

Neonatal abstinence syndrome

Delaware

2010 – 2018

Highlights

- The Council for State and Territorial Epidemiologists (CSTE) provided a case definition of NAS in 2019 for Tier 1 and Tier 2. The NAS case identification for previous briefs and the current brief is based on the Tier 2 definition recommended by CSTE “...a neonate whose healthcare record contains any diagnosis of neonatal drug withdrawal symptoms within the birth hospitalization or a hospitalization (or similar clinic admission” using ICD-10-CM codes.
- Neonatal abstinence syndrome (NAS) is a withdrawal syndrome in newborns occurring after birth that is primarily caused by maternal opiate use during pregnancy.
- According to hospital discharge data, during 2010 to 2018 in Delaware, 1,956 cases of NAS were identified with an incidence of 20.1 cases per 1,000 births. There were 263 NAS cases in 2017 updated to reflect year-end hospital discharge data (HDD). The total number of NAS cases in 2018 was 228, which is a slight underestimate due to 2018 end-of-year cut-off for HDD.
- A total of 18 iatrogenic cases were identified during the entire 2010-2018 time-period. The overall 2010-2018 NAS rate excluding these 18 cases was 21.0 per 1,000 births. There was a 10 percent drop in the incidence of NAS (excluding iatrogenic cases) from 25.6 cases per 1,000 births in 2017 to 23.2 cases per 1,000 births in 2018.
- Median length of stay of 17 days for a NAS affected newborn remained unchanged from previous years. The length of stay for a NAS affected newborn was 17 days as compared to two days for a non-NAS newborn. There was considerable variation in the length of stay between hospitals.



DELAWARE HEALTH AND SOCIAL SERVICES

Division of Public Health

Family Health Systems

What is neonatal abstinence syndrome (NAS)?

Neonatal abstinence syndrome (NAS) is a withdrawal syndrome in newborns following birth that is primarily caused by maternal opiate use during the prenatal period (antepartum).¹ First described by Dr. Loretta Finnegan in the 1970s, this condition is perhaps better described as neonatal withdrawal, given the implicit nature of abstinence as a choice to refrain from doing something and a newborn's inability to functionally abstain.² The National Institutes of Health (NIH) defines NAS as a group of problems that occurs in a newborn exposed to addictive illegal or prescription drugs while in the mother's womb (i.e., in utero exposure).³ Use of substances such as amphetamines, barbiturates, benzodiazepines, and opiates (e.g., diazepam, clonazepam, cocaine, marijuana, heroin, methadone, codeine, hydrocodone, Vicodin oxycodone, or OxyContin) by women during the prenatal period has been associated with both obstetrical and neonatal complications including NAS. A newborn's presentation of NAS varies (Figure 1) and may be influenced by factors that not only include licit and illicit exposures but also include maternal physiology, epigenetic modifications, and genetic predisposition.⁴ NAS infants are more likely to experience adverse neonatal outcomes such as low birthweight (LBW, <2,500 grams or 5 pounds, 8 ounces) than infants without NAS – a major risk factor for infant mortality.

Figure 1. Neonatal abstinence syndrome (NAS) characteristics²

- high-pitched cry / irritability
- respiratory distress
- sleep–wake disturbances
- alterations in infant tone and movement (hyperactive primitive reflexes, hypertonicity, and tremors with resultant skin excoriations)
- feeding difficulties, gastrointestinal disturbances (vomiting and loose stools)
- autonomic dysfunction (sweating, sneezing, fever, nasal stuffiness, and yawning)

Assessment of neonatal abstinence syndrome (NAS)

A typical mechanism for NAS assessment and evaluation is the Finnegan Scoring System and/or its variant. The objective of the assessment is to quantify the severity of symptoms to determine the need for intervention.³ While this type of data may be available at the hospital and/or clinic level, these data are not typically reported to population registries such as vital record systems or captured in hospital discharge datasets. To enumerate NAS incidence at a population level, 2010-2018 hospital discharge data from Delaware hospitals were utilized. Cases were identified using criteria based on the national incidence study by Patrick et al. using *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)*. The authors of this study utilized the Healthcare Cost and Utilization Project's Kids' Inpatient Database (KID) to identify newborns with NAS and the Nationwide Inpatient Sample (NIS) to identify women. Due to the changes in ICD-9-CM on 1st October, 2015 to ICD-10-CM, NAS code of P96.1 has

¹ Patrick SW, Schumacher RE, Benneyworth BD, Krans EE, McAllister JM, Davis MM. Neonatal Abstinence Syndrome and Associated Health Care Expenditures: United States, 2000-2009. *JAMA* 2012 May; 307(18):1934-1940.

² McQueen K, Murphy-Oikonen J. Neonatal Abstinence Syndrome. *N Engl J Med*. 2016 Dec; 375(25):2468-2479.

³ U.S. National Library of Medicine. Neonatal Abstinence Syndrome. National Library of Medicine Website. Available at <http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0004566/>. Accessed on September 7, 2012.

⁴ Jansson LM, Velez M. Neonatal abstinence syndrome. *Curr Opin Pediatr*. April 2012; 24(2):252-258.

also been used by several studies in the U.S.^{5,6,7} In 2019, the Council for State and Territorial Epidemiologists (CSTE) provided a case-definition for NAS. The NAS case definition in this research brief is consistent with CSTE Tier 2 recommendation.⁸

How is Neonatal abstinence syndrome (NAS) determined for this report?

