

Neonatal Abstinence Syndrome

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An Introduction to Neonatal Abstinence Syndrome

The capabilities of drugs are not to be underestimated. If mishandled, its repercussions are devastating. Even with all the knowledge and testimonies of the harmful effects of certain drugs, as well as drug abuse, people still fall victim of its fierce control. Gradually it becomes a beast that seems impossible to tame, and external factors such as school, work, family, and friends are unfortunately affected by the compulsive habit of one person. Drug abuse has been a topic of awareness for decades, but not often do we envision these addiction victims to be pregnant. The babies exposed to drugs in the womb by their addicted mothers are known to suffer from Neonatal Abstinence Syndrome (NAS), and the fight for their lives begins from the moment they are born. Unfortunately the widespread epidemic is not talked about enough, yet everyday hundreds of babies are being diagnosed with this condition. Current understanding of NAS is examined by digging deeper into the problem from several different perspectives.

Neonatal abstinence syndrome has been a problem that has been around for an extended period of time. With rules and regulations on drugs advancing day to day there is hope that NAS can potentially become a thing of the past. With research found on the history, diagnosis, treatment and prevention a literature review has been created. NAS is a syndrome that could be a result of recreational uses of drugs or even due to the addiction of prescribed drugs from the pharmaceutical companies. There has been a substantial increase in research pertaining to NAS over the years and many new changes in both the exposure substance and clinical management of neonatal abstinence syndrome. A considerable amount of research in this syndrome has been conducted in the effort to help with treatment and diagnosis of babies suffering from NAS.

History and Trends

Opioids were not as notorious as they are today. In fact, for decades, opioids had the reputation of being useful for pain relief and was legally available for recreational use. Researchers mention that morphine is said to have been marketed for pain relief and actually used to combat other addiction such as opium addiction and alcoholism, it's abuse became more common with the evolution of the needle. Neonatal abstinence syndrome: historical perspective, current focus, future directions. Morphine's. After morphine became a social problem, diacetylmorphine, known under its trade name as heroin, was marketed as a substitute for morphine, and the recreational use of the drug only become illegal after the 1914 Harrison Act. The first records of the condition were recognized in Germany in 1875. The first documented cases in the US appeared around 1892, and the condition was identified as "congenital morphinism" then. Over time as more cases were documented and more studies were done on the condition, its name changed from "infant addiction" to "congenital neonatal addiction," and subsequently kept changing into a label that best described the understanding of what it was. The establishment of the Neonatal Abstinence Scoring System (NASS) became a pivotal role in accessing NAS babies by the symptoms they were exhibiting, with or without knowledge of the mother's hand in drug abuse (H.E. Jones, A. Fielder, 2015).

Drug abuse is known to be one of the oldest practices, but today, striking statistics show that there lies a problem that is in desperate need of a solution. Researchers have found that "the percentage of non-medical use of opioids among pregnant women is 5%," and this may seem like a very small quantity when described in these terms, but the reality is that this is a much more grand number on a larger scale, and the more statistics provided, the worse the situation

presents itself. From 2000 to 2014, the results of the comparison because the percentage of infants reported to the child welfare system with neonatal abstinence syndrome (NAS) versus fetal alcoholism spectrum disorder (FASD) show that NAS reports increased strikingly, whereas FASD reports have not shown much change over the duration of the study. Researchers attempted to predict that based on the laws and stricter authority states are now taking on drug abuse, especially for pregnant women, they expect this percentage to decline. However, based on the evidence that reports of NAS increased over time, this prediction seems unrealistic (Lynch et al, 2018). Even with the present restrictions and laws that support the protection of unborn children and incriminate negligent mothers, these results stand as evidence that government intervention has little to no effect on improving the epidemic. Much of the problem stems from women not even wanting to seek help for their addiction because of fear of the law, and so if laws are too strict, a blameless life is impacted in a very harsh way; their health suffers more everyday that their dependent mother does not seek health. Many testimonies of addicted pregnant women demonstrate why the problem seems to not only be a cycle, but is becoming an increasingly popular issue that cannot seem to be managed. In one study alone, 1424 infants with NAS were recorded as a sample size from 14 different states across U.S. children's hospitals from between 2004 to 2011 (Patrick, Kaplan, Passarella, Davis, and Lorch, 2014). If such a large sample size was able to be assembled even over the span of 7 years, it stands to represent a small percentage out a big scope. In addition, who is in that scope, and where they are mostly identified also has a big role on representation.

