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## Wide Variation Found in Care of Opioid-Exposed Newborns

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### Abstract

**Background**—Standardized practices for the management of neonatal abstinence syndrome (NAS) are associated with shorter lengths of stay, but optimal protocols are not established.

**Aim**—Identify practice variations for newborns with in-utero chronic opioid exposure among hospitals in the Better Outcomes through Research for Newborns (BORN) network.

**Methods**—Nursery site leaders completed a survey about hospitals' policies and practices regarding care for infants with chronic opioid exposure (< 3 weeks).

**Results**—The 76/95 (80%) respondent hospitals were in 34 states, varied in size (<500–>8000 births and <10–>200 opioid-exposed infants/year), with most affiliated with academic centers (89%). Most (85%) had protocols for newborn drug exposure screening; 95% used risk-based approaches. Specimens included urine (81%), meconium (73%) and umbilical cords (10%). Of sites (88%) with NAS management protocols, 77% addressed medical management, 72% nursing care, 72% pharmacologic treatment and 58% supportive care. Morphine was the most common

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first-line pharmacotherapy followed by methadone. Observation periods for opioid-exposed newborns varied; 57% observed short-acting opioid exposure for 2–3 days while 30% observed for 5 days. For long-acting opioids, 71% observed for 4–5 days, 19% for 2–3 days and 8% for 7 days. Observation for NAS occurred mostly in Level 1 nurseries (86%); however most (84%) transferred to NICUs when pharmacologic treatment was indicated.

**Conclusion**—Most BORN hospitals had protocols for the care of opioid-exposed infants, but policies varied widely and characterize areas of needed research. Identification of variation is the first step toward establishing best practice standards to improve care for this rapidly growing population.

### Keywords

Neonatal Abstinence Syndrome (NAS); Opioid; newborn nursery; NICU; variation-in-care

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## BACKGROUND

The nationwide epidemic of opioid use does not spare pregnant women; the prevalence in this population more than quadrupled within the past decade.<sup>1</sup> Consequently, many more infants require treatment for neonatal abstinence syndrome (NAS), a syndrome of opioid withdrawal that results in significant healthcare costs related to prolonged newborn hospital stays.<sup>2,3</sup> Significant variation in the care of opioid-exposed newborns exists with many institutions providing care in neonatal intensive care units (NICUs).<sup>3–7</sup> When NAS care is given in NICUs, focus is often on pharmacologic treatment with frequent separation of mothers and infants. NICU treatment is expensive and perhaps unnecessary for these not critically ill infants. Limited data suggest low rates of serious adverse outcomes.<sup>2,8</sup> Furthermore, the resulting separation of mother and child may be counterproductive to optimal care. For these reasons, there is ongoing debate as to the optimal location for the care of these newborns.<sup>9</sup> Mounting evidence suggests that care may be more optimal in non-NICU settings where the mother and baby may continue to room-in together through the entire NAS hospitalization.<sup>10–14</sup> Some have found benefit of home management once infants are stable.<sup>15,16</sup> Furthermore, recent studies have also shown that standardized protocols for NAS management are associated with shorter lengths of stay and decreased hospital costs.<sup>17,18</sup>

In a Delphi study conducted by members of the *Better Outcomes through Research for Newborns (BORN) Network* of the Academic Pediatric Association, optimal management of NAS was identified as a priority area of research.<sup>19</sup> The BORN Network ([https://www.academicpeds.org/research/research\\_BORN.cfm](https://www.academicpeds.org/research/research_BORN.cfm)) is a national collaborative of pediatric clinicians and researchers who evaluate neonatal care in the birth setting and in the transition to home. The goal of the BORN Network is to conduct collaborative research to establish a firm evidence-base for routine care of the term and late preterm infant.

As a first step toward identification of best practices for NAS, we aimed to identify to what extent variations in practice existed in care provided by BORN hospitals in non-NICU as well as NICU settings. We hypothesized that care provided in non-NICU settings would be more conducive to non-pharmacologic supportive-care of opioid-exposed newborns than that

provided in NICU settings. We aimed to assess comprehensive NAS care across all care settings – including variation in infant drug screening, pharmacologic treatment, rooming-in, infant feeding practices and discharge planning.

