Statewide Descriptive Analysis of Neonatal Abstinence Syndrome and Newborn Length of Stay in Indiana Using Hospital Discharge Data from 2017-2020

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Abstract

Introduction: Neonatal abstinence syndrome (NAS) is a condition in which a fetus is exposed to drugs in utero and undergoes withdrawal symptoms after birth. This study fills a gap by conducting a comprehensive descriptive analysis of characteristics and trends of NAS, with a particular focus on hospital length of stay (LOS) and drug exposures, in Indiana infants from 2017 to 2020.

Methods: This serial cross-sectional study utilized hospital discharge data from the state of Indiana from 2017 to 2020. The inclusion criteria for this study included infants who were admitted to an Indiana hospital within 30 days of birth and had no missing data on demographic and clinical characteristics (n=235,043). A logistic regression analysis was performed to analyze LOS and NAS.

Results: A larger proportion of infants diagnosed with NAS were non-Hispanic white (n=2,217 or 92.24%) compared to infants without NAS (n=187,602 or 80.61%). Since 2017, NAS incidence has decreased with 7.76 cases per 1,000 infant births in 2020. After adjusting for demographic factors (sex, race, ethnicity), the primary source of payment, and birth weight, an infant having an increased LOS has 1.036 times the odds of being diagnosed with NAS (95% CI: 1.034-1.038).

Conclusion: NAS incidence is decreasing in Indiana while drug exposure incidence is remaining consistent. An increased LOS is a consequence of NAS and adjusting for clinical and demographic characteristics did not drastically change the odds of developing NAS when LOS increased. Improving NAS surveillance will be important for future research.

Dedication

I would like to dedicate my project to my family, friends, professors, mentors, and bunnies who supported me during my journey at Grand Valley these past six years. I am truly thankful to have you all in my corner.

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Background

The American opioid epidemic has worsened in recent years as the United States utilizes over 80% of the world's opioid supply despite being 4.6% of the global population (Terplan, 2017; Krans & Patrick, 2016). In 2012, providers in the United States had prescribed the equivalent of over one opioid prescription filled per adult with over 259 million prescriptions (Pryor et al., 2017). Women are particularly vulnerable to opioid use due to having higher rates of physical abuse, sexual abuse, behavioral health issues, higher healthcare utilization rates, and rising mortality rates (Terplan, 2017).

While non-medical opioid usage is concerning for anyone, pregnant women are a high-risk group, whether the use is illicit or prescribed by a provider. This is due to the delicate placental connection between a mother and fetus before birth. During pregnancy, white non-Hispanic women are especially susceptible as they fill outpatient opioid prescriptions at the highest rate, have the fastest growing heroin usage rate, and have the highest overdose mortality rate compared to other races including Black, white-Hispanic, Asian, and other women (Krans & Patrick, 2016; Metz et al., 2018; Terplan, 2017). The 2019 National Survey on Drug Use and Health conducted by the Substance Abuse and Mental Health Services Administration (SAMHSA) found that the prevalence of opioid use in the past month among pregnant women had peaked at 1.4% in 2017 (Substance Abuse and Mental Health Services Administration [SAMHSA], 2020).

An opioid-exposed newborn (OEN) is at risk of developing neonatal drug withdrawal symptoms and/or being diagnosed with neonatal abstinence syndrome (NAS) after birth depending on the severity of symptoms. The Council of State and Territorial Epidemiologists (CSTE) defines NAS as the withdrawal process after exposure to substances in utero with contributing medications and other drugs for infants less than 28 days old (Council of State and Territorial Epidemiologists [CSTE], 2019).

NAS presents as a condition with a multitude of different symptoms that can all appear at different times. NAS symptoms may be increasingly severe depending on which substances were used during pregnancy. Infants may experience excessive crying, irritability in the central nervous system, poor sleep, gastrointestinal disturbances, yawning, tremors, excessive movement, and other symptoms. Approximately 2-11% of severe cases of NAS may lead to infants having seizures (Stover & Davis, 2015). The appearance of NAS symptoms may vary depending on which substances the infant was exposed to in-utero with on-set ranging from 24 hours to 5 days (Stover & Davis, 2015).

Common characteristics of NAS include birth weight, race, infant sex, type of drug exposure, and the presence of certain comorbidities, such as seizures, feeding difficulties, and respiratory complications (Batra et al., 2020; Harward et al., 2022). The incidence of NAS has increased rapidly from approximately ten cases per 1,000 hospital admissions in 2004 to 27 cases per 1,000 hospital admissions in 2014 (Gomez-Pomar & Finnegan, 2018). Davies et al. (2016) compared the United States NAS incidence rate to other countries and found that the United States NAS rate of 3.6 births per 1,000 hospital admissions was lower than Canada's rate of 5.1 births per 1,000 hospital admissions. This serves as an indication that the United States is not the only country with a growing rate of NAS.

According to SAMSHA, non-pharmacological treatment is best for treating infants diagnosed with NAS as this encourages the bond between mother and infant to form and develop (SAMHSA, 2016). This is a crucial aspect of care given the numerous barriers that a mother with opioid use disorder (OUD) faces, which can include but are not limited to, social, emotional, environmental, and financial barriers (SAMHSA, 2016). Additionally, the result of pharmacological treatment options for pregnant women can result in a higher incidence of NAS, as infants face additional exposure to opioids perinatally.

Literature Review

NAS is a growing public health concern due to the widespread prevalence of maternal substance use for both legal and illicit substances. A nationwide cross-sectional analysis by Hirai et al. (2021) examined hospitalization data from 48 states and the District of Columbia to evaluate the prevalence and incidence rates of NAS in the United States. An overwhelming majority of NAS infants are non-Hispanic white which is consistent with previous findings from other studies that report non-Hispanic white women as having the highest prevalence of OUD (Hirai et al., 2021). Indiana was not a state of interest in this study however, the incidence rate of NAS was slightly above the United States average of 7.1 cases per 1,000 birth hospitalizations (Hirai et al., 2021).

