The Growing Burden of Disability Related to Chronic Liver Disease in the United States: Data From the Global Burden of Disease Study 2007-2017

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Chronic liver disease (CLD) causes significant morbidity and mortality in the United States with regional variations. Comparable and consistent state-level measures of CLD-related morbidity and disability among U.S. states have not been well studied. Our aim was to assess the CLD burden within the United States between 2007 and 2017 based on the most common causes of CLD: hepatitis B virus, hepatitis C virus (HCV), alcoholic liver disease (ALD), and nonalcoholic fatty liver disease (NAFLD). The Global Burden of Disease database was used for the years 2007-2017. International Classification of Diseases, Tenth Revision, codes were used to identify liver cancer (LC) and cirrhosis. Disability-adjusted life years (DALYs) were computed by the summation of years of life lost and years lived with disability. All rates reported here were age-standardized rates per 100,000 population. In 2017, there were 167,324 incident CLDs, 21% from LC and 79% from cirrhosis; this number was 30% higher than in 2007. The highest rate increases were seen in Kentucky, New York, and Pennsylvania. In 2017, there were 90,046 CLD-related deaths, which was 34% higher than in 2007. Highest rank increases were seen in Kentucky, Montana, and Washington. The rate of CLD incidence and death due to NAFLD was higher than other causes of CLD. In 2017, CLD caused 2.33 million DALYs, which was 27% higher than in 2007 and was mainly driven by HCV (37.2%), ALD (27.7%), and NAFLD (10.6%). California, Texas, and Florida had the highest DALYs; however, the highest CLD-DALY rates per 100,000 population were seen in New Mexico, District of Columbia, and Oklahoma. *Conclusion:* The CLD-related burden is increasing in the majority of U.S. states at an unprecedented rate. The impact of this burden on individual states is heterogeneous, and there are important disparities among states that merit further investigation. (*Hepatology Communications* 2021;5:749-759).

Chronic liver disease (CLD) is increasingly being recognized as an important contributor to the burden of disease in the United States and the rest of the world.[1-4] CLD is now regarded as one of the leading causes of morbidity and mortality. In fact, in 2017, CLD was the tenth leading cause of death among men in the United States.[5] Furthermore, CLD was the fifth cause of death among 45-64 year olds, which are the most productive years of life.[6]

In the United States, the most common etiologies of CLD have been chronic hepatitis C virus (HCV) and hepatitis B virus (HBV) infections, alcoholic liver

Abbreviations: ALD, alcoholic liver disease; CLD, chronic liver disease; DALY, disability-adjusted life year; GBD, Global Burden of Disease, Injuries, and Risk Factor; HBV, hepatitis B virus; HCV, hepatitis C virus; ICD-10, International Classification of Diseases, Tenth Revision; IHME, Institute for Health Metrics and Evaluation; LC, liver cancer; NAFLD, nonalcoholic fatty liver disease; SDI, sociodemographic index; UI, uncertainty interval; YLD, years lived with disability; YLL, years of life lost.

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disease (ALD), and nonalcoholic fatty liver disease (NAFLD).[3,4] Less commonly, other liver diseases, such as hereditary hemochromatosis, Wilson disease, autoimmune hepatitis, primary biliary cholangitis, and primary sclerosing cholangitis, can also lead to advanced liver disease and associated complications.[1,7]

In recent years, the global burden of CLD and its complications have been described.[8-10] In this context, mortality and morbidity of CLD is primarily driven by its complications related to liver cancer (LC) and cirrhosis.[1-5] On the other hand, the burden of disease is defined as disability-adjusted life years (DALYs), which combines the years of life lost (YLL) and years lived with disability (YLD).[10] The global burden of disease data related to CLD suggest that different types of liver disease are responsible for the burden of CLD across different regions of the world.[2,4,10,11] For example, chronic HBV is the leading cause of LC and cirrhosis in most parts of Africa, while ALD plays a significant role in Central Europe and North America and NAFLD has been on the rise in most parts of the globe.[2,4,10,11] Data about CLD burden at the U.S. state level are scarce, and few studies have focused on this important topic, especially for U.S. policy makers.

Therefore, the aim of this study was to determine the burden of the most common causes of CLD in the United States at the state level and assess any changes that may have occurred between 2007 and 2017.

