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Very early disengagement and subsequent re-engagement in primary care Office Based Opioid Treatment (OBOT) with buprenorphine

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Abstract

Introduction—Patients with opioid use disorder often require multiple treatment attempts before achieving stable recovery. Rates of disengagement from buprenorphine are highest in the first month of treatment and termination of buprenorphine therapy results in return to use rates as high as 90%. To better characterize these at-risk patients, this study aims to describe: 1) the frequency and characteristics of patients with very early disengagement (≤1 month) from Office Based Opioid Treatment (OBOT) with buprenorphine and 2) the frequency and characteristics of patients who re-engage in care at this same OBOT clinic within 2 years, among the subset of very early disengagers.

Methods—This is a retrospective cohort study of adult patients enrolled in a large urban OBOT program. Descriptive statistics were used to characterize the sample and the proportion of patients with very early (≤1 month) disengagement and their re-engagement. Multivariable logistic regression models were used to identify patient characteristics associated with the outcomes of very early disengagement and re-engagement. Potential predictors included: sex, age, race/

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ethnicity, education, employment, opioid use history, prior substance use treatments, urine drug testing, and psychiatric diagnoses.

Results—Overall, very early disengagement was unusual, with only 8.4% (104/1234) of patients disengaging within the first month. Among the subset of very early disengagers with 2 years of follow-up, the proportion who re-engaged with this OBOT program in the subsequent 2 years was 11.9% (10/84). Urine drug test positive for opiates within the first month (AOR: 2.01, 95% CI: 1.02–3.93) was associated with increased odds of very early disengagement. Transferring from another buprenorphine prescriber (AOR: 0.09, 95% CI: 0.01–0.70) was associated with decreased odds of very early disengagement. No characteristics were significantly associated with re-engagement.

Conclusions—Early disengagement is uncommon; however, continued opioid use appeared to be associated with higher odds of treatment disengagement and these patients may warrant additional support. Re-engagement was uncommon, suggesting the need for a more formal explicit system to encourage and facilitate re-engagement among patients who disengage.

Keywords

buprenorphine; patient dropout; reengagement; Office Based Opioid Treatment (OBOT); opioid-related disorders; substance users

1.0 Introduction

Opioid use disorder (OUD) affects more than 2 million patients in the United States, causing significant morbidity, mortality, and costs to society. (Kraus et al., 2011) Opioid overdose mortality has skyrocketed in recent years due to increased use of illicit prescription opioid analgesics(Chen, Hedegaard, & Warner, 2014), heroin(Hedegaard, Chen, & Warner, 2015), and fentanyl use. (Warner, Trinidad, Bastian, Minino, & Hedegaard, 2016) Patients with OUD benefit from long term treatment with opioid agonist therapies such as buprenorphine. (Bart, 2012; Dunn, Sigmon, Strain, Heil, & Higgins, 2011; Fudala et al., 2003; Kakko, Svanborg, Kreek, & Heilig, 2003; Sordo et al., 2017) Successful buprenorphine treatment retention is associated with reduced mortality, improved social function, decreased illicit drug use, and improved quality of life. (Bart, 2012) In contrast, termination of buprenorphine therapy, particularly early in the course of treatment, is usually followed by return to use, with 50–90% of patients relapsing just one month after discontinuation. (Bentzley, Barth, Back, & Book, 2015) Moreover, the risk of overdose is greatly increased immediately following discontinuation of therapy, likely due to loss of opioid tolerance. (Cornish, Macleod, Strang, Vickerman, & Hickman, 2010; Davoli et al., 2007; White & Irvine, 1999; Woody, Kane, Lewis, & Thompson, 2007) Unfortunately, the highest rate of buprenorphine treatment disengagement often occurs in the first month. (Gryczynski et al., 2013; Soeffing, Martin, Fingerhood, Jasinski, & Rastegar, 2009; Stein, Patricia Cioe, & Friedmann, 2005)

Prior buprenorphine maintenance studies showed a reported or estimated 1-month disengagement rate between 8–48%. (Amass et al., 2012; Cunningham, Roose, Starrels, Giovanniello, & Sohler, 2013; Fiellin et al., 2006; Hser et al., 2014; Lee, Grossman,

DiRocco, & Gourevitch, 2009; Mattick et al., 2003; Schuman-Olivier, Weiss, Hoeppner, Borodovsky, & Albanese, 2014; Sohler et al., 2010; Warden et al., 2012) Few studies specifically reported 1-month disengagement rates. (Amass et al., 2012; Sohler et al., 2010) Most reported disengagement rates at 3-months (Mattick et al., 2003; Warden et al., 2012) or 6-months (Cunningham et al., 2013; Hser et al., 2014) as their primary outcome for treatment success and included 1-month disengagement rates only in passing. Some studies included 1-month disengagement rates only in the form of a Kaplan-Meier graph from which 1-month disengagement rates could be extrapolated. (Fiellin et al., 2006; Schuman-Olivier et al., 2014) Therefore a comprehensive exploration of patient characteristics associated with 1-month disengagement outcome has not been a past focus. We aim to identify the patients who are at high risk for very early disengagement in order to gain a better understanding of this subgroup of patients given their high risk of morbidity and mortality. (Cornish et al., 2010; Woody et al., 2007)

This study is part of the Disenrollment and Re-engagement in an OBOT (Office Based Opioid Treatment) Program (DROP) study. (Weinstein et al., 2017) It will assess the following: 1) the proportion and characteristics of patients in an urban safety net hospital OBOT program who leave care in less than 1 month (i.e., very early disengagement); and 2) the proportion and characteristics of those who re-engage in care with the same clinic within 2 years among those with very early disengagement.

