What is Neonatal Abstinence Syndrome (NAS)?

Neonatal abstinence syndrome (NAS) is withdrawal syndrome in newborns following birth and is primarily caused by maternal opiate use.[1] National Institute of Health (NIH) and Jansson et al. define NAS as a group of problems that occur in a newborn exposed to addictive illegal or prescription drugs while in the mother's womb (in utero-exposure).[2,3] Jansson et al. also note that a newborn's display of NAS varies and perhaps is influenced by factors that not only include licit and illicit exposures, but also maternal physiology, epigenetic modifications, and genetic predisposition. This syndrome is primarily associated with use of opiates during the prenatal period (antepartum): amphetamines, barbiturates, benzodiazepines: diazepam, clonazepam; cocaine, marijuana, opiates and/or narcotics: heroin, methadone, codeine/hydrocodone: vicodin or oxycodone (e.g., oxycontin). Other substances including alcohol have also been linked to this syndrome. Alcohol exposure during pregnancy and its impact on the fetus has been described by the umbrella term Fetal Alcohol Spectrum Disorders (FASD). However, this research brief does not focus on alcohol specifically, rather it examines NAS within the context defined above. Other drug exposures have been incorporated as a section to this brief.

Box 1

Neonatal Abstinence Syndrome (NAS) characteristics:

- 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), and failure to thrive

NAS infants are more likely to have adverse neonatal outcomes including low birthweight (LBW) — a major risk factor for infant mortality. Characteristics associated with NAS are summarized in box 1.

Assessment of Neonatal Abstinence Syndrome (NAS)

A typical mechanism for NAS assessment and evaluation is the Finnegan Scoring System and/or its variant to assess opioid-induced withdrawal. The objective is to quantify the severity of symptoms to determine the need intervention.[3] While this type of data is perhaps available at the individual hospital and/or clinic level, these are not typically reported at a population registry level such as Vital Records data and/or Hospital Discharge Data (HDD). To enumerate the case incidence of NAS at population level, HDD data for 2008 to 2013 time-period was utilized. Cases were identified based on the national incidence study by Patrick et al. for NAS using *International Classification of Diseases, Ninth Revision, Clinical Modification* (*ICD-9-CM*) code. The authors of this study utilized the Kid's Inpatient Database (KID) for newborns with NAS and utilized the Nationwide Inpatient Sample (NIS) to identify mothers.

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[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* May 2012; 307(18):1934-1940.
[2] 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.
[3] Jansson LM, Velez M. Neonatal abstinence syndrome. *Curr Opin Pediatr*. April 2012; 24(2):252-258.

How is Neonatal Abstinence Syndrome (NAS) determined in Arizona?

The identification of NAS cases was based on *ICD-9-CM* codes and the study by Patrick et al. using Hospital Discharge Data (HDD) for Arizona. The Arizona Department of Health Services (ADHS) collects hospital discharge records for inpatient and emergency department visits from all Arizona licensed hospitals. This collection is required by Arizona Revised Statute (A.R.S.) § 36-125-05, and Arizona Administrative Code Title 9, Chapter 11, Articles 4 and 5. The records are collected twice each year based upon patient discharge date, January 1 through June 30 discharges comprising the first data reporting and July 1 through December 31 comprising the second. Approximately 3 million discharge records are collected annually. ADHS requires and enforces accuracy and completeness in reporting. All Arizona licensed hospitals (i.e. regulated by the Arizona Department of Health Services), are required to report. However, hospitals such as Veteran's Administration, Department of Defense, and those located on tribal land are not included in the reporting.

Box 2

NAS: The number of newborns in Arizona during 2008-2012 with any underlying ***ICD-9-CM*** diagnosis code of 779.5 "drug withdrawal syndrome in a newborn."

Other substances including alcohol: The number of newborns in Arizona during 2008-2011 with any underlying ***ICD-9-CM*** diagnosis codes: 760.71 (Alcohol), 760.72 (Narcotics), and 760.75 (Cocaine).

