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## Do out-of-pocket costs influence retention and adherence to medications for opioid use disorder?

Christopher Dunphy\*, Cora Peterson, Kun Zhang, Christopher M. Jones

National Center for Injury Prevention and Control, Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA

### Abstract

**Background:** Availability of medications for opioid use disorder (MOUD) has increased during the past two decades but treatment retention and adherence remain low. This study aimed to measure the impact of out-of-pocket buprenorphine cost on treatment retention and adherence among US commercially insured patients.

**Methods:** Medical payment records from IBM MarketScan were analyzed for 6,439 adults age 18–64 years with commercial insurance who initiated buprenorphine treatment during January 1, 2016 to June 30, 2017. Regression models analyzed the relationship between patients' average daily out-of-pocket buprenorphine cost and buprenorphine retention (at least 80 % days covered by buprenorphine) at three different thresholds (180, 360, and 540 days) and adherence (the number of days of buprenorphine coverage) within each retention threshold. Models controlled for patient demographic and clinical characteristics including age, sex, presence of other substance use disorders, psychiatric and pain diagnoses, and receipt of prescription medications.

**Results:** A one dollar increase in daily out-of-pocket buprenorphine cost was associated with a 12–14 % decrease in the odds of retention and a 5–8 % increase in the number of days without buprenorphine coverage during each analyzed retention threshold.

**Conclusion:** Recent policies have attempted to address supply-side barriers to MOUD treatment. This study highlights patient cost-sharing as a demand-side barrier to MOUD. While the average out-of-pocket buprenorphine cost is lower than two decades ago, this study suggests even at current levels such costs decrease retention and adherence among commercially insured patients.

\*Corresponding author at: Mailstop 106-8, 4770 Buford Highway, CDC National Center for Injury Prevention and Control, Atlanta, GA, 30341, USA., ppz1@cdc.hhs.gov (C. Dunphy).

#### Author contributions

Christopher Dunphy conducted the analysis, study design, and manuscript drafting. Cora Peterson assisted in drafting the manuscript, developing the research design, and interpreting the results. Kun Zhang assisted in data preparation, research design, manuscript drafting, and interpretation of results. Christopher Jones assisted in providing clinical expertise and assisted in interpretation of results. All authors provided critical revisions to the manuscript and approved the final manuscript as submitted. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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The authors have no relevant financial relationships interest to disclose.

#### Declaration of Competing Interest

The authors report no declarations of interest.

#### Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.drugalcdep.2021.108784>.

Efforts to address demand-side barriers could help maximize the health and social benefits of buprenorphine-based MOUD.

## Keywords

Opioid-related disorders; Medication adherence; Health expenditures

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## 1. Introduction

Expanding use of medications for opioid use disorder (MOUD) such as buprenorphine is a major component of the public health response to the opioid overdose epidemic, which caused nearly 50,000 drug overdose deaths in 2019 (Mattson et al., 2021). More recent provisional data suggest that annual deaths continue to rise in 2020 (Centers for Disease Control and Prevention, 2020). Escalating OUD-related mortality has been explicitly tied to an inability to fully deploy proven strategies including MOUD (National Academies of Sciences and Medicine, 2019). Buprenorphine has been available as an evidence-based treatment via prescription since 2002 and legislation in the past two decades has expanded access to buprenorphine (SAMHSA, 2020).

Longer buprenorphine retention (12–18 months with treatment) and better adherence (more days with buprenorphine supply) are associated with less opioid use, fewer costly opioid-related health care events such as inpatient admissions, and fewer overdoses (Ruetsch et al., 2017; Samples et al., 2020; Williams et al., 2020). Still, buprenorphine remains underutilized (Andrilla et al., 2017; Beetham et al., 2019). Less than one third of patients are retained at 180 days and over half of commercially-insured patients discontinue buprenorphine before 12 months (Agbese et al., 2020; American Society of Addiction Medicine, 2020; Olfson et al., 2020). Low utilization has been attributed to the limited number of clinicians authorized to prescribe buprenorphine, as well as a limit on the number of patients that can be treated per clinician (SAMHSA, 2020). In recent years in most US states the number of people with OUD exceeded buprenorphine prescribing capacity (Jones et al., 2015).

