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Risk factors for discontinuation of buprenorphine treatment for opioid use disorders in a multi-state sample of Medicaid enrollees

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Abstract

Introduction: Recent U.S. trends demonstrate sharp rises in adverse opioid-related health outcomes, including opioid use disorder (OUD), overdose, and death. Yet few affected people receive treatment for OUD and a minority of those who receive treatment are effectively retained in care. The purpose of this study was to examine duration of buprenorphine treatment for OUD following treatment initiation to identify risk factors for early discontinuation.

Methods: We analyzed insurance claims from the 2013–2015 MarketScan multi-state Medicaid database. The sample included adults 18–64 years old with an OUD diagnosis in the 6 months before initiating buprenorphine treatment, defined as 6 months without a buprenorphine claim prior to the index buprenorphine claim (N=17,329 individuals). We used Cox proportional hazards regression to estimate risk of discontinuing treatment (>30 days without buprenorphine supply), and logistic regression to estimate the odds of persistent treatment for a minimum of 180 days.

Results: Over one-quarter of the sample discontinued buprenorphine in the first month of treatment (N=4,928; 28.4%) and most discontinued before 180 days (N=11,189; 64.6%). In the proportional hazards model, risk factors for discontinuation included a lower initial buprenorphine dose (4mg; Hazard Ratio [HR]=1.72, p<.001), male sex (HR=1.19, p<.001), younger age (HR=1.34, p<.001), minority race/ethnicity (black HR=1.31, p<.001; Hispanic HR=1.24, p=.01; other HR=1.09, p<.001), capitated insurance (HR=1.21, p<.001), comorbid substance use disorders (alcohol HR=1.07, p=.04; non-opioid drugs HR=1.14, p<.001), hepatitis C (HR=1.06, p=.01), opioid overdose history (HR=1.20, p=.001), or any inpatient care (HR=1.22, p<.001) in

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the 6-month baseline period. In logistic models, these risk factors were similarly associated with significantly lower odds of treatment retention for at least 180 days.

Conclusion: For Medicaid beneficiaries with OUD treated with buprenorphine, there is a need to implement treatment models that more effectively address barriers to treatment retention. These barriers are particularly challenging for minorities, younger individuals, and those with additional substance use disorders.

Keywords

opioid use disorders; Buprenorphine; medication-assisted treatment; Medicaid

1. Introduction

Over the last two decades, opioid use disorder (OUD) has become one of the most pervasive threats to health in the U.S. In 2016, over 2 million adolescents and adults met criteria for an OUD (Center for Behavioral Health Statistics and Quality, Substance Abuse and Mental Health Services Administration, 2017), and individuals with OUD are a high-risk group for overdose and other adverse opioid-related health outcomes including opioid-related death (Rudd, Aleshire, Zibbell, & Gladden, 2016). Although prevention efforts focused on reducing incident OUD through reductions in opioid prescribing (and, therefore, availability, use, and misuse) have made progress (Guy et al., 2017), research focusing on treatment of OUD is urgently needed to inform a comprehensive approach to addressing the opioid epidemic.

Medication is the gold standard treatment for individuals with OUD, and buprenorphine has demonstrated effectiveness in both clinical trials and observational studies (Fiellin et al., 2014; Lo-Ciganic et al., 2016; Murphy & Polsky, 2016; Parran et al., 2010). Buprenorphine treatment is associated with reductions in prescription opioid use, risk of overdose and all-cause mortality as well as higher utilization of addiction treatment and lower rates of treatment dropout (Murphy & Polsky, 2016). Moreover, the association between buprenorphine treatment and improved clinical outcomes is stronger with longer treatment duration (Fiellin et al., 2014; Lo-Ciganic et al., 2016; Parran et al., 2010). Based on the effectiveness of longer treatment, the National Quality Forum (NQF) recently endorsed a measure of minimum OUD treatment duration as at least 180 days of continuous pharmacotherapy (National Quality Forum (NQF), 2017).

Despite robust evidence supporting the effectiveness of medications for OUD, treatment initiation and retention remain a challenge. Less than one-third of adults with prescription OUD ever receive treatment (Blanco et al., 2013). Among those who receive treatment, retention rates are discouragingly low and vary considerably across different follow-up periods and between studies measuring retention at the same follow-up time (Timko, Schultz, Cucciare, Vittorio, & Garrison-Diehn, 2016). Provider characteristics (e.g. specialization, training) (Morgan, Schackman, Leff, Linas, & Walley, 2017; Saloner, Daubresse, Caleb Alexander, & Alexander, 2017; Wisniewski, Dlugosz, & Blondell, 2013) and treatment practices (e.g. buprenorphine dose, program requirements) (Fareed, Vayalapalli, Casarella, & Drexler, 2012; Gryczynski et al., 2014; Walley et al., 2008) may

contribute to variation in retention. Health systems factors can also impede treatment, such as care fragmentation, payment structures (Lembke, 2012; Wisniewski et al., 2013), prescriber and caseload restrictions (Walley et al., 2008), and other resource limitations (Walley et al., 2008). In addition, inadequate health insurance coverage for substance use services can be a barrier to treatment initiation and retention (Mckenna, 2017), and may explain why longer retention has been reported for individuals paying out-of-pocket compared to those with either public or private insurance coverage (Saloner et al., 2017).

