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Psychiatric comorbidities and their treatment predict buprenorphine continuation among postpartum people with opioid use disorder

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Abstract

Background: Opioid use disorder (OUD) is a growing crisis among pregnant and postpartum people. Psychiatric comorbidities are common, yet how they impact OUD treatment outcomes is not well characterized. The aim of this study was to assess the association of psychiatric comorbidities and receipt of psychiatric treatment with buprenorphine continuation through one year postpartum among a sample of people with OUD.

Methods: A subsample was identified from a larger retrospective cohort of patients receiving buprenorphine for OUD at the time of delivery from an academic medical center between 2017 and 2020. Medical record abstractions were conducted during pregnancy through one year postpartum. Independent variables included any psychiatric diagnosis and postpartum receipt of psychiatric treatment (medication or behavioral health). The primary outcome was week of buprenorphine discontinuation. Cox Proportional Hazard models were used.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Hannah Shadowen: Conceptualization, Formal analysis, Writing – original draft, Writing – review & editing. **Stephanie Violante:** Methodology, Data curation, Writing – review & editing. **Andrea Gataric:** Conceptualization, Data curation, Writing – review & editing. **Alison N. Goulding:** Visualization, Writing – review & editing. **Caitlin E. Martin:** Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing, Funding acquisition.

Results: Of 138 patients, 71.8% had a psychiatric condition and 35.5% continued buprenorphine for a full year postpartum. Postpartum buprenorphine continuation was associated with (a) Psychiatric co-morbidity (buprenorphine discontinuation HR 0.49; 95% CI 0.29, 0.82), (b) Receipt of psychiatric medications in weeks 39–52 postpartum (buprenorphine discontinuation HR 0.21; 95% CI 0.06, 0.83), and (c) Receipt of behavioral health therapy in weeks 9–38 postpartum (buprenorphine discontinuation HR 0.40; 95% CI 0.18, 0.90).

Conclusion: Our work suggests a dynamic relationship between OUD treatment outcomes, psychiatric comorbidities and receipt of psychiatric treatments through the highly vulnerable postpartum period. Clinicians and researchers alike should work to advance patient-centered engagement in integrated care models tailored for this unique population.

Keywords

Opioid use disorder; Postpartum; Perinatal; Mental illness

1. Introduction

Opioid use disorder (OUD) during pregnancy and postpartum presents a growing public health concern for both the infant and parent (Kern-Goldberger et al., 2020; Hirai et al., 2021). Drug related deaths, including overdose, have become a leading cause of pregnancy-associated mortality in the United States, and especially in the 12 months after delivery due to the unique stressors during this postpartum time period (Nielsen et al., 2020; Smid et al., 2019; Wallace et al. (2020); Margerison et al., 2022).

Promisingly, OUD is a treatable chronic medical condition, with the potential for optimal outcomes resulting from the use of evidence-based OUD treatments (Klaman et al., 2017). Medication for OUD (MOUD), including buprenorphine and methadone, is the standard of care for individuals with OUD, including pregnant and postpartum people (Kampman and Jarvis, 2015; Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants 2018). OUD treatments that include MOUD are superior to treatments without MOUD in reducing overdose risk and increasing treatment continuation (Kampman and Jarvis, 2015; Wakeman et al., 2020). Unfortunately, MOUD discontinuation is common in the postpartum period, with discontinuation rates reported as high as 66% (Schiff et al., 2021; Wilder et al., 2015; Krans et al., 2021). Lapses in MOUD continuity can place individuals with OUD at increased risk of overdose, morbidity and mortality in the already vulnerable postpartum period (Schiff et al., 2018; Nielsen et al., 2020).

Psychiatric conditions, such as major depression and anxiety disorders, are common comorbidities among individuals with OUD, especially females (Jones and McCance-Katz, 2019; Arnaudo et al., 2017). Psychiatric conditions in the postpartum period are associated with poor outcomes for the parent-infant dyad, such as greater postpartum weight retention, worse physical health (weight retention, overall physical health), and poorer social function among postpartum parents with psychiatric conditions compared to parents without (Vesga-Lopez et al., 2008; Slomian et al., 2019). In non-pregnant/postpartum samples, evidence for the relationship between psychiatric comorbidities and MOUD retention is mixed, with some studies suggesting that individuals with a psychiatric diagnosis are less likely to

be retained in buprenorphine treatment and others finding that buprenorphine treatment retention is more likely among these individuals (Slomian et al., 2019; O'Connor et al., 2018; Shadowen et al., 2021). Additionally, little is known about the impact of psychiatric treatment on MOUD retention in the postpartum period. One retrospective cohort study of postpartum patients receiving buprenorphine at delivery found that the provision of an antidepressant prescription during the third trimester was associated with higher odds of buprenorphine continuation at 6 months postpartum (O'Conner et al., 2018). While there may be sparse literature on buprenorphine continuation and psychiatric conditions, continuity of diabetes care and HIV care has been examined in the context of psychiatric comorbidities. Greater nonadherence to HIV medication was associated with depression in one meta-analysis, and antidepressant treatment for depression was associated with a reduction in HIV medication nonadherence (Gonzalez et al., 2007; El-Halabi et al., 2022). Similarly, depression is associated with diabetes regimen non-adherence across diet, exercise and pharmacological treatment modalities (Gonzalez et al., 2011).

There remains a gap in knowledge regarding how psychiatric comorbidities and their treatments impact buprenorphine continuation after infant delivery through the high risk one-year postpartum period for birthing parents with OUD. Investigations to identify clinical and psychosocial factors that heighten or mitigate the risk of postpartum MOUD discontinuation are urgently needed to inform targeted evidence-based improvements in the quality of OUD treatments and MOUD continuity. Thus, the aims of the current study are to examine the association of (1) the presence of a psychiatric comorbidity, (2) the receipt of psychiatric medication in the postpartum period, and (3) the receipt of behavioral health therapy in the postpartum period on buprenorphine discontinuation among postpartum people with OUD who were receiving buprenorphine at the time of delivery.

2. Materials and methods

2.1. Design

The current study is a secondary analysis of a retrospective cohort study exploring health and addiction outcomes for pregnant and postpartum patients who received buprenorphine for OUD at an academic medical center. The retrospective cohort study was approved by the University's Institute Review Board. Methods for the parent study are described elsewhere (Shadowen et al., 2021). Briefly, patients receiving buprenorphine at any point during pregnancy and/or through one year postpartum from January 2017 to March 2020 at an academic medical center were identified through a query of the electronic medical records. It is important to note that this academic medical center has an integrated obstetric and gynecological clinic that provides prenatal, postnatal and gynecological care along with treatment for substance use disorder. In addition to these services, the clinic provides social work/case management services and in-house behavioral health services. Receiving care in this clinic was not required to be a part of this study, but many patients in this study were patients at this clinic. A study team performed a manual abstraction of the electronic medical records from the academic medical center, which included review of buprenorphine prescriptions documented by the state Prescription Monitoring Program.

