BRIEF REPORT

Hospital Variation in Neonatal Abstinence Syndrome Incidence, Treatment Modalities, Resource Use, and Costs Across Pediatric Hospitals in the United States, 2013 to 2016

Carly E. Milliren, MPH,[a] Munish Gupta, MD,[b] Dionne A. Graham, PhD,[a] Patrice Melvin, MPH,[a] Maria Jorina, PhD,[a] Al Ozonoff, PhD[a]

ABSTRACT

BACKGROUND: The national incidence of neonatal abstinence syndrome (NAS) has increased with the opioid epidemic in the United States. The impact of pharmacologic treatment on hospital use is not well established. We examined the recent population of neonates with NAS admitted to pediatric hospitals, hospital variation in pharmacologic treatment, and the effect of treatment on resource use during neonatal hospitalization, including length of stay (LOS), readmission, and cost-of-living adjusted hospital costs.

METHODS: We included inpatients discharged between January 2013 and March 2016 from hospitals in the Pediatric Health Information System. We compared neonates with NAS to those without on demographic, socioeconomic, clinical characteristics and hospital resource use. We also compared neonates with NAS on these characteristics by pharmacologic treatment.

RESULTS: This analysis included 136 762 neonatal encounters from 23 hospitals. Of these, 2% had a diagnosis of NAS. Compared with other neonates, neonates with NAS had a longer LOS (18.7 vs 2.9 days; $P = .004$). Average costs per admission were 10 times higher for neonates with NAS ($37 584 vs $3536; $P = .003$). Of neonates with NAS, 70% were treated pharmacologically with wide variation in hospital rates of pharmacotherapy (range: 13%–90%). Pharmacologically-treated neonates with NAS experienced a longer LOS (22.0 vs 10.9 days; $P = .004$) than other neonates with NAS. Total costs for pharmacologically-treated neonates with NAS were over 2 times higher ($44 720 vs $20 708; $P = .002$) than neonates with NAS treated without pharmacotherapy.

CONCLUSIONS: Neonates with NAS, particularly those treated pharmacologically, have lengthier, more expensive hospital stays. Significant variation in pharmacologic treatment reflects opportunities for practice standardization and substantial reductions in resource use.

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Address correspondence to Carly E. Milliren, MPH, Center for Applied Pediatric Quality Analytics, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115. E-mail: carly.milliren@childrens.harvard.edu

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[a]Center for Applied Pediatric Quality Analytics, Boston Children's Hospital, Boston, Massachusetts; and [b]Department of Neonatology, Beth Israel Deaconess Medical Center, Boston, Massachusetts

Rates of opioid use among pregnant women are high, with estimated rates of 5.63 hospital births in 1000 being to mothers with diagnosed opiate dependence or use at the time of delivery[1] and with 14% of mothers having any exposure to prescription opioids during pregnancy.[2] Prenatal exposure to opioids may lead to opioid withdrawal in the newborn with central and autonomic nervous system dysfunction, also known as neonatal abstinence syndrome (NAS),[3,4] which often results in morbidity and lengthy hospital stays.[5] Rates of opioid use and abuse are correlated with the incidence of NAS,[6–8] and between 2000 and 2009, NAS incidence increased threefold, accompanied by rising costs for NAS discharges caused primarily by complications.[1]

Approaches to treating NAS involve pharmacologic therapy, management without pharmacotherapy, and, more recently, specific nonpharmacologic interventions, with the choice of treatment depending on symptom severity, specific opioid exposure, and institutional or provider variation.[9–14] Management without pharmacotherapy includes minimizing stimulation, frequent small volume feeds, and comforting.[15] Nonpharmacologic therapy may involve a number of interventions (including rooming-in, which promotes breastfeeding and maternal attachment) that have shown promising results in reducing the length of stay (LOS) and admission to the NICU, as well as in reducing the need for pharmacologic therapy.[12,16–18] Pharmacologic treatment agents include morphine, methadone, barbiturates, and benzodiazepines, which are often accompanied by admission to the NICU.[9,16] The standardization of pharmacologic treatment protocols has shown promising results with the potential for reductions in resource use and cost, in addition to reducing the duration of exposure to therapeutic opioids.[13] Wide variation in practice across geographic regions and institutions has been reported,[5,8,9,16] although studies have shown that implementation of standardized protocols for the evaluation and treatment of NAS can decrease the need for pharmacologic treatment and lower costs.[14,17,18]