The identification of NAS cases was based on ICD-9-CM and ICD-10-CM codes for all inpatient hospital births in Delaware using hospital discharge data. The Division of Public Health (DPH) collects hospital discharge records for inpatients from all Delaware licensed hospitals. Hospitals are required by Delaware law (16 Del.C. Ch. 20, § 2001-2009) to submit inpatient hospital discharge data from the uniform claims and billing dataset (UB-82 or successor form) to the Delaware Health Statistics Center on a quarterly basis. Hospital births from Bayhealth, Beebe, Christiana Care, Nanticoke, and St. Francis are part of the data that are collected.

Figure 2. Estimating the incidence of Neonatal abstinence syndrome

NAS (numerator): The number of newborns in Delaware during 2010-2018 with any underlying *ICD-9-CM* diagnosis code of 779.5 “drug withdrawal syndrome in a newborn.” Changes in *ICD-10-CM* in October 2015 led to incorporation of P96.1 in enumeration.

Denominator: All hospital births in Delaware during 2010-2018.

Neonatal abstinence syndrome rates for Delaware were estimated using the formula provided in Figure 2. The numerator is defined as babies born meeting the NAS case definition; the denominator includes all reported hospital births in Delaware for the calendar year. It is important to note that in theory all hospital births from the inpatient hospital discharge records to Delawareans should match all hospital births in the birth certificate data. However, due to different cut-off dates in both these administrative datasets the total number of records in each of these datasets typically don't match; however, the differences in the number of records are typically very low.

iatrogenic cases were identified based on Patrick et al.'s study and also includes CSTE criteria. A total of 18 cases were identified during the entire 2010-2018 time-period and the results presented exclude these 18 cases as there was no significant difference in NAS rates after exclusion. In addition to enumerating the

⁵ Maalouf FI, Cooper WO, Stratton SM, Dudley JA, Ko J, Banerji A, Patrick SW. Positive Predictive Value of Administrative Data for Neonatal Abstinence Syndrome. *Pediatrics*, 2019 Jan; 143(1). pii: e20174183.

⁶ Lind JN, Ailes EC, Alter CC, et al. Leveraging Existing Birth Defects Surveillance Infrastructure to Build Neonatal Abstinence Syndrome Surveillance Systems — Illinois, New Mexico, and Vermont, 2015–2016. *MMWR Morb Mortal Wkly Rep* 2019;68:177–180

⁷ Patrick SW, Faherty LJ, Dick AW, Scott TA, Dudley J, Stein BD. Association Among County-Level Economic Factors, Clinician Supply, Metropolitan or Rural Location, and Neonatal Abstinence Syndrome. *JAMA*. 2019;321(4):385–393. doi:10.1001/jama.2018.20851

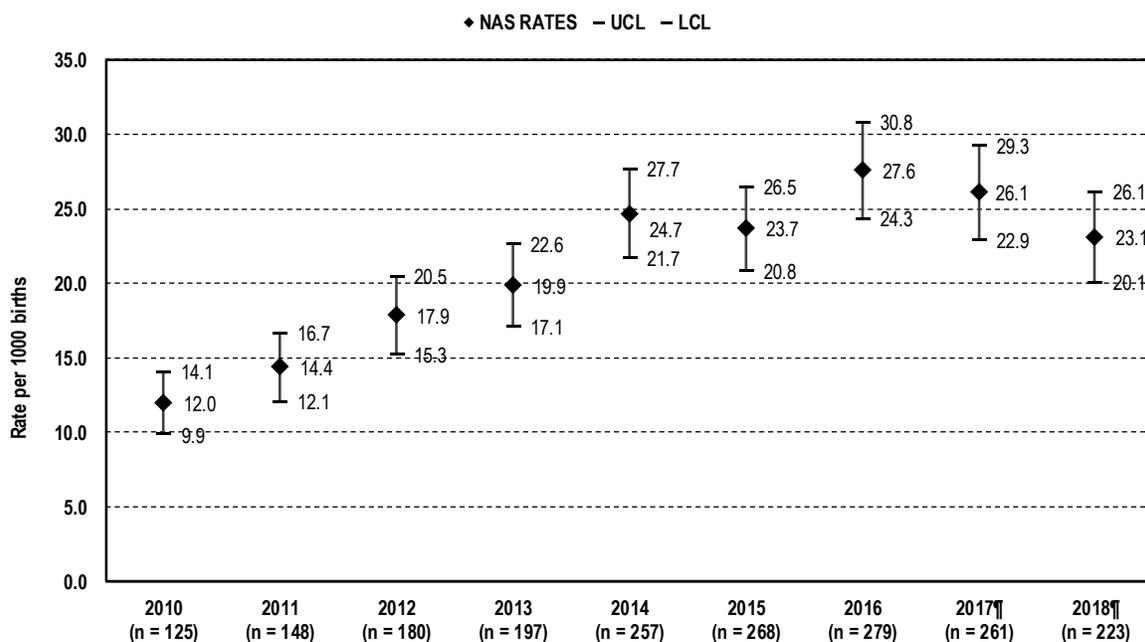
⁸ Council for State and Territorial Epidemiologists. Neonatal Abstinence Syndrome Standardized Case Definition. Available at: https://cdn.ymaws.com/www.cste.org/resource/resmgr/2019ps/final/19-MCH-01_final_7.31.19.pdf

