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# Characterizing initiation, use, and discontinuation of extended-release buprenorphine in a nationally representative United States commercially insured cohort

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## Abstract

**Background and Aims:** While the United States is in the midst of an overdose epidemic, effective treatments are underutilized and commonly discontinued. Innovations in medication delivery, including an extended-release formulations, have the potential to improve treatment access and reduce discontinuation. We sought to assess extended-release buprenorphine discontinuation among individuals with opioid use disorder (OUD) in a real-world, nationally representative cohort.

**Setting:** United States

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Contributors: All authors contributed to the design of the study. JRM wrote the first draft of the manuscript. JRM managed the statistical analysis. All authors made contributions to the interpretation of the data including clinical and epidemiological inferences. All authors contributed to the discussion section, revised, and approved the final manuscript.



Conflict of interest: None

**Participants:** Commercially insured individuals initiating one of four FDA-approved medications for opioid use disorder (MOUD) in 2018: extended-release buprenorphine, extended-release naltrexone, mucosal buprenorphine (mono- or co-formulated with naloxone), or methadone.

**Measurements:** Our primary outcome was medication discontinuation, defined as a gap of more than 14 days between the end of one prescription or administration and the subsequent dose.

**Findings:** We identified 14,358 individuals initiating MOUD in 2018, including 204 (1%) extended-release buprenorphine, 1,173 (8%) extended-release naltrexone, 12,171 (85%) mucosal buprenorphine, and 810 (6%) methadone initiations. Three months after initiation, 50% (95% confidence interval [CI] 40%−60%) of extended-release buprenorphine, 64% (95% CI 61%−69%) of extended-release naltrexone, 34% (95% CI 33%−35%) of mucosal buprenorphine, and 58% (95% CI 54%−62%) of methadone initiators had discontinued treatment.

**Conclusions:** Across all treatment groups, medication discontinuation was high, and in this sample of early adopters with limited follow-up time, we found no evidence that extended-release buprenorphine offered a retention advantage compared to other MOUD in real-world settings. Retention continues to represent a major obstacle to treatment effectiveness, and interventions are needed to address this challenge even as new MOUD formulations become available.

### Keywords

opioid use disorder; extended-release buprenorphine; medication for opioid use disorder; retention

## 1. Introduction

Since the 1980s, drug overdose rates in the United States (US) have been rising at alarming rates, driven in the 2010s by the presence of illicitly produced fentanyl—a potent synthetic opioid—in the illicit drug supply.[1–3] A synthesis of multiple data sets estimated at least 1.5 million insured people in the U.S. have an opioid use disorder (OUD) balanced between commercial (41%) and public (16% Medicare and 43% Medicaid) beneficiaries,[4] and this number is increasing.[5,6] Medications for opioid use disorder (MOUD) substantially reduce the risk of opioid overdose,[7] but less than 25% of individuals with OUD initiate MOUD.[8,9] Additionally, among those who do initiate treatment, discontinuation is common – 50% or greater by 12 months in many clinical cohorts.[8–12] There are three MOUD approved for use by the Food and Drug Administration (FDA), and multiple formulations are available: mucosal buprenorphine (M-BUP, mono- or co-formulated with naloxone), dosed daily; methadone, dosed daily often in a supervised clinical setting; extended-release injectable naltrexone, dosed monthly (XR-NTX); and an extended-release buprenorphine implant, dosed every 6 months. A formulation of buprenorphine approved in the United States in 2017, extended-release depot buprenorphine (XR-BUP), dosed monthly, may offer an attractive alternative that could increase retention.[13–15] Randomized controlled trials have demonstrated the efficacy of XR-BUP over placebo,[16] and non-inferiority compared to M-BUP combinations,[17–19] for abstinence from opioid use. Qualitative research suggests that XR-BUP may be appealing to individuals because of its convenient dosing schedule.[20] While additional clinical trials are ongoing in several populations who might benefit

from a depot injection, including individuals with prior overdose or exposed to fentanyl, individuals released from correctional settings,[21,22] veterans,[23] and pregnant women,[24] there is a lack of evidence comparing XR-BUP to other MOUD or characterizing its initiation, use, and discontinuation in real-world settings. This is important given potential challenges of XR-BUP including increased cost and rigorous storage requirements as a controlled substance.[19,24,25]

In this study, we characterize initiation, use, and discontinuation of XR-BUP in a real-world cohort to understand the lessons from early adoption and compare discontinuation rates to established alternatives of M-BUP, XR-NTX, and methadone. These emerging real-world data can begin to build the evidence base to inform the MOUD treatment decisions faced by patients, clinicians, payers, and policymakers.

