



**H·CUP**  
HEALTHCARE COST AND UTILIZATION PROJECT

**DISTRIBUTION AND CORRELATES OF NEONATAL ABSTINENCE  
SYNDROME ACROSS US COUNTIES, 2016**

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## ABSTRACT

### Background

Understanding geographic variation and correlates of neonatal abstinence syndrome (NAS) across US counties can inform efforts to reduce the incidence of NAS. We examine county-level factors associated with rates of NAS.

### Methods

This cross-sectional study includes birth hospitalizations from Healthcare Cost and Utilization Project 2016 State Inpatient Databases for 47 states (2439 counties). Log-linear regression models examine the association of 26 county-level factors related to social context, access to health care, insurance coverage, and sociodemographics with NAS rates.

### Results

Counties with high NAS rates (>80th percentile, 38.3 per 1000 births) were more often in the Northeast and South than other regions. Compared with counties with low NAS rates (<20th percentile, 2.3 per 1000 births), counties with high rates had more mental health-related hospitalizations (mean 4989 vs 3118 per 100 000 population), yet fewer mental health professionals. The average opioid prescribing rate was higher in counties with high, compared with low, NAS rates (96 vs. 73 per 100 population); however, in multivariate analyses, higher opioid prescribing rates were not associated with higher NAS rates. Factors associated with higher NAS rates included more mental health-related hospitalizations, mental health professional shortages, white race, unemployment, and poverty. Findings varied by census region.

### Conclusion

National NAS estimates may mask variations in local experiences of mothers and infants affected by the opioid epidemic. Local efforts, particularly those that expand access to substance use treatment, are needed to reduce the incidence of NAS.

## INTRODUCTION

Neonatal abstinence syndrome (NAS) in infants is characterized by signs and symptoms of withdrawal most commonly caused by abrupt cessation of opioids at birth, following in utero exposure. Maternal opioid use during pregnancy may occur either illicitly or as pharmacotherapy for pain or opioid use disorder (OUD). The incidence of NAS in the United States increased sevenfold from 2000 to 2014,[1,2] in parallel with increases in opioid-related hospital utilization and deaths.[3,4] Newborn hospital stays for NAS—which cost \$315 million in 2012—are about three times longer and costlier than other births.[5]

NAS rates have been reported as higher in Appalachia and the New England and East South Central census divisions than in other regions.[6,7] However, NAS rarely is examined at substate geographic levels,[8,9] and the extent to which NAS rates vary at the county level across the United States is largely unknown.[10] Research suggests that NAS rates may be higher in areas with higher opioid prescribing rates,[6] long-term unemployment,[10] and mental health professional shortages,[10] but no studies have used national data to examine a broader set of factors distinguishing counties with high NAS rates from those with low or zero rates.

Local patterns in NAS rates may differ from other opioid outcomes that have been more widely examined at the county level, such as hospitalizations[11] and deaths from overdoses.[12,13] Opioid-related hospitalization and mortality rates may reflect the degree of illicit opioid use, availability of more lethal opioids, availability of naloxone, substance use disorder (SUD) treatment options, and/or access to hospitals in a county. Higher NAS rates may reflect these factors, but also may indicate that pregnant women are accessing pharmacotherapy, such as methadone or buprenorphine, which is the standard of care for OUD in pregnancy and has been shown to improve outcomes.[15,16] Regardless of its cause, NAS reflects a wider public health problem for reproductive-aged women, mothers, and infants. Support required by these populations may differ from that required by others affected by the opioid crisis, including preconception health counseling, postpartum treatment, and relapse-prevention programs.[17-19]

An understanding of county-level factors associated with NAS rates may inform local policymakers and programs to better target resources to the specific needs of reproductive-aged women, mothers, and infants. This study aimed to describe characteristics of counties with high compared with low NAS rates and determine county-level factors associated with NAS rates in multivariate analyses.

## METHODS

### Study Population

We included birth hospitalizations from Healthcare Cost and Utilization Project (HCUP) State Inpatient Databases (SID)[20] from 46 states and the District of Columbia in 2016, the first full year implementing International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes. NAS was defined by the ICD-10-CM code P96.1. Newborn records with presumed iatrogenic opioid withdrawal, including infants with very low birth weight, were excluded (see eTables 1 and 2 in the Appendix). Births were identified using the ICD-10-CM code Z38, excluding transfers into hospitals to avoid double counting infants.

To obtain stable county-level NAS rates, we excluded 572 counties with populations of women aged 15-44 years and birth hospitalizations with counts in the bottom 10th percentile ( $\leq 761$

women and  $\leq 82$  births). The remaining 2439 counties included in the study represented 98.8% of the population in the 47 SID and 96.2% of the US population overall in 2016.

### Primary Dependent Variable

The primary dependent variable in multivariate models was the county-level NAS rate per 1000 birth hospitalizations, based on patient's county of residence. In descriptive analyses, we categorized this rate by ranking counties nationally: zero, low (<20th percentile, 3.7 per 1000 births), moderate (20th-80th percentile), and high (>80th percentile, 18.3 per 1000 births). The percentile distribution was calculated after excluding counties with a rate of 0 (n = 607).

### Other Variables

As a point of reference, we calculated the population rate of nonmaternal hospitalizations with any listed opioid-related diagnosis for women aged 15-44 years (per 100 000 population), a group of focus for the primary prevention of NAS (see eTable 3 in the Appendix). The opioid-related hospitalization rate was categorized as zero, low, moderate, or high, using the same percentile thresholds as the NAS rates.

We used a conceptual framework developed through a structured literature review to identify other county- and state-level variables potentially associated with NAS. Because a public health approach to preventing NAS relies on reducing opioid use and misuse before and during pregnancy,[17-19] we focused on factors associated with opioid use and OUD among reproductive-aged women. Sources included the SID, Uniform Crime Reporting Program Data, Area Health Resources Files, Substance Abuse and Mental Health Services Administration, Centers for Disease Control and Prevention, Medicaid and Children's Health Insurance Program (CHIP) Payment and Access Commission, Prescription Drug Abuse Policy System, Census Bureau, Bureau of Labor Statistics, Appalachian Regional Commission, and US-Mexico Border Health Commission. The Appendix (eTable 4) contains further information on data sources and variable specifications. We selected variables falling into the following broad categories:

- **Social context:** violence and property crime, inpatient hospitalizations involving opioid-related diagnoses and mental health conditions among women of reproductive age, teen births
- **Access to physicians and specialists:** primary care physicians, obstetrician-gynecologists (OB-GYNs), chiropractors, physical therapists, mental health professionals
- **Access to opioids and SUD treatment:** facilities with certified opioid treatment programs, specialized programs for women in SUD treatment facilities, opioid prescriptions, physicians licensed to prescribe buprenorphine in office-based settings, state Medicaid coverage of methadone, whether physicians in the state are required to check prescription drug monitoring program (PDMP) databases
- **Insurance coverage:** uninsured population, Medicaid enrollment in relation to individuals in poverty (a proxy for Medicaid access)
- **Sociodemographic characteristics:** unemployment; income inequality; poverty; education, sex, age, and racial distributions; population density and growth; census region (Northeast, Midwest, South, West); Appalachia location; location along the US-Mexico border (shown in descriptive tables only)

## Analytic Approach

We categorized NAS rates in the descriptive analysis (zero, low, moderate, high) and examined means across these categories to determine the relationship between study variables and the outcome. In regression models, we treated the NAS rate as a continuous outcome. We estimated log-linear regression models, nationally and stratified by census region. The overall US model had an R-squared of 0.51.

## RESULTS

The average county-level NAS rate was highest in the Northeast (16.0 per 1000 birth hospitalizations) and in the South (11.5) and lowest in the Midwest (7.2) and West (7.5) (Table 1). More than 30% of counties in the Northeast had a NAS rate above the 80<sup>th</sup> percentile (>18.3) when ranked nationally, compared with 18.8% of counties in the South and less than 10% of counties in the Midwest and West.

