

Feeding Infants with Neonatal Abstinence Syndrome: Finding the Sweet Spot

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ABSTRACT

Purpose: The purpose of this study is to learn how caregivers who are expert in feeding infants with neonatal abstinence syndrome (NAS) successfully feed these infants during withdrawal.

Design/Sample: Focus group methodology was used to gather information from self-identified experts from three large regional NICUs. Twelve NICU nurses and speech therapists participated in open-ended, recorded discussions. Detailed flip chart notes were taken, reviewed, and verified by the participants before the group ended.

Results: Four major themes emerged verified by the participants: (1) optimal medication management, (2) follow the baby's cues, (3) calm and comfortable, and (4) nurture the relationship. Participants reported using both common and creative techniques. Keeping the infant calm was crucial to being successful, as well as maintaining good control of withdrawal signs. Feeding the infant facing away from them to avoid eye contact was used, as well as vertical rocking, continuous butt patting, bundling, "shhing" sound, and a novel feeding position.

Keywords: abstinence; withdrawal; feeding; neonatal abstinence syndrome (NAS)

NEARLY 10,000 INFANTS ARE BORN annually to mothers addicted to opioids, a rate that tripled between 2000 and 2009. The Florida Department of Health reports that the number of infants discharged with this diagnosis has increased tenfold since 1995.¹ Nationally, the incidence of neonatal abstinence syndrome (NAS) increased from 1.20 to 3.39 per 1,000 hospital births per year.² In a 2014 study conducted by the Centers for Disease Control and Prevention (CDC) in Florida, 97.1 percent of infants with NAS were admitted to a NICU, where they reported a mean length of stay of 26.1 days.³ Nationally, hospital charges were

estimated to be \$720 million in 2009, with 77.6 percent charged to state Medicaid programs.² Infants with this disorder characteristically demonstrate signs of withdrawal within 1–6 days of birth, depending upon the type of drug exposure.⁴ Signs of withdrawal reflect irritability of the central nervous and gastrointestinal systems, as well as changes in metabolic, vasomotor, and respiratory systems.

Signs of NAS occur in newborns within days of birth after exposure to opiates during gestation. These infants are innocent victims who suffer from inconsolable crying, poor sleeping, and resistance to feeding,⁵ which present significant challenges to attachment

and successful parenting.⁶ Several studies^{5,7,8} confirm the challenges caregivers face when feeding infants with NAS. The sucking reflex has been reported to be uncoordinated with swallowing and breathing,⁷ whereas others have reported infants spending more time crying than feeding during a scheduled feeding.⁵ There is, however, little empiric evidence about how to manage these infants' nursing care.⁹ Management in the NICU typically includes both pharmacologic and nonpharmacologic treatment.¹⁰ In a recent study, mother-infant dyads were observed in regard to the behaviors that occur in infants with NAS during feeding. Half of the feeding time was spent fussing or crying, and about 25 percent of the infants were unable to complete the feeding.⁵ Other investigators have confirmed that feeding patterns and/or the mechanics of sucking can be different in infants with NAS.^{7,8}

Feeding is perhaps the first and most important parenting task that mothers of infants with NAS are expected to master shortly after birth. Feeding success is an important indicator of a mother's ability to successfully parent her child,¹¹ and the mother's level of success in this task contributes significantly in the discharge decisions for the infant. The lack of empiric evidence about how to be successful in the important task of feeding is the problem we sought to investigate. Although these behaviors present significant challenges to successful parenting, there is little evidence basis as to the skill set or "tips" to managing feedings with infants with NAS.

Because infants with NAS do not demonstrate clear feeding cues,⁵ we believe that caregivers who are experts in feeding these babies can provide an important source of information about how to keep an infant focused on the task of feeding. We hypothesized that experienced nurses and therapists employ interventions based on subtle infant cues that help the newborn feed successfully. We were interested in identifying that characteristic skill set, so we could develop an intervention for mothers of these infants to be more successful in this important and challenging parenting skill. Using focus groups, we sought to identify that characteristic skill set. The specific aim of this study was to identify behaviors that optimize feeding outcomes in infants with NAS using focus groups with expert caregivers.