With the lack of consensus and the need for care standardization in mind, we analyzed data from pediatric hospitals across the United States to describe the population of neonates with NAS, hospital variation in treatment modalities (pharmacologic treatment versus no pharmacologic treatment; type of pharmacologic agent), and the effect of pharmacologic treatment on resource use and neonatal hospitalization outcomes, including LOS, NICU admission, cost of care, readmissions, and mortality.

METHODS

Study Design

We used administrative data from the Pediatric Health Information System (PHIS) on inpatients in 48 tertiary care pediatric hospitals and compared neonates with NAS to other neonates admitted during the same time period. Among neonates with NAS, we compared those treated pharmacologically to those treated without pharmacotherapy. The study was determined not human subjects research by the Boston Children's Hospital Institutional Review Board.

Patient Selection and Inclusion and Exclusion Criteria

All inpatient encounters with patients discharged between January 1, 2013 and March 31, 2016, and patients aged <30 days at admission were included. On the basis of flags provided within PHIS, we excluded neonates with mechanical ventilation, extracorporeal membrane oxygenation, congenital or genetic abnormalities, or preterm or low birth weight (by diagnosis code) and patients who underwent any surgical procedure after admission. These exclusions were chosen to limit comorbidities and allow for comparisons within a relatively healthy and more homogenous group of neonates. Rates of preterm birth or low birth weight were similar between neonates with and without NAS (23% vs 22%), and we therefore opted to exclude these neonates. We determined NAS status by using *International Classification of Diseases* diagnosis codes (*Ninth Revision* code 779.5: drug withdrawal syndrome in infant of dependent mother; and *10th Revision* code P96.1: neonatal withdrawal symptoms from maternal use of drugs of addiction). Hospitals caring for fewer than 20 NAS discharges over the study period were excluded given that the findings in these might not be generalizable to the other PHIS hospitals. This approach is similar to other articles examining NAS by using PHIS.[9] We further stratified NAS by treatment group by using pharmacologic billing codes. Neonates who received opioids, opioid agonists, barbiturates, or benzodiazepines were classified as pharmacologically-treated; all others were classified as treated without pharmacologic agents.

Dependent Variables

Resource use during neonatal hospitalization included total LOS in days, admission to the NICU, NICU LOS in days, readmissions (30- and 90-day), and adjusted total cost. Cost data from the PHIS database are derived from charges that are converted to costs (direct and indirect) according to hospital-specific ratios of costs to charges; these are adjusted for geographic region by using the Centers for Medicare and Medicaid Services wage index. We also examined in-hospital mortality.

Statistical Analysis

We reported frequencies (percent) for categorical variables and mean (SD) for continuous variables. We compared neonates with NAS to those without NAS on demographic, socioeconomic, clinical characteristics, and use. For analyses, we used generalized estimating equations (GEEs) for continuous variables and Cochran-Mantel-Haenszel χ^2 tests for categorical variables to account for clustering by hospital. We made similar comparisons among neonates with NAS by treatment modality. All analyses were performed by using SAS version 9.4 (SAS Institute, Inc, Cary, NC). We considered $P < .05$ statistically significant.