2.0 Methods

We performed a retrospective cohort study of adult patients treated with buprenorphine at the OBOT Program at Boston Medical Center from the clinic's inception on January 2002 through February 2014. This study was approved by the Boston University Medical Campus Institutional Review Board.

2.1 Study Setting

This OBOT program is housed within a primary care clinic at the largest safety-net medical center in New England, and has been previously described as a collaborative nurse care manager (NCM) model(Alford et al., 2011) and subsequently dubbed the Massachusetts Model of office-based opioid treatment. (Korthuis et al., 2016; Substance Abuse and Mental Health Services Administration, 2014) Patients are induced on a buprenorphine protocol specified by federal guidelines with on-site direct observation. (McNicholas, 2004) Special care was taken to minimize precipitated withdrawal in patients transitioning from methadone maintenance therapy. The standard protocol involved slowly tapering patients down to 30mg of methadone daily for 1 week followed by a 72-hour period of abstinence with comfort medications if desired before buprenorphine induction; however, a methadone negative urine was not required for induction. During the stabilization period of the first 4–6 weeks, patients have a minimum of once per week clinic visits with the NCM in addition to telephone communication. During these interactions, NCM provide education and support to patients and ensure patient's adherence to treatment guidelines. Patients are also required to engage in weekly behavior health counseling, which may be obtained off site. (LaBelle, Han, Bergeron, & Samet, 2016)

Patients may leave treatment for many reasons. Patients who desire treatment cessation may request a buprenorphine taper at any time, although they are encouraged to have at least six months of abstinence prior to tapering. Patients may be administratively discharged for a multitude of reasons including persistent opioid use as determined by three or more consecutive opioid positive urine drug tests despite buprenorphine dose adjustment, high suspicion for medication misuse, non-adherence with three or more consecutive appointments or monitoring requests (i.e. producing urine samples for testing or presenting remaining buprenorphine prescription for pill counting), or disruptive behavior prompting safety concerns. Usually these patients are first offered assisted transfer to methadone maintenance treatment where they may obtain more structured care and observed daily dosing – refusing to transfer may result in involuntary discharge from the clinic. (Alford et al., 2011) If patients are lost to follow-up, NCMs attempt multiple times by phone to reach patients, significant others, counselors, current housing programs and other contacts before formally discharging them from the program.

2.1.1 Study Population—For the primary analyses, the study sample included patients' first engagement in buprenorphine treatment at Boston Medical Center, as evidenced by a concurrent buprenorphine prescription and an OBOT visit. Only patients who initiated treatment at least one month before the end of the study period were included in the study to allow adequate time to assess for very early disengagement (i.e., initiated before January 28, 2014). A total 1,308 patients were initially included in this study, based on dates of entry. As this study focused on describing patients who dropped out of treatment altogether, patients who reported their intention to transfer to another outpatient buprenorphine or naltrexone program, as indicated by a chart review of clinic notes, were excluded from the primary analysis. Seventy-four patients were excluded on this basis. A total of 1,234 patients were included in the final sample for the primary objective.

The analyses of the secondary outcome re-engagement within 2-years of disengagement included only patients who experienced very early disengagement at least 2 years before the end of the study period (i.e., those with their first disengagement before February 28, 2012). Twenty of the very early disengagers were excluded from this analysis as they did not have a full 2-year follow-up.

2.2 Data Collection

We abstracted clinical data from the Electronic Medical Record (EMR), including patient demographics, medical characteristics, substance use history, urine drug tests, buprenorphine prescriptions, and visit notes. For information that could not be automatically converted to data amenable to statistical analysis, two trained reviewers assessed clinic notes to manually abstract data to accurately obtain details such as previous history of buprenorphine treatment or years of substance use.