An interesting observation was noted in the article on the historical perspective of NAS, which took a look into the trends in ethnic background of the mothers, where majority of them profiled

to be white which was about 64% to 76%, blacks at about 5% to 10%, and hispanics at about 10% to 18%. Which makes one question the demographics of the few particular states the study drew its data from. Is it fair to conclude that based on what their results provided, addicted white women are most likely to subject their unborn child to NAS? Or, do most of the states they collected their data from have a very high percentage of whites, making the comparison of the other ethnic groups an unfair juxtaposition? Interestingly the answer to these question may lie in the fact that "NAS seems to be concentrated in states where opioid prescriptions are also highest," and so their findings may truly be justified.

Methodology

In order to effectively understand and write about Neonatal Abstinence syndrome, I researched articles via google scholar. Upon reading through articles that examined symptoms and/or outcomes, I realized that either the information was too broad and I wouldn't have been able to reproduce enough to fit 6 pages. I then took to the CCNY library and looked up NAS through Academic Search Complete. Once I looked it up, I then set up parameters to only yield results that included, articles, peer reviewed journals, and papers written from 2015 to 2018. After doing this, I was able to find articles that explored both the symptoms and childhood outcomes of NAS. Each article/peer reviewed journal that I decided to use had its own distinct central idea and this helped me to better fully comprehend the topics that I would be writing about.

The article entitled "The Epidemic of Neonatal Abstinence Syndrome, Historical References of its Origins, Assessment, and Management" by Enrique Gomez-Pomar and Loretta

P. Finnegan was used to analyze the symptoms associated with NAS. The article gave an overview of how NAS is caused as well as signs and symptoms that may present itself as NAS. In addition, the article remained objective in its analysis of the disease and gave extensive information on the history as well as the treatments involved with NAS. I also used the article called “Comparison of Neonatal Abstinence Syndrome Manifestations in Pre-term versus Term opioid-exposed infants” by Elizabeth Allocco and Marjorie Melker to analyze the symptoms of NAS, as well as childhood outcomes. While this article focused on pre-term infants suffering from NAS, it further served as a way for me to see how the outcomes of children with NAS develops and changes overtime. This article was also effective because it contained a study that was done to examine secondary outcomes of child growth development as well as treatment efficiency outcomes. This article, as well as another article I reviewed called “Neonatal Opioid Withdrawal Syndrome” by Anne Johnston provided great information about the NAS scoring tool known as the MOTHER score. Furthermore, both of these articles thoroughly explained the symptoms and outcomes that are derived from NAS.

The last article that I reviewed was called “Opioid dependence and Pregnancy: Minimizing Stress on the Fetal Brain” by JJ McCarthy and MH Leamon was cited by several PubMed central articles and examined the importance of researching NAS more and finding more effective management techniques to manage it. This article helped me understand the interactions between doctors and patients with opioid dependency issues, by providing a survey that analyzed these doctor-patient interactions, how they helped with pain management, and

neonate development. These four articles together gave me insight into how NAS is developed, the ways in which it manifests itself, and the issues and outcomes that result from it.

Symptoms

The use of opioids or other psychoactive drugs, whether illegally or for medicinal purposes during pregnancy has been shown to breed a host of dysfunctions in the fetus and results in physiological and neurological deficits once the baby is born. Neonatal Abstinence Syndrome, or NAS, is a widespread epidemic that affects women and their infants all over the world. According to researchers, 20-40% of mothers who chronically use psychoactive drugs during pregnancy tend to deliver prematurely. While premature infants do not typically develop NAS due to an underdeveloped nervous system and a decreased duration of in-utero opioid exposure, NAS can still manifest itself in these infants, or neonates, as well as full-term infants. (Allocco, Melker, 2016.)

In the case of Neonatal Abstinence Syndrome (NAS), the most common drug that causes it is opioids. This is because opioids are low in their molecular weight and are soluble in the lipid layers; therefore it can easily pass through the placenta and into the fetus in-utero. When the baby is born, and the umbilical cord is severed, the baby's access to the drug is also cut off. By this time the baby has adapted to the effects of the drug, and without it, the baby begins to feel withdrawal. In other words, the infant's central nervous system becomes dysregulated and hypersensitive to stimuli. NAS also causes autonomic abnormalities as well as major respiratory problems.

