formulations of: Butrans™ (Purdue Pharma, CT), Belbuca™ (Titan Pharmaceuticals, Inc., CA), and Buprenex™ (Reckitt Benckiser, NJ). Included buprenorphine products are listed in Supplemental Table 1.

2.2. Key measures

The primary outcome was retention in buprenorphine treatment over the 12-months following initiation, defined as a medication possession ratio ≥ 80% during the follow-up period (Pizzicato et al., 2020). Sensitivity analyses were also performed using a follow-up period of 6-months. The medication possession ratio was calculated by adding the total days supply of medication dispensed during the follow-up period and dividing by the number of days in the follow-up period.

Additional covariates included: 1) patient sociodemographic characteristics obtained from their initial buprenorphine prescription, including age, sex, insurance coverage, year of treatment initiation, and the distance from their home to the pharmacy (based on ZIP Code centroids); 2) initial buprenorphine prescription characteristics, including the buprenorphine formulation, daily dose, and days' supply dispensed; and 3) other prescribing characteristics obtained from prescriptions filled during the follow-up period, including the first stable dose of buprenorphine (defined as the first dose an individual received for 7 continuous days), receipt of overlapping benzodiazepine and buprenorphine prescriptions (defined as any overlapping days' supply during follow-up) (Rose et al., 2018), and receipt of an opioid prescription other than buprenorphine during follow-up. Highly skewed continuous variables (distance from home to pharmacy, days' supply, and daily dose) were collapsed into clinically meaningful categories prior to analysis.

2.3. Statistical Methods

Descriptive and inferential statistics were performed using SAS 9.4 (Cary, North Carolina). Patient and prescription characteristics between those with and without long-term buprenorphine retention were compared using chi-square tests. Bivariate associations

are presented with unadjusted odds ratios (ORs) and 95% confidence intervals (CIs). A multivariable logistic regression model was used to identify characteristics independently associated with treatment retention. No variables were forced into the multivariable model based on a priori assumptions given the exploratory nature of this analysis. Rather, all variables with significant bivariate associations were included in the final multivariable model. Multicollinearity was assessed by evaluating the correlation between covariates. Model fit was verified using the Hosmer and Lemeshow test. This study was deemed exempt by the Intuitional Review Board of the Rhode Island Department of Health.

3. Results

During the study period, 4898 unique RI-residents initiated buprenorphine treatment, of whom 45% continued treatment for ≥ 6 months (Supplemental Table 2) and 38% continued treatment for ≥ 12 months (Table 1). Most patients were male (61%), aged 25–44 years (56%), and covered through private insurance (46%) or Medicaid (35%). Based on their initial buprenorphine prescription, 42% of patients lived in the same ZIP Code as their pharmacy, 31% lived < 5 miles away, and 28% lived ≥ 5 miles away. Most individuals were initially dispensed a film buprenorphine formulation (59%). The initial days' supply dispensed varied, with 61% of patients receiving medication to cover ≤ 7 days, 30% receiving medication to cover 8–29 days, and 9% receiving medication to cover ≥ 30 days. Additionally, 14% of individuals were started on a daily dose < 8 mg, 26% between 8 and < 16 mg, 51% between 16 and < 24 mg, and 10% received a daily dose ≥ 24 mg. During the 12-month follow-up period, 18% of individuals were dispensed at least one benzodiazepine prescription that overlapped with a buprenorphine prescription, and 17% of individuals were dispensed one or more other opioid prescriptions. In bivariate analyses, individuals with and without long-term buprenorphine retention differed by age, sex, insurance coverage, distance to pharmacy, initial buprenorphine formulation and days' supply, receipt of overlapping benzodiazepine and buprenorphine prescriptions, and receipt of any other opioid during follow-up.

In multivariable analyses, select characteristics of the patient, initial buprenorphine prescription, and other prescribing practices during follow-up were associated with 12-month treatment retention (Table 2). Specifically, individuals who were older, female, had Medicaid insurance (versus private insurance), and lived closer to their pharmacy had higher odds of treatment retention. Individuals who initially received the tablet formulation had lower odds of treatment retention compared to those receiving the film formulation (adjusted OR [aOR]: 0.82; 95% CI: 0.72, 0.93). Individuals dispensed any other opioid prescription during follow-up also had lower odds of treatment retention compared to those who did not (aOR: 0.37; 95% CI: 0.31, 0.44). Individuals dispensed overlapping benzodiazepine and buprenorphine prescriptions during follow-up (aOR: 1.99; 95% CI: 1.71, 2.34) and individuals given a days supply of 30 days or greater had higher odds of retention than those started on a days' supply of seven days or less.