## 2. Methods

### 2.1 Population and cohort design

We utilized the IBM Watson MarketScan Commercial Claims and Encounters Database (MarketScan) to identify MOUD use. MarketScan is a nationally representative data set of US individuals covered by employer-sponsored health insurance, and contains detailed data on inpatient and outpatient medical claims, and outpatient pharmacy administrative claims. Given that XR-BUP was not approved until late 2017 (on November 30, 2017), we use 2018 data covering over 27 million unique individuals to establish our cohort. We compared XR-BUP to three other FDA-approved medication treatments for OUD: methadone, XR-NTX, and M-BUP. We identified MOUD treatment using national drug code numbers in outpatient pharmacy claims that included details of the date the prescription was filled and the number of days supply. For extended-release products and methadone, Health Common Procedure Coding System (HCPCS) codes for in-office administration (supplemental appendix). To identify the initiating prescribing event, we isolated the first prescribing or administration event preceded by a three-month washout period for all MOUDs,[8] so each individual was enrolled in the dataset from three months prior to their index prescribing event (as early as October 1st, 2017 for initiation in January 1, 2018) through December 31st, 2018. For methadone, XR-NTX, and M-BUP we defined the washout period as free of any other MOUD prescriptions or initiations, while for XR-BUP we allowed for induction with M-BUP as recommended in the prescribing information package insert.[26] As XR-NTX is also used to treat alcohol use disorder, we required XR-NTX to be preceded by a diagnosis of OUD in the 30 days prior to initiation as evidence that the medication was being used to treat this condition. We excluded implantable buprenorphine as there were only claims for three documented administrations in two individuals in 2018.

### 2.2 Outcome measures and analysis

**2.2.1 Characterizing the XR-BUP cohort.—**We first characterized the uptake and utilization of XR-BUP and compared the cohort of individuals prescribed XR-BUP with those prescribed other MOUD, using a chi-square or Fisher's exact test. We compared the composition of each medication cohort based on demographic and clinical characteristics available in claims data including sex, age (under 30 vs. 30 and older as in previous

literature[8,27]), region of residence (Northeast, Midwest, South, West), as well as whether the beneficiary was the primary holder of the plan, or a spouse or dependent. We also included a modified Elixhauser comorbidity score[27,28] from the 30 days prior to initiation, which captures general comorbidity burden, but excludes illicit drug and alcohol use (which are captured separately). This is important to capture as individuals with competing health priorities may be more likely to discontinue treatment, and to understand MOUD prescribing patterns as the potential convenience of a monthly dosed medication may be helpful for these individuals. We also assessed differences in individual components of the comorbidity index as a supplemental analysis. We included the presence of non-opioid concurrent illicit drug (including amphetamines, cocaine, non-medical marijuana, hallucinogens, and sedatives) use and alcohol use in the 30 days prior to initiation as a dichotomous variable.

**2.2.2 Discontinuation: XR-BUP and other MOUD.—**Next, we compared the uptake of XR-BUP with the utilization of M-BUP, XR-NTX, and methadone over the same period by calculating the time on treatment of each medication. We also characterized the length of gaps between prescriptions. We calculated the proportion who discontinued by three months, defined as consistent medication coverage, via in-office administration or filled prescription, with a gap of no more than 14 days in coverage, and calculated the 95% confidence interval for each proportion. We assessed the effect of censorship in two ways. First, we included all medication initiations from January 1st through December 31st, 2018 and looked for discontinuation by three months – those who initiated the medication with fewer than 3 months left in the calendar year, but had not discontinued by December 31st, 2018, were included among those who did not discontinue. Second, we included only those initiating before October 1st, 2018 so that we only measured 3-month discontinuation among those we observed for three months. We report both of these measures to transparently describe the emerging use of XR-BUP. The first discontinuation measure provides a snapshot of discontinuation as of December 31st, 2018, recognizing that uptake of XR-BUP was increasing through the calendar year. The second discontinuation measure fully accounts for person-time in the three-month discontinuation definition. Finally, we summarized the number of individuals who initiated a different MOUD within 14 days of discontinuing their initial medication to measure the frequency of medication switching.

**2.2.3 Characterizing XR-BUP prescribing guidance concordance.—**We then examined concordance with XR-BUP prescribing information instructions as of December 2018: (1) recommended dosing schedule of two 300 mg injections followed by 100 mg injections; (2) initiation with mucosal buprenorphine for at least 7 days prior to XR-BUP initiation, and; (3) a gap of at least 26 days and not more than 45 days between administrations.[29] The XR-BUP package insert was later updated to allow for a 300mg dose to cover 60 days as needed for travel, etc.[26] We assessed how often this occurred in our data, although these updated guidelines were not published until February 2020, outside of our observation period.

**2.2.4 Ethical approval.—**Because these data are de-identified, the Boston University Institutional Review Board ruled this study Not Human Subjects Research.