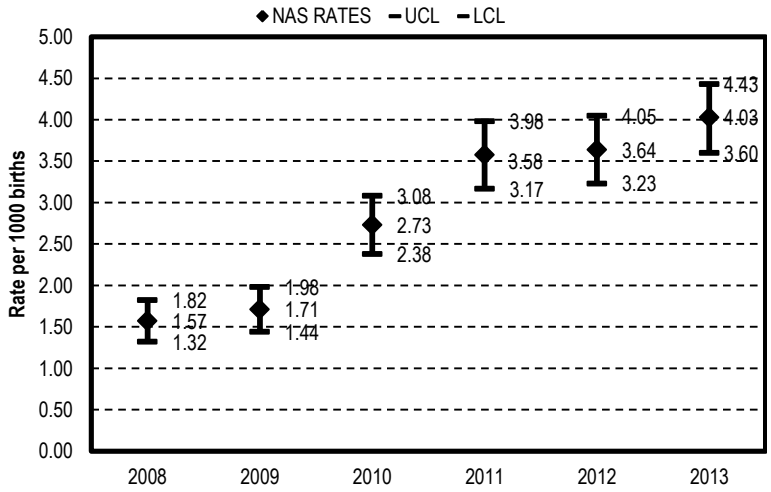
The description of case identification is given in Box 2. Neonatal Abstinence Syndrome rates for Arizona and other substance use related rate was estimated using the *ICD-9-CM* codes described in Box 2. For other conditions relating to alcohol and other substances, case identification was based upon *ICD-9-CM* "760 - Fetus or newborn affected by maternal conditions, which may be unrelated to present pregnancy."

Numerators are NAS case incidents and all reported births for the calendar year serve as denominators. Rates were expressed per 1000 births for any given year (e.g. denominators for 2008 comprised of all hospital births in 2008).

Neonatal Abstinence Syndrome (NAS) in Arizona

During 2008-2013 there were a total of 1,472 cases of NAS in Arizona. Figure 1 displays the NAS rates for 2008-2013 time-period. The overall NAS rate for Arizona during 2008-2013 was 2.83 (95% CI, 2.68- 2.97) per 1000 cases. It is evident that there was a significant increase (156%) in NAS rates in 2008 from 1.57 per 1000 births to 4.03 per 1000 births in 2013. The U.S. rate for the most recent data available for 2009 was

Figure 1. Neonatal Abstinence Syndrome Rates for 2008-2013 with 95% Confidence Intervals



3.39 per 1000 births. Table 1 compares the characteristics of newborns with NAS compare with all other hospital births by year.

Table 1. Characteristics of Newborns Diagnosed With Neonatal Abstinence Syndrome (NAS) in Arizona

Characteristics	Total (N = 520,564)	
	Neonatal Abstinence Syndrome (NAS) (N = 1,472)	All other hospital births in Arizona (N = 519,092)
Gender (Male)	807 (54.82%)	264,831 (51.02%)
Clinical conditions		
Low birth weight (<2500 grams)	264 (18%)	36,624 (7.06%)
Respiratory diagnoses	246 (16.71%)	25,288 (4.87%)
Seizures	20 (1.36%)	434 (0.08%)
Feeding difficulties	76 (5.16%)	5,901 (1.14%)
Insurance Status		
Medicaid	1,144 (77.72%)	274,502 (52.88%)
Private payers	198 (13.45%)	189,477 (36.5%)
Self-pay	54 (3.67%)	18,308 (3.53%)
Indian Health Services	20 (1.36%)	3,838 (0.74%)
Commercial Indemnity	26 (1.77%)	24,117 (4.65%)
Other	30 (2.04%)	8,850 (1.7%)
Race and Ethnicity		
American Indian or Alaskan Native	71 (4.82%)	19,300 (3.71%)
Asian	5 (0.34%)	13,039 (2.51%)
African American or Black	63 (4.28%)	19,906 (4.56%)
Hispanic or Latino	305 (20.72%)	202,813 (39.07%)
Native Hawaiian or Pacific Islander	2 (0.14%)	3,859 (0.74%)
White	1,007 (68.41%)	246,029 (47.4%)
Two or more races	1 (0.07%)	270 (0.05%)
Unknown/Refused	18 (1.22%)	9,496 (1.83%)
Median cost in dollars (IQR)	$31,070 ($61,295.5)	$2,518 ($1,859)
Median length of stay in days (IQR)	13 (21)	2 (2)

