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Trends in Premature Deaths From Alcoholic Liver Disease in the U.S., 1999–2018

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Abstract

Introduction: So-called "deaths of despair"—those involving drug overdoses, alcohol-related liver disease, and suicide—have been rising in the U.S. among middle-aged non-Hispanic white adults without a college degree. Premature deaths (ages 25–69) from alcoholic liver disease were examined specifically in this study from 1999 to 2018, by sex, race/Hispanic origin, and age group.

Methods: Data were drawn from the 1999–2018 Multiple Cause of Death database and bridged-race estimates of the U.S. resident population, including 281,243 alcoholic liver disease deaths or an average of eight deaths per 100,000 population. Analyses examined alcoholic liver disease death rates for sex differences among three age groups (25–49, 50–59, and 60–69 years), by race/Hispanic origin, from 1999 to 2018, as well as age-adjusted and age-specific annual percentage changes (accounted for cohorts), years of potential life lost, and age of death for sociodemographic backgrounds, alcoholic liver disease clinical courses, and comortalities.

Results: Non-Hispanic whites increasingly experienced greater alcoholic liver disease mortality than non-Hispanic blacks and Hispanics, confirming the racial/ethnic crossover observed in previous studies. Although men consistently had higher rates of mortality, male-to-female ratios decreased in the past 2 decades and were the lowest among ages 25–49 years and especially among ages 25–34 years. Although women generally had longer life expectancies, women died of alcoholic liver disease on average about 2–3 years earlier than men.

Conclusions: Prevention and intervention efforts are imperative to address the narrowing sex gap and widening racial disparities in alcoholic liver disease premature deaths.

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INTRODUCTION

Premature mortality, or unfulfilled life expectancy, has increased in recent years.[1–4] Life expectancy in the U.S. has not kept pace with other industrialized nations[5,6] and has declined since 2015.[6–8] Kochanek et al.[9] reported that increasing death rates from drug overdoses, suicides, and alcoholic (alcohol-associated) liver disease (ALD) were responsible for the increased all-cause death rate among non-Hispanic whites. Case and Deaton[2] referred to these three causes as "deaths of despair," which stemmed from cumulative disadvantages to some people (e.g., middle-aged non-Hispanic whites with a high school or less education) as a result of economic stagnation and social disintegration since the 1970s. Rehm and Probst[10,11] suggested that alcohol use was a direct or indirect cause of these deaths. Increasing social inequality may have exacerbated alcohol use problems, thereby increasing premature mortality.[10–14]

With defining characteristics including alcoholic fatty liver (i.e., steatosis), alcoholic hepatitis, and fibrosis/liver cirrhosis, ALD is a significant burden on health in the U.S. and substantially contributes to premature mortality.[15,16] ALD is associated with greater premature mortality than all causes.[17] In 2018, the percentage of premature deaths from all causes was 33%, which paled in comparison to the 87% for ALD. Premature deaths from overall chronic liver disease and cirrhosis are projected to increase until 2030 for all racial and ethnic groups except non-Hispanic black men.[18] ALD risk is determined by the interaction of alcohol consumption with both host factors (e.g., sex, race, genetic variants, SES) and comorbidities (e.g., metabolic syndrome, hepatitis C virus [HCV], malnutrition, hemochromatosis).[19] Concurrent unhealthy behaviors or conditions (e.g., smoking, drug use, poor dietary habits, obesity) often exacerbate the extent and severity of ALD, thereby contributing to mortality.[16,20]

Expanding upon the "deaths of despair" literature,[21–25] this study examines ALD premature mortality trends from 1999 to 2018. In light of the narrowing sex gap in alcohol-related emergency department visits,[26] hospitalizations,[27] and mortality[6,28–30] in recent years, this study focuses on sex differences in ALD, by race/Hispanic origin, with respect to age-specific death rates, annual percentage changes (APCs), years of potential life lost (YPLL), and age of death. Age-specific death rates are compared across three age groups (25–49, 50–59, and 60–69 years).

METHODS

Analyses were based on 1999–2018 Multiple Cause of Death data (www.cdc.gov/nchs/data_access/Vitalstatsonline.htm) and bridged-race estimates of the U.S. resident population (www.cdc.gov/nchs/nvss/bridged_race.htm) from the National Center for Health Statistics (NCHS). Multiple Cause of Death data compiled by the NCHS's National Vital Statistics System from death certificates for U.S. residents provided information on ALD deaths. Mid-year population data produced by the U.S. Census Bureau for NCHS provided denominators in rate calculations. Each death certificate contains a single underlying cause of death, up to 20 additional contributing causes, and sociodemographic data. During 1999–2018, causes of death were coded in accordance with ICD-10.[31] However, the coding rule change

discontinuing the use of ICD-10: F10.0 (mental and behavioral disorders due to use of alcohol, acute intoxication) contributed to an unusually large increase in ALD deaths from 2006 to 2007.[32]

According to the underlying cause of death, "the disease or injury which initiated the train of morbid events leading directly or indirectly to death or circumstances of the accident or violence which produced the fatal injury,"[33] a total of 281,243 decedents died prematurely of ALD at ages 25–69 years, ranging from 10,210 in 1999 to 20,180 in 2018. Premature mortality was defined as death before age 70 years, following the age threshold used by the UN Sustainable Development Goals for health.[34] The lower age threshold was set at 25 years because decedents rarely died of ALD at younger ages.