However, clinicians have also reported low patient demand for buprenorphine (Jones and McCance-Katz, 2019; Louie et al., 2019). Shorter retention in buprenorphine treatment has been linked to patients' perceived inflexibility of treatment (Gryczynski et al., 2014), low daily dosage (Lo-Ciganic et al., 2019; Muruganandam et al., 2019), patient stress and emotions (Panlilio et al., 2019), other substance use disorders (Samples et al., 2018), exposure to actively using peers (Velasquez et al., 2019) and stigma surrounding MOUD treatment (Barry et al., 2014). Patients and clinicians also identify insurance factors and cost as inhibiting factors (Jones and McCance-Katz, 2019; Timko et al., 2016). There is some evidence that insurers impose more restrictions and require more cost-sharing at a higher rate for buprenorphine than medication treatment for alcohol use disorder and that some patients lower their buprenorphine fill rate in response to higher out-of-pocket costs (McClellan et al., 2019; Peters and Wengle, 2016).

The average out-of-pocket expenditure for a 30-day buprenorphine prescription among patients with commercial insurance was \$32 in 2013–2015 compared to \$67 in 2003

(Agbese et al., 2020; Roberts et al., 2018). It is important to contextualize this amount—already intuitively a non-trivial amount for patients to face every month—with evidence that the average total out-of-pocket health care cost among patients with commercial insurance still taking buprenorphine at 12 months was nearly \$3,000 in 2013 (Agbese et al., 2020). Given recent changes to address supply-side issues that have hindered prescribing of buprenorphine (SAMHSA, 2020), it is critical to further analyze demand-side issues that may inhibit use of MOUD despite expanded access. This study aimed to measure the impact of out-of-pocket buprenorphine cost on treatment retention and adherence among US commercially insured patients.

## 2. Material and methods

This study examined health insurance payments (inpatient, outpatient, outpatient pharmacy dispensing) from IBM MarketScan Commercial Claims and Encounters Database. MarketScan includes commercial health plans and self-insured employers and is one of the largest data sources on the US commercially insured population. Patients were analyzed if they: 1) initiated buprenorphine-based MOUD (identified by National Drug Codes [NDC] excluding buprenorphine pain formulations, Belbuca and Butrans) with 7-day total supply (to potentially exclude treatment for short-term opioid withdrawal) during January 1, 2016 to June 30, 2017 (index prescription); 2) had continuous insurance enrollment including prescription drug coverage for 6 months before and 18 months after the index prescription; and 3) had no buprenorphine prescriptions 6 months before the index prescription.

The main outcome measures were buprenorphine retention and adherence. Retention was defined as 80 % days with buprenorphine supply (observed through patients' prescription fill date and days' supply) and 60 days' gap (no buprenorphine possession) using three retention thresholds: 180, 360, and 540 days. Overlapping buprenorphine prescriptions were separately counted. Adherence was defined by the number of days with buprenorphine supply among retained patients during each analyzed retention threshold.

Patients' out-of-pocket buprenorphine cost was the sum of the associated co-pay, co-insurance, and deductible. Patients' average daily out-of-pocket buprenorphine cost was calculated as the total out-of-pocket buprenorphine cost divided by the total days supplied. Patient sex, age, and residential Census region were analyzed as reported in the MarketScan enrollment file. Patients' other substance use disorder diagnoses, psychiatric diagnoses, and pain diagnoses (inpatient or outpatient) 3 months before the index prescription were identified by ICD-10-CM diagnosis codes (Supplemental Table 1). Patients' buprenorphine dosage was converted to Suboxone dosage (Supplemental Table 2). Patients' outpatient prescriptions for four other drug classes—antidepressants, opioid analgesics, benzodiazepines, and stimulants—3 months before index prescription were identified by NDC.

A multivariable logistic regression model estimated the association between patients' average daily out-of-pocket buprenorphine cost and treatment retention for each analyzed retention threshold, controlling for patient demographic and clinical characteristics. A multivariable Poisson regression model estimated the association between patients' average

daily out-of-pocket buprenorphine cost and treatment gaps (or, days patients were without buprenorphine supply) for each analyzed retention threshold. Sensitivity analysis examined results using: 1) retention defined by 70 % and 90 % of days with buprenorphine supply, 2) restricting analysis to patients with continuous insurance enrollment in 2016, 2017, and 2018; and 3) restricting analysis to patients with 1 OUD clinical diagnosis 3 before the index prescription. This study used publicly available data and no human subjects. Analysis was conducted using SAS Software Version 9.4.