METHODS

Institutional Review Board Approval and Written Informed Consent

University institutional review IRB approval was obtained before recruitment of participants for the focus groups. An IRB-approved flyer was posted in the NICU lounges to recruit NICU nurses, occupational therapists, and speech therapists who consider themselves to be expert in feeding infants with NAS. Nurses and therapists interested in participating were asked to contact one of the investigators, who explained the study, answered all questions, and invited them to participate in the focus groups. Written consent was obtained from participants before the focus group.

Settings

Data were collected from participants working in three regional hospitals with Level III NICUs. Each NICU had 80–100 beds and a large population of infants with NAS (greater than 100 annual discharges).

Sample

NICU nurses, occupational therapists, and speech therapists who self-identified as experienced in feeding infants with NAS were invited to participate. We utilized a mostly homogeneous group of participants, as one's professional role had to include primarily caring for infants with NAS in order to effectively answer the questions posed. A total of 12 participants (10 RNs and two speech therapists) were enrolled across the three hospitals. We enrolled four participants from each hospital ($n = 12$). All were female, and most (11) worked full time. Their ages ranged from 31 to 65 years (mean = 47.8, $SD = 12$), years working in the NICU ranged from 2 to 43 (mean = 17.3, $SD = 12.9$), and years in their profession ranged from 2 to 43 (mean 18.2, $SD = 13$).

Procedures

Focus group methodology was used to gather information from participants, in which a group discussion was arranged around specific sets of questions/topics posed by a facilitator.¹² Focus groups lasted 40–60 minutes, and were concluded when there was no new information forthcoming. The recorder took extensive notes on a flip chart, which were reviewed and verified by the participants before leaving the focus group. The final (fourth) focus group yielded information that reflected responses from the previous groups, providing evidence of data saturation.¹³

Two investigators conducted the focus groups: one led the questioning, whereas the other wrote down and summarized participants' statements. The sessions were digitally recorded and later transcribed using a transcription service. Participants were assigned a number for transcription purposes (i.e., "Speaker 1," "Speaker 2") to maintain confidentiality. Participants were given a \$50 gift card at the end of the focus group.

Demographics were collected to describe the sample, and a series of questions and probes were presented to the focus groups. The questions included: (1) Please tell me about one of the most challenging infants with NAS that you fed. (2) Why do you think you were more successful than others in completing the feeding? (3) When do you know that you *won't* be successful feeding a baby with NAS? (4) Do you do anything to "turn that around"? (5) How would you describe what you do to get a fussing baby who has NAS to feed? (6) Do you have any additional tips you can share about how mothers can be more successful in feeding their infant with NAS?

The principal investigator verified the transcripts against the digital recording. Themes were derived directly and inductively from the raw data using grounded theory

TABLE 1 ■ Themes and Subthemes with Definitions

Theme	Subthemes	Definition
Optimal medication management		A baseline requirement for successful feeding is having the signs of neonatal abstinence syndrome well controlled with opioid replacement therapy.
Follow the baby's cues and be flexible with techniques	Follow the baby's cues	Pay attention to the baby's cues to guide your interventions.
	Flexibility with techniques	Be responsive to infant individuality; try different techniques until one works.
Calm and comfortable	Calm the caregiver	The caregiver needs to be calm and comfortable during feeding so that the baby does not sense anxiety.
	A calm and comfortable baby before and during feeding	Try different strategies to keep the baby calm, such as "C" positioning, patting, massage, decreased eye contact, swaddling, burping, pacifier, decreased stimulation, and dark environment.
Nurture the relationship	Encourage caregivers to be there	Emphasize how important mothers are to help the baby recover.
	Provide continuity in caregiving	Consistency is needed to learn their baby's unique cues.
	Build parents' confidence	Help mothers to feel empowered by being with their baby.
	Develop trust and avoid judgmental attitudes	Work with the mother as you would with any other parent.

techniques.^{14,15} The research team first read the transcripts and field notes to identify emerging themes. Codes were applied to the data, which consisted of a word or short phrase that symbolically assigned a summative or salient attribute to a participant's response.¹⁶ Codes were then organized and grouped into meaningful categories of similarly coded data that shared some characteristic. Patterns were identified and grouped into emerging themes, defined as phrases that provide meaningful representation of the explicit data that was coded and categorized.¹⁶ Informative quotes were used to illustrate main themes. The investigators then reviewed the themes and related quotations to validate the identified themes or to recommend alternatives.

