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Authors
Desai, Archita P
Mohan, Prashanthinie
Roubal, Anne M
et al.

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Geographic variability in liver disease related mortality rates in the United States

Archita P. Desai, MD[1], **Prashanthinie Mohan, MBA**[2], **Anne M. Roubal, PhD**[2], **Ricki Bettencourt, MS**[3], and **Rohit Loomba, MD, MHSc**[4]

[1]Division of Gastroenterology and Hepatology, Liver Research Institute, University of Arizona, Tucson, AZ, USA

[2]Center for Population Science and Discovery, University of Arizona, Tucson, AZ, USA

[3]NAFLD Translational Research Unit, Department of Medicine and Division of Epidemiology, Department of Family and Preventive Medicine, University of California at San Diego, La Jolla, CA, USA

[4]NAFLD Translational Research Unit, Division of Gastroenterology and Epidemiology, University of California at San Diego, La Jolla, CA, USA

Abstract

Purpose—Liver disease is an important cause of morbidity and mortality in the United States (US). Geographic variations in the burden of chronic liver disease may have significant impact on public health policies but have not been explored at the national level. The objective of this study is to examine inter-state variability in liver disease mortality in the US.

Methods—We compared liver disease mortality from the 2010 National Vital Statistics Report on a state level. States in each quartile of liver disease mortality were compared with regard to viral hepatitis death rates, alcohol consumption, obesity, ethnic and racial composition, and household income. Race, ethnicity, and median household income data was derived from the 2010 US Census. Alcohol consumption and obesity data was obtained from the 2010 Behavioral Risk Factor Surveillance System Survey.

Please address correspondence to: Rohit Loomba, MD, MHSc, 9500 Gilman Drive, MC 0063, NAFLD Translational Research Unit, Division of Gastroenterology and Epidemiology, University of California at San Diego, La Jolla, CA 92093, Ph: 858-534-2624, Fax: 858-534-3338, roloomba@ucsd.edu.

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Author contributions:
Archita Desai - study concept and design, analysis and interpretation of data, drafting of the manuscript, critical revision of the manuscript, approved final submission
Prashanthinie Mohan - Statistical analysis, drafting of the manuscript, approve final version submission
Anne Roubal - Statistical analysis, drafting of the manuscript, approve final version submission
Ricki Bettencourt - Statistical analysis, critical revision of the manuscript, approved final submission
Rohit Loomba - study concept and design, analysis and interpretation of data, critical revision of the manuscript, obtained funding, study supervision, approved final submission

Results and Conclusion—We found significant inter-state variability in liver disease mortality, ranging from 6.4 to 17.0 per 100,000. The South and Mid-West carry the highest rates of liver disease mortality. In addition to viral hepatitis death rates, there is a strong correlation between higher percent Hispanic population and a state's liver disease mortality rate ($r = 0.538$, $p < 0.001$). Greater racial diversity ($p < 0.001$) and lower household income ($r = 0.405$, $p=0.003$) was associated with the higher liver disease mortality. While there was a trend between higher obesity rates and higher liver disease mortality, the correlation was not strong and there was no clear association between alcohol consumption and liver disease mortality rates.

Keywords

Cirrhosis; liver disease; death; population-based factors; geographic variability

INTRODUCTION

While chronic liver disease is the twelfth leading cause of death in all Americans, it is the fourth leading cause of death in those 45 – 54 years of age and the sixth leading cause of death in Hispanics Americans[1]. In the US, liver disease mortality has been attributed to individual characteristics such as ethnicity, race, obesity, and alcohol consumption[2–5]. Beyond the impact of individual characteristics on liver disease mortality, assessment of geographic variations may inform health promotion strategies, intervention programs, resource allocation, and health policies. In other disease states, geographic variations have led to impactful preventive measures. For example, description of the "Stroke Belt" in Southern states led to better understanding of demographic and healthcare system determinants of health with the establishment of research and clinical collaboratives aimed at reducing health disparities[6,7]. Similarly in an analysis of geographic variations, heart healthy policies and built environment characteristics significantly impacted cardiovascular mortality[8]. Currently, there are no prior studies describing the geographic variation in liver disease across the US. Therefore, the aim of this study was to examine inter-state geographic variability in liver disease mortality in relation to important co-morbid conditions.

