HHS Public Access
Author manuscript
J Subst Use. Author manuscript; available in PMC 2024 May 15.

Published in final edited form as:
J Subst Use. 2023 ; 28(5): 789–796. doi:10.1080/14659891.2022.2098841.

A population-based descriptive study of neonatal abstinence syndrome using hospital discharge and birth certificate data

Jacob C. Rainey, MPH[a,b], **Lacee Satcher, BS, PhD**[b,c], **Sarah J. Nechuta, MPH, PhD**[b,d]

[a]Johns Hopkins University, Bloomberg School of Public Health, Department of Mental Health, 615 North Wolfe Street, Baltimore, MD 21205, United States

[b]Tennessee Department of Health, Office of Informatics and Analytics, 710 James Robertson Parkway, Nashville, TN 37243, United States

[c]Vanderbilt University, Department of Sociology, PMB 351811, Nashville, TN 37235, United States

[d]Grand Valley State University, College of Health Professions, Department of Public Health, 500 Lafayette Street, Grand Rapids, MI 49503, United States

Abstract

BACKGROUND: Neonatal abstinence syndrome (NAS), largely a consequence of prenatal opioid exposure, results in substantial morbidity. Population-based studies of NAS going beyond Medicaid populations and hospital discharge data (HDD) alone are limited. Using statewide Tennessee (TN) HDD and birth certificate (BC) data, we examined trends and evaluated maternal and infant factors associated with NAS.

METHODS: We conducted a population-based descriptive study during 2013–2017 in TN. NAS infants were identified with International Classification of Diseases (ICD)-9-Clinical Modification (CM) and ICD-10-CM codes in HDD and linked to BC data using iterative deterministic matching algorithms. Descriptive analyses were conducted for infant and maternal factors (exposures) by NAS (outcome). Multivariable logistic regression models were used to estimate adjusted ORs and 95% CIs.

RESULTS: NAS incidence increased from 13.4 to 15.4 per 1,000 live births between 2013–2017 (15% increase; p_{trend}<0.001), but remained stable in 2017. In adjusted models, maternal factors associated with reduced odds of NAS included breastfeeding (OR:0.55, 95%CI:0.52–0.59) and prenatal care (OR:0.36, 95%CI:0.32–0.41). Smoking, preterm birth and lower birthweight were associated with increased odds of NAS.

CONCLUSIONS: This study highlights the value of utilizing surveillance data to monitor trends and correlates of NAS to inform prevention efforts and targeting of public health resources.

[*]**Corresponding author**: Sarah Nechuta, MPH PhD, Grand Valley State University, College of Health Professions, Department of Public Health, Grand Rapids, MI, USA; nechutas@gvsu.edu;.

DECLARATIONS

Conflicts of interest: The authors' declare they have no conflicts of interest.

Keywords

neonatal abstinence syndrome; epidemiology; newborn; retrospective cohort; birth certificates

Introduction

Over the last 20 years, opioid use disorder (OUD) and maternal opioid use have increased in the United States (U.S.) (Desai et al., 2014; Epstein et al., 2013; Haight et al., 2018). From 1994 to 2014, the national prevalence of OUD during pregnancy increased from 1.5 to 6.5 cases per 1,000 delivery hospitalizations (Haight et al., 2018). According to the National Survey on Drug Use and Health, past month illicit drug use among pregnant women aged 15–44 years increased from 4.7% in 2015 to 8.5% in 2017 (U.S. Department of Health and Human Services, 2018). Neonatal abstinence syndrome (NAS) is a withdrawal syndrome in infants caused by *in-utero* exposure to drugs. NAS is particularly prevalent among women with OUD and women being treated for OUD with methadone or buprenorphine during pregnancy (Brogly et al., 2014; McQueen and Murphy-Oikonen, 2016). NAS is characterized by a complex array of individually-varying symptoms, including fever, respiratory distress, gastrointestinal manifestations (e.g., feeding difficulties), and central nervous system manifestations (e.g., tremors, irritability) (McQueen and Murphy-Oikonen, 2016; Patrick et al., 2012). NAS has become one of the most rapidly growing causes of newborn hospital admissions in the U.S. in the last 15–20 years and is associated with substantial economic costs (Ko et al., 2016; Patrick et al., 2012; Tolia et al., 2015; Winkelman et al., 2018). More recently, evidence has begun to accumulate regarding the long-term adverse impact of NAS on short- and long-term childhood mental and physical health outcomes (Corr et al., 2018; Oei et al., 2017; Witt et al., 2017).

To date, most studies of NAS trends, characteristics, and risk factors have focused primarily on Medicaid populations and/or used only administrative data or hospital discharge data only (Atwell et al., 2016; Charles et al., 2017; Hussaini and Garcia Saavedra, 2018; Ko et al., 2016; Milliren et al., 2018; Strahan et al., 2019). NAS shows substantial geographic variation in the U.S., and has a greater burden in the southern U.S., including in Tennessee (TN) (Patrick et al., 2012; Warren, 2015). Therefore, it is important to understand recent trends and risk and protective factors in TN.

Statewide surveillance data can be valuable for maternal and infant public health research, and as a resource for continued monitoring of trends and risk factors. Our study had two primary objectives. First, we described trends among infants with a diagnosis of NAS using TN population-based statewide hospital discharge data (HDD). Second, we linked NAS infants from HDD data to their birth certificate (BC) data to construct a retrospective cohort study among all live births in TN to evaluate descriptive associations between maternal and infant factors and NAS.

Methods

Study design overview

We conducted a population-based statewide serial cross-sectional study using HDD data for TN resident infants to describe trends in NAS and potential NAS from 2013 to 2017. We then linked NAS infants from the HDD to their BC data to conduct a retrospective population-based cohort of NAS and non-NAS infants for all infants born to TN resident mothers from 2013 to 2017. This study was approved by the Tennessee Department of Health (TDH) Institutional Review Board.

