

ARTICLE



Neonatal abstinence syndrome and mother's own milk at discharge

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OBJECTIVE: To describe factors impacting receipt of mother's own milk (MOM) at discharge among California infants diagnosed with neonatal abstinence syndrome (NAS).

STUDY DESIGN: Cohort study of the California Perinatal Quality Care Collaborative's Maternal Substance Exposure Database for infants with NAS and gestational age ≥ 34 weeks from 2019 to 2020.

RESULT: 245 infants with NAS were identified. Variables with an increased likelihood of being discharged on MOM included maternal medication assisted treatment ($p = 0.001$), use of maternal addiction services ($p < 0.001$), receiving donor human milk ($p = 0.001$), being treated in the well baby unit ($p < 0.001$), rooming-in ($p < 0.001$), and kangaroo care ($p < 0.001$). Among infants with NAS for whom MOM was recommended ($n = 84$), rooming-in was the only factor associated with being discharged on MOM ($p = 0.002$); receiving formula was the only inversely associated factor ($p < 0.001$).

CONCLUSION: Results suggest supporting the mother-infant dyad and using non-pharmacologic treatment methods, such as rooming-in, increase receipt of MOM at discharge.

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INTRODUCTION

Neonatal abstinence syndrome (NAS), also known as neonatal opioid withdrawal syndrome (NOWS), is characterized by withdrawal symptoms present in infants due to exposure to opioids in utero [1]. Although difficult to quantify, it is estimated that between 1999 and 2014, maternal opioid use disorder (OUD) rates at delivery increased fourfold [2]. This rise in use among child-bearing aged women has led to an increase in NAS incidence [3]. In addition to medical complications related to NAS, opioid use during pregnancy has been linked to adverse health outcomes such as maternal death, fetal loss, or preterm birth [3]. Studies have shown that infants of women undergoing treatment for opioid use can benefit significantly from breastfeeding such as decreased severity of NAS and decreased length of hospital stay [4–7]. This benefit is hypothesized to be linked to the dual benefits of skin-to-skin contact and the low concentrations of maternal opioid agonist pharmacotherapy in the breastmilk, though no studies have definitively substantiated this assumption. The Academy of Breastfeeding Medicine (ABM), the American College of Obstetricians and Gynecologists (ACOG), and the American Academy of Pediatrics (AAP) strongly encourage breastfeeding and the use of mother's own milk (MOM) for infants with NAS while mothers are enrolled in medication assisted treatment (MAT) [4–6]. Despite the strong support, breastfeeding rates among mothers on MAT are lower compared to other lactating women [4, 7]. These low rates are likely due to a lack of knowledge or adherence to

recommendations among hospital staff and patients, negative stigma surrounding mothers who have exposed their infants to opioids, and an overall lack of support for these women [8–12].

Despite encouragement from medical experts and the demonstrated level of safety of breastfeeding for some infants with NAS, variation in NAS management has resulted in limited use of MOM. Variations in resources, treatment plans, and knowledge regarding NAS have impeded the creation of a unified NAS standard of care and the discovery of critical factors to breastfeeding success. Being able to understand the association between pharmacologic and non-pharmacologic factors, maternal characteristics, and breastfeeding rates will ultimately help improve the quality of care for mother-infant dyads affected by NAS. The objective of this study was to describe the relationships and predictors associated with receipt of MOM for infants with NAS. Throughout this paper, the authors use terms such as mother, maternal, or pregnant woman when referring to birthing or lactating individuals. The authors acknowledge that not all birthing or lactating people refer to themselves as mothers or women and believe that all individuals deserve patient-centered care that enables them to lead healthy authentic lives.

METHODS

Data source

California Perinatal Quality Care Collaborative's (CPQCC) extensive neonatal intensive care unit (NICU) database is used to inform quality

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improvement and research efforts, monitor improvement interventions, and identify strong and weak performance areas, aiding in the advancement of quality neonatal care. A subsection of the NICU database is the Maternal Substance Exposure (MatEx) database; this optional database focuses on collecting and identifying maternal substance exposure and NAS management data to identify variations and improve healthcare for infants with NAS. Infants exposed to substances in utero may be included in the MatEx database whether treatment was received in the NICU or the well baby/newborn nursery unit.