2.3 Outcomes

2.3.1 Very Early Disengagement—The study's primary outcome was very early disengagement, defined as disengaging from OBOT treatment within 30-days of initiating care. Since an exact date of disengagement was not recorded in the EMR even in cases of

administrative discharge, retrospectively establishing very early disengagement required a 2-step process. First, disengagement in general was strictly determined by a lapse in treatment in the medical record. A lapse was defined as having neither clinic visits nor active prescription for a period of 60-days or longer. A standard of 60-days was used to maximize capture of true disengagement while minimizing false positives – a 60-day lapse in clinic visits or prescriptions allowed room for real world variability in provider tolerance or individual patient circumstances. Second, a patient was determined to have experienced very early disengagement only if their last active prescription or visit date occurred within the first 30-days of initiating treatment. A manual review of clinic notes was performed to identify patient-reported reasons for disengagement as part of a separate study. (Weinstein et al., 2017) Descriptive statistics were used to characterize the reasons for disengagement among the very early disengagers, which included broad categories such as health contraindications, insurance problems, clinic problems, and legal issues.

2.3.2 Re-engagement—Our secondary outcome was re-engagement in OBOT treatment within 2-years of disengagement among the subgroup of patients with very early disengagement. Re-engagement was defined as receipt of a new buprenorphine prescription after disengagement. A cutoff of 2-years was used to determine re-engagement based on clinical judgement in order to allow ample opportunity for very early disengagers to reengage in treatment.

2.4 Potential Predictors

2.4.1 Demographics & Clinical Characteristics—Demographic data included age, sex, race/ethnicity, education, and employment status collected at treatment initiation. Clinical characteristics included current alcohol use and current smoker status at the time of intake. Two physicians reviewed all psychiatric diagnoses from the patient problem list and categorized them as follows: Anxiety; Attention-deficit/hyperactivity disorder (ADHD); Bipolar/Mania; Depression; and Schizophrenia.

2.4.2 Opioid Use History—Substance use history was recorded as part of a standardized intake interview during the patient's initial interaction with the clinic prior to buprenorphine induction. Pertinent information included type of opioids used, length of addiction history in years, any prior buprenorphine or methadone maintenance treatments, and current buprenorphine or methadone maintenance at time of intake. Every patient had an intake performed by nurses that was highly structured, and answers to the key substance use history questions were documented nearly universally. The uncommon absence of a recorded response to individual questions was assumed to be negative, although the frequency of this occurrence was not tracked. This self-reported data was manually abstracted from the clinical documentation by trained reviewers. For types of opioids used, patients were categorized based on whether they indicated having ever used heroin only, prescription opioid analgesics only, or both.

2.4.3 Urine Drug Test—Patients have weekly urine drug tests (UDT) with each NCM visit for at least the first month of treatment. UDT initially included a standard toxicology panel (i.e., opiates, cocaine, amphetamines, benzodiazepines, barbiturates). Opiate in this

context refers to a specific subset of natural or semi-synthetic opioids including codeine, morphine, and heroin that can be reliably detected with a single test. In 2007, an expanded opioid panel (i.e., oxycodone, methadone, and buprenorphine) was added to the standard toxicology panel for the remainder of the study period. Results from UDTs in the first month of treatment were aggregated and dichotomized as either positive if there were ever any positive test for the individual substance (except buprenorphine) or negative if all tests were negative. Each substance as noted above was treated as a separate independent variable in the analysis.

2.5 Statistical analysis

We calculated the proportion of patients with very early disengagement and the proportion of very early disengagers who experienced re-engagement within 2 years. Then we calculated frequencies and percentages for categorical patient characteristics, means and standard deviations for continuous variables, and median and interquartile ranges for lengths of time in initial treatment by study group. We also calculated median and interquartile ranges for average time to re-engagement and average time of length of the second episode of treatment. For descriptive purposes, we compared characteristics between groups using chi-square or Fisher's exact tests for dichotomous variables and t-tests or Wilcoxon Rank Sum tests for continuous variables as appropriate.

We used multivariable logistic regression models to examine baseline demographics, clinical characteristics, and substance use history as potential predictors for very early disengagement and re-engagement. In preliminary analyses, we constructed separate unadjusted models for each independent variable and covariate. Next, we fit an adjusted model for each independent variable controlling for age, race, and sex as covariates. Finally, we constructed multivariable logistic regression models for each outcome including any statistically significant independent variables from the initial adjusted analyses ($p < 0.05$). In this final model, we also included year of treatment initiation, divided in three discrete periods, in the model as another covariate in order to control for possible secular trends, operationalized as the categories: enrolled in 2002 to 2007, 2008 to 2010 and 2011 to 2014.

For the re-engagement outcome, we used exact logistic regression due to the limited number of events. Prior to final regression analyses, we calculated Spearman correlation coefficients for each pair of independent variables and covariates to avoid including variables that were highly correlated with one another. In the two cases where the correlation was >0.40, we used clinical judgment to select the variable that would be included in the final regression model. Positive methadone UDT and transferring from methadone maintenance therapy were found to be highly correlated by Spearman's analysis ($r=0.51$). In this case, we chose to include "transferring from methadone maintenance therapy" in the final multivariable model because, in our experience, the majority of methadone positive UDT were from patients coming from a methadone clinic rather than from the illicit street use of methadone. Methadone metabolites can be excreted in the urine typically up to 2–4 days after last use, which can be captured by UDT performed early in the treatment course – potentially explaining the collinearity.

