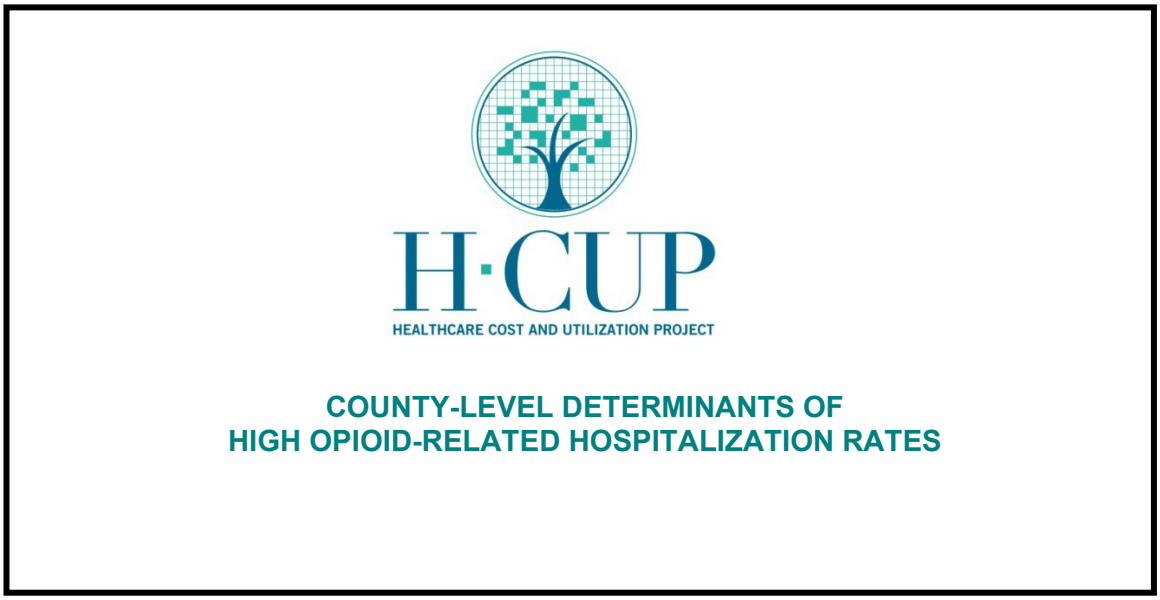

Recommended Citation: Weiss AJ, Owens PL, Karaca Z, Heslin KC, Henke RM, McDermott KW, Pickens G, Barrett ML. County-Level Determinants of High Opioid-Related Hospitalization Rates. ONLINE. January 7, 2022. U.S. Agency for Healthcare Research and Quality. Available: www.hcup-us.ahrq.gov/reports.jsp.

The authors are or were affiliated with the following organizations at the time this manuscript was developed: Agency for Healthcare Research and Quality (Pamela L. Owens, PhD; Zeynal Karaca, PhD; Kevin C. Heslin, PhD), IBM Watson Health (Audrey J. Weiss, PhD; Rachel M Henke, PhD; Kimberly W. McDermott, PhD; Gary Pickens, PhD), and ML Barrett, Inc. (Marguerite L. Barrett, MS). The authors gratefully acknowledge assistance with data management, programming, and statistical support from the following individuals who are or were affiliated with IBM Watson Health at the time this manuscript was developed: Eli Cutler, PhD; Thomas Flottemesch, PhD; Shannon Harrer, MA; Minya Sheng, MS; Halcyon Skinner, PhD, MPH; and Frank Yoon, PhD. The authors also acknowledge Teryl Nuckols, MD, MSHS (RAND Corporation, Cedars-Sinai Medical Center) for sharing topical expertise and insights and Paige Jackson, MS and Mary Beth Schaefer, MS (IBM Watson Health) for providing editorial review of the manuscript.

We also wish to acknowledge the HCUP Partner organizations that contributed to the data used in this study: **Alaska** Department of Health and Social Services, **Alaska** State Hospital and Nursing Home Association, **Arizona** Department of Health Services, **Arkansas** Department of Health, **California** Office of Statewide Health Planning and Development, **Colorado** Hospital Association, **Connecticut** Hospital Association, **District of Columbia** Hospital Association, **Florida** Agency for Health Care Administration, **Hawaii** Laulima Data Alliance, **Hawaii** University of Hawai'i at Hilo, **Illinois** Department of Public Health, **Indiana** Hospital Association, **Iowa** Hospital Association, **Kansas** Hospital Association, **Kentucky** Cabinet for Health and Family Services, **Louisiana** Department of Health, **Maine** Health Data Organization, **Maryland** Health Services Cost Review Commission, **Massachusetts** Center for Health Information and Analysis, **Michigan** Health & Hospital Association, **Minnesota** Hospital Association, **Mississippi** State Department of Health, **Missouri** Hospital Industry Data Institute, **Montana** Hospital Association, **Nebraska** Hospital Association, **Nevada** Department of Health and Human Services, **New Jersey** Department of Health, **New Mexico** Department of Health, **New York** State Department of Health, **North Carolina** Department of Health and Human Services, **North Dakota** (data provided by the Minnesota Hospital Association), **Ohio** Hospital Association, **Oklahoma** State Department of Health, **Oregon** Association of Hospitals and Health Systems, **Oregon** Office of Health Analytics, **Pennsylvania** Health Care Cost Containment Council, **Rhode Island** Department of Health, **South Carolina** Revenue and Fiscal Affairs Office, **South Dakota** Association of Healthcare Organizations, **Tennessee** Hospital Association, **Texas** Department of State Health Services, **Utah** Department of Health, **Vermont** Association of Hospitals and Health Systems, **Virginia** Health Information, **Washington** State Department of Health, **West Virginia** Department of Health and Human Resources, **West Virginia** Health Care Authority, **Wisconsin** Department of Health Services, and **Wyoming** Hospital Association.

ABSTRACT

Background and Objective

Despite substantial geographic variation in opioid-related health outcomes, the role of county-level characteristics in differentiating areas affected by the opioid crisis is largely unknown. This study sought to understand the relationship between opioid-related hospitalization rates and county-level characteristics.

Research Design

Using data from the Agency for Healthcare Research and Quality (AHRQ) Healthcare Cost and Utilization Project (HCUP) 2016 State Inpatient Databases (SID) from 45 states and the District of Columbia, we examined opioid-related hospitalization rates for individuals aged 15 years and older in 2,851 counties. Our outcome was the county population rate of opioid-related hospitalizations, classified as high (top 10 percent) versus low (bottom 20 percent). Covariates included 44 county-level characteristics covering social and economic factors, physical infrastructure of the community, clinical care and healthcare delivery, and opioid public policy. We used logistic regression to model county-level factors associated with high population rates of opioid-related hospitalizations.

