Impact of Coronavirus Disease-2019 on Hospital Care for Neonatal Opioid Withdrawal Syndrome

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Objective To compare prenatal exposures, hospital care processes, and hospitalization outcomes for opioid-exposed newborns before and during the coronavirus disease 2019 (COVID-19) pandemic.

Study design In this multicenter retrospective analysis, data were collected from 19 Massachusetts hospitals, including 5 academic and 14 community hospitals. The pre-COVID-19 cohort was defined as births occurring during March 1, 2019-February 28, 2020, and the COVID-19 cohort was defined as births occurring during March 1, 2020-December 31, 2020. Opioid-exposed newborns born at ≥35 weeks of gestation were included. Differences in prenatal substance exposures, hospital care processes, and neonatal opioid withdrawal syndrome (NOWS) outcomes, including pharmacologic treatment for NOWS (PharmTx), length of stay (LOS), and as-needed (prn) treatment failure rates, were evaluated.

Results There were 663 opioid-exposed newborns in the pre-COVID-19 group and 476 in the COVID-19 group. No between-group differences were seen in prenatal substance exposures or the need for PharmTx. Compared with the pre-COVID-19 group, in the COVID-19 group there was less rooming-in after maternal discharge (53.8% vs 63.0%; P = .001) and less care in the pediatric unit setting (23.5% vs 25.3%; P = .001), longer LOS (adjusted risk ratio, 1.04; 95% CI, 1.01-1.08), and a higher rate of breast milk receipt at discharge (aOR, 2.03; 95% CI, 1.22-3.39). Within the subset of academic centers, more infants failed prn treatment in the COVID-19 group (53.8% vs 26.5%, P = .02; aOR, 3.77; 95% CI, 0.98-14.5).

Conclusions Among the hospitals in our collaborative, hospital processes for NOWS, including care setting, rooming-in, and LOS were negatively impacted in the COVID-19 group, particularly in academic medical centers. (J Pediatr 2022;245:47-55).

Neonatal opioid withdrawal syndrome (NOWS) refers to a pattern of withdrawal signs in newborns resulting from chronic in utero opioid exposure and characterized by behavioral dysregulation of the central nervous, autonomic nervous, respiratory, and gastrointestinal systems.[1,2] Rates have increased significantly in recent years with the overall incidence of NOWS estimated at 8 per 1000 hospital births in the US in 2014.[3,4] Wide geographic variation also exists, with the Northeast having the highest regional rate, at 9.5 per 1000 births.[4,5]

Supporting nonpharmacologic care is a priority in management of NOWS and should be considered the foundation of care for all opioid-exposed newborns.[2] Numerous quality improvement reports and several small randomized control trials have shown that nonpharmacologic interventions, such as rooming-in with parents, increasing parental presence at the bedside, breast milk feeding, decreasing environmental stimulation, and a variety of soothing techniques, improve NOWS outcomes, such as the need for pharmacologic treatment for NOWS (PharmTx), hospital length of stay (LOS), and weight trajectory.[6-10]

Early recommendations encouraged separating newborns from mothers with confirmed or suspected COVID-19 to reduce the risk of transmission and potential risks of transmission associated with breastfeeding.[11] As the understanding of COVID-19 has developed, clinical guidelines also have evolved, with greater emphasis on keeping biological parents and babies together and supporting lactation.[12,13] However, other hospital-level

COVID-19	Coronavirus disease 2019
ER	Emergency room
ESC	Eat, Sleep, Console
LOS	Length of stay
NICU	Neonatal intensive care unit
NOWS	Neonatal opioid withdrawal syndrome
OUD	Opioid use disorder
PharmTx	Pharmacologic treatment for neonatal opioid withdrawal syndrome
PNQIN	Perinatal-Neonatal Quality Improvement Network of Massachusetts
Prn	As necessary

policies aimed at infection control also may adversely affect nonpharmacologic care for opioid-exposed newborns, including visitor restrictions, loss of volunteer cuddler programs, staff redeployment, and conversion of pediatric units into COVID-19 units, decreasing the space and opportunity for parental rooming-in.[13-15]

At the same time, during the COVID-19 pandemic there have been increases in the reported rates of community substance use and overdose, reflecting increased social and economic stressors.[16-18] Although telehealth and updated guidance from the Substance Abuse and Mental Health Services Administration have provided opportunities for access to medication-assisted therapy through take-home dosing, access to other services may have been limited, with a decrease in attendance to group therapy reported among pregnant women in treatment programs for opioid use disorder (OUD).[19-21] Data from the Massachusetts Department of Public Health indicate that the rate of NOWS increased from 11.7 to 14 per 1000 live births between 2018 and 2020-2021.

