County-level Vulnerability Assessment for Rapid Dissemination of HIV or HCV Infection Among Persons who Inject Drugs, United States – Supplemental Appendix

Contents

Supplemental Methods

We identified indicators associated with acute hepatitis C virus (HCV) infection to develop a composite index score (vulnerability score) ranking each county's vulnerability to rapid dissemination of IDU-associated HIV if introduced, and new or continuing high numbers of HCV infections among persons who inject drugs (PWID). We chose acute HCV infection as the outcome that best serves our purpose because it is collected at the county-level for almost all states.

Regression Modeling Analyses

We modeled the number of acute HCV infections by county using a multilevel Poisson model with the county population set as the offset.[1] Our data have a multilevel structure with the ith year (2012, 2013) nested in the jth county and jth county nested in the kth state. The Poisson distribution is defined as:

$$Pr(Y = y) = \frac{\lambda^y e^{-\lambda}}{y!}$$

where y = 0, 1, 2, ..., and λ is the expected rate. The Poisson model uses the $\log_e$ function that relates the expected value of the response variable to the linear predictor. Hence, the expected rate, λ, is modeled using the link function $\log_e$ as:

$$log_e(\lambda) = \eta = log_e(Population) + \beta_0 + \beta_1 X_1 + ... + \beta_p X_p$$

where X is the ith indicator and β is the associated model parameter, and β_0 the intercept (i.e., overall mean). The offset, *log_e(Population)*, is the county population. We have multilevel data and we model the levels (i.e., state and county nested within a state) as random effects to account for spatial heterogeneity (i.e., overdispersion). We modified our model so the log_e link function relates the conditional mean (i.e., conditional on the random effects) of the response variable (i.e., acute HCV rate) to the linear indicator of the fixed and random effects. Our model including random effects for the county and state is given by:

$$log_e(\lambda|b) = \eta = log_e(Population) + \beta_0 + \beta_1 X_1 + ... + \beta_p X_p + b_0 Z_{jk} + b_1 Z_k$$

Where the random effects, b_0 and b_1, are assumed to be $N(0, \sigma^2_{jk})$ and $N(0, \sigma^2_k)$, respectively. We used SAS GLIMMIX[2] and the residual subject-specific pseudo-likelihood (RSPL) model estimation method.

Modeling Procedure

We fit a univariable Poisson random-effects models for each of the 15 considered indicators. Figure S1 depicts county-level data by class for each of the 15 considered indicators. Per capita income and population density were modeled on log_{10} scale. Aside from urgent care and highway exit, which were coded as yes/no, the other indicators were treated as continuous variables. Our goal was to develop a parsimonious model that is significantly associated with acute HCV infection rate. We entered all 15 indicators in the multivariable model and removed the indicators with the highest p-value. We removed and added indicators in a backwards stepwise procedure until all remaining indicators had a p-value<0.05.

Continuous Indicators Linearity Assessment

We assessed linearity for the 13 continuous indicators. Our assumption was that these indicators were linear on the log_e(acute HCV rate) scale. To assess the assumption of linearity of the rate on the log-scale we used the following procedure.

1. Calculate the quintiles for the indicator
2. Calculate the acute HCV rate by quintile
3. Plot the log_e(acute HCV rate) versus the quintile for the indicator

4. Estimate the slope and intercept of the log_e(acute HCV rate) versus quintile

5. Visually assess the assumption of linearity of the indicator

Collinearity Assessment of Indicators

If an indicator is nearly a linear combination of other indicators in the model, the affected estimates may be unstable and have high standard errors. This situation is usually referred to as collinearity or multicollinearity. We used a generalized linear model (GLM) with counts as the outcome, which required a different procedure to assess collinearity than for a linear regression model. To assess collinearity we relied on three calculated statistics: eigenvalue, condition index, and principal component proportion of variation. An eigenvalue is a computed value that characterizes the essential properties and numerical relationships within a matrix. Eigenvalues that are close to zero may be indicative of a matrix that is close to singular, which indicates collinearity. Eigenvalues <0.01 are usually thought to be close to zero. The condition index is defined as the square root of the ratio of the largest eigenvalue to each individual eigenvalue. The largest condition index (i.e., the square root of the ratio of the largest to the smallest eigenvalue) is the condition number of the scaled X matrix which, as noted by Belsley et al (1990), suggest that when this number is nearing 10, weak dependencies might start to affect the regression estimates.[3] When this number is larger than 100, the estimates likely include significant numerical error.

To calculate the eigenvalues, condition indices, and proportions of variation we used a two-step process in SAS.[2] First, we fit the Poisson model using PROC GENMOD and output the Hessian weights. Secondly, we fit a linear model, using PROC REG, with the Hessian weights defined in the weight statement to obtain the collinearity diagnostics.

Standardized Regression Coefficients

Standardized regression coefficients for our final multivariable model were calculated to determine the relative importance of each indicator. We calculated the standardized regression coefficients using:

$$\beta_p^s = \frac{Std(X_p)}{Std(y^{pseudo})}\beta_p$$

Where β_p is the estimated regression coefficient from the final multivariable model, *Std* is the standard deviation of the X^{th} indicator and *pseudo* outcome *y*. The *pseudo* outcome is the outcome estimated on the log_e scale from the estimated regression model.

Composite Index (Vulnerability) Score and Rank

Our primary goal was to develop a composite index score for ranking the county vulnerability to rapid dissemination of IDU-associated HIV if introduced, and new or continuing high numbers of acute HCV infection among PWID. We developed a vulnerability score using data from the indicators identified in the final multivariable model and the following method to rank counties from lowest to highest vulnerability. We used regression coefficients and observed values to compute the index score for each county. The score for the j^{th} county was calculated using the regression coefficients (β) and indicators (*X*) as given by:

$$S_j^u = \beta_1 X_1 + \ldots + \beta_p X_p$$

The intercept, β_0, is not used because it is a constant and has no impact on the ranking of counties based on the scores. Once the vulnerability score was calculated for each county, including those not used in fitting the model, they were ranked from 1 - 3143 with higher scores interpreted as being more vulnerable. Ranks using regression coefficients include uncertainty. To account for uncertainty in the ranks we used simulation to estimate the 90% confidence interval (CI) for each county's rank. We drew 10,000 samples from a normal distribution for each regression coefficient using their estimate and standard error of the estimate. For each of the 10,000 samples we calculated the county's vulnerability score and rank and then obtained a CI for each county's rank.

The threshold for classifying the most vulnerable counties was set at the 95th percentile (top 5%). The 95th percentile threshold of the ranks was calculated using all 3,143 counties as 0.95 * 3,143 = 2985.85. We used the upper bound of the 90% CI to determine if a county's rank was within the 95th percentile. Once we determined the counties that were within the threshold we ranked them using the inverse of their mean estimated rank (1=highest vulnerability).

Supplemental Results

Model Fit Results

The final multivariable model with the 6 indicators closely aligned the reported HCV rates with the model-estimated HCV rates. To illustrate the model fit we mapped the reported and model-estimated rates of acute HCV infection per 10,000 population (Figure S2). Fewer than 15% (469 of 3,143) of counties varied by more than 1 class when comparing the reported and model-estimated rate of acute HCV infection. The average absolute difference in the model-estimated rates was 0.011 per 10,000 population lower than the actual rates.

Composite Index (Vulnerability) Score and Rank

Figure S3a shows a histogram of the vulnerability scores by number of counties in each score group (e.g., 0 to 0.25). Figure S3b shows a sigmoid curve of the vulnerability scores by county rank.

Using the mean average rank, 157 counties were ranked above the inclusion threshold. The red circle identifies the counties that border the top 5% cut-off. Figure S3c shows a caterpillar curve of the 90% confidence intervals (CIs) bordering the top 5% cut-off. An additional 63 counties were identified above the threshold based on their 90% CI for a total of 220 vulnerable counties.

Counties Identified as Vulnerable

Table S1 lists the counties identified within the top 5% threshold of vulnerability ranks by state and rank. Table S2 summarizes information on the 220 counties by state; including information on the number of counties identified. Seven states had 10 or more vulnerable counties: Indiana, Kentucky, Michigan, Missouri, Ohio, Tennessee, and West Virginia.

References

1. Gelman, A and Hill, J. Data Analysis Using Regression and Multilevel/Hierarchical Models. (2007). Cambridge University Press. 625 p.
2. SAS Institute, Inc. SAS®: Version 9.3 for Windows. Cary (NC): SAS Institute, Inc.; 2012.
3. Belsley DA, Kuh E, Welsch RE. Regression Diagnostics: Identifying Influential Data and Sources of Collinearity. (1990). John Wiley & Sons Inc.

