RESEARCH ARTICLE

The ACT NOW Clinical Practice Survey: Gaps in the Care of Infants With Neonatal Opioid Withdrawal Syndrome

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ABSTRACT

OBJECTIVES: The incidence of neonatal opioid withdrawal syndrome (NOWS) has increased fivefold over the last 10 years. Standardized NOWS care protocols have revealed many improved patient outcomes. Our objective for this study is to describe results of a clinical practice survey of NOWS management practices designed to inform future clinical studies in the diagnosis and management of NOWS.

METHODS: A cross-sectional survey was administered to medical unit directors at 32 Institutional Development Award States Pediatric Clinical Trial Network and 22 Neonatal Research Network sites in the fall of 2017. Results are presented as both the number and percentage of positive responses. Ninety-five percent Wilson confidence intervals (CIs) were generated around estimates, and χ^2 and Fisher's exact tests were used to compare the association between unit type and reporting of each protocol.

RESULTS: Sixty-two responses representing 54 medical centers were received. Most participating NICU and non-ICU sites reported protocols for NOWS management, including NOWS scoring (98% NICU; 86% non-ICU), pharmacologic treatment (92% NICU; 64% non-ICU), and nonpharmacologic care (79% NICU; 79% non-ICU). Standardized protocols for pharmacologic care and weaning were reported more frequently in the NICU (92% [95% CI: 80%–97%] and 94% [95% CI: 83%–98%], respectively) compared with non-ICU settings (64% [95% CI: 39%–84%] for both) ($P < .05$ for both comparisons). Most medical centers reported morphine as first-line therapy (82%; 95% CI: 69%–90%) and level 3 and level 4 NICUs as the location of pharmacologic treatment (83%; 95% CI: 71%–91%).

CONCLUSIONS: Observed variations in care between NICUs and non-ICUs revealed opportunities for targeted interventions in training and standardized care plans in non-ICU sites.

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The incidence of neonatal opioid withdrawal syndrome (NOWS) has increased fivefold over the last decade because of increased opioid use in women of childbearing age.[1–5] From 1999 to 2014, the prevalence of opioid use disorder among delivery hospitalizations in the United States increased from 1.5 to 6.5 per 1000 events.[6] The Centers for Disease Control and Prevention recommends that hospitals have protocols to identify and manage infants with NOWS as a public health–level intervention.[7] Inpatient NOWS care protocols have revealed benefits in improving outcomes, such as shorter time to diagnosis, reduced therapeutic opioid exposure, and decreased length of stay, for infants with NOWS.[8–16] The number of hospital units implementing standardized care protocols has been examined in surveys during the last 10 years.[17–19] Patrick et al[17] reported an increase in the number of centers with a protocol for NOWS evaluation and management from 76% to 95% between 2013 and 2014 in NICUs participating in the Vermont Oxford Network. A survey of NICUs by Mehta et al[18] similarly revealed that 72% of NICUs had protocols for NOWS management. Bogen et al[19] performed a survey of US academic and community hospitals in the Academic Pediatric Association's Better Outcomes through Research for Newborns (BORN) Network in 2015. At that time, 88% of BORN Network sites had NOWS management protocols for addressing medical management, nursing care, pharmacologic treatment, and supportive care.[19] However, these estimates have varied, potentially because of differences in hospitals surveys but also likely because of changes over time, with the most recent estimates from 2015. As the scope of the opioid crisis increases, so also do the number and types of health care providers involved in treating the symptoms of neonatal opioid withdrawal.[20,21] A more recent reevaluation of the clinical practices guiding the care of infants with NOWS at the institutional level may identify new areas for engagement and intervention to improve the quality of care. In this study, we describe more recent data from a clinical practice survey of NOWS management practices in 54 Institutional Development Award States Pediatric Clinical Trial Network (ISPCTN) and National Institutes of Health *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN) sites designed to inform future clinical trials in the diagnosis and management of NOWS.

METHODS

The ISPCTN and NRN convened a cross-disciplinary team in September 2017 to address the growing neonatal opioid crisis.[22,23] This collaboration between the ISPCTN and NRN resulted in the formation of the Advancing Clinical Trials in Neonatal Opioid Withdrawal (ACT NOW) initiative, a research alliance designed to evaluate diagnostic and treatment options for neonates experiencing withdrawal from prenatal opioid exposure. The ACT NOW collaborative is implementing a multifaceted clinical research program designed to fill these gaps, building on clinical practice surveys and observational data collection to direct future clinical trials across the United States in both urban and rural sites.