2.2. Data collection

Our dataset consisted of chart abstractions performed in four-week intervals for each patient which collected data about pregnancy, OUD treatment, psychiatric diagnoses, and psychiatric treatment. The maximum number of four-week intervals abstracted for a patient was 22 (9 intervals during pregnancy and 13 intervals during the postpartum period). The four-week interval was used to reflect clinical practices where a monthly provider visit typically occurs in conjunction with buprenorphine prescribing. Chart abstractions started when patients first enrolled in the study during pregnancy and continued until they either (1) had discontinued buprenorphine for at least two consecutive intervals, or (2) reached 52 weeks (one year) postpartum. A patient was considered 'continuing' buprenorphine for a given interval if they received buprenorphine at any point during that interval. Patients were no longer included in the parent study after buprenorphine discontinuation (no receipt of buprenorphine for at least two consecutive intervals). For example, a patient could enroll in the parent study at 14 weeks pregnant, have their delivery at 35 weeks, and stop taking buprenorphine at 16 weeks postpartum. Their first interval would include weeks 14 through 17 of pregnancy; the interval during which they delivered would include week 34 of pregnancy through the 2nd week postpartum; the interval during which they stopped taking buprenorphine would include weeks 15 through 18 postpartum (though they would still be considered to be continuing buprenorphine in that interval because buprenorphine was received at some point during the interval); and the week in which they would be considered 'discontinued' would be week 18 (the last week of the last interval during which buprenorphine was taken).

2.3. Sample

Patients were included in the current secondary analysis if they (1) were pregnant upon entering the parent study, (2) had data for at least two intervals in the parent study, and (3) continued buprenorphine through infant delivery and at least one week postpartum. Patients were excluded if they had missing data for our main variables of interest or included covariates ($n = 4$). Altogether, of the parent study's sample of 233 patients, the current study included $N = 138$ patients (see Fig. 1).

2.4. Exposure and outcome variables

The primary outcome was time to discontinuation of buprenorphine after infant delivery (in weeks). Buprenorphine continuation for each four-week interval was defined as either (1) identification of a buprenorphine prescription/order in the electronic medical record or (2) filled buprenorphine prescription reported on the state Prescription Monitoring Program in the four-week interval. The last week of the four-week interval in which a patient was included in the study was considered the week they discontinued buprenorphine. If the patient continued buprenorphine until 52 weeks postpartum, the end of the follow-up time, they were considered censored at week 52 (Rich et al., 2010).

Independent variables include presence of a psychiatric diagnosis and receipt of psychiatric treatment (medication and/or behavioral health). A patient was considered to have a comorbid psychiatric condition if they had any provider-rendered psychiatric diagnosis (e.g., ADHD, anxiety, bipolar disorder, depression, schizophrenia, PTSD) reported in

their electronic medical record (i.e., in medical history, problem list, and/or provider documentation) at the time of initial enrollment in the parent study. Due to the small sample, no distinction was made between mood disorders such as depression and anxiety and severe psychiatric conditions such as schizophrenia and PTSD. Psychiatric treatment (medication and/or behavioral health) is time varying and was collected at each interval. A patient was considered to have received psychiatric medication treatment during an interval if they were prescribed antidepressant, anxiolytic, or antipsychotic medication treatment (e.g., Paroxetine, Bupropion, dextroamphetamine, antidepressants, benzodiazepine) per documentation in their electronic medical record. A patient was considered to have received behavioral health therapy if they participated in group and/or individual sessions identified either by the behavioral health clinician (at same institution) note or per other provider documentation (if receiving therapy outside institution).

The psychiatric treatment variables were lagged four weeks such that buprenorphine continuation/discontinuation in an interval was predicted by receipt of psychiatric treatment in the prior interval. The lag of the treatment variable was taken to recognize the reciprocal causation and the delay in which the effect of the variable (psychiatric treatments) may be observed on the outcome (Masyn, 2003). For example, a patient's buprenorphine continuation/discontinuation in weeks 7–10 was predicted by the receipt of psychiatric medication and/or behavioral health treatment in weeks 3–6. This lag was included in order to establish temporal precedence.

2.5. Analytic plan

Chi-squared tests and Student's t-tests were conducted for demographic, clinical, and psychosocial variables comparing two groups: (1) patients who remained on buprenorphine for 52 weeks postpartum and (2) patients who discontinued buprenorphine before 52 weeks postpartum.

Next, Kaplan-Meier survival curves were generated to visually examine the distribution of the discontinuation of MOUD by week from delivery (the index event) for the sample by 1) presence of psychiatric comorbidity 2) receipt of psychiatric medication, and 3) receipt of behavioral health therapy using the Wilcoxon Rank test.

Lastly, Cox proportional hazard models were used to assess for associations between our independent variables (psychiatric comorbidity, receipt of psychiatric medication, and receipt of behavioral health therapy) and time (in weeks) to postpartum buprenorphine discontinuation adjusting for important covariates. This method is similar to prior work done in postpartum populations (Schiff et al., 2021). Two models of the outcome of time to postpartum buprenorphine discontinuation were performed for our independent variables of interest: (1) Presence of comorbid psychiatric condition (operationalized as yes/no), (2) Receipt of prior psychiatric treatment including medication (operationalized as yes/no) and behavioral health therapy (operationalized as yes/no). Model 1 (presence of comorbid psychiatric condition predicting discontinuation) included the total sample and model 2 (receipt of psychiatric treatment) included only the sub-sample with a psychiatric comorbidity. For both models, delivery marked the start of the time-to-event analyses, and censoring occurred either at the 52nd postpartum week (if they did not discontinue

buprenorphine) or the last week of the study interval (if they did discontinue buprenorphine) (Rich et al., 2010).

The following covariates were included in the models: (1) incarceration status at delivery (not incarcerated or incarcerated), (2) race (non-White vs. White), (3) age (in years, continuous, integer), (4) the number of weeks patients received buprenorphine before delivery (continuous, integer). Covariates were selected based on existing literature that has identified factors associated with MOUD outcomes: incarceration status at delivery, race, age, and the number of weeks patients received buprenorphine before delivery (Schiff et al., 2021; Goodman et al., 2022). While we recognize that race is not a biological variable, rather a reflection of societal grouping, we included race in our models given reported wide disparities in OUD outcomes between Black and White birthing parents (Schiff et al., 2020). Proportionality assumptions were tested by examining both adjusted log-log plots and Schoenfeld residuals for each outcome of interest (Kuitmen et al., 2021). Receipt of psychiatric medications and receipt of behavioral health therapy violated the proportional hazard assumption. Due to this violation, we provide estimates of the hazards for three distinct time periods that reflect where the hazards cross, weeks 0–8, 9–38 weeks, and 39–52 weeks postpartum. All analysis was done with STATA 16.

