Vulnerability Assessment of Oklahoma Counties to an Outbreak of Hepatitis C and Human Immunodeficiency Virus

Final Report

Submitted by

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August 2019

ACKNOWLEDGEMENTS

This project was supported by a contract between the Oklahoma State Department of Health (OSDH) and the College of Public Health and College of Medicine at the University of Oklahoma Health Sciences Center (OUHSC).

These efforts are supported by funding from the Centers for Disease Control and Prevention (TP18-1802- Cooperative Agreement for Emergency Response: Public Health Crisis Response).

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Executive Summary

The opioid epidemic has impacted Oklahomans and their communities, similar to many others throughout the US. As prescription opioids are designed to be taken orally, the association between injection drug use (IDU) and the opioid epidemic has been under-appreciated until a large outbreak of HIV occurred in Indiana, where disease was spread by users crushing their opioids and injecting them with shared/contaminated needles. This prompted public health officials to investigate the extent to which their communities may be at risk for an outbreak of HIV, hepatitis C virus (HCV), or other poor outcomes associated with IDU.

We designed an ecologic analysis of county-level characteristics associated with diseases spread via IDU. These characteristics included the distributions of age, sex, race/ethnicity, poverty, health insurance status, education level, population density, rates of drug-related crimes, rates of opioids being prescribed, number of buprenorphine prescribing facilities, and death rates from prescription opioid overdose. The number of acute HIV and acute HCV infections in each county served as the outcome marker for IDU. Populations of chronic HCV cases were included in sensitivity analyses to assess the robustness of results. Poisson regression modeling was used to identify associations and estimate vulnerability scores. Heat maps were generated to visually summarize the results by county.

There were 389 acute HIV-IDU and acute HCV cases across 49 of Oklahoma's 77 counties during 2015–2017. County-level characteristics associated with these cases of disease included the percent of the county that is Native American, prescription opioid death rate, rate that opioids are prescribed, percent of the county population without health insurance, and the percent of the county with less than a high school education among those age 18–24 years. When conducting sensitivity analyses including either all chronic HCV cases or chronic HCV cases aged ≤ 54 years, other potential county-level characteristics include a higher percentage

of those who are: male, age 25–44 years, and age 60+ years, identify two or more races, living below the federal poverty level and counties with a higher drug-related crime rate and increased population density. A curvilinear group of counties running from northeast Oklahoma to southcentral Oklahoma tended to have the highest vulnerability scores and predicted rates of infection of HIV-IDU and HCV.

Public health and other government officials, healthcare providers, community members, or other stakeholders, may wish to examine further which factors can be addressed to not only decrease the risk of an outbreak of HIV or HCV, but also benefit the county in other ways. The impact of race on these results needs to be interpreted with caution because the Cherokee Nation has been engaged in enhanced detection and treatment of HIV and HCV. Hence, the increased vulnerability in counties within the Cherokee Nation jurisdictional area may be an artifact of heightened awareness rather than of increased risk. A dissemination plan for these findings may facilitate dialogue among stakeholders and prioritize resources to address community needs.

INTRODUCTION

1. Hepatitis C virus Prevalence and Incidence in Oklahoma

Hepatitis C virus (HCV) causes a substantial burden of morbidity and mortality in Oklahoma and the United States (US). Oklahoma has a higher incidence rate of acute cases of HCV compared to the national rate. In 2016, there were 85 cases reported and confirmed as acute HCV in the state of Oklahoma. Males accounted for 47.1% (n=40) and females accounted for 52.9% (n=45) of these acute cases.[1] The rate of acute HCV in Oklahoma was 2.2 per 100,000 population, with the rate among females slightly higher (2.3 per 100,000) than males (2.1 per 100,000). Injection drug use (IDU) is the primary mode of HCV transmission with the majority (56.5%) of acute HCV cases in 2016 reported a history of using needles for street drugs. Nationally, the overall incidence rate for 2016 was 1.0 case per 100,000 population, an increase from 2015 (0.8 cases per 100,000 population).

2. Burden of New HIV Cases in Oklahoma

In 2016, 295 HIV cases were newly diagnosed in Oklahoma,[1] representing a rate of 7.5 cases per 100,000 population. Of these cases, 26.1% (n=77) were also diagnosed with AIDS in 2016. A quarter (n=74; 25.1%) of the newly diagnosed HIV cases were classified as late testers, which is defined as having an AIDS diagnosis within 3 months of HIV diagnosis. Approximately 6% (n=18; 6.1%) of the newly diagnosed cases were classified as HIV stage 0, or early HIV infection.

Nationally, from 2011 through 2015, the annual number and the rate of diagnoses of HIV infection in the US decreased. In 2016, the CDC estimated the rate of new HIV diagnoses was 12.3 per 100,000. In contrast, as of 2014, Oklahoma began to observe an increased rate of HIV infection.[2]

3. Opioid Prescriptions and Opioid-related Overdose Deaths

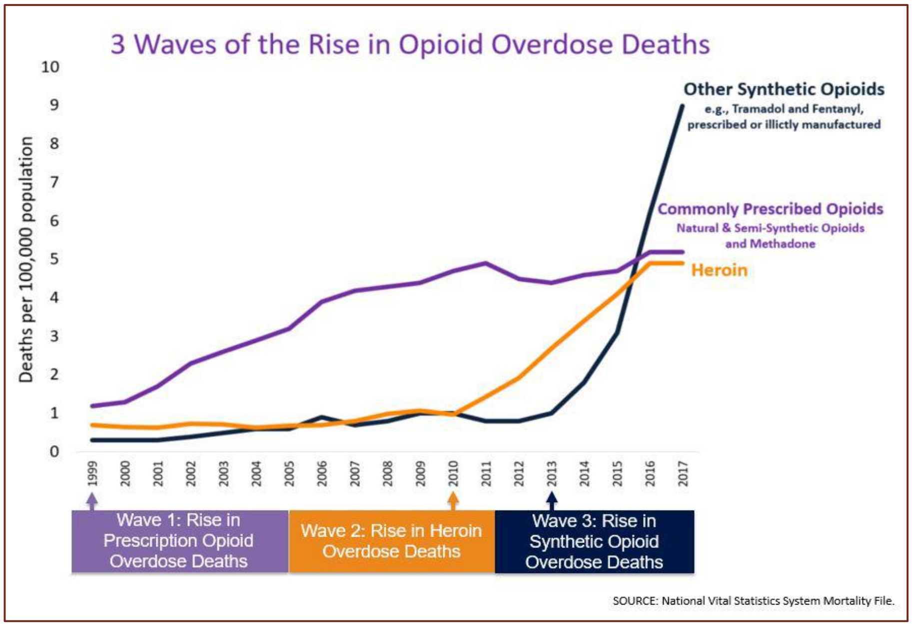
The use of prescription and illicit opioids has reached an epidemic proportion. According to CDC reports, more than 191 million opioid prescriptions were dispensed in the US in 2017, with wide variations across states.[3,4] Even with short term use, addiction to opioids can occur and as many as one in four of those receiving long term opioid therapy in a primary care setting struggles with addiction. In 2016, Oklahoma ranked sixth overall in the prevalence of opioid prescriptions, with almost 98 prescriptions per 100 population (Table 1).

Table 1. Prevalence of Opioid Prescription across the US in 2016.

State	Prevalence Opioid Prescription per 100	State	Prevalence Opioid Prescription per 100
Alabama	121.0	Maine*	66.9
Arkansas	114.6	Florida	66.6
Tennessee	107.5	New Mexico*	65.1
Mississippi	105.6	Washington*	64.9
Louisiana	98.1	New Hampshire*	64.3
Oklahoma	97.9	Iowa	64.0
Kentucky	97.2	Virginia	63.4
West Virginia	96.0	Nebraska	62.8
South Carolina	89.4	Wisconsin	62.2
Michigan*	84.9	Rhode Island*	60.3
Indiana	83.9	Colorado*	59.8
North Carolina	82.5	Alaska*	58.9
Nevada*	80.7	Maryland*	58.7
Missouri	80.4	Vermont*	58.6
Delaware*	79.2	Texas	57.6
Georgia	77.8	Illinois*	56.8
Idaho	77.6	Connecticut*	55.9
Kansas	76.9	South Dakota	54.8
Oregon*	76.3	New Jersey*	52.6
Ohio	75.3	North Dakota	47.8
Wyoming	71.1	Massachusetts*	47.1
Utah	70.4	Minnesota*	46.9
Arizona*	70.2	California*	44.8
Montana*	69.8	New York*	42.7
Pennsylvania	69.5	Hawaii*	41.9

*State has legalized medical or recreational marijuana, which can be used as substitute to opioids for pain management.