RESULTS

Among 48 hospitals and 313 664 neonatal discharges in the study period, 176 902 discharges were excluded, including those from 24 hospitals caring for fewer than 20 NAS discharges and 1 hospital without cost data (Supplemental Fig 2). Among 136 762 eligible neonatal encounters

from 23 pediatric hospitals, 2% ($n = 3264$) had a diagnosis of NAS. Among 23 included hospitals, the number of neonatal encounters with NAS per hospital ranged from 21 to 516 (mean: 141.9; median: 61), and the percentage of neonatal encounters with NAS per hospital ranged from <1% to 18% (mean: 4%; median: 2%).

Demographic and clinical characteristics are presented in Table 1. Compared with neonates without NAS, neonates with NAS were more likely to be white, have public insurance, and reside in zip codes with lower median household income. Neonates with NAS had slightly lower birth weights, marginally higher Apgar scores at birth, longer LOSs, and more frequent admissions to the NICU with longer stays. Adjusted total costs per admission for neonates with NAS were over 10 times those of other neonates. Neonates with NAS had lower readmission rates than neonates without NAS at both 30 and 90 days. There were no significant differences in hospital mortality.

A total of 2294 (70%) of the neonates with NAS were treated pharmacologically, and this varied by hospital (mean: 65%; median: 71%; range: 13%–90%; $P < .001$; Fig 1). Table 2 shows the demographic and clinical characteristics of neonates with NAS by treatment group. Treatment groups differed by sex, race, and insurance, but not by Apgar score or birth weight. Pharmacologically-treated neonates with NAS experienced longer LOSs and more frequent NICU admissions. Pharmacotherapy was highly concordant with NICU admission, with 93% of pharmacologically-treated neonates with NAS admitted to the NICU, although variation by hospital was observed (mean: 82%; median: 100%; range: 0%–100%; $P < .001$; Fig 1). Adjusted total costs for pharmacologically-treated neonates were more than double those of other neonates with NAS. Readmissions and in-hospital mortality did not differ by pharmacologic treatment. The pharmacologic agents used most commonly were morphine (90%), phenobarbital (23%), and methadone (13%), and 20% of pharmacologically-treated neonates received both morphine and phenobarbital.

DISCUSSION

We observed differences between neonates with and without NAS and by NAS treatment

TABLE 1 Demographic and Clinical Characteristics and Hospital Resource Use of Neonates by NAS Status in 23 Tertiary Care Children's Hospitals in the United States

	All Neonates ($N = 136\,762$)	Neonates With NAS ($n = 3264$)	Neonates Without NAS ($n = 133\,498$)	P[a]
Female sex, *n* (%)	64 295 (47)	1520 (47)	62 775 (47)	.32
Race, *n* (%)				<.001
White, non-Hispanic	66 085 (48)	2367 (73)	63 718 (48)	
African American, non-Hispanic	19 326 (14)	162 (5)	19 164 (14)	
Hispanic, any race	20 432 (15)	220 (7)	20 212 (15)	
Other, non-Hispanic	25 694 (19)	291 (9)	25 403 (19)	
Unknown	5225 (4)	224 (7)	5001 (4)	
Insurance payor, *n* (%)				<.001
Commercial	61 861 (45)	269 (8)	61 592 (46)	
Public	66 363 (49)	2904 (89)	63 459 (48)	
Other	8219 (6)	90 (3)	8129 (6)	
Unknown	319 (<1)	1 (<1)	318 (<1)	
Median household income, $, mean (SD)	46 174 (19 913)	39 508 (12 637)	46 336 (20 030)	.04
Apgar score, mean (SD)				
1 min ($N = 80\,727$)	7.85 (1.82)	8.11 (1.30)	7.84 (1.83)	.03
5 min ($N = 80\,698$)	8.65 (1.34)	8.82 (0.71)	8.64 (1.35)	.03
Birth weight, g, mean (SD) ($N = 110\,984$)	3353 (528.8)	3084 (492.3)	3361 (527.8)	.002
LOS, d, mean (SD)	2.85 (4.2)	18.7 (14.9)	2.46 (2.46)	.004
NICU admission, *n* (%)	35 507 (26)	2831 (87)	32 676 (24)	<.001
NICU LOS, d, mean (SD)[b]	4.96 (7.1)	18.4 (15.3)	3.79 (4.1)	.008
Adjusted total cost, $, mean (SD)[c]	4349 (10 542)	37 584 (34 469)	3536 (7560)	.003
Readmissions, d, n (%)				
Within 30	26 277 (19)	300 (9)	25 977 (19)	<.001
Within 90	36 372 (27)	613 (19)	35 759 (27)	<.001
Hospital mortality, *n* (%)	65 (<1)	1 (<1)	64 (<1)	.46