3. Results

Our final sample included 138 patients; 100 (71.8%) had a psychiatric comorbidity. Of the 138 patients, 49 (35.5%) continued buprenorphine until 52 weeks postpartum, and 89 (64.5%) discontinued buprenorphine before 52 weeks postpartum. These results and the following can be found in Table 1. The proportion of patients discontinuing buprenorphine before 1-year postpartum did not differ by presence of psychiatric comorbidity (81.6% for patients who continued vs. 67.2% for patients that did not continue; $p = 0.074$), yet did differ by race (46.9% Black for patients who continued vs. 20.2% for patients who did not continue; $p < 0.001$) and being incarcerated at the time of delivery (12.2% of patients who continued vs. 27.0% for patients who did not continue; $p = 0.045$) for the total sample. Among patients with any psychiatric comorbidity ($n = 100$), anxiety was the most common diagnosis (76%) followed closely by depression (72%), and schizophrenia was the least common (5%). There were no differences in postpartum buprenorphine continuation by type of psychiatric diagnosis.

Kaplan-Meier curves of the unadjusted weekly probability of continued buprenorphine in the total sample as well as the subsample of patients with a psychiatric comorbidity are shown in Fig. 2. There was a significant difference in the probability of discontinuation between patients with and without a psychiatric comorbidity ($p = 0.0014$). Among patients with a psychiatric comorbidity, there was a significant difference in the probability of discontinuation between patients with receipt of psychiatric medications compared to patients without receipt ($p = 0.036$), and no significant difference in the probability of discontinuation between patients with receipt of behavioral health therapy and patients without ($p = 0.1236$).

In the Cox proportional hazard models, patients with any psychiatric comorbidity were less likely to discontinue buprenorphine than patients without a psychiatric comorbidity (HR 0.54; 95% CI 0.34, 0.86; Table 2). This finding remained after adjustments for race, incarceration at delivery and time taking buprenorphine before delivery = (HR 0.49; 95% CI 0.29, 0.82).

Among the subsample of patients with a psychiatric comorbidity, receipt of psychiatric medication was associated with a decreased likelihood of discontinuing buprenorphine in weeks 39–52 postpartum (HR 0.21; 95% CI 0.06, 0.83 in adjusted model 2; Table 3). However, prior to week 39, there was no significant relationship between receipt of psychiatric medication and discontinuation of buprenorphine (HR 1.18; 95% CI 0.32, 4.37 and HR 0.62 95% CI 0.26, 1.47 in adjusted model 2 respectively; Table 3). Receipt of behavioral health therapy was associated with a significantly lower likelihood of discontinuation of buprenorphine in postpartum weeks 9–38 (HR 0.40; 95% CI 0.18, 0.90) but not for weeks 0–8 postpartum or 39–52 postpartum (Table 3).

4. Discussion

The current study included a unique sample consisting of pregnant patients receiving buprenorphine at the time of delivery to understand how psychiatric comorbidities and treatments for psychiatric conditions affect postpartum buprenorphine continuation. In summary, the prevalence of psychiatric conditions (including both mood disorder and severe psychiatric comorbidities) among our sample is similar to the upper range of psychiatric condition prevalence reported among patients with OUD in the literature (Arnaudo et al., 2017). Further, our results indicated that patients with any psychiatric comorbidity were less likely to discontinue buprenorphine over the course of the postpartum period compared to patients without a psychiatric comorbidity. Among patients with a psychiatric comorbidity, receiving psychiatric medication decreased the subsequent likelihood of buprenorphine discontinuation for weeks 39–52 postpartum, and receiving behavioral health therapy decreased the subsequent likelihood of buprenorphine discontinuation for weeks 9–38 in the postpartum period.

Prior work has presented conflicting evidence about the relationship between psychiatric diagnoses and buprenorphine continuation across various samples. For example, in a study of individuals discharged from addiction centers in the US, psychiatric comorbidity was found to increase the odds of treatment completion (Friesen and Kurdyak, 2020). In another study of 321 patients from a behavioral health clinic between age 18 and 65 who received buprenorphine, patients who had a diagnosis of depression or other mood disorders had a higher probability of being retained in treatment for a full year (Montalvo et al., 2019). Other work suggests that having a psychiatric comorbidity may make buprenorphine treatment continuation more difficult. For example, among a sample of veteran patients who received buprenorphine, having a psychiatric comorbidity was associated with less adherence to buprenorphine treatment (Fareed et al., 2014). Additionally, in a sample of pregnant individuals, anxiety disorder was significantly associated with buprenorphine discontinuation in the year postpartum compared to not having an anxiety diagnosis (Schiff et al., 2021). Similar to our work, Arnaudo et al. (2017) found, in a literature review, that

individuals with moderate psychopathology had the least OUD treatment attrition compared to those with the least severe psychopathology or no psychopathology. Our findings add to the evidence that having a psychiatric comorbidity may increase buprenorphine continuation among individuals with OUD, including during the high risk one year postpartum period. Importantly, though, the impact that psychiatric co-morbidities can have on perinatal OUD outcomes can vary substantially by factors related to both patient characteristics and treatment settings.

There are multiple potential explanations for our finding of longer buprenorphine duration among our sample of postpartum patients with a psychiatric comorbidity than patients without. First, this finding may be related to how our academic center houses a comprehensive program for pregnant and postpartum individuals with substance use disorder. Integrated models providing medical, addiction treatment, mental health and recovery support care, like ours, are associated with superior health outcomes for parent-infant dyads affected by OUD (Klaman et al., 2017). Thus, our finding of increased buprenorphine continuation among individuals with, rather than without, a psychiatric diagnosis may reflect superior patient engagement in care, including OUD treatment, due to these robust services available. Specifically, patients with a psychiatric diagnosis may have (1) had more appointments/contacts with the clinic, or (2) felt they were receiving more comprehensive care, both of which may result in improved treatment engagement and continuity of buprenorphine. Additionally, individuals with a comorbid psychiatric diagnosis may be more used to having a chronic condition that requires daily management. For example, patients with comorbid mental illness and diabetes, conditions that both require daily management, achieved better hemoglobin control than patients with diabetes without a comorbid mental illness (Nieuwenjuijse et al., 2022). Patients with a psychiatric diagnosis may have already overcome the difficulties in establishing a routine of care management, making it easier to add OUD treatment into their daily lives.