There are different cases in how the symptoms of NAS presents itself. Some cases depend on the amount of time the baby was in utero, whether the mother took prenatal vitamins while pregnant, maternal and infant metabolism, etc. NAS will manifest itself from a span of 72 hours to a week after the baby is born. Signs of the syndrome are classified as three signs, neurological, gastrointestinal, and autonomic. The neurological symptoms include tremors, seizures, increased muscle tone, sleep disturbances, irritability, or frequent crying. These symptoms also result in alterations to the Central nervous system. The gastrointestinal symptoms are comprised of diarrhea, poor feeding, and vomiting. The least common stage which is autonomic includes fever, sweating, yawning and sneezing, nasal congestion, and increased respiratory rate. (Pomar, Finnegan, 2018.) The symptoms associated with NAS vary with each neonate, because of factors such as duration of prenatal exposure, and term length. Hepatic drug clearance, which is the interval of time in which a drug metabolizes as it passes through the liver, is also a factor in determining the severity of symptoms in a neonate. The hepatic drug clearance is based on the hepatic extraction ratio, which tells the liver's capability of eliminating that drug. Common drugs that cause NAS such as opioids and morphine have a high hepatic extraction ratio; hence they stay in the system of the mother as well as the fetus for a prolonged period. The symptoms of NAS, in this case, will present itself more, especially if the infant is full-term. (Allocco, Melker, 2016.)

A scoring system for NAS has been created and used as both a clinical and investigative device. The score is symptom-based and monitors the infant suffering from NAS in a way that

has been deemed more extensive and inclusive. The most common scoring tool is called the MOTHER score, or the modified Finnegan score. This tool constitutes 19 items which are weighted differently and serves as a guideline for treatments. Each item represents a symptom that is commonly associated with NAS (Johnston, 2015.) In a study that compared symptoms present in pre-term neonates vs. full-term neonates, the MOTHER score was used. There were crucial differences in the frequency of scoring for many items on the scale. For example, pre-term infants were shown to have a decreased ability in tone and reflexes, as well as inadequate self-regulation and increased stress than term infants. The use of the Finnegan tool has been proven to decrease hospital stay as well as the need for treatment. The score can be affected in many ways, by examining the severity of NAS present in the infant, painful stimuli, and the order of score. While the scoring system has been shown to be successful in accurately obtaining NAS symptoms, it still is still a work in progress because it does not prospectively determine NAS factors in pre-term babies.

Outcomes

The number of opioid-dependent pregnant women delivering babies who are at risk of developing NAS has sky-rocketed in the past ten years. “Opioid dependence and pregnancy: minimizing stress on the fetal brain,” documentation which was conducted by the US Government Accountability Office “noted that there are three sources of dependence: untreated opioid use disorder, pain management, and medication-assisted treatment with methadone or buprenorphine.” A study of methadone patients' experiences when telling a doctor of their

pregnancy and addiction to opioids showed that doctors were not sure about adequately caring for the mothers, they also had numerous negative encounters during appointments, and failures to provide an adequate referral. Methadone and buprenorphine were seen negatively because they were perceived to be the cause of neonatal abstinence syndrome. Most mothers that were interviewed ended up having to find opioid treatment elsewhere. The outcomes of opioid withdrawal stress and maternal emotional stress on neonatal and developmental outcomes are explored. Simultaneously, efforts have been made to prohibit maternal opioid dependence and to persuade pregnant women to undergo withdrawal in order to save their babies from developing NAS. This practice, however, poses the risk of fetal hypoxia, wherein the fetus is deprived of an adequate amount of oxygen. Studies of the effects of withdrawal stress on the developing fetal brain have not been conducted and can be instrumental in fully gauging the risks involved. There has been a close observation on the disparity with hospital management of fetuses at risk for NAS. Neglecting the crucial role of maternal comforting in neonatal abstinence syndrome management is necessarily a preventable cause of poor outcomes and extended hospital stays. Hospital stay allows for continuous care of the baby and maternal/neonatal bonding, frequently unintentionally disrupted by the neonatal intensive care unit environment.

Further research is imperative in order to give the optimal dosing of methadone and buprenorphine to minimize and possibly eliminate maternal/fetal withdrawal (McCarthy, Leamon, Finnegan, 2017.) Methadone and Buprenorphine, which are used to treat opioid-related disorders such as NAS, have been shown to stabilize and prevent relapse in a pregnant woman.