Findings were generally similar in sensitivity analyses of 6-month treatment retention (Supplemental Table 2 and 3). However, in the final multivariable model, year of treatment initiation was also significantly associated with 6-month retention.

4. Discussion

In this population-based, retrospective cohort study, over one-third (38%) of patients newly initiating buprenorphine treatment for OUD remained engaged in treatment for at least 12-months. Older age, female sex, having Medicaid insurance, residing close to the pharmacy where they filled their prescription, initially receiving film buprenorphine formulation, receiving a longer days' supply, and not receiving any other opioid prescriptions in the 12 months after initiating buprenorphine treatment were associated with long-term retention. Importantly, buprenorphine formulation, days' supply, pharmacy distance, and co-prescribing practices are modifiable, suggesting that clinicians and public health practitioners can help remove barriers to long-term retention.

Specific prescribing practices may improve long-term treatment retention. Aligning with prior work, individuals dispensed a film formulation of buprenorphine had higher treatment retention when compared to individuals who received tablets, suggesting that film formulations should be considered first line (Pizzicato et al., 2020; Clay et al., 2014). This study also suggests that facilitating easy access to medications is critical for improving treatment retention. To help remove access barriers for patients, it is imperative for providers to work with patients to provide a longer days' supply and identify preferred pharmacies and promote access to mail-order buprenorphine and/or telemedicine for individuals with transportation barriers when possible (Barnett et al., 2021; Wang et al., 2021).

In this cohort, approximately 1 in 6 patients were provided an opioid prescription in the 12 months after starting buprenorphine treatment for OUD, and results suggest that this negatively impacted treatment retention. This finding again highlights the complexity of treating acute and/or chronic pain episodes among individuals in treatment for OUD (Pizzicato et al., 2020). Additional research and practice improvement is needed to successfully manage concomitant pain among patients with OUD while supporting continued treatment engagement.

In contrast to prescription opioids, individuals who were co-prescribed buprenorphine and benzodiazepines had higher treatment retention when compared to individuals who were not. This unexpected finding should be interpreted cautiously but does question the practice of discontinuing previously prescribed benzodiazepines when initiation to buprenorphine treatment. In 2016, the Food and Drug Administration issued a black box warning against co-prescribing any opioid and benzodiazepines due to increased fatal and non-fatal overdose risk, which continues to be supported with recent work (Weinstein et al., 2017). This warning has led providers to not initiate buprenorphine treatment among patients on benzodiazepines or work with patients to taper down and off benzodiazepines prior to initiating buprenorphine treatment. This practice is evident in prior work which has shown lower buprenorphine retention rates among individuals dispensed benzodiazepine prescriptions (Pizzicato et al., 2020). However, recent work has found that while individuals co-prescribed buprenorphine and benzodiazepines had higher overdose risk than those on buprenorphine alone, these individuals still had a net lower risk when compared to individuals taking benzodiazepines in the absence of buprenorphine (Xu et al., 2021). In review of quality data from 2018 to 2020 in Rhode Island, 905 opioid overdose deaths

occurred among Rhode Island residents, however, < 5 occurred among individuals with an active buprenorphine and benzodiazepine prescription at the time of death. During this period, around 7500 Rhode Island residents were taking buprenorphine each year, of whom about 1800 (~25%) were co-prescribed benzodiazepines. Future work is needed to examine the risks and benefits of co-prescribing of MOUD and benzodiazepines.

Although study methods and measures vary, the 6- and 12-month long-term buprenorphine retention rates in our study (45% and 38%, respectively) generally align with previous work (Ronquest et al., 2018; Ruetsch et al., 2017; Kinsky et al., 2019; Pizzicato et al., 2020). Additionally, prior studies also found higher long-term buprenorphine treatment retention among older individuals and women (Pizzicato et al., 2020; Hasan et al., 2021). The RI PDMP does not include data on patient race and ethnicity, so this could not be evaluated in our study, but prior work has shown lower retention among Black or Hispanic individuals when compared to White individuals (Hasan et al., 2021). While most prior studies were limited to specific payer populations (e.g. only Medicaid, or only commercially insured), we were able to compare treatment retention by health insurance type and found that patients with Medicaid insurance had higher retention than those with private insurance.

This work aligns with prior studies that found relatively high levels of opioid prescribing among individuals engaged with buprenorphine treatment (Pizzicato et al., 2020; Williams et al., 2020). Future work should evaluate the medical conditions for which these opioid prescriptions are prescribed and evaluate if non-opioid alternatives could have been more appropriate. Additionally, subsequent work should evaluate the temporality of opioid prescribing, and determine if these prescriptions are being prescribed following successful completion of opioid use disorder treatment or are being provided during the treatment window and reducing long-term buprenorphine treatment engagement.

