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Assessment of risk factors for Neonatal Abstinence Syndrome (NAS) using a Standardized Surveillance Case Definition in Clark County, NV

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ABSTRACT

Background: Neonatal Abstinence Syndrome (NAS) is a withdrawal syndrome in neonates that can occur due to drug exposure during pregnancy. This study had two objectives: (1) Assess the implementation of the Council of State and Territorial Epidemiologists (CSTE) Tier 2 case definition for NAS surveillance in Clark County, Nevada and (2) Identify risk factors for NAS.
Subjects and Method: This study utilized hospital discharge data. Claim-based records from non-federal acute care hospitals located in Clark County during 2016-2022 were analyzed. All newborn inpatient discharge records from January 1, 2016 to September 30, 2022 in Clark County, Nevada were selected. *ICD-10-CM* codes were utilized based on the CSTE Tier 2 case definition. Any neonate record that met the case definition, including any record with the diagnosis code P96.1, was considered a NAS confirmed case. Codes for suspect cases, maternal history of substance use, unspecified maternal medication, and transmitted noxious-substances were also assessed. A multiple logistic regression model using backward stepwise selection was developed to find risk factors related to NAS-confirmed births.
Results: In Clark County, Nevada, the NAS incidence rate from January 2016 to September 2022 was 7.4 per 1,000 births. In 2022 alone, the rate of NAS was 8.9 per 1,000 births. Estimated rates of NAS were highest among neonates who were White at 13 per 1,000 births. Hospital J, the largest academic medical center in Southern Nevada, had the highest NAS confirmed case rate at 11.3 per 1000 newborn hospitalizations. Results from the multiple logistic regression model showed the odds of being born with NAS among neonates who identified as White were 5.0 (OR=5.17; 95% CI= 4.29 to 6.24; p <0.001) times more likely to have NAS compared to the Hispanic group.
Conclusion: Given that 2022 had the highest rate of confirmed NAS cases there is a need to collect substance and diagnosis-specific data about prenatal substance use to identify unmet service care and disparities.

Keywords: neonatal abstinence syndrome, opioids, substance dependence.

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BACKGROUND

The opioid epidemic continues to be a significant public health concern. Many societal and economic factors have impacted the severity of the epidemic. Two important causes are: (1) The increase in opioid prescriptions and (2) access and decreased price point of heroin and other synthetic opioids (Volkow et al., 2021). Consequently, the number of women with opioid-related diagnoses documented at delivery increased by 131% from 2010-2017 (Hirai et al., 2021). As a result, infants born with Neonatal Abstinence Syndrome (NAS) have been a growing concern.

NAS results from chronic in-utero exposure of the neonate to certain drugs or substances. Cessation at birth results in withdrawal symptoms such as irritability, tremors, sweating, and more (Weller et al., 2021). Opioid use disorder (OUD) has been seen to be a leading cause of NAS. However, NAS can also result from synthetic and semi-synthetic opioids like methadone and buprenorphine, which have been the standard for opioid addiction (medication-assisted therapy or MAT) during pregnancy (Anbalagan et al., 2023). The term NAS has also been intermittently exchangeable with Neonatal Opioid Withdrawal Syndrome (NOWS), a recent term for neonates born with confirmed maternal opioid use (Weller et al., 2021). Infants born to mothers with polysubstance use are more commonly referred as NAS cases (Weller et al., 2021). Opioid-exposed infants may also be at an increased mortality risk (Leyenaar et al., 2021). For purposes of this paper referral will utilize NAS due to the definition adderssing polysubstance use. From 2016-2018, the state of Nevada had a NAS incidence rate of 8.0 per 1000 births with Clark County specifically having an incidence rate of 8.2 per 1000 births (Batra et al., 2021). The population of Clark County accounts for roughly 70% of the state's total population, standing approximately at 2.3 million.

