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# Nutritional Intake and Weight Gain in Infants with Neonatal Abstinence Syndrome: A Literature Review

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# NUTRITIONAL INTAKE AND WEIGHT GAIN IN INFANTS WITH NEONATAL ABSTINENCE SYNDROME: A LITERATURE REVIEW

by

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# ABSTRACT

Neonatal abstinence syndrome (NAS) in infants presents unique challenges in feeding and weight gain. The unpredictable clinical manifestations associated with the newborns withdrawal from exposure to drugs in utero can lead to costly delays in transition of the infant out of the Neonatal Intensive Care Unit (NICU).The purpose of this review of literature was to explore feeding positions and nutritional intake with the greatest impact on weight gain in infants with neonatal abstinence syndrome (NAS) following delivery. The secondary purpose was to compare the clinical manifestations of infants with NAS that influence nutritional intake and their relationship to length of time and cost of stay in the NICU. A review of literature was performed using multiple databases. Articles focusing on feeding position and nutrition intake were identified for interventions to effectively promote weight gain, while reducing clinical manifestations common in infants with NAS. Articles exploring improved feeding and weight gain in infants with NAS and reduced length of stay in the NICU were also synthesized for cost reductions to the facility. Results from 12 studies comparing various feeding positions that optimized nutrition, and reduced negative clinical manifestations in infants with NAS were synthesized for content relevant to the research questions. Results suggest a relationship between placing infants in the c-position, and side-lying position to reduce sensory stimulation, with reducing clinical manifestations for infants actively experiencing withdrawal symptoms from NAS. Providing chin and cheek support as needed, decreasing eye contact during feeding periods, and providing darker quiet environments all play an important role in allowing infants with NAS to optimize their weight gain. As previously stated, to manage nutritional intake and optimize weight gain, reduction of clinical manifestations through pharmacological and non-pharmacological interventions must be actively incorporated into the infants' plan of care.

## DEDICATION

For my Lord and Savior, who calls me to have a strong passion for such a vulnerable population, and allows me to give my life to love and care for His children, as His Son has done for us.
For my fiancé Matthew Chambers, for his never-ending love and support, his unwavering patience, and for always believing in me, each and every day.
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# INTRODUCTION

Neonatal abstinence syndrome (NAS), in conjunction with the opioid epidemic, has seen a successive incremental rise in the United States (US) in the past 20 years, with an increase of 300% from 1.5 hospital births in 1999 to 6 per 1,000 hospital births as of 2013 (Ko et al., 2016). This is the equivalent of one opioid dependent infant born every 25 minutes ("Dramatic Increases in Maternal", 2019). The treatment of NAS in infants born addicted often involve pharmacologic and non-pharmacological therapies to manage the individualized clinical manifestations. Clinical manifestations include central nervous system deficits such as irritability, autonomic dysfunction, and gastrointestinal signs such as excessive sucking, reduced quality and quantity of feeding resulting in poor weight gain, vomiting, and loose stools (Logan, Brown, Hayes, 2013). Interventions aimed at reducing the negative effects of addiction involve consistent care regimens that promote weight gain and growth, while minimizing CNS disturbances. In most instances, a multidisciplinary approach is instituted using drug therapy and scheduled care routines, however implementation of care related to feedings can be inconsistent and vary between health care providers.

The use of pharmacological agents to reduce the severity of CNS clinical manifestations in infants with NAS is well established. However, interventions aimed at feeding methods to improve digestion and increase nutrition levels have not been adequately studied in the context of overall weight gain. According to a study conducted by Wachman, Byun, & Philipp (2010), breastfeeding rates among opioid-dependent women were low, with 75% of eligible women electing not to breastfeed. Colostrum and breast milk via breastfeeding in comparison to high calorie formula via bottle feeding warrants further exploration in relation to weight gain and nutrition intake for infants with NAS. Equally important is the reduction of clinical

manifestations interfering with nutritional intake and proper positioning of infants with NAS during feeding, with regards to breast-feeding or formula feeding methods.

# PROBLEM

There are many physiologic and psychosocial causes of failure to thrive that can potentially affect an infant's weight. Failure to thrive is defined as "a state of undernutrition due to inadequate caloric intake, inadequate caloric absorption, or excessive caloric expenditure. In the United States, unintentional weight loss and poor nutritional intake is prevalent in 5 to 10 percent of children in primary care settings" (Cole & Lanham, 2011).

Physiologic causes of failure to thrive can include, damage to the brain or central nervous system, anemia, metabolic disturbances, chronic infections, cardiovascular or pulmonary disturbances, organ dysfunction, hormone dysfunction, or low birth weight (Failure to thrive, 2019). Psychosocial causes can include, psychological, social, or economic problems within the family dynamic. Additionally, "emotional or maternal deprivation, substance abuse, or lack of knowledge about proper feeding techniques are also related to nutritional deprivation" (Pediatric Poor Growth, 2019). Often times, the specific cause of failure to thrive cannot be determined.

However, infants affected by NAS have unique concerns regarding weight gain. Common clinical manifestations that impact infants affected by NAS include diarrhea, vomiting, irritability, inadequate nutrition, leading to poor weight gain. Clinical manifestations associated with infants born with NAS present challenges to improving feeding patterns and styles, promoting weight gain, and ultimately meeting neonatal milestones, to transition out of the Neonatal Intensive Care Unit (NICU).

The research question in this literature review focused on the socio-economic factors to identify, promote, and implement efficient feeding positions and styles, as well as quality of nutritional intake for infants with NAS in order to decrease overall time spent in the NICU, and cost.

# PURPOSE

The purpose of this literature review was to examine current research regarding factors that had the greatest impact on weight gain in infants with NAS following delivery, with respect to various feeding positions and styles, and the quality of nutritional intake.

The outcome of this review was to understand how interventions can be implemented to decrease the amount of central nervous system disturbances to prevent, maintain, and improve overall weight gain, and the health of infants affected by NAS. Additionally, this review explored various socio-economic factors, to identify, promote, and implement interventions that potentially lead to an overall decrease in time and cost spent in the NICU. Sufficient evidence exists to suggest that increased weight gain is correspondent with shorter duration in the NICU. However, more support is needed to determine how these various feeding positions, and quality of nutritional intake, whether it be breast milk or formula, promote greater overall health, increased weight gain, and decreased overall time spent in the NICU.

# METHOD

A literature review was performed using research articles from 1999 to present**,** regarding factors that have the greatest impact on weight gain in infants with NAS associated with feeding positioning, and styles, quality of nutritional intake, and reduction of clinical manifestations. The focus was also to relate to various socio-economic factors to identify, promote, and implement interventions that will potentially lead to an overall decrease in time and cost spent in the NICU. Databases used to search for articles included Cumulative Index to Nursing & Allied Health Literature (CINAHL), Elton B. Stephens Co. (EBSCOhost), Education Resources Information Center (ERIC), Medical Literature Analysis and Retrieval System Online (Medline), and PsycINFO databases. Searches used a combination of the following terms: Neonatal abstinence syndrome*, clinical manifestations*, symptoms*, benefit*, NICU*, weight gain*, feeding*, nutrition*, high-calorie formula*, breast feeding*, CNS disturbances*, vomiting*, irritability*, diarrhea*, cost*, and duration*. Inclusion criteria consisted of 1) published research in English, 2) positions and styles of feeding approach, quality of nutrition, and 3) identified interventions effectively promoting weight gain, while reducing clinical manifestations common in infants with NAS.

The data was conformed into tables that synthesized the relationship between the various feeding positions, and styles, as well as the quality of nutrition related to the reduction of clinical manifestations in infants with NAS. Any additional information on NAS based on reduction of clinical manifestations, reduced duration of stay in the NICU, and cost-effectiveness, was tabled based on the obtained data. The data was used to reveal evidence that could be used to develop guidelines for promoting overall weight gain, and the reduction of clinical manifestations in infants with NAS.

# BACKGROUND

Neonatal abstinence syndrome (NAS), is the result of behavioral and physiological clinical manifestations that an infant may experience while withdrawing from narcotics (opioids) and other pharmacologic agents from exposure in utero (Rojan, 2017). Though there are recurring clinical manifestations that occur throughout most cases of NAS, the presentation of NAS is unpredictable, and infants will display individualized manifestations dependent upon the severity of withdrawal, type of drug, and age of the infant (MacMullen, Dulski & Blobaum, 2014).

There are two major types of NAS (MacMullen, Dulski & Blobaum, 2014). Prenatal NAS is widely recognized, and is due to the prenatal maternal use of substances. Withdrawal symptoms will occur once the placenta no longer has access to the substance provided during pregnancy. Common pharmacological agents used during pregnancy that are implicated in prenatal NAS consist of: opiates, barbiturates, stimulants such as cocaine, sedatives, ethanol, marijuana, and nicotine (MacMullen, Dulski & Blobaum, 2014). Postnatal NAS occurs when there is an abrupt discontinuation of analgesia, such as fentanyl or morphine. It usually occurs after prolonged drug exposure for post-procedure pain management and/or sedation. However, chronic opioid exposure is the most common source of NAS (MacMullen, Dulski & Blobaum, 2014).

Maternal substance abuse is a preventable cause of mental, physical, and psychological problems in infants and children, which can lead to classification of prenatal NAS. Drug abuse in pregnancy, and neonatal psychomotor behavior consistent with withdrawal from opiate and polydrug withdrawal is currently a significant clinical and social problem. An estimated average of 5.4% of pregnant women between 15 to 44 years of age used illicit drugs in 2012-2013. The

highest rate occurred in those 15to 17 years of age, (14.6%), followed by women 18 to 25 years of age (8.6%), and those between 26 to 44 years (3.2%) ("Substance Use and Mental Health Estimates", 2014).

Postnatal NAS occurs when an abrupt discontinuation of opioid analgesia occurs, usually after prolonged drug exposure. In the Neonatal Intensive Care Unit (NICU), fentanyl is the most commonly administered analgesic. This is a potent, rapid acting, synthetic opioid with a relative lack of hemodynamic side effects. Fentanyl and morphine have shown to produce a high rate of opioid withdrawal when administered to critically ill infants. Tolerance and withdrawal symptoms may occur after 5 or more days of continuous infusion of fentanyl, and may occur more often with fentanyl than morphine (Hamdan, 2017).

Common opiates and narcotics associated with NAS include: Codeine, fentanyl, heroin, methadone, meperidine, oxycodone, morphine, hydromorphone, butorphanol, pentazocine, propoxyphene, chlordiazepoxide, buprenorphine, barbiturates, caffeine, cocaine, selective serotonin reuptake inhibitors, antihistamines, ethanol, marijuana, nicotine, phencyclidine, meprobamate, glutethimide, ethchlorvynol, diazepam and lorazepam (Hamdan, 2017).

Drugs are transferred from the mother to the fetus via the placenta through active transport which requires energy to move fluids into the cell. Passive diffusion requires no energy for movement. Pinocytosis, moves fluid by invagination of the cell membrane. The ease of transport depends on the size of the drug molecule, its lipophilicity, the pKa (acid ionization constant) of the compound, and the pH of the blood. During delivery of the fetus, the passage of the drug is interrupted, resulting in the development of a withdrawal symptom in the neonate. It is theorized that withdrawal can cause molecular alterations that may produce systemic,

behavioral, and cognitive symptoms. However, the mechanisms of withdrawal in a neonate are poorly understood (MacMullen, Dulski & Blobaum, 2014).