Using CPQCC's MatEx database, a cohort of infants was identified for this study. Within the research period Jan 2019-Dec 2020, there were 20 participating hospitals, all level 3 or 4 NICUs, that submitted data to MatEx, 14 of which were Baby-Friendly Hospitals. No information regarding infant race or ethnicity was collected for this specific database and therefore limits the opportunity for data disaggregation with these categories. This information is collected in the CPQCC NICU database, but not all MatEx infants are eligible for CPQCC NICU database entry.

The primary outcome was the use of MOM within 24 h of discharge and included both pumped MOM and infants feeding at the breast. The term MOM was specified to distinguish from the use of donor human milk (DHM) while also remaining inclusive of pumped breast milk. MOM is also a commonly used outcome among other studies involving neonates with NAS [13]. Variables of interest modeled continuously included gestational age, birthweight, and length of stay. Variables modeled as binary included maternal medication assisted treatment, maternal medication assisted treatment with methadone, maternal medication assisted treatment with buprenorphine, treatment of the infant in the well baby unit, NICU level 3 or 4, rooming-in, Eat, Sleep, and Console (ESC) approach, low stimulation, kangaroo care, cuddlers, pacifiers, swaddling, high calorie formula, low lactose formula, formula, donor milk, and pharmacologic treatment for NAS. Categorically modeled variables included primary drug treatment for NAS, insurance type, and final disposition.

Population criteria

Data were submitted to the MatEx database for infants exposed to any substance in utero with NAS withdrawal symptoms by Day of Life 7. Additional inclusion criteria for this study included a gestational age ≥ 34 weeks and at least one of the following: mother was exposed to opioids, mother's toxicology screen tested positive for opioids, or infant's toxicology screen tested positive for opioids. This analysis only included late preterm and term infants who would have an increased ability to receive non-pharmacologic interventions such as rooming-in and a decreased likelihood of breastfeeding challenges due to very preterm birth. Information on the severity of NAS withdrawal symptoms was not collected as centers use a variety of methods to ascertain this including both the Finnegan Neonatal Abstinence Scoring System and the Eat, Sleep, Console method (which does not yield a numerical score) [14].

While according to AAP/ABM/ACOG recommendations [4–6], MOM may not be indicated for all infants in this population, we included analysis on the full NAS population because hospital policies and practices on which infants are allowed to receive MOM vary. In order to more fully understand the factors that increase the likelihood of MOM at discharge, a subset of infants with NAS for whom MOM was explicitly recommended by AAP/ABM/ACOG was created [6]. We also analyzed pairwise correlations between modalities of care for NAS using *corrplot* package in order to describe which treatments were being delivered together. To do this, we calculated a correlation matrix, and Spearman's statistics were used to test the significance of correlations. All analyses were conducted using R 4.0.0 [15].

Statistical analysis

Means and standard deviations were calculated for continuous variables; frequency and percentages were used for binary and categorical variables. Differences between the population receiving or not receiving MOM at discharge were tested. Student's *t*-tests were used to test differences between groups for continuous variables, while chi-squared tests and Fisher's exact tests were used to test categorical or binary variables. For any variable that had 7 or fewer observations in a category, Fisher's exact test was used. All statistical tests were two-sided and evaluated at an α -level of 0.002 to account for multiple testing. Complete-case analysis was used for all statistical tests, though there were high levels of missing data ($>15\%$) regarding whether infants were treated with an ESC approach, whether the mother received methadone, and whether the mother received addiction services. Addiction services include but are not limited

to case management, psychiatry, psychology, social work, facilitated group therapy, or facilitated family therapy. Approval for this study was given by the Stanford Institutional Review Board, protocol number 14746.

RESULTS

Between 2019 and 2020, 449 infant records from 20 hospitals across California were submitted to the MatEx database. Of these 449 records, 245 records were identified as infants with NAS. From this population of all infants with NAS, 33% were discharged on MOM ($n = 81$), 62% were not discharged on MOM ($n = 151$), and 5% had unknown MOM status at discharge ($n = 13$). MOM at discharge was associated with 8.9 fewer days of hospital stay (95% CI: 5.9, 11.9). Factors associated with an increased likelihood of infants discharged on MOM included maternal MAT ($p < 0.001$), use of maternal addiction services ($p < 0.001$), receiving donor human milk (DHM) ($p < 0.001$), being inborn ($p < 0.001$), and being treated in the well baby unit ($p < 0.001$) (Table 1). Non-pharmacologic approaches found to be associated with being discharged on MOM included rooming-in ($p < 0.001$) and kangaroo care ($p < 0.001$). Factors associated with a lower likelihood of being discharged on MOM included use of any type of formula ($p < 0.001$) and, more specifically, low lactose formula ($p < 0.001$). There was also a lower likelihood of being discharged on MOM if the infant received any pharmacologic treatments ($p < 0.001$). Use of ESC, low stimulation, cuddlers, pacifiers, swaddling, and high calorie formula were not significantly associated with being discharged on MOM.