Results

The following characteristics were associated with a county having *higher* odds of high population rates of opioid-related hospitalizations: a higher proportion of the population aged 45–64 years, higher property crime rates, a higher proportion of hospitalizations involving chronic conditions, higher opioid prescribing rates, more primary care physicians per capita, more psychiatric hospital beds per capita, more buprenorphine treatment providers per capita, and more Federally Qualified Health Centers. The following characteristics were associated with *lower* odds of a county having high population rates of opioid-related hospitalizations: larger black and Hispanic/Latino populations, more manual labor industry employment, more postsecondary education, greater rurality, and designation as a mental health professional shortage area.

Conclusions

The findings suggest that characteristics of counties may be useful in identifying areas in most need, designing effective interventions, and implementing policies to address the opioid crisis.

INTRODUCTION

Increasing misuse of and addiction to prescription and nonprescription opioids have led to a U.S. opioid epidemic. The opioid-related overdose death rate in 2017 was 3.6 times higher than in 1999 and represented a nearly 10% increase from 2016.[1] In response to this public health crisis, the federal government budgeted a record $4.6 billion in 2018,[2] targeting opioid abuse prevention, treatment, and research.[3]

The Centers for Disease Control and Prevention estimated the total annual economic burden of prescription opioid abuse, dependence, and overdose at $78.5 billion—more than a third of which is attributed to substance use disorder (SUD) treatment and healthcare costs, including inpatient hospital utilization.[4] Between 2005 and 2014, the national rate of opioid-related hospitalizations increased by 64.1 percent,[5] and by 2016 it was 296.9 per 100,000 population.[6]

There is extensive geographic variation in opioid-related hospital utilization.[5,7,8] In 2014, the rate of opioid-related hospitalizations varied more than five-fold across states—from 72.7 hospitalizations per 100,000 population in Iowa to 403.8 in Maryland.[5] Even within states, patterns of opioid-related hospital use vary widely across rural and urban areas and counties.[7,8] Despite this geographic variation, little is known about differences in characteristics of counties with high versus low rates of opioid-related hospitalization. Previous work has focused on variation in other opioid-related outcomes, including opioid abuse,[9] fatal opioid intoxication,[10] and emergency department visits for prescription opioid overdose.[11] Few studies have examined the relationship between opioid-related outcomes and substate area-level predictors, and all were limited in focus to 1 state.[7,12,13]

The purpose of this study was to identify factors associated with counties with high population rates of opioid-related hospitalizations, which can inform decisions on where and how to target county-level interventions aimed at reducing exposure to opioids and increasing access to treatment. Hospitalizations are a key component of the continuum of services provided for SUD, particularly for individuals who require crisis care. We focused on hospital use involving any opioid-related diagnosis (including abuse/dependence, adverse effects, and poisoning/self-harm) to fully encapsulate the resource use and burden of the opioid epidemic in the hospital setting. In addition, preliminary state-level analyses (not shown) suggested that diagnosis codes for adverse effects and poisoning of opioids may be used interchangeably.

Conceptual Framework

The link between community factors and healthcare utilization is well established,[14] specifically at the county level.[15,16] For this study, we drew from several conceptual frameworks of social factors related to healthcare utilization[17,18,19] to select 4 conceptual domains of particular relevance to opioid-related hospitalizations. *Social and economic factors* include race, ethnicity, age, and sex distributions as well as economic stability, employment, education, and social cohesion. Several studies found that certain demographic groups are particularly likely to be prescribed opioids or to misuse opioids (see Wright et al.[20] for a review). Research has demonstrated that higher rates of poverty and income inequality are related to poor health outcomes[21] and more drug events[22] and that higher educational attainment and social capital are associated with lower likelihood of opioid abuse[23] or drug overdose.[24] *Physical infrastructure of the community* represents physical conditions and safety. Environmental factors such as urbanicity have been linked to higher rates of opioid prescribing[25] and higher rates of opioid-related misuse and overdose.[26] *Clinical care and healthcare delivery* refers to both the population health status (e.g., prevalence of conditions commonly treated with opioids)

and healthcare coverage and treatment availability (e.g., access to preventive care and treatment for SUDs). *Opioid-related policy factors* capture opioid supply and state laws and regulations targeting opioid prescribing and availability of opioid overdose reversal drugs.

METHODS

Data Sources

We used 2016 inpatient discharge data from nonfederal community acute care hospitals in 45 states and the District of Columbia obtained from the Healthcare Cost and Utilization Project (HCUP)[27] State Inpatient Databases (SID),[28] encompassing 26.2 million discharges for patients from 2,851 counties in the United States (90.6 percent of U.S. counties). We excluded 5 states: Delaware and New Hampshire (2016 SID were not available at the time of the analysis); Georgia (restrictions on reporting of adverse effects of opiates); and Alabama and Idaho (no statewide data collection of inpatient discharges). We used the U.S. Census American Community Survey (Table S0101, Age and Sex, 2016, 5-Year Estimates) to determine the county population of 15+-year-olds.

We obtained data on county-level characteristics from a number of external data sources, much of which is now available through the AHRQ's Social Determinants of Health database[29] (Table 1). Opioid-related policy data were at the state rather than county level. With a few exceptions, data from other sources were based on calendar year 2016.

Study Population

We included discharges for patients aged 15 years and older, regardless of payer. We defined location on the basis of the county of the patient's residence and included only discharges for patients treated near their residence (i.e., hospital was located in the same state as patient residence or within 100 miles of patient residence in another state). Distance was calculated using the centroids for the patient's and hospital's ZIP Codes. We excluded the few discharges that were missing patient county (0.8%). To avoid double counting, we excluded discharges for patients transferred to the hospital from another acute care facility (6.9%). Focusing on acute care for patients with opioid-related disorders, we limited the study to discharges at community hospitals, excluding long-term acute care and rehabilitation hospitals.

Outcome of Interest

Our outcome of interest was the county population rate of opioid-related hospitalizations identified using any-listed (principal or secondary) diagnosis of opioid abuse/dependence, opioid adverse effects, opioid poisoning/self-harm, or unspecified opioid use. Specific codes used are provided in the Appendix, Table A-1. Rates are reported per 100,000 population.

We used the population rate of opioid-related hospitalizations to classify counties as low, moderate, or high rate by comparing each county rate with the rate for the respective U.S. census region (Table 2). We used the regional population rate, rather than the national rate, because preliminary analyses revealed substantial differences in the range and distribution of opioid hospitalization population rates across regions. Using a regional comparative point ensured an adequate representation of counties designated as high- and low-rate areas in each region. We classified the top 10% of counties with the highest rates in each region as *high-rate* areas (n = 283) and the bottom 20% of counties with the lowest rates in each region as *low-rate* areas (n = 568). The middle 70% of counties in each region were designated as *moderate-rate* areas (n = 2,000). Using the 10% (top) and 20% (bottom) thresholds followed observed

inflection points in the data distribution, ensuring sufficient representation of counties clustered at the lower end of the distribution, as well as adequate separation of the high- and low-rate areas.