# 3. Results

## 3.1. Overall MOUD initiation

We identified 14,358 individuals initiating medications for opioid use disorder in 2018, including 204 (1%) XR-BUP, 1,173 (8%) XR-NTX, 12,171 (85%) M-BUP, and 810 (6%) methadone initiations (Table 1). The days of medication supplied at initiation was 4-weeks for injectable formulations (defined by package insert), one day for dispensed methadone (defined by the HCPCS code), and varied for M-BUP, with 13% initiating with a prescription covering 7 or fewer days, 15% 8–14 days, and the remainder initiated with a 30 day prescription. There were several notable differences among the initiating cohorts.

## 3.2. Demographic differences among MOUD initiations

First, younger individuals were more often initiating injectable MOUD, particularly XR-NTX, evidenced by a higher proportion of individuals under 30 (59% XR-NTX and 37% XR-BUP vs. 32% in M-BUP and 26% for methadone, $p<0.01$). Next, a higher proportion of individuals who were listed as dependents on the insurance plan, rather than primary plan holder or spouses, were represented among those receiving injectable MOUD (48% XR-NTX and 26% XR-BUP vs. 20% M-BUP and 17% methadone, $p<0.01$, Table 1).

## 3.3. Clinical differences among MOUD initiations

For each non-opioid substance, individuals initiating XR-NTX had the highest prevalence of documented concurrent substance use (ranging from 3% with hallucinogen use, to 61% with alcohol use), followed by XR-BUP (ranging from 2% with hallucinogen use to 24% with alcohol use). In addition, individuals treated with injectable MOUD had higher comorbidity burden; 10% of XR-NTX initiators had 3 or more non-drug use Elixhauser comorbidities in the month prior to MOUD initiation, followed by 8% of the XR-BUP cohort, 7% in M-BUP, and 5% in methadone, ($p<0.01$). This difference was largely driven by increased documented prevalence of depression in those receiving XR-NTX (supplemental appendix).

## 3.4. Discontinuation differences among MOUD initiations

The majority of individuals initiating an MOUD discontinued (a gap of more than 14 days between medications) before the end of follow-up, including 51% (n=105, 95% confidence interval [CI] 45%−58%)) of those starting XR-BUP, 74% (868, 95% CI 71%−77%)) of XR-NTX initiations, 53% (6,493, 95% CI 52%−54%) of M-BUP starts, and 69% (557, 95% CI 66%−72%) of individuals who initiated methadone. Figure 1 presents the Kaplan-Meier curves showing time to discontinuation, while incorporating differences in follow-up time. The median time from initiation until discontinuation among those who discontinued was 47 days for those starting XR-BUP (interquartile range [IQR] 28–73 days), 48 days for XR-NTX (IQR 28–84 days), 71 days for M-BUP (IQR 36–122 days), and 32 days for methadone (IQR 29–60 days). A Wilcoxon rank test of homogeneity indicated a significant ($p<0.01$) difference in discontinuation time among the treatments. Among those enrolled for at least three months after initiation, 64% (95% CI 55%−73%) of those initiating XR-BUP, 67% (95% CI 64%−70%) of those initiating XR-NTX, 34% (95% CI 33%−35%) of those initiating M-BUP, and 59% (95% CI 55%−62%) of those initiating methadone discontinued.

The sample size of those enrolled for at least 3 months after initiation was markedly smaller than the unrestricted cohort, but the differences among discontinuation rates at 3 months was significantly different (chi-square test $p<0.01$) (n=100 XR-BUP, 839 XR-NTX, 8,888 M-BUP, 628 methadone). In general, those who discontinued by 3 months were more often under 30 years of age, managing multiple comorbidities, and diagnosed with concurrent substance use (supplemental appendix).

### 3.5. Characterizing medication "switching" and the effect on discontinuation

Few individuals initiated a different MOUD within 14 days of discontinuing the initial MOUD ("switched"); this occurred in 3% of XR-NTX discontinuations (27 individuals switched to M-BUP), 1% of methadone discontinuations (4 to M-BUP), and 1% of M-BUP discontinuations (52 to XR-NTX and 2 to methadone). Among those discontinuing XR-BUP, 15% (16 individuals) switched to another MOUD, all to M-BUP. We then excluded switches from the discontinuation numbers to estimate discontinuation from *any* medication rather than discontinuation from the *initiating* medication as was estimated in section 3.4. This implies 44% (95% CI 37%−50%) discontinuation among those initiating with XR-BUP; 72% (95% CI 69%−74%) for XR-NTX; 53% (95% CI 52%−54%) for M-BUP, and; 68% (95% CI 65%−71%) for methadone. Among those with at least three months of follow-up, the revised discontinuation proportions are: 50% (95% CI 40%−60%) for XR-BUP; 65% (95% CI 61%−68%) for XR-NTX; 34% (95% CI 33%−35%) for M-BUP, and; 58% (95% CI 54%−62%) in methadone.