### 3. Results

The total number of patients identified as initiating buprenorphine treatment was 6,439. The likelihood that patients were retained in MOUD treatment decreased as the retention threshold increased, with 49 % of analyzed patients retained in treatment at 180 days, 41 % at 360 days, and 37 % at 540 days (Table 1). Over 94 % of patients faced some out-of-pocket buprenorphine cost but patients retained in treatment had lower average daily out-of-pocket costs than those who discontinued treatment for all three analyzed retention thresholds. The average daily out-of-pocket buprenorphine cost was \$1.91/day for patients retained in treatment at the 180-day threshold compared to \$2.63/day for those who discontinued treatment within 180 days, \$1.76/day compared to \$2.38/day at 360 days, and \$1.74/day compared to \$2.27 at 540 days ( $p < 0.05$  for all) (Table 1). Patients that discontinued treatment during all analyzed retention thresholds also had a lower average buprenorphine dose, were younger (aged 18–34 years), more often resided in the South or West region of the country, more often had other substance use disorder diagnoses (alcohol, cannabis, sedatives, cocaine, stimulants), psychiatric diagnoses (bipolar disorder, major depression, post-traumatic stress disorder), more often dispensed a prescription stimulant, and were less likely to have an osteoarthritis diagnosis or an opioid prescription prior to starting buprenorphine ( $p < 0.05$  for all) (Table 1).

In multivariable analysis, a \$1 increase in patients' average daily out-of-pocket buprenorphine cost was associated with a 12 %, 14 %, and 13 % decrease ( $p < 0.05$  for all) in the odds of treatment retention at 180, 360, and 540 days, respectively, controlling for patients' demographic characteristics, other prescriptions, and SUD, psychiatric, and pain diagnoses (Table 2). For patients retained in treatment, a \$1 increase in patients' average daily out-of-pocket buprenorphine cost was associated with a 5%, 8%, and 8% increase ( $p < 0.05$  for all) in the number of days without buprenorphine supply (roughly equivalent to missing 1.5 weeks, 1 month, and 1.5 months) during retention periods at the 180-, 360-, and 540-day thresholds, respectively, again controlling for patients' demographic and clinical characteristics (Table 2 and Supplemental Table 3 [complete model estimates]). The direction and magnitude of base case results was not substantively changed in the sensitivity analyses (data available upon request).

### 4. Discussion

This study's primary contribution is directly quantifying the association between patients' average daily out-of-pocket buprenorphine cost and retention and adherence. Controlling for observable factors previously identified to be associated with buprenorphine use, this study

found that higher average out-of-pocket buprenorphine cost is associated with reduced buprenorphine retention and increased gaps in treatment coverage. For example, a \$1 dollar increase in the daily out-of-pocket cost for buprenorphine decreased the likelihood of retention at 360 days by 14 % and increased the number of days without coverage by roughly one month for those still in treatment at 360 days.

These findings are important in the context of recent policymaking to expand access to office-based outpatient buprenorphine treatment as well as clinical recommendations on the minimum retention of 180 days for desired treatment outcomes (National Quality Forum, 2017). Longer buprenorphine retention and better adherence are linked to less opioid use, fewer costly opioid-related health care events, and fewer overdoses (Ruetsch et al., 2017; Samples et al., 2020; Williams et al., 2020). This study supports other recent research in concluding that demand-side factors inhibiting buprenorphine use, including patient out-of-pocket cost, must be addressed to fully realize the benefits of MOUD. The results of this study could be applied in cost-benefit analysis among commercial insurance providers—that is, weighing revenue from patient buprenorphine cost-sharing against the consequences of high-cost healthcare events that are more likely among patients with shorter retention in buprenorphine treatment (Samples et al., 2018.). The cost of a single ED visit or inpatient admission with principal diagnosis of opioid-related disorder is approximately \$1,700 and \$9,000 respectively (2017 USD) (Peterson et al., 2021), whereas this study's estimated average out-of-pocket cost for buprenorphine treatment for 360 days is \$765.

