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Systematic Review: The Effects of Nonpharmacological and Pharmacological Measures in

Neonates with Neonatal Abstinence Syndrome

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Abstract

With the increasing incidence of drug addiction among pregnant women, neonatal abstinence syndrome (NAS) has become a significant problem in the United States and has led to increased hospital costs, longer lengths of stay, and more serious health problems in neonates. This systematic review will explore the evidence about outcome differences for neonates with NAS that receive breastfeeding, rooming-in, and acupuncture in addition to pharmacological agents when compared to infants only receiving pharmacological agents. Twenty-one articles, retrieved from the databases PubMed and CINAHL and published between the years 2000-2017, were described in an integrated review, analyzed with critical appraisal, and synthesized for this systematic review. In general, researchers have found that breastfeeding, rooming-in, and acupuncture have positive effects of decreasing the need for pharmacological treatment, NAS symptoms, hospital costs, and length of hospital stay for infants with NAS when used in conjunction with pharmacologic agents.

Systematic Review: The Effects of Pharmacological and Nonpharmacological Measures in Neonates with Neonatal Abstinence Syndrome

The use or abuse of illicit drugs by mothers during pregnancy puts infants at risk for neonatal abstinence syndrome. Illicit drugs cross the placentas and the fetuses can become dependent on these substances. At birth, neonates are no longer exposed to these substances and are then at risk for a wide range of withdrawal symptoms, known as neonatal abstinence syndrome (NAS). NAS is a condition which primarily affects the autonomic and central nervous systems, as well as the gastrointestinal system (Johnson, 2017). NAS causes many issues in neonates and clinical manifestations of NAS can vary in both severity and timing (McQueen & Murphy-Oikonen, 2016). Clinical manifestations of NAS typically develop within the first few days of life and can range in severity from mild tremors and irritability to fever, excessive weight loss, and seizures (McQueen & Murphy-Oikonen, 2016).

Neonatal abstinence syndrome is a significant problem in the United States (Corr & Hollenbeak, 2017). Corr and Hollenbeak, (2017) revealed a 413% increase in the admissions of neonates suffering from NAS from 2003 to 2012. Along with the large increase in admissions of neonatal abstinence syndrome, the hospital lengths of stay also increased to the extent that neonates with NAS had lengths of stay that were about three times higher than those neonates not suffering from the syndrome. In 2003, NAS admissions cost the United States \$60,643,042. In 2012, this financial load reached an astounding value of \$315,665,913 (Corr & Hollenbeak, 2017).

Neonatal abstinence syndrome not only affects health care costs, number of admissions, and lengths of stay, but also has many detrimental effects on neonates (Corr & Hollenbeak, 2017). Approximately 225,000 neonates are exposed to illicit substances each year (MacMullen,

Dulski, & Blobaum, 2014). Of the neonates exposed to drugs in utero, greater than 75% have major medical problems, compared with 27% of unexposed infants (MacMullen et al., 2014). Because infants suffering from NAS tend to have major medical problems, these infants require extensive nursing care consisting of a number of interventions. Common interventions used to treat infants suffering from NAS include pharmacological measures, such as methadone and buprenorphine, and nonpharmacological measures, such as rooming-in, acupuncture, low-stimulation environment, and encouraging mothers to breastfeed neonates.

This systematic review was guided by the following PICOT question: In neonates with neonatal abstinence syndrome, how do supplemental nonpharmacological measures, compared with treatment as usual (pharmacological measure alone), affect outcomes? The purpose of this systematic review is to describe and critically appraise the evidence about outcomes of supplemental breastfeeding, rooming-in, and acupuncture in neonates with NAS, when compared to neonates with NAS that received only pharmacological agents.

Methods

A systematic review of the literature was conducted to answer the PICOT question. The databases PubMed and CINAHL were used to collect 21 peer reviewed journal articles published between the year 2000 and 2017. Intervention types included pharmacological agents, breastfeeding, and supportive interventions, including acupuncture, rooming-in, and reducing stimulation in the environment. Key words were “breastfeeding,” “neonatal abstinence syndrome,” “pregnancy and drug dependence and breastfeeding,” “neonatal abstinence syndrome and medications,” “maternal methadone use and neonatal abstinence syndrome,” “neonatal withdrawal syndrome and treatments,” “methadone maintenance program and neonatal abstinence syndrome,” “neonatal abstinence syndrome and acupuncture,” “neonatal abstinence

syndrome and interventions,” and “neonatal abstinence syndrome and rooming-in.” MeSH, or Medical Subject Headings, is the National Library of Medicine’s controlled vocabulary thesaurus that is used to index articles for Pubmed. MeSH included “neonatal abstinence syndrome,” “drug therapy,” and “breastfeeding.” Integrated review, analysis with critical appraisal, and synthesis of the reviewed articles were accomplished through the use of a matrix of evidence which included the article’s title, author, purpose statement, research question, clinical practice setting, sampling methods, sample size, research design, level of evidence, research findings, practice/research implications, and limitations of findings (Appendix A).

Review of the Literature

Pharmacological interventions aimed at treating the symptoms of NAS have been studied extensively. Opioid maintenance programs using methadone and buprenorphine are critical to preventing NAS in order to improve the health of neonates (Kakko, Heilig, & Sarman, 2008). In addition to pharmacological management of NAS, researchers have examined the effect of many nonpharmacological methods on outcomes in neonates with NAS. For the purpose of this systematic review, the interventions include breastfeeding, rooming-in, and acupuncture. This systematic review of literature will provide an in-depth discussion of the studies that have evaluated these interventions on NAS-related outcomes.

Pharmacological measures. In order to compare the treatments and outcomes for babies with NAS, it is important to know the standard treatment provided today. Buprenorphine and Methadone are the two most common pharmacological measures to reduce the severity of NAS seen in babies born to opioid-dependant mothers (Kakko et al., 2008).

Target action. Opioid-dependent mothers are given Buprenorphine or Methadone early in their pregnancy to reduce the effects of opioids on their unborn infants as part of an opioid

maintenance program (Kakko et al., 2008). Opioid maintenance programs are very important to the health of infants and the prevention of neonatal abstinence syndrome. Ebnar, Rohrmeister, Winklbaaur, Baewert, Jagsch, Peternell, and Fischer (2007) demonstrated that infants born to mothers with drug addiction who were on an opioid maintenance program (N=53) showed comparable APGAR scores with infants born to non-opioid dependent mothers (N=53). The APGAR score is an assessment done at birth to determine if newborns are ready to live without additional medical assistance. APGAR assessment focuses on five important factors of neonate health: (1) baby's appearance, (2) pulse, (3) muscle activity, (4) breathing and (5) responsiveness.

Buprenorphine and Methadone are two drugs that are used to help persons addicted to drugs avoid using illicit drugs. They target the same receptors that drugs, such as heroin, target, therefore making persons with addiction feel satisfied, but in a more controlled and regulated state to prevent the harmful side effect of withdrawal. Methadone is an opioid agonist, which means that the drug binds to the central μ receptors and reduces pain impulses. It is used in maintenance programs because it is easy to control and has a similar effect of illicit drugs but does not give the euphoria, in turn decreasing reward responses and likelihood of addiction. This drug is a schedule II, which means it is controlled and can potentially be very dangerous if abused. On the other hand, Buprenorphine is a partial opioid agonist, which means that it is weaker and there is less chance of abuse. An opioid antagonist, such as Narcan, is an antidote for opioid agonists. Therefore, when Buprenorphine and Methadone are used in combination, the persons feel as if they are on an opioid, but it is, in essence, a safe opioid used to prevent them from abusing or overdosing. Buprenorphine is a schedule III, which means it has a lower risk of

addiction than methadone, but still has potential to become dangerous (Kee, Hayes, & McCuiston, 2009).

Research findings. Between Buprenorphine and Methadone, as used for opioid maintenance, Buprenorphine has been found to be more effective (Jones, Kaltenbach, Heil, Stine, Coyle, Arria, & Fischer, 2010; Kakko, et al., 2008). When mothers were given Buprenorphine early in pregnancies, neonates are less likely to experience withdrawal, less Morphine is required for treatment, higher birth weights and full term pregnancies result, and hospital stays are shorter (Jones et al, 2010; Kakko et al, 2008). Ebnar et al. (2007) found that in cases where mothers were not compliant with treatment or infants were experiencing withdrawal symptoms, morphine, when given to the neonates, was the most effective treatment for neonatal abstinence syndrome.