Women undergo many physiologic changes throughout their pregnancy. Examples of common physiologic changes that new mothers may face include nausea, vomiting, sensitivity to odors, gastric reflux, and constipation. This pregnancy-related constipation is the result of decreasing peristalsis in the gastrointestinal tract. Peristalsis is the involuntary wave-like movement that moves food throughout the gastrointestinal tract (Peristalsis, 2019). "Smooth muscle relaxation and decreased peristalsis occur related to the influence of progesterone. Elevated progesterone levels cause smooth muscle relaxation, which results in delayed gastric emptying and decreased peristalsis" (Kyle & Ricci, 2009).

Many women use some type of drug, substance, or medication during pregnancy, and often times don't recognize or understand the effects that these substances may have on their developing fetus. With decreasing peristalsis throughout the gastrointestinal tract, the rate of absorption for these substances is prolonged, and therefore poses a greater risk for negative teratogenic effects. Though clinical manifestations are individualized for each infant affected by NAS, there are general effects that will present themselves due to generalized use of drugs, substances, or medications during pregnancy. These general effects include, but are not limited to: interfering with normal fetal development, damaging the infant's organs, damaging the placenta and putting the infant's life at risk, increasing the risk of miscarriage, or bringing on premature labor (Pregnancy- medication, drugs, and alcohol, 2012). Bowel function and rooting in the infant are impaired as a result of use of substances during pregnancy. NAS infants lose the drive to root, or the will to suckle, and have impaired bowel function, resulting in lethargy, which can lead to poor weight gain.

As previously stated, NAS is individualized, and infants will present with varying manifestations. However, there are common manifestations that are recognized and associated with infants experiencing NAS. The manifestations exhibited are heavily dependent upon the type of drug used during pregnancy, as well as the amount of exposure the fetus had in utero. The effect of drugs on body systems is influenced by the type of drug, the combination of drugs, the amount and frequency of use, the trimester in which the drug is used, the timing of withdrawal, and the genetic susceptibility of the fetus/neonate (MacMullen, Dulski & Blobaum, 2014). Infants exposed to opioids in utero are likely to present with manifestations such as: hyperirritability, GI dysfunctions such as excessive sucking, poor feeding, regurgitation, and diarrhea. They may also experience tremors, high-pitched crying, increased muscle tone, seizures, nasal congestion, hyperthermia, and tachypnea. Unfortunately, it is not widely known how healthcare professionals and those caring for infants with NAS can decrease GI disturbances, and increase opportunities for weight gain. Increased awareness among healthcare professionals is essential when caring for infants with NAS in relation to feeding quality, and positioning, to decrease the clinical manifestations related to poor weight gain.

Infants exposed to cocaine in utero may not experience any significant withdrawal syndromes due to the short period of time in which a withdrawal related to cocaine may occur. Similarly, infants exposed to benzodiazepines may not experience a withdrawal syndrome. Though Cannabis/Marijuana is a substance that has been known to be used during pregnancy, the current effects of Cannabis/Marijuana on the infant, and infant feeding are not yet fully understood. Alcohol exposed infants may present with hyperactivity, central nervous system (CNS) dysfunction, fetal alcohol syndrome (FAS), jitteriness, irritability, hyperreflexia, hypertonia, poor suck, tremors, seizures, poor sleep patterns, hyperphagia, and diaphoresis.

Infants exposed to selective secretion reuptake inhibitors (SSRIs) may present with jitteriness, respiratory distress, and sleep disturbances (MacMullen, Dulski & Blobaum, 2014).

**Summary**

Neonatal abstinence syndrome is an individualized condition that varies between infants. Though there are many common clinical manifestations, each infant will present with their own challenges based on type and duration of drug exposure in utero (MacMullen, Dulski & Blobaum, 2014). Many women use some type of drug, substance, or medication during pregnancy, and often times don't recognize or understand the effects that these substances may have on their developing fetus. It is not widely understood how healthcare professionals can decrease gastrointestinal disturbances and other manifestations, while increasing opportunities for weight gain.

# RESULTS

Twelve studies related to neonatal abstinence syndrome and reduction of clinical manifestations were included in this review of literature. All studies were published in the past twenty years. Seven articles provided follow-up data on previously conducted cohort studies, one case study was included, one mixed-methods pilot study was included, one article included a focus group methodology, one article was composed of a case series, and one prospective cohort study was also included. Mixtures of both qualitative and quantitative studies were included in this literature review.

## Neonatal Abstinence Syndrome and Related Outcomes

The literature review revealed major themes pertaining to neonatal abstinence syndrome and the reduction of clinical manifestations to optimize weight gain in infants with this condition. Studies described self-reported data trends and outcomes related to breastfeeding promotion, rooming-in promotion, pharmacological interventions, and non-pharmacological interventions.

## Breastfeeding Promotion

Seven studies focused on the promotion of breastfeeding by mothers whose infants are affected with neonatal abstinence syndrome, so long as there are no outstanding contraindications, and appropriate therapies have been commenced (Abdel-Latif et al., 2006; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Pritham, 2012; Pritham, Paul, & Hayes, 2012; Short, Gannon, & Abatemarco, 2016). In a retrospective cohort study, the effects of breast milk feeding were assessed in comparison with the severity of neonatal abstinence syndrome in a population of affected infants. Among 190 infants, the length of stay for those who were

breastfed was 14.7 days, compared to 19.1 days for those infants who were non-breastfed (Abdel-Latif et al., 2006). Infants were assessed using the Finnegan Scoring System. The mean scores for the first 9 days of life were considerably lower in infants with breastmilk intake. Additionally, the median time to withdrawal occurred considerably later in breastmilk infants when compared to infants in the formula group (Abdel-Latif et al., 2006).

One infant in a case study was monitored to track tolerance to feedings, daily weight gain, growth patterns, velocity goals, head circumferences, length measurements, changes in electrolytes, and implementation of nutrition-related medications. These goals were continually adjusted to lessen the severity of NAS, and the clinical manifestations associated with it, that the infant was experiencing. The infant started with transitional formula for intake at the beginning of the study, then moved to a 20-calorie per ounce term formula, where weight gain (36.2 g/d) increased. Then, the infant moved to 24- calorie per ounce term formula, where weight (7.4 g/d) continued to increase. The benefits of breastfeeding for this vulnerable group outweigh any of the potential risks, granted that the mother is on a stable dose of methadone or buprenorphine, and is actively involved in an opioid management program (Gottesman, Chang, Feldman, & Ziegler, 2018).

In a retrospective cohort study, maternal breast milk feedings were associated with shorter median duration of methadone therapy in both term and preterm infants. Compared to infants who were formula-fed (median 18.5 days), consumption of maternal breast milk was associated with shorter length of stay (median 12.5 days) (Isemann, Meinzen-Derr, & Akinbi, 2011).

In a mixed-methods pilot study, thematic analysis generated 5 key themes relating to breastfeeding support and substance exposure. These themes included: breastfeeding skill and

knowledge, psychological factors, person-centered approach, environmental modifications, and postnatal experience on breastfeeding. Breastfed infants in this study had a shorter hospital stay than infants who were formula-fed (10.8 and 30.0 days, respectively). These infants were also less likely to require pharmacotherapy, and displayed a less significant course of withdrawal (MacVicar, Humphrey, & Forbes-McKay, 2017).

In an additional retrospective study, there were statistically significant differences between infants who were formula-fed and infants who were breastfed in relation to the commencement of pharmacological treatment. Three infant feeding methods included in this study (formula, breast, or mixed formula and breast) revealed significant differences in neonatal abstinence syndrome treatment between formula and breastfed infants, but not between the formula-fed infants and infants who received a mixture of formula and breastmilk. Opioid-dependent women that are actively participating in buprenorphine maintenance therapy were encouraged to breastfeed, so long as there are no outstanding contraindications present (Pritham, 2012).

Furthermore, in another retrospective study, infants with prenatal exposure to methadone who were breastfed were discharged home earlier than those infants who were formula-fed. It is suggested that breastfeeding may be protective for neonates withdrawing from opioids. Overall breastfeeding is associated with a decreased rate of infant treatment for withdrawal from prenatal methadone or buprenorphine exposure. Breastfeeding should be permitted and encouraged so long as the maternal urine drug screen is negative for illicit substances upon admission (Pritham, Paul, & Hayes, 2012).

Correspondingly, in another retrospective cohort study, it was found that NAS infants who are breastfed have a significantly shorter length of stay than non-breastfed NAS infants,

even after controlling for differences in maternal and infant characteristics. Lower rates of breastfeeding among NAS infants were not unexpected, this tendency could be due to higher NICU admission rates and/or the physical manifestations more commonly found in this population, making breastfeeding an additional challenge. However, the act of breastfeeding plays an additional role in impacting NAS infants, rather than the breast milk intake alone (Short, Gannon, & Abatemarco, 2016).

**Rooming-in Promotion**

Three studies described the promotion of mothers and infants rooming-in, and the benefits that may prevail with infants with NAS.

A retrospective cohort study was conducted to evaluate the effects of rooming-in on the incidence and severity of NAS among opioid-exposed newborns and on the proportion of mothers who regain custody of their babies at hospital discharge. Rooming-in was associated with substantially reduced rates of newborn treatment with morphine, length of morphine treatment, vomiting, admission to a level II nursery, and length of stay in the hospital. Mothers who roomed-in were much more likely to retain custody of their newborns. Newborns who roomed-in were much more likely to be discharged in the custody of their mothers than infants in other groups. This study found that overall, rooming-in is associated with easing newborns' transition and promotes better care from the mother (Abrahams et al., 2007).

In a case series, a rooming-in program was implemented to support close uninterrupted contact between opioid-dependent women and their infants in order to decrease the severity of NAS scores, lessen the need for pharmacotherapy, and shorten hospital stays. The mean length of stay was significantly shorter among those in the rooming-in cohort (7.9 days vs 24.8 days). Rooming-in could potentially reduce bed use and save hospital resources, while preventing

patients from dealing with negative psychosocial stressors. Rooming-in was also associated with a decreased need for pharmacotherapy from 88.3% of infants receiving care in the NICU, to only 14.3% of those rooming-in (Newman et al., 2015).

In a retrospective cohort study, the association between breastfeeding and length of hospital stay among infants diagnosed with NAS was examined. This study found that rooming-in and uninterrupted post-partum contact between mother and infant has shown to positively affect infants by NAS (Short, Gannon, & Abatemarco, 2016).

**Pharmacological Interventions**

Nine studies discussed the importance of pharmacological interventions in the treatment regimen for infants with NAS.

In a retrospective cohort study previously discussed, pharmacological treatment began if Finnegan scores exceeded 8 on 2 occasions or was greater than 10 on 1 occasion. Morphine commenced for poly-drug and opiate-exposed infants and increased or decreased 10% every 2-3 days to maintain a Finnegan score of less than 8. Phenobarbital was given in addition to morphine if symptoms were uncontrolled. Overall treatment in the breast milk group was 20 days less than those in the formula group, while the maximum amount of morphine was lower in the breast milk group (Abdel-Latif et al., 2006).