This study is subject to several limitations. First, this work assumes that individuals who filled any buprenorphine, benzodiazepine, or opioid prescriptions took them as prescribed, which is not present in the PDMP data. Second, in this study, we exclusively looked at long-term retention in buprenorphine treatment, and it is plausible that individuals who were not retained in buprenorphine treatment transitioned to other pharmacological (e.g., methadone) or non-pharmacological (e.g., group therapy) treatments. Third, this work used an administrative dataset, so we did not have information on individual's experiences on buprenorphine or reasons for discontinuation, including information on the copay cost which likely impacted long-term retention. Fourth, to align with prior work (Pizzicato et al., 2020) prescriptions dispensed with a days' supply surpassing the follow-up end date were not truncated which may influence the findings. Finally, we acknowledge that it is rare to start individuals on buprenorphine with a 30 + day supply, and it is possible that these individuals may have recently been in buprenorphine treatment at a facility from which the RI PDMP does not receive data (e.g., a correctional or inpatient treatment facility).

5. Conclusion

This work demonstrates the utility of state PDMPs to identify modifiable prescribing practices that may improve long-term buprenorphine treatment retention at the population

level. These findings suggest that treatment retention may be improved by removing barriers to treatment initiation, such as providing a longer day supply and exploring mailed prescriptions for those further from the pharmacy. When prescribing, initial use of the film formulation may also improve treatment retention for some patients. Finally, additional research to understand the risks and benefits of co-prescribing buprenorphine and benzodiazepines for different patients, as well as optimal pain management approaches for patients taking buprenorphine, would be useful to inform tailored management of co-morbid conditions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Demographic and prescription characteristics of Rhode Island residents who initiated buprenorphine treatment, stratified by long-term buprenorphine retention — Rhode Island, July 1, 2017-June 30, 2020 (n = 4898).

	Overall	Prescriptions for buprenorphine for ≥ 80% of the 365 days following treatment initiation			Bivariate associations with sustained treatment	
		Yes	No	Chi-sq	Odds ratio	95% CI
Demographics						
Age						
18–24	391 (8.0)	64 (3.5)	327 (10.7)	< 0.0001	0.428	0.320, 0.572
25–34	1451 (29.6)	456 (24.6)	995 (32.7)		Ref	–
35–44	1312 (26.8)	529 (28.6)	783 (25.7)		**1.476**	**1.262, 1.726**
45–54	900 (18.4)	407 (22.0)	493 (16.2)		**1.809**	**1.523, 2.149**
55–64	658 (13.4)	315 (17.0)	343 (11.3)		**1.994**	**1.651, 2.409**
≥ 65	186 (3.8)	80 (4.3)	106 (3.5)		**1.624**	**1.189, 2.218**
Sex						
Male	2998 (61.2)	1100 (59.4)	1898 (62.3)	0.0153	Ref	–
Female	1799 (36.7)	721 (39.0)	1078 (35.4)		**1.149**	**1.019, 1.295**
Missing	101 (2.1)	30 (1.6)	71 (2.3)		0.726	0.471, 1.120
Year of Initiation						
2017	1019 (20.8)	395 (21.3)	624 (20.5)	0.4048	Ref.	–
2018	1863 (38.0)	697 (37.7)	1166 (38.3)		0.944	0.807, 1.105
2019	1414 (27.9)	517 (27.9)	897 (29.4)		0.911	0.771, 1.075
2020	602 (12.3)	242 (13.1)	360 (11.8)		1.062	0.864, 1.305
Insurance Coverage[a]						
Private Insurance	2247 (45.9)	790 (42.7)	1457 (47.8)	0.0002	Ref	–
Medicaid	1715 (35.0)	687 (37.1)	1028 (33.7)		**1.231**	**1.081, 1.401**
Medicare	448 (9.2)	199 (10.8)	249 (8.2)		**1.470**	**1.197, 1.806**
Other	488 (10.0)	175 (9.5)	313 (10.3)		1.027	0.836, 1.261
Initial Prescription						
Distance from Home to Pharmacy (based on zip)						
0 Miles	2037 (41.6)	835 (45.1)	1202 (39.5)	< 0.0001	Ref	–
< 5 Miles	1499 (30.6)	582 (31.4)	917 (30.1)		0.910	0.794, 1.044
≥ 5 Miles	1348 (27.5)	432 (23.3)	916 (30.1)		**0.677**	**0.586, 0.782**
Missing	14 (0.3)	<5	12 (0.4)			
Days' Supply						
7 days or less	2977 (60.8)	1116 (60.3)	1861 (61.1)	0.0157	Ref	–
8–29 days	1490 (30.4)	545 (29.4)	945 (31.0)		0.970	0.853, 1.104
30 + days	431 (8.8)	190 (10.3)	241 (7.9)		**1.320**	**1.076, 1.620**
Buprenorphine Formulation						
FIL	2909 (59.4)	1170 (63.2)	1739 (57.1)	0.0001	Ref	–