**Table 1. Rates of Neonatal Abstinence Syndrome and Opioid-Related Hospitalizations Among Reproductive-Aged Women by Region, 2016**

Measure	All Counties	Region			
		Northeast	Midwest	South	West
Total counties, N	2439	201	792	1168	278
NAS rate per 1000 birth hospitalizations					
Mean	10.0	16.0	7.2	11.5	7.5
Category, % <sup>a</sup>					
Zero	24.9	2.5	30.4	26.9	16.9
Low (<20 <sup>th</sup> percentile, 3.7)	15.0	8.0	14.3	15.4	20.5
Moderate (20 <sup>th</sup> -80 <sup>th</sup> percentile)	45.1	59.2	46.8	38.9	55.7
High (>80 <sup>th</sup> percentile, 18.3)	15.0	30.3	8.5	18.8	6.8
Opioid-related hospitalizations per 100 000 women aged 15-44 y					
Mean	196.5	351.3	168.9	206.5	156.0
Category, %					
Zero	6.4	0.5	9.3	6.0	4.3
Low (<20 <sup>th</sup> percentile, 80.6)	18.7	1.5	19.7	20.5	20.5
Moderate (20 <sup>th</sup> -80 <sup>th</sup> percentile)	56.2	55.7	55.8	54.8	63.3
High (>80 <sup>th</sup> percentile, 342.0)	18.7	42.3	15.2	18.7	11.9
High NAS rate and high opioid-related hospitalization rate among reproductive-aged women, %	8.4	14.4	4.5	11.1	3.2
High NAS rate but not high opioid-related hospitalization rate among reproductive-aged women, %	6.7	15.9	3.9	7.7	3.6
High opioid-related hospitalization rate among reproductive-aged women but not high NAS rate, %	10.3	27.9	10.6	7.5	8.6

Abbreviation: NAS, neonatal abstinence syndrome.

<sup>a</sup> Percentages may not add to 100% because of rounding.

Nonmaternal hospitalization rates among reproductive-aged women with any listed opioid-related diagnoses followed a similar pattern as NAS rates, with some exceptions. For instance, 15.9% of counties in the Northeast had a high NAS rate (>80<sup>th</sup> percentile) but not a high opioid-related hospitalization rate among women of reproductive age, compared with less than 10% of counties in other regions. Additionally, 27.9% of counties in the Northeast had a high rate of hospitalizations with opioid-related diagnoses among reproductive-aged women but not a high NAS rate, compared with less than 11% of counties in other regions.

Table 2 presents characteristics of counties by NAS rate categories. Counties with no NAS hospitalizations differed from other counties. Notably, they were more often rural with a mean population density per square mile of 56.2. In comparison, the population density per square mile was 1062.4 for counties with low NAS rates (<20<sup>th</sup> percentile) and 126.5 for counties with high NAS rates.

**Table 2. Characteristics of Counties by Rate of NAS and Region, 2016<sup>a</sup>**

County Characteristic	All Counties	Categories of NAS Rates per 1000 Birth Hospitalizations				Region			
		Zero	Low	Mod- erate	High	North- east	Mid- west	South	West
Total counties, N	2439	607	366	1099	367	201	792	1168	278
NAS rate per 1000 birth hospitalizations, mean	10.0	0.0	2.3	8.7	38.3	16.0	7.2	11.5	7.5
<b>Social Context</b>									
Violent plus property crime rate, mean	720.0	599.8	805.0	782.8	645.7	539.3	680.1	803.3	613.9
Mental health inpatient stay rate, women 15-44 y, mean	3844.3	3331.4	3118.2	3987.1	4989.1	4167.7	4061.0	3788.7	3226.3
Teen birth rate, women 15-19 y, mean	2408.7	2611.3	2239.4	2248.6	2721.9	1388.2	1842.5	3003.0	2262.6
<b>Access to Physicians and Specialists</b>									
Rate of primary care physicians, mean	48.1	39.3	56.8	50.5	46.5	63.9	46.6	43.6	59.8
Rate of OB-GYNs, mean	32.2	18.0	46.4	36.6	28.1	53.6	26.9	30.4	39.0
Rate of chiropractors and physical therapists, mean	65.8	56.4	73.6	69.5	62.3	105.1	79.1	46.8	79.2
Mental health shortage area, %									
None	10.6	6.8	12.8	12.5	9.0	16.4	11.2	11.4	1.1
Whole	62.0	85.5	45.4	55.3	59.7	23.4	66.7	63.9	68.7
Partial	27.4	7.7	41.8	32.2	31.3	60.2	22.1	24.7	30.2
<b>Access to Opioids and SUD Treatment</b>									
Rate of facilities with certified opioid treatment program, mean	0.2	0.1	0.2	0.2	0.3	0.5	0.1	0.2	0.2
Rate of treatment facilities with a program for women, mean	1.9	1.6	1.7	2.1	2.4	2.6	2.0	1.5	3.1
Opioid prescriptions per 100 population, mean	78.8	67.9	73.3	81.0	95.7	62.4	68.9	90.3	70.7
Rate of physicians licensed to prescribe buprenorphine, mean	5.4	2.2	4.6	5.8	10.1	11.7	3.3	5.1	8.0
Medicaid covers methadone, %	58.0	45.6	61.8	65.5	52.0	100.0	50.4	53.2	69.4
Prescribers required to check PDMP, %	33.2	13.7	17.5	37.3	68.9	92.0	22.2	35.5	12.6
<b>Insurance Coverage</b>									
Population uninsured, mean, %	12.0	13.1	12.6	11.5	11.1	7.8	9.3	14.3	13.1
Medicaid enrollees per 100 population in poverty, mean	128.1	124.2	123.7	129.7	134.2	160.5	134.4	116.1	137.0
<b>Sociodemographic Characteristics</b>									
Unemployment rate, mean	5.3	5.3	5.0	5.2	6.1	5.1	4.7	5.6	6.0
Gini index of income inequality, mean	44.5	44.6	44.8	44.2	44.8	44.4	42.9	45.7	44.2

County Characteristic	All Counties	Categories of NAS Rates per 1000 Birth Hospitalizations				Region			
		Zero	Low	Mod-erate	High	North-east	Mid-west	South	West
Population in poverty, mean, %	16.6	17.3	15.8	15.9	18.3	12.9	14.0	19.1	16.1
Population with a college degree, mean, %	8.5	8.4	8.2	8.8	8.1	9.1	9.9	7.3	9.0
Population, female, mean, %	50.2	49.6	50.4	50.3	50.3	50.6	50.0	50.4	49.4
Population by age, y, mean, %									
<18	22.6	22.9	23.9	22.5	20.9	20.2	22.8	22.6	23.5
18-24	9.1	8.9	10.2	9.1	8.3	9.6	9.1	9.0	9.3
25-44	23.8	23.0	25.6	23.9	22.8	23.3	22.9	24.2	24.5
45+	44.6	45.2	40.3	44.5	48.0	46.9	45.2	44.2	42.7
Population by race/ethnicity, mean, %									
White	73.8	72.2	61.3	74.4	87.2	80.3	86.7	67.3	59.6
Black	9.5	11.7	12.7	9.2	3.8	5.5	3.0	16.6	1.7
Hispanic	9.0	9.8	14.8	8.4	3.8	6.8	4.5	9.7	20.4
API	1.6	0.7	3.6	1.6	0.7	2.7	1.1	1.2	3.7
AI/AN	1.7	1.8	1.1	1.9	1.9	0.3	1.7	1.0	5.9
Other	4.4	3.7	6.4	4.6	2.7	4.4	3.0	4.2	8.7
Population density per square mile, mean	335.3	56.2	1062.4	317.1	126.5	1558.7	166.4	258.8	253.7
Percent change in population, 2000-2010, mean	2.8	-0.2	7.7	3.6	0.2	0.0	0.3	3.8	7.3
Appalachia, %	14.4	4.5	4.6	10.3	53.1	31.3	4.0	22.0	0.0
Border county, %	1.2	2.0	1.9	0.9	0.3	0.0	0.0	1.6	4.0
Region, %									
Northeast	8.2	0.8	4.4	10.8	16.6	100.0	0.0	0.0	0.0
Midwest	32.5	39.7	30.9	33.8	18.3	0.0	100.0	0.0	0.0
South	47.9	51.7	49.2	41.3	60.0	0.0	0.0	100.0	0.0
West	11.4	7.7	15.6	14.1	5.2	0.0	0.0	0.0	100.0

Abbreviations: AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; NAS, neonatal abstinence syndrome; OB-GYN, obstetrician-gynecologist; PDMP, prescription drug monitoring program; SUD, substance use disorder.

Note: Six counties were missing data on the rate of opioid prescriptions. All other variables had no missing data.

<sup>a</sup> Rates are per 100 000 individuals in the general population unless a different scale (eg, per 100) or population group (eg, women aged 15-44 years) is noted. Publicly available mortality data are suppressed if the numerator or denominator reflects <10 persons. The 20<sup>th</sup> and 80<sup>th</sup> percentile cut-offs used to categorize the NAS rate as low, medium, and high were 3.7 and 18.3, respectively.