Some studies that examine NAS in one state include Batra et al. (2020) who examined predictors of NAS in Nevada from 2016 to 2018 (n=100,845, NAS infants n= 796). Factors that contributed to an increased odds of being diagnosed with NAS include race, payment source, feeding difficulties, neonatal jaundice, seizures, transient tachypnoea, and sepsis. Consistent with previous literature and national NAS incidence trends, infants who utilized Medicaid (OR: 2.88, 95% CI: 1.2-4.2) and infants who are white (OR: 6.16, 95% CI: 4.7-8.1) were more likely to be diagnosed with NAS (Batra et al., 2020).

A recent study conducted by Harward et al. (2022) in North Carolina examined the incidence and characteristics of NAS infants and their mothers using North Carolina's State Inpatient Database (SID) from 2016 with comparisons to data from 2000 through 2013 (n=114,517, NAS infants n= 1,120). The predictors of interest examined included race, ethnicity, birth weight, payment source, length of stay, county of residence and respective county population size, and income quartile. Similar to other studies already mentioned, white infants (Other races [OR: 0.43, 95% CI: 0.31-0.61], Black [OR 0.11, 95% CI: 0.08-1.16]) and infants on Medicaid and Medicare (Other insurance [OR: 0.35, 95% CI: 0.24-0.52], private insurance [OR: 0.07, 95% CI: 0.05-0.10]) were more likely to be diagnosed with NAS compared to other groups. However, low birth weight was not found to be a predictor of NAS (OR 0.87, 95% CI: 0.78-0.98). Notably, infants who lived in areas with a population of 50,000 to 249,000 were more likely to be diagnosed with NAS compared to larger areas with a population of greater than one million individuals (Harward et al., 2022).

Studies using nationwide data to examine inpatient hospital length of stay and predictors of NAS include Bhatt et al. (2021) who utilized the Healthcare Cost and Utilization Project's (HCUP) National Inpatient Sample (NIS) database in 2018 to look at predictors of length of stay and cost of hospitalization of NAS. Conditions alongside NAS such as seizure, sepsis, respiratory complications, feeding issues, and low birth weight were attributed to a longer LOS (Bhatt et al., 2021).

There are currently few studies in Indiana that focus on NAS. A study conducted by Joshi (2020) used Indiana Medicaid claims data to model the impact of OUD in Medicaid-enrolled pregnant women to determine if opioid intake pattern impacts the odds of giving birth to an infant with NAS. This study found that women in Indiana are more likely to give birth to an infant with NAS if they have a history of nicotine or pain medication dependence, consume alcohol, or have mental health diagnoses prior to their pregnancy (Joshi, 2020).

An additional study by López-Soto and Griffin (2021) also looked at Indiana Medicaid claims data and found that three NAS interventions (mandatory opioid testing [MOT], patient navigators, and peer recovery coaches) significantly decreased Medicaid incremental by a combined 26%. Another study by Scott (2018) used a retrospective medical record review in Indiana to examine the factors associated with the need for neonatal medication among infants born to opioid-dependent mothers. Scott (2018) found that factors pertaining to the mother's drug use (opioid usage, type of opioid used, tobacco usage, benzodiazepine usage), infant gestational age, feeding characteristics, and caregiver involvement are statistically significant in determining neonatal medication initiation.

In 2015, the International Classification of Diseases (ICD) transitioned from ICD-9-CM codes (for diagnoses prior to October 1st, 2015) to ICD-10-CM (for diagnoses on or after October 1st, 2015) (Centers for Medicare and Medicaid Services, 2015). With the introduction of ICD-10-CM, there have been several benefits to public health research including an increased level of detail when reporting health conditions and managing healthcare utilization (Centers for Disease Control and Prevention [CDC], 2015). However, the transition from ICD-9-CM to ICD-10-CM serves as a limitation in comparing more recent studies to studies that utilize ICD-9-CM codes from previous years (Batra et al., 2020).

Indiana is a state of interest for maternal and child health given their outcomes in most recent years. Approximately 623 infants died in Indiana in 2016 which is the 8th highest infant mortality rate in the United States (Indiana University School of Medicine, n.d.). In 2014, 657 Indiana infants were diagnosed with NAS (Indiana University School of Medicine, n.d.). While studies exist on the characteristics of NAS infants in the United States, there are none that currently focus on the entire state of Indiana. Additionally, there are few studies across the United States that examine data beyond the year 2018. This study fills a gap in existing knowledge by conducting a comprehensive descriptive analysis of characteristics and trends of NAS with a particular focus on inpatient length of stay (LOS) and drug exposures, in Indiana infants from 2017 to 2020.

Methodology

Study Design

This serial cross-sectional study utilizes hospital discharge data (HDD) in Indiana. The inclusion criteria for this study included infants born in Indiana from 2017 to 2020 in inpatient settings. The study protocol was reviewed and approved by Grand Valley State University's (GVSU) Institutional Review Board and determined to be non-human subjects' research. Non-federal acute care hospitals must report inpatient HDD to the Indiana Hospital Association (IHA) (Indiana Department of Health, n.d). These hospitals include a variety of healthcare settings that range from rural to larger, statewide systems that encompass over 170 hospitals across the state of Indiana (Indiana Hospital Association [IHA], n.d.).

Study Population

Figure 1 in Appendix B visualizes the inclusion and exclusion criteria of this study. In order to be eligible for the study, infants were born in Indiana and admitted to an Indiana hospital prior to 30 days of age. Additionally, infants diagnosed with NAS were diagnosed prior to 30 days of age based on recommendations by the Joint Commission (The Joint Commission, n.d). Infants who have data on age (in days), sex, race, ethnicity, residency status, the year they were admitted to the hospital, and their primary source of payment for services were considered eligible for the study.

