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RESEARCH ARTICLE

Concurrent Prescription Fills of Opioids and Benzodiazepines Among Postpartum Women During COVID-19

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Introduction: Concurrent prescribing of opioids and benzodiazepines is associated with increased risk of emergency department visits and overdose. Postpartum women commonly receive opioids for pain after delivery and are at risk for postpartum depression/anxiety. Although prior research finds increases in opioid prescribing and symptoms of depression/anxiety during COVID-19, concurrent prescribing among postpartum women has not been examined in the context of COVID-19.

Methods: Using data from a large sample of privately insured postpartum women (N=514,120), the authors compared concurrent prescription fills of opioids and benzodiazepines before March 1, 2020, and after March 1, 2020. Primary outcome variables measured whether a patient ever filled concurrent opioid and benzodiazepine prescriptions and the number of concurrent prescription fills per patient in the 6 months after delivery.

Results: Roughly 46.4% of postpartum women filled an opioid prescription, 2.4% filled a benzodiazepine prescription, and 1.2% of women filled a concurrent prescription. Among postpartum women filling a benzodiazepine prescription, 50.7% filled a concurrent opioid prescription. The number of concurrent fills among postpartum women significantly increased during the early period of COVID-19. On average, postpartum women filled 0.009 more concurrent prescriptions than expected on the basis of the preexisting trend, representing a 22.0% increase in the number of concurrent prescriptions relative to the sample mean.

Conclusions: Concurrent prescribing of opioids and benzodiazepines places postpartum women at higher risk of emergency department visits and overdose. To reduce the harms associated with concurrent prescribing, clinicians should carefully consider whether opioids and/or benzodiazepines are clinically necessary for treatment and consult their state prescription drug monitoring program prior to prescribing these medications.

INTRODUCTION

Concurrent prescribing of opioids and benzodiazepines is associated with increased risk of emergency department (ED) visits and overdose.[1–3] An estimated 83.5% of deaths related to benzodiazepines in the U.S. also involved opioids,[4] and one fourth to one half of opioid-related

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overdoses also involved benzodiazepines.[1,3] Despite clinical guidelines and boxed warnings discouraging concurrent prescribing of opioids and benzodiazepines, concurrent prescribing of these medications remains common.[5–9]

Disruptions to health care and worsening mental health during the coronavirus disease 2019 (COVID-19) pandemic likely exacerbated the risk of receiving concurrent prescriptions of opioids and benzodiazepines. Postpartum women may have been particularly impacted because they are frequently prescribed opioids for pain after delivery[10] and commonly experience postpartum depression and/or anxiety.[11] In addition, research found significant increases in both opioid prescribing[12] and reported symptoms of depression and anxiety[13,14] among postpartum women during COVID-19. However, there is no prior research examining how concurrent prescribing of opioids and benzodiazepines evolved in this population during the pandemic.

To address this gap, this cross-sectional study of 514,120 commercially insured postpartum women examines concurrent prescribing of opioids and benzodiazepines before and during the early period of the COVID-19 pandemic.

METHODS

Study Sample

Data are from Optum's deidentified Clinformatics® Data Mart Database (2016–2020), which is derived from a database of administrative health claims for members of large commercial and Medicare Advantage health plans. This retrospective cross-sectional study includes 514,120 postpartum women observed between January 1, 2016 and December 31, 2020. Inclusion criteria required 6 months of continuous plan enrollment (with at least 3 months postpartum) and delivery of a single live birth. Delivering individuals aged <18 years and >50 years were excluded.

Claims for medical diagnoses, medical services, and prescription drug fills were aggregated at the patient level. Births were identified using Current Procedural Terminology and ICD-10-CM codes (Appendix Table 1, available online). To be defined as giving birth, patients had to have either an ICD-10-CM or a Current Procedural Terminology code indicating birth.

The authors followed the STROBE reporting guidelines for cross-sectional studies. The University of Georgia IRB approved this study and waived the need for informed consent owing to the deidentified nature of the data.

