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Defining Sepsis Mortality Clusters in the United States

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Abstract

Objective—In the United States (US) sepsis is a major public health problem accounting for over 200,000 annual deaths. The aims of this study were to identify US counties with high sepsis mortality and to assess the community characteristics associated with sepsis mortality.

Design—We performed a descriptive analysis of 2003 through 2012 Compressed Mortality File (CMF) data summarized at the county level. We defined sepsis deaths as deaths associated with an infection as the CMF is derived from death certificates and classified according to the International Classification of Diseases, Version 10 (ICD-10).

Measurements—We identified county-level sepsis clustering groups: strongly clustered, moderately clustered, and non-clustered. We approximated the mean crude, age-adjusted, and community-adjusted sepsis mortality rates nationally and for clustering groups. We contrasted demographic and community characteristics between clustering groups. We performed logistic regression for the association between strongly clustered counties and community characteristics.

Main Results—Among 3,108 US counties, the age-adjusted sepsis mortality rate was 59.6 deaths per 100,000 persons (95% CI: 58.9 – 60.4). Among 161 (5.2%) counties categorized as strongly clustered, the age-adjusted sepsis mortality rate was 93.1 deaths per 100,000 persons (95% CI: 90.5 – 95.7). Strongly clustered sepsis counties were more likely to be located in the South (92.6%, p <0.001), had lower education, larger population in poverty, without medical insurance, and higher unemployment rates (p < 0.001).

Conclusion—Sepsis mortality clustering is prevalent in Southern US, with three definitive sepsis clusters: "Mississippi Valley", "Middle Georgia", and "Central Appalachia," characterized by lower education, income, employment and insurance coverage.

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Keywords

Sepsis; Geographic locations; Spatial Autocorrelation; Disease Clustering; mortality

Introduction

Sepsis is a clinical syndrome characterized by an overwhelming inflammatory response that develops following severe infection. Sepsis is associated with a high mortality rate and poses an overwhelming burden of healthcare utilization in the United States.[1-4] In the United States sepsis is a major public health problem responsible for over 750,000 hospitalizations and 215,000 deaths annually.[1] Past studies have investigated the epidemiology of sepsis.[1,3-6] However, less is known about the factors influencing regional disparities in sepsis, thus it is imperative that we determine and target the specific areas within the United States that are devastated by this syndrome with healthcare interventions.

Prior research indicates geographic variations in sepsis and infections.[4,7] Burton et al. (2010) found that people living in impoverished census tracts were at an increased risk of developing infections.[7] Wang et al. (2010) found that there was variation of sepsis mortality across the United States, and observed a high sepsis mortality cluster that ranged from the southeast to mid-Atlantic United States.[4] However, in the latter study, regional differences in sepsis mortality were measured at the state level, limiting the ability to find community-level factors that influenced sepsis disparities. Thus, it may be more feasible to examine community characteristics at a more granular level.

Identifying spatial patterns of sepsis cases may provide insights into the underlying causes of disease.[8] Many questions remained unanswered about the demographic and socioeconomic differences that may explain sepsis mortality clusters. The objectives of the current study were to identify US counties with high sepsis mortality and to assess the county-level characteristics associated with sepsis mortality. We hypothesized that there are regional differences in highly clustered sepsis counties within the United States, and that community-level characteristics may explain the observed differences.

Methods

Ethics Statement

This study was considered exempt by the institutional review board of the University of Alabama at Birmingham, as we used existing secondary data that are publicly available and non-identifiable.

Study Design & Data Source

We analyzed 2003 through 2012 Compressed Mortality File (CMF) data from the National Center for Health Statistics (NCHS) summarized at the county level.[9] Mortality data in the CMF are derived from death certificates and include a record for every death of a U.S. resident recorded in the United States.[9] We complemented the county-level sepsis mortality data with county-level community characteristics obtained from the 2010 American

Community Survey (ACS) through the National Historical Geographic Information System (NHGIS).[9,10] We obtained demographic data for each county using the 2010 ACS 5-year data for years 2006-2010.