Compared with counties with low NAS rates, those with high NAS rates had lower crime rates (645.7 vs 805.0 per 100 000 population), higher rates of mental health inpatient stays among reproductive-aged women (4989.1 vs 3118.2 per 100 000 women aged 15-44 years), and higher teen birth rates (2721.9 vs 2239.4 per 100 000 women aged 15-19 years).

Compared with counties with low NAS rates, on average, counties with high NAS rates had fewer primary care physicians per 100 000 population (46.5 vs 56.8), OB-GYNs (28.1 vs 46.4), and chiropractors and physical therapists (62.3 vs 73.6) and were more likely to be whole<sup>1</sup> mental health shortage areas (59.7% vs 45.4%). Despite having fewer physicians, the average opioid prescribing rate (excluding pharmacotherapy for SUD) was higher in counties with high NAS rates than in those with low NAS rates (95.7 vs 73.3 per 100 population).

Generally, opioid-related treatment resources were more readily available in counties with high NAS rates than in counties with low NAS rates. Buprenorphine-waivered physicians were more than twice as common in counties with high NAS rates than in those with low rates (10.1 vs 4.6 physicians per 100 000 population). There also were more SUD treatment facilities with a program for women in counties with high versus low NAS rates (2.4 vs 1.7 per 100 000 population). More than two-thirds of counties with high NAS rates (68.9%) were in states requiring prescribers to check PDMPs, compared with 17.5% of counties with low NAS rates. Counties with high NAS rates also had a higher mean rate of Medicaid enrollees per 100 individuals in poverty (134.2 vs 123.7).

On average, counties with high NAS rates had higher percentages of white residents (87.2% vs 61.3%) and lower percentages of black, Hispanic, and Asian/Pacific Islander (API) residents. Counties with high NAS rates also had higher rates of unemployment (6.1% vs 5.0%) and poverty (18.3% vs 15.8%), more adults aged 45+ years (48.0% vs 40.3%), and slower population growth from 2000 to 2010 (0.2% vs 7.7%). Counties with high versus low NAS rates were more likely to be in Appalachia and less likely to be along the US-Mexico border.

County characteristics varied by census region. The opioid prescribing rate was highest in the South (90.3 per 100 population) and lowest in the Northeast (62.4). In contrast, buprenorphine-waivered physicians were more common in the Northeast (11.7 per 100 000 population) than the South (5.1).

The regression results in Table 3 include statistically significant ( $P < 0.05$ ) associations. Full regression results for all variables included in the model are in eTables 5 and 6 in the Appendix, which display models that included and excluded, respectively, counties with NAS rates of 0. In the full US multivariate models, higher county-level rates of crime and mental health hospital inpatient stays were associated with higher NAS rates, as were designation as a partial mental health shortage area, more buprenorphine-waivered physicians, Medicaid coverage of methadone, state policies requiring prescribers to check PDMPs, and a higher ratio of Medicaid enrollees to individuals in poverty. Higher county percentages of unemployment, poverty, and female residents also were associated with higher NAS rates, as was designation as an Appalachian county. A higher percentage of minority residents, including black and API populations, was associated with lower NAS rates, as was being in the Northeast, Midwest, and

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<sup>1</sup> Health Professional Shortage Area designations are used to identify areas and population groups within the United States that are experiencing a shortage of health professionals. To be designated as a mental health professional shortage area, the population-to-provider ratio in a county must be at least 30 000 to 1 (20 000 to 1 if there are unusually high needs in the community). Counties that do not meet this threshold but have population group(s) with access barriers may be designated partial shortage areas.<sup>21</sup>

West versus the South. Generally, results were similar in models excluding counties with a NAS rate of 0 (eTable 6 in the Appendix).

**Table 3. Regression Results<sup>a</sup>**

County Characteristic	US, $\beta$	Region, $\beta$			
		North-east	Mid-west	South	West
<b>Total counties, N</b>	<b>2433</b>	<b>201</b>	<b>791</b>	<b>1163</b>	<b>278</b>
<b>Social Context</b>					
Violent plus property crime rate	0.0001		-0.0002	0.0002	
Mental health inpatient stay rate, women 15-44 y	0.0001		0.0002	0.0001	0.0006
Teen birth rate, women 15-19 y			0.0001	-0.0001	
<b>Access to Physicians and Specialists</b>					
Rate of primary care physicians			0.0081		
Rate of OB-GYNs		-0.0029	-0.0059		-0.0118
Rate of chiropractors plus physical therapists			-0.0054		-0.0144
Partial mental health shortage area (REF=No shortage)	0.1694	0.3581			
<b>Access to Opioids and SUD Treatment</b>					
Rate of facilities with certified opioid treatment program			0.2048		
Rate of facilities with a program for women		-0.0577	0.0248		-0.0826
Opioid prescriptions per 100 population		0.0077	-0.0029	0.0010	
Rate of physicians licensed to prescribe buprenorphine	0.0034	0.0138	0.0270		
Medicaid covers methadone (REF=No)	0.2466				-1.0926
Prescribers required to check PDMP (REF=No)	0.4442	-0.5220	0.6975	0.2596	
<b>Insurance Coverage</b>					
Uninsured, %			-0.0487	-0.0236	0.1352
Medicaid enrollees per 100 population in poverty	0.0077	0.0066	0.0070	0.0053	
<b>Sociodemographic Characteristics</b>					
Unemployment rate	0.0324	0.1461	0.1475		
Gini index of income inequality				-0.0274	
Population in poverty, %	0.0318	0.0642	0.0364	0.0248	
Population with a college degree, %	-0.0191	-0.1385			
Female, %	0.0274		0.1848		0.4945
Age, y, %					
<18	-0.0795		-0.1955	-0.0299	-0.4586
18-24			-0.0369		
25-44	0.0489			0.0485	0.2698
<b>Race/ethnicity, %</b>					
Black	-0.0311		-0.0475	-0.0332	
Hispanic		-0.0567		-0.0440	0.0596
API	-0.0668			-0.0889	0.1078
AI/AN	0.0126	-0.1875	0.0299	0.0344	
Other	-0.0315			-0.0717	-0.0820
Population density per square mile				0.0001	
Percent change in population, 2000-2010			0.0385		
<b>Region</b>					
Northeast (REF=South)	-0.6491				
Midwest (REF=South)	-0.3503				

County Characteristic	US, $\beta$	Region, $\beta$			
		North-east	Mid-west	South	West
West (REF=South)	-0.2523				
Appalachia (REF=Non-Appalachia)	0.6152			0.8349	

Abbreviations: AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; NAS, neonatal abstinence syndrome; OB-GYN, obstetrician-gynecologist; PDMP, prescription drug monitoring program; SUD, substance use disorder.

Note: Six counties were missing data on the rate of opioid prescriptions and were not included in the model. All other variables had no missing data.

<sup>a</sup> Rates are per 100 000 individuals in the general population unless a different scale (eg, per 100) or population group (eg, women aged 15-44 years) is noted.  $\beta$  is the estimate from the log-linear regression model and can be interpreted as the percentage change in the county-level NAS rate associated with a 1-unit increase in the county characteristic. Only those variables with statistically significant associations with the NAS rate ( $P < 0.05$ ) are shown; full model results can be found in the Appendix. Cells highlighted in red signify increasing the county characteristic is associated with higher rates of NAS. Cells highlighted in green signify increasing the county characteristic is associated with lower rates of NAS.

Findings from multivariate models varied by census region; however, some results were consistent. Higher rates of inpatient mental health hospital stays were associated with higher NAS rates in all regions except the Northeast. More OB-GYNs were associated with lower NAS rates in the Northeast, Midwest, and West, as were more chiropractors and physical therapists in the latter two regions. In the Northeast, several other access-related variables also were associated with lower NAS rates: no shortage of mental health professionals (relative to being designated a partial shortage area), more SUD treatment facilities with a program for women, and requirements for prescribers to check PDMPs. Higher levels of Medicaid enrollment and poverty were associated with higher NAS rates in the Northeast, Midwest, and South, as was greater unemployment in the Northeast and Midwest. Only in the Northeast and South were higher opioid prescribing rates associated with higher NAS rates; opioid prescribing rates were not associated with NAS rates in the full US model.

## DISCUSSION

We found marked variation in county-level NAS rates across the country. Clusters of counties had NAS rates above 18.3 per 1000 births (the 80<sup>th</sup> percentile), most notably in the Northeast and the South, where 30% and 19% of counties, respectively, had NAS rates in the highest quintile.

