

# Buprenorphine-naloxone versus Buprenorphine for Treatment of Opioid Use Disorder in Pregnancy

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**Objectives:** Data regarding treatment outcomes with the use of buprenorphine-naloxone (BUP-NX) in pregnancy are scarce. The objective of this study is to examine the outcomes in a cohort of pregnancies treated with BUP-NX versus buprenorphine (BUP).

**Methods:** This single-center, retrospective cohort study examined birthing person-infant dyads treated with BUP-NX versus BUP. The primary birthing person outcome was return to opioid use in pregnancy. The primary neonatal outcome was the need for pharmacologic treatment for neonatal opioid withdrawal syndrome (NOWS).

**Results:** The BUP-NX and the BUP treatment groups included 33 and 73 dyads, respectively. Except for psychiatric medication use, all demographics were similar between groups. In the final regression models, neither the birthing person nor the neonatal outcomes differed. The adjusted odds ratio for return to use during pregnancy for the BUP-NX versus BUP groups was 1.93 (95% confidence interval, 0.78–4.76). The adjusted odds ratio for pharmacologic treatment of NOWS for the BUP-NX versus BUP groups was 0.65 (95% confidence interval, 0.27–1.54). Among a subgroup of persons who transitioned from BUP to BUP-NX mid-pregnancy, there was no proximate return to use or need for dose increase.

**Conclusions:** Compared with BUP, the use of BUP-NX in pregnancy is not associated with a higher risk of return to opioid use or a higher need for pharmacological treatment for NOWS.

**Key Words:** buprenorphine, BUP, buprenorphine-naloxone, BUP-NX, naloxone, NX, methadone, MTD, opioid agonist, opioid antagonist, opioid use disorder, OUD, opioid relapse, pregnancy, birthing persons, neonatal opioid withdrawal syndrome, NOWS, neonatal outcomes, project RESPECT, Clinical Opioid Withdrawal Scale, COWS, eat sleep console, Boston Medical Center, BMC, Boston University, BU

(*J Addict Med* 2022;00: 00–00)

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Received for publication September 7, 2021; accepted February 14, 2022.

The authors report no conflicts of interest.

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ISSN: 1932-0620/22/0000-0000

DOI: 10.1097/ADM.0000000000001004

The opioid epidemic in the United States continues to have a significant effect on birthing persons and their neonates. From 2010 to 2017, the number of birthing persons with opioid-related diagnoses documented at delivery increased by 131%. In 2017, the national estimated rate of neonatal opioid withdrawal syndrome (NOWS) was 7.3 per 1000 births, and the rate of opioid use disorder (OUD) in birthing persons was 8.2 per 10,000 delivery hospitalizations.<sup>1</sup>

Current guidance from the American College of Obstetrics and Gynecology for the care of birthing persons with OUD includes the following: (1) universal screening for substance use during pregnancy; (2) provision of medications for OUD (MOUD) and behavioral counseling during pregnancy and the postpartum period; (3) anticipation and management of NOWS for infants prenatally exposed to substances; and (4) multidisciplinary, long-term follow-up care for the birthing persons and infants.<sup>2</sup>

The standard of care for MOUD in pregnancy centers on the use of the long-acting opioids methadone (MTD) and buprenorphine (BUP), which have been proven to decrease the risk for overdose, return to use, mortality, pregnancy loss, and preterm birth.<sup>3,4</sup> Numerous studies have compared MTD and BUP use in pregnancy with a systematic review and meta-analysis, concluding that the use of BUP was associated with a lower risk of preterm birth, greater birth weight, larger head circumference, and less severe NOWS compared with the use of MTD. Further, birthing persons treated with BUP are less likely to use illicit opioids near delivery compared with those treated with MTD.<sup>1</sup> Data regarding alternative therapeutic options, such as the use of the opioid antagonist naltrexone, are also beginning to emerge.<sup>5</sup>

The 2 most common formulations of BUP are BUP monotherapy and BUP with naloxone (BUP-NX), both of which are designed to be administered sublingually.<sup>6,7</sup> The addition of the -NX component to BUP was engineered to deter intranasal or intravenous medication use in pursuit of euphoric effects.<sup>8</sup> When BUP-NX is taken sublingually, the BUP is absorbed providing therapeutic effect, whereas the -NX remains inert given low oral bioavailability. If BUP-NX is altered (crushed or dissolved), however, for intranasal or intravenous ingestion, then the -NX is activated, blocking the opioid receptors and preventing euphoric effects.