Race/ethnicity and type of opioid use (prescription opioid analgesics and/or heroin) were also found to be highly correlated by Spearman's analysis (r=−0.41). We selected race for use in the final model because previous studies have implicated racial disparities as a factor predicting substance use treatment outcomes. (Mennis & Stahler, 2015; Weinstein et al., 2017; Wells, Klap, Koike, & Sherbourne, 2001)

We reported odds ratios and 95% confidence intervals for each independent variable and covariate included in the multivariable models. We conducted all analyses using two-sided tests and a significance level of 0.05. Due to the exploratory, hypothesis-generating nature of these analyses, we made no adjustment for multiple comparisons. We performed the statistical analysis using SAS version 9.4 (SAS Institute, Inc., NC, USA).

3.0 Results

3.1 Sample Characteristics

In this 12-year retrospective assessment of patients receiving care in the OBOT clinic, we reviewed clinical data for 1,234 individuals. The mean age at enrollment was 38 years (range: 18–76). The majority of patients were white (67.3%), male (62.1%), unemployed (64.1%), high school educated (64.0%), current smokers (78.1%), and current non-drinkers (81.8%). Patients began using opioids at the mean age of 22 and most frequently reported a history of using both prescription opioid analgesics and heroin (45.8%). (Table 1)

3.2 Very Early Disengagement

Very early disengagement occurred in 8.4% (95% CI: 6.9–9.9%) of patients who engaged in OBOT buprenorphine treatment. The median length of this first episode of OBOT treatment for patients who experienced early disengagement was 15 days (IQR: 8–26). Median length of treatment for patients who did not experience very early disengagement was 376 days (IQR: 149–1092). Compared with those who were retained in care for greater than 1-month, very early disengagers were more likely to have the following characteristics: non-white ($p=0.006$); diagnosed with schizophrenia ($p=0.002$); UDT positive for opiates ($p<0.001$), oxycodone ($p=0.007$), cocaine ($p<0.001$), and methadone ($p<0.001$); transfer from methadone maintenance ($p=0.004$); and used heroin exclusively (global $p=0.03$). Very early disengagers were less likely to have transferred from buprenorphine maintenance treatment at a different clinic ($p<0.001$). (Table 1)

In the final multivariable logistic regression model, having positive UDT for opiates within the first month of treatment remained significantly associated with greater odds of very early disengagement (AOR: 2.01, 95% CI: 1.02–3.93); being prescribed buprenorphine immediately prior to OBOT treatment initiation also remained associated with lower odds of very early disengagement (AOR: 0.09, 95% CI: 0.01–0.70). Among covariates, initiating treatment in more recent years appeared to be associated with very early disengagement (enrolled in calendar years 2011–2014 vs. 2002–2007, AOR: 4.39, 95% CI: 1.21–15.93). (Table 2)

Descriptive statistics were used to characterize the reasons for disengagement among the very early disengagers. Out of 104 very early disengagers, we retrospectively found

documentation that four patients (3.8%) reported disengagement due to medical reasons, which may include precipitated withdrawal; zero reported disengagement due to health insurance problems; three patients (2.9%) reported disengagement due to clinic problems; one patient (1.0%) reported disengagement due to incarceration/legal issues. However, we were unable to find any documentation for 71 (68%) very early disengagers. (data not shown)

3.3 Re-engagement

Ten out of 84 very early disengagers (11.9%, 95% CI: 5.0%–18.8%) re-engaged in the same OBOT program within two years. Median time to re-engagement (also considered the length of lapse in treatment) was 338 days (IQR: 151–471), and the median length of very early disengagers' second episode of treatment was 271 days (IQR: 77–664). No patient characteristics were associated with re-engagement in unadjusted or adjusted analyses. (Table 3, Table 4)

4.0 Discussion

This study found that very early disengagement (≤1 month) from buprenorphine treatment was uncommon (8.4%) at this office based opioid treatment (OBOT) program in a primary care clinic. The proportion of those with very early disengagement in this clinic falls on the lower end of the range of those with disengagement within one month from other studies (8–48%). (Amass et al., 2012; Cunningham et al., 2013; Fiellin et al., 2006; Hser et al., 2014; Mattick et al., 2003; Schuman-Olivier et al., 2014; Sohler et al., 2010; Stein et al., 2005) These results are encouraging when considering the evidence that patients leaving OUD treatment experience high rates of return to opioid use and mortality. (Cornish et al., 2010; Davoli et al., 2007; White & Irvine, 1999; Woody et al., 2007) The success of this clinic at short-term treatment retention could be attributed to the multidisciplinary team providing extensive individualized support for patients. (LaBelle et al., 2016) The proportion of patients who experience very early disengagement may be useful in OBOT practice as a performance metric by which clinics can benchmark progress and drive improvement in patient outcomes. (Thomas et al., 2013) One caveat, however, is recognizing the possibility that the relatively low very early disengagement rates are due to more stringent criteria for initial entry into care (i.e., subjectively screening out patients deemed unsuitable candidates for treatment).