Tables

Table S1. Counties identified in the top 5% of vulnerability ranks by state and rank

FIPS	County	Rank
Alabama		
01127	Walker	37
01093	Marion	100
01133	Winston	109
01059	Franklin	206
Arizona		
04015	Mohave	208
Arkansas		
05135	Sharp	157
05075	Lawrence	201
California		
06063	Plumas	152
06033	Lake	199
Colorado		
08025	Crowley	220
Georgia		
13111	Fannin	82
13281	Towns	120
13213	Murray	159
13143	Haralson	200
Illinois		
17069	Hardin	68
Indiana		
18143	Scott	32
18175	Washington	57
18149	Starke	70
18041	Fayette	81
18155	Switzerland	94
18025	Crawford	112
18065	Henry	128
18079	Jennings	158
18137	Ripley	195
18029	Dearborn	213
Kansas		
20207	Woodson	144
20001	Allen	171
20205	Wilson	181
20153	Rawlins	218
Kentucky		
21237	Wolfe	1
21025	Breathitt	3
21193	Perry	4
21051	Clay	5
21013	Bell	6
21131	Leslie	8
21121	Knox	9
21071	Floyd	10
21053	Clinton	11
21189	Owsley	12
21235	Whitley	14
21197	Powell	15
21119	Knott	17
21195	Pike	21
21153	Magoffin	23
21065	Estill	25
21129	Lee	30
21165	Menifee	31
21159	Martin	34
21021	Boyle	35
21127	Lawrence	39
21203	Rockcastle	40
21095	Harlan	45
21147	McCreary	48
Kentucky (cont.)		
21133	Letcher	50
21115	Johnson	53
21207	Russell	54
21063	Elliott	56
21125	Laurel	65
21041	Carroll	67
21217	Taylor	75
21081	Grant	77
21001	Adair	93
21137	Lincoln	97
21231	Wayne	99
21057	Cumberland	101
21077	Gallatin	108
21011	Bath	125
21085	Grayson	126
21089	Greenup	129
21087	Green	132
21045	Casey	153
21043	Carter	154
21171	Monroe	163
21079	Garrard	167
21201	Robertson	175
21135	Lewis	178
21061	Edmonson	179
21003	Allen	180
21019	Boyd	187
21105	Hickman	191
21027	Breckinridge	202
21037	Campbell	212
21167	Mercer	214
Maine		
23027	Waldo	135
23025	Somerset	145
23029	Washington	170
23011	Kennebec	193
Michigan		
26129	Ogemaw	86
26035	Clare	87
26135	Oscoda	88
26119	Montmorency	91
26085	Lake	137
26141	Presque Isle	174
26001	Alcona	184
26143	Roscommon	192
26039	Crawford	197
26079	Kalkaska	207
26031	Cheboygan	215
Mississippi		
28141	Tishomingo	164
Missouri		
29179	Reynolds	55
29123	Madison	58
29187	St. Francois	69
29039	Cedar	107
29093	Iron	117
29223	Wayne	119
29221	Washington	130
29055	Crawford	148
29085	Hickory	156
29013	Bates	177
29181	Ripley	183
Missouri (cont.)		
29153	Ozark	185
29229	Wright	194
Montana		
30061	Mineral	161
30103	Treasure	211
Nevada		
32029	Storey	52
32009	Esmeralda	118
North Carolina		
37043	Clay	63
37193	Wilkes	104
37075	Graham	124
37023	Burke	176
37039	Cherokee	189
Ohio		
39001	Adams	51
39131	Pike	72
39079	Jackson	111
39105	Meigs	123
39015	Brown	127
39145	Scioto	136
39163	Vinton	146
39053	Gallia	155
39009	Athens	173
39027	Clinton	190
39071	Highland	196
Oklahoma		
40067	Jefferson	89
40025	Cimarron	217
Pennsylvania		
42079	Luzerne	38
42021	Cambria	131
42039	Crawford	188
Tennessee		
47067	Hancock	13
47087	Jackson	19
47005	Benton	24
47151	Scott	26
47135	Perry	33
47071	Hardin	36
47029	Cocke	41
47015	Cannon	42
47137	Pickett	43
47013	Campbell	46
47019	Carter	59
47027	Clay	64
47057	Grainger	66
47073	Hawkins	71
47173	Union	74
47059	Greene	79
47025	Claiborne	80
47085	Humphreys	83
47145	Roane	92
47133	Overton	95
47041	DeKalb	102
47143	Rhea	103
47121	Meigs	105
47129	Morgan	106
47049	Fentress	115
47111	Macon	116
47185	White	134
Tennessee (cont.)		
47063	Hamblen	138
47007	Bledsoe	139
47159	Smith	140
47109	McNairy	141
47139	Polk	142
47089	Jefferson	149
47163	Sullivan	151
47181	Wayne	160
47101	Lewis	168
47091	Johnson	169
47099	Lawrence	172
47179	Washington	198
47177	Warren	203
47095	Lake	216
Texas		
48155	Foard	204
Utah		
49007	Carbon	84
49001	Beaver	114
49015	Emery	186
Vermont		
50009	Essex	143
50025	Windham	219
Virginia		
51027	Buchanan	28
51051	Dickenson	29
51167	Russell	61
51105	Lee	73
51195	Wise	78
51185	Tazewell	96
51141	Patrick	166
51197	Wythe	210
West Virginia		
54047	McDowell	2
54059	Mingo	7
54109	Wyoming	16
54081	Raleigh	18
54045	Logan	20
54005	Boone	22
54019	Fayette	27
54065	Morgan	44
54063	Monroe	47
54029	Hancock	49
54015	Clay	60
54099	Wayne	62
54009	Brooke	76
54053	Mason	85
54013	Calhoun	90
54067	Nicholas	98
54089	Summers	110
54101	Webster	113
54043	Lincoln	121
54011	Cabell	122
54091	Taylor	133
54055	Mercer	147
54007	Braxton	150
54095	Tyler	162
54087	Roane	165
54051	Marshall	182
54003	Berkeley	205
54039	Kanawha	209

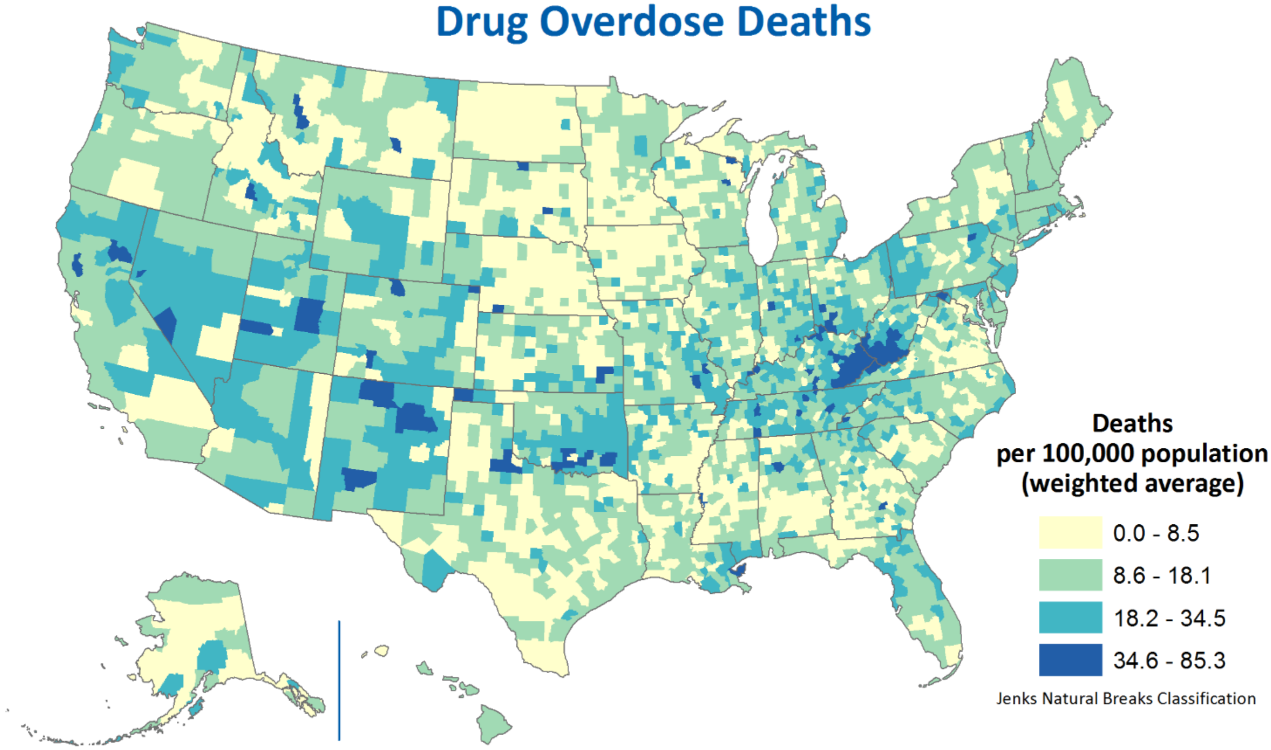
Table S2. States with at least one county identified in the top 5% of highest vulnerability ranks by number of vulnerable counties and percentage of all state counties identified as vulnerable.

