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Neonatal Abstinence Syndrome: An Evidence-Based Review for the Family Nurse Practitioner

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Chapter 1: Introduction

The number of infants born with symptoms of withdrawal related to passive drug exposure in-utero has been steadily increasing in the United States. In 2012, approximately one infant was born every hour with signs of drug withdrawal as a result of maternal opioid use (Patrick, et al., 2012). Maternal use of opioids may cause neonatal withdrawal or acute toxicity that may lead to long-term neurodevelopmental effects. Intrauterine exposure to opioids causes symptoms of withdrawal in 55 to 94 percent of infants. This pattern of withdrawal is universally known as Neonatal Abstinence Syndrome (Newman, 2014).

Neonatal Abstinence Syndrome (NAS) is a constellation of clinical findings associated with drug withdrawal in neonates exposed to drugs in-utero, most commonly opioids (Backes, et al., 2011). In 1975, a syndrome of opiate withdrawal in newborns was first described by Finnegan et al (Hudak & Tan, 2012). The syndrome is characterized by dysregulation of central, autonomic, and gastrointestinal functioning. Central nervous system symptoms include an excessive high pitched cry, poor sleep quality following feedings, increased muscle tone, tremors, and convulsions. Autonomic dysregulation symptoms exhibited include increased sweating, yawning and sneezing, and increased respirations. Gastrointestinal signs including excessive sucking, poor feeding, regurgitation or vomiting and loose stools are also common (Logan, Brown, & Hayes, 2013).

The use of both licit and illicit drugs can lead to a substantial burden on the health of a society. The epidemic of opioid use in the United States has resulted in increased numbers of maternal opioid dependence resulting in neonatal withdrawal syndrome; ICD-9 code 779.5

(Hudak & Tan, 2012). Between 2000 and 2009, the incidence of NAS tripled with over 13,000 babies diagnosed with the condition in 2009 (Ordean & Chisamore, 2014).

Description of the Problem

Use of opioid pain relievers in the United States is higher than any other nation, with prescribing rates for opioids twice as high as the second ranking nation, Canada. The state of Tennessee has been ranked as the second highest in the United States, following Alabama, for prescribing rates for opioid pain relievers.(Paulozzi, Mack, & Hockenberry, 2014). Illicit drug use is prevalent in 16.2% of pregnant teens and 7.4% in pregnant women aged 18-25 years. The rate of maternal opiate use has increased nearly 5-fold in the last decade (Patrick, et al., 2012). Maternal reporting of illicit drug use is most likely lower when self-reporting when compared to results of biologic screening, leading to underestimated actual rates of intrauterine drug exposure (Hudak & Tan, 2012).

The financial burdens of NAS on society are considerable. The cost in the neonatal intensive care unit (NICU) for an infant with NAS is an average of $3,500 per day, with an average length of stay of 30 days. In 2009, 77.6% of infants with NAS were covered by state Medicaid programs (Patrick, et al., 2012). Public health and medical costs related to the care of infants diagnosed with NAS in 2009 was estimated between $70.6 million and $112.6 million in the United States (Jones, et al., 2010).

The quality of care the mother receives during pregnancy can greatly affect the outcome of the infant exposed to drugs in-utero (Jensen, 2014). The substance-using woman is at risk for complications due to the exposure affecting not only her own health and wellbeing, but the passive exposure of her developing fetus as well (Paltrow & Flavin, 2013). This high-risk

population may fail to attend regular gynecologic appointments or obtain prenatal care due to fears related to substance abuse revelation, resulting in possible punitive action including loss of child custody (Murphy-Oikonen, Montelpare, Bertoldo, Southon, & Persichino, 2012). In a drastic move to control the epidemic the state of Tennessee passed the controversial Pregnancy Criminalization Law, SB1391 on May 16, 2014 (Tn.gov, 2014). This legislative action stipulates that a woman can be prosecuted for assault charges due to the illegal use of a narcotic drug while pregnant if her child is born addicted to or harmed by the narcotic drug (DuBois, 2014).

Rationale for Review

Evidence found in the literature review reflects factors related to this growing epidemic and public health concern of NAS, but there is limited data that evaluates the role of the Family Nurse Practitioner specifically. The rationale for this review of literature is to examine the etiology, pathophysiology, clinical manifestations, tools of assessment, management, and strategies for the prevention of NAS within the scope of practice of the Family Nurse Practitioner, utilizing concepts applied from the perspective of Sister Callista Roy's Adaptation Model. No particular nursing theory was provided in the articles evaluated for this literature review.

Definition of Terms

Adaptation: A process of responding to environmental changes (Current Nursing, 2012).

Neonatal Abstinence Syndrome: NAS is a cluster of symptoms exhibited by the baby which indicates physiological response to the immediate withdrawal of maternal drug use (Ramakrishnan, 2014).

Opioid: A class of drug that binds to opioid receptors (mu, delta, kappa) to produce supraspinal analgesia by acutely inhibiting the release of noradrenaline at synaptic terminals (Hudak & Tan, 2012).

Roy's Adaptation Model: A nursing theory that recognizes an individual as a combination of spiritual, biological, and psychological systems attempting to maintain equilibrium between the environment and these systems (Current Nursing, 2012).

Theoretical Framework

The theoretical framework chosen for this review is based on Sister Callista Roy's Adaptation Model. Major assumptions of this theory are based on the hypothesis that an individual is in constant interaction with a changing environment and attempts to cope with this using both innate and acquired mechanisms which are biological, psychological, and social in origin (Roy, 2011). Roy's Adaptation Model focuses on the person as an open, adaptive system using coping skills to deal with stressors (Alligood, 2010). Roy sees the environment as a factor that surrounds and affecst the development of the person. Health is manifested by the person's ability to adapt, and an unhealthy state is a result of three types of stressors: focal, contextual, or residual. In the case of NAS, an infant is exposed to an environmental stressor, opiates, in-utero. Maternal opiate use subjects the fetus to exposure through equilibrium between the maternal and fetal circulation, and the fetus undergoes adaptation to the in-utero environment. The cessation of the maternal supply of the drug at birth can result in the onset of withdrawal symptoms in the neonate, resulting in focal stimuli stressors that can lead to an unhealthy state for the neonate. The presenting symptoms of withdrawal are a result of dysregulation of central, autonomic, and gastrointestinal functioning, and these symptoms can lead to a state of poor adaptation. The goal

of intervention is to promote adaptation and achieve a state of optimal health. Table A1 outlines the four concepts defined by Roy's Adaptation Model (Current Nursing, 2012)

Statement of Purpose

The purpose of this literature review is to present current knowledge of Neonatal Abstinence Syndrome to promote awareness among Family Nurse Practitioners. This information will serve as a guide in intervention and prevention strategies, utilizing best evidence, toward reduction in the occurrence of NAS applying concepts from Roy's Adaptation Model.

Chapter 2: Literature Review

Methods

Criteria for the literature review was limited to current articles that targeted all issues related to Neonatal Abstinence Syndrome and management thereof. The literature search was completed using the online CINAHL, Ovid, and MEDLINE information sources. Current demographic information was obtained through a web-based search. The phrases used in the literature search contained the following; "neonatal abstinence syndrome," "primary care and neonatal abstinence syndrome," "opioid abuse," "maternal drug use," and "substance abuse during pregnancy," with a date range of 2009 through 2014. The study selection process included only material that is scholarly and peer-reviewed.

Results

The information obtained through the literature review was divided into the following categories: background, etiology, pathophysiology, clinical manifestations, tools of assessment, management, outcomes, and prevention strategies.