Measures

This study identified decedents with ALD reported as the underlying cause of death; co-occurring conditions reported as contributing causes of death; and sociodemographic characteristics, which acted as covariates (e.g., education, marital status) or stratifiers (e.g., sex, race/Hispanic origin, age group) depending on the analysis. ALD included ICD-10 codes for alcoholic fatty liver (K70.0); alcoholic hepatitis (K70.1); alcoholic fibrosis and sclerosis of liver (K70.2); alcoholic cirrhosis of liver (K70.3); alcoholic hepatic failure (K70.4); and alcoholic liver disease, unspecified (K70.9). Selected co-occurring conditions included alcohol use disorder (AUD) (F10), tobacco use disorder (F17), HCV infection (B17.1 and B18.2), diabetes (E10–E14), hypertension (I10–I13), and unnatural death (V01–Y89).

Statistical Analysis

Data were initially analyzed for 1999–2017 in 2019 and reanalyzed for 1999–2018 in March 2020. Descriptive analyses graphically examined trends in sex-specific ALD death rates and male-to-female rate ratios from 1999 to 2018, by race/Hispanic origin (i.e., [non-Hispanic] whites and blacks and Hispanics), comparing three age groups (25–49, 50–59, and 60–69 years); trendlines were fitted using generalized additive models implemented in R, version 3.5.3 mgcv.[35] Age-period-cohort analyses, implemented in R code provided by the National Cancer Institute,[36] examined age-adjusted and age-specific APCs (i.e., net and local drifts, respectively) accounting for cohorts. Stata, version 15.1 was used to calculate YPLL and mean age of ALD death (the latter is a complement to average YPLL per decedent such that the two measures sum to 70 years). For YPLL, the total number and the age-adjusted rate in each year using APCs derived from Poisson models quantified the magnitude of change from 1999 to 2006 and 2007 to 2018. Mean ages of death for each covariate adjusted for other covariates were based on predictive margins derived from truncated Poisson regression with robust variance and truncations at ages 24 and 70 years.[37]

RESULTS

From 1999 to 2018, age-specific ALD death rates were consistently lower for women than men and lower for ages 25–49 years than ages 50–59 and 60–69 years (Figure 1). However, male-to-female rate ratios decreased during the period, particularly among those aged 25–49

years. According to the age-period-cohort analysis (Figure 2), the ALD death rate increased more rapidly for women. The respective age-adjusted APCs (net drifts) for women versus men were 4.91 vs 2.70 for whites, 2.20 vs −0.24 for Hispanics, and −0.13 vs −2.61 for blacks. Despite wide 95% CIs, increases in ALD death rates (local drifts) were notable among people aged <35 years. Both the total number and rate of YPLL increased from 2007 to 2018 and increased more rapidly for women than men (Table 1). For example, the respective APCs in YPLL rate for women versus men were 5.6 vs 2.9 for whites, 3.7 vs −0.1 for blacks, and 3.3 vs 0.7 for Hispanics.

With some fluctuations, mean age of ALD death steadily increased between 1999 and 2018 and increased more among men (Table 2). On average, decedents died of alcoholic fatty liver disease at a younger age than other types of ALD. Women died of ALD about 2–3 years earlier than men, but the sex difference was smaller among Hispanics, who died younger than whites and blacks, and much larger for blacks who died of alcoholic fatty liver and alcoholic hepatitis and who died in 2012–2018. Having a college degree tended to raise the mean age of death, except among Hispanic women. Co-occurring AUD reduced the mean age of death among white and Hispanic men; co-occurring injury (unnatural death) reduced the mean age of death among Hispanic men. By contrast, co-occurring tobacco use disorder, diabetes, and hypertension were generally associated with older mean ages of death.

