

Neonatal Abstinence Syndrome

Delaware Profile 2010-2020

This research brief provides an overview of neonatal abstinence syndrome in Delaware during 2010-2020. Neonatal abstinence syndrome (NAS) is a withdrawal syndrome and a complex multisystem disorder that varies in signs, symptoms, and severity among infants. NAS occurs shortly after birth in infants born to women with chronic opioid use (heroin, prescription pain medicines), or with maternal medications for opioid use disorder such as methadone or buprenorphine, as well as exposures to cocaine, selective serotonin reuptake inhibitors (SSRIs) and nicotine [1-10]. The rates of NAS and maternal opioid use disorder (OUD) have shown to vary across states in the U.S. and Delaware's NAS rate is among top five in the U.S. [9].

Overview

Neonatal abstinence syndrome (NAS) and neonatal opioid withdrawal syndrome (NOWS) have been used interchangeably since the time period from 2012-2016 when the US Food and Drug Administration introduced NOWS terminology; however, NOWS is considered a subset of NAS [12]. The expert panel consisting of 20 clinical experts specializing in care for the substance-exposed mother-neonate dyad concluded that:

in utero exposure (known by history, not necessarily by toxicology testing) to opioids with or without the presence of other psychotropic substances, and the presence of at least two of the most common clinical signs characteristic of withdrawal (excessive crying, fragmented sleep, tremors, increased muscle tone, gastrointestinal dysfunction) are required for diagnosis of NAS/NOWs [11; p. 1]

Assessment of NAS/NOWs

Expert consensus emphasizes the clinical criteria for diagnosis of NAS/NOWS independent of scoring and assessment tools, non-pharmacological and pharmacological care, and administrative coding,



Importance

On average 45 opioid prescriptions are dispensed per 100 persons in Delaware compared to 43.3 in the U.S. [11]. The growing opioid crisis has impacted various populations in Delaware differently. One such population group are women and their infants. In utero exposure to opioids during pregnancy may result in withdrawal in newborns known as NAS. On average, in the U.S., NAS infants as compared to non-NAS infants have longer length of stay (9.2 days vs. 1.6 days) and greater average cost (\$14,000 vs. \$4,200) per stay [9].

Key findings

- During 2010 to 2020 there were 2,323 NAS cases in Delaware excluding 23 iatrogenic cases with an overall rate of 20.9 (95%CI: 20.0-21.7) per 1,000 births. Alternatively, 1 in 50 newborns (~2.0%) in Delaware were diagnosed with NAS during 2010-2020.
- The most recent published 2017 national and statewide estimate of NAS suggest that the U.S. NAS rate was 7.3 per 1,000 birth hospitalizations. Delaware's NAS rate was three times that of the U.S. rate.
- NAS rates increased by 105% during 2010 to 2014 and decreased by 29% during 2016 to 2020.
- In 2020, the OUD rate of 22.2 (95%CI: 19.4-25.2) per 1,000 delivery hospitalizations was similar to the NAS rate of 19.6 (95%CI: 16.7-22.4).



while acknowledging that although toxicology testing for the mother and neonate was not required for NAS/NOWS, testing could be helpful for a better understanding of the clinical presentation [12]. Assuming an accurate clinical diagnosis, the panel indicated that while claims data has a high positive predictive value it may miss mild withdrawal [12].

Use of all-payer claims administrative data such as the hospital discharge data (HDD) is the predominant mechanism in identifying NAS cases for surveillance [13-14]. 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 discharge data from the uniform claims and billing dataset (UB-82/UB-40 or successor form) to the Delaware Health Statistics Center on a quarterly basis. Hospital births from six birthing facilities: Bayhealth (Kent and Sussex), Beebe, ChristianaCare, Nanticoke, and St. Francis are included. To enumerate NAS incidence at a population level, 2010-2020 HDD from Delaware hospitals were used. The ICD-9-CM 779.5 and ICD-10-CM P96.1 codes were used based on the Council for State and Territorial Epidemiologists (CSTE) Tier 2 recommendation of confirmed cases [12].

The numerator is comprised of newborns meeting the NAS case definition; the denominator includes all reported hospital births in Delaware for the calendar year. In addition to enumerating the NAS cases from hospital discharge data, all hospital births were matched to birth certificate data for the 2010-2020 period using a previously described methodology [14-15]. 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 dataset may not match. However, the differences in the number of records are typically very low. Based on Patrick et al.'s study criteria [6] iatrogenic cases (newborns who require opioids to prevent or treat signs of withdrawal) were excluded for ICD-9-CM [9, 12] but not for ICD-10-CM as they contain a specific code P96.2 (i.e., withdrawal symptoms from therapeutic use of drugs in newborn). A total of 23 iatrogenic cases were identified during the entire 2010-2020 time-period and the results presented exclude these 23 cases.