In a repeated cross-sectional analysis including 11.8 million hospitalizations from 47 states and the District of Columbia, the national estimated rate of NAS was 7.3 per 1000 births and the rate of maternal opioid-related diagnoses was 8.2 per births in 2017 (Hirai et al., 2021). From 2010 to 2017, estimated rates significantly increased nationally and some states, with a substantial state-level variation (Hirai et al., 2021). Both studies utilized ICD codes for neonatal withdrawal symptoms from maternal use of drugs of addiction in determining cases. The cost associated with NAS is also substantial. A study in 2016 noted that the average cost per infant with NAS was $22,552 (Strahan et al., 2020). NAS rates were highest among Medicaid-covered births (12.3 per 1000) and those without insurance (7.0 per 1000) (Strahan et al., 2020). Total costs were highest for births covered by Medicaid ($477.0 million) (Strahan et al., 2020). Therefore, the need for surveillance of NAS and intervention is necessary from both medical and financial standpoints.

In efforts for standardization of surveillance practice, the Council of State and Territorial Epidemiologists (CSTE) released a position statement for the proposition of a uniform case definition for NAS (CSTE, 2019). This definition is currently in revision, but multiple states have begun piloting the case definition procedures in their surveillance systems. The definition is divided into two tiers of classification. Tier 1 focuses on real time case reporting based on public health legal authority (i.e., clinicians, health care settings, clinical records) and Tier 2 is case reporting based on claims-based administrative data (e.g., identified from Medicaid, all payer claims, hospital discharge) (CSTE, 2019). This surveillance analysis used the CSTE NAS case definition Tier 2 to

analyze the rate of NAS in Clark County, Nevada.

SUBJECTS AND METHOD

1. Study Design

This study is a retrospective observational study design using hospital discharge data. Claim-based records from non-federal acute care hospitals located in Clark County, Nevada during 2016-2022 were analyzed.

2. Population and Sample

This study utilized hospital claim-based data from the Center for Health Information Analysis for Nevada (CHIA), which is contracted by the Nevada Department of Health and Human Services (DHHS) to collect billing records from hospital inpatient, outpatient, and ambulatory surgical centers Click or tap here to enter text. Non-federal, acute care, hospital centers in Clark County, NV were analyzed.

The sample selection included all newborn hospital (inpatient) discharge records from Clark County, Nevada, from January 1, 2016, to September 30, 2022. *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM) codes were utilized based on the CSTE Tier 2 case definition (CSTE, 2019). Any neonate record with the ICD-10-CM code P96.1 was seen as NAS confirmed. Suspected NAS cases were classified as any neonate record with ICD-10-CM codes P04.14, P04.17, or P04.1A. Suspect cases involve neonates expressing no clinical symptoms of withdrawal but had a documented maternal history of substance use. NAS cases were classified as unspecified when maternal medications or drug use indicated in-utero exposure but substance was unknown. These ICD-10-CM codes may have been used to capture polysubstance use of opioids or medical-assisted treatment with opioids, which are not defined in ICD-10 in-utero exposure code (Bauer et al., 2021). NAS unspecified ICD-10-CM codes P04.1, P04.18, P04.19, P04.40, P04.49 were used to assess newborns affected by unspecified maternal medication or drugs. Hospital admission year, birth hospital, length of stay, urban/rural status, ethnicity, insurance, and gender were also included in the analysis. Additionally, the following NAS unspecified ICD-10-CM codes were also explored based on CSTE recommendation: P04.11, P04.12 P04.13, P04.15, P04.16, P04.2, P04.41, P04.42, P04.5, P04.6, P04.81, and P04.89. All missing data was excluded (Appendix A).

3. Study Variables

The dependent variable was NAS-confirmed case. The independent variables were hospital admission year, birth hospital, length of stay, urban/ rural status, race/ ethnicity, payer status (insurance), and gender.

4. Operational Definition of Variables

NAS-confirmed cases were coded into binary variables with presence (NAS=1) and absence (NAS=0) to identify factors between NAS and non-NAS births.