State	Vulnerable #	Total #	Identified Vulnerable (%)
Alabama	4	67	6.0
Arizona	1	15	6.7
Arkansas	2	75	2.7
California	2	58	3.5
Colorado	1	64	1.6
Georgia	4	159	2.5
Illinois	1	102	1.0
Indiana	10	92	10.9
Kansas	4	105	3.8
Kentucky	54	120	45.0
Maine	4	16	25.0
Michigan	11	83	13.3
Mississippi	1	82	1.2
Missouri	13	115	11.3
Montana	2	56	3.6
Nevada	2	17	11.8
North Carolina	5	100	5.0
Ohio	11	88	12.5
Oklahoma	2	77	2.6
Pennsylvania	3	67	4.5
Tennessee	41	95	43.2
Texas	1	254	0.4
Utah	3	29	10.3
Vermont	2	14	14.3
Virginia	8	134	6.0
West Virginia	28	55	50.9
Total	**220**	**2139**	**10.3%**

Figures

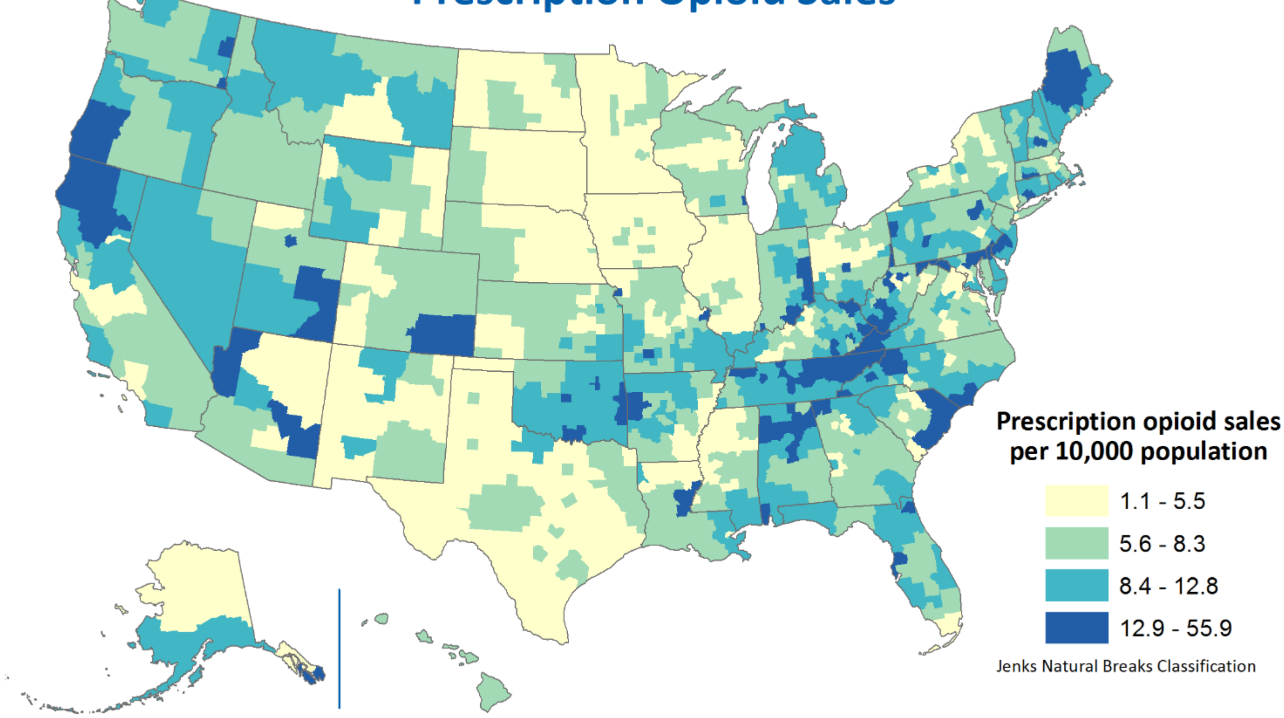
Figure S1. County-level indicators investigated for association with acute HCV infection.

Drug Overdose Deaths



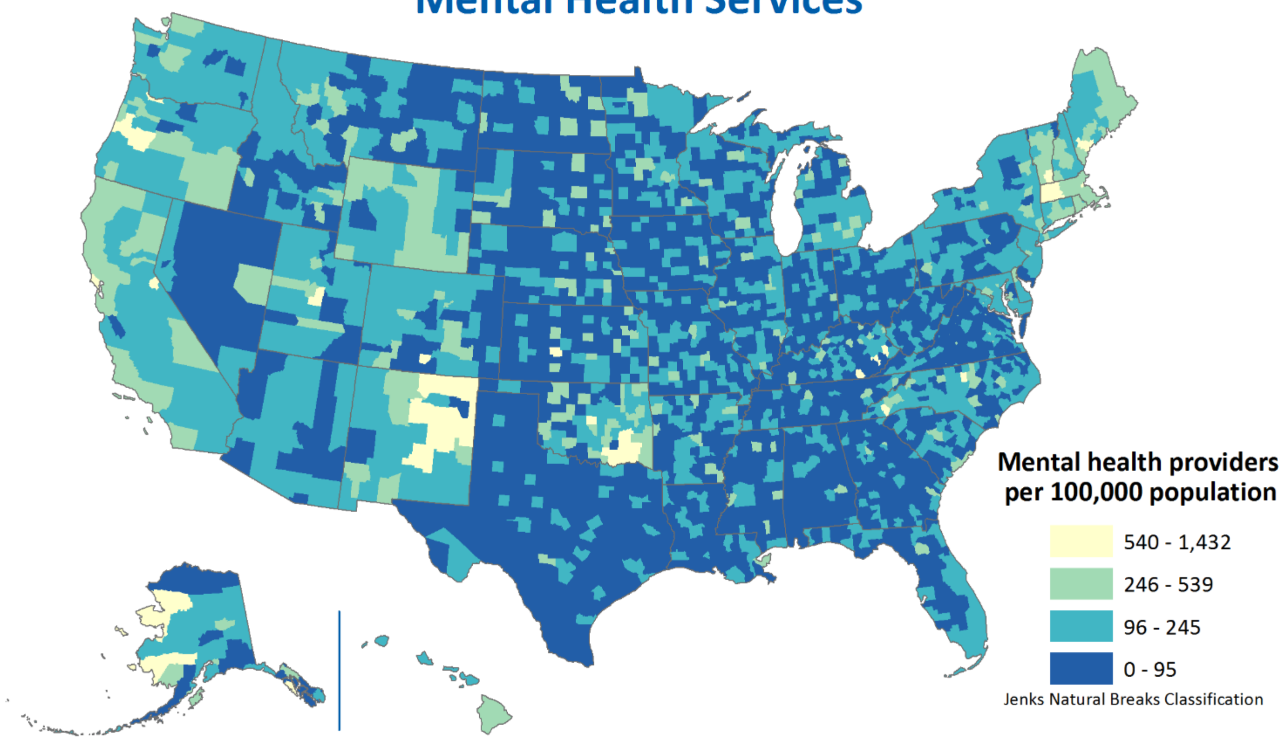
Source: National Center for Health Statistics (NCHS)/National Vital Statistics, 2012 and 2013