METHODS

Data Sources

This is a cross-sectional analysis of state-specific liver disease mortality rates and factors predicted to be associated with liver disease mortality at a population level. This study was considered exempt from oversight by the University of Arizona Institutional Review Board because it did not meet the definition of research and/or human subject research. Age-adjusted liver disease mortality rate was derived from the National Vital Statistics in 2010[1].

Death rates due to viral hepatitis were derived from CDC reporting of cause of death for 2010[9]. Alcohol consumption is defined as an adult reporting having at least one alcoholic drink in the last 30 days in the 2010 Behavioral Risk Factor Surveillance Survey. Obesity is defined as having a body mass index (BMI) great than 30.0. BMI is calculated by dividing an adult's self-reported weight in kilograms by the square of their height in meters obtained from the 2010 Behavioral Risk Factor Surveillance System.[10]

Race and Ethnicity were obtained from 2010 Census data. Data reported are weighted averages based on each state's total population. Ethnicity was broken into two large categories – Hispanic or non-Hispanic. Race categories include "White", "Black or African American", "American Indian or Alaska Native", "Asian", "Native Hawaiian or Other Pacific Islander", or "Some Other Race"[11]. Median Household Income is derived from the 2010 U.S. Census. It is the median household income for all household in the state over the past 12 months at 2010 inflation-adjusted dollars[12].

Statistical analysis

Age-adjusted liver disease mortality was categorized into quartiles. Each state was assigned its' corresponding outcome quartile value. This quartile value was then used as an outcome variable. Raw values of each of the independent variables were obtained from the data sources previously described. Quartile cut off values (Q1, Q2, Q3, Q4) were calculated for each variable. Mean values of each independent variable were calculated for the states grouped into each of the liver disease mortality quartiles. Box plots of each independent variable (% viral hepatitis, % alcohol consumption, % obese, % Hispanic, and median household income) were created by the outcome variable categories (mortality quartile). Kruskal-Wallis tests tested for across group differences. For race, the population-weighted percentage of each race category was averaged across the states within each of the 4 quartiles of liver disease mortality and compared by Chisquared test. All analyses were performed in SAS 9.4 (Cary, NC).

RESULTS

Inter-state Variability in Liver Disease Mortality

Figure 1 and Table 1 show significant variability in age-adjusted liver disease mortality at a state level. Age-adjusted liver disease mortality ranges from 6.4 to 17.0 per 100,000. In the northeast US, rates of age-adjusted liver disease mortality are the lowest in the country. New Hampshire and New York have the lowest rates in the US (6.4 and 6.5/100,000, respectively). In contradiction to this general assumption, West Virginia rate is the highest quartile with a rate of 10.7/100,000. States in the south- and mid-west carry the some of the highest liver disease mortality rates with New Mexico reporting the highest liver disease mortality, 17.0/100,000. The southern state of Georgia does not fit this assumption and falls into the lowest quartile with a rate of 7.5/100,000. States size did not impact the variability in mortality rates.

Associations between Individual Factor Geographic Variability and Liver Disease Mortality

Viral Hepatitis

We assessed individual-level factors that have been implicated in prior studies to affect liver disease mortality. Death rates due to viral hepatitis vary across the US with rates as low as 1% in Wisconsin and Illinois to as high as 5.9% in Delaware. There was a strong correlation between death rates due to viral hepatitis and liver disease mortality. Mean death rates from viral hepatitis increased from 2.0% in the states in the lowest quartile of liver disease mortality to 3.1% in the states within the highest mortality quartile ($r = 0.55$, $p<0.0001$, Figure 2a, Table 2).