Supply-side barriers to buprenorphine treatment for OUD have been widely documented, but less is known about associations between patient characteristics and treatment retention. Patients' expectations about treatment have been found to be largely unrelated to discontinuation, though continued opioid use and conflicts with staff may play an important role (Gryczynski et al., 2014). In contrast, treatment duration may be related to demographic characteristics, such as sex, age, and race/ethnicity (Manhapa, Petrakis, & Rosenheck, 2017; Morgan et al., 2017; Saloner et al., 2017; Weinstein et al., 2017). However, results vary in the direction and magnitude of risk attributable to each characteristic (Manhapa et al., 2017; Saloner et al., 2017; Weinstein et al., 2017). Treatment duration may also be related to clinical characteristics, such as medical and behavioral health comorbidities (Manhapa et al., 2017; Weinstein et al., 2017) or health services received after initiating buprenorphine (Manhapa et al., 2017; Timko et al., 2016).

To date, research examining risk factors for buprenorphine treatment discontinuation among Medicaid enrollees is limited to one single-state study (Lo-Ciganic et al., 2016), despite the high burden of OUD in this population and broad coverage of buprenorphine in Medicaid programs. Adults with Medicaid insurance have elevated rates of OUD compared to adults with private insurance (Medicaid and CHIP Payment and Access Commission (MACPAC), 2017). Although insurance requirements (e.g. prior authorization) and coverage for substance use services varies across states, all state Medicaid programs include coverage for buprenorphine (Grogan et al., 2016). Medicaid spending on prescription medications used to treat OUD has increased substantially in recent years, to nearly a billion dollars in 2016 (Clemans-Cope, Epstein, & Kenney, 2017). With growing demand and investment in medications for OUD treatment, understanding factors related to retention within the Medicaid program is critical to develop practices and policies that improve outcomes and maximize resources. The purpose of this study was to examine continuous buprenorphine treatment in Medicaid and provide more extensive data about risk factors for discontinuation.

2. Material and Methods

2.1. Data source

We analyzed data from the MarketScan® database of Medicaid claims, which is a multi-state sample of insurance claims for approximately 12 million Medicaid enrollees each year from 2013–2015. All claims are de-identified and include a unique identification code that can be used to link enrollee claims across settings and time periods, allowing for longitudinal analyses. MarketScan® data include enrollment information as well as comprehensive inpatient, outpatient, and prescription drug utilization.

2.2. Study sample

We included patients with an opioid use disorder (OUD) diagnosis who were 18–64 years old when they initiated buprenorphine treatment and who were observed for at least 6 months before and after initiating buprenorphine treatment. We excluded individuals if they were eligible for Medicare or if mental health/substance abuse coverage and prescription drug coverage was otherwise not captured in the MarketScan® data.

2.3. Measures

2.3.1. Buprenorphine treatment and other prescription medications—We identified prescription drugs using RedBook® to match drug names with National Drug Codes (NDC) listed on prescription claims (“Red Book,” 2017). Similar to prior studies (Lo-Ciganic et al., 2016; Shcherbakova, Tereso, Spain, & Roose, 2018), we defined buprenorphine treatment initiation as an index buprenorphine claim preceded by at least a 6-month baseline period without any claims for buprenorphine to capture incident treatment episodes. To ensure we included buprenorphine prescribed for OUD and not pain, buprenorphine products that may be used off-label to treat OUD but with approval only to treat pain such as injectables (e.g. Buprenex) and the transdermal patch (e.g. Butrans) were excluded (see Appendix Table A.1). We used the index claim to categorize the initial buprenorphine dose as low (≤ 4 mg) or high (>4 mg) based on guidelines for buprenorphine treatment, which recommend dosage on the first day of treatment as a minimum of 2 mg for those addicted to long-acting opioids or 4 mg for those addicted to short-acting opioids and a maximum of 8 mg (Center for Substance Abuse Treatment, 2004).

We defined buprenorphine treatment discontinuation as >30 days without buprenorphine supply. Previous studies examining buprenorphine treatment episodes used longer, 60-day (Saloner et al., 2017) and 90-day (Hui et al., 2017) definitions of discontinuation. Our goal was to capture discontinuation, rather than gaps in treatment, while also producing results that correspond to the relatively short period after discontinuing treatment in which risk for adverse opioid-related outcomes (e.g. relapse, overdose) is elevated.

We identified opioid and psychotropic medications using prescription drug claims in the baseline 6-month period prior to initiating buprenorphine treatment. Appendix Table A.1 includes a complete list of drug names used to define opioids and psychotropic medications (antidepressants, antipsychotics, mood stabilizers, benzodiazepines, and stimulants).

2.3.2. Opioid use disorders and other comorbid conditions—We used codes from the International Classification of Diseases, 9th and 10th revisions (ICD-9 and ICD-10) to classify opioid use disorders and comorbid conditions (“ICD-9-CM: International Classification of Diseases, 9th revision, clinical modification,” 2015; World Health Organization, 2015). We identified opioid use disorders using primary and secondary diagnoses for opioid dependence or opioid abuse from all inpatient and outpatient claims in the baseline 6-month period prior to initiating buprenorphine treatment and the month in which buprenorphine was initiated (ICD-9 codes: 304.0, 304.7, 305.5; ICD-10 codes: F11).

