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Hospitalized Opioid-Dependent Patients: Exploring Predictors of Buprenorphine Treatment entry and retention After Discharge

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Abstract

Objectives—Few studies have explored predictors of entry into and retention in buprenorphine treatment following linkage from an acute medical hospitalization.

Methods—This secondary analysis of a completed clinical trial focuses on medically hospitalized, opioid dependent patients (n=72) who were randomized to an intervention including buprenorphine induction and dose stabilization during hospitalization followed by post-discharge transition to office-based buprenorphine treatment (OBOT)).

Predictors included—demographics, days hospitalized, prior buprenorphine/methadone treatment, PTSD symptoms, social support, and readiness for drug use cessation. Outcome variables were treatment entry and retention (number of days in OBOT).

Results—Previous buprenorphine treatment, more days hospitalized, and higher PTSD symptoms predicted OBOT entry. Prior treatment, older age, and non-minority status were associated with a higher mean number of days in OBOT.

Conclusions—OBOT may appeal to patients who have tried buprenorphine in other settings. Linking hospitalized patients to OBOT may improve utilization of addiction treatment. Scientific Significance: Prior substance treatment, longer hospital stay, and mental health should be examined in future linkage studies.

Introduction

The dramatic increase in scope and severity of opioid use disorder (OUD) in the U.S is reflected in the increase in the population of hospitalized opioid users ^{1,2}. Opioid-related visits to the emergency department increased 183% (488,004) within 8 years, and up to a

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quarter of those visits resulted in hospital admissions^{3,4}. Office-based opioid treatment with buprenorphine-naloxone (noted hereafter as buprenorphine) offers flexible, responsive management of recovery-related addiction and medical issues^{1,5-7}. A linkage model that initiates buprenorphine treatment during hospitalization, then facilitates transition of patients to primary care-based buprenorphine treatment has shown promise^{5,8-10}. We have recently shown that compared to a detoxification protocol, the linkage model was an effective means for engaging some hospital inpatients¹. The current analysis explores what factors influence entry and retention in a secondary analysis of this earlier randomized clinical trial of linkage¹.

Regarding treatment entry to OAT (from needle exchange programs), social support and type of social network have been identified as predictors¹¹. Injection drug users who lived with a partner, family, or friends, were three times more likely to enter OAT than those who lived alone or in non-stable (e.g., streets, abandoned house) or controlled (e.g., transitional housing program), environments¹². With regard to social network influences, buying drugs for one's social network at treatment entry strongly predicted early drop-out¹³. Readiness for cessation of drug use was predictive of entry to substance use treatment among injection drug users¹⁴.

Retention in opioid treatment leads to positive clinical outcomes¹⁵⁻¹⁹: reduced opioid use^{20,21} improved social and physical functioning^{11,16,22-24}, and increased abstinence^{25,26}. Predictors of buprenorphine treatment retention include: older age^{13,16}, longer history of opioid use¹⁵ and treatment experience^{13,27,28}. Non-white racial/ethnic group membership predicts early drop out^{1,15}. Gender has not consistently predicted entry or retention^{1,29-31}, although there is some evidence to suggest that men are more likely to be retained^{28,32}. While some studies have found treatment readiness for cessation of drug use to be an important influence on retention¹¹ in different treatment modalities (e.g., long term residential, outpatient, methadone)^{20,25,33,34}, others have not found this relationship^{35,36}, particularly among samples of African-American patients^{35,37}. Similarly, poor mental health may worsen retention in buprenorphine treatment in some studies³⁸, while other studies have suggested a link between depressive symptomatology and retention^{47,48}. Because being hospitalized is the unique defining aspect of the linkage treatment model, days of hospitalization was included as a predictor as well.

In this secondary analysis we used an exploratory approach which considers both significant and non-significant trends⁶. We hypothesize that age, gender, ethnicity, days hospitalized, social support, readiness for drug use cessation, employment, PTSD symptomatology, and prior use of treatment with buprenorphine or methadone, will influence who initiates and who remains in office-based buprenorphine treatment.