Identification of County-Level Sepsis Mortality

We determined county-level sepsis-related deaths using methods by Wang et al. (2010) as deaths associated with an infection (Appendix A).[4] We included sepsis-related deaths for all persons ≥ 15 years of age during the period 2003-2012. We included deaths in individuals aged 15-19 years because the CMF uses a single reference standard population for ages 15-24, and thus the inclusion of the 15-19 year groups is necessary for the estimation of age-adjusted rates.[4] The CMF includes data on the age, race, sex, year and causes of all U.S. deaths.[9]

County-Level Demographic Characteristics

We obtained county-level demographic statistics (e.g., age, sex, and race) for the years 2006 through 2010 from the ACS. We categorized race into five groups: White (non-Hispanic), Black (non-Hispanic), Asian/Pacific Islander (non-Hispanic), Hispanic, and Other (including Native Americans).

County-Level Community Characteristics

We obtained county-level community variables from the ACS that included median household income, median home value in dollars, percentage of the population that completed college, percentage of the population below the poverty line, percentage of the population that is urban, population density, percentage of population without medical insurance coverage (in 2010), and unemployment rate. We also included the county-level ratio per 100,000 persons for number of hospitals, hospital beds, medical doctors, and primary care physician (PCP). We estimated the ratio per 100,000 by dividing each characteristic by the county population and then multiplied the quotient by 100,000 to obtain the ratio per 100,000 persons (all measured for year 2010). Geographic region was defined using the Census definition (i.e., Midwest, Northeast, South, and West).[11] We did not include Alaska, Hawaii, and other US Territories in this analysis.

Defining Sepsis Mortality Clusters

Disease clustering is defined as the spatial aggregation of cases in an identifiable subpopulation.[8] Further, cluster investigations provide an opportunity to understand the etiology and causes of disease.[8] Currently there is no consensus on the best clustering approach; therefore we adopted novel geospatial autocorrelation methods to define highly clustered sepsis mortality counties. Introduced by Nassel et al. (2014), we combined three separate analytical spatial clustering methods to identify areas that were hot spots for sepsis mortality.[12] We categorized county-level sepsis clustering into three groups: strongly clustered, moderately clustered, and non-clustered. We considered a county to be strongly clustered if it was identified as high risk or sepsis hot spot using all three geospatial metrics (5th quartile of Empirical Bayes (EB) smoothed sepsis mortality rates, high-high cluster using Local Moran's I, and sepsis hot spot as defined by Getis-Ord Gi*). In order to be considered as a moderately clustered county, a county had to be identified high-risk using two out of three geospatial metrics. All other U.S. counties were categorized as being non-clustered.

First, we estimated Empirical Bayes (EB) smoothed sepsis mortality rates for the 10-year study period using the total number of sepsis-mortality events in each county divided by the county population, with smoothing performed using the EB tools in GeoDa 1.6.7.9 (http://geodacenter.asu.edu).[12] We further categorized the EB smoothed sepsis mortality rates into quintiles, and we defined counties as high-risk if the EB sepsis mortality rates were in the top quintile. Second, we used Local Indicators of Spatial Autocorrelation [13] to measure similarity between counties and calculate values both within and across geographic boundaries, additionally identifying spatial outliers.[12,14,15] For each US county, we estimated Local Moran's I Statistic values, using associated z-scores and p-values to assess the magnitude of spatial autocorrelation and statistical significance, respectively.[12] Counties with statistically significant positive z-scores indicate areas surrounded by areas with similar sepsis-mortality rates – either similarly high or similarly low (positive spatial autocorrelation).[12] Lastly, we used the Gi* statistic to identify areas where sepsis mortality rates with either high or low values clustered within the context of the neighboring county.[12,16,17] In contrast to LISA, Gi* does not identify the similarity of values to the surrounding counties. Further details to the geospatial autocorrelation analysis were introduced by Nassel et al. (2014) and are described elsewhere.[12]