Several researchers have compared the effect of different opioid maintenance program dosing schedules on NAS-related outcomes in neonates. Findings demonstrate no differences in outcomes relative to program dosing schedules (Cleary, Reynolds, Eigan, O'connell, Fahey, Gallagher, & Murphy, 2013; Kuschel, Austerberry, Cornwell, Couch, & Rowley, 2004). Typically, some programs increase dosages of methadone in the later stages of pregnancy to reduce the likelihood of mothers going into withdrawal or drug relapse, and others decrease dosages in later stages to prevent neonates from going into neonatal abstinence syndrome. Cleary et al. (2013) categorized dosing patterns into three categories: (1) increasing Methadone dosages in later stages of pregnancies, (2) decreasing Methadone dosages in later stages of pregnancies, or (3) no change in Methadone dosing throughout pregnancies. The outcome of medically treated neonatal abstinence syndrome did not differ between groups (Cleary et al, 2013). However, according to Kuschel et al. (2004), Methadone-exposed infants who required treatment for

neonatal abstinence syndrome had lower amounts of methadone in their system than those who did not receive treatment. The results of these studies suggest that dosages can remain consistent throughout the opioid maintained pregnancies with little to no adverse effect on the neonate (Cleary et al., 2013).

Summary. When women are addicted to illicit drugs, such as heroin, and they find they are pregnant, they may be enrolled in opioid maintenance programs using either Buprenorphine or Methadone. Both of these medications target the same receptors targeted by drugs such as heroin, therefore decreasing the harmful side effect of withdrawal. When looking at these two drugs, Buprenorphine has been found to be the superior. This drug regime resulted in less infants going through withdrawal, less morphine required for treatment, higher birth weights due to infants going full term, and shorter hospital stays (Jones et al, 2010; Kakko et al, 2008). Although it is best to start on programs before conception, starting them as early as possible in the pregnancy is shown to yield better outcomes. If neonates are born and show severe signs of withdrawal, morphine has been shown to be the best drug for managing the symptoms (Ebnar et al, 2007).

Breastfeeding. The effect of breastfeeding on NAS has been researched extensively in the literature. Seven studies in this systematic review tested the effects of breastfeeding on NAS (Dryden, Young, Hepburn, & Mactier, 2009; Isemann, Meizen-Derr, & Akinbi, 2011; McQueen, Murphy-Oikonen, Gerlach K, & Montelpare, 2011; Mohamed, Abde-Latif, Pinner, Clews, Cooke, Lui, & Oei, 2006; O'Connor, Collett, Alto, & O'Brien, 2013; Pritham, Paul, & Hayes, 2012; Welle-Strand, Skurtveit, Jansson, Bakstad, Bjarko, & Ravndal, 2013). These researchers consistently showed that breastfeeding may reduce the incidence and duration of pharmacological treatment of neonates with NAS, reduce the length of hospitalization, and

reduce the severity of NAS. Description of studies in this integrated review are organized based on those three outcomes. Samples of these seven studies included neonates suffering from NAS ranging from 28 to 450 neonates; samples in five of the seven studies were greater than 120 neonates. Of the seven studies, the designs were retrospective cohort design, retrospective chart review, and prospective design. Studies were conducted at hospitals, ranging from rural to inner-city settings in the United States, Canada, United Kingdom, and Australia. Limitations of these studies included small samples of buprenorphine-exposed infants, potential Finnegan instrumentation bias, non-randomized group assignments due ethical considerations, and retrospective data collection from available medical records, often resulting in incomplete data.

Incidence and duration of pharmacological treatment. As stated above, researchers have consistently found that breastfeeding reduces incidence and duration of pharmacological treatment in neonates exposed to methadone in utero (Dryden et al., 2009; Mohamed et al., 2006; Welle-Strand et al., 2013). Breastfeeding for greater than 72 hours was associated independently with a 50% reduced need for pharmacological treatment of NAS in methadone-exposed infants (Dryden et al., 2009). According to Welle-Strand et al. (2013), only 53% of the methadone-exposed infants being breastfed required pharmacological treatment while 80% of the methadone-exposed infants not being breastfed required pharmacological treatment for NAS. Similarly, Mohamed et al. (2006), found that 52.9% of the breastfed infants required pharmacological treatment for withdrawal while 79.0% of the formula-fed infants required pharmacological treatment for withdrawal.

Breastfeeding has also been found to shorten length of pharmacological treatment of NAS in infants exposed to methadone (Isemann et al., 2011; Mohamed et al., 2006; Welle-Strand et al., 2013). According to Welle-Strand et al. (2013), a significantly shorter duration of

pharmacological treatment of NAS was found in methadone-exposed infants linked to lactation status. The duration of treatment for breastfed infants exposed to methadone was 31 days while the duration of treatment for methadone-exposed infants who were not breastfed was 48.9 days. Likewise, Isemann et al. (2011) discovered that maternal breast milk feedings decreased median duration of methadone therapy for NAS in both preterm and term infants. The median duration of methadone therapy for NAS in breastfed infants was less than ten days while the median duration of methadone therapy in formula-fed infants was greater than ten days. Lastly, Mohamed et al. (2006) found that overall NAS pharmacological treatment duration was almost 20 days less in breastfed infants compared to formula-fed infants. The duration of pharmacological treatment for breastfed infants was 85.4 days while the duration of treatment for formula-fed infants was 108.2 days.

Hospital stays. Additionally, researchers have found that infants suffering from NAS who were breastfed had shorter hospital stays than formula-fed infants suffering from NAS (Isemann et al., 2011; Mohamed et al., 2006; Pritham et al., 2012). According to Isemann, Meizen-Derr, and Akinbi (2011), maternal breast milk decreased hospital length of stay compared to formula-fed infants. The median length of hospital stay for breastfed infants suffering from NAS was 12.5 days while the median length of stay for formula-fed infants was 18.5 days. Mohamed, Abde-Latif, Pinner, Clews, Cooke, Lui, and Oei (2006) found similar results with a shorter length of hospitalization among breastfed infants compared to formula-fed infants. In their study, the length of hospitalization in breastfed infants was 14.7 days compared to 19.1 days in formula-fed infants.

Severity of NAS. Breastfeeding has also been found to reduce severity of NAS (Isemann et al., 2011; McQueen et al., 2011; Mohamed et al., 2006; O'Connor et al., 2013). The incidence

and severity of NAS is measured using the Finnegan objective scoring system. Finnegan scoring systems assess the severity of NAS by observing central nervous system, gastrointestinal, respiratory, and vague autonomic symptoms in infants. Finnegan scores determine whether or not pharmacological treatment for NAS will be initiated and also help to determine the dosing regimen of the chosen pharmacological method. It should be noted that the Finnegan scoring system is only validated for opiate withdrawal; therefore, it may not be an accurate scoring system for neonates exposed to other substances (Mohamed et al., 2006).

Isemann, Meinen-Derr, and Akinbi (2011) used the Finnegan abstinence scoring method to measure the severity of NAS. Their findings suggested that the volume of maternal breast milk ingested reduced incidence and severity of NAS in both preterm and term infants. Similarly, Mohamed, Abde-Latif, Pinner, Clews, Cooke, Lui, and Oei (2006) monitored infants for NAS using the Finnegan objective scoring system and found that breastfed infants exposed to multiple drugs in utero had worse Finnegan scores than infants exposed to only a single drug in utero, but had significantly better scores than formula-fed infants.

McQueen, Murphy-Oikonen, Gerlach, and Montelpare (2011) used a modified Finnegan Scoring Tool that consisted of 30 items used to measure withdrawal including central nervous system, metabolic, vasomotor, respiratory, and gastrointestinal symptoms. In this modified Finnegan Scoring Tool, the maximum score that could be recorded was 44 while the minimum score was 0. A score of eight or greater suggested withdrawal in neonates (McQueen et al., 2011). Initial scores were recorded at birth and every two hours after birth for the first 48 hours for the neonate exposed to methadone in utero. Afterwards, scores were recorded every 4 hours for 72 hours and then as required by hospital policy. If scores greater than 8 were recorded, further scores were recorded every two hours. The number of NAS scores recorded differed

between breastfed and formula-fed infants. The mean number of NAS scores recorded of predominantly breastfed infants was 25.0 while the mean number of scores recorded for formula-fed infants was 95.6 (McQueen et al., 2011). Additionally, the predominantly breastfed infants had a lower severity of NAS symptoms than the formula-fed infants indicated by a lower magnitude Finnegan score. The overall mean NAS score of breastfed infants was 4.9 while the mean overall NAS score of formula-fed infants was 6.9 (McQueen et al., 2011). A limitation to this study is that the reliability and validity of this tool was not established; therefore, some instrumentation bias may have existed (McQueen et al., 2011).

