



# Examining differences in retention on medication for opioid use disorder: An analysis of Ohio Medicaid data

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## ABSTRACT

**Background:** Medications for opioid use disorder (MOUDs), including methadone, buprenorphine and naltrexone, are associated with lower death rates and improved quality of life for people in recovery from opioid use disorder (OUD). Less is known about each MOUD modality's association with treatment retention and the contribution of behavioral health therapy (BHT). The objectives of the current study were to estimate the association between MOUD type and treatment retention and determine whether BHT was associated with length of time retained. **Methods:** We investigated the time from initiation to discontinuation from MOUD by medication type and exposure to BHT using statewide Medicaid Claims data (N = 81,752). We estimated covariate adjusted hazard ratios (AHR) using a Cox proportional hazards model.

**Results:** Compared to methadone, buprenorphine was associated with a higher risk of discontinuation at the time of initiation (AHR = 2.41, 95% CI = 2.28–2.55), however that difference decreased over one year of maintained retention (AHR = 1.44, 95% CI = 1.37–1.50). Compared to methadone and buprenorphine, naltrexone was associated with a higher risk of discontinuation at the time of initiation (naltrexone vs. methadone AHR = 2.49, 95% CI = 2.30–2.65; naltrexone vs. buprenorphine AHR 1.03, 95% CI = 1.00–1.07), and that relative risk increased over the course of one year of retention (naltrexone vs. methadone AHR = 3.85, 95% CI = 3.63–4.09; naltrexone vs. buprenorphine AHR = 2.67, 95% CI = 2.54–2.81). In general, independent of MOUD type, exposure to BHT during MOUD treatment was associated with a lower risk of discontinuation (AHR = 0.94, 95% CI = 0.92–0.96). However, BHT during the treatment episode was not associated with retention in the adolescent/young adult and pregnant women subpopulations.

**Discussion:** From the standpoint of early success, methadone was associated with the lowest risk of treatment discontinuation. While buprenorphine and naltrexone were associated with similar risks at the beginning of treatment, the relative discontinuation risk for buprenorphine was less than half that of naltrexone at one year of retention. In general, BHT with MOUD was associated with a lower risk of treatment discontinuation.

## 1. Introduction

Since the early 2000s, the United States has seen alarming increases in opioid-related mortality nationwide. The opioid epidemic has been particularly severe in Ohio, which has the third highest rate of opioid overdose deaths in the U.S. (Centers for Disease Control and Prevention

(CDC), 2021). The crisis, exacerbated by the COVID-19 pandemic, has been met with a call to action for increased treatment of Opioid Use Disorder (OUD). However, prescriber decision making around treatment options for OUD is weakly informed by the literature. While research has shown that medication treatment for opioid use disorder (MOUD) is generally more effective in treating OUD than not (Mattick, Breen,

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Kimber, & Davoli, 2014; Sordo et al., 2017), many studies offer contradictory evidence for effectiveness of specific types of MOUD. The aim of this study was to examine patterns of retention in treatment on three different types of MOUD using administrative claims data from the Ohio Department of Medicaid, in consideration of behavioral health treatment (BHT) and other covariates.

### 1.1. Background

Currently available MOUD includes three types of medication: methadone, a full opioid agonist which stimulates the opioid receptors; buprenorphine, a partial opioid agonist; and naltrexone, an opioid antagonist (Substance Abuse and Mental Health Services Administration, 2019). U.S. federal law 42.CFR 8.12 requires patients receive opioid agonist MOUD (methadone or buprenorphine/combination buprenorphine and naltrexone) in designated opioid treatment programs (OTPs) also receive counseling services (e.g. BHT) (Substance Abuse and Mental Health Services Administration, 2019). Federal regulations require methadone to be administered through a Substance Abuse and Mental Health Services Administration (SAMHSA)-certified OTP. Buprenorphine may be prescribed or administered through an OTP or by providers with a waiver to prescribe or dispense buprenorphine under the Drug Addiction Treatment Act of 2000 to a maximum of 100 to 275 patients per physician (National Association of State Alcohol and Drug Abuse Directors, 2019). Any licensed prescriber may provide naltrexone, although patients receiving naltrexone must go through a one- to two-week period of detoxification and/or abstinence from opioids, including buprenorphine and methadone. Additionally, SAMHSA-funded programs (e.g. drug courts, opioid treatment programs accessing grant funds, Screening, Behavioral Intervention, and Referral to Treatment programs) require naltrexone recipients to also receive BHT. Although federal rules require OTP and SAMHSA-funded programs to provide BHT, patients receiving MOUD may decline to use the service.

Large-scale administrative claims data have unique value for investigating retention on MOUD, as many of the most vulnerable OUD patient groups are under-represented in randomized control trials (RCTs) (Franklin & Schneeweiss, 2017; Wang et al., 2019). In large-scale administrative claims data, receipt of pharmaceuticals in office and from pharmacy claims can serve as a proxy for retention on MOUD. For instance, discontinuation may be defined as patients being without MOUD supply over a period (e.g., 60 days) after initiation (Saloner, Daubresse, & Caleb Alexander, 2017). Subsequently, multiple studies have examined risk factors for discontinuation from MOUD, including comorbid mental health and other substance use diagnoses, insurance type, criminal justice involvement, demographic factors such as age and gender, and MOUD type ((Lopian, Chebolu, Kulak, Kahn, & Blondell, 2019); (Manhapra, Agbese, Leslie, & Rosenheck, 2018); (Morgan, Schackman, Leff, Linas, & Walley, 2018); (Saloner et al., 2017); (Samples, Williams, Olfson, & Crystal, 2018); (Shcherbakova, Tereso, Spain, & Roose, 2018); and (Williams, Samples, Crystal, & Olfson, 2020)). However, there remains a need for additional research on the association of BHT on discontinuation by MOUD type.

Treatment retention is a primary goal in OUD treatment as it is associated with decreased drug use/misuse, improved social functioning and quality of life, and reduced mortality (Kampman & Jarvis, 2015; Ohio Department of Health Bureau of Vital Statistics, 2017). Previous studies have found MOUD to increase retention in outpatient addiction treatment (Scholl, Seth, Kariisa, Wilson, & Baldwin, 2018; Substance Abuse and Mental Health Services Administration, 2019; Wakeman et al., 2020). Individuals who received methadone or buprenorphine for longer than six months experienced fewer overdose and serious opioid-related acute care events as compared with those with shorter durations of treatment (Wakeman et al., 2020). Similarly, a recent meta-analysis observed that retention in MOUD of more than one year was associated with a lower mortality rate than retention of less than one year (Ma et al., 2019). The National Institute on Drug Abuse recommends a

minimum of one year in methadone maintenance treatment for best outcomes (Substance Abuse and Mental Health Services Administration, 2019). Specific length of treatment recommendations for other MOUD (buprenorphine and naltrexone) do not exist but instead are based on an individualized patient care approach (American Society of Addiction Medicine, 2015).

BHT for OUD is indicated when a patient is receiving MOUD (Substance Abuse and Mental Health Services Administration, 2019), although BHT administration can vary across settings and categories. Many studies have focused on specific types of BHT for OUD outcomes, including length of treatment, abstinence, and relapse. One meta-analysis (Carroll & Weiss, 2017) showed mixed results regarding the association of BHT with positive OUD treatment outcomes, however the analysis only included studies of people receiving buprenorphine, and mostly included small samples. For methadone, contingency management therapy was associated with lower drop-out rate ( $p = 0.02$ , (Gertra et al., 2011)), and supportive counseling was associated with lower rate of attrition from treatment (HR = 0.55, 95%, CI 0.39–0.80; (Gu et al., 2013)). For naltrexone, contingency management therapy was associated with improved retention rate for oral naltrexone ( $p < 0.01$ ; (Dunn et al., 2013)) and injectable naltrexone ( $ps < 0.004$ , (DeFulio et al., 2012)). Much of the discrepancy in understanding the impact of BHT in combination with MOUD may be due to differences in study populations, BHT modality, study design, and treatment outcome type (Carroll & Weiss, 2017).

From 2000 to 2017, Ohio's death rate due to unintentional drug poisonings increased 1081%; similar to national patterns, this increase was largely driven by opioid-related overdoses (Ohio Department of Health Bureau of Vital Statistics, 2017). While this decreased in 2018 by 22.5%, the 2018 age-adjusted death rate for overdoses involving opioids in Ohio was 29.6 per 100,000, compared to 20.7 per 100,000 in the U.S. (National Institute on Drug Abuse, 2020; Ohio Department of Health, 2018; Scholl et al., 2018).

### 1.2. Current study

Currently, few studies of treatment discontinuation have compared all three general types of MOUD: buprenorphine, methadone, and naltrexone. Many studies relied on limited sampling frames, including small samples or narrow populations, and often limited their study to people with private health insurance. Moreover, few studies took into account MOUD type, the presence of BHT, and several baseline and time-varying covariates. This study seeks to contribute to the body of knowledge surrounding MOUD treatment retention by comparing medication type and exposure to BHT prior to and during an MOUD treatment episode for people insured by Medicaid. The study contains two objectives: 1) to estimate the association between MOUD type and retention in MOUD treatment with consideration and accounting for observed confounding factors; and 2) to determine whether BHT is associated with length of time retained in treatment. The results have policy implications, as well as the potential to support the development of treatment guidelines for clinical decision-making at the point of service.

## 2. Methods

### 2.1. Data and measurements

#### 2.1.1. Institutional review board (IRB)

This retrospective observational study was reviewed by the institutional review boards at The Ohio State University and Case Western Reserve University. This project was implemented for the limited purpose of improving services within Ohio's Medicaid program; therefore, the boards determined that the study qualified for exemption. The study received approval by the primary IRB for the State of Ohio, managed by the Ohio Department of Health (ODH). The study was funded by the

Ohio Department of Medicaid (ODM) and administered by the Ohio Colleges of Medicine Government Resource Center. The views expressed in this paper are solely those of the authors and do not represent the views of the state of Ohio or federal Medicaid programs.

### 2.1.2. Data sources

We utilized administrative datasets from ODM (claims and enrollment information) linked with data from ODH (birth and death records) for the years 2012 to 2017. Health service utilization records at the individual level provide a relatively complete, temporally accurate record of diagnoses and treatment received by individuals enrolled in Medicaid over time and served as the analytical dataset for all models. The dataset included individual-level diagnosis codes, procedure codes, and pharmacy claims for approximately 3 million Ohio residents enrolled in Medicaid per year. Individuals enrolled in Medicaid with at least one diagnosis code related to OUD (see Appendix) and initiated on MOUD were included. Individuals with chronic pain and cancer diagnoses were excluded, as were those in hospice.

### 2.1.3. Dependent variable

The outcome measure used for this study was the duration of the earliest known MOUD treatment episode. An MOUD episode is calculated as the length of time between initiation and discontinuation. Initiation is the date when MOUD was first supplied. Discontinuation is the date when MOUD was last supplied (i.e., date of prescription + days of supply) and then being without MOUD for 60 days. This definition reflects clinical experience with long-term buprenorphine patients and prescriber habits (Williams et al., 2020). Individuals who had Medicaid claims for MOUD within 60 days of their last day of Medicaid enrollment or 12/31/2017 were censored. Individuals who dropped out of enrollment or died during the study period were also censored and treated accordingly in the models. For each eligible individual enrolled in Medicaid, we employed the earliest known MOUD episode initiated after 60-days of Medicaid enrollment. The study excludes episodes involving more than one type of MOUD (i.e. individuals who “switched” MOUD types). The 60-day enrollment allowed for the measurement of baseline variables. The final dataset included 81,752 earliest known MOUD episodes of unique individuals enrolled in Medicaid.