In the reviewed case study, the infant was given morphine and phenobarbital, and these medications were titrated accordingly based on Finnegan scores (Gottesman, Chang, Feldman, & Ziegler, 2018). In the second month of treatment, the infant switched to a 20-calorie per ounce term formula, and slowly began to wean from phenobarbital and morphine. However, the infant re-exhibited signs of withdrawal through hyperirritability, and high-pitched cries, therefore morphine and phenobarbital were continually titrated. The infant continued to show signs of

withdrawal at month 3. At month 4, phenobarbital was titrated, methadone was added to support withdrawal, and morphine was removed. At month 5, Finnegan scores were decreasing, while weight gain was increasing. At month 6, after transitioning to 24-calorie per ounce term formula with iron, the infant had a weight gain of 7.4 g/d, Finnegan scores were low, and methadone was discontinued (Gottesman, Chang, Feldman, & Ziegler, 2018). Pharmacological therapy is a necessity for the treatment regimen in helping infants with NAS.

A retrospective cohort study discussed the factors that impact maternal and neonatal factors that impact response to methadone therapy for neonatal abstinence syndrome (Isemann, Meinzen-Derr, & Akinbi, 2011). Infants were scored using the Finnegan Scoring System, and received methadone per protocol if signs of NAS continued, post-non-pharmacological management. Infants that required adjunctive therapy with phenobarbital were born of mothers on higher doses of methadone and had longer lengths of stay compared with infants managed with methadone therapy alone. Maternal methadone maintenance dose during pregnancy positively correlated with overall length of stay. There was an inverse relationship between the amount of mother's breast milk ingested, and overall length of stay (Isemann, Meinzen-Derr, & Akinbi, 2011).

A mixed-methods pilot study consisted of an intervention and a control group. The intervention group received support based on practical breastfeeding advice, promotion of maternal self-efficacy through encouragement and persuasion, and provision of neonatal self-consolation techniques within a low-stimuli environment. Of the intervention group, 28% required pharmacotherapy for severe withdrawal compared with 57% in the control group (MacVicar, Humphrey, & Forbes-McKay, 2017).

In a focus group methodology, information was gathered from 12 participants including NICU nurses and speech therapists through two separate focus group discussions (Maguire, Shaffer-Hudkins, Armstrong, & Clark, 2018). The study revealed that pharmacological management with opioid replacement therapy is of value, because it dampens the central nervous system irritability that leads to disrupted feeding, and therefore to increased mal-adaptive manifestations and poor weight gain (Maguire, Shaffer-Hudkins, Armstrong, & Clark, 2018).

A retrospective cohort study conducted by Pritham (2012) found that exposed neonates receiving NAS treatment either through receiving methadone maintenance therapy or buprenorphine maintenance therapy who were also breastfed began first line therapy with phenobarbital 1.1 days later and their length of stay was shorter by 9.4 days as compared to formula-fed neonates or neonates who received formula and breastmilk (Pritham, 2012).

An additional retrospective cohort study consisted of two groups, including: opioid-dependent pregnant women on methadone maintenance therapy (MMT), and opioid-dependent pregnant women on buprenorphine maintenance therapy (BMT). This study found that benzodiazepine use is a predictor variable for length of treatment for NAS. Neonates exposed to methadone and benzodiazepines while in utero and who were born at term had significantly longer length of treatment for NAS when compared with unexposed neonates or to exposed neonates born prematurely. Also, associated exposure to SSRIs with MMT did not prolong length of stay. Additionally, neonates exposed to buprenorphine experienced less severe NAS and shorter length of stay than those exposed to methadone by seven days (Pritham, Paul, & Hayes, 2012).

**Non-Pharmacological Interventions**

Five studies discussed the importance of non-pharmacological interventions in infants with neonatal abstinence syndrome.

A mixed-methods pilot study evaluated the feasibility of an intervention that included environmental modifications such as minimizing external stimuli through temperature control, reduced activity, and regulated noise (MacVicar, Humphrey, & Forbes-McKay, 2017). Infants in this study were nursed in a shielded cot and canopy to limit exposure to light. The mother was provided and instructed with consolation techniques including non-nutritive sucking, and loose swaddling for self-soothing purposes for the infant. The intervention group had higher breastfeeding rates, and higher confidence in terms of breastfeeding ability than those in the control group (MacVicar, Humphrey, & Forbes-McKay, 2017).

A focus group methodology by Maguire, Shaffer-Hudkins, Armstrong, and Clark (2018) showed that neurobehavioral organization plays an important role in successful feeding. Often times, the baby is not ready to feed when picked up, as a result nursing assessment of feeding cues were crucial for success when feeding infants with NAS. Additionally, a technique that achieved feeding goals on a certain day may not work again the next day, requiring continued trial and error by providers. Swaddling and decreasing environmental stimuli can assist in calming and comforting the infant during feeding, thereby increasing weight gain in a timely manner.

Swaddling is one of the few non-pharmacological interventions reported to be effective in infants with NAS to reduce crying. Swaddling can also decrease startles and sleep arousals, which leads to increased sleep time and continuity of restful states between feedings. The C-position holding method was discussed, where the infant is placed on his side, lying on the

informants' legs, with arms slightly flexed, keeping the head of the infant slightly elevated by crossing one leg over the other. Warm baths have been used to calm infants with NAS prior to feeding as well. Informants in this study emphasized the importance of vertical versus horizontal rocking to calm the infant. Most informants reported trying all available nipples until they found the nipple most effective for the infant, and most reported using chin and cheek support as needed (Maguire, Shaffer-Hudkins, Armstrong, & Clark, 2018) in infants with NAS to increase amount of time during feeding sessions.

A study randomized to intervention showed that even highly irritable infants can enjoy a significant reduction in distress by being laid in the prone position. Infants experiencing withdrawal showed significantly lower levels of distress and lower withdrawal scores when laid in the prone position compared with similar infants kept supine (Maichuk, Zahorodny, & Marshall, 1999).

A retrospective cohort study by Short, Gannon, and Abatemarco (2016) showed that other nonpharmacological interventions both compliment and support the act of breastfeeding, such as skin to skin contact, and kangaroo care. These positions can lead to optimized weight gain, and reduction in length of stay, and overall cost spent in infants with NAS having difficulty feeding (Short, Gannon, & Abatemarco, 2016).

A prospective design, with a random assignment of drug-exposed and non-exposed newborns to either a control or experimental group, showed that through auditory, tactile, visual, and vestibular (ATVV) intervention, the drug-exposed experimental group trended toward greater active sleep. The non-exposed infants who received ATVV intervention had 19% more alertness during the intervention period than the non-exposed control infants during the same period of observation. ATVV intervention consisted of a 15-minute procedure, consisting of

infant-directed talk, continuous throughout the procedure (auditory), 10 minutes of light stroking/infant massage (tactile), eye-to-eye contact during alert periods (visual), and vertical rocking of the swaddled infant for 5 minutes post massage (vestibular) (White-Traut et al., 2002). This intervention is to be conducted prior to feeding intervention to help dampen the central nervous system, and optimize greater weight gain during feeding periods.

# DISCUSSION

The studies reviewed in this work provide insight into the common clinical manifestations of infants with neonatal abstinence syndrome. Research findings revealed the main outcomes of interventions commonly used in treating infants with NAS, to increase the opportunity for weight gain. Though the reviewed literature did not have a confirmatory, singular agreement on the interventions for feeding positions with regard to NAS infant weight gain, there are main themes that prevailed through multiple articles that were shown to positively affect outcomes of infants with NAS, while optimizing periods for weight gain.

## Breastfeeding Promotion

In the absence of outstanding contraindications, including mothers currently using methadone maintenance therapy (MMT), buprenorphine maintenance therapy (BMT), or other appropriate and equal therapies, breastfeeding should be promoted by nurses and healthcare professionals in efforts to help reduce the severity of neonatal abstinence syndrome, and optimize weight gain in infants. Several studies had positive correlations with breastfeeding in comparison to reduction in length of stay, and reduction in likelihood of requiring pharmacological treatment than infants who were formula-fed (Abdel-Latif et al., 2006; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Pritham, 2012; Pritham, Paul, & Hayes, 2012; Short, Gannon, & Abatemarco, 2016).

Infants in multiple articles were assessed using the Finnegan Scoring System (Abdel-Latif et al., 2006; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Newman et al., 2015). This

scoring system is broken into three different systems including, central nervous system disturbances, metabolic vasomotor/respiratory disturbances, and gastrointestinal disturbances. Infants are scored with varying numbers of 1-3, dependent on the specific clinical manifestations in each system. Infants are assessed every 2 hours with the Finnegan Scoring System, while daily weights are additionally recorded. ("The Assessment and Management", 1992). During this time, healthcare providers can continually monitor an infants tolerance to feedings, daily weight gain, growth patterns, velocity goals, head circumferences, length measurements, changes in electrolytes, and implementation of pharmacological interventions. Health care providers can track changes, monitor interventions, and keep detailed records, about feeding and weight gain to advocate and support infants with NAS and their families.

Management of the clinical manifestations associated with infants exposed to drugs in utero is useful in promoting feeding and positioning during feeding to ensure weight gain. Promotion of breastfeeding and skin-to-skin feeding options are of value to feeding infants with NAS when safe. Though breastfeeding may not be desired, or possible in every case, education on the benefits and drawbacks directed at the infant's mother and how and the positive affect on their infants weight gain and immunologic protection is of value. The literature shows significant correlation between breastfeeding in infants with NAS and decreasing length of stay in the hospital, thereby reducing overall cost of stay. Breastfeeding also has been correlated with decreased need for pharmacological intervention in infants with NAS, and a less severe course of withdrawal.

Lower rates of breastfeeding among NAS infants is not unexpected and associated with higher NICU admission rates and/or the physical manifestations commonly found in women using drug therapy during pregnancy. Healthcare providers can assist in creating an environment

that is more feasible to breastfeeding, and promote the significance of breastfeeding for vulnerable populations, such as infants born to women using drugs during pregnancy. Discussion about the immunologic and protective benefits of breastfeeding can improve both the women's health and their infants. Education provided to families about interventions to help control the physical manifestations of NAS that can be barriers to the breastfeeding process should be explored. Understanding the mechanics of breastfeeding can be difficult for women after birth of their child however, healthcare can be prepared and willing to teach proper techniques conducive to breastfeeding an infant with NAS.

**Rooming-in Promotion**

Rooming-in has been positively correlated in three articles (Abrahams et al., 2007; Newman et al., 2015; Short, Gannon, & Abatemarco, 2016). Rooming-in is useful in infants with NAS that are transitioned from the NICU to the nursery or that are physiologically stable enough to require less monitoring. The process of rooming-in allows women to stay in the same room with their infants after delivery, rather than being placed on a different unit. Rooming-in has been shown to reduce pharmacological treatment, length of stay of infants, overall cost, and hospital resources. Rooming-in aids in the infants' transition to extra-uterine life and promotes better care from the mother. This approach allows the infant to be discharged in the custody of the mother in a timely manner compared to mother-child dyads not involved in rooming-in. Inspiring autonomy in women post-partum can be promoted by involving her in the care of her infant shortly after birth which is easier if the child is in direct proximity. Rooming-in is an important intervention for both the woman and the infant. Infants born with NAS can benefit

from multiple family members being present for feeding on demand and immediate soothing of the clinical manifestations of NAS.