Our findings also add to a very limited literature on the effect of mental health treatment on OUD treatment retention. Although psychiatric comorbidities are common in individuals with opioid use disorder, behavioral health treatment is underutilized in OUD treatment settings (Novak et al., 2019). Prior work examining the relationship between psychiatric treatments and buprenorphine continuation is sparse and inconsistent, with one study having found no relationship between prescription of antidepressants in the third trimester and treatment outcomes in the postpartum period, and another study finding significant positive associations between prescription of antidepressants in the third trimester and treatment retention 6 months postpartum (Ray-Griffith et al., 2021; O'Connor et al., 2018). The current study adds to the existing literature in several ways. Notably, it is the only one, to our knowledge, that examines the impact of psychiatric treatments in the postpartum period (rather than the prenatal period) on buprenorphine discontinuation. Additionally, our study employed robust methods using survival analysis with time varying factors reflecting the dynamic nature of mental health treatment found within the clinic setting. Analyses that do not use time varying factors treat mental health treatments as static and unchanging despite the fluidity of these treatments in reality.

In addition, we found that psychiatric treatments demonstrated varying associations with postpartum buprenorphine continuation among patients with a psychiatric diagnosis at different times in the postpartum period. We surmise that the non-significant effect of both psychiatric medications and behavioral health therapy in the first 8 weeks postpartum may be because individuals are receiving additional supports during that period, overpowering our ability to witness any benefits due specifically to the psychiatric treatments evaluated in our dataset. Additionally, development and recognition of postpartum conditions such as postpartum depression or psychosis may not occur until after 8 weeks, leading to treatment initiation and gain of treatment benefit after the first 8 weeks postpartum. Only during the postpartum weeks 8–39, we found an association with a reduced risk of buprenorphine discontinuation among patients receiving behavioral health therapies. This finding may be reflective of how some behavioral therapies may be especially beneficial to patients during times of life transitions that necessitate learning new behaviors and roles, such as the early postpartum period where there is a high concentration of transitions occurring for the parent-infant dyad (e.g., new life routines, situations prompting use of coping mechanisms, changes in relationships). Additionally, some behavioral health treatments, such cognitive behavioral therapy, provide skills and tools for behavioral change that can be immediately applied, leading to our ability to detect treatment benefit during postpartum weeks 9–38. Lastly, only during the latest postpartum weeks were psychiatric medications significantly associated with a reduced risk of buprenorphine discontinuation. This may be because psychiatric medications can take several weeks to work effectively. Therefore, receipt of medication benefit may require individuals to be engaged in treatment for a long enough duration to be prescribed a medication plus an additional time period of consistent medication adherence, leading to our findings of medication treatment benefit during postpartum weeks 39–52.

Encouragingly, clinical care has started to integrate care and remove barriers to siloed medical and behavioral health services (Schiff et al., 2022). Prior work has suggested that collaboration and shared decision making between providers in the perinatal period can encourage treatment for both psychiatric conditions and OUD in this critical time period (Raffi et al., 2021). In addition, prior work has shown greater treatment engagement among patients with OUD who are receiving care that includes wraparound services that involves behavioral health and care coordination (Ganetsky et al., 2022). Although prior work has called attention to the need for integrated care, the evidence of the efficacy of this care remains limited. Our work provides supporting evidence that psychiatric comorbidities may increase buprenorphine continuation when patients have access to integrated care services that address both their addiction and psychiatric needs. We also demonstrate that treatment for psychiatric comorbidities may improve OUD outcomes in the postpartum period. With the continued overdose crisis and increasing contribution of OUD to pregnancy-associated deaths, further evidence is urgently needed to guide the implementation of evidence-based care models addressing the complex medical and psychosocial needs of birthing parents with OUD.

While we address gaps in the literature, we do face limitations in our study. First, we are limited to individuals who received care at a single academic medical center so our findings may not be generalizable to a larger audience. This single academic medical center has a designated addiction clinic staffed by Obstetricians that provide integrated care for many

of the individuals in this study, including incarcerated pregnant people; making the results less generalizable to populations that do not have access to this type of clinical care model. Our data did not include information about individuals' self-reported engagement in care, either with this integrated clinic or other addiction services, nor treatment outcomes beyond variables captured consistently in the medical record (i.e., buprenorphine prescription receipt), such as self-reported abstinence and toxicology testing. Future research evaluating healthcare models for this patient population should incorporate patient-reported OUD treatment and recovery outcomes. Further, we have a small sample that is missing key information for many individuals on important potential covariates (i.e. education and income) and outcomes (specifically neonatal outcomes), so we cannot explore these factors. Our small sample precluded our ability to assess differences in outcomes by mood disorders, such as anxiety, depression or others, compared to severe psychiatric conditions, such as schizophrenia or PTSD which have illustrated differing associations in other clinical samples (Fitzsimons et al., 2007; Tuten et al., 2018). These differences should be investigated further in subsequent studies of pregnant and postpartum people. In addition, we are relying on medical record data that may be incomplete if, for example, an individual saw providers outside of our medical center's electronic medical record system. This may have particularly impacted the mental health treatment variables as many individuals seek psychiatric care from community or private providers. Finally, the data only reflect prescribed buprenorphine and does not reflect if the patient actually took the medication or not.

5. Conclusions

Our work expands a body of evidence that suggests psychiatric comorbidities may serve as a driver for OUD treatment continuation, and psychiatric treatment may actually increase treatment continuation when evidence-based treatments are available and accessible. Further qualitative work may better illuminate underlying mechanisms of our findings and illuminate potential targets for adjunctive interventions aimed to improve OUD outcomes. Ultimately, our results add to the evidence about the critical interplay between the receipt of treatment for psychiatric comorbidities and OUD in the one-year postpartum period.

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References

Arnaudo CL, Andraka-Christou B, Allgood K, 2017. Psychiatric co-morbidities in pregnant women with opioid use disorders: prevalence, impact, and implications for treatment. Curr. Addict. Rep 4 (1), 1–13. doi:10.1007/s40429-017-0132-4. [PubMed: 28357191]

El-Halabi S, Cooper DH, Cha DS, Rosenblat JD, Gill B, Rodrigues NB, Lipsitz O, McIntyre RS, Gill H, 2022. The effects of antidepressant medications on antiretroviral treatment adherence in HIV-positive individuals with depression. J. Affect. Disord 300, 219–225. doi:10.1016/j.jad.2021.12.083. [PubMed: 34952118]

Fareed A, Eilender P, Ketchen B, Buchanan-Cummings AM, Scheinberg K, Crampton K, Nash A, Shongo-Hiango H, Drexler K, 2014. Factors affecting noncompliance with buprenorphine

maintenance treatment. J. Addict. Med 8 (5), 345–350. doi:10.1097/ADM.0000000000000057. [PubMed: 25072677]