The ACT NOW Clinical Practice Survey was a cross-sectional, clinical unit–level exploratory survey conducted October 2017 to November 2017. The purpose of the survey was to identify current practice in the ISPCTN and NRN sites that would potentially participate in future ACT NOW clinical trials. The survey content was adapted in part from the 2015 Bogen et al[19] survey of NOWS care and is detailed in Supplemental Table 4. The ISPCTN Data Coordinating and Operations Center (DCOC) sent the survey to principal investigators of 17 ISPCTN and 15 NRN sites with instructions for the survey to be completed by the medical director of any unit caring for infants with NOWS at their associated clinical sites. The ISPCTN DCOC used Research Electronic Data Capture to build the data collection instrument.[24] ISPCTN investigators received a unique link to the ACT NOW Clinical Practice Survey that allowed for individual tracking of receipt and response. At the request of the NRN coordinating center, the NRN investigators received a generic link that did not allow for individual tracking of receipt and response among NRN investigators. For a complete list of participating institutions, please see the Acknowledgments.

Results are presented as a both a number and percentage of "yes" responses. The respondent indicated which protocols and/or care measures were in place in their unit for the diagnosis and management of NOWS, including screening protocols, scoring systems used to aid in clinical decision-making, and types and weaning of pharmacologic treatment. They additionally indicated which nonpharmacologic care measures were used, the location of pharmacologic care, and first- and second-line pharmacologic treatments used when pharmacologic treatment was initiated. Respondents self-identified their unit as "NICU/PICU," "delivery unit," or "other." The latter 2 categories were collapsed, and practice data are hereafter displayed as "NICU" and "non-ICU." Respondents were able to select >1 option in any category and, in some instances, had the option to provide more detail using free text. Ninety-five percent Wilson confidence intervals (CIs) were generated around estimates, and χ^2 and Fisher's exact tests were used to compare the association between unit type (NICU versus non-ICU) and reporting of each standardized protocol guiding NOWS care in each domain. The statistical software R version 3.5.3 (R Foundation for Statistical Computing, Vienna, Austria) was used for computing statistics and performing tests. No adjustments were made for multiple comparisons.

RESULTS

Sixty-two unit respondents, representing 54 medical centers across 28 states, responded to the ACT NOW Clinical Practice Survey. Thirty-eight ISPCTN unit respondents and 24 NRN units submitted responses, representing 32 ISPCTN medical centers and 22 NRN medical centers. All ISPCTN and NRN investigators responded to the survey for at least 1 unit in their catchment area (100% response rate). Five ISPCTN sites and 2 NRN sites submitted responses from >1 unit within a single medical center. Three centers (1 in New Mexico and 2 in Rhode Island) participate in both the ISPCTN and the NRN; all 3 centers are categorized with

the ISPCTN in this survey on the basis of the initial survey invitation. Respondents self-identified as NICU ($n = 48$) and as delivery unit or other (combined as non-ICU; $n = 14$), which could include mother-infant units, inpatient general pediatric wards, or other units that provide care for infants with NOWS.

Standardized Care Protocols for NOWS by Inpatient Setting

Most of the participating NICU and non-ICU sites reported standard care protocols for many NOWS management domains (Table 1). NICU representatives reported protocols for 79% to 98% of domains queried; by inspection, non-ICU units appeared slightly less likely to report protocols for NOWS care in the queried domains (64%–86%). Standardized protocols for pharmacologic care and weaning were reported more frequently in the NICU setting (92% [95% CI: 80%–97%] and 94% [95% CI: 83%–98%], respectively) compared with in the non-ICU settings (64% [95% CI: 39%–84%] for both) ($P < .05$ for both comparisons). Tools for monitoring infant withdrawal symptoms are characterized in Table 2. Seventy-three percent (95% CI: 59%–83%) of respondents used the modified Finnegan scoring system, 4% (95% CI: 1%–14%) used the Neonatal Withdrawal Inventory (a Finnegan-related scoring system), and the remainder used either the original Finnegan or the Neonatal Abstinence Scoring System (another Finnegan-related system).[25–27]