NAS cases from hospital discharge data, all hospital births were matched to birth certificate data for the 2010-2018 period using a similar methodology noted in a previous brief.⁹

Neonatal abstinence syndrome (NAS) in Delaware

There were 1,956 cases of NAS identified in Delaware and included 18 iatrogenic cases. Figure 3 displays the NAS rates for 2010-2018 excluding the iatrogenic cases and the overall NAS rate for Delaware during 2010-2018 was 21.0 (95% CI: 20.1–22.0) per 1,000 births. Although there was a significant increase in NAS rates (~105 percent), from 12.0 per 1,000 births in 2010 to 24.7 per 1,000 births in 2014, the NAS rates seem to decline. For example, the NAS rate in 2016 was 27.6 per 1,000 births and in 2017 the NAS rate was 26.1 per 1,000 births (~5% decline). In 2018, the NAS rate was 23.1 per 1,000 births (~16% decline) as compared with 2016, although this may be a slight underestimate. It is also important to note that 2016-2018 time-period contains a complete transition from ICD-9-CM to ICD-10-CM.

Figure 3. Neonatal Abstinence Syndrome Rates* Delaware, 2010-2018 Intervals



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, Hospital Discharge and Vital Records Data, 2010-2018.

*Rates are presented with 95% confidence intervals; UCL = upper confidence limit; LCL = lower confidence limit
 2015 data contains ICD-9-CM and ICD-10-CM changes. Excludes iatrogenic cases.

† 2017 data are updated to reflect updated HDD records. 2018 NAS rate may be a **slight underestimate** as 2018 data contains less overall newborn records (<43 births) for Delaware Residents.

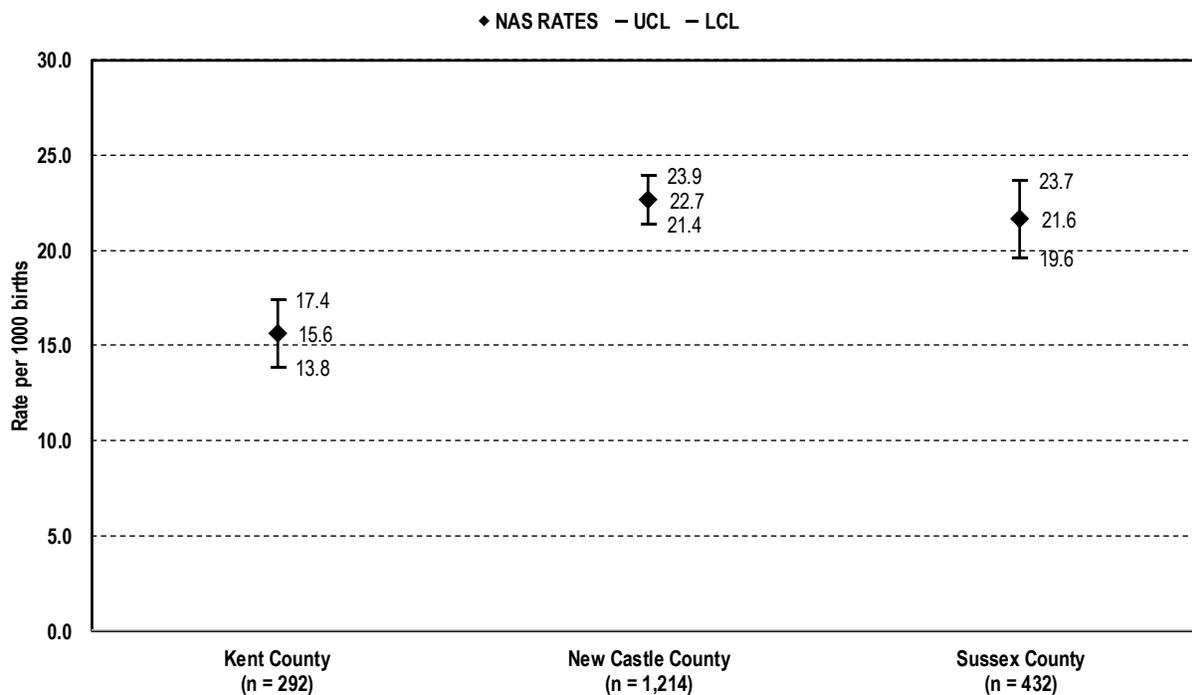
The latest data released by the U.S. Centers of Disease Control and Prevention (CDC) for 28 states indicates that “the overall incidence of NAS in the states has increased almost 300 percent during 1999–

⁹ Hussaini, SK. Neonatal abstinence syndrome: Delaware, 2010-2013. *Research Brief*. Delaware Department of Health and Social Services, Division of Public Health. Published May 2017. Available at: http://dethrives.com/wp-content/uploads/2013/06/Neonatal-abstinence-syndrome-Delaware-2010-2013_final_approved.pdf

2015, from 1.5 to 6.0 cases per 1,000 hospital births.”¹⁰ The U.S. rate for the most recent data available for 2013 was 5.8 per 1,000 births per year.¹¹ Following changes in ICD-9-CM to ICD-10-CM, no national estimates for NAS are currently available, except estimates from the CDC for 2015, from a tri-state analyses that suggests that the NAS incidence during 2015 were 3.0 per 1,000 births for Illinois, 7.5 for New Mexico, and 30.8 for Vermont.⁶ Delaware’s 2013 NAS rate (19.9 per 1,000 births) was more than three times that of the 2013 U.S. rate.