Materials and Methods

DATA SOURCES

This study was based on data from the Global Burden of Disease, Injuries, and Risk Factor (GBD) study, coordinated by the Institute for Health Metrics and Evaluation (IHME). The IHME is an independent population health research center at the University of Washington College of Medicine. Its vision is to provide the world high-quality information on population health, its determinants, and the performance of health systems. The GBD study annually produces estimates of cause-specific incidence, mortality, and morbidity for age, sex, and worldwide location from at least 1990 onward, using standardized statistical estimation techniques instead of simply presenting data points. As a continuous quality improvement, each annual GBD study re-estimates the entire time series by including all known advances in data, modeling, estimation methods, and health knowledge, ensuring that each GBD study contains the most up-to-date estimates. In 2018, the GBD 2017 study published epidemiologic assessments of 359 diseases (including LC and cirrhosis) and injuries and 84 risk factors from 195 countries and territories; for certain countries, subnational estimates (including the 50 states and one district of the United States) were published. Notably, compared to the previous GBD 2016 study, GBD 2017 added NAFLD as the fifth cause of LC and cirrhosis along with HBV, HCV, ALD, and other causes. For this study, we obtained the publication estimates of incidences, deaths, and DALYs for LC and cirrhosis as well as five etiology groups (HBV, HCV, ALD, NAFLD, and other causes) from GBD 2017.[11]

GBD STUDY ESTIMATION FRAMEWORK

General methodologies as well as the specific LC and cirrhosis methodology have been published.[10-13]

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Herein, we briefly present the GBD study estimation process for LC and cirrhosis as well as their etiology.

Death data, which were used to estimate mortality due to LC and cirrhosis, were obtained from the National Center for Health Statistics for each state. The International Classification of Diseases, Tenth Revision (ICD-10), codes were used to identify LC and cirrhosis (Supporting Table S1). ICD-10 codes for acute hepatitis were excluded. To estimate LC and cirrhosis mortality with uncertainty by age, sex, location, and year, the GBD study used the Cause of Death Ensemble models, which is an approach that incorporates a wide variety of individual models and combinations of covariates.[11,14,15] All individual and ensemble models were evaluated using out-of-sample predictive validity tests vetted by experts in each disease and validated by IHME and their collaborators from around the world. Mortality estimates were then scaled with other causes of deaths to sum to 100% of all-cause mortality estimates within each age, sex, year, and location.

Because ICD-10 coding is valid for defining LC and cirrhosis and not for etiologic estimates, the GBD study used the models to split the parent cause "liver cancer and cirrhosis" mortality and morbidity into the five causes, comprising HBV, HCV, ALD, NAFLD or steatohepatitis (hereafter referred to as NAFLD), and other causes, such as hemochromatosis, autoimmune hepatitis, Wilson's disease, cryptogenic, idiopathic, or unknown.[11] The proportions of LC and cirrhosis cases and deaths due to different liver diseases were identified by systematic literature review and modeled in the DisMod-MR model, an integrative meta-regression method to obtain age-sex-location and year-specific estimates.[16,17] A complete list of covariates used in the models can be found in Supporting Table S2. Relevant metadata can be retrieved through the publicly available Data Input Sources Tool (http://ghdx.healthdata.org/gbd-2017/data-input-sources).

DALYs were computed by the summation of YLL and YLD, which quantifies health loss due to specific diseases and injuries. YLL was calculated by multiplying the estimated number of deaths by age with a standard life expectancy at that age. YLD was calculated by multiplying prevalence by a disability weight, ranging from 0 to 1, where 0 is a state of full health and 1 is death. A disability weight represents the magnitude of health loss associated with a disease. LC and cirrhosis due to any cause have a disability weight of 0.451 (95% uncertainty interval [UI], 0.307-0.600) and 0.178 (95% UI, 0.377-0.687), respectively.[18] The total amount of DALYs in a population is useful for measuring the disease burden experienced by that population as a whole.

The sociodemographic index (SDI), a measure of average income per capita, educational attainment, and total fertility rate at the state level, is also available in the GBD study (Supporting Table S3).[19] The value of SDI is between 0 and 1, with a higher index indicating greater sociodemographic development. Population size for each state was obtained from the U.S. Census Bureau. Age-standardized rates were based on the world standard population developed for the GBD study. Flow charts for database, input data and methodologic summary for the models, and statistical codes are publicly available in compliance with the Guidelines for Accurate and Transparent Health Estimates Reporting developed by the World Health Organization and others.

DATA ANALYSIS

GBD study estimates for a disease burden are reported with the 95% UIs, including the true value of a parameter with 95% probability. UIs account for not only variance in parameter estimation but also uncertainty from data collection, model selection, and other sources of uncertainty under the parameter estimation process. All rates reported here were age-standardized rates per 100,000 population. Percentage change was based on the difference between the value in 2017 and in 2007 divided by the value in 2007 and was considered to be significant when the 95% UIs did not include zero. We performed a decomposition analysis of change in age-standardized rates of CLD-related DALYs from 2007 to 2017 by each liver disease. The association between SDI and CLD-related DALYs was displayed in a scatterplot. For this study, a CLD-related burden was defined by combining the burden of LC and cirrhosis. All analyses were performed using SAS, version 9.4 (SAS Institute, Cary, NC). Microsoft Excel was used for data visualization.

Results

Results and findings of the GBD 2017 study can be explored interactively through GBD Compare

Visualization Hub.[20] U.S. state-level estimates of LC and cirrhosis incidences, deaths, YLL, YLD, and DALYs attributable to different liver diseases from 2007 to 2017 are summarized in Supporting Tables S4-S8.