Alcohol Consumption

Alcohol consumption varies across the US. The prevalence of individuals reporting at least one alcoholic drink in the last 30 days ranged from 25% in Utah to 66% in Wisconsin and Connecticut. There was no statistically significant association between liver disease mortality and alcohol consumption (Figure 2b, Table 2, r = 0.205, p = 0.148). Of the 13 states in the lowest quartile for liver disease mortality, 6 states were in the third or fourth quartile for alcohol consumption. Looked at another way, of the 13 states in the highest quartile of alcohol consumption, 10 were not in the fourth highest quartile for liver disease mortality. In fact, mean alcohol consumption rates were higher in the lowest quartile of liver disease mortality compared to the higher quartile (55.1% in quartile 1 of liver disease mortality vs. 50% in quartile 4). This relationship was also true when prevalence of heavy drinking behavior was used as the measure of alcohol consumption (data not reported).

Obesity

There was a trend between higher obesity rates and liver disease mortality, although this was not statistically significant (Figure 2c, Table 2, r = 0.16, p = 0.25). Of 13 states in the highest quartile of liver disease mortality, 4 states were in the highest quartile for obesity rate while the rest were either in the first or second quartiles. Similarly, of the 13 states in the lowest quartile for liver disease mortality, 6 states were in the lowest quartile for obesity rates and 5 states were in the third or fourth quartile. Looked at another way, mean obesity rates in the lowest quartile of liver disease mortality were similar to that in the highest quartile of liver disease mortality (25.7% vs. 27%).

Ethnicity & Race

There is a strong correlation between increasing percent of the population reporting Hispanic ethnicity and higher liver disease mortality within states (Figure 2d, Table 2 r = 0.538, p < 0.001). Compared to the overall US population, which is 16.3% Hispanic, 7 of the 13 states in the highest quartile of liver disease mortality reported a higher prevalence of individuals reporting Hispanic ethnicity. Of the 13 states in the lowest quartile of liver disease mortality, only 2 states exceeded the national average percentage Hispanic population, New York (17.6%) and New Jersey (17.7%).

Overall, states in the highest quartile of liver disease mortality also showed the greatest diversity of racial make-up (Figure 3). This is largely due to a significant increase in the proportion of individual reporting “Other” as their race in states in the highest quartile of liver disease mortality. Overall, states with higher proportion of minorities experienced higher prevalence of liver disease.

Economic factors

We found a statistically significant association between liver disease mortality and median household income (Figure 2e, Table 2, r = 0.405, p=0.003). Income is lower in states with higher liver disease mortality. Compared to the overall US median household income of $51,194, 9 of the 13 states in the highest quartile of liver disease mortality had a lower median income. Furthermore, 6 of the 13 states in the first quartile for liver disease mortality are in the highest quartile for income, 12 of the 13 are in the top half.

DISCUSSION

In this study, we sought to determine whether there was geographic variability in liver disease related mortality rates at the state level in the US. Using publicly reported data, we report significant state-by-state variation. States in the highest quartile of liver disease mortality tend to be in the Southern US and states in the lowest quartile of liver disease mortality tend to be in the Northern US. Specifically, in the lowest quartile of liver disease mortality, 8 of 13 states are in the northeast and 3 are in the northwest. In the highest quartile of liver disease mortality, 7 of the 13 states are in the south and 3 are in the west. Exceptions exist to these general statements such as West Virginia. The Appalachian region of West Virginia, a traditionally unhealthy region of the US, could potentially be the reason for this discrepancy.