Figure 4 displays the overall NAS rates for Delaware by county. Although the overall rate of NAS was highest in New Castle County during the eight-year period (22.2 cases per 1,000 births; 95% CI:20.8–23.5), the Sussex County NAS rate was similar to the New Castle County NAS rate during same time- period (21.4 per 1,000 births; 95%CI: 19.3-23.6).

Figure 4. Neonatal Abstinence Syndrome Rates* by County, Delaware, 2010-2018



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, Hospital Discharge and Vital Records Data, 2010-2018.

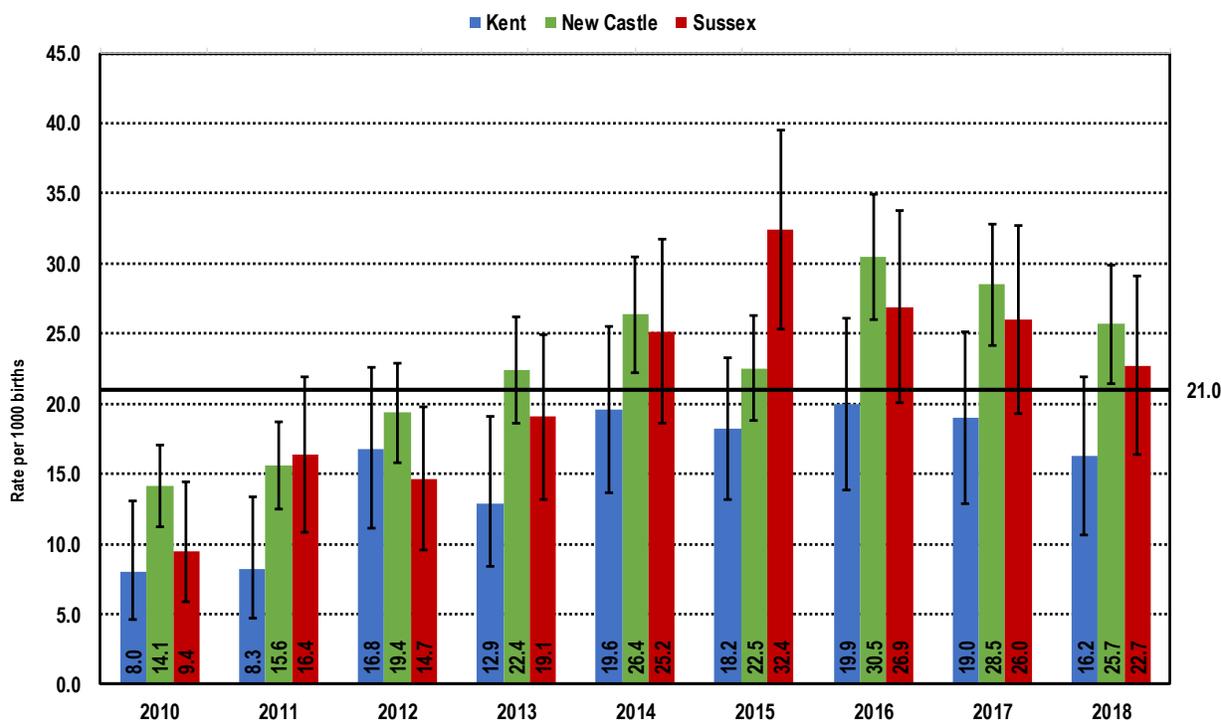
*Rates are presented with 95% confidence intervals; UCL = upper confidence limit; LCL = lower confidence limit
 2015 data contains ICD-9-CM and ICD-10-CM changes. Excludes iatrogenic cases. 2017 data are updated to reflect updated HDD records. 2018 NAS rate may be a slight underestimate as 2018 data contains less overall newborn records (<43 births) for Delaware Residents.

Figure 5 displays NAS rates by county by year. It is evident that in general, NAS rates were higher in New Castle County, followed by Sussex County.

¹⁰ Ko JY, Patrick SW, Tong VT, Patel R, Lind JN, Barfield WD. Incidence of Neonatal Abstinence Syndrome – 28 States, 1999-2015. *Morbidity and Mortality Weekly Report (MMWR)*. 2016 Aug; 65(31):799-802.

¹¹ Patrick SW, Davis MM, Lehmann CU, et al. *J Perinatol*. 2015 Aug; 35(8):650-5.