### 3.6. Describing concordance with prescribing guidelines for XR-BUP

We captured several measures of utilization of XR-BUP among the 204 early adopters. Based on prescriptions filled, XR-BUP demonstrated a ramp-up of utilization over calendar-year 2018, while other treatments were stable or slightly decreasing (Figure 2). Overall, 527 total administrations were observed among the 204 individuals initiating XR-BUP. XR-BUP dosing guidelines recommend 300 mg for the first two administrations followed by 100 mg every administration after that, and our real-world data showed broad adherence to these instructions. Ninety-four percent of first administrations were 300 mg, 88% of second administrations were 300 mg, then 74% of third administrations were 100 mg, and 81% of fourth and fifth administrations were 100 mg (Figure 3). Just four individuals (2%) were given 100mg for each of the first three doses, and 17 (8%) received 300mg for all three first doses (a 300 mg maintenance dose is guideline-recommended for patients for which the benefits outweigh the harms[26]). To assess how often individuals were receiving a 300 mg dose every other month we examined individuals with at least three doses that were between 6 and 10 weeks apart. We only found one individual with this schedule, and those doses were 300 mg, 100 mg, and 100 mg – we did not find evidence of 300 mg used every other month as allowed in updated guidelines. Next, we examined how often initiation of XR-BUP was preceded by a prescription of M-BUP. In the 90 days prior to XR-BUP initiation, 171 (84%) individuals received at least one prescription for M-BUP, while 33 (16%) had no evidence of M-BUP. Finally, we assessed overlap and gaps between doses of XR-BUP. In the 313 cases of subsequent XR-BUP doses, 44 (14%) were administered before 26 days had passed from the prior administration (among these the median time from the prior administration was 23 days ranging from 14 to 25 days). Thirty-seven (12%) were

administered after more than 45 days had elapsed from the prior administration (median of 83 days between administrations ranging from 47 to 128 days). Based on our definition of discontinuation, any dose that was administered more than 6 weeks apart (4 weeks of medication coverage plus a two week gap) met the criteria for discontinuation.

## 4. Discussion

While it is clear that new approaches are needed to address the opioid overdose epidemic in the US, retention on MOUD continues to be a major barrier to OUD treatment efficacy at the population level. In our assessment of emerging XR-BUP data in a nationally representative, commercially insured population, we found discontinuation, defined as a 14-or-more day gap in medication coverage, was common across all MOUD studied. There is an urgent need to address discontinuation across MOUD given recent work, highlighted by the National Institute on Drug Abuse,[30] showing that current low adherence rates are one of the primary barriers to reducing opioid-related overdose on an individual and population level.[31] As in previous work,[27] we found that M-BUP was by far the most common MOUD, representing 85% of the sample. We did find that those initiating on XR-BUP more often switched to another MOUD upon discontinuation of XR-BUP compared to other MOUDs, and that fact made XR-BUP look attractive as of December 31, 2018 with the lowest proportion discontinued at that point in time (44% vs. 53% for M-BUP with non-overlapping confidence intervals). However, this was due in part to the significant ramp up of XR-BUP uptake at the end of the year, so on average those on XR-BUP had less follow-up time (and thus less time to discontinue). This ramp up in uptake has been seen among Medicaid-covered individuals as well[32], and a positive sign for increasing MOUD access and choice. Assessing those with at least three months of follow-up, M-BUP had the lowest rate of discontinuation by a substantive margin over XR-BUP (34% vs. 50%, $p<0.01$).

Our research reveals patient-centered flexibility of choice of MOUD, via shared decision making, for example, is likely key to improving adherence as more than 15% of those leaving XR-BUP were later initiated on M-BUP. Some of the patient-centered aspects of shared decision making that warrant further study include attention to cost barriers, accommodating dose adjustment or co-prescribing with M-BUP, or using XR-BUP as a taper off MOUD for patients desiring that option.[33] We saw the most dramatic discontinuation in the first month after initiation, so this may be the most clinically relevant time to provide that flexibility and support.

Even with important retention obstacles to overcome, development of novel medication options remains an important piece of addressing the opioid crisis at an individual level. Qualitative research exploring the medication preferences of patients has found that opinions are diverse and that treatment characteristics that may be appealing for one patient (long-acting formulations reducing treatment) are a disadvantage for another (long-acting formulations remove the morning routine and “purpose” provided by daily dosing).[34] For this reason, it is important that all MOUD are available during the patient-clinician decision-making process such that treatment decisions can meet the unique needs of individual patients. Previous work has shown that more than half (59%) of patients receive behavioral

health treatment for OUD, and just as many seek inpatient care as do MOUD (both approximately 15%).[35] Combinations of MOUD with behavioral and residential treatment should be considered in shared decision-making treatment planning.