Data sources

The two data sources for this study were the TN hospital discharge data system (2013–2017) and the TN birth statistical files (2013–2017). TN HDD is collected by the TDH and contains information on all TN hospital admissions and discharges. On October 1st, 2015 hospitals implemented a transition from International Classification of Diseases (ICD)-9-Clinical Modification (CM) to ICD-10-CM diagnostic coding (Khera et al., 2018). HDD data provided ICD-9-CM diagnosis codes for discharges that occurred January 1st 2013 to September 30th 2015, and ICD-10-CM diagnosis codes for discharges from October 1st 2015 to end of the study. HDD data also provided infant date of birth (DOB), date of discharge, infant first and last name, infant medical record number, maternal first and last name, maternal address, and infant sex, length of hospital stay, and insurance type.

The TN birth statistical files include data for all TN live births, regardless of residence status, and births to TN residents who delivered at out-of-state hospitals. TN BC data is collected by TDH and follows the National Center for Health Statistics (NCHS) standards for data items and data quality (CDC, 2019). This study excluded non-TN resident live births. The data items available from the TN BC data for this study (for data linkage and analysis) included the following: maternal and infant name, address, maternal and infant date of birth (DOB), maternal race, maternal education, maternal income, parity, maternal pre-pregnancy weight and height, maternal smoking during pregnancy, breastfeeding at birth hospitalization discharge, receipt and timing of prenatal care, weeks of gestation, infant sex and birthweight.

Creation of retrospective cohort

We linked NAS infant HDD records (identified using ICD-9 and ICD-10 codes described below) with BC data to create a retrospective cohort of NAS infants and non-NAS infants for all live TN resident births during 2013 to 2017. Available linkage variables included infant first and last name, DOB, and medical record number (social security number was too incomplete for infants in the HDD for linkage, close to 70% missing/invalid for patients aged <30 days). Infant names in the HDD were cleaned and parsed for matching. We first used an iterative deterministic matching approach with several algorithms using identifiers and then used fuzzy matching for non-matches with manual review for all potential incorrect matches (i.e., false positives) and for duplicate matches (i.e., an HDD NAS record linked to more than one birth record) (Dusetzina et al., 2014). Manual review involved using additional identifiers including maternal names, addresses, and infant sex. Overall, 96% of eligible NAS infants were linked to their BC data.

Study Variables

Maternal and infant factors were selected based on literature review (Creanga et al., 2012; Lind et al., 2015; Patrick et al., 2015c; Short et al., 2016; Wang et al., 2017). Maternal demographics were defined as follows: age in years (<20, 20–24, 25–29, 30–34, ≥35), education (< high school, high school, ≥high school), race (white, Black, other race/ ethnicities), and household income (<$10,000, $10,000-<25,000, ≥$25,000). Pregnancy and infant characteristics included prenatal care (none, received during first trimester, received (not during first trimester), received (unknown timing)), breastfeeding at discharge (yes, no), parity (0, 1, 2, ≥3), pre-pregnancy height and weight (used to create pre-pregnancy body mass index (BMI) categorized as <21.5 kg/m^2, 21.5-<24.99 kg/m^2, 24.99-<29.99 kg/m^2, ≥30 kg/m^2), number of cigarettes smoked by trimester (categorized as <10 and ≥ 10 per day during pregnancy), preterm birth (defined as <37 weeks gestation) (Nguyen and Wilcox, 2005), infant sex (male, female), and birthweight in grams (<2,500, 2,500-<2977, 2977-<3260, 3260-<3572, ≥3572). Birthweights <400g were considered unreliable and excluded (Patrick et al., 2015c).

Newborn hospitalizations with a NAS diagnosis in the HDD were identified with the ICD-9-CM diagnosis code 779.5 (drug withdrawal syndrome in newborn) from January 1st 2013 to September 30th, 2015 (Lind et al., 2015; Patrick et al., 2012). The ICD-10-CM diagnosis code P96.1 (neonatal withdrawal symptoms from maternal use of drugs of addiction) was used to identify newborns with NAS from October 1st, 2015 to December 31st, 2017 (Maalouf et al., 2019). Following previous studies, the NAS diagnoses had to occur among infants aged ≤30 days at discharge (Atwell et al., 2016; Patrick et al., 2015a). We also considered diagnoses of potential NAS (Grossman et al., 2017; Lind et al., 2015), defined using ICD-9-CM code 760.72 and the available equivalent ICD-10-CM code P04.49. This ICD-10-CM code encompasses two ICD-9-CM codes 760.72 and 760.73.

We identified potential iatrogenic NAS cases for exclusion following previous research (Corr et al., 2018; Crane et al., 2019; Patrick et al., 2012). These included very low birthweight (<1500 grams), any intraventricular hemorrhage, periventricular leukomalacia, necrotizing enterocolitis, spontaneous intestinal perforation, and chronic respiratory disease arising from the perinatal period (codes shown in Table S1). We excluded infants missing DOB, aged >30 days (Atwell et al., 2016; Patrick et al., 2015a) and iatrogenic cases.

For NAS cases only using HDD data, we classified newborn clinical outcomes using ICD-9-CM and ICD-10-CM codes based on previous research (Atwell et al., 2016; Corr et al., 2018; Crane et al., 2019; Patrick et al., 2012) with specific codes shown in Table S1. These included low birthweight (1500g-2500g), preterm (24-<37 weeks gestation), feeding difficulties, respiratory symptoms, and seizures.

Statistical analysis

Rates for NAS were calculated as the number of NAS infants per 1,000 live resident births in TN by quarter from 2013–2017 and displayed on a graph with a line delineating the transition from ICD-9-CM to ICD-10-CM, as recommended when analyzing trends across the transition (Denham et al., 2019; Elixhauser et al., 2017; Salemi et al., 2019). Two-sided Cochran-Armitage trend tests were performed on NAS rates by discharge quarter. Descriptive chi-square analyses were conducted to obtain percentages and frequencies for categorical variables. Logistic regression models were used to estimate multivariable adjusted odd ratios (ORs) and 95% confidence intervals (CIs) to examine maternal factors and infant factors in association with NAS. We conducted a sensitivity analysis to determine the influence of excluding missing data for maternal and infant factors on logistic regression results. All analyses were conducted using Statistical Analysis Software (SAS) version 9.4 (Cary, NC, SAS Institute). P-values <0.05 were considered statistically significant.