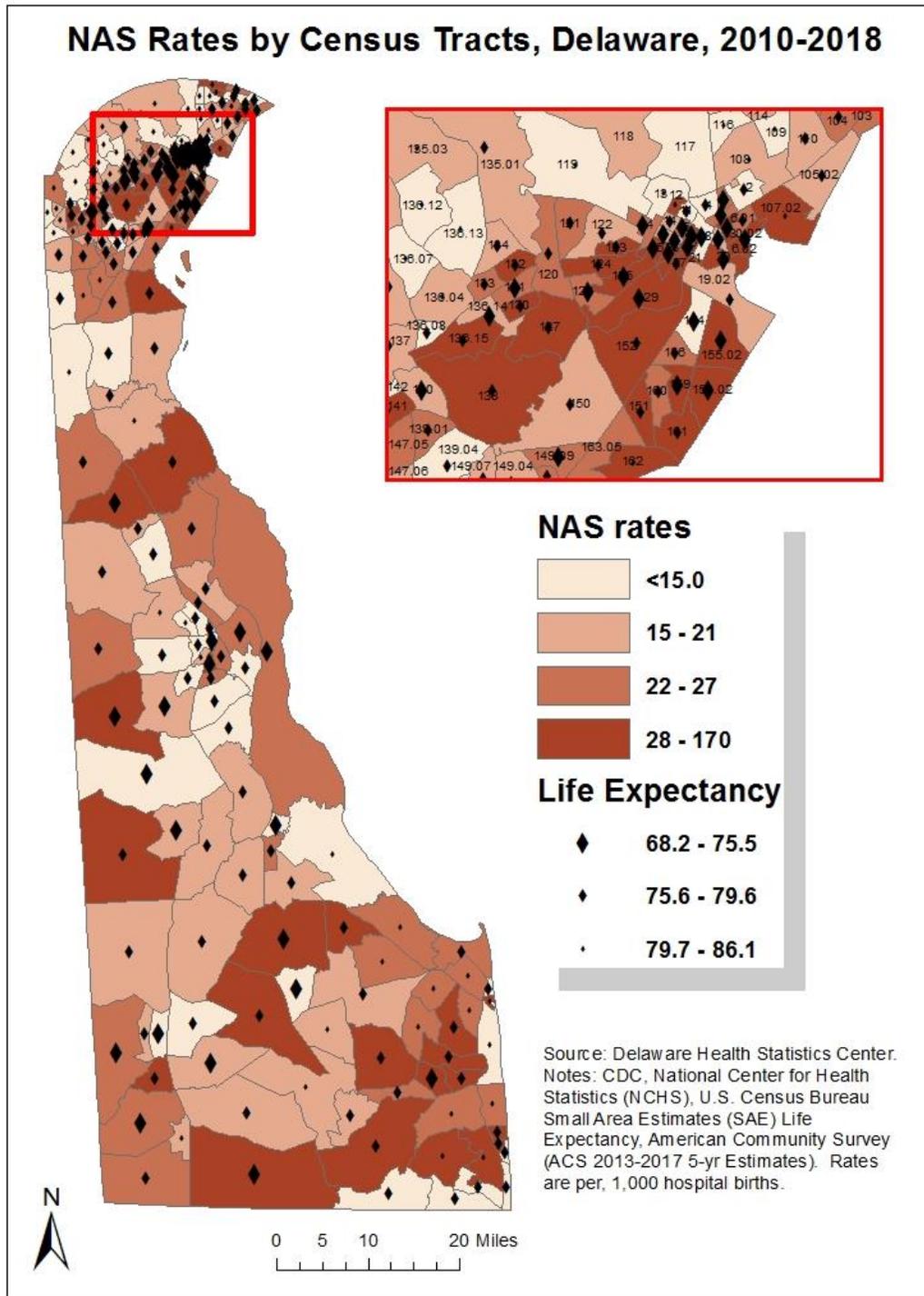
Figure 5. Annual Neonatal Abstinence Syndrome Rates, by County, Delaware, 2010-2018



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, Hospital Discharge and Vital Records Data, 2010-2018.
 *Rates are presented with 95% confidence intervals; UCL = upper confidence limit; LCL = lower confidence limit
 2015 data contains ICD-9-CM and ICD-10-CM changes. Excludes iatrogenic cases. 2017 data are updated to reflect updated HDD records. 2018 NAS rate may be a slight underestimate as 2018 data contains less overall newborn records (<43 births) for Delaware Residents.

To further identify the sub-county level NAS cases, a Census Tracts data map for NAS cases was developed for the 2010-2018 period (Figure 6) overlaid with average life expectancy for Delaware residents developed by the CDC. Darker shades in the map represent higher number of NAS rates during the nine-year period time-period with larger size of the diamond representing “lower life-expectancy.” At the census tracts lower life-expectancy was associated with overall rates of NAS ($r = -0.21$; $p = 0.0017$). While some areas seem to have ‘higher rates’ of NAS, the total number of cases during the entire time-period could have been very low. Hence, the sub-county level NAS rates need to be interpreted with caution. The overlay of life-expectancy on the NAS census tracts is utilized to provide a snapshot of a “quality of life” (QOL) measure rather than attribute any causal factors.