Measures

The authors used several measures of opioid and benzodiazepine prescription fills in the postpartum period, defined as the first 6 months after delivery date. They identified all benzodiazepines included in the anxiolytics, sedatives, and hypnotics therapeutic classes using American Hospital Formulary Service Classification Code 282408. All opioids were identified using National Drug Codes from the Centers for Disease Control and Prevention's Opioid National Drug Codes and Oral Morphine Milligram Equivalent Conversion File.[15] The authors measured whether a patient ever filled a benzodiazepine prescription, ever filled an opioid prescription, and ever filled a concurrent prescription of opioids and benzodiazepines in the postpartum period. Consistent with prior research, concurrent fills were defined as an opioid–benzodiazepine overlap of at least 1 day according to the fill date and the number of days' supply of each prescription.[2,16] The authors also measured the average number of benzodiazepine, opioid, and concurrent fills per patient in the postpartum period.

Statistical Analysis

Analyses were performed from April to November of 2023. Descriptive statistics were calculated for all variables. Data were aggregated to the patient-birth level. The authors used ordinary least squares regression to fit the time trend for each outcome variable using data from patients giving birth prior to the COVID-19 pandemic (January 2016–February 2020). Regressions included indicator variables for calendar month to capture seasonality in outcomes and calendar year to address potential changes in sample composition due to changes in participation in Clinformatics Data Mart Database. The authors used ordinary least squares regression models to predict expected outcomes during the COVID-19 period (March 2020–December 2020) on the basis of the pre-existing trend. Data were analyzed using Stata 17.0.

RESULTS

Opioid and benzodiazepine prescription fills were examined for 514,120 postpartum women. Over the study period, 46.4% of the sampled women filled an opioid prescription, 2.4% filled a benzodiazepine prescription, and 1.2% filled a concurrent prescription (Table 1). Of women filling an opioid prescription, 3.4% filled a concurrent benzodiazepine prescription. Of women filling a benzodiazepine prescription, 50.7% filled a concurrent opioid prescription.

Figure 1 shows deseasonalized actual and predicted values for the proportion of postpartum women with opioid, benzodiazepine, and concurrent prescriptions before and during the early period of the COVID-19 pandemic. Of note, Figure 1 indicates that opioid prescription fills, benzodiazepine prescription fills, and concurrent fills of opioid and benzodiazepines were all decreasing prior to the COVID-19 pandemic.

Table 1. Descriptive Statistics (N=514,120)

Variables	% (n) or mean (SD)
Percentage of women ever filling a concurrent opioid and benzodiazepine prescription	1.2 (6,169)
Percentage of women ever filling a benzodiazepine prescription	2.4 (12,339)
Percentage of women ever filling an opioid prescription	46.4 (258,645)
Percentage of women with an opioid prescription fill who filled a concurrent benzodiazepine prescription[a] (*n*=258,645)	3.4 (8,794)
Percentage of women with a benzodiazepine prescription fill who filled a concurrent opioid prescription[a] (*n*=12,339)	50.7 (6,256)
Number of concurrent opioid and benzodiazepine prescription fills per patient, mean (SD)	0.041 (0.405)
Number of benzodiazepine prescription fills per patient, mean (SD)	0.079 (0.637)
Number of opioid prescription fills per patient, mean (SD)	0.767 (1.39)
Percentage of women with vaginal delivery	65.8 (338,060)
Percentage of women with Cesarean delivery	34.2 (175,697)
Age at delivery, mean (SD)	31.206 (5.139)

[a]For the percentage of women with an opioid prescription fill who also filled concurrent benzodiazepine prescription, the total number of women with an opioid prescription fill is 258,645. For the percentage of women with a benzodiazepine prescription fill who also filled a concurrent opioid prescription, the total number of women with a benzodiazepine prescription fill is 12,339.

Postpartum women were 2.5 percentage points more likely to fill an opioid prescription and 0.3 percentage points more likely to fill a benzodiazepine prescription during the COVID-19 period than expected on the basis of the preexisting trend (Table 2). The average number of opioid prescriptions significantly increased during COVID-19, with women receiving 0.06 more opioid prescriptions than expected relative to the preexisting trend. There was no significant change in the average number of benzodiazepine prescriptions.

The share of postpartum women filling concurrent opioid and benzodiazepine prescriptions during COVID-19 was not statistically different from the share expected on the basis of the preexisting trend, although several months in late 2020 did fall above the 95% CI (Figure 1). The average number of concurrent opioid and benzodiazepine prescriptions filled significantly increased during the early period of the COVID-19 period. On average, postpartum women filled 0.009 more concurrent prescriptions than expected on the basis of the preexisting trend (Table 2), representing a 22.0% increase relative to the sample mean.