Statistical Analysis

We used mean crude and age-adjusted mortality rates provided by CMF, which uses intercensal (2003-2009), actual (2010), and postcensal (2011-2012) US Census population estimates. All standardization was performed relative to the 2000 US standard population. We conducted a weighted (i.e., by county population) multivariable linear regression to assess the association between each county-level sepsis-clustering group and sepsis mortality rate after adjustment for age and all significant ($p \leq 0.05$) community-level community characteristics. We additionally calculated the national community-adjusted sepsis mortality rate. We compared regional differences in high-risk sepsis categories (EB, LISA, Gi*) using a Chi-square test of association. We performed the non-parametric Kruskal Wallis test to examine the distribution of community characteristics across county-level clustering groups (e.g., strongly clustered, moderately clustered, and non-clustered).

In a sensitivity analysis, we performed logistic regression to examine the association between strongly clustered sepsis counties and county-level community characteristics. We adjusted the logistic regression model by community characteristics found statistically significant (≤0.05) in crude logistic regression. We examined temporal changes in sepsis mortality using multivariable linear regression for two 5-year periods nested within our study period (i.e., 2003 – 2007 and 2008 – 2012). We used SAS version 9.4, QGIS version 2.8.1-Wien, and GeoDa version 1.6.7.9 for all statistical analyses and geographic mapping. We considered p-values ≤ 0.05 to be statistically significant.

Results

LISA, Gi*, and EB analysis

The LISA analysis identified that 246 of the 352 (69.9%) “high-high” sepsis cluster counties by LISA criteria were located in the South (Appendix B, Table 1). The Gi* analysis identified 516 counties as sepsis “hot spots” (16.6%) [Appendix C, Table 1]. Counties within the South were more likely to be in a sepsis “hot spot” (34.3%) by Gi* criteria ($p < 0.001$). There were 622 (20.0%) counties categorized within the highest quintile for EB smoothed sepsis mortality rate (Appendix D, Table 1). Counties located within the South were more likely to have EB smoothed sepsis mortality rates in the highest quintile (27.4%), corresponding to an EB smoothed sepsis mortality rate of 76.4 deaths per 100,000 persons (95% CI: 58.9 – 60.4) [$p < 0.001$].

Demographic Characteristics

Among 3,108 counties included in the analysis, 161 (5.2%) were categorized as strongly clustered counties and 2,714 (87.3%) counties were categorized as non-clustered counties (Figure 1). Strongly and moderately clustered counties were more likely to have a larger proportion of older adults than non-clustered counties (Table 2). Strongly clustered counties had the largest black population (13.4% vs. 3.7% and 1.7%) and the lowest white population (76.8% vs. 87.5% and 86.5%) compared to moderately and non-clustered counties, respectively. Non-clustered counties had the largest Hispanic population (3.3% vs. 1.4% and 1.8%) and other population (3.0% vs. 2.4% and 2.0%) compared to moderately and strongly clustered counties, respectively.

Community Characteristics

The clustering groups had similar population density ($p = 0.7$), PCP per 100,000 persons ($p = 0.3$), beds per 100,000 persons ($p=0.2$), and medical doctors per 100,000 persons ($p = 0.5$) [Table 2]. However, there were differences in all other county-level community characteristics. Strongly clustered and moderately clustered counties had lower median household income, median value of housing units, and were less urban when compared to counties within the non-clustered group. Moreover, strongly clustered sepsis counties had lower education represented by a lower college completion percentage ($p<0.001$). Strongly clustered sepsis counties had a higher percentage of persons living in poverty, without medical insurance, and higher unemployment rates ($p < 0.001$). Strongly and moderately clustered counties were more likely to be located in the South (92.6%, $p < 0.0001$).