This study identified only one factor associated with significantly increased risk of very early disengagement after adjusting for covariates. Patients with at least one urine drug test (UDT) positive for opiates had higher odds of very early disengagement (AOR: 2.01, 95% CI: 1.02–3.93). Positive opiate UDT may be a proxy for early failure to respond to buprenorphine treatment, and is consistent with other studies showing that early positive UDT for opiates was a predictor of treatment disengagement at 3, 6, and 14-months. (Campbell, Kolodner, Spencer, & DuPont, 2016; Marcovitz, McHugh, Volpe, Votaw, & Connery, 2016; Stein et al., 2005) Some patients may continue to use opioids suggesting that they require more structure and support than an office-based buprenorphine treatment can offer. Others may find buprenorphine ineffective at controlling cravings, or they cannot

tolerate side effects. (Gryczynski et al., 2014; Ramdurg, Ambekar, & Lal, 2012) These results affirm existing practices of buprenorphine programs that escalate treatment intensity for patients who test positive for opiates as they are the most unstable and vulnerable. (Alford et al., 2011) Physicians and other prescribers should consider offering these patients both intensification of buprenorphine treatment (e.g., increased clinic visits, counseling, buprenorphine dosage) or facilitated transfer to a methadone program, if needed.

Being prescribed buprenorphine immediately prior to OBOT enrollment and treatment initiation from another provider was found to be significantly associated with decreased odds of very early disengagement (AOR: 0.09, 95% CI: 0.01–0.70). Notably, simply having a history of ever having prior buprenorphine treatment was not a significant predictor in our study. Some previous studies have shown that any prior buprenorphine experience, illicit or prescribed, conferred protection against disengagement at 6-months while other studies have found that only previous illicit buprenorphine use and not-prescribed buprenorphine use was associated with treatment success at 12-months. (Alford et al., 2011; Cunningham et al., 2013) It is possible that the type of previous buprenorphine experience affects the risk of disengagement differently at various points in treatment. Patients who are directly transferring from another provider may have advantages in very short-term retention due to ongoing treatment of cravings and withdrawal symptoms through the transition period between treatment programs. Patients who have prior history of buprenorphine use but are not transferring from another clinic do not appear to have similar protection against very early disengagement for this reason. Instead, these patients may derive benefit in terms of long-term treatment retention for other reasons such as having a history of positive experience with buprenorphine that motivates them to succeed in the long term.

Transitioning from methadone maintenance therapy was not associated with decreased risk of very early disengagement. Surprisingly, our results showed that transitioning from methadone maintenance therapy was associated with more very early disengagement on the bivariate analysis (p=0.004), though this association did not reach significance in the multivariate analysis (AOR: 2.60, CI: 0.95–7.14). Patients may not have the benefit of a smooth transition as the pharmacology of methadone, a full mu-opioid receptor agonist, differs compared with buprenorphine, a partial mu-opioid receptor agonist, which may not fully treat cravings and can precipitate withdrawal complicating induction. (Breen et al., 2003; Rosado, Walsh, Bigelow, & Strain, 2007) This side effect is not exclusive to transitioning from methadone maintenance therapy as recent use of other opioids may also provoke precipitated withdrawal during induction. One study found that complicated induction was observed in 16% of patients receiving buprenorphine therapy and was also associated with lower 30-day treatment retention outcome. (Whitley et al., 2010) Reassuringly, we found that only 3.8% of very early disengagers reported leaving treatment due to nonspecific medical issues, which may include medication side effects. However, the incidence of precipitated withdrawal was not specifically documented in our EMR at time of induction, making it difficult to draw any reliable conclusions on the effect of precipitated withdrawal on very early disengagement, specifically in regards to transitioning from methadone therapy. Future research aimed at exploring this fragile transition of care would be of interest because of the risk of return to use. (Cousins et al., 2011)

Health insurance is an important factor that may reflect a patient's ability to access and continue substance use treatment. Massachusetts, however, passed healthcare reform in 2006, allowing consistent and expansive medical coverage for most patients regardless of their ability to pay. (Van Der Wees, Zaslavsky, & Ayanian, 2013) Consequentially, the uninsured rate in Massachusetts was very low compared to national average during this study period, down to 1.9% in 2010. ("Health Care in Massachusetts: Key Indicators May 2011 Edition," 2011) In addition, the majority (73% in 2014) of patients at Boston Medical Center have government insurance. (Weinstein, Battaglia, & Baranoski, 2016) Despite this scenario, it is a study limitation that insurance status was not collected. We instead attempted to identify very early disengagers who reported insurance as reason for disengagement. No such cases were found, although as many as 68% of very early disengagers had no reported reason for disengagement – raising the possibility of reporting bias. Future studies should include insurance status as a predictor of treatment retention if they draw from national data sets or are performed in states with less robust insurance coverage.