Of the 245 infants in the entire NAS population, a smaller cohort was created to analyze information on infants with NAS for whom MOM was recommended according to AAP/ABM/ACOG guidelines. In accordance with these guidelines, infants were excluded due to a lack of maternal MAT ($n = 134$) or exposure to illicit drugs and/or positive HIV status ($n = 27$) (Fig. 1). The remaining 84 infants were included in the cohort description of infants with NAS and for whom MOM was recommended.

Within this population, 51 infants were discharged on MOM (60.7%), 31 infants were not discharged on MOM (36.9%), and 2 infants (2.4%) were missing MOM at discharge data (Fig. 1). MOM at discharge was associated with 12.4 fewer days of hospital stay (95% CI: 4.8, 20.5). In this cohort, rooming-in ($p = 0.002$) and being inborn ($p < 0.001$) were the only significant factors associated with being discharged on MOM, while receiving formula was the only significant factor inversely associated with being discharged on MOM ($p < 0.001$) (Table 2).

For this smaller cohort, correlations between treatment factors are presented in Fig. 2. Rooming-in was correlated with being treated in the well baby unit ($p < 0.001$). Rooming-in was negatively correlated with use of cuddlers ($p < 0.001$), pharmacological treatments ($p < 0.001$), and using formula ($p < 0.001$). Pacifier use was correlated with swaddling ($p < 0.001$) and low stimulation ($p < 0.001$). Swaddling was also correlated with low stimulation ($p = 0.01$). Being treated in the well-baby unit was negatively correlated with pharmacological treatments for NAS ($p < 0.001$) and receiving donor milk was negatively correlated with receiving formula ($p = 0.01$).

DISCUSSION

Between 2019 and 2020, 449 infant records were recorded in the MatEx Database from 20 California hospitals. 245 infants were categorized into the population of infants with NAS. Of those, 84 infants had no apparent maternal contraindications and were identified as infants with NAS for whom MOM was recommended. For infants with NAS, use of maternal MAT, maternal addiction services use, donor human milk use, and well-baby unit treatment were associated with being discharged on MOM. Rooming-in and kangaroo care were also associated with being discharged on

Table 1. Descriptive Characteristics of All Infants with NAS.