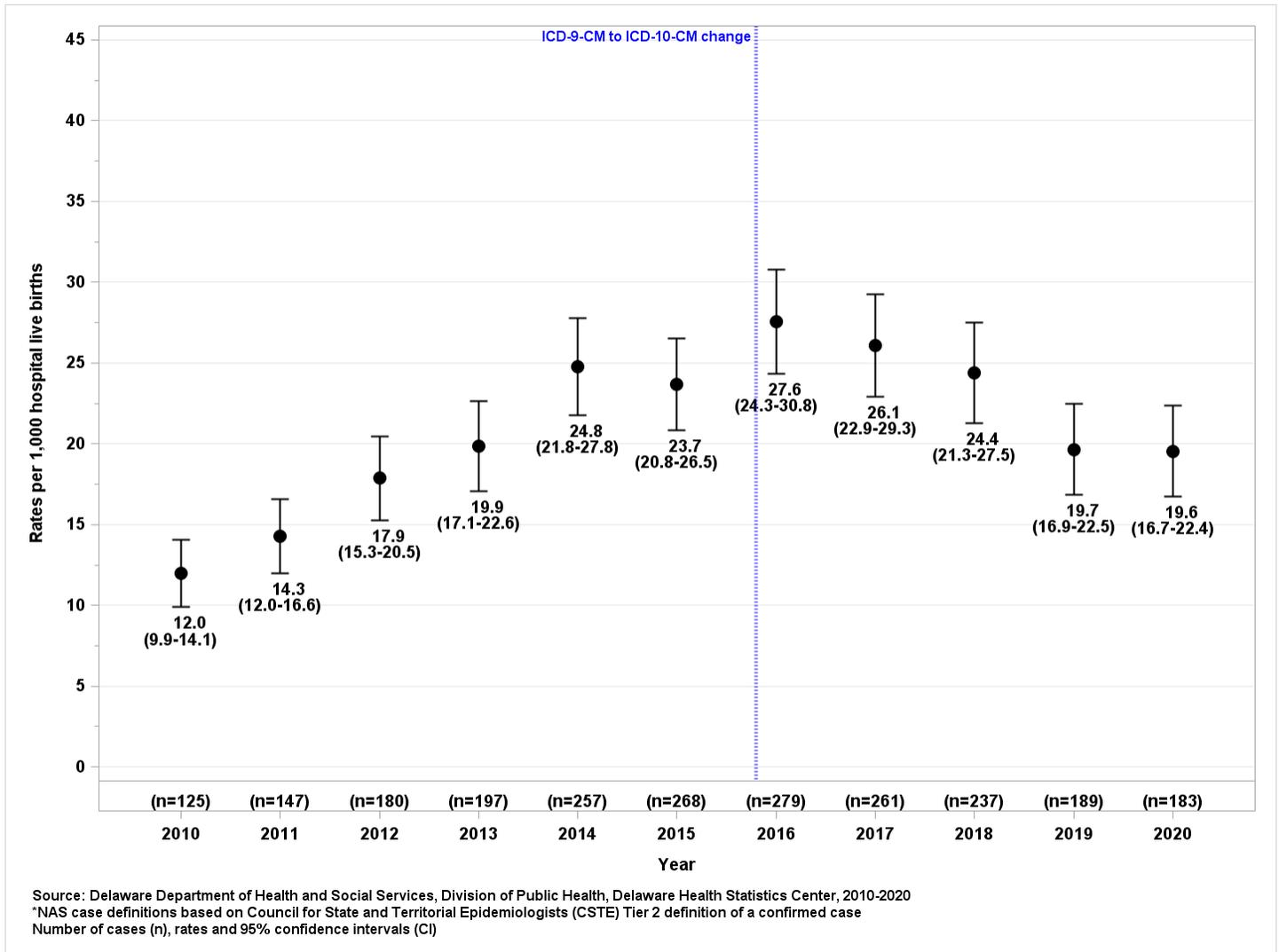
Neonatal abstinence syndrome (NAS) in Delaware

During 2010 to 2020 there were 2,323 NAS cases in Delaware excluding 23 iatrogenic cases with an overall rate of 20.9 (95%CI: 20.0-21.7) per 1,000 hospital births. Alternatively, 1 in 50 newborns (~2.0%) in Delaware were diagnosed with NAS during 2010-2020.

Figure 1 displays the number of NAS cases and rates per 1,000 hospital births for 2010-2020. Although there was a significant increase in NAS rates (~105 percent), from 12.0 per 1,000 hospital births in 2010 to 24.7 per 1,000 hospital births in 2014, the NAS rates declined between 2016 and 2020. For instance, there was a 29% decline in NAS rates between 2016 (27.6; 95%CI: 24.3-30.8 per 1,000 hospital births), and 2020 (19.6; 95%CI: 16.7-22.4 per 1,000 hospital births). The most recent published 2017 national and statewide estimates of NAS suggest that the NAS rate was 7.3 per 1,000 birth hospitalizations and the 2017 Delaware rate as per this estimate was 24.3 per 1,000 birth hospitalizations [9] as compared to our estimate of 26.1 per 1,000 births. The NAS rate derived from the national data was a slight underestimate due to reporting differences to Health Care Utilization Project (HCUP), National Inpatient Sample (NIS). Irrespective of the source, Delaware's NAS rate was three times that of the U.S. rate.



Figure 1. Neonatal Abstinence Syndrome (NAS)* rates per 1,000 hospital live births in Delaware, 2010-2020



During 2010-2020, there were 351 NAS cases in Kent county with an overall rate of 15.6 (95%CI: 14.0-17.2) per 1,000 hospital births. There were 1,431 NAS cases in New Castle county with an overall rate of 22.2 (95%CI: 21.0-23.3) per 1,000 hospital births, and 540 NAS cases in Sussex county with an overall rate of 22.3 (95%CI: 20.4-24.2). Figure 2 displays the NAS rates by county and by year in Delaware for 2010-2020. NAS rates increased in all counties with highest increase in Sussex county (244%) during 2010-2015, followed by Kent county (124%) and New Castle county (59%). After 2016, New Castle county saw a 36% change in NAS rates during 2016-2020, followed by Kent county (23%) and Sussex county (13%).

Figure 3 displays the NAS rates by census tracts for 2010-2020 overlayed by pharmacies in Delaware. NAS rates were highest in tracts surrounding zipcodes 19711, 19716, and 19717 in New Castle county.

Figure 2. Neonatal Abstinence Syndrome (NAS) rates per 1,000 hospital live births by county in Delaware, 2010-2020