Results

Study sample size and exclusions are shown in Figure 1. The figure shows exclusions prior to and after linkage of NAS infants identified in HDD data to BC data. After study exclusions, a total of 5,899 NAS infants and 395,059 non-NAS infants were available for analysis.

Table 1 shows maternal and infant characteristics for NAS and non-NAS infants. Compared to mothers with non-NAS newborns, more mothers of NAS newborns were 25–29 years-old (37.9% vs. 30.0%), white (93.8% vs. 68.6%), had attained less education, had a lower household income, and had not received prenatal care (8.1% vs. 1.8%). Compared to mothers with non-NAS newborns, fewer mothers of NAS newborns were breastfeeding at discharge (48.1% vs. 75.7%) or primiparous (22.7% vs. 38.6%). Moreover, a higher proportion of NAS mothers had a pre-pregnancy BMI of <21.5 kg/m^2 (37.7% vs. 22.3%) and smoked ≥10 cigarettes/day during pregnancy (66.3% vs. 10.8%). More newborns with NAS were preterm (15.4% vs. 10.8%), male (54.3% vs. 51.2%), and of lower birthweight (<2500 g: 18.3% vs. 8.8%).

As shown in Figure 2, from 2013–2017, the rate of NAS (per 1,000 live births) increased from 13.4 to 15.4 (15% increase; p_{trend} <0.001). By ICD coding period, there was an increase in the rate of NAS (per 1,000 live births) from the beginning to the end of the ICD-9-CM period—from 13.4 to 16.4 (22% increase; p_{trend} <0.001). From the beginning of the ICD-10-CM period to the end of 2017, the NAS rate (per 1,000 live births) decreased from 17.1 to 15.4 (10% decrease; p_{trend} <0.018).

Figure 3 provides adjusted ORs and 95% CIs for associations of maternal and infant factors and NAS. In multivariable logistic regression models adjusted for age, maternal demographics and pregnancy characteristics, the odds of having a newborn with NAS decreased with any prenatal care. Specifically, compared to not receiving prenatal care, the odds of NAS when receiving prenatal care during the first trimester was 0.17 (95% CI: 0.15–0.19), when receiving prenatal care after the first trimester was 0.36 (95% CI: 0.32–0.41), and when receiving prenatal care with timing unknown was 0.49 (95% CI: 0.42–0.56). Breastfeeding at discharge was associated with reduced odds of NAS (OR: 0.55, 95% CI: 0.52–0.58). Smoking during pregnancy was associated with increased odds of NAS (<10 cigarettes/day (reference: none): OR: 4.03, 95% CI: 3.46–4.69; ≥10 cigarettes/day OR: 10.4, 95% CI: 9.73–11.1). Preterm birth and infant sex were both associated with increased odds of NAS (OR: 1.15, 95% CI: 1.06–1.24; and OR: 1.13, 95% CI: 1.06–1.24, respectively). Lower birthweight was associated with increased odds of NAS, while higher birthweights were associated with reduced odds of NAS. We conducted sensitivity analyses to determine the influence of missing data on associations, and results were similar when excluding missing data (data not shown).

Discussion

Rates of NAS measured based on validated ICD-CM codes increased overall in TN during our study period, which crosses the ICD-9-CM to ICD-10-CM transition, from 13.4 in 2013 to 15.4 per 1,000 live births in 2017 (a 15% increase). However, looking at rates after the ICD-CM transition, a decrease from the first quarter of 2016 was observed, followed by almost no change in rates through 2017. Male sex, cigarette smoking, preterm birth, and lower birthweight were associated with increased odds of NAS, while women who were breastfeeding at discharge and those receiving prenatal care had reduced odds of NAS. Providing education and resources to support breastfeeding at the hospital and after returning home is critically important for mothers with NAS infants and infants exposed to maternal drug use (Klaman et al., 2017; Paterno et al., 2019).

NAS rates vary substantially geographically (Creanga et al., 2012; Patrick et al., 2015b; Winkelman et al., 2018), and our results, which show almost twice the burden of U.S. rates (for example, U.S. rates were 6.6 per 1,000 births in 2016), highlight the need to examine geographically diverse populations to understand NAS morbidity. Our findings for male sex and cigarette smoking with NAS are consistent with previous findings among largely Medicaid only populations (Atwell et al., 2016; Charles et al., 2017; Creanga et al., 2012; Erwin et al., 2017; Patrick et al., 2015c). We also found that increased parity, low birthweight and preterm birth were associated with increased odds of NAS, shown previously in largely Medicaid populations (Erwin et al., 2017; Lind et al., 2015; Patrick et al., 2015c). As many pregnancies among women with OUD are unintended (Heil et al., 2011), access for women of reproductive age who use drugs to contraception can potentially reduce maternal and infant morbidity and mortality due to drug use (Fischbein et al., 2018).

Prenatal care use, even prenatal care initiated after the first trimester, was independently associated with reduced odds of NAS. Based on the most recently available live birth data from the NCHS, about 77.5% of women who gave birth in 2018 received prenatal care in the first trimester and about 6% of women had late or no prenatal care (Martin et al., 2019). In our study 8.1% of NAS infants did not receive prenatal care compared to 1.8% of non-NAS infants. Resources to enable prenatal care initiation early and throughout pregnancy through education, support (e.g., transportation, childcare for other children, lack of judgment for reporting drug use), and health care access is critically needed.

Key strengths of this study include the large sample size, statewide population-based data sources, five years of data, and utilization of both HDD and BC data. This study also has several limitations. First, the use of administrative billing codes to define NAS may result in misclassification. A recent study comparing HDD with medical records found that hospital administrative data had a high positive predictive value (91% for ICD-9-CM and 98.2% for ICD-10-CM) for identifying clinically diagnosed NAS cases (Maalouf et al., 2019). Second, we did not have data on maternal opioid use, which was beyond the scope of the present study. Finally, this study was designed to be descriptive, and findings should not be interpreted as causal as temporality cannot be established due to the retrospective nature of the data.

