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Surveillance of Intrauterine Opioid Exposures Using Electronic Health Records

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Abstract

The objective was to use population-based electronic health records for surveillance of intrauterine exposures to substances of abuse, including opioids, and to monitor changes in exposure rates over time. This retrospective, descriptive analysis utilized geocoded neonatal physician billing records representing intrauterine exposures to substances of abuse detected through universal maternal drug testing. Census tract-level exposure rates were identified among the newborn population of Hamilton County, Ohio between 2014 and 2016. Among 27,896 newborns, the authors detected an intrauterine opioid exposure rate of 37.9 per 1000 infants, with 10.5 per 1000 experiencing severe opioid withdrawal (neonatal abstinence syndrome). Individual data were mapped to 222 US census tracts. Tract-level opioid exposure rates ranged from 0.0 to 607.1 (median: 32.9) per 1000 live births. Secondary use of electronic health record data has potential to aid in intrauterine opioid exposure and other public health surveillance efforts without disrupting clinical workflows or placing an additional burden on limited resources. Surveillance of intrauterine opioid exposures may inform stakeholders and enable targeting of interventions and prevention strategies toward the highest risk populations.

Keywords: neonatal abstinence syndrome, opioid, newborn, electronic health records, public health surveillance

Introduction

Withdrawal among newborn infants following intrauterine opioid exposure known as neonatal opioid withdrawal syndrome, or traditionally as neonatal abstinence syndrome (NAS), has emerged as a national epidemic.[1,2] Between 2000 and 2013, US NAS rates rose an estimated 400%, increasing from 1.2 to 6.0 per 1000 infants.[3,4] According to recent reports, some states estimate that more than 30 of every 1000 newborns are affected, with increases in incidence impacting rural communities disproportionally.[5–7] Increasing incidence of in utero opioid exposures has led to surges in the reported expenditures for NAS management in neonatal intensive care units (NICUs) as well as corresponding increases in the diagnoses of conditions related to opioid use such as neonatal hepatitis C.[6,8,9]

Collection of NAS surveillance and monitoring data is crucial for informing policy makers and targeting interventions where they may be most effective.[5,10,11] In 2013, Tennessee established the first statewide public health surveillance system aimed at monitoring NAS, which identified regions, predominantly rural Appalachian counties, most impacted.[12] Hospital staff were required to report data using an online system involving cases in which opioid withdrawal produced clinically significant symptoms. However, intrauterine exposures that did not lead to clinically significant symptoms of withdrawal likely were not reported.

In response to dramatic increases in NAS rates throughout Ohio,[13] all maternity hospitals in the greater Cincinnati region have implemented universal drug testing of maternal urine provided at the time of parturition.[14] Test results facilitate the timely identification and treatment of infants at risk for opioid withdrawal according to regional guidelines.[15] Additionally, test results enable identification of subclinical exposures to opioids as well as other substances of abuse.

In combination with universal drug testing, Cincinnati's Maternal and Infant Data Hub (MIDH) is a unique resource to support surveillance of intrauterine drug exposures. Housed at Cincinnati Children's Hospital Medical Center (CCHMC), MIDH integrates electronic health records (EHRs) from a vast majority of maternity hospital-based neonatal encounters throughout the region.[16] Records represent all infants treated for NAS as well as those who experienced intrauterine exposures to opioids or other substances of abuse. In addition, the

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repository contains geocoded address information facilitating census tract-level reporting and analyses. This study aims to demonstrate the utility of MIDH to support public health surveillance at the county and subcounty level by identifying geographic regions (census tracts) with the highest exposure incidence as well as regions experiencing increases in exposure rates over time. The overall objective is to provide actionable information to policy makers and stakeholders, including members of state and county health departments, members of state Departments of Medicaid and Mental Health and Addiction Services, the Ohio Hospital Association, and care providers including obstetricians, neonatologists, and pediatricians. This information will enable timely and efficient public health responses that include targeted interventions and a focus on primary prevention.[17]

Table 1. Diagnosis Codes Corresponding to Substance of Abuse Exposures

Diagnosis description	*Relevant diagnosis codes*
Drug Exposed	ICD-9-CM: 760.70, 760.72, 760.73, 760.75, 779.5 ICD-10-CM: F11.23, P04.1, P04.41, P04.49, P04.8, P04.9, P96.1
Opioid Exposed	ICD-9-CM: 760.72, 779.5 ICD-10-CM: P04.49
Neonatal Abstinence Syndrome	ICD-9-CM: 779.5 ICD-10-CM: F11.23, P96.1

ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; ICD-10-CM, *International Classification of Diseases, Tenth Revision, Clinical Modification.*

Methods

Population

CCHMC neonatologists and pediatricians are contracted to direct newborn care in each of 13 maternity hospitals in greater Cincinnati. As a result, approximately 80% of infants in the region receive newborn care from CCHMC physicians in the maternity hospital setting, including all newborn admissions to regional special care nurseries and NICUs. Within Hamilton County, Ohio, a county with an estimated population of 804,000[18] in which CCHMC and the city of Cincinnati are located, CCHMC physicians provide newborn care for more than 92% of resident births. These neonatal encounters produce physician billing records maintained by the CCHMC EHR system, which function as a backbone for population-based record linkage within the MIDH data system. This retrospective, descriptive study incorporates newborn encounter data representing Hamilton County, Ohio resident births from January 1, 2014, through December 31, 2016. The Institutional Review Board at CCHMC approved this study and granted a waiver of informed consent.

Data sets

The principal source of patient data used in this study was physician billing records originating from the Epic EHR (Epic Systems Corporation, Verona, WI) installed at CCHMC. Source data elements captured during the initial neonatal encounter were extracted, transformed, and loaded into the MIDH system including: infant race and ethnicity (recoded as: black, non-Hispanic; white, non-Hispanic; other, non-Hispanic; or Hispanic), insurance provider (recoded as: public, self-pay, or private), gestational age, birth weight, residence address, and diagnosis codes related to in utero exposures to substances of abuse as well as to the hepatitis C virus (HCV). The study team also captured length of initial hospitalization as well as an indicator of admission to a regional NICU.

Regional universal maternal testing for drug use was implemented in September 2013, 4 months prior to the study period, and was performed for 98% of mothers delivering in regional maternity hospitals.[14] Throughout the region, consent for drug testing was obtained and urine samples were collected during the routine hospital admission process at the time of delivery. Samples testing positive using an on-site immunoassay test were sent for confirmation using mass spectrometry at CCHMC. Test results were grouped into 3 exposure categories based on standardized regional use of exposure-related diagnosis codes: (1) Drug exposure – intrauterine exposures to substances of abuse (including amphetamines, benzodiazepines, barbiturates, cannabinoids, cocaine, and phencyclidine as well as short-acting opioids, including heroin or prescription pain medications, and long-acting opioids including buprenorphine or methadone); (2) Opioid exposure – intrauterine exposures to short- or long-acting opioids; and (3) NAS. *International Classification of Diseases, Ninth or Tenth Edition, Clinical Modification* codes were used to capture exposures (Table 1).

Nationally, the term NAS is used to refer to varying severities of opioid withdrawal.[4] However, in the greater Cincinnati region the diagnosis is consistently used to represent infants who received pharmacologic treatment with a first-line opioid weaning medication, typically methadone, morphine, or buprenorphine. No distinction was made between legal or illicit use in this analysis. Depending on exposures, a single patient could receive multiple diagnoses codes and could be included in more than 1 category. For example, an infant exposed in utero to marijuana and buprenorphine would be classified into both categories 1 and 2. If the infant experienced severe opioid withdrawal requiring pharmacologic treatment with opioid weaning, he or she also would be classified in category 3.

Maternal residence at time of birth was geocoded and each individual record was associated with a corresponding census tract identifier enabling linkage to area-level community measures. To maintain Health Insurance Portability and Accountability Act compliance, the geocoding software runs on a server inside CCHMC and individual addresses are never transmitted externally. Address information was translated to latitude and longitude coordinates using the 2015 TIGER/Line Shapefiles, and coordinates were subsequently mapped to corresponding census tract identifiers.[19,20] Along with the census tract identifier, the geocoding program produced a precision value indicating the level of geocoding accuracy. In order of decreasing accuracy, precision values included: (1) Range - interpolated based on address ranges from street segments; (2) Street - center of matched street; (3) Intersection - intersection of 2 streets; (4) Zip - centroid of the matched zip code; and (5) City - centroid of the matched city. Only geocodes at the range level and within Hamilton County, Ohio were included in the analysis (Fig. 1).