We are encouraged by the close alignment we found between treatment dosing guidelines for XR-BUP and real-world use of this novel medication, but findings of two specific populations need further study. First, we found that younger aged individuals more likely to initiate injectable medications. Previous literature has demonstrated younger age is associated with higher discontinuation,[8,27] and while a sophisticated adjusted analysis is beyond the scope of this paper, we found that individuals under 30 had higher discontinuation through the study period (supplemental appendix). More research is needed to understand why younger individuals are disproportionately initiating injectable medications, whether by choice, family pressure, generational differences in MOUD preference, or other barriers to or stigma surrounding non-injectable MOUD. Second, individuals with current non-OUD substance use and higher comorbidity burden were more represented in injectable MOUD, and it is not immediately obvious why this would be the case. It could be that some providers interpret long-acting drugs as more suitable for individuals with multiple use disorder or "complex cases," or it could be that these individuals tried other MOUDs in the past before our washout and we are capturing a new treatment attempt. Previous research has not shown compelling evidence that XR-NTX was beneficial for those with concurrent substance use,[27] but as more data emerges this hypothesis could be tested among those receiving XR-BUP. Our finding that discontinuation is high across MOUD has been shown in previous studies. We also report factors such as age, comorbidities, utilization of inpatient care, as well as variation in provider specialty and place of treatment initiation that have been previously described.[8,27] Further work should contextualize these findings to develop relevant interventions. More evidence is also needed to understand the disconnect between qualitative studies suggesting that injectable medications are acceptable and may provide a convenience benefit, and emerging real-world data showing a high rate of discontinuation in injectable MOUD. Earlier research of XR-NTX hypothesized that this difference could be driven by the lack of withdrawal symptoms when discontinuing an antagonist compared to an agonist such as M-BUP.[8] While there is little data available yet for XR-BUP, reduced withdrawal symptoms have been reported in at least one case series among people treated with XR-BUP seeking to discontinue.[36]

A major strength of this study is that our large, nationally representative cohort allows us to track the emerging utilization of XR-BUP in the real-world and compare that utilization to existing MOUD, using data from actual medication administrations and filled prescriptions. However, there are several limitations inherent to this type of commercial claims data. First, our cohort includes those who are commercially insured, and it is possible that retention patterns we observed may be different among those with public insurance, particularly for methadone which is more difficult to receive under commercial insurance due to a burdensome pre-authorization process.[37] Additionally, we identified methadone administration with a procedure code specific to OUD rather than pain.[38] This approach does not allow us to see the formulation or dosage given. And while not common in the U.S., there may be differences in injectable versus oral methadone administration that should be considered, particularly in places where injectable methadone treatment is an established

practice, such as the United Kingdom.[39] Second, while we observe administration of long-acting medications and methadone in either outpatient or inpatient settings, for M-BUP we are limited to outpatient pharmacy records, so may be missing initiation of M-BUP in inpatient settings such as drug detoxification centers or inpatient hospital settings. Third, we did not account for inpatient addiction care or psychosocial interventions. In examining XR-BUP, other MOUD are the most relevant comparators. MOUD treatments have demonstrated better outcomes than inpatient[40] or psychosocial[35] care alone, specifically associated with better survival. The National Academy of Sciences Engineering and Medicine has specifically concluded that MOUD saves lives and should not be withheld due to a lack of availability of behavioral interventions.[41] However, many individuals with OUD have comorbid mental health diagnoses and psychosocial concerns,[42] and both the American Society of Addiction Medicine (ASAM)[43] and the National Institute for Health and Care Excellence (NICE)[44] recommend psychosocial support and treatment in conjunction with pharmacological treatment. For patients for whom MOUD is not enough, psychosocial components of care warrant strengthening with approaches like cognitive behavioral therapy, contingency management, and residential treatment. Fourth, we are only able to measure what is documented in administrative billing records. For example, polysubstance use is common among individuals with OUD, and the prevalence of concurrent use we find, particularly for M-BUP and methadone patients, is lower that we might expect[45] – studies of methadone maintenance programs have found concurrent cocaine use of over 20%, for example.[46,47] Instead, our estimates should be interpreted as concurrent use that was severe enough or particularly relevant to the course of care to be documented by the provider. Our type of data also precludes us from examining shared decision making as we might with chart review. Understanding how patients and clinicians work together to establish the approach to OUD treatment is important for developing strategies to promote access and retention.