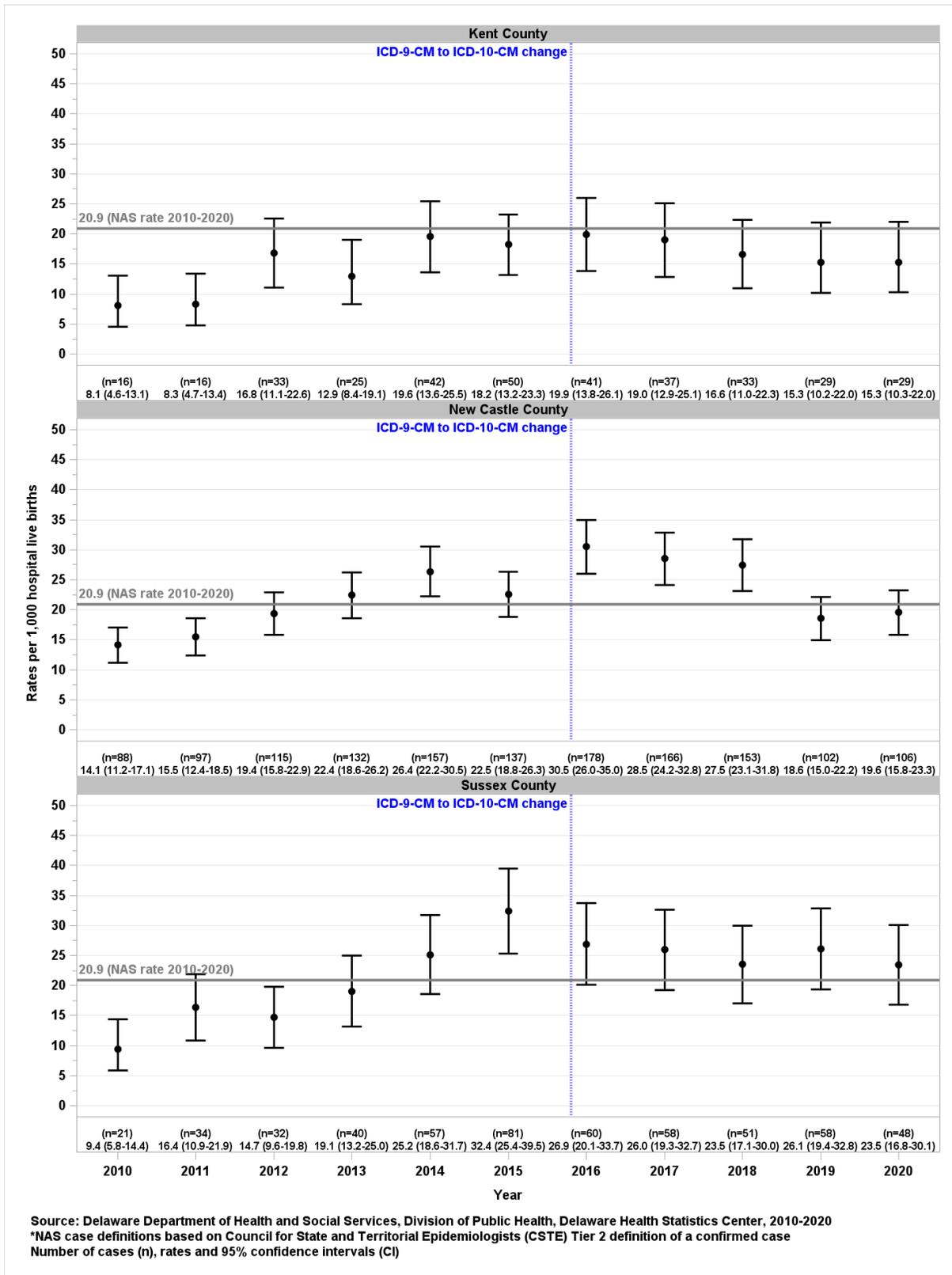


Figure 3. Neonatal Abstinence Syndrome (NAS) rates per 1,000 hospital live births by census tracts in Delaware, 2010-2020

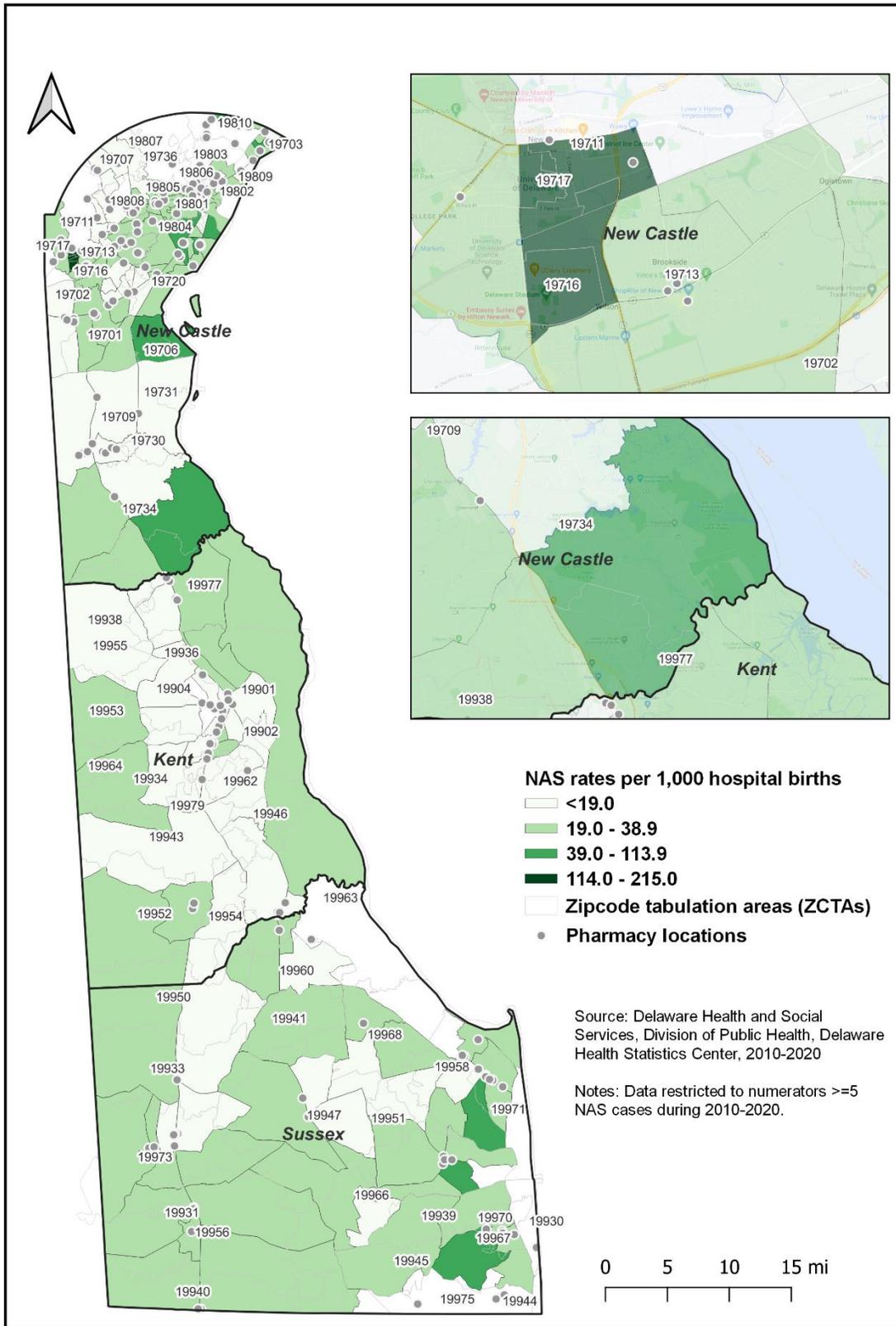


Figure 4 displays the average length of stay (LOS) in days, which is days between date of admission and date of discharge for NAS infants during 2010-2020 in Delaware. The median length of stay in Delaware increased from 8 days in 2010 to 19 days in 2020, which was greater than the U.S. median of 11 days [9].