County-Level Factors

We considered a wide range of county-level factors in the 4 domains previously described: (1) social and economic factors, (2) physical infrastructure of the community, (3) clinical care and healthcare delivery, and (4) opioid-related policy factors. After reviewing numerous concepts and variables within each domain, we selected 44 variables relevant to the opioid epidemic, on the basis of existing literature, clinical judgment, variable properties (missingness, correlations with other variables, distribution), and preliminary analyses of the association with opioid hospitalization rate. Table 1 lists the 44 selected covariates and data sources. Data were linked at the county level using Federal Information Processing Standards (FIPS) codes.

Three variables had missing data for some counties. Opioid prescribing rate, which measures prescription fills at retail pharmacies, was missing for 166 counties, of which 145 had no pharmacies and so were assigned a zero rate. For the remaining counties with missing information (21 counties missing opioid prescribing rate [0.7% of the sample], 2 counties missing religious congregation affiliation, 1 county missing property crime rate), we assigned an imputed value based on the average of adjacent counties or used the state average when adjacent county data were unavailable.

Data Analyses

We used a 2-step modeling approach. First, we used least absolute shrinkage and selection operation (lasso) methods to identify the most important factors to include in the model. Unlike stepwise selection methods, the lasso method reduces prediction error and provides variable selection, leading to a more interpretable model and better prediction error performance.[30] Shrinking the absolute size of regression coefficients drives coefficients for noninformative covariates to zero. We modeled the relationship between all covariates and the dichotomous county-level outcome of the population rate of opioid-related hospitalizations (1 = high rates and 0 = low rates) (n = 851 counties). We selected covariates for our final model starting with the variables deemed informative in the lasso model as initial guidance, and then removing additional variables because of concerns such as multicollinearity and lack of variance across counties (e.g., state-level variables) to ensure the final covariate set was analytically and conceptually sound.

After finalizing the set of covariates, we used logistic regression to estimate the association between these covariates and counties with high population rates of opioid-related hospitalizations. We report results using odds ratios, which can be interpreted as the increase (decrease) in the odds of a county having high population rates of opioid-related hospitalizations on the basis of a unit change in the covariate. For continuous variables, the scale of the covariate affects the odds ratio and its interpretation, because not all covariates are scaled identically. As a sensitivity analysis, we also ran the model including region as a covariate and obtained similar results.

The Agency for Healthcare Research and Quality (AHRQ) human protections administrator has determined this project does not constitute research involving human subjects; thus, it was not required by the Agency to be submitted to an institutional review board (IRB).

Table 1. County-Level Covariates: Description, Year, and Data Source

Variable	Year	Source*
Social and economic factors		
Race distribution (% White, Black, American Indian/Alaska Native, Asian/Pacific Islander, Other/2 or more races)	2016	A
Hispanic, Latino (%)	2016	A
Age distribution (% 15–17 years, 18–44 years, 45–64 years, 65+ years)	2016	A
Sex distribution (% female)	2016	A
Religious congregation affiliation in population (%)	2010	B
Employment in manual labor industry occupations among employed population aged 16 years and older (%)	2016	A
Households that are vacant (%)	2016	A
Single-occupant households (%)	2016	A
Poverty in population (%)	2016	A
Gini index of income inequality (0–100)	2016	A
Associate's degree or higher among population aged 25 years and older (%)	2016	A
Physical infrastructure of the community		
Population density per square mile	2016	A
Urban/rural designation	2016	C
Reported property crime rate per 1,000 population	2014	D
Clinical care and healthcare delivery		
Access and quality of healthcare		
Medicare enrollment in noninstitutionalized population (%)	2016	A
Medicaid enrollment in noninstitutionalized population (%)	2016	A
Medicaid managed care enrollment among Medicaid enrollees (%)	2016	E
Uninsured in noninstitutionalized population (%)	2016	A
Primary care physicians per 1,000 population	2015	F
Federally Qualified Health Centers (n)	2016	F
Teaching hospitals (n)	2016	G
Pharmacy density (number of pharmacies per square mile)	2016	H
Access and quality of mental health and substance abuse treatment		
Psychiatric physicians per 1,000 population	2015	F
Psychiatric hospital beds per 1,000 population	2016	G
Mental health professional shortage area designation (whole county or partial county/no designation)	2016	F
Buprenorphine treatment providers per 1,000 population	2018	I
Hospitalizations in the county with select comorbidities†		
Hospitalizations with chronic pulmonary disease (%)	2016	J

Variable	Year	Source*
Hospitalizations with diabetes with chronic complications (%)	2016	J
Hospitalizations with renal failure (%)	2016	J
Hospitalizations with rheumatoid arthritis/collagen vascular diseases (%)	2016	J
Opioid-related policy factors‡		
Opioid prescribing rate (excluding medication-assisted treatment) per 100 residents per year	2016	K
Pain management prescribing restrictions: at least 2 restrictions on Schedule II drugs, state-level (yes/no)	2016	L
Pain management prescribing restrictions: at least 1 restriction on Schedule III drugs, state-level (yes/no)	2016	L
Prescribers required to check prescription drug monitoring program (PDMP) before prescribing controlled substances, state-level (yes/no)	2016	M
Naloxone prescriptions authorized to third parties, state-level (authorized full year or authorized only partial year/not authorized)	2016	M
Buprenorphine prescription payments paid out of pocket, state-level (%)	2016	N
Law enforcement illicit drug seizures tested and confirmed to contain fentanyl, state-level (n)	2016	O

*Data sources:

A: Census Bureau American Community Survey (https://data.census.gov/cedsci/)

B: Association of Statisticians of American Religious Bodies U.S. Religion Census (www.usreligioncensus.org)

C: U.S. Department of Agriculture, Economic Research Service (www.ers.usda.gov/data-products/rural-urban-continuum-codes/)

D: Inter-university Consortium for Political and Social Research Uniform Crime Reporting Program Data (www.icpsr.umich.edu)

E: Decision Resources Group Managed Market Surveyor (https://decisionresourcesgroup.com/solutions)

F: Area Health Resources File (https://data.hrsa.gov/topics/health-workforce/ahrf)

G: American Hospital Association Annual Survey (www.ahadata.com/aha-annual-survey-database-asdb/)

H: Census Bureau County Business Patterns (www.census.gov/programs-surveys/cbp.html)