Sepsis Mortality Rates

During 2003-2012, and among people aged ≥15 years, there were a total of 1,451,986 sepsis-related deaths, corresponding to a national crude mortality rate of 69.9 deaths per 100,000 persons (95% CI: 68.9 – 70.9) [Table 3]. Among 3,108 United States counties included in the analysis, the age-adjusted sepsis mortality rate was 59.6 deaths per 100,000 persons (95% CI: 58.9 – 60.4). The national community-adjusted sepsis mortality rate was 58.0 deaths per 100,000 persons (95% CI: 57.4 – 58.7).

During the observation period, the age-adjusted sepsis mortality rate was lowest for non-clustered counties, corresponding to a rate of 55.9 deaths per 100,000 persons (95%CI: 55.1 – 56.6). However, the age-adjusted sepsis mortality rate was highest for strongly clustered counties, with a corresponding rate of 93.1 deaths per 100,000 persons (95% CI: 90.5 – 95.7). The community-adjusted sepsis mortality rate was lowest for non-clustered counties, corresponding to a rate of 56.8 deaths per 100,000 persons (95%CI: 56.2 – 57.4). The community-adjusted sepsis mortality rate was highest for strongly clustered counties, corresponding to a rate of 85.7 deaths per 100,000 persons (95%CI: 82.1 – 89.4).

Sensitivity Analysis

After adjustment for significant county-level community characteristics (i.e., median household income, and median home value) none of the community characteristics remained associated with odds of strongly sepsis clustering (Appendix E). After adjustment for age and county-level community characteristics there were no temporal differences in sepsis mortality (Appendix F).

Discussion

Our results also indicate that sepsis remains a major public health burden responsible for greater than 140,000 deaths annually. These results also suggest that sepsis mortality clustering is prevalent in counties located in the southeastern US with three specific clusters: 1) “Mississippi Valley” - counties bordering the southern Mississippi river in three southern states (Louisianna, Arkansas, and Mississippi); 2) “Middle Georgia” - a belt of counties expanding from southwest Georgia through middle to southeast Georgia; 3) and “Central Appalachia” - a cluster of counties in southeastern Kentucky and southwest Virginia (Figure 1). Over the ten-year observation period, 5.2% (161 of 3,108) of US counties were defined as strongly clustered counties. After adjustment for age and community level characteristics, those living in the strongly clustered counties were about 1.5 times more likely to have a sepsis related death than people living in non-clustering counties. Demographic and socio-economic characteristics associated with sepsis mortality clustering were race, household income, value of housing property, education, rural population, poverty, ratio of hospitals per 100,000 persons, insurance coverage, and higher unemployment rate. The odds of strongly sepsis clustering was non-significant after multivariate adjustment for community characteristics.

This study builds upon previous work by Wang et al (2010)[4], and to our knowledge, this is the first study to utilize geospatial analysis to identifiy county-level sepsis clustering groups. Wang et al. identified the first “sepsis cluster” consisting of 11 contiguous states from Southeastern to Mid-Atlantic US.[4] Wang et al.'s sepsis cluster had increased sepsis mortality compared other US regions (80.1 vs. 61.9 deaths per 100,000 persons).[4] Comparatively, this study further describes that sepsis mortality is prevalent within these same states, with three prominent clusters (e.g., Mississippi Valley, Middle Georgia, and Central Appalachia). Moreover, we further delineate that the counties within these states are part of our strongly clustered counties, corresponding with an increased sepsis mortality compared to other US counties of 93.1 vs. 55.9 deaths per 100,000 persons.

Regional differences in sepsis mortality may be explained by community and socio-demographic characteristics.[18-21] Numerous studies have shown that uninsured critically ill patients are less likely to receive life-saving critical care procedures, receive less post acute care during critical illness recovery, and have increased mortality compared to those with insurance.[22-27] As seen in our study, strongly clustered counties had greater socioeconomic and access to care disparities. Analogously, Mendu et al. (2012) elucidated that neighborhoods with greater than 20% poverty rates had 32% increased odds of community-acquired infections compared to those with neighborhood poverty rate <5%.[18] Additionally, we found that race was a significant determinant in regional disparities of sepsis mortality. Many epidemiolgic studies based on hospital discharge records have reported that black persons have higher rates of sepsis, hospitalization mortality, and are twice as likely to develop sepsis as white persons.[20,28-36] In contrast, while using prospective data from the REasons for Geographic and Racial Differences in Stroke (REGARDS) we found that black participants were less likely to develop sepsis when compared to white participants.[37] Nevertheless, higher community-level proportion of black race may serves as a proxy to overall lower socio-economic status and access to care, and thus our efforts should focus on establishing healthcare coverage for those currently living in these underserved communities.