Some of the characteristics of the newborns diagnosed with NAS was consistent with Patrick et al.'s national study on NAS. For instance, percent males diagnosed with NAS (55%), percent low birthweight diagnosed with NAS (18%), percent on Medicaid diagnosed with NAS (77%), percent on private insurance diagnosed with NAS (15%) were similar to the most recent estimates available for the U.S.[4] There were

[4] See footnote 1 and table 1 of the article.

also differences in Arizona estimates and the U.S. estimates. For instance, Arizona's estimate for respiratory diagnoses was 17 percent compared to the U.S. (31%); Arizona's estimate for feeding difficulties was five percent compared to the U.S. (18%); and finally Arizona's estimate for seizures was approximately one percent compared to the U.S. (2.3%).

The median cost in dollars for a NAS stay was approximately $31,000 and the median length of stay in Arizona was 13 days, which is similar to the average length of stay in the U.S. (~16 days). The differences in some of the characteristics is perhaps related to geographic variability as well as variability in the quality of *ICD-9-CM* data coding.

Table 2 gives an overview of the five-year NAS case incidents by county with 95% confidence intervals (CI). Because these births are hospital births in Arizona, residency typically defined as mother's state of residence is difficult to establish and therefore a patient's county (i.e. newborn) is used for enumeration.

Table 2. Neonatal Abstinence Syndrome Case Incidents by County

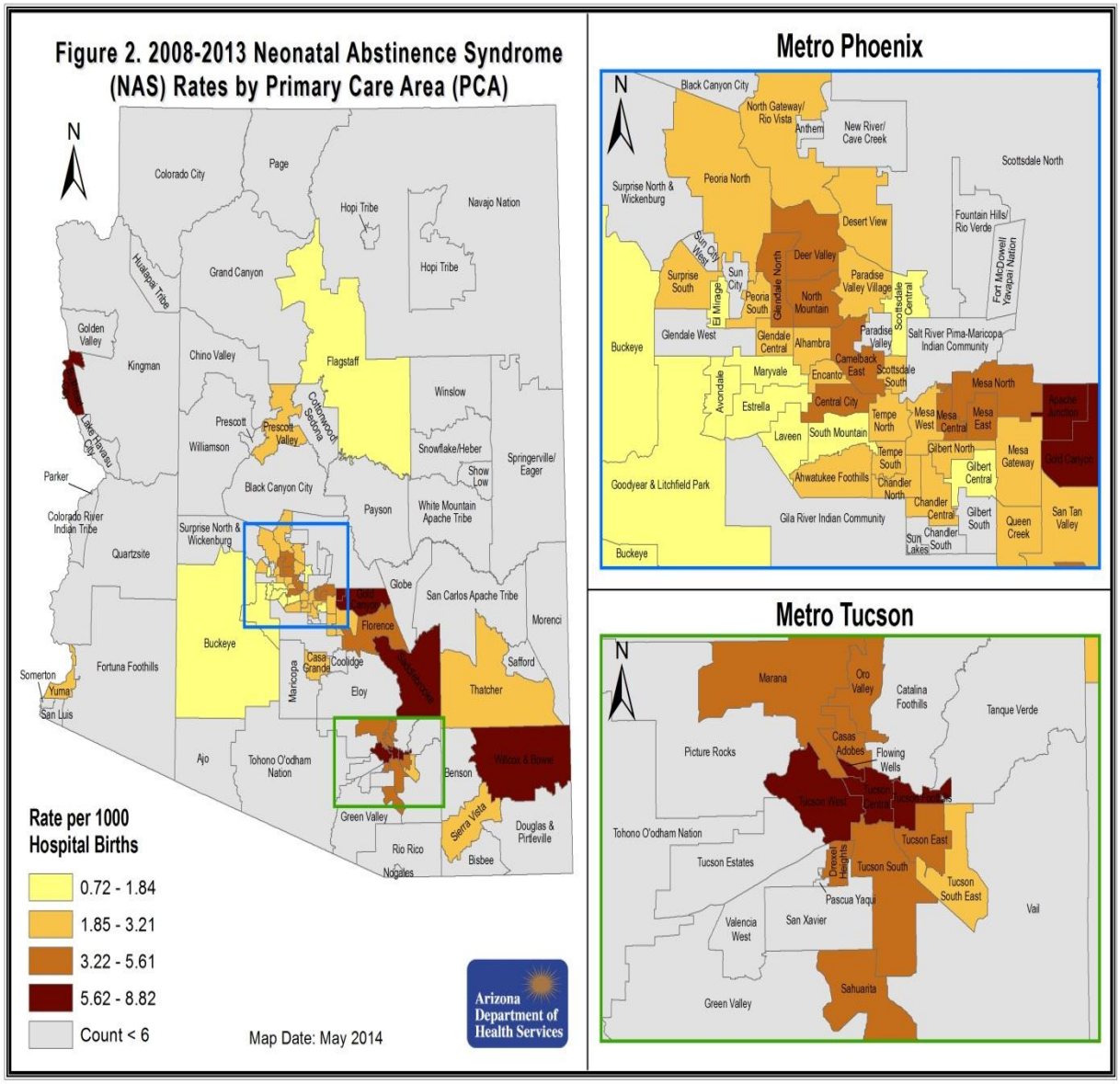
County	Neonatal Abstinence Syndrome (NAS) 2008-2013		
	Cases	Rates	95% CI
Apache County	2	1.32	0.16 - 4.77
Cochise County	26	2.58	1.69 - 3.78
Coconino County	8	0.93	0.4 - 1.83
Gila County	6	1.92	0.7 - 4.18
Graham County	13	3.11	1.65 - 5.31
Greenlee County	1	1.40	0.04 - 7.79
La Paz County	0	0.00	0 - 3.15
Maricopa County	843	2.56	2.39 - 2.73
Mohave County	39	3.65	2.5 - 4.79
Navajo County	10	1.35	0.65 - 2.49
Pima County	371	5.08	4.56 - 5.59
Pinal County	84	2.83	2.23 - 3.44
Santa Cruz County	2	0.47	0.06 - 1.69
Yavapai County	19	1.72	1.04 - 2.69
Yuma County	38	1.89	1.29 - 2.49
Unknown	10		
Border region[§]	437	4.06	3.68 - 4.44
Non-border region	1025	2.51	2.36 - 2.67
Total	**1,472**	**2.83**	**2.68 - 2.97**