O'Connor, Collett, Alto, and O'Brien (2013) also used a modified Finnegan Scoring System to measure the degree of withdrawal symptoms in buprenorphine-exposed neonates. The results suggest that breastfeeding may reduce the severity of NAS in infants exposed to buprenorphine. The mean peak NAS score of breastfed infants was 8.83 while the mean peak NAS score of non-breastfed infants was 9.65. If three or more consecutive scores greater than or equal to 8 were recorded for infants, pharmacological treatment of NAS was indicated. Breastfed infants were less likely to score greater than or equal to 8 than non-breastfed infants. Additionally, symptoms of NAS were found to resolve about two hours earlier in breastfed infants than in formula-fed infants. A limitation to this study was the ability to control all variables. Some nonpharmacological interventions for NAS occur with breastfeeding, so it is not possible to distinguish the potential impact of breastfeeding from interventions such as swaddling or kangaroo care on the reduction of NAS symptoms (O'Connor et al., 2013).

Multiple studies have found reduced need for pharmacological treatment for NAS in breastfed infants exposed to buprenorphine (O'Connor et al., 2013; Pritham et al., 2012). According to O'Connor et al. (2013), buprenorphine-exposed neonates who were breastfed were

less likely to require pharmacological management of NAS than buprenorphine-exposed infants who were not breastfed. They discovered that 23.1% of breastfed infants of mothers maintained on buprenorphine during pregnancy required treatment for NAS while 30.0% of non-breastfed infants required treatment for NAS.

While some researchers have found decreased incidence of pharmacological treatment for NAS in breastfed infants exposed to buprenorphine, Welle-Strand, Skurtveit, Jansson, Bakstad, Bjarko, and Ravndal (2013) found no reduced need for pharmacological management of NAS in buprenorphine-exposed infants when breastfeeding was introduced. In their study, 64% of breastfed infants exposed to buprenorphine required pharmacological treatment for NAS while 44% of buprenorphine-exposed infants who were not breastfed required treatment for NAS. The cohort in their study consisted of both women in methadone maintenance treatment and women in buprenorphine maintenance treatment which allowed for the comparison of the effects of both drugs on the neonate; however, the study groups, especially for buprenorphine, were small. The study group consisted of 78 infants exposed to methadone and 46 infants exposed to buprenorphine. The small study groups made it difficult to detect any significant differences between buprenorphine-exposed infants who were breastfed and buprenorphine-exposed infants who were not breastfeed (Welle-Strand et al., 2013). Future research needs to examine if breastfeeding reduces the need for pharmacological treatment for NAS in infants exposed to buprenorphine (O'Connor et al., 2013; Welle-Strand et al., 2013).

Summary. Researchers studying the effects of breastfeeding consistently found that breastfeeding may reduce the incidence and duration of pharmacological treatment of NAS, reduce the length of hospitalization, and reduce the severity of NAS (Dryden et al., 2009;

Isemann et al., 2011; McQueen et al., 2011; Mohamed et al., 2006; O'Connor et al., 2013; Pritham et al., 2012; Welle-Strand et al., 2013).

Rooming-In. Non-pharmacological measures such as rooming-in are commonly used along with pharmacological measures to treat neonatal abstinence syndrome. Four studies in this systematic review tested the effects of rooming-in on neonatal abstinence syndrome (Abrahams, Kelly, Payne, Thiessen, Mackintosh, & Janssen, 2007; Grossman, Berkwitt, Osborn, Xu, Esserman, Shapiro, & Bizzaro, 2017; Holmes, Atwood, Whalen, Beliveau, Jarvis, Matulis, & Ralston, 2016; Newman, Davies, Dow, Holmes, Macdonald, Mcknight, & Newton, 2015). The researchers measured outcomes of length of hospital stay, hospital cost, severity of NAS symptoms, and need for pharmacological treatment. Samples included neonates suffering from NAS with sample sizes ranging from 26 to 287 neonates. Three of the four studies included had sample sizes under 45 neonates. Of the four studies, the designs were retrospective cohort design and retrospective chart review. Each study took place in single-site hospitals, ranging from rural to inner-city settings. The studies took place in British Columbia, United States, and Ontario. Limitations of these studies included small samples, potential biases in NAS scoring systems due to the scoring tool relying on some subjective data, inconsistencies in pharmacological treatment, changes in hospital policies during the course of the study, and non-randomized group assignment.

Across studies researchers consistently found that admitting neonates directly to inpatient rooms, by-passing neonatal intensive care units (NICU), led to shorter lengths of hospital stay, decreased hospital costs, reduced severity of NAS symptoms, and decreased need for pharmacological treatment (Abraham et al., 2007; Grossman et al., 2017; Holmes et al., 2016; Newman et al., 2015). For example, Grossman et al. (2017) studied 287 neonates with NAS at

Yale New Haven Children's Hospital and investigated the effects of implementing nonpharmacological interventions, administering morphine, and transferring infants directly to the inpatient unit on the average length of hospital stay for infants with NAS. This was a long-term study in which the researchers collected data from January 2008 until June 2016. In March 2010 a quality improvement (QI) project was implemented at this hospital. The QI project had neonates placed in a low stimulation environment, and encouraged parents to room-in, continuously care for their neonates, feed their neonates on demand, and tend to neonates if crying. Mothers were encouraged to breastfeed infants as long as there were no contraindications, such as HIV. Staff was trained to view nonpharmacological interventions as equal to pharmacological interventions, and to increase parent involvement before implementing pharmacological treatment. The use of the Finnegan Neonatal Abstinence Scoring system (FNASS) was discontinued and instead a functional assessment was developed that focused on the infant's ability to eat, sleep, and be consoled. The scores of this functional assessment determined whether or not the infant needed to be given morphine. Of the 421 infants over the gestational age of 35 weeks that were diagnosed with NAS during the study period, only 287 were included in the study. Those excluded were infants either not exposed to methadone or those with serious comorbid conditions. Of the 287 infants, 55 were in the pre-implementation period, 188 in the intervention period, and 44 in the post-implementation period. The pre-implementation and post-implementation periods had to do with the QI project that was implemented in March 2010. Infants born before March 2010 were part of the pre-implementation period, and infants born after May 2015 were considered part of the post-implementation period. The average length of stay (ALOS) decreased from 22.4 days in the pre-

implementation to 5.9 days in the post-implementation period; and the proportion of infants treated with morphine decreased from 98% to 14%.

Grossman et al. (2017)'s findings about decreased length of hospital stay are in line with those of Abrahams et al. (2007), who examined the effects of rooming-in on need for pharmacological treatment, need for admission to a neonatal intensive care nursery, and ALOS, all of which represented severity of NAS symptoms. Specifically, Abrahams et al (2007) conducted the study at a hospital in Vancouver, British Columbia and compared outcomes of three subsamples of mothers who used heroin or methadone during pregnancy (Abrahams et al., 2007). The study cohort consisting of 32 new mothers admitted to BC Women's Hospital (BCWH) between October 2001 and December 2002, was compared to two historical cohorts that consisted of women who gave birth between January 1999 and September 2001. The study cohort took place after the implementation of rooming-in at BCWH. Mothers were instructed by nurses about how to care for infants and how to identify symptoms of NAS. The first historical cohort consisted of 38 women who disclosed use of heroin or methadone during pregnancy. The second historical cohort consisted of 36 women who also reported use of heroin or methadone. The women in the historical cohorts received the same care as those in the study cohort, but had not had rooming-in; instead, infants were admitted to a level II nursery. Outcomes of this study demonstrate that rooming-in was associated with a decreased need for pharmacological treatment, decreased need for admission to a neonatal intensive care nursery, and decreased ALOS. A limitation of this study was that the effects of rooming-in could not be separated from the effects of breastfeeding. Sixty percent of women in the study cohort breastfed, while only 10% of women in the comparison groups breastfed.

Summary. Researchers consistently found that rooming-in led to shorter length of hospital stay, decreased hospital costs, reduced severity of NAS symptoms, and decreased need for pharmacological treatment, suggesting reliability of this group of studies.

Acupuncture. Another non-pharmacological intervention used for infants suffering from NAS is acupuncture. Two studies tested the effects of acupuncture on the treatment of NAS (Filippeli, White, Spellman, Broderick, Highfield, Sommers, & Gardiner, 2012; Raith, Schmolzer, Resch, Reiterer, Avian, Koestenberger, & Urlesberger, 2015). Raith et al. (2015) examined the effect of laser acupuncture on length of morphine treatment and average length of hospital stay in 28 neonates at a hospital in Austria. Laser acupuncture increases the levels of endomorphin, endorphins, enkephalin, and serotonin and causes analgesia and sedation. The design of the study was a randomized, controlled, blinded, single-center study. The study was blinded by having both the control group and the test group spend time in the treatment room where the test group received acupuncture treatment and the control group simply spent time lying in bed. The use of laser acupuncture was found to significantly decrease the duration of morphine therapy in newborns with NAS. The median drug treatment for the acupuncture group was 28 days compared to 39 days for the control group. Neonates who received laser acupuncture also had shorter lengths of hospital stay. The ALOS for the acupuncture group was 35 days compared to 50 days for the control group. While this study suggests that laser acupuncture is a safe way to reduce length of morphine treatment and ALOS, the small sample must be taken into consideration as a limitation to this study.