## METHODS

A comprehensive survey was developed, pilot tested among BORN leadership and colleagues, revised, and reviewed again by BORN Network Research Committee members. The survey was created using Qualtrics® and included up to 70 items, depending on skip patterns. The survey included single item response as well as “all that apply.” Most items included an option for “unsure”. The survey included questions on hospital characteristics and all areas of NAS management (complete survey is available on-line in supplemental materials).

In autumn 2015, BORN site leaders were emailed a link to the study’s online survey, a study identification number, and a request to forward the survey to the person most knowledgeable about NAS care at their site. Up to four reminders were sent to site leaders and BORN staff sent individual emails to encourage participation.

The analysis included descriptive statistics – frequencies and proportions. We compared number of births per year to numbers of infants born chronically exposed to opioids using Pearson correlation. We defined chronic exposure as opioid-exposure for at least the last 3 weeks before delivery. When questions referred to short- or long acting opioids, the following examples were provided (short-acting: morphine, oxycodone and Percocet; long-acting: methadone and buprenorphine).

We examined the association between a variety of hospital characteristics (number of births/year grouped as <4000 or 4000/year; number of opioid-exposed infants/year grouped as <20, 20–69, 70/year; geographic location grouped as urban, suburban, rural and aspects of NAS care (dichotomous variables including infant drug screening policy, NAS written protocol, staff education for NAS, minimum observation time policy, cuddler program, and discharge on medications) using Fisher’s exact test (due to small sizes in some cells). Statistics were performed with SPSS V22 (IBM).

Exempt IRB approval was obtained from the University of Pittsburgh.

## RESULTS

Among the 95 hospitals that participated in the BORN Network in autumn 2015, 81 sites initiated and 76 (80%) completed the survey; 4 sites did not complete the survey as they transferred at-risk infants to another area hospital for NAS care. Participating sites were located in 34 states and diverse settings – 64% urban, 28% suburban and 8% rural. Most (89%) were affiliated with an academic medical center. Number of annual births varied widely – ranging from < 500 to > 8000 births/year; most ranged from 2000 to 6000/year. The number of infants chronically exposed to opioids at each site also varied, ranging from < 10 to > 200/year. The number of infants born with chronic opioid exposure did not

correlate with number of deliveries (correlation coefficient 0.08,  $p=.5$ ). Variation in individual NAS care practices are described below.

### Infant Drug Screening

When asked, “Does your hospital have a written protocol for drug screening newborns?” 80% answered yes. Of those, 90% reported they use risk-based screening, 3% screened all infants, 1% did not screen and 6% were unsure or were missing a response. Factors used for risk-based screening varied. Most screened for positive maternal drug screen at delivery (100%) or in pregnancy (96%), maternal history of substance use disorder (94%) or limited prenatal care (87%). Fewer also used the following risk criteria: maternal legal involvement (62%), placental abruption (52%), preterm labor (21%) and maternal tobacco use (3%). Infant drug screening was most commonly performed by testing meconium (85%) and urine (76%); 10% used umbilical cord testing.

### Scoring and Pharmacologic Treatment for NAS

Most BORN sites (88%) had a written NAS management protocol. Protocols most commonly addressed medical management (77%), nursing care (72%), pharmacologic treatment (72%) and non-pharmacological supportive care (58%). Most hospitals (93%) used a formal scoring system to assess for signs and symptoms of NAS with the majority (92%) using a version of the “Finnegan Scale” (22% “Original Finnegan Scale” and 70% “Modified Finnegan Scale”). One site used parental report. Formal staff education programs to ensure standardization of NAS scores occurred in 63% of sites, while 12% did not have specific training and 25% were unsure or did not answer. Among sites with formal training, most commonly employed methods included video training (32%), structured observation using an NAS checklist (33%), and formal (26%) or informal (18%) observation by an experienced nurse.

Initiation of pharmacologic management was dictated most commonly by a combination of clinical assessments and formal scoring (75%), while 20% of sites relied on formal scoring alone, 3% did not have specific criteria and one site used clinical assessments alone. One site started all infants exposed to long-acting opioids on methadone within 24 hours of life regardless of scoring or clinical assessment while all other exposures at that site were managed by a combination of criteria. When asked, “How often do you use your formal scoring system to decide when to make pharmacologic dose changes?” 74% responded “always” or “almost always”, 9% “usually”, 3% “sometimes” or “never” and 14% were “unsure.” To terminate pharmacologic therapy, 69% “always or almost always” used the formal scoring system, 9% “usually” used it, 6% “sometimes to never” used it and 17% were “unsure.”