The impact of increased psychosocial stressors on medication for OUD dosing and unprescribed substance use in pregnancy remains unclear. We sought to utilize an ongoing statewide collaborative seeking to improve the care of families affected by perinatal opioid use to examine the impact of the COVID-19 pandemic on NOWS inpatient care.

Methods

This study was conducted under the umbrella of the Massachusetts Perinatal-Neonatal Quality Improvement Network (PNQIN), a statewide quality collaborative that includes birthing hospitals, community organizations, and state agencies, such as the Department of Children and Families and the Department of Public Health.[22] Since 2016, the PNQIN has been involved in leading a NOWS improvement initiative focused on improving NOWS hospitalization outcomes through the increase of nonpharmacologic care measures, such as breast milk receipt and rooming-in. The initiative has included voluntary in-kind participation by multidisciplinary teams from 37 hospitals across the state of Massachusetts.

Hospitals participating in the PNQIN including a mix of academic medical centers and community hospitals that care for infants with NOWS in a variety of care settings. The majority of pregnant people with OUD in the PNQIN are receiving medication for OUD with methadone, buprenorphine, buprenorphine-naloxone, or naltrexone at the time of delivery.[23] There was no uniform monitoring or treatment protocol required for centers for NOWS management, although many centers adapted a family-centered care approach focused on the use of nonpharmacologic care methods with use of the Eat, Sleep, Console (ESC) NOWS care tool.[24] Infants were treated with either morphine or methadone as first-line pharmacotherapy, with clonidine or phenobarbital used as second-line agents. Some centers used prn ("as needed") dosing of opioids.[25] All infants were monitored in the hospital for 24-48 hours after the last dose of morphine or methadone before discharge to home.

Data Collection

Hospitals participating in the PNQIN collaborative voluntarily enter patient-level data into a statewide deidentified REDCap database on a monthly basis. Data points collected include birthing parent demographics, birthing parent drug exposures according to chart review data, birth demographics, details of the NOWS care setting and protocol, NOWS PharmTx details, nonpharmacologic care measures (eg, breastfeeding, rooming-in, skin-to-skin), discharge destination, and readmissions and emergency room (ER) visits within 30 days of infant discharge. All data are hand-abstracted by the hospital teams. This statewide quality improvement project was deemed nonhuman subjects research by the Institutional Review Boards at the PNQIN leadership team hospitals. All participating centers completed data use agreements with the PNQIN to be able to submit these deidentified data to the secure statewide database.

Criteria for inclusion of hospitals in this analysis were complete data entry into REDCap during both the pre-COVID-19 and COVID-19 periods. The pre-COVID-19 period was defined as births occurring during March 1, 2019-February 28, 2020, and the COVID-19 period was defined as births occurring during March 1, 2020-December 31, 2020, based on when the first surge of COVID-19 in Massachusetts occurred in March 2020. Infants had to have a known opioid exposure in pregnancy, as determined by a chart review of maternal records and/or maternal and infant toxicology screening, were cared for with a site-specific NOWS protocol, and to be at ≥35 weeks of gestational age at delivery for inclusion. Exclusion criteria included the birthing parent on naltrexone for the treatment of OUD. Data were reviewed for completeness, and sites were contacted about missing data before the final analysis.

Outcome Measures

Our primary outcome measures were related to NOWS hospitalization outcomes, specifically receipt of any PharmTx for NOWS, infant hospital LOS in days, days of opioid treatment, prn opioid treatment failure rates (defined as the transition from prn to standing opioid dosing), and any breast milk receipt at the time of discharge. Secondary outcome measures included infant custody at discharge and infant ER or hospital readmissions within 30 days of discharge. We also examined hospital process variables, including breastfeeding eligibility and initiation rates, rooming-in, skin-to-skin receipt, and location of infant care.

Data Analyses

We compared birthing parent and infant characteristics in the pre-COVID-19 and COVID-19 cohorts. Birthing parental variables examined included race and ethnicity, type of in utero opioid exposure including medication for OUD, unprescribed substance exposures, psychiatric medications, and eligibility to provide breast milk according to hospital guidelines. Infant variables included sex, gestational age at delivery, birth weight, location of care, receipt of breast milk, and NOWS hospital outcome measures.