Fitzsimons HE, Tuten M, Vaidya V, Jones HE, 2007. Mood disorders affect drug treatment success of drug-dependent pregnant women. J. Subst. Abuse Treat 32 (1), 19–25. doi:10.1016/j.jsat.2006.06.015. [PubMed: 17175395]

Friesen EL, Kurdyak P, 2020. The impact of psychiatric comorbidity on treatment discontinuation among individuals receiving medications for opioid use disorder. Drug Alcohol Depend. 216, 108244. doi:10.1016/j.drugalcdep.2020.108244. [PubMed: 32861134]

Ganetsky VS, Heil J, Yates B, Jones I, Hunter K, Rivera B, Wilson L, Salzman M, Baston KE, 2022. A low-threshold comprehensive shared medical appointment program for perinatal substance use in an underserved population. J. Addict. Med 16 (3), e203–e209. doi:10.1097/ADM.0000000000000912. [PubMed: 34510086]

Gonzalez JS, Safren SA, Cagliero E, Wexler DJ, Delahanty L, Wittenberg E, Blais MA, Meigs JB, Grant RW, 2007. Depression, self-care, and medication adherence in type 2 diabetes: relationships across the full range of symptom severity. Diabetes Care. 30 (9), 2222–2227. doi:10.2337/dc07-0158. [PubMed: 17536067]

Gonzalez JS, Batchelder AW, Psaros C, Safren SA, 2011. Depression and HIV/AIDS treatment nonadherence: a review and meta-analysis. J. Acquir. Immune Defic. Syndr 58 (2), 181–187. doi:10.1097/QAI.0b013e31822d490a. [PubMed: 21857529]

Goodman DJ, Saunders EC, Frew JR, Arsan C, Xie H, Bonasia KL, Flanagan VA, Lord SE, Brunette MF, 2022. Integrated vs nonintegrated treatment for perinatal opioid use disorder: retrospective cohort study. AM. J. Obstetr. Gynecol. MFM 4 (1), 100489. doi:10.1016/j.ajogmf.2021.100489.

Hirai AH, Ko JY, Owens PL, Stocks C, Patrick SW, 2021. Neonatal abstinence syndrome and maternal opioid-related diagnoses in the US, 2010-2017. JAMA 325 (2), 146–155. doi:10.1001/jama.2020.24991. [PubMed: 33433576]

Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants. HHS Administration; 2018. https://store.samhsa.gov/sites/default/files/d7/priv/sma18-5054.pdf

Jones CM, McCance-Katz EF, 2019. Co-occurring substance use and mental disorders among adults with opioid use disorder. Drug Alcohol Depend. 197, 78–82. doi:10.1016/j.drugalcdep.2018.12.030. [PubMed: 30784952]

Kampman K, Jarvis M, 2015. American Society of Addiction Medicine (ASAM) National practice guideline for the use of medications in the treatment of addiction involving opioid use. J. Addict. Med 9 (5), 358–367. doi:10.1097/ADM.0000000000000166. [PubMed: 26406300]

Kern-Goldberger AR, Huang Y, Polin M, Siddiq Z, Wright JD, D'Alton ME, Friedman AM, 2020. Opioid use disorder during antepartum and postpartum hospitalizations. Am. J. Perinatol 37 (14), 1467–1475. doi:10.1055/s-0039-1694725. [PubMed: 31421640]

Klaman SL, Isaacs K, Leopold A, Perpich J, Hayashi S, Vender J, Campopiano M, Jones HE, 2017. Treating women who are pregnant and parenting for opioid use disorder and the concurrent care of their infants and children: literature review to support national Guidance. J. Addict. Med 11 (3), 178–190. doi:10.1097/ADM.0000000000000308. [PubMed: 28406856]

Krans EE, Kim JY, Chen Q, Rothenberger SD, James AE 3rd, Kelley D, Jarlenski MP, 2021. Outcomes associated with the use of medications for opioid use disorder during pregnancy. Addiction 116 (12), 3504–3514. doi:10.1111/add.15582. [PubMed: 34033170]

Kuitunen I, Ponkilainen VT, Uimonen MM, Eskelinen A, Reito A, 2021. Testing the proportional hazards assumption in cox regression and dealing with possible non-proportionality in total joint arthroplasty research: methodological perspectives and review. BMC Musculoskelet. Disord 22 (1), 489. doi:10.1186/s12891-021-04379-2. [PubMed: 34049528]

Margerison CE, Roberts MH, Gemmill A, Goldman-Mellor S, 2022. Pregnancy associated deaths due to drugs, suicide, and homicide in the United States, 2010-2019. Obstet. Gynecol 139 (2), 172–180. doi:10.1097/AOG.0000000000004649. [PubMed: 34991132]

Masyn KE, 2003. Discrete-Time Survival Mixture Analysis for Single and Recurrent Events Using Latent Variables. Doctoral dissertation, University of California, Los Angeles.

Montalvo C, Stankiewicz B, Brochier A, Henderson DC, Borba C, 2019. Long-term retention in an outpatient behavioral health clinic with buprenorphine. Am. J. Addict 28 (5), 339–346. doi:10.mi/ajad.12896. [PubMed: 31066985]

Nielsen T, Bernson D, Terplan M, Wakeman SE, Yule AM, Mehta PK, Bharel M, Diop H, Taveras EM, Wilens TE, Schiff DM, 2020. Maternal and infant characteristics associated with maternal opioid overdose in the year following delivery. Addiction 115 (2), 291–301. doi:10.1111/add.14825. [PubMed: 31692133]

Nieuwenhuijse EA, Struijs JN, Sutch SP, Numans ME, Vos RC, 2022. Achieving diabetes treatment targets in people with registered mental illness is similar or improved compared with those without: analyses of linked observational datasets. Diabetic Med. 39 (6), e14835. doi:10.1111/dme.14835, a journal of the British Diabetic Association. [PubMed: 35342984]

Novak P, Feder KA, Ali MM, Chen J, 2019. Behavioral health treatment utilization among individuals with co-occurring opioid use disorder and mental illness: evidence from a national survey. J. Subst. Abuse Treat 98, 47–52. doi:10.1016/j.jsat.2018.12.006. [PubMed: 30665603]

O'Connor AB, Uhler B, O'Brien LM, Knuppel K, 2018. Predictors of treatment retention in postpartum women prescribed buprenorphine during pregnancy. J. Subst. Abuse Treat 86, 26–29. doi:10.1016/j.jsat.2017.12.001. [PubMed: 29415847]

Raffi ER, Gray J, Conteh N, Kane M, Cohen LS, Schiff DM, 2021. Low barrier perinatal psychiatric care for patients with substance use disorder: meeting patients across the perinatal continuum where they are. Int. Rev. Psychiatry 33 (6), 543–552. doi:10.1080/09540261.2021.1898351. [PubMed: 34406106]

Ray-Griffith S, Tharp E, Coker JL, Catlin D, Knight B, Stowe ZN, 2021. Buprenorphine medication for opioid use disorder: a study of factors associated with postpartum treatment retention. Am. J. Addict 30 (1), 43–48. doi:10.1111/ajad.13084. [PubMed: 32673447]

Rich JT, Neely JG, Paniello RC, Voelker CC, Nussenbaum B, Wang EW, 2010. A practical guide to understanding Kaplan-Meier curves. Otolaryngology 143 (3), 331–336. doi:10.1016/j.otohns.2010.05.007, head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery.