We asked sites about their first- and second-line pharmacologic therapies for NAS by exposure to either opioids alone or combined exposure with other illicit drugs (see Table 1). Morphine was the most common first-line pharmacotherapy with methadone the next most common regardless of exposure type. However, 17% of hospitals reported using another medication as first-line. Phenobarbital was the most commonly reported medication used to

treat NAS-related seizures, followed by benzodiazepines. Notably, there was a significant proportion of “unsure” responses.

### Who Cares for Infants with NAS

Most commonly, infants observed for NAS were cared for by general pediatricians (59%) and newborn hospitalists (34%) and less often by pediatric hospitalists (22%), neonatologists (16%) and “other” (8%, mostly family physicians and nurse practitioners). Infants being treated for NAS were most commonly cared for by neonatologists (68%) and less often by pediatric hospitalists (20%), general pediatricians (17%), newborn hospitalists (12%), and “other” (4%, mostly nurse practitioners).

### Monitoring for NAS

Most hospitals (74%) required a minimum observation period prior to discharge for newborns with perinatal chronic opioid exposure; 18% did not have a policy and 8% were “unsure”. Among those with a policy (see Table 2), more than half observed infants with exposure to short-acting opioids for 2–3 days while almost a third observed for 5 or more days. For long-acting opioid exposures, most (71%) observed infants for 4–5 days, while some observed only for 2–3 days (19%) and others 7 days or more (8%). Hospitals estimated the average length of observation for short- and long-acting opioid exposure (see Table 2).

Most hospitals (86%) provided care for infants being observed, but not yet treated for NAS, in their Level 1 Nursery. In contrast, most infants receiving pharmacologic therapy for NAS were cared for in either Level 2 (33%) or 3 (54%) NICUs; few reported NAS treatment occurred in the Level 1 Nursery (12%) or their pediatric inpatient (16%) (total >100% because could select more than one location).

Most hospitals (77%) utilized monitoring of infants once they were started on pharmacologic therapy, 10% did not start monitoring and 10% were unsure. Among those that reported monitoring and asked how they monitor (all that apply), most used full cardiorespiratory monitoring (89%) and fewer used pulse oximetry alone (14%). Of those that monitored infants, 57% did so for the full duration of pharmacologic treatment, 15% until the infant was on a stable treatment dose, 9% until the infant was weaning from pharmacologic treatment and 11% monitored until discharge.

### Supportive-care Approaches

Supportive-care practices reported by BORN nurseries were diverse (see Table 3) and included modifications to the environment, parental care and alternative interventions. Rooming-in and other supportive-care measures that promoted maternal contact (e.g., skin-to-skin contact) were reduced during pharmacologic treatment in many participating centers, whereas measures not utilizing human contact were increased. Although most sites (73%) almost always offered rooming-in during observation for NAS, only 11% did so during pharmacologic treatment; 41% never offered rooming-in and 31% only rarely did. Volunteer cuddler programs were used by 33% of sites. Training for “cuddlers” included the general hospital volunteer training (23 sites) while 7 sites provided some special NAS training.

## Feeding Practices

Most sites (70%) had a policy or guideline regarding breastfeeding or feeding expressed breastmilk to infants being observed or treated for NAS, while 13% did not and 17% were unsure. Breastfeeding guideline criteria included negative drug screen at delivery (50%), mother enrolled in drug treatment program (40%), and confirmed adherence to a drug treatment program (36%). Sites were nearly evenly distributed with regards to how long before delivery women must have 1) negative drug screens and 2) be enrolled in a drug treatment program to breastfeed (1–2 weeks 13% and 13%; 3–4 weeks 12% and 10%; 5–6 weeks 9% and 10%; 7–8 weeks 9% and 10%; 9–10 weeks 8% and 9%; 11–12 weeks 9% and 9%; and more than 12 weeks 7% and 12%, respectively). Hospitals used a wide variety of feeding practices for infants being observed or treated for NAS, as described in Table 4.