I: Substance Abuse and Mental Health Services Administration Buprenorphine Treatment Practitioner Locator (www.samhsa.gov/medication-assisted-treatment/physician-program-data/treatment-physician-locator)

J: Healthcare Cost and Utilization Project State Inpatient Databases (https://www.hcup-us.ahrq.gov/sidoverview.jsp)

K: Centers for Disease Control and Prevention U.S. Opioid Prescribing Rate Maps (www.cdc.gov/drugoverdose/maps/rxcounty2016.html)

L: National Alliance for Model State Drug Laws Overview of Pain Management and Prescribing Policies (https://namsdl.org/wp-content/uploads/Overview-of-State-Pain-Management-and-Prescribing-Policies-1.pdf)

M: Prescription Drug Abuse Policy System (https://pdaps.org)

N: IQVIA Institute for Human Data Science Report: Use of Opioid Recovery Medications (https://www.iqvia.com/-/media/iqvia/pdfs/institute-reports/use-of-opioid-recovery-medications.pdf?_=1639076836896)

O: amfAR Opioid & Health Indicators Database (https://opioid.amfar.org/indicator/fentanyl_seize)

†Comorbidities were defined using the Healthcare Cost and Utilization Project (HCUP) Elixhauser Comorbidity Software (beta version v2018.1) modified to only use diagnoses that were present on admission.

‡All opioid-related policy factors consist of state-level data, with the exception of opioid prescribing rate, which was county-level data.

RESULTS

Population Rate of Opioid-Related Hospitalizations

Overall, the average population rate of opioid-related hospitalizations ranged from 127.7 per 100,000 population in counties with low rates to 632.6 in counties with high rates (Table 2). By region, the average rate per 100,000 population ranged from 299.4 in the West to 438.0 in the Northeast. Population rates for opioid-related hospitalizations differed by specific opioid diagnosis. The population rate of hospitalizations for unspecified opioid use was 1.6 times higher in counties with high overall rates than in counties with low rates. In comparison, the population rate of hospitalizations for opioid abuse/dependence was 6.8 times higher in counties with high overall rates than in counties with low rates.

Table 2. Population Rates of Opioid-Related Hospitalizations per 100,000 Population, by County Classification, 2016*

Characteristic	All Counties (N = 2,851)	Counties with Low Rates (n = 568)	Counties with Moderate Rates (n = 2,000)	Counties with High Rates (n = 283)	Ratio of County Population Rates: High vs. Low
All opioid-related hospitalizations	**339.1**	**127.7**	**301.1**	**632.6**	**5.0**
Geographic region					
Northeast (n = 207)	438.0	221.2	420.8	721.9	3.3
Midwest (n = 1,055)	360.7	79.2	258.3	561.7	7.1
South (n = 1,186)	300.9	102.9	280.2	749.8	7.3
West (n = 403)	299.4	113.3	274.8	608.8	5.4
Opioid diagnosis type					
Abuse/dependence	227.7	69.0	194.3	470.2	6.8
Adverse effect	73.1	41.0	70.8	101.7	2.5
Poisoning/self-harm	35.6	15.9	33.1	57.9	3.6
Unspecified use	2.7	1.7	2.8	2.7	1.6

*Rate is per 100,000 population. Some discharges included more than 1 opioid diagnosis type. For this table, discharges were categorized into only 1 opioid diagnosis type category using the following hierarchy: abuse/dependence, adverse effect, poisoning/self-harm, unspecified use.

Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) from 45 states and the District of Columbia, 2016.

Bivariate Analysis

Table 3 shows the county classification based on population rates of opioid-related hospitalizations (low, moderate, or high) and county characteristics. From a social and economic perspective, counties with high population rates of opioid-related hospitalizations (relative to counties with low rates) exhibited the following population characteristics: lower proportion of Hispanic/Latino individuals, less likely to be affiliated with religious congregations, less likely to be employed in manual labor, smaller percentage of vacant households, and more likely to live in poverty and in areas of income inequality. In terms of physical location and infrastructure, counties with high population rates of opioid-related hospitalizations were more likely located in large metropolitan areas and had higher property crime rates compared with counties with low rates. Relative to counties with low rates, counites with high population rates of opioid-related hospitalizations were more likely to have a healthcare infrastructure to support treatment of opioid use disorders (i.e., higher rates of Medicare, Medicaid, and Medicaid

managed care enrollment; more primary care physicians per capita; more Federally Qualified Health Centers [FQHCs]; more pharmacies per square mile; more psychiatrists, psychiatric hospital beds, and buprenorphine treatment providers per capita; more likely to have a teaching hospital; and less likely to be a mental health professional shortage area). In addition, counties with high population rates of opioid-related hospitalizations had a higher proportion of hospitalizations with chronic pulmonary disease, diabetes with chronic complications, and renal failure. In terms of opioid-related policy factors, counites with high population rates of opioid-related hospitalizations had higher opioid prescribing rates than counties with low rates and were more likely to have at least one of the following: restrictions for prescribing Schedule II controlled substances, requirements for prescribers to check the prescription drug monitoring program (PDMP), naloxone prescriptions authorized to third parties, lower out-of-pocket share of buprenorphine prescription payments, and a higher number of law enforcement seizures of fentanyl.

Table 3. Bivariate Association of County Classification Based on Population Rates of Opioid-Related Hospitalizations and County Characteristics, 2016

County Characteristic (mean value across counties or percentage of counties)	Counties with Low Rates (n = 568)	Counties with Moderate Rates (n = 2,000)	Counties with High Rates (n = 283)	Low Rate vs. High Rate Ratio	Low Rate vs. High Rate *P*-value
Social and economic factors					
Race (% of population)					
White	83.9	84.7	85.4	1.02	0.213
Black	7.2	7.8	6.7	0.93	0.541
American Indian, Alaska Native American; Asian, Pacific Islander; and Other (2 or more races)	8.9	7.5	7.9	0.90	0.252
Hispanic, Latino (% of population)	13.5	8.4	6.1	0.46	<.0001
Age, y (% of population)					
15–17	4.9	4.9	4.7	0.97	0.026
18–44	39.9	39.5	39.9	1.00	0.913
45–64	33.4	34.0	34.1	1.02	0.001
65+	21.8	21.7	21.3	0.98	0.118
Female (% of population)	49.0	50.1	50.4	1.03	<.0001
Religious congregation affiliation in population (%)	56.0	51.0	44.7	0.80	<.0001
Manual labor industry employment in employed population aged 16 years and older (%)	30.0	28.2	26.6	0.89	<.0001
Households that are vacant (%)	20.8	17.6	16.7	0.80	<.0001
Single-occupant households (%)	28.5	28.0	29.0	1.02	0.123
Poverty in population (%)	15.7	15.8	18.5	1.18	<.0001
Gini index of income inequality (0-100)	44.4	44.2	45.2	1.02	0.003