Prescription Opioid Sales



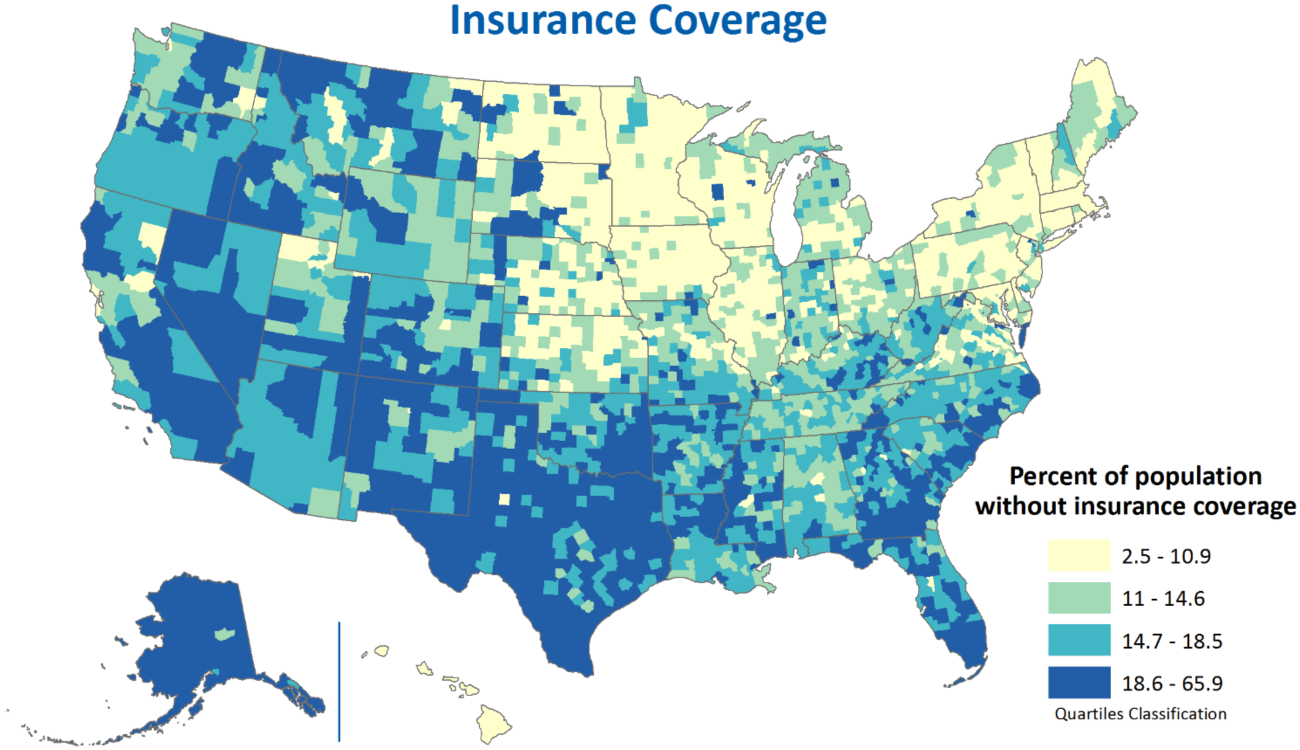
Source: Drug Enforcement Administration (DEA) – Automation of Reports and Consolidated Orders System (ARCOS), 2013. DEA provided 3-digit ZIP data and authors transformed data to 5-digit county FIPS.

Mental Health Services



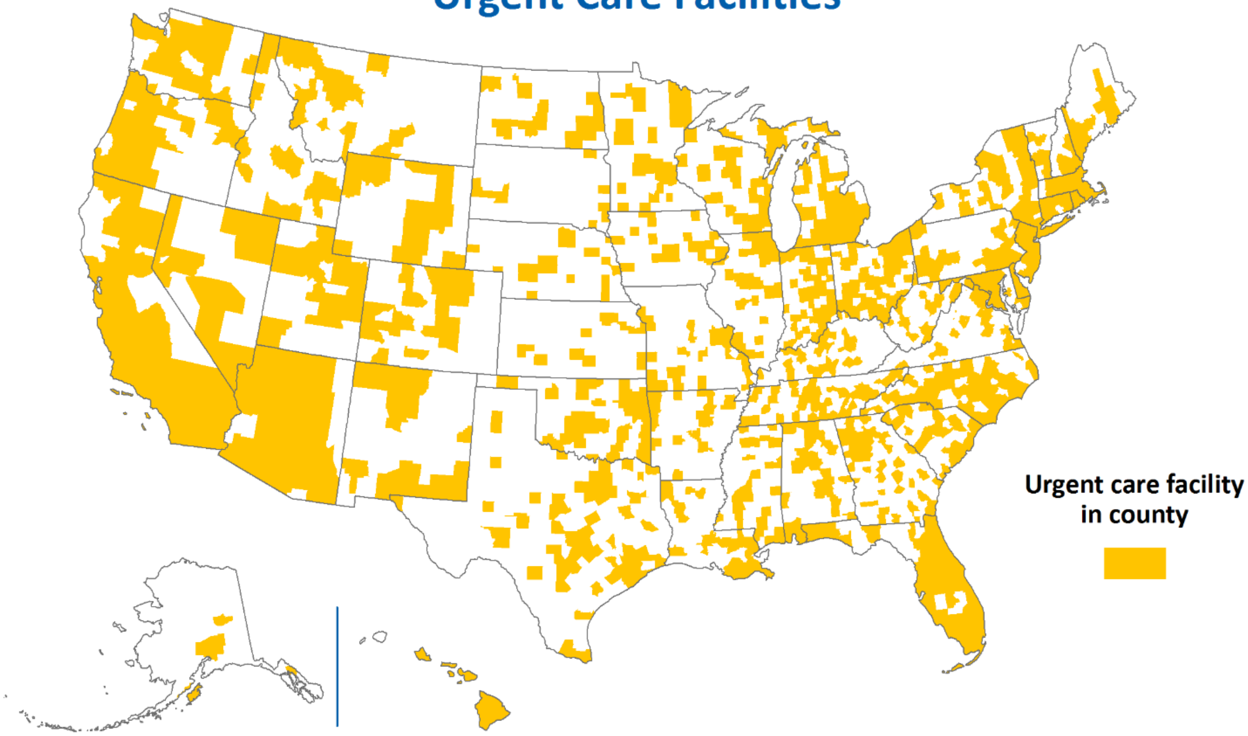
Source: CMS, National Provider Identification, 2014

Insurance Coverage



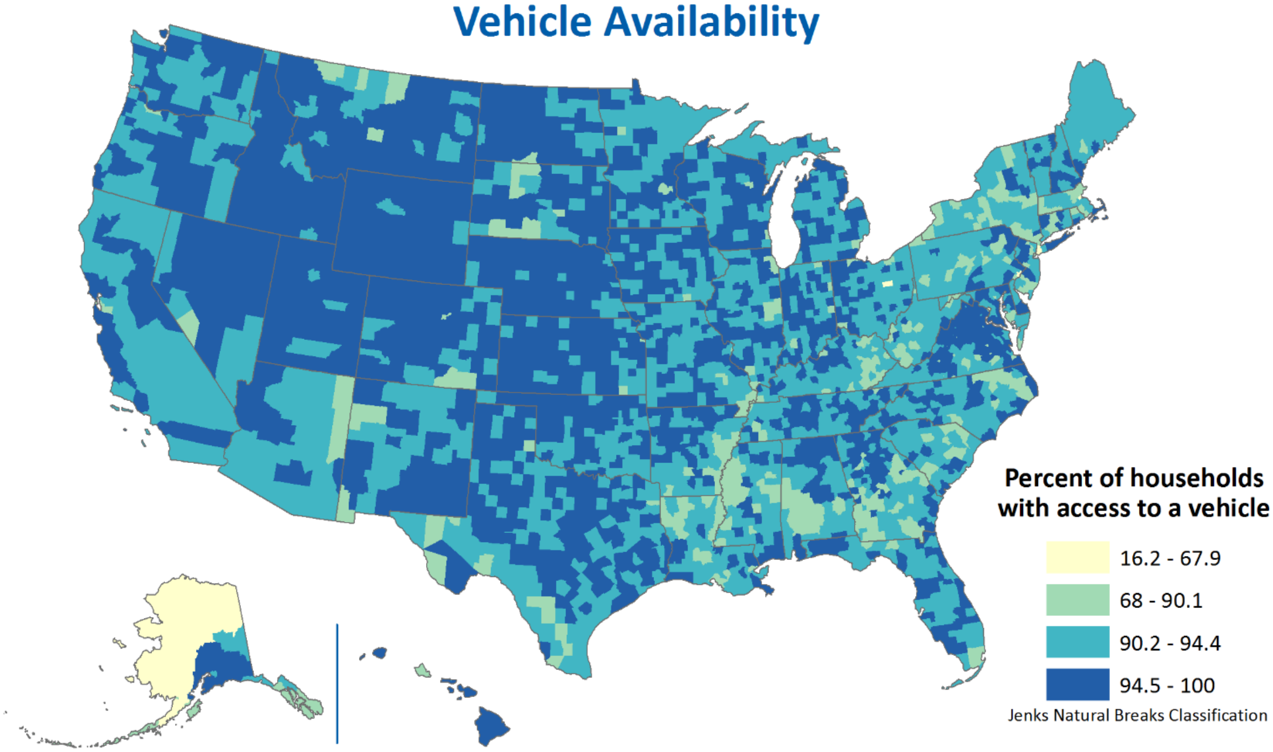
Source: American Community Survey, 2012 and 2013 5-year estimates
Notes: Map and Analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Urgent Care Facilities