In the nonpregnant population, BUP-NX is favored to BUP because of the decreased risk of misuse. In the 2004 guidelines by the Substance Abuse and Mental Health Services Administration, BUP-NX was recommended over BUP for induction, stabilization, and maintenance of “most patients” receiving BUP for OUD.<sup>9,10</sup>

Birthing persons, however, are an exception to this recommendation given concerns regarding the potential for fetal harm if the birthing person were to precipitate withdrawal by misusing BUP-NX. Historically, these concerns have stemmed from 2 case reports from the 1970s, which reported that detoxification during pregnancy increases the risk of stillbirth, fetal distress, and premature labor.<sup>11,12</sup> Although opioid detoxification during pregnancy is no longer recommended, previous studies examining this process reported minimal fetal harm.<sup>12</sup> Given these concerns and limited data on the use of -NX in pregnancy, some patients receiving BUP-NX before pregnancy have been transitioned to BUP once pregnant in accordance with the 2014 WHO Guidelines.<sup>13</sup> Birthing persons therefore may be uniquely prescribed BUP, increasing their vulnerability for misuse, coercion, theft, and violence. To mitigate risk, many providers have begun treating birthing persons with OUD with BUP-NX, and initial observational studies have been reassuring. Furthermore, several small retrospective studies examining the use of BUP-NX in pregnancy have not found adverse birthing person or neonatal outcomes.<sup>14–16</sup>

The purpose of this study was to retrospectively examine birthing person and infant outcomes for a cohort of birthing person-infant dyads treated with BUP-NX versus BUP at a single institution. Currently, only 1 published study has compared these 2 cohorts, and this limited data leave providers with a lack of clarity regarding the safety and efficacy of BUP-NX in pregnancy, thereby limiting treatment options for birthing people.<sup>17</sup>

## METHODS

This was a retrospective study that received approval from the Institutional Review Board at Boston University Medical Campus/Boston Medical Center (BMC) to explore the effect of MOUD in pregnancy on birthing person and neonatal outcomes. This pilot study was completed with the goal of analyzing the experiences of all of the patients within our practice to provide a preliminary analysis of the different effect of the MOUDs on their pregnancies.

To be included in this study, birthing persons had to be prescribed BUP in the form of either BUP or BUP-NX, to be receiving prenatal care from Project RESPECT for at least 1 week before delivery, and to have delivered at BMC between October 2016 and March 2020. Persons who transitioned to MTD therapy during pregnancy were excluded. Project RESPECT is a multidisciplinary program at BMC that focuses on providing prenatal and postpartum care to persons with substance use disorders. Through this program, patients are seen every 1 to 2 weeks throughout pregnancy for routine antepartum care, as well as for additional psychiatric and social work care, as indicated. Beginning in June 2018, BMC transitioned from primarily prescribing BUP to primarily prescribing BUP-NX for the treatment of OUD in pregnancy. This study examines pregnancies of people with OUD treated before, during, and after this transition.