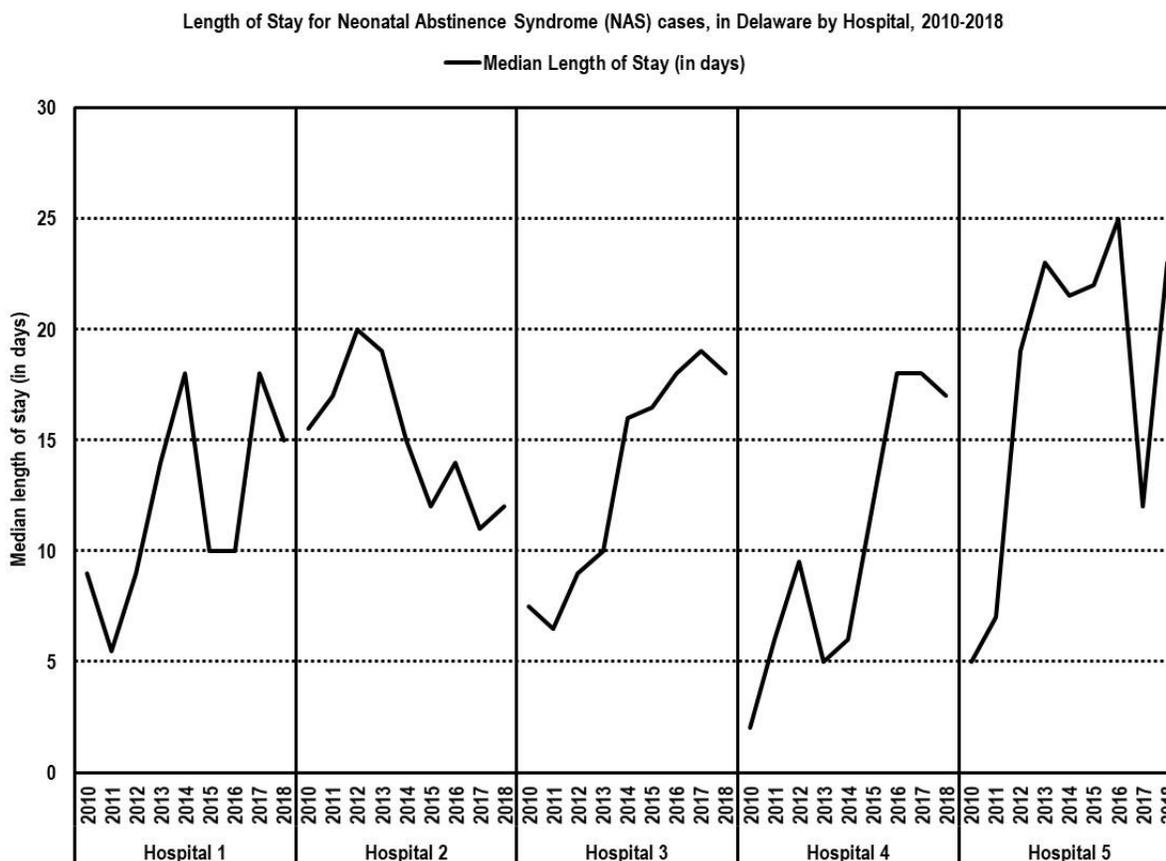
Figure 6. Neonatal Abstinence Syndrome (NAS) Rates by Census Tracts in Delaware, 2010-2018



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, Hospital Discharge and Vital Records Data, 2010-2018.

The median length of stay for NAS affected newborn was 17 days in 2018 as compared to 2 days for a non-NAS newborn. The median length of stay for NAS newborns increased 112 percent during 2010-2018 time-period from 8 days in 2010 to 17 days in 2018. There was considerable year-to-year variation in the length of stay within and between hospitals (Figure 7). Variation in length of stay (LOS) for newborns affected by NAS is partly contingent on standard treatment protocol, severity of the symptoms, maternal opioid dose,¹² and perhaps most importantly associated hospital costs and charges. While LOS is a major driver of cost, as such prolonged LOS may lead to poor mother-infant bonding, increased risk adverse events for newborns and hence decreasing LOS and/or reducing variation in LOS provides opportunities for quality improvement.

Figure 7. Length of Stay (LOS) for Neonatal Abstinence Syndrome (NAS) cases by hospitals in Delaware, 2010-2017



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, Hospital Discharge and Vital Records Data, 2010-2018.

¹² Asti L, Magers JS, Keels E, Wispe J, McClead RE Jr. A quality improvement project to reduce length of stay for neonatal abstinence syndrome. *Pediatrics*. 2015 Jun;135(6): e1494-500. doi: 10.1542/peds.2014-1269.

Mother and infant characteristics of NAS in Delaware

The matched hospital discharge and birth certificate dataset was utilized to further examine the newborn as well as maternal characteristics. Over 98 percent of the total NAS cases (n = 1,850) for singleton deliveries was available for analyses for the 2010-2018 period. There were significant differences in maternal characteristics of NAS and non-NAS infants (Table 2). For instance, women were more likely to be younger (~62%), with low levels of education (~70%), more likely to be white (81%), more likely to have Medicaid as the payor of the birth, more likely to have no prenatal care and/or entered prenatal care in the second and/or third trimester, more likely to have smoked during pregnancy. Women who delivered NAS affected infants were more likely to have received WIC services during pregnancy (37%) as compared to women who delivered non-NAS affected infants (32%), which was a positive attribute as many women who deliver NAS affected infants do not typically have access to resources such as early prenatal care.

Table 2. Characteristics of women delivering singleton infants with neonatal abstinence syndrome (NAS) in Delaware, 2010-2018.