**Pharmacological Interventions**

Pharmacological interventions are often necessary in infants experiencing NAS. Nine studies discussed the importance of pharmacological intervention in the treatment regimen for infants with NAS (Abdel-Latif et al., 2006; Abrahams et al., 2007; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Maguire, Shaffer-Hudkins, Armstrong, & Clark, 2018; Newman et al., 2015; Pritham, 2012; Pritham, Paul, & Hayes, 2012). Phenobarbital, methadone, and morphine are consistently used in the treatment regimen for infants with NAS exposed to opioids during pregnancy, and are used according to a facility's policy. Other interventions can be used prior to, and in conjunction with pharmacological interventions. Benefits and drawbacks of drug therapy in infants with NAS should be explained in depth to families. Pharmacological management with opioid replacement therapy can reduce the central nervous system irritability that leads to disrupted feeding, and therefore poor weight gain. Pharmacological intervention has been associated with decreased length of stay, treatment duration, clinical manifestations and overall cost.

**Non-Pharmacological Interventions**

Non-pharmacological interventions should be explored early in the development of the treatment regimen for an infant with NAS to improve physiologic outcomes, such as weight gain. Across five separate studies (MacVicar, Humphrey, & Forbes-McKay, 2017; Maguire, Shaffer-

Hudkins, Armstrong, & Clark, 2018; Maichuk, Zahorodny, & Marshall, 1999; Short, Gannon, & Abatemarco, 2016; White-Traut et al., 2002), various interventions are discussed to improve physiologic outcomes for infants with NAS. Minimizing external stimuli, maintaining temperature control, reducing activity, regulating noise, loose swaddling, limiting exposure to light, warm baths, C-positioning, and horizontal rocking are examples of non-pharmacological interventions that had positive outcomes for improved feeding and weight gain. Education about different methods of consoling infants with NAS to improve length of time during each feeding, and how to read feeding cues that are different from NAS symptoms can improve weight gain and decrease the amount of time spent in the NICU or facility. Women and families not educated about feeding infants with NAS can become easily frustrated and struggle to maintain motivation to feed their infants. This can lead to less than optimal weight gain and failure to thrive, increased need for health care services, and costly health care.

Skin to skin contact, chin to cheek support, and ATVV intervention can promote improved physiologic outcomes in infants with NAS. Non-pharmacological interventions to increase length of time feeding can assist with lowering levels of distress, optimizing weight gain, reducing length of stay, and therefore reducing overall cost spent (White-Traut et al., 2002).

**Length of Stay & Overall Cost**

Nine articles reflect on the interventions previously mentioned, and their effects on decreasing length of stay, and therefore, reducing overall cost for families of infants with NAS (Abdel-Latif et al., 2006; Abrahams et al., 2007; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Newman et al., 2015; Pritham, 2012; Pritham, Paul, & Hayes, 2012; Short, Gannon, &

Abatemarco, 2016). “According to The March of Dimes, the length of an average NICU stay hovers at around 13.2 days. That’s an average cost of $39,600, not factoring in the pregnancy and birthing costs” (Norsworthy, 2017). Optimizing feeding position and greater nutrient intake in an infant with NAS to improve weight gain can reduce length of stay in the NICU. It can also provide an opportunity for autonomy to the woman in caring for her infant and less exposure of the infant to potential pathogens found in acute care facilities.

## LIMITATIONS

Several limitations were noted in this review of literature. Initial search results revealed numerous findings on keywords neonatal abstinence syndrome, clinical manifestations, NICU, weight gain, feeding, nutrition, breast feeding, CNS disturbances, vomiting, irritability, diarrhea, cost, and duration; however, fewer original research articles remained relevant to the purpose of this literature review. Search terms were expanded to include keywords symptoms, benefit, high-calorie formula, in order to provide more relevant search results. Inclusion and exclusion vary between studies and are not defined by concrete widespread criteria used across all articles, therefore limiting the definitive review of specific topics discussed in this literature review.

Many studies were limited by the lack of research in a wider drug-regimen including non-opiate effects with drugs including amphetamines, and cannabinoids (Abdel-Latif et al., 2006; Maguire, Shaffer-Hudkins, Armstrong, & Clark, 2018; Maichuk, Zahorodny, & Marshall, 1999; Pritham, Paul, & Hayes, 2012; Short, Gannon, & Abatemarco, 2016). The limitation on analyzing effects of a wider range of drugs should be taken into consideration, reflecting that maternal substance abuse is inclusive of a wide array of narcotics including, but not limited to: stimulants, barbiturates, opiates, cocaine, sedatives, marijuana, and nicotine. It is estimated that about five percent of pregnant women will use one or more addictive substances throughout their pregnancy ("Substance Use in Women", 2018). With a 300% increase from 1.5 hospital births to 6 per 1,000 hospital births as of 2013, it is evident that we must take a stand as healthcare professionals to educate and provide resources in the community setting (Ko et al., 2016).

Furthermore, the degree and duration of prenatal narcotic exposure needs to be taken into consideration. A limitation in many studies in this literature review was the varying degree and duration of exposure to medications in utero. As previously discussed, NAS is individualized and

will present differently amongst infants. Therefore, the varying degrees of narcotic exposure, if known, should be recorded and considered when implementing appropriate interventions.

There are difficulties obtaining information about drug use during pregnancy in suspected cases due to the fear of incarceration or lawful repercussions. The limited availability of medical records, and accuracy of documentation to exposure history is a limitation that must be taken into consideration (Pritham, Paul, & Hayes, 2012). A major limitation in this literature review was the essence of self-reporting. Often times, women feel judged by healthcare providers for a history of substance abuse, whether drug therapy was taken throughout pregnancy, or not. This presents a major challenge for healthcare providers due to the necessity of the data in implementing appropriate interventions for infants with NAS. For example, cannabis or marijuana is not fully researched on the effects or the health impact during developmental milestones of infants in utero. Due to the unreliable nature of self-reporting, the number of women using marijuana during pregnancy is unknown, though there has been substantial evidence of statistical significance between marijuana smoking throughout pregnancy, and low birth weight ("Substance Use in Women", 2018). Data regarding stimulant use during pregnancy and the effects on the neonate are not fully understood. There have been effects linked to low birth weight, smaller head circumference, irritability, hyperactivity, tremors, high-pitched cries, and excessive sucking at birth ("Substance Use in Women", 2018) due to stimulant use during pregancy.

Furthermore, pregnant women are not aware of the damage opioid abuse and prescription drug therapy during pregnancy can have on the fetus and in some instances the disadvantages to the fetus are not clearly defined. A limitation in this literature review dealt with the lack of differentiation between legitimate use of an opioid prescription and maternal opioid abuse

(Short, Gannon, & Abatemarco, 2016). In-depth information about prescriptive drug regimens during pregnancy and the teratogenic effects that can result in fetal deprivation of nutrients are unknown for many drugs. There were also limitations in two studies that focused on the lack of identification in maternal opioid dependence drug regimens used for treatment, which may have influenced length of stay, and overall cost spent for the NAS infants time in NICU (Pritham, Paul, & Hayes, 2012; Short, Gannon, & Abatemarco, 2016). Commencement and duration of maternal treatment (MMT and BMT) during pregnancy varied greatly, and should also be taken into consideration.

There was a widespread limitation across articles that used single sites to conduct their studies. Additionally, the lack of prospective studies became evident while determining articles to utilize in this literature review.

Lastly, the use of scoring tools to assess NAS withdrawal severity posed challenges when regarding possible subjective observer bias. This variability in the assessment of NAS changes implementation of appropriate interventions for infants, and may contribute to greater length of stay and overall cost, based on the differing interpretations of the condition. Six articles discussed the use of the Finnegan Scoring System, and/or the Neonatal Abstinence Scoring System (Abdel-Latif et al., 2006; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Maichuk, Zahorodny, & Marshall, 1999; Newman et al., 2015).

## Recommendations for Feeding Management to Promote Weight Gain in Infants with NAS

### Implementation of Breastfeeding Promotion

Breastfeeding practices should be promoted by healthcare professionals so long as no outstanding contraindications are present, urine drug screens are negative, and mothers are actively participating in methadone maintenance therapy, buprenorphine maintenance therapy, or other appropriate and equally substantial therapies (Pritham, Paul, & Hayes, 2012). Studies in this literature review have shown that breastfeeding should be encouraged to aid in the reduction of clinical manifestations regarding neonatal abstinence syndrome, decreasing the need for pharmacological interventions, reducing length of stay, while also optimizing weight gain in infants.

### Implementation of Rooming-in Promotion

Rooming-in, when appropriate, is an intervention that can be explored regarding the reduction of clinical manifestations of NAS, and improving weight gain in infants with NAS. Furthermore, rooming-in has been associated with greater likelihood of retaining custody of the infant, reduction of pharmacological treatment, length of stay, overall cost, and hospital resources.

### Implementation of Pharmacological and Non-Pharmacological Interventions

Pharmacological interventions are often necessary in the plan of care for infants with NAS. The use of both pharmacological and non-pharmacological interventions are important in reducing clinical manifestations of NAS, and therefore increasing opportunities to optimize weight gain. These interventions are also associated with decreased length of stay, treatment duration, and overall cost. The use of skin to skin contact, auditory, tactile, visual & vestibular

(ATVV) intervention, C-positioning, warm baths, decreased eye contact, and reduced environmental stimuli should be used frequently in conjunction with pharmacological treatment.

**Research**

Further research is needed to determine the correlation between dose-related effects of prenatal narcotic and stimulant exposure, regarding their effects on NAS, and how they affect clinical manifestations displayed by infants, and infant's ability to feed in different positions for weight gain. The effects of non-opiate drugs on infants with NAS is not widely understood. Though the rise in opiate use during pregnancy is a serious concern, exploring the gaps in research regarding non-opiate drugs use during pregnancy, and their effects on NAS and infant feeding and weight gain is of value.

Though the articles included in this literature review were helpful in identifying current challenges in the management of NAS to improve feeding and weight gain, further qualitative research from the nurses' perspective, as well as the perception of the many families, regarding infant feeding to promote weight gain would be of value to decreasing length of time and cost. The psychosocial stressors of financial duty regarding severity of NAS, and length of stay were present in these articles, but should be further explored from a psychological standpoint. Additionally, the challenges of self-reporting should be researched further, so that proper interventions may be implemented according to not only clinical manifestations present during interaction with the pregnant woman, but through quantitative data related to commencement during gestational age, type of drug, and duration of use.

**Education**

Successful implement of meaningful feeding interventions to improve weight gain in infants with NAS include decreasing the clinical manifestations of NAS, optimize weight gain

with a nutrient dense formula or breast-milk, and reducing the need for pharmacological treatment. Health care providers are effective in providing communication and consolation techniques with not only the infant with NAS, but the families of the infant as well, to promote better bonding patterns, which can improve feeding. Families, if present, can be included during treatment plans to promote autonomy and to make preparations to care for the infant after discharge. There is a need for prevention and resource education regarding maternal substance abuse, as well as prescribed drug therapy throughout pregnancy.

**Nursing Practice**

Research findings have many implications for nursing practice. The responsibility of not only a nurse, but a healthcare professional is to stay knowledgeable with current evidence-based research, and implement the research into their daily practice. It has been proven that nurses who are caring for infants who are actively experiencing withdrawal symptoms from neonatal abstinence syndrome can reduce clinical manifestations by laying the infant prone for "tummy time." There are many variables to consider when configuring the best feeding practice for infants with NAS. Often times, feeding position preference can change daily, or during every intervention period. What works one day, may not work the next, and it's imperative that nurses find the right position to soothe the infant, and optimize weight gain. Additionally, there are multiple factors regarding the fluctuation of severity of neonatal abstinence syndrome. Medications are often titrated, and environmental factors may not remain the same each day. Therefore, the severity of NAS can be highly influenced by changes in the environment, and can pose as further challenges in managing the positioning and intake of infants with NAS.