Through BMC protocol, if the person presented to care with their OUD in remission, then they were immediately transitioned to prenatal care with Project RESPECT where they are offered MOUD titration outpatient. Conversely, if the person presented to care actively using opioids, then they were offered a hospital admission for obstetric and OUD stabilization. While

admitted, withdrawal symptoms were monitored using the Clinical Opioid Withdrawal Scale (COWS) for 24 hours with initial and subsequent BUP or BUP-NX doses per COWS scores. The BMC Addiction service was consulted for patients with a history of complex withdrawal (eg, seizures), with concurrent withdrawal from other substances (eg, alcohol or benzodiazepines), or for whom greater than 16 mg of BUP was required in the first 24 hours of titration. All patients were connected with community recovery support systems depending on acuity, including residential treatment programs, intensive outpatient programs, and group and/or individual therapy. After discharge, BUP dose adjustments were made on an individual basis in the RESPECT clinic. At outpatient visits, urine samples were collected to qualitatively analyze for opiates, benzodiazepines, cocaine, amphetamines, barbiturates, BUP, MTD, fentanyl, and oxycodone. If fentanyl was detected, then a confirmatory quantitative test was performed.

Routine NOWS care per BMC protocol was used for the duration of this study and centered on a rooming-in model emphasizing nonpharmacologic care. All opioid-exposed infants were monitored for 5 to 7 days in the inpatient, pediatric unit. Infants were monitored with a standardized NOWS assessment tool (Eat, Sleep, and Console NOWS Tool) and treated with MTD per protocol. From October 2016 to October 2017, the protocol indicated using MTD every 8 hours with a 10% taper each day, as tolerated.<sup>16</sup> From October 2017 to March 2020, a symptom-triggered MTD protocol was adopted, which gave infants 1 dose of MTD for symptoms as needed, with an average of 2 doses given per infant.<sup>18</sup> Regardless of protocol iteration, all infants were monitored inpatient for a minimum of 48 hours after their last dose of MTD.

Data were reviewed retrospectively from the electronic medical record. Birthing person data points included patient age, race, smoking status, psychiatric medication use, illicit drug use, presence of comorbid medical conditions, gestational age (GA) at enrollment into Project RESPECT, BUP dose at treatment initiation, number of obstetrical provider visits, number of total prenatal visits, number of urine drug tests, number of returns to opioid use, GA at delivery, BUP dose at delivery, mode of delivery, and breastfeeding status. For the purpose of this study, the term “obstetrical provider visits” refers only to outpatient prenatal visits with obstetricians, family medicine doctors, and midwives within Project RESPECT, whereas the term “prenatal visits” refers to all outpatient prenatal appointments with Project RESPECT, including those with affiliated social workers, nurses, and psychiatric providers. For the purpose of this study, it was decided to focus on the presence of these factors in the immediate weeks preceding delivery because NOWS was the primary neonatal outcome and neonates are not expected to display signs of withdrawal from exposures earlier in pregnancy given the various half-lives of different substances. For example, if a patient quit smoking cigarettes or stopped taking psychiatric medications before 36w0d of pregnancy, then they were considered a person with no active nicotine use and not to be prescribed psychiatric medications, as long as their pregnancy continued for 2 weeks after stopping. Similarly, if a patient transitioned from BUP to BUP-NX before 36w0d, then they were analyzed as part of the BUP-NX study arm, as long as their pregnancy continued for at least another 2 weeks after transition.

**TABLE 1.** Birthing Person Demographics

Demographics	BUP-NX (n = 33)	BUP (n = 73)	P
Age, mean ± SD, years	30 ± 4	30 ± 5	0.99
Race, n (%)			0.09*
White	30 (91)	67 (92)	
Black	2 (6)	0	
Hispanic	1 (3)	6 (8)	
Cigarette use, n (%)	24 (73)	63 (86)	0.15
Psychiatric medication use, n (%)	15 (45)	41 (56)	0.04
Breastfeeding, n (%)	16 (48)	38 (52)	0.89
Medical comorbidities, n (%)			
Human immunodeficiency virus	0	1 (1)	1.00*
Hepatitis C virus	19 (58)	49 (67)	0.46
Preexisting diabetes mellitus	0	1 (1)	1.00*
Gestational diabetes mellitus	1 (3)	3 (4)	1.00*
Chronic hypertension	0	3 (4)	0.55*
Gestational hypertension	15 (45)	25 (31)	0.24

P values were generated by  $\chi^2$  tests and Fisher exact tests, with the later indicated by a (\*). All ages are in years.