CLD-RELATED INCIDENCE AND DEATH RATES IN THE UNITED STATES

In 2017, there were 167,324 incident cases of CLD in the United States (21% from LC and 79% from cirrhosis) and 90,046 CLD-related deaths (30.6% death from LC and 69.4% death from cirrhosis). This represented increases of 30% and 34% from 2007, respectively (Supporting Tables S4 and S5). Between 2007 and 2017, age-standardized incidence rate for CLD increased by 11.6% (Supporting Figs. S1 and S2; Supporting Table S9), while the increase in the CLD-related death rate was 9.5% (Supporting Figs. S9 and S10; Supporting Table S10). During this period, the age-standardized incidence rate and death rate due to NAFLD increased more than any other etiology (Supporting Figs. S3 and S11).

Geographically, the highest increases in the incidence rate of CLD were observed in Kentucky, New York, Pennsylvania, and Tennessee (Supporting Figs. S4-S8), while the highest increases in CLD-related death rates were seen in Kentucky, Montana, Washington, and Indiana (Supporting Figs. S12-S16).

CLD-RELATED DALYs ACROSS THE U.S. STATES

In 2017, there were 2.33 million CLD-related DALYs in the United States, which was a 27.3% increase from 2007. CLD-related DALYS were related to HCV (37.2%), ALD (27.7%), NAFLD (10.6%), and HBV (8.4%) (Supporting Tables S6 and S11). The majority of CLD-related DALYs came from YLL (96.1%) and only 3.9% came from YLD (Supporting Tables S7 and S8).

As expected, highly populated states had the highest CLD-related DALYs in 2017, with California, Texas, Florida, and New York having ≥100,000 DALYs (Fig. 1). However, New Mexico (857 per 100,000 population), District of Columbia (672 per 100,000), Oklahoma (619 per 100,000), and Alabama (600 per 100,000) had the highest rates. The states with the lowest rates of CLD-related DALYs were Vermont, Iowa, Minnesota, and New York (≤380 per 100,000). Between 2007 and 2017, there were variations across states in terms of DALY rate increase or decrease. For example, North Dakota (+28%), South Dakota (+22.2%), Kentucky (+20%), and Iowa (+19.6%) had the highest rate increments in DALYs, whereas Nevada (−3.0%) and District of Columbia (−2.2%) were the only states with a decline in DALY rates.

Changes in LC and cirrhosis DALY rates are provided in Supporting Figs. S17 and S18. The age-standardized rate of cirrhosis DALYs was 2 times to 5 times higher than that of LC DALYs across U.S. states (Supporting Table S5).

DALYs ACCORDING TO ETIOLOGY OF CLD

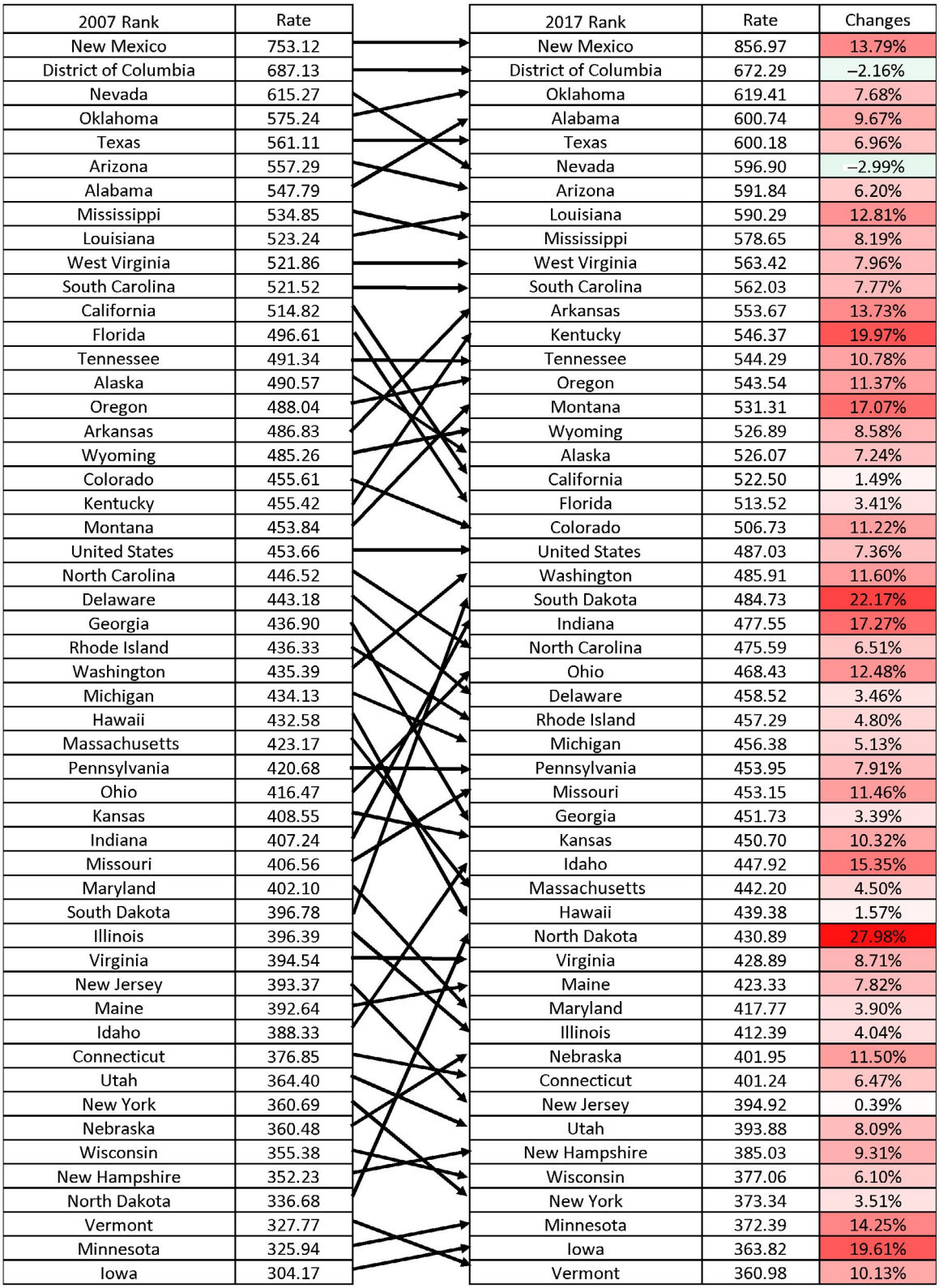
In 2017, HCV was the leading cause of CLD-related DALYs in all states (ranging from 22.2% in Indiana to more than 40% in Michigan, California, and Tennessee) (Fig. 2; Supporting Table S11). Nevertheless, improving trends in HCV-related DALYs (negative percentage change) were observed in New Jersey, District of Columbia, and Nevada.