Engaging in first OBOT treatment in later years (2011–2014) appeared to be associated with increased odds (AOR: 4.39, 95% CI: 1.21–15.93) of very early disengagement. This may be a consequence of the clinic's efforts to create greater access for at risk individuals as the opioid epidemic expanded and overdose mortality increased.

Among patients with 2-years of follow-up, 12% of the very early disengagers subsequently re-engaged with this OBOT clinic within 2-years. Re-engagement has not received focused past attention and thus the comparable rate of re-engagement in other settings is unknown. In this study, it is concerning that so few patients returned to care. The average time to re-engagement (i.e., 318 days) demonstrates a significant lapse in care between episodes of treatment, a lapse that could have exposed patients to the risks of return to use, overdose, and death. Multiple large-scale studies have found all-cause mortality to be significantly higher in patients after disengagement from buprenorphine or methadone maintenance therapy compared with all-cause mortality during treatment. (Bell, Trinh, Butler, Randall, & Rubin, 2009; Clausen, Anchersen, & Waal, 2008; Cousins et al., 2016) Although some very early disengagers may have sought buprenorphine or methadone treatment elsewhere, some patients may have died without treatment. This may partially explain this clinic's low re-engagement rates of very early disengagers. (Cornish et al., 2010; Davoli et al., 2007; White & Irvine, 1999; Woody et al., 2007) Future research should attempt to investigate subsequent substance use treatments, rates of return to use, and mortality after treatment disengagement.

Although relatively few very early disengagers returned to the same clinic for a second episode of care, as OUD is a chronic relapsing disease, understanding subsequent treatment attempts is critical in addressing this disease. In this study the median length of first episode of care of 15 days as compared with the median length of second episode of care of 271 days. Increased experience with buprenorphine or the clinic may improve future treatment retention and success. (Cunningham et al., 2013; Monico et al., 2015) This observation suggests the need for better outreach through measures such as telephone-based recovery assistance programs or harm reduction programs to encourage and facilitate treatment re-entry. (Proctor, Wainwright, Herschman, & Kopak, 2017; Shah, BS, Sohler, PhD, MPH, López, BA, Fox, MD, & Cunningham, MD, MS, 2013) Such outreach may ultimately

benefit patients by reducing mortality and morbidity associated with being out of treatment. (Bart, 2012)

4.1 Limitations

This study includes only retrospective data collected for clinical purposes. Although the single site and specific model of care potentially limit the generalizability of the results, the increasing dissemination of this Massachusetts collaborative care model makes it an important one to understand. (LaBelle et al., 2016) Our study was unable to account for some factors that may confound our disengagement analysis. Psychiatric diagnoses are likely under-reported by patients due to patients being under-diagnosed or the associated stigma. (Takayanagi et al., 2014) Patients with pending legal issues or incarceration dates are probably less likely to engage as buprenorphine will not be continued in jail or prison, although unexpected legal problems may arise in the course of the early treatment period. (Wakeman & Rich, 2015) This did not appear to be a common driver for very early disengagement as only one very early disengager reported treatment cessation due to legal issues, although reporting bias may distort this conclusion.

Our re-engagement analysis is limited by its small sample size and a lack of larger statewide or insurance-level data and thus could not capture receipt of care elsewhere. However, this is an exploratory analysis attempting to highlight the importance of discussing re-engagement in the context of OUD as a chronic disease. Future studies should include attempts at post-treatment monitoring to follow patients through all care settings or seek to obtain access to state records concerning substance use services.

5.0 Conclusion

This study found that very early (≤1 month) disengagement from buprenorphine treatment was uncommon. However, having a positive opiate urine drug test was associated with increased odds of very early disengagement, suggesting that patients with continued active opiate use are the most vulnerable to leaving treatment. While transitioning into OBOT with a previous active buprenorphine prescription was associated with decreased odds of very early disengagement, transitioning into OBOT from previous methadone maintenance treatment was associated with very early disengagement in bivariate analyses. These findings suggest that they specific type of medication impacts the care transition for patients with OUD. Additionally, a low proportion of very early disengagers ultimately returned to this same OBOT program to re-engage in care within two years, suggesting a need to both explicitly inform early-departing patients that returning to care is an option that the treatment site supports and enact specific clinic guidelines for reducing system-based barriers to re-engagement. Monitoring for very early disengagers could be considered as a clinical quality marker that might advance more integrated treatment and patient-tracking systems leading to both practice-improvements and enhancement of patient care.

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Abbreviations

OUD	opioid use disorder
OBOT	office based opioid treatment
UDT	urine drug test

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Highlights

1. Only 8.4% of patients left buprenorphine treatment within the first month.
2. Continued opiate use was associated with increased odds of early disengagement.
3. Transferring from another buprenorphine clinic reduced early disengagement risk.
4. Only 11.9% of patients returned to buprenorphine treatment within 2 years.