Univariate comparisons were made between the pre-COVID-19 and COVID-19 groups using the χ^2 test or Fisher exact test for categorical variables and the *t* test for continuous variables. The Wilcoxon–Mann–Whitney test was used for medians. A subgroup analysis for NOWS outcomes was conducted among the 5 academic medical centers to examine potential effects from institutional pressures faced by larger centers converting pediatric spaces to accommodate adult COVID-19 patients, in addition to general physical space restrictions and COVID-19 precautions. Process measures and outcome measures were examined by univariate comparisons. Multivariate models were then used to examine determinants of primary outcome measures using mixed-effects logistic regression, including random intercepts for control of clustering by delivery hospital. Variables significantly associated with primary NOWS outcomes ($P < .05$) in univariate analyses were included in the regression models. All analyses were performed using SAS version 9.4 (SAS Institute).

Results

Of the 37 centers in the PNQIN, 26 participated in REDCap data entry to some degree since the start of the database. Of those 26, 7 were excluded from this analysis due to lack of data entry during the COVID-19 time period. This included 3 major academic medical centers and 4 smaller community hospitals that historically had a low volume of NOWS cases. From the remaining 19 centers, there were 1139 parent–infant dyads in our cohort, including 663 in the pre-COVID-19 group and 476 in the COVID-19 group. Five academic medical centers and 14 community hospitals were included, with a mix of level I, II, and III nurseries. Demographic characteristics of our cohort are summarized in Table I. There were slight differences in age of the birthing parent, race, and ethnicity between the 2 cohorts. Prenatal substances exposures did not differ significantly between the 2 groups, with the exception of other opioid exposures in the month before delivery (Table I). Infant birth outcomes of gestational age and birth weight did not differ between the 2 time periods.

Process measures and comparison of NOWS treatment protocols in the pre-COVID-19 and COVID-19 groups are displayed in Table II. All results were adjusted for clustering by center. In the COVID-19 group, there were significant decreases in rooming-in after parental discharge (53.8% vs 63.0%; $P = .001$) and in pediatric unit care during that time period (23.5% vs 25.3%; $P = .001$) (Table II). No significant differences in skin-to-skin receipt and breastfeeding eligibility and initiation rates were seen. More infants in the COVID-19 group were assessed with the ESC assessment method (71.6% vs 67.0%; $P = .002$). Of the 398 infants who received PharmTx, 348 (87.4%) were treated with morphine and 44 (11.1%) were treated with methadone in accordance with hospital guidelines. In addition, 118 of the 398 treated infants (29.6%) received prn dosing. Phenobarbital (n = 4) and clonidine (n = 1) were used as second-line agents.

Primary NOWS outcome measures are shown in Table II. There were no differences between the pre-COVID-19 and COVID-19 groups in NOWS PharmTx, LOS, days of opioid treatment, prn dosing failure rates, or receipt of breast milk at discharge in bivariate analyses. There also were no differences in our secondary outcomes of hospital readmissions or ER visits within 30 days or in infant custody status at discharge.

The association of covariates with our primary NOWS outcomes of PharmTx, LOS, and breast milk receipt at discharge were then examined (data not shown). There were significant differences by center, region, and center level for all primary outcomes. In addition, maternal medication for OUD was associated with multiple outcomes; specifically, methadone treatment was associated with higher rates of PharmTx and longer LOS, and buprenorphine treatment and no medication for OUD were associated with less PharmTx and shorter LOS. The rate of breast milk receipt was higher in buprenorphine-treated pregnant women and lower in those not on medication for OUD. Care location was significantly associated with differences, with infants cared for in a neonatal intensive care unit (NICU)/special care nursery and those cared for at academic centers having higher rates of PharmTx and longer LOS. Male infants had worse NOWS outcomes for both PharmTx and LOS. Exposures to unprescribed drugs, nicotine, and psychiatric medications were associated with higher rates of PharmTx, longer LOS, and lower rates of breast milk receipt at discharge. Any breast milk receipt during hospitalization was associated with less PharmTx and shorter LOS.