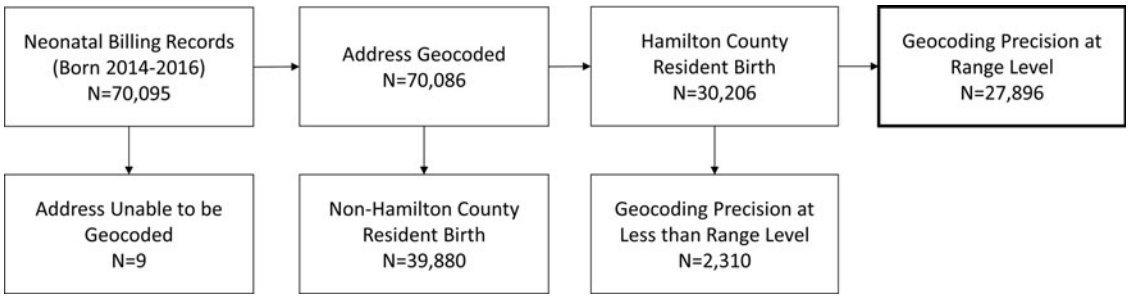

FIG. 1. Determination of study population.

Finally, total population estimates for each census tract were obtained from the 2015 American Communities Survey and linked using census tract identifier fields.[18]

Analysis

The study team computed descriptive statistics for the study population including annual regional rates for each exposure category and patient outcomes within each exposure category. Next, the team described exposure rates among the county's 222 census tracts. A *t* test was used to detect differences in birth and exposure rates among tracts within the highest and lowest quartiles of opioid exposure over the entire study period, whereby each tract was weighted equally regardless of population. Next, the study team identified regions with increasing opioid exposure rates (as well as tracts with cases in 2016 and none in 2014) by calculating the percent of change in rates for each tract between 2014 and 2016. The team generated maps representing regional opioid exposure rates as well as changes in rates between 2014 and 2016 using Google Fusion Tables,[21] and census tract cartographic boundary files obtained from the US Census Bureau.[22] Statistical calculations were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

During the study period, CCHMC physician billing records were generated for 30,206 of the 32,658 births (Hamilton County Public Health, unpublished data, August 2017) among county residents (approximately 92.5%). Further, 27,896 records contained an address that could be geocoded at the highest level of precision and mapped to a corresponding census tract (85.4% of all county resident births). Characteristics of the population as well as annual exposure cases and rates among racial and insurance type subgroups are listed in Table 2.

The overall drug exposure rate was 98.3 per 1000 births. Of the infants experiencing intrauterine drug exposures, 38.6% involved opioids (1058 of 2742), resulting in an opioid exposure rate of 37.9 per 1000 newborns. More than 10 in every 1000 infants born in the county experienced severe opioid withdrawal. Exposure rates were much lower among the privately insured compared to the publicly insured or self-pay. Also, although a higher rate of exposure to all substances of abuse was detected among the black, non-Hispanic population, the highest rates of opioid exposure and NAS were detected among the white, non-Hispanic population.

Table 3 presents newborn outcomes among infants in each drug exposure category. Consistent with previous findings in Ohio, 45.4% of infants treated for NAS were exposed to HCV.[8] HCV rates also were elevated for drug-exposed and opioid-exposed infants compared to those in the general county newborn population. As expected, mean length of initial hospitalization and rate of NICU admission increased from exposure category 1 to 3.

Total population, birth, and exposure rate characteristics among the county's 222 census tracts are listed in Table 4. Notably, the census tract with the highest exposure rate for opioids and NAS, as well as rate of exposure for any substance of abuse, contains a live-in maternal medication-

Table 2. Study Population Demographics and Exposure Rates, 2014–2016

	Births N *(%)*	*Drug exposed* N *(rate per 1000)*	*Opioid exposed* N *(rate per 1000)*	*NAS* N *(rate per 1000)*
Total Population	27,896 (100.0)	2742 (98.3)	1058 (37.9)	293 (10.5)
2014	9121 (32.7)	884 (96.9)	345 (37.8)	72 (7.9)
2015	9348 (33.5)	787 (84.1)	362 (38.7)	93 (9.9)
2016	9426 (33.8)	1071 (113.6)	351 (37.2)	128 (13.6)
Race and Ethnicity				
Black, non-Hispanic	7181 (25.7)	1154 (160.7)	237 (33.0)	28 (3.9)
White, non-Hispanic	8647 (31.0)	615 (71.1)	402 (46.5)	147 (17.0)
Other Race, non-Hispanic	1127 (4.0)	83 (73.6)	36 (31.9)	13 (11.5)
Hispanic	1458 (5.2)	55 (37.7)	29 (19.9)	7 (4.8)
Unknown	9483 (34.0)	835 (88.1)	354 (37.3)	98 (10.3)
Insurance				
Public or Self-pay	15,626 (56.0)	2489 (159.3)	952 (60.9)	287 (18.4)
Private	12,270 (44.0)	253 (20.6)	106 (8.6)	6 (0.5)

NAS, neonatal abstinence syndrome.