We also identified comorbidities using primary and secondary diagnoses from all inpatient and outpatient claims in the baseline 6-month period prior to initiating buprenorphine treatment. Appendix Table A.2 includes ICD-9 and ICD-10 codes for comorbid conditions. Mental health comorbidities included measures for depression, anxiety, Post Traumatic Stress Disorder (PTSD), bipolar disorder, and schizophrenia. Substance use comorbidities included measures for alcohol use disorders and non-opioid drug use disorders. Medical comorbidities included measures for chronic pain and hepatitis C.

Finally, we calculated a modified Agency for Healthcare Research and Quality (AHRQ) Elixhauser Comorbidity Index score to adjust for overall medical burden (Moore, White, Washington, Coenen, & Elixhauser, 2017). The index score accounts for 29 medical and mental comorbidities (e.g. HIV, hypertension, obesity, diabetes, heart failure, liver failure, pulmonary disease) and applies weights to each comorbidity according to its predictive relationship with mortality (Moore et al., 2017). We excluded duplicative diagnoses of mental health, substance use, and medical conditions from the final index (i.e. alcohol and drug abuse, depression, bipolar disorder, schizophrenia, hepatitis C).

2.3.3. Health services—We identified health services for opioid and non-opioid drug overdoses using primary and secondary diagnoses from inpatient and outpatient claims in the baseline 6-month period prior to incident buprenorphine treatment. We coded overdoses using all inpatient and outpatient claims and defined them according to a guide from the Centers for Disease Control and Prevention (CDC) National Center for Injury Prevention and Control (Dowell, Haegerich, & Chou, 2016). Appendix Table A.3 includes ICD-9 and ICD-10 codes for overdose services.

We identified inpatient, emergency, and outpatient services using claims in the baseline 6-month period prior to incident buprenorphine treatment. We defined inpatient services as any inpatient claim. We defined emergency services using revenue codes. We defined outpatient therapy and medication management services using procedure codes (Centers for Medicare & Medicaid Services, 2015). Therapy services included individual and group psychotherapy or counseling. Appendix Table A.3 includes procedure codes for outpatient therapy and medication management.

2.4. Analyses

2.4.1. Time to discontinuation—We used Cox proportional hazards regression to estimate the number of days from buprenorphine initiation to discontinuation and to assess risk factors for discontinuation. Covariates included patient demographic characteristics (sex, age, race/ethnicity, insurance plan type), comorbidities (Elixhauser Index, depression, anxiety, bipolar disorder, schizophrenia, alcohol use disorder, non-opioid drug use disorder, chronic pain, hepatitis C), health service use (medically treated opioid and non-opioid drug overdoses, inpatient, emergency, outpatient therapy, outpatient medication management, prescription opioids and psychotropic medications), and initial buprenorphine dose.

2.4.2. Minimum treatment duration—Based on the NQF measure defining minimum treatment duration for OUD as at least 180 days (6 months) of continuous pharmacotherapy (National Quality Forum (NQF), 2017), we used logistic regression to compare individuals

with continuous buprenorphine treatment for a minimum of 6 months to those who discontinued buprenorphine earlier, including the same covariates described above.

3. Results

3.1. Sample characteristics

The sample (N=17,329) was mostly female (64.2%), white (84.5%) and young, with nearly half of individuals aged 25–34 years old (48.9%; Table 1). Most had a comorbid mental health or substance use disorder diagnosis (N=12,368; 71.4%) and nearly half had a chronic pain condition (48.9%). Rates of general health service use were high, with 25.3% receiving inpatient services, 14.9% receiving emergency services, 48.0% receiving outpatient therapy services, and 9.9% receiving medication management services during the 6 months prior to the index buprenorphine prescription fill. Health services for non-opioid drug-related overdose and for opioid-related overdose were received by 4.9% and 3.4% of the sample, respectively. Most individuals had a prescription for at least one psychotropic medication (57.8%), and most also had a prescription for at least one opioid (52.7%).

3.2. Time to discontinuation

Ten percent of the sample discontinued buprenorphine in the first week of treatment (N=1,808, 10.4%), over one-quarter discontinued in the first month (N=4,928; 28.4%) and nearly two-thirds discontinued before 180 days (N=11,189; 64.6%). In the Cox model (Table 2), the strongest risk factor for discontinuation was a low initial dose of buprenorphine (4mg; adjusted Hazard Ratio [HR] = 1.72, $p < .001$). Figure 1 shows the results of time to buprenorphine discontinuation through the first 180 days, stratified by initial dose (low and high).

3.2.1. Demographic characteristics—Compared to females, males had a higher hazard of discontinuation (HR=1.19, $p < .001$). Compared to adults 55–64 years old, three younger age groups had higher hazards of discontinuation (18–24 years HR=1.34, $p < .001$; 25–34 years HR=1.14, $p = .002$; 35–44 years HR = 1.11, $p = .02$). Compared to whites, all minority racial/ethnic groups had higher hazards of discontinuation (black HR=1.31, $p < .001$; Hispanic HR=1.24, $p = .01$; other race/ethnicity HR=1.09, $p < .001$). Compared to those with a FFS insurance plan at baseline, those with capitated insurance plans had a higher hazard of discontinuation (HR=1.21, $p < .001$).