Infants must have clinical data on their birth weight in grams (g) and the ICD-10-CM code for their principal diagnosis. Infants who weigh less than 1,000g were considered to be extremely low birth weight (ELBW) and thus were excluded from the study (University of Rochester Medical Center, n.d.).The principal diagnosis is the condition that is chiefly responsible for the admission of the patient after a review from providers. This is utilized rather than the admitting diagnosis as the admitting diagnosis can differ based on further evaluation. Completed data on the type and source of the hospital admission, the discharge status, whether emergency services were needed, and LOS were also required to meet the inclusion criteria. Missing data on any of the demographic, clinical, and administrative characteristics results in the infant being excluded from the study. After applying the inclusion and exclusion criteria to the study sample, 235,043 infants were eligible for the study.

Study Variables

Due to some groups having a smaller sample size, some groups within certain variables were recoded into a separate group within each variable. These variables include other races (including newborns that were Asian and Pacific Islander, American Indian and Alaskan Native, and multiple races), "other government insurance" (includes Medicare), an admission classified as "urgent" (includes trauma center admissions), and "other discharge status" (includes discharges to home care, nursing facilities, and against medical advice). All of these recodes are denoted by table notes.

The exposure of interest was LOS and this was calculated by the IHA. A separate binary LOS variable was recoded into two categories. These two categories include a LOS less than or equal to three days and a LOS greater than three days for data analysis to test for statistical differences in the sample. LOS was unmodified during additional analyses in this study.

Infants with a birth weight ranging from 1,000g to 2,500g were categorized as low birth weight infants for the analysis of this study (University of Rochester Medical Center, n.d.). Table 1 in Appendix B displays the definitions of ICD-10-CM codes that were used in this study. Any drug exposure was recorded as the presence of any of the following ICD-10-CM drug usage codes: P04.14 (opiates), P04.4 (drugs of addiction), P04.40 (unspecified drugs of addiction), P04.41 (cocaine), and P04.49 (other drugs of addiction). This variable was recoded as yes or no based on the binary findings within each of the aforementioned drug exposure variables.

Study Outcomes

The outcome of this study was NAS which was coded as a binary variable as yes or no. The presence of ICD-10-CM code P96.1 ("neonatal withdrawal symptoms from maternal use of drugs of addiction" was used to determine whether the infant was diagnosed with NAS based on recommendations from previous literature and the Indiana Department of Health (Elmore et al. 2020; Doherty et al. 2021). Code P96.1 may have been the principal diagnosis or one of up sixty potential secondary diagnoses ICD-10-CM codes in order to be considered an infant diagnosed with NAS.

Statistical Analysis

Data analyses were conducted in Microsoft Excel and Statistical Analysis System (SAS) software version 9.4. Incidence rates for NAS and newborn drug exposure based on prenatal maternal drug use were calculated. NAS incidence rates were calculated per 1,000 infant birth hospitalizations for the entire sample and both sexes by year of the study. Newborn drug exposure incidence rates were calculated by year per 1,000 infant birth hospitalizations. Percent change was calculated based on the incidence rates calculated for NAS and overall newborn drug exposure during the four-year study period. Percent change was not calculated for specific types of drugs due to the small sample size and lack of data for some years (e.g. opiate use was only accurately available for two years).

A chi-square analysis was used to determine if there were any statistical differences in the sample between a LOS beyond three days and the diagnosis of NAS. A logistic regression analysis was performed on LOS and NAS to estimate odds ratios and 95% confidence intervals.

The first model was unadjusted by any study variables. The second model was adjusted by sex, race, and ethnicity. The third model was adjusted by the variables in model 2, the primary source of payment and birth weight. An additional model was adjusted for the same factors as the third model, however, birth weight was replaced by low birth weight.

Results

Demographic Characteristics of Infants in Indiana

Table 2 in Appendix C displays the demographic characteristics of infants within 30 days of birth in Indiana from 2017 to 2020. The year 2019 had the largest number of infant hospitalizations (n=61,795 or 26.55%) and the year 2017 had the largest number of infant hospitalizations with NAS (n=691 or 29.97%). While both groups of infants were composed of infants who were predominantly white, infants diagnosed with NAS had a higher distribution of white infants (n=2,127 or 92.24%) compared to infants without NAS (n=187,602 or 80.61%). A higher proportion of infants diagnosed with NAS receive Medicaid (n=1,806 or 78.32%) compared to infants without NAS who receive commercial insurance more commonly (n=118,889 or 51.08%).

Clinical Characteristics of Infants in Indiana

Table 3 in Appendix C displays the clinical characteristics of infants by the diagnosis of NAS within 30 days of birth in Indiana from 2017 to 2020. Infants diagnosed with NAS comprised a higher proportion of being urgent (n=56 or 2.43%) or emergency hospital admissions (n=113 or 4.90%) compared to infants without NAS (emergency [n=3,058 or 1.31%] and urgent [n=1,324 or 0.57%]). Infants diagnosed with NAS were transferred to other hospitals or institutions at a higher proportion (n=166 or 7.20%) compared to infants without NAS (n=3,600 or 1.55%). Infants without NAS had an average length of stay of 3.6 days (SD: 7.923) compared to infants diagnosed with NAS having an average length of stay of 15.491 days (SD: 15.017) despite the lower range. Infants without NAS also weighed an average of 3,509.271g (SD: 1,403g) compared to infants diagnosed with NAS weighing an average of 3,324.059g (SD: 1,452g).

Newborn Drug Exposure Characteristics of Infants in Indiana

Table 4 in Appendix C displays the drug exposures in utero for infants with (n=2,306) and without NAS (n=232,737) within 30 days of birth in Indiana from 2017 to 2020. As anticipated, infants diagnosed with NAS were exposed to any drug at a higher proportion (n=917 or 39.77%) compared to infants without NAS (n=3,045 or 1.31%). Drug exposure for the five ICD-10-CM codes did not go above 1.14% of the sample without NAS while infants diagnosed with NAS had a greater range of 1.52-29.97% between the codes. The code for other drug use exposure (P04.4) was the ICD-10-CM code used most frequently by both groups. For infants diagnosed with NAS, opiate exposure (P04.14) had the highest proportion of exposed infants out of the two exposure codes that name a specific substance (n=259 or 11.23%). Approximately 427 infants who were exposed to opioids in utero (0.18%) did not develop NAS.