## Discharge planning

About a third of sites (n=26, 34%) allowed for discharge home on pharmacologic treatment for NAS. When asked how often infants were discharged on medication, 61% indicated it was rare (< 10% of the time) while only 11% indicated it was common (90–99% of the time). Sites varied on which medications they sent infants home on – phenobarbital (13 sites), methadone (12 sites), morphine (4 sites), clonidine (2 sites) and buprenorphine (1 site). Nearly all sites that allowed discharge home on medication indicated that the following criteria had to be met before discharge: family demonstrates appropriate response to and care of the baby, family has stable social situation, family has access to a phone and transportation, and primary care provider comfortable monitoring infant on medication.

## Associations between Hospital Characteristics and NAS Management

Presence of formal staff training was associated with higher births/year (p=0.01) and urban location (p=0.05). No other significant associations between hospital characteristics and NAS care were found.

## DISCUSSION

Among hospitals participating in the BORN Network, most had protocols for drug screening and management of the opioid-exposed infant, but the policies varied widely. Our survey addressed areas of NAS care not previously evaluated, including supportive-care, infant feeding, monitoring, nurse training and discharge planning. Standardization of care practices can lead to improved care, so identification of this variation is the first step toward improving care for this rapidly growing population of infants.

Ours was the first national survey among well newborn nurseries. Crocetti conducted a telephone survey in 2007 to Maryland hospitals with nurseries (27/33 responded) and found that 52% used a standardized evaluation and treatment protocol for NAS.<sup>4</sup> Other surveys were of neonatologists and focused on pharmacologic therapy. A 2005 survey of neonatology division chiefs with accredited fellowship programs in neonatal-perinatal medicine in the US (75/102 responded) found that 55% of programs had a written NAS policy; most used a form of the Finnegan scoring tool yet varied in their treatment approaches.<sup>7</sup> A survey in England was mailed to 235 neonatal units with telephone follow-

up for non-responders; 96% of responders reported that they have formal NAS guidelines, Finnegan was the most widely used scoring system, and morphine was the most common first line pharmacotherapy with phenobarbital the most common second line treatment.<sup>6</sup> In that study, 29% of NICUs allowed infants to be discharged home on medication. Similarly, most BORN nurseries used Finnegan scoring to monitor signs and symptoms of NAS and to guide treatment, and a third allowed discharge of infants home on medications. In 2011, Mehta *et al.* surveyed medical directors or charge nurses at 383 US NICUs with a 47% response.<sup>5</sup> They reported that 72.5% had written NAS protocols; nearly all used risk-based toxicology screening and 98.7% used a formal NAS scoring system. We found that 77% of BORN nurseries had standard protocols; the continued increase in having written protocols for management of NAS likely reflects the increasing rates of NAS nationally.

Unlike most previous surveys, we assessed infant drug screening and specifically criteria used for screening. Although most hospitals screen based on risk criteria, the criteria used to identify risk were variable. Furthermore, risk-based screening is associated with under-diagnosis and is prone to bias.<sup>20</sup> Wexelblatt and colleagues found that 20% of drug-exposed infants are missed using risk-based screening.<sup>21</sup> Drug screening methods also varied widely, which also has implications both for identification of at-risk infants as well as referrals to child protective services. Urine drug screening most often only detects exposures in the prior few days while meconium and cord testing detect exposures at least through the third trimester. Zellman and colleagues reviewed perinatal drug screening protocols and found that they lack clarity, which precludes most from encouraging standardized care.<sup>22</sup> They concluded that legislative mandates could shape their development and features.

We found significant variation in observation periods for short- and long-acting opioids. Expert recommendations suggest that infants exposed to short- and long-acting opioids should be observed for up to 3 days and 5–7 days respectively.<sup>23</sup> We found that 44% of sites observed infants exposed to short-acting opioids for longer than 3 days and 47% observed infants exposed to long-acting opioids shorter than 5 days. Lack of high quality data to support these recommendations, implications for separation of mother and infant, as well as costs associated with prolonged hospitalization, all render this as an important area for future research.