We further sought to identify whether factors such as viral hepatitis prevalence, alcohol consumption, obesity, ethnicity, race, and socioeconomic status may be associated with liver disease mortality. While alcohol consumption and obesity are causative agents of liver disease and likely do contribute to mortality, our analysis shows that these factors do not explain the geographic variability of liver disease mortality noted in our study. Importantly, our results show that Hispanic ethnicity and median household income are strong predictors of liver disease mortality and as strongly associated with liver disease mortality as prevalence of death due to viral hepatitis. In many disease states including cardiovascular disease, Hispanics benefit from the “Hispanic paradox” but this mortality benefit does not extend to liver disease[2]. Specifically, liver disease was the sixth leading cause of death in the Hispanic population compared the twelfth leading cause of death for all Americans[1]. Race impacts liver mortality as well with African Americans having the lowest risk of liver disease mortality while Native Americans and Alaskan Natives carry the highest risk[3,13]. Our results confirm prior reports with states in the highest quartile of liver disease mortality showing higher racial diversity. Race and ethnicity, which are characterized not only by differences in genetics and biology but also by variation in environmental, psychosocial, cultural, and behavioral factors, may affect an individual’s interaction to medical care system on a variety of levels. Therefore, differences in death rates among various demographic sub-populations may be due to differences in genetic predisposition or due to social factors such as socioeconomic status, access to medical care, and the prevalence of specific risk factors in a particular subpopulation[3,14].

Geographic variability in liver disease mortality is likely due to various factors ranging from public health policy over major contributors to chronic liver disease such as HCV and alcohol consumption to religious and sociocultural attitudes that vary by state. A prior study looking at per capita alcohol consumption had similar findings. A study by Polednak showed higher liver disease mortality rates in states with high per capita alcohol (PCA) consumption for those under the age of 65 but also found exceptions on both spectrums - states with average or low PCA but high liver disease mortality (New Mexico, California) and states with high PCA but low liver disease mortality (New Hampshire, Wisconsin)[4]. While there is a clear link between chronic liver diseases and alcohol consumption at an individual level, geographic variability in liver disease mortality in not fully explained by per capita alcohol consumption.

The association between liver disease mortality and income is also complex. While median household income serves as an indicator of socioeconomic status, many other individual level factors likely impact the association between household income and liver disease mortality. These associations require more investigation. A prior study of geographic variation in hepatocellular cancer found an initial association between socioeconomic variation and death rates due to hepatocellular cancer, however, this association weakened when adjusting for other individual factors such as education attainment, diabetes, alcohol consumption, and other health behaviors[5]. In another study, unemployment rate by state was a predictor of state specific liver cirrhosis mortality rate in both time series and cross-sectional analyses of US state-specific cirrhosis mortality rates, along with PCA[15]. Variation in access to liver transplantation is well described and may play role in the variability in liver disease mortality. The average model for end-stage liver disease at transplant varies by more than 10 points between donor service areas and more than 7 points between regions[16]. While some of these disparities were addressed with regional sharing addressed by the Share 30 policy, differential access to liver transplant continues to exist[17].

Our study found that ethnicity, race and income correlate with liver disease mortality do not fully explain the geographic variability of liver disease mortality as exceptions to the relationship exist. Future work is needed to explain the trends described in our study. We suspect that factors such as employment status, educational level, health insurance status, community socioeconomic status (income), access to health care and subspecialty care may all be associated with liver disease mortality through various pathways. We further hypothesize that these factors may all play a role and need to be addressed through more targeted public policy driven changes and preventive care in order to impact liver disease mortality around the country in ethnic-specific strategies. In addition, these efforts will need to take into account ethnic disparity. These factors might all decrease mortality and increase quality of life.

Limitations

Our unit of geographic variation, namely US state, was relatively large, meaning that fine resolution of geographic variation, such as at that which might be present at the level of a county or postal code, was not possible using our analytic strategy. In addition, liver disease mortality rates are based on data gleaned from death certificates, which have traditionally underestimated chronic liver disease as a cause of death[18]. Furthermore, self-reported measures of drinking and obesity from the BRFSS. These health factors have a negative stigma attached to them such that participants are likely to underreport their alcohol consumption and weight in order to appear healthier. There may be confounding present in that the study is being performed at the state level but looking at individual characteristics. Lastly, there is also an assumed time-lag between these health factors and liver disease mortality, such that an individual who was a heavy drinker in their 20’s might have chronic liver disease in their 60’s. We used 2010 data on health outcomes and risk factors, which was unable to adjust for this time-lag.