Chi-Square

Table 5 in Appendix D displays the results of an independent chi-square analysis conducted on the sample. There is a statistically significant difference between LOS and the diagnosis of NAS, X^2 (1, N=235,043) = 12,772.4983, $p < .0001$. Infants diagnosed with NAS were more likely to have a LOS greater than 3 days based on expected values per each category within the sample (n=2,023 or 87.73%). This is contrary to 11.15% of infants not diagnosed with NAS requiring a LOS greater than 3 days (n=25,947).

NAS Incidence in Indiana

Figure 2 in Appendix D displays the incidence of NAS in Indiana from 2017 to 2020. The incidence of NAS was highest in 2017 at 11.44 cases per 1,000 infant hospitalizations. Since 2017, NAS incidence has decreased with 7.76 cases per 1,000 infant hospitalizations in 2020. NAS incidence is higher in male infants every year except in 2018 with a four-year incidence of 10.23 cases per 1,000 infant hospitalizations from 2017 to 2020. Female NAS incidence was highest in 2018 at 11.26 cases per 1,000 infant hospitalizations and a four-year incidence of 9.28 cases per 1,000 infant hospitalizations. The overall incidence of NAS has decreased by 35.75% from 2017 to 2020.

Newborn Drug Exposure Due to Maternal Prenatal Drug Use Incidence

Figure 3 in Appendix D displays the incidence of newborn drug exposure due to maternal prenatal drug use in Indiana from 2017 to 2020. No consistent trends were observed among the incidence of any drug exposure from year to year. There were higher incidence rates in 2017 and 2019 with above 17 exposures per 1,000 infant hospitalizations. The years 2018 and 2020 had lower rates that fall below the four-year incidence rate of 16.91 exposures per 1,000 infant hospitalizations. Other drug use (P04.4) had the highest four-year incidence rate but declined by 2020. The overall incidence of any drug exposure had a 2.53% decrease from 2017 to 2020.

Logistic Regression

Table 7 in Appendix E displays the results of the logistic regression analysis of LOS and the diagnosis of NAS among infants born in Indiana from 2017 to 2020. The first model was unadjusted for any covariates and found that as LOS increases, an infant has 1.037 times the odds of being diagnosed with NAS (95% CI: 1.035-1.039). The odds ratio of an infant being diagnosed with NAS did not change when adjusting for sex, race, and ethnicity in the second model. However, there was a slight shift in the 95% confidence interval of the second model from 1.035-1.039 to 1.036-1.039. After adjusting for the factors in the second model, the primary source of payment, and birth weight, an infant having an increased LOS has 1.036 times the odds of being diagnosed with NAS which is a slight decrease from the previous two models (95% CI: 1.034-1.038). The fourth model replaced birth weight with low birth weight and this did not drastically change the model which resulted in the same odds ratio as the first unadjusted model (OR: 1.037, 95% CI: 1.035-1.039). All four models were statistically significant.

Discussion

The findings in this study are consistent with previous research as the sample of infants diagnosed with NAS is predominantly non-Hispanic white and NAS is more prevalent in male infants compared to female infants. However, it is notable that NAS was more prevalent in female infants in 2018 when compared to male infants. Overall, in Indiana, NAS is trending downwards with a percent change of 35.75% from 2017 to 2020. Females saw a greater change in percent change from 2017 to 2020 with a 35.83% decrease when compared to males during the same time period with a 35.68% decrease.

Drug exposure incidence rates saw a small percent change decrease of 2.53% from 2017 to 2020. Drug exposure percent changes were not calculated per type of drug exposure due to the small sample size which may explain why codes such as P04.4 (other drug use) and P04.49 (other drugs of addiction) have slightly higher incidence rates compared to the following years, but it is not certain as there was no independent check or replication conducted after the data were received. Both codes existed in 2017 according to CMS, so it is unknown why they were not utilized (CMS, 2021). Results for these drug types should be interpreted with caution as the changes in trends may be due to data inaccuracy, not actual changes in infant exposure.

In comparison to NAS trends in the United States, Indiana was ranked 14th highest according to Healthcare Cost and Utilization Project (HCUP) Fast Stats data in 2017. HCUP Fast Stats data on NAS incidence is publicly available through the Agency for Healthcare Research and Quality (AHRQ) from the years 2008 through 2019 (Healthcare Cost and Utilization Project [HCUP], 2021). In the year 2017, Indiana had a NAS incidence rate of 10.4 cases per 1,000 birth hospitalizations compared to the United States average of 7.3 cases per 1,000 birth hospitalizations. As of 2018, the United States has an overall NAS incidence rate of 6.8 cases per 1,000 birth hospitalizations compared to Indiana's 9.1 cases per 1,000 birth hospitalizations (HCUP, 2021). While there are no national trends for the year 2019, Indiana decreased its ranking to 18th in the United States at 7.4 cases per 1,000 birth hospitalizations. These trends are similar to the findings in this study where NAS is decreasing overall in the state of Indiana in 2017 and 2018.

Previous studies found that characteristics of NAS infants included identifying as non-Hispanic white, being male, being considered low birth weight, and utilizing Medicaid as a payment source (Hirai et al., 2021). This study found a difference within the sample when comparing infants diagnosed with NAS compared to infants not diagnosed with NAS when looking at hospital LOS. More infants with NAS were expected to have a hospital LOS of less than three days similar to infants without NAS. However, this was not the case as a majority of infants diagnosed with NAS had a hospital LOS greater than three days. The association between LOS and NAS did not change when adjusting for characteristics of NAS.