Rural/urban status was defined using the 2010 Rural-Urban Commuting Area (RUCA) codes from the Economic Research Service of the U.S. Department of Agriculture Click or tap here to enter text. Data was obtained from the 2010 decennial census and the 2006-2010 American Community Survey (ACS). RUCA codes are based on the theoretical concepts used by the Office of Management and Budget (OMB) to define county-level metropolitan and micropolitan areas Click or tap here to enter text.. The coding classification system ranges from 1-10 with 1 representing areas with high commuting (urban) and 10 representing low commuting areas (rural). NAS confirmed cases were separated by ZIP code and were labeled according to their RUCA status.

Payer systems were also separated by public, private and uninsured Click or tap here to enter text. Medicare, CHAMPUS or

CHAMPVA, Nevada Medicaid, Other Medicaid, HMO, Medicare HMO, and Nevada Medicaid HMO were all categorized as public insurance. Commercial Insurer, Negotiated Discounts (e.g., PPO) were categorized as private insurers. Charity, self-pay, miscellaneous, unknown, and not provided were categorized as uninsured.

Hospital facilities were also categorized by teaching and non-teaching institutions distinguished by CHIA's data dictionary. Teaching hospitals partner with medical schools, nursing schools, and other education programs to facilitate training and research to students.

Length of stay was calculated by the difference of discharge and admit date.

5. Study Instruments

This study utilized hospital claim-based data from the Center for Health Information Analysis for Nevada (CHIA), which is contracted by the Nevada Department of Health and Human Services (DHHS) to collect billing records from hospital inpatient, outpatient, and ambulatory surgical centers Click or tap here to enter text. Electronic medical records were also reviewed during the exploratory study.

5. Data analysis

An unweighted multiple logistic regression model using backward stepwise selection was formed to find potential predictors related to NAS-confirmed births. NAS-confirmed cases were coded into binary variables with presence (NAS=1) and absence (NAS=0) to identify factors between NAS and non-NAS births. Factors analyzed were rural/ urban status, payer system, hospital facility, race/ ethnicity, and gender. Descriptive and logistic regression statistics were performed. All statistical procedures utilized the SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA). All variables were binary coded for analysis. All missing data was removed.

6. Research Ethics

Given the absence of an Institutional Review Board (IRB) at the Southern Nevada Health District, ethical oversight was ensured through the completion of HIPAA trainings by all research staff involved in the project. Additionally, this study exclusively utilizes secondary data.

The Southern Nevada Health District has an agreement with CHIA to utilize data. The Disease Surveillance Team was also aware of medical record exploration and subjects were de-identified.

A short explorative review was also conducted with a Disease Data Collection Specialist (DDCS) at SNHD. This explorative review used the CSTE Tier 1 Case definition in confirming NAS confirmed cases (i.e., utilizing patient records to determine if the Tier 1 definition was in concordance with Tier 2). Records for all ICD-10-CM P96.1 NAS confirmed infants were collapsed into one document and subjects were randomly selected for review. Based on availability of hospital records, neonate subjects were continuously, randomly selected until 12 records had enough data to analyze. Maternal records were also analyzed if linked to neonate cases. Cases that met NAS confirmed Tier 1 definition used Table VII from the Neonatal Abstinence Syndrome Standardize Case Definition.

RESULTS

1. Sample Characteristics

The study population comprised of 167,118 newborns discharged from 16 Clark County hospitals from January 1, 2016, to September 30, 2022. Of these, 1,237 neonates were NAS confirmed based on ICD-10-CM coding of P96.1 within 10 of the 16 hospitals. Making the overall NAS incidence rate 7.4 per 1000 hospital births. Hospital J, the largest academic medical center in Southern Nevada, had the highest NAS confirmed

