

ARTICLE



Accuracy of diagnostic codes for prenatal opioid exposure and neonatal opioid withdrawal syndrome

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OBJECTIVE: Determine the accuracy of diagnostic codes in identifying Prenatal Opioid Exposure (POE) and Neonatal Opioid Withdrawal Syndrome (NOWS).

STUDY DESIGN: A cross-sectional study of 374,222 mother-infant dyads with delivery from 01/01/2010 to 12/31/2019. We ascertained maternal diagnostic codes for opioid use during pregnancy and infant diagnostic codes for drug exposure and withdrawal. We assessed sensitivity and positive predictive value (PPV) for POE and NOWS, defined using laboratory, pharmacy, and clinical data.

RESULTS: Maternal codes had low sensitivity (36.4%) and PPV (34.7%) for POE. Infant codes for drug exposure were neither sensitive for POE (14%) nor NOWS (31.6%) and had low PPV. Codes for newborn withdrawal had low sensitivity (31.6%) for detecting NOWS, but high PPV (85%). Sensitivity improved (95.1%) for NOWS requiring pharmacologic treatment.

CONCLUSIONS: Diagnostic codes identify POE and NOWS poorly. Improved case identification would include pharmacy and laboratory results, and clearly defined criteria for evidence of withdrawal.

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INTRODUCTION

The opioid epidemic is a public health emergency that has extended to pregnant mothers and infants. Among women of reproductive age in 2017, 19.5% with private insurance had claims for opioid prescriptions, and among women enrolled in Medicaid, 24.7% [1]. From 2010–2017, the incidence of neonatal opioid withdrawal syndrome (NOWS) in the United States nearly doubled from 4.0 to 7.3 per 1000 hospital births [2]. Compared with other birth hospitalizations, infants with NOWS have a nine day longer median length of stay and \$14,600 in additional costs in 2017 [2].

The Centers for Disease Control have advocated for longitudinal linked surveillance of mother-infant pairs to elucidate physical and neurodevelopmental outcomes later in childhood from POE [3, 4]. Many states have implemented NOWS surveillance to assess trends, but clinical case and surveillance definitions vary across jurisdictions [5, 6]. Passive surveillance is the primary methodology employed, with 25 states using International Classification of Diseases, Clinical Modification (ICD-CM) codes from hospital discharge databases [5]. ICD codes for drug-exposure and newborn withdrawal are not specific to opioids and may indicate exposure to a variety of drugs [7, 8].

Inconsistent case definitions can result in inaccurate comparisons, misinformed conclusions and an ineffective response. In August 2019, the Council of State and Territorial Epidemiologists

released a position statement proposing a uniform case definition for NOWS [9].

Our objective was to determine sensitivity, specificity, and positive and negative predictive value (PPV and NPV) of maternal diagnostic codes for opioid use and infant diagnostic codes for drug exposure and newborn withdrawal, in identifying POE and NOWS, within an integrated health care delivery system.

SUBJECTS AND METHODS

Study design and population

We performed a population-based cross-sectional study of mother/infant dyads born at 15 Kaiser Permanente Northern California (KPNC) hospitals from 2010 to 2019. KPNC is an integrated healthcare system serving over 4.5 million members. The sociodemographic distribution of the KPNC membership is broadly similar to California, though the extremes of income distribution are underrepresented [10]. We included infants born at ≥35 weeks' gestation in whom withdrawal could be reliably assessed. We excluded delivery room deaths and infants transferred out of KPNC. We excluded infants with major congenital anomalies and hypoxic ischemic encephalopathy (HIE). The KPNC Institutional Review Board and California Committee for the Protection of Human Subjects approved the study.

Data source and diagnostic codes

The KPNC Virtual Data Warehouse (VDW) contains diagnostic codes for inpatient and outpatient encounters within KPNC [11].