Our study leveraged large, statewide population-based surveillance data over five years to describe NAS trends and characteristics, as well as maternal and infant factors associated with NAS during 2013 to 2017. Our study is unique by going beyond Medicaid only populations (using all NAS discharges and all live births) and using data both before and after the ICD-10-CM transition. To our knowledge, this is the first study using TN BC data for the entire state to evaluate factors associated with NAS and utilize multiple years of data after the ICD transition.

Over the five-year study period, which crossed the ICD-9-to-ICD-10-CM transition, NAS rates increased from 13.4 to 15.4 (15% increase) but remained stable in 2017. Despite the stabilization of rates in TN, the magnitude of rates in TN (15.4 per 1,000 births) remain nearly twice overall U.S. rates. Using population-based statewide data for all NAS discharges and live births, we found maternal and infant factors associated with NAS among TN infants. These factors overall are known risk factors for adverse maternal and infant health outcomes (lack of breastfeeding, maternal smoking, and infant preterm birth) (Bartick et al., 2017; Ratnasiri et al., 2020; Tita et al., 2018). These data contribute to the literature that supports a critical need for access to comprehensive prenatal and postpartum health care, improved education and support services for women with a history of substance use and/or those being treatment for OUD, and the need for continued follow-up and close monitoring of NAS infants (e.g., through home visiting and early parenting interventions) (Labella et al., 2021; Rayce et al., 2017). While this study was descriptive, it highlights the value of utilizing existing statewide surveillance data sources to monitor both trends and correlates of NAS and related outcomes, which is needed to inform prevention efforts and targeting of public health resources. Future studies should link to other data sources, such as Prescription Drug Monitoring Programs data for prescription data both before and after birth and maternal medical records for substance use history.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Funding:

This work was partly supported by the Centers for Disease Control & Prevention [Prescription Drug Overdose Prevention for States Program (5 NU17CE002731–02-00)] to the Tennessee Department of Health. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention or the Tennessee Department of Health.

Abbreviations

BC	Birth Certificate

BMI	Body Mass Index
HDD	Hospital Discharge Data
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
ICD-10-CM	International Classification of Diseases, Tenth Revision, Clinical Modification
LOS	Length of Stay
NAS	Neonatal Abstinence Syndrome
OUD	Opioid Use Disorder
SAS	Statistical Analysis Software
TN	Tennessee
TDH	Tennessee Department of Health
U.S.	United States

References

Atwell KA, Weiss HB, Gibson C, Miller R, Corden TE (2016). Neonatal Abstinence Syndrome and Maternal Substance Use in Wisconsin, 2009–2014. WMJ 115(6), 287–294. [PubMed: 29094858]

Bartick MC, Schwarz EB, Green BD, Jegier BJ, Reinhold AG, Colaizy TT, Bogen DL, Schaefer AJ, Stuebe AM (2017). Suboptimal breastfeeding in the United States: Maternal and pediatric health outcomes and costs. Matern Child Nutr 13(1), 1–13.

Brogly SB, Saia KA, Walley AY, Du HM, Sebastiani P (2014). Prenatal buprenorphine versus methadone exposure and neonatal outcomes: systematic review and meta-analysis. Am J Epidemiol 180(7), 673–686. [PubMed: 25150272]

Centers for Disease Control and Prevention. (2019). National Center for Health Statistics: National Vital Statistics System. Guide to Completing the Facility Worksheets for the Certificate of Live Birth and Report of Fetal Death. Available at: https://www.cdc.gov/nchs/data/dvs/GuidetoCompleteFacilityWks.pdf

Charles MK, Cooper WO, Jansson LM, Dudley J, Slaughter JC, Patrick SW (2017). Male Sex Associated With Increased Risk of Neonatal Abstinence Syndrome. Hosp Pediatr 7(6), 328–334. [PubMed: 28465360]

Corr TE, Schaefer EW, Paul IM (2018). Growth during the first year in infants affected by neonatal abstinence syndrome. BMC Pediatr 18(1), 343. [PubMed: 30396334]

Crane D, Marcotte M, Applegate M, Massatti R, Hurst M, Menegay M, Mauk R, Williams S (2019). A statewide quality improvement (QI) initiative for better health outcomes and family stability among pregnant women with opioid use disorder (OUD) and their infants. J Subst Abuse Treat 102, 53–59. [PubMed: 31202289]

Creanga AA, Sabel JC, Ko JY, Wasserman CR, Shapiro-Mendoza CK, Taylor P, Barfield W, Cawthon L, Paulozzi LJ (2012). Maternal drug use and its effect on neonates: a population-based study in Washington State. Obstet Gynecol 119(5), 924–933. [PubMed: 22525903]

Denham A, Mullaney T, Hill EL, Veazie PJ (2019). Are Increasing Trends in Opioid-Related Hospitalizations Attributable to Increases in Diagnosis Recordability? Evidence from 2 Large States. Health Serv Insights 12, 1178632919861338.

Desai RJ, Hernandez-Diaz S, Bateman BT, Huybrechts KF (2014). Increase in prescription opioid use during pregnancy among Medicaid-enrolled women. Obstet Gynecol 123(5), 997–1002. [PubMed: 24785852]

Dusetzina S, Tyree S, Meyer A, Meyer A, Green L, Carpenter W (2014). Linking Data for Health Services Research A Framework and Instructional Guide [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US). Available at: https://www.ncbi.nlm.nih.gov/books/NBK253313/.

Elixhauser A, Heslin K, Owens P (2017). Healthcare Cost and Utilization Project (HCUP) Recommendations for Reporting Trends Using ICD-9-CM and ICD-10-CM/PCS Data. U.S. Agency for Healthcare Research and Quality. Available at: https://www.hcupus.ahrq.gov/datainnovations/icd10_resources.jsp.