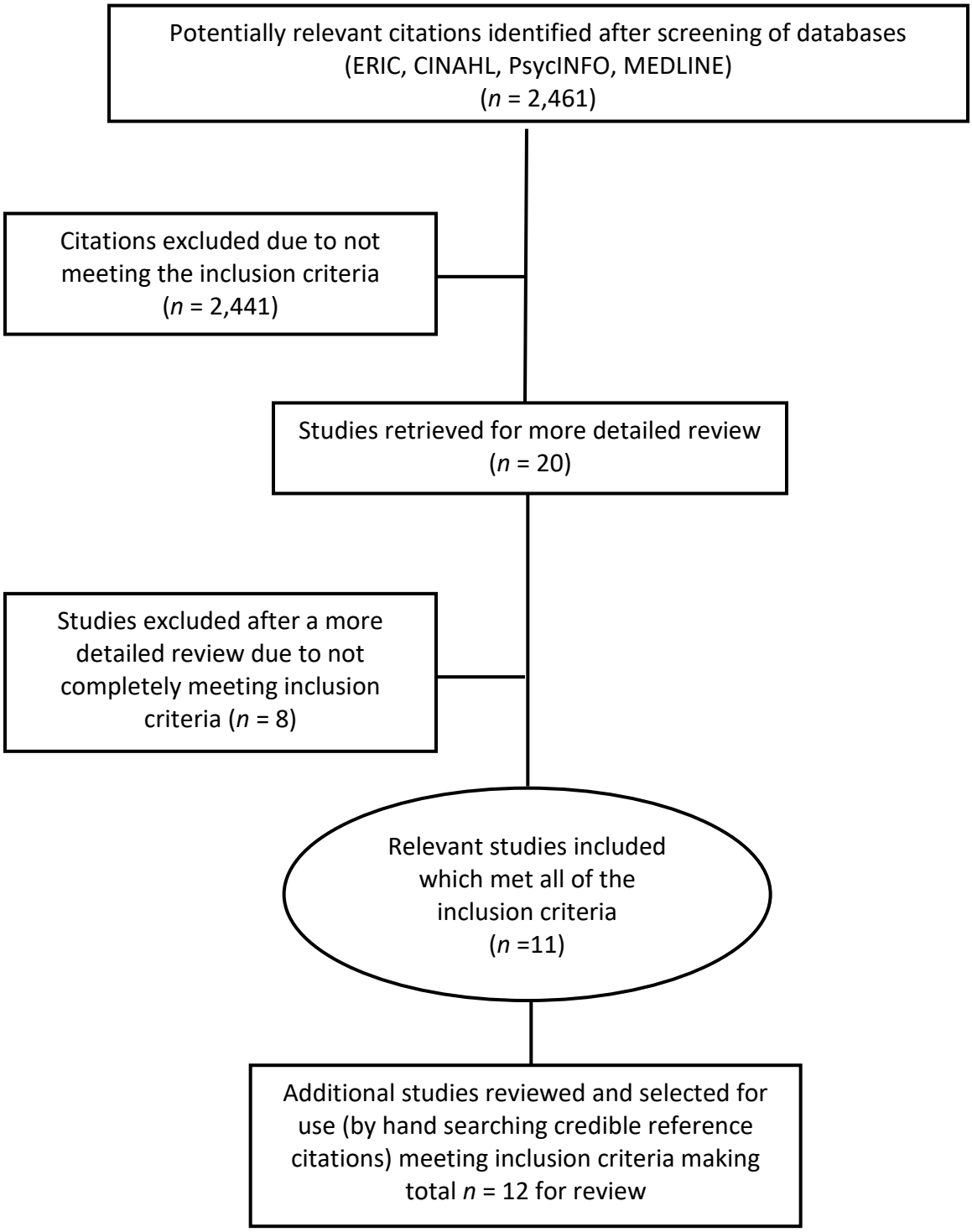
Regarding feeding, the C-position, where the infant is placed on its side, lying on the caregiver's legs, with arms slightly flexed, keeping the head of the infant slightly elevated by

crossing one leg over the other has been proven to be helpful in the optimization of weight gain. Additionally, while holding the infant, placing the infant in a side-lying position while supporting their weight on your chest or stomach, and using chin and cheek support has been especially helpful in managing nutritional intake for infants with NAS.

**Conclusion**

Current research regarding breastfeeding promotion, rooming-in, pharmacological and non-pharmacological treatments has potential to influence nursing practice in the management of feeding positions, nutritional intake, and weight gain in infants with neonatal abstinence syndrome. The literature suggests various approaches to feeding techniques are required and can benefit the infant and post-partum woman through reduction in the severity of clinical manifestations for infants with NAS, reduced length of stay, reduced cost, and improved weight gain in infants (Abdel-Latif et al., 2006; Abrahams et al., 2007; Gottesman, Chang, Feldman, & Ziegler, 2018; Isemann, Meinzen-Derr, & Akinbi, 2011; MacVicar, Humphrey, & Forbes-McKay, 2017; Maguire, Shaffer-Hudkins, Armstrong, & Clark, 2018; Newman et al., 2015; Pritham, 2012; Pritham, Paul, & Hayes, 2012; Short, Gannon, & Abatemarco, 2016). However, the correlation between dose-related effects of both opiate and non-opiate exposure in utero on optimization of weight gain through improved feeding techniques and nutrient intake is unclear. Though the reduction of clinical manifestations can improve breastfeeding promotion, rooming-in, pharmacological and non-pharmacological interventions has been established in the literature, further research must be conducted to fill the gaps of knowledge on subtopics that aren't fully understood. The use of these interventions has been associated with improved health-related outcomes, and reduced clinical manifestations, leading to optimized weight gain in infants with NAS.

# APPENDIX A: FIGURE




Key Search Terms = Neonatal abstinence syndrome*, clinical manifestations*, symptoms*, benefit*, NICU*, weight gain*, feeding*, nutrition*, high-calorie formula*, breast feeding*, CNS disturbances*, vomiting*, irritability*, diarrhea*, cost*, and duration*
Limiters = English language, peer-reviewed, published between 1995-2018

Figure 1: Selection Method of Literature

# APPENDIX B: TABLE OF EVIDENCE

Table 1: Table of Evidence

| Author(s) Year Location | Study Design and Purpose | Sample Size | Intervention Protocol | Screening Measures | Outcome Measures | Key Findings and Limitations |
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| Abdel-Latif et al. (2006) Australia | Retrospective cohort study<br><br>The purpose of this study was to assess the effects of breast milk feeding on the severity of neonatal abstinence syndrome (NAS) in a population of infants of drug-dependent mothers who were at risk of NAS. | n=190<br><br>Breast milk n=85<br><br>Formula n=105 | Infants were assessed with the Finnegan objective Scoring System before the first feed, and were assessed before every feed for the duration of admission.<br><br>Swaddling, frequent feeds, and nursing in quiet environments were applied from birth.<br><br>Pharmacological treatment began if the Finnegan score exceeded 8 on 2 occasions or was >10 on 1 occasion.<br><br>Morphine was started at 0.5 mg/kg per day in 4 divided doses for polydrug and opiate-exposed infants and increased or decreased 10% every 2-3 days to maintain an average | This study included infants of drug dependent mothers admitted to a local Australian hospital, between 1998 and 2004.<br><br>190 total consecutive charts were reviewed for maternal and infant data for this study.<br><br>In this specific hospital, infants born to drug-dependent mothers were nursed with their mothers in the postnatal wards unless there were medical or social contraindications.<br><br>All mothers were encouraged to breastfeed or express their milk for bottle or gavage feedings unless it was contraindicated. | The mean Finnegan scores for the first 9 days of life were considerably lower in breast milk infants.<br><br>The median time to withdrawal occurred considerably later in breast milk infants in comparison to the formula group (10 vs 3 days; $P < .001$).<br><br>Breast milk infants were less likely to require pharmacologic treatment for withdrawal (59.0% vs 79.0%, respectively $P < .001$).<br><br>6 (7.0%) infants from the breast milk group, and 18 (17.1%) from the formula group required phenobarbital in addition to the morphine to control NAS. | Among 190 infants born to drug-dependent mothers in New South Wales, breast milk significantly reduced the severity of NAS and reduced the length of hospital stay. The length of stay among infants who were breastfed was 14.7 days compared to 19.1 days for non-breastfed infants ($p = 0.049$).<br><br>The Finnegan scores for the formula group were consistently higher in the groups of premature infants and those who were exposed to polydrug, methadone, opioid, or maternal methadone use >80 mg/kg per day. There was no difference in Finnegan scores between breastfed infants and those given breast milk by bottle or gavage tube within the breast milk group.<br><br>Overall treatment in the breast milk group was 20 days less than those in the formula group. The maximum amount of morphine was lower in the breast milk group. Breast milk was found to be independently associated with a lessened need for pharmacologic treatment for NAS.<br><br>Limitations: The majority of the infants in the study were exposed to opiates, and only a few were exposed to stimulants such as cocaine and amphetamines. No reliable system has been found for |

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| | | | Finnegan score of <8.<br><br>Phenobarbital was given to polydrug opiate-exposed infants in addition to morphine if symptoms were uncontrolled. | | | accurately assessing non-opiate effects, resulting from those such as cocaine, cannabinoids, and amphetamines. |
| Abrahams et al. (2007) Canada | Retrospective cohort study<br><br>The purpose of this study was to evaluate the effect of rooming-in (rather than standard nursery care) on the incidence and severity of neonatal abstinence syndrome among opioid-exposed newborns and on the proportion of mothers who retain custody of their babies at | n=106 Total sample of methadone or heroin using women<br><br>n=32 Rooming-in mothers<br><br>n=38 Mothers who gave birth at a local hospital before the rooming-in program<br><br>n=36 Mothers who reported use of heroin or methadone, | A rooming-in care program. Routine care, instruction by nursing staff on how to care for the baby and how to identify symptoms of NAS. Parenting skills and symptoms of NAS were assessed and observed. Mothers were consulted about their observation of NAS in their newborns.<br><br>Before rooming-in group: The same approach to obstetric care as the study group, with no rooming-in. Babies were kept in a nursery, separate from their mothers during the first week of life. | This study included women referred by a local hospital who were identified as users of illicit drugs such as heroin or methadone, or whose newborns were identified as showing symptoms of opiate withdrawal. | Among women who had had children previously, fewer in the rooming-in group had retained custody of at least 1 child (7.7%) than in the local hospital comparison group (15.6%) or the additional local hospital group (22.6%).<br><br>More women in the rooming-in group were breastfeeding (62.5%) than women in the BCWH group (7.9%) or the Surrey group (11.1%) were.<br><br>Newborn length of stay in hospital was significantly shorter in the rooming-in group compared with the BCWH comparison group (β- | Rooming-in was associated with substantially reduced rates of newborn treatment with morphine, length of morphine treatment, vomiting, admission to a level II nursery, and length of stay in hospital. Mothers who roomed in were much more likely to retain custody of their newborns.<br><br>Newborns who roomed-in at BCWH were much more likely to be discharged in the custody of their mothers than infants in the other groups.<br><br>Overall, rooming-in is associated with easing a newborns' transition and promote better care from the mother.<br><br>Limitations:<br>The subjects were non-randomly allocated. The subjects didn't choose their study groups. The research cannot exclude the possibility that mothers of newborns who didn't show signs of NAS weren't included in this study. The mother-infant dyad was included if the newborn showed signs of NAS within the first few days of life. |