This study's finding that out-of-pocket buprenorphine cost is negatively associated with buprenorphine use is supported by analytic methods presented here that addressed both the extensive (treatment retention) and intensive margins (treatment adherence during retention). Previous research on the price elasticity of demand for pharmaceuticals based on the intensive margin has demonstrated that patients may respond differently to price changes based on drug class (Gatwood et al., 2014). Previous research on buprenorphine cost-sharing demonstrated a statistically significant reduction in buprenorphine prescription fills during 2011–2015 associated with increased cost sharing only among some patient subgroups (patients age 45–64 years, those with rural or South region residence, and those enrolled in a health maintenance organization) (McClellan et al., 2019). The present study's finding with more recent data that average out-of-pocket buprenorphine cost is associated with shorter retention in buprenorphine treatment and less adherence among patients overall suggests that even though the average out-of-pocket buprenorphine price is lower now than 20 years ago, more patients with OUD are less willing or able to sustain that cost and continue buprenorphine treatment.

This study is subject to several limitations. First, this study was not able to control for patients' OUD duration and severity, which might affect MOUD initiation and continuation. Second, this study was not able to examine socioeconomic differences that might account for some patients' greater sensitivity to out-of-pocket costs. Third, this study examined prescription fills but could not observe actual use. Fourth, this study did not examine concurrent services such as behavioral therapy that might be associated with patients' MOUD retention and adherence. Finally, this study is limited to commercially insured patients and results may not be generalizable to different health insurance.

## 5. Conclusions

Recent policies have addressed supply-side inhibitors of MOUD treatment by making it easier for clinicians to prescribe buprenorphine to a greater number of patients. This study highlights cost as a demand-side barrier, suggesting that public health and insurer strategies aimed at reducing patient cost-sharing could improve buprenorphine treatment retention. Although the average out-of-pocket buprenorphine cost is lower than two decades ago, even at current levels such costs decrease retention and adherence among commercially insured patients. Efforts to address demand-side barriers, such as reducing patient cost-sharing, could help fully maximize the health and social benefits of buprenorphine-based MOUD.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Funding source

No external funding.

## Abbreviations:

<b>ADHD</b>	attention deficit hyperactivity disorder
<b>IRR</b>	incidence rate ratio
<b>MOUD</b>	medications for opioid use disorder
<b>PTSD</b>	post-traumatic stress disorder
<b>SUD</b>	substance use disorder

## References

- Agbese E, Leslie DL, Manhapra A, Rosenheck R, 2020. Early discontinuation of buprenorphine therapy for opioid use disorder among privately insured adults. *Psychiatr. Serv. (Washington, D.C.)* 71 (8), 779–788.
- American Society of Addiction Medicine, 2020. The ASAM national practice guideline for the treatment of opioid use disorder: 2020 focused update. *J. Addict. Med* 14 (2S Suppl 1), 1–91.
- Andrilla CHA, Coulthard C, Larson EH, 2017. Barriers rural physicians face prescribing buprenorphine for opioid use disorder. *Ann. Fam. Med* 15, 359–362. [PubMed: 28694273]
- Barry CL, McGinty EE, Pescosolido BA, Goldman HH, 2014. Stigma, discrimination, treatment effectiveness, and policy: public views about drug addiction and mental illness. *Psychiatr. Serv. (Washington, D.C.)* 65 (10), 1269–1272.
- Beetham T, Saloner B, Wakeman SE, Gaye M, Barnett ML, 2019. Access to office-based buprenorphine treatment in areas with high rates of opioid-related mortality. *Ann. Intern. Med* 171, 1–9. [PubMed: 31158849]
- Centers for Disease Control and Prevention, 2020. 12 Month-Ending Provisional Number of Drug Overdose Deaths by Drug or Drug Class. <https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm>.
- Gatwood J, Gibson TB, Chernew ME, Farr AM, Vogtmann E, Fendrick AM, 2014. Price elasticity and medication use: cost sharing across multiple clinical conditions. *J. Manag. Care Spec. Pharm* 20 (11), 1102–1107. [PubMed: 25351971]