DISCUSSION

This study documented and confirmed an upward trend in premature deaths from ALD by sex and race/Hispanic origin from 1999–2018. As suggested in a previous study,[6] ALD death rates were higher among men, but relative increases were greater among women, resulting in narrowing sex gaps. Accounted for cohort effects, premature mortality mainly increased among whites and Hispanic women, as indicated by net drift in Figure 2 and confirmed by age-adjusted YPLL rates in Table 1. The narrowing sex gaps in ALD death rates reflect the increasing trends in women's drinking, high-risk drinking, and AUD[38] and possible relatively higher occurrence of alcoholic hepatitis in women at younger ages. Similar sex differences in alcohol-related harms have been observed globally.[39]

The impact of ALD on women was further reflected in lower mean ages of ALD death than men regardless of sociodemographics, clinical courses of ALD, and comortalities. Although women are known to have longer life expectancies than men, women die of ALD at younger ages, presumably because women are at greater risk for developing ALD at lower lifetime alcohol intakes and shorter drinking histories. Women are more susceptible to ALD because of differences in hepatic ethanol metabolism and in mechanisms by which the body reacts to alcohol, such as endotoxin levels,[40] gut permeability to endotoxins,[41–46] effects of estrogen and androgens on endotoxin- and alcohol-mediated liver injury,[44,47] and alcohol elimination rates.[48,49] These variations are due to differences in first-pass metabolism, enzymatic activities,[44,50–54] volumes of distribution, and peak blood alcohol levels.[41,44,53] Given greater vulnerability to physiological consequences of high-risk drinking for women, narrowing sex gaps in prevalence of high-risk drinking may have contributed to the increasing sex disparity in mean age of ALD death over time. The rising trends in ALD deaths also coincide with those in severe obesity, which is more prevalent in women.[55]

Because of few symptoms at early disease stages and stigma attached to heavy alcohol use, most people with ALD are not diagnosed until later stages, when symptoms appear.[16] Consequently, ALD is usually diagnosed among middle-aged adults, and survival rates are quite low once diagnosed.[56] The finding of higher prevalence of ALD death among people aged 50 years and older reflects disease progression from morbidity to mortality. This age trend also parallels recent increases in alcohol use and binge drinking among middle-aged adults.[57] Larger increases in binge and heavy drinking among older Americans[57–59] may account for rising ALD death rates among black and Hispanic men from the mid-2000s for ages 60–69 years.

Unexpectedly, adults aged 25–34 years showed faster growth in ALD mortality (from 259 deaths in 1999 to 832 deaths in 2018) than older counterparts, as indicated by net drift (Figure 2) and rising death rates since 2007.[60] Because it usually takes 10 or more years of drinking to develop liver diseases, premature mortality before age 35 years is quite unusual and cause for serious public health concerns. Cholankeril et al.[61] reported that young adults (aged 18–39 years) on the liver transplantation waiting list had significantly greater severity of liver disease compared with their older counterparts. Increasing ALD mortality rates among young adults could be attributed to increases in extreme binge drinking, or high-intensity drinking, among heavy drinkers.[62–69] One study found that certain birth cohorts aged younger than 50 years (men born between 1976 and 1985 and women born between 1981 and 1985) had the highest alcohol consumption.[70] Changes in drinking patterns and more pronounced sex convergence in alcohol consumption among younger age cohorts[38,39,57,71–75] contribute to the narrowing sex gap in ALD deaths. The hypothesis also is consistent with the same phenomenon observed in alcohol-related emergency department visits[26] and hospitalization.[27]

Historically, sex disparities in drinking were more pronounced in Hispanics than other racial/ethnic groups. Hispanic women typically had much lower ALD death rates than men because heavy and binge drinking were male-dominated activities, whereas abstention and infrequent light drinking were common patterns among women.[76–79] In this study, despite Hispanics' lower all-cause mortality, Hispanic men maintained higher ALD death rates than their non-Hispanic counterparts. Lower SES, as reflected in lower educational attainment, might be a contributing factor to the higher ALD death rates observed in Hispanic men.[80] Heightened rates among Hispanic women may be attributed to increases in female drinking associated with acculturation.[81,82]

The ALD death rates for whites surpassed those for blacks in the early 2000s. For several prior decades, blacks had much higher rates of cirrhosis mortality than whites.[83,84] Scholars attributed these earlier racial disparities to differences in drinking behaviors. Compared with whites, blacks had a greater propensity for continued heavy drinking into their 30s and 40s despite later onset,[85–87] as well as greater consumption of spirits.[88,89] However, the higher rates in earlier years could also be due to the "alcohol harm paradox," in which drinkers with lower SES experience more alcohol-related harms because of harmful alcohol consumption patterns, other unhealthy behaviors, and lack of access to healthcare resources.[90] Increases in educational attainment among blacks could be one potential factor besides changes in drinking patterns. Higher college completion rates may have improved economic, social, and

behavioral circumstances, leading to healthier lifestyles, better access to quality health care, and ultimately reductions in premature deaths from ALD. Yoon and colleagues[91] found that college-educated blacks were less likely to drink beyond daily or weekly drinking limits than their counterparts with a high school education or less. Recent declines in mortality from HIV, HCV, and tobacco-related conditions, which are cofactors of ALD, also likely contributed to decreases in ALD deaths among blacks.[3]