County Characteristic (mean value across counties or percentage of counties)	Counties with Low Rates (n = 568)	Counties with Moderate Rates (n = 2,000)	Counties with High Rates (n = 283)	Low Rate vs. High Rate Ratio	Low Rate vs. High Rate *P*-value
Associate's degree or higher in population aged 25 years and older (%)	29.0	29.9	28.7	0.99	0.658
Physical infrastructure of the community					
Population density per square mile	128.7	275.7	596.9	4.64	0.002
Urban/rural population (% of counties)					
Metro	17.6	39.4	54.8	3.11	<.0001
Rural, adjacent to metro	30.5	33.4	25.4	0.84	0.128
Rural, remote	51.9	27.3	19.8	0.38	<.0001
Property crime rate per 1,000 population	13.6	17.7	22.3	1.64	<.0001
Clinical care and healthcare delivery					
Access and quality of healthcare					
Medicare enrollment in noninstitutionalized population (%)	19.9	20.3	20.9	1.05	0.004
Medicaid enrollment in noninstitutionalized population (%)	18.0	19.4	23.1	1.29	<.0001
Medicaid managed care enrollment among Medicaid enrollees (%)	53.5	59.4	67.0	1.25	<.0001
Uninsured in noninstitutionalized population (%)	13.5	11.7	11.2	0.84	<.0001
Primary care physicians per 10,000 population	3.8	4.7	5.3	1.40	<.0001
Federally Qualified Health Centers (no.)	1.1	2.5	5.3	4.86	<.0001
Any teaching hospital (% of counties)	8.1	21.3	32.5	4.01	<.0001
Pharmacy density (no. of pharmacies per 10 square miles)	0.3	0.6	1.2	4.00	0.024
Access and quality of mental health and substance use care					
Psychiatrists per 10,000 population	0.2	0.4	0.6	2.50	<.0001
Psychiatric hospital beds per 10,000 population	0.6	0.8	1.4	2.46	0.001

County Characteristic (mean value across counties or percentage of counties)	Counties with Low Rates (n = 568)	Counties with Moderate Rates (n = 2,000)	Counties with High Rates (n = 283)	Low Rate vs. High Rate Ratio	Low Rate vs. High Rate *P*-value
Mental health professional shortage area, whole county (% of counties)	84.9	64.0	51.2	0.60	<.0001
Buprenorphine treatment providers per 10,000 population	0.3	0.5	1.0	3.33	<.0001
Hospitalizations in the county with select comorbidities (%)					
Chronic pulmonary disease	17.5	20.6	24.3	1.39	<.0001
Diabetes with chronic complications	9.0	10.3	11.9	1.31	<.0001
Renal failure	11.9	13.1	13.9	1.17	<.0001
Rheumatoid arthritis/collagen vascular diseases	3.0	3.0	3.0	1.01	0.856
Opioid-related policy factors					
Opioid prescribing rate per 100 residents per year	49.7	72.9	96.3	1.94	<.0001
State-level policies					
Pain management prescribing restrictions, at least 2 Schedule II restrictions (% of counties)	47.5	65.4	67.5	1.42	<.0001
Pain management prescribing restrictions, at least 1 Schedule III restriction (% of counties)	62.1	69.0	68.6	1.10	0.066
Prescribers required to check prescription drug monitoring program before prescribing controlled substances (% of counties)	18.8	31.6	53.7	2.85	<.0001
Naloxone prescriptions authorized to third parties, full year (% of counties)	68.5	75.3	81.3	1.19	<.0001
Out-of-pocket share of buprenorphine prescription payments (%)	12. 5	12.4	10.9	0.88	<.0001
Law enforcement seizures of fentanyl (no.)	286.6	653.2	1,420.6	4.96	<.0001

Notes: Unless specified as "% of counties," the values presented are the means for all counties classified as having low, moderate, or high population rates of opioid-related hospitalizations. For the characteristics specified as "% of counties," the values presented are the percentage of counties classified as low, moderate, or high rate that have the specified characteristic.

Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) from 45 states and the District of Columbia, 2016.

Multivariate Analysis

Table 4 shows our multivariate analysis results, focusing on a comparison of counties with high population rates of opioid-related hospitalizations to counties with low rates. In the adjusted model, the following county characteristics were associated with *lower* odds of a county having high (vs. low) rates: larger percentage of black and Hispanic/Latino residents (odds ratio [OR]: 0.919, 95% confidence interval [CI]: 0.890, 0.949; OR: 0.969, 95% CI: 0.944, 0.995, respectively), larger percentage of the population employed in the manual labor industry (OR: 0.869, 95% CI: 0.807, 0.936), larger percentage of the population with an associate's degree or higher (OR: 0.892, 95% CI: 0.831, 0.957), being located in rural areas (rural, adjacent to metro area, OR: 0.125, 95% CI: 0.053, 0.296; rural, remote area, OR: 0.436, 95% CI: 0.208, 0.912), and designation as a mental health professional shortage area (OR: 0.518, CI: 0.270, 0.993).

Table 4. Multivariate Results: Association of County Population Rates of Opioid-Related Hospitalizations and County Characteristics, 2016 (n = 851)

County Characteristic	Odds Ratio	95% CI
Social and economic factors		
Race		
White (reference)	—	—
Black	0.919	0.890–0.949
American Indian, Alaska Native American; Asian, Pacific Islander; and Other (2 or more races)	1.008	0.976–1.042
Hispanic, Latino	0.969	0.944–0.995
Age, y		
15–17	1.415	0.961–2.085
18–44 (reference)	—	—
45–64	1.181	1.054–1.323
65+	1.032	0.948–1.124
Female	1.049	0.900–1.224
Religious congregation affiliation in population	0.991	0.974–1.008
Manual labor industry employment in employed population aged 16 years and older	0.869	0.807–0.936
Poverty in population	1.052	0.976–1.133
Associate's degree or higher in population aged 25 years and older	0.892	0.831–0.957
Physical infrastructure of the community		
Urban/rural population		
Metro (reference)	—	—
Rural, adjacent to metro	0.125	0.053–0.296
Rural, remote	0.436	0.208–0.912
Property crime rate per 1,000 population	1.048	1.019–1.079
Clinical care and healthcare delivery		
Access and quality of care		
Uninsured in noninstitutionalized population	0.950	0.878–1.029