RESULTS

The following is a summary of the combined findings from the focus groups. The data yielded four overarching themes related to success with feeding infants with NAS (Table 1).

Theme 1: Optimal Medication Management

A theme emerged that was not specifically tied to strategies a nurse or other feeding caregiver could implement, but was still an important component to successful feeding. The need for infants with NAS to have appropriate pharmaceutical management of their withdrawal symptoms was described as one of the most significant needs. This was often just referred to as "proper management" and was viewed as a baseline requirement for feeding success, as shared in this example: "She really wasn't managed the way she needed to be yet because they were still trying to figure out what was going on with her. I felt pretty confident that once we got her managed from a pharmaceutical standpoint to where she needed to be and—and got her to an organized calm level that she would be okay" (P1, FG3).

Feedings could also be unsuccessful when pharmaceutical management had not started ("that usually happens in the beginning, sometimes before they have medication on board" [P1, FG4]) or was not optimal ("it's just not working and you've tried, and that's when then I'll go to the physician too . . . to rethink plan of care . . . or a different medication" [P3, FG3]). Sucking behaviors were most disorganized before optimal medication management, and described as frantic ("It's [sucking] disorganized and frantic (when) not well managed pharmacologically" [P4, FG4]).

Theme 2: Follow the Baby's Cues and Be Flexible with Techniques

Across all groups, participants expressed the need to be responsive to each individual baby and use cues and problem solving to determine the most effective approach.

Subtheme: Follow the Baby's Cues. Many nurses shared that learning and following each individual baby's cues was critical to successful feedings, particularly when many challenges were present. One participant stated this as "follow the baby's cues a little bit. The baby [is] not ready as soon as you hold [him], you have to follow their cues" (P4, FG4). This was also expressed as letting the infant be in control, "You let [the baby] control the situation as much as possible; find that window where you feel like they're ready" (P2, FG2). Nurses also discussed the importance for mothers to be attuned to each individual baby's cues to make feeding more successful. "Once you know their cues, once you have taken care of them for a few times, it's easier" (P3, FG1).

Subtheme: Flexibility with Techniques (Respond to Individuality). All groups emphasized the need to be open to trying different techniques that may be specific to each

baby. A sense for the infant's individual style and needs related to feeding was shared. Even well-established techniques were not "one size fits all." Although many specific techniques were shared across groups, the need to be flexible with which techniques to use based on the individual baby was a consistent factor.

One participant, when discussing burping, described it this way: "It just depends on the baby, but sometimes when they have that motion they over exaggerated rooting and sucking where they do get more air; some of those do need more frequent burping, I find. But then other ones I guess you just read the baby. Other ones you burp and it causes a total disruption, so I just decide if you're not a vomiter you don't get to burp until you're done because then you have to start all over. I can't explain how it is that I know that. I just know after I know the baby a few times" (P1, FG3).

Theme 3: Calm and Comfortable

Creating a calm and relaxed environment, and helping the feeding caregiver and the infant to get and remain calm, was found to be necessary in light of the consistent occurrence in which infants are disorganized and agitated, and thus unable to coordinate their movements smoothly. Participants described this problem as "they're out of control and they can't bring anything together . . . they are very hungry, but they just can't bring themselves midline" (P3, FG1) and "the babies are just frantic or just so agitated, so upset" (P2, FG2). To remedy this, the following specific subthemes were used.

Subtheme: Calm the Caregiver. Participants expressed the need for the caregiver feeding the baby to also remain calm because "every baby can sense what the person that's holding them or talking to them, how they feel" (P3, FG3). Participants described the anxiety mothers often felt and the need to help and teach them to relax: "Once I get mom and baby sitting together and I'm about to leave them alone to have some time just to work as a dyad, I always do say . . . 'Are you comfortable? Is there anything I can do to help you be more comfortable?' And that will help them relax" (P1, FG3).

Subtheme: A Calm and Comfortable Baby Before and During Feeding. All participants expressed the need to do whatever strategies are needed to calm the baby before attempting to begin a feeding: "Just try to calm them first" (P1, FG4). Numerous strategies aimed at making the baby comfortable were discussed:

1. Positioning. Using a variety of positions to hold the baby that may differ from those used for typical babies, such as the C positioning or vertical rocking, was mentioned across groups. Nurses at one NICU used a form of facilitated tucking they call the C position: The nurse lays the baby on her leg, with the spine slightly curved, knees bent, and arms flexed not only to relax an irritable baby, but also to feed one. ("I usually start sideline but with my leg up so sideline head up, because when I relax my leg

and get them on my nice, warm relaxed leg, usually they will relax" [P1, FG3]. "We teach them the up and down [rocking]" [P2, FG3]. "You rock them this way, like this" [positioned vertically on the chest] [P3, FG1]. "Not just that bouncing, but just slow, up and down" [P3, FG2].)