Background

As early as 1969, pediatrician Loretta Finnegan began documenting withdrawal symptoms of newborns born to mothers that were drug dependent (Nelson, 2013). An emerging rise in the incidence of newborns with a passive addiction to heroin was observed in 1974, and Finnegan and MacNew identified a need for specific assessment and management of the condition (Maguire, Cline, Parnell, & Tai, 2013). The expression of NAS symptoms depends on the substance or combination of substances, extent of exposure, and timing of maternal exposure prior to delivery, with 50 to 90 percent experiencing withdrawal after opiate exposure alone (Bio, Siu, & Poon, 2011). The transient withdrawal associated with maternal drug use could have long-term neurodevelopmental effects on the neonate (Newman, 2014).

Etiology

NAS is a result of either iatrogenic or passive exposure to opioids. The focus of this review is passive exposure through maternal use of opioids or opioid derivatives, which results in the development of physical dependence on the substance by the infant. When the cord is clamped at birth, the combination of the sudden withdrawal from the drug, change in metabolism, and increased excretion result in elimination of the drug from the infant's system. This process leads to the onset of symptom development in the neonate. The diagnosis of NAS is made based on the infant's history and evidence of exposure obtained from infant and/or maternal drug screen and clinical signs of exposure (Lucas & Knobel, 2012).

Opioids, the causative agent of NAS, include agonists and mixed agonists-antagonists. The agonists include heroin, morphine (including prodrug codeine), fentanyl, methadone, oxycodone, meperidine, hydromorphone, tramadol, and propoxyphene. Mixed agonists-antagonists include buprenorphine, butorphanol, nalbuphine, and pentazocine (Jansson, Velez, & Harrow, 2009). The agonist effects of opioids include supraspinal analgesia, sedation, euphoria, respiratory depression, and decreased gastrointestinal motility. Opioids inhibit the release of noradrenaline at synaptic terminals (Ordean & Chisamore, 2014). Opiates are known to rapidly cross the placenta, creating equilibrium between the maternal and fetal circulation (Behnke & Smith, 2013).

Pathophysiology

The pathophysiology of NAS involves mechanisms that facilitate transplacental passage: active transport, passive diffusion, and pinocytosis. Factors that affect transport include the size of the drug molecule, its lipophilicity, the acid ionization constant of the compound, and pH of the blood. Upon clamping of the cord at delivery, the transport of the drug is discontinued leading to the onset of a withdrawal syndrome in the neonate (MacMullen, Dulski, & Blobaum, 2014). Opioid receptors are located in the central nervous system and the gastrointestinal tract. Therefore, the cessation of opioids leads to withdrawal causing central nervous system irritability, over-reactivity in the autonomic nervous system, and gastrointestinal dysfunction (Hudak & Tan, 2012).

Clinical Manifestations

When assessing the clinical manifestations of NAS, it is important to consider that many infants are poly-drug exposed to licit and illicit substances, as well as alcohol and nicotine, and

this contributes to the overall symptoms exhibited by a neonate (Jansson, Velez, & Harrow, 2009). This complicates medical management due to the exacerbation of signs and symptoms of NAS (Lucas & Knobel, 2012). Full term infants exhibit more severe and earlier onset of symptoms when compared to preterm infants due to the developmental immaturity of central nervous system functioning (Newman, 2014). Decreased severity of symptoms in the preterm infant may be related to differences in drug exposure totals and decreased fat deposits of the drug (Hudak & Tan, 2012). The presentation of clinical symptoms varies with the opioid used, the history and timing of maternal use, maternal poly-drug abuse, maternal and infant metabolism, transplacental passage of the drug, placental metabolism, and infant excretion. The expression of NAS is also affected by environmental factors and infant hunger (Lucas & Knobel, 2012).

Symptoms are unpredictable and can be related to many factors at the time of delivery, or for weeks after delivery. These symptoms can be subacute for a period as long as six months with potential neurodevelopmental problems evident until approximately 12 months of age (Lucas & Knobel, 2012). NAS symptoms are manifested in a multi-system presentation related to the location of opioid receptors. Central nervous system (CNS) symptoms include: irritability, increased wakefulness, high-pitched cry, tremors, increased muscle tone, hyperactive deep tendon reflexes, frequent yawning, frequent sneezing, and seizures. Gastrointestinal symptoms include: vomiting, diarrhea, dehydration, poor weight gain, and poor feeding. Autonomic symptoms include: diaphoresis, nasal stuffiness, mottling, fever, temperature regulation issues, tachypnea, hypertension, and piloerection (Hudak & Tan, 2012).

Underlying medical conditions can present with symptoms similar to the clinical manifestations of NAS. A thorough assessment is required to exclude possible differential diagnoses. These conditions include: infections, hyperthyroidism, hypoglycemia, hypocalcemia,

hypomagnesaemia, trauma, anoxic brain injury, or intracranial hemorrhage (Bio, Siu, & Poon, 2011). Other conditions requiring consideration as potential differential diagnoses are hypoxic ischemic encephalopathy and polycythemia hyperviscosity syndrome (Ordean & Chisamore, 2014).

T**ools of Assessment**

In 1975, pediatrician Loretta Finnegan developed a scoring system, known today as the Finnegan Score, to assess clinical symptoms exhibited by newborns (Ordean & Chisamore, 2014). The American Academy of Pediatrics recommends utilizing standardized assessment tools for scoring clinical symptoms such as the Finnegan method, the Ostrea system, or the Lipsitz tool (Lucas & Knobel, 2012).

The Finnegan Neonatal Abstinence Scoring Tool, FNAST, is an instrument used to determine the severity of symptoms of withdrawal in infants subjected to opioids in-utero. The FNAST is the most frequently used assessment tool used in clinical practice management of NAS (D'Apolito, 2014). The tool can be seen in Table A2.

Management

Overall management of NAS begins with appropriate maternal screening during pregnancy. Gathering information regarding potential drug exposure when obtaining prenatal patient histories is essential in identification of NAS risk. Self-reporting is a practical method of obtaining information, yet a biological specimen can more accurately determine substance use during pregnancy (Behnke & Smith, 2013). The American College of Obstetricians and Gynecologists (ACOG) recommends the use of a screening tool to assist in identification of drug use risk. Signs of a substance use disorder in a pregnant woman include seeking prenatal care

late in pregnancy, poor adherence to appointments, poor weight gain, symptoms of sedation, intoxication, withdrawal, or erratic behavior (Nelson, 2013). The 4P's Plus and the Substance Use Risk Profile, Pregnancy Scale were designed specifically for screening pregnant women. Regulatory guidelines regarding maternal drug screening using biological methods vary by state and practice policies (Goodman & Wolff, 2013). The 4P's Plus is a four-question tool designed to identify patients at risk for alcohol or illicit drug use (Chasnoff, et al., 2005). The questionnaire can be seen in Table A3.

Untreated withdrawal of the opioid exposed fetus is linked to preterm labor and fetal death. The risk of fetal loss has been successfully abated with the use of methadone and buprenorphine replacement therapy during pregnancy. Maternal treatment for opioid abuse during pregnancy has demonstrated improved prenatal care and participation adherence in substance abuse counseling (Pritham, 2013). In 2005, only six percent of pregnant women that were categorized as needing substance abuse treatment received it as recommended (Ramakrishnan, 2014).