We found similar pharmacologic management as previous surveys<sup>4–7</sup> – with morphine and methadone being the most common first line treatments. There are currently no FDA approved medications to treat NAS and little data to support the best medication(s) to use. This lack of evidence is reflected in the variation found in pharmacologic therapy. However, there are federally-funded studies currently being conducted to add to this evidence base. We also found variation in duration and method of infant cardio-respiratory monitoring during treatment. While the purpose of monitoring infants is to ensure patient safety, there is no evidence in the literature that documents this effect among infants with NAS. Because monitoring can impact overall cost as well as parents' comfort and ease holding their infants, it is a valid area for future study.

Supportive-care has long been included as an important component of care for infants with opioid exposure.<sup>24</sup> We found important variation in separation of mother and infant (i.e.,



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lack of rooming-in). In many hospitals, infants receiving pharmacologic treatment for NAS are not able to room in with their mothers – perhaps because the mothers have been discharged and/or the babies are in the NICU without rooming-in capability. Some sites are able to move the infant to a pediatric hospital bed and out of the NICU –which can support ongoing rooming-in. However, this is a challenge for infants born in free-standing maternity hospitals. In a quality improvement project, rooming-in with continuous maternal presence as the first-line of treatment was associated with lower pharmacologic treatment rates, shorter length of stay and improved maternal satisfaction and cost.<sup>10</sup> A minority of hospitals discharge infants being treated for NAS while still weaning from pharmacotherapy. Kelly and colleagues in Canada conducted a retrospective study to compare the experience of infants who completed their morphine wean in hospital with those who completed it at home.<sup>16</sup> They found that the 65% of infants who completed their morphine weaning at home were significantly less likely to return to the hospital for further withdrawal treatment but remained on morphine longer (32 vs. 19 days,  $p < 0.01$ ). Backes *et al.* in Ohio conducted a similar study and found that infants who were discharged while still on treatment had shorter hospital stays and higher breastfeeding rates but longer treatment durations (37 vs 21 days,  $p < 0.001$ ).<sup>15</sup> These retrospective studies suggest a benefit to this approach but are prone to selection bias – that is, who is eligible for early discharge – which should be assessed carefully in future studies. However, it is also unclear whether prolonged exposure to opioids may impact infant neurodevelopment. There is a need for high quality, long-term studies that evaluate neurodevelopmental outcomes to ensure no unintended consequences of the treatment.

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Feeding practices for infants prenatally exposed to opioids are also highly variable across sites – from breastfeeding policies to type of formula used. Breastmilk feeding is associated with lower treatment rates for and severity of NAS and, of course, with maternal and infant health benefits.<sup>13,25–29</sup> However, not all programs have a policy about breastfeeding for drug-exposed infants. Among those with a policy, wide variation in criteria for breastfeeding were reported, which likely reflects variations in expert recommendations (e.g. AAP, ABM, WHO) and lack of supporting evidence.<sup>23,30,31</sup> More than half of hospitals with a policy require that women have a drug screen negative at delivery for all drugs, except those prescribed, in order to support breastfeeding. This recommendation, based on expert opinion, assumes that women who have illicit drugs in their urine at delivery are not adherent to their drug treatment program and could potentially use illicit drugs when breastfeeding which could be dangerous to their infant. Infants with NAS are at increased risk for excessive weight loss and/or slower return to birth weight.<sup>32–34</sup> For these reasons, given lack of data to support use of special formulas (e.g., hypoallergenic formula) or timing for the introduction of high-calorie formula for infants with NAS, hospitals have developed their own procedures. If criteria for discharge readiness includes an appropriate weight pattern, improved feeding protocols have the potential to reduce hospital length of stay. However, the use of specialty formulas, such as hypoallergenic formula, may increase costs without necessarily improving outcomes and thus is another area for future research.

Our study was limited by a response rate of 77%. It is possible that nurseries that did not respond to our survey were systematically different from respondent nurseries, thus biasing our results. The survey was also generally completed by one individual, and it is possible

that variation exists not only across hospitals but also among providers within an institution, especially given that some items in our survey had a high rate of “unsure” responses. The high rate of unsure responses can also be seen as a study strength as it may reduce survey bias by allowing responders to report uncertainty rather than forcing them to guess. Additionally, our survey did not measure actual practices at the surveyed nurseries, so it is possible that responses represent an ideal or average practice pattern.