Neonatal data points included sex, birth weight, head circumference, APGAR scores, and NICU admission. NOWS outcomes included whether the neonate received pharmacologic treatment for NOWS, whether in addition to first-line treatment (ie, MTD) the neonate also received second-line treatment (ie, phenobarbital and/or clonidine), length of time receiving pharmacotherapy, and length of hospital stay because of NOWS. NOWS outcomes were selected based on a review article of the existing neonatal abstinence syndromes literature.<sup>19</sup> Low birth weight was defined as weight at birth of less than 2500 grams (ie, 5.5 lb) based on the definition set by the World Health Organization.

The primary birthing person outcome was the number of returns to opioid use in pregnancy. For the purpose of this study, all returns to use were identified by urine drug tests collected in Project RESPECT that were positive for a substance that the participant was not prescribed. If fentanyl was detected on the initial qualitative test (presumptive positive test), then a confirmatory test was performed to quantify fentanyl and norfentanyl (an inactive fentanyl metabolite). If the amount of fentanyl and/

**TABLE 2.** Prenatal and Delivery Characteristics

Characteristics	BUP-NX (n = 33)	BUP (n = 73)	P
BUP dose at initiation (mg/day), mean ± SD	12 ± 5	13 ± 6	0.23
GA at initiation (in weeks), median(IQR)	0 (0–0)	0 (0–12)	0.37*
GA at enrollment (in weeks), median (IQR)	12 (9–16)	14 (10–23)	0.21*
Number of prenatal visits, mean ± SD	20 ± 8	21 ± 11	0.67
Number of obstetrical provider visits, mean ± SD	10 ± 5	9 ± 4	0.23
BUP dose at delivery (in mg/day), mean ± SD	15 ± 6	16 ± 7	0.46
GA at delivery (in weeks), median (IQR)	39 (38–40)	39 (38–41)	0.78*
Delivery timing, n (%)			
Term (≥37 weeks GA)	29 (88)	66 (90)	0.73*
Preterm	4 (12)	7 (10)	
Mode of delivery, n (%)			
Vaginal delivery	21 (64)	36 (49)	0.25
Cesarean section	12 (36)	37 (51)	
Vaginal Deliveries with Neuraxial Anesthesia, n (%)	17 (81)	30 (83)	1*

P values were generated by t tests,  $\chi^2$  tests, Fisher's exact tests, or Wilcoxon rank sum tests, with the later indicated by a (\*). GA, gestational age; IQR, interquartile range.

**TABLE 3.** Return-to-use Outcomes in Birthing Persons Treated With BUP-NX Versus BUP

Outcomes	BUP-NX (n = 33)	BUP (n = 73)	P
Number of urine drug tests, mean ± SD	17 ± 6	16 ± 7	0.60
Return(s) to opioid use, n (%)			
Yes	12 (36)	17 (23)	0.17
• 1 return	• 5 (42)	• 11 (65)	
• 2 returns	• 1 (8)	• 2 (12)	
• 3 or more returns	• 6 (50)	• 4 (24)	
No	21 (64)	56 (77)	
Return(s) to nonopioid use, n (%)			0.87
Yes	10 (30)	21 (29)	
• 1 return	• 5 (50)	• 8 (38)	
• 2 returns	• 2 (20)	• 4 (19)	
• 3 or more returns	• 3 (30)	• 9 (43)	
No	23 (70)	52 (71)	

The nonopioids tested included amphetamines, barbiturates, benzodiazepines, and cocaine.

or norfentanyl present on the confirmatory test was lower than the previous test, then this was not considered a return to use. Conversely, if the amount was higher, then this was considered an additional return to use. Nonopioid drug misuse was recognized by urine drug tests inappropriately positive for amphetamines, barbiturates, benzodiazepines, or cocaine. Each drug test positive for one of these substances was considered an additional return to use. Our primary neonatal outcome was receipt of pharmacologic treatment for NOWS. For neonates who had NOWS treatment for at least a day, we further determined if the treatment type (BUP-NX vs BUP) was associated with total opioid treatment days for NOWS.