Filippeli et al. (2012) looked at the effects of non-insertive acupuncture (NIA) on the symptoms associated with NAS in a retrospective chart review of 54 neonates with NAS. The neonates received a total of 92 NIA sessions, which involved an acupuncturist stimulating seven

acupuncture points with a teishin or finger. The researchers found that 28 neonates slept through the treatment or fell asleep immediately after the treatment. Of those who slept through the treatment, one neonate experienced deeper sleep following treatment. Effects were more prominent in neonates who were agitated prior to treatment. Additionally, 13 neonates exhibited signs of released tension during NIA treatment. Findings also revealed that better feeding followed NIA treatment, with eight neonates showing higher caloric intake for the days following treatment. The infants receiving NIA as an adjunctive treatment along with pharmacological interventions were found to reveal deeper sleep, better feedings, and more even breathing. A limitation of this study was that acupuncturists were only available one day a week resulting in some infants being treated early in their stay and others being treated later in their stay.

Critical Appraisal

In general, researchers have found that breastfeeding, rooming-in, and acupuncture have positive effects of decreasing the need for pharmacological treatment, NAS symptoms, hospital costs, and length of hospital stay for infants with NAS when used in conjunction with pharmacologic agents. In this section, quality (validity and reliability) of the studies is discussed with pharmacology studies discussed first, followed by studies about breastfeeding, rooming, and then acupuncture.

Pharmacological methods. There is an abundant amount of research about pharmacological interventions of babies with NAS. The six studies that were included in this systematic review were appraised on validity and reliability (Cleary et al., 2013; Dryden et al., 2009; Ebnar et al., 2007; Jones et al., 2010; Kakko, et al., 2008; Kuschel et al., 2004). Because the findings across studies were consistent, it can be concluded that they are reliable. Validity

was questioned with the studies relating to small samples (Cleary et al., 2013; Ebner et al., 2007; Kakko, et al., 2008; Kuschel et al., 2004), no group randomization (Ebner et al., 2007; Kakko et al., 2008; Kuschel et al., 2004), dosages not being stated (Jones et al., 2010), attrition, e.g., participants not showing to follow up appointments (Dryden et al., 2009), and varying severities of addiction and age of the pregnant women (Kakko et al., 2008).

Designs of these studies show many strengths and include: prospective cohort (Cleary et al., 2013; Kakko et al., 2008), retrospective (Dryden et al., 2009), double-blind, double-dummy (Jones et al., 2010) random and controlled (Jones et al., 2010). The level of evidence on these studies is also something to consider when discussing validity and limitations. Levels of evidence were: level III (Dryden et al., 2009), level V (Jones et al., 2010), level VI (Ebner et al., 2007; Kakko et al., 2008; Kuschel et al., 2004), and level VII (Cleary et al., 2013). Internal validity was also increased when participants were all on the same medication, because it was easier to conclude findings of the particular medication. In three of the studies, researchers looked at women who were only on Methadone, which allowed researchers to compare data pertaining to this specific drug along with other variables that may be present (Cleary et al., 2013; Dryden et al., 2009; Kuschel et al., 2004).

Breastfeeding. Breastfeeding and its effects on NAS has been researched extensively in the literature. Researchers of seven studies in this systematic review tested the effects of breastfeeding on abstinence syndrome (Dryden et al., 2009; Isemann et al., 2011; McQueen et al., 2011; Mohamed et al., 2006; O'Connor et al., 2013; Pritham et al., 2012; Welle-Strand et al., 2013). The consistent findings across studies suggest the reliability of studies. As previously noted, limitations of study and threats to internal and external validity included small samples of buprenorphine-exposed neonates (Welle-Strand et al., 2013), affecting the statistical conclusion

validity of findings; however, breastfeeding in larger samples of methadone-exposed infants were studied in the literature. Researchers found that breastfeeding had positive outcomes whether using smaller samples of buprenorphine-exposed or larger samples of methadone-exposed infants (Dryden et al., 2009; Isemann et al., 2011; Mohamed et al., 2006; Pritham et al., 2012; Welle-Strand et al., 2013).

Potential Finnegan instrumentation bias was also noted and contributes to threats to internal validity (Isemann et al., 2011). A modified Finnegan scoring tool was used by researchers in two studies (O'Connor et al., 2013; McQueen et al., 2011). The reliability and validity of the modified Finnegan scoring tool is not well-established but it has been used in numerous studies to guide and compare various treatments for NAS (McQueen et al., 2011). The Finnegan abstinence scoring method is a subjective assessment of NAS designed for term infants and may not be sensitive to detecting NAS in preterm infants. However, more term neonates were included in the research than preterm neonates (Isemann et al., 2013). Additionally, while the Finnegan scoring system is only validated for opiate withdrawal, no reliable system has been created to assess non-opiate effects. However, the majority of the participants in the samples were exposed to opiates (Mohamed et al., 2006).

Researchers also used retrospective data collection from available medical records, which may have resulted in missing data (Dryden et al., 2009; Isemann et al., 2011; McQueen et al., 2011; Mohamed et al., 2006; O'Connor et al., 2013; Pritham et al., 2012; Welle-Strand et al., 2013). However, retrospective data collection is an efficient way to collect data from larger samples and it minimizes recall bias. Retrospective data collection is valuable and is often used to direct future retrospective data collection in research. While the majority of the researchers used retrospective data collection from available medical records, researchers of one cohort

study used a prospective data collection. The researchers compared background characteristics, pregnancy variables, and neonatal outcomes linked to feeding method across the three study groups (Welle-Strand et al., 2013).

Rooming-in. Researchers of four studies researched the effects of rooming-in on outcomes in neonates with NAS (Abrahams et al., 2007; Grossman et al., 2017; Holmes et al., 2016; Newman et al., 2015), measuring outcomes of average length of hospital stay, average hospital cost, severity of NAS symptoms, and need for pharmacological treatment. Sample sizes across studies ranged from 26 to 287 infants, with samples in three of the four studies of less than 45 infants. Researchers consistently found that rooming-in led to shorter length of hospital stay, decreased hospital costs, reduced severity of NAS symptoms, and decreased need for pharmacological treatment, suggesting reliability of this group of studies. Because findings of these studies are consistent despite having different settings and populations, these practices can likely be applied to other populations and have similar outcomes. Limitations of these studies included small samples (Abraham et al., 2007; Newman et al., 2017), potential biases in NAS scoring systems due to the scoring tool relying on some subjective data (Newman et al., 2015), inconsistencies in pharmacological treatment (Holmes et al., 2016), changes in hospital policies during the course of the study (Grossman et al., 2017), and non-randomized allocation of subjects to study groups (Abrahams et al., 2007).

Acupuncture. Another non-pharmacological intervention used for neonates with NAS is acupuncture. Researchers of two studies examined the effects of acupuncture on outcomes in neonates with NAS (Filippeli et al., 2012; Raith et al., 2015). One group of researchers examined the effect of laser acupuncture in 28 newborns to test two outcomes: length of morphine treatment and average length of hospital stay (Raith et al., 2015). The use of laser acupuncture

was found to increase endorphins and lead to analgesia, which significantly decreased duration of morphine therapy and length of hospital stay in newborns with NAS. While these researchers found that the use of laser acupuncture has favorable outcomes, the small sample must be taken into consideration as a limitation to this study and threat to external validity.

In another study regarding acupuncture, researchers also looked at the effects of non-insertive acupuncture (NIA) on the symptoms associated with NAS (Filippeli et al., 2012). In the study, 54 infants received a total of 92 NIA sessions, which involved an acupuncturist stimulating seven acupuncture points with a teishin or finger. The infants receiving NIA as an adjunctive treatment along with pharmacological interventions were found to have deeper sleep, better feedings, and more even breathing. A limitation of this study was that acupuncturists were only available one day a week, resulting in some infants being treated early in their stay and others being treated later in their stay. While the findings in this study demonstrated reliability and internal validity, this single study is not enough to conclude external validity.