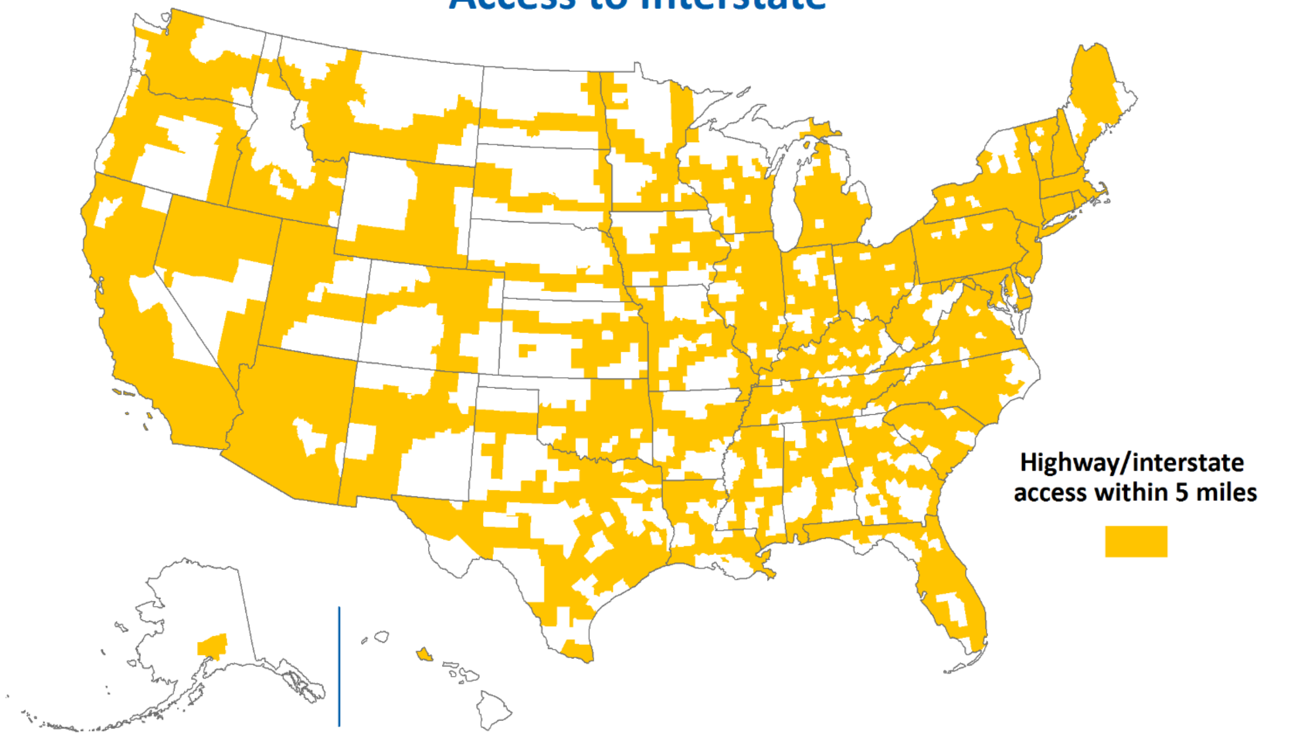
Source: HSIP 2012 Gold; last updated 2009

Vehicle Availability



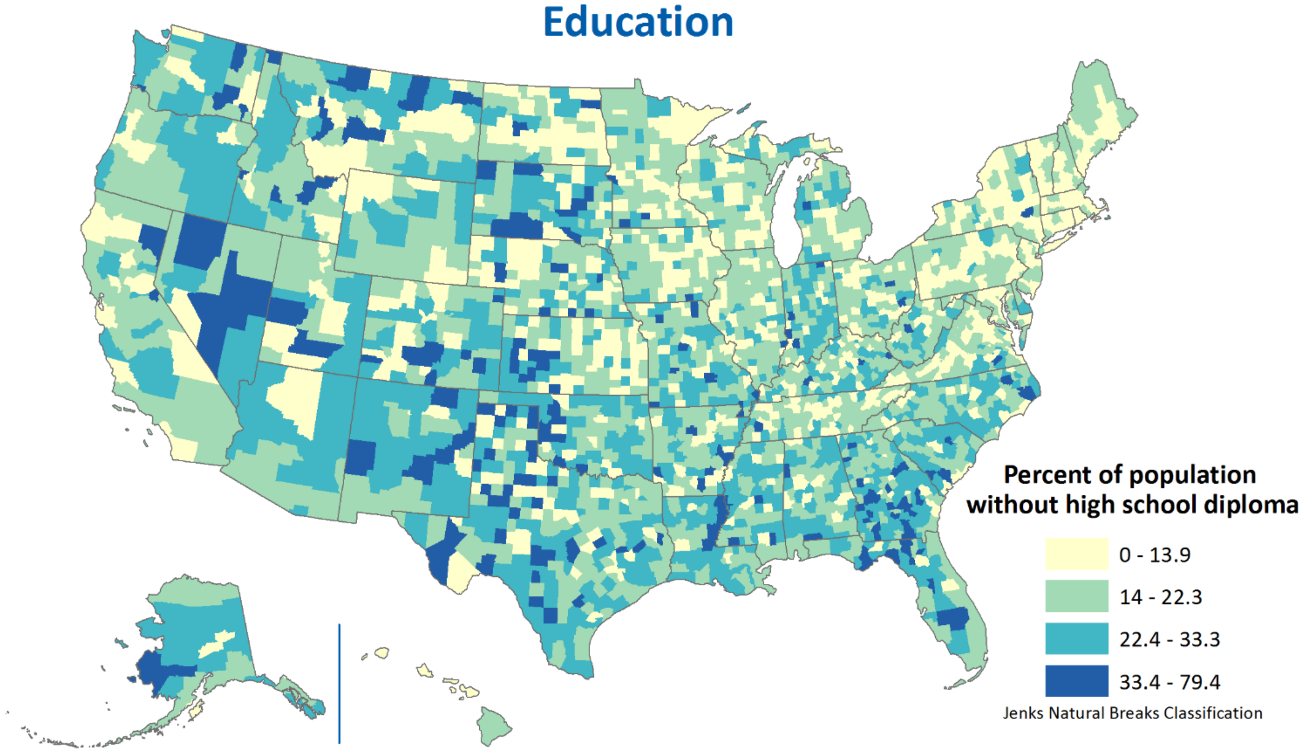
Source: American Community Survey, 2012 and 2013 5-year estimates
Notes: Map and Analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Access to Interstate