## 5. Conclusion

OUD presents a major public health challenge, and treatment discontinuation is an important barrier to the effectiveness of MOUD. We assessed the uptake, use, and adherence to a new MOUD, XR-BUP, in a real-world setting. While XR-BUP was the least prescribed of the MOUD we examined, uptake increased over 2018 and use of the medication was largely concordant with induction and dosing instructions. However, we found that all MOUD, including XR-BUP, had low retention over the analysis period. Long-acting depot formulations of medications for opioid use disorder are an important advance, but they are not a panacea. The effectiveness of MOUD to address the opioid overdose epidemic will be severely limited unless the discontinuation challenge is addressed, even as new medications enter the market.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Author disclosures

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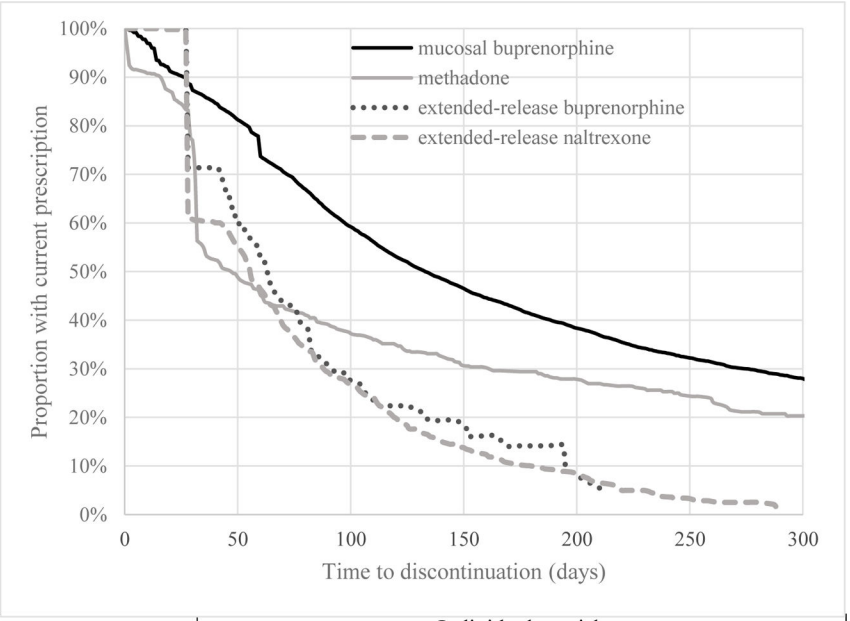
## Highlights

- Studied 204 early adopters of injectable buprenorphine compared to other medications
- Discontinuation is common across opioid use disorder medications
- No evidence that injectable buprenorphine offered a retention advantage
- Good concordance with injectable buprenorphine prescribing guidelines




| | Individuals at risk | | | | | |
|---|---|---|---|---|---|---|
| | 50 days | 100 days | 150 days | 200 days | 250 days | 300 days |
| Mucosal buprenorphine | 8573 | 5377 | 3521 | 2344 | 1438 | 778 |
| Methadone | 369 | 244 | 172 | 122 | 74 | 42 |
| Extended-release buprenorphine | 78 | 26 | 13 | 3 | 0 | 0 |
| Extended-release naltrexone | 530 | 223 | 99 | 50 | 14 | 2 |

**Figure 1: Time-to-medication discontinuation among individuals treated for opioid use disorder in a 2018 United States commercially insured population.**

This Kaplan–Meier survival curve displays the time to discontinuation for individuals prescribed injectable buprenorphine, injectable naltrexone, mucosal buprenorphine (mono- or co-formulated with naloxone), and methadone. Injectable formulations have no discontinuation prior to 4-weeks, reflecting the fact that once the medication is injected, an individuals is adherent for the duration of the extended-release medication, compared to mucosal buprenorphine, which may be prescribed for different lengths of time, and methadone, which is dispensed daily. The horizontal axis displays the time to discontinuation in days while the vertical axis displays the proportion of the population with a current prescription.