Strengths and Limitations

This study used a large HDD dataset over a four-year period with over 235,000 inpatient infants in the sample after the inclusion and exclusion criteria were applied. Additionally, there are very few studies in Indiana that look at NAS within the state with no studies that focus on characteristics of NAS infants based on newborn health outcomes within 30 days of age. This study utilizes more recent data than other similar studies in Indiana and other state-specific studies that look at NAS-related characteristics and trends.

The large sample size of this study combined with data collected by the IHA from over 170 acute care hospitals in Indiana has created a dataset that is representative of the state of Indiana which is important for the external validity of this study. This study also utilizes ICD-10-CM codes which provide greater specificity when compared to ICD-9-CM codes. This higher degree of specificity allows for more precise reporting in medical records and in public health research (American Medical Association, 2014; CDC, 2015). This is especially notable given that this study evaluated the presence of five ICD-10-CM neonatal drug exposure codes throughout the sample. The ICD-10-CM code used to identify cases of NAS was P96.1 and this code has high sensitivity, and specificity (Goyal et al., 2020). Code P96.1 is also included in Indiana's clinical case definition of NAS (Chiang et al., 2019).

This study had some limitations. Over 102,000 infants in the study were missing data and were excluded from the study. The transition from ICD-9 to ICD-10 codes in late 2015 has potential implications as facilities and coders began transitioning to the new coding system. Additionally, physicians had to provide more specific documentation beyond what was required for ICD-9. ICD-10 codes abstracted from medical records can be used for billing and reimbursement purposes and do not provide as much information as a medical record review or other clinical data sources (CDC, 2015). Drug and alcohol dependence are some of the most commonly reported conditions with unspecified diagnosis codes which create issues for data quality, surveillance, and limiting claim denials (American Health Information Management Association [AHIMA], n.d.). There are also some limitations surrounding the drug exposure codes examined in this study as the disclosure of maternal substance use may be underreported based on stigma and legal concerns which impact the sensitivity of these codes (Goyal et al., 2020).

Another limitation is the lack of recent national data on NAS trends. This makes the comparison to previous studies that utilize ICD-9 codes more difficult and also limits the comparison to other similar studies in other states (Batra et al., 2020). There was only publicly available HCUP data through 2018 so only the years 2017 and 2018 were utilized in the national comparison (HCUP, 2021). This can be an area where a future study investigates this topic further as HCUP or other data sources release more current data on NAS trends in the United States.

Conclusion and Future Directions

Public Health Implications

This study highlights the characteristics of NAS infants in Indiana and can help highlight areas of interest for clinical monitoring after birth. Since this study is one of the few studies in Indiana to look at NAS trends and characteristics, it provides an overview of NAS in Indiana and how certain factors impact hospital LOS. As non-Hispanic white women fill the most opioid prescriptions and have the highest opioid-related mortality rate, they have become a population of interest for OUD (Terplan, 2017). Non-Hispanic white infants are diagnosed with NAS at a higher prevalence than other races in Indiana and this will continue to be a population of interest for developing more targeted interventions.

By studying the characteristics of NAS infants, researchers can determine populations at risk. This can assist in creating targeted programs for treatment and rehabilitation while a mother is still pregnant. OUD is not an issue that will see improvement without several contributions from policymakers, public health, and medical professionals. There are several areas for future research and development that will benefit not only pregnant women but also marginalized and vulnerable women. Stover and Davis (2015) are suggesting that more resources need to be dedicated to improving maternal OUD outcomes during drug treatment throughout pregnancy. This helps to reduce the severity of NAS if it is diagnosed upon the birth of the infant.

Lastly, studying the characteristics of NAS infants will help facilitate a better understanding of healthcare utilization in Indiana. A longer length of stay is a consequence of NAS as infants with NAS require more care based on their condition. Additional resources can be dedicated to mothers and infants during their prolonged hospital visits. These resources can assist in providing support for mothers after they leave the hospital, drug therapy and rehabilitation, and additional assistance in follow-up visits with their providers. Since infants with NAS have been found to utilize healthcare resources at a higher frequency long-term compared to infants without NAS, this is a critical area to consider and support (Liu et al., 2019).

Future Directions

NAS and maternal OUD are both growing public health issues when it comes to implementing new methods of supporting at-risk mothers and infants. The history of the opioid epidemic has influenced some of the barriers that exist today for pregnant women with substance use disorder (SUD) and/or OUD. In many states, the law severely punishes pregnant women who use illicit substances. This can make it challenging to reach this population of women and can lead to more infants being diagnosed with NAS once they are born.

Due to these policies, it is inevitable to run into barriers when attempting to monitor illicit drug usage among women of reproductive age. According to Angelotta et al. (2016), as of 2012, nineteen states classified illicit substance misuse during pregnancy as a form of either civil or criminal child abuse. Fear of being charged with child abuse can attribute to the number of misrepresented and underreported SUD cases. These critical decisions by each state play a huge role in determining access to care, funding, and other resources for pregnant women seeking assistance for SUD.

Dedicating more resources toward addiction medicine for pregnant women, the negative stigma of being pregnant and using substances, the fear of legal consequences in the aforementioned states, and the lack of transportation for prenatal care are all areas where policymakers need to improve and expand support. While many of these changes are substantial social and policy-level changes, some changes also need to occur on the patient-provider level as well. NAS is a public health issue with many barriers that intersect medical ethics, health policy, and negative social stigma. Placing the fear of prosecution over safety and personal health is far from the solution.

While Hirai et al. (2021) found the growth of maternal OUD is rising at a higher rate than NAS, there is a positive side. Despite having in-utero exposure to opioids, not all OENs will meet the diagnosis criteria to be formally diagnosed with NAS. In January 2022, the United States Department of Health and Human Services (HHS) announced a new standardized clinical definition of NAS (Office of the Assistant Secretary for Health, 2022). The new standardized clinical definition has numerous benefits for NAS data collection, treatment, research, and surveillance. This definition was developed after a study by Jilani et al. (2022) evaluated NAS surveillance efforts in six states. Elements assessed include the type of drug exposure in utero, clinical signs of withdrawal, and other signs of interest (Jilani et al., 2022).