[a] P value accounting for within-hospital clustering; Cochran-Mantel-Haenszel χ^2 test for categorical variables; GEEs for continuous variables.
[b] Of the neonates with NICU admission in each column.
[c] Derived from charges that are converted to costs according to hospital-specific ratios of costs to charges.

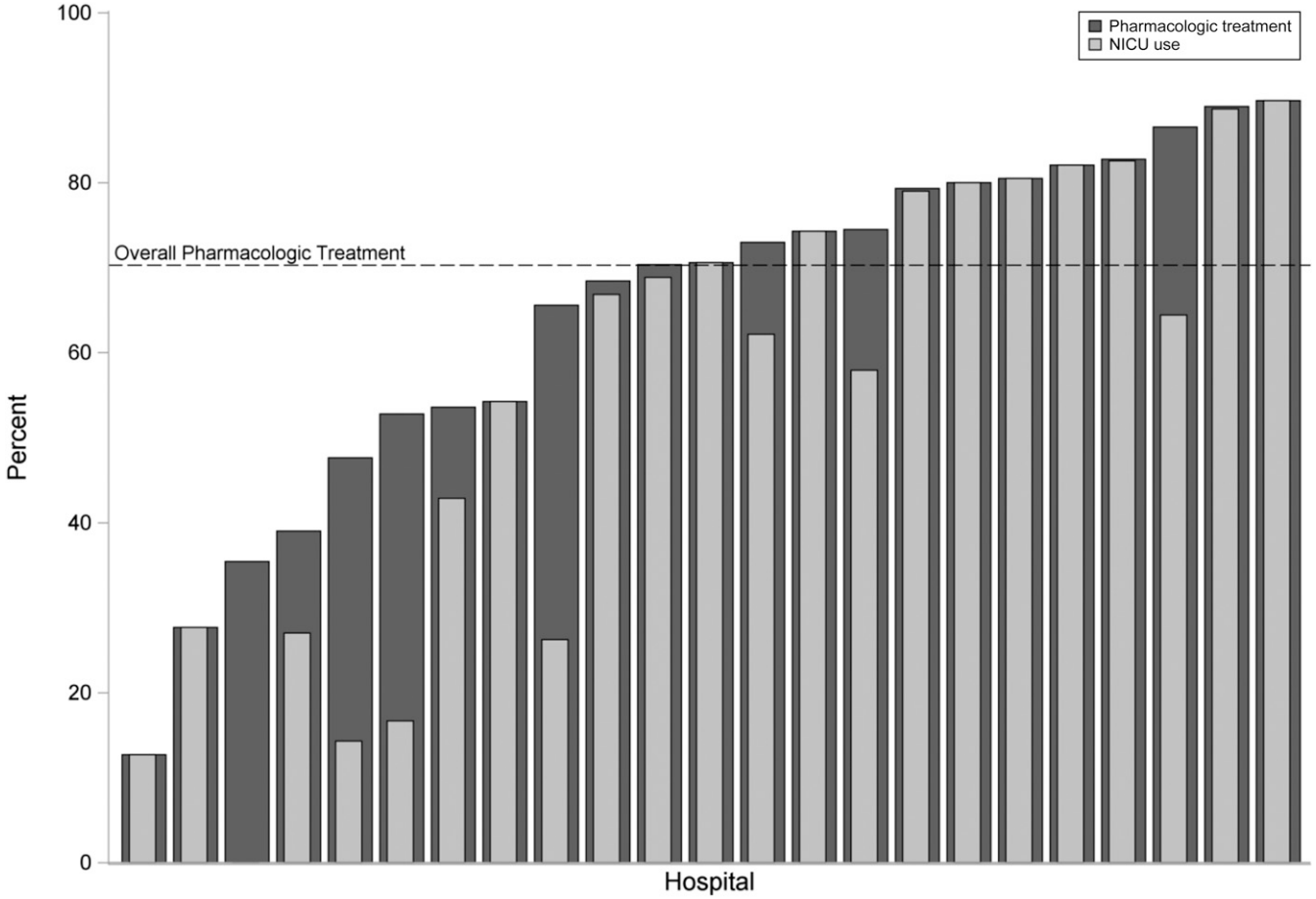

FIGURE 1 Interhospital variation in pharmacologic treatment of neonates with NAS and NICU admission among pharmacologically-treated neonates with NAS from 2013 to 2016 across 23 tertiary care children's hospitals in the United States. The dark gray bars represent hospital percentage of neonates with NAS treated pharmacologically, and the light gray bars represent the percentage of neonates with NAS treated pharmacologically and with NICU admission. Hospitals with dark gray and light gray bars of equal lengths had all pharmacologically-treated neonates with NAS admitted to the NICU. A horizontal dashed line indicates the overall percentage of pharmacologically-treated neonates with NAS across all hospitals.

modality at tertiary care pediatric hospitals in the United States during the 2013–2016 period. Compared with other neonates, those with NAS incurred higher costs of care and use of services. Neonates with NAS cost $34 000 more per admission and stayed a cumulative excess of 52 000 hospital bed days compared with other infants, representing a cumulative cost burden of $111 000 000. These results agree with other studies suggesting high costs of care for these infants and increased use of health care resources.[1,2,5,7] Our findings underscore the economic burden of the opioid epidemic via increased health care use and costs related to in-utero substance exposure. Of note, the vast majority of neonates with NAS receive public insurance (89%), resulting in increased hospital use and costs covered primarily by public payors.