case rate at 11.3 per 1000 newborn hospitalizations. The majority of NAS confirmed cases were classified as metropolitan area core urban status. Out of the additional NAS unspecified ICD-10-CM codes, maternal noxious substance unspecified, maternal cannabis use, and maternal tobacco use all ranged between 30 to 40 occurrences of NAS cases. The mean length of stay was also higher for neonates diagnosed with NAS staying in the hospital for an average of 18 days compared to non-NAS diagnosed neonates only at 4 days. Infants who were White had the highest NAS rate (13.0 per 1000 births) compared to other ethnicities. Infant's ethnicity identified as Native American or Alaskan Native, Asian, Black, and Hispanic had NAS rates 9.3, 2.2, 6.4, and 3.1 per 1000 births respectively (Appendix B). There was no significant difference in NAS rates by birth gender.

Multiple Logistic Regression Analysis

An unweighted multiple logistic regression model using backward stepwise selection was used to find potential predictors related to NAS-confirmed births. The final model of the multiple logistic regression included ethnicity, private and public insurance payer, gender, and teaching hospitals. Based on this model, White neonates were 5 times the odds to have NAS compared to the Hispanic neonates (OR=5.17; 95% CI= 4.29 to 6.24; p <0.001). In addition, family of infants with public insurance were 2.2 times more likely to have of NAS (OR=2.20; 95% CI= 4.29 to 6.24; p <0.001) compared to those who had private insurance. Patients at teaching hospitals also had increased odds of NAS with an OR of 1.9 compared to those who delivered at non-teaching hospitals (OR=1.88; 95% CI= 1.63 to 2.19; p<0.001) (Appendix B).

Exploratory Review Analysis

Regarding the exploratory review, a large proportion of patient records had no data. Only certain hospital systems had full patient records due to reasons unknown. This explorative review utilized patient records to determine if the Tier 1 definition was in concordance with Tier 2 definition. The exploratory review included 12 patient records with documented NAS data. Of the patient records that had documented NAS data, 50% of the criteria were present. All except one of the patient records documented displayed neonate lab results and 42% of the patient records documented symptoms at delivery and stay. However, some patient charts only had laboratory results with no provider notes. A few had "other congenital difficulties" listed in discharge notes but used the NAS confirmed ICD-10-CM diagnosis code P96.1 even when NAS was not noted. One third of the medical charts also utilized the Finnegan NAS scaling chart; however, exact symptoms were not always listed. Overall, 12 subjects' charts were analyzed with roughly 1/3 meeting qualifications of NAS based on CSTE Tier 1 definition.

Table 1. ICD-10-CM Utilized for use of Neonatal Abstinence/ NAS Surveillance (Appendix A)

ICD-10-CM Utilized for use of Neonatal Abstinence/NAS Surveillance	
Confirmed Case	
P96.1	Neonatal withdrawal symptoms from maternal use of drugs of addiction
Suspect Case	
P04.14	Newborn affected by maternal use of opiates
P04.17	Newborn affected by maternal use of sedative hypnotics
P04.1A	Newborn affected by maternal use of anxiolytics
Unspecified newborn affected by maternal medication/drug use codes	
P04.1	Newborn affected by other maternal medication

ICD-10-CM Utilized for use of Neonatal Abstinence/NAS Surveillance	
P04.11	Newborn affected by maternal antineoplastic chemotherapy
P04.12	Newborn affected by maternal cytotoxic drugs
P04.13	Newborn affected by maternal use of anticonvulsants
P04.15	Newborn affected by maternal use of antidepressants
P04.16	Newborn affected by maternal use of amphetamines
P04.18	Newborn affected by other maternal medication
P04.19	Newborn affected by maternal use of unspecified medication
P04.2	Newborn affected by maternal use of tobacco
P04.3	Newborn affected by maternal use of alcohol
P04.40	Newborn affected by maternal use of unspecified drugs of addiction
P04.41	Newborn affected by maternal use of cocaine
P04.42	Newborn affected by maternal use of hallucinogens
P04.49	Newborn affected by maternal use of other drugs of addiction
P04.5	Newborn affected by maternal use of nutritional chemical substances
P04.6	Newborn affected by maternal exposure to environmental chemical substances
P04.81	Newborn affected by maternal use of cannabis
P04.89	Newborn affected by other maternal noxious substances
P04.9	Newborn affected by maternal noxious substance, unspecified