Table 3. Outcomes Among Exposure Groups, 2014–2016

	Births N = *27,896*	*Drug exposed* N = *2742*	*Opioid exposed* N = *1058*	*NAS* N = *293*
Exposed to Hepatitis C Virus, N (%)	392 (1.4)	295 (10.8)	255 (24.1)	133 (45.4)
Gestational Age, mean ± SD, weeks	38.4 ± 2.1	37.9 ± 2.4	37.8 ± 2.5	37.5 ± 2.6
Birthweight, mean ± SD, grams	3224.5 ± 617.0	2968.2 ± 595.9	2979.1 ± 618.6	2906.6 ± 580.7
Length of Initial Hospitalization, mean ± SD, days	4.1 ± 7.9	6.3 ± 10.3	8.7 ± 9.9	17.1 ± 9.3
Neonatal Intensive Care Unit Admission, N (%)	2790 (10.0)	542 (19.8)	369 (34.9)	225 (76.8)

NAS, neonatal abstinence syndrome; SD, standard deviation.

assisted treatment facility. Of the 222 tracts, 95 (42.8%) had no measured cases of NAS, 20 (9.0%) had no cases of opioid exposure, and only 4 tracts (1.8%) had no cases of exposure to any substances of abuse during the study period.

Among the 56 census tracts comprising the highest quartile of opioid exposure rates, the per 1000 drug-exposed, opioid-exposed, and NAS rates ± standard deviation (SD) were 173.4 ± 94.3, 88.1 ± 77.1, and 25.8 ± 35.2, respectively, compared to 49.5 ± 50.3, 7.5 ± 6.3, and 1.8 ± 3.9 among infants in the lowest quartile of census tracts. Comparing the highest and lowest quartiles, all differences in exposure rates were significant ($P < 0.001$). On average, tracts in the quartile with the highest rates of opioid exposure were approximately 30% less populous than tracts in the quartile with the lowest opioid exposure rates (mean population ± SD: 2765.7 ± 1332.4 versus 3936.3 ± 1906.9, $P < 0.001$). No difference was detected in the number of births per tract in the 2 quartiles (mean births ± SD: 108.7 ± 68.5 versus 120.5 ± 65.8, $P = 0.36$).

Figure 2A presents a map of opioid exposure rates among the Hamilton County, Ohio newborn population. Shading indicates tracts by exposure rate quartile. However, the fourth quartile was subdivided to indicate tracts with rates exceeding 100 per 1000 births. Figure 2B shows differences in census tract-level opioid exposure rates comparing 2014 to 2016. Between 2014 and 2016, 34 tracts (15.3%) experienced no change in opioid exposure rates, 101 (45.5%) experienced a decline, and 87 (39.2%) experienced an increase, including 41 tracts (18.5%) in which no cases were measured in 2014. On average, tracts experienced a slight 1.5% decline in opioid exposure rates from 2014 to 2016.

Discussion

Using internally developed geocoding technology, this study leveraged population-based EHR data for surveillance and monitoring of drug exposures affecting a countywide newborn population. This analysis included the identification of geographic areas with high and low incidence of intrauterine opioid exposures, as well as areas with noteworthy changes in exposure rates over time. Comparing maps side by side enables identification of additional trends, such as lower incidence tracts with dramatic increases over time, higher incidence tracts with declining rates, or already high incidence tracts with continued increases in exposure rates. The maps also reveal the broad and spanning impact of opioid use in the county. Despite variation in rates from tract to tract, intrauterine exposures were not concentrated in 1 particular neighborhood or subcounty region – both high- and low-income areas were impacted as were both urban and rural regions. The EHR-based data set also was linked with publically available population measures, which led to the discovery that those areas most impacted were significantly less populous (approximately 30% fewer residents) than tracts with lower opioid exposure rates.