County Characteristic	Odds Ratio	95% CI
Primary care physicians per 1,000 population	1.013	1.003–1.023
Federally Qualified Health Centers	1.088	1.026–1.155
Access and quality of mental health and substance use care		
Psychiatric hospital beds per 1,000 population	3.472	1.442–8.359
Mental health professional shortage area, whole county	0.518	0.270–0.993
Buprenorphine treatment providers per 1,000 population	1.034	1.009–1.059
Hospitalizations in the county with select comorbidities		
Chronic pulmonary disease	1.246	1.153–1.346
Diabetes with chronic complications	1.168	1.030–1.324
Renal failure	1.108	0.994–1.234
Rheumatoid arthritis/collagen vascular diseases	0.849	0.667–1.081
Opioid-related policy factors		
Opioid prescribing rate per 100 residents per year	1.017	1.008–1.025
State-level policies		
Pain management prescribing restrictions, at least 2 Schedule II restrictions	1.750	0.970–3.158
Prescribers required to check prescription drug monitoring program before prescribing controlled substances	0.767	0.401–1.467
Naloxone prescriptions authorized to third parties, full year	0.753	0.368–1.541

Notes: The odds ratio compares counties with high population rates of opioid-related hospitalizations to counties with the low rates. The following four covariates, which were reported in Table 3 in terms of the percentage of counties with the characteristic, were included in the logistic regression model as dichotomous (0/1) variables: mental health professional shortage area, whole county; pain management prescribing restrictions, at least 2 Schedule II restrictions; prescribers required to check prescription drug monitoring program before prescribing controlled substances; and naloxone prescriptions authorized to third parties, full year.

Source: Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), State Inpatient Databases (SID) from 45 states and the District of Columbia, 2016.

Conversely, after controlling for other characteristics, the following characteristics were associated with *higher* odds of a county having high (vs. low) population rates of opioid-related hospitalizations: higher proportion of the population aged 45–64 years (OR:1.181, 95% CI: 1.054, 1.323), higher property crime rates (OR: 1.048, 95% CI: 1.019,1.079), more primary care physicians per capita (OR: 1.013, 95% CI: 1.003, 1.023), more FQHCs (OR: 1.088, 95% CI: 1.026, 1.155), more psychiatric hospital beds per capita (OR: 3.472, 95% CI: 1.442, 8.359), more buprenorphine treatment providers per capita (OR: 1.034, 95% CI: 1.009, 1.059), higher proportion of hospitalizations with chronic pulmonary disease or diabetes with chronic complications (OR: 1.246, 95% CI: 1.153, 1.346 and OR: 1.168, 95% CI: 1.030, 1.324, respectively), and higher opioid prescribing rates (OR=1.017, 95% CI=1.008, 1.025).

DISCUSSION

Counties with high population rates of opioid-related hospitalizations differed from counties with low rates on factors in all 4 domains we examined: social and economic factors, physical infrastructure of the community, clinical care and healthcare delivery, and opioid-related policies. This is one of the first studies to our knowledge to examine the relationship between a wide array of county-level factors and opioid-related hospitalizations across most of the United States.

Demographically, we found an association between counties with high rates of opioid-related hospitalizations and lower black and Hispanic/Latino populations and a higher population aged 45–64 years. This is consistent with statistics from the Centers for Disease Control and Prevention (CDC): in 2015, nonfatal opioid-related hospitalizations were highest among those aged 45–64 years; in 2016, reported opioid misuse was highest among whites, and rates of prescription opioid overdose deaths were highest among those aged 45–54 years and non-Hispanic whites.[21] Our results also indicated an inverse relationship between population education level and opioid-related hospitalizations. Platts-Mills et al. (2012)[31] found that patients with lower levels of education were more likely to receive opioids in the emergency department than were those with higher education.

One unexpected finding in our study was that counites with high population rates of opioid-related hospitalizations had a lower percentage of the population employed in manual labor industries, even after controlling for a number of other county characteristics. A 2017 study by Cerdá et al.[7] found higher hospital discharge rates for prescription opioid poisoning in areas of California with more manual labor industries. Our differing result was surprising because employees in manual labor industries are more likely to have work-related injuries that might be treated with opioids.[32] Because opioids now are commonly prescribed for chronic conditions that afflict all employees, this relationship may no longer exist. Further, we examined all types of opioid-related hospitalizations, most of which are abuse/dependence, whereas Cerdá et al.'s 2017 study[7] focused on prescription opioid poisonings. More research is needed to explore the relationship between manual labor industries and opioid outcomes.

We found that counties with high population rates of opioid-related hospitalizations were located in urban areas, consistent with CDC statistics on opioid misuse and opioid overdose deaths.[21] Hester et al. (2012)[25] found that areas of New Hampshire with no fatal prescription opioid poisonings had more rural populations than areas with fatal poisonings. People in urban areas have greater proximity access to the healthcare system when experiencing opioid-related complications or overdose. Indeed, we found greater access to healthcare professionals and facilities in counties with high population rates of opioid-related hospitalizations. We also found a link between the number of FQHCs and these counties, presumably because FQHCs enable needed access to inpatient care. Longitudinal research is necessary to tease apart the mechanisms of this relationship. Our findings also indicated that counties with high population rates of opioid-related disorders had higher community property crime rates. A 2013 Cerdá et al. study[13] found higher fatality rates involving opioid analgesic overdoses in neighborhoods of New York City with lower-quality built environments.

We found that counties with a higher percentage of hospitalizations involving chronic pulmonary disease and diabetes with chronic complications were more likely to be counties with high population rates of opioid-related hospitalizations. This result was expected because opioids may be prescribed for these conditions, but are complex to administer because of decreased kidney function and increased risk for respiratory complications.[33,34] Higher rates of these conditions may also be indicative of communities that do not adequately address the problem of ambulatory care sensitive conditions[35]; thus, these communities also may be less equipped to address opioid misuse. Unlike the 2017 Cerdá et al. study,[7] we found no link between arthritis and opioid hospitalizations.

In terms of opioid-related policies, we found an association between opioid hospitalizations and opioid supply (as measured by county-level opioid prescribing rate), but not any of the state-level opioid policies. Prior research[36] found that implementation of a PDMP was associated with reduced opioid prescribing. However, evidence that PDMP implementation affects opioid-

related health outcomes is inconsistent.[37,38,39] Although one study found that PDMP mandatory-access provisions were associated with reduced treatment admissions related to prescription drug abuse,[39] we found no link between state-level requirements for prescribers to check the PDMP and opioid-related hospitalizations. The lack of a statistically significant association could be due to our inability to examine the timing, extent, and fidelity to PDMP implementation.

The association we found between counties with high rates of opioid-related hospitalizations and buprenorphine provider availability was significant and policy relevant. As part of medication-assisted therapy, buprenorphine is an evidence-based treatment for opioid use disorder and may be preferred to methadone and naltrexone for its convenience and effectiveness.[40] However, there is a dearth of providers with a waiver to provide this treatment.[41] Our findings suggest that providers in areas with greatest need are more likely to apply for buprenorphine waivers, that waivered providers are attracted to areas with greatest need, or both.