Despite the recommendations of the American Academy of Pediatrics and others for standardization of NAS treatment,[14,15] our findings and others suggest persistent variation that is unlikely explained by case mix alone, particularly with regards to the use of pharmacologic therapy for NAS.[9,16,19] This variation may be amenable to standardization of practices, with the added benefit that a more conservative approach to first-line treatment, potentially without the use of pharmacotherapy, could result in savings in terms of both hospital use and cost.[17] Over two-thirds of neonates with NAS in these hospitals received pharmacotherapy. If overall rates of pharmacologic therapy were reduced by 25% to the first quartile rate of 53%, this would result in nearly 600 fewer infants receiving pharmacotherapy, resulting in a savings of ~6300 hospital bed days, 3700 NICU bed days, and $13 500 000 over the 3.25-year study period. A more substantial reduction of 50% would result in 660 fewer infants receiving pharmacotherapy and a potential savings of 7400 hospital bed days, 4300 NICU bed days, and nearly $16 000 000 over the study period.

Interestingly, a number of hospitals provided pharmacotherapy to a proportion of neonates outside of the NICU setting, with 1 hospital completely shifting

TABLE 2 Demographic and Clinical Characteristics and Hospital Resource Use of Neonates With NAS by Treatment Modality in 23 Tertiary Care Children's Hospitals in the United States ($N = 3264$)