Our final multivariate regression models for the primary outcome measures for the entire cohort, adjusting for type of center (academic vs nonacademic), type of medication for OUD, care within a NICU/special care nursery (yes/no), selective serotonin reuptake inhibitor exposure (yes/no), benzodiazepine exposure (yes/no), and receipt of any breast milk (yes/no), and taking hospital-level clustering into account, are shown in Table III. There was no difference in PharmTx between the pre-COVID-19 and COVID-19 groups. There were higher rates of breast milk receipt at discharge (aOR, 2.03; 95% CI, 1.22-3.39) and longer hospital LOS (adjusted risk ratio, 1.04; 95% CI, 1.01-1.08) in the COVID-19 group. The prn treatment failure rate did not differ significantly between the 2 groups.

A subgroup analysis of the 5 academic medical centers (n = 479 infants; 305 in the pre-COVID-19 group and 177 in the COVID-19 group) did not indicate any differences in NOWS outcomes (bivariate data not shown), with the exception of a higher prn treatment failure rate in the COVID-19 cohort (14 of 26 [53.8%] vs 22 of 73 [30.1%]; $P = .02$) within these centers. Final multivariate regression models for the academic center subgroup are shown in Table IV. There were no differences in PharmTx or LOS between the pre-COVID-19 and COVID-19 groups. There was a higher rate of breast milk receipt at discharge in the COVID-19 group, as was seen in the larger cohort (aOR,

Table I. Demographic characteristics

Characteristics	Overall (N = 1139)		Pre-COVID-19 group (N = 663)		COVID-19 group (N = 476)		P value
Region, n (%)							.004
Western Massachusetts	242	(21.2)	164	(24.7)	78	(16.4)	
Central Massachusetts	183	(16.1)	106	(16.0)	77	(16.2)	
Northeast Massachusetts	162	(14.2)	97	(14.6)	65	(13.7)	
Boston metropolitan areas	208	(18.3)	118	(17.8)	90	(18.9)	
Southeast Massachusetts	344	(30.2)	178	(26.8)	166	(34.9)	
NICU level, n (%)							.13
Level I	220	(19.3)	118	(17.8)	102	(21.4)	
Level II/III	919	(80.7)	545	(82.2)	374	(78.6)	
Center type, n (%)							.003
Academic center	482	(42.3)	305	(46.0)	177	(37.2)	
Nonacademic center	657	(57.7)	358	(54.0)	299	(62.8)	
Birthing parent age, y, mean (SD)	31.2	(4.7)	30.9	(4.9)	31.5	(4.4)	.03
Birthing parent race and ethnicity, n (%)							.01
Hispanic	102	(9.0)	71	(10.7)	31	(6.5)	
Non-Hispanic Black	38	(3.3)	24	(3.6)	14	(2.9)	
Non-Hispanic White	931	(81.7)	542	(81.7)	389	(81.7)	
Other	34	(3.0)	14	(2.1)	20	(4.2)	
Unknown	34	(3.0)	12	(1.8)	22	(4.6)	
Opioid exposure group, n (%)							.19
Medication for OUD alone	679	(59.6)	390	(58.8)	289	(60.7)	
Unprescribed opioids without medication for OUD	124	(10.9)	65	(9.8)	59	(12.4)	
Medication for OUD and unprescribed opioids	295	(25.9)	182	(27.5)	113	(23.7)	
Other opioids prescribed	41	(3.6)	26	(3.9)	15	(3.2)	
Medication for OUD, n (%)							.21
Methadone	449	(39.4)	280	(42.2)	169	(35.5)	
Buprenorphine	510	(44.8)	284	(42.8)	226	(47.5)	
Methadone and buprenorphine	15	(1.3)	8	(1.2)	7	(1.5)	
Neither	165	(14.5)	91	(13.6)	74	(15.5)	
Unprescribed substances (opioids or cocaine), n (%)	457	(40.1)	268	(40.4)	189	(39.7)	.68
Which unprescribed substance, n (%)							
Cannabis	333	(29.2)	197	(29.7)	136	(28.6)	.46
Amphetamines/methamphetamine	105	(9.2)	57	(8.6)	48	(10.1)	.62
Heroin (1 mo before delivery)	102	(9.0)	59	(8.9)	43	(9.0)	.80
Other opioids (1 mo before delivery)	66	(5.8)	47	(7.1)	19	(4.0)	.02
Cocaine	221	(19.4)	124	(18.7)	97	(20.4)	.37
Selective serotonin reuptake inhibitor, n (%)	135	(11.9)	77	(11.6)	58	(12.2)	.60
Benzodiazepines, n (%)	183	(16.1)	109	(16.4)	74	(15.5)	.66
Gabapentin, n (%)	115	(10.1)	69	(10.4)	46	(9.7)	.72
Nicotine smoking, n (%)	649	(57.0)	390	(58.8)	259	(54.4)	.07
Eligible to provide breast milk, n (%)	781	(68.7)	445	(67.3)	336	(70.6)	.36
Male infant, n (%)	591	(51.9)	333	(50.2)	258	(54.2)	.193
Gestational age at delivery, wk, mean (SD)	38.3	(1.5)	38.2	(1.5)	38.3	(1.6)	.341
Preterm <37 weeks of gestational age, n (%)	166	(14.6)	98	(14.8)	68	(14.3)	.705
Birth weight, g, mean (SD)	3027.8	(521.3)	3022.02	(520.9)	3035.86	(522.3)	.659