In this study, middle-aged whites with lower educational attainment contributed to increases in premature mortality from ALD, as Case and Deaton[2] suggested. However, middle-aged Hispanics with lower educational attainment also contributed to this increase. Educational attainment was inversely associated with ALD death rates overall. The ALD death rate escalated more rapidly after the economic recession in 2008 for all those with a high school or less education, and the associated male-to-female ratio of ALD death rates was higher for this educational group and decreased more drastically than for other groups after 2008 (Appendix Figure 1). Education was positively associated with mean age of death among whites, blacks, and Hispanic men, but not necessarily among female Hispanics, who received no beneficial effect of college education on health. Similar to a lack of education, never being married was associated with death at younger ages compared with other marital statuses, partly because lack of social integration increases mortality risks.[92,93]

Age-specific death rates and age-adjusted YPLL rates showed changes in direction (i.e., from modest declines to significant increases) in the mid-2000s. The first change from 2006 to 2007 was due to an ICD-10 coding rule change.[32] Accelerated increases in ALD death rates after 2007, however, could be a lingering consequence of heavy drinking associated with economic hardship during the 2008–2009 recession. Previous studies reported that rising foreclosures, unemployment, and poverty coincided with an increase in heavy drinking occasions among heavy drinkers.[94–96] Furthermore, resources to finance AUD treatment may have been depleted, adversely impacting ALD treatment options for financially vulnerable individuals.

The opioid epidemic beginning around 2010 and the new era of direct-acting antivirals for HCV infection beginning in 2011 have affected ALD mortality trends. Alcohol may interact with certain drugs to accentuate liver injury because the liver metabolizes, eliminates, and detoxifies both substances.[97] Further analysis confirmed that the percentage of ALD deaths with drug-induced causes increased considerably during the study period and was greater among non-Hispanics (Appendix Figure 2). Alcohol use, in combination with coinfections with HIV-1 or hepatitis B virus, fosters progression of HCV infection in the development and severity of liver cirrhosis and mortality.[98,99] Successful antiviral treatments for HCV have reduced the contribution of HCV to ALD deaths and prolonged longevity, particularly for non-Hispanic blacks. However, drug-induced causes (8.5%) and HCV (7.8%) are not very prevalent among ALD deaths.

Limitations

This study has several limitations, including use of death certificates, which are subject to under-reporting[100–106]; misclassification of race/ethnicity[107,108]; and lack of information on ALD onset, drinking histories, and treatment experiences and effectiveness. The high degree

of selectivity in liver transplantation based on many psychosocial criteria, including 6-month abstinence from alcohol, may have prevented survival of ALD patients on the waiting list and those who had AUD but could not abstain from alcohol.[61,109] Moreover, as in other observational studies, inferences are subject to measurement bias and confounding, and a cross-sectional study cannot investigate differential ALD progression among subgroups with various drinking patterns and durations. Large-scale prospective studies are needed to follow patients from diagnosis to death.

It is not clear whether there has been any improvement in under-reporting in general or due to stigma, as the NCHS medical examiners' and coroners' handbook[110] has always encouraged reporting alcohol use on death certificates when it is believed to be a contributory cause. In the extreme scenario in which all the non-alcoholic liver disease deaths were indeed ALD deaths and were misclassified due to underreporting, the narrowing sex gaps would have been less pronounced. To accurately identify the pathologies associated with ALD deaths, a thorough macroscopic and microscopic post-mortem examination is desired. However, autopsies were performed on only a small percentage (8.9%) of ALD decedents and disproportionately on decedents with alcoholic fatty liver disease.

CONCLUSIONS

Although some studies have evaluated sex differences in alcohol consumption and cirrhosis mortality,[111–117] this study examined ALD mortality directly by drawing upon all death certificates in the U.S. spanning 2 decades. Findings reported here provide empirical evidence of increases in premature mortality from ALD and demonstrate that longevity of men and women with ALD could be affected by demographic factors (e.g., race/Hispanic origin, marital status, and education) and comortalities. These findings encourage future research to examine whether environmental factors or alcohol policies may reduce premature mortality from ALD by reducing alcohol consumption or eliminating socioeconomic inequalities that imperil the health of economically disadvantaged populations. Destigmatizing AUD will also increase treatment utilization and prevent death from ALD. Future studies analyzing ALD mortality by sex and race/ethnicity should also take genetic and environmental risk factors into consideration, as they affect alcohol metabolism and subsequent liver injury.[99,118–120] To address narrowing sex gaps in premature death from ALD, greater emphasis must be placed on implementation of abstinence programs, early detection of ALD, and education about hazardous drinking levels for women, as Saunders et al.[121] suggested a few decades ago.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Y-HY, CMC, MES, and AMW conceptualized the study. Y-HY led the drafting of the article. CMC performed data analysis. All authors (including MKJ) interpreted the findings, reviewed and edited drafts of the article, and approved the final version. Susanne Hiller-Sturmhöfel and Hunter Barret provided editorial support.