3.2.2. Comorbid conditions—Comorbid substance use disorders were associated with higher hazards of discontinuation (alcohol HR=1.07, $p = .04$; non-opioid drugs HR=1.14, $p < .001$). Comorbid chronic pain conditions were associated with a lower hazard of discontinuation (HR=0.97, $p = .05$), while hepatitis C was associated with a higher hazard of discontinuation (HR=1.06, $p = .01$).

3.2.3. Health service use—Receipt of health services for opioid overdose were associated with a higher hazard of discontinuation (HR=1.20, $p = .001$), but this was not the case for non-opioid drug overdoses. Inpatient service use was associated with a higher hazard of discontinuation (HR=1.22, $p < .001$), but emergency service use, outpatient therapy,

and outpatient medication management were not associated with treatment duration. Prescription opioids and psychotropic medications were not associated with treatment duration of use, except antidepressant use was associated with a lower hazard of discontinuation (HR=0.96, p=.05).

3.3. Minimum treatment duration

We present logistic model results in the right panel of Table 2 (N=17,329). The strongest risk factor for premature discontinuation was a low initial dose of buprenorphine (4mg; Odds Ratio [OR]=0.46, p<.001). With few exceptions, the pattern of results resembled those in the Cox models.

4. Discussion

In this study of adult Medicaid enrollees with OUD, about 10% discontinued buprenorphine in the first week, over 25% discontinued in the first month and nearly two-thirds discontinued in the first 6 months following buprenorphine initiation. The high frequency of early buprenorphine discontinuation underscores the challenges of retaining patients with OUD in treatment. Those who discontinued in the first week may also represent patients who underwent detoxification without being inducted into buprenorphine maintenance treatment, although detoxification alone is not recommended because it is inadequate to treat OUD and increases the risk of subsequent overdose (Center for Substance Abuse Treatment, 2004; O'Connor, 2005; Schuckit, 2016). Demographic characteristics associated with earlier discontinuation included male sex, younger age, minority race/ethnicity, and capitated insurance plans. Clinical risk factors included a history of alcohol and non-opioid drug use disorders, opioid overdose, hepatitis C and inpatient health care utilization. The strongest risk factor for discontinuation was a low initial dose of buprenorphine (4mg or less).

Guidelines for buprenorphine treatment induction recommend up to 8 mg on the first day of treatment with a target to reach 12–16 mg per day within the first week (Center for Substance Abuse Treatment, 2004). In previous research, higher average daily doses of buprenorphine (approximately 16 mg) predicted better treatment retention (Hser et al., 2014; Khemiri, Kharitonova, Zah, Ruby, & Toumi, 2014; Timko et al., 2016), and higher doses received early in treatment were shown to be particularly important for stabilizing and retaining patients (Gryczynski et al., 2014; Timko et al., 2016). Furthermore, higher doses of buprenorphine are associated with lower rates of opioid use during treatment, which is a risk factor for relapse and premature discontinuation (Hser et al., 2014; Hui et al., 2017; Mattick, Breen, Kimber, & Davoli, 2014). A recent study of medical records identified relapse as the most common reason for early discontinuation, particularly among those who discontinued in the first year compared to those with longer treatment (Weinstein et al., 2017). For cases in which treatment with higher doses is clinically appropriate (e.g. patients with more severe substance use disorder histories or prior failed attempts at recovery), prescribing higher doses could improve retention by both better controlling withdrawal symptoms and reducing opioid use (Volkow, Frieden, Hyde, & Cha, 2014).

The observed age gradient in risk for buprenorphine discontinuation is consistent with previous research across settings, which has shown that younger age is associated with

premature discontinuation (Lo-Ciganic et al., 2016; Saloner et al., 2017; Weinstein et al., 2017). The youngest age group had the highest risk and successive age groups had progressively smaller increases in risk of discontinuation compared to adults 55–64 years old. One explanation for the consistent findings that young adults have elevated risk of discontinuation could be developmental, as the young adult brain has not fully matured in regions associated with executive function (e.g. self-control, planning/goal-oriented behavior) (Brorson, Arnevik, Rand-Hendriksen, & Duckert, 2013). However, the age gradient suggests that other factors that are more salient for younger groups, such as the cost of treatment, may also play a role in risk of discontinuation. All individuals in the sample were covered by Medicaid insurance, but out-of-pocket costs likely remain a barrier to buprenorphine treatment retention (Gryczynski et al., 2014). Among those with out-of-pocket spending for buprenorphine medication in this study (N=4,312; 30.1%), mean spending per person on buprenorphine medication alone was \$68, with a median of \$39. Although out-of-pocket spending on buprenorphine medication is distributed over the treatment period, research has shown that cost sharing as low as \$1-\$5 among Medicaid enrollees is associated with reductions in service use (Artiga, Ubri, & Zur, 2017). Furthermore, cost sharing for physician visits, psychotherapy, urinalysis, or other services received as part of treatment may represent additional financial barriers to treatment retention. In combination with findings that most individuals who discontinue treatment relapse within one month and that young adults have particularly high relapse rates (Bentzley, Barth, Back, & Book, 2015), development and evaluation of programs focused on retaining younger people is needed.