Despite, these limitations, this is the first study to establish geographic variability in liver disease mortality. Epidemiological studies such as ours are essential mechanisms for development of public health policies and guidelines. They can also serve to target resources for research focused at dissecting disease mechanisms, testing treatments, implementing preventive strategies and ultimately optimizing the quality of health care delivered. Given the strong influence of region on liver disease mortality, future work assessing variation in state and national public funding of chronic liver disease care is important. Availability of specialists and transplant centers may be important health delivery variables that impact the geographic variation seen in our study and need to be explored. Variation in alcohol related public policy as well as public health resources to manage substance need to be explored further. Finally, investigation of other socioeconomic variables such as health insurance, income inequality, build environment resources will be meaningful in understanding the variations in liver disease mortality seen in our study.

CONCLUSIONS

There is significant inter-state variability in liver disease mortality. We find an association between viral hepatitis death rates, Hispanic ethnicity, racial diversity, and household income but not obesity or alcohol consumption and liver disease mortality. Understanding the variations in liver disease mortality throughout the US should inform public health policy and guide research, education, and resource allocation to reduce existing health care disparities in liver disease.

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AD had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Abbreviations

BMI	Body Mass Index
CDC	Center for Disease Control and Prevention
HCUP	Health Care Cost and Utilization Project
LD-M	Liver Disease-related mortality
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NHAMCS	National Hospital Ambulatory Medical Care Survey

NIS	Nationwide Inpatient Sample
OMB	Office of Management and Budget's
PCA	Per capita alcohol
US	United States

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Clinical Significance

- Liver disease is an important cause of morbidity and mortality in the U.S. Understanding the geographic variations in liver disease mortality (LD-M) is essential to reducing existing health care disparities.
- There is significant inter-state variability in liver disease mortality rates with the South and Mid-West carry the highest rates of liver disease mortality.
- There is significant association between a state's liver disease mortality rate and higher proportion of Hispanic population, racial diversity, and household income.

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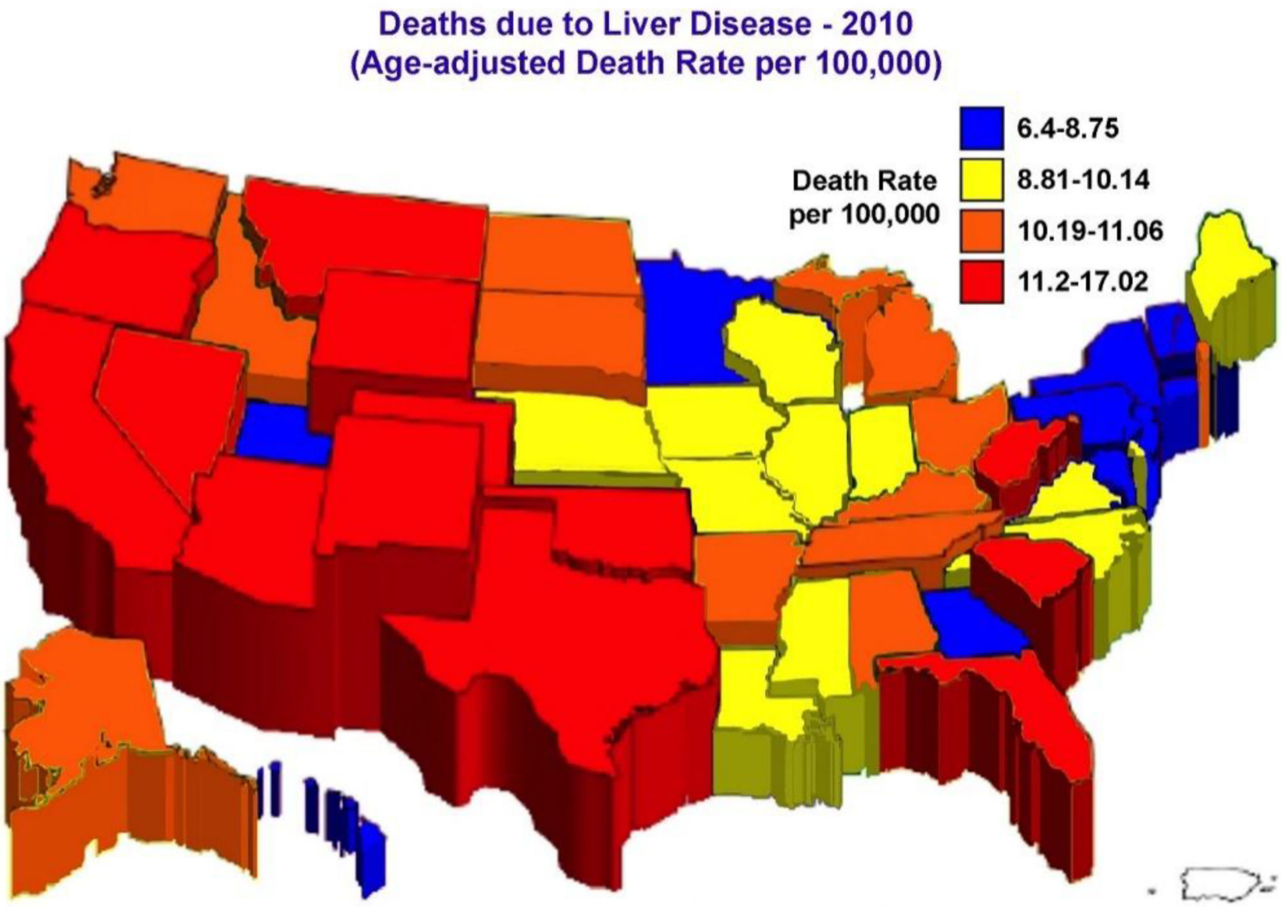