Figure 1. Opioid Overdose Deaths 1999-2017



Opioid abuse or misuse has led to a significant increase in opioid-related overdose death (Figure 1). Almost 400,000 people died from an overdose involving an opioid of any kind over the period of 1999–2017. In 2017, 47,746 overdose deaths were attributed to opioid abuse, which accounts for 68% of all drug overdose deaths in that year. Moreover, opioid-related overdose deaths in 2017 were six times higher than that in 1999.[5-7]

In Oklahoma, there were 444 opioid-related overdose deaths identified in 2016. This corresponds to a mortality rate of 11.6/100,000 population. Additionally, heroin-related overdose deaths have doubled since 2012.

4. Vulnerability Assessment

In January of 2015, Scott County, a rural county in Indiana, experienced the largest outbreak of HIV in the recent two decades. The 2014–15 HIV outbreak in Indiana, which was caused by shared needles and injection paraphernalia, showed that 92% of the 181 cases were individuals co-infected with HIV and HCV.[8] To address and prepare for possible future outbreaks, the CDC developed a vulnerability index to identify counties at similar risk for a syndemic of drug overdose, HIV and HCV. Variables included in the index included racial, socioeconomic, drug overdose, prescription opioid sales in morphine milligram equivalents, and buprenorphine prescribing potential characteristics.[9]

Applying the vulnerability index, CDC identified 220 counties across 26 states that are at high risk for the rapid spread of HIV, particularly among those who inject drugs by identifying factors associated with the rate of acute HCV infection as a proxy for unsafe IDU, and used these factors to create a vulnerability score.[10] A survey of these counties found that the majority are rural, with few resources or access to health care. Among the 220 counties, CDC identified two Oklahoma counties that ranked in the top 5% of counties nationwide as the most vulnerable for an HCV and HIV outbreak. These counties were Jefferson County (in the south) and Cimarron County (in the panhandle). Preliminary analyses to examine factors that were related to the risk of an HCV/HIV outbreak in Oklahoma pointed to race, ethnicity, drug-related arrests, prescribed opioid dose, and poverty as predicators.

OBJECTIVE

Using HIV infections with evidence of IDU (HIV-IDU) and confirmed acute HCV cases as a proxy measure of IDU, for which surveillance data are not available, the OSDH and OUHSC team conducted an updated, statewide vulnerability assessment of an HIV/HCV outbreak among persons who inject drugs in Oklahoma.

METHODS

1. Study Design

We designed an epidemiological ecologic study at the county level to assess the association between acute HCV infection and acute HIV infection from IDU and population-level characteristics to assess counties in Oklahoma that may be more vulnerable to experiencing an outbreak of an infection from IDU.

2. Data Sources

This study included datasets from the American Community Survey, U.S. Census Bureau, CDC, National Center for Health Statistics, the HIV/STD Service at the Oklahoma State Department of Health (OSDH), the Oklahoma State Bureau of Investigation, and the Oklahoma State Bureau of Narcotics and Dangerous Drugs Control. In addition, we made a Freedom of Information Act (FOIA) request to the Substance Abuse and Mental Health Administration (SAMHSA) to acquire data for buprenorphine prescription capacity by DATA 2000 waiver per 10,000 population for the years 2015 to 2017. Surveillance data were obtained from the HIV/STD Service at OSDH for HCV infection and HIV infection for the years 2015 to 2017. Acute HCV cases, classified as either confirmed or probable, were included. Acute HIV cases whose primary mode of transmission was identified as either "IDU" or "IDU and men who have sex with men (MSM)". The number of eligible acute cases for both conditions were summed for each county.

Predictor variables were selected based on analyses identified from previous vulnerability analyses that have been published.[9,11,12] These variables include: age (15–24, 25–44, 45–59, and ≥60 years), sex (male and female), ethnicity/race (Hispanic [any] and non-Hispanic: white, black, Native American, Asian, Pacific Islander, and two or more races), poverty (percent at or below the federal poverty level), education level (percent of the county age 18–24 years with less than a high school education), population density (number of people living per square mile), health insurance status (percent uninsured), adult drug related crime rate (number of crimes per county population), opioid-related death rate (number of deaths per county population), opioid prescribing rates, and buprenorphine prescription capacity were hypothesized predictor variables. The population for 2016, the median year of the analysis, was used for the population denominator, age, sex, race, poverty, insurance status, education level, and population density.

Table 2. Data Sources, Outcome and Predictor Variables

Source	Variable	Years
Enhanced Hepatitis Surveillance	Acute HCV infection	2015–2017
HIV and AIDS surveillance (eHARS)	Acute HIV infection with injection drug use transmission risk factor	2015–2017
American Community Survey[13]	Age group	2016
	Sex	
	Race	
	Poverty	
	Insurance status	
	Education level	
	Population density	
	County population	
Oklahoma State Bureau of Investigation[14]	Adult drug-related crimes	2016
National Center for Injury Prevention and Control[15]	Opioid prescribing rate	2015–2017
Oklahoma State Bureau of Narcotics and Dangerous Drugs Control[16]	Prescription opioid deaths	2014–2016
Substance Abuse and Mental Health Services Administration	Buprenorphine prescription capacity	2015–2017

Average rates for 2014–2016 were used for prescription opioid deaths, the number of arrests for 2016 were used, and the average rates for 2015–2017 for opioid prescriptions were used. The data and sources are summarized in Table 2.

3. Statistical Analysis

County-level characteristics were categorized as either the percent of the county with a given characteristic or the rate (i.e., number of events divided by the county population) for that county. As a proxy measure for IDU, the primary outcome of interest was all reported acute HIV cases with evidence of IDU and all reported acute HCV cases. Collinearity of variables was assessed by using Pearson's correlation. In the case of highly correlated variables (e.g., age variables and race/ethnicity variables), the variable with larger numbers that was also significant was selected. Poisson regression was used to estimate the association between predictors and the number of acute infections in the county. A backwards stepwise model-building approach was implemented. A crude analysis of each predictor, except the buprenorphine prescription capacity data, and the outcome was performed; variables with an *a priori* $p \leq 0.10$ were considered for the next step in the full model. An *a priori* $p > 0.2$ criteria for excluding variables from the multivariable model was employed. Predicted acute infection rates and 95% confidence intervals (CI) were generated for each county from the final multivariable Poisson model. Specifically, estimated log-counts of acute infections were derived in SAS v.9.4 (Cary, NC) with PROC GENMOD, converted to log-rates and exponentiated in PROC PLM for final interpretation. These predicted acute infection rates served as our metric for vulnerability scores, and counties were directly ranked from highest to lowest vulnerability based on descending acute infection rate values.

Three separate models were run using variations of the population included in the outcome variable. The outcome variables for each of the three models are:

- Model 1: All acute HCV and HIV-IDU cases;
- Model 2: All HCV, chronic and acute, and HIV-IDU cases;
- Model 3: All acute HCV, chronic HCV cases aged ≤54 years, and HIV-IDU cases.

All acute HIV-IDU cases and acute HCV cases were included in all three models. Results from each model were compared to assess the sensitivity to model changes. Heat maps of counties by predicted infection rate quintile were generated for each model.

Counties with at least one facility with buprenorphine prescription capacity were identified. However, the buprenorphine prescription capacity data were not included in the regression models because 34 (44%) counties did not have any facilities with buprenorphine prescription capacity. If buprenorphine was included in regression models, these counties with zero facilities would fall out of the model in the analysis. A Pearson correlation coefficient was calculated to assess the correlation of the mean number of buprenorphine-prescribing facilities per population and the number of acute HIV-IDU and acute HCV cases per population by county.

RESULTS

Of the 77 counties in Oklahoma, 49 (63.6%) have ≥ 1 acute infection of HCV or HIV-IDU during 2015–2017. In all, there were 389 cases in the outcome category, "acute HIV-IDU and acute HCV", 9,436 in the outcome category "acute HIV-IDU and all HCV", and 8,674 in the outcome category "acute HIV-IDU, acute HCV, and chronic HCV age ≤54 years". Across Oklahoma, 21 counties (27%) reported more than 100 cases of HCV (both acute and chronic) and HIV (Appendix 1). These include Beckham, Bryan, Canadian, Cherokee, Comanche, Cleveland, Creek, La Flore, Mayes, Muskogee, Oklahoma, Okmulgee, Osage, Payne, Pittsburg, Pottawatomie, Rogers, Sequoyah, Tulsa, and Wagoner. Not surprisingly, the three counties that are most populated in the state reported the highest number of cases, Cleveland (n=903), Oklahoma (n=1,446), and Tulsa (n=1,633).