In the full US model, we did not find an association between county-level opioid prescribing rates and NAS rates in multivariate analysis. However, it should be noted that counties with high NAS rates tended to have fewer physicians. Policymakers and payers have invested in programs to restrict prescriptions, increase access to SUD treatment, and educate providers and patients about opioid addiction.[22] However, the effects of these programs often are measured in terms of other more general opioid-related measures, including mortality and hospitalization rates. Less is known about effects on reproductive-aged or pregnant women, uniquely vulnerable populations. It is unknown whether prescribing rates affect pregnant women in the same way they do the rest of the population. Indeed, although intense efforts over recent years seem to have reduced overall opioid prescription rates,[23] physicians already may have been prescribing fewer opioids during pregnancy. It also is possible that reducing prescribing rates has not resulted in the intended decrease in OUD during pregnancy, particularly when diverted prescription and illegal drugs are easily accessible.[24]

NAS rates generally followed a similar pattern as opioid-related hospitalization rates among reproductive-aged women, but there were some differences. This finding is important because it suggests that both measures are uniquely informative for targeting resources toward primary and secondary prevention of NAS. Some counties, most notably in the Northeast, had high NAS rates but did not have opioid hospitalization rates among reproductive-aged women that were above the 80<sup>th</sup> percentile. Prior literature indicates that some states in this region, including Maine and Vermont, have the highest rates of buprenorphine-waivered physicians relative to individuals with opioid addiction.[25] In these areas known to have a severe opioid problem,[26-28] expanded access to pharmacotherapy for OUD may not reduce NAS rates but may reduce risk of hospitalization.

Higher rates of buprenorphine-waivered physicians were associated with higher NAS rates. This may suggest that areas with greater access to buprenorphine-waivered physicians have more pregnant women receiving pharmacotherapy for OUD, potentially contributing to higher NAS rates but less severe NAS symptoms.[29-31] However, compared with methadone, buprenorphine is a relatively new treatment for OUD during pregnancy, and it is unclear how quickly its use is being adopted. Another explanation for this association could be that buprenorphine-waivered physicians are concentrated in areas with greater need. These areas may have more women with untreated OUD during pregnancy with difficulty accessing buprenorphine-waivered physicians or programs administering methadone.[25,32] These findings support the need for additional data that track the maternal source of opioid exposure among infants born with NAS. Such data would help tailor outreach toward women with illicit drug use, who may face barriers to accessing treatment during pregnancy, and toward women already receiving pharmacotherapy.

Several of our results suggest that fewer health care professionals in a county may contribute to higher NAS rates, raising concerns about access to care, particularly for individuals with mental disorders who are at greater risk of SUDs. In the Northeast, designation as a partial shortage area of mental health professionals, fewer SUD treatment facilities with a program for women, and absence of state policies requiring physicians to check PDMPs before prescribing opioids were associated with higher NAS rates. Also, fewer OB-GYNs were associated with higher NAS rates in the Northeast, Midwest, and West, as were fewer chiropractors and physical therapists in two of these regions. Our findings are consistent with a recent study of eight states that also found an association between mental health professional shortages and higher NAS rates.[10] More research is needed to identify whether improved access to SUD treatment, mental health care and other types of health care could reduce NAS incidence.

To some extent, our results are consistent with research showing that disadvantaged populations experience worse health outcomes. For instance, unemployment and poverty were associated with higher NAS rates, consistent with established links between socioeconomic status and rates of SUDs.[10,33] However, other findings show that variation in NAS rates do not follow traditional patterns previously associated with poor health outcomes, such as for racial/ethnic minorities. For example, we found that counties with higher percentages of black and API populations had lower NAS rates. Conversely, populations with a higher percentage of white residents had higher NAS rates, which corresponds with previous research showing that 90% of individuals initiating heroin use in the past decade were white.[24] Additionally, white individuals have the highest mortality rates from prescription opioid use, whereas black individuals have the lowest.[35]

## Limitations

Our study had several limitations. First, this cross-sectional study using 1 year of data was not designed to identify causal relationships or provide insight on the temporal sequence of cause and effect. Although we included many variables in our models related to several important dimensions associated with opioid outcomes, we could not measure some unobservable variables, such as quality of primary and prenatal care. Even variables that we included may not completely capture constructs of interest. For example, inpatient stays with opioid- and mental health-related diagnoses may reflect hospital bed capacity rather than true burden in a community. Buprenorphine-waivered physicians may not fully capture access because not all licensed providers actively provide treatment, and some do not accept certain types of insurance or populations, such as women covered by Medicaid or who are pregnant.[21,28] Finally, births outside reporting hospitals (eg, birthing centers, federal hospitals), stillbirths, and miscarriages are not captured.

## CONCLUSIONS

In this cross-sectional study of nearly all US states with county-level data on potential predictors of NAS, we found that county rates of NAS vary widely and did not always align with opioid-related hospitalization rates among reproductive-aged women. Across regions, predictors of NAS rates often differed. The variability of our findings suggests that efforts to reduce the incidence of NAS should be tailored to local contexts. We examined various factors that may be relevant to policymakers in making evidence-based decisions, on the basis of local data, that aim to reduce NAS incidence and improve maternal and infant outcomes.

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## APPENDIX

**eTable 1. ICD-10-CM Codes Defining Birth Hospitalizations<sup>a</sup>**

ICD-10-CM Code	Description
Z38.00	Single liveborn infant, delivered vaginally, born in hospital
Z38.01	Single liveborn infant, delivered cesarean, born in hospital
Z38.1	Single liveborn infant, born outside hospital
Z38.2	Single liveborn infant, unspecified as to place of birth
Z38.30	Twin liveborn infant, delivered vaginally, born in hospital
Z38.31	Twin liveborn infant, delivered by cesarean, born in hospital
Z38.4	Twin liveborn infant, born outside hospital
Z38.5	Twin liveborn infant, unspecified as to place of birth
Z38.61	Triplet liveborn infant, delivered vaginally, born in hospital
Z38.62	Triplet liveborn infant, delivered by cesarean
Z38.63	Quadruplet liveborn infant, delivered vaginally
Z38.64	Quadruplet liveborn infant, delivered by cesarean
Z38.65	Quintuplet liveborn infant, delivered vaginally
Z38.66	Quintuplet liveborn infant, delivered by cesarean
Z38.68	Other multiple liveborn infant, delivered vaginally
Z38.69	Other multiple liveborn infant, delivered by cesarean
Z38.7	Other multiple liveborn infant, born outside hospital
Z38.8	Other multiple liveborn infant, unspecified as to place of birth

Abbreviation: ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

<sup>a</sup> Excluded transfers in (ASOURCE = 2 or 3, PointOfOriginUB04 = 4, B, D, E, or F, regardless of ATYPE coding, PointOfOriginUB04 = 5, 6 when ATYPE is not equal to 4).

**eTable 2. ICD-10-CM Codes Defining NAS Among Birth Hospitalizations**

<b>ICD-10-CM Code</b>	<b>Description</b>
P96.1	Neonatal withdrawal symptoms from maternal use of drugs of addiction
<b>Iatrogenic Exclusions</b>	
P27.0	Wilson-Mikity syndrome
P27.1	Bronchopulmonary dysplasia originating in the perinatal period
P27.8	Other chronic respiratory diseases originating in the perinatal period
P52.3	Unspecified intraventricular (nontraumatic) hemorrhage of newborn
P52.0	Intraventricular (nontraumatic) hemorrhage, grade 1, of newborn
P52.1	Intraventricular (nontraumatic) hemorrhage, grade 2, of newborn
P52.21	Intraventricular (nontraumatic) hemorrhage, grade 3, of newborn
P52.22	Intraventricular (nontraumatic) hemorrhage, grade 4, of newborn
P77.9	Necrotizing enterocolitis in newborn, unspecified
P77.1	Stage 1 necrotizing enterocolitis in newborn
P77.2	Stage 2 necrotizing enterocolitis in newborn
P77.3	Stage 3 necrotizing enterocolitis in newborn
P78.0	Perinatal intestinal perforation
P91.2	Neonatal cerebral leukomalacia
P96.2	Withdrawal symptoms from therapeutic use of drugs in newborn
P07.00	Extremely low birth weight newborn, unspecified weight
P07.10	Other low birth weight newborn, unspecified weight
P07.01	Extremely low birth weight newborn, less than 500 grams
P07.02	Extremely low birth weight newborn, 500-749 grams
P07.03	Extremely low birth weight newborn, 750-999 grams
P07.14	Other low birth weight newborn, 1,000-1,249 grams
P07.15	Other low birth weight newborn, 1,250-1,499 grams

Abbreviations: ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NAS, neonatal abstinence syndrome.