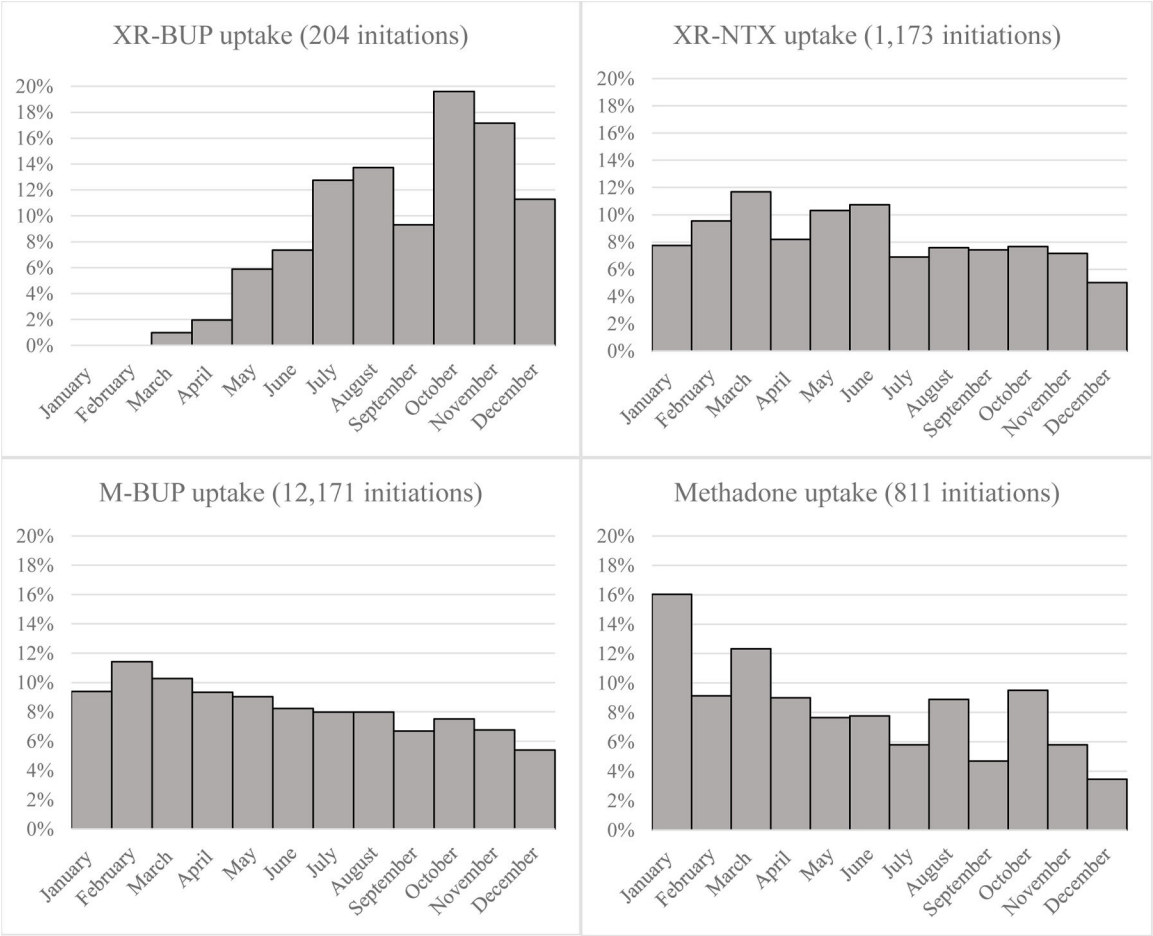
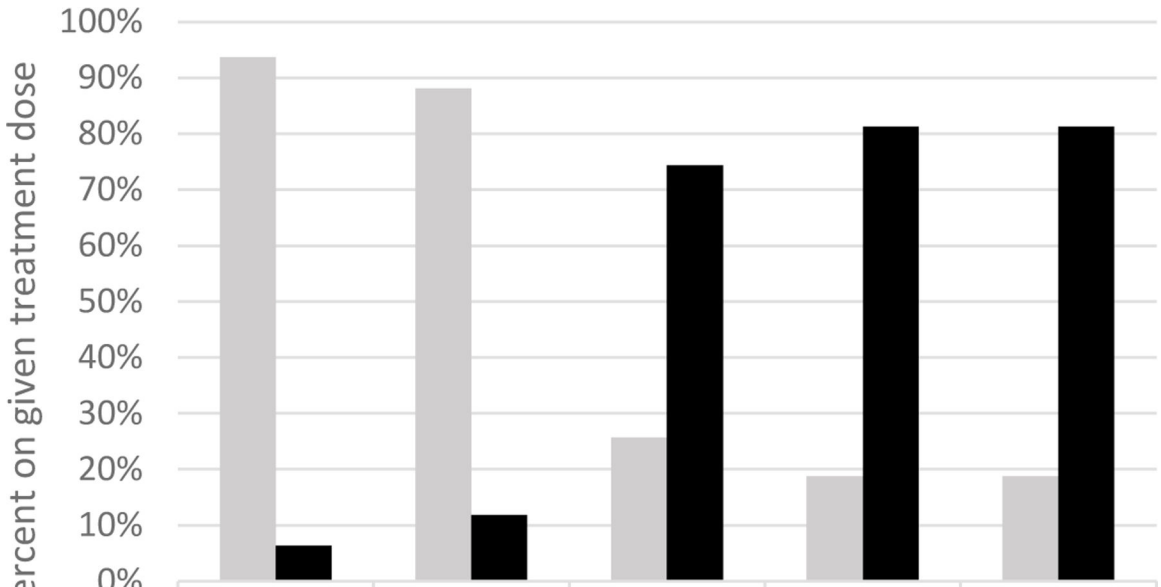