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Maternal diagnostic codes for opioid use during pregnancy

Diagnostic codes for maternal opioid use included any ICD-9-CM or ICD-10-CM during the pregnancy indicating unspecified or chronic opioid use, opioid dependence, opioid abuse, opioid poisoning or overdose, adverse effects of opioids, or long-term (current) use of opioids (Supplementary Table 1).

Infant diagnostic codes for drug exposure

Newborns exposed to drugs were identified by the following diagnostic codes from their birth hospitalization: ICD-9-CM 760.21 Newborn affected by maternal use of unspecified drugs of addiction, ICD-10-CM P04.40 Newborn affected by maternal use of unspecified drugs of addiction, P04.49 Newborn affected by maternal use of drugs of addiction, or P04.14 Newborn affected by maternal use of opiates.

Infant diagnostic codes for newborn withdrawal

Newborn withdrawal was identified from diagnostic codes: ICD-9-CM 779.5 Drug Withdrawal Syndrome in Newborn, ICD-10-CM P96.1 Newborn withdrawal symptoms from maternal drugs of addiction, or P96.2 Withdrawal symptoms from (maternal) therapeutic use of drugs in newborn.

Case ascertainment for prenatal opioid exposure

We used a combination of pharmacy records, urine drug screen (UDS) results, and chart review, to determine POE. KPNC's pharmacies provide members with nearly all of their prescriptions [12]. Maternal prescriptions for opioid medications (Supplementary Table 2), methadone, and buprenorphine, dispensed during the pregnancy, were extracted from pharmacy records. We identified methadone and buprenorphine administered from the electronic medication administration record. Maternal and infant UDS results were extracted from the KPNC VDW. KPNC conducts universal UDS during the first trimester. Additional UDS are performed if there is suspected substance abuse. Infants are tested if maternal testing is not available, or the infant displays symptoms of drug intoxication or withdrawal. At least one UDS was performed in 95% of the women in the study.

POE was defined by any of the following criteria: (1) opioid pain medications dispensed to the mother within 60 days prior to delivery, with a ≥ 10 -day supply, (2) methadone or buprenorphine dispensed within 60 days prior to delivery or received during the delivery encounter, (3) maternal delivery UDS or infant UDS positive for methadone, (4) maternal delivery or infant UDS positive for opioids, and a UDS during the pregnancy positive for opioids. The threshold of 10 days was chosen because it represented >75th percentile of the distribution of opioid pain medications filled in the 60 days prior to delivery. To avoid misclassification of mothers who received opioids during labor, positive UDS during pregnancy was required, if the maternal delivery or infant UDS was positive for opioids.

We reviewed maternal and infant electronic health records to assess for maternal opioid use in infants that received Finnegan Neonatal Abstinence Scoring System (FNASS) scores [13] for more than two days. We identified FNASS scoring from electronic nursing flowsheets.

Case ascertainment for neonatal opioid withdrawal syndrome (NOWS)

We defined NOWS as an infant with POE and withdrawal evidenced by either (1) FNASS score >4 or (2) pharmacologic treatment for withdrawal [14]. Pharmacologic therapy included methadone, clonidine, phenobarbital, or morphine within the first week of life. Our definition of NOWS aligns closely with the definition recently proposed by an expert panel, convened by the Department of Health and Human Services [15].

Additional data

From KPNC databases, we obtained maternal and infant race/ethnicity, payer source, infant sex, birthweight, delivery mode, neonatal intensive care unit (NICU) admission, and infant length of stay [16]. We identified maternal selective serotonin reuptake inhibitor (SSRIs) use during the pregnancy from pharmacy records. Maternal depression was identified by diagnostic codes for depression in the VDW [11]. Maternal education was obtained from Birth Certificate data.