Epstein RA, Bobo WV, Martin PR, Morrow JA, Wang W, Chandrasekhar R, Cooper WO (2013). Increasing pregnancy-related use of prescribed opioid analgesics. Ann Epidemiol 23(8), 498–503. [PubMed: 23889859]

Erwin PC, Meschke LL, Ehrlich SF, Lindley LC (2017). Neonatal Abstinence Syndrome in East Tennessee: Characteristics and Risk Factors among Mothers and Infants in One Area of Appalachia. J Health Care Poor Underserved 28(4), 1393–1408. [PubMed: 29176103]

Fischbein RL, Lanese BG, Falletta L, Hamilton K, King JA, Kenne DR (2018). Pregnant or recently pregnant opioid users: contraception decisions, perceptions and preferences. Contracept Reprod Med 3, 4. [PubMed: 29610676]

Grossman MR, Berkwitt AK, Osborn RR, Xu Y, Esserman DA, Shapiro ED, Bizzarro MJ (2017). An Initiative to Improve the Quality of Care of Infants With Neonatal Abstinence Syndrome. Pediatrics 139(6).

Haight SC, Ko JY, Tong VT, Bohm MK, Callaghan WM (2018). Opioid Use Disorder Documented at Delivery Hospitalization - United States, 1999–2014. MMWR Morb Mortal Wkly Rep 67(31), 845–849. [PubMed: 30091969]

Heil SH, Jones HE, Arria A, Kaltenbach K, Coyle M, Fischer G, Stine S, Selby P, Martin PR (2011). Unintended pregnancy in opioid-abusing women. J Subst Abuse Treat 40(2), 199–202. [PubMed: 21036512]

Hussaini KS, Garcia Saavedra LF (2018). Neonatal Abstinence Syndrome (NAS) in Southwestern Border States: Examining Trends, Population Correlates, and Implications for Policy. Matern Child Health J 22(9), 1352–1359. [PubMed: 29572587]

Khera R, Dorsey KB, Krumholz HM (2018). Transition to the ICD-10 in the United States: An Emerging Data Chasm. JAMA 320(2), 133–134. [PubMed: 29868861]

Klaman SL, Isaacs K, Leopold A, Perpich J, Hayashi S, Vender J, Campopiano M, Jones HE (2017). Treating Women Who Are Pregnant and Parenting for Opioid Use Disorder and the Concurrent Care of Their Infants and Children: Literature Review to Support National Guidance. J Addict Med 11(3), 178–190. [PubMed: 28406856]

Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD (2016). Incidence of Neonatal Abstinence Syndrome - 28 States, 1999–2013. MMWR Morb Mortal Wkly Rep 65(31), 799–802. [PubMed: 27513154]

Labella MH, Eiden RD, Roben CKP, Dozier M (2021). Adapting an Evidence-Based Home Visiting Intervention for Mothers With Opioid Dependence: Modified Attachment and Biobehavioral Catch-up. Front Psychol 12, 675866. [PubMed: 34489793]

Lind JN, Petersen EE, Lederer PA, Phillips-Bell GS, Perrine CG, Li R, Hudak M, Correia JA, Creanga AA, Sappenfield WM, Curran J, Blackmore C, Watkins SM, Anjohrin S, Centers for Disease, C., Prevention. (2015). Infant and maternal characteristics in neonatal abstinence syndrome--selected hospitals in Florida, 2010–2011. MMWR Morb Mortal Wkly Rep 64(8), 213–216. [PubMed: 25742381]

Maalouf FI, Cooper WO, Stratton SM, Dudley JA, Ko J, Banerji A, Patrick SW (2019). Positive Predictive Value of Administrative Data for Neonatal Abstinence Syndrome. Pediatrics 143(1).

Martin JA, Hamilton BE, Osterman MJK, Driscoll AK (2019). Births: Final Data for 2018. Natl Vital Stat Rep 68(13), 1–47.

McQueen K, Murphy-Oikonen J (2016). Neonatal Abstinence Syndrome. N Engl J Med 375(25), 2468–2479. [PubMed: 28002715]

Milliren CE, Gupta M, Graham DA, Melvin P, Jorina M, Ozonoff A (2018). Hospital Variation in Neonatal Abstinence Syndrome Incidence, Treatment Modalities, Resource Use, and Costs Across Pediatric Hospitals in the United States, 2013 to 2016. Hosp Pediatr 8(1), 15–20. [PubMed: 29263122]

Nguyen RH, Wilcox AJ (2005). Terms in reproductive and perinatal epidemiology: 2. Perinatal terms. J Epidemiol Community Health 59(12), 1019–1021. [PubMed: 16286486]

Oei JL, Melhuish E, Uebel H, Azzam N, Breen C, Burns L, Hilder L, Bajuk B, Abdel-Latif ME, Ward M, Feller JM, Falconer J, Clews S, Eastwood J, Li A, Wright IM. (2017). Neonatal Abstinence Syndrome and High School Performance. Pediatrics 139(2).

Paterno MT, Jablonski L, Klepacki A, Friedmann PD (2019). Evaluation of a Nurse-Led Program for Rural Pregnant Women With Opioid Use Disorder to Improve Maternal-Neonatal Outcomes. J Obstet Gynecol Neonatal Nurs 48(5), 495–506.

Patrick SW, Burke JF, Biel TJ, Auger KA, Goyal NK, Cooper WO (2015a). Risk of Hospital Readmission Among Infants With Neonatal Abstinence Syndrome. Hosp Pediatr 5(10), 513–519. [PubMed: 26427919]

Patrick SW, Davis MM, Lehman CU, Cooper WO (2015b). Increasing incidence and geographic distribution of neonatal abstinence syndrome: United States 2009 to 2012. J Perinatol 35(8), 667.

Patrick SW, Dudley J, Martin PR, Harrell FE, Warren MD, Hartmann KE, Ely EW, Grijalva CG, Cooper WO (2015c). Prescription opioid epidemic and infant outcomes. Pediatrics 135(5), 842–850. [PubMed: 25869370]

Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM (2012). Neonatal abstinence syndrome and associated health care expenditures: United States, 2000–2009. JAMA 307(18), 1934–1940. [PubMed: 22546608]

Ratnasiri AWG, Gordon L, Dieckmann RA, Lee HC, Parry SS, Arief VN, DeLacy IH, Lakshminrusimha S, DiLibero RJ, Basford KE (2020). Smoking during Pregnancy and Adverse Birth and Maternal Outcomes in California, 2007 to 2016. Am J Perinatol 37(13), 1364–1376. [PubMed: 31365931]

Rayce SB, Rasmussen IS, Klest SK, Patras J, Pontoppidan M (2017). Effects of parenting interventions for at-risk parents with infants: a systematic review and meta-analyses. BMJ Open 7(12), e015707.