	Overall	Prescriptions for buprenorphine for ≥ 80% of the 365 days following treatment initiation		Bivariate associations with sustained treatment		
		Yes	No	Chi-sq	Odds ratio	95% CI
TAB	1978 (40.4)	678 (36.6)	1300 (42.7)		0.556	0.147, 2.100
ERS	11 (0.2)	<5	8 (0.3)		0.773	0.686, 0.871
Daily Dose						
0 to <8 mg	678 (13.8)	257 (13.9)	421 (13.8)	0.0682	Ref	–
8 to < 16 mg	1275 (26.0)	506 (27.3)	769 (25.2)		1.085	0.896, 1.315
16 to < 24 mg	2479 (50.6)	896 (48.4)	1583 (52.0)		0.928	0.779, 1.107
24 + mg	466 (9.5)	192 (10.4)	274 (9.0)		1.158	0.910, 1.474
First Stable Daily Dose[b]						
0 to <8 mg	641 (13.1)	236 (12.8)	405 (13.3)	0.1194	Ref	–
8 to < 16 mg	1207 (24.6)	478 (25.8)	729 (23.9)		1.133	0.930, 1.382
16 to < 24	2558 (52.2)	935 (50.5)	1623 (53.3)		0.990	0.827, 1.185
24 + mg	492 (10.0)	202 (10.9)	290 (9.5)		1.206	0.947, 1.535
Overall Follow Flags[c]						
Overlapping benzodiazepine and buprenorphine prescription						
Yes	861 (17.6)	451 (24.4)	410 (13.5)	< 0.0001	2.063	1.777, 2.394
No	4037 (82.4)	1400 (75.6)	2637 (86.5)		Ref	–
Opioid dispensed in treatment period						
Yes	820 (16.7)	208 (112)	612 (20.1)	< 0.0001	0.502	0.423, 0.595
No	4078 (83.3)	1643 (88.8)	2435 (79.9)		Ref	–

[a]Obtained from first buprenorphine prescription.

[b]Defined as the first dose an individual received for 7 or more continuous days. Individuals who never received a daily dose > 6 days were listed as the first dose.

[c]Based on prescriptions filled during the follow-up period.

Table 2

Multivariable associations between demographic and prescription characteristics and 12-month sustained engagement in buprenorphine treatment among Rhode Island residents who initiated buprenorphine treatment — Rhode Island, July 1, 2017-June 30, 2020.

	Adjusted Odds Ratio	95% CI
Demographics		
Age		
18–24	**0.450**	**0.335, 0.603**
25–34	Ref	–
35–44	**1.520**	**1.295, 1.785**
45–54	**1.924**	**1.608, 2.302**
55–64	**2.244**	**1.832, 2.750**
≥ 65	**1.849**	**1.312, 2.606**
Sex		
Male	Ref	–
Female	**1.137**	**1.001, 1.292**
Missing	**0.914**	**0.576, 1.450**
Insurance Coverage[a]		
Private Insurance	Ref	–
Medicaid	**1.235**	**1.076, 1.419**
Medicare	1.068	0.852, 1.339
Other	1.036	0.835, 1.287
Initial Prescription		
Distance from Home to Pharmacy (based on zip)		
0 Miles	Ref	–
< 5 Miles	0.914	0.793, 1.054
≥ 5 Miles	**0.719**	**0.617, 0.838**
Days' Supply		
7 days or less	Ref	–
8–29 days	1.002	0.872, 1.152
30 + days	**1.256**	**1.009, 1.563**
Buprenorphine Formulation		
FIL	Ref	–
TAB	**0.817**	**0.721, 0.927**
ERS	0.707	0.179, 2.785
Overlapping Flags[b]		
Overlapping benzodiazepine and buprenorphine prescription		
No	Ref	–
Yes	**1.999**	**1.705, 2.344**
Opioid dispensed in treatment period		
No	Ref	–
Yes	**0.366**	**0.306, 0.439**

[a] Obtained from first buprenorphine prescription.

[b] Based on prescriptions filled during the follow-up period.