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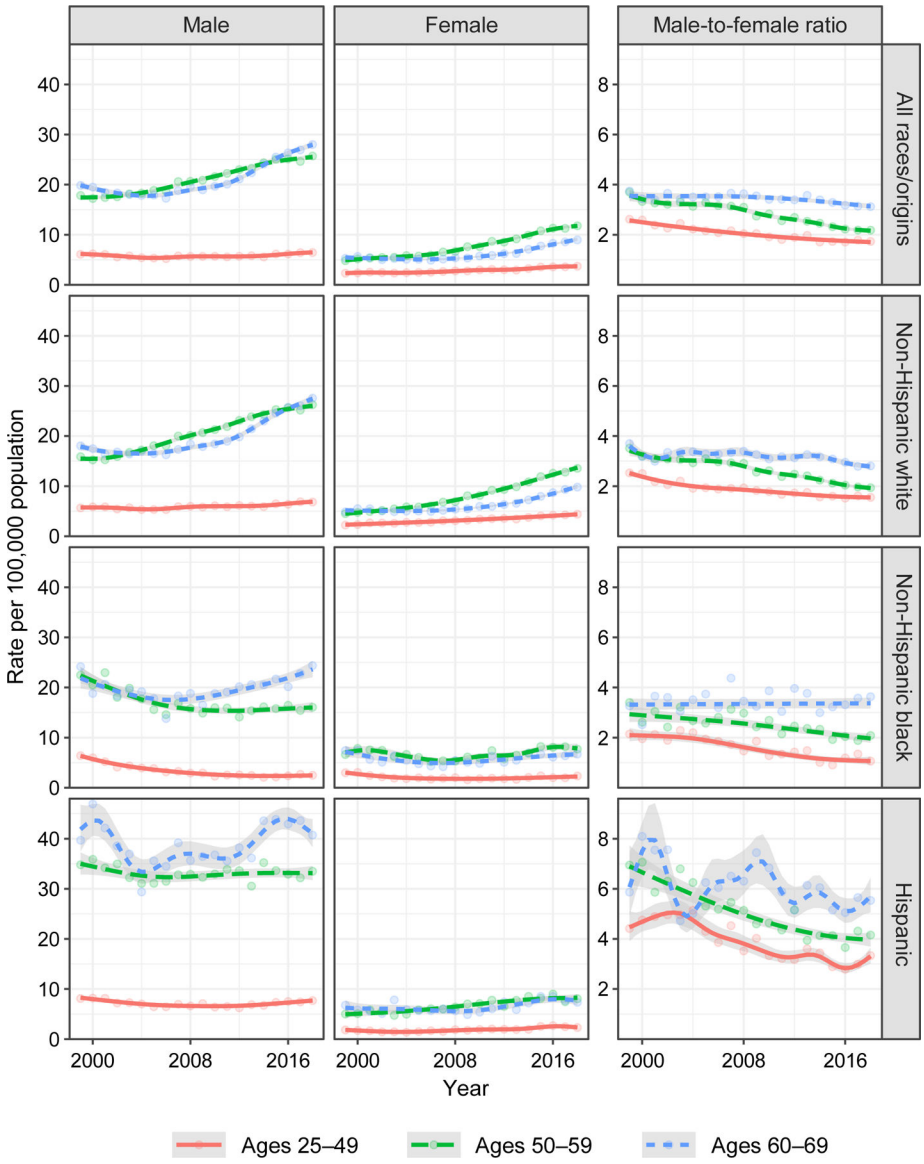

Figure 1.

Sex-specific death rate (per 100,000 population) and male-to-female rate ratio for alcoholic liver disease, by age group and race/Hispanic origin, in the U.S., 1999–2018.

Note: Gray areas indicate 95% CIs.