Figure 4. Average length of stay in days for NAS infants in Delaware, 2010-2020

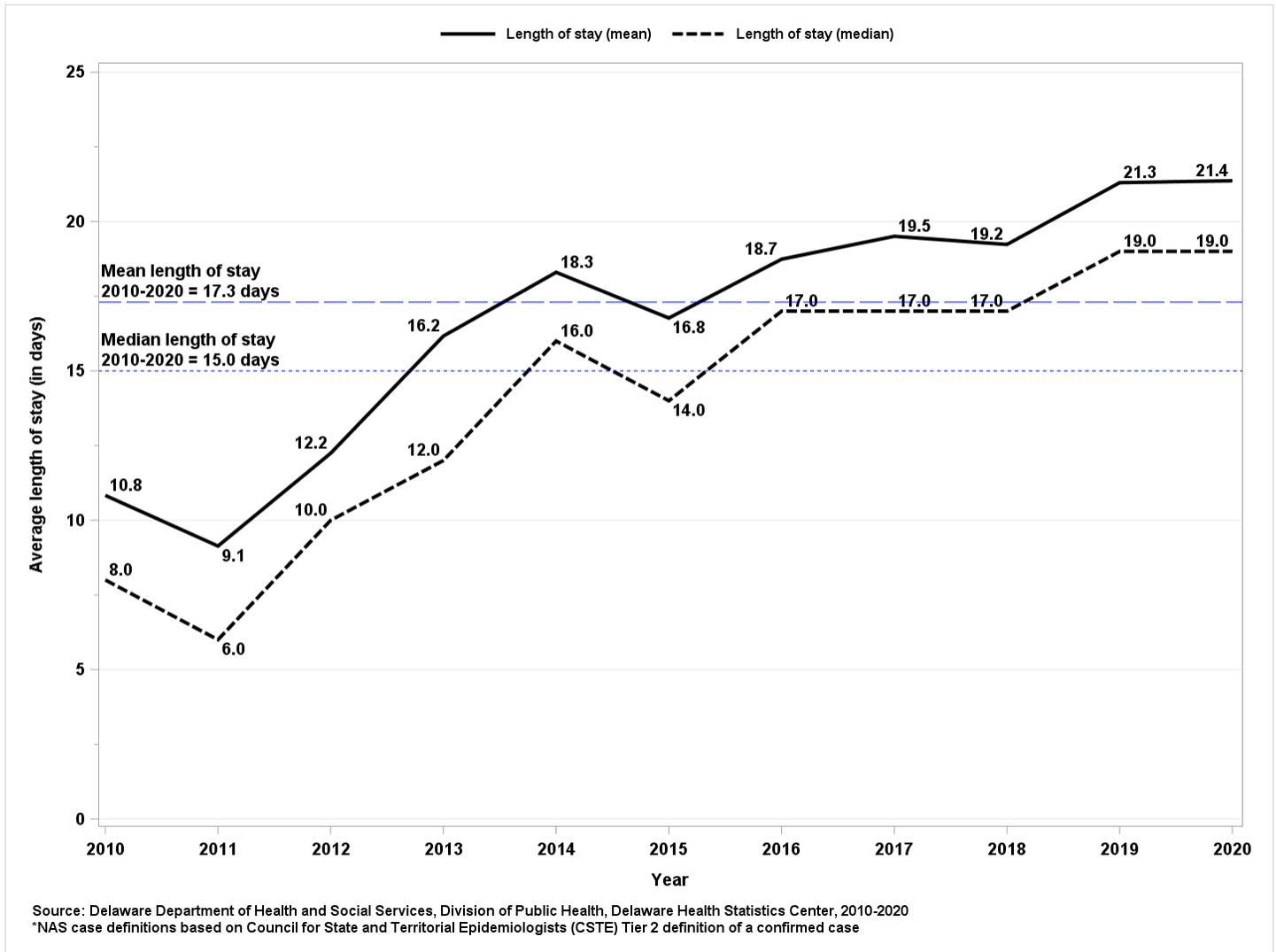
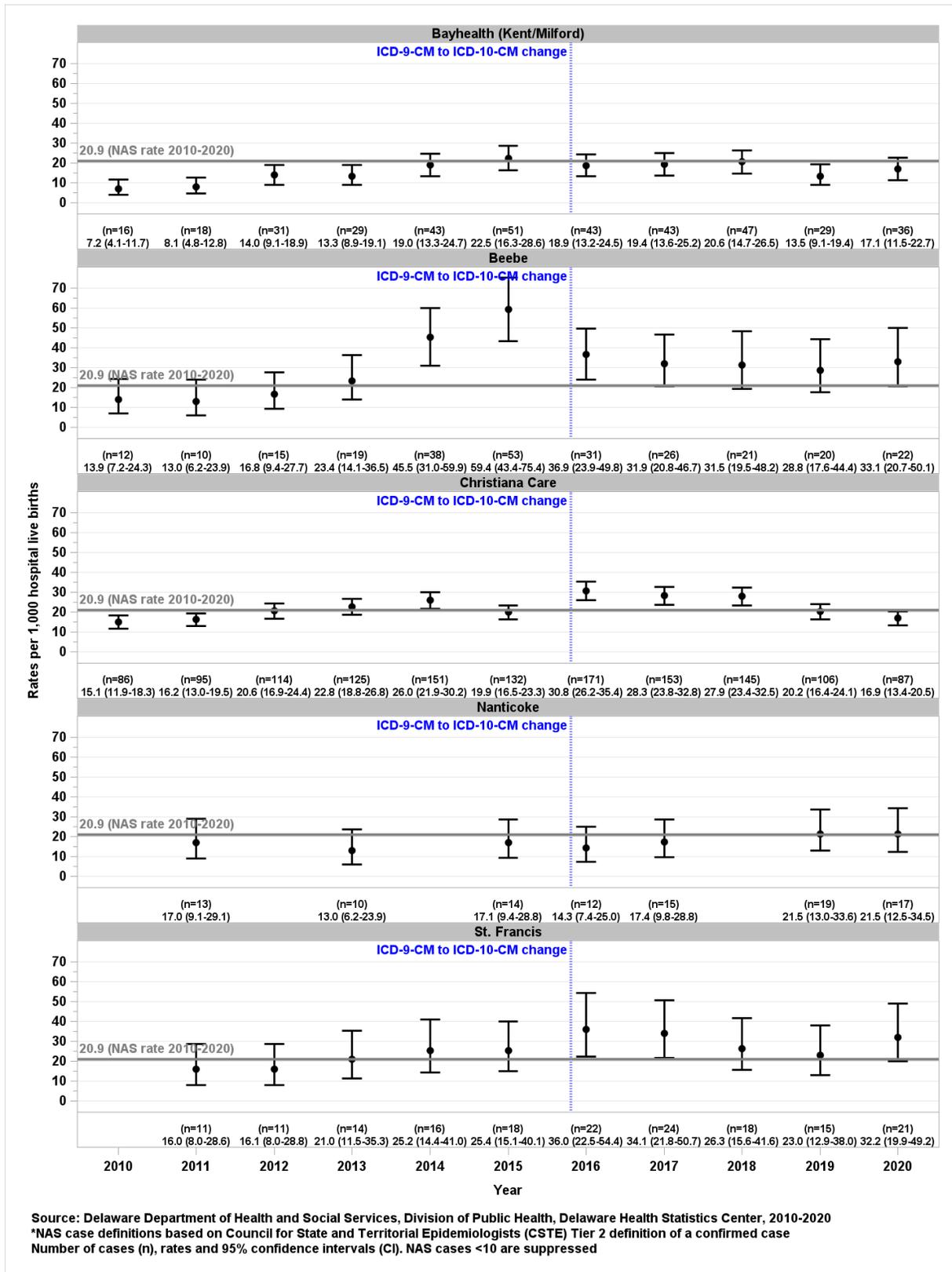