### 2.1.4. Independent variables

Focal independent variables were limited to type of MOUD: methadone, buprenorphine or naltrexone; and BHT during the MOUD treatment episode. We combined buprenorphine and buprenorphine/naloxone into a single category, as recommended by data and policy experts at ODM and clinical expert opinion. We identified pharmacy prescriptions of MOUD by using the generic drug names: “naltrexone hcl” with Medicaid therapeutic class h3t, “naltrexone hydrochloride dihydrate” with Medicaid therapeutic class h3t, “naltrexone microspheres” with Medicaid therapeutic class c0d, “buprenorphine hcl / naloxone hcl” with Medicaid therapeutic class h3w, “buprenorphine hcl” with Medicaid therapeutic class h3w, and “buprenorphine” with Medicaid therapeutic class h3w. We intentionally did not include buprenorphine under therapeutic class h3a, which is opioid analgesics and would include buprenorphine used for pain management. We identified office administrations of MOUD by employing HCPCS codes: H0020 for methadone; J8499, S5000, S5001, T1502, J0570, J0571, J0572, J0573, J0574, J0575 for buprenorphine; and J2315 for naltrexone. Continuous MOUD of the same type but different modalities (e.g. prescription buprenorphine and office administered buprenorphine) and formulations (buprenorphine and buprenorphine/naloxone) were considered part of the same MOUD treatment episode, as the modalities and formulations might in some cases be mixed for induction and maintenance but are part of the same treatment episode.

The variable BHT after MOUD initiation is a time-dependent binary indicator. The variable equals 0 at treatment episode start and equals 1 after any BHT received during the MOUD treatment episode. Each

MOUD type is treated the same with regard to BHT indication. However, in compliance with Federal guidelines methadone treatment included BHT in every episode in our data. Thus, our estimate of the effect of methadone MOUD alone assumes that the BHT that is provided with it has the same effect as BHT that tends to accompany buprenorphine and naltrexone MOUD treatment. BHT exposure is limited to BHT captured by Medicaid claims, and includes the following types of treatment: 1) Individual Counseling, 2) Group Counseling, 3) Intensive Outpatient Hospitalization, 4) Partial Hospitalization, and 5) Case Management. Procedure codes used for BHT were derived from the MODRN Behavioral Health Therapy with MOUD metric codeset, and were refined based on input from clinical, policy, and research team members (The Medicaid Outcomes Distributed Research Network (MODRN), 2021). It is possible that we are not capturing all BHT modalities during the treatment episode such as participation in 12-step or mutual aid programs, or services billed to other funders as described in the Limitations section of this paper.

### 2.1.5. Control covariates

We included the following covariates in the model to control for confounding between treatment indicators and retention. The covariates included: 1) demographics including age and gender; 2) comorbidities (i.e., behavioral health diagnoses received any time prior to initiation) including ADHD, anxiety disorder, bipolar disorder, depression, other substance use disorder (SUD), opioid overdose, post-traumatic stress disorder (PTSD) and schizophrenia/psychosis; and 3) previous exposure (within 60 days preceding MOUD initiation) to prescribed opioids, benzodiazepines, stimulants and BHT. The comorbidities and previous exposures were determined by the health history prior to MOUD initiation, meaning baseline exposure of BHT could be different from the time-dependent variable BHT after MOUD initiation.

The International Classification of Diseases (ICD) and drug codes used can be found in Tables 14–15.

## 2.2. Analysis

We built Cox proportional hazards models of the hazard of discontinuation (Cox, 1972) to accommodate the outcome of time in treatment and right censored data. For each variable, we built a Cox model to estimate an *unadjusted* hazard ratio (HR), 95% confidence interval (CI), and *p*-value. Subsequently, a similar model was fitted with all covariates included to estimate *adjusted* HRs (AHR), 95% CIs and *p*-values. In the adjusted Cox model, the baseline covariates included types of MOUD, demographic variables, comorbidities, time-dependent BHT variable, and baseline exposure status. Lastly, we introduced covariate-time interactions for the variables that did not satisfy the proportional hazard assumption. The covariate adjusted Cox model allows the adjusted hazard ratios (AHRs) to vary over time. For a covariate with both a time-fixed AHR and a time-varying AHR, the time-fixed AHR represents the AHR at MOUD initiation and the time-varying AHR represents the ratio of hazard rates for the same group at two adjacent 30-day time periods (e.g., the ratio of the hazard rate at the second 30-day period and the first 30-day period). The AHR at any specific time (except the initial 30-day period) is determined by both time-fixed AHR (a starting point), time-varying AHR (describing how the AHR varies with time), and the amount of time that has passed.

We investigated the weighted residuals and used an alpha ( $\alpha$ ) threshold of 0.05 to identify covariates that violated the proportional hazard assumption. For the violators, we used Akaike Information Criterion (AIC) to determine the best functional form of the hazard ratio over time (Klein & Moeschberger, 2003; Therneau, Crowson, & Atkinson, 2019) and determined that a logarithmic step-function (i.e.  $\log([t/30] + 1)$ , where  $[x]$  is the floor function) was appropriate.

We performed four analyses: entire population ( $n = 91,752$ ), youth and young adults (ages  $<27$ ,  $n = 18,471$ ), pregnant women ( $n = 3627$ ), and postpartum women ( $n = 3367$ ). Specifically, the youth and young

adult analysis included people enrolled in Medicaid who initiated MOUD before the age of 27. The pregnant dataset included individuals who initiated MOUD while they were pregnant (i.e., between pregnancy and delivery). The postpartum dataset included individuals who initiated MOUD within 365 days of delivery. Deliveries were identified through Medicaid claims, and pregnancy start dates were calculated with gestational age on vital statistics birth records. Procedure codes to identify pregnancy and delivery can be found in the Appendix.

### 3. Results

Tables 1–3 and Fig. 1 present the results of the main analyses on the entire study population. Table 1 shows the demographic characteristics by MOUD type at baseline. Table 2 presents the MOUDs' AHRs at day-1, day-91, day-181, and day-361 after MOUD initiation, which we interpret as day 1, 3 months, 6 months, and 12 months. Additionally, AHRs of discontinuation from treatment over time are shown graphically in Fig. 1. We present demographics and AHRs for youth and young adults, pregnant women, and postpartum women in Tables 4–6. Tables 7–13 present full results for these three subpopulations.

Table 1 presents a detailed quantitative summary of the sample ( $N = 81,752$ ). The majority of the sample was prescribed buprenorphine during their earliest known treatment episode (76.00%,  $n = 62,135$ ; Table 1), followed by naltrexone (15.37%,  $n = 12,568$ ), and then methadone (8.62%,  $n = 7049$ ). Almost 2/3 (65.18%,  $n = 53,286$ ) had a comorbid behavioral health disorder diagnosis of which anxiety (30.71%,  $n = 25,111$ ) and depression (29.08%,  $n = 23,485$ ) were most common. In the 60 days prior to the treatment episode, 21.40% ( $n = 17,495$ ) were prescribed opioids. During the treatment episode, 68.38% ( $n = 55,902$ ) received some form of BHT.

After adjusting for covariates, buprenorphine was associated with a higher risk of discontinuation compared to methadone at the beginning of a treatment episode (AHR = 2.41, 95% CI: 2.27–2.55; Table 2). However, consistent with the time-varying AHR for buprenorphine being below one (AHR = 0.82, 95% CI: 0.80, 0.84), the AHR of discontinuation for buprenorphine decreased at 3 months (AHR = 1.82, 95% CI: 1.77–1.88) and 6 months (AHR = 1.63, 95% CI: 1.58–1.68). After 12 months, the AHR of discontinuation for buprenorphine compared with methadone was 1.44 (95% CI: 1.37–1.50). As time progressed during a treatment episode, the risk of discontinuation between individuals using methadone versus buprenorphine moved toward convergence (Fig. 1).

After adjusting for observed confounding covariates, naltrexone was also associated with a higher risk of discontinuation compared with methadone at the beginning of an episode (AHR = 2.49, 95% CI: 2.30–2.65; Table 2). Unlike buprenorphine, the AHR of discontinuation for naltrexone increased at 3 months (3-month AHR = 3.15, 95% CI: 3.03–3.28) and 6 months (AHR = 3.47, 95% CI: 3.31–3.63). At 12 months, the AHR of discontinuation for naltrexone was 3.85 (95% CI: 3.63–4.09). The comparative rates of discontinuation between individuals using methadone and naltrexone diverged further as treatment episodes progressed (Fig. 1).

With regards to the comparison of the risk of discontinuation of buprenorphine versus naltrexone, at the beginning of an MOUD treatment episode, the discontinuation risk for individuals treated with naltrexone was slightly higher compared to buprenorphine (AHR = 1.03, 95% CI: 1.00–1.07; Table 2). At 3 and 6 months, the AHR increased for naltrexone compared to buprenorphine (AHR at 3 months = 1.73, 95% CI: 1.68–1.77, AHR at 6 months = 2.13, 95% CI: 2.05–2.20). At 12 months, the discontinuation AHR for naltrexone was more than two and a half times the AHR for buprenorphine (AHR = 2.67, 95% CI: 2.54–2.81).

Table 3 shows the full adjusted model including the fixed and time-varying AHRs. Male sex, younger age, and presence of other SUD were associated with higher risk of treatment discontinuation, as were baseline exposure to opioids and benzodiazepines. The presence of anxiety and exposure to stimulants were associated with decreased risk of treatment discontinuation. With regards to BHT, while BHT prior to MOUD initiation was associated with a higher risk of discontinuing MOUD (AHR = 1.11, 95% CI: 1.09–1.13), BHT after MOUD initiation was associated with a lower risk of discontinuing treatment (AHR = 0.94, 95% CI: 0.92–0.96). We also conducted univariate Cox regression analyses which demonstrated similar findings to the covariate adjusted analysis shown in Table 3.

Table 4 shows full adjusted model for the adolescent and young adult subpopulation. Similar to the results in the entire population, after adjusting for covariates and confounders, buprenorphine was associated with a higher risk of discontinuation compared with methadone at the beginning of a treatment episode (AHR 2.23, 95% CI: 1.96, 2.54); however, consistent with a time-varying AHR below one (AHR = 0.83, 95% CI: 0.78, 0.89), the AHR of discontinuation for buprenorphine decreased over time. Naltrexone was associated with a higher risk of discontinuation compared with methadone at the beginning of an episode (AHR = 1.90, 95% CI: 1.65, 2.18), but with a time-varying AHR

**Table 1**  
Demographics by medication for opioid use disorder (MOUD) type ( $N = 81,752$ ).

|                    | Variable                                                | Total Sample (n) | Methadone n =<br>7049 | Buprenorphine n =<br>62,135 | Naltrexone n =<br>12,568 |
|--------------------|---------------------------------------------------------|------------------|-----------------------|-----------------------------|--------------------------|
| Sex                | Male                                                    | 47.20% (38,633)  | 40.47%                | 46.82%                      | 53.22%                   |
|                    | Female                                                  | 52.80% (43,119)  | 59.53%                | 53.18%                      | 46.78%                   |
| Age                | 0 < Age < 18                                            | 0.19% (161)      | 0.14%                 | 0.14%                       | 0.51%                    |
|                    | 18 ≤ Age < 27                                           | 22.40% (18,314)  | 14.39%                | 22.40%                      | 26.90%                   |
|                    | 27 ≤ Age < 35                                           | 37.90% (30,946)  | 35.74%                | 39.35%                      | 37.72%                   |
|                    | ≥ 35                                                    | 38.6% (31,575)   | 49.74%                | 38.12%                      | 34.87%                   |
| Baseline diagnosis | No comorbid BH diagnosis                                | 34.82% (28,468)  | 42.98%                | 37.06%                      | 19.18%                   |
|                    | Other SUD                                               | 51.84% (42,384)  | 43.78%                | 49.51%                      | 67.91%                   |
|                    | Anxiety                                                 | 30.71% (25,111)  | 22.36%                | 29.61%                      | 40.87%                   |
|                    | Bipolar                                                 | 5.67% (4637)     | 11.7%                 | 14.33%                      | 23.34%                   |
|                    | Depression                                              | 29.08% (23,485)  | 23.19%                | 27.01%                      | 40.32%                   |
|                    | Schizophrenia/Psychosis                                 | 4.52% (3694)     | 3.86%                 | 4.02%                       | 7.35%                    |
|                    | PTSD                                                    | 7.50% (6133)     | 5.50%                 | 6.74%                       | 12.39%                   |
|                    | ADHD                                                    | 6.42% (5249)     | 3.25%                 | 4.56%                       | 6.62%                    |
|                    | Opioid overdose                                         | 1.14% (1157)     | 0.92%                 | 1.68%                       | 3.81%                    |
|                    | Opioids                                                 | 21.40% (17,491)  | 19.92%                | 23.18%                      | 13.40%                   |
|                    | Benzodiazepines                                         | 10.72% (8764)    | 9.04%                 | 11.05%                      | 10.03%                   |
|                    | Stimulants                                              | 2.40% (1962)     | 1.86%                 | 2.45%                       | 2.46%                    |
| Baseline exposure  | Behavioral health therapy (BHT) before the MOUD episode | 50.42% (41,222)  | 57.64%                | 45.38%                      | 71.31%                   |
|                    | BHT during the MOUD episode                             | 68.36% (55,890)  | 90.95%                | 64.19%                      | 76.34%                   |