Males were not only at increased risk of discontinuation, but also comprised a minority of the sample. The predominantly female sample is similar to those in prior studies specifically examining Medicaid enrollees (Gordon et al., 2015; Khemiri et al., 2014; Lo-Ciganic et al., 2016). In part, the differences observed in treatment duration and risk of premature discontinuation may be related to sex differences in the mechanisms and effects of buprenorphine, along with other social and psychological factors that may vary by sex. Although pharmacological sex differences have not been studied extensively, women may have higher blood concentrations of buprenorphine than men at the same dosage (Moody, Fang, Morrison, & Mccance-Katz, 2011). These differences may be inconsequential at intermediate (i.e. maintenance) doses, but may have important implications at low doses (Moody et al., 2011). Since women are effectively exposed to more buprenorphine than men at the same dosage level, the association between lower initial doses and premature discontinuation may disproportionately impact men. Another potential explanation for the observed sex difference in treatment duration may be related to the antidepressant qualities of buprenorphine (Fava et al., 2016). While the relationship between sex and depression diagnosis and treatment were not examined in this study, antidepressants were associated with a small but significant reduced risk of buprenorphine discontinuation. Since women have higher rates of depression (Eaton et al., 2012; Kessler, 2003) and are more likely to take antidepressants at all levels of depression severity (Pratt, Brody, & Gu, 2011), future studies could examine the relationships between sex, the prevalence and treatment of depression, and retention in buprenorphine treatment.

Similar to prior research (Lo-Ciganic et al., 2016; Saloner et al., 2017; Weinstein et al., 2017), minority racial/ethnic groups had higher risk of premature buprenorphine discontinuation, with black individuals at particularly increased risk. These differences could reflect persistent disparities in access to evidence-based addiction treatment (Substance Abuse and Mental Health Services Administration, 2006). Although we studied a sample of Medicaid beneficiaries, which includes buprenorphine coverage (Grogan et al., 2016), whites remained the overwhelming majority of those receiving services. Thus, factors other than insurance coverage and practices (e.g. prior authorization and reauthorization processes) may also impact treatment retention among minority groups. Specifically, minority populations may have disproportionately less accessible addiction treatment options. Prior research has shown that the proportion of minorities in substance use treatment center patient populations is negatively associated with the availability of medication-based treatments for substance use disorders (Knudsen & Roman, 2009) and that the proportion of minorities in neighborhood populations is negatively associated with buprenorphine availability (Hansen, Siegel, Wanderling, & DiRocco, 2016). Those who initiate treatment may have to travel farther for care, putting them at risk of premature buprenorphine discontinuation (Saloner et al., 2017). Similar to prior studies of buprenorphine treatment duration, we did not examine the specific relationship between race/ethnicity and geographic distance to treatment, but future research could consider treatment availability as one potential source of disparities across racial/ethnic groups. Further research is also needed to identify clinical and service strategies to improve access and quality of care for minority groups potentially facing multiple challenges that could adversely affect their ability to remain in treatment, such as housing or transportation difficulties, competing or untreated health care needs, and lack of provider, peer and social support for recovery.

A history of non-opioid substance use disorders was associated with increased risk of premature buprenorphine discontinuation. By initiating buprenorphine, individuals in this study are among a small minority of those with substance use disorders who receive treatment (Substance Abuse and Mental Health Services Administration, 2017), and are therefore well-positioned to benefit from comprehensive, evidence-based care for other substance use disorders in addition to OUD (Socías, Volkow, & Wood, 2016). Among individuals with substance use disorders, the presence of multiple substance use disorders is not only common but also associated with more persistent problems (McCabe & West, 2017). Among individuals in opioid treatment programs, multiple substance use and disorders may be more widespread and negatively impact OUD treatment, suggesting a need to account for multiple substance use disorders in treatment protocols (Center for Substance Abuse Treatment, 2005). While successful buprenorphine treatment has been linked to reductions in patients' use of other substances, there is no evidence that buprenorphine is an effective treatment for substance use disorders other than OUD (Center for Substance Abuse Treatment, 2005). Rather than discontinue treatment for patients whose substance use is complex or interferes with treatment goals, providing services that address specific co-occurring substance use disorders as well as general substance use problems may improve treatment retention and outcomes (Center for Substance Abuse Treatment, 2005).

We found no association between baseline emergency service use and duration of buprenorphine treatment, but inpatient service use was associated with increased risk of premature discontinuation. Previous research showed associations between earlier treatment discontinuation and both inpatient hospitalizations and emergency department visits (Lo-Ciganic et al., 2016). However, previous research measured emergency services concurrently with buprenorphine treatment (i.e. not isolated to the baseline period), which could explain the discrepancy in findings (Lo-Ciganic et al., 2016). Though patients with a history of emergency service use may not have higher risk of treatment discontinuation, monitoring emergency treatment following medication initiation for OUD may be important to identify individuals who could benefit from targeted interventions to improve retention.

4.1. Limitations

We analyzed data from a multi-state sample of Medicaid administrative claims that are not representative of individuals with no insurance or private coverage. Although the dataset includes around 12 million Medicaid enrollees each year, the results are not representative of all state programs or of all individuals covered by Medicaid insurance who receive treatment for OUD. The results are not generalizable to individuals receiving treatment without an OUD diagnosis who were excluded from the sample to provide confidence that the sample was receiving treatment for OUD rather than for pain. In addition, the results are not generalizable to children and adolescents under age 18, who are less likely to receive medication for OUD (Hadland et al., 2017) and whose medication use may be dependent on caregiver relationships, beliefs, and behaviors (Santer, Ring, Yardley, Geraghty, & Wyke, 2014).