Figure 1.

Significant inter-state variability exists in liver disease related mortality. States color and height represent liver disease mortality

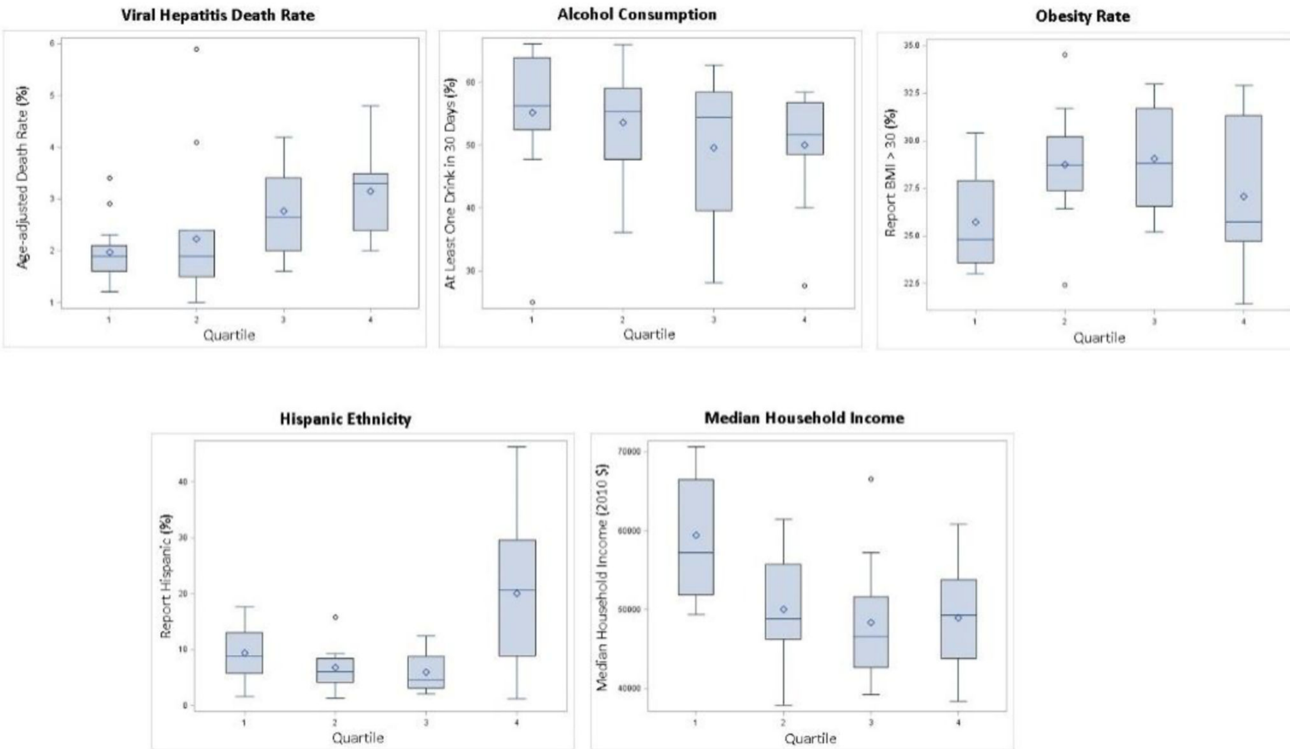

Figure 2.

Box plots of displaying rates of (a) viral