Our survey found wide variation in care for most aspects of care for the opioid-exposed infant. The challenge is that many areas of care lack evidence to drive best practices. Areas that are amenable to change at most sites deserve immediate study. For example, most hospitals could adopt standard observation times for short- and long-acting opioid exposures based on pharmacokinetics of the opioid and expert recommendations (AAP) and could standardize pharmacologic treatment initiation and weaning to help reduce length of stay. Rooming-in and continuous maternal presence should be a focus of all care, during both the observation and pharmacologic treatment portions of the hospital stay. However, this area needs to be addressed based on the hospital characteristics and local resources. Our survey suggests some important areas of future research and quality improvement initiatives to decrease variation in care for opioid-exposed infants and treatment of NAS.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Abbreviations

<b>BORN</b>	Better Outcomes through Research for Newborns
<b>NAS</b>	neonatal abstinence syndrome
<b>NICU</b>	neonatal intensive care unit

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**What's New**

With prenatal opioid use increasing, most newborn nurseries have written protocols for NAS screening and management. Our survey demonstrates significant variations in NAS care among US nurseries related to observation time, supportive-care approaches, infant feeding and discharge planning.

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**Table 1**  
First and Second Line Pharmacologic Treatment Choices for NAS by Exposure Type

Pharmacologic Treatment	Opioid Exposure			Poly-drug Exposure		
	1st line %	2nd line %	Seizure treatment %	1st line %	2nd line %	Seizure treatment %
Morphine (oral)	53	10	1.4	47	7	1.4
Morphine (IV)	8	1	1.4	7	1	
Methadone	22	4		21	4	
Clonidine	1	25		1	19	
Phenobarbital	3	33	45*	4	33	43*
Buprenorphine	1			1		
Diazepam			13 <sup>†</sup>		1	8 <sup>‡</sup>
Other	7 <sup>‡</sup>	6	7	4 <sup>‡</sup>	4	
Unsure	4	21	32	14	29	

\* For treatment of seizures among infants with opioid-only exposure, oral and IV phenobarbital were used 11.3% and 33.8% respectively. For poly-drug exposure, oral and IV phenobarbital were 9.9% and 33.8% respectively.

<sup>†</sup> For treatment of seizures for infants with opioid-only exposure, this number included all responses for a benzodiazepine. Individual responses were 2.8% diazepam, 8.5% lorazepam, and 1.4% midazolam. For poly-drug exposure, individual responses were 1.4% diazepam and 7% lorazepam.

<sup>‡</sup> When noted, other treatments included combinations of the above medications (e.g. morphine + clonidine or morphine + phenobarbital)

**Table 2**

Among hospitals with a policy, minimum length of observation periods for short- and long-acting opioid exposures

Minimum Length of Observation		
Days	Short-acting opioid %	Long-acting opioid %
2-3	57	19
4	14	28
5	28	43
7	2	6
8	0	2
Average Length of Observation		
2-3	34	9
4-5	26	43
6-7	4	10
Unsure	34	36

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**Table 3**

Supportive care provided during observation for and treatment of NAS

	<b>Observation %</b>	<b>Treatment %</b>
<b>Environment</b>		
Low level lighting	63	74
Quiet environment	79	84
Vibrating or moving seat/bed	30	42
Non-nutritive sucking (pacifier)	76	82
<b>Parental care</b>		
Skin to skin	75	59
Breastfeeding when appropriate	86	76
Rooming-in	71	40
Holding	82	74
<b>Interventions</b>		
Music therapy	5	8
Infant massage	11	12
<b>Other</b>	7	10



**Table 4**

Infant feeding for infants being observed or treated for NAS

<b>Calorie-enhanced BM or special formula fed to infants observed or treated for NAS?</b>	<b>%</b>
Yes	33
No	57
Unsure	10
<b>How often are infants who are observed or treated for NAS routinely fed calorie-enhanced breastmilk or special formula?</b>	
<10%	22
10–25%	26
26–50%	26
51–75%	13
76–100%	9
<b>Type of special diet usually used</b>	
Calorie-enhanced donor breastmilk	4
Calorie-enhanced mother's breastmilk	44
Calorie-enhanced standard formula	61
Elemental formula	9
Lactose-reduced cow milk based formula	22
Soy formula	9
Protein hydrolysate formula	17
Preterm formula 22 kcal/oz	30
Preterm formula 24 kcal/oz	4
Other	4