Predictor data were complete for all counties with the exception that there were no data regarding the opioid prescribing rates for Beaver County. The β-estimates, standard errors (SE), and p-values for each variable entered into the crude Poisson regression models are summarized in Tables 3 and 4.

Each of the age group variables were significantly correlated with each other (p<0.001) with absolute values for the correlation coefficients ranging from 0.39–0.82. The correlation among the race/ethnicity variables was less consistent, where percent white, percent Native American, and percent two-or-more races were largely correlated with each other race/ethnicity variable, while percent black, percent Asian, percent Pacific Islander, and percent Hispanic tended to not be correlated with each other.

Table 3 presents the crude results identifying county-level predictors that are associated with the number of acute HCV and all HIV-IDU infections from drug use in the county (Model 1 referenced above). Counties with higher percent of residents identified as Native American, of those in two or more racial categories, below the poverty line, uninsured, have an education level of high school or below, and prescription opioid-related death rate were significantly associated with the outcome. There is an observed inverse relationship between the percent of white residents and the number of infections. Moreover, it is worth noting that the magnitude of association is much larger for the variable, prescription opioid-related death rate, with the number of infections, compared to all other variables.

Table 3. Estimates from Crude Poisson Regression Models (Model 1)

Predictor	Acute HCV + All HIV-IDU		
	Estimate	SE	p-value
Percent male	0.058	0.039	0.131
Percent age 15–24 years	-0.014	0.017	0.401
Percent age 25–44 years	-0.020	0.016	0.228
Percent age 45+ years	0.015	0.014	0.301
Percent age 45–59 years	0.053	0.038	0.160
Percent age 60+ years	0.028	0.014	0.052
Percent white	-0.019	0.007	0.004
Percent black	-0.010	0.010	0.312
Percent Native American	0.022	0.006	0.000
Percent Asian	-0.067	0.045	0.135
Percent Pacific Islander	-0.402	0.264	0.128
Percent Hispanic	-0.644	1.000	0.520
Percent two or more races	0.156	0.030	<0.0001
Prescription opioid-related death rate	1260.062	387.553	0.001
Opioid prescribing rate	0.003	0.002	0.092
Percent below poverty line	0.034	0.016	0.035
Drug crime rate	19.578	27.224	0.472
Percent uninsured	0.037	0.016	0.022
Percent with less than high school education in age group 18–24	0.021	0.010	0.040
Population Density	0.000	0.000	0.394

Table 4 presents two sets of results identifying county-level predictors that are associated with the number of infections in our two sensitivity analyses: (1) all HCV and all HIV-IDU infections (Model 2), and (2) acute HCV, chronic HCV for those aged ≤54 years, and all HIV-IDU infections (Model 3).

Table 4. Estimates from Crude Poisson Regression Models (Model 2 and Model 3)

Predictor	All HCV+ HIV-IDU			Chronic HCV aged ≤54 +Acute HCV+ HIV-IDU		
	Estimate	SE	p-value	Estimate	SE	p-value
Percent male	0.062	0.008	<0.001	0.073	0.008	<0.001
Percent age 15–24 years	0.010	0.003	0.001	0.012	0.003	0.002
Percent age 25–44 years	-0.022	0.003	<0.001	-0.022	0.003	<0.001
Percent age 45+ years	-0.007	0.003	0.018	-0.008	0.003	0.012
Percent age 45–59 years	0.003	0.008	0.699	0.002	0.008	0.804
Percent age 60+ years	0.017	0.003	<0.001	0.017	0.003	<0.001
Percent white	-0.580	0.119	<0.001	-0.444	0.124	<0.001
Percent black	-1.174	0.192	<0.001	-1.455	0.201	<0.001
Percent Native American	2.552	0.131	<0.001	2.595	0.136	<0.001
Percent Asian	-3.891	0.709	<0.001	-4.185	0.740	<0.001
Percent Pacific Islander	-22.588	3.705	<0.001	-22.290	3.817	<0.001
Percent Hispanic	-0.266	0.199	0.181	-0.084	0.205	0.682
Percent two or more races	13.168	0.634	<0.001	13.220	0.662	<0.001
Prescription opioid-related death rate	1206.840	78.860	<0.001	1213.480	82.229	<0.001
Opioid prescribing rate	12.000	0.000	<0.001	0.001	0.000	0.002
Percent below poverty line	0.045	0.003	<0.001	0.043	0.003	<0.001
Drug crime rate	55.909	5.179	<0.001	57.383	5.387	<0.001
Percent uninsured	0.047	0.003	<0.001	0.046	0.003	<0.001
Percent with less than high school education in age group 18–24	0.006	0.002	0.005	0.005	0.002	0.153
Population Density	0.000	0.000	<0.001	0.000	0.000	<0.001

Similar to results for acute HCV and HIV-IDU infections, counties with higher percent of male residents, residents who are in the age ranges of 15–24, 60 or older, those identified as Native American, those in two or more racial categories, below the poverty line, uninsured, drug crime rate, and prescription opioid-related death rate. The association between percent of those with education level of high school or below remained significant for all HCV and HIV-IDU infections but not when the sample that was diagnosed with HCV was limited to those who are 54 years and younger with chronic HCV. On the other hand, the percent of those aged 25–44, 45 and older, or who are white, black, Asian, Pacific Islander were inversely associated with the number of infections. In addition, the magnitude of association with the number of infections is much larger for the variables, prescription opioid-related death rate and drug crime rate.

When applying the stepwise backwards selection to identify the most useful predictors, prescription opioid death rate and mean opioid prescription rate are common predictors that were retained across all three models. Other socio-demographic predictors varied across models (Table 5). The race/ethnicity variables for percent white, black, Asian, Pacific Islander, and Hispanic fell out of each model, whereas percent Native American and percent two or more races showed associations with HIV-IDU and HCV counts.

Table 5. List of Variables Selected via Stepwise Backward Selection for Each Models

Model 1 (Acute HCV and HIV-IDU)	Model 2 (All HCV+ HIV-IDU)	Model 3 (Chronic HCV age ≤54 years + Acute HCV + HIV-IDU)
• Percent Native American • Prescription opioid death rate • Mean opioid prescription rate • Percent uninsured (healthcare) • Percent of age 18–24 years with less than High School education	• Percent male • Percent aged 60+ years • Percent two or more races • Prescription opioid death rate • Mean opioid prescription rate • Percent below the federal poverty line • Population density	• Percent male • Percent aged 25–44 years • Percent two or more races • Prescription opioid death rate • Mean opioid prescription rate • Percent below the federal poverty line • Adult drug crime rate

Table 6 ranks the counties in Oklahoma in terms of their predicted rates of acute HCV and IDU-associated HIV infection. The top ten counties, Adair, Mayes, Muskogee, Carter, Murray, Cherokee, Pushmataha, Pittsburg, Craig, and Bryan, are concentrated in the northeastern part of the state, bordering Arkansas, or southcentral part of Oklahoma, near Texas.

Table 6. Predicted rates and of acute HCV and IDU-associated acute HIV infection

			95% Confidence Intervals (CI)	
Rank	COUNTY	Rate/100,000	Lower	Upper
1	Adair County	20.00	12.25	32.66
2	Mayes County	18.61	13.43	25.79
3	Muskogee County	16.17	12.15	21.53
4	Carter County	15.78	11.22	22.18
5	Murray County	15.18	11.74	19.63
6	Cherokee County	14.91	9.84	22.57
7	Pushmataha County	14.71	8.48	25.52
8	Pittsburg County	14.26	11.29	18.01