**Table 2**

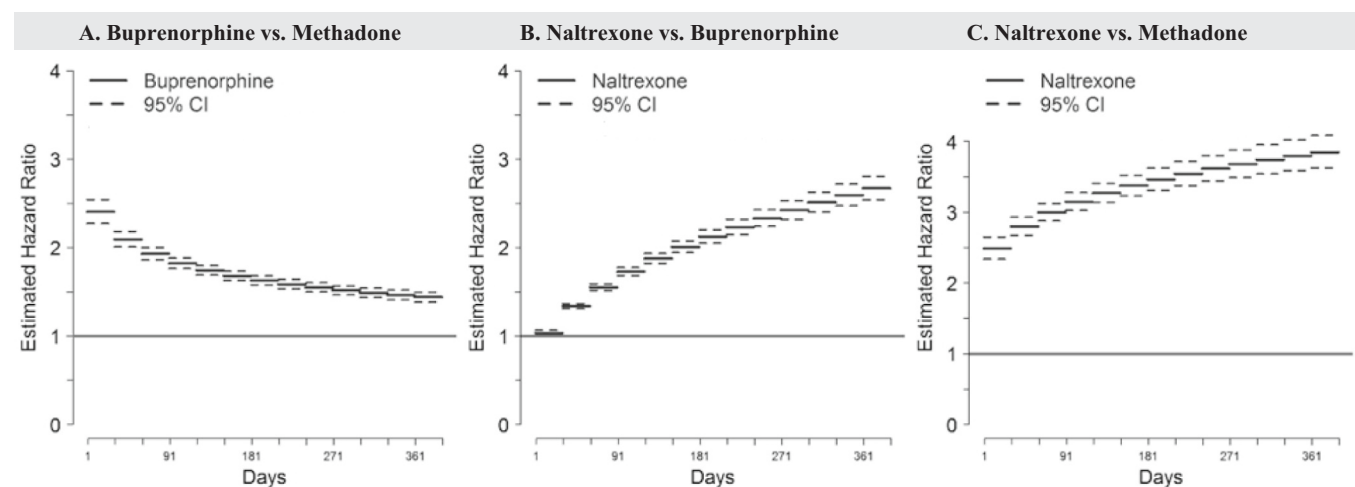
Adjusted hazard ratio (AHR) at 3, 6, and 12 months: Treatment retention for people enrolled in Medicaid (N = 81,752).

|                              | Start (day 1) |             | 3 months (day 91) |             | 6 months (day 181) |             | 12 months (day 361) |             |
|------------------------------|---------------|-------------|-------------------|-------------|--------------------|-------------|---------------------|-------------|
|                              | AHR           | 95% CI      | AHR               | 95% CI      | AHR                | 95% CI      | AHR                 | 95% CI      |
| Buprenorphine vs. methadone  | 2.41          | (2.28–2.55) | 1.82              | (1.77–1.88) | 1.63               | (1.58–1.68) | 1.44                | (1.37–1.50) |
| Naltrexone vs. methadone     | 2.49          | (2.30–2.65) | 3.15              | (3.03–3.28) | 3.47               | (3.31–3.63) | 3.85                | (3.63–4.09) |
| Naltrexone vs. buprenorphine | 1.03          | (1.00–1.07) | 1.73              | (1.68–1.77) | 2.13               | (2.05–2.20) | 2.67                | (2.54–2.81) |

**Table 3**

Demographics and results from multivariate Cox analysis: Treatment retention for people enrolled in Ohio Medicaid (N = 81,752).

| Type of risk factor (reference group)           | Risk factor                                       | N      | Percentage | Adjusted hazard ratio (AHR) | 95% confidence interval (CI) | p-value |
|-------------------------------------------------|---------------------------------------------------|--------|------------|-----------------------------|------------------------------|---------|
| MOUD (ref: methadone)                           | Buprenorphine                                     | 62,135 | 76.00%     | 2.41                        | (2.27–2.55)                  | <0.001  |
|                                                 | Buprenorphine×time <sup>a</sup>                   | NA     | NA         | 0.82                        | (0.80–0.84)                  | <0.001  |
|                                                 | Naltrexone                                        | 12,568 | 15.37%     | 2.49                        | (2.34–2.65)                  | <0.001  |
|                                                 | Naltrexone×time <sup>a</sup>                      | NA     | NA         | 1.19                        | (1.14–1.23)                  | <0.001  |
| Sex (ref: female)                               | Male                                              | 38,636 | 47.26%     | 1.15                        | (1.13–1.17)                  | <0.001  |
| Age (ref: age ≥35)                              | 0 < Age < 18                                      | 160    | 0.20%      | 1.48                        | (1.25–1.75)                  | <0.001  |
|                                                 | 18 ≤ Age < 27                                     | 18,311 | 22.40%     | 1.33                        | (1.31–1.36)                  | <0.001  |
|                                                 | 27 ≤ Age < 35                                     | 31,709 | 38.79%     | 1.07                        | (1.05–1.10)                  | <0.001  |
|                                                 | 27 ≤ Age < 35 × time <sup>a</sup>                 | NA     | NA         | 1.03                        | (1.02–1.05)                  | <0.001  |
| Baseline diagnosis (ref: no other BH diagnosis) | Other SUD                                         | 42,386 | 51.85%     | 1.44                        | (1.40–1.47)                  | <0.001  |
|                                                 | Other SUD×time <sup>a</sup>                       | NA     | NA         | 0.85                        | (0.84–0.86)                  | <0.001  |
|                                                 | Anxiety                                           | 25,113 | 30.72%     | 0.97                        | (0.95–0.99)                  | 0.005   |
|                                                 | Bipolar                                           | 12,660 | 15.49%     | 1.10                        | (1.07–1.14)                  | <0.001  |
|                                                 | Bipolar ×time <sup>a</sup>                        | NA     | NA         | 0.97                        | (0.95–0.99)                  | 0.004   |
|                                                 | Depression                                        | 23,486 | 28.73%     | 1.02                        | (1.00–1.04)                  | 0.046   |
|                                                 | Schizophrenia/Psychosis                           | 3696   | 4.52%      | 1.08                        | (1.03–1.12)                  | <0.001  |
|                                                 | PTSD                                              | 6130   | 7.50%      | 1.02                        | (0.99–1.06)                  | 0.134   |
|                                                 | ADHD                                              | 3892   | 4.76%      | 1.02                        | (0.98–1.06)                  | 0.449   |
|                                                 | Opioid overdose                                   | 1590   | 1.94%      | 1.06                        | (1.00–1.13)                  | 0.052   |
|                                                 | Opioids                                           | 17,492 | 21.40%     | 1.15                        | (1.11–1.18)                  | <0.001  |
|                                                 | Opioids×time <sup>a</sup>                         | NA     | NA         | 0.96                        | (0.95–0.98)                  | <0.001  |
| Baseline exposure (ref: no exposure)            | Benzodiazepines                                   | 8761   | 10.72%     | 1.07                        | (1.04–1.10)                  | <0.001  |
|                                                 | Stimulants                                        | 1962   | 2.40%      | 0.92                        | (0.87–0.98)                  | 0.006   |
|                                                 | Behavioral health therapy (BHT) before initiation | 41,222 | 50.42%     | 1.11                        | (1.09–1.13)                  | <0.001  |
| Exposure during treatment episode               | BHT after initiation <sup>b</sup>                 | NA     | NA         | 0.94                        | (0.92–0.96)                  | <0.001  |

<sup>a</sup> Time-covariate interaction. Time scale =  $\log([t/30] + 1)$ ,  $[x]$  is the floor function.<sup>b</sup> The hazard ratio applies when a patient is exposed to behavioral therapy after initiation of MOUD.**Fig. 1.** Estimated adjusted hazard ratio (AHR) of MOUD discontinuation (N = 81,752) for A. Buprenorphine vs. Methadone, B. Buprenorphine vs. Naltrexone, and C. Naltrexone vs. Methadone in the first year (2012–2017).

above one (AHR = 1.28, 95% CI: 1.18–1.38), indicating that the risk of discontinuation from naltrexone increased over time. BHT during the treatment episode was not significantly associated with treatment retention in this subpopulation (AHR = 0.97, 95% CI: 0.94, 1.02).

Table 5 shows full adjusted model for the pregnant women

subpopulation. Similar to findings in the entire population, after adjusting for covariates and confounders, buprenorphine was associated with a higher risk of discontinuation compared with methadone at the beginning of a treatment episode (AHR = 1.91, 95% CI: 1.54, 2.37), and the time-varying AHR for buprenorphine was below one (AHR = 0.87,

**Table 4**

Demographics and results from multivariate Cox analysis: treatment retention for the adolescents and young adult subpopulation enrolled in Ohio Medicaid (age < 27, n = 18,471).

| Type of risk factor<br>(reference group)              | Risk factor/time varying<br>covariate interaction <sup>c</sup> | n      | Percentage | Single Cox regression analysis <sup>a</sup> |                                 |         | Multiple Cox regression analysis <sup>b</sup> |             |         |
|-------------------------------------------------------|----------------------------------------------------------------|--------|------------|---------------------------------------------|---------------------------------|---------|-----------------------------------------------|-------------|---------|
|                                                       |                                                                |        |            | Hazard<br>Ratio (HR)                        | 95% Confidence<br>Interval (CI) | p-value | Adjusted<br>Hazard Ratio<br>(AHR)             | 95% CI      | p-value |
| MOUD<br>(ref: Methadone)                              | Buprenorphine                                                  | 14,002 | 75.81%     | 1.73                                        | (1.61–1.86)                     | <0.001  | 2.23                                          | (1.96–2.54) | <0.001  |
|                                                       | Buprenorphine×time <sup>c</sup>                                | NA     | NA         | NA                                          | NA                              | NA      | 0.83                                          | (0.78–0.89) | <0.001  |
|                                                       | Naltrexone                                                     | 3445   | 18.65%     | 2.31                                        | (2.13–2.51)                     | <0.001  | 1.90                                          | (1.65–2.18) | <0.001  |
|                                                       | Naltrexone×time <sup>c</sup>                                   | NA     | NA         | NA                                          | NA                              | NA      | 1.28                                          | (1.18–1.38) | <0.001  |
| Gender (ref: Female)                                  | Male                                                           | 7167   | 38.80%     | 1.18                                        | (1.15–1.22)                     | <0.001  | 1.14                                          | (1.10–1.18) | <0.001  |
| Age (ref: 22 ≤ Age < 27)                              | 0 < Age < 18                                                   | 160    | 0.87%      | 1.24                                        | (1.05–1.47)                     | 0.011   | 1.19                                          | (1.00–1.41) | 0.045   |
|                                                       | 18 ≤ Age < 22                                                  | 3595   | 19.46%     | 1.25                                        | (1.20–1.30)                     | <0.001  | 1.25                                          | (1.20–1.29) | <0.001  |
|                                                       | Other SUD                                                      | 9527   | 51.58%     | 1.24                                        | (1.20–1.28)                     | <0.001  | 1.36                                          | (1.29–1.43) | <0.001  |
| Baseline diagnosis (ref:<br>No other BH<br>diagnosis) | Other SUD ×time <sup>c</sup>                                   | NA     | NA         | NA                                          | NA                              | NA      | 0.86                                          | (0.84–0.89) | <0.001  |
|                                                       | Anxiety                                                        | 5031   | 27.24%     | 1.14                                        | (1.10–1.18)                     | <0.001  | 1.02                                          | (0.97–1.06) | 0.471   |
|                                                       | Bipolar                                                        | 2644   | 14.31%     | 1.20                                        | (1.15–1.26)                     | <0.001  | 1.04                                          | (0.99–1.09) | 0.15    |
|                                                       | Depression                                                     | 4814   | 26.06%     | 1.13                                        | (1.09–1.18)                     | <0.001  | 1.00                                          | (0.95–1.04) | 0.869   |
|                                                       | Schizophrenia/Psychosis                                        | 690    | 3.74%      | 1.43                                        | (1.32–1.56)                     | <0.001  | 1.21                                          | (1.11–1.33) | <0.001  |
|                                                       | PTSD                                                           | 1206   | 6.53%      | 1.22                                        | (1.14–1.30)                     | <0.001  | 1.06                                          | (0.99–1.14) | 0.108   |
|                                                       | ADHD                                                           | 1136   | 6.15%      | 1.21                                        | (1.13–1.29)                     | <0.001  | 1.02                                          | (0.94–1.09) | 0.667   |
|                                                       | Opioid overdose                                                | 354    | 1.92%      | 1.39                                        | (1.23–1.57)                     | <0.001  | 1.13                                          | (1.00–1.28) | 0.045   |
|                                                       | Opioids                                                        | 2988   | 16.18%     | 1.05                                        | (1.01–1.10)                     | 0.018   | 1.06                                          | (1.01–1.11) | 0.009   |
|                                                       | Benzodiazepines                                                | 1210   | 6.55%      | 1.06                                        | (0.99–1.13)                     | 0.085   | 1.03                                          | (0.96–1.10) | 0.375   |
| Exposure (ref: no<br>exposure)                        | Stimulants                                                     | 441    | 2.39%      | 1.06                                        | (0.95–1.17)                     | 0.279   | 0.97                                          | (0.87–1.08) | 0.572   |
|                                                       | Behavioral health therapy (BHT)<br>before the MOUD episode     | 9744   | 52.75%     | 1.16                                        | (1.13–1.20)                     | <0.001  | 1.09                                          | (1.05–1.13) | <0.001  |
|                                                       | BHT during the MOUD episode <sup>d</sup>                       | NA     | NA         | NA                                          | NA                              | NA      | 0.98                                          | (0.94–1.02) | 0.227   |
|                                                       | Exposure during<br>treatment episode                           |        |            |                                             |                                 |         |                                               |             |         |