hepatitis, (b) alcohol consumption, (c) obesity, (d) Hispanic ethnicity and (e) median household income (y-axis) by quartile of liver diseaserelated mortality (x-axis). Q1 = lowest quartile, Q4 = highest quartile.

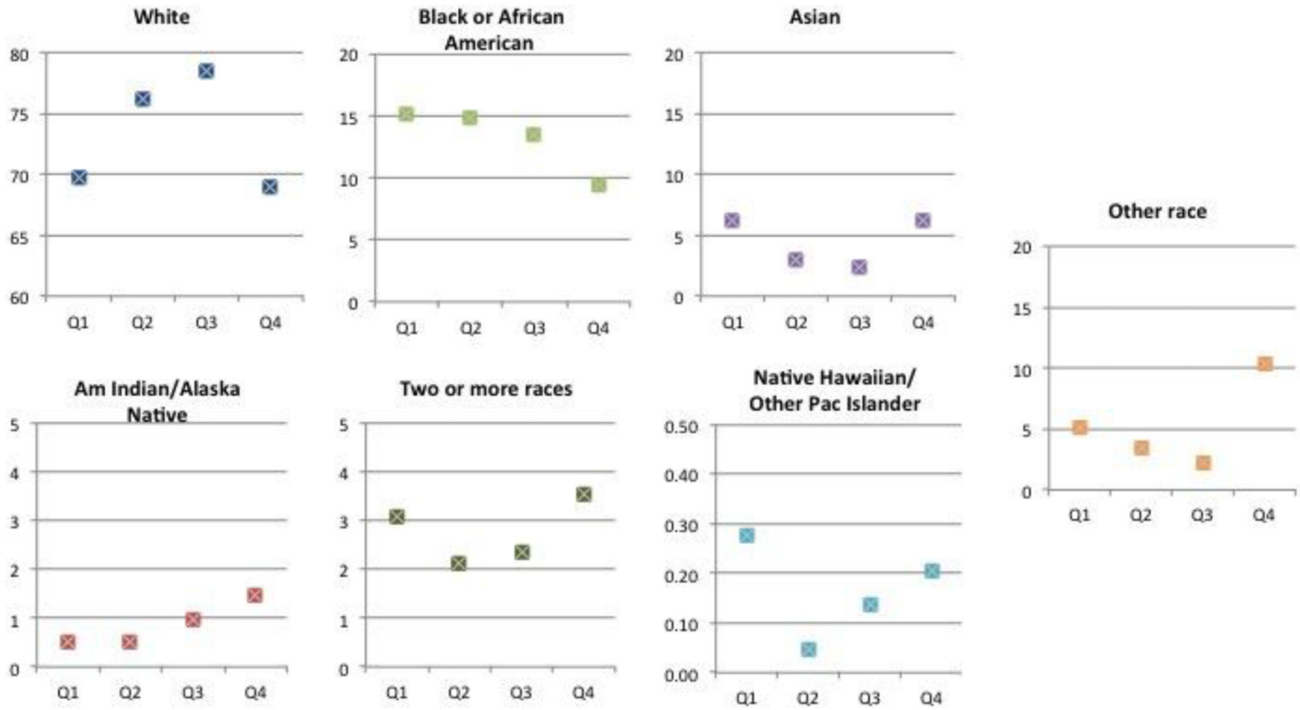

Figure 3.