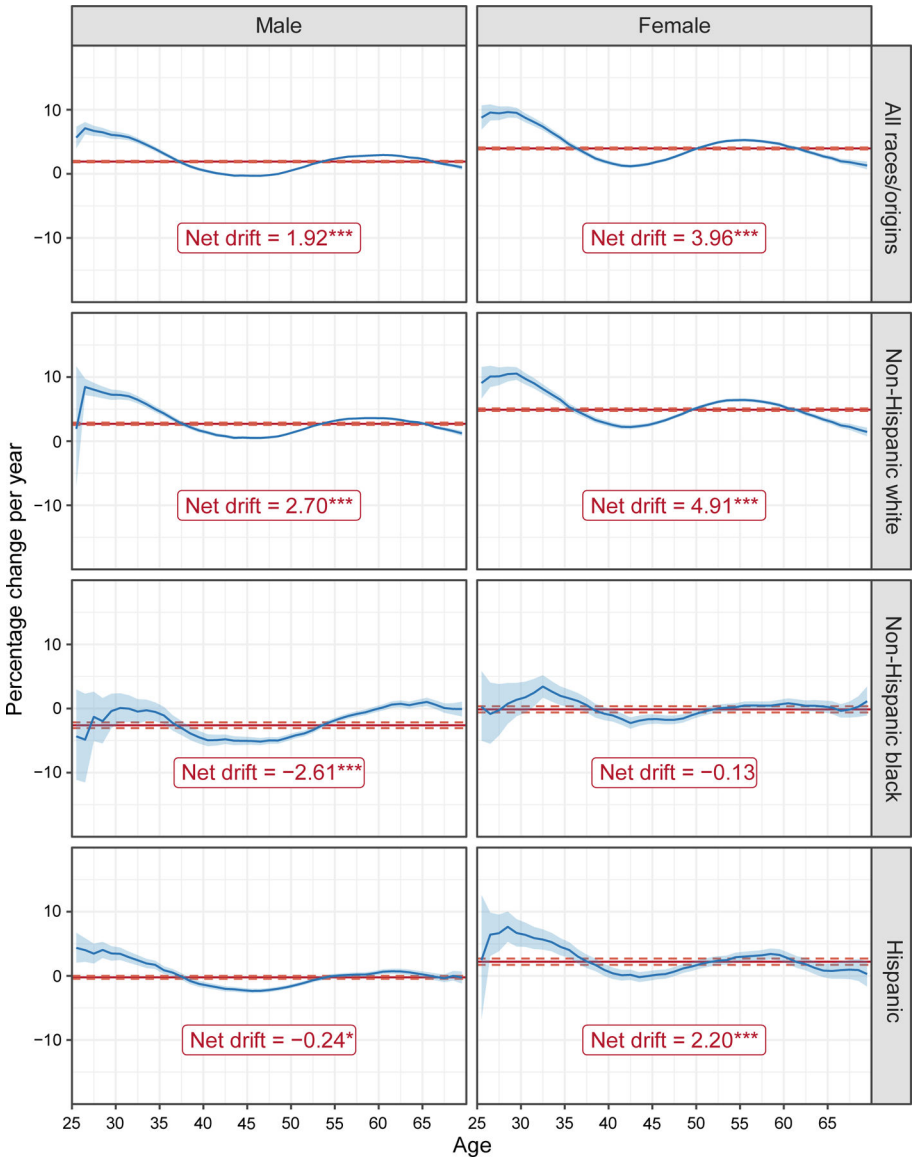

Figure 2.

Age-adjusted (net drift) and age-specific annual percentage changes (APC) for alcoholic liver disease mortality, by sex and race/Hispanic origin, in the U.S., 1999–2018.

Note: Dashed lines and gray areas indicate 95% CIs for age-adjusted and age-specific APC, respectively (*p<0.05; ***p<0.001).

Table 1.