Significant P values are in bold type.

2.93; 95% CI, 1.28-6.73). In the COVID-19 group, the aOR for prn treatment failure rate was 3.77 (95% CI, 0.98-14.50), which was no longer statistically significant.

Discussion

This study demonstrates changes in hospital care processes for newborns with prenatal opioid exposure in the COVID-19 era. Most notably, there was a significant decrease in opioid-exposed newborns who roomed-in with their parent after hospital discharge. Rooming-in of the parent–infant dyad is an important nonpharmacologic intervention that facilitates parental presence at the bedside and has been associated with improved hospital outcomes for opioid-exposed newborns.[7] This decrease in rooming-in following discharge may reflect a decreased availability of bedspaces in areas of the hospital where rooming-in was not possible as the hospital's COVID-19 patient load increased.[15] Alternatively, this may reflect the impact of more stringent visitor policies in place to limit COVID-19 spread. Previous studies have demonstrated a negative impact of visitor restrictions on parental presence in the NICU and other pediatric units, as well as on parent experience during their child's hospitalization.[13-15,26,27] In some cases, limits on the number of visitors may have decreased the ability of fathers and other family members or support persons to visit, impacting the feasibility of an extended maternal stay at bedside. In other cases, the change in maternal status from patient to visitor might have precluded the mother's ability to stay overnight with limited visitation hours.

Table II. System process variables and NOWS outcomes

Variables	Overall (N = 1139)		Pre-COVID-19 group (N = 663)		COVID-19 group (N = 476)		P value
Process measures and NOWS treatment protocol							
Room-in before parental discharge, n (%)	948	(83.5)	552	(83.6)	396	(83.2)	.54
Rooming-in after parental discharge, n (%)	662	(59.1)	408	(63.0)	254	(53.8)	**.001**
Received skin to skin, n (%)	930	(81.9)	546	(82.6)	384	(80.8)	.26
Location of care, n (%)							
NICU/SCN	423	(37.1)	253	(38.2)	170	(35.7)	.71
Nursery	1020	(89.6)	589	(57.8)	431	(42.3)	.64
Pediatric unit	280	(24.6)	168	(25.3)	112	(23.5)	**.001**
Parent eligible to provide breast milk, n (%)	781	(68.7)	445	(67.3)	336	(70.6)	.36
Received breast milk, n (%)	613	(53.9)	365	(55.1)	248	(52.1)	.56
NOWS assessment method, n (%)							
Finnegan	354	(31.1)	219	(33.0)	135	(28.4)	**.002**
ESC	785	(68.9)	444	(67.0)	341	(71.6)	
NOWS medications, n (%)							
Morphine	350	(87.5)	208	(87.8)	142	(87.1)	.65
Methadone	44	(11.0)	25	(10.5)	19	(11.7)	
Clonidine	1	(0.3)	1	(0.4)	0	(0.0)	
Phenobarbital	4	(1.0)	3	(1.3)	1	(0.6)	
Primary outcome measures							
Feeding breast milk at discharge, n (%)	528	(46.5)	303	(46.0)	225	(47.3)	.29
PharmTx, n (%)	400	(35.5)	237	(36.2)	163	(34.5)	.80
Prn opioid treatment of those with PharmTx, n (%)	119	(29.8)	73	(30.8)	46	(28.2)	.55
Prn treatment failure rate, n (%)	42	(35.3)	22	(30.1)	20	(43.5)	.14
Opioid treatment days, mean (SD)	15.5	(10.9)	15.5	(10.6)	15.5	(11.3)	.99
Hospital LOS, d, mean (SD)	12.3	(10.3)	12.2	(9.9)	12.5	(10.9)	.66
Secondary outcome measures							
Discharged in parental custody, n (%)	856	(75.2)	498	(75.1)	358	(75.4)	.52
ER visit within 30 d, n (%)	38	(3.3)	24	(3.6)	14	(2.9)	.39
Inpatient readmission within 30 d, n (%)	18	(1.6)	13	(2.0)	5	(1.1)	.66

SCN, special care nursery.
P values account for hospital-level clustering using the Cochran–Mantel–Haenszel χ^2 test and mixed-effects regression analysis. Significant *P* values are in bold type.