Salemi JL, Tanner JP, Kirby RS, Cragan JD (2019). The impact of the ICD-9-CM to ICD-10-CM transition on the prevalence of birth defects among infant hospitalizations in the United States. Birth Defects Res 111(18), 1365–1379. [PubMed: 31414582]

Short VL, Gannon M, Abatemarco DJ (2016). The Association Between Breastfeeding and Length of Hospital Stay Among Infants Diagnosed with Neonatal Abstinence Syndrome: A Population-Based Study of In-Hospital Births. Breastfeed Med 11, 343–349. [PubMed: 27529500]

Strahan AE, Guy GP Jr., Bohm M, Frey M, Ko JY (2019). Neonatal Abstinence Syndrome Incidence and Health Care Costs in the United States, 2016. JAMA Pediatr. 174 (2), 200–202.

Tita AT, Doherty L, Roberts JM, Myatt L, Leveno KJ, Varner MW, Wapner RJ, Thorp JM Jr., Mercer BM, Peaceman A, Ramin SM, Carpenter MW, Iams J, Sciscione A, Harper M, Tolosa JE, Saade GR, Sorokin Y, Eunice Kennedy Shriver National Institute of Child, H., Human Development Maternal-Fetal Medicine Units, N. (2018). Adverse Maternal and Neonatal Outcomes in Indicated Compared with Spontaneous Preterm Birth in Healthy Nulliparas: A Secondary Analysis of a Randomized Trial. Am J Perinatol 35(7), 624–631. [PubMed: 29190847]

Tolia VN, Patrick SW, Bennett MM, Murthy K, Sousa J, Smith PB, Clark RH, Spitzer AR, 2015. Increasing incidence of the neonatal abstinence syndrome in U.S. neonatal ICUs. N Engl J Med 372(22), 2118–2126. [PubMed: 25913111]

U.S Department of Health and Human Services, 2018. Substance Abuse and Mental Health Services Administration. The National Survey on Drug Use and Health. Available at: https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/Assistant-Secretary-nsduh2018_presentation.pdf.

Wang X, Zhu Y, Dave CV, Alrwisan AA, Voils SA, Winterstein AG, 2017. Trends of Neonatal Abstinence Syndrome Epidemic and Maternal Risk Factors in Florida. Pharmacotherapy 37(7), 806–813. [PubMed: 28500694]

Warren MD, Miller Angela M., Traylor Julie, Bauer Audrey, and Patrick Stephen W., 2015. Implementation of a Statewide Surveillance System for Neonatal Abstinence Syndrome — Tennessee, 2013. CDC Morbidity and Mortality Weekly Report 64(5), 125–128. [PubMed: 25674995]

Winkelman TNA, Villapiano N, Kozhimannil KB, Davis MM, Patrick SW, 2018. Incidence and Costs of Neonatal Abstinence Syndrome Among Infants With Medicaid: 2004–2014. Pediatrics 141(4).

Witt CE, Rudd KE, Bhatraju P, Rivara FP, Hawes SE, Weiss NS, 2017. Neonatal abstinence syndrome and early childhood morbidity and mortality in Washington state: a retrospective cohort study. J Perinatol 37(10), 1124–1129. [PubMed: 28682319]