With the exception of Arkansas and Kentucky, the identified clustered sepsis counties were in states that did not adopt the Affordable Care Act (ACA).[22] Historically, regional disparities in health outcomes have been found in the three geographic regions observed in this study.[38-48] Similar to our sepsis cluster found in the Mississippi Valley, studies have shown that the Mississippi Valley also has higher rates for coronary heart disease.[43] Howard et al. elucidated that there is a “Stroke-Belt” located in the Southeastern US, which comprises of our “Middle Georgia” and Mississippi Valley sepsis clusters.[40,48] Lastly, the Central Appalachia sepsis cluster has been previously described as a very vulnerable population with limited access to health care.[49] These geographic regions could generally be representable of overall poor health, increased health risk, and low access to care areas within the US. These geographic areas have consistently faced healthcare disparities and should be specifically targeted for future health care interventions, such as the adoption of the ACA.[22,49]

Limitations

The results of this study should be interpreted in the light of certain limitations. We used publicly available death records, and as a result, missclassification of the listed causes of death could affect the sepsis mortality rates observed in this study. We did not use the SIRS criteria for identification of sepsis; however we used methods perfomed in previous sepsis invesigations.[4] Additionally, the compressed mortality file suppressed sub-national data representing fewer than ten persons for years 1989 and later [9], and as result we were unable to determine differences in infections types by cluster status. We identified sepsis deaths using ICD-10 codes for infections and consequently the rates presented may be underestimates of the true number for sepsis mortality in the US. We used the mean community characteristic estimates for years 2006 through 2010 to approximate the association between sepsis mortality and county-level demographic information; however the population estimates were adequate because they are within median time of the overall observation period. Lastly, this study is an ecological analysis, thus individual level factors associated with sepsis were not attainable.

Although the data used in this study are from a national representative sample, a future study investigating regional variation in sepsis among a longitudinal cohort may give further details regarding the lifestyle and community factors that explain differences in sepsis mortality. Sepsis mortality is a function of both case-fatality and sepsis incidence[4]; therefore, a prospective analysis will provide an opportunity to differentiate whether incident sepsis cases or case-fatality are driving these differences in sepsis mortality among the counties observed in this study. We are currently investigating these objectives within the REGARDS cohort, one of the largest ongoing national longitudinal cohorts of community-dwelling adults in the United States.[40]