Population-weight average rates of each race category (y-axis) by quartile of liver disease-related mortality (x-axis). Q1 = lowest quartile, Q4 = highest quartile. Note the varying y-axis values.

Table 1

State variation in liver disease mortality by state

		Deaths (age adjusted rate per 100,000)	
State	**Total Population**	**All-cause**	**Chronic Liver Disease and Cirrhosis**
Alabama	4,779,736	939.7	9.4
Alaska	710,231	771.5	9.8
Arizona	6,392,017	693.1	12.7
Arkansas	2,915,918	892.7	9.9
California	37,253,956	646.7	11.3
Colorado	5,029,196	682.7	11.2
Connecticut	3,574,097	652.9	7.3
Delaware	897,934	769.9	8.8
D of Columbia	601,723	792.4	8.9
Florida	18,801,310	701.1	10.6
Georgia	9,687,653	845.4	7.5
Hawaii	1,360,301	589.6	6.5
Idaho	1,567,582	731.6	9.3
Illinois	12,830,632	736.9	8.2
Indiana	6,483,802	820.6	9.0
Iowa	3,046,355	721.7	7.9
Kansas	2,853,118	762.2	7.8
Kentucky	4,339,367	915	9.4
Louisiana	4,533,372	903.8	7.9
Maine	1,328,361	749.6	8.8
Maryland	5,773,552	728.6	7.0
Massachusetts	6,547,629	675	7.7
Michigan	9,883,640	786.2	10.0
Minnesota	5,303,925	661.5	7.0
Mississippi	2,967,297	962	9.0
Missouri	5,988,927	819.5	7.8
Montana	989,415	754.7	10.7
Nebraska	1,826,341	717.8	8.1
Nevada	2,700,551	795.4	11.1
New Hampshire	1,316,470	690.4	6.4
New Jersey	8,791,894	691.1	7.3
New Mexico	2,059,179	749	17.0
New York	19,378,102	665.5	6.6
North Carolina	9,535,483	804.9	8.9
North Dakota	672,591	704.3	10.1
Ohio	11,536,504	815.7	9.4

		Deaths (age adjusted rate per 100,000)	
State	**Total Population**	**All-cause**	**Chronic Liver Disease and Cirrhosis**
Oklahoma	3,751,351	915.5	12.5
Oregon	3,831,074	723.1	11.3
Pennsylvania	12,702,379	765.9	7.8
Rhode Island	1,052,567	721.7	9.7
South Carolina	4,625,364	854.8	10.8
South Dakota	814,180	715.1	10.1
Tennessee	6,346,105	890.8	10.2
Texas	25,145,561	772.3	11.7
Utah	2,763,885	703.2	7.3
Vermont	625,741	718.7	7.2
Virginia	8,001,024	741.6	7.9
Washington	6,724,540	692.3	10.5
West Virginia	1,852,994	933.6	10.7
Wisconsin	5,686,986	719	8.2
Wyoming	563,626	778.8	12.5

Table 2

Correlation between individual-level factors and liver disease-related mortality.

	Correlation to LD-M	p-value¶
Viral Hepatitis*	0.548	<0.001
Alcohol Use†	0.205	0.148
Obese‡	0.164	0.251
Hispanic§	0.538	<0.001
Income//	0.405	0.003

*% with viral hepatitis in the state, n = 49

†% reporting any drink in the last 30 days, negative correlation, n = 51

‡% Obese in state, negative correlation, n = 51

§% Hispanic in state, n = 51

//median household income in stage, negative correlation, n = 51

¶Kruskal–Wallis test