This study's EHR-based system provides actionable data that are essential to informing local stakeholders and in shaping health policy to local population needs. Further, this system has several advantages over approaches described previously. Unlike the Tennessee NAS surveillance system, which only captures clinically significant neonatal withdrawal signs,[12] the present system also is able to report on laboratory-verified drug exposures that have the potential to cause neonatal harm. Additionally, the data capture is integrated into existing workflows. Other previous reports have made use of national- and state-level hospital discharge data to track increasing rates of NAS over time and in specific geographies.[3,5,23] Although hospital discharge data sets may represent trends over a much larger geography, the data are frequently subject to multiple year delays, limiting their utility to local stakeholders. Similarly, in Massachusetts, investigators used linked EHRs to identify adverse perinatal outcomes (including intrauterine growth restriction; cardiac, respiratory, neurologic, infectious, hematologic, and feeding/nutrition problems; prolonged hospital stay; and higher mortality) among infants born to mothers with documented substance use disorders.[24] However, time

Table 4. Exposure Characteristics Among 222 Hamilton County, Ohio Census Tracts, 2014–2016

	Minimum	*Median*	*Maximum*	*Mean ± SD*
Drug Exposed (rate per 1000)	0	84.1	642.9	102.9 ± 79.7
Opioid Exposed (rate per 1000)	0	32.9	607.1	40.4 ± 49.2
Neonatal Abstinence Syndrome (rate per 1000)	0	6.1	214.3	11.3 ± 20.8
Births, N	14	112	432	122.1 ± 67.6
Total Population, N	822	3363.5	8316	3622.5 ± 1740.0

SD, standard deviation.