Schiff DM, Nielsen T, Terplan M, Hood M, Bernson D, Diop H, Bharel M, Wilens TE, LaRochelle M, Walley AY, Land T, 2018. Fatal and nonfatal overdose among pregnant and postpartum women in massachusetts. Obstet. Gynecol 132 (2), 466–474. doi:10.1097/AOG.0000000000002734. [PubMed: 29995730]

Schiff DM, Nielsen T, Hoeppner BB, Terplan M, Hansen H, Bernson D, Diop H, Bharel M, Krans EE, Selk S, Kelly JF, Wilens TE, Taveras EM, 2020. Assessment of racial and ethnic disparities in the use of medication to treat opioid use disorder among pregnant women in massachusetts. JAMA Netw. Open 3 (5), e205734. doi:10.1001/jamanetworkopen.2020.5734. [PubMed: 32453384]

Schiff DM, Nielsen TC, Hoeppner BB, Terplan M, Hadland SE, Bernson D, Greenfield SF, Bernstein J, Bharel M, Reddy J, Taveras EM, Kelly JF, Wilens TE, 2021. Methadone and buprenorphine discontinuation among postpartum women with opioid use disorder. Am. J. Obstet. Gynecol 225 (4), 424. doi:10.1016/j.ajog.2021.04.210, e1–424.e12.

Schiff DM, Partridge S, Gummadi NH, Gray JR, Stulac S, Costello E, Wachman EM, Jones HE, Greenfield SF, Taveras EM, Bernstein JA, 2022. Caring for families impacted by opioid use: a qualitative analysis of integrated program designs. Acad. Pediatr 22 (1), 125–136. doi:10.1016/j.acap.2021.04.016. [PubMed: 33901729]

Shadowen C, Moeller FG, Martin CE, 2021. The use of once-monthly injectable buprenorphine for the treatment of opioid use disorder in postpartum women: a case series. J. Addict. Med 15 (4), 292–296. doi:10.1097/ADM.0000000000000835. [PubMed: 34397780]

Smid MC, Stone NM, Baksh L, Debbink MP, Einerson BD, Varner MW, Gordon AJ, Clark E, 2019. Pregnancy-associated death in utah: contribution of drug-induced deaths. Obstet. Gynecol 133 (6), 1131–1140. doi:10.1097/AOG.0000000000003279. [PubMed: 31135726]

Slomian J, Honvo G, Emonts P, Reginster JY, Bruyère O, 2019. Consequences of maternal postpartum depression: a systematic review of maternal and infant outcomes. Womens Health 15, 1745506519844044. doi:10.1177/1745506519844044, (Lond Engl).

Tuten M, Fitzsimons H, Hochheimer M, Jones HE, Chisolm MS, 2018. The impact of early substance use disorder treatment response on treatment outcomes among pregnant women with primary

opioid use. J. Addict. Med 12 (4), 300–307. doi:10.1097/ADM.0000000000000397. [PubMed: 29538089]

Vesga-López O, Blanco C, Keyes K, Olfson M, Grant BF, Hasin DS, 2008. Psychiatric disorders in pregnant and postpartum women in the United States. Arch. Gen. Psychiatry 65 (7), 805–815. doi:10.1001/archpsyc.65.7.805. [PubMed: 18606953]

Wakeman SE, Larochelle MR, Ameli O, Chaisson CE, McPheeters JT, Crown WH, Azocar F, Sanghavi DM, 2020. Comparative effectiveness of different treatment pathways for opioid use disorder. JAMA Netw. Open 3 (2), e1920622. doi:10.1001/jamanetworkopen.2019.20622. [PubMed: 32022884]

Wallace ME, Crear-Perry J, Mehta PK, Theall KP, 2020. Homicide during pregnancy and the postpartum period in Louisiana, 2016-2017. JAMA Pediatr. 174 (4), 387–388. doi:10.1001/jamapediatrics.2019.5853. [PubMed: 32011644]

Wilder C, Lewis D, Winhusen T, 2015. Medication assisted treatment discontinuation in pregnant and postpartum women with opioid use disorder. Drug Alcohol Depend. 149, 225–231. doi:10.1016/j.drugalcdep.2015.02.012. [PubMed: 25735465]