Management of infants at risk for NAS begins at birth with observation, monitoring of vital signs, and utilization of scoring tools to assess for symptom development (Jansson, Velez, & Harrow, 2009). The timing and expression of NAS symptoms are variable and depend on the substance the neonate was exposed to (Bio, Siu, & Poon, 2011). Nonpharmacologic treatment of NAS includes reduction of environmental stimuli, positioning, swaddling, and breastfeeding. Breastfeeding, by women that are without contraindications, is supported by The American College of Obstetricians and Gynecologists, the American Academy of Pediatrics, and the Academy of Breastfeeding Medicine. Breastfeeding offers improved outcomes for the NAS affected neonate related to decreased severity and duration of symptoms, as well as enhanced

maternal attachment and bonding (Pritham, 2013). Rooming in with mothers has improved the outcome for NAS infants and demonstrated a diminished need for pharmacologic therapy (Ramakrishnan, 2014).

The first line pharmacologic treatment of the infant with NAS are opiates, Neonatal Morphine Solution (NMS), or combinations of opiates and phenobarbital or clonidine, to diminish symptom duration. Dosages are based on symptoms and infant weight. The overall length of hospital stay is dependent on the successful weaning of the infant from the opiates (Pritham, 2013). Medication regimens that are specific to poly-drug exposure provide beneficial adjunct therapy for infants with atypical NAS presentation (Ramakrishnan, 2014).

The average hospitalization for an infant with NAS is 30 days, followed by further outpatient monitoring by a primary care provider to assess infant growth and neurodevelopment (Backes, et al., 2011). Long-term management of infants with NAS should include sensory processing with occupational therapy, speech therapy, and physical therapy for improved motor function. Behavior modification management may be necessary and provision of a consistent environment with support of family, day care, or school programs is suggested. Medications are recommended on an individualized basis as needed for management of issues related to risk of attention deficits/hyperactivity, impulsivity control, and aggressive behaviors (Behnke & Smith, 2013).

Outcomes

The major short-term effect of opiate exposure in-utero is neonatal abstinence syndrome. The long-term outcome of opiate exposure has led to documented delayed fetal growth as well as long-term effects on neurocognitive function, sensory integration, mood and temperament, and

dysregulation from birth through three years of age. There is not a consensus on the effects, long-term, on cognition. There have been limited studies of the long-term effects of intrauterine opiate exposure on language and achievement (Behnke & Smith, 2013). There is an increased risk of both motor and cognitive developmental delays after methadone exposure in-utero. Logan, Brown, & Hayes (2013) studied drug exposed infants at nine months of age, and found that 37.5% of the sample had documented motor delays. The study also confirms that other factors, including poly-drug exposure, environmental, and medical issues, may play a role in the negative outcomes in this population (Logan, Brown, & Hayes, 2013).

Prevention Strategies

The American Nurses Association has issued a position statement encouraging the promotion of addiction treatment and social support over criminalization of women with substance abuse problems. Their position also focuses on a primary solution to perinatal substance abuse by supporting rehabilitation and therapy for treatment (American Nurses Association, 2011). Strategies of NAS prevention include promoting awareness of the effects of drug use during pregnancy, screening, intervention and referrals to treatment, and the promotion of regular prenatal care (Ramakrishnan, 2014). An understanding of the pathophysiology of NAS can lead to optimal outcomes for infants (Jansson, Velez, & Harrow, 2009). Other strategies of prevention include the promotion and maintenance of optimal health by primary care providers through the process of obtaining thorough and complete patient histories and screening those at risk for substance abuse (Behnke & Smith, 2013). Nelson states “Neonatal Abstinence Syndrome is a growing nursing, medical, social and psychological issue. Though this problem is 100% preventable, it is an issue that needs to be addressed from all disciplines” (Nelson, 2013). The Maternal Opioid Treatment: Human Experimental Research study, MOTHER, discussed the

significant consequences of opiate dependence on both maternal and infant health, determining that appropriate treatment would improve patient outcomes (Jones, et al., 2010). Dr. Michael Warren, Division of Family Health and Wellness for the State of Tennessee Department of Health, adapted a CDC framework into a chart with recommended Levels of Prevention of NAS. The chart is presented in table A4.

Chapter 3: Discussion

Synthesis of Research

This literature review has provided an overview of the neonatal drug withdrawal condition known as Neonatal Abstinence Syndrome. The literature identifies the increasing prevalence of NAS and the correlation of the condition with maternal opioid use. The clinical manifestations of NAS are identified to assist the primary care provider in early diagnosis to promote improved outcomes for the infant. Tools used to assess the risk of maternal substance abuse and scoring tools to monitor the severity of the symptoms experienced by the infant were reviewed and serve as evidenced-based guidelines in management of the condition. Management techniques presented in the literature included pharmacologic and non-pharmacologic methods. The findings of this review support the importance of prevention, early recognition, and follow up for improved long-term outcomes.

Limitations

The major limitation of this literature review is the lack of data regarding the long-term effects of NAS on children. Multiple studies were found regarding the short-term effects of NAS, but there were limited studies found that provide information regarding the overall

longitudinal effects and management of the condition. Further studies that explore the long-term issues related to NAS would be necessary to improve outcomes.

Chapter 4: Conclusion

Neonatal Abstinence Syndrome is a growing concern due to the increasing number of infants diagnosed with the condition. Caring for infants with NAS, their families, or caregivers, can present a challenge for primary care providers. Family Nurse Practitioners have the opportunity to assess the pregnant woman for risks of opiate use and to observe and intervene when signs and symptoms are observed in their fragile infants. Evidence supports the continuation of management of NAS after hospitalization and the need for comprehensive care by primary care providers through a multidisciplinary approach. Providing primary care to women of childbearing age and integrating screening techniques with appropriate early intervention can decrease the risk of NAS. Establishing consistent quality care with a nonjudgmental attitude, compassion, and an evidenced-based approach can lead to improved outcomes for NAS-affected infants and their families.

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Appendix A

Table A1 Definition of Domain Concepts by Sister Callista Roy

Person	Nursing	Health	Environment
The Person is a biopsychosocial being in constant interaction with a changing environment. The person is an open, adaptive system who uses coping skills to deal with stressors. The NAS infant faces challenges in adaptation when transitioning after drug exposure in the intrauterine environment.	The goal of nursing is to promote adaptation in the four adaptive modes, thus contributing to health, quality of life, by assessing behaviors and factors that influence adaptive abilities and by intervening to enhance environmental interactions. Intervention assists the NAS infant in coping to achieve optimal health through pharmacologic and non-pharmacologic techniques.	An inevitable dimension of a person's life, represented by a health-illness continuum. A state and a process of being and becoming integrated and whole. Attaining a state of health for the NAS infant is represented by being symptom-free and appropriately reaching growth and neurodevelopmental milestones.	All conditions, circumstances, and influences surrounding and affecting the development and behavior of persons and groups with particular consideration of mutuality of person and earth resources, including focal, contextual and residual stimuli. Optimal Health for the NAS infant is obtained through a drug-free environment.