2. Calm their body and reduce rigidity. "Before we [put] a bottle in their mouth, we might hold them tight and put a pacifier in their mouth and try to get the rigidity and the hypertonicity to just ease up a little bit just so they can take the bottle" (P1, FG4). Calming sounds, patting, and massage were the other physically calming techniques participants described. One participant shared, "They love the sound of 'shh shh shh' . . . they love that wooshing sound while I'm patting (their bottom)" (P1, FG3). Two participants used warm baths, one stating, "to calm them down a little bit I [might] bathe them before the feed" (P1, FG1).
3. Decreasing stimulation. One way in which stimulation was decreased was by creating a dark, calm environment ("We keep the lights dimmed down" [P3, FG4]). In addition, caregivers discussed holding the baby out/facing away from them in the beginning as a way to decrease stimulation, "because it's just too much for them to take in (looking at you too)" (P3, FG1).
4. Swaddling. Swaddling was one of the most common strategies discussed for helping to calm and organize infants before and during a feeding. "I think one of the first things that we probably would all do is swaddle them. You know, because if they have their hands out, good Lord, forget it. They're not going to eat . . . we try warm blankets" (P3, FG4). Swaddling only the baby's arms was mentioned across two groups: "With older children I like to only swaddle the uppers . . . they like to kick and so they like to be free at the lower extremities" (P4, FG3).
5. Support the infant's disorganized sucking ability. This included introducing the bottle slowly ("I introduce the bottle and might give them a little bit so they don't dribble, because a lot of them, if they're disorganized, they're spitting milk out the side of their mouth" [P4, FG4]) and providing chin support, which was mentioned across two of the groups. One nurse's remark, which met with head nods of others in the group, was "put your [gloved] finger in to find that sweet spot so you know where to put the nipple" (P2, FG2). Experimenting with a variety of nipples was also a common strategy, with a slow flow nipple endorsed as most commonly helpful: "We have three different nipples on the floor. You try a fast flow, you try a slow flow; we usually go with the slow flow because they suck so hard" (P3, FG1). "Some of the babies going through withdrawal . . . have such a strong suck that they need a slow flow or they start drowning themselves with a regular nipple" (P3, FG2).
6. Burping. Specific tips for burping the infant included more frequent burping, burping even before feeding, and helping the baby relax enough to burp. One participant

shared, “A technique that I’ve found is I actually give them their pacifier while I’m burping and that relaxes them enough; they can let the burp out” (P1, FG2).

Theme 4: Nurture the Relationship

Subtheme: Encourage the Caregivers to Be There. Participants expressed that they welcomed mothers to be present as much as possible in order to learn their babies’ cues and feel empowered. “I try to stress to them how important they are to that baby” (P1, FG2). Another nurse shared, “I think one of the most important things is being able to encourage the moms to be there as much as they can to be able to participate in the feeding times, and not just the feeding times but to stay there with their baby. The more the better, because . . . the more experience they have with how their baby responds to different things, then the better off I think baby and mom are going to be at discharge” (P2, FG3).

Subtheme: Provide Continuity in Caregiving. Nurses expressed a desire for mothers to be more consistently present with the baby while in the NICU in order to learn their cues and bond with them. “*Continuity. I mean, spending time with the baby consistently. You know, we NAS moms that come in and bring breast milk. They’ll come in for an hour and then leave, and then maybe six hours later they come in for an hour, and then they leave*” (P3, FG4).

Subtheme: Build Parent’s Confidence. Helping mothers to feel empowered as the primary caregiver and giving them a chance to participate in the feedings was readily shared by participants. In regard to empowerment, one nurse shared what she may say to mothers: “You’re the mommy. You’re the one going home with the baby. And there’s no reason why you couldn’t do it any differently than I could” (P1, FG3). Having mothers be the ones feeding was described in one example as: “We’ll sit there with Mom and work with Mom to feed. If . . . things I’m telling her, it’s just not connecting, maybe then I show, I’ll say: ‘here, let me try this and see if it works.’ And if it does, then I’ll say: ‘okay, now you try it.’ I don’t take over a feeding. I may feel that I need to show her something but then it goes back to her” (P3, FG2).