<sup>a</sup> Cox model only using the specific covariate.

<sup>b</sup> Cox model with all covariates.

<sup>c</sup> Time interaction. Time scale =  $\log([t/30] + 1)$ , where  $[t/30]$  is the integer part of  $t/30$ .

<sup>d</sup> The hazard ratio applies when a patient is exposed to BHT after initiation of MOUD.

**Table 5**

Demographics and results from multivariate Cox analysis: treatment retention for the pregnant subpopulation enrolled in Ohio Medicaid (N = 3595)<sup>a</sup>.

| Type of risk factor<br>(reference group)           | Risk factor                                                | N    | Percentage | Single Cox regression analysis <sup>b</sup> |             |        | Multiple Cox regression analysis <sup>c</sup> |             |        |
|----------------------------------------------------|------------------------------------------------------------|------|------------|---------------------------------------------|-------------|--------|-----------------------------------------------|-------------|--------|
|                                                    |                                                            |      |            | Hazard<br>ratio (HR)                        | 95% CI      | P      | Adjusted hazard<br>ratio (AHR)                | 95% CI      | P      |
| MOUD<br>(ref: methadone)                           | Buprenorphine                                              | 3042 | 84.62%     | 1.43                                        | (1.28–1.59) | <0.001 | 1.91                                          | (1.54–2.37) | <0.001 |
|                                                    | Buprenorphine×time <sup>d</sup>                            | NA   | NA         | NA                                          | NA          | NA     | 0.87                                          | (0.79–0.96) | 0.004  |
| Baseline diagnosis (ref: No<br>other BH diagnosis) | Other SUD                                                  | 1738 | 48.34%     | 1.11                                        | (1.03–1.20) | 0.006  | 1.12                                          | (1.04–1.22) | 0.005  |
|                                                    | Anxiety                                                    | 930  | 25.87%     | 1.03                                        | (0.94–1.12) | 0.512  | 0.96                                          | (0.87–1.06) | 0.429  |
|                                                    | Bipolar                                                    | 428  | 11.91%     | 1.03                                        | (0.92–1.16) | 0.567  | 0.96                                          | (0.84–1.09) | 0.523  |
|                                                    | Depression                                                 | 863  | 24.01%     | 1.05                                        | (0.96–1.14) | 0.307  | 1.01                                          | (0.91–1.12) | 0.843  |
|                                                    | Schizophrenia/Psychosis                                    | 90   | 2.50%      | 1.15                                        | (0.90–1.47) | 0.251  | 1.08                                          | (0.84–1.39) | 0.554  |
|                                                    | PTSD                                                       | 234  | 6.51%      | 1.09                                        | (0.94–1.27) | 0.245  | 1.02                                          | (0.87–1.20) | 0.786  |
|                                                    | ADHD                                                       | 150  | 4.17%      | 1.17                                        | (0.98–1.41) | 0.09   | 1.14                                          | (0.93–1.39) | 0.207  |
|                                                    | Opioid overdose                                            | 34   | 0.95%      | 1.66                                        | (1.15–2.41) | 0.008  | 1.75                                          | (1.20–2.55) | 0.004  |
|                                                    | Opioids                                                    | 486  | 13.52%     | 1.03                                        | (0.93–1.15) | 0.547  | 1                                             | (0.89–1.11) | 0.925  |
| Baseline exposure<br>(ref: no exposure)            | Benzodiazepines                                            | 214  | 5.95%      | 1.07                                        | (0.91–1.25) | 0.409  | 1.06                                          | (0.90–1.25) | 0.472  |
|                                                    | Stimulants                                                 | 65   | 1.81%      | 0.90                                        | (0.67–1.20) | 0.472  | 0.82                                          | (0.60–1.11) | 0.198  |
|                                                    | Behavioral health therapy (BHT)<br>before the MOUD episode | 1439 | 40.03%     | 1.07                                        | (0.99–1.15) | 0.09   | 1.06                                          | (0.98–1.15) | 0.174  |
|                                                    | BHT during the MOUD episode <sup>e</sup>                   | NA   | NA         | NA                                          | NA          | NA     | 1.04                                          | (0.94–1.14) | 0.435  |
| Exposure during<br>treatment episode               |                                                            |      |            |                                             |             |        |                                               |             |        |

<sup>a</sup> 32 observations using naltrexone were removed.

<sup>b</sup> Cox model only using the specific covariate.

<sup>c</sup> Cox model with all covariates.

<sup>d</sup> Time interaction. Time scale =  $\log([t/30] + 1)$ , where  $[t/30]$  is the integer part of  $t/30$ .

<sup>e</sup> The hazard ratio applies when a patient is exposed to behavior therapy after initiation of MOUD.

95% CI: 0.79, 0.96), indicating that the risk of discontinuation decreased over time. Like in adolescents and young adults, BHT during the treatment episode was not significantly associated with retention in treatment in the pregnant population (AHR = 1.04, 95% CI: 0.94, 1.14).

Table 6 shows full adjusted model for the postpartum women subpopulation. After adjusting for covariates and confounders, buprenorphine was associated with a higher risk of discontinuation compared with methadone (AHR = 1.60, 95% CI: 1.39, 1.85), and that difference

did not change over time. Naltrexone was also associated with a higher risk of discontinuation compared with methadone at the beginning of an episode (AHR = 1.99, 95% CI: 1.60, 2.47), and after initiation with a time-varying AHR above one (AHR = 1.44, 95% CI: 1.24–1.67) indicating that the risk of discontinuation from naltrexone increased over time. BHT during the treatment episode was associated with reduced risk of discontinuation (AHR = 0.88, 95% CI: 0.80, 0.98).

Additional results include adolescent and young adults (Tables 7–8

**Table 6**

Demographics and results from multivariate Cox analysis: Treatment retention for the Postpartum Subpopulation enrolled in Ohio Medicaid (N = 3367).

| Type of risk factor<br>(reference group)        | Risk factor                                             | N    | Percentage | Single Cox regression analysis <sup>a</sup> |             |        | Multiple Cox regression analysis <sup>b</sup> |             |        |
|-------------------------------------------------|---------------------------------------------------------|------|------------|---------------------------------------------|-------------|--------|-----------------------------------------------|-------------|--------|
|                                                 |                                                         |      |            | Hazard ratio (HR)                           | 95% CI      | P      | Adjusted hazard ratio (AHR)                   | 95% CI      | P      |
| MOUD (ref: methadone)                           | Buprenorphine                                           | 2675 | 79.45%     | 1.61                                        | (1.40–1.85) | <0.001 | 1.60                                          | (1.39–1.84) | <0.001 |
|                                                 | Naltrexone                                              | 387  | 11.49%     | 2.88                                        | (2.42–3.43) | <0.001 | 1.99                                          | (1.60–2.47) | <0.001 |
|                                                 | Naltrexone×time                                         | NA   | NA         | NA                                          | NA          | NA     | 1.44                                          | (1.24–1.67) | <0.001 |
| Baseline diagnosis (ref: no other BH diagnosis) | Other SUD                                               | 1898 | 56.37%     | 1.20                                        | (1.11–1.30) | <0.001 | 1.34                                          | (1.18–1.52) | <0.001 |
|                                                 | Other SUD×time                                          | NA   | NA         | NA                                          | NA          | NA     | 0.88                                          | (0.82–0.94) | <0.001 |
|                                                 | Anxiety                                                 | 1095 | 32.52%     | 1.12                                        | (1.03–1.21) | 0.008  | 1.00                                          | (0.90–1.10) | 0.923  |
|                                                 | Bipolar                                                 | 483  | 14.35%     | 1.18                                        | (1.06–1.32) | 0.003  | 1.04                                          | (0.92–1.18) | 0.488  |
|                                                 | Depression                                              | 1009 | 29.97%     | 1.10                                        | (1.01–1.20) | 0.023  | 0.95                                          | (0.86–1.05) | 0.309  |
|                                                 | Schizophrenia/Psychosis                                 | 84   | 2.49%      | 1.39                                        | (1.09–1.78) | 0.008  | 1.18                                          | (0.91–1.52) | 0.202  |
|                                                 | PTSD                                                    | 270  | 8.02%      | 1.28                                        | (1.11–1.47) | 0.001  | 1.12                                          | (0.96–1.30) | 0.146  |
|                                                 | ADHD                                                    | 142  | 4.22%      | 1.17                                        | (0.97–1.42) | 0.102  | 1.08                                          | (0.88–1.32) | 0.48   |
|                                                 | Opioid overdose                                         | 31   | 0.92%      | 1.40                                        | (0.92–2.13) | 0.117  | 1.17                                          | (0.77–1.78) | 0.47   |
| Exposure (ref: no exposure)                     | Opioid                                                  | 973  | 28.90%     | 1.00                                        | (0.92–1.09) | 0.911  | 0.98                                          | (0.90–1.07) | 0.622  |
|                                                 | Benzodiazepines                                         | 269  | 7.99%      | 1.14                                        | (0.99–1.31) | 0.062  | 1.07                                          | (0.93–1.24) | 0.328  |
|                                                 | Stimulant                                               | 65   | 1.93%      | 1.05                                        | (0.80–1.38) | 0.732  | 0.94                                          | (0.71–1.26) | 0.702  |
|                                                 | Behavioral health therapy (BHT) before the MOUD episode | 1766 | 52.45%     | 1.19                                        | (1.10–1.28) | <0.001 | 1.16                                          | (1.06–1.28) | 0.001  |
| Exposure during treatment episode               | BHT during the MOUD episode <sup>c</sup>                | NA   | NA         | NA                                          | NA          | NA     | 0.88                                          | (0.80–0.98) | 0.015  |

<sup>a</sup> Cox model only using the specific covariate.<sup>b</sup> Cox model with all covariates.<sup>c</sup> The adjusted hazard ratio applies when a patient is exposed to behavior therapy after initiation of MOUD.**Table 7**

Adolescent and young adults subpopulation demographics (Age &lt; 27).