- Gryczynski J, Mitchell SG, Jaffe JH, O'Grady KE, Olsen YK, Schwartz RP, 2014. Leaving buprenorphine treatment: patients' reasons for cessation of care. *J. Subst. Abuse Treat* 46 (3), 356–361. [PubMed: 24238714]
- Jones CM, McCance-Katz EF, 2019. Characteristics and prescribing practices of clinicians recently waived to prescribe buprenorphine for the treatment of opioid use disorder. *Addiction* (Abingdon, England) 114 (3), 471–482.
- Jones CM, Campopiano M, Baldwin G, McCance-Katz E, 2015. National and state treatment need and capacity for opioid agonist medication-assisted treatment. *Am. J. Public Health* 105 (8), e55–63.
- Lo-Ciganic WH, Donohue JM, Kim JY, Krans EE, Jones BL, Kelley D, James AE, Jarlenski MP, 2019. Adherence trajectories of buprenorphine therapy among pregnant women in a large state Medicaid program in the United States. *Pharmacoepidemiol. Drug Saf.* 28 (1), 80–89. [PubMed: 30192041]
- Louie DL, Assefa MT, McGovern MP, 2019. Attitudes of primary care physicians toward prescribing buprenorphine: a narrative review. *BMC Fam. Pract* 20 (1), 1–8. [PubMed: 30606122]
- Mattson CL, Tanz LJ, Quinn K, Kariisa M, Patel P, Davis NL, 2021. Trends and geographic patterns in drug and synthetic opioid overdose deaths - United States, 2013–2019. *Morbidity and Mortality Weekly Rep.* 70 (6), 202–207.
- McClellan C, Fingar KR, Ali MM, Olesiuk WJ, Mutter R, Gibson TB, 2019. Price elasticity of demand for buprenorphine/naloxone prescriptions. *J. Subst. Abuse Treat* 106, 4–11. [PubMed: 31540610]
- Muruganandam P, Shukla L, Sharma P, Kandasamy A, Chand P, Murthy P, 2019. 'Too little dose - too early discontinuation?'-Effect of buprenorphine dose on short term treatment adherence in opioid dependence. *Asian J. Psychiatr* 44, 58–60. [PubMed: 31325758]
- National Academies of Sciences, E., Medicine, 2019. *Medications for Opioid Use Disorder Save Lives*. The National Academies Press, Washington, DC.
- National Quality Forum, 2017. Behavioral Health 2016–2017: Technical Report, [https://www.qualityforum.org/Publications/2017/08/Behavioral\\_Health\\_2016-2017\\_Final\\_Report.aspx](https://www.qualityforum.org/Publications/2017/08/Behavioral_Health_2016-2017_Final_Report.aspx).
- Olfson M, Zhang V, Schoenbaum M, King M, 2020. Buprenorphine treatment by primary care providers, psychiatrists, addiction specialists, and others. *Health Aff.* 39 (6), 984–992.
- Panlilio LV, Stull SW, Kowalczyk WJ, Phillips KA, Schroeder JR, Bertz JW, Vahabzadeh M, Lin JL, Mezghanni M, Nunes EV, Epstein DH, Preston KL, 2019. Stress, craving and mood as predictors of early dropout from opioid agonist therapy. *Drug Alcohol Depend.* 202, 200–208. [PubMed: 31357121]
- Peters R, Wengle E, 2016. Coverage of Substance-Use Disorder Treatments in Marketplace Plans in Six cCities. Urban Institute, Washington, DC.
- Peterson C, Li M, Xu L, Mikosz CA, Luo F, 2021. Annual cost of substance use disorder in US hospitals. *Jama Netw. Open* 4 (3), e210242. [PubMed: 33666661]
- Roberts AW, Saloner B, Dusetzina SB, 2018. Buprenorphine Use and Spending for Opioid Use Disorder Treatment: Trends From 2003 to 2015. *Psychiatr. Serv. (Washington, D.C.)* 69 (7), 832–835.
- Ruetsch C, Tkacz J, Nadipelli VR, Brady BL, Ronquest N, Un H, Volpicelli J, 2017. Heterogeneity of nonadherent buprenorphine patients: subgroup characteristics and outcomes. *Am. J. Manag. Care* 23 (6), e172–e179. [PubMed: 28817294]
- SAMHSA, 2020. Statutes, Regulations, and Guidelines (Accessed November 16 2020). <https://www.samhsa.gov/medication-assisted-treatment/statutes-regulations-guidelines>.
- Samples H, Williams AR, Olfson M, Crystal S, 2018. Risk factors for discontinuation of buprenorphine treatment for opioid use disorders in a multi-state sample of Medicaid enrollees. *J. Subst. Abuse Treat* 95, 9–17. [PubMed: 30352671]
- Samples H, Williams AR, Crystal S, Olfson M, 2020. Impact Of Long-Term Buprenorphine Treatment On Adverse Health Care Outcomes In Medicaid. *Health Aff. (Project Hope)* 39 (5), 747–755.
- Timko C, Schultz NR, Cucciare MA, Vittorio L, Garrison-Diehn C, 2016. Retention in medication-assisted treatment for opiate dependence: a systematic review. *J. Addict. Dis* 35 (1), 22–35. [PubMed: 26467975]