One participant remarked how hard it was for the mothers to breastfeed. “A lot of moms pump. Or they pump while they are here, and everyone starts off, ‘I want to breast feed’, but after a while, in the NICU, it’s very difficult to keep up. And, these moms, especially, they have other issues going on, so it’s really difficult” (P3, FG1).

Subtheme: Develop Trust and Avoid Judgmental Attitudes. Establishing trust and rapport with mothers was discussed as important to feeding success in three of the groups. For example, one nurse shared that she communicates “*that the mom is doing nothing wrong. It’s not them. I think taking that off of them helps*” (P2, FG2). Nurses also expressed the need to be mindful of the stigma that the mothers experience

and how this can impact their feeding success with their baby. One nurse stated this as: “*We need to not have the judgmental attitude . . . body language, verbal language, they read it all, the moms do. We can’t think of it as how could you do this to your baby? Because it’s really not a choice for a lot of them. And it is a disease*” (P2, FG3).

DISCUSSION

This study investigated strategies that nurses use to successfully feed infants with NAS in the NICU. Results showed that a baseline of appropriate pharmacologic management with opioid replacement therapy is very important, because it dampens the central nervous system irritability that disrupts feeding. Sucking behaviors were described as being disorganized and frantic before optimal medication management was achieved. Nurses did not expect to be successful in feeding infants with NAS whose signs were not well under control, and usually collaborated with the medical team to re-evaluate the plan of care. Many experts believe that the infant’s neuro-behavioral organization plays an important role in successful feeding,^{17–19} which is reflected by findings describing factors that disrupt feeding in infants with NAS.⁵

The informers readily shared their expertise about how to increase success in feeding infants with NAS. We asked them about their most challenging infant to feed so that they would begin thinking about their strategies for success. All participants discussed the importance of recognizing infant cues. Informants reported that the baby is often not ready to feed when he is picked up, so nursing assessment of feeding cues were important for success. There was respect for allowing the infant some control, and helping the infant to prepare for feeding. They recognized that each infant was an individual and that even well-established techniques do not work in everyone. A technique that works one day may not work the next day, so continued trial and error is needed. We expect that even after an infant’s signs of NAS are well controlled, the infant will continue to recover and may experience some blunting of responses if the opioid dose lags behind his recovery. Thus, the infant’s cues can be confusing throughout the hospitalization. Unclear cues have been reported in the literature in this population,²⁰ as well as decreased responsiveness of mothers to infant cues.⁸

The third theme that emerged, and which participants spent the most time defining, was “Calm and comfortable.” This theme emerged from two subthemes: calm the caregiver and a calm and comfortable baby. The informants strongly believed that anxiety in a caregiver could be felt by the infant, who was likely to react negatively. They helped the mothers relax by helping them to find a comfortable position in which to feed the infant. They ask about their comfort, and for anything they can do before leaving them alone.

Keeping the infant calm was crucial to being successful, and they used many techniques to that end. Several strategies to calm the infant and keep him comfortable were mentioned, some of which are described in the literature, such as swaddling and decreasing environmental stimulation.^{21–23}

Swaddling is one of the few nonpharmacologic interventions that has been reported to be effective in infants with NAS to reduce crying.²⁴ van Sleuwen and colleagues²⁴ also reported that swaddling decreased startles and sleep arousals, enabling infants to increase sleep time and continuity. Informants also talked about an intervention called the C position they adapted for feeding. They place the infant on his side lying on their leg and arms slightly flexed, keeping the head slightly elevated by crossing one leg over the other. Searches for “C position” in the scientific literature as well as the Internet only revealed information about breastfeeding positions. We found no references to feeding infants in the position they described, although we acknowledge that it might appear in a paper without that keyword.