Source: Neonatal Abstinence Syndrome Case Definition, Council of State and Territorial Epidemiologists, 2019

Table 2. NAS-Confirmed rate from January 2016 to September 2022 per 1,000 hospital births (Appendix B)

Birth Year	Number of Hospital Visits	Rate per 1,000 births
2016	228	8.7
2017	195	7.6
2018	202	7.9
2019	147	5.9
2020	148	6.2
2021	165	6.9
2022	152	8.9
Total	1237	7.4

Source: Hospital Discharge Data, Center for Health Information Analysis for Nevada, Southern Nevada Health District, 2016-2022

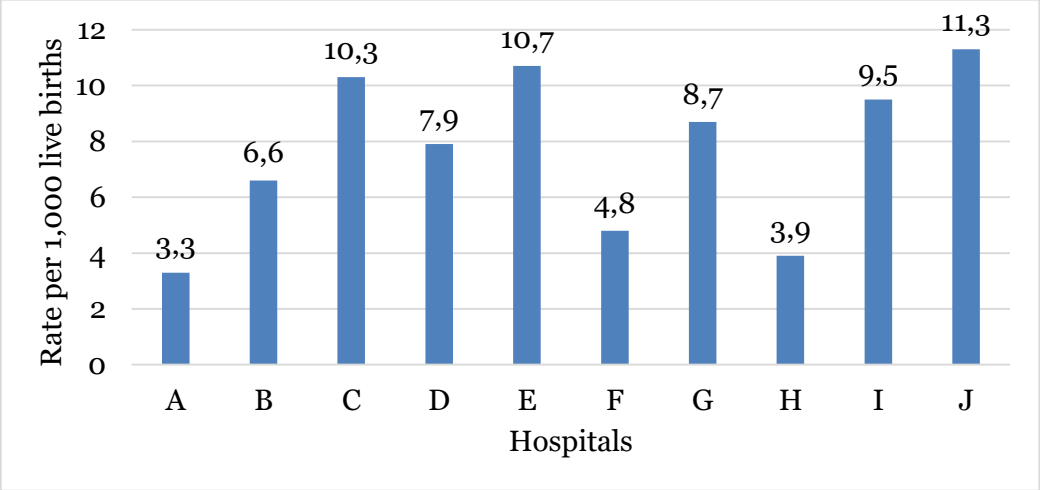

Figure 1. The NAS hospital-visits rate in non-federal acute care hospitals in Clark County, NV from 2016-2022

Source: Hospital Discharge Data, Center for Health Information Analysis for Nevada, Southern Nevada Health District, 2016-2022