(Alligood, 2010)

Table A2 Finnegan Neonatal Abstinence Scoring Tool

NEONATAL ABSTINENCE SCORING SYSTEM

SYSTEM	SIGNS AND SYMPTOMS	SCORE	AM						PM						COMMENTS
CENTRAL NERVOUS SYSTEM DISTURBANCES	Continuous High Pitched (or other) Cry	2													Daily Weight:
	Continuous High Pitched (or other) Cry	3													
	Sleeps <1 Hour After Feeding	3													
	Sleeps <2 Hours After Feeding	2													
	Sleeps <3 Hours After Feeding	1													
	Hyperactive Moro Reflex	2													
	Markedly Hyperactive Moro Reflex	3													
	Mild Tremors Disturbed	1													
	Moderate-Severe Tremors Disturbed	2													
	Mild Tremors Undisturbed	3													
	Moderate-Severe Tremors Undisturbed	4													
	Increased Muscle Tone	2													
	Excoriation (Specific Area)	1													
	Myoclonic Jerks	3													
	Generalized Convulsions	5													
METABOLIC/VASOMOTOR/RESPIRATORY DISTURBANCES	Sweating	1													
	Fever 100.4°-101°F (38°-38.3°C)	1													
	Fever > 101°F (38.3°C)	2													
	Frequent Yawning (>3-4 times/interval)	1													
	Mottling	1													
	Nasal Stuffiness	1													
	Sneezing (>3-4 times/interval)	1													
	Nasal Flaring	2													
	Respiratory Rate >60/min	1													
	Respiratory Rate > 60/min with Retractions	2													
GASTRO-INTESTIONAL DISTURBANCES	Excessive Sucking	1													
	Poor Feeding	2													
	Regurgitation	2													
	Projectile Vomiting	3													
	Loose Stools	2													
	Watery Stools	3													
	TOTAL SCORE														
	INITIALS OF SCORER														

(D'Apolito, 2014)

Table A3 4 P's Plus

• Parents	Did either of your parents have a problem with alcohol or drugs?
• Partner	Does your partner have a problem with alcohol or drugs?
• Past	Have you ever drank beer, wine, or liquor?
• Pregnancy	In the month before you knew you were pregnant, how many cigarettes did you smoke? In the month before you knew you were pregnant, how many beers/how much wine/how much liquor did you drink?

(Chasnoff, et al., 2005)

Table A4

The Levels of Prevention

	PRIMARY Prevention	**SECONDARY** Prevention	**TERTIARY** Prevention
Definition	An intervention implemented before there is evidence of a disease or injury	An intervention implemented after a disease has begun, but before it is symptomatic.	An intervention implemented after a disease or injury is established
Intent	Reduce or eliminate causative risk factors (risk reduction)	Early identification (through screening) and treatment	Prevent sequelae (stop bad things from getting worse)
NAS Example	Prevent addiction from occurring Prevent pregnancy	Screen pregnant women for substance use during prenatal visits and refer for treatment	Treat addicted women Treat babies with NAS

(Warren, 2013)

Appendix B Matrices

Title	**Purpose** Objective, Hypotheses, or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Study Design/ Level of Evidence**	**Findings/ Limitations**
Article 1 Backes, C. H., Backes, C. R., Gardener, D., Nankervis, C. A., Giannone, P. J., & Cordero, L. (2011). Neonatal abstinence syndrome: transitioning methadone-treated infants from an inpatient to an outpatient setting. *Journal of Perinatology, 425-430.*	To compare safety and efficacy of a traditional inpatient only approach with a combined inpatient and outpatient methadone treatment program for pharmacologic treatment of NAS.	**Population characterization:** Infants born to mothers maintained on methadone. **Sample Size:** N=121 Inpatient: 75 infants Combined: 46 infants **Inclusion**: Infants with history of maternal methadone use. **Exclusion**: Infants with history of maternal illicit drug use (cocaine, heroin, etc.)	**IV**: Demographics, Obstetrical Risk Factors, Birth Weight, Gestational Age, Incidence of prematurity **DV:** Duration of Hospital Stay, Length of Treatment, Outpatient Follow up **Instrument:** Finnegan Scoring System	Retrospective Review Level of Evidence: IV	**Findings:** The average hospitalization for an infant with NAS is 30 days, followed by further outpatient monitoring by a primary care provider to assess infant growth and neurodevelopment. Hospital stay was shorter in the combined group (13 vs 25 days; P<0.001) Treatment was longer for infants in the combined group (37 vs 21 days; P<0.01) Combined treatment decreases hospital stay and substantially reduces cost in treatment of NAS. **Limitations:** • Retrospective Design • Small study Population

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Article 2 Behnke, M., & Smith, V. C. (2013). Prenatal Substance Abuse: Short and Long-term Effects on the Exposed Fetus. *Pediatrics*, e1009-e1024.	To review data regarding the prevalence of prenatal substance abuse and the short and long-term effects on exposed infants. The aim of the study was to facilitate pediatricians in promotion and maintenance of infant and child health.	**Population Characterization:** Infants born to substance abusing women between 15 and 45 years old. **Inclusion criteria:** Exposure to: nicotine, alcohol, marijuana, opiates, cocaine, and methamphetamine.	**IV:** Maternal history, Drugs or combinations of drugs used, Testing of biological specimens, Biological specimen type; hair, urine, or meconium, Screening techniques **DV:** Fetal growth, congenital anomalies, withdrawal symptoms, neurobehavioral, cognitive functioning, language, achievement, Predisposed to drug use. **Instruments:** Maternal survey forms for self-reporting Biological specimen screening (immunoassay)	Systematic Review Level of Evidence: V	**Findings:** Opiates are known to rapidly cross the placenta, creating equilibrium between the maternal and fetal circulation. The findings were broken down into short-term and long-term effects by specific drug exposure. The most significant effect of prenatal opiate exposure is neonatal abstinence syndrome. **Limitations:** Methodological differences between studies and limited data in the extant literature make generalizations of the results difficult.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Study Design/ Level of Evidence**	**Findings/ Limitations**
Article 3 Bio, L. L., Siu, A., & Poon, C. Y. (2011). Update on the Pharmacologic Management of Neonatal Abstinence Syndrome. *Journal of*	To review the management of infants diagnosed with NAS due to opioid or polysubstance exposure.	**Population Characterization:** Neonates exposed to opioid or polysubstance exposure.	**IV:** Pharmacokinetics of the agent, Gestational Age, Total amount of exposure (time), Fetal Growth, Prematurity, Birth Weight **DV:** Manifestations of NAS	**Design:** Systematic Review of Literature Level of Evidence: V	**Findings:** A thorough assessment is required to exclude possible differential diagnoses. These conditions include infections, hyperthyroidism, hypoglycemia, hypocalcemia, hypomagnesaemia, trauma, anoxic brain injury, or intracranial hemorrhage. Oral morphine solution was found to be the preferred

Perinatology, 695-701			• Neurological • Gastrointestinal • Autonomic **Instruments:** Finnegan Scoring System		drug to treat NAS and is recommended by AAP. Non-opioid therapies can be beneficial in treatment of NAS.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design Level of Evidence**	**Findings/ Limitations**
Article 4 Chasnoff, I. J., McGourty, R. F., Bailey, G. W., Hutchins, E., Lightfoot, S. O., Pawson, L., & Campbell, J. (2005). The 4P's Plus© screen for substance use in pregnancy: clinical application and outcomes. *Journal of Perinatology*, 25(6), 368-374.	To determine the prevalence of substance use among pregnant women in five diverse communities utilizing the 4P's Plus© screen for alcohol, tobacco, and other drug use.	**Population Characterization:** Pregnant women enrolled in prenatal care clinics with positive screen. **Sample size:** N=1548 **Inclusion Criteria:** Any woman who had evidence of any alcohol or illicit substance abuse during pregnancy. **Exclusion Criteria:** Non-substance using pregnant woman.	**IV:** Alcohol use, cigarette use, alcohol and cigarette use reported on screening tool. **DV:** Screening results determining substance abuse. **Instrument:** 4P's Plus© Screening Tool	**Study Design:** Non-randomized, well designed study **Level of Evidence:** III	**Findings:** The 4P's Plus is a four-question tool designed to identify patients at risk for alcohol or illicit drug use. Among the population with a positive screen, 717 (15%) of the population continued using the substance after learning of the pregnancy. Overall, 21% of the women used alcohol prior to the recognition of pregnancy and 11% continued to use after knowledge of the pregnancy. The rates of marijuana and other illicit drug use among the women were 7 and 2%, respectively, prior to pregnancy, and dropped to 3 to 1% after learning of the pregnancy. The