Some informants reported that they start with techniques such as a warm bath to calm the infant, whereas others reported that they start by helping the infant to burp. Many different techniques were described, such as burping before the feeding, whispering a “shh” sound in baby’s ear, and using a pacifier to help the infant relax to release a burp. Most informants reported that they try all available nipples until they find the one that works the best, and most reported using chin and cheek support as needed. Informants described using their gloved finger to find the “sweet spot” on the palate that helped infants form a good suck. They emphasized the importance of vertical versus horizontal rocking to calm the infant. They teach mothers to hold the infant vertically on their chest to rock, rather than rocking the infant horizontally in their arms. The vertical rocking intervention is mentioned in the literature,²² although to our knowledge it has not been tested.

Some informants reported that they often bottle feed with the infant facing away from them when the infant cannot tolerate eye-to-eye contact. This maneuver is meant to decrease stimulation associated with eye contact, and is often successful if the infant opens his eyes. However, since eye-to-eye contact is an important element of attachment,²⁵ mothers may need to be reassured that their infant’s inability to tolerate eye-to-eye contact is a temporary effect of withdrawal. As the infant begins to recover from withdrawal, he will be able to tolerate more face-to-face moments, which must be encouraged. Weber²⁶ contends that inadequate eye-to-eye contact between mothers and infants may “result in the loss of a vital emotional connection.”^(p205)

The final theme that emerged was “Nurture the relationship.” These caregivers encouraged the mothers to be available for as many feedings as possible, and use that time to engage the mother in learning infant cues and how their infant responds to different interventions. Most had a strong message to avoid being judgmental toward the women, helping them as you would any other new mother. If a mother is made to feel uncomfortable in the NICU, she may not visit as often, creating missed opportunities to help the mother develop a healthy relationship with her baby, learn valuable parenting skills, build her confidence, and be encouraged to

continue her own drug treatment. Caregivers explained that it was important to provide continuity of care so that they could develop a trusting relationship with the mother. Morris and colleagues²⁷ found that as the quality of relationships between midwives and their drug-dependent pregnant clients improved, patient care outcomes improved.

An intervention not reported by our expert informants was a discussion of breastfeeding. It was mentioned by only one participant, and she remarked that mothers often pump while they are in the NICU, but it is difficult to sustain because the infants are hospitalized for so long. Breastfeeding is recommended in this population, however, as long as the mother is abstaining from alcohol, illicit drugs, and amphetamines; has a negative screening for human immunodeficiency virus (HIV); and has no other contraindications for breastfeeding.²⁸ There is evidence that breastfeeding infants with NAS results in shorter treatment duration and less severe withdrawal signs,²⁹ and conflicting evidence that it has no specific effect on NAS.³⁰ Even if breastfeeding has little effect on NAS, it has many other beneficial effects for both mother and baby that should not be overlooked.³¹

Additionally, rooming-in as an intervention has appeared in the literature as demonstrating improved infant outcomes,³² but was not mentioned by any participant. Holmes and colleagues³² implemented a multidisciplinary quality improvement project, and found that in comparison to baseline levels, infants with NAS who roomed-in with their mothers used less morphine and phenobarbital, had a shorter length of stay with decreased costs, and had no adverse events. Their interventions were parent- and infant-focused, in a calm, family-centered environment. For example, infants were not awoken for scheduled assessments, and many care activities were conducted with the infant skin-to-skin. Others have reported similar findings.^{32,33}

This study provides the first insight into a characteristic skill set used by NICU caregivers to promote feeding success for infants with NAS. The first question, “Tell us about the most challenging infant with NAS that you have fed,” helped to establish the shared experience among the clinicians at three hospitals. These experts were faced with similar challenges across this population of infants. In general, about 80 percent of infants with NAS in this region are born to women in a methadone program. Drug addiction is treated as a chronic disease in Florida rather than a crime as in some communities. Although it is not uncommon to care for infants whose mothers are poly-substance abusers, there is not a big culture of methamphetamines or heroin that other communities are facing. Because of these regional characteristics, the tips from these experts may not be generalizable beyond this region, or to regions that do not share these unique characteristics.

More work needs to be done to learn how to best manage infants exposed to a wide range of street drugs, and we welcome opportunities to learn more about that from expert caregivers. Although using strategies that are individualized to each infant was a prevalent theme, many specific techniques matched to

the NAS population were identified across every group. These techniques or considerations can be used to develop a training protocol to assist NICU staff in promoting the best feeding outcomes for these infants. Our goal is to develop a standardized intervention based on these findings and others in the literature that can be tested for efficacy in this population.

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