Figure 5 displays NAS rates per 1,000 hospital births by birthing facility in Delaware. NAS rates increased across all hospitals during 2010-2020. In 2015, Beebe’s NAS rate (59.4; 95%CI: 43.4-75.4) was 3 times higher than the overall state rate of 20.9. In 2016, all three birthing facilities: Beebe, ChristianaCare, and St. Francis had NAS rates above the state average. Between 2016 and 2020, ChristianaCare saw a 45% decline in NAS rates from 30.8 (95%CI: 26.2-35.4) per 1,000 hospital births to 16.9 (95%CI: 13.4-20.5) per 1,000 hospital births.

Figure 5. Neonatal Abstinence Syndrome (NAS) rates per 1,000 hospital live births by birthing facilities in Delaware, 2010-2020



Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, 2010-2020
 *NAS case definitions based on Council for State and Territorial Epidemiologists (CSTE) Tier 2 definition of a confirmed case
 Number of cases (n), rates and 95% confidence intervals (CI). NAS cases <10 are suppressed

Figure 6 displays the average length of stay in days for NAS infants by birthing facilities during 2010-2020 in Delaware. Average length of stay varied between birthing facilities during this period with LOS increasing for ChristianaCare during this period, and LOS decreasing for Beebe. By 2020, Beebe’s median LOS of 13 days and ChristianaCare’s was at 23 days as compared to the state average of 15 days.

Figure 6. Average length of stay in days for NAS infants by birthing facilities in Delaware, 2010-2020