Methods

Full details of the randomized clinical trial (RCT) have been described elsewhere (Lieschutz et al., 2014). Between August 1, 2009, through October 31, 2012, 663 opioid-dependent inpatients on the general medical wards of an urban safety-net hospital were identified, of whom 294 were eligible for the study. Of the 145 eligible patients who

consented to participate in the randomized clinical trial, 139 completed the baseline interview and were assigned to the Detoxification (five days of tapering buprenorphine, $n = 67$) or Linkage (buprenorphine begun during hospitalization with a facilitated transition to the first outpatient buprenorphine hospital-based (OBOT) clinic visit, $n = 72$) group of the parent study. The primary outcome, treatment initiation, was measured by the proportion of participants who presented to an initial visit at OBOT after hospital discharge. A secondary outcome, retention, was measured by number of days engaged in OBOT, as defined by days with an active buprenorphine prescription. Study outcomes were obtained by review of documentation in the electronic health record at the referral buprenorphine outpatient treatment site six months after study recruitment. Predictors of initiation and retention, measured during hospitalization, included: social support (MOS Social Support Survey³⁹), readiness to change (Thoughts about Abstinence scale⁴⁰), and PTSD symptoms (PTSD Checklist-Civilian (PCL-C) using a cut-off of 44 to correlate with a PTSD diagnosis⁴¹).

Analytical Methods

We summarize sample characteristics with descriptive statistics. We employed bivariate and multivariate logistic regression to evaluate the unadjusted and adjusted associations of background characteristics and treatment history with OBOT entry. For persons entering OBOT, we used OLS regression to estimate unadjusted and adjusted associations of these same characteristics with days of OBOT treatment. Because of small sample sizes and failure to well approximate distributional assumptions, all standard errors and confidence intervals were estimated by bootstrap resampling with 2500 replications. All continuous variables were standardized to zero mean and unit variance prior to the analysis. For continuous correlates, the estimated odds-ratios give the expected change in the odds of OBOT entry for a 1-standard deviation change in the correlate. For days of OBOT treatment, the reported coefficients for continuous correlates are fully standardized and the coefficients for categorical correlates are y -standardized. Because the small sample size limits statistical power and increases the likelihood of Type II error in this exploratory study, we present only adjusted associations because the unadjusted were similar in magnitude in all cases.

Results

Participants ($n=72$) averaged 41.4 (± 12.1) years of age, 70.8% were male, 44.4% non-Latino Caucasian, 30.6% African-American, 19.4% Latino, and 5.6% were of other racial or ethnic origins (Table 1). About 26.8% and 46.5% had ever been in buprenorphine or methadone maintenance treatment. The mean length of hospitalization was 4.26 (± 7.07) days. Fifty-two (72.2%) entered OBOT and the mean number of days in OBOT was 64.4 (± 61.7).

Persons who had ever been in buprenorphine treatment had a substantially ($OR = 3.50$, 95%CI 0.41; 29.65) higher likelihood of entry to OBOT (Table 2). Adjusting for other covariates in the model, a 1 standard deviation increase in days hospitalized was associated with a 2.37 (95%CI 0.11; 50.92) fold increase in the expected odds of OBOT entry. And a 1 standard deviation increase in PCL-C total scores was associated with an estimated 1.85 (95%CI 0.50; 6.89) factor increase in the expected odds of OBOT entry.

Persons with a history of buprenorphine treatment tended to have more days of OBOT treatment ($b = .52$, 95%CI -0.16 ; 1.19) than those with no history of buprenorphine treatment. These standardized differences in adjusted means corresponds to 28.5 (95%CI -8.70 ; 65.74) difference in days of OBOT treatment. Days of OBOT treatment tended to be associated positively with older age ($b = 0.34$, 95%CI -0.10 ; 0.78); and non-Latino Caucasians tended to have a higher adjusted mean number of OBOT treatment days ($b = 0.55$, 95%CI -0.25 ; 1.35).