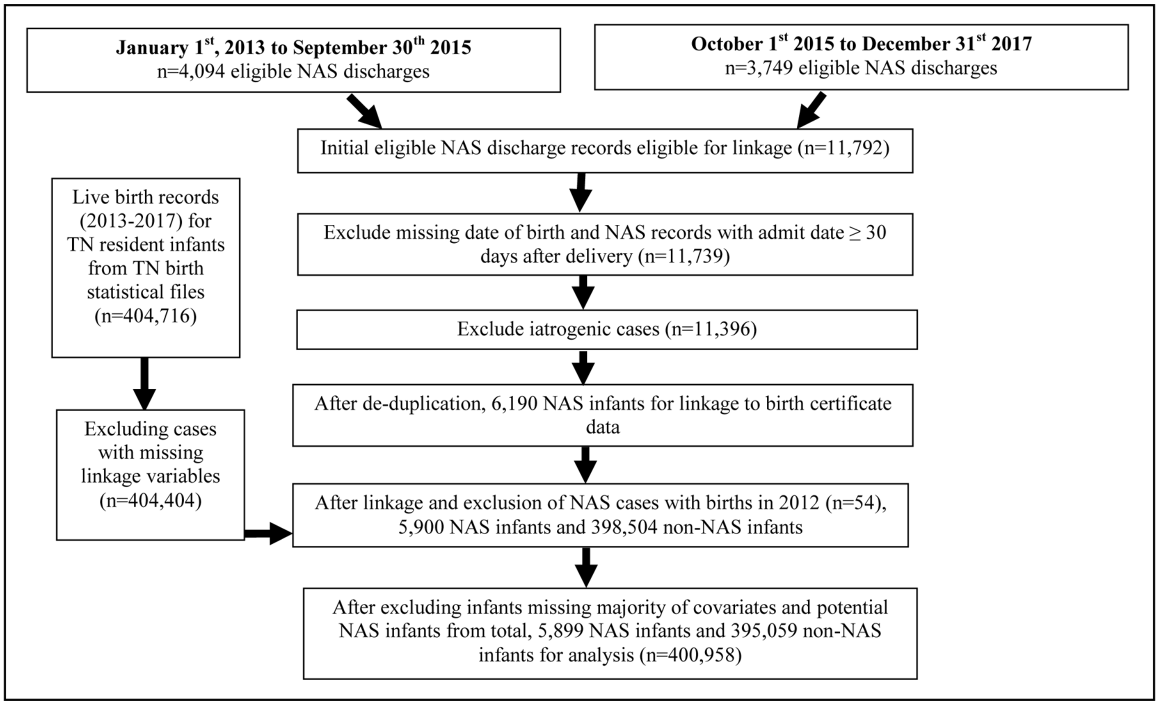

Figure 1.
Study design, exclusions and final analytic sample

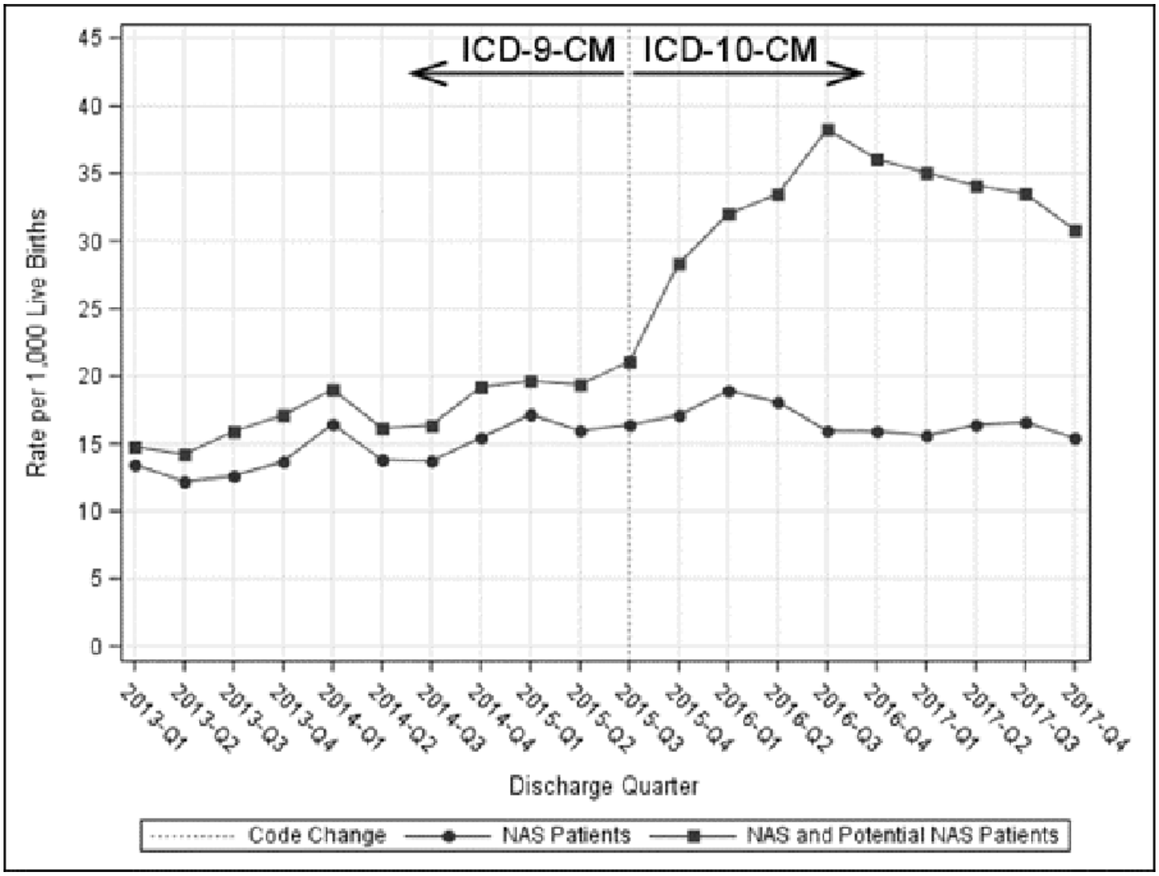

Figure 2.

Incidence rate of newborns diagnosed with neonatal abstinence syndrome and potential neonatal abstinence syndrome in Tennessee before and after the ICD-9-CM to ICD-10 CM Transition per 1,000 live births, 2013–2017*

*The dotted line indicates when the U.S. transitioned from the ICD-9-CM to ICD-10-CM diagnosis coding system on October 1, 2015.