Statistical analysis

We used descriptive statistics to summarize maternal and infant characteristics. We calculated sensitivity, specificity, PPV, NPV and 95%

confidence intervals (CI) for diagnostic codes for maternal opioid use during pregnancy, newborns exposed to drugs, and newborn withdrawal, for three conditions: POE, NOWS, and NOWS receiving pharmacologic treatment. Since our study included both ICD-9-CM and ICD-10-CM, we performed a sensitivity analysis, using only the ICD-10-CM period.

RESULTS

During the study period, 376,930 infants were born in KPNC at ≥ 35 weeks' gestation. Our final cohort included 374,222 maternal/infant dyads, after excluding delivery room deaths ($n = 406$), transfers out of KPNC ($n = 1075$), major congenital anomalies ($n = 925$), and HIE cases ($n = 302$). The prevalence of POE was 8.7 per 1000 births ($n = 3259$). We identified NOWS in 3.1 per 1000 births ($n = 1163$), among which 24% (284) received pharmacologic treatment. Mothers of infants with POE were more likely to be insured by Medicare/Medicaid, be White (non-Hispanic) or Black, have a diagnosis of depression during pregnancy, and have lower education levels, compared to mothers of infants without POE (Table 1). Mothers of infants with POE were more likely to be prescribed SSRIs and have positive UDS for non-opioid drugs. Infants with POE were more likely to be delivered by caesarean, preterm, and admitted to NICU.

Maternal diagnostic codes for opioid use during pregnancy were present in 9.1 per 1000 births ($n = 3422$). Codes for newborns exposed to drugs were present in 3.1 per 1000 births ($n = 1167$), and codes for newborn withdrawal in 1.4 per 1000 births ($n = 511$). The frequencies of individual diagnostic codes are presented in Supplementary Table 3. Despite receiving a diagnostic code during pregnancy for opioid use, most of these pregnancies had no evidence of opioid use by UDS or pharmacy data (Table 2). Similarly, in infants with a code for drug exposure, opioid exposure was low. These infants had a high percentage of NICU admission (33.4%), nearly half with length of stay >3 days. Among infants with a code for newborn withdrawal, there were substantially higher rates of POE, abstinence scoring (93.7%), NICU admission (81.2%), and a median length of stay of 11.1 days.

Maternal diagnostic codes for opioid use had low sensitivity for POE (36.4%) but higher sensitivity for NOWS (69.7%). PPV was poor, at $<40\%$, for both (Table 3). Infant codes for drug exposure were not sensitive for POE (14%). These codes were more sensitive for NOWS but still low. Sensitivity was similar for all NOWS cases and NOWS cases requiring pharmacologic treatment (31.6% versus 39.1%). These codes also had low PPV ($<40\%$) for POE and NOWS. Diagnostic codes for newborn withdrawal had low sensitivity (31.6%) for NOWS, but high PPV 85%. The sensitivity improved to 95.1% when identifying NOWS cases requiring pharmacologic treatment. Combining infant codes for drug exposure and newborn withdrawal, marginally increased the sensitivity for NOWS to 57.3%, but with a low PPV of 43.7%. The combined infant codes had high sensitivity (97.5%) for detecting NOWS requiring pharmacologic treatment. Combining maternal and infant codes identified nearly all NOWS cases (85%) but at the expense of extremely poor PPV (22.8%). Specificity and negative predictive values were extremely high ($\geq 99\%$) for all diagnostic code groups and outcomes. This was expected given the relatively low prevalence of the outcomes and large cohort size. Restricting our analysis to ICD-10-CM diagnostic codes yielded similar results (Table 4).

DISCUSSION

In our population, both maternal and infant diagnostic codes identified POE poorly, even when combined. Infant codes for drug exposure had poor sensitivity and PPV for NOWS. A primary driver of the poor PPV is that most codes are not specific for opioids. In 57.4% of infants with drug exposure codes, maternal UDS was positive for drugs other than opioids. Only 52.5% of these infants

Table 1. Maternal and infant characteristics by prenatal opioid exposure (POE) status.