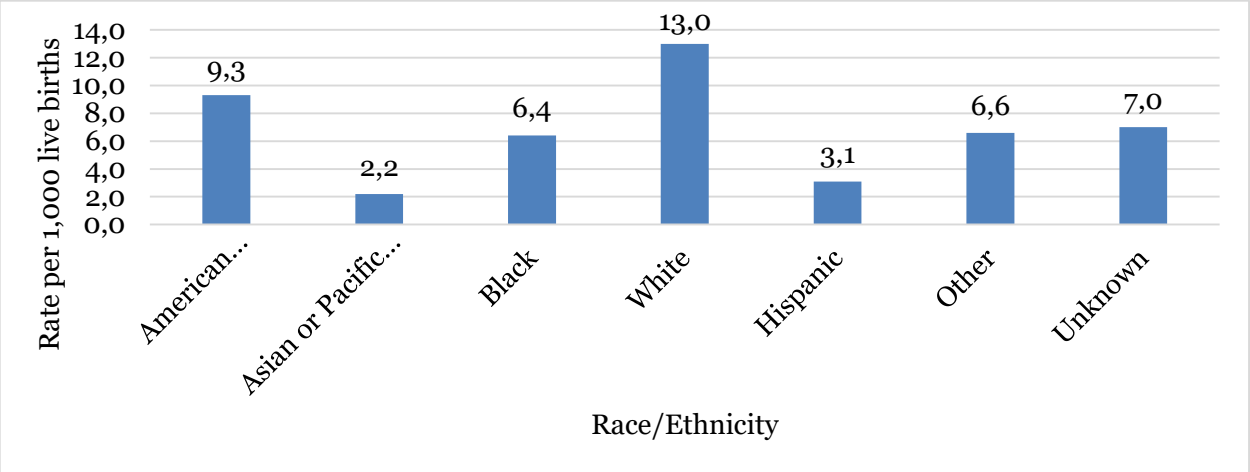

Figure 2. The NAS-Confirmed rate by Race/Ethnicity in Clark County, NV from January 2016 to September 2022 per 1,000 hospital births

Source: Hospital Discharge Data, Center for Health Information Analysis for Nevada, Southern Nevada Health District, 2016-2022

Table 3. Results of the multiple logistic models assessing risk factors for NAS in Clark County, NV

Independent Variables	OR	95% CI		p
		Lower limit	Upper limit	
Ethnicity				
Hispanic	ref	ref	ref	ref
Asian or Pacific Islander	0.15	0.61	1.34	<0.001
Black	2.16	1.73	2.69	0.011
White	5.17	4.29	6.24	<0.001
Other[a]	2.23	1.77	2.81	0.021
Payer Insurance				
Private	ref	ref	ref	ref
Public	2.20	1.83	2.64	<0.001
Self-pay/uninsured	1.46	1.01	2.11	0.930
Gender[b]				
Female	ref	ref	ref	ref
Male	0.94	0.84	1.05	0.280
Hospital Type[c]				
Non-Teaching	ref	ref	ref	ref
Teaching	1.89	1.63	2.19	<0.001
N observation= 1,237				

a - Other categorized as: American Indian/Alaskan Native 3 NAS-Confirmed Cases, Other 126 NAS-Confirmed Cases, Unknown: 25 NAS-Confirmed cases

b - Total for Gender does not equal 1237 due to 4 unclassified children

c - Teaching hospitals include Hospitals I and J

Source: Hospital Discharge Data, Center for Health Information Analysis for Nevada, Southern Nevada Health District, 2016-2022

DISCUSSION

As of 2020, the national NAS incidence rate among newborn hospitalizations in the United States was about 6.0 per 1000 newborn hospitalizations reported by the Healthcare Cost and Utilization Project

(HCUP) Fast Stats (Healthcare Cost and Utilization Project, 2022). From this study, Clark County, NV, the NAS incidence rate from January 1, 2016, to September 30, 2022, was 7.4 per 1000 newborn hospitalizations. For the first three quarters of 2022, the rate of NAS was 8.9 per 1000 newborn hospitalizations. Infants who were White had the highest rate of NAS. However, based on the U.S. Census for Clark County, non-Hispanic Whites account for 42% of the population (U.S. Census Bureau, 2022). Maternal use codes had low frequencies for any significant conclusions. The results obtained from the multiple logistic regression model may be partially attributed to lower socioeconomic status (SES). This is evident due to a higher prevalence of lower SES among public insured clients and the presence of teaching hospitals in economically disadvantaged regions.

In 2022, the Centers for Disease Control and Prevention (CDC) released a Morbidity and Mortality Weekly Report (MMWR) evaluating state-led surveillance of NAS in six U.S. states (Jilani et al., 2022). Although many of these states were moving to the CSTE case definition, data collection and infrastructural gaps challenge the capabilities of long-term surveillance beyond initial case reporting. From the brief exploratory study done at SNHD to compare CSTE Tier 1 and Tier 2 case definitions: half had the necessary requirements to match both Tier 1 and Tier 2 definitions; many subjects selected lacked details on neonate symptoms and lab reports which are criteria needed for Tier 1. This was also dependent on the medical record system utilized. Due to unknown circumstances some records were unavailable even though they were coded as P96.1. Further investigation is needed to determine exact specificity and sensitivity of CHIA. Currently, the CSTE is amending the case definition based on further clinical and expert recommendations.