ALD was the second leading cause of CLD-related DALYs, with 30% in Texas, Ohio, and Minnesota. Again, improving trends in DALYs related to ALD were noted for Hawaii, California, and New Jersey.

DALYs caused by NAFLD ranged between 8.3% in Texas and 17.8% in Indiana. On the other hand, between 2007 and 2017, all states showed increasing rates in DALYs due to NAFLD, with the highest rate being reported for North Dakota (+23.4%) and the lowest for Nevada (0.9%) (Fig. 3). Decomposition analyses of LC and cirrhosis DALYs are provided in Supporting Figs. S19 and S20.

ASSOCIATIONS BETWEEN CLD-RELATED BURDEN AND SOCIODEMOGRAPHIC FACTORS

The lowest LC and cirrhosis DALYs were seen in states with a high SDI, such as Vermont, Iowa, and Minnesota, while low SDI states, such as New Mexico,



2007 Rank	Rate	2017 Rank	Rate	Changes
New Mexico	753.12	New Mexico	856.97	13.79%
District of Columbia	687.13	District of Columbia	672.29	–2.16%
Nevada	615.27	Oklahoma	619.41	7.68%
Oklahoma	575.24	Alabama	600.74	9.67%
Texas	561.11	Texas	600.18	6.96%
Arizona	557.29	Nevada	596.90	–2.99%
Alabama	547.79	Arizona	591.84	6.20%
Mississippi	534.85	Louisiana	590.29	12.81%
Louisiana	523.24	Mississippi	578.65	8.19%
West Virginia	521.86	West Virginia	563.42	7.96%
South Carolina	521.52	South Carolina	562.03	7.77%
California	514.82	Arkansas	553.67	13.73%
Florida	496.61	Kentucky	546.37	19.97%
Tennessee	491.34	Tennessee	544.29	10.78%
Alaska	490.57	Oregon	543.54	11.37%
Oregon	488.04	Montana	531.31	17.07%
Arkansas	486.83	Wyoming	526.89	8.58%
Wyoming	485.26	Alaska	526.07	7.24%
Colorado	455.61	California	522.50	1.49%
Kentucky	455.42	Florida	513.52	3.41%
Montana	453.84	Colorado	506.73	11.22%
United States	453.66	United States	487.03	7.36%
North Carolina	446.52	Washington	485.91	11.60%
Delaware	443.18	South Dakota	484.73	22.17%
Georgia	436.90	Indiana	477.55	17.27%
Rhode Island	436.33	North Carolina	475.59	6.51%
Washington	435.39	Ohio	468.43	12.48%
Michigan	434.13	Delaware	458.52	3.46%
Hawaii	432.58	Rhode Island	457.29	4.80%
Massachusetts	423.17	Michigan	456.38	5.13%
Pennsylvania	420.68	Pennsylvania	453.95	7.91%
Ohio	416.47	Missouri	453.15	11.46%
Kansas	408.55	Georgia	451.73	3.39%
Indiana	407.24	Kansas	450.70	10.32%
Missouri	406.56	Idaho	447.92	15.35%
Maryland	402.10	Massachusetts	442.20	4.50%
South Dakota	396.78	Hawaii	439.38	1.57%
Illinois	396.39	North Dakota	430.89	27.98%
Virginia	394.54	Virginia	428.89	8.71%
New Jersey	393.37	Maine	423.33	7.82%
Maine	392.64	Maryland	417.77	3.90%
Idaho	388.33	Illinois	412.39	4.04%
Connecticut	376.85	Nebraska	401.95	11.50%
Utah	364.40	Connecticut	401.24	6.47%
New York	360.69	New Jersey	394.92	0.39%
Nebraska	360.48	Utah	393.88	8.09%
Wisconsin	355.38	New Hampshire	385.03	9.31%
New Hampshire	352.23	Wisconsin	377.06	6.10%
North Dakota	336.68	New York	373.34	3.51%
Vermont	327.77	Minnesota	372.39	14.25%
Minnesota	325.94	Iowa	363.82	19.61%
Iowa	304.17	Vermont	360.98	10.13%