Discussion

We found that history of buprenorphine experience, longer hospitalization stay, and increased trauma symptoms, appeared to increase the odds of treatment entry following hospital discharge. Older age, non-Hispanic-Caucasian, and history of buprenorphine treatment seemed to be associated with treatment retention.

Patients who had previously received buprenorphine treatment were nearly four times more likely to enter OBOT compared to those who had not. Familiarity with a medication through prior exposure may encourage preference^{13,42,43}. For example, heroin users who chose buprenorphine over methadone (in outpatient treatment), reported that their first hand experiences with using buprenorphine in non-medical contexts (i.e., used for self-management of withdrawal), strongly influenced their choice⁴². From this, it is also possible to infer that patients with prior buprenorphine treatment exposure have clearer expectations of both the process and benefits of maintenance treatment and are thus more predisposed towards treatment entry.

Patients with longer hospitalization stays had double the odds of entering OBOT compared to those with shorter hospitalization. Hospitalization presents an important opportunity to recruit patients into treatment. Medically admitted patients (for their opioid-related problems) may relate their hospitalization to their opioid use, thus providing a “teachable moment”^{44–46} when patients are willing to consider making changes. Rapport may also be augmented during an extended hospital stay—thus encouraging patient consideration of treatment. Relatedly, patients who require longer hospitalization may be more severely ill; this may promote greater motivation for treatment. For patients who have not yet tried OUD treatment, education during hospitalization may be helpful. Future research should investigate what elements of the longer hospitalization experience may impact on entry and retention.

Surprisingly, elevated PTSD symptoms did not predict drop-out among our sample, but nearly doubled the likelihood of OBOT entry. These findings are of interest because of the high prevalence of PTSD among opioid users compared to other drug classes^{1,38}. It is also known that poor mental health is co-morbid with opioid use dependence⁴⁷, with depression most commonly studied. Of note, some studies have reported that patients with elevated depression are more likely to remain in buprenorphine treatment^{47,48}. Relatedly, individuals with a history of suicide attempts were less likely to drop out of buprenorphine treatment⁴⁹. Yet, a prospective randomized trial found that reductions in depressive symptoms among heroin users who were given escitalopram, did not predict improved retention compared to

those who did not receive escitalopram¹⁸. Given that depressive symptoms are now part of a core symptom cluster for PTSD in the DSM-5, and that dysphoria is a common emotional state in recovery, we were interested that participants with PTSD were more likely to enter OBOT. This aligns with findings from prior studies^{38,49} where opioid dependent individuals with emotional issues were receptive to buprenorphine treatment. The linkage model may provide needed structure to people who have experienced traumatic situations to access care.

Participants who initiated OBOT stayed in treatment for 64 days on average. We found that prior history of buprenorphine/methadone treatment^{13,27,28}, (older) age⁴⁹, and non-minority status, predicted improved treatment retention. Because addiction is a chronic relapsing condition, multiple treatment attempts may be necessary to achieve abstinence. In one study, opioid dependent individuals achieved long-term successes only after four failed attempts at completing a treatment program⁵⁰. Older age may be a predictor of treatment retention because older patients have had more treatment episodes, which cumulatively increase the likelihood of treatment retention⁵¹. Younger patients, who have not experienced as many substance-related negative consequences relative to older patients³², are more likely to drop out early from methadone maintenance and opiate agonist treatment^{13,15,16,27,49,52}. Racial/ethnic minorities are more likely to drop out of treatment early^{29,52}, suggesting the need for further research to improve treatment retention.

We did not find associations between readiness or social support and treatment entry or retention. As in other studies of opioid dependent individuals, our hospitalized study participants reported high levels of readiness for opioid cessation. Readiness to change has not been found to consistently predict treatment entry or retention³⁷, possibly due to the ceiling effect. Social support was not associated with either treatment entry or retention here. Other studies have documented that stability of residence or network type composition played a greater role in encouraging treatment entry and retention than did individual perception of social support¹².