We defined treatment discontinuation as >30 days without buprenorphine supply. Alternate definitions might produce different patterns of results with varying implications for improving retention and outcomes. We measured patient characteristics using information from the 6-month period prior to initiating buprenorphine to assess baseline risk factors that could be used to identify individuals at risk of discontinuation, but longer term medical history and information about health services received after buprenorphine initiation could also help to identify those in need of programs or other resources to improve retention. Furthermore, health insurance claims are somewhat limited in terms of additional patient characteristics that could be important factors related to treatment duration. Patient preferences regarding treatment, illicit drug use behaviors, and psychosocial characteristics (e.g. housing, relationships and legal issues) were not measured.

5. Conclusions

As interventions aimed at reducing incident OUD through reductions in opioid use and misuse continue to make strides (Guy et al., 2017), strategies are also needed to focus on treatment retention among patients identified with OUD along with initiatives to increase the initiation of buprenorphine treatment. Identifying risk factors for buprenorphine discontinuation is important for targeting patients who could benefit from more intensive approaches to improve outcomes. In addition to medical management, evidence-based behavioral therapies (e.g. contingency management) and established care models show great

promise (Carroll & Weiss, 2017; Socías et al., 2016; Williams, Nunes, & Olfson, 2017), and demographic and clinical risk factors should be considered in the development and evaluation of these programs. Within the Medicaid program, increased attention should be given to populations at particularly high risk of early treatment discontinuation, including young, male, and minority patients as well as those with other substance use disorders, prior opioid overdose, and hospital-based service use. Improving their treatment retention may translate into improved outcomes. In addition, future research is needed to understand the relationship between these patient characteristics and patients' treatment perspectives and experiences, which may reveal specific groups for which reducing the burdens of treatment and communicating the benefits of treatment are likely to improve retention (Bentzley, Barth, Back, Aronson, & Book, 2015; Winstock, Lintzeris, & Lea, 2011). Finally, identifying and addressing structural barriers to care, such as insurance coverage limitations, may facilitate treatment initiation and retention.

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Appendix A

Table A.1.

Drugs used to define baseline prescription drug use

Drug Category	Drug Name
Buprenorphine	Buprenorphine Hydrochloride, Buprenorphine/naloxone, and their brand name equivalents
Opioids	Alfentanil, Codeine, Fentanyl, Hydrocodone, Hydromorphone, Levorphanol, Meperidine, Morphine, Nalbuphine, Opium, Oxycodone, Oxymorphone, Pentazocine, Propoxyphene, Remifentanyl, Sufentanyl, Tapentadol, Tramadol, and their brand name equivalents
Antidepressants	Amitriptyline, Amoxapine, Bupropion, Citalopram, Clomipramine, Desipramine, Desvenlafaxine, Doxepin, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Imipramine, Isocarboxazid, Levomilnacipran, Maprotiline, Milnacipran, Mirtazapine, Nefazodone, Nortriptyline, Paroxetine, Phenelzine, Protriptyline, Reboxetine, Selegiline, Sertraline, Tranylcypromine, Trazodone, Trimipramine, Venlafaxine, Vilazodone, Vortioxetine, and their brand name equivalents
Antipsychotics	Aripiprazole, Asenapine, Brexpiprazole, Cariprazine, Chlorpromazine, Clozapine, Fluphenazine, Haloperidol, Iloperidone, Loxapine succinate, Lurasidone, Mesoridazine, Molindone, Olanzapine, Paliperidone, Perphenazine, Pimozide, Promazine, Quetiapine, Risperidone, Thioridazine, Thiothixene, Trifluoperazine, Triflupromazine, Ziprasidone, and their brand name equivalents
Mood stabilizers	Carbamazepine, Cariprazine, Gabapentin, Lamotrigine, Lithium, Oxcarbazepine, Topiramate, Valproic acid/sodium valproate/divalproex sodium, and their brand name equivalents
Benzodiazepines	Adinazolam, Alprazolam, Bentazepam, Bretazenil, Bromazepam, Brotizolam, Camazepam, Chlordiazepoxide, Cinazepam, Cinolazepam, Clobazam, Clonazepam, Clonazolam, Clorazepate, Clotiazepam, Cloxazolam, Delorazepam, Diazepam, Diclazepam, Estazolam, Ethyl carfluzepate, Etizolam, Ethyl Loflazepate, Flubromazepam, Flubromazolam, Flunitrazepam, Flurazepam, Flutazolam, Flutoprazepam, Halazepam, Ketazolam, Loprazolam, Lorazepam, Lormetazepam, Medazepam, Mexazolam, Midazolam, Nifoxipam, Nimetazepam, Nitrazepam, Nordiazepam, Oxazepam, Premazepam, Phenazepam, Pinazepam, Prazepam, Pyrazolam, Rilmazafone, Quazepam, Temazepam, Tetrazepam, Thienalprazolam, Triazolam, and their brand name equivalents
Stimulants	Amphetamine, Armodafinil, Atomoxetine, Dexmethylphenidate, Dextroamphetamine, Lisdexamfetamine, Methamphetamine, Methylphenidate, Modafinil, and their brand name equivalents

Table A.2.