FIG. 1. Change in the absolute number of age-standardized CLD-related DALY rates: U.S. states from 2007 through 2017.

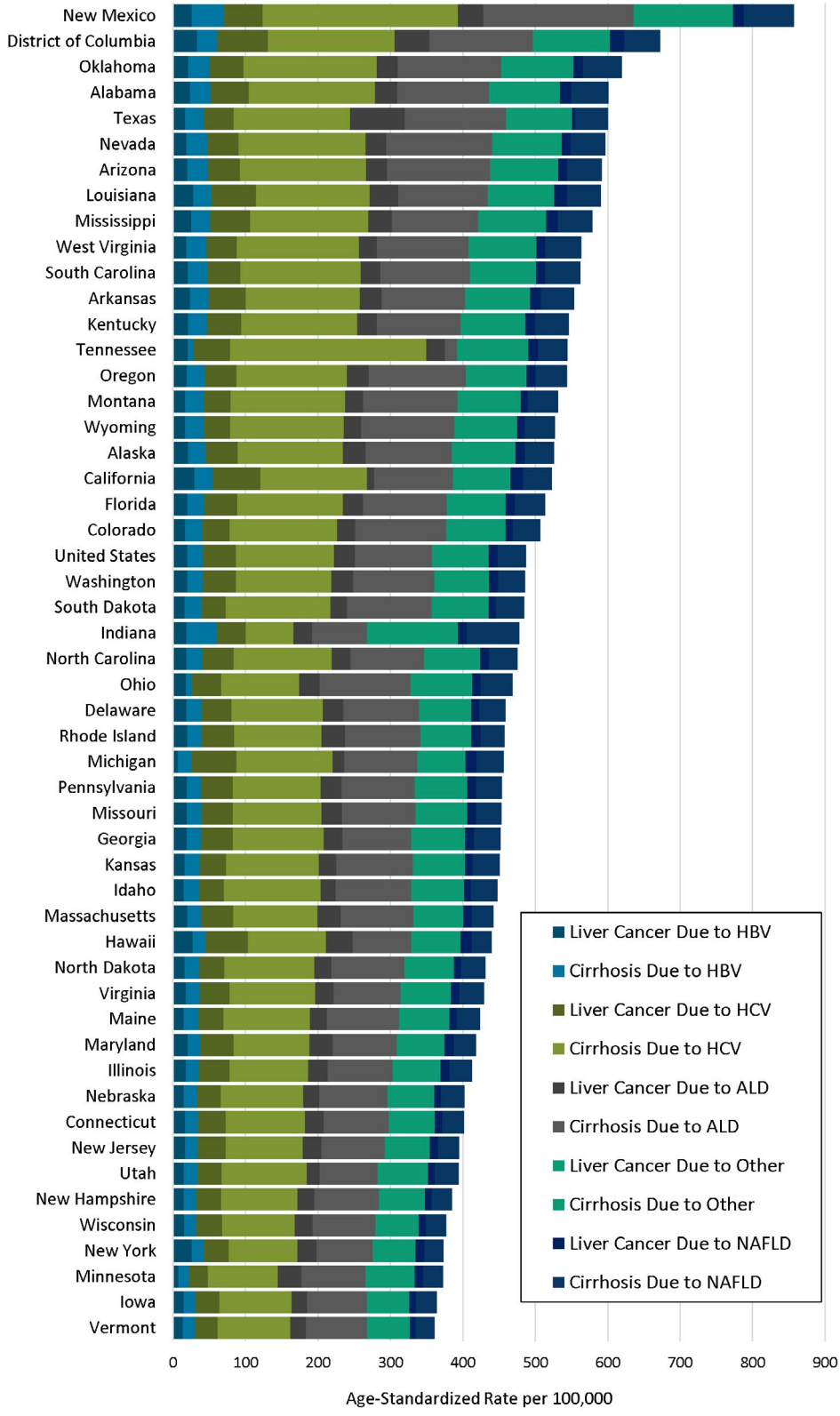


FIG. 2. Age-standardized rates of CLD-related DALYs per 100,000 population due to different liver diseases by U.S. state in 2017.