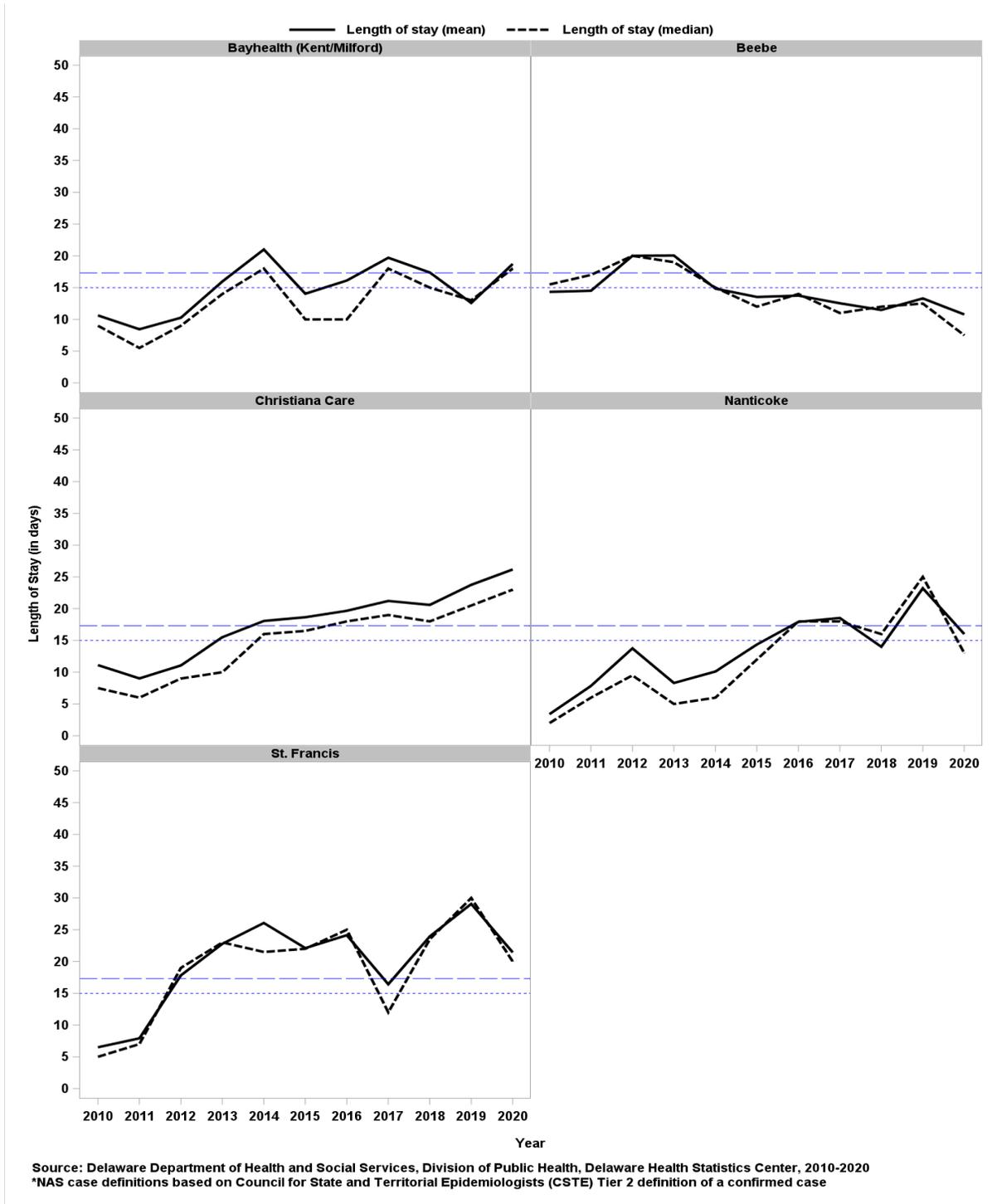
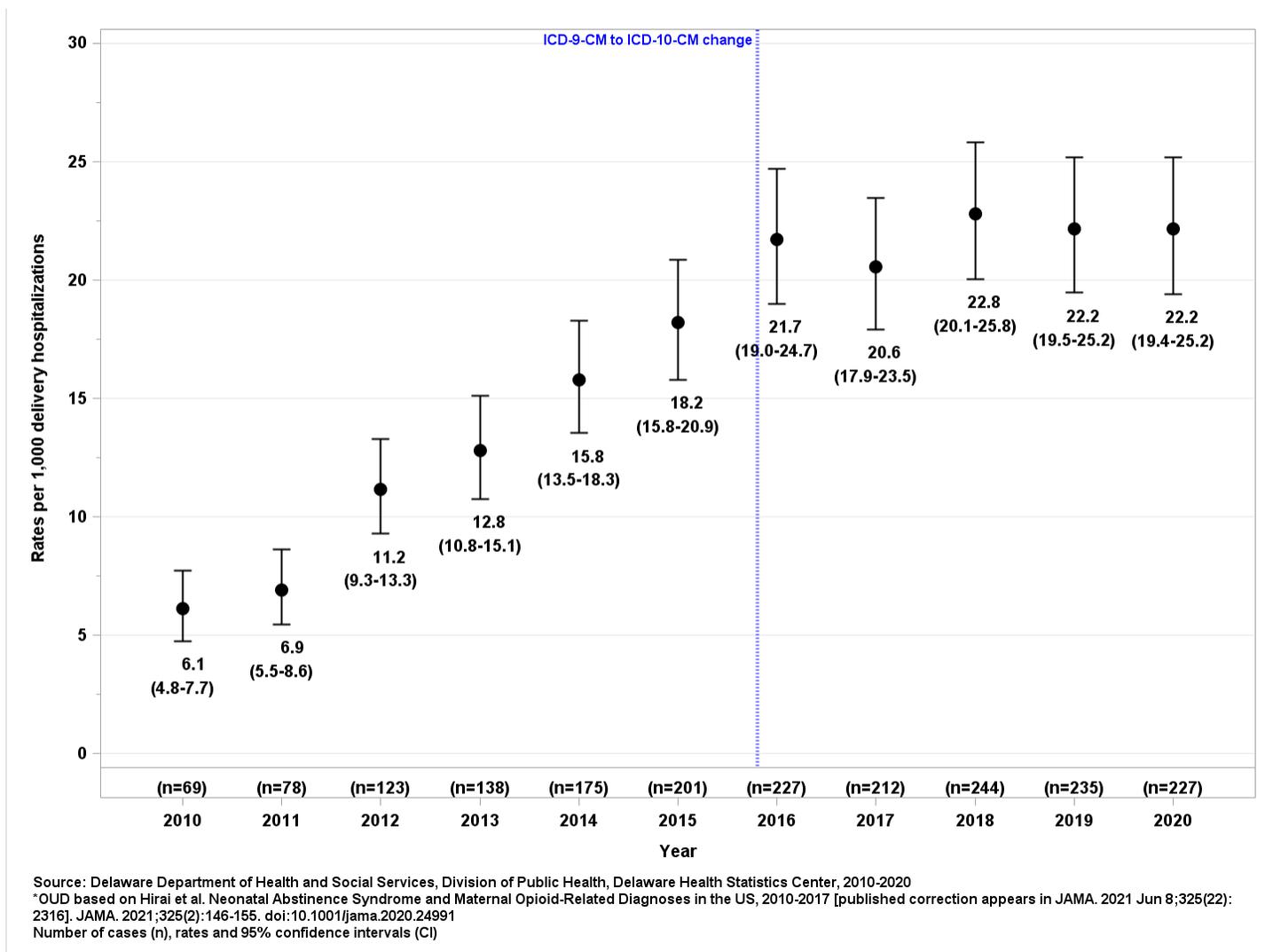


Figure 7 displays delivery hospitalizations of women with an opioid use disorder (OUD) in Delaware during 2010-2020. It is evident that the OUD rate of 22.2 (95%CI: 19.4-25.2) per 1,000 delivery hospitalizations is similar to the NAS rate of 19.6 (95%CI: 16.7-22.4) in 2020.

Figure 7. Maternal Opioid Use Disorder (MOUD) rates per 1,000 delivery hospitalizations in Delaware, 2010-2020



Characteristics of mother-infant dyads with and without NAS in Delaware

The matched hospital discharge and birth certificate dataset from 2010-2020 was used to further examine the maternal characteristics of those who delivered an infant with and without NAS. The cohort was comprised of 105,292 (~98% matched) mother-infant pairs. A total of 2,165 NAS cases with singleton gestation was available for analyses for the 2010-2020 period. There were significant differences in maternal and newborn characteristics of NAS and non-NAS infants (Table 1). Women with a NAS-affected infant as compared with women without a NAS-affected infant had: more than one pregnancy (75% vs. 60%); were non-Hispanic White (79% vs. 59%); had Medicaid (85% vs. 47%) as the payor of the birth; had no prenatal care (8% vs.

2%) and/or entered prenatal care in the second (26% vs. 17%) and/or third trimester (7% vs. 4%); had hepatitis C infection (13% vs. <1%); smoked during pregnancy (68% vs. 9%); had OUD (53% vs. 1%); had serious mental illness (14% vs. 4%); had infants with birth weight less than 2,500 grams or low birth weight (19% vs. 7%); had infants with less than 37 weeks gestation or preterm (15% vs. 8%); and had birth weights below the 10th percentile or smaller than other babies of the same gestational known as small for gestational age (26% vs. 11%).