	Sample size for each variable	Discharged on Mother's Own Milk ^a		Difference in means or odds ratios (95% CI) ^b		p-value ^c
	<i>n</i>	No <i>n</i> = 151	Yes <i>n</i> = 81			
Gestational Age in weeks, mean ± SD	232	37.52 ± 2.01	37.65 ± 1.62	0.13	(−0.34, 0.62)	0.596
Birthweight in kg, mean ± SD	232	2.93 ± 0.54	2.99 ± 0.48	−0.09	(−0.07, 0.20)	0.357
Sex, <i>n</i> (%)	229			0.92	(0.53, 1.58)	0.862
Female		74 (49.7)	38 (47.5)			
Male		75 (50.3)	42 (52.5)			
Location of Birth, <i>n</i> (%)	230			5.01	(2.19, 12.96)	<0.001
Inborn		96 (64.4)	73 (90.1)			
Outborn		53 (35.6)	8 (9.9)			
MAT, <i>n</i> (%)	222	58 (40.6)	51 (64.6)	2.67	(1.52, 4.76)	0.001
Methadone MAT, <i>n</i> (%)	108	37 (64.9)	32 (62.7)	0.91	(0.41, 2.00)	0.973
Buprenorphine MAT, <i>n</i> (%)	108	23 (40.4)	19 (37.3)	0.88	(0.74, 0.40)	0.895
Maternal Addiction Services, <i>n</i> (%)	190	34 (27.9)	38 (55.9)	3.28	(1.77, 6.15)	<0.001
NAS Location: Well Baby, <i>n</i> (%)	230	16 (10.7)	28 (34.6)	4.39	(2.22, 8.94)	<0.001
NICU level, <i>n</i> (%)	232			0.36	(0.19, 0.66)	0.002
Level 4		64 (42.4)	17 (21.0)			
Level 3		87 (57.6)	64 (79.0)			
Rooming-in, <i>n</i> (%)	232	9 (6.0)	34 (42.0)	11.4	(5.3, 26.9)	<0.001
ESC Approach, <i>n</i> (%)	110	35 (48.6)	25 (65.8)	2.03	(0.91, 4.69)	0.129
Low Stimulation, <i>n</i> (%)	232	110 (72.8)	49 (60.5)	0.57	(0.32, 1.01)	0.075
Kangaroo Care, <i>n</i> (%)	232	47 (31.1)	55 (67.9)	4.68	(2.65, 8.46)	<0.001
Cuddlers, <i>n</i> (%)	232	63 (41.7)	29 (35.8)	0.78	(0.44, 1.35)	0.461
Pacifier, <i>n</i> (%)	232	131 (86.8)	72 (88.9)	1.22	(0.54, 2.95)	0.795
Swaddling, <i>n</i> (%)	232	139 (92.1)	75 (92.6)	1.07	(0.36, 3.65)	1.000
High Calorie Formula, <i>n</i> (%)	232	29 (19.2)	8 (9.9)	0.46	(0.19, 1.02)	0.097
Low Lactose Formula, <i>n</i> (%)	232	35 (23.2)	5 (6.2)	0.22	(0.06, 0.60)	0.001
Formula, <i>n</i> (%)	232	151 (100.0)	48 (59.3)	-		<0.001
Donor milk, <i>n</i> (%)	232	1 (0.7)	8 (9.9)	16.26	(2.11, 731.39)	0.001
Pharmacologic Treatment, <i>n</i> (%)	232	105 (69.5)	31 (38.3)	0.27	(0.15, 0.48)	<0.001
Primary Drug: NAS Treatment, <i>n</i> (%)	134					
Clonidine		8 (7.6)	0 (0.0)	-		0.662
Phenobarbital		2 (1.9)	0 (0.0)			
Methadone (707)		7 (6.7)	2 (6.5)			
Morphine (710)		86 (81.9)	29 (93.5)			
Insurance, <i>n</i> (%)	221					0.001
CCS		23 (16.4)	22 (27.2)	-		
Commercial HMO		0 (0.0)	3 (3.7)			
Commercial PPO		3 (2.1)	7 (8.6)			
Medi-Cal		112 (80.0)	49 (60.5)			
Disposition, <i>n</i> (%)	232					<0.001
Transported to another hospital		9 (6.0)	0 (0.0)	-		
Home to mom		31 (20.5)	76 (93.8)			
Home to family member		27 (17.9)	2 (2.5)			
Social Service/Foster care		81 (53.6)	3 (3.7)			
Adoption		3 (2.0)	0 (0.0)			
Length of stay in days, mean ± SD	230	17.6 ± 15.3	8.7 ± 7.8	−8.9	(−11.9, −5.9)	<0.001

The main descriptive characteristics are in bold and the *n*(%) is in italics to ease reading comprehension.

^a13 individuals were missing information on whether they were discharged on MOM and were not included in this table.

^bDifferences in means were calculated for the continuous variables of birthweight and gestational age describing the difference between the mean of the population discharged on MOM and the mean of the population not discharged on MOM. Confidence intervals were calculated assuming unequal variances. For binary variables, odds ratios were calculated describing the change in odds of being discharged on MOM associated with the variable. For variables with cells smaller than 7, confidence intervals were calculated based on Fisher's exact test. For other binary variables, Wald confidence intervals were calculated. Odds ratios and confidence intervals were not provided for variables with zero cells.

^c*P*-values were calculated to test the difference between groups discharged on MOM and not discharged on MOM. T-tests with unequal variances were used to test the differences in continuous variable means. Chi-square tests with continuity corrections were used to test the difference between binary and categorical variables. For variables with cells of 7 or less, Fisher's exact test was used.