					screening tool provides an opportunity for early intervention. **Limitations:** Screening tools are often focused on targeted populations rather than the general population.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 5 D'Apolito, K. (2014). Assessing Neonates for Neonatal Abstinence. *Journal of Perinatology and Neonatal Nursing*, 220-231.	To review the elements of the Finnegan Scoring Tool and describe a way to improve the accuracy and consistency of scoring infants for signs of withdrawal using an interobserver reliability approach.	**Population Characterization:** Nurses, (raters/observers) taking care of infants exposed to opioids in-utero that are exhibiting withdrawal symptoms. **Sample Size:** N=1647 **Inclusion criteria:** Participant training utilizing videos and testing with 90% reliability. **Exclusion criteria:** Participant fails to achieve 90% on testing after training.	**IV:** Assessment of signs of withdrawal: Central Nervous System Crying, Sleep patterns, Moro Reflex, Tremors, Increased muscle tone, Excoriation, Myoclonic jerks, Generalized Convulsions Metabolic, vasomotor, and respiratory Sweating, Fever, Frequent yawning, Mottling, Nasal Stuffiness, Respiratory Rate Gastrointestinal Excessive sucking, Poor feeding,	**Study Design:** Descriptive design examining relationships. **Level of Evidence:** VI	**Findings:** The FNAST is the most frequently used assessment tool used in clinical practice management of NAS. Results revealed that our of 1647 interobserver reliability checks, 45% were not performed at the same time. Findings determine that it is important to perform the interobserver reliability assessment at the same time between the two observers. **Limitations:** Timing of the interobserver reliability check is critical in obtaining accurate results.

			Regurgitation, Projectile Vomiting, Loose stools/Watery Stools **DV:** Equal scoring by each observer **Instruments:** Finnegan Scoring Tool used by 2 independent raters.		

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 6 Goodman, D. J., & Wolff, K. B. (2013). Screening for Substance Abuse in Women's Health: A Public Health Imperative. *Journal of Midwifery & Women's Health,* 278-287.	To provide a review of screening tools available to providers in both prenatal and primary women's health care settings.	**Population Characterization:** Women's Health Care Providers providing primary care and care during pregnancy.	**IV:** Prevalence of drug and alcohol use during pregnancy, variations in practice, screening integration, follow up, screening tools, intervention techniques, referral for treatment, and comorbid conditions. **DV:** Improved perinatal outcomes **Instruments:** Multiple screening tools were reviewed: ASSIST AUDIT-C CRAFFT 4P's Plus© Substance Use Risk Profile Pregnancy Scale T-ACE	**Study Design:** Retrospective **Level of Evidence:** IV	**Findings:** Screening for substance use and dependence is an essential component of women's health care. Addressing the problem leads reduces lifelong morbidity and mortality for women, and prevents or reduces exposure during pregnancy. Perinatal outcomes are improved with substance abuse screening and appropriate treatment. The 4P's Plus© screening tool is developed specifically for pregnant women. Approximately 11% of pregnant women reported using alcohol, tobacco, or illicit substances during pregnancy in 2009 National Survey on Drug Use and Health. **Limitations:** Screening can have ethical implications.

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Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 7 Hudak, M. L., & Tan, R. C. (2012). Neonatal Drug Withdrawal. *Pediatrics*, 540-560.	To provide information about the clinical presentation of infants exposed to intrauterine drugs and the therapeutic, evidence-based options for treatment and management of withdrawal.	**Population Characterization:** Infants exposed to intrauterine illicit drugs. **Inclusion criteria:** Infants exposed to Drugs of Abuse: Opioids, CNS Stimulants, CNS Depressants, Hallucinogens. **Exclusion criteria:** Non-exposed infants or iatrogenic exposed infants.	**IV:** Clinical Symptoms: Central Nervous System Crying, Sleep patterns, Moro Reflex, Tremors, Increased muscle tone, Excoriation, Myoclonic jerks, Generalized Convulsions Metabolic, vasomotor, and respiratory Sweating, Fever, Frequent yawning, Mottling, Nasal Stuffiness, Respiratory Rate Gastrointestinal Excessive sucking, Poor feeding, Regurgitation, Projectile Vomiting, Loose stools/Watery Stools Medication management using medications per protocols to affect response. **DV:** Decreased severity of symptoms with medication management. **Instruments:**	**Study Design:** Quasi-experimental Design **Level of Evidence:** III	**Findings:** In 1975, a syndrome of opiate withdrawal in newborns was first described by Finnegan. Protocols should be standardized for each nursery caring for infants with NAS. Screening for maternal substance abuse is essential. Maternal reporting of illicit drug use is most likely lower when self-reporting when compared to results of biologic screening, leading to underestimated actual rates of intrauterine drug exposure. Rule out differential diagnosis for infants with symptoms of NAS. Use scoring tool to measure symptoms of drug withdrawal. Breastfeeding should be encouraged. Tables with recommended dosing of oral morphine, methadone, and clonidine are provided. Outpatient follow up of infants with

			Weaning protocols: Four tables provided Finnegan Scoring		NAS is critical. **Limitations:** Further randomized controlled studies to measure pharmacologic therapy and weaning strategies should are necessary to assess short-term outcomes and provide for long-term follow up.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 8 Jansson, L. M., Velez, M., & Harrow, C. (2009). The Opioid Exposed Newborn: Assessment and Pharmacologic Management. *Journal of Opioid Management*, 47-55.	To provide the health care provider with a review of current evidence and practical guidelines for optimal evaluation and pharmacologic management of the opiate exposed newborn.	**Population Characterization:** Opiate exposed newborns with withdrawal symptoms. **Inclusion criteria:** Maternal history of opiate use during pregnancy. **Exclusion criteria:** Non-opiate exposed infant	**IV:** Symptoms exhibited: <u>Central Nervous System</u> Crying, Sleep patterns, Moro Reflex, Tremors, Increased muscle tone, Excoriation, Myoclonic jerks, Generalized Convulsions <u>Metabolic, vasomotor, and respiratory</u> Sweating, Fever, Frequent yawning, Mottling, Nasal Stuffiness, Respiratory Rate <u>Gastrointestinal</u> Excessive sucking, Poor feeding, Regurgitation, Projectile Vomiting, Loose stools/Watery Stools	**Study Design:** Systematic Review **Level of Evidence:** V	**Findings:** Standardized assessment and treatment protocols for early identification and appropriate treatment for opioid exposed infants are needed for optimal management. Symptom based treatment would be optimal when compared to weight based treatment to reduce replacement medication therapy. **Limitations:** Small numbers and use of convenience sampling could present limitations.