Limitations and Strengths

Our study had several important limitations. This was a cross-sectional study and was not designed to assess the interrelated connectedness of all of the factors and population rates of opioid-related hospitalization or opioid use disorders. Because we measured covariates and outcomes at a single point in time, determining the temporal order of the associations was not possible. Although we included many factors related to important dimensions thought to be associated with opioid-related hospitalizations, there also are unobservable factors that we could not measure. Even the characteristics we included may not completely capture intended constructs. For example, our measure of buprenorphine-waivered physicians may not accurately capture access to buprenorphine treatment because not all licensed providers actively provide this treatment, and many restrict their patient panel. The opioid-related policies we examined were at the state level. Variation in the implementation of these state policies across counties could have weakened observed relationships. Finally, most hospitalizations in our sample (83.7%) were identified by a secondary opioid-related diagnosis. This meant that we included hospitalizations that were primarily for other non-opioid-related reasons or for non-opioid-related treatment for patients with opioid dependence. We deliberately chose this approach to be comprehensive in our identification of opioid-related hospitalizations. In 2016, hospitals were in the first year of implementing the *International Classification of Diseases, Tenth Revision, Clinical Modification* coding system, and coding distinctions among different opioid-related codes may not be consistently or uniformly reported.[42] A notable strength of our study was the inclusion of nearly all U.S. states and the District of Columbia and our examination of county-level data including a variety of potential predictors of opioid-related hospitalizations.

Conclusions

Results from this study demonstrate that substantial county-level variation in opioid-related hospitalization rates exists and that counties with high population rates differ in a number of ways from counties with low rates. We found that the odds of a county having high population rates of opioid-related hospitalizations were *higher* in counties with a higher proportion of adults aged 45–64 years, more property crime, and higher opioid prescribing rates, and *lower* in counties with a higher proportion of black and Hispanic/Latino populations and with more postsecondary education, manual labor industry employment, and rurality. These findings suggest that particular communities may be at greater risk of poor opioid-related outcomes and that the design and implementation of opioid-related interventions should be targeted at the local level. Our findings also suggest that policymakers, particularly in areas with high rates of opioid-related hospitalizations, should continue efforts to regulate opioid supply while balancing

legitimate need for opioids in these communities. Future research should use a longitudinal design to understand factors that differentiate counties that have successfully reduced (or slowed the increase of) opioid-related hospitalizations over time.

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APPENDIX

Table A-1. ICD-10-CM Codes Defining Opioid-Related Diagnoses

ICD-10-CM Code	Description
	Opioid Abuse/Dependence
F11.10	Opioid abuse, uncomplicated
F11.120	Opioid abuse with intoxication, uncomplicated
F11.121	Opioid abuse with intoxication delirium
F11.122	Opioid abuse with intoxication with perceptual disturbance
F11.129	Opioid abuse with intoxication, unspecified
F11.14	Opioid abuse with opioid-induced mood disorder
F11.150	Opioid abuse with opioid-induced psychotic disorder with delusions
F11.151	Opioid abuse with opioid-induced psychotic disorder with hallucinations
F11.159	Opioid abuse with opioid-induced psychotic disorder, unspecified
F11.181	Opioid abuse with opioid-induced sexual dysfunction
F11.182	Opioid abuse with opioid-induced sleep disorder
F11.188	Opioid abuse with other opioid-induced disorder
F11.19	Opioid abuse with unspecified opioid-induced disorder
F11.20	Opioid dependence, uncomplicated
F11.220	Opioid dependence with intoxication, uncomplicated
F11.221	Opioid dependence with intoxication delirium
F11.222	Opioid dependence with intoxication with perceptual disturbance
F11.229	Opioid dependence with intoxication, unspecified
F11.23	Opioid dependence with withdrawal
F11.24	Opioid dependence with opioid-induced mood disorder
F11.250	Opioid dependence with opioid-induced psychotic disorder with delusions
F11.251	Opioid dependence with opioid-induced psychotic disorder with hallucinations
F11.259	Opioid dependence with opioid-induced psychotic disorder, unspecified
F11.281	Opioid dependence with opioid-induced sexual dysfunction
F11.282	Opioid dependence with opioid-induced sleep disorder
F11.288	Opioid dependence with other opioid-induced disorder
F11.29	Opioid dependence with unspecified opioid-induced disorder
	Opioid Adverse Effects
T40.0X5A	Adverse effect of opium, initial encounter
T40.0X5D	Adverse effect of opium, subsequent encounter
T40.0X5S	Adverse effect of opium, sequela
T40.2X5A	Adverse effect of other opioids, initial encounter
T40.2X5D	Adverse effect of other opioids, subsequent encounter
T40.2X5S	Adverse effect of other opioids, sequela
T40.3X5A	Adverse effect of methadone, initial encounter
T40.3X5D	Adverse effect of methadone, subsequent encounter

ICD-10-CM Code	Description
T40.3X5S	Adverse effect of methadone, sequela
T40.4X5A	Adverse effect of synthetic narcotics, initial encounter
T40.4X5D	Adverse effect of synthetic narcotic, subsequent encounter
T40.4X5S	Adverse effect of synthetic narcotic, sequela
T40.605A	Adverse effect of unspecified narcotics, initial encounter
T40.605D	Adverse effect of unspecified narcotics, subsequent encounter
T40.605S	Adverse effect of unspecified narcotics, sequela
T40.695A	Adverse effect of other narcotics, initial encounter
T40.695D	Adverse effect of other narcotics, subsequent encounter
T40.695S	Adverse effect of other narcotics, sequela
	Opioid Poisoning/Self-Harm
T40.0X1A	Poisoning by opium, accidental (unintentional), initial encounter
T40.0X1D	Poisoning by opium, accidental (unintentional), subsequent encounter
T40.0X1S	Poisoning by opium, accidental (unintentional), sequela
T40.0X2A	Poisoning by opium, intentional self-harm, initial encounter
T40.0X2D	Poisoning by opium, intentional self-harm, subsequent encounter
T40.0X2S	Poisoning by opium, intentional l self-harm, sequela
T40.0X3A	Poisoning by opium, assault, initial encounter
T40.0X3D	Poisoning by opium, assault subsequent encounter
T40.0X3S	Poisoning by opium, assault, sequela
T40.0X4A	Poisoning by opium, undetermined, initial encounter
T40.0X4D	Poisoning by opium, undetermined, subsequent encounter
T40.0X4S	Poisoning by opium, undetermined, sequela
T40.1X1A	Poisoning by heroin, accidental (unintentional), initial encounter
T40.1X1D	Poisoning by heroin, accidental (unintentional), subsequent encounter
T40.1X1S	Poisoning by heroin, accidental (unintentional), sequela
T40.1X2A	Poisoning by heroin, intentional self-harm, initial encounter
T40.1X2D	Poisoning by heroin, intentional self-harm, subsequent encounter
T40.1X2S	Poisoning by heroin, intentional self-harm, sequela
T40.1X3A	Poisoning by heroin, assault, initial encounter
T40.1X3D	Poisoning by heroin, assault, subsequent encounter
T40.1X3S	Poisoning by heroin, assault, sequela
T40.1X4A	Poisoning by heroin, undetermined, initial encounter
T40.1X4D	Poisoning by heroin, undetermined, subsequent encounter
T40.1X4S	Poisoning by heroin, undetermined, sequela
T40.2X1A	Poisoning by other opioids, accidental (unintentional), initial encounter
T40.2X1D	Poisoning by other opioids, accidental (unintentional), subsequent encounter
T40.2X1S	Poisoning by other opioids, accidental (unintentional), sequela
T40.2X2A	Poisoning by other opioids, intentional self-harm, initial encounter