Conclusion

Sepsis mortality clustering is prevalent in Southern US counties, with three definitive sepsis clusters: the Mississippi Valley, Middle Georgia, and Central Appalachia. Regional variations in sepsis mortality are important because they allow explanation for susceptibility and case-fatality. This study reiterates that sepsis mortality varies by region, while further illuminating that high risk sepsis counties are differentiated by lower education, income, employment, insurance coverage, and race. As these risk factors are highly related to health care access, enhancements of community-level access to care for the defined areas may contribute to a reduction in sepsis mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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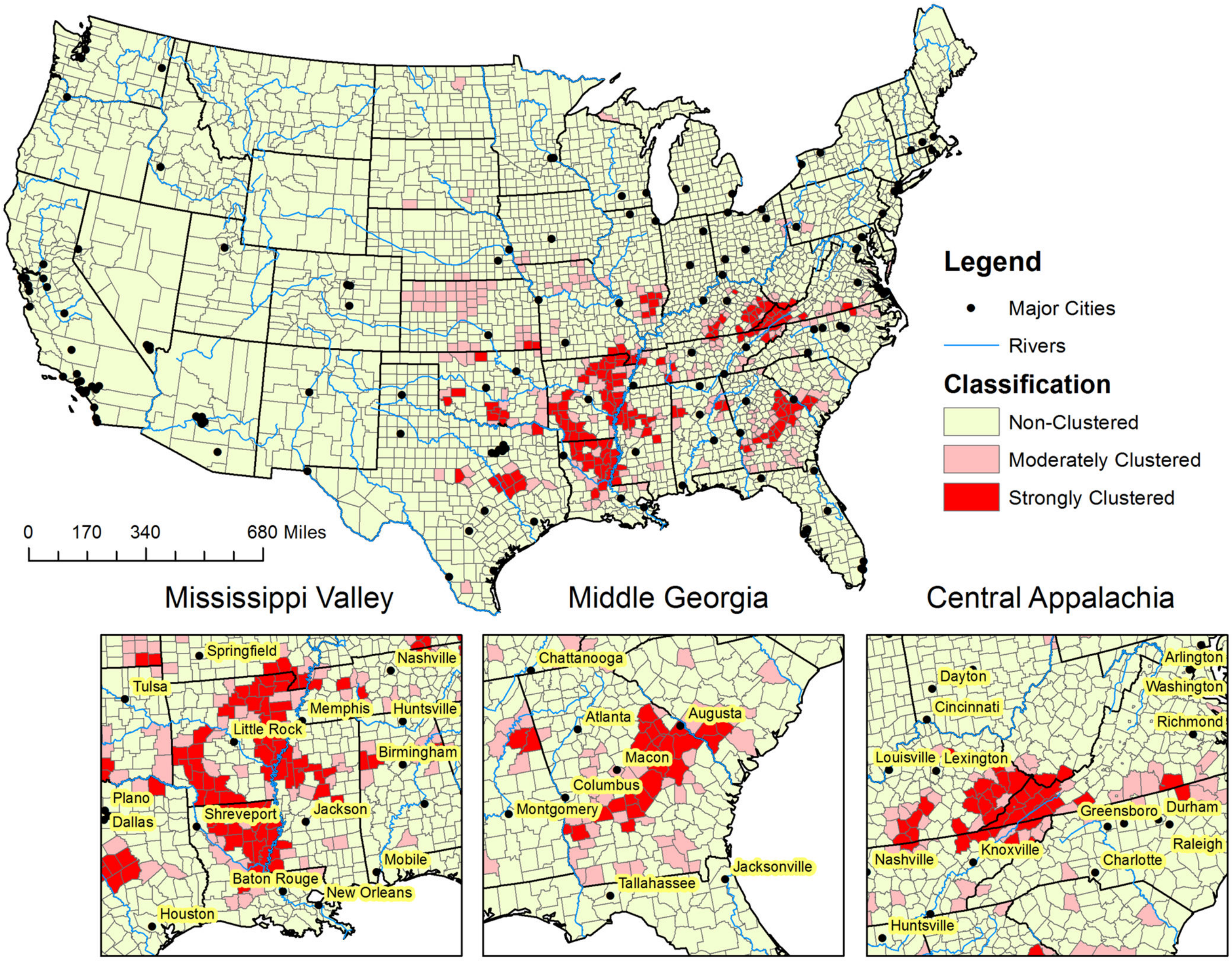

Figure 1. Moderately and strongly clustered sepsis mortality groups for county-level regional variation in sepsis, United States, 2003-2012. Excludes Alaska and Hawaii

Table 1

Comparison of county-level sepsis clustering category by United States region, 2003-2012