|                                   |                                                         | Methadone n = 1024 | Buprenorphine n = 14,002 | Naltrexone n = 3445 |
|-----------------------------------|---------------------------------------------------------|--------------------|--------------------------|---------------------|
| Sex                               | Male                                                    | 25.39%             | 37.45%                   | 48.27%              |
|                                   | Female                                                  | 74.61%             | 62.55%                   | 51.73%              |
| Age                               | 0 < Age < 18                                            | 0.98%              | 0.61%                    | 1.86%               |
|                                   | 18 ≤ Age < 22                                           | 14.26%             | 19.55%                   | 20.64%              |
|                                   | 22 ≤ Age < 27                                           | 15.23%             | 20.17%                   | 22.5%               |
| Baseline Diagnosis                | No other BH diagnosis                                   | 42.97%             | 39.07%                   | 20.73%              |
|                                   | Other SUD                                               | 46.29%             | 48.31%                   | 66.42%              |
|                                   | Anxiety                                                 | 22.36%             | 25.4%                    | 36.17%              |
|                                   | Bipolar                                                 | 10.06%             | 12.89%                   | 21.36%              |
|                                   | Depression                                              | 20.21%             | 24.05%                   | 35.99%              |
|                                   | Schizophrenia/Psychosis                                 | 3.12%              | 3.22%                    | 6.01%               |
|                                   | PTSD                                                    | 4.69%              | 5.41%                    | 11.61%              |
|                                   | ADHD                                                    | 4.59%              | 5.46%                    | 9.4%                |
|                                   | Opioid overdose                                         | 0.59%              | 1.54%                    | 3.83%               |
| Baseline exposure                 | Opioids                                                 | 13.48%             | 18.05%                   | 9.38%               |
|                                   | Benzodiazepines                                         | 5.18%              | 6.86%                    | 5.72%               |
|                                   | Stimulants                                              | 1.76%              | 2.37%                    | 2.64%               |
|                                   | Behavioral health therapy (BHT) before the MOUD episode | 61.43%             | 46.79%                   | 74.43%              |
| Exposure during treatment episode | BHT during the MOUD episode                             | 88.96%             | 63.56%                   | 78.37%              |

**Table 8**

Adjusted hazard ratios at day 1, 31, 91 and 361: Treatment retention for adolescent and young adults enrolled in Medicaid (Age &lt; 27).

|                              | Start (day 1) |             | 3 months (day 91) |             | 6 months (day 181) |             | 12 months (day 361) |             |
|------------------------------|---------------|-------------|-------------------|-------------|--------------------|-------------|---------------------|-------------|
|                              | AHR           | 95% CI      | AHR               | 95% CI      | AHR                | 95% CI      | AHR                 | 95% CI      |
| Buprenorphine vs. methadone  | 2.23          | (1.96–2.54) | 1.73              | (1.60–1.87) | 1.56               | (1.44–1.68) | 1.39                | (1.26–1.53) |
| Naltrexone vs. methadone     | 1.90          | (1.65–2.18) | 2.67              | (2.45–2.91) | 3.06               | (2.77–3.38) | 3.56                | (3.13–4.05) |
| Naltrexone vs. buprenorphine | 0.85          | (0.80–0.91) | 1.54              | (1.47–1.62) | 1.96               | (1.83–2.10) | 2.56                | (2.33–2.82) |

and Fig. 2), pregnant women (Tables 9–10 and Fig. 3), and postpartum women (Table 11–12 and Fig. 4). We also evaluated the impact of covariate adjustment. In the unadjusted analyses, using methadone as the referent, both buprenorphine and naltrexone had high hazards of discontinuation, whereas when adjusted both adjusted and unadjusted analyses show buprenorphine and naltrexone associated with higher hazard of discontinuation than methadone. In Ohio, Medicaid coverage for buprenorphine treatment is limited to a 6-month period with the option to renew (American Society of Addiction Medicine, n.d.), and

prior authorization during the study period was required for both fee-for-service and managed care. Therefore, we evaluated the probability of discontinuation over time for all MOUDs to ensure that prior authorization did not impact treatment episodes. We observed no dramatic change in the probability of discontinuation at 6 months for buprenorphine.

**Table 9**

Demographics for women enrolled on Medicaid who began an MOUD treatment episode during pregnancy.

|                    |                                                         | Methadone (n = 555) | Buprenorphine (n = 3042) | Naltrexone (n = 32) |
|--------------------|---------------------------------------------------------|---------------------|--------------------------|---------------------|
| Baseline diagnosis | No other BH diagnosis                                   | 34.18%              | 40.34%                   | 9.38%               |
|                    | Other SUD                                               | 55.15%              | 47.11%                   | 78.12%              |
|                    | Anxiety                                                 | 25.14%              | 26%                      | 37.5%               |
|                    | Bipolar                                                 | 11.93%              | 11.9%                    | 21.88%              |
|                    | Depression                                              | 24.23%              | 23.96%                   | 31.25%              |
|                    | Schizophrenia/Psychosis                                 | 2.53%               | 2.5%                     | 6.25%               |
|                    | PTSD                                                    | 6.15%               | 6.57%                    | 12.5%               |
|                    | ADHD                                                    | 3.07%               | 4.37%                    | 0%                  |
|                    | Opioid overdose                                         | 1.81%               | 0.79%                    | 6.25%               |
|                    | Opioids                                                 | 10.31%              | 14.1%                    | 15.62%              |
| Baseline exposure  | Benzodiazepines                                         | 5.24%               | 6.08%                    | 6.25%               |
|                    | Stimulants                                              | 1.08%               | 1.94%                    | 6.25%               |
|                    | Behavioral health therapy (BHT) before the MOUD episode | 50.45%              | 38.13%                   | 68.75%              |
|                    | BHT during the MOUD episode                             | 92.59%              | 68.93%                   | 81.25%              |

**Table 10**

Estimated adjusted hazard ratios at day 1, 31, 91 and 361: Treatment retention for pregnant women enrolled in Medicaid.

|                             | Start   |             | 3 months |             | 6 months  |             | 12 months |             |
|-----------------------------|---------|-------------|----------|-------------|-----------|-------------|-----------|-------------|
|                             | (day 1) |             | (day 91) |             | (day 181) |             | (day 361) |             |
|                             | AHR     | 95% CI      | AHR      | 95% CI      | AHR       | 95% CI      | AHR       | 95% CI      |
| Buprenorphine vs. methadone | 1.91    | (1.54–2.37) | 1.57     | (1.39–1.78) | 1.45      | (1.30–1.62) | 1.33      | (1.17–1.51) |

**Table 11**

Demographics for women enrolled on Medicaid who began an MOUD treatment episode during postpartum period.

|                    |                                                         | Methadone n = 305 | Buprenorphine n = 2675 | Naltrexone n = 387 |
|--------------------|---------------------------------------------------------|-------------------|------------------------|--------------------|
| Baseline diagnosis | No other BH diagnosis                                   | 29.84%            | 32.71%                 | 11.11%             |
|                    | Other SUD                                               | 56.07%            | 53.76%                 | 74.68%             |
|                    | Anxiety                                                 | 27.87%            | 31.4%                  | 43.93%             |
|                    | Bipolar                                                 | 15.08%            | 13.01%                 | 23%                |
|                    | Depression                                              | 24.26%            | 28.19%                 | 46.77%             |
|                    | Schizophrenia/Psychosis                                 | 2.62%             | 2.06%                  | 5.43%              |
|                    | PTSD                                                    | 7.21%             | 7.1%                   | 14.99%             |
|                    | ADHD                                                    | 3.93%             | 4.07%                  | 5.43%              |
|                    | Opioid overdose                                         | 0.33%             | 0.75%                  | 2.58%              |
|                    | Opioids                                                 | 22.3%             | 30.88%                 | 20.41%             |
| Baseline exposure  | Benzodiazepines                                         | 3.93%             | 8.56%                  | 7.24%              |
|                    | Stimulants                                              | 1.64%             | 1.83%                  | 2.84%              |
|                    | Behavioral health therapy (BHT) before the MOUD episode | 59.67%            | 48.3%                  | 75.45%             |
|                    | BHT during the MOUD episode                             | 89.51%            | 66.88%                 | 79.07%             |

**Table 12**

Adjusted hazard ratios at day 1, 31, 91 and 361: Treatment retention for postpartum women enrolled in Medicaid.

|                              | Start   |             | 3 months |             | 6 months  |             | 12 months |             |
|------------------------------|---------|-------------|----------|-------------|-----------|-------------|-----------|-------------|
|                              | (day 1) |             | (day 91) |             | (day 181) |             | (day 361) |             |
|                              | AHR     | 95% CI      | AHR      | 95% CI      | AHR       | 95% CI      | AHR       | 95% CI      |
| Buprenorphine vs. methadone  | 1.6     | (1.39–1.85) | 1.6      | (1.39–1.85) | 1.6       | (1.39–1.85) | 1.6       | (1.39–1.85) |
| Naltrexone vs. methadone     | 1.99    | (1.60–2.47) | 3.3      | (2.73–4.00) | 4.05      | (3.20–5.13) | 5.08      | (3.75–6.89) |
| Naltrexone vs. buprenorphine | 1.24    | (1.04–1.48) | 2.06     | (1.78–2.38) | 2.53      | (2.07–3.09) | 3.17      | (2.40–4.19) |

#### 4. Discussion

This study highlights novel findings that point to new avenues for research about how treatment for OUD among populations served by Medicaid might be improved. In general, we found that methadone was associated with the lowest risk of treatment discontinuation, followed by buprenorphine, and then naltrexone. Furthermore, the relative discontinuation risk among the MOUD types changed over time with discontinuation risks of methadone and buprenorphine converging while the discontinuation risks of methadone and naltrexone diverged even further apart over time. This dynamic relationship could be related to intrinsic differences in the three medication types, such as mode of

delivery, action at the opioid receptor, prescription period, or half-life, or extrinsic factors like the clinical settings in which they are provided. Provision of methadone requires significantly more structure with imbedded BHT and regular contact with programs; it is possible that the frequent contact required for methadone per federal regulations plays an important role in its difference to successfully retain clients in treatment as compared to buprenorphine and naltrexone. Furthermore, differences in the patient populations that access distinct forms of MOUD could also contribute to the study findings. As access barriers are greater for methadone, perhaps patients who seek out this medication are more motivated in their recovery or have more resources at their disposal to overcome barriers to treatment such as reliable

**Table 13**

Demographics and results: univariate analysis versus. Multivariate analysis.

| Type of risk factor<br>(reference group)  | Risk factor                                | N      | Percentage | Univariate analysis <sup>a</sup> |               |        | Multivariate analysis <sup>b</sup> |               |        |
|-------------------------------------------|--------------------------------------------|--------|------------|----------------------------------|---------------|--------|------------------------------------|---------------|--------|
|                                           |                                            |        |            | Hazard ratio<br>(HR)             | 95% CI        | P      | Hazard ratio<br>(HR)               | 95% CI        | P      |
| MOUD (ref: Methadone)                     | Buprenorphine                              | 62,135 | 76.00%     | 1.819                            | (1.765–1.875) | <0.001 | 1.750                              | (1.695–1.805) | <0.001 |
|                                           | Naltrexone                                 | 12,568 | 15.37%     | 2.819                            | (2.720–2.921) | <0.001 | 2.492                              | (2.401–2.586) | <0.001 |
| Gender (ref: Female)                      | Male                                       | 38,636 | 47.26%     | 1.142                            | (1.124–1.161) | <0.001 | 1.154                              | (1.136–1.172) | <0.001 |
| Age (ref: Age ≥35)                        | 0 < Age < 18                               | 160    | 0.20%      | 1.696                            | (1.435–2.005) | <0.001 | 1.490                              | (1.259–1.764) | <0.001 |
|                                           | 18 ≤ Age < 27                              | 18,311 | 22.40%     | 1.36                             | (1.332–1.389) | <0.001 | 1.337                              | (1.308–1.366) | <0.001 |
|                                           | 27 ≤ Age < 35                              | 31,709 | 38.79%     | 1.124                            | (1.103–1.144) | <0.001 | 1.115                              | (1.096–1.135) | <0.001 |
|                                           | Other SUD                                  | 42,386 | 51.85%     | 1.282                            | (1.262–1.303) | <0.001 | 1.186                              | (1.166–1.208) | <0.001 |
| Baseline Diagnosis (ref: no<br>Diagnosis) | Anxiety                                    | 25,113 | 30.72%     | 1.128                            | (1.109–1.148) | <0.001 | 0.970                              | (0.950–0.992) | 0.005  |
|                                           | Bipolar                                    | 12,660 | 15.49%     | 1.207                            | (1.181–1.234) | <0.001 | 1.067                              | (1.040–1.095) | <0.001 |
|                                           | Depression                                 | 23,486 | 28.73%     | 1.149                            | (1.129–1.169) | <0.001 | 1.025                              | (1.003–1.048) | 0.019  |
|                                           | Schizophrenia/Psychosis                    | 3696   | 4.52%      | 1.258                            | (1.211–1.307) | <0.001 | 1.083                              | (1.039–1.128) | <0.001 |
|                                           | PTSD                                       | 6130   | 7.50%      | 1.174                            | (1.139–1.211) | <0.001 | 1.029                              | (0.995–1.063) | 0.09   |
|                                           | ADHD                                       | 3892   | 4.76%      | 1.159                            | (1.116–1.203) | <0.001 | 1.017                              | (0.976–1.060) | 0.423  |
|                                           | Opioid overdose                            | 1590   | 1.94%      | 1.329                            | (1.251–1.411) | <0.001 | 1.079                              | (1.015–1.147) | 0.014  |
|                                           | Opioids                                    | 17,492 | 21.40%     | 1.084                            | (1.063–1.104) | <0.001 | 1.095                              | (1.074–1.117) | <0.001 |
|                                           | Benzodiazepines                            | 8761   | 10.72%     | 1.073                            | (1.047–1.101) | <0.001 | 1.061                              | (1.032–1.090) | <0.001 |
|                                           | Stimulants                                 | 1962   | 2.40%      | 0.978                            | (0.929–1.030) | 0.407  | 0.924                              | (0.875–0.976) | 0.005  |
| Exposure (ref: no<br>Exposure)            | Behavior therapy (BT) before<br>initiation | 41,222 | 50.42%     | 1.179                            | (1.160–1.198) | <0.001 | 1.102                              | (1.080–1.124) | <0.001 |
|                                           | BT after initiation <sup>c</sup>           | NA     | NA         | NA                               | NA            | NA     | 0.947                              | (0.929–0.966) | <0.001 |