	Opioid unexposed N = 370,963	POE N = 3259	NOWS* N = 1163	NOWS Rx Treated* [†] N = 284
MATERNAL				
Maternal age (years) - mean (SD)	30.7 (5.5)	31.0 (5.4)	30.4 (5.4)	29.5 (5.5)
Medicare/Medicaid	8.6%	25.0%	31.8%	30.3%
Race				
White, non-Hispanic	38.2%	59.1%	63.9%	62.3%
Black	6.8%	11.1%	11.0%	9.2%
Hispanic	25.5%	21.7%	18.2%	18.3%
Asian	25.9%	6.3%	3.6%	6.0%
Other/Unknown	3.6%	2.9%	3.3%	4.2%
Depression Dx during pregnancy	14.0%	47.1%	59.2%	63.7%
Maternal SSRI Rx	3.3%	17.5%	21.8%	19.0%
Education				
<High school	3.2%	4.4%	6.2%	6.0%
High school	31.8%	53.0%	56.1%	60.6%
College degree	46.0%	30.1%	21.6%	15.1%
Unknown	19.0%	12.6%	16.2%	18.3%
UDS during Pregnancy	95.1%	95.1%	93.2%	84.5%
UDS positive non-opioids	5.2%	8.0%	10.0%	11.3%
INFANT				
Caesarean delivery	25.9%	39.4%	36.9%	30.3%
Male	51.1%	50.5%	49.9%	49.3%
Preterm <37 weeks	5.1%	9.5%	11.1%	10.9%
SGA < 10th%	7.7%	8.2%	11.3%	13.4%
Neonatal Intensive Care Unit	7.4%	25.6%	52.0%	96.8%
Length of stay* (days)	2.1 (1.9)	4.5 (6.5)	8.3 (9.7)	19.9 (12.8)

*Subset of POE.

[†]NOWS Rx Treated—pharmacologic treatment with opioids.**Table 2.** Maternal and infant characteristics by diagnostic codes.

	ICD-9/ICD-10 Diagnostic codes			
	Maternal opioid use during pregnancy N = 3422	Newborns exposed to drugs N = 1167	Newborn withdrawal N = 511	No drug/opioid diagnostic codes N = 369,891
Pregnancy UDS + Opioids	949 (27.7%)	328 (28.1%)	284 (55.6%)	1406 (0.4%)
Delivery UDS + Opioids	455 (13.3%)	238 (20.4%)	228 (44.6%)	768 (0.2%)
Perinatal opioid pain medications ^a	529 (15.5%)	167 (14.3%)	127 (24.9%)	1720 (0.5%)
Buprenorphine or methadone use	576 (16.8%)	216 (18.5%)	256 (50.1%)	32 (0.01%)
FNASS scoring	1103 (32.2%)	616 (52.8%)	479 (93.7%)	781 (0.2%)
Length of stay > 3 days	1210 (35.4%)	560 (48.0%)	464 (90.8%)	46,680 (12.6%)
Length of stay: median days (IQR)	2.3 (1.7–3.5)	3.0 (2.1–4.5)	11.1 (4.3–17.8)	1.8 (1.3–2.4)
NICU admission	752 (22.0%)	390 (33.4%)	415 (81.2%)	27,190 (7.4%)
UDS positive non- opioid drugs	560 (16.4%)	670 (57.4%)	80 (15.7%)	18,218 (4.9%)

UDS urine drug screen, FNASS Finnegan neonatal abstinence scoring system, NICU neonatal intensive care unit.

^aprescription for opioid pain medications ≥10-day supply within 60 days of delivery.

Table 3. Sensitivity, specificity, and predictive value of ICD-9 and ICD-10 diagnostic codes.