Years of Potential Life Lost (YPPL) to Alcoholic Liver Disease, 1999–2018

Year	All races, both sexes	Non-Hispanic white		Non-Hispanic black		Hispanic	
		Male	Female	Male	Female	Male	Female
	Total YPLL (Rate)[a]	YPLL (Rate)[a]	YPLL (Rate)[a]	YPLL (Rate)[a]	YPLL (Rate)[a]	YPLL (Rate)[a]	YPLL (Rate)[a]
1999	186,630 (123)	92,415 (163)	33,797 (59)	16,250 (212)	7,887 (86)	22,208 (332)	4,397 (63)
2000	191,404 (123)	93,765 (163)	35,341 (61)	15,540 (194)	8,409 (89)	24,265 (339)	4,345 (59)
2001	194,048 (122)	93,433 (160)	39,127 (67)	15,063 (184)	7,232 (75)	24,837 (328)	4,564 (60)
2002	187,834 (116)	91,312 (154)	38,661 (66)	12,309 (146)	6,593 (67)	24,000 (304)	4,233 (53)
2003	193,366 (118)	95,642 (160)	38,587 (65)	13,602 (157)	6,085 (61)	24,625 (294)	4,457 (52)
2004	192,773 (115)	94,148 (156)	41,491 (69)	12,282 (139)	5,906 (57)	24,415 (278)	4,334 (49)
2005	196,164 (115)	96,278 (157)	41,113 (68)	11,741 (128)	6,203 (59)	24,511 (266)	5,152 (55)
2006	197,638 (114)	96,578 (156)	42,338 (70)	10,481 (111)	5,561 (52)	25,717 (266)	5,862 (59)
APC	**0.6** ** **(−1.2** **)**	**0.6** ** **(−0.7** **)**	**3.0** ** **(2.1** **)**	**−5.7** ** **(−8.4** **)**	**−5.5** ** **(−7.4** **)**	**1.2** * **(−3.8** **)**	**3.6** ** (−1.4)
2007	219,359 (125)	107,289 (173)	47,182 (78)	11,939 (123)	5,849 (53)	28,708 (284)	5,736 (56)
2008	224,086 (127)	110,161 (178)	47,374 (79)	11,387 (115)	6,244 (56)	28,879 (272)	6,876 (64)
2009	230,054 (129)	110,121 (177)	51,424 (85)	11,117 (110)	5,904 (51)	30,902 (276)	6,989 (62)
2010	238,725 (133)	114,026 (183)	53,720 (89)	10,940 (105)	6,515 (56)	30,566 (265)	7,694 (66)
2011	247,184 (136)	114,614 (183)	57,290 (95)	11,720 (110)	7,373 (62)	31,813 (267)	8,480 (70)
2012	253,814 (139)	121,365 (196)	57,986 (97)	11,162 (104)	6,436 (54)	32,461 (262)	8,242 (66)
2013	262,459 (143)	123,682 (200)	59,109 (100)	11,947 (109)	6,875 (58)	33,878 (263)	8,803 (68)
2014	273,779 (149)	124,003 (201)	64,786 (111)	11,547 (104)	7,889 (66)	37,580 (283)	9,443 (71)
2015	296,736 (162)	133,336 (221)	70,029 (120)	11,894 (106)	9,242 (76)	39,692 (288)	11,559 (84)
2016	303,942 (165)	133,389 (221)	73,949 (129)	12,592 (111)	8,514 (70)	41,582 (291)	12,737 (90)
2017	307,210 (167)	135,261 (229)	74,821(131)	13,256 (117)	8,604 (70)	41,922 (286)	11,633 (80)
2018	315,951 (172)	136,712 (232)	76,803 (136)	13,364 (117)	9,370 (78)	44,388 (293)	11,588 (77)
APC	**3.7** ** **(3.2** **)**	**2.4** ** **(2.9** **)**	**4.9** ** **(5.6** **)**	**1.4** ** (−0.1)	**4.6** ** **(3.7** **)**	**4.4** ** **(0.7** **)**	**6.8** ** **(3.3** **)**

Note: Boldface indicates statistical significance

* $p<0.05$;

** $p<0.01$.

[a] Age-adjusted YPLL rate per 100,000 population.

APC, annual percentage change.

Table 2.

Predictive Margins for Mean Age of Death From Alcoholic Liver Disease, 1999–2018

Predictors for mean age of death	Non-Hispanic white			Non-Hispanic black			Hispanic		
	Male	Female	Dif.	Male	Female	Dif.	Male	Female	Dif.
Alcoholic liver disease	55.2	52.4	**2.8****	55.4	52.5	**3.0****	52.6	51.1	**1.5****
K70.0 Alcoholic fatty liver	**50.0****	**47.8****	**2.2****	**50.3****	**45.4****	**4.9****	**45.8****	**47.1****	−1.3
K70.1 Alcoholic hepatitis	**52.4****	**49.7****	**2.7****	**54.0****	**50.0****	**4.0****	**49.0****	**46.7****	**2.3****
K70.2 Alcoholic fibrosis and sclerosis of liver	**53.2****	50.2	3.0	51.4	51.5	−0.2	54.6	-	-
K70.3 Alcoholic cirrhosis of liver (ref)	55.9	53.1	**2.8****	55.8	53.2	**2.6****	53.2	51.8	**1.5****
K70.4 Alcoholic hepatic failure	**54.1****	**51.4****	**2.7****	**54.8****	**51.6****	**3.2****	**51.1****	**48.8****	**2.3****
K70.9 Alcoholic liver disease, unspecified	**55.0****	**52.2****	**2.8****	55.7	**52.2****	**3.5****	**52.0****	**50.8****	**1.3****
Educational achievement									
High school or less (ref)	54.8	51.9	**2.9****	55.4	52.3	**3.1****	52.5	51.3	**1.2****
Some college	54.9	**52.3****	**2.6****	55.1	52.3	**2.9****	52.2	**49.6****	**2.6****
College	**56.8****	**54.5****	**2.3****	**56.2***	**54.3****	**1.9****	**54.0****	**50.2***	**3.8****
Unknown	**56.6****	**52.7****	**3.9****	56.1	53.2	**2.9****	**54.6****	52.4	**2.2****
Marital status									
Never married (ref)	49.5	47.1	**2.4****	51.7	49.2	**2.5****	48.0	46.9	**1.1****
Married	**56.5****	**53.4****	**3.2****	**56.6****	**52.6****	**4.0****	**54.1****	**52.3****	**1.8****
Widowed	**61.9****	**59.9****	**2.0****	**62.3****	**60.0****	**2.2****	**60.8****	**58.9****	**1.9****
Divorced	**55.7****	**52.9****	**2.8****	**57.2****	**54.6****	**2.6****	**54.2****	**52.7****	**1.5****
Unknown	**54.7****	**53.4****	**1.3****	**55.8****	**52.7****	**3.0****	**51.4****	**51.3****	0.1
Co-occurring condition									
Alcohol use disorder									
No (ref)	55.2	52.4	**2.8****	55.4	52.5	**2.9****	52.7	51.1	**1.6****
Yes	**54.8****	52.3	**2.5****	55.4	52.2	**3.2****	**51.9****	51.1	**0.8***
Tobacco use disorder									
No (ref)	55.0	52.3	**2.7****	55.3	52.3	**3.0****	52.6	51.1	**1.5****
Yes	**56.9****	**53.0****	**3.8****	**56.6****	**54.6****	**2.0****	**53.8****	51.8	**2.0****
Hepatitis C virus infection									
No (ref)	55.2	52.5	**2.7****	55.3	52.3	**3.0****	52.6	51.1	**1.5****
Yes	**54.7****	**51.5****	**3.2****	**56.5****	**53.7****	**2.7****	**53.1****	51.3	**1.9****
Diabetes									
No (ref)	55.1	52.3	**2.8****	55.4	52.4	**3.0****	52.5	50.9	**1.6****
Yes	**57.4****	**55.7****	**1.8****	**56.6****	**53.9****	**2.7****	**55.1****	**55.0****	0.1
Hypertension									
No (ref)	55.1	52.2	**2.9****	55.3	52.3	**3.1****	52.5	50.9	**1.6****
Yes	**56.8****	**55.8****	**0.9****	**56.6****	**54.9****	**1.8****	**55.1****	**55.1****	0.0