**Figure 2: Histograms of medication uptake by month and medication type in a commercially insured cohort of individuals initiating medication for opioid use disorder in 2018**

XR-BUP=Extended-release buprenorphine; XR-NTX=extended-release naltrexone; M-BUP=sublingual buprenorphine (mono- or co-formulated with naloxone). For each histogram, the vertical axis is the percent of total initiations of the given medication that occurred on a given month. For example, of all M-BUP initiations, just under 10% occurred in January.




| | 1st dose | 2nd dose | 3rd dose | 4th dose | 5th dose |
|---|---|---|---|---|---|
| 300mg | 94% | 88% | 26% | 19% | 19% |
| 100mg | 6% | 12% | 74% | 81% | 81% |
| Total n | 204 | 126 | 74 | 48 | 32 |

**Figure 3: Extended-release buprenorphine strength over dosing time in a commercially insured cohort of 204 individuals in 2018**

**Table 1:**

Characteristics of individuals initiating medication for opioid use disorder in 2018

| | XR-BUP | | XR-NTX | | M-BUP | | Methadone | | p-value of difference* |
|---|---|---|---|---|---|---|---|---|---|
| | n | % | n | % | n | % | n | % | |
| Total | 204 | 100% | 1,173 | 100% | 12,171 | 100% | 810 | 100% | |
| Sex | | | | | | | | | |
| Male | 128 | 63% | 715 | 61% | 7,802 | 64% | 496 | 61% | 0.08 |
| Female | 76 | 37% | 458 | 39% | 4,369 | 36% | 314 | 39% | |
| Age | | | | | | | | | |
| <30 | 76 | 37% | 696 | 59% | 3,924 | 32% | 213 | 26% | <0.01 |
| 30 or older | 128 | 63% | 477 | 41% | 8,247 | 68% | 597 | 74% | |
| Region | | | | | | | | | |
| Northeast | 53 | 26% | 397 | 34% | 2,529 | 21% | 223 | 28% | |
| Midwest | 30 | 15% | 233 | 20% | 2,290 | 19% | 115 | 14% | |
| South | 102 | 50% | 388 | 33% | 5,522 | 45% | 367 | 45% | <0.01 |
| West | 19 | 9% | 154 | 13% | 1,808 | 15% | 105 | 13% | |
| Unknown | 0 | 0% | 1 | 0% | 13 | 0% | 0 | 0% | |
| Concurrent substance use at initiation** | | | | | | | | | |
| Alcohol | 49 | 24% | 720 | 61% | 2,005 | 16% | 76 | 9% | <0.01 |
| Amphetamines | 22 | 11% | 320 | 27% | 1,111 | 9% | 28 | 3% | <0.01 |
| Marijuana | 29 | 14% | 237 | 20% | 932 | 8% | 31 | 4% | <0.01 |
| Cocaine | 39 | 19% | 387 | 33% | 1,128 | 9% | 54 | 7% | <0.01 |
| Hallucinogens | 5 | 2% | 34 | 3% | 96 | 1% | 2 | 0% | <0.01 |
| Sedatives | 35 | 17% | 440 | 38% | 1,550 | 13% | 45 | 6% | <0.01 |
| Elixhauser comorbidity index*** | | | | | | | | | |
| 0 | 119 | 58% | 493 | 42% | 7,743 | 64% | 593 | 73% | |
| 1 | 49 | 24% | 391 | 33% | 2,564 | 21% | 118 | 15% | <0.01 |
| 2 | 20 | 10% | 173 | 15% | 1,034 | 8% | 58 | 7% | |
| 3+ | 16 | 8% | 116 | 10% | 830 | 7% | 41 | 5% | |
| Insurance Coverage | | | | | | | | | |
| Primary holder | 103 | 50% | 428 | 36% | 6,688 | 55% | 497 | 61% | |
| Spouse | 48 | 24% | 186 | 16% | 3,031 | 25% | 174 | 21% | <0.01 |
| Dependent | 53 | 26% | 559 | 48% | 2,452 | 20% | 139 | 17% | |

XR-BUP = extended-release buprenorphine; XR-NTX = extended-release naltrexone; M-BUP = sublingual buprenorphine (mono- or co-formulated with naloxone)

*The p-value of difference is based on the chi-square statistic from the distribution difference in the given characteristic among the medications initiated. Taking age as an example, the p-value indicates there is a statistically significantly difference in the distribution of individuals under 30 and those 30 and over among each medication initiation type.

**Diagnosis code in 30 days before first initiation, only includes use documented in the billing record

***Diagnosis code in 30 days before first initiation and modified to exclude drug use as a comorbidity