			DV: Symptom relief or improvement of symptoms **Instruments:** Finnegan Scoring Lipsitz Neonatal Drug-Withdrawal Scoring System Neonatal Withdrawal Inventory Neonatal Narcotic Withdrawal Index		

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 9 Jensen, C. (2014). Improving outcomes for infants with NAS. *The Clinical Advisor*, 85-91.	To present strategies that will improve outcomes for infants with NAS.	**Population Characterization:** Newborns exposed to illegal or prescription drugs during pregnancy. **Inclusion criteria:** Infants diagnosed with NAS **Exclusion criteria:** Non-exposed infants	**IV:** Symptoms of NAS: <u>Central Nervous System</u> Crying, Sleep patterns, Moro Reflex, Tremors, Increased muscle tone, Excoriation, Myoclonic jerks, Generalized Convulsions <u>Metabolic, vasomotor, and respiratory</u> Sweating, Fever, Frequent yawning, Mottling, Nasal Stuffiness, Respiratory Rate <u>Gastrointestinal</u> Excessive sucking, Poor feeding, Regurgitation, Projectile Vomiting, Loose stools/Watery Stools	**Study Design:** Systematic Review **Level of Evidence:** V	**Findings:** Prevalence of NAS is increasing due to increased use of illicit drugs by pregnant women. NAS symptoms can be managed with pharmacologic and non-pharmacologic measures. The quality of care the mother receives during pregnancy can greatly affect the outcome of the infant exposed to drugs in-utero. **Limitations:** Confounding variables may affect outcomes such as environmental factors, dysfunctional caregivers,

			DV: Improvement or reduction of symptoms of NAS **Instruments:** Finnegan Scoring		fetal growth problems, and polydrug exposure.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population** **Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 10 Jones, H. E., Kaltenbak, K., Heil, S. H., Stine, S. M., Coyle, M. G., Arria, A. M., O'Grady, K. E., Selby, M. B., Martin, P. R., & Fischer, G. (2010). Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure. *The New England Journal of Medicine*, 2320-2331.	To conduct a randomized controlled trial comparing buprenorphine with methadone for treatment of opioid-dependent pregnant patients.	**Population Characterization:** Opioid-dependent pregnant women between the ages of 18-41 years old with a singleton pregnancy between 6 and 36 weeks gestation at eight international sites. **Sample**: N=175 **Inclusion criteria:** Women were eligible if they had no medical or other conditions contraindicating participation, no pending legal action, no disorders related to the use of benzodiazepines or alcohol, and did not plan to give birth outside the hospital at the study site. **Exclusion criteria:** No consent. Failed to meet inclusion criteria. Gestational age outside range. Benzodiazepine use.	**IV:** Randomized dosing of Buprenorphine or Methadone **DV:** Neonates requiring treatment for NAS, Peak NAS Score, Total amount of morphine to treat NAS, Length of hospital stay, Neonatal head circumference **Instruments:** • Screening tests to meet inclusion criteria. • Finnegan	**Study Design:** Descriptive/ RCT **Level of Evidence:** I	**Findings:** Buprenorphine is an alternative to methadone for treatment of opioid dependency during pregnancy and should be considered as a first-line treatment in pregnancy. Public health and medical costs related to the care of infants diagnosed with NAS in 2009 was estimated between $70.6 million and $112.6 million in the United States. Detailed primary and secondary outcomes were broken down into tables. **Limitations:** Subpopulations of pregnant patients may likely have a variable response to one medication over another which could contribute to nonadherence.

		Medical complications Alcohol use. Legal issues. Psychological/psychiatric reason. Multiple-fetus pregnancy Outside age range. Detoxification. Did not speak English/German. Not opioid dependent.	scoring		

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 11 Logan, B. A., Brown, M. S., & Hayes, M. J. (2013). Neonatal Abstinence Syndrome: Treatment and Pediatric Outcomes. *Clinical Obstetrics and Gynecology*, 186-192.	To examine the treatment and outcomes of prenatal opiate exposure on the neonate.	**Population Characterization:** Infants exposed to maternal opiate use during pregnancy. **Inclusion criteria:** Maternal opiate dependence with prenatal fetal exposure.	**IV:** Maternal Methadone dose-Low vs high Gestational exposure to benzodiazepines Breastfeeding **DV:** Length of stay, NAS severity Longer gestation **Instruments:** • Finnegan Scoring • NICU Network Neurobehavioral Scale • Bayley Scales of Infant	**Study Design:** Descriptive-Longitudinal/ Cohort study **Level of Evidence:** IV	**Findings:** Maternal opiate dependence and fetal exposure presents complications; most notably NAS. Methadone is associated with improved stability of maternal and infant health when compared to illicit opiate use. Titration of methadone, prenatal care, and breastfeeding are recommended. Early intervention to manage treatment of NAS are recommended. **Limitations:** Further longitudinal studies of development are critical.

			Development II		

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 12 Lucas, K., & Knobel, R. (2012). Implementing Practice Guidelines and Education to Improve Care of Infants with Neonatal Abstinence Syndrome. *Advances in Neonatal Care*, 40-45.	To evaluate change in nursing knowledge about NAS and the use of Finnegan Scoring after implementation of clinical guidelines and an educational program.	**Population Characterization:** Nurses employed in NICU at single facility **Sample Size-** N=68 **Inclusion criteria:** Nurses employed in NICU at site.	**Methods:** Nurses were tested before and after participation in the educational presentation about NAS. **Instruments:** Finnegan Scoring System	**Study Design:** Descriptive, non-experimental **Level of Evidence:** V	**Findings:** The diagnosis of NAS is made based on the infants history of exposure, evidence of exposure obtained from infant and/or maternal drug screen, and clinical signs of exposure. Symptoms of NAS can be subacute for a period delayed as long as six months with potential neurodevelopmental problems evident until approximately 12 months of age. Evidence-based guidelines and education provide caregivers with tools to provide quality and accurate care to infants diagnosed with NAS. **Limitations:** Post-testing was done immediately after the educational presentation and may

					not represent knowledge retained over any length of time.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 13 MacMullen, N. J., Dulski, L. A., & Blobaum, P. (2014). Evidence-Based Interventions For Neonatal Abstinence Syndrome. *Pediatric Nursing*, 165-172.	To identify best nursing practice by systematically and critically reviewing the literature regarding interventions in Neonatal Abstinence Syndrome	**Population Characterization:** Neonates with NAS **Inclusion criteria:** Infants with prenatal NAS **Exclusion criteria:** Infants with postnatal NAS	**IV:** Drug classes: • Opiates • Cocaine • Benzodiazepines • Cannabis/marijuana • Alcohol • SSRIs **DV:** Neonatal symptoms of NAS **Instruments:**	**Study Design:** Descriptive/ Systematic Review **Level of Evidence:** V	**Findings:** Upon clamping of the cord at delivery, the transport of the drug is discontinued leading to the onset of a withdrawal syndrome in the neonate. Traditional supportive interventions have evidence for their use. **Limitations:** Future research of NAS should be at a higher level of evidence.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 14 Maguire, D., Cline, G. J., Parnell, L., & Tai, C.-Y. (2013). Validation of the Finnegan Neonatal Abstinence Syndrome Tool-Short Form. *Advances in Neonatal Care*, 430-437.	To reduce items in the Modified Finnegan Scoring Tool-Short Form to the minimum possible to retain validity in a shorter version.	**Population Characterization:** Infants diagnosed with NAS admitted to a specific NICU during designated time period. **Sample Size:** N=171 (Males-92, Females-79) **Inclusion criteria:** All infants admitted with a diagnosis of NAS during specified time period.	**IV:** NAS Symptoms: • CNS Disturbances • MVR Disturbances • GI Disturbances **DV:** Scores obtained using the M-FNAST **Instruments:** Modified Finnegan Neonatal Abstinence Syndrome Tool (M-FNAST)	**Study Design:** Correlational/ Psychometric **Level of Evidence:** IV	**Findings:** An emerging rise in the incidence of newborns with a passive addiction to heroin was observed in 1974, and Finnegan and MacNew identified a need for specific assessment and management of the condition. The M-FNAST scores ranged from 0-29 with a mean of 3.5 (SD=2.5). Utilizing the short form when assessing NAS symptoms is reliable. **Limitations:** Further analysis on a larger scale with diverse populations in multiple settings will increase validity.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 15	To evaluate the	**Population**	**IV:**	**Study Design:**	**Findings:**