[§]Border region is defined as counties bordering U.S. Mexico southern border as per U.S. Mexico Border Region Commission and comprises Cochise, Pima, Santa Cruz, and Yuma.

[¶]Rates are per 1000 hospital births in Arizona during 2008-2012. Rates based on numerators (i.e. case incidents) of less than 10 use Poisson distribution and should be interpreted cautiously.

The overall state rate for neonatal abstinence syndrome during 2008-2013 was 2.83 per 1000 births. Maricopa county had a significantly lower NAS rate (2.56 per 1000 births) compared to the state, and Pima county had a significantly higher NAS rate (5.06 per 1000 births) compared to the state. Border region had significantly higher NAS rates (4.06 per 1000 births) compared to the non-border region (2.51 per 1000 births) and the state rate.

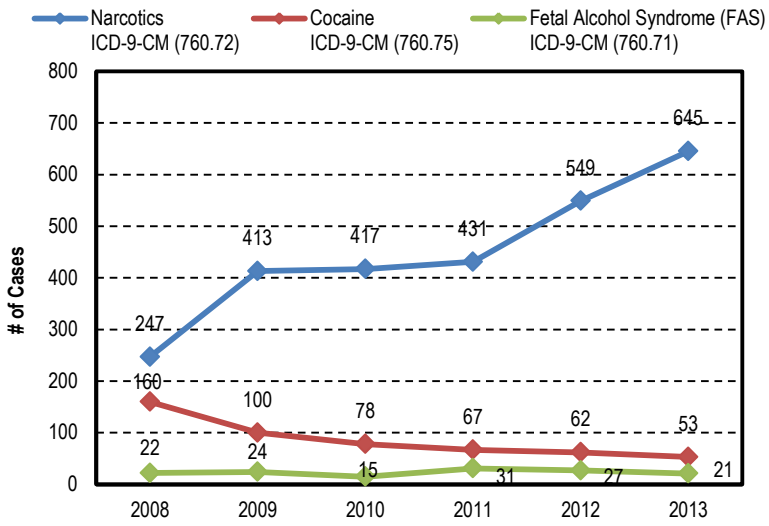
Figure 2 below displays NAS rates by primary care areas (PCAs)[5] for 2008-2013 time-period.