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| | hospital discharge. | or whose babies were admitted to a level II observation nursery at an additional local hospital. | Heroin/methadone use &/or observation nursery: Babies were kept in a nursery, separate from their mothers during the first week of life.<br><br>Morphine was prescribed as needed for all 3 groups, and was titrated to control symptoms. | | coefficient for cohort membership 1.17, standard error 0.46, *P* = .01), adjusted for maternal methadone dose at delivery and involvement of the father. | |
| Gottesman et al. (2018) United States of America | Case Study<br><br>The purpose of this study was to expand the research on a vulnerable population in regard to neonatal abstinence syndrome and nutritional challenges many neonates affected by NAS face. | n=1 infant | Baby N was started on a transitional formula initially. Baby N received a full nutrition assessment (recommendation for oral feeding modifications, adjustment of formula goal rate, and evaluation of growth patterns) on day 2 of life, and was reassessed every 3-5 days while he remained in the intermediate nursery.<br><br>Monitoring of tolerance to feedings, daily weight gain, tracking of growth | Baby N was admitted to an intermediate nursery in July of 2016, born at 38 weeks and 4 days' gestation and was delivered via C-section. Apgar scores at 1 minute and 5 minutes were recorded, and were 8 and 9 respectively.<br><br>Baby N displayed signs and symptoms of NAS including: tremors, jitteriness, and high-pitched cries postnatally.<br><br>Baby N's anthropometric measurements at birth were a weight of 2355 g, length of | Each month, Baby N experienced a change in feeding regimen to lessen the severity of NAS, and to meet goals for anthropometric measurements, which were additionally recorded each month.<br><br>Initially, Baby N started on a transitional formula. At month 2, he switched to a 20-calorie per ounce term formula, which lead to a weight gain of 36.2g/d. He slowly began to wean from phenobarbital and morphine. However, he re-exhibited signs of withdrawal | The experience of Baby N displays the challenges that many infants with NAS face. He was small for gestational age, had poor growth, was irritable at meal times, had an increased length of stay in the hospital, and showed poor growth.<br><br>Though Baby N's formula goals were continually adjusted to promote better weight gain, total gains in length, head circumference, and weight remained less than desired.<br><br>Breastfeeding has shown to be best for the infant with NAS. Breastfeeding has been associated with clinical outcomes through reductions in the severity of NAS, duration of treatment, and overall length of stay. The benefits of breastfeeding for this vulnerable group outweigh any of the potential risks, granted that the mother is on a stable dose of methadone or buprenorphine, and is actively involved in an opioid management program. |

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| | | | velocity goals, weekly head circumference and length measurements, monitoring changes in electrolytes, and implementation of nutrition-related medications (vitamins, and minerals).<br><br>Each month, feeding regimens were changed, anthropometric measurements were recorded, Baby N was continually assessed by the Finnegan scoring system, and pharmacological regimens were added in accordingly.<br><br>Morphine and phenobarbital were ordered, administered, and titrated based on Finnegan scores. | 46.5 cm, and head circumference of 32.5 cm. | through hyperirritability and high-pitched cries, therefore morphine and phenobarbital were titrated accordingly. At month 3, Baby N stayed on the 20-calorie per ounce term formula, and had a weight gain of 25 g/d. He continued to show signs of withdrawal. At month 4, Baby N continued to receive 20-calorie per ounce term formula. He gained 25.7g/d, and Finnegan scores remained elevated. Phenobarbital was titrated, methadone was added to support withdrawal, and morphine was removed. At month 5, Baby N transitioned to a 24-calorie per ounce preterm formula to promote weight gain. He had a weight gain of 11.5 g/d. Finnegan scores were decreasing, and phenobarbital and methadone were titrated. At month 6, | Limitations in NAS research:<br>Few studies have addressed nutrition interventions for infants with NAS when breastfeeding is not an option. There are limited prospective studies or clinical trials available to base NAS nutritional management decisions. |

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| | | | | | Baby N remained on the 24-calorie per ounce term formula with iron. He had a weight gain of 7.4 g/d. Finnegan scores were low, and methadone was discontinued. | |
| Isemann et al. (2011) United States of America | Retrospective cohort study<br><br>The purpose of this study was to identify maternal and neonatal factors that impact response to methadone therapy for neonatal abstinence syndrome. | n=142 total infants<br><br>n=128 infants' post-exclusion<br><br>n=36 preterm infants<br><br>n=92 term infants | Pharmacotherapy for opiate withdrawal to identify factors associated with favorable response to methadone therapy.<br><br>Infants were scored with the Finnegan Scoring System. Infants received methadone per protocol if signs of NAS continued. Post-non-pharmacologic management (swaddling, minimal tactile stimulation, dimmed lighting and frequent feeding).<br><br>Methadone therapy started at 0.1 mg kg orally every 4 hours, following two consecutive Finnegan scores | Inclusion: Most infants (82%) were born to mothers that received prenatal care. All patients were managed with methadone therapy. Other infants were born to mothers with a history of dependence on opiates or had urine drug screen positive for opiates. All newborn infants who were treated with at least one dose of methadone were eligible.<br><br>Exclusion: If infants had no documentation of methadone on their medical record, if opiates were administered before initiating methadone protocol, if the methadone protocol | Infants that required adjunctive therapy with phenobarbital were born of mothers on higher doses of methadone (median 90 (0 to 150) vs 60 (0 to 160) mg per day, P.0.04) and they had longer LOS (median 24.5 (12 to 93) vs 13.0 (3 to 43) days, P<0.0001) compared with infants managed with methadone therapy alone.<br><br>Methadone therapy was initiated at a later time (P = 0.04), was accelerated more frequently (P<0.01) and was supplemented with phenobarbital less frequently (P=0.002) in preterm infants compared with term infants. | There were no significant differences in the length of stay between neonates exposed to methadone in utero compared with infants that were additionally exposed to other classes of drugs such as benzodiazepines (n = 17), barbiturates (n = 7), cocaine (n = 23), selective serotonin reuptake inhibitors (n = 17), marijuana (n = 12), additional opiates (n = 29) or tobacco (n = 98).<br><br>Maternal breast milk feedings were associated with shorter median duration of methadone therapy in both term and preterm infants.<br><br>Compared with infants who were formula-fed, consumption of maternal breast milk was associated with shorter length of stay (median 12.5 (3 to 51) vs 18.5 (9 to 43) days, P= 0.01).<br><br>Limitations:<br>Incomplete collection of data from medical records.<br><br>The use of the Finnegan Scoring System to assess NAS was designed for term infants, and may not be sensitive in the assessment of NAS in preterm infants. |

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| | | | above 8. An eight-step tapered dosing regimen was followed, which was guided by Finnegan scores assessed every 4 hours.<br><br>If doses or steps in the eight-step tapered dosing regimen were skipped, infants were seen as having accelerated the taper. Infants unable to progress with continuously elevated Finnegan scores were seen as non-responders, and were additionally treated with phenobarbital at 10 mg/kg orally every 12 hours. | for initial dosing was not adhered to, if the infant was transferred to another hospital, or if the infant perished before the completion of methadone tapering. | Maternal methadone maintenance dose during pregnancy correlated with overall length of stay (P = 0.009). There was an inverse correlation between the amount of mother's breast milk ingested and length of stay (B = -0.03, P = 0.02). | Possible bias in initiating MBM therapy at lower doses, and more aggressive weaning of infants fed MBM, which may have contributed to earlier discharge. |
| MacVicar et al. (2017) United Kingdom | Mixed-methods pilot study<br><br>The purpose of this study was to evaluate the feasibility of the intervention and to assess whether a | n=53 total assessed for eligibility<br><br>n=14 total neonates' post-exclusion<br><br>n=7 intervention neonates | The intervention group received support based on practical breastfeeding advice, promotion of maternal self-efficacy through encouragement and persuasion, and provision of neonatal self-consolation | The subjects in this study were recruited from a combined specialist obstetric or substance abuse clinic.<br><br>Inclusion criteria included: Opioid substation medication therapy during pregnancy, intention to | On the fifth postnatal day, 100% (7 of 7) of the intervention group was still breastfeeding compared with 57% (4 of 7) of control participants.<br><br>Of the intervention group, 28% (2 of 7) required pharmacotherapy for | Questionnaire: Thematic analysis generated 5 key themes relating to breastfeeding support and substance exposure: (1) breastfeeding skill and knowledge, (2) psychological factors, (3) person-centered approach, (4) environmental modifications, and (5) postnatal experience on breastfeeding.<br><br>There was a demonstrated trend for continued breastfeeding on the fifth postnatal day, and intervention |

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| | future adequately powered randomized controlled trial was warranted. | n=7 control neonates | techniques within a low-stimuli environment. A scheduled session with a support worker was included, where collaboration resulted between mothers and support workers to identify breastfeeding barriers, opportunities to problem solve, and set individualized, family-centered goals. Additionally, environmental modifications took place, such as minimizing external stimuli through temperature control, reduced activity, and regulated noise.<br><br>The infants were nursed in a shielded cot and canopy to limit exposure to light. The mother was provided and instructed with consolation techniques including non-nutritive sucking, and loose swaddling for self- | breastfeed, > 36 weeks' gestation, and over 16 years of age.<br><br>Exclusion criteria included: Those who were HIV positive, ongoing illicit psychoactive drug or alcohol use, and had a child removal order in force. | severe withdrawal compared with 57% (4 of 7) in the control group.<br><br>The intervention group also had a shorter duration of hospitalization (mean 10.5 days) than the control group (mean 19.4 days). Collectively breastfed infants were less likely to require pharmacotherapy (3 of 11 breastfeeding vs 3 of 3 formula feeding). | participants reported increased breastfeeding confidence and satisfaction.<br><br>The intervention group had higher breastfeeding rates, and higher confidence in terms of breastfeeding ability than those in the control group.<br><br>Breastfed infants were less likely to require pharmacotherapy for neonatal withdrawal and had a shorter hospital stay than infants who were formula-fed (10.8 and 30.0 days, respectively).<br><br>Maternal experience of health care practices, attitudes, and postnatal environment influenced their perceptions of breastfeeding support.<br><br>Breastfed infants displayed a less significant course of withdrawal.<br><br>Limitations:<br>This study used a single site only, and there was homogeneity of the population. The research may not be representative of other locations, other than Scotland, where service in health care differs. |