Murphy-Oikonen, J., Montelpare, W. J., Bertoldo, L., Southon, S., & Persichino, N. (2012). The impact of a clinical practice guideline on infants with neonatal abstinence syndrome. *British Journal of Midwifery*, 493-501.	effectiveness of clinical practice guidelines (CPGs) when managing neonates diagnosed with NAS.	**Characterization:** Infants diagnosed NAS following exposure to opiates in-utero. **Sample:** N=90 (20 pre-intervention, 70 post-intervention) **Inclusion criteria:** Infants with two documented Finnegan NAS scores with symptoms of NAS.	NAS Symptoms: • CNS Disturbances • MVR Disturbances • GI Disturbances **DV:** NAS Scores **Instruments:** • Finnegan Scoring Tool • Clinical Practice Guidelines (Toxicology Screening, Pharmacologic and weaning protocols)	Retrospective/ cohort **Level of Evidence:** IV	CPGs successfully benefit management of infants with NAS. Future research is needed to assess the impact of specific substances and interaction of various substances on neonatal withdrawal. This high-risk population may fail to attend regular gynecologic appointments or obtain prenatal care due to fears related to substance abuse revelation, resulting in possible punitive action including loss of child custody. **Limitations:** • Includes the inability to identify neonates exposed only to methadone. • Concern related to the impact of smoking/nicotine withdrawal on the neonate.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 16 Nelson, M. (2013). Neonatal	To address the nurse's role in assessing withdrawal	**Population Characterization:** Nurses that care for	**IV:** Nursing Interventions to decrease symptoms	**Study Design:** Descriptive	**Findings:** Collaboration is needed for prevention of NAS and

Abstinence Syndrome: The Nurses Role. *International Journal of Childbirth Education*, 42.	symptoms that can be evidenced at varying degrees in drug-dependent neonates.	infants diagnosed with NAS **Inclusion criteria:** Nurses that care for infants with symptoms of NAS.	of NAS. **DV:** Improvement in symptoms of NAS in neonate. NAS Symptoms: • CNS Disturbances • MVR Disturbances • GI Disturbances	**Level of Evidence:** VI	involves prevention and care for the mother and the child. Signs of a substance use disorder in a pregnant woman include seeking prenatal care late in pregnancy, poor adherence to appointments, poor weight gain, symptoms of sedation, intoxication, withdrawal, or erratic behavior. **Limitations:** Lack of quality nursing literature on NAS.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 17 Newman, K. (2014). The Right Tool at the Right Time. *Advances in Neonatal Care*, 181-186.	To identify the superior tool used to guide identification, assessment, and treatment of NAS.	**Population Characterization:** Tools used to measure symptoms in infants diagnosed with NAS.	**Instruments:** • Finnegan Scale • Lipsitz Tool • Neonatal Withdrawal Inventory • Sophia Benzodiazepine and Opioid Withdrawal Checklist • Withdrawal Assessment Tool	**Study Design:** Systematic Review **Level of Evidence:** V	**Findings:** The transient withdrawal associated with maternal drug use could have long-term neurodevelopmental effects on the neonate. A consistent approach to the identification and assessment of infants with NAS is critical. The American Academy

					of Pediatrics recommends the modified Finnegan and the author suggest it be tested over time. Maternal use of opioids may cause neonatal withdrawal or acute toxicity that may lead to long-term neurodevelopmental effects. Intrauterine exposure to opioids causes symptoms of withdrawal in 55 to 94 percent of infants.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 18 Ordean, A., & Chisamore, B. C. (2014). Clinical presentation and management of neonatal abstinence syndrome: an update. *Research and Reports in Neonatology*, 75-86.	To provide an evidence-based clinical review of the presentation and management of NAS.	**Population Characterization:** Infants with Neonatal Abstinence Syndrome.	**IV:** Symptoms of NAS: <u>Central Nervous System</u> Crying, Sleep patterns, Moro Reflex, Tremors, Increased muscle tone, Excoriation, Myoclonic jerks, Generalized Convulsions <u>Metabolic, vasomotor, and respiratory</u> Sweating, Fever, Frequent yawning, Mottling, Nasal	**Study Design:** Systematic Review **Level of Evidence:** V	**Findings:** Between 2000 and 2009, the incidence of NAS tripled with over 13,000 babies diagnosed with the condition in 2009. The agonist effects of opioids include supraspinal analgesia, sedation, euphoria, respiratory depression, and decreased

			Stuffiness, Respiratory Rate <u>Gastrointestinal</u> Excessive sucking, Poor feeding, Regurgitation, Projectile Vomiting, Loose stools/Watery Stools **DV:** Appropriate recognition and treatment of symptoms. **Instruments:** • Finnegan Scoring • Lipsitz Scoring		gastrointestinal motility. Opioids inhibit the release of noradrenaline at synaptic terminals. Current knowledge gaps in assessment tools and management protocols exist in identification and treatment of infants with NAS.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 19 Paltrow, L. M., & Flavin, J. (2013). Arrests of and Forced Interventions on Pregnant Women in the United States, 1973-2005: Implications for Women's Legal Status and Public Health. *Journal of Health Politics, Policy and Law*, 299-343.	Description of arrests and forced interventions of pregnant women, the role of health care providers, the implications on pregnant women's liberty and maternal, fetal, and child health.	**Population Characterization:** Pregnant women with a history of attempted and actual deprivation of their physical liberty. **Sample:** N=413	**IV:** • Socioeconomic factors • Race	**Study Design:** Case Report **Level of Evidence:** V	**Findings:** The substance-using woman is at risk for complications due to the exposure affecting not only her own health and wellbeing, but the passive exposure of her developing fetus as well. Multiple demographic and case characteristics are provided in

					tables. Findings challenge the notion that forced interventions promote maternal, fetal and child health. Interventions are happening in every region of the country and affect women of all races.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 20 Patrick, S. W., Schumacher, R. E., Benneyworth, B. D., Krans, E. E., McAllister, J. M., & Davis, M. M. (2012). Neonatal Abstinence Syndrome and Associated Health Care Expenditures United States, 2000-2009. *JAMA*, E1-E7.	To determine the national incidence of NAS and maternal opiate use and to identify trends in US health care expenditures associated with NAS.	**Population Characterization:** Infants diagnosed with NAS	**Main Outcome Measures:** • Incidence of NAS • Maternal Opiate Use • Related Hospital Charges	**Study Design:** Retrospective, serial, cross-sectional analysis **Level of Evidence:** III	**Findings:** Between 2000 and 2009, a substantial increase in the incidence of NAS and maternal opiate use in the US was observed in addition to the hospital charges related to NAS. The number of infants born with symptoms of withdrawal related to passive drug exposure in-utero has been steadily increasing in the United States. In 2012, approximately one infant was born every hour with signs of drug withdrawal as a result of maternal opioid use **Limitations:**

					Hospital discharge abstracts rely on accurate coding and errors of omission and commission may occur. Incidence and hospital related expenditures might be underestimated.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 21 Paulozzi, L. J., Mack, K. A., & Hockenberry, J. M. (2014, July 4). *Vital Signs: Variation Among States in Prescribing of Opioid Pain Relievers and Benzodiazepines - United States, 2012*. Retrieved from CDC: www.cdc.gov/mmwr/preview/mmwrhtml/mm6326a2.htm?s_cid=mm6326a2_w	To examine variation among prescription rates of opioid pain relievers and benzodiazepines in the United States.	**Population Characterization:** Persons consuming opioid pain relievers and benzodiazepines in the US in 2012. **Inclusion criteria:** Data was chosen by the CDC reflecting current information from 2012 databases.	**CDC Commercial Database-IMS Health Rankings by** • State • Opioid Pain Relievers • Benzodiazepines	**Study Design:** Retrospective study **Level of Evidence:** IV	**Findings:** Opioid pain relievers and benzodiazepines are commonly prescribed in the United States. Overprescribing of opioid pain relievers can result in adverse health outcomes. Wide variation exists from one state to another in prescribing rates for these drugs. An urgent change in prescribing practices is necessary.