[5] A Primary Care Area (PCA) is a geographic area in which most residents seek primary health services from the same place(s). The PCA is meant to depict the "primary care service seeking patterns" of the residents. Based on the 2010 Census Data, Arizona has 126 PCAs.

Narcotics, Cocaine, and Alcohol Exposures in Arizona Newborns

Figure 3. Number of Arizona Newborns with Drug Exposure, 2008-2013



Other substances including narcotics, cocaine, and alcohol in newborns were estimated using the same criteria described in Box 2. Figure 3 displays the case incidents by year for these substances. There were a total of 2,702 cases of newborns diagnosed with narcotics during 2008-2013; 520 cases of newborns diagnosed with cocaine; and 140 cases of newborns diagnosed with alcohol also referred to as Fetal Alcohol Syndrome (FAS) during 2008-2013. In total, there were 3,239 newborns identified during 2008-2013 with presence of either narcotics, cocaine, and/or alcohol (FAS) in Arizona hospital births. Table 3 shows the rates for narcotics, cocaine, and FAS during 2008-2013 with 95% CI.

Table 3. Rates of Narcotics, Cocaine, and FAS in Arizona Newborns during 2008-2013

Year	Substance (Rates per 1000 births)[¶]		
	Narcotics[†]	Cocaine[‡]	FAS[φ]
2008	2.56 (2.24 - 2.88)	1.66 (1.4 - 1.91)	0.23 (0.14 - 0.34)
2009	4.59 (4.15 - 5.04)	1.11 (0.89 - 1.33)	0.27 (0.17 - 0.4)
2010	4.91 (4.44 - 5.38)	0.92 (0.71 - 1.12)	0.18 (0.1 - 0.29)
2011	5.21 (4.71 - 5.70)	0.81 (0.62 - 1.00)	0.37 (0.24 - 0.51)
2012	6.55 (6.00 - 7.10)	0.74 (0.56 - 0.92)	0.32 (0.21 - 0.47)
2013	7.81 (7.20 - 8.41)	0.64 (0.47 - 0.81)	0.25 (0.16 - 0.39)
2008-2013	5.19 (4.99 - 5.39)	1.00 (0.91 - 1.08)	0.27 (0.22 - 0.31)
% Change (2012 to 2013)	**19%**	**-14%**	**-22%**
% Change (2008 to 2013)	**205%**	**-61%**	**9%**

[¶]Rates are per 1000 hospital births in Arizona during 2008-2013. Annual rates based on numerators (i.e. case incidents) of less than 20 are not stable and reliable. Poisson distribution was used to calculate 95% CI for cases less than 30.

[†]Narcotics diagnosis in newborns are reported using ICD-9-CM 760.72.

[‡]Cocaine diagnosis in newborns are reported using ICD-9-CM 760.75.

[φ]Fetal Alcohol Syndrome (FAS) is presence of alcohol in newborns, and are reported using ICD-9-CM codes 760.71.

The overall rate for narcotics during 2008-2013 was 5.19 (95% CI, 4.99 – 5.39) per 1000 hospital births. There was a 19 percent increase in the rate from 2012 and there was a 205 percent increase in this rate from 2008. Similarly, the overall rate for cocaine was 1.00 (95% CI, 0.91 – 1.08) per 1000 births. The cocaine rate declined by 14 percent from 2012 and there was a 61 percent decline in cocaine rate from 2008. With regards to Fetal Alcohol Syndrome (FAS), the overall rate during 2008-2013 was 0.27 (95% CI, 0.22 – 0.31) per 1000 births. There was a 22 percent decline in FAS rate from 2012; however, FAS rate increased nine percent from 2008.