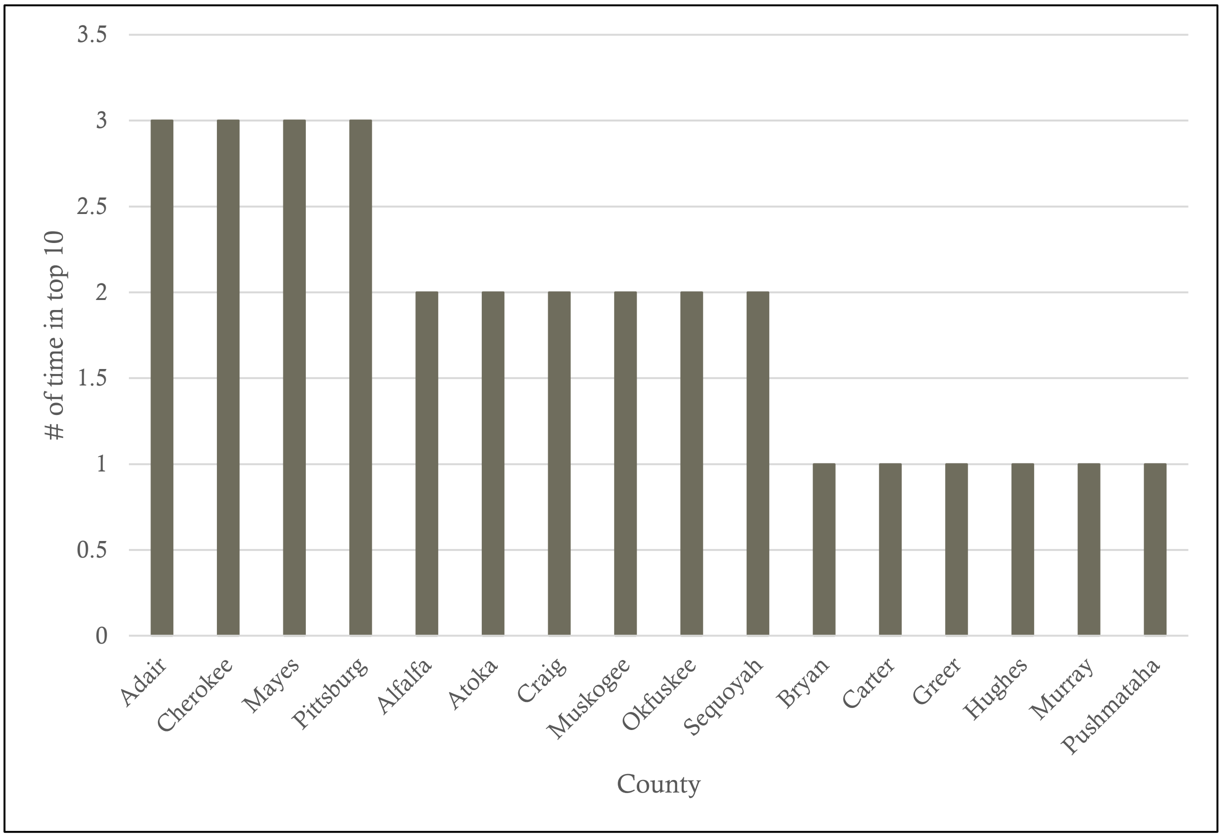
			95% Confidence Intervals (CI)	
Rank	COUNTY	Rate/100,000	Lower	Upper
9	Craig County	13.26	10.12	17.39
10	Bryan County	13.20	10.26	16.98
11	Sequoyah County	12.84	10.11	16.32
12	Latimer County	12.81	10.36	15.83
13	Creek County	12.52	10.50	14.92
14	Delaware County	12.50	10.02	15.58
15	McIntosh County	11.87	9.84	14.32
16	Stephens County	11.76	9.72	14.24
17	Pottawatomie County	11.63	9.89	13.69
18	McClain County	11.59	9.41	14.27
19	Rogers County	11.58	8.94	15.00
20	Ottawa County	11.28	9.16	13.90
21	Wagoner County	11.22	8.71	14.45
22	Pawnee County	11.22	9.98	12.61
23	Blaine County	11.11	6.59	18.74
24	Pontotoc County	11.05	8.80	13.87
25	Caddo County	10.92	7.40	16.12
26	Okmulgee County	10.86	9.22	12.79
27	Washington County	10.58	9.23	12.13
28	Tulsa County	10.27	8.94	11.79
29	Love County	10.22	8.30	12.58
30	Le Flore County	10.14	8.20	12.54
31	Beckham County	10.12	7.78	13.16
32	Kay County	10.04	7.97	12.65
33	Seminole County	9.96	7.56	13.13
34	Nowata County	9.92	7.53	13.08
35	Choctaw County	9.80	5.33	18.01
36	Haskell County	9.78	7.08	13.50
37	Washita County	9.77	5.79	16.46
38	Okfuskee County	9.61	6.16	14.99
39	Coal County	9.56	6.60	13.85
40	Atoka County	9.53	7.07	12.84
41	McCurtain County	9.47	6.89	13.02
42	Woodward County	9.31	7.83	11.08
43	Noble County	9.23	5.94	14.34
44	Marshall County	9.18	7.23	11.64
45	Hughes County	8.96	6.26	12.84

			95% Confidence Intervals (CI)	
Rank	COUNTY	Rate/100,000	Lower	Upper
46	Harmon County	8.91	4.61	17.23
47	Grady County	8.84	7.11	10.99
48	Tillman County	8.67	6.81	11.04
49	Oklahoma County	8.53	7.26	10.03
50	Osage County	8.53	6.03	12.05
51	Garvin County	8.46	6.77	10.57
52	Johnston County	8.37	4.86	14.43
53	Cimarron County	8.32	6.22	11.13
54	Canadian County	8.26	6.65	10.25
55	Comanche County	8.15	6.58	10.11
56	Cleveland County	7.92	6.09	10.28
57	Lincoln County	7.92	5.82	10.77
58	Roger Mills County	7.88	5.37	11.55
59	Kingfisher County	7.52	5.52	10.25
60	Jackson County	7.49	6.23	9.00
61	Grant County	7.24	5.07	10.35
62	Custer County	7.23	5.56	9.39
63	Jefferson County	7.21	4.62	11.26
64	Garfield County	7.10	5.64	8.93
65	Woods County	7.06	5.20	9.59
66	Cotton County	7.00	4.68	10.47
67	Major County	6.87	3.87	12.19
68	Payne County	6.78	5.01	9.17
69	Ellis County	6.69	4.46	10.04
70	Logan County	6.63	5.25	8.38
71	Kiowa County	6.54	4.90	8.73
72	Texas County	6.46	4.62	9.04
73	Alfalfa County	6.19	4.34	8.84
74	Greer County	6.13	4.06	9.25
75	Harper County	5.68	3.19	10.11
76	Dewey County	5.49	3.52	8.54

* Beaver County is excluded due to missing opioid prescribing rate data.

Sixteen counties ranked among the 10 most vulnerable counties in one or more Poisson models. Four counties, Adair, Cherokee, Mayes, and Pittsburg, remained in the top 10 most vulnerable counties, regardless of the how the outcome variable was defined (e.g., inclusion of chronic HCV cases) for the analyses (Figure 2).

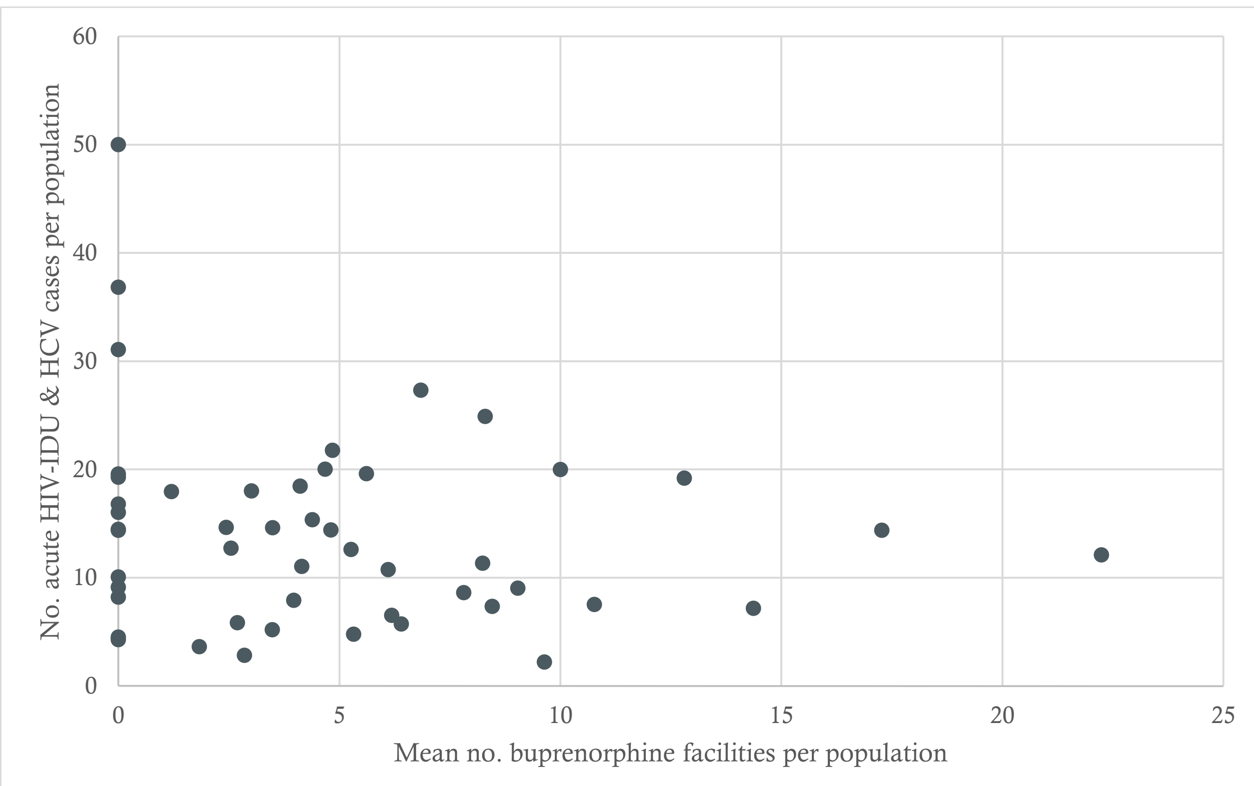
Figure 2. Of the three models, the number of Poisson models in which the county ranked among the top 10 most vulnerable