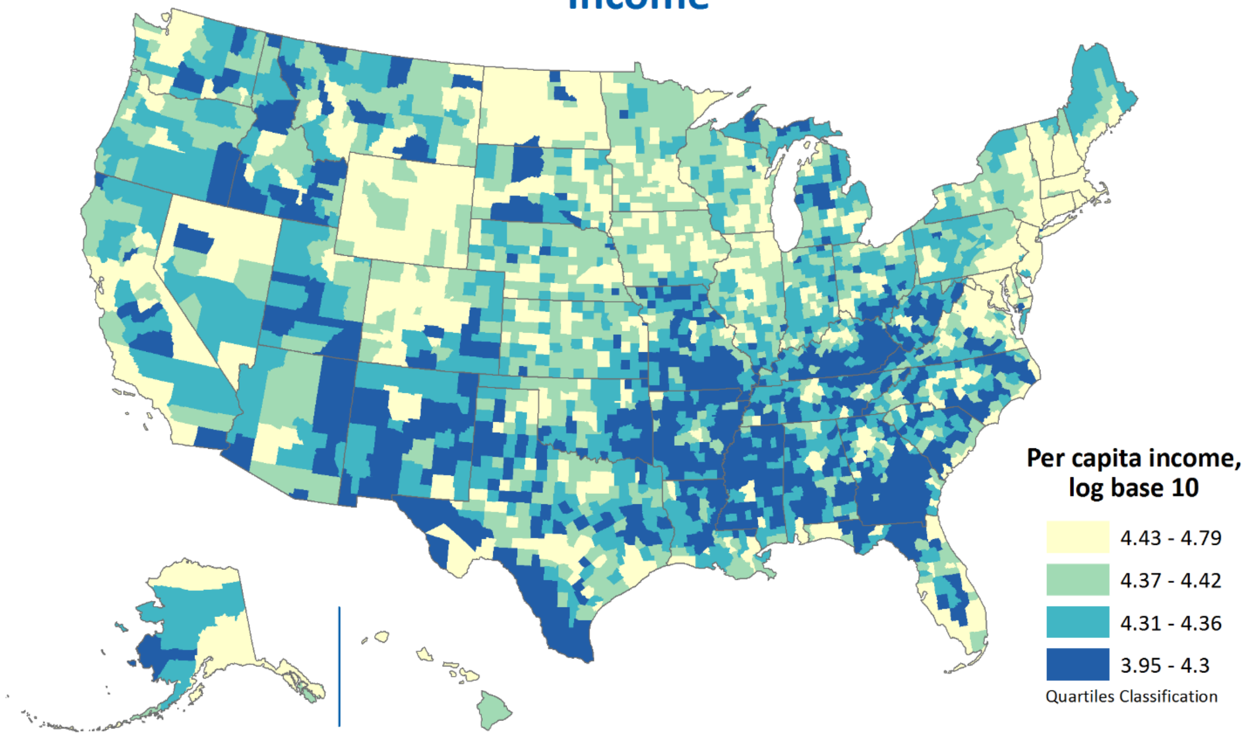
Source: ESRI maps and data 2014; last updated 2010

Education



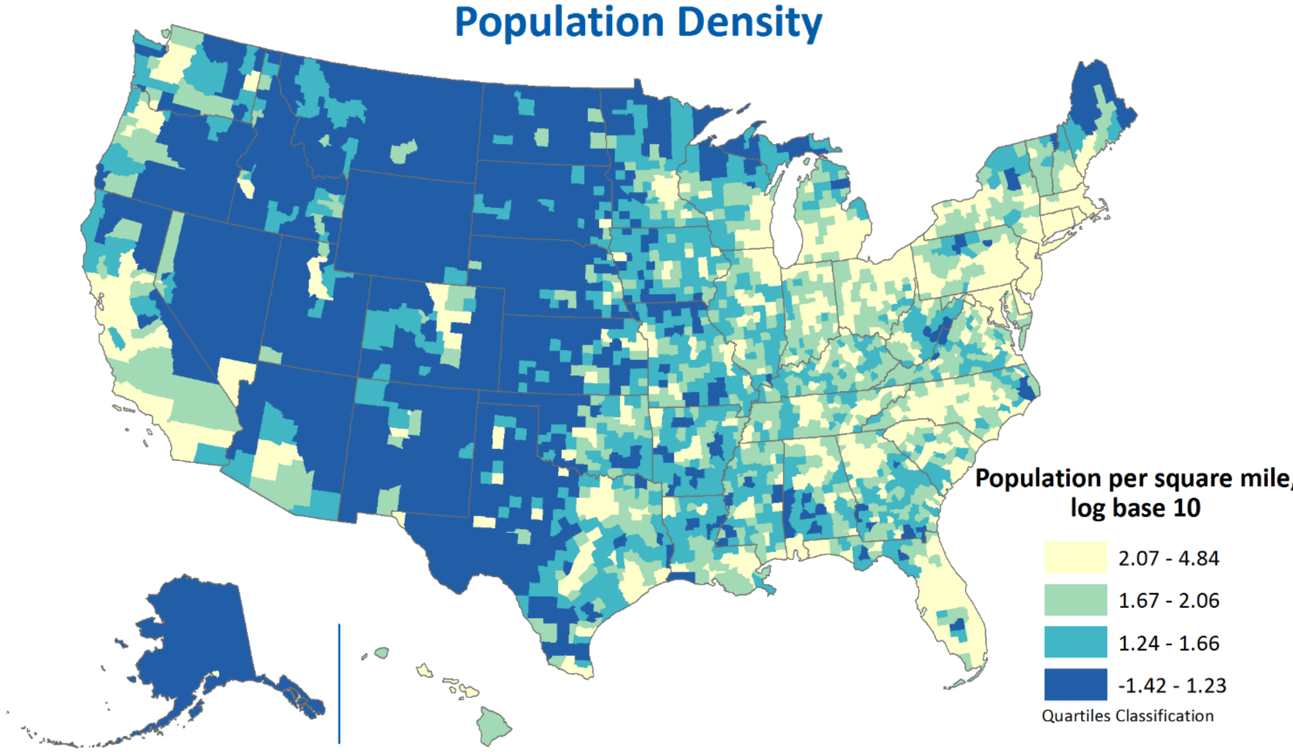
Source: American Community Survey, 2012 and 2013 5-year estimates
Notes: Map and Analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Income



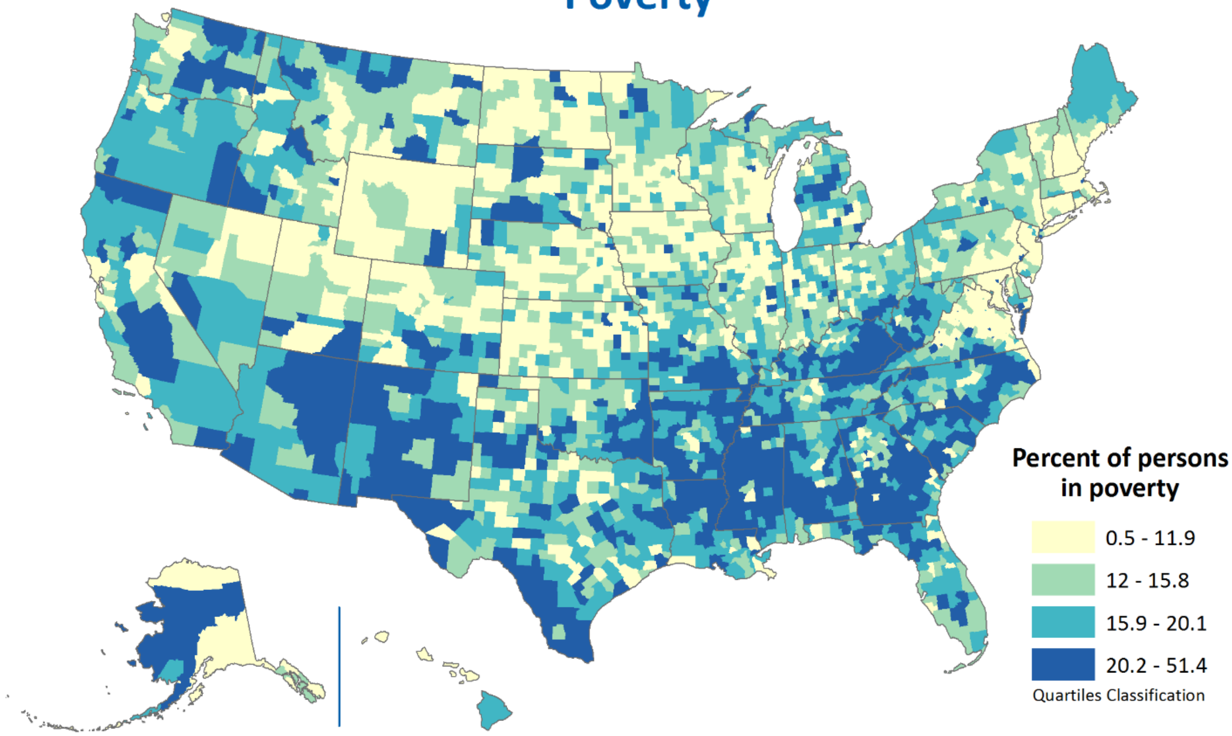
Source: American Community Survey, 2012 and 2013 5-year estimates