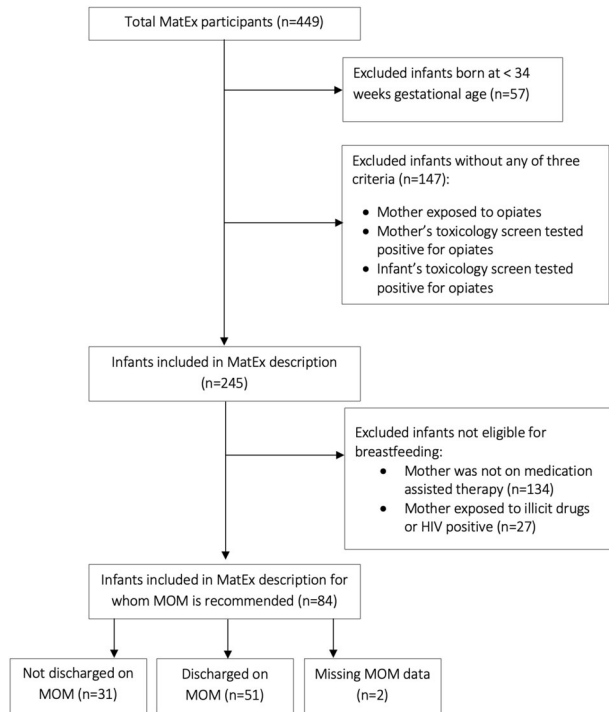


Fig. 1 Population Chart. This chart shows the population breakdown for infants with NAS for whom MOM is recommended.

MOM. Use of formula, low lactose formula, and pharmacologic treatment were associated with not being discharged on MOM. For the smaller cohort of infants with NAS for whom MOM was recommended, rooming-in and being inborn were the only factors positively associated with MOM at discharge, while formula was the only factor negatively associated. Additionally, rooming-in was correlated with being treated in the well baby unit, and both factors were negatively correlated to pharmacologic treatment.

Rooming-in

We found that infants able to room-in with their mothers were significantly more likely to be discharged on MOM. As the literature would suggest, this may reflect the benefits of mother/infant bonding and a lower acuity setting which reduces the stress and anxiety for the mother and leads to increased likelihood of breastfeeding success [9, 16, 17]. While some hospitals may have rooming-in options in both the NICU and the well baby unit, the decision to treat the infant in a particular unit may be driven by hospital policies and procedures for care.

Maternal MAT/Addiction services

Infants with NAS whose mothers received addiction services (which includes case management, psychiatry, psychology, social work, facilitated group therapy, or facilitated family therapy at any time during the pregnancy and prior to admission in labor and delivery) also showed an increase in the likelihood of being discharged on MOM. Although ACOG recommends that those receiving MAT engage in behavioral therapy [6], only 66.1% of mothers on MAT received addiction services in this dataset. The correlation between receiving addiction services and MOM outcomes at discharge may stem from the fact that these mothers experienced more controlled withdrawal and were provided increased prenatal care as part of the addiction services. It could also reflect the quality of care provided, as addiction services are not available in all regions, particularly rural locations.

Low lactose formula

The data showed that the use of low lactose formula negatively correlated with MOM use at discharge. This is particularly important because in 2018, the Ohio Perinatal Quality Collaborative compared outcomes in centers utilizing non-pharmacologic standardized bundles, including the use of low lactose formula in non-breastfeeding infants [5] and this was subsequently recommended by the AAP. However, our data aligns with other studies that have since found that low lactose formula had no impact on length of stay/treatment or weight gain among infants with NAS [18–20].

Pharmacologic treatment

At least two rationales exist as to why infants with NAS who received pharmacologic therapy were less likely to be discharged home on MOM. One reason is that more severe NAS patients are transferred to the NICU for treatment- which increases the likelihood of separation of mother and baby. Alternatively, many authors have previously found that reduced breastfeeding or use of MOM has been linked to more severe symptoms associated with NAS [18, 21, 22]. Receiving pharmacotherapy is not necessarily indicative of symptom severity as it may simply reflect hospital protocol or failure to promote proven non-pharmacologic treatments such as ESC. Further research is needed to determine the influence of these factors on the likelihood of receiving MOM at discharge.

Barriers to breastfeeding

One of the most common barriers to breastfeeding among infants with NAS is misinformation among healthcare workers understanding which mother-infant dyads meet the recommendations for safe breastfeeding [23, 24]. AAP, ABM, and ACOG encourage breastfeeding in women who are stable on MAT opioid agonists (methadone or buprenorphine) and are not using illicit drugs nor have other contraindications, such as HIV infection [4–6]. AAP does note that in animal studies, buprenorphine may decrease milk production and offspring viability [25]. Although trace amounts of these substances in breastmilk are not sufficient to prevent NAS symptoms, abrupt discontinuation may aggravate symptoms; therefore, gradual weaning when discontinuing breastfeeding is advised [25].