There is currently no national monitoring and surveillance system in the United States which creates difficulties in identifying and following up with cases of NAS long-term (Jilani et al., 2021). In collaboration with CSTE, the National Center on Birth Defects and Developmental Disabilities (NCBDDD) is working on standardizing the surveillance definition for NAS. Six U.S. states, including Arizona, Florida, Georgia, Massachusetts, Pennsylvania, and Tennessee currently have NAS surveillance programs (National Center on Birth Defects and Developmental Disabilities [NCBDDD], 2021). Additionally, there are six states where NAS is a legally reportable condition and these states include Arizona, Florida, Georgia, Kentucky, Tennessee, and Virginia (Jilani et al., 2021). This is important as these states are focusing on NAS surveillance and will need to focus on identifying cases of NAS in their respective states.

Though Indiana is not currently among the six states with established NAS surveillance programs, Indiana is implementing their own interventions for NAS. Community Hospital East in Indianapolis, Indiana is piloting the Change, Hope, Overcome, Inspire, Compassion, Educate (CHOICE) program which is a substance use disorder program for pregnant women (Community Health Network, n.d.; Association of University Centers on Disabilities [AUCD]; 2020). The CHOICE program was implemented in 2016 and assists pregnant women in creating treatment programs that include access to medications, medical care, therapy, and community-based assistance (Community Health Network, n.d.). This program is accessible to mothers who utilize Medicaid which is a high proportion of infants diagnosed with NAS. The goals of this program are to provide care without stigmatization for a safe recovery process in order to combat NAS and other severe opioid-withdrawal symptoms in newborns.

Another program in Indiana is the CARE Plus program at Indiana University (IU) Health Methodist Hospital. This program is open to mothers who give birth to an infant with NAS that is currently receiving care in the neonatal intensive care unit (NICU). A community health worker and therapist assist the mother in learning how to take care of her infant after they leave the NICU and techniques and resources for fostering a healthy relationship and environment after they are discharged from the hospital (Indiana University School of Medicine, n.d.).

Future Research

While characteristics of NAS infants are well-studied, patterns and trends can change over time, and a more detailed and updated analysis should be conducted in Indiana that utilizes more complex data compared to HDD. This data can include an analysis of newborn inpatient data through reviewing medical records. Additionally, further studies that expand on healthcare utilization in Indiana will be crucial and help contribute to short and long-term health outcome research. This study is descriptive in nature and merely provides an overview of infant hospitalizations within 30 days of birth in Indiana. While this study focuses on infants diagnosed with NAS, there is the potential for another study that can further expand on NAS infants and potential co-morbidities. Additional research that evaluates data beyond HHD can paint a clearer picture of NAS and related health outcomes in Indiana in more recent years and in the future.

Due to the varying treatment options available for treating OENs and NAS infants, healthcare utilization research for NAS is lacking for both short and long-term outcomes of NAS infants, and the results of what little research exists are mixed. Children with NAS had a greater number of claims filed in inpatient hospitalizations, outpatient visits, and emergency department visits (Liu et al., 2019). When compared to non-exposed infants, OENs and infants diagnosed with NAS were also more likely to be hospitalized again within four weeks after birth and one year after birth (Liu et al., 2019). Future research should be directed towards understanding how to standardize and conduct NAS surveillance in a streamlined manner that supports mothers while pregnant and throughout early childhood.

Conclusions

NAS incidence in Indiana has decreased from 2017 to 2020 which is encouraging and consistent with national trends in the United States. When comparing NAS rates across the United States, Indiana has decreased its ranking from 14th to 18th in a four-year span. Infant opiate exposure has increased drastically in Indiana over recent years despite the rates of NAS decreasing. The incidence rates of other and unspecified drug exposure have decreased which may be due to data quality and specificity requirements that stem from ICD-10 implementation. As LOS increases, the odds of an infant being diagnosed with NAS slightly increases when adjusting for contributing demographic and clinical factors.

Characteristics of NAS infants in Indiana may be consistent with other states, however, there is little research conducted in Indiana on NAS and related health outcomes. Additional research in Indiana will provide further insight on how effective NAS interventions are such as the CHOICE program and CARE Plus. While several states are dedicating resources toward improving surveillance efforts and assisting pregnant women with SUD and/or OUD, more research needs to be conducted on identifying pregnant women who are at risk of having infants with NAS. Additional follow-up with mothers of infants who are diagnosed with NAS will be crucial in future monitoring and research on long-term health outcomes where a significant gap in knowledge still exists.

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Appendix A

Project Objectives and Competencies

Project Objectives	MPH Project Competencies
Interpret results of data analysis to identify trends of NAS in Indiana from 2017 to 2020	4
Compare Indiana NAS trends to national NAS trends in 2017 and 2018	E1
Conduct data analyses in SAS 9.4 software for NAS trends and ICD-10-CM code usage	E4