Table 4 presents the total case incidents of drug exposures to Arizona newborns by county during 2008-2013 with 95% CI. Maricopa and Pima county accounted for 75 percent of the total cases relating to narcotic exposure, 90 percent cocaine exposure in newborns, and approximately 60 percent of the cases of Fetal Alcohol Syndrome.

Table 4. Arizona Newborns with Drug Exposures by County, 2008-2013

County	Type of Drug Exposure during 2008-2013 (Rates per 1000 birth)[¶]					
	Narcotics (N = 2,702)[†]		Cocaine (N = 520)[‡]		FAS (N = 140)[φ]	
	Counts	Rates	Counts	Rates	Counts	Rates
Apache County	15	9.9 (5.54 - 16.33)	1	0.66 (0.02 - 3.68)	3	1.98 (0.41 - 5.79)
Cochise County	29	2.88 (1.93 - 4.13)	6	0.6 (0.22 - 1.3)	4	0.4 (0.11 - 1.02)
Coconino County	25	2.9 (1.88 - 4.29)	0	0 (0 - 0.43)	8	0.93 (0.4 - 1.83)
Gila County	23	7.36 (4.67 - 11.05)	0	0 (0 - 1.18)	1	0.32 (0.01 - 1.78)
Graham County	30	7.17 (4.84 - 10.24)	0	0 (0 - 0.88)	1	0.24 (0.01 - 1.33)
Greenlee County	5	6.99 (2.27 - 16.32)	0	0 (0 - 5.16)	0	0 (0 - 5.16)
La Paz County	22	18.79 (11.77 - 28.44)	0	0 (0 - 3.15)	1	0.85 (0.02 - 4.76)
Maricopa County	1,757	5.33 (5.08 - 5.58)	295	0.9 (0.79 - 1)	61	0.19 (0.14 - 0.23)
Mohave County	77	7.2 (5.59 - 8.8)	1	0.09 (0 - 0.52)	1	0.09 (0 - 0.52)
Navajo County	59	7.97 (5.94 - 10.01)	7	0.95 (0.38 - 1.95)	25	3.38 (2.19 - 4.99)
Pima County	272	3.72 (3.28 - 4.16)	177	2.42 (2.06 - 2.78)	21	0.29 (0.18 - 0.44)
Pinal County	246	8.3 (7.26 - 9.33)	24	0.81 (0.52 - 1.2)	8	0.27 (0.12 - 0.53)
Santa Cruz County	1	0.23 (0.01 - 1.3)	1	0.23 (0.01 - 1.3)	1	0.23 (0.01 - 1.3)
Yavapai County	35	3.17 (2.12 - 4.22)	1	0.09 (0 - 0.51)	0	0 (0 - 0.33)
Yuma County	60	2.98 (2.22 - 3.73)	3	0.15 (0.03 - 0.44)	1	0.05 (0 - 0.28)
Unknown	46		4		4	
Border region[§]	362	3.36 (3.02 - 3.71)	187	1.74 (1.49 - 1.99)	27	0.25 (0.17 - 0.37)
Non-border region	2,294	5.63 (5.4 - 5.86)	329	0.81 (0.72 - 0.89)	109	0.27 (0.22 - 0.32)
Total	**2,702**	**5.19 (4.99 - 5.39)**	**520**	**1.00 (0.91 - 1.08)**	**140**	**0.27 (0.22 - 0.31)**

[¶]Rates are per 1000 hospital births in Arizona during 2008-2013. Annual rates based on numerators (i.e. case incidents) of less than 20 are not stable and reliable. Poisson distribution was used to calculate 95% CI for cases less than 30.

[§]Border region is defined as counties bordering U.S. Mexico southern border as per U.S. Mexico Border Region Commission and comprises Cochise, Pima, Santa Cruz, and Yuma.

[†]Narcotics diagnosis in newborns are reported using *ICD-9-CM* 760.72

[‡]Cocaine diagnosis in newborns are reported using *ICD-9-CM* 760.75

[φ]Fetal Alcohol Syndrome (FAS) is presence of alcohol in newborns, and are reported using *ICD-9-CM* codes 760.71

Pinal county accounted for approximately nine percent of the cases relating to narcotic exposure and four percent of the cases relating to cocaine exposure in newborns. Narcotic exposure was higher (5.6 per 1000 births) in non-border regions compared to the overall state rate (5.2 per 1000 births). In contrast, cocaine exposure (1.7 per 1000 births) was higher in border regions compared to the overall state rate.