Synthesis

Breastfeeding. Researchers have found that breastfeeding as a nonpharmacological measure reduced the incidence and length of pharmacological management of NAS, reduced the length of hospital stay, and reduced the incidence and severity of NAS symptoms (Dryden et al., 2009; Isemann et al., 2011; McQueen et al., 2011; Mohamed et al., 2006; O'Connor et al., 2013; Pritham et al., 2012; Welle-Strand et al., 2013). Strengths of studies included large samples of methadone-exposed neonates with NAS and the reduction of recall bias through the use of retrospective data collection. Instruments used to measure the severity of NAS were consistent across studies. Based on the critical appraisal of these studies, breastfeeding as a

nonpharmacological method should be used in addition to pharmacological methods to reduce the incidence, length, and severity of NAS as well as reduce the length of hospital stay for NAS.

Rooming-in. Researchers found that the use of nonpharmacological method of rooming-in has reduced average length of stay, reduced hospital costs, reduced severity of NAS symptoms, and decreased the need for pharmacological treatments (Abrahams et al., 2007; Grossman et al., 2017; Holmes et al., 2016; Newman et al., 2015). Based on the critical appraisal of these studies, findings were consistent across studies, therefore suggesting reliability. Researchers of these studies did see a change in anticipated outcomes, therefore confirming that rooming-in leads to favorable outcomes.

Acupuncture. Researchers have found that the use of different acupuncture techniques as an adjunctive therapy reduced length of stay, decreased need for pharmacological treatment, decreased signs of discomfort in neonates, and increased feeding times (Filippeli et al., 2012; Raith et al., 2015). The purpose of acupuncture is to achieve pain relief. These studies supported this theory by examining for signs of increased comfort following acupuncture therapy, and examining the effect acupuncture has on length of stay, and need for pharmacological treatment. Although these preliminary findings are promising and consistent for effects on positive outcomes, external validity cannot be implied from these two studies alone.

Implications and Recommendations for Practice

Pharmacological methods. Based on the evidence, it is important for nurses to motivate and enroll new mothers in opioid maintenance programs for the health and safety of their babies (Ebnar et al., 2007). It is important to start them as early as they can, even before pregnancy if possible (Kakko et al., 2008). If a mother is noncompliant and the neonate goes into withdrawal, it is important for nurses to use morphine to manage symptoms (Ebnar et al., 2007). Future

researchers should conduct studies with larger samples, control groups, and control statistically for extraneous variables, since randomized group assignment is rarely used in research about this topic. There should also be research about compliance to opioid maintenance programs and effectiveness of interventions, e.g., motivational interviewing, on outcomes to increase compliance rates.

Breastfeeding. Based on quality of evidence of this systematic review, pregnant women who misuse drugs should be strongly encouraged and supported to breastfeed in the absence of any contraindications (Dryden et al., 2013; Isemann et al., 2011; McQueen et al., 2011; Mohamed et al., 2006; Pritham et al., 2012; Welle-Strand et al., 2013). Breastfeeding education should be provided to these women during the prenatal period, early in their pregnancies (O'Connor et al., 2013; McQueen et al., 2011; Welle-Strand et al., 2013). Information about breastfeeding from interdisciplinary healthcare professions should be consistent (Welle-Strand et al., 2013). An extended postnatal stay may also be beneficial so nurses can watch for signs of NAS and it would also allow healthcare professionals to continue to support breastfeeding and provide parenting support (Dryden et al., 2013). Future research needs to be conducted to continue to examine effects of breastfeeding on outcomes in neonates with NAS, especially in those exposed to buprenorphine (Welle-Strand et al., 2013). Additional research should be conducted to explore issues such as reasons for low breastfeeding rates among drug-misusing women and effective interventions to support these women to breastfeed (McQueen et al., 2011).

Rooming-in. Based on the evidence, rooming-in contributes to favorable outcomes for neonates with NAS and therefore should be implemented in hospital settings (Abrahams et al., 2007; Grossman et al., 2017; Holmes et al., 2016; Newman et al., 2015). Further research would be beneficial to provide more evidence. Future studies should consider using randomized groups

and larger samples. Researchers should also ensure consistencies in pharmacological treatment and the use of breastfeeding in participants. Further, researchers should look into the effects rooming-in has on medium and long-term childhood outcomes, such as growth, development, and behavioral outcomes of participants (Grossman et al., 2017; Newman et al., 2015). Future studies could also examine quality of mother-infant bonding and other longer term outcomes, such as involvement of child protective services (Newman et al.,2015).

Acupuncture. Based on evidence, the use of laser acupuncture reduced length of pharmacological treatment and reduced length of hospital stay (Raith et al., 2015). Evidence has also shown that non-insertive acupuncture increased comfort, deeper sleep, and better feedings in neonates with NAS (Filippeli et al., 2012). Findings suggest that both laser acupuncture and NIA could be used as an adjunct to other standard treatment. Acupuncture could be especially useful in hospitals in areas with high prevalence of drug use, in which there is higher occurrences of neonates with NAS (Filipelli et al., 2012). While research has shown favorable outcomes from both laser acupuncture and NIA, more research should be conducted to ensure safety and efficacy of acupuncture in neonates. Further research should include larger randomized controlled studies. Future studies should consider investigating mother-delivered NIA and its effects on mother-neonate bonding (Filippeli et al., 2012) and also the possibility of at home laser acupuncture treatment programs (Raith et al., 2015).

Conclusion

The management of neonates with NAS has evolved and improved greatly over the past twenty years. These advances have been supported by evidence about the effects of nonpharmacological interventions on outcomes of neonates with NAS. Breastfeeding may reduce the incidence and duration of pharmacological treatment of neonates with NAS, reduce

the length of hospitalization, and reduce the severity of NAS (Dryden et al., 2009; Isemann et al., 2011; McQueen et al., 2011; Mohamed, Abde-Latif et al., 2006; O'Connor et al., 2013; Pritham et al., 2012; Welle-Strand et al., 2013). When combined with Buprenorphine, the best choice for a pharmacological treatment, outcomes in this population have significantly improved. Infants with NAS receiving nonpharmacological interventions, such as rooming-in and acupuncture, are found to have better outcomes than infants receiving only pharmacological treatment (Abrahams et al., 2007; Filippeli et al., 2012; Grossman et al., 2017; Holmes et al., 2016; Newman et al., 2015; Raith et al., 2015). Overall, researchers have found that breastfeeding, rooming-in, and acupuncture have positive effects of decreasing the need for pharmacological treatment, NAS symptoms, hospital costs, and length of hospital stay for infants with NAS when used in conjunction with pharmacologic agents.

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Appendix A

APA formatted reference	Purpose statement, Research question.	Clinical Practice Setting, Sampling methods, Sample size	Design. Level of Evidence	Findings, Conclusion	Practice & Research Implications	Limitations of Findings
Abrahams, R., Kelly, S., Payne, S., Thiessen, P., Mackintosh, J., & Janssen, P. (2007). Rooming-in compared with standard care for newborns of mothers using methadone or heroin. <i>Canadian Family Physician</i> , 53(10), 1722-1730.	<p>Purpose Statement: To evaluate the effect of rooming-in rather than standard nursery care on the severity of NAS.</p> <p>Research Question: Does rooming-in reduce the severity of NAS?</p>	<p>Setting: British Columbia</p> <p>Sampling Method: convenience</p> <p>Sample Size: 32 women who used heroin or methadone during pregnancy</p>	<p>Design: retrospective cohort study</p> <p>Level of Evidence: level III</p>	<p>Rooming-in was associated with a significant decrease in need for treatment of NAS compared with the control. Rooming-in was also associated with shorter newborn LOS and newborns were more likely to be discharged in the custody of their mothers.</p>	<p>Rooming-in might ease newborns' transition to extrauterine life and promote more effective mothering.</p>	<p>Non-random allocation of subjects to study groups</p>
Cleary, B. J., Reynolds, K., Eogan, M., O'Connell, M. P., Fahey, T., Gallagher, P. J., & ... Murphy, D. J. (2013). Methadone dosing and prescribed medication use in a prospective cohort of opioid-dependent pregnant women.	<p>Purpose statement: To describe methadone dosing during and after pregnancy, to compare occurrences of NAS between those with dose decreases and those with steady or increasing doses, and to describe</p>	<p>Setting: Two Irish tertiary care maternity hospitals</p> <p>Sampling Method: not stated</p> <p>Sample Size: 117 pregnant women on methadone maintenance treatment</p>	<p>Design: prospective cohort study</p> <p>Level of Evidence: level VII</p>	<p>Incidence of treatment of NAS did not differ between dosage groups.</p>	<p>There is no need to decrease the methadone dosing during pregnancy because the dosing has no effect on the outcome of the neonate with NAS.</p>	<p>Maternal noncompliance, sample size limitations.</p>