Appendix B

Figure 1

Study inclusion and exclusion criteria

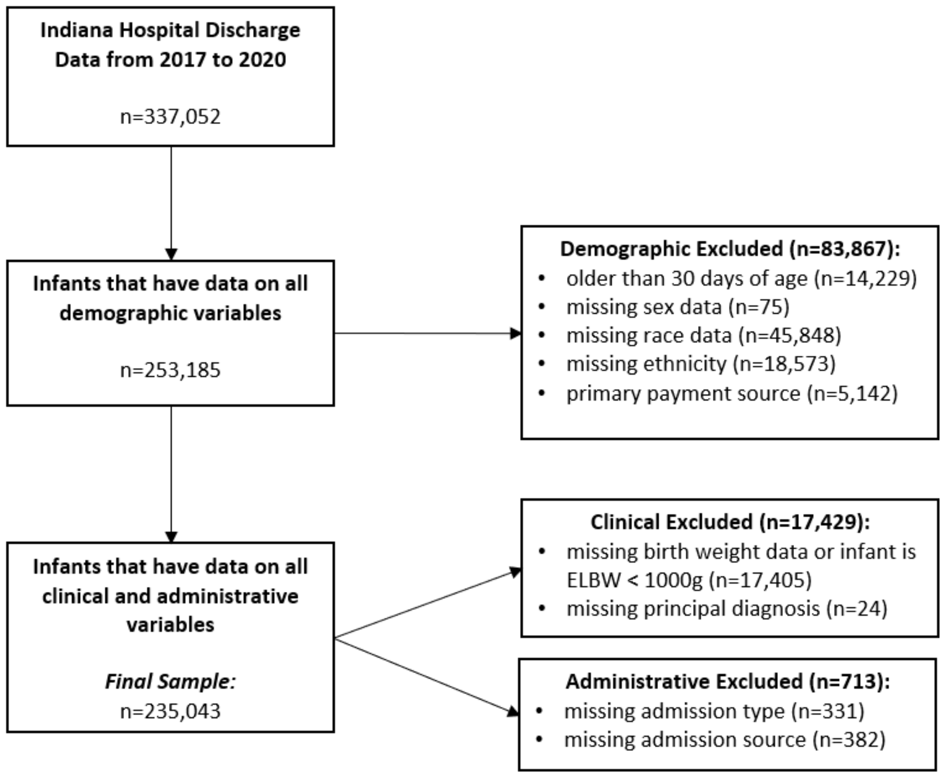


Table 1

ICD-10-CM Code Description Table

ICD-10-CM Code	Definition
P96.1	Neonatal withdrawal symptoms from maternal use of drugs of addiction
P04.14	Newborn affected by maternal use of opiates
P04.4	Newborn affected by maternal use of drugs of addiction
P04.40	Newborn affected by maternal use of unspecified drugs of addiction
P04.41	Newborn affected by maternal use of cocaine
P04.49	Newborn affected by maternal use of other drugs of addiction

Note. Data source: Centers for Medicare and Medicaid Services (2021)

Appendix C

Table 2

Demographic characteristics of infants by the diagnosis of NAS within 30 days of birth in Indiana from 2017 to 2020 (n=235,043)

	Infants Without NAS (n=232,737)		Infants Diagnosed with NAS (n=2,306)	
Variable	n	%	n	%
Year of Admission				
2017	55,654	23.91	691	29.97
2018	58,300	25.05	641	27.80
2019	61,795	26.55	530	22.98
2020	56,988	24.49	444	19.25
Sex				
Male	119,404	51.30	1,239	53.73
Female	113,333	48.70	1,067	46.27
Race				
White	187,602	80.61	2,127	92.24
Black or African American	34,283	14.73	139	6.03
Other[a]	10,852	4.66	40	1.73
Ethnicity				
Hispanic or Latino	8,238	3.54	16	0.69
Not Hispanic or Latino	224,499	96.46	2,290	99.31
Primary Source of Payment				
Medicaid	97,415	41.86	1,806	78.32
Other Government[b]	1,992	0.86	4	0.17
Commercial Insurance	118,889	51.08	336	14.57
Self Pay	14,441	6.20	160	6.94
Indiana Resident				
Yes	225,167	96.75	2,249	97.53
No	7,570	3.25	57	2.47

Note. Data source: Indiana Hospital Discharge Data

[a]Includes multiple races, Asian and Pacific Islander, and American Indian/Alaskan Native

[b]Includes Medicare due to smaller sample size

Table 3

Clinical characteristics of infants by the diagnosis of NAS within 30 days of birth in Indiana from 2017 to 2020 (n=235,043)

	Infants Without NAS (n=232,737)		Infants Diagnosed with NAS (n=2,306)	
Variable	n	%	n	%
Admission Type				
Newborn	227,910	97.93	2,119	91.89
Emergency	3,058	1.31	113	4.90
Urgent[a]	1,324	0.57	56	2.43
Elective	445	0.19	18	0.78
Admission Source				
Routine	227,743	97.85	2,104	91.24
Transfer	4,712	2.02	184	7.98
Other	282	0.12	18	0.78
Emergency Services				
Yes	1,195	0.51	20	0.87
No	231,542	99.49	2,287	99.13
Discharge Status				
Routine	228,301	98.09	2,115	91.72
Expired	369	0.16	3	0.13
Other Hospital or Institution	3,600	1.55	166	7.20
Other[b]	467	0.20	22	0.95
	Mean (SD)	Range	Mean (SD)	Range
Length of Stay	3.564 (7.923)	1-276	15.491 (15.017)	1-237
Birth Weight (g)	3,509.271 (1,403)	1,000-9,996	3,324.059 (1,452)	1,012-9,723

Note. Data source: Indiana Hospital Discharge Data

[a]Includes trauma center admissions

[b]Includes discharges to home care, nursing facilities, and against medical advice

Table 4

Newborn drug exposure due to maternal prenatal drug use of infants by the diagnosis of NAS within 30 days of birth in Indiana from 2017 to 2020 (n=235,043)

	Infants Without NAS (n=232,737)				Infants Diagnosed With NAS (n=2,306)			
	Exposure		No Exposure		Exposure		No Exposure	
Newborn Drug Exposure	n	%	n	%	n	%	n	%
Other Drug Use (P04.4)	2,647	1.14	230,090	98.86	691	29.97	1,615	70.03
Cocaine (P04.41)	187	0.08	232,550	99.92	63	2.73	2,243	97.27
Other Drug Addiction (P04.49)	2,299	0.99	230,438	99.01	625	27.09	1,681	72.91
Opioids (P04.14)	427	0.18	232,310	99.82	259	11.23	2,047	88.77
Unspecified (P04.40)	203	0.09	232,534	99.91	35	1.52	2,271	98.48
Any Drug Exposure[a]	3,045	1.31	229,692	98.69	917	39.77	1,389	60.25

Note. Data source: Indiana Hospital Discharge Data

[a]Any drug exposure includes the presence of any of the above newborn drug exposure codes