**eTable 3. ICD-10-CM Codes Defining Nonmaternal Opioid-Related Hospitalizations Among Women Aged 15-44 Years<sup>a</sup>**

<b>ICD-10-CM Code</b>	<b>Description</b>
<b>Opioid Abuse/Dependence</b>	
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
<b>Opioid Poisoning/Self-Harm</b>	
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 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

<b>ICD-10-CM Code</b>	<b>Description</b>
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
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

<b>ICD-10-CM Code</b>	<b>Description</b>
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
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
<b>Opioid Use, Unspecified</b>	
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

Abbreviation: ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification.

<sup>a</sup> Inclusion/exclusion criteria: Women aged 15-44 years with no pregnancy-related code in any position (O00-O9A).

**eTable 4. Variable Specifications and Data Sources**

<b>County Characteristic</b>	<b>Source</b>	<b>Year</b>	<b>Link</b>
NAS rate per 1000 birth hospitalizations	HCUP SID	2016	<a href="http://www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp">www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp</a>
Nonmaternal opioid-related hospitalizations per 100 000 women aged 15-44 y	HCUP SID	2007-2016	<a href="https://wonder.cdc.gov/natality.html">https://wonder.cdc.gov/natality.html</a>
<b>Social Context</b>			
Violent plus property crime rate	ICPSR Uniform Crime Reporting Program Data	2016	<a href="https://www.icpsr.umich.edu/icpsrweb/ICPSR/series/00057">https://www.icpsr.umich.edu/icpsrweb/ICPSR/series/00057</a> . Note that data were not available at the county level for Florida or Illinois. For these states, we imputed the state rate for each county.
Mental health inpatient stays per 100 000 women aged 15-44 y	HCUP SID	2016	<a href="http://www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp">www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp</a>
Teen birth hospitalizations per 100 000 women aged 15-19 y	HCUP SID	2016	<a href="http://www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp">www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp</a>
<b>Access to Physicians and Specialists</b>			
Primary care physicians per 100 000 population	AHRF	2016	<a href="https://datawarehouse.hrsa.gov/data/datadownload.aspx">https://datawarehouse.hrsa.gov/data/datadownload.aspx</a>
OB-GYNs per 100 000 population	AHRF	2016	<a href="https://datawarehouse.hrsa.gov/data/datadownload.aspx">https://datawarehouse.hrsa.gov/data/datadownload.aspx</a>
Chiropractors plus physical therapists per 100 000 population	AHRF	2016	<a href="https://datawarehouse.hrsa.gov/data/datadownload.aspx">https://datawarehouse.hrsa.gov/data/datadownload.aspx</a>
Mental health shortage area	AHRF	2016	<a href="https://datawarehouse.hrsa.gov/data/datadownload.aspx">https://datawarehouse.hrsa.gov/data/datadownload.aspx</a>
<b>Access to Opioids and SUD Treatment</b>			
Facilities with certified opioid treatment program per 100 000 population	SAMHSA NSSATs	2016	<a href="https://www.samhsa.gov/data/data-we-collect/nssats-national-survey-substance-abuse-treatment-services">https://www.samhsa.gov/data/data-we-collect/nssats-national-survey-substance-abuse-treatment-services</a>
Facilities with a targeted program for women per 100 000 population	SAMHSA Directory of Drug and Alcohol Abuse Treatment Centers (NSSATs)	2016	<a href="https://www.samhsa.gov/data/data-we-collect/nssats-national-survey-substance-abuse-treatment-services">https://www.samhsa.gov/data/data-we-collect/nssats-national-survey-substance-abuse-treatment-services</a>
Opioid prescriptions per 100 population	CDC US Prescribing Rate Maps	2016	<a href="https://www.cdc.gov/drugoverdose/maps/rxcounty2016.html">https://www.cdc.gov/drugoverdose/maps/rxcounty2016.html</a>
Physicians licensed to prescribe buprenorphine per 100 000 population	SAMHSA Treatment Locator	2016	<a href="https://findtreatment.samhsa.gov/">https://findtreatment.samhsa.gov/</a>
State Medicaid program covers methadone	MACPAC	Sept 2015	<a href="https://www.macpac.gov/state-coverage-of-fda-approved-drugs-to-treat-addiction-2015/">https://www.macpac.gov/state-coverage-of-fda-approved-drugs-to-treat-addiction-2015/</a>
State requires prescribers to check PDMP	Prescription Drug Abuse Policy System	2016	<a href="http://www.pdaps.org">www.pdaps.org</a>

County Characteristic	Source	Year	Link
<b>Insurance Coverage</b>			
Uninsured, %	Census Bureau Small Area Health Insurance Estimates	2016	<a href="https://www.census.gov/data/datasets/time-series/demo/sahie/estimates-acs.html">https://www.census.gov/data/datasets/time-series/demo/sahie/estimates-acs.html</a>
Medicaid enrollees per 100 population in poverty	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
<b>Sociodemographic Characteristics</b>			
Unemployment rate	Bureau of Labor Statistics	2016	<a href="https://www.bls.gov/">https://www.bls.gov/</a>
Gini index of income inequality on a scale of 0 to 100	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Population in poverty, %	Census Bureau SAIPE	2016	<a href="https://www.census.gov/programs-surveys/saipe/data/datasets.html">https://www.census.gov/programs-surveys/saipe/data/datasets.html</a>
Population aged 25+ y with a college degree (associate's or higher)	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Female, %	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Age, y, %	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Race/ethnicity, %	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Population density per square mile	Census	2016	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Percent change in population, 2000-2010	Census	2000, 2010	<a href="https://data.census.gov/cedsci/">https://data.census.gov/cedsci/</a>
Appalachia	Appalachian Regional Commission	N/A	<a href="https://www.arc.gov/about-the-appalachian-region/">https://www.arc.gov/about-the-appalachian-region/</a>
Border county	US-Mexico Border Health Commission	N/A	<a href="https://www.hhs.gov/about/agencies/oga/about-oga/what-we-do/international-relations-division/americas/border-health-commission/us-mexico-border-region/index.html">https://www.hhs.gov/about/agencies/oga/about-oga/what-we-do/international-relations-division/americas/border-health-commission/us-mexico-border-region/index.html</a>
Region	HCUP SID	N/A	<a href="http://www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp">www.hcup-us.ahrq.gov/db/state/siddbdocumentation.jsp</a>

Abbreviations: ACS, American Community Survey; AHRF, Area Health Resources Files; CDC, Centers for Disease Control and Prevention; HCUP, Healthcare Cost and Utilization Project; ICPSR, Inter-university Consortium for Political and Social Research; MACPAC, Medicaid and CHIP Payment and Access Commission; N/A, not applicable; NAS, neonatal abstinence syndrome; N-SSATS, National Survey of Substance Abuse Treatment Services; SAIPE, Small Area Income and Poverty Estimates; SAMHSA, Substance Abuse and Mental Health Services Administration; SID, State Inpatient Databases.