Diagnostic codes	N	Per 1 K Births	POE		NOWS		NOWS Rx Treated ^a	
			metric	estimate	95% CI	estimate	95% CI	estimate
Maternal opioid use during pregnancy	3422	9.1	Sensitivity	36.4%	(34.7–38.0%)	69.7%	(67.0–72.3%)	79.2%
			Specificity	99.4%	(99.4–99.4%)	99.3%	(99.3–99.3%)	99.2%
			PPV	34.7%	(33.1–36.3%)	23.7%	(22.3–25.1%)	6.6%
			NPV	99.4%	(99.4–99.5%)	99.9%	(99.9–99.9%)	100.0%
Newborns exposed to drugs	1167	3.1	Sensitivity	14.0%	(12.8–15.2%)	31.6%	(28.9–34.2%)	39.1%
			Specificity	99.8%	(99.8–99.8%)	99.8%	(99.8–99.8%)	99.7%
			PPV	39.2%	(36.4–42.0%)	31.5%	(28.8–34.1%)	9.5%
			NPV	99.3%	(99.2–99.3%)	99.8%	(99.8–99.8%)	100%
Newborn withdrawal	511	1.4	Sensitivity	13.8%	(12.6–15.0%)	37.9%	(35.1–40.7%)	95.1%
			Specificity	100%	n/a	100%	n/a	99.9%
			PPV	88.1%	(85.3–90.9%)	86.3%	(83.3–89.3%)	52.8%
			NPV	99.3%	(99.2–99.3%)	99.8%	(99.8–99.8%)	100%
Newborns exposed to drugs or withdrawal	1524	4.1	Sensitivity	23.4%	(22.0–24.9%)	57.3%	(54.4–60.1%)	97.5%
			Specificity	99.8%	(99.8–99.8%)	99.8%	(99.8–99.8%)	99.7%
			PPV	50.1%	(47.6–52.6%)	43.7%	(41.2–46.2%)	18.2%
			NPV	99.3%	(99.3–99.4%)	99.9%	(99.9–99.9%)	100%
Maternal opioid use or newborns exposed to drugs or withdrawal	4331	11.6	Sensitivity	43.3%	(41.6–45.0%)	85.0%	(83.0–87.1%)	100.0%
			Specificity	99.2%	(99.2–99.2%)	99.1%	(99.1–99.1%)	98.9%
			PPV	32.6%	(31.2–34.0%)	22.8%	(21.6–24.1%)	6.6%
			NPV	99.5%	(99.5–99.5%)	100%	n/a	100%

PPV positive predictive value, NPV negative predictive value.

^aNOWS Rx Treated – pharmacologic treatment with opioids.

Table 4. Sensitivity, specificity, and predictive value of ICD-10 diagnostic codes.

Diagnostic codes	N	Per 1 K Births	POE		NOWS		NOWS Rx Treated ^a	
			metric	estimate	95% CI	estimate	95% CI	estimate
Maternal opioid use during pregnancy	1839	10.5	Sensitivity	57.1%	(54.1–60.1%)	80.0%	(76.5–83.4%)	85.8%
			Specificity	99.3%	(99.2–99.3%)	99.2%	(99.1–99.2%)	99.0%
			PPV	32.0%	(29.9–34.2%)	22.6%	(20.7–24.5%)	6.9%
			NPV	99.7%	(99.7–99.8%)	99.9%	(99.9–100.0%)	100.0%
Newborns exposed to drugs	772	4.4	Sensitivity	26.3%	(23.6–28.9%)	44.3%	(40.0–48.6%)	57.4%
			Specificity	99.7%	(99.7–99.7%)	99.7%	(99.7–99.7%)	99.6%
			PPV	35.1%	(31.7–38.5%)	29.8%	(26.6–33.0%)	11.0%
			NPV	99.6%	(99.5–99.6%)	99.8%	(99.8–99.9%)	100.0%
Newborn withdrawal	231	1.3	Sensitivity	19.6%	(17.2–22.0%)	38.2%	(34.0–42.3%)	96.0%
			Specificity	100.0%	n/a	100.0%	n/a	100.0%
			PPV	87.5%	(83.2–91.7%)	85.7%	(81.2–90.2%)	61.5%
			NPV	99.5%	(99.5–99.6%)	99.8%	(99.8–99.8%)	100.0%
Newborns exposed to drugs or withdrawal	887	5.1	Sensitivity	35.4%	(32.5–38.3%)	62.2%	(58.1–66.4%)	98.7%
			Specificity	99.7%	(99.7–99.7%)	99.7%	(99.7–99.7%)	99.6%
			PPV	41.2%	(37.9–44.4%)	36.4%	(33.3–39.6%)	16.5%
			NPV	99.6%	(99.6–99.6%)	99.9%	(99.9–99.9%)	100.0%
Maternal opioid use or newborns exposed to drugs or withdrawal	2032	11.6	Sensitivity	60.0%	(57.0–63.0%)	88.3%	(85.5–91.0%)	99.3%
			Specificity	99.3%	(99.3–99.4%)	99.3%	(99.2–99.3%)	99.1%
			PPV	35.2%	(33.0–37.5%)	26.1%	(24.0–28.1%)	8.4%
			NPV	99.8%	(99.7–99.8%)	100.0%	n/a	100.0%