Table 1. Maternal characteristics of newborns with and without neonatal abstinence syndrome in Delaware, 2010-2020

Maternal and newborn characteristics for singleton births	Neonatal Abstinence Syndrome,* no. (%)		
	Total	NAS	Non-NAS
Total	105,292	2,165 (2.1%)	103,127 (97.9%)
Parity[†]			
Missing/Unknown	66 (0.1%)	3 (0.1%)	63 (0.1%)
Nulliparous	42,071 (40.0%)	542 (25.0%)	41,529 (40.3%)
Multiparous	63,155 (60.0%)	1,620 (74.8%)	61,535 (59.7%)
Maternal age (mean [SD])	28.3 (±5.8)	28.3 (±5.0)	28.3 (±5.8)
Maternal age-groups (years)			
<20	6,690 (6.4%)	42 (1.9%)	6,648 (6.4%)
20-24	22,636 (21.5%)	476 (22.0%)	22,160 (21.5%)
25-29	31,398 (29.8%)	775 (35.8%)	30,623 (29.7%)
30-34	28,685 (27.2%)	625 (28.9%)	28,060 (27.2%)
>=35	15,883 (15.1%)	247 (11.4%)	15,636 (15.2%)
Race and ethnicity			
Missing/Unknown	40 (0.0%)	1 (0.0%)	39 (0.0%)
White (non-Hispanic)	54,223 (51.5%)	1,710 (79.0%)	52,513 (50.9%)
Black (non-Hispanic)	28,729 (27.3%)	329 (15.2%)	28,400 (27.5%)
Hispanic	15,279 (14.5%)	93 (4.3%)	15,186 (14.7%)
Other races	7,021 (6.7%)	32 (1.5%)	6,989 (6.8%)
Payor of birth			
Missing/Unknown	305 (0.3%)	3 (0.1%)	302 (0.3%)
Medicaid	50,689 (48.1%)	1,846 (85.3%)	48,843 (47.4%)
Private Insurance	49,941 (47.4%)	248 (11.5%)	49,693 (48.2%)
Self Pay	1,210 (1.1%)	34 (1.6%)	1,176 (1.1%)
Other	3,147 (3.0%)	34 (1.6%)	3,113 (3.0%)
Trimester of prenatal care			
Missing/Unknown	1,930 (1.8%)	102 (4.7%)	1,828 (1.8%)
No Prenatal Care	2,334 (2.2%)	182 (8.4%)	2,152 (2.1%)
First Trimester	78,991 (75.0%)	1,177 (54.4%)	77,814 (75.5%)
Second Trimester	17,639 (16.8%)	551 (25.5%)	17,088 (16.6%)
Third Trimester	4,398 (4.2%)	153 (7.1%)	4,245 (4.1%)

Table contd/.

Maternal and newborn characteristics for singleton births	Neonatal Abstinence Syndrome,* no. (%)		
	Total	NAS	Non-NAS
Prepregnancy body mass index (BMI)[§]			
Missing/Unknown	1,789 (1.7%)	51 (2.4%)	1,738 (1.7%)
Underweight	4,182 (4.0%)	122 (5.6%)	4,060 (3.9%)
Normal weight	42,884 (40.7%)	1,017 (47.0%)	41,867 (40.6%)
Overweight	27,297 (25.9%)	549 (25.4%)	26,748 (25.9%)
Obese	29,140 (27.7%)	426 (19.7%)	28,714 (27.8%)
Hepatitis			
Yes	629 (0.6%)	279 (12.9%)	350 (0.3%)
No	104,663 (99.4%)	1,886 (87.1%)	102,777 (99.7%)
Cigarette use during pregnancy			
Missing/Unknown	31 (0.0%)	3 (0.1%)	28 (0.0%)
Yes	10,794 (10.3%)	1,472 (68.0%)	9,322 (9.0%)
No	94,467 (89.7%)	690 (31.9%)	93,777 (90.9%)
Opioid use disorder[¶]			
Yes	1,836 (1.7%)	1,136 (52.5%)	700 (0.7%)
No	103,456 (98.3%)	1,029 (47.5%)	102,427 (99.3%)
Serious mental illness (SMI)**			
Yes	4,642 (4.4%)	293 (13.5%)	4,349 (4.2%)
No	100,650 (95.6%)	1,872 (86.5%)	98,778 (95.8%)
Low birth weight (<2,500 grams)			
Missing/Unknown	10 (0.0%)	0 (0.0%)	10 (0.0%)
Yes	7,648 (7.3%)	415 (19.2%)	7,233 (7.0%)
No	97,634 (92.7%)	1,750 (80.8%)	95,884 (93.0%)
Preterm birth (<37 weeks gestations)			
Missing/Unknown	73 (0.1%)	11 (0.5%)	62 (0.1%)
Yes	8,712 (8.3%)	331 (15.3%)	8,381 (8.1%)
No	96,507 (91.7%)	1,823 (84.2%)	94,684 (91.8%)
Small for gestational age			
Missing/Unknown	1,634 (1.6%)	48 (2.2%)	1,586 (1.5%)
Yes	11,891 (11.3%)	552 (25.5%)	11,339 (11.0%)
No	91,767 (87.2%)	1,565 (72.3%)	90,202 (87.5%)

Source: Delaware Department of Health and Social Services, Division of Public Health, Delaware Health Statistics Center, 2010-2020

*NAS case definitions based on Council for State and Territorial Epidemiologists (CSTE) Tier 2 recommendation of confirmed cases

†Number of pregnancies reaching 20 weeks and 0 days of gestation or beyond, regardless of the number of fetuses or outcomes

§Body Mass Index (BMI) is a person's weight in kilograms (or pounds) divided by the square of height in meters (or feet)

¶OUD based on Hirai et al. Neonatal Abstinence Syndrome and Maternal Opioid-Related Diagnoses in the US, 2010-2017 [published correction appears in JAMA. 2021 Jun 8;325(22):2316]. JAMA. 2021;325(2):146-155. doi:10.1001/jama.2020.24991