Predictors for mean age of death	Non-Hispanic white			Non-Hispanic black			Hispanic		
	Male	Female	Dif.	Male	Female	Dif.	Male	Female	Dif.
Unnatural death									
No (ref)	55.2	52.4	**2.8****	55.4	52.5	**3.0****	52.7	51.1	**1.5****
Yes	54.9	52.4	**2.5****	55.0	53.7	1.3	**51.3****	49.6	1.7
Year									
1999	**53.3****	**50.7****	**2.6****	**52.3****	**50.0****	**2.3****	**51.1***	49.4	**1.7***
2000	**53.2****	51.3	**1.9****	**51.4****	**50.4***	**1.1***	51.6	49.8	**1.9***
2001	**53.2****	**51.0****	**2.2****	**52.6****	**50.6***	**2.1****	51.5	49.8	**1.7***
2002	**53.7****	**51.2***	**2.5****	**53.1****	51.1	**2.0****	51.7	50.5	1.2
2003	**53.6****	**51.3***	**2.4****	**53.2****	51.9	**1.2***	**51.3***	51.6	−0.3
2004	**54.0***	51.3	**2.7****	53.9	52.2	**1.7****	**50.9****	51.2	−0.2
2005	54.2	51.6	**2.5****	**53.8***	51.3	**2.5****	51.8	50.6	1.2
2006	54.3	51.8	**2.6****	54.1	51.3	**2.8****	52.0	50.2	**1.8****
2007 (ref)	54.5	51.8	**2.7****	54.7	51.9	**2.8****	52.0	50.8	**1.2***
2008	54.7	52.1	**2.6****	55.4	52.3	**3.1****	52.1	50.3	**1.8****
2009	**55.0****	52.2	**2.7****	55.2	53.2	**2.0****	52.1	50.8	**1.3***
2010	**55.2****	**52.5****	**2.7****	**56.2****	52.5	**3.8****	52.5	50.4	**2.1****
2011	**55.4****	**52.6****	**2.8****	**56.0****	**53.8****	**2.3****	**53.0****	51.3	**1.7****
2012	**55.5****	**52.9****	**2.7****	**56.8****	53.1	**3.7****	**53.5****	52.1	**1.4****
2013	**55.9****	**53.0****	**2.9****	**56.9****	53.1	**3.9****	**52.9****	51.0	**1.8****
2014	**56.3****	**53.0****	**3.3****	**57.7****	**54.0****	**3.7****	**53.5****	**52.6****	0.9
2015	**56.2****	**53.3****	**2.9****	**58.1****	**53.6****	**4.5****	**53.6****	51.6	**2.0****
2016	**56.6****	**53.4****	**3.2****	**57.7****	**53.7****	**4.0****	**53.3****	51.6	**1.6****
2017	**56.5****	**53.5****	**3.0****	**57.7****	**54.1****	**3.5****	**53.8****	51.5	**2.3****
2018	**56.9****	**53.7****	**3.1****	**58.5****	**53.8****	**4.8****	**53.6****	52.0	**1.6****

Note: Boldface indicates statistical significance

* $p<0.05$;

** $p<0.01$.