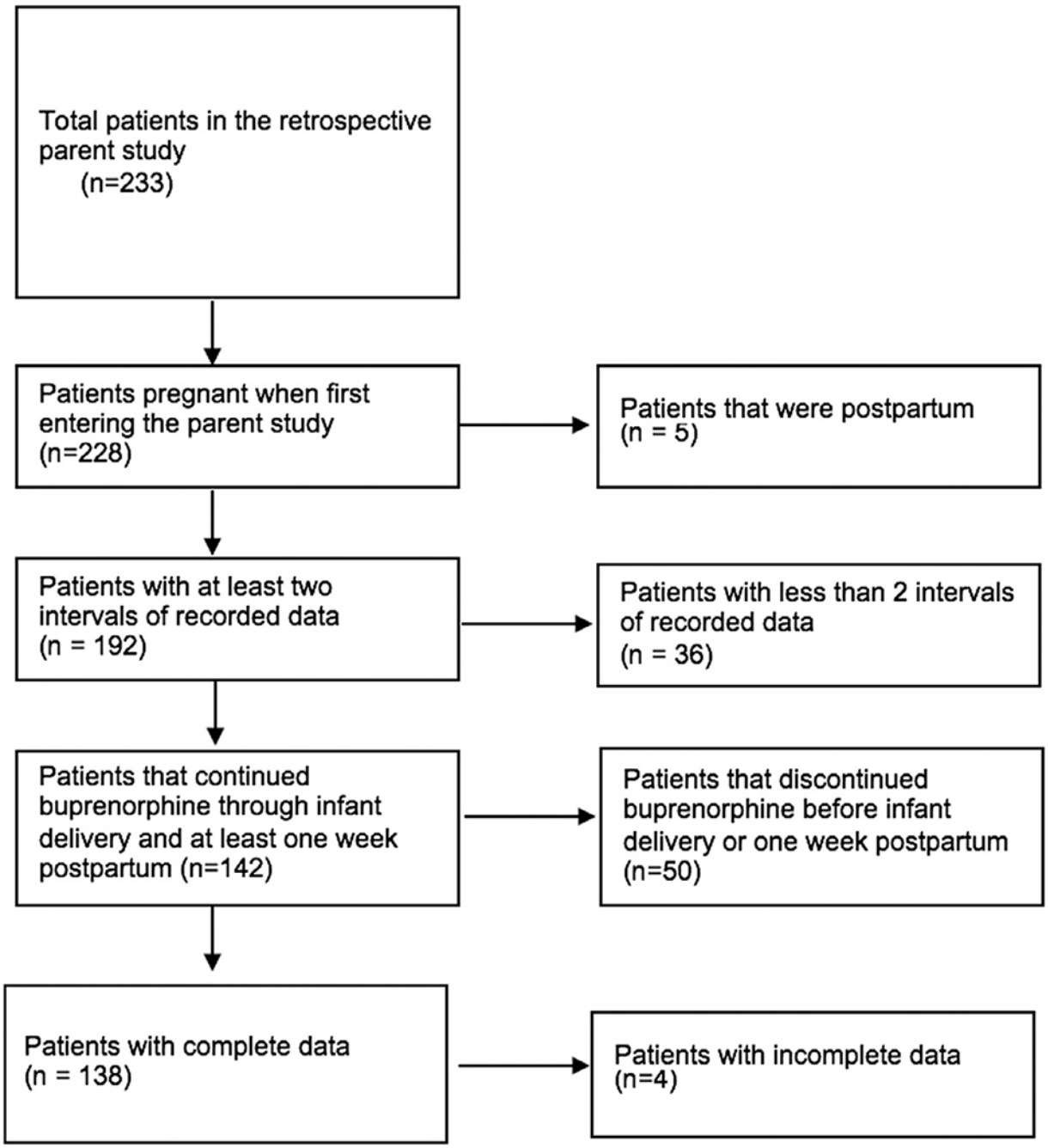

Fig. 1.
Study Schema and final sample size.

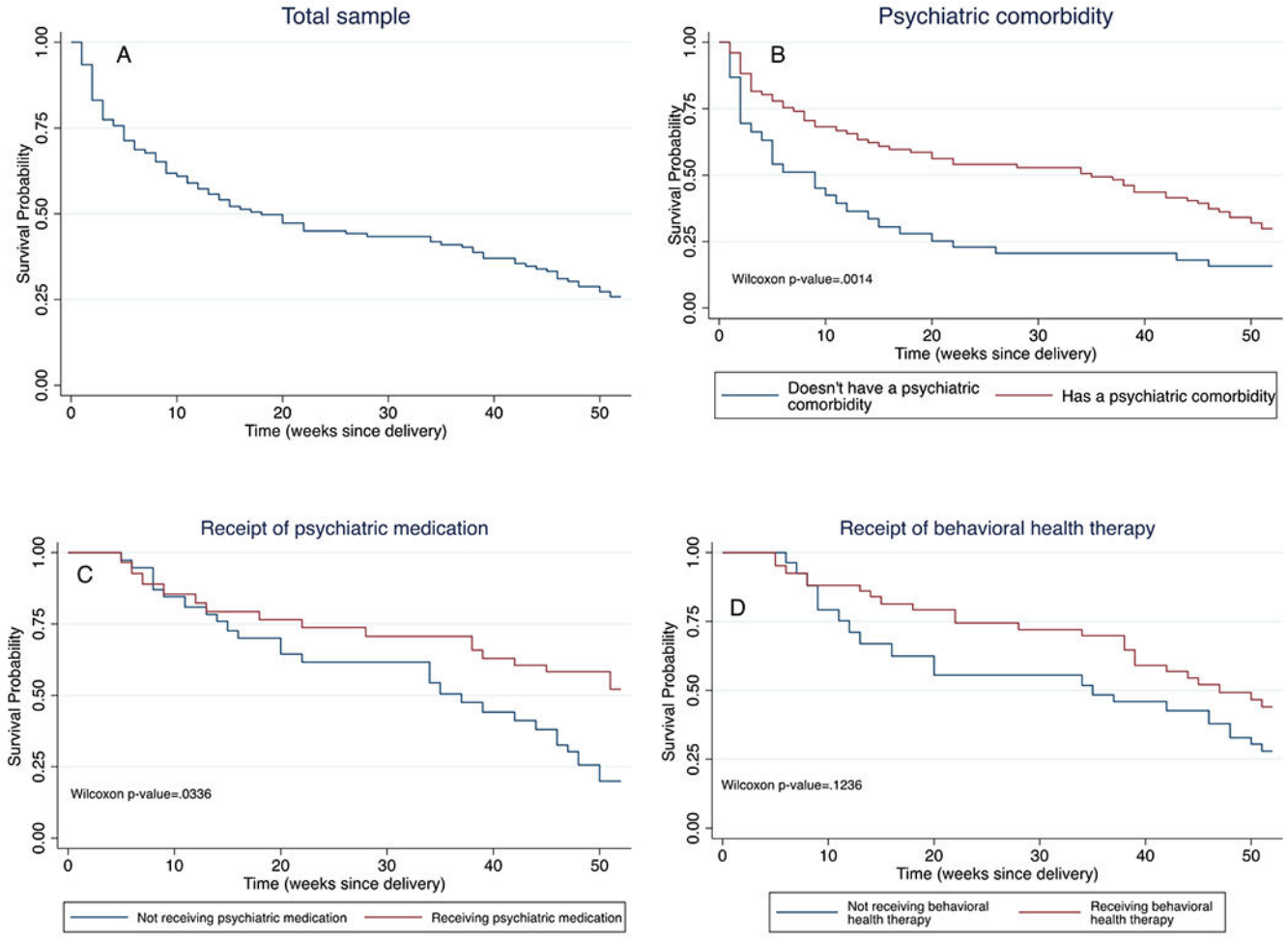

Fig. 2.

Kaplan-Meier Survival Curves of time to buprenorphine discontinuation through 52 weeks postpartum among the total sample and the subsample of patients with a psychiatric diagnosis.

Graphs illustrate buprenorphine continuation trajectories through the 52 week postpartum period for the (A) total sample, (B) total sample by presence of any psychiatric diagnosis, (C) the sub-sample with a psychiatric diagnosis by receipt of postpartum psychiatric medication, (D) the sub-sample with a psychiatric diagnosis by receipt of postpartum behavioral health therapy. For A-D, x axis represents time from delivery to discontinuation of buprenorphine (weeks) or until censored at 52 weeks. For A-D, y-axis represents the number of individuals remaining on buprenorphine at that week over the number of individuals at risk of discontinuing buprenorphine.