Table 1

Characteristics of Patients Receiving Office-Based Opioid Treatment with Buprenorphine at Boston Medical Center Primary Care - Overall and Stratified by Very Early Disengagement Status

Patient Characteristic	Overall (N = 1234) N(%) or mean (SD)	Disengaged within 1 Month (N = 104) N(%) or mean (SD)	Remained in Treatment for > 1 month (N = 1130) N(%) or mean (SD)	p-value
Age at Enrollment (N = 1218)	38 (11)	38 (11)	38 (11)	0.70
Male Sex (N = 1218)	756 (62.1%)	61 (64.2%)	695 (61.9%)	0.65
Race (N = 1197)				
White	806 (67.3%)	46 (50.5%)	760 (68.7%)	
Black	182 (15.2%)	21 (23.1%)	161 (14.6%)	**0.006**
Hispanic	191 (16.0%)	22 (24.2%)	169 (15.3%)	
Other	18 (1.5%)	2 (2.2%)	16 (1.4%)	
HS/GED[†] or Greater Level of Education (N = 980)	627 (64.0%)	41 (69.5%)	586 (63.6%)	0.36
Unemployed (N = 1157)	748 (64.1%)	62 (70.5%)	686 (63.6%)	0.20
Comorbid Psychiatric Diagnosis at Initiation				
ADHD[‡] (N = 1234)	28 (2.3%)	1 (1.0%)	27 (2.4%)	0.35
Anxiety (N = 1234)	231 (18.7%)	18 (17.3%)	213 (18.8%)	0.70
Bipolar/Mania (N = 1234)	99 (8.0%)	8 (7.7%)	91 (8.1%)	0.90
Depression (N = 1234)	397 (32.2%)	39 (37.5%)	358 (31.7%)	0.22
Schizophrenia (N = 1234)	42 (3.4%)	9 (8.7%)	33 (2.9%)	**0.002**
Urine Test Positive				
Amphetamines (N = 1127)	37 (3.3%)	3 (4.8%)	34 (3.2%)	0.48
Benzodiazepines (N = 1127)	131 (11.6%)	7 (11.3%)	124 (11.6%)	0.91
Cocaine (N = 1127)	213 (18.9%)	22 (35.5%)	191 (17.9%)	**<0.001**
Methadone (N = 888)	73 (8.2%)	11 (21.2%)	62 (7.4%)	**<0.001**
Opiates (N = 1127)	433 (38.4%)	39 (62.9%)	394 (37.0%)	**<0.001**
Oxycodone (N = 838)	71 (8.5%)	9 (19.1%)	62 (7.8%)	**0.007**
Current Smoker (N = 388)	303 (78.1%)	19 (73.1%)	284 (78.5%)	0.52
Current Alcohol Use (N = 1234)	224 (18.2%)	20 (19.2%)	204 (18.1%)	0.77
Age of First Opioid Exposure (N = 1169)	22 (8)	23 (9)	22 (8)	0.72
Length of Addiction History in Years (N = 1153)	15 (11)	16 (11)	15 (10)	0.54
Prior History of Buprenorphine Treatment (N = 1234)	409 (33.1%)	27 (26.0%)	382 (33.8%)	0.10
Prior History of Methadone Treatment (N = 1234)	398 (32.3%)	37 (35.6%)	361 (31.9%)	0.45
Transferring from Buprenorphine Maintenance Treatment (N = 1234) [*]	238 (19.3%)	2 (1.9%)	236 (20.9%)	**<0.001**

Patient Characteristic	Overall (N = 1234) N(%) or mean (SD)	Disengaged within 1 Month (N = 104) N(%) or mean (SD)	Remained in Treatment for > 1 month (N = 1130) N(%) or mean (SD)	p-value
Transferring from Methadone Maintenance Treatment (N = 1234)	90 (7.3%)	15 (14.4%)	75 (6.6%)	**0.004**
Types of Opioids Used (N = 1234)				
Used Heroin Only	512 (41.5%)	56 (53.8%)	456 (40.4%)	
Used Opioid Pills Only	157 (12.7%)	9 (8.7%)	148 (13.1%)	**0.03**
Used Heroin and Opioid Pills	565 (45.8%)	39 (37.5%)	526 (46.5%)	

† High School/General Education Development

‡ Attention Deficit Hyperactive Disorder

* Fisher's exact test was used

Table 2

Multivariable Logistic Regression Model Evaluating the Association Between Patient Characteristics and Very Early Disengagement for OBOT with Buprenorphine (N=1,234)

Independent Variable	Adjusted OR (95% CI)
Age *	0.98 (0.95, 1.02)
Male Sex	1.11 (0.54, 2.27)
Race	
White	Reference
Black	1.51 (0.59, 3.90)
Hispanic	1.51 (0.66, 3.45)
Other Race	4.10 (0.80, 21.11)
Schizophrenia	2.11 (0.55, 8.08)
Urine Test Positives	
Opiates	2.01 (1.02, 3.93)
Oxycodone	1.94 (0.80, 4.66)
Cocaine	1.48 (0.73, 3.01)
Transferring from Buprenorphine Maintenance Treatment	0.09 (0.01, 0.70)
Transferring from Methadone Maintenance Treatment	2.60 (0.95, 7.14)
Calendar Year of Treatment Initiation	
2002–2007	Reference
2008–2010	1.59 (0.44, 5.71)
2011–2014	4.39 (1.21, 15.93)