There was also a significant decrease in opioid-exposed newborns cared for in pediatric inpatient units. Presumably, this reflects in part the decreased availability of bedspaces on these units as hospitals' COVID-19 census increased. In several locations, adult patients with Covid-19 were cared for on units previously designated for pediatric care.[15] This decrease in pediatric unit utilization likely contributed to the decrease in rooming-in after maternal discharge. Of note, a higher proportion of opioid-exposed newborns were cared for at nonacademic sites during the COVID-19 period, and many of these sites do not have inpatient pediatric units available.

Overall, NOWS hospitalization outcomes were stable from the pre-COVID-19 period to the COVID-19 period, with no significant changes in the overall rate of pharmacotherapy or any clinically significant differences in hospital LOS. A greater proportion of newborns in the COVID-19 period were managed using ESC assessment. This likely reflects a temporal trend as the selection of NOWS assessment model is made at the hospital level, with increased adoption of ESC over time.[24] Management using ESC has been associated with a decreased need for PharmTx and decreased LOS, which might have balanced some of the impact of pandemic-associated decrease in rooming-in and decreased utilization of inpatient pediatric units at the care site on these outcomes.[24,28-31]

Prn opioid dosing for NOWS in combination with nonpharmacologic interventions may be associated with decreased LOS and decreased NICU transfers.[25,28] Rates of

failed prn dosing and conversion to standing opioids for NOWS treatment increased during the COVID-19 time period in the subanalysis of academic hospital settings, which might have been more subject to system-level pressures as many became dedicated centers for COVID-19 care, converting units to accommodate transfers.[15] We hypothesize that the decreased success of limited prn doses may have been driven by changes in care settings, as well as other potential changes in provision of nonpharmacologic care.

There was a significant increase in the rate of breast milk receipt during the COVID-19 period. This finding was unexpected, given that previous studies reflected early concerns about potential COVID-19 transmission related to breast milk and demonstrated a decrease in hospital practices supporting breastfeeding.[32-36] The reason for this association is uncertain. It is possible that with birthing parents anticipating more time at home owing to quarantine restrictions, increased availability of remote work for those working from home, and the promise of financial support for those not working, more mothers felt confident that they would be able to maintain a breastfeeding relationship after discharge.[13,37,38] It is also possible that some parents may have hoped to provide immunologic protection for their newborn.[39] Finally, there may have been another unidentified temporal trend toward greater breastfeeding education and support within this quality improvement network unrelated to the pandemic over this period.