With FDA approval in 2002, buprenorphine, an opioid partial agonist, is the first medication to treat opioid dependency that can be prescribed or dispensed in physician offices or clinics, which significantly increases access to treatment. According to SAMHSA, under the Drug Addiction Treatment Act of 2000 (DATA 2000), qualified US physicians and mid-level practitioners with an X-license can prescribe buprenorphine in various settings, including a physician's office, community hospital, health department, or correctional facility. Given the significant associations between infections and opioid-related variables, it is reasonable to assume that availability of facilities offering buprenorphine can be used as a proxy to examine access to care.

When analyzing the relationship between buprenorphine prescription capacity and cases of infection in Oklahoma, there was a negative, though not significant, correlation between the mean number of facilities offering buprenorphine per population and the rate of acute HIV-IDU and HCV infection (r=-0.17, p=0.23) among counties with at least one case of disease (Figure 3).

Figure 3. Correlation between the mean number of buprenorphine facilities per population and number of acute HIV-IDU and HCV cases per population in each county with one or more acute case in 2015-2017.



However, of the most vulnerable counties, Adair, Alfalfa, Atoka, Okfuskee, Greer, and Hughes Counties did not have any buprenorphine prescription capacity during 2015–2017. Table 7 presents the prescription opioid rates and access to buprenorphine.

Table 7. Prescription Opioid Rate and Access to Buprenorphine

		Access to Buprenorphine	
COUNTY	Prescription Opioid Rate	Mean number of clinics prescribing 2015-2017	Mean number of clinics prescribing per 100,000 population
Counties with at least 1 buprenorphine prescribing facility			
Carter County	163	2.3	4.81
Murray County	149	2	14.37
Bryan County	143	2	4.39
Muskogee County	122	12	17.27
Cherokee County	104	2	4.11
Craig County	104	1	6.84
Mayes County	99	1	2.44
Sequoyah County	67	2	4.8
Pushmataha County	13	1	9.04
Pittsburg County	6	3.7	8.30
Counties without any buprenorphine prescribing facilities			
Adair County	68	0	0
Atoka County	37	0	0
Hughes County	34	0	0
Greer County	23	0	0
Okfuskee County	4	0	0
Alfalfa County	2	0	0

Heat maps for each of the three Poisson models (Figures 4–6) report the predicted rates of HIV-IDU/HCV infection by quintile. Although there is a certain degree of variability across the three models, a pattern is clearly observed that counties in the northeast trending toward the southcentral are among the most vulnerable counties.

Figure 4. Predicted incidence of an infection from injection drug use based on reports of all acute HIV-IDU cases and acute HCV cases in Oklahoma, 2015-2017

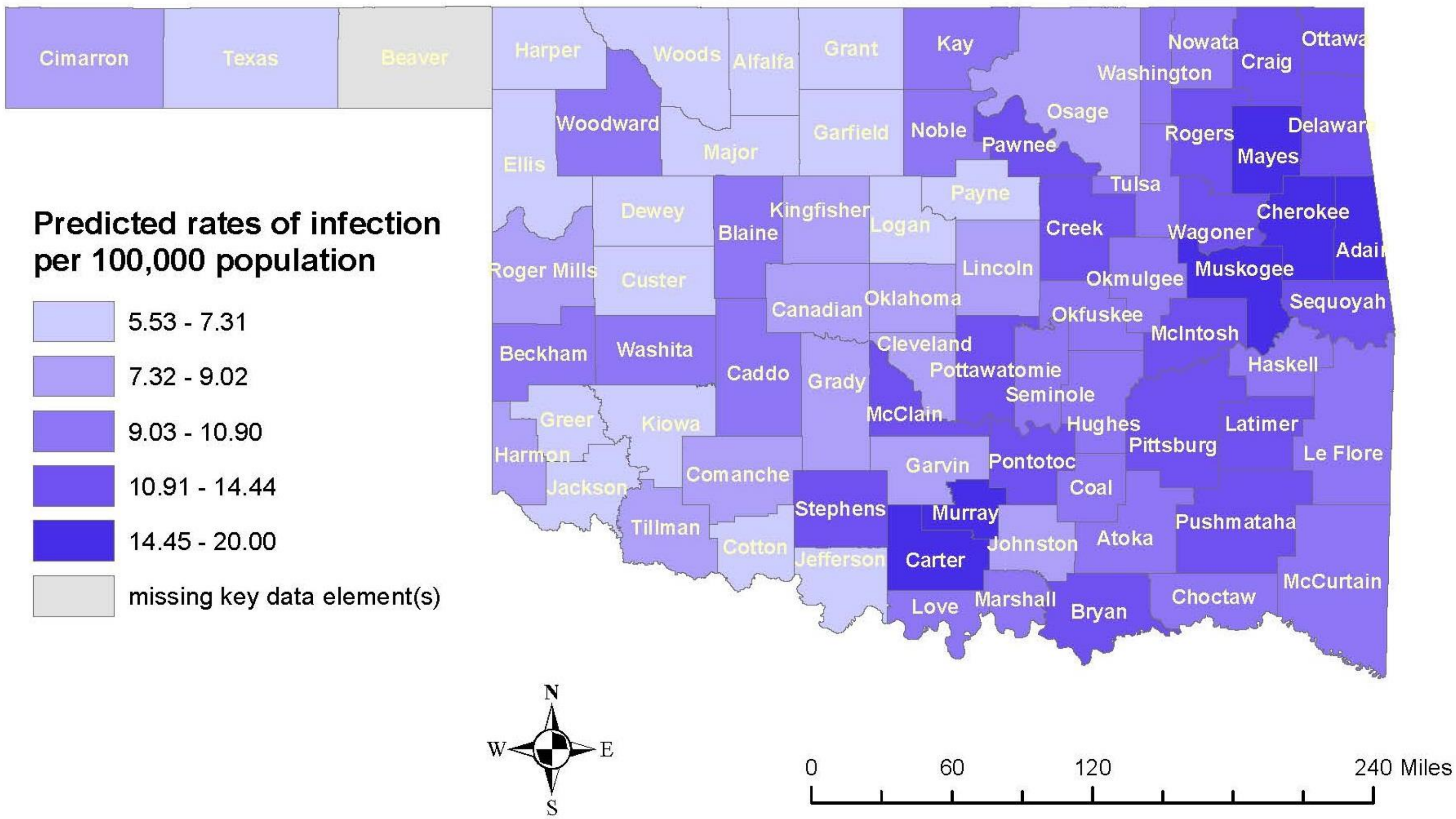


Figure 5. Predicted incidence of an infection from injection drug use based on reports of all acute HIV-IDU cases and all acute and chronic HCV cases in Oklahoma, 2015-2017