Because infants cared for in NICUs that have access to DHM tend to have a higher percentage of infants discharged on MOM, in cases where mothers are unable to breastfeed initially or use of MOM is not recommended, temporary use of DHM may ultimately improve MOM at discharge [26]. While nearly one-fifth of Level I nurseries in the U.S. regularly use DHM for various reasons [27], DHM is a limited resource and as such may not be ideal for all circumstances. Due to financial constraints, NICUs may reserve their DHM for high-risk infant populations such as those with a birth weight of <1500 g or a gestational age <32 weeks. Even though a primary benefit of breastmilk in infants with NAS is the soothing and calming effect that comes directly from feeding at breast [18], a NICU culture that communicates that breastmilk is both a priority and a critical part of the infant's care may lead to mothers receiving more support around lactation in general. Lactation support and services require a multi-disciplinary approach and close contact with the infant's mother. Unfortunately, due to the stigma that mothers with OUD often experience from healthcare staff, the mother may be less likely to have all the support she needs to be successful with breastfeeding [28]. Allowing the opportunity for mothers to ask candid questions in a non-judgmental environment may provide more clarity to families and lead to increased opportunities for infants to be discharged home on MOM. Data from this study demonstrates that both a strong culture of breastmilk promotion and encouraging human connection (between the infant and mother through rooming-in as well as between healthcare staff and mothers through lactation

Table 2. Descriptive Characteristics of Infants with NAS for whom MOM is Recommended.

	Sample size for each variable <i>n</i>	Discharged on Mother's Own Milk ^a		Difference in means or Odds Ratios (95% CI) ^b		<i>p</i> -value ^c
		No <i>n</i> = 31	Yes <i>n</i> = 51			
Gestational Age in weeks, mean ± SD	82	38.10 ± 1.66	37.90 ± 1.73	−0.20	(−0.96, 0.57)	0.618
Birthweight in kg, mean ± SD	82	3.07 ± 0.53	3.04 ± 0.44	−0.02	(−0.24, 0.21)	0.888
Sex, <i>n</i> (%)	81			1.55	(0.63, 3.85)	0.471
Female		14 (45.2)	28 (54.9)			
Male		17 (54.8)	22 (43.1)			
Location of Birth, <i>n</i> (%)	82			7.36	(2.11, 30.29)	<0.001
Inborn		17 (54.8)	46 (90.2)			
Outborn		14 (45.2)	5 (9.8)			
Methadone MAT, <i>n</i> (%)	82	20 (64.5)	32 (62.7)	0.93	(0.36, 2.33)	1.000
Buprenorphine MAT, <i>n</i> (%)	82	13 (41.9)	19 (37.3)	0.82	(0.33, 2.06)	0.851
Maternal Addiction Services, <i>n</i> (%)	64	17 (73.9)	37 (90.2)	3.20	(0.66, 17.56)	0.148
NAS Location: Well Baby, <i>n</i> (%)	82	3 (9.7)	17 (33.3)	4.59	(1.15, 26.91)	0.018
NICU level, <i>n</i> (%)	82			0.26	(0.10, 0.67)	0.010
Level 4		16 (51.6)	11 (21.6)			
Level 3		15 (48.4)	40 (78.4)			
Rooming-in, <i>n</i> (%)	82	2 (6.5)	19 (37.3)	8.42	(1.78, 80.81)	0.002
ESC Approach, <i>n</i> (%)	42	11 (57.9)	13 (56.5)	0.95	(0.27, 3.25)	1.000
Low Stimulation, <i>n</i> (%)	82	23 (74.2)	35 (68.6)	0.76	(27, 2.03)	0.774
Kangaroo Care, <i>n</i> (%)	82	12 (38.7)	33 (64.7)	2.90	(1.17, 7.48)	0.039
Cuddlers, <i>n</i> (%)	82	11 (35.5)	20 (39.2)	1.17	(0.47, 3.02)	0.918
Pacifier, <i>n</i> (%)	82	24 (77.4)	46 (90.2)	2.65	(0.65, 11.80)	0.196
Swaddling, <i>n</i> (%)	82	27 (87.1)	47 (92.2)	1.73	(0.30, 10.09)	0.469
High Calorie Formula, <i>n</i> (%)	82	9 (29.0)	7 (13.7)	0.39	(0.11, 1.37)	0.149
Low Lactose Formula, <i>n</i> (%)	82	11 (35.5)	5 (9.8)	0.20	(0.05, 0.73)	0.008
Formula, <i>n</i> (%)	82	31 (100.0)	32 (62.7)	-	-	<0.001
Donor milk, <i>n</i> (%)	82	0 (0.0)	6 (11.8)	-	-	0.078
Pharmacologic Treatment, <i>n</i> (%)	82	23 (74.2)	25 (49.0)	0.33	(0.12, 0.86)	0.044
Primary Drug: NAS Treatment, <i>n</i> (%)	48			-	-	0.267
Clonidine		3 (13.0)	0 (0.0)			
Methadone (707)		2 (8.7)	2 (8.0)			
Morphine (710)		18 (78.3)	23 (92.0)			
Insurance, <i>n</i> (%)	81			-	-	1.000
CCS		9 (30.0)	14 (27.5)			
Commercial HMO		0 (0.0)	1 (2.0)			
Commercial PPO		1 (3.3)	3 (5.9)			
Medi-Cal		20 (66.7)	33 (64.7)			
Disposition, <i>n</i> (%)	82			-	-	<0.001
Transported to another hospital		2 (6.5)	0 (0.0)			
Home to mom		10 (32.3)	47 (92.2)			
Home to family member		7 (22.6)	1 (2.0)			
Social Service/Foster care		11 (35.5)	3 (5.9)			
Adoption		1 (3.2)	0 (0.0)			
Length of stay in days, mean ± SD	82	21.4 ± 20.9	8.8 ± 6.5	−12.4	(−20.5, −4.8)	<0.001