Maternal and newborn characteristics for singleton births [¶]	Total (N = 88,208) [¶]	
	Neonatal Abstinence Syndrome (NAS) (N = 1,850)	All other non-NAS in Delaware (N = 86,358)
Maternal Age		
Less than 19 years	36 (2%)	5,853 (6.8%)
20-24 years	424 (22.9%)	18,802 (21.8%)
25-29 years	678 (36.7%)	25,362 (29.4%)
30-34 years	507 (27.4%)	23,409 (27.1%)
35 or more	205 (11.1%)	12,932 (15%)
Maternal Education		
Less than 12 years of schooling	502 (27.1%)	15,290 (17.7%)
High school graduate	796 (43%)	22,369 (25.9%)
12 or more years of schooling	529 (28.6%)	48,221 (55.8%)
Unknown/Refused	23 (1.2%)	478 (0.6%)
Maternal Race and Ethnicity		
White	1,476 (79.8%)	44,329 (51.3%)
African American or Black	260 (14.1%)	23,698 (27.4%)
Hispanic	90 (4.9%)	12,794 (14.8%)
Other	21 (1.1%)	5,500 (6.4%)
Unknown/Refused	3 (0.2%)	37 (0%)

Table 2 contd/.

Maternal and newborn characteristics for singleton births [¶]	Total (N = 88,208) [¶]	
	Neonatal Abstinence Syndrome (NAS) (N = 1,850)	All other non-NAS in Delaware (N = 86,358)
Maternal Insurance Status		
Medicaid	1,359 (83.7%)	37,358 (48.5%)
Private payers	205 (12.6%)	36,275 (47.1%)
Self Pay	22 (1.4%)	875 (1.1%)
Other	36 (2.2%)	2,398 (3.1%)
Unknown/Refused	2 (0.1%)	129 (0.2%)
Maternal County of Residence		
Kent	293 (15.8%)	17,823 (20.6%)
New Castle	1,162 (62.8%)	50,988 (59%)
Sussex	395 (21.4%)	17,547 (20.3%)
Prenatal Care		
No prenatal care	167 (9%)	2,098 (2.4%)
First Trimester	1,039 (56.2%)	64,823 (75.1%)
Second Trimester	434 (23.5%)	14,229 (16.5%)
Third Trimester	137 (7.4%)	3,710 (4.3%)
Unknown/Refused	73 (4%)	1,498 (1.7%)
Received WIC during pregnancy		
Received WIC services	677 (36.6%)	27,157 (31.5%)
Pre-pregnancy weight		
Underweight	113 (6.1%)	3,635 (4.2%)
Normal weight	892 (48.2%)	35,683 (41.3%)
Overweight	454 (24.5%)	22,274 (25.8%)
Obesity	352 (19%)	23,323 (27%)
Unknown/Refused	39 (2.1%)	1,443 (1.7%)
Cigarette Use		
Smoked during pregnancy	1,271 (68.7%)	8,374 (9.7%)
Hepatitis		
Hep C	223 (12.1%)	274 (0.3%)

Table 2 contd/.

Maternal and newborn characteristics for singleton births [¶]	Total (N = 88,208) [¶]	
	Neonatal Abstinence Syndrome (NAS) (N = 1,850)	All other non-NAS in Delaware (N = 86,358)
Previous poor outcome		
Previous preterm birth	229 (12.4%)	4750 (5.5%)
Infant outcomes		
Low birth weight	356 (19.2%)	5,988 (6.9%)
Preterm birth	298 (16.1%)	6,937 (8%)
Small for gestational age	476 (25.7%)	10,001 (11.6%)
Neonatal deaths	4 (0.2%)	368 (0.4%)
Postneonatal deaths	7 (0.4%)	113 (0.1%)

Source: Delaware Department Health and Social Services, Division of Public Health, Hospital Discharge Data, Vital Records Data, 2010-2018

[¶]Data for singleton births obtained from birth certificate data for 2010-2018

Consistent with Patrick et al.'s study, 19 percent of the infants were low birthweight during the 2010-2018 period. While Patrick et al.'s study did not characterize the gestational age in their study, 16 percent of NAS infants in Delaware were preterm (<37 weeks of gestation), and 26 percent were small for gestational age (infants whose weight is less than the 10th percentile for gestation). Further, women who smoked cigarettes during pregnancy were almost 20 times more likely to have their infants be diagnosed with NAS, compared to those who did not smoke (unadjusted OR: 20.7; 95% CI:18.7–22.9). According to Janson et al.,¹³ “exposures such as cocaine, nicotine, serotonin reuptake inhibitors [SRIs], and polydrugs can potentiate the infant’s expression of opioid-induced NAS.” Maternal cigarette use (adjusted OR = 15.7; 95%CI: 14.3-17.2), race and ethnicity (i.e., non-Hispanic white vs. other race and ethnicity AOR = 3.9; 95%CI: 2.5-6.1; non-Hispanic black vs. other race and ethnicity AOR = 1.7; 95%CI: 1.1-2.7; Hispanics vs. other race and ethnicity AOR = 1.8; 95%CI: 1.1-2.9), and having hepatitis C (AOR = 11.7; 95%CI: 9.5-14.6) had strong discriminatory power in predicting whether an infant was diagnosed with NAS or not.