* Per 10-year increase in age

Table 3

Characteristics of Very Early Disengagers from an Office-Based Opioid Treatment with Buprenorphine Stratified by Re-engagement Status

Patient Characteristic	Overall (N=84) N(%) or mean (SD)	Re-engaged (N=10) N(%) or mean (SD)	Never Re-engaged (N=74) N(%) or mean (SD)	p-value
Age at Enrollment (N = 78)	37 (11)	34 (11)	38 (11)	0.25
Male Sex (N = 78)	51 (65.4%)	5 (50.0%)	46 (67.6%)	0.27
Race (N = 75)				
White	40 (53.3%)	5 (50.0%)	35 (53.8%)	
Black	16 (21.3%)	2 (20.0%)	14 (21.5%)	
Hispanic	18 (24.0%)	3 (30.0%)	15 (23.1%)	0.95
Other	1 (1.3%)	0 (0.0%)	1 (1.5%)	
HS/GED[†] **or Greater Level of Education** (N = 45)	34 (75.6%)	5 (62.5%)	29 (78.4%)	0.34
Unemployed (N = 72)	49 (68.1%)	6 (60.0%)	43 (69.4%)	0.56
Comorbid Psychiatric Diagnosis at Initiation				
ADHD[≠] (N = 84)	1 (1.2%)	0 (0.0%)	1 (1.4%)	0.71
Anxiety (N = 84)	14 (16.7%)	2 (20.0%)	12 (16.2%)	0.76
Bipolar/Mania (N = 84)	6 (7.1%)	1 (10.0%)	5 (6.8%)	0.71
Depression (N = 84)	34 (40.5%)	3 (30.0%)	31 (41.9%)	0.47
Schizophrenia (N = 84)	9 (10.7%)	3 (30.0%)	6 (8.1%)	**0.04**
Urine Test Positive				
Amphetamines (N = 45)	3 (6.7%)	0 (0.0%)	3 (7.3%)	0.58
Benzodiazepines (N = 45)	6 (13.3%)	0 (0.0%)	6 (14.6%)	0.41
Cocaine (N = 45)	15 (33.3%)	2 (50.0%)	13 (31.7%)	0.46
Methadone (N = 35)	8 (22.9%)	0 (0.0%)	8 (24.2%)	0.43
Opiates (N = 45)	26 (57.8%)	3 (75.0%)	23 (56.1%)	0.46
Oxycodone (N = 30)	8 (26.7%)	0 (0.0%)	8 (28.6%)	0.38
Current Smoker (N = 20)	14 (70.0%)	1 (50.0%)	13 (72.2%)	0.52
Current Alcohol Use (N = 84)	13 (15.5%)	0 (0.0%)	13 (17.6%)	0.15
Age of First Opioid Exposure (N = 81)	22 (8)	18 (7)	22 (9)	0.18
Length of Addiction History in Years (N = 75)	16 (11)	13 (10)	17 (11)	0.42
Prior History of Buprenorphine Treatment (N = 84)	18 (21.4%)	2 (20.0%)	16 (21.6%)	0.91
Prior History of Methadone Treatment (N = 84)	33 (39.3%)	4 (40.0%)	29 (39.2%)	0.96
Transferring from Buprenorphine Maintenance Treatment (N = 84)	2 (2.4%)	1 (10.0%)	1 (1.4%)	0.09

Patient Characteristic	Overall (N=84) N(%) or mean (SD)	Re-engaged (N=10) N(%) or mean (SD)	Never Re-engaged (N=74) N(%) or mean (SD)	p-value
Transferring from Methadone Maintenance Treatment (N = 84)	14 (16.7%)	2 (20.0%)	12 (16.2%)	0.76
Types of Opioids Used (N = 84)				
Used Heroin Only	46 (54.8%)	5 (50.0%)	41 (55.4%)	
Used Opioid Pills Only	8 (9.5%)	0 (0.0%)	8 (10.8%)	0.41
Used Heroin and Opioid Pills	30 (35.7%)	5 (50.0%)	25 (33.8%)	

†High School/General Education Development

‡Attention Deficit Hyperactive Disorder

Table 4

Multivariable Logistic Regression Model Evaluating the Association Between Patient Characteristics and Re-engagement Among Very Early Disengagers from Office-Based Opioid Treatment with Buprenorphine (N=84)

Independent Variable	Adjusted Odds Ratio (95% Confidence Interval)
Age *	0.92 (0.82, 1.00)
Male Sex	0.88 (0.38, 2.13)
White	Reference
Non-White	1.19 (0.40, 3.49)
Comorbid Schizophrenic Psych Diagnosis	2.81 (0.81, 11.53)

*:per 10-year increase in age