<p><i>Addiction</i>, 108(4), 762-770. doi:10.1111/add.12078</p>	<p>prescribed medication use among opioid-dependent pregnant women.</p> <p>Research Question: What dose of methadone is most effective for neonates suffering from NAS?</p>	<p>between July 2009 to July 2010</p>				
<p>Corr, T. E., & Hollenbeak, C. S. (2017). The economic burden of neonatal abstinence syndrome in the United States. <i>Addiction</i>, 112(9), 1590-1599. doi:10.1111/add.13842</p>	<p>Purpose Statement: To describe the NAS population and compare with the non-NAS population, determine the incidence of NAS in the United States and estimate the total annual costs and hospital days of NAS admissions, and estimate the incremental costs and length of stay of an NAS admission compared with a non-NAS admission.</p> <p>Research Question: What effect does NAS have on the united states</p>	<p>Setting: United States hospitals from states that used KID (Kids' Inpatient Database) - a program that nationally represents a sample of pediatric discharges.</p> <p>Sampling Method: randomly from the KID</p> <p>Sample Size: patients diagnosed with NAS (27,943) compared to non-NAS patients (3,783,629)</p>	<p>Design: retrospective, observational study</p> <p>Level of Evidence: level III</p>	<p>From 2003 to 2012, NAS admissions increased by nearly 4 times, causing a major increase in costs for the United States (around \$61 to 316 million). Hospital stays were three times longer.</p>	<p>Research implications: to reduce healthcare costs, NAS needs to be treated better. The use of opioid maintenance programs should be implemented and people should be educated on the effects of opioids and other illicit drugs.</p>	<p>No limitations</p>

	economic system?					
<p>Dryden, C., Young, D., Hepburn, M., & Mactier, H. (2009). Maternal methadone use in pregnancy: factors associated with the development of neonatal abstinence syndrome and implications for healthcare resources. <i>BJOG: An International Journal Of Obstetrics & Gynaecology</i>, 116(5), 665-671. doi:10.1111/j.1471-0528.2008.02073.x</p>	<p>Purpose Statement: To investigate factors associated with the development of neonatal abstinence syndrome (NAS) and to assess the implications for health care resources of infants born to drug-misusing women.</p> <p>Research Questions: What factors are associated with NAS? What are the implications for health care resources of infants born to drug-misusing mothers?</p>	<p>Setting: Neonatal Unit, Princess Royal Maternity, Glasgow, UK (Inner-city maternity hospital providing dedicated multidisciplinary care to drug-misusing women)</p> <p>Sampling Method: the charts of all singleton infants born to drug-misusing women prescribed substitute methadone and delivered at Princess Royal Maternity in Glasgow over the 3-year period from 1 January 2004 to 31 December 2006 were reviewed</p> <p>Sample Size: 450 singleton</p>	<p>Design: retrospective cohort study from 1 January 2004 to 31 December 2006</p> <p>Level of Evidence: level III</p>	<p>Breastfeeding was associated with reduced odds of requiring treatment for NAS.</p> <p>Breastfeeding for greater than 72 hours was independently associated with a halving of the odds of the infant receiving pharmacologic treatment of NAS.</p>	<p>Practice Implications: pregnant drug-misusing women should be encouraged and supported to breastfeed</p> <p>An extended postnatal stay would be beneficial to be able to watch for signs of NAS, to be able to support breastfeeding, and to be able to provide parenting support.</p>	<p>Over half the infants given appointments for the outpatient clinic defaulted on two or more occasions.</p>

		pregnancies of drug-misusing women prescribed substitute methadone in pregnancy				
Ebner, N., Rohrmeister, K., Winklbaaur, B., Baewert, A., Jagsch, R., Peternell, A., & ... Fischer, G. (2007). Management of neonatal abstinence syndrome in neonates born to opioid maintained women. <i>Drug & Alcohol Dependence</i> , 87(2/3), 131-138.	<p>Purpose Statement: To examine the effects of opioid maintenance treatment on the incidence and timing of NAS compared to two different NAS treatment (Phenobarbital v. morphine).</p> <p>Research Question: What is the best medication regimen to treat pregnant mothers with drug addiction?</p>	<p>Setting: addiction clinic, medical university of Vienna</p> <p>Sampling Method: not stated</p> <p>Sample Size: 53 neonates born to mothers with drug addiction. 22 received methadone, 17 received slow-release morphine, and 14 received buprenorphine</p>	<p>Design: Not stated</p> <p>Level of Evidence: level VI</p>	All of the neonates born to mother treated with the opioid maintenance program showed APGAR scores comparable to babes of non-opioid dependent mothers. No differences were found with weight, length of head circumference between the three groups. Morphine is the best drug for neonates suffering from NAS.	Nursing implications: treat mother with drug addiction with morphine during pregnancy to improve outcomes of neonates.	Study did not exclude women using nicotine and/or cannabis, the portion of babies into the NAS groups was not randomized but dependent on when they were entered into the study, the two medications have different durations of actions, the Finnegan score was not rated under double-blind conditions
Filippeli, A., White, L., Spellman, L., Broderick, M., Highfield, E., Sommers, E., & Gardiner, P. (2012). Non-	<p>Purpose Statement: To examine the potential of non-insertive acupuncture as an adjunctive treatment for</p>	<p>Setting: BMC Pediatric Ward</p> <p>Sampling Method: convenience</p>	<p>Design: retrospective chart review</p> <p>Level of Evidence: level III</p>	Neonates receiving NIA treatments revealed a deeper sleep, had better feedings, and demonstrated	The chart review shows potential for use of NIA as an adjunctive treatment in newborns with NAS.	Acupuncturists were only available one day a week resulting in some babies being treated early in their

<p>insertive acupuncture and neonatal abstinence syndrome: A case series from an inner-city safety net hospital. <i>Global Advances in Health and Medicine</i>. 1(4), 48-52.</p>	<p>newborns with NAS. Research Question: Does NIA provide treatment of symptoms associated with NAS?</p>	<p>Sample Size: 54 newborns with NAS</p>		<p>more even breathing.</p>		<p>stay and others later in their stay.</p>
<p>Grossman, M., Berkwitz, A., Osborn, R., Xu, Y., Esserman, D., Shapiro, E., & Bizzaro, M. (2017). An initiative to improve the quality of care of infants with neonatal abstinence syndrome. <i>Pediatrics</i>, 139(6). doi:10.1542/peds.2016-3360</p>	<p>Purpose Statement: To reduce the ALOS for infants with NAS by implementing nonpharmacological interventions. Research Question: Will implementing nonpharmacological interventions, administration of morphine as needed, and transfer of infants directly to the inpatient unit reduce the ALOS for</p>	<p>Setting: Yale New Haven Children’s Hospital Sampling Method: convenience Sample Size: 287 infants with NAS</p>	<p>Design: retrospective cohort study Level of Evidence: level III</p>	<p>ALOS decreased from 22.4 to 5.9 days. Proportions of methadone-exposed infants treated with morphine decreased from 98% to 14%; costs decreased from \$44 824 to \$10 289. No infants were readmitted for treatment of NAS and no adverse events were reported.</p>	<p>Admit infants directly to inpatient unit, administer as needed morphine, and implement nonpharmacological interventions such as placing in low stimulation environment, and rooming-in.</p>	<p>During implementation of the interventions there were changes in hospital policies that may have affected results.</p>

	infants with NAS?					
Holmes, A., Atwood, E., Whalen, B., Beliveau, J., Jarvis, D., Matulis, J., & Ralston, S. (2016). Rooming-in to treat neonatal abstinence syndrome: Improved family-centered care at lower cost. <i>Pediatrics</i> . 137(6).	<p>Purpose Statement: To implement a program for NAS including standardized protocols for scoring, medications and weaning, and a calm rooming-in environment, to improve family-centered care and to decrease both length of stay (LOS) and hospital costs.</p> <p>Research Question: Will implementing a coordinated program decrease the LOS and hospital costs of infants with NAS?</p>	<p>Setting: Children's Hospital at Dartmouth-Hitchcock</p> <p>Sampling Method: convenience</p> <p>Sample Size: 163 newborns with NAS</p>	<p>Design: retrospective cohort study</p> <p>Level of Evidence: level III</p>	Coordinated, standardized NAS program safely reduced pharmacologic therapy, LOS, and hospital costs.	Implementing a QI project including standardized scoring, rooming-in, and environmental management of NAS can reduce the use of pharmacologic therapy, decrease LOS, and reduce hospital costs.	Most mothers maintained on buprenorphine as opposed to methadone which can affect the length of treatment needed.
Isemann, B., Meinzen-Derr, J., & Akinbi, H. (2011). Maternal and neonatal factors impacting response to methadone therapy in infants treated for neonatal abstinence syndrome. <i>Journal Of</i>	<p>Purpose Statement: To identify maternal and neonatal factors that are independent predictors of response to methadone pharmacotherapy for NAS.</p> <p>Research Question: What</p>	<p>Setting: The University Hospital in Cincinnati, Ohio</p> <p>Sampling Method: the charts of all newborns that received methadone therapy for NAS in the</p>	<p>Design: retrospective review</p> <p>Level of Evidence: level III</p>	<p>Inverse relationship between the amount of mother's breast milk ingested and length of stay.</p> <p>Shorter median duration of methadone therapy in breastfed</p>	<p>Research Implications: future studies should be conducted to be able to identify infants at risk for rebound NAS, care plan for opiate-dependent women beginning early in pregnancy</p>	<p>Incomplete data collection from the medical records.</p> <p>Finnegan abstinence scoring method is designed for term infants, may not be</p>