Table III. **Multivariable regression of primary NOWS outcomes**

Factors	Breast milk at discharge*			PharmTx*			Hospital LOS[†]			Failed prn treatment*,[‡]		
	% Breastfed	aOR, 95% CI	P value	% PharmTx	aOR, 95% CI	P value	Mean LOS	aRR, 95% CI	P value	% Failed prn	aOR, 95% CI	P value
Group												
Pre-COVID-19	46.0	Reference	**.007**	36.2	Reference	.63	12.2	Reference	**.02**	30.1	Reference	.36
COVID-19	47.3	2.03 (1.22-3.39)		34.5	0.92 (0.65-1.30)		12.5	1.04 (1.01-1.08)		43.5	1.56 (0.60-4.09)	
Center type												
Academic	50.7	1.24 (0.54-2.87)	.62	39.4	0.65 (0.23-1.86)	.42	14.0	1.02 (0.79-1.31)	.90	36.0	0.08 (0.00-2.57)	.15
Nonacademic	43.4	Reference		32.6	Reference		11.1			34.1	Reference	
Medication for OUD												
Methadone	43.8	Reference	.86	44.3	Reference	**.002**	14.6	Reference	**<.001**	40.3	Reference	.11
Buprenorphine	55.1	1.22 (0.73-2.03)		25.8	0.51 (0.35-0.73)		10.0	0.80 (0.77-0.83)		23.8	0.31 (0.10-0.93)	
None	27.9	1.01 (0.44-2.32)		41.5	0.87 (0.53-1.44)		13.3	0.89 (0.84-0.93)		50.0	0.81 (0.16-4.08)	
NICU/SCN												
Yes	33.0	0.57 (0.33-0.97)	**.04**	72.4	24.10 (16.19-35.93)	**<.001**	12.2	2.46 (2.37-2.56)	**<.001**	37.5	2.20 (0.74-6.58)	.16
No	54.5	Reference		13.6	Reference		5.1	Reference		32.7	Reference	
SSRI												
Yes	45.2	1.51 (0.69-3.32)	.31	45.8	1.64 (0.97-2.75)	.06	9.5	1.05 (0.99-1.10)	.09	42.3	0.88 (0.27-2.84)	.83
No	46.7	Reference		34.1	Reference		10.4	Reference		33.3	Reference	
Benzodiazepines												
Yes	30.1	0.29 (0.16-0.52)	**<.001**	59.7	2.71 (1.72-4.26)	**<.001**	13.4	1.30 (1.25-1.35)	**<.001**	44.1	2.29 (0.76-6.88)	.14
No	49.7	Reference		30.9	Reference		9.1	Reference		31.8	Reference	
Any breast milk												
Yes	N/A	N/A	N/A	24.6	0.40 (0.28-0.56)	**<.001**	8.9	0.79 (0.76-0.82)	**<.001**	26.0	0.80 (0.28-2.31)	.67
No	N/A	N/A	N/A	48.3	Reference		11.1	Reference		42.0	Reference	

aRR, adjusted risk ratio; *N/A*, not appliable; *SSRI*, selective serotonin reuptake inhibitor.
Significant *P* values are in bold type.
*Multivariable mixed-effects logistic regression model, taking into account hospital-level clustering.
†Multivariable mixed-effects Poisson regression model, taking into account hospital-level clustering.
‡Among pharmacologically treated infants on prn (n = 75).

Table IV. Multivariable regression of primary NOWS outcomes at academic centers

Factors	Breast milk at discharge*			PharmTx*			Hospital LOS†			Failed prn treatment*,‡		
	% Breastfed	aOR, 95% CI	P value	% PharmTx	aOR, 95% CI	P value	Mean LOS	aRR, 95% CI	P value	% Failed prn	aOR, 95% CI	P value
Group												
Pre-COVID-19	48.7	Reference	**.01**	39.6	Reference	.13	13.2	Reference	.48	26.5	Reference	.05
COVID-19	54.2	2.93 (1.28-6.73)		39.0	0.66 (0.39-1.12)		15.3	1.02 (0.97-1.07)		53.9	3.77 (0.98-14.50)	
Medication for OUD												
Methadone	49.0	Reference	.92	46.2	Reference	.10	16.1	Reference	**<.001**	47.7	Reference	**.02**
Buprenorphine	57.4	0.82 (0.38-1.77)		29.8	0.52 (0.30-0.88)		11.5	0.78 (0.74-0.82)		20.8	0.17 (0.04-0.72)	
None	32.8	0.68 (0.21-2.24)		46.6	0.73 (0.34-1.57)		14.9	0.81 (0.75-0.88)		14.3	0.05 (0.00-0.83)	
NICU/SCN												
Yes	37.6	0.52 (0.25-1.09)	.08	68.9	16.49 (9.69-28.07)	**<.001**	21.2	2.59 (2.45-2.75)	**<.001**	36.7	2.64 (0.60-11.55)	.20
No	62.5	Reference		12.7	Reference		7.4	Reference		34.6		
SSRI												
Yes	47.3	1.50 (0.46-4.89)	.51	50.0	1.22 (0.54-2.75)	.63	15.3	0.99 (0.91-1.07)	.77	27.8	0.43 (0.10-1.84)	.25
No	51.2	Reference		38.0	Reference		13.8	Reference		38.6	Reference	
Benzodiazepines												
Yes	30.7	0.17 (0.07-0.39)	**<.001**	63.4	3.49 (1.89-6.46)	**<.001**	20.1	1.31 (1.24-1.39)	**<.001**	42.9	2.42 (0.61-9.54)	.20
No	56.1	Reference		33.0	Reference		12.3	Reference		31.9	Reference	
Any breast milk												
Yes	N/A	N/A	N/A	27.1	0.35 (0.21-0.57)	**<.001**	10.6	0.74 (0.70-0.77)	**<.001**	24.2	0.51 (0.13-2.00)	.33
No	N/A	N/A	N/A	57.1	Reference		18.7	Reference		45.2	Reference	

Significant P values are in bold type.
*Multivariable mixed-effects logistic regression model, taking into account hospital-level clustering.
†Multivariable mixed-effects Poisson regression model, taking into account hospital-level clustering.
‡Among pharmacologically treated infants on prn (n = 75).