<sup>a</sup> Cox model only using the specific covariate.<sup>b</sup> Cox model with all covariates.<sup>c</sup> the hazard ratio applies when a patient is exposed to behavior therapy after initiation of MOUD.

transportation, social support, etc.

We found that people with a naltrexone prescription had the highest rate of treatment discontinuation. Similarly, recent work demonstrated that methadone and buprenorphine were associated with reduced overdose and opioid-related morbidity compared with naltrexone therapy, inpatient treatment, or intensive outpatient behavioral interventions (Wakeman et al., 2020). Treatment with buprenorphine or methadone was associated with a 59% reduction in overdose at 12 months (Wakeman et al., 2020). With regards to our findings, unobserved differences in the underlying population characteristics of the treatment groups could have contributed to this higher rate of discontinuation among those on naltrexone. While we adjusted for observed covariates, the naltrexone cohort may represent a group with complex health care needs or individuals involved with the criminal justice system, potentially confounding factors we were unable to adequately measure. Importantly, in 2013, the Ohio Addiction Treatment Pilot Program (ATPP) began to support addiction treatment pilot interventions for ten substance use specialty docket courts (also known as “drug courts”) across Ohio. One of the outcomes of ATPP included findings that naltrexone was the most prevalent MOUD in the Ohio drug court system and was not associated with successful drug court completion (Baughman, Tossone, Singer, & Flannery, 2019). Furthermore, the ATPP group initiated on naltrexone had higher rates of baseline substance use disorder diagnoses, behavioral health diagnoses, and exposure to benzodiazepines than those on methadone or buprenorphine. Keeping in mind that naltrexone is widely employed in some regions in Ohio (Baughman et al., 2019), the results of this study have implications for efforts to expand access to all modalities of MOUD, both in Ohio and similar U.S. regions and states. In this context, our findings also point to a need for closer partnerships with court systems and additional research to determine whether and when naltrexone should be utilized over other MOUD options. It should be stated, however, that while naltrexone was associated with the highest overall chance of discontinuing treatment earlier, prior research has found that all forms of MOUD, including naltrexone, are superior to no treatment at all (RR of no MAT 2.56 compared to MAT for overdose death; Ma et al., 2019). Therefore, it is necessary that future research identifies for which populations naltrexone is most effective in treating OUD. To the extent that buprenorphine does support retention in treatment more effectively

than naltrexone, health care providers could benefit their patients by offering buprenorphine in the outpatient setting. Because treatment regimens for buprenorphine and buprenorphine/naloxone are easier to access and comply with (including integration with primary care and other outpatient care settings), they may benefit groups that cannot easily comply with the relatively intense requirements of methadone treatment regimens. However, it is likely that expanding outpatient prescribing of buprenorphine will require addressing the barriers to buprenorphine provision such as regulatory burden, comprehensive education and training, and stigma. Nevertheless, efforts should continue to expand the number and type of providers who have sufficient screening, support and administrative services to offer buprenorphine, including primary care providers who treat underlying health issues associated with OUD. An important next step is to identify groups or the conditions in which the cost-benefit tradeoff of methadone versus buprenorphine may favor the use of buprenorphine. We combined buprenorphine and buprenorphine-naloxone in our analysis for a few reasons. First, buprenorphine and buprenorphine-naloxone had very similar probabilities on treatment retention over time. Second, in the claims data, some patients on buprenorphine and buprenorphine-naloxone that alternated between the two medications. We did not believe that these individuals should be categorized as discontinuing treatment when claims reflected a different formulation of buprenorphine. For the purpose of this study, we aimed to capture treatment induction, maintenance, and formulation adjustment as reflected in claims as part of a continuous course of MOUD.

Our data demonstrate that methadone is associated with the lowest risk of treatment discontinuation, supporting continued (or expanded) access to methadone treatment for those who require a higher level of care. This recommendation is tempered with the understanding that there are known restrictions to methadone prescribing, which are less restrictive for buprenorphine, and not present for naltrexone. Both buprenorphine and naltrexone can be provided in medical care settings where methadone cannot, such as primary care offices, allowing more opportunities for patients to access these medications. Relatedly, evaluating mode of delivery (i.e. injectable vs. oral) for buprenorphine and naltrexone is warranted. Doing so would require larger and more recent data, as injectable buprenorphine only became available in Ohio in 2018 and the number of individuals receiving oral naltrexone was very low for

**Table 14**  
International Classification of Diseases (ICD) and drug codes used.

| Variable                     | Definition                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
|------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Opioid use disorder          | ICD-9: 3040, 30400, 304000, 30401, 30402, 30403, 30470, 30471, 30472, 30473, 3055, 30550, 30551, 30552, 30553<br>ICD-10: F11, F111, F1110, F1111, F1112, F11120, F11121, F11122, F11129, F1114, F11150, F11151, F11159, F1118, F11181, F11182, F11188, F1119, F112, F1120, F1121, F1122, F11220, F11221, F11222, F11229, F1123, F1124, F11250, F11251, F11259, F11281, F11282, F11288, F1129, F119, F1190, F11920, F11921, F11922, F11929, F1193, F1194, F11950, F11951, F11959, F11981, F11982, F11988, F1199                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
| Opioid overdose              | ICD-9: E9500<br>ICD-10: T400X2A, T400X2D, T401X2, T401X2A, T401X2D, T401X2S, T402X2A, T402X2D, T402X2S, T403X2A, T403X2D, T404X2A, T404X2D, T405X2, T405X2A, T405X2D, T405X2S, T40602, T40602A, T40602D, T40602S, T40692A, T40692S, T407X2A, T407X2D, T408X2A, T40902A, T40992A, T40992D                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Other substance use disorder | ICD-9: 2910, 2911, 2912, 2913, 2914, 2915, 29181, 29182, 29189, 2919, 2920, 29200, 29211, 29212, 2922, 29281, 29282, 29283, 29284, 29285, 29289, 2929, 29290, 303, 30300, 30301, 30302, 30303, 30320, 30330, 3039, 30390, 30391, 30392, 30393, 304, 3041, 30410, 30411, 30412, 30413, 3042, 30420, 30421, 30422, 30423, 3043, 30430, 30431, 30432, 30433, 30440, 30441, 30442, 30443, 30450, 30451, 30452, 30453, 30460, 30461, 30462, 30463, 30480, 30481, 30482, 30483, 3049, 30490, 30491, 30492, 30493, 305, 3050, 30500, 30501, 30502, 30503, 3051, 30510, 30511, 30512, 3052, 30520, 30521, 30522, 30523, 30530, 30531, 30532, 30533, 30540, 30541, 30542, 30543, 3056, 30560, 30561, 30562, 30563, 30570, 30571, 30572, 30573, 30580, 30581, 30582, 30583, 3059, 30590, 30591, 30592, 30593<br>ICD-10: F10, F100, F101, F1010, F1011, F1012, F10120, F10121, F10129, F1014, F10150, F10151, F10159, F10180, F10181, F10182, F10188, F1019, F102, F1020, F1021, F1022, F10220, F10221, F10229, F10230, F10231, F10232, F10239, F1024, F10250, F10251, F10259, F1026, F1027, F10280, F10281, F10282, F10288, F1029, F109, F1092, F10920, F10921, F10929, F1094, F10950, F10951, F10959, F1096, F1097, F10980, F10981, F10982, F10988, F1099, F121, F1210, F1211, F1212, F12120, F12121, F12122, F12129, F12150, F12151, F12159, F12180, F12188, F1219, F122, F1220, F1220F1, F1221, F1222, F12220, F12221, F12222, F12229, F12250, F12251, F12259, F12280, F12288, F1229, F129, F1290, F12920, F12921, F12922, F12929, F1295, F12950, F12951, F12959, F1298, F12980, F12988, F1299, F131, F1310, F1311, F1312, F13120, F13121, F13129, F1314, F13150, F13151, F13159, F13180, F13182, F13188, F1319, F132, F1320, F1321, F13220, F13221, F13229, F13230, F13231, F13232, F13239, F1324, F13250, F13251, F13259, F1326, F1327, F13280, F13281, F13282, F13288, F1329, F1390, F13920, F13921, F13929, F13930, F13931, F13932, F13939, F1394, F13950, F13951, F13959, F1396, F13980, F13981, F13982, F13988, F1399, F141, F1410, F1411, F1412, F14120, F14121, F14122, F14129, F1414, F14150, F14151, F14159, F14180, F14181, F14182, F14188, F1419, F142, F1420, F14208, F1420, F1421, F1422, F14220, F14221, F14222, F14229, F1423, F1424, F14250, F14251, F14259, F14280, F14281, F14282, F14288, F1429, F149, F1490, F1491, F14920, F14921, F14922, F14929, F1494, F14950, F14951, F14959, F14980, F14981, F14982, F14988, F1499, F151, F1510, F1511, F15120, F15121, F15122, F15129, F1514, F1515, F15150, F15151, F15159, |