However, it begs the question of whether the effects of this exposure can have a long-term or short-term effect on infants born with NAS. Studies have shown that exposure to opioids in the prenatal stage of life has resulted in deficits in the cognitive, psychomotor, and behavioral development in infants. Other studies have yielded outcomes of long-term behavioral deficits but no problems with cognition. A consolidation of studies and examinations have derived that the use of buprenorphine instead of methadone as a treatment for NAS yielded a more favorable outcome for infants. It was found that these infants were delivered at term, had a higher birth weight as well as a larger head circumference. While these studies are sporadic, they give insight as to which treatment should be the better option when it comes to the developmental outcomes of neonates.

A study that examined the secondary outcomes of child growth development by focusing on cognitive processing, language, sensory development and character, maternal stress, home environment, and severity of NAS within the initial 36 months of life was conducted in 2015. 96 children and their mothers were asked to participate in the Maternal Opioid Treatment: human experimental research (MOTHER) study. The goal of the study was to see if the severity of prenatal opioid exposure affected neonates differently in their first few years of life as well as factors of maternal stress and home environment, and also to gauge whether the use of opioid agonists (methadone or buprenorphine) breeds different developmental outcomes in children suffering from NAS. The study concluded that prenatal exposure to methadone or buprenorphine

did not have a harmful effect on growth, language ability or cognitive development, as well as the use of the opioid agonists as a treatment for NAS. (Allocco, Melker, 2016.)

Diagnosis Methodology

For this literature review on neonatal abstinence syndrome, I was able to find four articles pertaining to the diagnosis of NAS. These four scholarly articles were published between the years of 2015-2018. Using recent articles for this literature review is important in the sense that it is the most updated studies on this matter. I used several scientific journals to obtain information on diagnosis of NAS. It was difficult for me to find much information about the diagnosis of this topic but after using several medical journals and databases I was able to obtain information about the diagnosis and the scoring system; the way they can tell if NAS is present in the infant.

Some articles I used were found using the NovelNY database this was a helpful database due to its credibility and reliable sources from notable medical professors with a phd such as Patt F. Bass. Other scholarly article search engines such as Pubmed, JAMA and Frontiers were used. Extensive searching was needed to sort through the articles presented, it was very difficult to gather much information on the diagnosis of NAS during the time frame of 2015-2018 it appears that many studies done in the past were not heavily advanced on, luckily I found articles that fell in the time block and were reliable and suitable for this review. While doing advanced searching I used specific key terms to help narrow down the search and really get exactly what I was looking for. These terms included: Neonatal abstinence syndrome, neonatal abstinence syndrome diagnosis, finnegan scoring system, lipsitz scoring system and prenatal exposure to narcotics. While using scholarly article search engines it could be crucial which key terms you use because

you can get many results that may not even pertain to what you are trying to research if you don't use the correct terminology. I experimented with other engines such as BMJ, which was not as helpful because it would not allow me to access full articles, although some information was helpful I did not use any articles from BMJ. I also ran into the same issue with google scholar.

An important factor of having different sources, is being able to see the different standpoints from the different authors; whom are all in the medical field. In this literature review I will be dissecting the different articles to summarize and synthesize the information while also analyzing the author's writing techniques and how they orchestrate their knowledge on the topic to explain to the reader.

Diagnosis

Infants born with NAS can be tested in different ways. An article posted in 2018, by ARUP, explains the two ways infants can be tested, one being by umbilical cord tissue and the other by meconium. Umbilical cord tissue testing is best used to detect drug use during the third trimester of a full-term pregnancy. It can be used to detect drugs such as opioids, stimulants, sedatives and other drugs such as PCP. Some downfalls of umbilical testing is that "Concentrations of some drug analytes are lower in cord than in meconium" (ARUP 2018). Meconium is the more commonly used testing, it is the testing of the dark green substance forming the first feces of a newborn infant. This article opens up with explaining the importance of timely detection of NAS to be able to treat the neonate early and effectively. Many signs in the infant indicate the need for drug testing; sometimes simple birth complications can be misinterpreted as symptoms of NAS, but most doctors proceed on the safe route and continue

with diagnosis methods regardless of definity. The use of umbilical cord tissue or meconium are best for results over other methods like urine tests. This being because often first urination by the infant can happen quickly after birth and is only helpful for detecting drug use within the few days before birth, and not long term drug usage. ARUP is a good source because they provide interpretive case research that helps with the better understanding of the umbilical cord tissue test. The information gathered from this study is a good example of primary data because it is straight out of a lab report. The drugs administered to the birth giver may be present in the test and also this test cannot show to frequency of drug use. This testing method can be very spotty because detection of drugs such as oxycodone, heroin, etc. really depend on extent of use and often time may not even appear on the test and this causes complications when it comes to treatment, due to the maternal character denying drug use. The more effective way to detect NAS is to administer a meconium test because it can detect drug use in the last 4-5 months of pregnancy. This article was good for getting a basis of the information, although complications arose in trying to decipher the medical terms being used throughout.