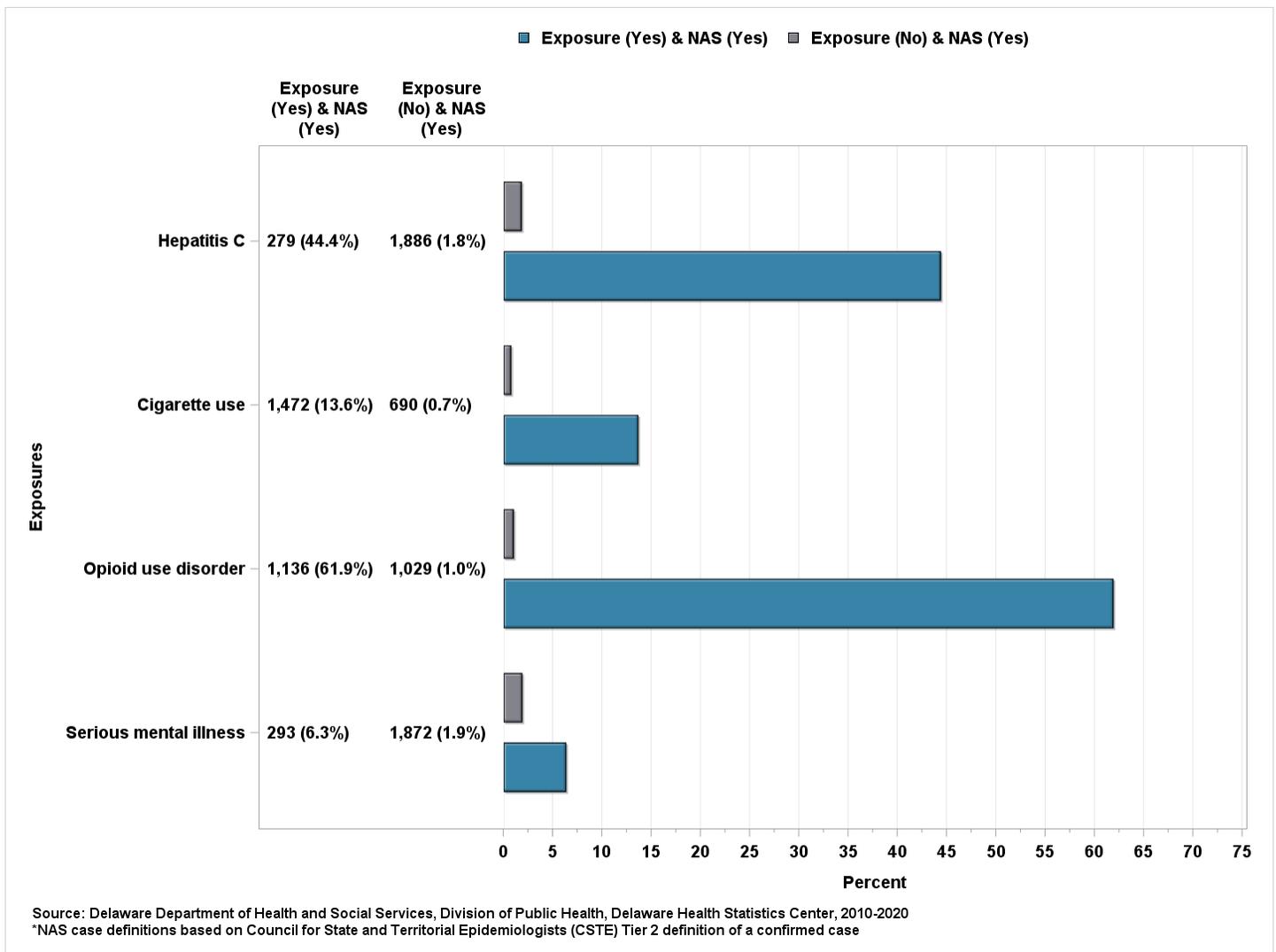
**SMI categories include schizophrenia and other psychotic disorders, bipolar and related disorders, depressive disorders, anxiety disorders, obsessive-compulsive disorders, trauma-and stressor related disorders, and dissociative disorders.



Consistent with other studies [3,6,7,10] infants with NAS had poor birth outcomes such as low birthweight, premature birth and were small for gestational age.

Figure 8 displays the percentage of women who had Hepatitis C, smoked cigarettes during pregnancy, had OUD, and SMI and delivered a NAS-affected infant. Women with Hepatitis C were 25 times more likely to deliver a NAS-affected infant as compared to those without (unadjusted RR = 24.6; 95%CI: 22.3-27.2). Women who smoked during pregnancy were 19 times more likely to deliver a NAS-affected infant as compared to those who didn't (unadjusted RR = 18.7; 95%CI:17.1-20.4). Women with OUD were 62 times more likely to deliver an NAS-affected infant as compared to those without an OUD (unadjusted RR = 62.2; 95%CI: 58.0-66.8). And women who were diagnosed with SMI were 3 times more likely to deliver an NAS-affected infant as compared to those without SMI (unadjusted RR = 3.4; 95%CI: 3.0-3.8).

Figure 8. Number and percentage of women who delivered a NAS-affected infant with Hepatitis C, smoked cigarettes during pregnancy, had an opioid use disorder, and had serious mental illness in Delaware, 2010-2020



Implications of findings and future steps

During 2010-2020, 2,323 NAS cases in Delaware excluding 23 iatrogenic cases were identified with an overall rate of 20.9 (95%CI: 20.0-21.7) per 1,000 hospital live births. Alternatively, 1 in 50 newborns (~2.0%) in Delaware were diagnosed with NAS during 2010-2020. Although there was an increase in NAS rates between 2010 to 2014, the NAS rates declined by 29% between 2016 and 2020.

This research brief also adds to the previous research brief [15] by describing the relationship between maternal OUD and NAS using linked data. We estimated two measures of associations the ϕ coefficient (r_{ϕ}) and the tetrachoric correlation (r_{tc}) between maternal OUD and diagnosis of NAS. The r_{ϕ} was 0.56 and the r_{tc} was 0.89 indicating a strong association between OUD and NAS. While surveillance of NAS is limited due to use of administrative data sources such as the hospital discharge data and may miss mild cases of NAS withdrawal and may potentially misclassify it, this source is likely the best available source of data. Based on the expert panel's emphasis on clinical criteria of diagnosis for NAS/NOWS, it may be useful to examine differences in clinical diagnoses between different birthing facilities.

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Mission — Protect and Promote the Health of all People in Delaware

Vision — Healthy People in Healthy Communities

Core Values — Integrity—Respect—Participation—Accountability—Teamwork—Excellence

Division of Public Health
Family Health Systems Section
1351 W. North Street | Suite 103
Dover, DE 19904
Phone: 302-608-5735 | Fax: 302-608-5731
www.dhss.delaware.gov/dhss/dph

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