Categorical variables were reported as percentages [n (%)] and continuous variables were reported as either means with standard deviations (mean ± SD) or medians with interquartile ranges (median ± interquartile range) where appropriate. For categorical variables, the Pearson  $\chi^2$  test of independence and the Fisher exact test were used. For continuous outcomes, independent 2-sample t-tests and the Wilcoxon rank sum test were used.

**TABLE 4.** Neonatal Outcomes

Outcomes	BUP-NX (n = 33)	BUP (n = 73)	P
Male sex, n (%)	18 (54)	37 (50)	0.87
Low birth weight*, n (%)	4 (12)	10 (14)	1*
Birth weight, mean ± SD, kg	3147 ± 638	3142 ± 600	0.96
Head circumference, mean ± SD, cm	34 ± 2	34 ± 2	0.67
APGAR score at 1 minute of life, median (IQR)	8 (8–9)	8 (8–9)	0.62*
APGAR score at 5 minutes of life, median (IQR)	9 (9–9)	9 (9–9)	0.67*
Received pharmacologic treatment for NOWS, n (%)	13 (40)	33 (45)	0.77*
Received secondary pharmacologic treatment for NOWS, n (%)	2 (6)	7 (10)	0.71*
Total length of hospital stay because of NOWS (in days), median (IQR)	7 (6–7)	7 (6–7)	0.87*
Received PRN MTD treatment, n (%)	10 (30)	11 (15)	0.02
NICU admission, n (%)	10 (30)	14 (20)	0.40

For continuous variables, *P* values were generated using independent *t*-tests except for those with a (\*), which were generated using Wilcoxon rank sum tests. For all categorical variables, *P* values were generated using  $\chi^2$  tests.

\*Low birth weight was defined as weight at birth of less than 2500 grams (5.5 lb), based on definitions set by the World Health Organization.

IQR, interquartile range; NOWS, neonatal opioid withdrawal syndrome; PRN, “pro re nata” (as needed); NICU, neonatal intensive care unit; MTD, methadone.

Statistical significance was considered for  $P < 0.05$ . Binary and multivariable logistic regression analyses were used to calculate the crude and adjusted odds ratio comparing categorical outcomes between the 2 treatment groups. Simple and multiple linear regression models were used to test for association between treatment groups and continuous outcomes and their Beta ( $\beta$ ) and 95% confidence interval reported. The covariates selected for possible inclusion in multivariable regression analysis were chosen based on literature review and an understanding of the clinical significance of these variables on the study outcomes. We further used the forward selection method of change in estimate analysis to develop a logistic regression model, selecting only variables with a relative risk due to confounding greater than 1.1 or less than 0.9. There were no missing values for key demographic, prenatal, or delivery characteristics; therefore, no adjustments were performed for missingness. The BUP treatment group was used as the reference group in all regression analyses. No formal power calculation was done as this was a pilot study to identify preliminary associations. A subgroup analysis was completed exploring the effect of transitioning from BUP to BUP-NX during pregnancy. This subanalysis focused on information regarding returns to use, hospital readmissions, and dose increases after the patient transitioned therapies. All analyses were done using R version 3.6.1.

## RESULTS

In total, 106 dyads met study criteria, of which 33 and 73 were in the BUP-NX and BUP treatment groups, respectively.

We completely excluded from our analysis 2 twin pregnancies and 2 patients who had multiple deliveries within the study period.

Demographics are shown in Table 1, and birthing person prenatal and delivery characteristics are shown in Table 2. All demographic parameters were equally distributed across treatment groups, except for psychiatric medication use which differed significantly (45% vs 56%,  $P = 0.04$ ). Birthing person prenatal and delivery characteristics did not differ significantly between the 2 treatment groups.