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| | | | soothing purposes for the infant.<br><br>This intervention lasted from birth up to and including the fifth postnatal day.<br><br>Severity of neonatal withdrawal was assessed every 4-6 hours with the Finnegan Scoring System. | | | |
| Maguire et al. (2018) United States of America | Focus group methodology<br><br>The purpose of this study was to learn how caregivers who are expert in feeding infants with neonatal abstinence syndrome (NAS) successfully feed these infants during withdrawal. | n=12 total<br><br>n=10 RNs<br><br>n=2 occupational therapists | Information was gathered from 12 participants including NICU nurses and speech therapists, through two separate focus group discussions. | Data were collected from participants working in three regional hospitals with Level III NICUs.<br><br>NICU nurses, occupational therapists, and speech therapists who self-identified as experienced in feeding infants with NAS were included.<br><br>Four participants from each hospital.<br><br>All were female, most (11) worked full time. Their ages ranged from 31 to 65 years, years working in the | There were 4 overarching themes, and 8 subthemes that the data resulted in.<br><br>Overarching themes:<br>(1) Optimal medication management.<br>(2) Follow the baby's cues and be flexible with techniques.<br>(3) Calm and comfortable.<br>(4) Nurture the relationship.<br><br>Subthemes:<br>(1) Follow the baby's cues<br>(2) Flexibility with techniques | Results showed that pharmacologic management with opioid replacement therapy is very important, because it dampens the central nervous system irritability that leads to disrupted feeding.<br><br>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 collaborated with the medical team to re-evaluate the plan of care to achieve these goals.<br><br>Neurobehavioral organization plays an important role in successful feeding.<br><br>Informants reported that the baby is often not ready to feed when he is picked up, so nursing assessment of feeding cues was crucial for success. |

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| | | | | NICU ranged from 2-43, and years in their profession ranged from 2-43. | (3) Calm the caregiver<br>(4) A calm and comfortable baby before and during feeding.<br>(5) Encourage caregivers to be there.<br>(6) Provide continuity in caregiving.<br>(7) Build parent's confidence.<br>(8) Develop trust and avoid judgmental attitudes. | A technique that works one day may not work the next day, so continued trial and error is needed.<br><br>The informants strongly believed that anxiety in a caregiver could be felt by the infant, who was likely to react negatively.<br><br>Swaddling and decreasing environmental stimulation help calm the infant and keep him comfortable. Swaddling is one of the few nonpharmacologic interventions that has been reported to be effective in infants with NAS to reduce crying. Swaddling has been known to decrease startles and sleep arousals, which leads to an increase in sleep time, and continuity.<br><br>Informants also talked about an intervention called the C position they adapted for feeding. The infant is placed on his side lying on the informants' legs and arms slightly flexed, keeping the head of the infant slightly elevated by crossing one leg over the other.<br><br>Warm baths have been used to calm the infant, whereas others reported that they start by helping the infant to burp.<br><br>Most informants reported that they try all available nipples until they find the one that works the best for the infant, and most reported using chin and cheek support as needed. Informants used their gloved finger to find the "sweet spot" on the palate that helped infants form a good suck. |

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| | | | | | | Informants emphasized the importance of vertical versus horizontal rocking to calm the infant.<br><br>Some informants reported that they often bottle feed with the infant facing away from them when the infant cannot tolerate eye-to-eye contact, to decrease stimulation associated with eye contact, and is often successful if the infant opens his eyes.<br><br>Mothers were encouraged to nurture the relationship by being available for as many feedings as possible. Mothers were encouraged to learn infant cues and how their infant responds to different interventions.<br><br>Limitations:<br>Research needs to include more information on managing a wider range of street drugs. |
| Maichuk et al. (1999) United States of America | Randomized to intervention<br><br>The purpose of this study was to test the hypothesis that highly fretful, narcotic-withdrawing neonates experience less distress | n=48 total<br><br>n=25 prone-lying infants<br><br>n=23 supine-lying infants | Subjects in this study were assessed for withdrawal severity with the Neonatal Abstinence Scoring System (NASS), and through daily caloric intake.<br><br>Infants showing initial signs of withdrawal (2 successive NASS scores of $\geq 5$) were randomly assigned | Subjects were recruited through admissions from an Intermediate Care Nursery in New Jersey. All subjects had urine toxicology findings that were positive for heroin and/or methadone.<br><br>Exclusion: Neonates with sepsis, congenital anomalies, respiratory disease, | Mean caloric intake was compared between groups by the paired t-test. Significance was set at $p < 0.05$.<br><br>Supine-lying, narcotic-withdrawing infants had significantly higher peak withdrawal severity (NASS) scores ($13.17 \pm 2.03$) compared with those in the prone group | Even highly irritable infants can enjoy a significant reduction in distress by being laid prone.<br><br>Infants experiencing withdrawal showed significantly lower levels of distress and lower withdrawal scores when laid face down (prone) compared with similar infants kept face up (supine).<br><br>The difference (30%) between the prone- and supine- lying groups was clinically significant and was matched by a symmetrical increase in feeding by supine-lying newborns (30%). |

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| | in a prone-lying position than comparable, supine-lying neonates. | | to the prone (n = 25) or supine-lying (n = 23) condition.<br><br>Infants in the prone group were swaddled and laid belly down for sleep, while infants in the supine group were swaddled and laid on their backs.<br><br>Per usual practice, subjects were fed every 3 to 4 hours, ≤800 calories per 24 hours. Caloric intake was recorded at each feeding. Infant weight was recorded daily at 8:00 AM. Subjects' withdrawal severity was assessed by standard administration of the NASS every 2 or 4 hours, depending on time from onset of withdrawal.<br><br>Caloric intake was summed on a 24-hour basis and divided by the daily weight (cal/kg per 24 hours). Subjects' | metabolic disorder, gastroesophageal reflux, and intraventricular hemorrhage. | (10.52 ± 2.08); p < 0.0001.<br><br>Mean NASS scores were also significantly higher in the supine-lying group (7.60 ± 0.70) compared with the prone-lying group (5.11 ± 0.64); p < 0.0001.<br><br>Supine-lying subjects had higher mean caloric intake (133 ± 11.2 cal/kg per 24 hours) than prone-lying neonates (100 ± 9.4 cal/kg per 24 hours), a significant difference (p <0.001).<br><br>There were no episodes of apnea, aspiration, or seizures. | Limitations:<br>This study was predestined by the use of the NASS to assess withdrawal severity. As designed and administered, the NASS does not allow for case-blind evaluation of neonatal withdrawal. In consideration that withdrawal scoring would be conducted by the nurses involved in an affected infant's care, the NASS introduces the possibility of observer bias.<br><br>The dose-related effects of prenatal narcotic and stimulant exposure on neonatal distress was beyond the scope of this study. The degree of prenatal narcotic and cocaine exposure regarding the infants in this study was not quantified. |

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| | | | mean and peak NASS scores, caloric intake, and rate of daily weight gain were determined. | | | |
| Newman et al. (2015) Canada | Case series<br><br>The purpose of this study was to implement a rooming-in program to support close uninterrupted contact between opioid-dependent women and their infants in order to decrease the severity of NAS scores, lessen the need for pharmacotherapy, and shorten hospital stays. | n = 24 NICU group<br><br>n = 21 rooming-in group | Opioid-dependent pregnant women were assessed before giving birth, and were provided with education and support.<br><br>Psychosocial issues were addressed in collaboration with a community program developed to support addicted mothers. The mother-infant dyad was admitted postpartum to a private room and attended by nurses trained in Finnegan scoring.<br><br>Infants remained with their mothers unless persistently elevated Finnegan scores deemed it necessary for transfer to neonatal intensive care units for commencement of pharmacotherapy. | Inclusion:<br>Women in chronic opioid therapy, who delivered single full-term infants who were not apprehended by child protection services.<br><br>Exclusion:<br>Women whose infants were apprehended at birth by child protective services. | The requirement for oral morphine therapy for the neonates in the rooming-in cohort was significantly lower than those admitted directly to the NICU (3 of 21 [14.3%] vs 20 of 24 [83.3%]; P < .001).<br><br>The mean (SD) length of stay was also significantly shorter among those in the rooming-in cohort (7.9 [7.8] days vs 24.8 [15.6] days; P < .001). | Women who participated in the rooming-in program completed a survey after discharge. Anonymous responses were obtained from 14 of the 21 participating women. On a 5-point scale (1= least satisfied, 5 = most satisfied), 100% of women rated their overall experience as a 4 or higher and 86% reported breastfeeding their infants for an average duration of 2.5 months.<br><br>A decrease in the need for pharmacotherapy was shown, from 88.3% of infants receiving usual care in the NICU to only 14.3% of those rooming-in.<br><br>Rooming-in could potentially reduce bed use and save hospital resources, while preventing patients from dealing with negative psychosocial stressors.<br><br>The length of stay for subjects in this study decreased from 24.8 to 7.9 days.<br><br>With the implementation of this program, a multidisciplinary team had taken the approach of permitting rooming-in for infants who were born to opioid-dependent women, rather than sending them straight to the NICU. Additionally, NICU admission was resorted to only if pharmacotherapy was required. Within the first year of implementation, this |

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| | | | | | | program resulted in decreased length of stay, and decreased need for pharmacotherapy, while mothers favorably rated their experience.<br><br>Limitations: The NAS scoring tool that was used to quantify withdrawal severity somewhat relies on subjective judgement, and might contribute to a possible source of bias. |
| Pritham (2012) United States of America | Retrospective study<br><br>The purpose of this study was to examine the effect of infant feeding methods on neonatal abstinence syndrome. | n=152 total<br><br>n=136 opioid-dependent pregnant women on methadone maintenance therapy (MMT)<br><br>n=16 opioid-dependent pregnant women on buprenorphine maintenance therapy (BMT). | Electronic medical records of all opioid-dependent women who were on methadone maintenance therapy (n=136) or buprenorphine therapy (n=16) during pregnancy, and their neonates. were reviewed. | Inclusion:<br>Women on methadone maintenance therapy (n=136) or buprenorphine maintenance therapy (n=16) who labored and delivered at a hospital in Maine, or at an outlying community hospital during the same time-period and whose neonates were directly admitted to the Neonatal Intensive Care Unit at the hospital in Maine were used for the study.<br><br>Exclusion:<br>Opioid-dependent women not on prescribed replacement therapy with methadone | Exposed neonates receiving neonatal abstinence syndrome treatment either through receiving methadone maintenance therapy or buprenorphine maintenance therapy who were also breastfed began first line therapy with phenobarbital 1.1 days later (p=0.008_ and their length of stay was shorter by 9.4 days p= .016) as compared to formula-fed neonates or neonates who received formula and breast milk. | Infant feeding method did not predict length of stay for neonatal abstinence syndrome.<br><br>However, there were statistically significant differences between infants who were formula-fed and infants who were breastfeed in relation to the commencement of pharmacologic treatment such as phenobarbital for neonatal abstinence syndrome.<br><br>The three infant feeding methods included in this study (formula, breast and mixed formula and breast) revealed significant differences in neonatal abstinence syndrome treatment between formula, and breastfed infants but not between the formula-fed infants and infants fed a mixture of formula and breastmilk.<br><br>Overall, opioid-dependent women who are actively participating in methadone or buprenorphine maintenance therapy should be encouraged to breastfeed, so long as there are no contraindications present. |