The slight drop from 2016 to 2019 could be the outcome of the implementation of Assembly Bill 474 or Controlled Substance Abuse Prevention Act, for the state of Nevada (Sisolak et al., 2019). This bill was effective January 1, 2018. This bill established procedures and regulations when prescribing controlled substances for pain. Confirmed and suspected cases of drug overdose were to be reported to the Chief Medical Officer. Statistics from Nevada's Office of Analytics Department of Health and Human Services reported January 2017 to October 2019, there was a 38% decrease in the rate of opioid prescriptions per 100 Nevada residents (Sisolak et al., 2019). This drop of prescriptions could be an indicator as to why NAS rates dropped within this time frame.

The COVID-19 Pandemic also could have been the cause of increased rates starting in 2020 onward. A survey assessing mental health, substance use, and suicide ideation was conducted by the CDC (Czeisler et al., 2022). Adults ages ≥18 in the United States during June 24-30, 2020, were evaluated. Of those who participated, 13% reported starting or increasing substance use as a way of coping with stress or emotions related to COVID-19 (Czeisler et al., 2022). For Clark County, opioid-related deaths increased by 56.6 percent from 2019-2021 (Southern Nevada Health District, 2022).

This study is not generalizable to the entire U.S. or counties located outside of Clark County, NV. This study was conducted using the original CSTE case definition before the 2023 revision. The lack of NAS data found in the patient records during the exploratory review contributes to missing data bias. Data from CHIA for 2022 only contained the first three quarters –January to September 30th, 2022. This study was unable to link CHIA maternal records from

neonate data thus maternal risk factors, such as age, were not analyzed. The CHIA database does not differentiate between white non-Hispanic and white Hispanic which could impact the categorization between race/ ethnicity. Misclassification bias due to coding errors from administrative data could have occurred.

As NAS rates are above the national average in Clark County, it is imperative that there be measures to address the issue of maternal and child health. Future recommendations include implementation of reporting system within Clark County. Hospitals need to collect substance and diagnosis-specific data about prenatal substance use to understand local treatment needs and capacity. Substance and diagnosis-specific data about prenatal substance could be used to identify unmet service care and any disparities in the area (Astho, 2021). Knowledge and awareness of NAS is needed at the provider and patient level to reduce stigma and barriers to care. There are needs to increase conversations between community partners to address mothers at risk. The Nevada Department of Health and Human Services (DDHS) have included plans to reduce NAS in their Nevada Opioid Needs Assessment and Statewide Plan 2022 which should provide beneficial changes in the following (State of Nevada Department of Health and Human Services, 2022). Overall, this surveillance analysis cannot uncover underlying risk factors of NAS in the populations analyzed. More studies are needed to contribute to a better understanding of disparities within Clark County, NV specifically concerning pregnant individuals.

AUTHOR CONTRIBUTION

The authors contributed to this research project in distinct capacities. Bryant played a central role in conceptualization, taking the lead in defining the research scope and objectives. Methodological aspects were jointly developed by Bryant and Delise with Bryant primarily responsible for data collection and initial analysis. Beckford contributed to data collection during the exploratory review of medical records looking for concordance between case definition tier 1 and tier 2. Delise and Zhang significantly contributed to formal analysis and offered critical insights during the manuscript's drafting. Writing of the original draft was undertaken by Bryant with subsequent input and revisions provided by Lockett, Delise, and Zhang. Lockett focused on data curation and contributed to the finalization of the manuscript through thorough review and editing.

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CONFLICT OF INTEREST

There are no conflicts of interest.

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