Diagnosis codes used to define baseline mental health and medical comorbidities

Comorbid Condition	ICD-9 Codes	ICD-10 Codes
Depression	296.2, 296.3, 300.4, 311	F32, F33, F34.1
Anxiety	300.0, 300.2, 300.3	F40-F42
PTSD	309.81	F43.1
BPD	296.0, 296.1, 296.4–296.8, 301.13	F31, F34.0
Schizophrenia	295	F20-F21, F25
Alcohol	291, 303, 305.0	F10
Non-opioid drugs	304.1–304.6, 304.8–304.9, 305.2–305.4, 305.6–305.9	F12-F19
Chronic pain	307.81, 337.0, 337.1, 338.0, 338.2, 338.4, 339, 346, 350.2, 354.0, 354.4, 355–357, 377, 710–739, 784.0	E0842, E0942, E1042, E1142, E1342, G43-G44, G50.1, G56.0, G56.4, G57, G58.9, G60-G65, G89.0, G89.2, G89.4, G90.0, G99.0, H46-H47, M00-M02, M05-M08, M11-M25, M30-M99, R26.2, R29.4, R29.898, R51
Hepatitis C	070.41, 070.44, 070.51, 070.54, 070.70, 070.71	B17.10, B17.11, B18.2, B19.20, B19.21

ICD-9 = International Classification of Diseases, 9th Revision (ICD-9); ICD-10 = International Classification of Diseases, 10th Revision (ICD-10)

Note: Opioid use disorders and comorbid conditions were coded using the International Classification of Diseases, applying clinical codes from the Ninth Revision (ICD-9) (“ICD-9-CM: International Classification of Diseases, 9th revision, clinical modification,” 2015) to all claims preceding October 15th, 2015 and codes from the Tenth Revision (ICD-10) (World Health Organization, 2015) to all subsequent claims.

Table A.3.

Procedure codes used to define baseline health service use

Health Service	ICD-9 Codes	ICD-10 Codes	CPT Codes	HCPCS Codes
Opioid overdose	965.0, E850.0-E850.2	T40.0-T40.4		
Non-opioid drug overdose	960–964, 965.1–979, E850.3-E850.9, E851-E858, E950.0-E950.5, E962.0, E980.0-E980.5	T36-T39, T40.5-T40.9, T41-T50		
Therapy	94.3–94.4	GZ5-GZ7, HZ3-HZ6	90785, 90832–90834, 90836–90840, 90845–90847, 90849, 90853	G0409-G0411, H0004-H0005, H0038, H2027, T1006
Medication management	V5883	HZ8	99605–99607, 90863	G0459, M0064

ICD-9 = International Classification of Diseases, 9th Revision; ICD-10 = International Classification of Diseases, 10th Revision; CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System

Note: Outpatient therapy and medication management services were coded using the International Classification of Diseases, applying clinical codes from the Ninth Revision (ICD-9) (“ICD-9-CM: International Classification of Diseases, 9th revision, clinical modification,” 2015) to all claims preceding October 15th, 2015 and codes from the Tenth Revision (ICD-10) (World Health Organization, 2015) to all subsequent claims and applying Level I (Current Procedural Terminology; CPT) and Level II codes from the Healthcare Common Procedure Coding System (HCPCS) to all claims (Centers for Medicare & Medicaid Services, 2015).

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Highlights:

- A minority of individuals with OUD are effectively retained on buprenorphine
- Discontinuation soon after initiation warrants further study to assess potential buprenorphine use for detoxification rather than treatment
- Low initial dose (4 mg) is a particularly strong risk factor for discontinuation
- Younger age, minority race/ethnicity, and a history of non-opioid substance use disorders are also risk factors for discontinuation
- Psychiatric comorbidities are *not* significant risk factors for discontinuation

Figure 1.
Proportion of adults 18–64 years old with OUD who were retained on buprenorphine during the first 180 days following treatment initiation (starting N=17,329)

Table 1.

Baseline demographic and clinical characteristics of adults 18–64 years old with OUD who initiated buprenorphine treatment between 2013–2015 (N=17,329)

	N	%
Demographics		
<i>Sex</i>		
Female	6,198	35.8
Male	11,131	64.2
<i>Age</i>		
18–24	2,339	13.5
25–34	8,466	48.9
35–44	4,165	24.0
45–54	1,722	9.9
55–64	637	3.7
<i>Race/ethnicity</i>		
White	14,649	84.5
Black	836	4.8
Hispanic	177	1.0
Other	1,667	9.6
<i>Insurance</i>		
FFS	3,868	22.3
Capitation	13,461	77.7
Comorbidities		
<i>Mental Health</i>		
Depression	4,580	26.4
Anxiety	5,682	32.8
PTSD	621	3.6
Bipolar Disorder	2,319	13.4
Schizophrenia	359	2.1
<i>Substance Use</i>		
Alcohol	1,648	9.5
Non-opioid drugs	7,624	44.0
<i>Medical</i>		
Pain	8,470	48.9
Hepatitis C	2,366	13.7
Health Services		
<i>Overdose treatment</i>		
Non-opioid drugs	857	4.9
Opioids	590	3.4
<i>Inpatient</i>	4,379	25.3

	N	%
<i>Emergency</i>	2,578	14.9
<i>Outpatient</i>		
Therapy	8,314	48.0
Medication management	1,708	9.9
Prescription drugs		
<i>Psychotropic drugs</i>	10,018	57.8
Antidepressants	7,577	43.7
Antipsychotics	2,535	14.6
Mood stabilizers	4,222	24.4
Benzodiazepines	4,299	24.8
Stimulants	792	4.6
<i>Opioids</i>	9,135	52.7
<i>Buprenorphine</i>		
Initial dose >4 MG	2,155	12.4
Initial dose ≤ 4 MG	15,174	87.6

Source: Authors' analysis of MarketScan Medicaid claims, 2013–2015

Table 2.