Title	**Purpose** Objective, Hypotheses	**Population Sample**	**Interventions/ Variables**	**Design/ Level of**	**Findings/ Limitations**

	or Study Questions	Inclusion / Exclusion Criteria	**Measurements**	**Evidence**	
Article 22 Pritham, U. (2013). Breastfeeding Promotion for Management of Neonatal Abstinence Syndrome. *Journal of Obstetric, Gynecologic. and Neonatal Nursing*, 517-526.	To educate perinatal clinicians through a review literature regarding the association between breastfeeding and NAS severity, the need for pharmacologic treatment of NAS, and length of hospital stay with in-utero exposure to methadone or buprenorphine opioid replacement therapy.	**Population Characterization:** Breastfed, opiate-exposed infants with NAS **Inclusion criteria:** Literature was chosen that included studies written in English on the topic of breastfeeding for management of NAS.	**IV:** In-utero exposure to opioids Breastfeeding Opioid Maintenance Therapy Maternal contact • Skin-to-skin contact • Swaddling • Rooming in **DV:** NAS Symptoms Length of Hospital Stay	**Study Design:** Systematic Review **Level of Evidence:** V	**Findings:** Maternal treatment for opioid abuse during pregnancy has demonstrated improved prenatal care and participation adherence in substance abuse counseling. Breastfeeding for infants with opiate exposure in-utero is beneficial for maternal and infant health. The severity and duration of NAS symptoms are decreased. Length of stay is shortened when compared to formula feeding. The overall length of hospital stay is dependent on the successful weaning of the infant from the opiate. **Limitations:** Breastfeeding rates are low in this high-risk population of women and many stop breastfeeding within one week.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 23	To provide intervention	**Population**	**IV:**	**Study Design:**	**Findings:**

Ramakrishnan, M. (2014, August). *Neonatal Abstinence Syndrome: How States Can Help Advance the Knowledge Base for Primary Prevention and Best Practices of Care.* Retrieved from ASTHO: http://www.astho.org/Prevention/NAS-Neonatal-Abstinence-Report/	strategies through state health agencies to prevent prenatal substance exposure and ameliorate the impacts of substance-exposure in infancy	**Characterization:** Substance using pregnant women in the United States and their exposed neonates diagnosed with NAS.	Substance Abuse in pregnancy **DV:** Incidence of infants diagnosed with NAS **Instruments:** Data obtained through Department of Health, Policy, Planning and Assessment Birth Statistical and Hospital Discharge Data Systems	Clinical Guidelines/ Program Evaluation **Level of Evidence:** V	State-levels of intervention are suggested: • Surveillance for NAS-affected infants and sources of maternal opiate use • Early screening for substance abuse in pregnancy • Follow-up care for opioid-dependent women • Clinical standards for identification, management, and follow-up of NAS-affected infants/families.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 24 Roy, C. (2011), Research Based on the Roy Adaptation Model*:* Last 25 Years. *Nursing Science Quarterly, pp 312-320.*	To present an overview of Roy Adaptation Model (RAM) based research.	**Theory/Subject:** Roy's Adaptation Model **Inclusion:** Research based on RAM	Variables include major theoretical concepts of Roy's Adaptation Model. **Instrument:** CAPS- Coping and Adaptation Processing Scale • 47 item Likert	**Study Design:** Descriptive Study **Level of Evidence:** V	**Findings:** The categories physiologic, self-concept, role function, and interdependence have remained useful for education, practice, and research. Coping is recognized as a critical variable in understanding the effect of

			CAPS Scale interpreted with psychometric analysis		stress on physical and mental health. The middle-range theory of coping and adaptation processing is defined in detail.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 25 (2013). *TennCare.* Nashville: State of Tennessee. Retrieved from State of Tennessee: http://health.tn.gov/MCH/NAS/	To provide data from the state of Tennessee regarding incidence of NAS among TennCare enrollees, demographic characteristics of NAS others, impact of NAS on health care expenditures, and percentage of newborns in DCS custody, narcotic prescriptions for NAS mothers, and contraceptive use among all women in CY 2012.	**Population Characterization:** TennCare recipients **Inclusion criteria:** Enrollees on TennCare with diagnosis of NAS, mothers of NAS infants **Exclusion criteria:** Privately insured, out-of-state Medicaid coverage, non-NAS infants/mothers	**IV:** NAS diagnosis TennCare status • At time of delivery • Year prior to birth • Paid narcotic prescriptions • Newborns in DCS custody • Contraceptive use **DV:** Incidence Cost **Instruments:** ICD-9 Coding records TennCare Interchange Records (using social security numbers)	**Study Design:** Descriptive/ Report of Program Evaluation **Level of Evidence:** VI	**Findings:** The incidence of NAS among TennCare recipients has risen in the state of Tennessee of 39.4% in 2012. The majority of cases are in east TN; 76%. Demographic data are reflected in several charts and graphs. Percentage of newborns in DCS custody within one year of birth is 24.3%. Women with NAS babies who received narcotics aid for by TennCare appeared to be receiving treatment for dependence/addiction. **Limitations:** Mother's receiving methadone treatment

					would not be covered by TennCare therefore those services were not reflected in this study.

Title	**Purpose** Objective, Hypotheses or Study Questions	**Population Sample** Inclusion / Exclusion Criteria	**Interventions/ Variables Measurements**	**Design/ Level of Evidence**	**Findings/ Limitations**
Article 26 Warren, M. (2013). *Tennessee Efforts to Prevent Neonatal Abstinence Syndrome.* Retrieved from State of Tennessee: http://www.tn.gov/tccy/pres-CAD-13-NAS.pdf	• To review the etiology, diagnosis, and treatment of NAS. • To describe scope of NAS in Tennessee and US • To share TN efforts related to NAS prevention.	**Population Characterization:** Neonates with history of intrauterine opioid exposure. **Inclusion criteria:** Neonates with history of intrauterine opioid exposure in the state of Tennessee. **Exclusion criteria:** Infants without history of intrauterine exposure. Infants born outside of the state of Tennessee.	**IV:** History of maternal opiate use during pregnancy Specific substance abused CNS symptoms GI symptoms Social/environmental issues **DV:** Short and long-term consequences of NAS **Instruments:**	**Study Design:** Descriptive/ Systematic Review **Level of Evidence:** V	**Findings:** No definitive log-term consequences of NAS. Social/environmental variables may confound outcomes. Incidence of NAS has increased 2.8-fold in the US. Hospital costs are high with 78% of charges to state Medicaid programs. Incidence has sharply increased in Tennessee with highest incidence in East TN with nearly all covered by TennCare. Prevention efforts have been initiated to help control epidemic.