**Table 14 (continued)**

| Variable   | Definition                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
|------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|            | F15180, F15181, F15182, F15188, F1519, F152, F1520, F1521, F15220, F15221, F15222, F15229, F1523, F1524, F15250, F15251, F15259, F15280, F15282, F15288, F1529, F159, F1590, F15920, F15921, F15922, F15929, F1593, F1594, F15950, F15951, F15959, F15980, F15981, F15982, F15988, F1599, F1610, F1611, F16120, F16121, F16122, F16129, F1614, F16150, F16151, F16159, F16180, F16183, F16188, F1619, F1620, F1621, F16220, F16221, F16229, F1624, F16250, F16251, F16259, F16280, F16283, F16288, F1629, F1690, F16920, F16921, F16929, F1694, F16950, F16951, F16959, F16980, F16983, F16988, F1699, F17, F172, F1720, F17200, F17201, F17203, F17208, F17209, F1721, F17210, F17211, F17213, F17218, F17219, F1722, F17220, F17221, F17223, F17228, F17229, F1729, F17290, F17291, F17293, F17298, F17299, F181, F1810, F1811, F18120, F18121, F18129, F1814, F18150, F18151, F18159, F1817, F18180, F18188, F1819, F1820, F1821, F18220, F18221, F18229, F1824, F18251, F18280, F18288, F1829, F1890, F18920, F18921, F18929, F1894, F18959, F1897, F18980, F18988, F1899, F19, F191, F1910, F1911, F1912, F19120, F19121, F19122, F19129, F1914, F19150, F19151, F19159, F1916, F1917, F19180, F19181, F19182, F19188, F1919, F192, F1920, F1921, F19220, F19221, F19222, F19229, F1923, F19230, F19231, F19232, F19239, F1924, F1925, F19250, F19251, F19259, F1926, F1927, F19280, F19281, F19282, F19288, F1929, F199, F1990, F19920, F19921, F19922, F19929, F19930, F19931, F19932, F19939, F1994, F19950, F19951, F19959, F1996, F1997, F19980, F19981, F19982, F19988, F1999 |
| Anxiety    | ICD-9: 3000, 30000, 30001, 30002, 30004, 30009, 3001, 30010, 30011, 30012, 30013, 30014, 30015, 30016, 30019, 3002, 30020, 30021, 30022, 30023, 30024, 30027, 30029, 3003, 30030, 3083<br>ICD-10: F40, F400, F4000, F4001, F4002, F401, F4010, F4011, F402, F4020, F40210, F40218, F40220, F40228, F4023, F40230, F40231, F40232, F40233, F40240, F40241, F40242, F40243, F40248, F40290, F40291, F40298, F408, F409, F41, F410, F4100, F411, F4110, F412, F4120, F413, F418, F419, F4190, F42, F420, F422, F4225, F423, F424, F428, F429, F43, F430, F431, F4310, F4311, F4312, F4313, F432, F4320, F4321, F4322, F4323, F4324, F4325, F4329, F4333, F4339, F438, F4381, F439, F440, F441, F442, F444, F445, F446, F447, F4481, F4489, F449, F450, F451, F4520, F4521, F4522, F4529, F454, F4541, F4542, F458, F459, F481, F482, F488, F489                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Bipolar    | ICD-9: 2960, 29600, 29601, 29602, 29603, 29604, 29605, 29606, 29610, 29611, 29612, 29613, 29614, 29615, 29616, 29618, 29640, 29641, 29642, 29643, 29644, 29645, 29646, 2965, 29650, 29651, 29652, 29653, 29654, 29655, 29656, 2966, 29660, 29661, 29662, 29663, 29664, 29665, 29666, 2967, 29670, 2968, 29680, 29681, 29682, 29683, 29689, 2969, 29690, 29692, 29695, 29696, 29699, 30113<br>ICD-10: F30, F301, F3010, F3011, F3012, F3013, F302, F303, F304, F308, F309, F31, F310, F311, F3110, F3111, F3112, F3113, F312, F3121, F313, F3130, F3131, F3132, F314, F3141, F315, F3150, F316, F3160, F3161, F3162, F3163, F3164, F3170, F3171, F3172, F3173, F3174, F3175, F3176, F3177, F3178, F318, F3181, F3187, F3189, F319, F3191, F34, F340, F341, F347, F348, F3481, F3482, F3489, F349, F39, F390, F3900                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                        |
| Depression | ICD-9: 2962, 29620, 29621, 29622, 29623, 29624, 29625, 29626, 29620, 2963, 29630, 29631, 29632, 29633, 29634, 29635, 29636, 3004, 30040, 311, 3110, 31100, 31101, 3111<br>ICD-10: F32, F320, F3201, F321, F322, F3220, F323, F3232, F324, F325, F328, F3281, F3289,                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |

(continued on next page)

Table 14 (continued)

| Variable                     | Definition                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| ADHD                         | F32899, F329, F33, F330, F331, F3310, F332, F3320, F333, F334, F3340, F3341, F3342, F3373, F338, F339, F3393<br>ICD-9: 31400, 31401, 3142<br>ICD-10: F90, F900, F9002, F901, F902, F904, F908, F9080, F909                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Schizophrenia/psychosis      | ICD-9: 29510, 29520, 29521, 29522, 29523, 29524, 29525, 29530, 29560, 29570, 29590, 2970, 2971, 2972, 2973, 2983, 2984, 2988, 2989, 30122<br>ICD-10: F20, F200, F2009, F201, F202, F203, F205, F208, F2081, F2089, F209, F2091, F21, F22, F23, F24, F25, F250, F251, F258, F259, F28, F29, F290<br>HCPCS: 720, 721, 7221, 7229, 7231, 7239, 724, 7251, 7252, 7253, 7254, 726, 7271, 7279, 728, 729, 7301, 7309, 731, 7321, 7322, 733, 734, 7351, 7359, 736, 738, 7391, 7392, 7393, 7394, 7399, 740, 741, 742, 744, 7499, 10D00Z0, 10D00Z1, 10D00Z2, 10D07Z3, 10D07Z4, 10D07Z5, 10D07Z6, 10D07Z7, 10D07Z8, 10E0XZZ, 59400, 59409, 59410, 59510, 59514, 59515, 59610, 59612, 59614, 59618, 59620, 59622 |
| Opioids                      | Generic name: Alfentanil, Codeine, Fentanyl, Hydrocodone, Hydromorphone, Levorphanol, Meperidine, Morphine, Nalbuphine, Opium, Oxycodone, Oxymorphone, Pentazocine, Propoxyphene, Remifentanil, Sufentanil, Tapentadol, Tramadol                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Benzodiazepines              | Generic name: Adinazolam, Alprazolam, Bentazepam, Bretazenil, Bromazepam, Brotizolam, Camazepam, Chlordiazepoxide, Cinazepam, Cinolazepam, Clobazam, Clonazepam, Clonazolam, Clorazepate, Clotiazepam, Cloxazolam, Delorazepam, Diazepam, Diclazepam, Estazolam, Ethylcarfluzepate, Etizolam, Ethylloflazepate, Flubromazepam, Flubromazolam, Flunitrazepam, Flurazepam, Flutazolam, Flutoprazepam, Halazepam, Ketazolam, Loprazepam, Lorazepam, Lormetazepam, Medazepam, Mexazolam, Midazolam, Nifoxipam, Nimetazepam, Nitrazepam, Nordiazepam, Oxazepam, Premazepam, Phenazepam, Pinazepam, Prazepam, Pyrazepam, Rilmafazone, Quazepam, Temazepam, Tetrazepam, Thienalprazolam, Triazolam           |
| Stimulant                    | Generic name: Amphetamine, Armodafinil, Atomoxetine, Dexamethylphenidate, Dextroamphetamine, Lisdexamphetamine, Methamphetamine, Methylphenidate, Modafinil                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Buprenorphine                | Generic name: “buprenorphine hcl / naloxone hcl” with Medicaid therapeutic class h3w, “buprenorphine hcl” with Medicaid therapeutic class h3w, and “buprenorphine” with Medicaid therapeutic class h3w<br>HCPCS code: J8499*, S5000*, S500*1, T1502*, J0570, J0571, J0572, J0573, J0574, J0575<br>*If billed by provider type 95                                                                                                                                                                                                                                                                                                                                                                      |
| Methadone                    | HCPCS code: H0020                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Naltrexone                   | Generic name: “naltrexone hcl” with Medicaid therapeutic class h3t, “naltrexone hydrochloride dihydrate” with Medicaid therapeutic class h3t, “naltrexone microspheres” with Medicaid therapeutic class c0d<br>HCPCS code: J2315                                                                                                                                                                                                                                                                                                                                                                                                                                                                      |
| Behavior therapy             | HCPCS code: H0001, H0004, H0005, H0006, H0007, H0010, H0011, H0012, H0014, H0015, S0201, S0281, G0396, G0397, 90804, 90806, 90808, 90810, 90812, 90814, 90832, 90833, 90834, 90837, 90839, 90840, 90846, 90847, H0036                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Delivery codes for pregnancy | Delivery Surgical Codes: 720, 721, 7221, 7229, 7231, 7239, 724, 7251, 7252, 7253, 7254, 726, 7271, 7279, 728, 729, 7301, 7309, 731, 7321, 7322, 733, 734, 7351, 7359, 736, 738, 7391, 7392, 7393, 7394, 7399, 740, 741, 742, 744, 7499, 10D00Z0, 10D00Z1, 10D00Z2, 10D07Z3, 10D07Z4, 10D07Z5, 10D07Z6, 10D07Z7, 10D07Z8, 10E0XZZ                                                                                                                                                                                                                                                                                                                                                                      |

Table 14 (continued)

| Variable                                         | Definition                                                                                                                                                                                                                                                                                                                                                                                           |
|--------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Non-fatal overdose diagnosis codes               | Delivery Procedure Codes: 59400, 59409, 59410, 59510, 59514, 59515, 59610, 59612, 59614, 59618, 59620, 59622<br>ICD9- E9500, ICD10- T400X2A, T400X2D, T401X2, T401X2A, T401X2D, T401X2S, T402X2A, T402X2D, T402X2S, T403X2A, T403X2D, T404X2A, T404X2D, T405X2, T405X2A, T405X2D, T405X2S, T40602, T40602A, T40602D, T40602S, T40692A, T40692S, T407X2A, T407X2D, T408X2A, T40902A, T40992A, T40992D |
| Fatal overdoses (vital statistics death records) | Underlying cause of death of acute drug poisoning (X40–44, X60–64, X85, Y10–14) and one of the following opioid codes among contributing cause of death codes: T40.0, T40.1, T40.2, T40.3, T40.4, T40.6                                                                                                                                                                                              |

Table 15

Annotation of behavioral health therapy codes.

|       |                                                                                                                                                                                                                                                                             |
|-------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| H0001 | Alcohol and/or drug assessment                                                                                                                                                                                                                                              |
| H0004 | Behavioral health counseling and therapy, per 15 min                                                                                                                                                                                                                        |
| H0005 | Alcohol and/or drug services; group counseling by a clinician                                                                                                                                                                                                               |
| H0006 | Alcohol and/or drug services; case management                                                                                                                                                                                                                               |
| H0007 | Alcohol and/or drug services; crisis intervention (outpatient)                                                                                                                                                                                                              |
| H0010 | Alcohol and/or drug services; sub-acute detoxification (residential addiction program inpatient)                                                                                                                                                                            |
| H0011 | Alcohol and/or drug services; acute detoxification (residential addiction program inpatient)                                                                                                                                                                                |
| H0012 | Alcohol and/or drug services; sub-acute detoxification (residential addiction program outpatient)                                                                                                                                                                           |
| H0014 | Alcohol and/or drug services; ambulatory detoxification                                                                                                                                                                                                                     |
| H0015 | Alcohol and/or drug services; intensive outpatient (treatment program that operates at least 3 h/day and at least 3 days/week and is based on an individualized treatment plan), including assessment, counseling; crisis intervention, and activity therapies or education |
| H0036 | Community psychiatric supportive treatment, face-to-face, per 15 min                                                                                                                                                                                                        |
| S0201 | Partial hospitalization services, less than 24 h, per diem                                                                                                                                                                                                                  |
| S0281 | Medical home program, comprehensive care coordination and planning, maintenance of plan                                                                                                                                                                                     |
| G0396 | Alcohol and/or substance (other than tobacco) misuse structured assessment (e.g., audit, dast), and brief intervention 15 to 30 min                                                                                                                                         |
| G0397 | Alcohol and/or substance (other than tobacco) misuse structured assessment (e.g., audit, dast), and intervention, greater than 30 min                                                                                                                                       |
| 90832 | Psychotherapy w/patient 30 minutes                                                                                                                                                                                                                                          |
| 90833 | Psychotherapy w/patient w/e&m srvc 30 min                                                                                                                                                                                                                                   |
| 90834 | Psychotherapy w/patient 45 minutes                                                                                                                                                                                                                                          |
| 90837 | Psychotherapy w/patient 60 minutes                                                                                                                                                                                                                                          |
| 90839 | Psychotherapy for crisis initial 60 minutes                                                                                                                                                                                                                                 |
| 90840 | Psychotherapy for crisis each addl 30 minutes                                                                                                                                                                                                                               |
| 90846 | Family psychotherapy w/o patient present 50 mins                                                                                                                                                                                                                            |
| 90847 | Family psychotherapy w/patient present 50 mins                                                                                                                                                                                                                              |
| 90804 | 20–30 min psychotherapy (pre-2013, now 90832)                                                                                                                                                                                                                               |
| 90806 | 45–50 min psychotherapy (pre-2013, now 90834)                                                                                                                                                                                                                               |
| 90808 | 75–80 min psychotherapy (pre-2013, now 90837)                                                                                                                                                                                                                               |
| 90810 | 20–30 min individual interactive psychotherapy (pre-2013, now 90832)                                                                                                                                                                                                        |
| 90812 | 45–50 min individual interactive psychotherapy (pre-2013, now 90834)                                                                                                                                                                                                        |
| 90814 | 75–80 min individual interactive psychotherapy (pre-2013, now 90837)                                                                                                                                                                                                        |

**Note:** We selected these codes as they were used in the MODRN BH counseling measure code set list. We also made adjustments as suggested by our clinical researchers. For example, we removed H0008 (detoxification).

the study period of 2012–2017. More robust knowledge on the effect of delivery mode has great potential to improve treatment retention rate, as it could help clinicians and patients make informed treatment decisions based on the availability, as well as the most appropriate treatment regimen.