PPV positive predictive value, NPV negative predictive value.

^aNOWS Rx Treated – pharmacologic treatment with opioids.

received FNASS scoring. Lack of abstinence scoring may indicate that clinicians were unaware of opioid exposure, as KPNC NOWS management guidelines state that there is no clearly defined maternal opioid intake below which a fetus is not at risk for NOWS, and that scoring should begin when a newborn is 12 h of age. Infant diagnostic codes for newborn withdrawal had excellent sensitivity for NOWS that required pharmacologic treatment, but when all NOWS was considered, sensitivity was 37.9%. These codes may be underutilized in infants managed non-pharmacologically which has important surveillance implications. As clinicians try to reduce postnatal opioid exposure by using functional assessments and maximizing non-pharmacologic interventions [17–19], it may erroneously appear that the incidence of NOWS is declining, if newborn withdrawal diagnostic codes are used preferentially when pharmacologic treatment is necessary.

Recent studies have sought to evaluate the accuracy of diagnostic codes related to NOWS and POE [7, 8, 20–23]. Two large studies in Florida [8] and Tennessee [23] were limited in that they only reviewed the records of infants with diagnostic codes for newborn withdrawal. While they both reported high PPV, the studies could not assess the sensitivity of the codes. PPV of these codes vary based upon the underlying prevalence of NOWS in the communities studied. As our study demonstrates, infants with NOWS requiring opioid replacement therapy and NICU admission may be more likely to receive codes than those that only received non-pharmacologic treatment. These studies may overestimate the PPV of diagnostic codes by preferentially including infants with severe withdrawal, requiring pharmacologic treatment.

A population-based study in Ontario, Canada, examined the prevalence of POE using three ascertainment methods: prenatal opioid prescriptions, maternal diagnostic codes, and infant diagnostic codes for withdrawal or drug exposure [20]. This study compared positive percent agreement among the methods, finding that the combination of methods identified a broader population of those with POE. This study had no standard case definition of POE, thus no way to assess sensitivity nor false positivity of these methods.

In a study of 121 opioid-exposed infants, Doherty et al. compared several definitions for NOWS and found diagnostic codes for newborn withdrawal present in 38% of their population and codes for drug exposure in 64% [21]. These data are consistent with our findings of poor sensitivity of codes for identifying opioid exposure that does not result in withdrawal requiring pharmacologic treatment.

A study of three hospitals in Florida examined the sensitivity of diagnostic codes; however, case ascertainment for NOWS relied on NICU admission logs and infant pharmacy records for medications used for opioid withdrawal, likely biasing their case definition to more severely affected infants [7]. Sensitivity was high 85.4% and consistent with our findings among infants with NOWS that required pharmacologic treatment.