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Table 1

Characteristics of patients continuing buprenorphine and discontinuing buprenorphine through 52 weeks postpartum.

	Total sample N(%) *N* = 138	**Continued buprenorphine for all 52 weeks N(%) *N* = 49**	**Discontinued buprenorphine before 52 weeks N(%) *N* = 89**	**p-value**
Gender				
Female	138 (100.0)	49 (100.0)	89 (100.0)	1.000
Race[*1,2]				<0.001
Black	41 (29.7)	23 (46.9)	18 (20.2)	
White	97 (70.3)	26 (53.1)	71 (79.8)	
Incarcerated at the time of delivery[*,2]				0.045
No	108 (78.3)	43 (87.8)	65 (73.0)	
Yes	30 (21.7)	6 (12.2)	24 (27.0)	
Receipt of buprenorphine before delivery (mean weeks, SD)[3]	18.43 (9.3)	19.4 (8.0)	17.61 (9.94	0.160
Age[3]	28.9 (4.8)	28.31 (4.3)	29.19 (5.0)	0.298
Psychiatric comorbidity[2]				0.074
No	38 (26.5)	9 (18.4)	29 (32.6)	
Yes	100 (72.5)	40 (81.6)	60 (67.2)	
Sub-sample with psychiatric comorbidities (*n* = 100)				
Type of psychiatric comorbidity[2,5]				
ADD/ADHD	8 (8.0)	1 (2.5)	7 (11.7)	0.098
Anxiety	76 (76.0)	30 (75.0)	46 (76.7)	0.848
Bipolar/Mania	26 (26.0)	13 (32.5)	13 (21.7)	0.226
Depression	72 (72.0)	30 (75.0)	42 (70.0)	0.585
Schizophrenia	5 (5.0)	3 (7.5)	2 (3.3)	0.349
PTSD	15 (15.0)	6 (15.0)	9 (15.0)	1.0
Percentage of postpartum months with receipt of psychiatric medications (mean, SD)[*,3,4]	51.4 (38.1)	64.7 (34.7)	39.4 (39.3)	0.0019
Percentage of postpartum months with receipt of therapy (mean, SD)[3,4]	61.3 (39.8)	64.1 (34.7)	58.7 (44.2)	0.5349

[1] Patients could be characterized as Native American or Alaska Native, Asia, Black or African American, Native Hawaiian or other Pacific Islander, White, Not reported.

[2] chi-squared tests used to assess the difference between patients who discontinued buprenorphine before 52 weeks and patients who continued buprenorphine before 52 weeks.

[3] Student *t*-test used to assess the difference between patients who discontinued buprenorphine before 52 weeks and patients who continued buprenorphine before 52 weeks.

[4] Although there were 100 individuals with a psychiatric condition, 16 had only one four-week interval in the postpartum period so they did not have any observations with receipt of treatment in the prior four weeks.

[5] Individuals could have more than one diagnosis so totals add up to more than 100%.

* p-value<0.05.

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Table 2

Association of psychiatric comorbidity with the likelihood of buprenorphine discontinuation in the postpartum period.

	Model 1: Presence of psychiatric comorbidity (Unadjusted) Number of subjects=138 HR (95% CI)	**Model 1: Presence of psychiatric comorbidity (Adjusted)[1] Number of subjects=138 HR (95% CI)**
Psychiatric comorbidity		
No	Ref	Ref
Yes	0.55 * (0.35, 0.87)	0.49 * (0.29, 0.82)
Race		
Black	—	Ref
White	—	2.22 * (1.29, 3.80)
Incarcerated at delivery		
No	—	Ref
Yes	—	1.98 * (1.14, 3.44)
Age		0.99 (0.97, 1.01)
Receipt of buprenorphine before delivery (weeks)		1.02 (0.98, 1.06)

[1] Adjusted for race, incarceration at delivery, age, and receipt of buprenorphine before delivery.

* indicates significance at p-value<0.05.

Table 3

Association of psychiatric treatment with the likelihood of buprenorphine discontinuation in the postpartum period among patients with a psychiatric comorbidity.

	Postpartum Weeks 0–8		Postpartum Weeks 9–38		Postpartum Weeks 39–52	
	Model 2: Treatments among patients with a psychiatric comorbidity (Unadjusted) *n* = 100 HR (95% CI)	**Model 2: Treatments among patients with a psychiatric comorbidity (Adjusted)[1] *n* = 100 HR (95% CI)**	**Model 2: Treatments among patients with a psychiatric comorbidity (Unadjusted) *n* = 76[2] HR (95% CI)**	**Model 2: Treatments among patients with a psychiatric comorbidity (Adjusted)[1] *n* = 76[2] HR (95% CI)**	**Model 2: Treatments among patients with a psychiatric comorbidity (Unadjusted) *n* = 53[3] HR (95% CI)**	**Model 2: Treatments among patients with a psychiatric comorbidity (Adjusted)[1] *n* = 53[3] HR (95% CI)**
Receipt of psychiatric medication						
No	Ref	Ref		Ref		Ref
Yes	1.29 (0.60, 2.79)	1.50 (0.72, 3.13)	0.62 (0.25, 1.50)	0.62 (0.26, 1.47)	0.25 * (0.08, 0.83)	0.21 * (0.06, 0.83)
Receipt of behavioral health therapy						
No	Ref	Ref	Ref	Ref	Ref	Ref
Yes	0.55 (0.26, 1.19)	0.76 (0.35, 1.64)	0.49 (0.22, 1.13)	0.40 * (0.18, 0.90)	0.76 (0.26, 2.24)	0.75 (0.26, 2.15)
Race						
Black	—	Ref		Ref		Ref
White	—	—[4]		3.69 * (1.17, 11.62)		1.86 (0.64, 5.46)
Incarcerated at delivery						
No	—	Ref		Ref		Ref
Yes	—	4.98 * (2.32, 10.70)		1.23 (0.58, 2.59)		—[4]
Age (years)		1.01 (0.94, 1.08)		1.09 (0.99, 1.19)		0.94 (0.79, 1.11)
Receipt of buprenorphine before delivery (weeks)		1.10 (0.96, 1.06)		0.98 (0.94, 1.02)		0.94 (0.86, 1.04)

[1] Adjusted for race, incarceration at delivery, age, and receipt of buprenorphine before delivery.

[2] Sample includes only patients who did not discontinue buprenorphine before 9 weeks.

[3] Sample includes only patients who did not discontinue buprenorphine before 30 weeks.

[4] Not able to be estimated due to insufficient variation.

* indicates significance at p-value<0.05.