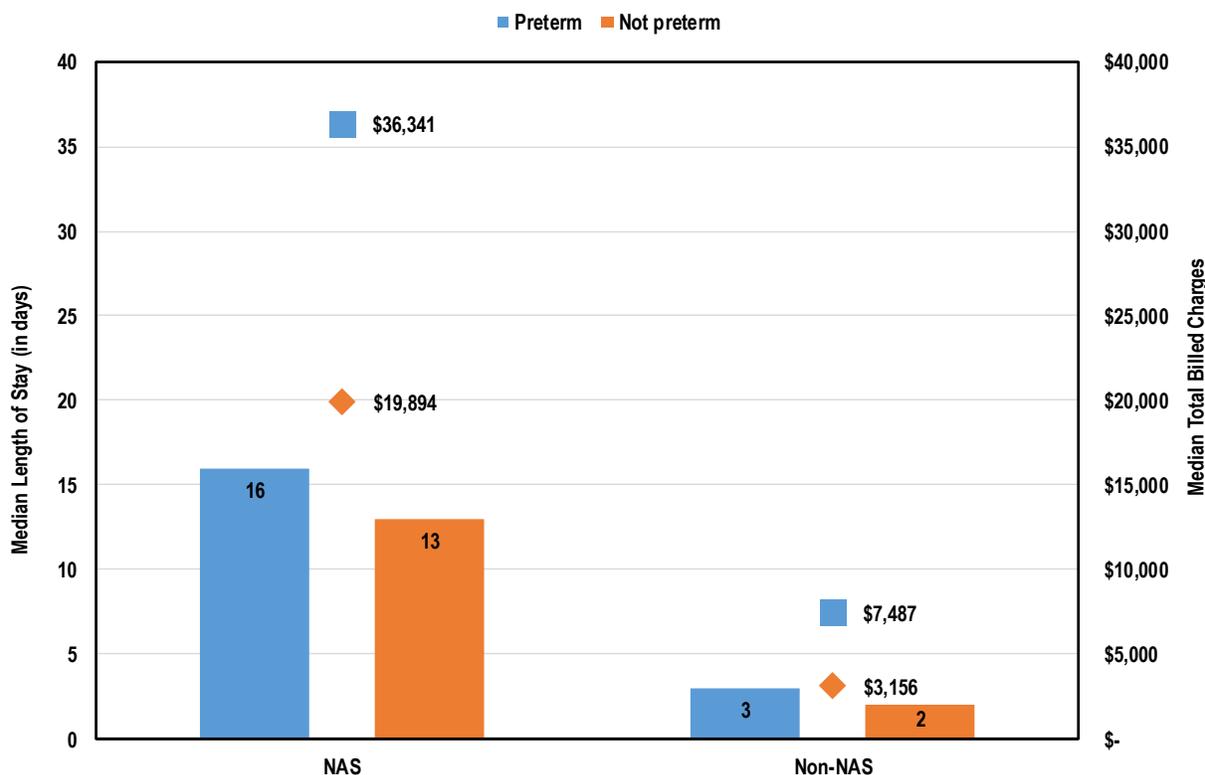
Implications of findings and future steps

During 2010-2018, 1,956 cases (including 18 iatrogenic cases) of NAS were identified in Delaware using the hospital discharge data. The overall NAS rate for Delaware during 2010-2018 was 21.0 (95% CI: 20.1–22.0) per 1,000 births. Although there was a significant increase in NAS rates (~105 percent), from 12.0 per 1,000 births in 2010 to 24.7 per 1,000 births in 2014, the NAS rates seem to decline. For example, the NAS rate in

¹³ See footnote 3 of this research brief.

2016 was 27.6 per 1,000 births and in 2017 the NAS rate was 26.1 per 1,000 births (~5% decline). In 2018, the NAS rate was 23.1 per 1,000 births (~16% decline) as compared with 2016, although this may be a slight underestimate.

Figure 8. Length of Stay and Billed Charges by Prematurity Status, Delaware, 2010-2018



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, Hospital Discharge and Vital Records Data, 2010-2018.

As length of stay is one of the biggest components and drivers of total costs and further, length of stay for newborn is also influenced prematurity status, it is important to account for them in estimating the financial burden. Although, hospital costs data are unavailable, total billed charges are available on the discharge record. Figure 8 provides the distribution of length of stay and total billed charges by prematurity status. It is evident from figure 8 that even after accounting for prematurity status LOS and billed charges on average were higher for NAS infants as compared to non-NAS infants.

This updated brief from the previous 2010-2013 research brief¹⁴ for Delaware has captured in detail the incidence of NAS among newborns and their maternal characteristics using hospital discharge data and matched vital records data. While this research brief highlights the incidence of NAS in Delaware newborns, it is difficult to estimate the ‘true incidence’ due to variability in reporting. For instance,

¹⁴ Hussaini, SK. Neonatal abstinence syndrome: Delaware, 2010-2013. Research Brief. Delaware Department of Health and Social Services, Division of Public Health. Published May 2017.

administrative data sources such as the hospital discharge data and vital records data are limited due to variability in coding within and between hospitals, between years (i.e., changes from ICD-9-CM to ICD-10-CM). In addition, there is considerable lag in availability of hospital discharge data to rapidly assess trends. Although over 99 percent of the births in Delaware occur at hospitals, the NAS analyses is limited to hospital births. Approximately 99 percent of the hospital births were matched to birth certificate data that also provided additional insights to the maternal and newborn characteristics and the epidemiological risks of NAS in newborns. Maternal race and ethnicity, maternal cigarette use, and hepatitis C were the strongest predictors of women delivering NAS infants.

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