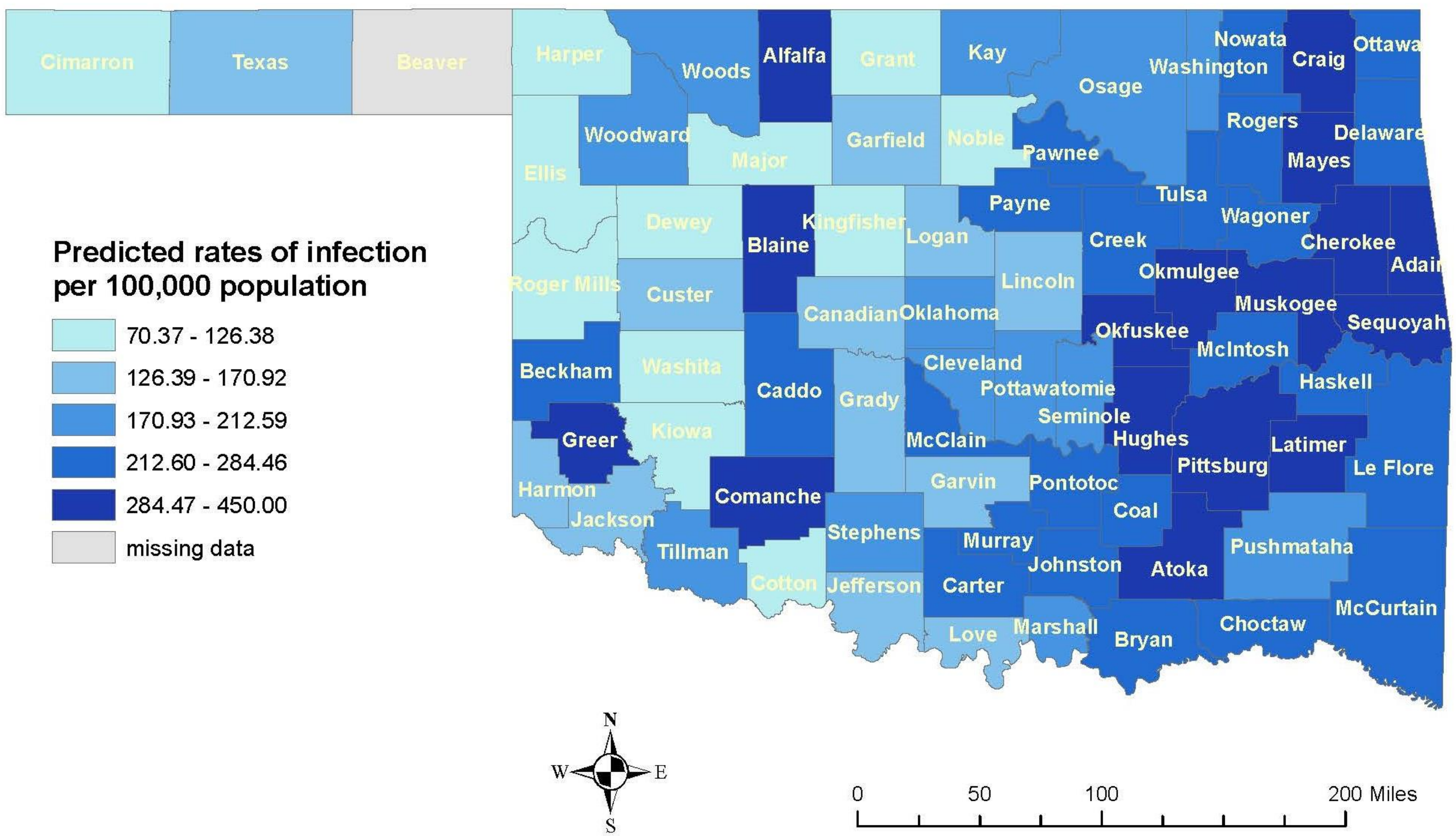
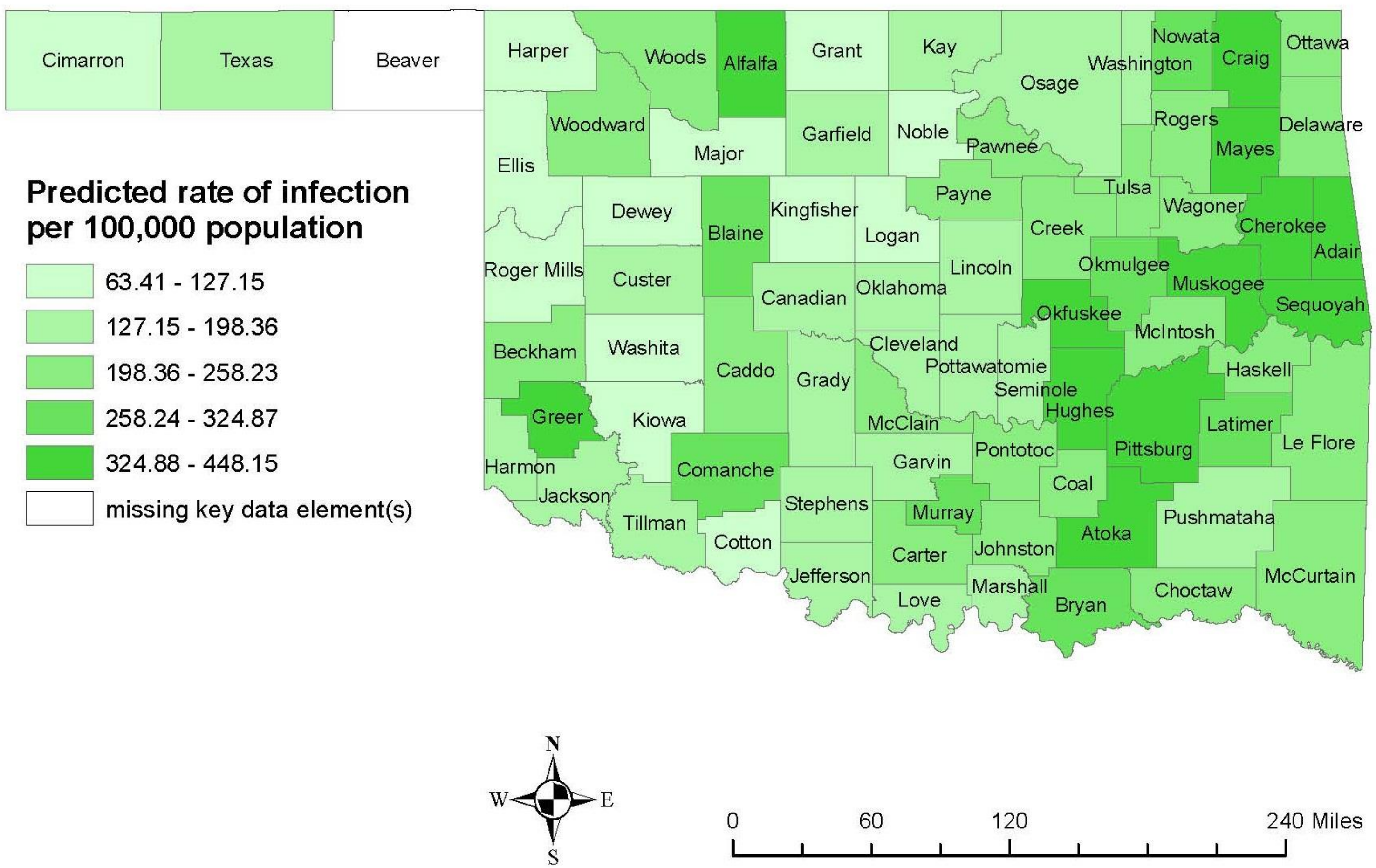


Figure 6. Predicted incidence of an infection from injection drug use based on reports of all acute HIV-IDU cases, all acute HCV cases, and chronic HCV cases age ≤54 years in Oklahoma, 2015-2017



DISCUSSION

1. Summary of Findings

This report presents the landscape of IDU-related infections, i.e., HCV and HIV, across the state of Oklahoma, computing predicted rates of infection for 76 of the 77 Oklahoma counties. Overall, counties located in the northeastern and southcentral part of the state are the most vulnerable, with the top ten most vulnerable counties identified in the primary analysis (acute HIV-IDU and acute HCV cases) being Adair, Mayes, Muskogee, Carter, Murray, Cherokee, Pushmataha, Pittsburg, Craig, and Bryan.

Chronic HCV cases and chronic HCV cases among those age ≤ 54 years were included in the outcome measure in sensitivity analyses because there was concern that that timing of diagnosing HCV may be inconsistent across age, county, and race/ethnicity. In addition, there was a hypothesis that the epidemiologic risk factors for chronic HCV cases age ≥ 55 years (roughly described as the Baby Boomers) may be different from younger cases of HCV. Another impact of including the chronic HCV cases in the sensitivity analyses was a dramatic increase in sample size and corresponding lower p-values. Despite these differences, the general geographic pattern of vulnerable counties remained consistent demonstrating robustness to the results.

Applying the Poisson regression models to identify predictors for HCV and HIV infections, socio-demographic predictors varied across outcome variables focusing on all, acute, and younger chronic HCV infections. Across the three models, a higher percent of residents who identify as American Indian/Native American, are of two or more racial groups, below the poverty line, uninsured, as well as the prescription opioid death rate were positively associated with the number of infections. In particular, the prescription opioid death rate is a very strong predictor, with a magnitude almost a thousand fold higher than those of other predictors.