The Opioid Exposed Newborn: Assessment and Pharmacologic Management, an article released by the National Center for Biotechnology delves into the different scoring systems used to diagnose infants with neonatal abstinence syndrome. The Finnegan neonatal abstinence scoring system; a 31 item scale is used to determine the severity of NAS and used as a guide to treatment. With the use of this system it allows the doctors to determine how they are going to help the infant, this system works on a scale from 1-5. In extreme cases some infants score an 8 or higher and this is when they are recommended to receive pharmacologic care. (Lauren Jansson MD, Martha Velez MD, Cheryl Harrow MD, 2016). The Lipsitz Neonatal

Drug-Withdrawal Scoring System is another system used by doctors. The Lipsitz scoring system is an 11 item scale which designates a score of 4 or higher as requirement for pharmacologic care; meaning the infant will either be given methadone or a very limited amount of the addictive drug for treatment. In scoring systems like the Lipsitz system and the Finnegan system the infant is tested on several things including measurements of sleep, crying and eating patterns. The authors then go to discuss the ostrea tool, as another type of scoring system deeming it not suitable for diagnosing infants. Having a comparison for different types of scoring systems and showing the advantages of one over the other is a systematic way for the authors to explain to the reader in a simple understandable matter. The Finnegan system is the most used by doctors in the U.S and is the most widely referenced, according to the doctors who constructed this article.

This article includes a copy of the Finnegan scoring system sheet to show the reader what they test for and how they do the scoring. Table 2, shows different signs of NAS such as, poor feeding, vomiting, loose stools and excessive irritability. While practicing this method the infant is monitored every three hours during their hospital stay to keep an updated version of how they are doing to insure timely discharge and proper treatment. The authors of this article express the importance of maternal cooperation during this time period although many mothers are not truthful of their drug use. This article continues on to breakdown the different symptoms and how you score them. This is extremely important information and is vital for the understanding of reading the scoring sheet. As mentioned previously symptoms like irritability and poor feeding are recorded. In the assessment of poor feeding the infant they monitor different factors such as tongue placement while feeding or gulping or clicking noises while sucking, infants who display poor feeding are given a score of 2. Irritability in the infant doesn't always mean crying ,

it could be portrayed in other ways like sensitivity to light, touch or sound. (Lauren Jansson MD, Martha Velez MD, Cheryl Harrow MD, 2016) After scoring of each symptom on the sheet they are added together and infants having a score of 8 or higher are then treated and remain in the hospital for the remainder of their treatment. This particular article was very clear in breaking down each aspect of the scoring and explaining how they do it from a doctor's point of view. This article was the most helpful in writing this review because it was a reliable source and was written in a simple but thorough way that aids to the complete understanding of the scoring system and its importance.

A scholarly article from 2016 from The New England Journal of Medicine titled "Neonatal Abstinence Syndrome", goes into detail to explain types of biologic testing in the neonate, something the other articles didn't do as well. Although the biologic testing is not as effective as other forms of testing; and the authors recognize this, they still deemed it important enough to include this information to establish point of views on the different types of testing. Table 3, shows the different types of biologic testing on specimens such as urine, meconium, hair and cord blood. Urine and cord blood seem to be the least reliable because the urine only detects drugs within the last few days of fetal life and only the last few hours in cord blood. Whereas, in hair it can detect drugs from the beginning of the third trimester and in meconium the beginning of the second trimester. (Table 3, Cotten, Farst and Hall). This is important information included because they infer that many organizations and doctors lack the qualification and knowledge to work with NAS cases. This article wasn't very helpful in gaining information on the diagnosis of NAS, the information gathered was similar to the other articles. The good thing about this article

was that it allowed the reader to see from a different point of view than the other articles and how these educated people with phds looked at the scenario.