	Pharmacologic Treatment ($n = 2294$)	No Pharmacologic Treatment ($n = 970$)	P[a]
Female sex, *n* (%)	1117 (49)	403 (42)	<.001
Race, *n* (%)			.002
White, non-Hispanic	1688 (74)	679 (70)	
African American, non-Hispanic	104 (5)	58 (6)	
Hispanic, any race	128 (6)	92 (9)	
Other, non-Hispanic	221 (10)	70 (7)	
Unknown	153 (7)	71 (7)	
Insurance payor, *n* (%)			.009
Commercial	173 (8)	96 (10)	
Public	2057 (90)	847 (87)	
Other	64 (3)	26 (3)	
Unknown	0 (0)	1 (<1)	
Median household income, $, mean (SD)	38 813 (12 289)	41 175 (13 292)	.71
Apgar score, mean (SD)			
1 min ($N = 2359$)	8.12 (1.30)	8.08 (1.30)	.55
5 min ($N = 2360$)	8.83 (0.70)	8.79 (0.74)	.46
Birth weight, grams ($N = 3065$)	3076.7 (470.6)	3103.2 (544.0)	.17
LOS, d	22.0 (14.8)	10.9 (12.1)	.004
NICU admission, *n* (%)	2133 (93)	698 (72)	<.001
NICU LOS, d, mean (SD)[b]	20.6 (15.3)	11.5 (13.1)	.013
Adjusted total cost, $, mean (SD)[c]	44 720 (34 539)	20 708 (27 791)	.002
Readmissions, d, *n* (%)			
Within 30	205 (9)	95 (10)	.51
Within 90	423 (18)	190 (20)	.44
Hospital mortality	1 (<1)	0 (0)	.18

[a] P value accounting for within-hospital clustering; Cochran-Mantel-Haenszel χ^2 test for categorical variables; GEEs for continuous variables.
[b] Of the neonates with NICU admission in each column.
[c] Derived from charges that are converted to costs according to hospital-specific ratios of costs to charges.

pharmacotherapy to outside the NICU ($n = 17$), providing another potential opportunity to reduce costs and use. The average cost for these 17 encounters was $38 687 (SD: $35 071), and the average LOS was 16.1 days (SD: 13.3). These indicate modest cost savings as well as small reductions in LOS relative to all pharmacologically-treated neonates with NAS, although conclusions are limited given the small sample. A shift toward providing pharmacotherapy outside of the NICU would save both NICU bed days as well as overall bed days and costs while fostering opportunities for rooming-in, breastfeeding, and other nonpharmacologic interventions that have demonstrated improved short-term outcomes.[4,11–14,16–18] Standardization of pharmacotherapy in terms of duration, location, and choice of treatment also offers an opportunity to reduce use along with duration of opioid exposure.[13,17]

This study is limited by the use of administrative data, which may include incomplete data on comorbidities and other clinical factors. By identifying neonates with NAS by diagnosis codes, we may have underestimated the incidence of NAS, particularly among those infants not requiring pharmacologic therapy whose admissions may not include a diagnosis code for NAS. However, other methods for identifying NAS are not well-established in the context of administrative data. Additionally, although nonpharmacologic interventions are becoming more common and show improved outcomes, this information is not coded, and we were therefore unable to determine the degree of use for these interventions.

Our analysis includes data from a subset of tertiary care pediatric hospitals within PHIS, which may reflect different NAS populations and care compared with delivery hospitals. Given the limitations of the data, we cannot generalize to NAS discharges at all delivery hospitals (ie, adult tertiary and community hospitals). The included hospitals all had birthing units or nurseries or were adjacent to or affiliated with a nearby birthing hospital. However, PHIS data allow for a more timely analysis of NAS care data and more accurate estimates of costs, and the size of the study population and its broad geographic distribution support the validity of this analysis.

CONCLUSIONS

Neonates with NAS use more hospital resources during lengthier, more expensive hospital stays and incur higher costs, without benefits in use or mortality during neonatal admission. Among neonates with NAS, there is significant variation in treatment choices across hospitals, reflecting opportunities for standardization of practices and improvement in care, particularly regarding the use of pharmacologic therapy, which is also a driver of increased usage and costs.

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