States	CLD-related DALY					
	ALL	HBV	HCV	ALD	NAFLD	Other
United States	7.4%	6.1%	6.0%	4.9%	9.2%	11.0%
North Dakota	28.0%	22.2%	21.3%	21.0%	23.4%	23.5%
South Dakota	22.2%	18.2%	17.6%	17.5%	18.2%	20.4%
Kentucky	20.0%	15.3%	15.6%	16.2%	17.9%	19.7%
Iowa	19.6%	15.8%	15.5%	15.4%	17.9%	19.5%
Indiana	17.3%	12.8%	13.9%	12.9%	14.3%	18.1%
Montana	17.1%	14.9%	13.6%	13.4%	16.0%	17.9%
Idaho	15.3%	12.5%	12.7%	12.7%	14.4%	15.4%
Minnesota	14.3%	11.3%	11.6%	11.2%	13.9%	15.8%
New Mexico	13.8%	11.0%	11.6%	10.6%	14.2%	15.3%
Arkansas	13.7%	10.2%	11.2%	10.8%	13.8%	15.9%
Louisiana	12.8%	10.4%	10.8%	10.1%	13.5%	13.9%
Ohio	12.5%	12.6%	10.5%	8.7%	12.7%	14.9%
Washington	11.6%	9.5%	10.1%	8.2%	12.9%	14.0%
Nebraska	11.5%	10.3%	8.9%	9.0%	12.6%	14.6%
Missouri	11.5%	9.3%	9.8%	8.8%	11.6%	13.7%
Oregon	11.4%	10.7%	9.1%	8.6%	13.5%	13.7%
Colorado	11.2%	9.6%	9.2%	8.0%	12.9%	14.5%
Tennessee	10.8%	8.1%	8.3%	10.6%	15.4%	11.2%
Kansas	10.3%	8.4%	8.1%	7.4%	12.9%	13.9%
Vermont	10.1%	9.1%	8.3%	7.9%	10.8%	12.7%
Alabama	9.7%	8.5%	8.0%	7.6%	8.8%	12.9%
New Hampshire	9.3%	8.6%	7.4%	6.7%	10.5%	13.1%
Virginia	8.7%	7.9%	6.9%	5.7%	11.6%	12.1%
Wyoming	8.6%	7.5%	7.0%	6.9%	9.3%	11.0%
Mississippi	8.2%	4.7%	7.0%	7.0%	7.0%	11.9%
Utah	8.1%	5.9%	6.2%	5.8%	9.5%	12.0%
West Virginia	8.0%	5.1%	6.0%	5.9%	8.7%	13.1%
Pennsylvania	7.9%	7.9%	6.3%	5.0%	10.3%	11.4%
Maine	7.8%	7.8%	6.5%	5.9%	7.6%	10.9%
South Carolina	7.8%	7.2%	6.2%	5.8%	8.0%	11.5%
Oklahoma	7.7%	7.0%	5.8%	5.9%	8.5%	11.5%
Alaska	7.2%	6.0%	6.0%	6.0%	7.0%	9.8%
Texas	7.0%	4.5%	5.5%	5.6%	8.1%	11.0%
North Carolina	6.5%	5.4%	5.2%	4.5%	7.0%	10.6%
Connecticut	6.5%	7.2%	5.2%	3.2%	11.3%	9.4%
Arizona	6.2%	4.4%	5.0%	3.4%	10.3%	10.2%
Wisconsin	6.1%	5.1%	5.2%	4.3%	8.0%	8.7%
Michigan	5.1%	2.3%	4.7%	1.8%	6.4%	10.7%
Rhode Island	4.8%	8.3%	3.3%	2.0%	8.6%	8.0%
Massachusetts	4.5%	5.9%	3.2%	1.4%	8.5%	9.1%
Illinois	4.0%	4.2%	3.1%	1.2%	8.1%	7.5%
Maryland	3.9%	6.2%	2.7%	1.1%	7.5%	7.0%
New York	3.5%	2.9%	2.4%	0.9%	6.7%	8.0%
Delaware	3.5%	3.0%	2.3%	0.9%	6.2%	8.6%
Florida	3.4%	1.9%	2.2%	0.5%	7.9%	8.3%
Georgia	3.4%	4.3%	2.5%	1.4%	5.1%	6.5%
Hawaii	1.6%	1.2%	0.8%	−0.2%	3.8%	5.2%
California	1.5%	1.0%	1.4%	−2.4%	4.2%	5.9%
New Jersey	0.4%	1.1%	−1.1%	−1.9%	5.2%	4.4%
District of Columbia	−2.2%	0.7%	−3.4%	−5.3%	3.6%	0.6%
Nevada	−3.0%	−4.5%	−4.4%	−6.3%	0.9%	4.1%

FIG. 3. Percentage change in age-standardized rates of CLD-related DALYs per 100,000 population attributable to different liver diseases: U.S. states from 2007 through 2017.