**eTable 5. Full Regression Results, Including Counties With NAS Rates Equal to 0<sup>a</sup>**

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Total counties, N</b>	<b>2433</b>		<b>201</b>		<b>791</b>		<b>1163</b>		<b>278</b>	
<b>Social Context</b>										
Violent plus property crime rate	0.0001	0.0000, 0.0001	-0.0001	-0.0006, 0.0004	-0.0002	-0.0004, 0.0000	0.0002	0.0002, 0.0003	-0.0008	-0.0018, 0.0003
Mental health inpatient stay rate, women 15-44 y	0.0001	0.0000, 0.0001	0.0000	0.0000, 0.0001	0.0002	0.0001, 0.0002	0.0001	0.0000, 0.0001	0.0006	0.0003, 0.0010
Teen birth rate, women 15-19 y	0.0000	-0.0001, 0.0000	-0.0001	-0.0003, 0.0001	0.0001	0.0000, 0.0002	-0.0001	-0.0001, 0.0000	0.0001	-0.0001, 0.0003
<b>Access to Physicians and Specialists</b>										
Rate of primary care physicians	0.0009	-0.0007, 0.0026	-0.0003	-0.0049, 0.0042	0.0081	0.0048, 0.0115	0.0000	-0.0022, 0.0022	0.0049	-0.0066, 0.0164
Rate of OB-GYNs	-0.0005	-0.0018, 0.0007	-0.0029	-0.0054, -0.0003	-0.0059	-0.0087, -0.0031	0.0008	-0.0008, 0.0024	-0.0118	-0.0196, -0.0039
Rate of chiropractors plus physical therapists	0.0003	-0.0012, 0.0019	0.0001	-0.0032, 0.0034	-0.0054	-0.0087, -0.0022	0.0006	-0.0015, 0.0027	-0.0144	-0.0231, -0.0058
<b>Mental health shortage area (REF=None)</b>										
Whole	-0.0391	-0.1687, 0.0904	0.0394	-0.2572, 0.3360	-0.0827	-0.3135, 0.1481	0.0120	-0.1413, 0.1653	-1.6302	-4.0856, 0.8253
Partial	0.1694	0.0406, 0.2982	0.3581	0.0937, 0.6224	-0.0909	-0.3281, 0.1463	0.1310	-0.0202, 0.2822	-2.6430	-5.4741, 0.1880
Rate of facilities with certified opioid treatment program	0.0064	-0.0164, 0.0292	-0.0305	-0.1154, 0.0545	0.2048	0.1562, 0.2533	-0.0013	-0.0330, 0.0305	-0.3726	-0.9380, 0.1929
Rate of facilities with a program for women	-0.0046	-0.0147, 0.0054	-0.0577	-0.0935, -0.0219	0.0248	0.0152, 0.0345	-0.0011	-0.0117, 0.0096	-0.0826	-0.1457, -0.0194
Opioid prescriptions per 100 population	0.0002	-0.0007, 0.0011	0.0077	0.0026, 0.0129	-0.0029	-0.0052, -0.0006	0.0010	0.0000, 0.0020	0.0075	-0.0038, 0.0188
Rate of physicians licensed to prescribe buprenorphine	0.0034	0.0004, 0.0063	0.0138	0.0032, 0.0244	0.0270	0.0203, 0.0336	-0.0001	-0.0035, 0.0032	0.0204	-0.0072, 0.0480
Medicaid covers methadone (REF=No)	0.2466	0.1475, 0.3457	N/A	N/A	0.0990	-0.1224, 0.3204	0.0942	-0.0478, 0.2363	-1.0926	-1.7459, -0.4392
Prescribers required to check PDMP (REF=No)	0.4442	0.3304, 0.5579	-0.5220	-0.8790, -0.1650	0.6975	0.4392, 0.9558	0.2596	0.1070, 0.4122	-0.3090	-1.1871, 0.5692

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Total counties, N</b>	<b>2433</b>		<b>201</b>		<b>791</b>		<b>1163</b>		<b>278</b>	
<b>Insurance Coverage</b>										
Uninsured, %	-0.0089	-0.0250, 0.0072	-0.0199	-0.0746, 0.0348	-0.0487	-0.0880, -0.0094	-0.0236	-0.0443, -0.0029	0.1352	0.0484, 0.2221
Medicaid enrollees per 100 population in poverty	0.0077	0.0062, 0.0092	0.0066	0.0033, 0.0099	0.0070	0.0033, 0.0106	0.0053	0.0025, 0.0082	0.0092	-0.0004, 0.0188
<b>Sociodemographic Characteristics</b>										
Unemployment rate	0.0324	0.0140, 0.0507	0.1461	0.0453, 0.2469	0.1475	0.0847, 0.2104	0.0204	-0.0005, 0.0413	-0.0747	-0.1914, 0.0421
Gini index of income inequality	-0.0101	-0.0263, 0.0061	0.0231	-0.0356, 0.0817	-0.0248	-0.0677, 0.0181	-0.0274	-0.0454, -0.0094	0.0140	-0.0729, 0.1009
Population in poverty, %	0.0318	0.0223, 0.0414	0.0642	0.0250, 0.1034	0.0364	0.0116, 0.0611	0.0248	0.0125, 0.0371	0.0590	-0.0125, 0.1305
Population with a college degree, %	-0.0191	-0.0380, -0.0002	-0.1385	-0.1989, -0.0782	0.0102	-0.0319, 0.0524	-0.0087	-0.0337, 0.0163	-0.0874	-0.1753, 0.0005
Female, %	0.0274	0.0034, 0.0514	0.0563	-0.0522, 0.1649	0.1848	0.1113, 0.2584	-0.0302	-0.0619, 0.0015	0.4945	0.2193, 0.7696
<b>Age, y, % (REF=45+)</b>										
<18	-0.0795	-0.0986, -0.0605	-0.0329	-0.0984, 0.0326	-0.1955	-0.2459, -0.1451	-0.0299	-0.0543, -0.0055	-0.4586	-0.7280, -0.1891
18-24	-0.0110	-0.0248, 0.0027	-0.0294	-0.0706, 0.0117	-0.0369	-0.0658, -0.0080	0.0021	-0.0159, 0.0201	-0.0240	-0.1156, 0.0676
25-44	0.0489	0.0294, 0.0683	0.0379	-0.0349, 0.1108	0.0407	-0.0108, 0.0922	0.0485	0.0219, 0.0750	0.2698	0.0874, 0.4521
<b>Race/ethnicity, % (REF=white)</b>										
Black	-0.0311	-0.0387, -0.0235	-0.0100	-0.0456, 0.0256	-0.0475	-0.0798, -0.0152	-0.0332	-0.0426, -0.0237	0.0832	-0.1010, 0.2675
Hispanic	-0.0076	-0.0171, 0.0019	-0.0567	-0.0955, -0.0180	-0.0516	-0.1038, 0.0006	-0.0440	-0.0711, -0.0168	0.0596	0.0203, 0.0989
API	-0.0668	-0.1218, -0.0118	-0.0480	-0.1376, 0.0416	0.0595	-0.0472, 0.1661	-0.0889	-0.1776, -0.0002	0.1078	0.0114, 0.2042
AI/AN	0.0126	0.0053, 0.0198	-0.1875	-0.3293, -0.0457	0.0299	0.0182, 0.0416	0.0344	0.0163, 0.0526	0.0119	-0.0112, 0.0350
Other	-0.0315	-0.0531, -0.0098	0.0487	-0.0362, 0.1337	0.0536	-0.0192, 0.1263	-0.0717	-0.1084, -0.0351	-0.0820	-0.1285, -0.0356

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Total counties, N</b>	<b>2433</b>		<b>201</b>		<b>791</b>		<b>1163</b>		<b>278</b>	
Population density per square mile	0.0000	0.0000, 0.0000	-0.0001	-0.0003, 0.0001	-0.0001	-0.0006, 0.0004	0.0001	0.0000, 0.0003	-0.0010	-0.0024, 0.0004
Population growth, 2010 vs 2000 census	-0.0010	-0.0078, 0.0058	-0.0218	-0.0512, 0.0075	0.0385	0.0214, 0.0557	-0.0062	-0.0148, 0.0025	-0.0229	-0.0634, 0.0176
Region (REF=South)										
Northeast	-0.6491	-0.8224, -0.4759	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Midwest	-0.3503	-0.4901, -0.2106	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
West	-0.2523	-0.5028, -0.0019	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Appalachia (REF=Non-Appalachia)	0.6152	0.5106, 0.7197	-0.2230	-0.4875, 0.0415	0.1716	-0.0642, 0.4074	0.8349	0.6808, 0.9889	N/A	N/A

Abbreviations: AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; CI, confidence interval; OB-GYN, obstetrician-gynecologist; N/A, not applicable; NAS, neonatal abstinence syndrome; PDMP, prescription drug monitoring program; SUD, substance use disorder.

<sup>a</sup> Rates are per 100 000 individuals in the general population unless a different scale (eg, per 100) or population group (eg, women aged 15-44 years) is noted.  $\beta$  is the estimate from the linear regression model and can be interpreted as the absolute change in the county-level NAS rate associated with a 1-unit increase in the county characteristic. Cells highlighted in red signify increasing the county characteristic is associated with higher rates of NAS. Cells highlighted in green signify increasing the county characteristic is associated with lower rates of NAS.