ICD-10-CM Code	Description
T40.2X2D	Poisoning by other opioids, intentional self-harm, subsequent encounter
T40.2X2S	Poisoning by other opioids, intentional self-harm, sequela
T40.2X3A	Poisoning by other opioids, assault, initial encounter
T40.2X3D	Poisoning by other opioids, assault, subsequent encounter
T40.2X3S	Poisoning by other opioids, assault, sequela
T40.2X4A	Poisoning by other opioids, undetermined, initial encounter
T40.2X4D	Poisoning by other opioids, undetermined, subsequent encounter
T40.2X4S	Poisoning by other opioids, undetermined, sequela
T40.3X1A	Poisoning by methadone, accidental (unintentional), initial encounter
T40.3X1D	Poisoning by methadone, accidental (unintentional), subsequent encounter
T40.3X1S	Poisoning by methadone, accidental (unintentional), sequela
T40.3X2A	Poisoning by methadone, intentional self-harm, initial encounter
T40.3X2D	Poisoning by methadone, intentional self-harm, subsequent encounter
T40.3X2S	Poisoning by methadone, intentional self-harm, sequela encounter
T40.3X3A	Poisoning by methadone, assault, initial encounter
T40.3X3D	Poisoning by methadone, assault, subsequent encounter
T40.3X3S	Poisoning by methadone, assault, sequela encounter
T40.3X4A	Poisoning by methadone, undetermined, initial encounter
T40.3X4D	Poisoning by methadone, undetermined, subsequent encounter
T40.3X4S	Poisoning by methadone, undetermined, sequela
T40.4X1A	Poisoning by synthetic narcotics, accidental (unintentional), initial encounter
T40.4X1D	Poisoning by synthetic narcotics, accidental (unintentional), subsequent encounter
T40.4X1S	Poisoning by synthetic narcotics, accidental (unintentional), sequela
T40.4X2A	Poisoning by other synthetic narcotics, intentional self-harm, initial encounter
T40.4X2D	Poisoning by other synthetic narcotics, intentional self-harm, subsequent encounter
T40.4X2S	Poisoning by other synthetic narcotics, intentional self-harm, sequela
T40.4X3A	Poisoning by other synthetic narcotics, assault, initial encounter
T40.4X3D	Poisoning by other synthetic narcotics, assault, subsequent encounter
T40.4X3S	Poisoning by other synthetic narcotics, assault, sequela
T40.4X4A	Poisoning by synthetic narcotics, undetermined, initial encounter
T40.4X4D	Poisoning by synthetic narcotics, undetermined, subsequent encounter
T40.4X4S	Poisoning by synthetic narcotics, undetermined, sequela
T40.601A	Poisoning by unspecified narcotics, accidental (unintentional), initial encounter
T40.601D	Poisoning by unspecified narcotics, accidental (unintentional), subsequent encounter
T40.601S	Poisoning by unspecified narcotics, accidental (unintentional), sequela
T40.602A	Poisoning by unspecified narcotics, intentional self-harm, initial encounter
T40.602D	Poisoning by unspecified narcotics, intentional self-harm, subsequent encounter
T40.602S	Poisoning by unspecified narcotics, intentional self-harm, sequela encounter
T40.603A	Poisoning by unspecified narcotics, assault, initial encounter

ICD-10-CM Code	Description
T40.603D	Poisoning by unspecified narcotics, assault, subsequent encounter
T40.603S	Poisoning by unspecified narcotics, assault, sequela
T40.604A	Poisoning by unspecified narcotics, undetermined, initial encounter
T40.604D	Poisoning by unspecified narcotics, undetermined, subsequent encounter
T40.604S	Poisoning by unspecified narcotics, undetermined, sequela
T40.691A	Poisoning by other narcotics, accidental (unintentional), initial encounter
T40.691D	Poisoning by other narcotics, accidental (unintentional), subsequent encounter
T40.691S	Poisoning by other narcotics, accidental (unintentional), sequela
T40.692A	Poisoning by other narcotics, intentional self-harm, initial encounter
T40.692D	Poisoning by other narcotics, intentional self-harm, subsequent encounter
T40.692S	Poisoning by other narcotics, intentional self-harm, sequela
T40.693A	Poisoning by other narcotics, assault, initial encounter
T40.693D	Poisoning by other narcotics, assault, subsequent encounter
T40.693S	Poisoning by other narcotics, assault, sequela
T40.694A	Poisoning by other narcotics, undetermined, initial encounter
T40.694D	Poisoning by other narcotics, undetermined, subsequent encounter
T40.694S	Poisoning by other narcotics, undetermined, sequela
	Opioid Use, Unspecified
F11.90	Opioid use, unspecified, uncomplicated
F11.920	Opioid use, unspecified, with intoxication, uncomplicated
F11.921	Opioid use, unspecified, with intoxication delirium
F11.922	Opioid use, unspecified, with intoxication with perceptual disturbance
F11.929	Opioid use, unspecified, with intoxication, unspecified
F11.93	Opioid use, unspecified with withdrawal
F11.94	Opioid use, unspecified with opioid-induced mood disorder
F11.950	Opioid use, unspecified with opioid-induced psychotic disorder with delusions
F11.951	Opioid use, unspecified with opioid-induced psychotic disorder with hallucinations
F11.959	Opioid use, unspecified with opioid-induced psychotic disorder, unspecified
F11.981	Opioid use, unspecified with opioid-induced sexual dysfunction
F11.982	Opioid use, unspecified with opioid-induced sleep disorder
F11.988	Opioid use, unspecified with other opioid-induced
F11.99	Opioid use, unspecified with unspecified opioid-induced disorder