Nonpharmacologic Care

Seventy-nine percent of both NICU and non-ICU sites reported having policies that support implementation of nonpharmacologic therapies for stabilization and treatment of infants with in utero opioid exposure (Table 1). Respondents identified all components of nonpharmacologic care used at their site. A summary of the reported nonpharmacologic care practices is presented in Table 3. Respondents from NICUs were significantly more likely to report using "cuddlers" (75% of NICUs [95% CI: 61%–85%] vs 43% of non-ICUs [95% CI: 21%–67%]; $P < .05$) and breastfeeding (98% [95% CI: 89%–100%] vs 71% [45% to 88%]; $P < .05$) as nonpharmacologic treatment of NOWS symptoms than respondents from non-ICUs. Swaddling (98% of NICUs and 86% of non-ICUs), positioning and comfort measures (88% of NICUs and 79% of non-ICUs), avoiding overstimulation (94% of NICUs and 86% of non-ICUs), and rooming-in (60% of NICUs and 64% of non-ICUs) were the most frequently reported nonpharmacologic care measures. Infant massage (21% of NICUs and 14% of non-ICUs) and high-calorie nutrition (40% of NICUs and 43% of non-ICUs) were reported less often. Seven units selected "other" and used free text to describe nonpharmacologic care, such as elemental formula if no breast milk was available, ear muffs, dark room, single room, skin-to-skin contact, environmental control, high-calorie nutrition only if significant weight loss was present, and nonpharmacologic therapies as directed by other providers (eg, physical or occupational therapy and child-life consultation).

TABLE 1 Number and Percentage of Units Reporting a Standardized Protocol in Each Domain

Does Your Unit Have a Standardized Protocol Specific to the Following Domains?	NICU		Non-ICU	
	No. Units ($n = 48$)	Units, % (95% CI)	No. Units ($n = 14$)	Units, % (95% CI)
Screening for maternal substances	38	79 (66–88)	9	64 (39–84)
Nonpharmacologic treatment	38	79 (66–88)	11	79 (52–92)
NOWS scoring	47	98 (89–100)	12	86 (60–96)
Breastfeeding for infants with in utero opioid exposure	43	90 (78–95)	11	79 (52–92)
Duration of observation for infants with in utero opioid exposure	41	85 (73–93)	12	86 (60–96)
Pharmacologic treatment of NOWS[a]	44	92 (80–97)	9	64 (39–84)
Weaning of pharmacologic therapy[a]	45	94 (83–98)	9	64 (39–84)

There were 62 responding units in total. Five sites selected "other" and reported standardized protocols such as mandated reporting, family involvement in assessments, NOWS assessments on the infant's schedule, parent information, prenatal consults, discharge planning, and a program to influence staff attitudes.

[a] $P < .05$; Fisher's exact test was used to compare the percentage of NICUs that responded affirmatively to each question with the percentage of non-ICUs that responded affirmatively to each question.

Pharmacologic Treatment

Respondents could select multiple locations in which pharmacologic treatment of NOWS occurred in the medical center. Overall, medical centers reported that pharmacologic care for infant exposed to opioids occurred in level 3 and level 4 NICUs (83%; 95% CI: 71%–91%) more frequently than they reported pharmacologic care occurring in other locations. Specifically, 48% (95% CI: 35%–61%) of medical centers reported pharmacologic treatment in level 2 intensive care nurseries, 15% reported pharmacologic treatment while rooming-in (95% CI: 8%–27%), 13% reported pharmacologic treatment on the pediatric ward (95% CI: 6%–24%), 7% reported pharmacologic treatment in the newborn nursery (95% CI: 3%–18%), and 7% reported pharmacologic treatment in other special NOWS care locations within the hospital (95% CI: 3%–18%). Two medical centers indicated "other" as a location of pharmacologic treatment and commented that care was provided in a dedicated NOWS unit within the NICU or in a rooming-in environment unless there were other medical indications for intensive care or no bed space available.

Morphine was the most commonly reported first-line therapy (82% of all reporting medical centers [95% CI: 69%–90%]; 40 NICUs and 9 non-ICUs); however, some centers use >1 drug as first-line therapy. Methadone (22% of all reporting medical centers [95% CI: 13%–35%]; 11 NICUs and 1 non-ICU), buprenorphine (4% of all reporting medical centers [95% CI: 1%–13%]; 2 NICUs), and clonidine (2% of all reporting medical centers [95% CI: 0%–10%]; 1 NICU) were also reported. The most commonly reported second-line pharmacologic therapies were clonidine

TABLE 2 Number and Percentage of Units Using Original Finnegan Scoring, Modified Finnegan Scoring, the Neonatal Withdrawal Inventory, the Neonatal Abstinence Scoring System, or Other Scoring Scales to Aid in Decision-making Regarding Management of Infants With NOWS