A 2018 article, “The Epidemic of Neonatal Abstinence Syndrome, Historical References of Its’ Origins, Assessment, and Management” Enrique gomez-pomar and Loretta P. Finnegan, they go into extensive detail the origins and mechanisms of the assessment tools for NAS. All the systems used are essentially derived from one another, basically simplified versions of one another. This article is very complex in breaking down the coefficients of the assessments. The finnegan scoring system has been reduced over time to make it easier for the doctors to assess the test on patients present with NAS. Further studies of the external factors in the experiment and testing with the finnegan neonatal abstinence scoring system show that it is the most reliable tool in the diagnostics part of NAS. The doctors responsible for this article go on to explaining the Lipsitz tool and the neonatal narcotic withdrawal index and how it was established around the same time as the FNASS. On the contrary, these assessments didn’t gain as much recognition in the medical field due to its error rate and just the pure fact that other tests are more reliable. This article breaks down the process of how other testing procedures were branched off and modified versions of FNASS such as the maternal opioid treatment: human experimental research (MOTHER). With this testing infants are monitored twice a day to determine treatment. Although an efficient way of testing, this system still awaits further studies. This idea was not seen in other articles evaluated in this literature review and it was beneficial reading this article because it introduced new ideas, even though not fully used yet it opens up opportunities in the medical field that may help further the understanding of the diagnosis of NAS. It was interesting reading into an idea not highly practiced yet but may be the future in diagnosing NAS.

Treatment and Prevention

Even though Neonatal Abstinence Syndrome has prevailed for many decades now, it caught the attention of medical researchers fairly recently. This makes it difficult to pin down its preventive measures and treatment guidelines because serious studies and research on the topic didn't begin until the 1970s. Until then, most of the data collected for research did not show a statistical difference between the variables to be tested. Even now, the research hasn't made drastic advancements regarding treatment and preventive measures remain health suggestions for the most part. The studies that are remotely close to treatment and prevention of Neonatal Abstinence Syndrome are further discussed amongst articles in this review from most recent to oldest, ranging over 2017 and 2016.

Amongst the latest studies, is one conducted by the Department of Pharmacy in Indianapolis, Indiana. This is more of an observational correlational study where they are comparing the gap of time when the first oral dose of Morphine was used as a treatment in a neonatal intensive care unit (NICU), versus a special care nursery (SCN). This article is presented in the manner of a lab report. Starting with a gist of the experiment, it goes on to elaborate on the methods, under which patient inclusion criteria is mentioned amongst objectives and statistical analysis. Further, the results take patient demographics and the complications of NAS into consideration, along with discussing outcomes in treatment provided under NICU vs. SCN. Next, the authors discuss what they initially hypothesized, what the result came out to be, whether it was what they expected, other related details about the similarities and differences of NICUs and SCNs, and the limitations of the study.

Mitchell, Costello and Nedderman conclude this article by stating that there was no statistical significance between the outcomes of the treatment when compared to the one provided in a NICU versus the one provided in a SCN. Listed towards the very end are references that were used to write this article but it is uncertain whether the authors are the researchers that carried out the experiment as well. Since this was carried out by the Department of Pharmacy in Indianapolis and later published by *Pharmacotherapy*, it is safe to say the researchers were credible enough to carry out this research. However, despite their initial hypothesis that the infants in NICUs receive a dose of oral morphine sooner than those in SCNs, their research and results were unable to prove it. Furthermore, there was an unequal number of patients included in the study, 19 from NICUs vs. 35 from SCNs, whereas there should have been an equal number. On the other hand, it is commendable that the study factored in other variables that could have caused a hinderance in the results, such as: infants with congenital abnormalities, those that were born outside the hospital, those that were readmitted, and those that did not receive a full treatment.

Following this is a “Facilitative Policy”, published in May 2017 by Harvard Journal on Legislature. This article starts by taking a step back to 1980s to take a look at the awareness regarding NAS amongst the American public at the time, only to go on further and stress on Massachusetts and where it stands currently regarding its drug situation. The Article is broken down into seven parts, after introducing the topic loosely focused around opioid usage, the article goes on to focus on NAS, its symptoms, history, and a cost tally estimate. The third part elaborates on the misuse and treatment, comparing methadone to buprenorphine, leading the fourth part into the role played by prescribed medications. The fifth part refers to the reformative

measures but this is further divided into two parts, where the first part discusses federal measures, the second one leans in on Massachusetts again, connecting the lines between what was initially mentioned regarding the state's statistics. Part six refers to preventive measures- also divided into two parts; the first one clarifies how self-reporting is an unreliable method to depends on and that instead there should be an aggressive identification system of young women that are capable of getting pregnant- as described in part two of this subsection. Part seven provides a neat wrap to this elaborately researched article.