The finding that BHT during an MOUD treatment episode is associated with a lower risk of discontinuation adds a data point to the mixed results found in the literature. Behavioral health treatment in combination with MOUD treatment has been associated with greater treatment retention (Weiss et al., 2015), although in some cases has shown to decrease time in treatment for people receiving naltrexone (Nunes,

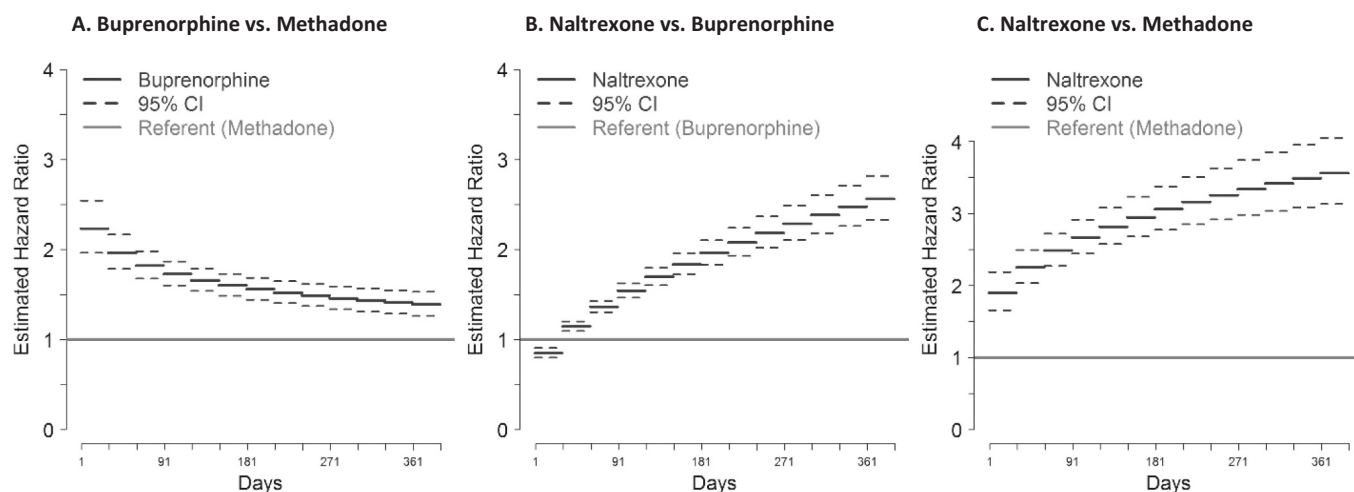


**Fig. 2.** Estimated adjusted hazard ratio of MOUD discontinuation in the adolescent and young adults subpopulation (Age < 27) for A. Buprenorphine vs. Methadone, B. Buprenorphine vs. Naltrexone, and C. Naltrexone vs. Methadone.

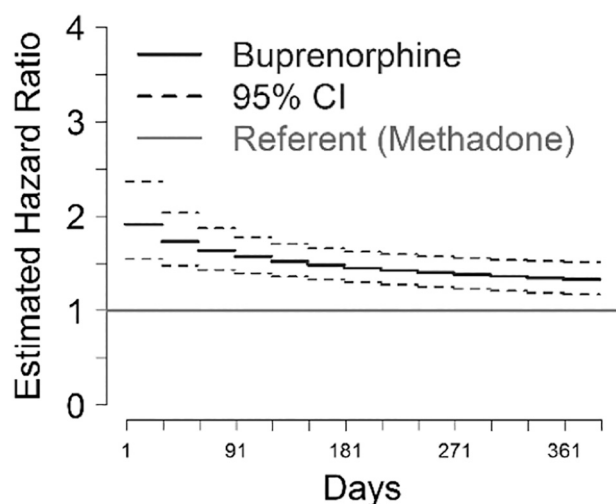


**Fig. 3.** Estimated adjusted hazard ratio of buprenorphine discontinuation (ref: methadone) in the pregnant subpopulation.

Rothenberg, Sullivan, Carpenter, & Kleber, 2006). However, other studies have found no difference in MOUD retention with the addition of BHT (Ling, Hillhouse, Ang, Jenkins, & Fahey, 2013). Further, medication treatment for opioid use disorder is generally more effective in treating OUD than no treatment at all (Mattick et al., 2014; Sordo et al., 2017). One reason for these conflicting results is likely related to the limited scope of BHT examined, limited mostly to medical management, contingency management, or cognitive behavioral therapy (Carroll & Weiss, 2017). Our study's scope covered many modalities and settings for BHT, although we assumed that they all had the same association. However, the results of the sub-analyses show some difference in the association of BHT with time to discontinuation from treatment based on specific sub-populations examined, underscoring the need to tailor treatment regimens to individual patient needs and challenging existing treatment regimen requirements. Specifically, we found that BHT had no significant association on risk of discontinuation for youth and young adults, and women who initiated treatment during pregnancy. Our finding that BHT in the 60 days prior to MOUD appears to be associated with a higher risk of discontinuing treatment was unexpected. We hypothesize that this is actually a marker of individuals who have already failed prior substance use treatment. Perhaps individuals who have struggled or failed at treatment programs where they received BHT are

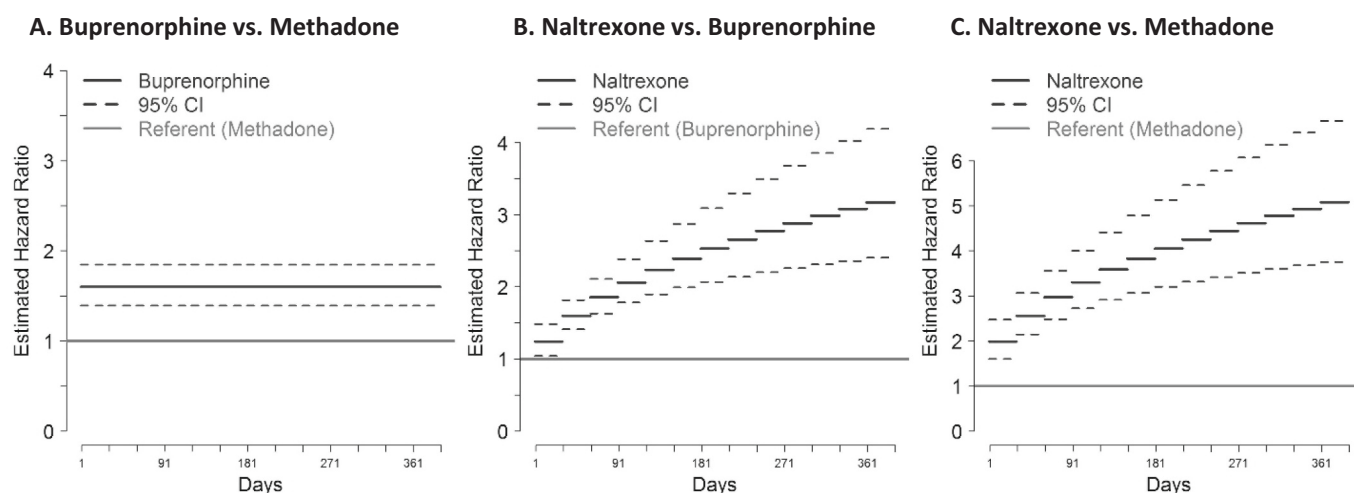


**Fig. 4.** Adjusted estimated hazard ratio of MOUD discontinuation for A. Buprenorphine vs. Methadone, B. Buprenorphine vs. Naltrexone, and C. Naltrexone vs. Methadone for MOUD episodes beginning in the postpartum period.

then referred to or are more open to MOUD.

#### 4.1. Limitations

This study has several limitations. First, administrative claims data is not intended for research purposes. Social determinants of health, such as housing, transportation, poverty, and lack of resources, are not explicitly measured in the data and likely have significant impacts on treatment retention. Further, claims data only represents OUD of individuals when such a diagnosis is present in a claim and service delivery when a payment claim is made. Accordingly, we could not account for BHT in the form of self-help or peer-oriented substance use or behavioral therapies that are not tied to a claim, such as a 12-step program, mutual aid, or residency in a sober living home. Likewise, opioid use can only be inferred if a prescription is filled through Medicaid and reflected in claims data. Sole use of claims data precludes observation of prescriptions obtained outside of Medicaid insurance. Additionally, any illicit substance use, such as heroin use, cannot be accounted for using this dataset.

A second notable limitation, also associated with the constraints of administrative data, is that we could not observe the reason for treatment discontinuation. Treatment may end for a multitude of reasons including non-compliance, overdose, or an agreement between a doctor and patient that services will end because they are no longer beneficial or needed. We largely assume longer treatment retention is better, but this may not always be true for an individual.

A third limitation is unobserved confounders. For example, court ordered MOUD treatment for people in Ohio was most likely to be naltrexone (Baughman et al., 2019), the treatment type that appears to have the shortest retention time among our sample. We were not able to measure which participants were previously incarcerated, so were unable to adjust for this factor. Additionally, treatment access varies based on location of residence, thus there may be geographic differences in access that are unaccounted for in our analysis. Other possible confounders that we were unable to measure include severity of OUD, illicit drug of choice, and length of time using illicit drugs prior to treatment. Data on race had a high level of missing values in the dataset, therefore race was not included as a variable in this analysis. Racial disparities are known to exist in MOUD access, treatment, and outcomes (Lagisetty, Ross, Bohnert, et al., 2019; Krawczyk, Feder, Fingerhoo, & Saloner, 2017).

A fourth limitation in the study is the exclusion of treatment episodes involving more than one type of MOUD (i.e. individuals who “switched” MOUD types). Individuals in treatment may experience changes in prescribed medication in response to adverse reactions, comorbidities, pregnancy, or other factors. Further research is needed to determine the role that switching between MOUDs may play in supporting or impeding treatment retention.

Finally, results of this study may only be generalizable to states with similar Medicaid policies and population profiles.

#### 4.2. Conclusion

In summary, we found that methadone was associated with the lowest risk of treatment discontinuation, followed by buprenorphine, and then naltrexone. We also found that over time, even though buprenorphine remained associated with a higher risk of treatment discontinuation compared to methadone, risk of discontinuation was lower for those that maintained treatment longer. In contrast, naltrexone over time was associated with an increasingly higher chance of discontinuing treatment compared to methadone and buprenorphine. These results were consistent across sub-populations of youth and young adults, pregnant women, and postpartum women. In general, BHT was associated with a lower chance of discontinuing MOUD treatment earlier, indicating a positive effect of BHT during the treatment episode, although this finding was not consistently found across all sub-

populations examined. Further study of these patterns is needed to rule out the important potential for confounding in our analyses, including unmeasured individual factors as well as state-specific treatment norms and regulations. With such verification, our hypotheses about effective changes to treatment policy can sit on firmer ground.

#### CRediT authorship contribution statement

Pengyue Zhang: Conceptualization; Methodology; Validation; Formal analysis; Writing - Original Draft; Writing - Review & Editing; Visualization; investigation.

Krystel Tossone: Conceptualization; Methodology; Writing - Original Draft; Writing - Review & Editing.

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Tina Bickert: Conceptualization; Writing - Review & Editing; Supervision.

Emelie Bailey Conceptualization; Writing - Original Draft; Writing - Review & Editing; Project Administration.

Nathan J. Doogan Conceptualization; Methodology; Validation; Writing - Original Draft; Writing - Review & Editing.

Aimee Mack: Methodology; Validation; Data Curation; Writing - Original Draft; Writing - Review & Editing.

Schuyler Schmidt: Conceptualization; Writing - Review & Editing.

Andrea E. Bonny: Writing - Original Draft; Writing - Review & Editing; Supervision.

#### Declaration of competing interest

None.

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