What Scoring System Does Your Unit Use to Aid in Management of Infants With In Utero Opiate Exposure?	NICU		Non-ICU	
	No. Units (n = 48)	Units, % (95% CI)	No. Units (n = 14)	Units, % (95% CI)
Finnegan scoring, original	8	17 (9–30)	2	14 (4–40)
Finnegan scoring, modified	35	73 (59–83)	10	71 (45–88)
NWI	2	4 (1–14)	0	0 (0–22)[a]
NASS	5	10 (5–22)	1	7 (1–31)

Adapted from Finnegan LP. Neonatal abstinence syndrome: assessment and pharmacotherapy. In: Nelson NM, ed. *Current Therapy in Neonatal-Perinatal Medicine*. 2nd ed. Hamilton, Canada: BC Decker; 1990; Zahorodny W, Rom C, Whitney W, et al. The neonatal withdrawal inventory: a simplified score of newborn withdrawal. *J Dev Behav Pediatr*. 1998;19(2):89–93; and Finnegan LP, Connaughton JF Jr, Kron RE, Emich JP. Neonatal abstinence syndrome: assessment and management. *Addict Dis*. 1975;2(1–2):141–158. There were 62 responding units in total. Units may have reported the use of >1 scoring system. Two non-ICUs reported other scoring scales to aid in decision-making; 1 of these units reported using the Eat, Sleep, Console assessment method. No statistical differences were observed between the percentage of NICUs that responded affirmatively to each question and the percentage of non-ICUs that responded affirmatively to each question. NASS, Neonatal Abstinence Scoring System; NWI, Neonatal Withdrawal Inventory.

[a] Modified Wilson CI.

(59% of all reporting medical centers [95% CI: 46%–71%]; 28 NICUs and 4 non-ICUs) and phenobarbital (57% of all reporting medical centers [95% CI: 44%–70%]; 26 NICUs and 5 non-ICUs), and, as with first-line therapy, some centers reported using >1 drug for second-line therapy. Methadone (11% of all reporting medical centers [95% CI: 5%–22%]; 6 NICUs) and morphine (6% of all reporting medical centers [95% CI: 2%–15%]; 3 NICUs) were also reported by a small number of sites as second-line therapy. Other second-line therapies included buprenorphine (2 NICUs), chlorpromazine (1 non-ICU), and lorazepam or other benzodiazepines (1 NICU).

DISCUSSION

The opioid crisis has affected many infants across the United States, and critical gaps remain in our knowledge of the best practices for diagnosis of NOWS and care of infants with NOWS. The strength of the ACT NOW collaborative is to join the neonatal expertise of the NRN with the ISPCTN's mission of engaging rural and underserved areas in clinical trials. This is of particular importance given the disproportionate increase of NOWS in rural compared with urban settings.[28] The ACT NOW Clinical Practice Survey sites reported protocols for many elements of NOWS care, including NOWS scoring (98% of NICUs and 86% of non-ICUs), pharmacologic treatment (92% of NICU and 64% of non-ICUs), and nonpharmacologic care (79% of NICUs and 79% non-ICUs). This appears to represent an increase in several domains compared with the results of the BORN survey in 2015, in which 93% of respondents had a NOWS scoring protocol and 72% had protocols for pharmacologic care.[19] Similarly, we observed a higher frequency of NOWS scoring protocols compared with that in a 2014 study in the Vermont Oxford Network, in which 77% of units reported NOWS scoring standardization.[17] A majority of sites in our survey used the Finnegan scoring system or a modification of it, similar to findings of previous studies.[17–20]

As the incidence of NOWS has increased so has the use of NICUs to care for these newborns, often separating the mother-infant dyad.[29] In this survey, pharmacologic treatment occurred most often in the intensive care setting, with the majority occurring in level 2 to level 4 NICUs, similar to that reported in other NOWS studies.[3,19,24]