- Velasquez M, Flannery M, Badolato R, Vittitow A, McDonald RD, Tofighi B, Garment AR, Giftos J, Lee JD, 2019. Perceptions of extended-release naltrexone, methadone, and buprenorphine treatments following release from jail. *Addict. Sci. Clin. Pract* 14 (1), 37. [PubMed: 31570100]
- Williams AR, Samples H, Crystal S, Olfson M, 2020. Acute care, prescription opioid use, and overdose following discontinuation of long-term buprenorphine treatment for opioid use disorder. *Am. J. Psychiatry* 177 (2), 117–124. [PubMed: 31786933]

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**Table 1**

Patient characteristics by buprenorphine retention period.

	Buprenorphine Retention Period			
	180 days	360 days	540 days	Retained <sup>a</sup>
Patients, n (%)	3,134 (49%)	3,305 (51%)	2,664 (41%)	3,805 (59%)
Buprenorphine				4,067 (62%)
Any out-of-pocket cost, n (%)	3,013 (96)	3,101 (94)*	2,626 (99)	3,605 (95)*
Out-of-pocket cost/day	\$1.91	\$2.63*	\$1.76	\$2.38*
Mean daily dose, mg	14.16	13.33*	14.18	13.43*
Demographics, n (%)				
Male	1,977 (63)	2,046 (62)	1,709 (64)	2,333 (61)*
Age: 18–34 years	1,238 (40)	1,733 (52)*	1,016 (38)	1,971 (52)*
Age: 35–44 years	867 (28)	645 (20)*	762 (29)	751 (20)*
Age: 45–54 years	610 (19)	559 (17)*	526 (20)	644 (17)*
Age: 55–64 years	419 (13)	368 (11)*	360 (14)	439 (12)*
Northeast region	666 (21)	763 (23)	574 (22)	864 (23)
Midwest region	604 (19)	659 (20)	519 (19)	745 (20)
South region	1,493 (48)	1,355 (41)*	1,266 (48)	1,600 (42)*
West region	371 (12)	528 (16)*	305 (11)	596 (16)*
Substance use disorders, n (%)				
Opioid	1,828 (58)	1,871 (57)	1,557 (58)	2,168 (57)
Alcohol	173 (6)	291 (9)*	141 (5)	328 (9)*
Cannabis	117 (4)	288 (9)*	103 (4)	309 (8)*
Sedatives	130 (4)	248 (8)*	109 (4)	272 (7)*
Cocaine	59 (2)	153 (5)*	51 (2)	165 (4)*
Stimulants	47 (2)	152 (5)*	37 (1)	169 (4)*
Nicotine	352 (11)	384 (12)	302 (11)	440 (12)
				266 (11)
				481 (12)
				2,324 (57)
				1,419 (58)
				133 (5)
				344 (8)*
				87 (4)
				332 (8)*
				94 (4)
				295 (7)*
				42 (2)
				180 (4)*
				27 (1)
				182 (4)*
				266 (11)
				481 (12)