All return-to-use data during pregnancy are shown in Table 3. The likelihood of returning to opioid or nonopioid use during pregnancy identified by inappropriate urine drug tests did not differ significantly between treatment groups, even after adjusting for coexposure to psychiatric medications. Overall, 12 persons (36%) on BUP-NX returned to opioid use at least once, whereas 17 persons (23%) on BUP returned to opioid use at least once.

Neonatal outcomes are shown in Table 4. There were more infants in the BUP-NX group treated with PRN MTD compared with the BUP group. Neonates of pregnancies treated with BUP-NX had significantly lower opioid treatment days for NOWS than did neonates of pregnancies treated with BUP in the bivariate analysis. This difference was no longer significant when adjusting for NOWS treatment protocol (standing vs symptom-triggered MTD), breastfeeding status, and psychiatric medication use (Table 5). All other neonatal outcomes analyzed did not differ significantly between treatment groups.

There were 10 people who transitioned from BUP to BUP-NX during their pregnancy. The decision to transition

**TABLE 5.** Multivariate Regression of Primary Outcomes for Pregnancies Treated With BUP-NX Versus BUP

	BUP-NX, n (%)	BUP, n (%)	Crude, OR (95% CI)	Adjusted OR* (95% CI)
Return-to-opioid use	12 (36)	17 (23)	1.88 (0.77 to 4.60)	1.93 (0.78 to 4.76)
Received pharmacologic treatment for NOWS	13 (39)	33 (45)	0.76 (0.32 to 1.76)	0.65 (0.27 to 1.54)
	BUP-NX, mean ± SD	BUP, mean ± SD	Crude $\beta$ (95% CI)	Adjusted $\beta^2$ (95% CI)
NOWS opioid treatment days	3 ± 6	8 ± 5	−4.18 (−8.07 to −0.30)	0.59 (−3.04 to 4.24)

<sup>1</sup>Adjusted for the use of psychiatric medications.

<sup>2</sup>Adjusted for the use of psychiatric medications, PRN methadone treatment, and breastfeeding.

CI, confidence interval; NOWS, neonatal opioid withdrawal syndrome.

their therapies was based on their prenatal care coinciding with a shift in BMC prescribing protocols in pregnancy. A subgroup analysis of these persons showed that the mean GA at transition was  $25.8 \pm 10.7$  weeks. Four (40%) of these patients needed a subsequent increase in their BUP-NX dosage at a mean of  $12.1 \pm 2.4$  weeks after transitioning. Two (20%) of the patients were identified as having a return to opioid use after transitioning, which happened at a mean of  $7 \pm 2.8$  weeks posttransition.

## DISCUSSION

In this retrospective, pilot study, we examined the use of BUP-NX versus BUP for the treatment of OUD in pregnancy. In adjusted models, we did not find significant differences in birthing person or neonatal outcomes between groups. These findings support the use of BUP-NX for the treatment of OUD in pregnancy.

To date, several small, retrospective studies have been published examining the use of BUP-NX in pregnancy. The largest of these studies, by Mullins et al.,<sup>17</sup> compared birthing person and neonatal outcomes from 85 dyads receiving BUP-NX to 108 dyads receiving BUP. In multivariate models, there were no significant differences between birthing person or neonatal outcomes.<sup>17</sup> The remaining studies mentioned found promising outcomes for a small number of pregnancies treated with BUP-NX<sup>15,16</sup> but did not directly compare the outcomes to those of pregnancies treated with BUP.