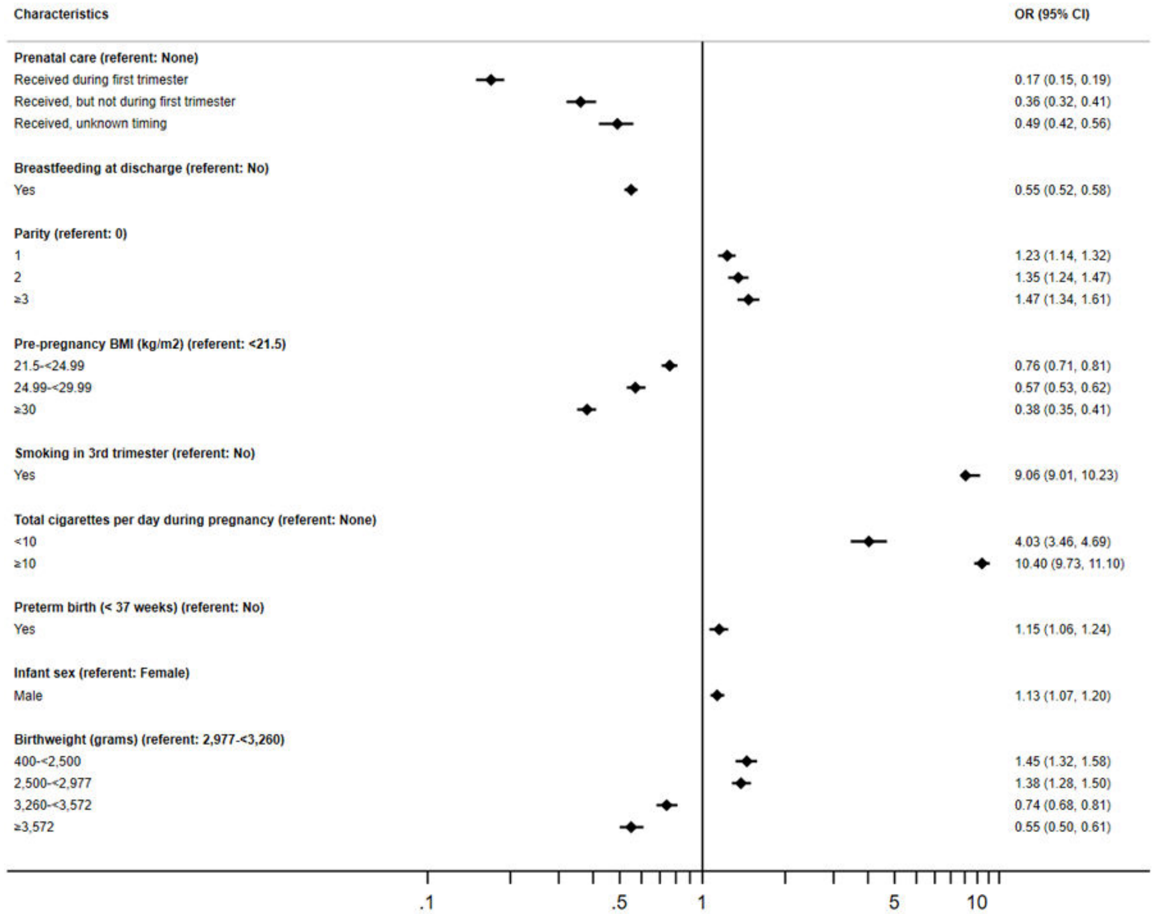

Figure 3.

Multivariable odds ratios (ORs) and 95% CIs for maternal factors and infant birth outcomes in association with NAS using linked birth and HDD data (n=400,958)*

*ORs were adjusted for maternal age at delivery, maternal education, maternal race, prenatal care, infant sex, parity, pre-pregnancy body mass index, and total cigarettes per day during pregnancy as appropriate. Birthweight was also adjusted for length of gestation.

Table 1.

Maternal and infant factors for NAS and non-NAS infants, retrospective cohort (n=400,958)[a]

	NAS infants		Non-NAS Infants		P-value
	n	(%)	n	(%)	
Maternal age at delivery (years)					
<20	137	(2.32)	31,385	(7.9)	< 0.001
20–24	1,580	(26.8)	104,796	(26.5)	
25–29	2,236	(37.9)	118,617	(30.0)	
30–34	1,344	(22.8)	93,146	(23.6)	
≥35	602	(10.2)	47,115	(11.9)	
Maternal education					
<High School	1,389	(23.6)	56,070	(14.2)	< 0.001
High School	2,647	(44.9)	110,048	(27.9)	
≥High School	1,832	(31.1)	168,002	(57.5)	
Missing	31	(0.53)	1,884	(0.48)	
Maternal race					
White	5,535	(93.8)	270,886	(68.6)	< 0.001
Black	273	(4.6)	82,521	(20.9)	
Other	68	(1.2)	38,813	(9.8)	
Missing	23	(0.39)	2,839	(0.72)	
Household income					
<$10,000	1,873	(31.8)	65,111	(16.5)	< 0.001
$10,000-<25,000	1,495	(25.3)	68,588	(17.4)	
≥$25,000	777	(13.2)	180,400	(45.7)	
Missing	1,754	(29.7)	80,960	(20.5)	
Prenatal care					
None	478	(8.1)	6,989	(1.8)	< 0.001
Received during first trimester	2,310	(39.2)	257,933	(65.2)	
Received, after first trimester	2,378	(40.3)	98,970	(25.1)	
Received, unknown timing	645	(10.9)	27,728	(7.02)	
Missing	88	(1.5)	3,439	(0.87)	
Breastfeeding at discharge					
No	2,873	(48.7)	82,780	(21.0)	< 0.001
Yes	2,836	(48.1)	299,149	(75.7)	
Missing	190	(3.2)	13,130	(3.3)	
Parity					
0	1,339	(22.7)	152,468	(38.6)	< 0.001
1	1,838	(31.2)	124,824	(31.6)	
2	1,354	(23.0)	65,486	(16.6)	
≥3	1,298	(22.0)	46,159	(11.7)	
Missing	70	(1.2)	6,122	(1.6)	
Pre-pregnancy body mass index (kg/m^2)					

	NAS infants		Non-NAS Infants		P-value
	n	(%)	n	(%)	
<21.5	2,225	(37.7)	87,913	(22.3)	< 0.001
21.5-<24.99	1,574	(26.7)	99,936	(25.3)	
24.99-<29.99	1,108	(18.8)	93,208	(23.6)	
≥ 30	805	(13.7)	100,916	(25.5)	
Missing	187	(3.2)	13,086	(3.3)	
Smoking in 3rd trimester					
No	2,001	(33.9)	352,123	(89.1)	< 0.001
Yes	3,829	(64.9)	40,126	(10.2)	
Missing	69	(1.2)	2810	(0.7)	
Total cigarettes per day during pregnancy					
None	1,723	(29.2)	340,826	(86.7)	< 0.001
<10	205	(3.5)	8,880	(2.3)	
≥10	3,912	(66.3)	42,794	(10.8)	
Missing	59	(1.0)	2,559	(0.65)	
Preterm Birth (<37 weeks)					
No	4897	(83.0)	350,654	(88.8)	< 0.001
Yes	911	(15.4)	42,744	(10.8)	
Missing	91	(1.5)	1,661	(0.42)	
Infant sex					
Female	2,696	(45.7)	192,942	(48.8)	< 0.001
Male	3,203	(54.3)	202,114	(51.2)	
Missing	0		3	(0.0)	
Birthweight (grams)					
400-<2,500	1,082	(18.3)	34,617	(8.8)	< 0.001
2,500-<2977	1,841	(31.2)	69,052	(17.5)	
2977-<3260	1,274	(21.6)	79,956	(20.2)	
3260-<3572	970	(16.4)	96,569	(24.4)	
≥ 3572	707	(12.0)	113,165	(28.7)	
Missing[b]	25	(0.42)	1,700	(0.43)	

[a]Table data source: Hospital discharge (for NAS diagnosis) and birth certificate data for both NAS and non-NAS infants born as TN residents.

[b]Missing includes implausible birthweights <400 grams.