Psychiatric diagnosis, n (%)	Buprenorphine Retention Period					
	180 days		360 days		540 days	
	Retained <sup>d</sup>	Not retained	Retained <sup>d</sup>	Not retained	Retained <sup>d</sup>	Not retained
Anxiety	777 (25)	855 (26)	644 (24)	994 (26)	572 (24)	1,077 (26)*
Bipolar disorder	132 (4)	195 (6)*	116 (4)	214 (6)*	94 (4)	238 (6)*
Major depression	597 (19)	712 (22)*	506 (19)	811 (21)*	453 (19)	874 (21)*
Other mood disorder	102 (3)	131 (4)	86 (3)	147 (4)	79 (3)	155 (4)
ADHD	182 (6)	215 (7)	154 (6)	246 (6)	128 (5)	275 (7)*
PTSD	45 (1)	81 (2)*	44 (2)	83 (2)	35 (1)	94 (2)*
Schizophrenia	17 (1)	29 (1)	16 (1)	30 (1)	14 (1)	33 (1)
Pain diagnosis						
Back pain	873 (28)	911 (28)	736 (28)	1,051 (28)	656 (27)	1,137 (28)
Neck pain	347 (11)	388 (12)	289 (11)	448 (12)	263 (11)	478 (12)
Migraine	119 (4)	136 (4)	98 (4)	158 (4)	92 (4)	164 (4)
Fibromyalgia	74 (2)	89 (3)	60 (2)	103 (3)	49 (2)	114 (3)
Osteoarthritis	250 (8)	193 (6)*	215 (8)	229 (6)*	187 (8)	257 (6)*
Inflammatory joint disorder	468 (15)	466 (14)	390 (15)	545 (14)	356 (15)	580 (14)
Periarticular	121 (4)	143 (4)	96 (4)	168 (4)	85 (4)	179 (4)
Other medications prior to treatment						
Opioids	1,428 (46)	1,402 (42)*	1,218 (46)	1,618 (43)*	1,107 (46)	1,731 (43)*
Antidepressants	1,227 (39)	1,332 (40)	1,033 (39)	1,540 (40)	935 (39)	1,652 (41)
Benzodiazepines	812 (26)	992 (30)*	667 (25)	1,144 (30)*	595 (25)	1,221 (30)*
Stimulants	268 (9)	333 (10)*	221 (8)	383 (10)*	194 (8)	411 (10)*

Notes. Data Source: IBM® MarketScan® commercial claims and encounters database.

ADHD = attention deficit hyperactivity disorder, PTSD = post-traumatic stress disorder.

\* p < 0.05. T-tests were conducted to test for statistically significant differences between the retention and non-retention group by retention threshold for each patient characteristic.

<sup>d</sup>Retained = Patient's buprenorphine prescriptions (days supplied) cover at least 80 % of the days within the retention window, which refers to the number of days since treatment inception during the analysis period.

**Table 2**

Impact of out-of-pocket cost for buprenorphine on treatment retention and gaps in treatment coverage.

Measure	Retained in treatment by retention period <sup>a</sup> aOR (95 % CI) <sup>b,d</sup>			Percentage increase in number of days without treatment coverage by retention period IRR (95 % CI) <sup>c,d</sup>		
	180 days	360 days	540 days	180 days	360 days	540 days
Daily out-of-pocket cost (\$)	0.88 (0.86, 0.90)	0.86 (0.84, 0.89)	0.87 (0.84, 0.89)	0.05 (0.05, 0.06)	0.08 (0.08, 0.09)	0.08 (0.08, 0.09)

Notes: Data Source: IBM® MarketScan® commercial claims and encounters database.

SUD diagnosis covariates: opioid, alcohol, cannabis, sedatives, cocaine, stimulants, and nicotine.

Psychiatric diagnosis covariates: anxiety, bipolar disorder, major depression, other mood disorders, ADHD, PTSD, and schizophrenia.

Pain diagnosis covariates: back pain, neck pain, migraine, fibromyalgia, osteoarthritis, inflammatory joint disorder, and periarticular.

Other prescription covariates: Opioids, antidepressants, benzodiazepines, and stimulants.

IRR = incidence rate ratio, SUD = substance use disorder.

<sup>a</sup>Retained = Patient's buprenorphine prescriptions (days supplied) cover at least 80 % of the days within the retention window, which refers to the number of days since treatment inception during the analysis period.<sup>b</sup>Multivariable logistic regression models with binary dependent variable (retained = 1, not retained = 0). Interpretation is: A \$1 increase in daily out-of-pocket cost is associated with the demonstrated decrease (aOR<1.0) in the odds of the dependent variable. Models controlled for demographic, SUD, psychiatric, pain, and other prescription covariates.<sup>c</sup>Multivariable Poisson regression models with count dependent variable representing the number of days a patient was without daily supply during the retention window. Interpretation is: A \$1 increase in daily out-of-pocket cost is associated with the demonstrated increase in the incidence of the dependent variable. Models includes only individuals defined as retained during the stated retention window. Models controlled for demographic, SUD, psychiatric, pain, and other prescription covariates.<sup>d</sup>Demographic covariates: age, sex, and census region.