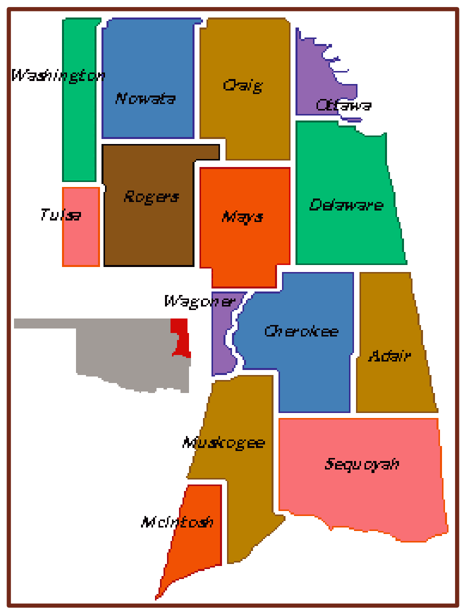
In addition to the previous vulnerability analyses conducted by CDC[9] and Tennessee[11] and an internal Oklahoma-specific vulnerability analysis conducted in 2016,[12] this vulnerability analysis was conducted in the context of approximately 40 other states, each of which was undertaking their own analysis. Although each state had flexibility in designing the methods of their analyses, regular conference calls were hosted by CDC and the Council of State and Territorial Epidemiologists (CSTE) to provide technical assistance and facilitate comparability across states. When comparing the results in the current report to those published and ongoing, there is a difference in the predictor variables identified as having significant associations. Among those analyses assessing the vulnerability of Oklahoma Counties,[9,11,12] there is also an observed difference in the most vulnerable counties. These differences are expected because each of these analyses (1) was conducted during a different timeframe, (2) used different outcome measures, and (3) had access to different predictor variables. Due to these differences, we caution against relying too heavily on the statistical significance of any one predictor variable or the numeric value of predicted rates of infection. Instead, the results from this report will be most helpful in identifying potential factors that can be addressed by public health officials, the medical community, and the general public.

It is noteworthy that, in contrast to national reports of having a higher representation of white and young population demonstrating association with increased vulnerability, the Oklahoma analyses showed a higher percent of Native American and those of two or more races as well as older age to be associated with increased vulnerability. To facilitate the comparison of our results to those from other states, we ran a number of exploratory models that retained certain predictors, such as white race and younger age groups, in the model regardless of their statistical significance. The distribution of vulnerability scores was similar to those presented in this report, thereby demonstrating the robustness of these results.

2. Limitations

There are a number of limitations to note for this analysis:

Figure 7. Overlap of the Cherokee Nation and Oklahoma Counties



- There may be possible diagnosis or surveillance bias in the 14 counties within the Cherokee Nation jurisdictional area (Figure 7). The Cherokee Nation has developed and implemented an extensive HCV elimination program in 2015. This program is ongoing with extensive screening of all those accessing the Cherokee Nation Health System aged 20–69 years, which may result in more cases identified. Subsequently, these counties may be more prepared to address the public health challenges associated with IDU. In addition, counties with the lowest reported rates of infection may be associated with external factors and not a result of having low infection rates.

- It is possible we double-counted some individuals who were co-infected with HIV and HCV. We did not have personal identifying information to determine uniqueness of each individual in the dataset. However, the robustness of the results with various models suggests the over-estimates may be non-differential.

- Counties without a single case may potentially introduce inflated variance in the Poisson regression model. We addressed this limitation is two ways. First, zero counts may have impacted the primary model (of acute cases only), but not the models including chronic HCV cases. The results were comparable across models. Second, we requested technical assistance from the CDC/CSTE who helped us arrive at our analytic plan.

- This vulnerability analysis is an ecologic study and includes data from multiple publically available sources. While the variables from these sources help identify important associations, they may not be designed to predict rates of infections.

- HCV and HIV infection status was used as a proxy for IDU. The assumption that HCV has been contracted via IDU may be flawed, as only about 60% of the acute HCV cases identified IDU as a mode of transmission. However, without a measure that captures the mode of acute HCV transmission, the analysis can only rely on the use of this proxy. Consistent across all currently available vulnerability analyses, the use of acute HCV infection as a proxy measure for IDU is an acceptable assumption.

3. Conclusions

This report serves to inform and educate medical providers and public health workers by identifying vulnerable counties with county-level predictors that are associated with an increased number of infections for targeted prevention and intervention efforts. Sixteen counties, Adair, Alfalfa, Atoka, Bryan, Carter, Cherokee, Craig, Greer, Hughes, Mayes, Muskogee, Murray, Okfuskee, Pittsburg, Pushmataha, and Sequoyah, were found to be among the most vulnerable counties across all analyses.

The American Indian/Native American communities may be at increased risk for poor outcomes associated with IDU, but may have higher awareness of HCV and HIV infections in their respective communities. Poverty, lower education, and increased crime rates contribute to counties being identified as more vulnerable.

Finally, the rate of opioid-related deaths is an important marker for communities which may also be at risk for an outbreak of disease associated with IDU. Many communities, including Scott County in Indiana, where the HIV outbreak occurred, have reduced the risk of disease transmission by instituting safe needle exchange programs. A dissemination plan will need to be developed to effectively communicate this information and engage stakeholders in identifying strategies for prevention that are tailored to the characteristics of the community and the needs of its members.

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Appendices

Appendix 1. Case counts in each outcome group by county

COUNTY	Acute HCV + HIV-IDU	All HCV + HIV-IDU	Acute HCV + Chronic HCV age ≤54 + HIV-IDU
Adair County	1	81	73
Alfalfa County	0	10	10
Atoka County	2	69	65
Beaver County	0	3	2
Beckham County	7	108	105
Blaine County	0	15	15
Bryan County	7	144	139
Caddo County	0	81	75
Canadian County	8	184	172
Carter County	7	99	90
Cherokee County	9	206	192
Choctaw County	0	23	19
Cimarron County	0	1	1
Cleveland County	30	903	856
Coal County	0	10	6
Comanche County	9	317	296
Cotton County	0	5	3
Craig County	4	47	39
Creek County	14	177	169
Custer County	0	39	38
Delaware County	7	79	74
Dewey County	0	4	4
Ellis County	0	8	8
Garfield County	3	71	64
Garvin County	5	73	69
Grady County	2	75	71
Grant County	0	2	1
Greer County	3	27	26
Harmon County	0	2	1

Harper County	0	0	0
Haskell County	0	53	50
Hughes County	5	78	77
Jackson County	5	30	26
Jefferson County	1	7	7
Johnston County	2	28	26
Kay County	1	93	86
Kingfisher County	0	18	18
Kiowa County	0	12	12
Latimer County	2	53	49
Le Flore County	10	216	200
Lincoln County	1	64	60
Logan County	2	59	51
Love County	2	13	11
McClain County	0	60	58
McCurtain County	3	50	48
McIntosh County	2	57	48
Major County	0	13	13
Marshall County	0	21	19
Mayes County	6	135	122
Murray County	1	16	16
Muskogee County	10	319	302
Noble County	0	14	13
Nowata County	0	12	10
Okfuskee County	1	38	33
Oklahoma County	59	1446	1276
Okmulgee County	5	111	92
Osage County	7	119	105
Ottawa County	4	88	83
Pawnee County	2	56	50
Payne County	7	188	175
Pittsburg County	11	260	249
Pontotoc County	2	76	68
Pottawatomie County	8	248	222
Pushmataha County	1	28	24
Roger Mills County	0	16	15
Rogers County	6	133	120
Seminole County	2	40	37

Sequoyah County	9	247	238
Stephens County	0	76	67
Texas County	0	39	38
Tillman County	0	2	2
Tulsa County	73	1633	1488
Wagoner County	15	165	151
Washington County	3	71	65
Washita County	0	11	10
Woods County	0	18	18
Woodward County	3	43	43

Appendix 2. Complete list of counties in Oklahoma ranked according to their predicted rates of acute HIV-IDU or HCV (all acute and all chronic) infection