Figure 4 examines Arizona newborns exposed to all drugs including alcohol (i.e. narcotics, cocaine, and alcohol) by primary care areas (PCA).

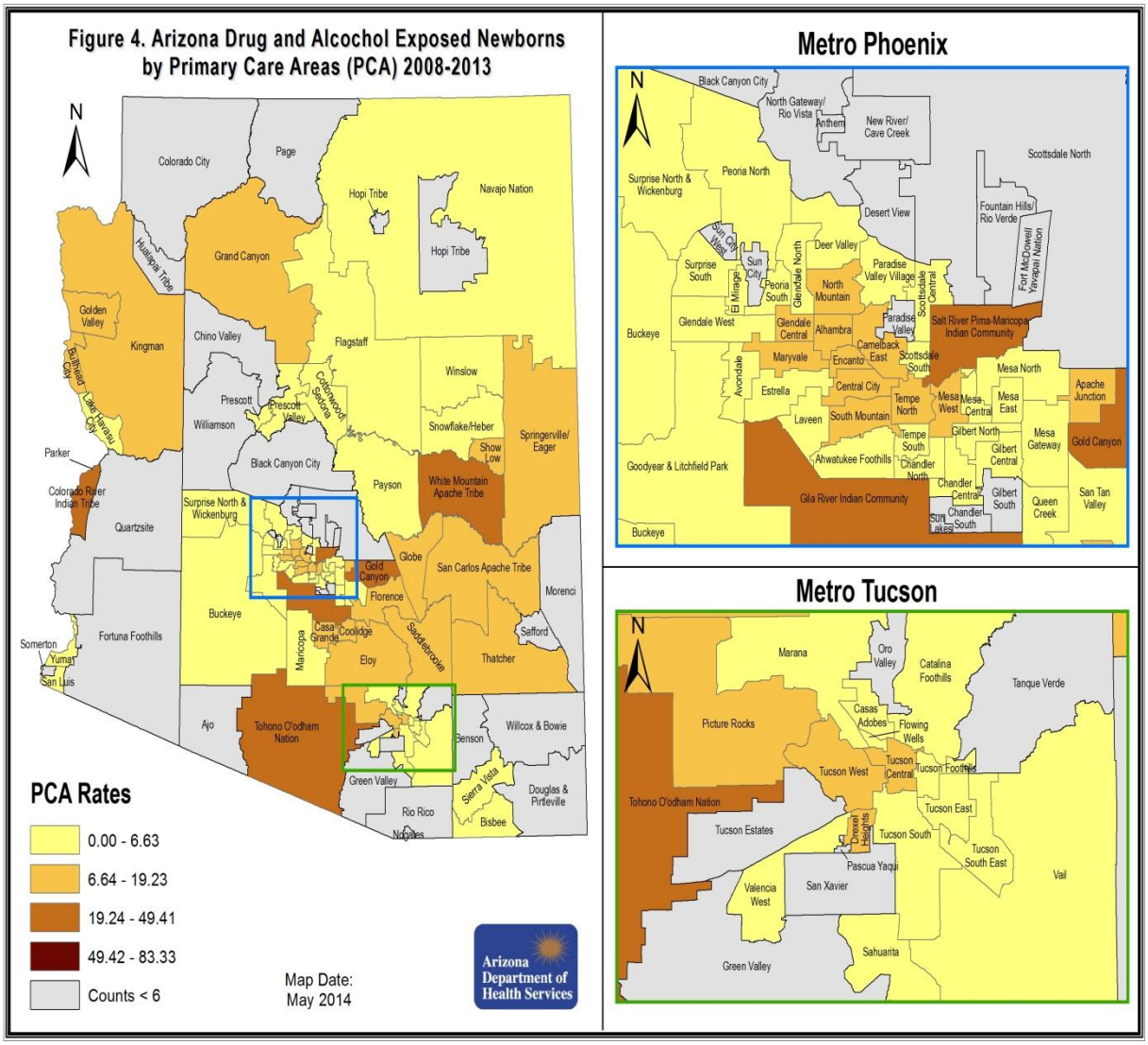


Table 5 on the following page displays the characteristics of Arizona newborns exposed to all drugs (i.e. substances including narcotics, cocaine, and alcohol) with all other hospital births during 2008-2013 time-periods. Because there are no other statistics available nationally that look at all the drug exposures combined, these estimates are specific to Arizona. For instance, newborns exposed to all drugs had higher incidence of low birthweight newborns (23.18%) compared to all other hospital births (7.02%), had higher incidence of respiratory symptoms (14.42%), had higher incidence of feeding difficulties (4.04%), were more likely to be paid for by Medicaid (75.52%). The median cost for total charges was twice high as compared to other hospital births.

Table 5. Characteristics of Arizona Newborns Exposed to All Drugs

Characteristics	Total (N = 520,564)	
	All Drug Exposures (N = 3,239)	All other hospital births in Arizona (N = 517,325)
Gender (Male)	1,688 (52.11%)	264,359 (51.02%)
Clinical conditions		
Low birth weight (<2500 grams)	747 (23.18%)	36,347 (7.02%)
Respiratory diagnoses	467 (14.42%)	25,274 (4.88%)
Seizures	17 (0.52%)	442 (0.09%)
Feeding difficulties	131 (4.04%)	5,964 (1.15%)
Insurance Status		
Medicaid	2,446 (75.52%)	273,563 (52.8%)
Private payers	263 (8.12%)	189,737 (36.62%)
Self-pay	292 (9.02%)	18,098 (3.49%)
Indian Health Services	185 (5.71%)	3,683 (0.71%)
Commercial Indemnity	19 (0.59%)	24,155 (4.66%)
Other	34 (1.05%)	8,865 (1.71%)
Race and Ethnicity		
American Indian or Alaskan Native	402 (12.41%)	18,984 (3.66%)
Asian	8 (0.25%)	13,043 (2.52%)
African American or Black	293 (9.05%)	24,007 (4.63%)
Hispanic or Latino	922 (28.47%)	202,503 (39.09%)
Native Hawaiian or Pacific Islander	17 (0.52%)	3,844 (0.74%)
White	1,545 (47.7%)	245,623 (47.4%)