	Midwest Counties† (N = 1,055)	Northeast Counties† (N = 217)	South Counties† (N = 1,422)	West Counties† (N = 414)	p-value§
LISA (%)					
Non-Significant	743 (70.4)	195 (89.9)	1,073 (75.5)	193 (46.6)	<0.001
High-High Cluster	101 (9.6)	4 (1.8)	246 (17.3)	1 (0.2)	
High-Low Outlier	22 (2.1)	0 (0.0)	10 (0.7)	25 (6.0)	
Low-High Outlier	19 (1.8)	0 (0.0)	47 (3.3)	1 (0.2)	
Low-Low Cluster	170 (16.1)	18 (8.3)	46 (3.2)	194 (46.9)	
EB (95% CI) *	68.1 (66.7 – 69.5)	67.2 (65.2 – 69.2)	76.4 (75.2 – 77.6)	52.6 (50.7 – 54.5)	
EB (%)					
1st quintile	241 (22.8)	31 (14.3)	158 (11.1)	192 (46.4)	<0.001
2nd quintile	239 (22.7)	45 (20.7)	220 (15.5)	117 (28.3)	
3rd quintile	189 (17.9)	71 (32.7)	304 (21.4)	58 (14.0)	
4th quintile	185 (17.5)	51 (23.5)	350 (24.6)	35 (8.5)	
5th quintile	201 (19.1)	19 (8.8)	390 (27.4)	12 (2.9)	
Gi* (%)					
Non-Significant	674 (63.9)	199 (91.7)	905 (63.6)	247 (59.7)	<0.001
Sepsis Hot Spot	25 (2.4)	2 (0.9)	487 (34.3)	2 (0.5)	
Sepsis Cold Spot	356 (33.7)	16 (7.4)	30 (2.1)	165 (39.9)	

§Significance determined using Chi-Square test.

†US regions as determined by the U.S. Census Bureau.

*Mean Empirical Bayes smoothed sepsis mortality rate and 95% confidence interval.

%Denotes column percentages.

Table 2

Comparison of county demographic characteristics and community characteristics and region by county-level sepsis clustering categories, 2003-2012