A population-based study in Massachusetts examined the accuracy of ICD-10-CM codes for POE and NOWS using clinical record review to confirm exposure and NOWS [22]. The study utilized a stratified sampling approach to select records for review and weighted data to assess the performance of ICD-10-CM codes. The study found that codes for substance-exposed infants had poor sensitivity (41.4%) for NOWS. Codes for newborn withdrawal had a high sensitivity (92.1% for NOWS). This was comparable to our sensitivity of identifying NOWS requiring pharmacologic treatment, but much higher than what we observed for all NOWS cases. Our study used a FNASS score >4 to confirm NOWS in opioid-exposed infants, while this study used a score ≥8. Differences in case definitions may account for differences in findings, with more prevalent use of codes for newborn withdrawal in infants with more severe symptoms.

Strengths of our study include comprehensive ascertainment of opioid prescriptions, including the timing and quantity of opioids

dispensed. Many studies don't have this granularity and consequently include short courses of opioids early in pregnancy as exposure [20, 24, 25]. Thus, studies report maternal prevalence of opioid use during pregnancy of 4–27% while we report prevalence of 0.6% [20, 24–27]. We used a minimum exposure of at least a 10-day supply and limited prescriptions to those dispensed within 60 days of delivery; usage more likely to result in NOWS. Universal UDS enhanced our ability to detect maternal opioid use. We reviewed all infants, not just those with diagnostic codes, allowing us to provide data on both false positives and false negatives. We identified infants with severe withdrawal requiring pharmacologic treatment, but also infants treated non-pharmacologically.

A limitation of our study is the retrospective identification of NOWS from clinical data. Additional information may have been available prospectively to categorize these infants. We did utilize standardized assessments such as FNASS scoring. Despite being the most widely used withdrawal assessment tool, FNASS is subjective with poor inter-rater reliability [28]. It has never been validated, nor its cutoff scores tested [28–30]. The overall prevalence of NOWS in KPNC is low, so our estimates of PPV are likely lower than in settings with higher prevalence. While our integrated medical system allows excellent ascertainment of opioid exposure and NOWS, such data is not readily available for public health surveillance.

Our analysis highlights the potential inaccuracy of surveillance data using solely diagnostic codes. For accurate estimations of the incidence of NOWS, it's essential that case reporting use clinical definitions requiring evidence of maternal opioid use as well as clearly defined criteria for evidence of withdrawal. Further standardization of definitions across jurisdictions is crucial for comparisons [15]. As management of infants with NOWS evolves, focusing on maximizing non-pharmacologic management, it is likely that passive surveillance using diagnostic codes will become even less reliable.

CODE AVAILABILITY

All analyses were performed using SAS version 9.4. The code used is available upon request.

DATA AVAILABILITY

The datasets generated for this study are stored at the KPNC Division of Research. Deidentified data can be provided upon reasonable request to the corresponding author, and with permission from the KPNC Institutional Review Board.

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AUTHOR CONTRIBUTIONS

MWK conceptualized and designed the study, obtained funding, acquired the data, carried out all data analysis, drafted the initial manuscript, and reviewed and revised the manuscript. CIC, SDC, LAC, SDP, and MH assisted in interpreting the analyses, assisted in writing the initial draft, and reviewed and revised the manuscript. SL was responsible for acquiring the data, building the datasets, and reviewing and revising the manuscript. EMW reviewed the data, performed chart review for data accuracy when needed, and reviewed and revised the manuscript. LSS assisted in the conceptualization and design of the study, obtained funding, reviewed data analyses, assisted in writing the initial draft and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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COMPETING INTERESTS

The authors declare no competing interests.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was reviewed and approved by the following boards. Individual consent of subjects was waived. Kaiser Permanente Northern California Institutional Review Board (#1507334). California Committee for the Protection of Human Subjects (#2021-043). The study is in accordance with the Declaration of Helsinki.

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