<p><i>Perinatology</i>, 31(1), 25-29. doi:10.1038/jp.2010.66</p>	<p>impact do maternal and neonatal factors impact response to methadone therapy for neonatal abstinence syndrome?</p>	<p>NICU at The University Hospital between January 2002 and December 2007 were reviewed</p> <p>Sample Size: 128 infants</p>		<p>preterm and term infants.</p> <p>Reduced incidence and severity of NAS in breastfed infants.</p>	<p>should include the risks of fetal drug exposure, the benefits of breastfeeding, and cautions against rapidly weaning infants from breast milk.</p>	<p>accurate in detecting the manifestation of NAS in preterm infants.</p>
<p>Jones, H., Kaltenbach, K., Heil, S., Stine, S., Coyle, M., Arria, A., & ... Fischer, G. (2010). Neonatal abstinence syndrome after methadone or buprenorphine exposure. <i>New England Journal Of Medicine</i>, 363(24), 2320-2331. doi:10.1056/NEJMoa1005359</p>	<p>Purpose Statement: To figure out which drug is the best treatment for neonates born to mothers with drug addiction.</p> <p>Research Question: Is Methadone or Buprenorphine a better treatment for neonates born to mothers with drug addiction?</p>	<p>Setting: 8 international sites</p> <p>Sampling Method: randomized, controlled</p> <p>Sample Size: 175 pregnant women with opioid dependence.</p>	<p>Design: double-blind, double-dummy, flexible-dosing study, comparing methadone and buprenorphine during opioid-dependent pregnancies.</p> <p>Level of Evidence: level V</p>	<p>Infants born to mothers treated with buprenorphine required substantially less morphine, required shorter hospital stays, and had a significantly shorter duration of treatment for NAS as opposed to mothers treated with methadone.</p>	<p>The preferred method of treatment for mothers with drug addiction is buprenorphine to decrease hospital stays, decreased morphine administration, and shorten the treatment of NAS care.</p>	<p>There were different rates of treatment, the amount of morphine given was important but not stated.</p>
<p>Kakko, J., Heilig, M., & Sarman, I. (2008). Buprenorphine and methadone treatment of opiate dependence during pregnancy: comparison of fetal growth and</p>	<p>Purpose statement: To compare the effects of fetal buprenorphine and methadone exposure during maintenance treatment of pregnant heroin dependent subjects?</p>	<p>Setting: Stockholm county, Sweden</p> <p>Sampling Method: non-randomized</p> <p>Sample Size: 47 pregnancies in 39 women</p>	<p>design: comparison of prospectively followed buprenorphine-exposed pregnancies to the former methadone-exposed pregnancies</p>	<p>Pregnancies exposed to buprenorphine, as opposed to methadone, resulted in less infants going through withdrawal syndrome and NAS, higher birth weights related to full</p>	<p>Start addicted women on buprenorphine, as opposed to Methadone, before they become pregnant to reduce the severity of NAS and withdrawal syndrome, decrease the</p>	<p>Not randomized, only 39 women were sampled, different addiction severities and ages, assessments of NAS were not blind, and</p>

<p>neonatal outcomes in two consecutive case series. <i>Drug & Alcohol Dependence</i>, 96(1/2), 69-78.</p>	<p>Research Question: is Methadone or Buprenorphine better for neonates born to addicted mothers in preventing withdrawal syndrome?</p>	<p>with opiate dependence and buprenorphine maintenance treatment (2001-2006), and all 35 methadone exposed pregnancies (26 women) 1982-2006</p>	<p>Level of evidence: level VI</p>	<p>term pregnancies, and shorter length of stay in the hospital. Using buprenorphine before conception further improved the health of the neonates.</p>	<p>length of stay in the hospital, and increase birth weights by improving length of pregnancies.</p>	<p>monitoring of illicit drug use was incomplete.</p>
<p>Kuschel, C., Austerberry, L., Cornwell, M., Couch, R., & Rowley, R. (2004). Can methadone concentrations predict the severity of withdrawal in infants at risk of neonatal abstinence syndrome?. <i>Archives Of Disease In Childhood -- Fetal & Neonatal Edition</i>, 89(5), F390-3</p>	<p>Purpose Statement: To determine the usefulness of methadone concentrations at 2 days of age in predicting the severity of NAS. Research Question: Can methadone concentrations predict the severity of withdrawal in infants at risk of neonatal abstinence syndrome?</p>	<p>Setting: National Women's Hospital Assessment of Drugs and Alcohol in Pregnancy Sampling Method: not stated Sample Size: 25 infants</p>	<p>Design: Not stated Level of Evidence: level VI</p>	<p>Maternal methadone dose does not predict the need for treatment of NAS. However, infants who required treatment for NAS had lower amounts of methadone in their system than those who did not receive treatment.</p>	<p>Methadone concentrations may identify infants at greater risk of developing NAS, but may not be accurate.</p>	<p>Small sample size, not randomized</p>
<p>McQueen K.A., Murphy-Oikonen J., Gerlach K., Montelpare W. (2011). The Impact of Feeding Method</p>	<p>Purpose Statement: To determine whether neonatal abstinence scores of infants exposed to methadone in</p>	<p>Setting: Northwestern Ontario Sampling Method: All methadone-exposed</p>	<p>Design: retrospective chart review Level of Evidence: level III</p>	<p>Predominantly breastfed infants had fewer NAS scores taken, lower severity scores, and lower area</p>	<p>Practice Implications: mothers on methadone maintenance programs should be encouraged and</p>	<p>Group allocation was self-selected according to the type of infant feeding,</p>

<p>on Neonatal Abstinence Scores of Methadone-Exposed Infants. <i>Advances in Neonatal Care</i>, 11(4), 282-290</p>	<p>utero differed by infant feeding method.</p> <p>Research Question: Does feeding method effect the NAS scores of infants exposed to methadone in utero?</p>	<p>infants born between March 2007 and March 2008 at the selected hospital and who were scored for NAS before discharge met the criteria to have their charts reviewed.</p> <p>Sample Size: 28 mother-infant pairs</p>		<p>scores than infants who were not predominantly breastfed.</p> <p>Breastfeeding may have helped to decrease the duration and intensity of NAS.</p>	<p>supported to breastfeed in the absence of contraindications, mothers should be educated during pregnancy on the benefits of breastfeeding, healthcare professionals should be aware of current breastfeeding recommendations for women on methadone.</p> <p>Research Implications: additional research should be conducted on breastfeeding among methadone-maintained women to explore issues such as reasons for low breastfeeding rates, healthcare providers' ideas and attitudes about breastfeeding on methadone, the effects of methadone on NAS, and effective interventions to support methadone-</p>	<p>limiting the ability to control for potentially confounding variables</p> <p>other confounding variables (SES, maternal education, etc.) were not evaluated because they were not included in the charts</p> <p>small group sizes</p> <p>instrument bias may exist (Modified Finnegan Scoring Tool)</p> <p>self-report was used to assess eligibility criteria for methadone use</p>
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					maintained mothers to breastfeed.	
<p>Mohamed E., Abde-Latif, Pinner J., Clews S., Cooke F., Lui K., Oei J. (2006). Effects of Breast Milk on the Severity and Outcome of Neonatal Abstinence Syndrome Among Infants of Drug-Dependent Mothers. <i>Pediatrics</i>, 117 (6)</p>	<p>Purpose Statement: To assess the effects of breast milk on the severity and outcome of neonatal abstinence syndrome.</p> <p>Research Question: Does breast milk reduce the severity and improve the outcome of neonatal abstinence syndrome?</p>	<p>Setting: Department of Newborn Care, Royal Hospital for Women, Randwick, New South Wales, Australia</p> <p>Sampling Method: the charts of all drug-dependent mothers who were admitted to the Department of Newborn Care between 1998 and 2004 were reviewed</p> <p>Sample Size: 190 drug-dependent mother-infant pairs</p>	<p>Design: retrospective chart review (cohort study)</p> <p>Level of Evidence: level III</p>	<p>Predominantly breastfed infants had significantly reduced mean NAS scores, delayed onset of withdrawal, a decreased need for pharmacologic interventions, and shorter hospitalization than formula-fed infants.</p> <p>No difference was found between infants fed breast milk by bottle or gavage tubes and infants who were exclusively breastfed.</p> <p>Breastfed infants exposed to multiple drugs had worse scores than infants exposed to single in utero drugs, but had considerably lower mean Finnegan scores during the entire 9</p>	<p>Practice Implications: Women should be encouraged to breastfeed</p>	<p>Finnegan scoring system was used (only validated for opiate withdrawal), some neonates may have been exposed to other substances</p> <p>institution relies on voluntary maternal disclosure as indicator of drug use, study could have been influenced by unidentified drugs</p>