	Strongly Clustered[a] Counties (N = 161)	Moderately Clustered[b] Counties (N = 233)	Non-Clustered Counties (N = 2,714)	p-value*
Age (%)†				
Under 18	23.4 (22.2 – 25.0)	23.4 (21.7 – 24.9)	23.7 (21.8 – 25.5)	0.05
18-29	14.2 (13.2 – 15.6)	13.9 (12.4 – 15.4)	14.0 (12.2 – 16.1)	0.1
30-44	18.5 (17.4 – 19.6)	18.1 (16.7 – 19.2)	18.5 (16.9 – 19.9)	0.006
45-64	27.2 (26.1 – 28.7)	27.5 (26.3 – 29.2)	27.6 (25.9 – 29.2)	0.4
65-79	11.7 (10.5 – 12.9)	11.9 (10.6 – 13.2)	10.9 (9.2 – 12.7)	<0.001
80+	4.2 (3.7 – 4.7)	4.5 (3.6 – 5.7)	4.0 (3.2 – 5.0)	<0.001
Sex (%)†				
Male	49.0 (48.1 – 50.0)	49.0 (48.3 – 49.8)	49.5 (48.8 – 50.4)	<0.001
Female	51.0 (50.0 – 51.9)	51.0 (50.2 – 51.7)	50.5 (49.6 – 51.2)	
Race (%)†				
Black (non-Hispanic)	13.4 (1.4 – 37.7)	3.7 (0.7 – 30.7)	1.7 (0.4 – 8.5)	<0.001
White (non-Hispanic)	76.8 (56.8 – 94.9)	87.5 (63.1 – 95.2)	86.5 (69.6 – 94.3)	0.02
Asian/ Pacific Islander	0.3 (0.1 – 0.5)	0.4 (0.2 – 0.6)	0.6 (0.2 – 1.2)	<0.001
Hispanic	1.4 (0.8 – 2.8)	1.8 (1.1 – 3.5)	3.3 (1.6 – 8.6)	<0.001
Other	2.0 (1.2 – 2.8)	2.4 (1.6 – 3.4)	3.0 (2.0 – 4.4)	<0.001
Community Characteristics				
Household Income†	37,061 (32,342 – 43,635)	39,574 (35.185 – 45,162)	42,882 (37,372 – 49,383)	<0.001
Value of housing units†	85,900 (72,100 – 110,700)	87,700 (74,400 – 123,500)	108,850 (81,650 – 155,900)	<0.001
% Completed college†	12.8 (11.0 – 17.2)	15.9 (11.6 – 20.2)	17.2 (13.5 – 23.1)	<0.001
% Below poverty line†	18.4 (14.9 – 22.1)	16.1 (11.9 – 20.3)	13.9 (10.7 – 17.9)	<0.001
% Urban†	32.2 (12.2 – 51.2)	35.6 (0.0 – 58.5)	41.6 (14.4 – 67.8)	<0.001
Population density†**	43.3 (29.0 – 84.1)	44.2 (22.6 – 97.7)	45.7 (16.3 – 120.5)	0.7
PCP€†	5.5 (2.3– 14.9)	6.2 (2.0 – 24.2)	5.2 (1.4 – 19.8)	0.3
Hospitals€†	0.7 (0.1 – 1.4)	0.7 (0.1 – 1.8)	0.4 (0.1 – 1.3)	0.01
Beds€†	31.0 (3.3 – 92.9)	37.8 (5.7 – 118.7)	23.7 (3.2 – 103.2)	0.2
Medical Doctors€†	9.5 (3.2– 24.7)	8.8 (2.3 – 46.8)	8.7 (2.0 – 42.1)	0.5
% Without insurance coverage†	20.3 (17.7 – 23.1)	18.9 (16.3 – 22.1)	17.9 (14.1 – 21.8)	<0.001
Unemployment rate†	0.05 (0.04 – 0.06)	0.05 (0.03 – 0.06)	0.04 (0.03 – 0.05)	0.01
Region (%)***				
Midwest	12 (7.5)	71 (30.5)	972 (35.8)	<0.001
Northeast	0 (0.0)	2 (0.9)	215 (7.9)	
South	149 (92.6)	160 (68.7)	1,113 (41.0)	
West	0 (0.0)	0 (0.0)	414 (15.3)	

[a]Defined as counties estimated as high risk by all definitions (LISA, EB, & Gi*)

[b]Defined as counties estimated as high risk by two of three definitions.

[†]Median (IQR)

[€]Ratio per 100,000 persons

[*]Significance determined using Kruskal-Wallis or Chi-Square test.

[**]Persons per square mile.

[***]US regions as determined by the U.S. Census Bureau

Table 3

Sepsis mortality† in the United States by county-level sepsis clustering category, 2003-2012, excluding Alaska and Hawaii

	Sepsis Clustering Category			Total
	Strongly Clustered (N = 161)	**Moderately Clustered (N = 233)**	**Non-Clustered (2,714)**	**All Counties (N = 3,108)**
Sepsis Deaths *	33,532	50,188	1,368,266	1,451,986
Mean Annual Population **	199,148	228,433	852,304	771,699
Crude Sepsis Mortality Rate (95% CI)	108.8 (105.9 – 111.6)	101.2 (98.1 – 111.6)	64.9 (64.0 – 65.8)	69.9 (68.9 – 70.9)
Age-Adjusted (95% CI) [a]	93.1 (90.5 – 95.7)	80.2 (77.6 – 82.8)	55.9 (55.1 – 56.6)	59.6 (58.9 – 60.4)
Community-Adjusted (95% CI) [b]	85.7 (82.1 – 89.4)	74.8 (71.9 – 77.6)	56.8 (56.2 – 57.4)	58.0 (57.4 – 58.7)

* Identified using IC10-codes for infection.

** Per County

† Annual Deaths per 100,000 persons.

[a] Adjusted for age.

[b] Additionally adjusted for county level - sex, race, household income, value of housing unit, % completed college, % below poverty line, % urban, number of hospitals, % without insurance coverage, unemployment rate.