**eTable 6. Full Regression Results, Excluding Counties With NAS Rates Equal to 0<sup>a</sup>**

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Total counties, N</b>	<b>1828</b>		<b>196</b>		<b>551</b>		<b>850</b>		<b>231</b>	
<b>Social Context</b>										
Violent plus property crime rate	0.0000	0.0000, 0.0001	-0.0001	-0.0006, 0.0004	-0.0001	-0.0003, 0.0001	0.0001	0.0000, 0.0002	-0.0002	-0.0006, 0.0003
Mental health inpatient stay rate, women 15-44 y	0.0000	0.0000, 0.0001	0.0000	0.0000, 0.0001	0.0001	0.0001, 0.0002	0.0000	0.0000, 0.0001	0.0003	0.0002, 0.0004
Teen birth rate, women 15-19 y	0.0000	0.0000, 0.0000	-0.0001	-0.0003, 0.0001	0.0001	0.0000, 0.0002	0.0000	-0.0001, 0.0000	-0.0001	-0.0002, 0.0000
<b>Access to Physicians and Specialists</b>										
Rate of primary care physicians	0.0015	-0.0002, 0.0032	-0.0001	-0.0046, 0.0043	0.0059	0.0023, 0.0094	0.0004	-0.0019, 0.0027	-0.0020	-0.0097, 0.0056
Rate of OB-GYNs	-0.0011	-0.0025, 0.0002	-0.0030	-0.0056, -0.0005	-0.0048	-0.0082, -0.0013	0.0003	-0.0014, 0.0020	-0.0092	-0.0131, -0.0052
Rate of chiropractors plus physical therapists	-0.0003	-0.0018, 0.0012	0.0008	-0.0025, 0.0040	-0.0057	-0.0088, -0.0025	0.0000	-0.0021, 0.0022	-0.0084	-0.0151, -0.0017
Mental health shortage area (REF=None)										
Whole	-0.0617	-0.1901, 0.0666	0.0011	-0.2885, 0.2907	-0.0066	-0.2347, 0.2215	-0.0385	-0.1963, 0.1193	-0.5298	-2.3034, 1.2437
Partial	0.0705	-0.0575, 0.1986	0.2745	0.0052, 0.5438	-0.1242	-0.3678, 0.1195	0.0299	-0.1269, 0.1867	-1.1000	-2.9507, 0.7508
<b>Access to Opioids and SUD Treatment</b>										
Rate of facilities with certified opioid treatment program	0.0099	-0.0129, 0.0327	-0.0183	-0.1041, 0.0674	0.1773	0.1278, 0.2268	0.0001	-0.0327, 0.0329	-0.3257	-0.5582, -0.0932
Rate of facilities with a program for women	-0.0050	-0.0148, 0.0048	-0.0590	-0.0953, -0.0227	0.0167	0.0073, 0.0261	-0.0020	-0.0129, 0.0088	-0.0035	-0.0419, 0.0350
Opioid prescriptions per 100 population	-0.0002	-0.0011, 0.0008	0.0078	0.0026, 0.0129	-0.0039	-0.0062, -0.0016	0.0010	-0.0001, 0.0020	0.0071	0.0018, 0.0123
Rate of physicians licensed to prescribe buprenorphine	0.0034	0.0005, 0.0064	0.0137	0.0034, 0.0240	0.0249	0.0184, 0.0315	0.0006	-0.0028, 0.0041	0.0341	0.0183, 0.0498
Medicaid covers methadone (REF=No)	0.0618	-0.0360, 0.1595	N/A	N/A	0.0535	-0.1647, 0.2718	-0.0439	-0.1867, 0.0989	-0.7296	-1.1718, -0.2874
Prescribers required to check PDMP (REF=No)	0.2691	0.1622, 0.3759	-0.5418	-0.8949, -0.1887	0.5034	0.2553, 0.7516	0.1023	-0.0546, 0.2592	0.1861	-0.1546, 0.5267

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Insurance Coverage</b>										
Uninsured, %	-0.0103	-0.0265, 0.0060	-0.0196	-0.0743, 0.0351	-0.0541	-0.0944, -0.0138	-0.0234	-0.0449, -0.0018	0.0710	0.0352, 0.1068
Medicaid enrollees per 100 population in poverty	0.0059	0.0044, 0.0075	0.0064	0.0030, 0.0097	0.0059	0.0020, 0.0099	0.0037	0.0009, 0.0065	0.0049	-0.0005, 0.0102
<b>Sociodemographic Characteristics</b>										
Unemployment rate	0.0183	-0.0015, 0.0381	0.1427	0.0420, 0.2434	0.0919	0.0317, 0.1520	0.0166	-0.0056, 0.0388	-0.1374	-0.2244, -0.0504
Gini index of income inequality	0.0048	-0.0109, 0.0206	0.0351	-0.0223, 0.0926	0.0214	-0.0192, 0.0621	-0.0164	-0.0346, 0.0019	0.0403	-0.0148, 0.0955
Population in poverty, %	0.0235	0.0139, 0.0332	0.0647	0.0254, 0.1039	0.0373	0.0120, 0.0626	0.0164	0.0038, 0.0290	0.0208	-0.0161, 0.0577
Population with a college degree, %	-0.0111	-0.0297, 0.0076	-0.1289	-0.1891, -0.0687	0.0288	-0.0129, 0.0705	-0.0077	-0.0331, 0.0176	-0.0362	-0.0907, 0.0184
Female, %	-0.0057	-0.0322, 0.0209	0.0100	-0.1022, 0.1222	0.1221	0.0411, 0.2031	-0.0482	-0.0801, -0.0164	0.1048	-0.0154, 0.2250
Age, y, % (REF=45+)										
<18	-0.0719	-0.0909, -0.0529	-0.0193	-0.0853, 0.0466	-0.1516	-0.2010, -0.1023	-0.0323	-0.0571, -0.0074	-0.1325	-0.2208, -0.0443
18-24	-0.0137	-0.0279, 0.0006	-0.0329	-0.0742, 0.0085	-0.0470	-0.0765, -0.0174	-0.0023	-0.0209, 0.0163	-0.0277	-0.0867, 0.0314
25-44	0.0181	-0.0024, 0.0386	0.0326	-0.0395, 0.1046	0.0169	-0.0355, 0.0692	0.0233	-0.0035, 0.0501	-0.0025	-0.0984, 0.0934
Race/ethnicity, % (REF=white)										
Black	-0.0229	-0.0298, -0.0159	-0.0091	-0.0437, 0.0255	-0.0356	-0.0679, -0.0032	-0.0244	-0.0330, -0.0159	-0.0522	-0.2087, 0.1044
Hispanic	-0.0019	-0.0102, 0.0065	-0.0522	-0.0902, -0.0142	-0.0433	-0.0906, 0.0040	-0.0370	-0.0658, -0.0082	0.0317	0.0177, 0.0457
API	-0.0684	-0.1257, -0.0110	-0.0534	-0.1422, 0.0354	0.0420	-0.0638, 0.1479	-0.0748	-0.1641, 0.0146	0.0514	0.0119, 0.0909
AI/AN	0.0153	0.0087, 0.0219	-0.1843	-0.3218, -0.0469	0.0246	0.0125, 0.0368	0.0322	0.0156, 0.0489	0.0032	-0.0145, 0.0208
Other	-0.0329	-0.0554, -0.0105	0.0397	-0.0443, 0.1237	0.0189	-0.0450, 0.0827	-0.0708	-0.1082, -0.0334	-0.0443	-0.0682, -0.0204
Population density per square mile	0.0000	0.0000, 0.0000	-0.0001	-0.0003, 0.0001	-0.0002	-0.0008, 0.0004	0.0001	0.0000, 0.0002	-0.0001	-0.0003, 0.0001

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
Population growth, 2010 vs 2000 census	-0.0088	-0.0157, -0.0018	-0.0168	-0.0465, 0.0130	0.0209	0.0031, 0.0387	-0.0113	-0.0202, -0.0024	-0.0020	-0.0319, 0.0279
Region (REF=South)										
Northeast	-0.5362	-0.7041, -0.3683	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Midwest	-0.2953	-0.4318, -0.1588	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
West	-0.3269	-0.5643, -0.0894	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Appalachia (REF=Non-Appalachia)	0.4709	0.3664, 0.5753	-0.2430	-0.5087, 0.0228	0.2448	0.0096, 0.4800	0.5989	0.4537, 0.7440	N/A	N/A

Abbreviations: AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; CI, confidence interval; OB-GYN, obstetrician-gynecologist; NAS, neonatal abstinence syndrome; PDMP, prescription drug monitoring program; SUD, substance use disorder.

<sup>a</sup> Rates are per 100 000 individuals in the general population unless a different scale (eg, per 100) or population group (eg, women aged 15-44 years) is noted.  $\beta$  is the estimate from the linear regression model and can be interpreted as the absolute change in the county-level NAS rate associated with a 1-unit increase in the county characteristic. Cells highlighted in red signify increasing the county characteristic is associated with higher rates of NAS. Cells highlighted in green signify increasing the county characteristic is associated with lower rates of NAS.