				days than formula-fed infants.		
<p>Newman, A., Davies, G., Dow, K., Holmes, B., Macdonald, J., Mcknight, S., & Newton, L. (2015). Rooming-in care for infants of opioid dependent mothers. <i>Canadian Family Physician</i>. 61(12), 555-561.</p>	<p>Purpose Statement: 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.</p> <p>Research Question: Does rooming-in decrease the severity of NAS scores, lessen the need for pharmacotherapy, and shorten hospital stays?</p>	<p>Setting: Ontario</p> <p>Sampling Method: convenience</p> <p>Sample Size: 45 women taking chronic opioid therapy</p>	<p>Design: retrospective cohort study</p> <p>Level of Evidence: level III</p>	<p>With the rooming-in program, the proportion of infants requiring pharmacotherapy decreased from 83.3% to 14.3% and the average length of stay decreased from 25 days to 8.</p>	<p>Rooming-in might decrease the need for pharmacotherapy and decrease the length of stay for infants with NAS.</p>	<p>Possible bias because the NAS scoring tool that was used to quantify severity relies on some subjective judgement.</p>
<p>O'Connor, A. B., Collett, A., Alto, W. A., & O'Brien, L. M. (2013). Breastfeeding Rates and the Relationship Between Breastfeeding and Neonatal Abstinence</p>	<p>Purpose Statement: To determine whether breastfeeding is related to the duration, severity, and frequency of pharmacologic treatment for neonatal</p>	<p>Setting: Maine General Medical Center, United States</p> <p>Sampling Method: office and hospital charts of all</p>	<p>Design: retrospective chart review</p> <p>Level of Evidence: level III</p>	<p>Infants who are breastfed experience less severe NAS than infants who are not breastfed.</p> <p>Infants who are breastfed are less likely to require</p>	<p>Clinical Implications: breastfeeding education should be provided during the prenatal period</p> <p>Research implications:</p>	<p>Since this study was a retrospective chart review, the results can only be used to generate potential hypotheses (cannot establish</p>

<p>Syndrome in Women Maintained on Buprenorphine During Pregnancy. <i>Journal Of Midwifery & Women's Health</i>, 58(4), 383-388. doi:10.1111/jmwh.12009</p>	<p>abstinence syndrome (NAS). Research Question: Does breastfeeding have an effect on the duration and severity of NAS and the frequency of pharmacologic treatment for neonatal abstinence syndrome?</p>	<p>opioid-dependent pregnant women maintained on buprenorphine and treated in an integrated maternal-infant opioid dependence treatment program from December 2007 to August 2012 were reviewed Sample Size: 85 maternal-infant pairs</p>		<p>pharmacologic treatment than infants who are not breastfed. Symptoms of NAS started to resolve about 2 hours earlier in the breastfeeding cohort.</p>	<p>further research to identify the effects of breastfeeding on NAS is necessary</p>	<p>cause and effect). Not possible to distinguish the potential impact of breastfeeding from other nonpharmacologic NAS interventions, swaddling and skin-to-skin contact may occur with breastfeeding.</p>
<p>Pritham, U. A., Paul, J. A., & Hayes, M. J. (2012). Opioid Dependency in Pregnancy and Length of Stay for Neonatal Abstinence Syndrome. <i>JOGNN: Journal Of Obstetric, Gynecologic & Neonatal Nursing</i>, 41(2), 180-190. doi:10.1111/j.1552-6909.2011.01330.x</p>	<p>Purpose Statement: To examine opioid replacement therapy in pregnancy and effect on neonatal outcomes, including length of hospital stay for neonatal abstinence syndrome. Research Question: What effects do opioid replacement therapy in pregnancy and breastfeeding</p>	<p>Setting: labor and delivery unit and neonatal intensive care unit, Eastern Maine Medical Center, Bangor, Maine Sampling Method: the EMRs of all opioid-dependent pregnant women and their newborns delivered</p>	<p>Design: retrospective descriptive study Level of Evidence: level III</p>	<p>Breastfeeding may be protective for neonates withdrawing from opioids length of stay was shorter in breastfed neonates than formula-fed neonates or neonates who received formula and breast milk. Breastfeeding was associated with a decreased rate</p>	<p>Practice Implications: Breastfeeding, which has been associated with a decreased need for NAS treatment and promotes infant attachment and bonding, should be encouraged. Research Implications: Future research is needed to determine the differences in NAS between neonates whose initial exposure</p>	<p>Maternal drug use was mostly self-reported (pregnant women often minimize report of drug use) confounding variables were not evaluated researcher was dependent on the availability of medical records</p>

	after birth have on neonatal outcomes?	between January 1, 2005 and December 31, 2007 were reviewed Sample Size: 152 opioid-dependent pregnant women on methadone maintenance therapy (n=136) or buprenorphine maintenance therapy (n=16) during pregnancy and their neonates		of infant treatment for withdrawal from prenatal methadone or buprenorphine exposure.	to opioid replacement therapy occurred at different gestational ages and with different durations of exposure.	
Raith, W., Schmolzer, G., Resch, B., Reiterer, F., Avian, A., Koestenberger, M., & Urlesberger, B. (2015). Laser acupuncture for neonatal abstinence syndrome: A randomized controlled trial. <i>Pediatrics</i> , 136(5), 876-884. doi:10.1542/peds.2015-0676	Purpose Statement: To reduce duration of morphine therapy and hospital stay by implementing adjuvant laser acupuncture. Research Question: Does adjuvant laser acupuncture reduce duration of morphine therapy and length of hospital stay?	Setting: Division of Neonatology, University Hospital of Graz Sampling Method: convenience Sample Size: 28 newborns with NAS	Design: prospective, randomized, controlled, blinded, single-center study Level of Evidence: level II	Adjuvant laser acupuncture significantly reduced the duration of morphine therapy in newborns with NAS.	Laser acupuncture can be used as adjuvant therapy along with morphine in order to reduce the duration of morphine therapy in infants with NAS.	Small sample size because Austria has a low incidence of NAS

<p>Welle-Strand, G.K., Skurtveit, S., Jansson, L.M., Bakstad, B., Bjarko, L., & Ravndal, E. (2013). Breastfeeding reduces the need for withdrawal treatment in opioid-exposed infants. <i>Acta Paediatrica</i>, 102(11), 1060-1066. doi:10.1111/apa.12378</p>	<p>Purpose Statement: To examine the rate and duration of breastfeeding in a cohort of women in opioid maintenance treatment (OMT) in Norway, as well as the effect of breastfeeding on the incidence and duration of NAS.</p> <p>Research Question: How do the outcomes differ for methadone and buprenorphine-exposed infants who are breastfed compared to methadone and buprenorphine-exposed infants who are not breastfed?</p>	<p>Setting: Norway</p> <p>Sampling Method: The participants were recruited through regional treatment centers for OMT and through users' organizations for patients in OMT.</p> <p>Sample Size: 124 women treated with either methadone or buprenorphine during pregnancy and their newborns.</p>	<p>Design: two retrospective studies, one prospective study</p> <p>Level of Evidence: level III, level II</p>	<p>Reduced need for pharmacological NAS treatment in breastfed compared to formula-fed methadone-exposed infants.</p> <p>Shorter length of pharmacological NAS treatment in breastfed infants compared to all exposed infants and methadone-exposed infants</p> <p>did not find decreased incidence or duration of pharmacological NAS treatment among buprenorphine-exposed infants.</p>	<p>Practice Implications: support to initiate and continue breastfeeding should begin early in pregnancy for OMT women, advice about breastfeeding from professionals should be consistent</p> <p>Research Implications: there is a need for more research, especially on the effects of breastfeeding on NAS for buprenorphine-exposed neonates</p>	<p>Only one part of the study had a prospective design</p> <p>retrospectively designed study period may be less accurate than the prospective design due to subject recall</p> <p>children in study were born at 18 different hospitals</p> <p>questionnaire did not cover the extent of breastfeeding</p> <p>study groups were small (especially for buprenorphine-exposed neonates)</p>