Since there is no experimental research at the base of this article, it is important to establish the credibility of the authors who found the necessary data to draw the conclusions and proposals regarding the treatment and prevention of NAS. It is interesting to note that both the authors have a law background, which serves as an important point considering the fact that they draw proposals- meaning they know what is in and out of the government's reach regarding its execution. Not only is the whole article strategically broken down to provide clarity, it is also well described in the sense that when the authors are discussing Methadone and Buprenorphine, they start by establishing how the drug set foot and is prevailing in the US society and how it works as a "replacement" mechanism in order to treat conditions like NAS. The authors go back and forth under all subtopics in order to expand on them so the readers understand it better. Preceding this was a shorter report compared to the other two, published in March 2017, by the Morbidity and Mortality Weekly Report (MMWR) under CDC. This is an informative report that starts by explaining what NAS is, along with descriptions of signs in the infant's behavior that can be ruled out as symptoms of NAS, leading in to the types of drugs to which exposure can

result in NAS. This is followed by the main topic of this article- prevention of NAS but the article goes on to explain factors that can hinder these proposed preventive measures.

This report is written by a collaboration of doctors that specialize in NAS and related fields like drug usage, which makes this report's sources credible. Furthermore, drugs, their outreach and exposure, that resulting in NAS is stressed by providing statistics from 1999-2010 and from 2010-2014, this astounding comparison between the time periods and their related statistics leads the readers to focus on preventive measure more. The article outdoes itself by discussing factors that serve as an obstacle in the prevention and spread of NAS and then further providing counteracting proposals in order to overcome those obstacles.

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Table 3. Biologic Testing in the Neonate.*

Biologic Specimen	Period of Detection	Collection Procedure	Special Considerations
Urine	Detects drug exposure within the last few days of fetal life	Immunoassay screening, noninvasive bag specimen collection	Efficient sample collection is necessary because the first urine specimen is the most highly concentrated; false negative results are possible because of drugs clearing rapidly from the urine and dilute urine samples.
Meconium	Detects drug exposure from the beginning of the second trimester	0.5-g stool sample collected and stored at -20°C to -80°C before drug measurement by means of organic-solvent extraction	Sample collection before contamination with human milk or formula yields most accurate results; avoid contamination with urine; specimen collection is difficult in neonates who have passed meconium in utero; results take time because a laboratory is used in most cases.
Hair	Detects drug exposure from the beginning of the third trimester	20 to 50 mg of hair cut close to the scalp required for adequate testing; stored at room temperature	Samples may be collected for several months after birth; method of detection is limited with insufficient hair sample; can be used to estimate approximate exposure period.
Cord blood	Detects drug exposure in the last few hours or days of fetal life	Sample of cord blood obtained from umbilical cord at time of birth	Testing is less sensitive than testing of other specimens because drug concentrations are lower.

* Data are from Cotten,⁵¹ Farst, Valentine, and Hall,⁵⁴ and Lozano et al.⁵⁵

Table 2. Clinical Manifestations and Outcomes of the Neonatal Abstinence Syndrome.*

Metabolic, vasomotor, and respiratory manifestations

Fever

Frequent yawning

Sneezing

Sweating

Nasal stuffiness

Respiratory rate >60 breaths per minute, with or without retractions

Mottling

Tachypnea

Gastrointestinal manifestations

Projectile vomiting

Regurgitation

Loose or watery stools

Weight loss

Poor feeding

Excessive sucking

Central nervous system manifestations

Tremors

High-pitched crying

Sleep disturbances

Increased muscle tone

Excoriation

Myoclonic jerks

Irritability

Seizures

Outcomes

Admission to neonatal intensive care unit

Pharmacologic treatment for 60–80% of infants

Prolonged hospitalization (average, 17 days)

Increased risk of birth complications (e.g., low birth weight, jaundice, and feeding difficulties)

Disrupted bonding

Child-safety concerns

* Data on manifestations are from Finnegan et al.,¹ Newnam et al.,³⁴ and D'Apollito,³⁵ and data on outcomes are from Patrick et al.,^{5,6} Jansson and Velez,²³ Lee et al.,²⁴ Uebel et al.,³⁶ Cleary et al.,³⁷ and Wachman et al.³⁸