COUNTY	Rate/100,000	Standard Error	95% CI	
			Lower	Upper
Adair County	485.76	0.000217	444.96	530.29
Mayes County	438.66	0.000114	416.86	461.60
Alfalfa County	430.58	0.000405	358.04	517.82
Okfuskee County	420.47	0.000195	384.02	460.38
Sequoyah County	404.69	0.000127	380.46	430.47
Atoka County	403.72	0.000139	377.42	431.85
Cherokee County	401.83	0.000104	382.01	422.68
Muskogee County	391.41	0.000122	368.22	416.05
Pittsburg County	390.50	0.000145	363.16	419.91
Craig County	382.05	0.000135	356.42	409.52
Hughes County	373.20	0.000163	342.56	406.59
Greer County	370.63	0.000295	317.05	433.27
Latimer County	362.64	9.25E-05	344.96	381.23
Blaine County	350.04	0.000228	308.14	397.64
Comanche County	331.02	9.31E-05	313.27	349.77
Okmulgee County	329.69	8.43E-05	313.58	346.62
Bryan County	301.34	8.86E-05	284.46	319.23
Murray County	300.79	0.000113	279.42	323.78
Nowata County	286.46	0.000116	264.52	310.21
Rogers County	285.55	9.67E-05	267.20	305.15
Caddo County	278.56	9.28E-05	260.96	297.35
Pontotoc County	272.89	5.69E-05	261.97	284.26
Le Flore County	272.01	7E-05	258.63	286.09
Johnston County	270.88	0.000133	246.07	298.19
Creek County	269.65	4.93E-05	260.16	279.49
Ottawa County	268.51	7.64E-05	253.94	283.91
Coal County	266.92	8.02E-05	251.64	283.12
Delaware County	264.37	0.0001	245.45	284.76
Payne County	263.33	9.78E-05	244.85	283.21
Choctaw County	263.00	0.000148	235.55	293.65
Haskell County	256.84	8.31E-05	241.06	273.65
Wagoner County	249.37	7.76E-05	234.62	265.06
Beckham County	247.94	0.000111	227.19	270.59
McIntosh County	247.77	0.000119	225.57	272.16
Carter County	246.80	8.19E-05	231.25	263.39

McClain County	245.96	8.11E-05	230.56	262.38
McCurtain County	239.86	7.57E-05	225.48	255.17
Tulsa County	239.60	4.5E-05	230.94	248.58
Pawnee County	237.92	5.31E-05	227.74	248.56
Seminole County	225.22	6.64E-05	212.59	238.61
Woods County	222.93	0.000101	204.00	243.63
Woodward County	216.89	8.91E-05	200.12	235.08
Pushmataha County	212.10	0.000138	186.72	240.93
Oklahoma County	212.06	3.84E-05	204.66	219.73
Cleveland County	209.52	4.82E-05	200.27	219.19
Washington County	205.85	4.92E-05	196.44	215.72
Pottawatomie County	203.17	5.84E-05	192.04	214.94
Tillman County	200.20	9.54E-05	182.36	219.80
Osage County	198.40	8.36E-05	182.67	215.49
Marshall County	193.43	5.43E-05	183.07	204.38
Stephens County	190.09	6.7E-05	177.39	203.69
Kay County	183.87	5.26E-05	173.84	194.47
Garvin County	179.81	4.65E-05	170.92	189.17
Texas County	175.07	7.87E-05	160.31	191.19
Love County	174.59	5.12E-05	164.84	184.92
Grady County	174.28	4.77E-05	165.18	183.87
Jefferson County	171.20	6.35E-05	159.20	184.10
Custer County	169.35	5.6E-05	158.73	180.69
Lincoln County	168.27	6.11E-05	156.71	180.68
Harmon County	163.38	0.00011	143.10	186.53
Jackson County	159.04	5.89E-05	147.90	171.02
Canadian County	158.39	4.89E-05	149.09	168.27
Garfield County	143.72	4.65E-05	134.89	153.12
Logan County	142.52	4.34E-05	134.27	151.28
Washita County	138.49	7.17E-05	125.14	153.27
Cotton County	137.87	6.12E-05	126.38	150.41
Kiowa County	133.89	6.93E-05	120.98	148.18
Cimarron County	129.33	8.35E-05	113.95	146.78
Dewey County	127.45	6.23E-05	115.81	140.25
Kingfisher County	126.67	4.4E-05	118.33	135.60
Noble County	122.32	5.33E-05	112.31	133.22
Grant County	117.16	6.15E-05	105.70	129.87
Major County	93.64	5.02E-05	84.31	104.00
Roger Mills County	91.82	5.24E-05	82.10	102.70
Ellis County	81.41	4.73E-05	72.66	91.22

Harper County	78.99	4.66E-05	70.37	88.67
Beaver County	No Data Reported			

Appendix 3. Complete list of counties in Oklahoma ranked according to their predicted rates of acute HIV-IDU or HCV infection among HCV cases age ≤54 years

COUNTY	Rate/100,000	Standard Error	95% CI	
			Lower	Upper
Alfalfa County	440.94	0.0004	373.12	521.08
Adair County	436.30	0.0002	399.05	477.03
Sequoyah County	426.36	0.0002	386.32	470.54
Atoka County	408.93	0.0002	379.98	440.08
Mayes County	394.71	0.0001	373.22	417.43
Pittsburg County	392.93	0.0001	365.96	421.90
Okfuskee County	377.16	0.0002	338.38	420.40
Cherokee County	363.31	0.0001	346.89	380.51
Greer County	361.88	0.0003	310.43	421.87
Hughes County	359.75	0.0002	329.36	392.94
Muskogee County	359.36	0.0001	338.14	381.92
Craig County	349.30	0.0001	326.02	374.25
Comanche County	324.87	0.0001	308.84	341.73
Latimer County	314.22	0.0001	297.85	331.49
Blaine County	307.10	0.0002	268.17	351.69
Nowata County	303.28	0.0002	271.81	338.40
Okmulgee County	300.94	0.0001	285.28	317.46
Murray County	287.74	0.0001	265.23	312.17
Bryan County	284.51	0.0001	269.99	299.81
Beckham County	258.23	0.0001	237.45	280.83
Ottawa County	255.45	0.0001	239.44	272.53
Rogers County	253.41	0.0001	236.22	271.85
Pontotoc County	252.88	0.0000	243.70	262.41
Caddo County	252.23	0.0001	235.08	270.63
McIntosh County	251.36	0.0001	232.00	272.34
Creek County	245.79	0.0001	236.12	255.86
Haskell County	245.47	0.0001	232.58	259.07
Carter County	242.94	0.0001	225.16	262.12
Johnston County	242.51	0.0001	219.01	268.53
Coal County	236.71	0.0001	223.98	250.17
Le Flore County	236.02	0.0001	222.31	250.59
Choctaw County	233.39	0.0001	208.14	261.71
Wagoner County	230.78	0.0001	216.22	246.33
McClain County	229.67	0.0001	215.02	245.31
Delaware County	227.67	0.0001	213.36	242.94

Payne County	227.00	0.0001	212.66	242.31
Woods County	225.50	0.0001	199.71	254.61
Pawnee County	218.35	0.0001	205.10	232.46
Tulsa County	208.60	0.0000	201.30	216.15
McCurtain County	206.15	0.0001	192.98	220.22
Woodward County	204.05	0.0001	188.21	221.21
Oklahoma County	198.36	0.0000	190.91	206.10
Cleveland County	197.03	0.0000	188.31	206.16
Seminole County	186.23	0.0001	173.08	200.38
Pottawatomie County	184.46	0.0000	176.33	192.97
Pushmataha County	181.73	0.0001	158.33	208.58
Washington County	181.36	0.0000	172.92	190.21
Osage County	176.04	0.0001	161.97	191.33
Tillman County	172.27	0.0001	155.54	190.79
Marshall County	166.87	0.0001	157.19	177.15
Stephens County	165.93	0.0001	154.24	178.50
Garvin County	165.35	0.0000	156.95	174.20
Texas County	165.24	0.0001	151.80	179.87
Canadian County	163.35	0.0001	153.57	173.75
Kay County	161.50	0.0001	151.70	171.94
Grady County	157.80	0.0000	149.28	166.80
Love County	153.64	0.0001	144.07	163.85
Jefferson County	150.41	0.0001	138.15	163.77
Custer County	146.03	0.0000	137.17	155.46
Lincoln County	142.31	0.0001	131.22	154.33
Harmon County	139.77	0.0001	122.31	159.73
Garfield County	136.70	0.0000	127.79	146.22
Jackson County	135.88	0.0000	127.10	145.26
Logan County	127.15	0.0000	119.79	134.97
Cotton County	119.12	0.0001	108.71	130.52
Washita County	116.92	0.0001	104.67	130.62
Kiowa County	115.93	0.0001	104.88	128.16
Noble County	112.03	0.0001	101.44	123.74
Kingfisher County	110.97	0.0000	102.78	119.81
Cimarron County	107.93	0.0001	95.26	122.28
Dewey County	105.57	0.0001	95.03	117.29
Grant County	99.96	0.0001	89.06	112.20
Major County	79.11	0.0000	70.74	88.47
Roger Mills County	77.30	0.0000	68.39	87.38
Ellis County	63.46	0.0000	55.73	72.26

Harper County	63.41	0.0000	55.83	72.03
Beaver County	No Data Reported			