Adjusted model results for buprenorphine discontinuation among adults 18–64 years old with OUD who initiated buprenorphine treatment between 2013–2015 (N=17,329)

	Time to discontinuation ^a			Minimum treatment duration ^b		
	HR	95% CI	p	OR	95% CI	p
Demographics						
<i>Sex</i>						
Female	Ref.	—	—	Ref.	—	—
Male	1.19	1.15–1.24	<.001	0.73	0.68–0.78	<.001
<i>Age</i>						
18–24	1.34	1.22–1.47	<.001	0.56	0.46–0.68	<.001
25–34	1.14	1.05–1.24	.002	0.74	0.62–0.88	.001
35–44	1.11	1.02–1.21	.02	0.80	0.67–0.96	.02
45–54	1.06	0.96–1.16	.25	0.82	0.67–1.00	.04
55–64	Ref.	—	—	Ref.	—	—
<i>Race/ethnicity</i>						
White	Ref.	—	—	Ref.	—	—
Black	1.31	1.19–1.43	<.001	0.59	0.50–0.69	<.001
Hispanic	1.24	1.06–1.46	.01	0.66	0.47–0.94	.02
Other	1.09	1.04–1.15	<.001	1.04	0.93–1.17	.45
<i>Insurance</i>						
FFS	Ref.	—	—	Ref.	—	—
Capitation	1.21	1.16–1.25	<.001	0.69	0.64–0.74	<.001
Comorbidities						
<i>Mental Health</i>						
Depression	0.99	0.95–1.03	.56	1.05	0.97–1.14	.24
Anxiety	0.98	0.94–1.02	.32	1.01	0.93–1.09	.80
PTSD	0.99	0.91–1.08	.83	0.98	0.82–1.17	.83
Bipolar Disorder	1.00	0.95–1.06	.93	1.01	0.91–1.13	.87
Schizophrenia	1.02	0.91–1.15	.76	0.96	0.75–1.22	.73
<i>Substance Use</i>						
Alcohol	1.07	1.00–1.13	.04	0.82	0.73–0.92	.001
Non-opioid drugs	1.14	1.11–1.18	<.001	0.84	0.78–0.90	<.001
<i>Medical</i>						
Pain	0.97	0.93–1.00	.05	1.03	0.96–1.11	.40
Hepatitis C	1.06	1.01–1.11	.01	0.97	0.88–1.07	.57
<i>Elixhauser Index</i>	1.00	1.00–1.00	.82	1.00	0.99–1.01	.59
Health Services						
<i>Overdose treatment</i>						

	Time to discontinuation ^a			Minimum treatment duration ^b		
	HR	95% CI	p	OR	95% CI	p
Non-opioid drugs	0.95	0.87–1.04	.30	1.02	0.85–1.23	.83
Opioids	1.20	1.08–1.34	.001	0.71	0.56–0.89	.003
<i>Inpatient</i>	1.22	1.16–1.29	<.001	0.71	0.64–0.79	<.001
<i>Emergency</i>	0.95	0.89–1.02	.19	1.01	0.88–1.16	.91
<i>Outpatient</i>						
Therapy	0.99	0.96–1.03	.76	0.98	0.92–1.05	.65
Medication management	0.99	0.93–1.06	.82	0.99	0.87–1.11	.83
Prescription drugs						
<i>Psychotropic drugs</i>						
Antidepressants	0.96	0.93–1.00	.05	1.06	0.98–1.14	.13
Antipsychotics	1.01	0.96–1.06	.80	0.97	0.87–1.08	.61
Mood stabilizers	1.03	0.98–1.07	.23	1.02	0.94–1.11	.67
Benzodiazepines	0.97	0.93–1.01	.16	1.01	0.93–1.10	.78
Stimulants	0.98	0.91–1.06	.63	0.96	0.82–1.11	.57
<i>Opioids</i>	1.01	0.97–1.05	.60	0.97	0.91–1.05	.49
<i>Buprenorphine</i>						
Initial dose >4 MG	Ref.	—	—	Ref.	—	—
Initial dose ≤4 MG	1.72	1.62–1.83	<.001	0.46	0.41–0.51	<.001

HR = hazard ratio; OR = odds ratio; CI = confidence interval

^aContinuous time to discontinuation was measured using Cox proportional hazard regression

^bMinimum treatment duration was measured using logistic regression to estimate continuous buprenorphine use for at least 180 days

Notes: For Cox regression, the proportional hazards assumption was assessed by visual inspection of log-log plots, plots of the Kaplan-Meier observed survival curves compared with the Cox predicted curve, and scaled Schoenfeld residual plots (Grambsch & Therneau, 1994). Model fit for logistic regression was tested using the Pearson goodness-of-fit test. The observed and predicted values are not significantly different ($p=.20$), indicating good model fit. Source: Authors' analysis of MarketScan Medicaid claims, 2013–2015