Appendix Figures 1–3 (available online) show that there is no evidence of coincident changes in observable characteristics of the mothers (average age at birth, proportion White) or proportion of Cesarean births.

DISCUSSION

This study adds to the literature on prescribing of opioids and benzodiazepines during the pandemic by examining concurrent prescribing of opioids and benzodiazepines among postpartum women.[17,18] This study found that half of the postpartum women who filled a benzodiazepine prescription filled a concurrent opioid prescription. The average number of concurrent fills of opioids and benzodiazepines among postpartum women increased significantly from March 2020 through December 2020. In addition, the results suggest that the onset of the COVID-19 pandemic may have reversed some of the progress made in reducing concurrent prescribing of opioids and benzodiazepines that occurred prior to the pandemic. These findings are concerning given the increased risk of ED visits and overdose associated with concurrent prescribing of these medications.

The Center for Disease Control and Prevention's Opioid Prescribing Guidelines and the U.S. Food and Drug Administration warn providers and patients about the harms of concurrent prescribing of opioids and benzodiazepines.[5–8] In 2016, the U.S. Food and Drug Administration added a boxed warning to opioid and benzodiazepine labels detailing the life-threatening risks associated with the combined use of these drugs.[7] In 2020, the boxed warning on benzodiazepines was updated to further warn against the serious risks of the medication as well as the risk of overdose death when combined with opioids.[8] Despite these warnings, this study found high rates of concurrent prescribing among women filling benzodiazepine prescriptions and increases in concurrent prescription fills during the pandemic. The increases in concurrent prescribing observed in the early period of the pandemic were likely driven in part by the increase in opioid prescribing during the pandemic[12] as well as an increase in anxiety experienced by postpartum women early in the pandemic.[14] Overall, the results suggest that additional efforts are needed to reduce potential harms associated with concurrent prescribing.

One policy tool showing promise in reducing concurrent prescribing of opioid and benzodiazepines is comprehensive mandatory-use Prescription Drug Monitoring Programs (PDMPs).[19,20] To reduce concurrent prescribing of opioids and benzodiazepines, states