Population Density



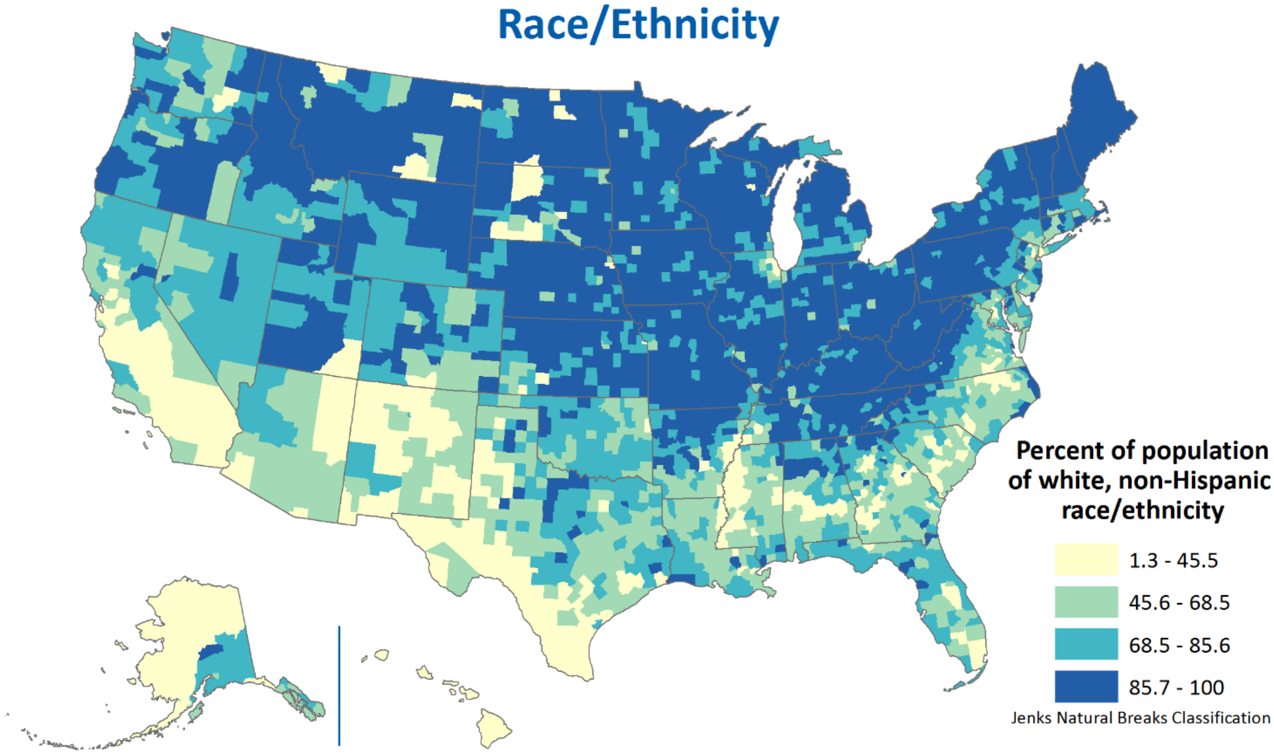
Source: U.S. Census
Notes: Map and Analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Poverty



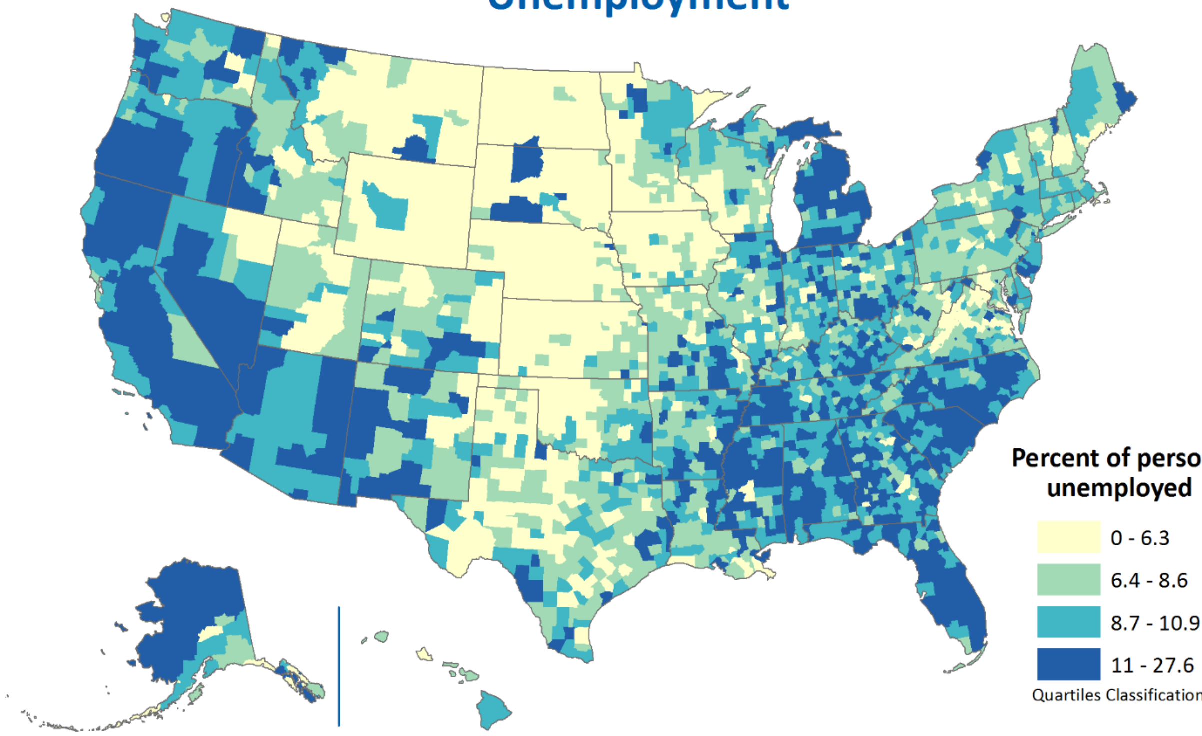
Source: American Community Survey, 2012 and 2013 5-year estimates

Race/Ethnicity



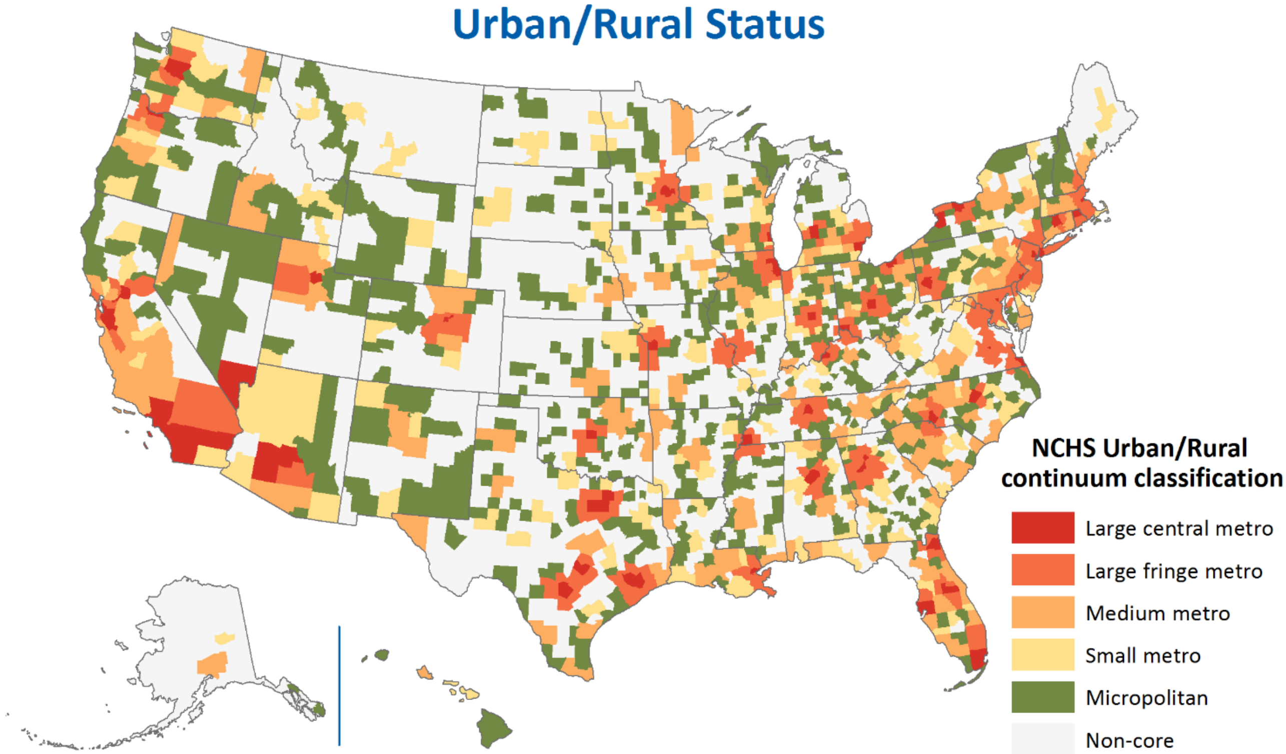
Source: American Community Survey, 2012 and 2013 5-year estimates
Notes: Map and Analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Unemployment