Table 5

Expected counts and chi-square analysis of length of stay and neonatal abstinence syndrome in Indiana from 2017 to 2020 (n=235,043)

	NAS Status			
	No NAS		NAS	
Length of Stay	n	%	n	%
≤ 3 days[a]	206,790 *205,041*	87.98 *88.85*	283 *2,031.6*	0.12 *12.27*
> 3 days[b]	25,947 *27,696*	11.04 *11.15*	2,023 *274.4*	0.86 *7.23*

$\chi 2$ (1) = 12,772.4983, p = .0001

Note. Data source: Indiana Hospital Discharge Data

[a, b]Expected counts are italicized

Appendix D

Figure 2

Incidence rate and percent change of neonatal abstinence syndrome by sex and admission year in Indiana from 2017 to 2020 per 1,000 infant hospitalizations (n=235,043)

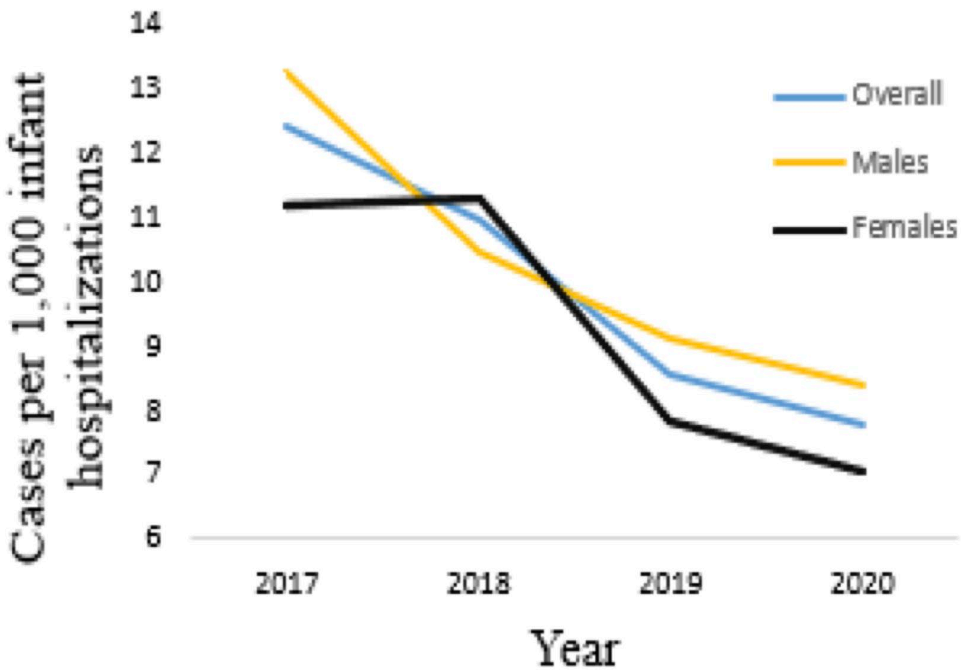
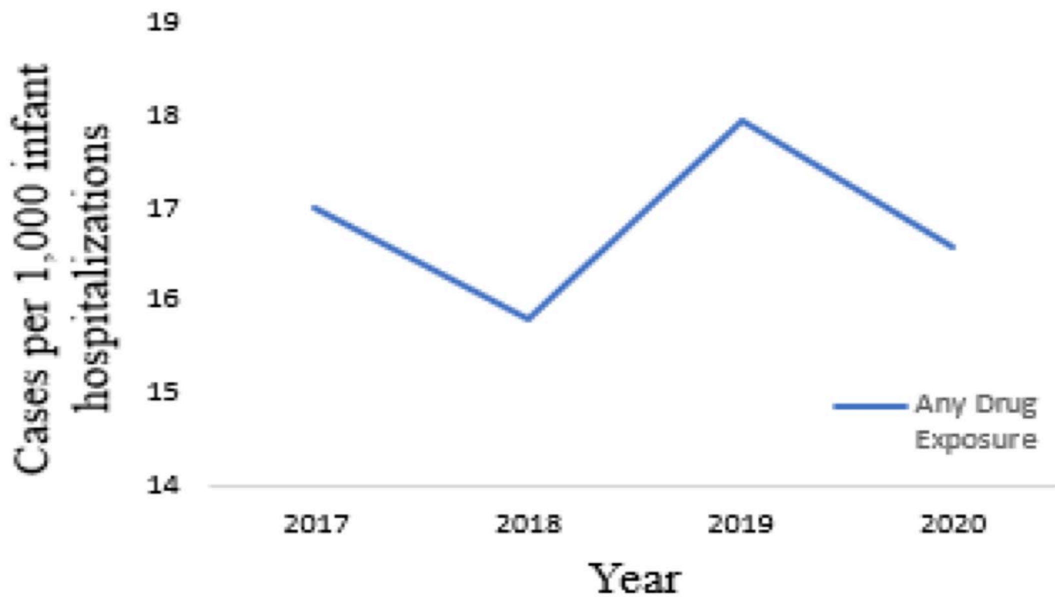


Figure 3

Incidence rates of newborn drug exposure due to maternal prenatal drug use by admission year in Indiana from 2017 to 2020 per 1,000 infant hospitalizations (n=235,043)



Appendix E

Table 7

Odds ratios and 95% confidence intervals for the association of hospital length of stay and the diagnosis of NAS among infants born in Indiana from 2017 to 2020 (n=235,043)

	Model 1[a]		Model 2[b]		Model 3[c]		Model 4[d]	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
NAS								
No	1.00	(reference)	1.00	(reference)	1.00	(reference)	1.00	(reference)
Yes	1.037	1.035-1.039	1.037	1.036-1.039	1.036	1.034-1.038	1.037	1.035-1.039

Note. Data source: Indiana Hospital Discharge Data

[a]Unadjusted

[b]Adjusted by sex, race, and ethnicity

[c] Adjusted by model 2 variables, the primary source of payment, and birth weight

[d] Adjusted by model 3 variables and low birth weight instead of birth weight