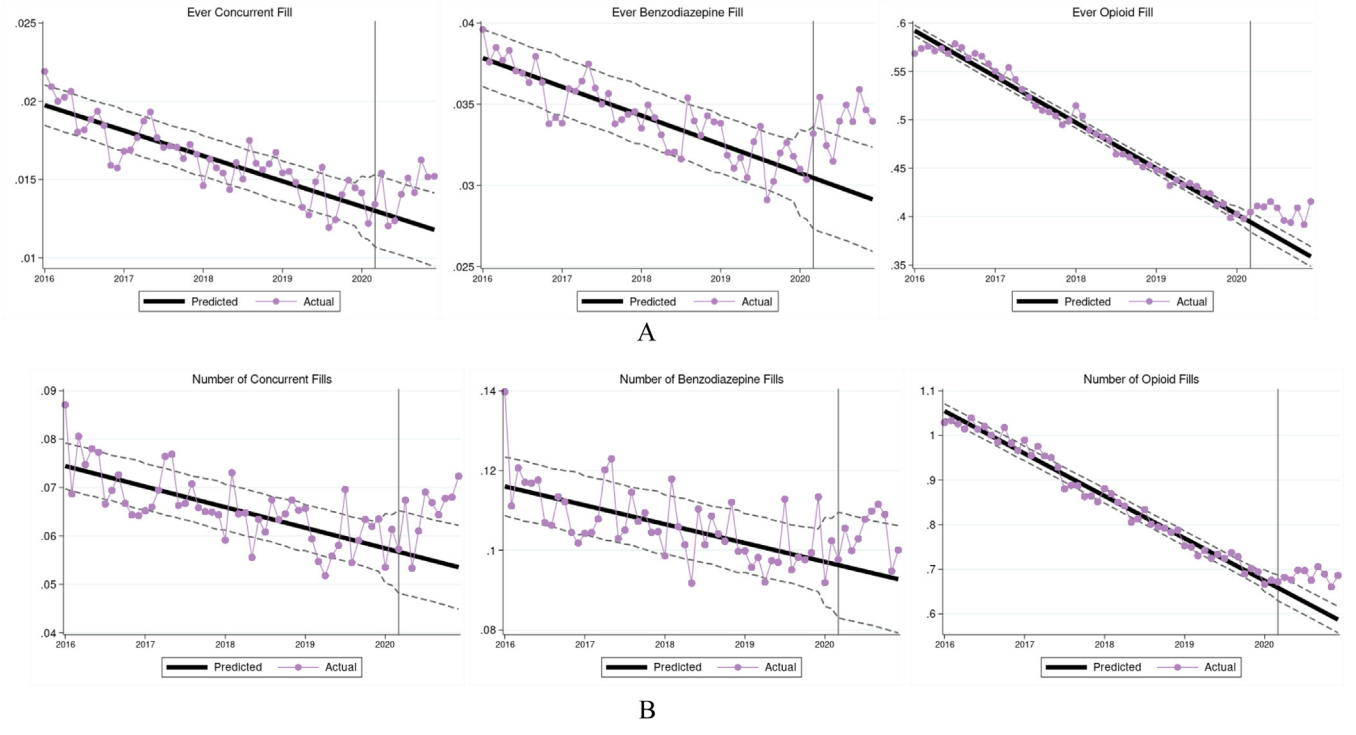

Figure 1. Patient fills of concurrent opioid and benzodiazepine prescriptions, benzodiazepine prescriptions, and opioid prescriptions before and after COVID-19 onset in March 2020. **(A)** Proportion of patients filling prescriptions**. (B)** Number of prescription fills per patient.

Panel A shows the share of postpartum women filling a concurrent prescription of opioids and benzodiazepines, filling a benzodiazepine prescription, and filling an opioid prescription. Panel B shows the number of prescriptions per patient (concurrent, benzodiazepine, and opioid). The solid diagonal lines and dashed lines represent the forecasted values from the regression models and the associated 95% CIs, respectively. The vertical line corresponds to March 2020.

Table 2. Deseasonalized Actual Values and Predicted Values Before and After March 2020

Outcome variables	Time period	Deseasonalized actual value	Predicted value	CI (LB, UB)	Difference
Ever fill concurrent opioid and benzodiazepine prescription	Before March 2020	0.017	0.017	(0.015, 0.018)	0.000
	After March 2020	0.014	0.013	(0.011, 0.015)	0.002
Ever fill benzodiazepine prescription	Before March 2020	0.035	0.035	(0.033, 0.036)	0.000
	After March 2020	0.034	0.031	(0.028, 0.033)	0.003[a]
Ever fill opioid prescription	Before March 2020	0.498	0.498	(0.492, 0.504)	0.000
	After March 2020	0.405	0.380	(0.372, 0.389)	0.025[a]
Number of concurrent opioid and benzodiazepine prescription fills per patient	Before March 2020	0.066	0.066	(0.061, 0.071)	0.000
	After March 2020	0.065	0.055	(0.048, 0.063)	0.009[a]
Number of benzodiazepine prescription fills per patient	Before March 2020	0.107	0.107	(0.099, 0.114)	0.000
	After March 2020	0.104	0.095	(0.084, 0.106)	0.009
Number of opioid prescription fills per patient	Before March 2020	0.865	0.865	(0.848, 0.881)	0.000
	After March 2020	0.684	0.628	(0.604, 0.653)	0.056[a]

[a]Deseasonalized actual value falls above or below the 95% CI for the predicted value on the basis of the pre-existing trend.
LB, lower bound; UB, upper bound.

without comprehensive PDMP mandated use laws should consider implementing more stringent PDMP requirements, such as requiring clinicians to check the PDMP prior to prescribing any Schedule II, III, or IV controlled substances.

Limitations

This study has several limitations. First, the outcomes measure whether patients filled a prescription but not actual use of opioids and/or benzodiazepines. Second, the authors only observe prescription fills; thus, they are unable to determine whether the results are due to changes in provider prescribing behavior or patient fill behavior. Third, this study excludes women aged <18 years and >50 years and women who are not commercially insured; thus, the findings may not generalize to other populations. Fourth, although the authors do not observe systematic changes in sample characteristics after the onset of the COVID-19 pandemic, they cannot rule out that the sample is changing in unobserved ways over this period.

CONCLUSIONS

Increased concurrent prescribing of opioids and benzodiazepines observed during the early period of the COVID-19 pandemic places postpartum women at higher risk of ED visits and overdose. To reduce the harms associated with concurrent prescribing, clinicians should carefully consider whether opioids and/or benzodiazepines are clinically necessary for treatment in the postpartum period as well as consult their state PDMP prior to prescribing these potentially dangerous medications.

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SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.focus.2024.100251.

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