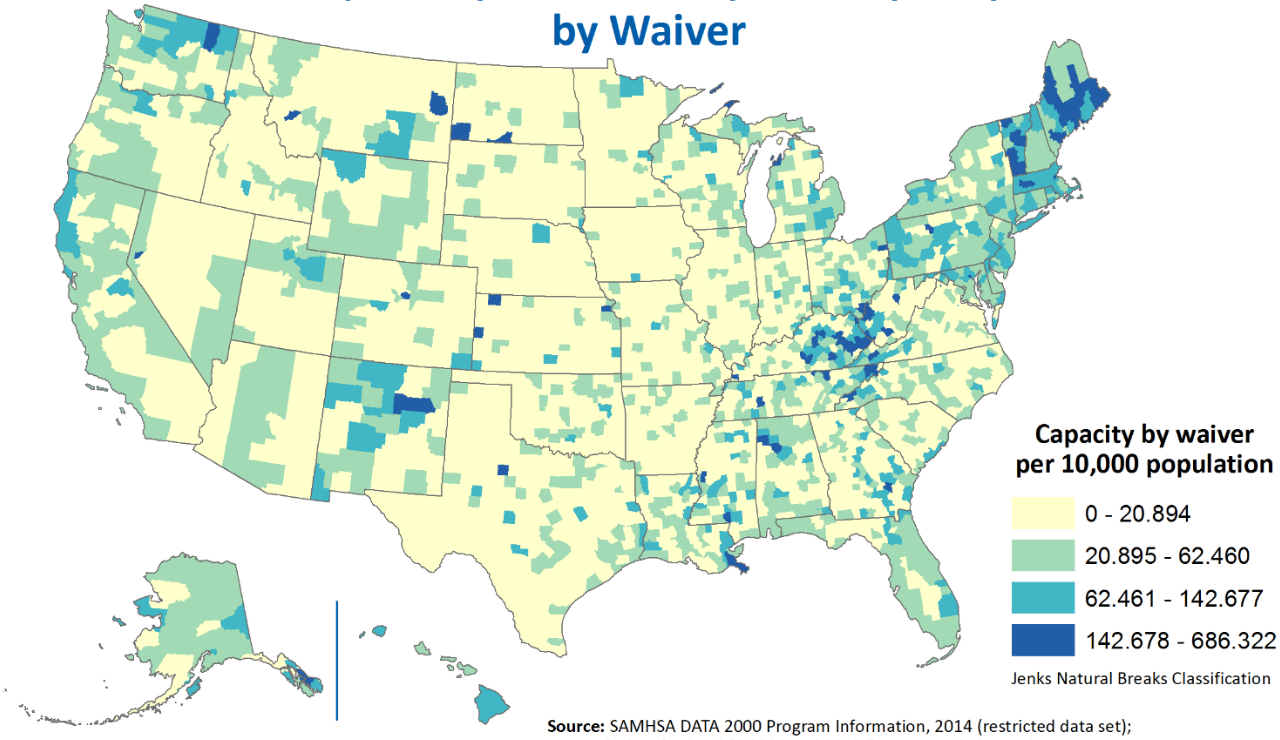
Source: American Community Survey, 2012 and 2013 5-year estimates

Urban/Rural Status



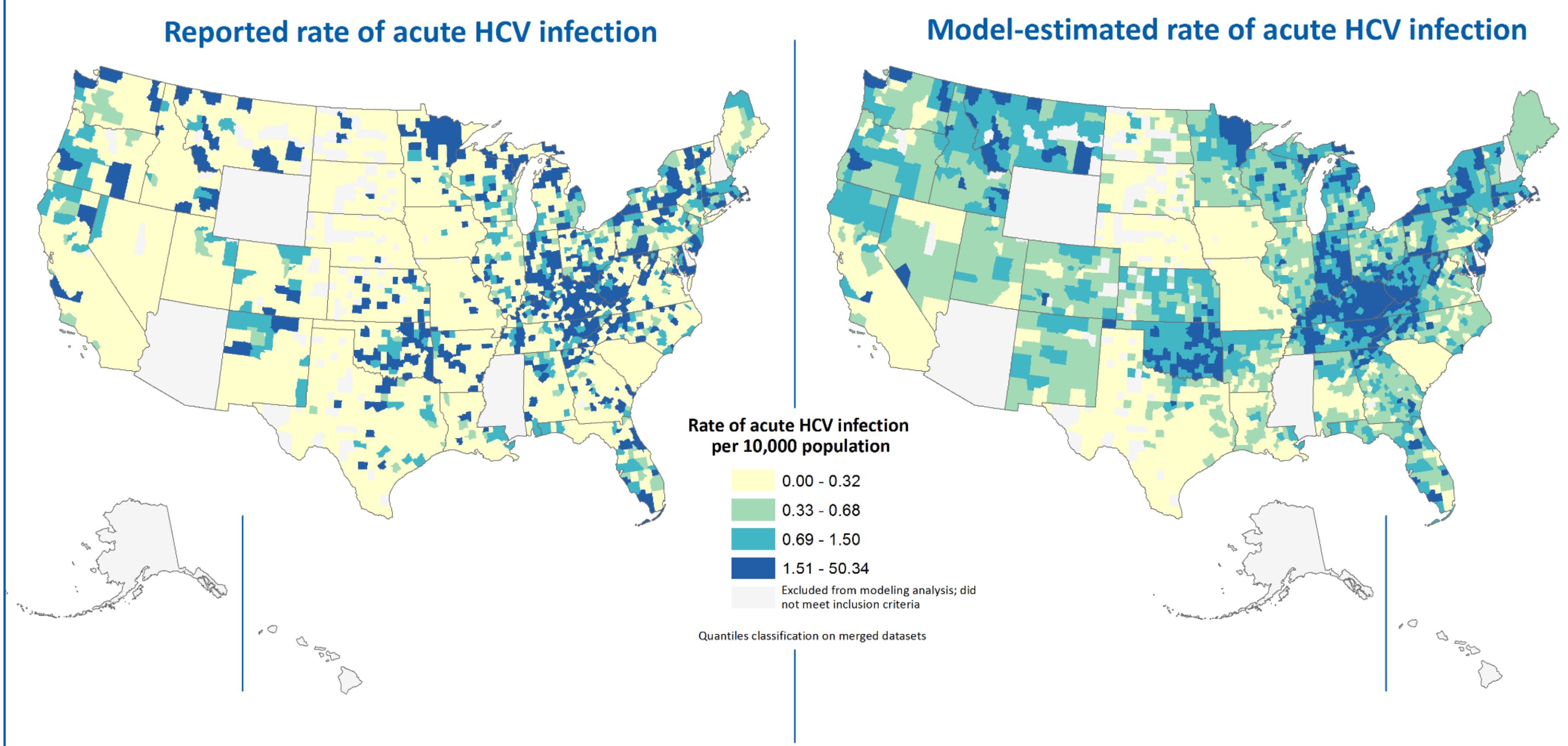
Source: NCHS, 2013
Notes: Map and Analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Buprenorphine Prescription Capacity by Waiver



Source: SAMHSA DATA 2000 Program Information, 2014 (restricted data set); rates calculated using ACS 2012 and 2013 5-year population estimates

Figure S2. Acute HCV infection rate by county. Reported rate of acute HCV infection by county, NNDSS 2012-2013 and model-estimated rate of acute HCV infection by county



Source: National Notifiable Disease Surveillance System, 2012 and 2013

Source: Multivariable Poisson regression model estimating the annual rate of acute HCV infection included 6 indicators: drug overdose deaths, prescription opioid sales, per capita income, percent of population of non-Hispanic white race/ethnicity, percent of population unemployed, and buprenorphine prescribing potential by waiver; average rates for 2012 and 2013
Notes: Map and analysis provided by the Geospatial Research, Analysis, and Services Program (GRASP), Div of Toxicology and Human Health Sciences, ATSDR (2015).

Figure S3. A. Histogram showing vulnerability scores by number of counties in each score group (eg, 0 to 0.25), B. Sigmoid curve showing vulnerability scores by county rank and identifying the scores bordering the top 5% cut-off, and C. Caterpillar curve of vulnerability scores by mean rank 90% confidence intervals bordering the top 5% rank cut-off (red dash line).