The main descriptive characteristics are in bold and the *n*(%) is in italics to ease reading comprehension.

^a2 individuals were missing information on whether they were discharged on MOM and were not included in this table.

^bDifferences in means were calculated for the continuous variables of birthweight and gestational age describing the difference between the mean of the population discharged on MOM and the mean of the population not discharged on MOM. Confidence intervals were calculated assuming unequal variances. For binary variables, odds ratios were calculated describing the change in odds of being discharged on MOM associated with the variable. For variables with cells smaller than 7, confidence intervals were calculated based on Fisher's exact test. For other binary variables, Wald confidence intervals were calculated. Odds ratios and confidence intervals were not provided for variables with zero cells.

^cP-values were calculated to test the difference between groups discharged on MOM and not discharged on MOM. T-tests with unequal variances were used to test the differences in continuous variable means. Chi-square tests with continuity corrections were used to test the difference between binary and categorical variables. For variables with cells of 7 or less, Fisher's exact test was used.

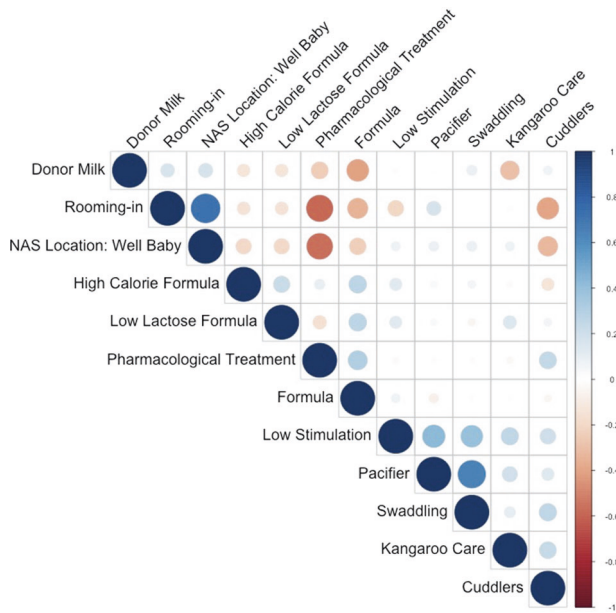


Fig. 2 This figure shows the correlation of different modalities of care for NAS. Red circles indicate negative correlations and blue circles indicate positive correlations. The size of the circle represents the size of the correlation with larger circles corresponding with stronger correlations.

and addiction services) serve to improve MOM outcomes at discharge for infants with NAS.