Our findings, concordant with those of the Mullins et al.<sup>17</sup> study, detected no differences in birthing person or neonatal outcomes between pregnancies treated with BUP-NX versus BUP. Our study differed from the Mullins et al.<sup>17</sup> study in several key ways. From the birthing person perspective, we were able to gather and analyze a greater amount of data regarding substance use and return to opioid use in pregnancy, including frequent urine drug tests that acted as objective evidence of ongoing substance misuse—a potentially important contributor to NOWS severity and marker of progress toward recovery. We also completed an exploratory subanalysis analyzing the effect of transitioning from BUP to BUP-NX mid-pregnancy. From the neonatal perspective, we were able to collect more detailed data regarding NOWS severity, including the number of days that pharmacologic treatment of NOWS was given and whether infants required a secondary medication for treatment of NOWS.

Ultimately 10 patients were examined in an exploratory subgroup analysis after transitioning from BUP to BUP-NX in pregnancy. Four (40%) of these patients required a dose increase at a mean of 12 weeks posttransition—a time lapse that suggests that the increased dose requirement was unrelated to the transition. Two (20%) of the patients had a return to opioid use at a mean of 7 weeks posttransition, suggesting that the return to use was also unrelated to the transition. The return to opioid use rate was also similar to the rate for all birthing persons in this study, as identified by inappropriate urine drug tests. Overall, these findings suggest that exposure to NX during pregnancy may not increase the required BUP dose or risk of return to use; however, given the small number of patients included in this group, these results are largely observational and are not powered sufficiently to be analyzed for significance.

One of the main limitations of this study is its small sample size. Though it is one of the largest studies of this population to date (only the Mullins et al.<sup>17</sup> study analyzed a greater number of pregnancies treated with BUP-NX), the size nevertheless limits the power to detect differences between groups, and the conclusions should be understood within this context.<sup>15,17</sup> The fact that one third of the patients in the BUP-NX group had transitioned from BUP to BUP-NX earlier in their pregnancies does limit the generalizability of our results. We decided to include this group within our final data analyses as our goal was to describe our clinic population, including those who made this transition during pregnancy. Their inclusion in the data analysis was further supported by our goal of focusing on the MOUD prescribed in the immediate weeks preceding delivery given that NOWS was the primary neonatal outcome and neonates are not expected to display signs of withdrawal from exposures earlier in pregnancy.

Our study was further limited by its retrospective design, which did not allow for us to control for changes in NOWS assessment and treatment protocols in our hospital over time. There were, however, key components of the protocols that did remain consistent over the study period including a consistent nonpharmacologic care bundle, consistent rooming-in model of care, support of breastfeeding in eligible individuals, and use of the Eat, Sleep, Console assessment method—all of which have been demonstrated to be the most influential factors affecting our primary outcome of NOWS pharmacologic treatment rates. Another study limitation includes our use of urine drug tests collected at prenatal visits to assess for return to substance use, as there is the potential for an ingested substance to be metabolically cleared between urine drug tests, especially with a lapse in prenatal care.

Finally, our study is limited by its lack of diversity. The population of patients both in our study and throughout Project RESPECT predominantly identify as White, Non-Hispanic persons. In Massachusetts in 2018, the overwhelming majority of recognized opioid overdose deaths (80%) occurred in people identifying as White and Non-Hispanic, compared with those identifying as Hispanic (13%) or Black (4%).<sup>20</sup> Nationwide, however, opioid overdoses in metropolitan areas are increasingly affecting Hispanic and Black populations.<sup>21</sup> Clinic leadership within Project RESPECT is actively engaged in the recruitment of patients identifying as Hispanic and Black in an effort to avoid perpetuating inequities in the clinical care and research of substance use disorders within these communities.

## CONCLUSIONS

Our findings add to the growing body of evidence that the use of BUP-NX for the treatment of OUD in pregnancy yields similar birthing person and neonatal outcomes to the use of BUP alone. These findings support the consideration of BUP-NX as a suitable treatment option for birthing persons with OUD.

## ACKNOWLEDGMENTS

*The authors thank all faculty and staff who work with Project RESPECT at BMC for the excellent care they provide to patients with substance use disorder. They also thank the Pediatrics Department at BMC for their expert support of neonates with NOWS.*

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