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| | | | | maintenance therapy or buprenorphine maintenance therapy were excluded from the study.<br><br>Neonates less than 28 weeks' gestation were excluded (n=2). The ability of the placenta to metabolize methadone or store buprenorphine prior to the third trimester is not yet fully understood. | | |
| Pritham et al., (2012) United States of America | Retrospective descriptive study<br><br>The purpose of this study was to examine opioid replacement therapy in pregnancy and maternal effects on neonatal outcomes including length of hospital stay for neonatal abstinence syndrome. | n=152 total<br><br>n=136 opioid-dependent pregnant women on methadone maintenance therapy (MMT)<br><br>n=16 opioid-dependent pregnant women on buprenorphine maintenance therapy (BMT). | A retrospective chart review was conducted of medical records for opioid-dependent pregnant women on MMT or BMT and their newborns delivered between January 1, 2005 and December 31, 2007. | Inclusion:<br>Women on methadone maintenance therapy (n=136) or buprenorphine maintenance therapy (n=16) who labored and delivered at a hospital in Maine, or at an outlying community hospital during the same time-period and whose neonates were directly admitted to the Neonatal Intensive Care Unit at the hospital in Maine, were used for the study. | Data analysis was generated using the Statistical Package for the Social Sciences version 19.<br><br>The model examined variables hypothesized to affect length of stay, such as: maternal methadone dose, smoking, SSRIs, benzodiazepines, alcohol, other opioids, and marijuana. In addition, infant feeding method was added because of the association with length of stay in other | Maternal:<br>The mean maternal age was 25.3 years (standard deviation [SD] 3.9, range 18-37).<br><br>The demographic characteristics of the two groups of women, those on methadone, and those on buprenorphine, were similar for age, gravidity, parity, gestational age at first prenatal visit, number of prenatal visits, reported use of tobacco, alcohol, and marijuana, and documentation of prescribed SSRIs and/or illicit use of benzodiazepines and other opioids.<br><br>Neonates:<br>The MMT group had significantly smaller head circumference ($p < .03$). There were also differences by group in size for gestational age ($p < .03$) with the MMT group showing more smaller for |

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| | | | | Exclusion:<br>Opioid-dependent women not on prescribed replacement therapy with methadone maintenance therapy or buprenorphine maintenance therapy were excluded from the study.<br><br>Neonates less than 28 weeks' gestation were excluded (n=2). The ability of the placenta to metabolize methadone or store buprenorphine prior to the third trimester is not yet fully understood. | studies. Significance was set at $p \leq .05$. | gestational age infants, and BMT showing more neonates with larger for gestational age diagnosis.<br><br>Length of Stay:<br>Maternal methadone dose and accompanying use of benzodiazepines increased the length of stay by 8.6 days while women on MMT who breastfed their neonates shortened their infants' length of stay. Infants with prenatal exposure to methadone who were breastfed were discharged home earlier than those infants who were formula-fed.<br><br>A positive relationship between maternal methadone dose and NAS was displayed in this study.<br><br>Benzodiazepine use is a predictor variable for length of treatment for NAS. Neonates exposed to methadone and benzodiazepines while in utero, and who were born at term had significantly longer length of treatment for NAS when compared with unexposed neonates or to exposed neonates born prematurely.<br><br>Associated exposure to SSRIs with MMT did not prolong length of stay.<br><br>Infant feeding method was negatively related to length of stay, suggesting that breastfeeding may be protective for neonates withdrawing from opioids.<br><br>Breastfeeding is associated with a decreased rate of infant treatment for withdrawal from prenatal methadone or |

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| | | | | | | buprenorphine exposure. If the maternal urine drug screen is negative for illicit substances upon admission, breastfeeding should be permitted and encouraged for mothers.<br><br>Neonates exposed to buprenorphine experienced less severe NAS and shorter length of stay than those exposed to methadone by seven days.<br><br>Limitations:<br>The study was dependent on the availability of medical records and the accuracy of documentation of exposure history to a number of substances of interest.<br><br>Maternal drug use was mostly determined by self-report, which may be unreliable, and should be taken in to consideration. There was difficulty finding information in the medical record about commencement dates regarding opioid replacement therapy, SSRIs, or benzodiazepines.<br><br>Maternal length of time in addiction treatment, number of treatment relapses, time of initiation of MMT or BMT relative to gestational age and duration of such therapy, also vary widely, and should be taken into consideration.<br><br>The study did not examine neonatal drug regimen, and it was not controlled across all groups. |

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| Short et al. (2016) United States of America | Retrospective cohort study<br><br>The purpose of this population-based study was to examine the association between breastfeeding and length of hospital stay among infants diagnosed with NAS. | n=3,725 | Breastfeeding at discharge was used to determine breastfeeding status.<br><br>Infant and maternal characteristics were compared by breastfeeding status and the association between breastfeeding and infant length of hospitalization was assessed. | Inclusion:<br>Single in-hospital births to resident mothers in Pennsylvania between January 1, 2012 and December 31, 2014.<br><br>A total of 20 matching iterations were performed using variables such as child date of birth, gender, race, ethnicity, zip code, facility/hospital number, gestation, and birth weight.<br><br>Exclusion:<br>Infants born less than 34 weeks of gestation were excluded to control for possible iatrogenic NAS. | Infants who were breastfed were significantly more likely to have a normal birth weight (86.9% versus 81.6%, $p < 0.0001$) and be born term (89.6% versus 86.2%, $p < 0.002$) than infants who were not breastfed.<br>They were also significantly more likely to have mothers who had greater than a high school education (44.9% versus 32.6%, $p < 0.0001$), were married (25.2% versus 16.9%, $p < 0.0001$), and had a history of prenatal care (98.8% versus 94.0%, $p < 0.0001$).<br><br>Breastfed infants were significantly less likely to have mothers who smoked (70.1% versus 81.0%, $p < 0.0001$) or received Medicaid (66.6% versus 72.6%, $p = 0.0001$) compared to non-breastfed infants. | NAS infants who are breastfed have shown to have a significantly shorter length of stay than non-breastfed NAS infants, even after controlling for differences in maternal and infant characteristics.<br><br>There is an inverse relationship between breastfeeding and length of hospital stay and other adverse outcomes among NAS infants.<br><br>The nearly 10% reduction associated with length of stay for infants who were breastfed represents as an opportunity for significant cost savings.<br><br>A shortened length of stay may equate to potential savings of more than $3,000 per inpatient treatment day.<br><br>Lower rates of breastfeeding among NAS infants are not unexpected and could be due to higher NICU admission rates and/or the physical symptoms more commonly found in this population, which could make breastfeeding difficult.<br><br>The act of breastfeeding, rather than the actual breast milk itself, is what likely impacts NAS infants.<br><br>Other nonpharmacological interventions both compliment and support the act of breastfeeding itself, such as skin to skin contact, and kangaroo care. Rooming-in and uninterrupted postpartum contact between mother and infant has shown to positively affect infants affected by NAS. |

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| | | | | | No differences in NICU admission or maternal age, race, ethnicity, or WIC use were found.<br><br>There was a significant inverse relationship between breastfeeding and length of stay (B = -0.085, p = 0.008). | Limitations:<br>The variability in assessment of NAS may lead to inaccuracies in the classification of NAS.<br><br>The lack of information regarding both in-utero exposure and postnatal treatment for NAS impacts the clinical presentation of NAS through: Substance(s), timing, and amount of last maternal use. This study also did not identify drugs used to treat maternal opioid dependence, although treatment may influence length of stay.<br><br>Maternal opioid abuse and the legitimate use of an opioid prescription was not differentiated in this study.<br><br>There was a lack of specific data about breastfeeding practices. There was only one question used to assess the breastfeeding status of the infant at discharge and it did not differentiate between exclusive breastfeeding, and mixed feeding of breast milk and formula. |
| White-Traut et al. (2002) United States of America | Prospective design with random assignment of drug-exposed and nonexposed newborns to control and experimental groups. | n=45 total drug-exposed newborns<br><br>n=21 drug-exposed control newborns<br><br>n=24 drug-exposed | ATVV intervention: A 15-minute procedure consisting of infant-directed talk, continuous throughout the procedure (auditory), 10 minutes of light stroking/infant massage (tactile), eye-to-eye contact | Inclusion:<br>Sample consisted of 72 nonexposed and 45 prenatally drug-exposed 24- to 48-hour-old neonates with a gestational age of 35 to 41 weeks.<br><br>Exclusion: | Both the drug-exposed newborn group, and the nonexposed newborn group were behaviorally similar at baseline. However, the experimental group (drug-exposed newborns) experienced a | The nonexposed infants who received the ATVV intervention had 19% more alertness during the intervention period than did the nonexposed control infants during the same period of observation.<br><br>The increased arousal of the drug-exposed experimental group was characterized by 13.66% more alertness than the drug-exposed control infants at the end of the extended postintervention period. |

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| | The purpose of this study was to compare responses of drug-exposed and nonexposed newborns to auditory, tactile, visual, and vestibular intervention. | experimental newborns.<br><br>n=72 total nonexposed newborns<br><br>n=29 nonexposed control newborns<br><br>n=43 nonexposed experimental newborns | during alert periods (visual), and vertical rocking of the swaddled infant for 5 minutes post massage (vestibular).<br><br>Infant behavioral state (quiet sleep, active sleep, drowsy, quiet alert, active alert, crying, and indeterminate state) were documented.<br><br>Pulse rate and pulse waveform were continuously recorded with a pulse oximeter. | Infants greater than 48 hours old, had symptoms of active withdrawal, were likely to be discharged before completion of the second ATVV intervention, had congenital malformations, or required medications, treatments, or intensive/intermediate care. | significant decrease in quiet sleep [$F(1,70)=14.83$, $p=0.000$] and an increase in alertness [$F(1,70)=5.18$, $p=0.026$] during the intervention.<br><br>In the experimental group during baseline, a trend toward an increased proportion of time spent in alert states ($p=0.051$) was noted.<br><br>During the administration of the ATVV intervention, the control group experienced more quiet sleep [$F(1,43)=9.04$, $p=0.004$] and less alertness [$F(1,43)=6.13$, $p=0.017$].<br><br>The increased arousal of the drug-exposed experimental group persisted throughout the immediate post [$F(1,43)=5.04$, $p=0.030$] and extended postintervention | The drug-exposed control infants displayed more active sleep than the nonexposed control infants during the time that their experimental counterparts received ATVV intervention [$F(1,49)=9.35$, $p=0.004$].<br><br>When compared at baseline, a trend toward greater active sleep ($p=0.092$) was shown for the drug-exposed experimental group.<br><br>The nonexposed experimental infants displayed greater alertness compared to the drug-exposed experimental infants but did not achieve statistical significance in this study. However, it supports the previously reported ability of the ATVV intervention to enhance both autonomic and behavioral function in infants.<br><br>Drug exposure alone, results in alterations in infant behavioral state, and suggests that the ATVV intervention modified the behavioral responses of drug-exposed experimental infants similar to what is seen in nonexposed experimental infants, which supports the findings that the ATVV intervention promotes optimal behavior in drug-exposed infants, and is of significant clinical value.<br><br>Limitations:<br>There was a smaller sample size of infants, and the research was conducted |

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| | | | | | [$F(1,43)=4.13$, $p=0.049$] periods.<br><br>The drug-exposed control infants had more active sleep [$F(1,49)=7.01$, $p=0.011$] and less alertness [$F(1,49)=7.42$, $p=0.009$] than the nonexposed control infants.<br><br>A strong, significant correlation between pulse rate and infant behavioral state was found for the combined group of nonexposed infants ($r=0.840$, $p=0.001$) whether they were assigned to the control ($r=0.938$, $p=0.006$) or experimental group ($r=0.979$, $p=0.001$). | over a 12-hour period during early postnatal adjustments.<br><br>The group of mothers who participated may be different from the mothers who refused to participate.<br><br>Self-reports are often unreliable, and were evident in this study.<br><br>Infants were considered "nonexposed" if maternal and/or infant urine toxicology was negative, and/or if a history of drug use during pregnancy was not identified through medical record screening.<br><br>Various lengths of exposure to a wide range of drugs may have contributed to affecting behavior. |

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