TABLE 3 Types of Nonpharmacologic Therapy Provided

Which Nonpharmacologic Therapies Does Your Unit Use for Stabilization and Treatment of Infants With In Utero Opioid Exposure?	NICU		Non-ICU	
	No. Units (n = 48)	Units, % (95% CI)	No. Units (n = 14)	Units, % (95% CI)
Rooming-in with mother	29	60 (46–73)	9	64 (39–84)
Breastfeeding[a]	47	98 (89–100)	10	71 (45–88)
Swaddling	47	98 (89–100)	12	86 (60–96)
Cuddlers[b]	36	75 (61–85)	6	43 (21–67)
Infant massage	10	21 (12–34)	2	14 (4–40)
Positioning and comfort measures	42	88 (75–94)	11	79 (52–92)
Avoiding overstimulation	45	94 (83–98)	12	86 (60–96)
High-calorie nutrition, hypercaloric formula	19	40 (27–54)	6	43 (21–67)

Units may have reported >1 type of nonpharmacologic care. There were 62 responding units in total. Seven sites indicated "other" and entered free text to describe other types of nonpharmacologic care, including elemental formula if no breast milk was available, ear muffs, dark rooms, single rooms, skin-to-skin contact, environmental control, high-calorie nutrition only if there is significant weight loss, and nonpharmacologic therapy as directed by physical and/or occupational therapy or child-life consultations.

[a] $P < .05$; Fisher's exact test.

[b] $P < .05$; the χ^2 test was used for comparison between the percentage of NICUs that responded affirmatively to each question and the percentage of non-ICUs that responded affirmatively to each question.

Buprenorphine, which has been associated with shortened length of stay in some studies, was not widely reported in this sample.[5]

The use of nonpharmacologic interventions (in particular, keeping the mother with her infant) has proven to ameliorate NOWS symptoms. Higher rates of nonpharmacologic care protocols were reported in this study compared with the BORN survey. We observed that 79% of units reported protocols for nonpharmacologic care, compared with 58% of units in the BORN survey.[19] More than 60% of the ACT NOW Clinical Practice Survey units reported using nonpharmacologic practices such as rooming-in, breastfeeding, positioning and comforting, swaddling, and avoiding overstimulation. The apparent increase in nonpharmacologic care practices reported may be attributable to the increasing evidence of their success, with recent studies revealing the benefits of parental presence and rooming-in on postnatal opioid exposure, hospital length of stay, breastfeeding rates, discharge from the hospital with family, and/or hospital cost.[12,30] However, only 15% of centers in the ACT NOW Clinical Practice Survey reported rooming-in during pharmacologic treatment. Overall, the non-ICUs in our survey reported fewer protocols for pharmacologic care and weaning compared with NICUs. This likely reflects the finding that pharmacologic care in general occurs more often in the NICU setting and that care in this setting is often more protocolized.[3,31,32] Non-ICU responders were also less likely to report the use of certain nonpharmacologic care measures, such as cuddlers and breastfeeding, which was somewhat unexpected and may be affected by the small number of non-ICU responders included in this sample.

There are several limitations to this survey. First, because this was intended as a clinical practice assessment for a specific clinical trial platform, only ISPCTN and NRN sites were surveyed, and the instrument was not validated, which limits the generalizability of our results. In particular, the oversampling of NICUs at academic medical centers may contribute to a higher proportion of sites with protocolized care and management in the ICU setting. There may be additional units at the participating institutions that provide care for infants with NOWS but did not respond to this survey. In addition, the brevity of the survey offered little opportunity for details regarding the implementation of protocols to guide NOWS care at the participating sites. Variability in respondents' perceptions and reporting of NOWS care in a particular unit may have influenced the results of the survey. In addition, respondents' reports may not account for practitioner variability within a given hospital or site. A follow-up study, ACT NOW Current Experience, is being used to obtain infant-level data on individual- and site-level variations in NOWS care within the ISPCTN and NRN collaborative to address several of these limitations.

CONCLUSIONS

The care of infants exposed to opioids is developing in response to the opioid crisis. These broad changes reflect a response by medical care providers to an evolving children's health problem. Observed variations in care between NICUs and non-ICUs reveal opportunities for targeted interventions in training and standardized care plans in non-ICU sites, given the benefits associated with standardization. However, many gaps remain in our understanding of which elements of standardized care may be most beneficial, of which variations might be beneficial for certain infants, and of the long-term effects of pharmacologic and nonpharmacologic treatment options for NOWS symptoms. This survey reveals the importance of multisite clinical studies, particularly those that engage participants in the highest-risk areas, to generate data that may be generalizable to a wide range of practices. Future ACT NOW studies can be used to assess the prevalence of NOWS in different regions of the country, describe individual- and site-level variations in care for infants with NOWS, and help develop clinical trials that impact the policies and practices that guide NOWS diagnosis and treatment in the United States.

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