Although previous studies have shown increases in community rates of opioid use and overdose,[16-19] our findings did not demonstrate a significant increase in newborns exposed to nonprescribed opioids or other substances. Overall rates of birthing parents on medication for OUD were stable. Previous studies have documented increased availability of telehealth and take-home dosing.[20,40] It is possible that improved maternal access to treatment of medication for OUD provided a balance to other social and financial pressures influencing unprescribed substance use during the pandemic. Alternatively, there is the potential that some cases of prenatal opioid exposure were missed in infants born to parents without a previously documented history of substance use disorder or treatment.

Strengths of this study include its coverage of multiple sites and care settings that are already routinely entering data on opioid-exposed newborns and therefore well-positioned to capture significant changes over time and its large number of parent–infant dyads. In addition, it included sites with different approaches to NOWS assessment and management. The baseline characteristics of birthing parents included in the pre-COVID-19 and COVID-19 periods were similar, including overall rates of medication for OUD and polysubstance exposures, which may influence neonatal outcomes. Of note, the percentage of infants exposed to medication for OUD was higher in our Massachusetts cohort compared with the general US population of pregnant individuals with OUD. Given the stable rate of medication for OUD over the pre-COVID-19 and COVID-19 periods and the identical NOWS treatment algorithm for all opioid-exposed infants regardless of type of opioid exposure, our results still would be generalizable to other settings.

This study has several limitations. Because this was not a controlled trial, there is a potential for other confounders or temporal trends impacting NOWS processes and outcomes in ways that we were unable to identify. It is possible that such data as maternal exposure to nicotine were underreported, given our reliance on chart abstraction owing to the limitations of our study design. Not all sites within the PNQIN network continued to enter data during the COVID-19 pandemic. Some enrolled sites had ceased regularly entering data before the pandemic; however, it is possible that sites more adversely affected by the pandemic had less staffing capacity to continue to enter data, or that sites that did continue to enter data had less infrastructure to support NOWS care in general. Of the 7 centers that stopped entering data during the pandemic, 3 were major academic medical centers in Boston significantly impacted by the COVID-19 patient burden. These centers historically have had low numbers of infants with NOWS, and data entry likely was not a high priority during the COVID-19 surge.

Additional limitations include the unclear proportion of newborns who were cared for in a level 1 infant-only nursery rather than a mother–baby room following maternal discharge versus being transferred to other units. It also is unclear whether newborns who otherwise might have been transferred to inpatient pediatric units were kept in mother–baby rooms longer or were transferred to level II/III nurseries. In addition, data on birthing parent COVID-19 status at or near delivery were not tracked as part of this study, and thus we were unable to draw any conclusions about how precautions to prevent transmission from birthing parent to baby may have impacted rooming-in, care site and other hospital processes, or NOWS outcomes for this subset of dyads.

Future directions include updated site practice surveys to better understand management of NOWS at each of the participating sites and site-identified facilitators and barriers to providing optimal care. In addition, parental questionnaires would help identify additional facilitators and barriers as perceived by the families. A better understanding of factors that promoted resiliency in this hospital network to pressures of the COVID-19 pandemic will be valuable for improving care as other areas of the country continue to experience surges in the COVID-19 pandemic, as well as preparing for possible future public health crises. It will be of interest to better understand facilitators and barriers to breastfeeding in this population and how these may have evolved with changes to community supports, interaction with the medical system through telehealth, and the potential impact of changes in remote versus onsite employment opportunities for parents who plan to return to work. The Massachusetts sites participating in the PNQIN have a history of quality improvement surrounding perinatal care of families impacted by OUD. In addition, even though Massachusetts experienced high rates of COVID-19 in the community and COVID-19–related hospitalizations earlier in the pandemic, later surges did not reach the same scale. It would be of interest to explore the impact of the COVID-19 pandemic on hospital care processes and outcomes for opioid-exposed newborns in other regions. ∎

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