Social determinants

Factors outside hospital setting, such as the involvement of Child Protective Services (CPS), can act as a structural barrier to breastfeeding. Although California state law does not consider prenatal substance exposure as a sole determinant of child abuse or neglect [29], referrals to CPS may create an environment that is not supportive or conducive for the mother to provide breastmilk. Even in situations where CPS involvement is necessary, it is critical to prioritize the care of the mother-infant dyad in order to promote breastmilk production. Further, demonstrating a maternal willingness to participate in infant care, a factor in the CPS determination of separation, can include the provision of breastmilk. Often a custodial determination is not made until several days or weeks after the infant is born which means there is a window of opportunity for many of these infants to bond with and/or be fed by their mother. Even once a decision is made that the infant will leave the hospital with someone other than the mother, mothers may still pump and provide breastmilk as a way of participating in the infant's caretaking. Exclusion and inclusion criteria for this data were based on AAP/ABM/ACOG recommendations of whether the mother's milk is appropriate for the infant, regardless of custodial dynamics.

Limitations

There is a lack of knowledge of how closely NICU staff are following AAP, ABM, or ACOG recommendations and whether they are encouraging appropriately screened mothers to breastfeed or provide breastmilk for their infants. There are likely inconsistencies between physician recommendations, hospital policies, and parental education on encouraging the use of breastmilk and whether mothers were provided with the most recent guidelines on its beneficial effects for their infants [30]. Further standardization of care practices would allow for more in-depth analysis and likely more mothers encouraged to offer breastmilk to their infants.

Additionally, it is important to note that although the dataset included information regarding whether infants were fed MOM at all during their stay, this study's primary outcome was the use of MOM at discharge. All California centers participating in the CPQCC database are familiar with this outcome, and these CPQCC-eligible NICU infants are identified at discharge. We did not analyze data based on those infants who received any MOM during their hospitalization since the ultimate goal is breastmilk provision beyond the hospital stay. The difference in breastmilk metrics is important to consider when designing future research.

It is also important to note that the timing and type of toxicology screenings are not standardized across California and, therefore, were not collected as part of this database. While length of stay data was taken, length of treatment was not analyzed. The non-pharmacologic treatment option of "kangaroo care or clothed cuddling" within the MatEx database does not delineate if this was performed by the infant's mother or other provider (nurse, cuddler, etc.). As kangaroo care is an effective practice for treating infants with NAS, further specification in future research is needed.

The study's ability to detect significant differences was limited by a small sample size and missing data for certain variables. Future research would need to reduce the occurrence of missing data entry values to ensure a more robust dataset and thus more well-supported results. The study, however, provides an important component of NAS treatment in California hospitals, and the results could potentially be used to design future causal studies.

CONCLUSIONS

The data demonstrated that opioid exposed infants cared for in centers that supported the mother through MAT and/or maternal addiction services and that promoted non-pharmacological measures—such as rooming-in, kangaroo care, and remaining in the well baby unit—were associated with increased MOM use at discharge. Utilizing formula or pharmacologic treatment was associated with a decrease in MOM use at discharge. Further research is needed regarding hospital-level variability (lack of facilities for rooming-in, lack of DHM available, etc.) which may systematically lead to an overall reduction in MOM. Similarly, the effects of stigma or lack of education among hospital staff on infants exposed to opioids need to be better understood. Measuring breastmilk provision at different points in the infant's hospitalization beyond discharge is another important area for future research. Lastly, with increased data on hospital alignment with AAP/ABM/ACOG recommendations on MOM for infants with NAS, additional opportunities for quality improvement will emerge that have the potential to improve MOM use.

DATA AVAILABILITY

Data for this study are not publicly available due to data use agreements with participating hospitals. Elements of the data can be made accessible based on purpose with appropriate permissions based on request to the authors.

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AUTHOR CONTRIBUTIONS

TTN conceptualized and designed the study, and drafted the initial manuscript; CTN coordinated the study, drafted the initial manuscript, and critically reviewed the manuscript; MKQ developed statistical models for the study, conducted data analyses, and critically reviewed the manuscript; JW, LC, and RC contributed to the study design and critically reviewed the manuscript; AH and PA-J contributed to the study design and critically reviewed the manuscript; HCL contributed to study design, supervised the study team, and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

COMPETING INTERESTS

The authors declare no competing interests.

ADDITIONAL INFORMATION

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