Two or more races	1 (0.03%)	257 (0.05%)
Unknown/Refused	51 (1.58%)	9491 (1.83%)
Median cost in dollars (IQR)	$4,932 ($11,394)	$2,514 ($1,857)
Median length of stay in days (IQR)	3 (4)	2 (2)

Implications of findings and future steps

One of the major findings of this brief is that there has been an increase in the number of NAS cases as well as other drug exposures. During the six-year time frame (i.e. 2008-2013), a total of 1,472 newborns in Arizona had NAS, and 3,239 newborns were exposed to either narcotics, cocaine, and/or alcohol.

Newborns in Arizona with neonatal abstinence syndrome were three times more likely to be low birthweight compared to those without NAS (i.e. COR 2.87, 95% CI, 2.51 – 3.28); were four times more likely to have respiratory symptoms to those without NAS (i.e. COR 3.90, 95% CI, 3.40 – 4.47); were 17 times more likely to have seizures to those without NAS (i.e. COR 17.08, 95% CI, 11.00 – 26.55); and were five times more likely to have feeding difficulties compared to those without NAS (i.e. COR 4.70, 95% CI, 3.73 – 5.90).

In terms of financial burden, the median cost of a NAS newborn was approximately $31,000 with a median length of stay of 13 days compared to a non-NAS newborn with a median cost of approximately $2,500 with a median length of stay of two days. While this brief highlights the importance of drug exposure in Arizona newborns, it is difficult to estimate the 'true incidence' due to variability in reporting. To adequately capture the incidence, an active surveillance for drug exposed infants is needed that can be supplemented with other administrative data such as vital records, birth defects registry that will enable a better understanding of the epidemiological risks of drug exposures in newborns. Nonetheless, this is the first research brief for Arizona that has captured in detail the incidences of newborns exposures to drugs.

Suggested citation: Hussaini SK. Neonatal Abstinence Syndrome: 2008-2013 Overview. *Research Brief,* 2014.