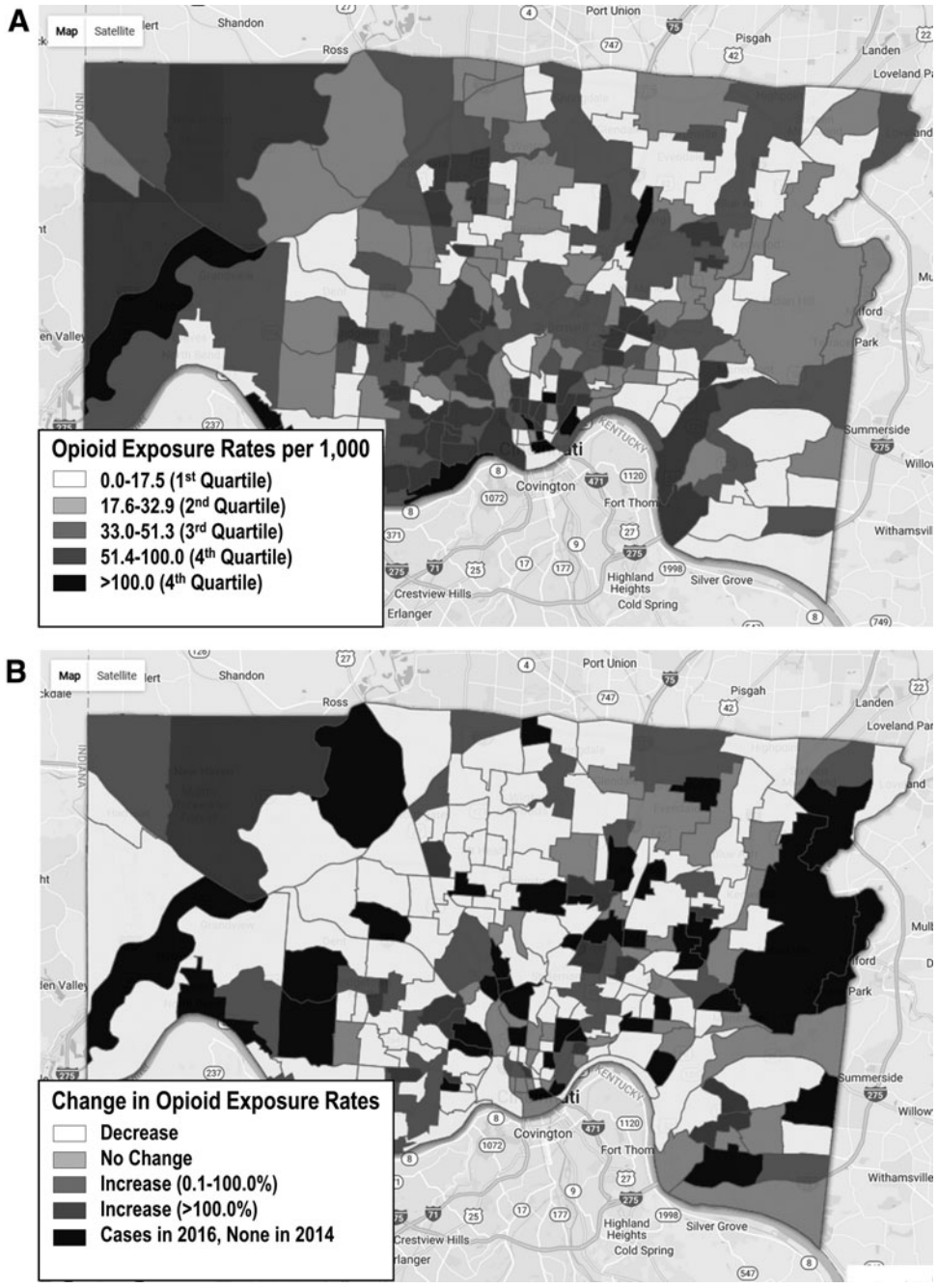

FIG. 2. Maps of intrauterine opioid exposure rates (Figure 2A) and change in opioid exposure rate (Figure 2B), Hamilton County, Ohio, 2014–2016.

requirements for data linkage limit the effectiveness of the particular approach in facilitating surveillance efforts. The present approach can provide more timely and actionable reports in monthly or quarterly intervals. Finally, data in these previous approaches were restricted to the county or zip code level of geographic precision whereas the present study data are available at a far more granular census-tract level, enabling strategic targeting of services and interventions within the jurisdiction of local health departments.

Although the model benefits from the high rate of clinical coverage within Hamilton County (92.5% of newborns), it may not be as reliable for supporting other nearby counties. Within CCHMC's 8-county primary market region – spanning portions of Ohio, Kentucky, and Indiana – county-level clinical coverage ranges from 50%-96% of newborns. Although all exposure cases detected have the potential to inform public health efforts in their respective counties, estimated exposure rates may be less reliable in the counties where a lesser percentage of the resident births are captured by the CCHMC EHR. Still, the model is generalizable to other regions in which a single provider captures a large majority of the relevant patient population, or in regions where multiple providers are able to combine records to establish a population-based data set that can drive surveillance efforts.

For the next stage of work, the study team has begun to schedule automated reports to provide regular, timely data about exposure rates and trends. Additionally, the team has engaged with the county health department to investigate potential geographic relationships between intrauterine opioid exposure, adult opioid overdoses, and sleep-related infant mortality. Other future work will focus on extending surveillance efforts to other perinatal conditions, including preterm birth, congenital malformations, and neonatal mortality, and will integrate individual-level data with additional area-level data sets representing measures of environmental exposures and neighborhood sociodemographic conditions.

Limitations

Although regional physicians and billing coders are trained for consistency in documenting exposure to substances of abuse, like other systems that utilize administrative data, there is potential for variation in coding patterns which would affect incidence calculations. This analysis also is limited by the physician coverage patterns provided by CCHMC physicians. Although an overwhelming majority of regional newborns are captured by the CCHMC EHR, newborns seen exclusively by non–CCHMC physicians in the maternity hospital setting are not represented in the study population. However, this population is estimated to be 7.5% of the county population. A large proportion of the MIDH newborn records were missing race and ethnicity data (34.0%), limiting the usefulness of that particular stratification in the analysis. Finally, approximately 7.6% of records were excluded from analysis because of insufficient geocoding precision. Although there is no obvious bias toward exclusion of exposed versus unexposed infants, these exclusions may have had a modest impact on tract-level exposure rate calculations. However, it is unlikely that the exclusions had a substantial impact on exposure patterns or trends over time.

Conclusions

Surveillance and monitoring data are of critical importance to formulating public health responses and prevention strategies. As demonstrated in this report, secondary use of regional EHR data has the potential to aid in intrauterine opioid exposure and other surveillance efforts without disrupting clinical workflows or placing an additional burden on limited resources. Identification of trends in the rates of exposure to substances of abuse will inform stakeholders and enable targeting of interventions and prevention strategies toward the highest risk populations.

Author Disclosure Statement

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