Oklahoma, and Alabama, had the highest LC and cirrhosis DALYs (Fig. 4). Between 2007 and 2017, the SDI increased across the United States, while all-cause DALY rates decreased.[21] The only exception was CLD-related DALYs, which followed the same direction as the SDI. The associations between SDI and CLD-related incidence and deaths are provided in Supporting Figs. S21 and S22.

Discussion

Over the past decade, the profile of liver disease in the United States has been changing.[22,23] In this context, the prevalence of HCV is declining while the prevalence of NAFLD is increasing.[24] Furthermore, ALD and NAFLD have now surpassed HCV as the most common indication for liver transplantation in the United States.[25]

The data from this analysis shows that CLD burden, as indicated by DALYs, in the United States has been increasing over the last decades, and these trends do not seem likely to change in the near future. Despite effective treatment for HCV and HBV and effective vaccines against HBV, the burden of CLD in the United States continues to worsen. In this context, the worsening trends in ALD and NAFLD are most likely responsible for fueling this burden and contributing to its morbidity and mortality. In this study, we were able to demonstrate the changing trends in cirrhosis and LC incidence and death and DALY rates for the United States at the level of different states.

Our data suggest a 30% increase in cirrhosis and LC incidence between 2007 and 2017 in the United States. Among different causes, the incidence rate for NAFLD was higher than other causes of CLD. Across the states, the highest increase in the incidence of cirrhosis and LC was observed in Kentucky, New York, and Pennsylvania. Similar to the incidence rates, death rates related to cirrhosis and LC also increased by 34%. Again, the increase in death rates due to NAFLD was also higher than other causes of CLD. Even though death rates related to cirrhosis and LC showed worsening trends across the United States, the highest increases were observed in Kentucky, Montana, and Washington. Indeed, the increasing burden of cirrhosis and LC mortality, which can also occur due to various extrahepatic complications of CLD, has been demonstrated.[26-28] As one would expect, the burden of CLD, mainly due to cirrhosis

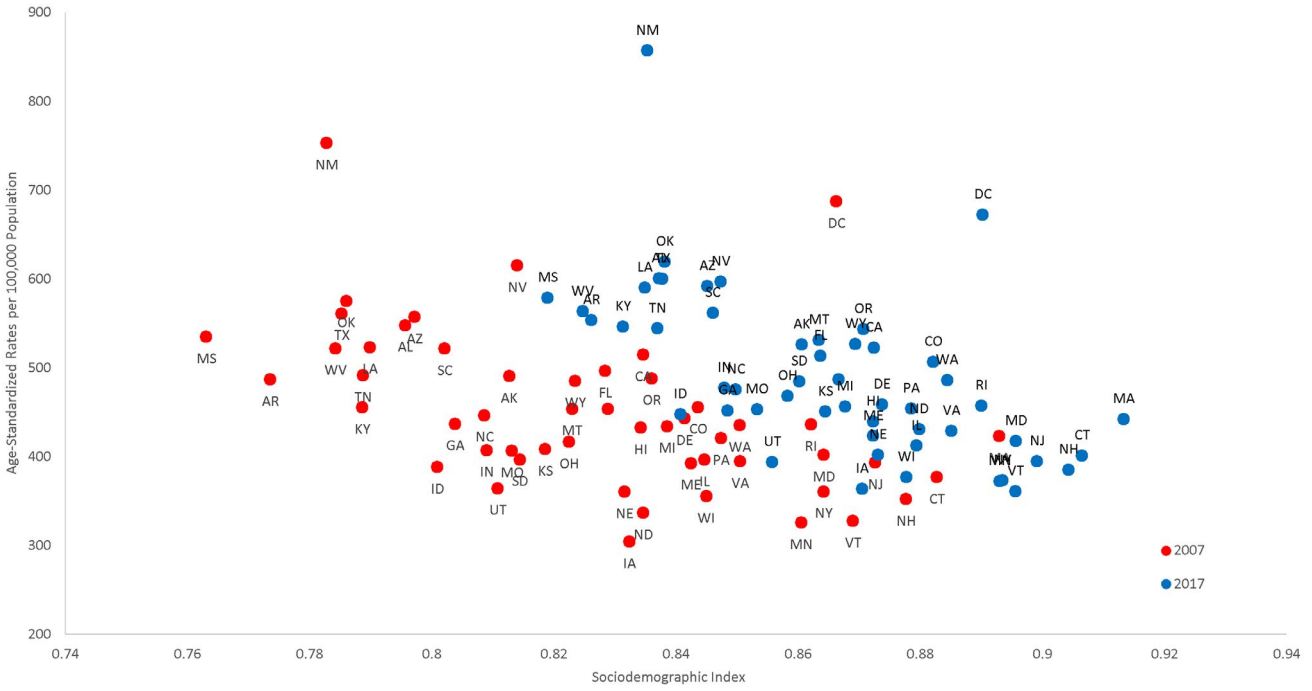


FIG. 4. Scatterplot of age-standardized CLD-related DALY rates and SDI in 2007 and 2017.