Our study had limitations. In addition to the small sample size were the single recruitment site and the enrollment only of persons interested in buprenorphine treatment. We were limited to variables used in the parent trial, so were unable to include all variables identified in prior studies. We did not collect urine drug toxicologies at baseline, an indicator of treatment severity⁴⁹, but nearly all (51/52) participants were injection drug users, another indicator of drug use severity which precluded testing injection use as a predictor. While many buprenorphine providers require abstinence from alcohol and benzodiazepines given dangerous interactions with opioid use, the exclusion criteria in the parent study (alcohol/benzodiazepine dependence, chronic pain, and cocaine dependence) may limit generalizability. Larger studies could explore whether type or severity of medical condition influences patient decisions to enter OBOT⁴⁹. Finally, our study did not include measures of mental disorders other than PTSD.

Conclusions

Individuals with opioid use disorder interact with the medical system at different times⁵¹, and programs linking addicted patients to substance use treatment opportunistically can

initiate long-term substance treatment. Maintenance buprenorphine treatment is an effective treatment², and educating hospitalized patients who may not have tried it before, initiating it during hospitalization, and establishing linkages with outpatient providers may improve access to addiction care.

Our findings, although limited by the small sample, suggest patient attributes that can be addressed during hospitalization in future investigation. Our linkage model provides the continuous structure and care that may have particular appeal to drug users with mental health symptoms. Because longer hospitalization predicted increased likelihood of treatment entry, the rush to discharge opiate users before aftercare treatment has been organized, could be counterproductive and may preclude taking advantage of this possible change moment.

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Table 1

Background Characteristics (n = 72).

	n (%)	Mean ($\pm$ SD)	Median	Range
Age		41 (12.1)	42.21	21 – 65
Gender (Male)	51 (70.8%)			
Race/Ethnicity				
Caucasian	32 (44.4%)			
African-American	22 (30.6%)			
Latino	14 (19.4%)			
Other	4 (5.6%)			
Ever in Buprenorphine Treatment	19 (26.8%)			
Ever in Methadone Treatment	33 (46.5%)			
Days Hospitalized		4.26 (7.07)	2.5	0 – 49
Social Support		60.5 (29.9)	61.2	0 – 100
PCL-C		44.9 (18.0)	44	17 – 81
Desire to Quit		9.13 (1.66)	10	2 – 10
Days in OBOT		64.4 (61.7)	49	0 – 183
Entered OBOT	52 (72.2%)			

Table 2

Baseline Predictors of Treatment Engagement.

	OBOT ENTRY (n = 72)	DAYS OBOT (n = 52)
	Adjusted OR ^a [95% CI] ^c	Adjusted b ^b [95% CI] ^c
Age	1.09 [0.42; 2.78]	0.34 [−0.10; 0.78]
Gender (Male)	0.79 [0.08; 7.99]	0.10 [−0.67; 0.88]
Non-Latino Caucasian	0.35 [0.05; 2.57]	0.55 [−0.25; 1.35]
Days Hospitalized	2.37 [0.11; 50.92]	−0.14 [−0.66; 0.39]
Ever Buprenorphine Treatment	3.50 [0.41; 29.65]	0.52 [−0.16; 1.19]
Ever MMT	0.99 [0.15; 6.72]	−0.24 [−0.88; 0.40]
Social Support	1.23 [0.46; 3.31]	0.18 [−0.15; 0.50]
PCL-C	1.85 [0.50; 6.89]	−0.25 [−0.55; 0.04]
Readiness to Quit	0.64 [0.19; 2.19]	0.03 [−0.20; 0.26]

^aContinuous correlates were standardized to zero mean and unit variance prior to analysis; the coefficients give the expected change in the odds of OBOT entry for a 1-standard deviation increase in the continuous predictor variable.

^bDays of OBOT treatment and all continuous correlates were standardized to zero mean and unit variance prior to analysis. The coefficients for continuous correlates are fully-standardized and the coefficients for categorical correlates are y-standardized.

^cConfidence interval estimates and standard errors were estimated by bootstrap resampling with 2500 replications.