**eTable 7. Unadjusted Regression Results, Including Counties With NAS Rates Equal to 0<sup>a</sup>**

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Social Context</b>										
Violent plus property crime rate	-0.0001	-0.0002, 0.0000	0.0003	-0.0001, 0.0008	-0.0002	-0.0004, 0.0000	0.0000	-0.0002, 0.0001	0.0004	-0.0002, 0.0010
Mental health inpatient stay rate, women 15-44 y	0.0002	0.0002, 0.0002	0.0001	0.0000, 0.0002	0.0002	0.0002, 0.0002	0.0002	0.0002, 0.0002	0.0001	0.0001, 0.0002
Teen birth rate, women 15–19 y	0.0001	0.0001, 0.0001	0.0003	0.0001, 0.0004	0.0003	0.0002, 0.0003	0.0000	0.0000, 0.0001	0.0001	0.0000, 0.0002
<b>Access to Physicians and Specialists</b>										
Rate of primary care physicians	-0.0007	-0.0027, 0.0012	-0.0016	-0.0051, 0.0019	-0.0015	-0.0054, 0.0025	-0.0003	-0.0032, 0.0026	-0.0031	-0.0090, 0.0029
Rate of OB–GYNs	-0.0015	-0.0033, 0.0003	-0.0038	-0.0071, -0.0005	-0.0014	-0.0049, 0.0020	-0.0024	-0.0053, 0.0005	-0.0045	-0.0102, 0.0012
Rate of chiropractors plus physical therapists	-0.0022	-0.0038, -0.0005	0.0009	-0.0023, 0.0041	-0.0091	-0.0127, -0.0056	0.0005	-0.0023, 0.0034	-0.0020	-0.0059, 0.0019
Mental health shortage area (REF=None)										
Whole	0.0014	-0.2105, 0.2133	0.3080	-0.1351, 0.7511	0.0649	-0.3295, 0.4594	0.0291	-0.2753, 0.3335	-0.0285	-1.3795, 1.3224
Partial	0.2145	-0.0046, 0.4336	0.3213	-0.0822, 0.7247	0.3080	-0.1076, 0.7237	0.2002	-0.1220, 0.5223	-0.4944	-1.8972, 0.9083
<b>Access to Opioids and SUD Treatment</b>										
Rate of facilities with certified opioid treatment program	0.0399	0.0178, 0.0620	0.2250	0.1240, 0.3260	0.2010	0.1381, 0.2639	0.0184	-0.0249, 0.0616	0.1838	0.0549, 0.3128
Rate of facilities with a program for women	0.0230	0.0143, 0.0318	0.0464	-0.0218, 0.1145	0.0203	0.0070, 0.0337	0.0323	0.0203, 0.0442	0.0125	-0.0227, 0.0477
Opioid prescriptions per 100 population	0.0062	0.0054, 0.0070	0.0178	0.0132, 0.0223	0.0060	0.0032, 0.0087	0.0060	0.0049, 0.0070	0.0083	0.0032, 0.0134
Rate of physicians licensed to prescribe buprenorphine	0.0348	0.0320, 0.0375	0.0220	0.0107, 0.0332	0.0449	0.0376, 0.0522	0.0321	0.0286, 0.0355	0.0375	0.0236, 0.0515
Medicaid covers methadone (REF=No)	-0.1328	-0.2522, -0.0134	N/A	N/A	0.7418	0.4801, 1.0035	-0.7011	-0.8989, -0.5032	-0.0284	-0.3782, 0.3213
Prescribers required to check PDMP (REF=No)	1.0766	0.9524, 1.2009	-0.8913	-1.1046, -0.6780	0.8688	0.6696, 1.0679	1.3164	1.1079, 1.5249	0.7853	0.4819, 1.0888

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
<b>Insurance Coverage</b>										
Uninsured, %	-0.0255	-0.0373, -0.0136	0.0013	-0.0402, 0.0427	0.0252	0.0099, 0.0406	-0.1060	-0.1247, -0.0872	0.0341	0.0114, 0.0568
Medicaid enrollees per 100 population in poverty	0.0042	0.0026, 0.0059	0.0049	0.0024, 0.0074	-0.0005	-0.0037, 0.0026	0.0119	0.0091, 0.0147	-0.0008	-0.0056, 0.0040
<b>Sociodemographic Characteristics</b>										
Unemployment rate	0.0955	0.0814, 0.1096	0.0869	-0.0166, 0.1903	0.2432	0.2008, 0.2855	0.1704	0.1487, 0.1922	0.0218	-0.0191, 0.0627
Gini index of income inequality	0.0189	0.0030, 0.0348	-0.0405	-0.0803, -0.0007	0.0527	0.0182, 0.0872	-0.0104	-0.0351, 0.0143	0.0756	0.0156, 0.1356
Population in poverty, %	0.0274	0.0203, 0.0346	0.0233	-0.0010, 0.0477	0.0375	0.0281, 0.0470	0.0194	0.0068, 0.0320	0.0348	0.0147, 0.0550
Population with a college degree, %	-0.0432	-0.0674, -0.0191	0.0058	-0.0421, 0.0538	-0.0496	-0.0913, -0.0079	-0.0030	-0.0490, 0.0431	0.0174	-0.0830, 0.1178
Female, %	0.0230	-0.0078, 0.0538	0.0014	-0.0793, 0.0821	0.0296	-0.0553, 0.1144	-0.0036	-0.0353, 0.0281	0.1830	0.0221, 0.3438
Age, y, % (REF=45+)										
<18	-0.0888	-0.1051, -0.0725	-0.0857	-0.1344, -0.0370	-0.0817	-0.1266, -0.0368	-0.0890	-0.1098, -0.0682	-0.0208	-0.0564, 0.0149
18-24	-0.0996	-0.1467, -0.0525	-0.1264	-0.2145, -0.0383	-0.0272	-0.0716, 0.0172	-0.2194	-0.3003, -0.1386	-0.0555	-0.1290, 0.0180
25-44	-0.0411	-0.0611, -0.0211	-0.1101	-0.1626, -0.0576	-0.0363	-0.0854, 0.0127	-0.0370	-0.0647, -0.0094	-0.1004	-0.1462, -0.0546
Race/ethnicity, % (REF=white)										
Black	-0.0308	-0.0402, -0.0215	-0.1066	-0.1638, -0.0495	-0.0062	-0.0320, 0.0196	-0.0746	-0.0945, -0.0547	-0.1467	-0.3269, 0.0335
Hispanic	-0.2412	-0.3081, -0.1744	-0.1058	-0.1661, -0.0455	-0.2185	-0.3405, -0.0966	-0.3214	-0.3947, -0.2480	0.0098	0.0019, 0.0177
API	-0.1969	-0.2752, -0.1187	-0.2611	-0.3913, -0.1309	-0.1346	-0.2626, -0.0067	-0.3009	-0.4490, -0.1529	-0.0945	-0.2128, 0.0238
AI/AN	0.0038	-0.0026, 0.0102	0.0427	-0.0927, 0.1781	0.0138	0.0091, 0.0185	-1.0008	-1.0008, -1.0008	0.0053	-0.0020, 0.0126
Other	-0.1453	-0.1863, -0.1044	-0.1078	-0.1658, -0.0498	-0.0410	-0.1016, 0.0196	-0.2980	-0.3670, -0.2291	0.0018	-0.0248, 0.0284
Population density per square mile	-0.0001	-0.0003, 0.0000	-0.0006	-0.0006, -0.0006	0.0000	-0.0003, 0.0002	-0.0002	-0.0005, 0.0001	-0.0008	-0.0020, 0.0005

County Characteristic	US		Northeast		Midwest		South		West	
	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI	$\beta$	95% CI
Population growth, 2010 vs 2000 census	-0.0265	-0.0343, -0.0186	-0.0768	-0.1069, -0.0468	-0.0153	-0.0337, 0.0032	-0.0256	-0.0353, -0.0159	-0.0518	-0.0712, -0.0324
Region (REF=South)										
Northeast	0.3308	0.1827, 0.4789	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Midwest	-0.4715	-0.6335, -0.3095	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
West	-0.4320	-0.6772, -0.1867	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Appalachia (REF=Non-Appalachia)	1.4064	1.3120, 1.5009	0.1516	-0.0885, 0.3917	1.5472	1.3767, 1.7176	1.6209	1.4550, 1.7868	N/A	N/A

Abbreviations: AI/AN, American Indian/Alaska Native; API, Asian/Pacific Islander; CI, confidence interval; OB-GYN, obstetrician-gynecologist; N/A, not applicable; NAS, neonatal abstinence syndrome; PDMP, prescription drug monitoring program; SUD, substance use disorder.

<sup>a</sup> Rates are per 100 000 individuals in the general population unless a different scale (eg, per 100) or population group (eg, women aged 15-44 years) is noted.  $\beta$  is the estimate from the linear regression model and can be interpreted as the absolute change in the county-level NAS rate associated with a 1-unit increase in the county characteristic. Cells highlighted in red signify increasing the county characteristic is associated with higher rates of NAS. Cells highlighted in green signify increasing the county characteristic is associated with lower rates of NAS.