and LC, is not uniform across the United States. Indeed, our findings are in agreement with a recent study by Tapper and Parikh[29] who reported changes in cirrhosis and hepatocellular carcinoma deaths at the state level between 2009 and 2017. Between the reported years of that study, Kentucky, New Mexico, Arkansas, Indiana, and Alabama were the states with the highest cirrhosis-related mortality rates; the results for hepatocellular cancer were not very different. There were also reports pointing out geographic variability and racial disparities as the responsible factor for across-state heterogeneity in CLD burden.[30] For example, a study from Atlanta, GA, reported that LC death rate is mainly affected by race and poverty level.[31] Other studies have also demonstrated higher liver disease mortality in southern and western states compared to the rest of the country, likely due to viral hepatitis death rates and a higher percentage of the Hispanic population in those areas.[32]

One crucial difference of this current study from Tapper and Parikh's paper[29] is that, besides cirrhosis and LC incidence and related deaths, our study also focused on DALYs caused by underlying liver disease. In this context, in 2017, there were 2.33 million cirrhosis and LC-related DALYs, which was 27.3% higher than 2007. In terms of etiology, HCV (37%), ALD (28%), and NAFLD (11%) were the main drivers of cirrhosis and LC-related DALYs. This is in contrast to the increasing prevalence of NAFLD recently reported for the United States.[3] This can be explained by the lag between cases of liver disease related to NAFLD and consequences related to mortality. In fact, despite highly effective treatment for HCV and a reduction in the number of complications, there is still a significant burden related to HCV-HCC and HCV-cirrhosis. In a recent study of liver transplant candidates listed for LC in the United States, HCV remains the most common indication for liver transplantation.[33] The scenario is different for ALD and NAFLD as both conditions are on the rise in the United States. In fact, the rapidity of increase in NAFLD is even faster than ALD.[33] In this context, NAFLD and ALD are expected to become responsible for most causes of cirrhosis, LC, and DALYs related to CLD over the next decade.[34,35]

When these 2.33 million cirrhosis and LC-related DALYs were distributed across the states, the highest DALY rates were observed in California, Texas, Florida, and New York, which is expected as those are the states with the highest populations. However, when focusing on the highest cirrhosis and LC-related DALY rates per 100,000 population, New Mexico, District of Columbia, Oklahoma, and Alabama were at the top of the list. Among those states, New Mexico and the District of Columbia merit special attention. In this context, our finding is strongly supported by previous studies that separated New Mexico from others as it carried the highest CLD-related mortality rate in the United States.[32,36] In fact, Centers for Disease Control and Prevention data demonstrated that New Mexico had the highest CLD-related death rate, with 24.9 per 100,000 population, while the average rate in the country was 10.7 per 100,000.[37] On the other hand, data from the District of Columbia may suggest some disparity in access to health care as well as other factors, such as a high prevalence of viral hepatitis. LC death rate in the District of Columbia is the highest in the United States for both men and women, and the black population had 5 times higher rates than whites.[31] As these data suggest, the burden of disease related to CLD is not uniform across the country, and further studies are needed to understand root causes of these significant variations.

The most important strength of the current study is that we used the data from GBD study estimates. GBD study estimates provide the only peer-reviewed estimates of cause-specific mortality available for each age, sex, year, and location under the same computational framework. The decomposition analyses provided insight into each liver disease as contributors to change in the CLD-related burden over the last decade. Disparities attributed to states may, in fact, reflect differences in demographic, social, and economic circumstances. The concentration of CLD-related burden at the state level may be important because many health and social policy decisions are made uniformly at the state level. However, these data also have a few limitations. Our analysis relied heavily on GBD study estimates so we share the limitations of these estimates. The accuracy of the GBD study estimates was limited by the quality of the available data even though the data and method are considered to be robust and reliable. However, the United States has the highest data quality rating (5 out of 5) for causes of death data,[10,18] resulting in similarities in the burden of LC and cirrhosis between the vital registration data and the GBD study estimates (https://vizhub.healthdata.org/cod). The current GBD study

estimates up to the state level do not capture differences between other geographic categories, such as urban and rural regions. Because of the dependence on the administrative data, underreporting of LC and cirrhosis using death certificates, and differences in definitions and diagnostic methods, both LC and cirrhosis may have been underestimated. Also, estimates for LC and cirrhosis due to NAFLD must be interpreted with caution in that the age-standardized prevalence of NAFLD that leads to LC or cirrhosis was 10.9%, which was lower than the global prevalence of 24%[38]; this was most likely due to different adjustments for alcohol use.

In conclusion, in the United States, CLD incidence, death rates, and DALYs increased between 2007 and 2017. The impact of this burden on individual states varies across the country. Although some of this variation may be related to the prevalence of different liver diseases (e.g., HCV, NAFLD, ALD), others are probably related to the disparity in accessing heath care and other socioeconomic factors. These data should provide insight to providers and health care policy makers to develop better strategies to deal with this important cause of mortality and morbidity in the United States.

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