




Increased mortality from alcohol use disorder, alcohol-associated liver disease, and liver cancer from alcohol among older adults in the United States: 2000 to 2021

Pojasorn Danpanichkul¹  | Kwanjit Duangsonk² | Ethan Kai Jun Tham³ | Primrose Tothanasrunroj⁴ | Thanida Auttapracha⁴ | Vitchapong Prasitsumrit⁵ | Benedix Sim^{3,6} | Daniel Tung^{3,6} | Romelia Barba¹ | Robert J. Wong^{7,8} | Lorenzo Leggio⁹  | Ju Dong Yang¹⁰ | Vincent L. Chen¹¹ | Mazen Nouredin¹² | Luis Antonio Díaz^{13,14,15} | Juan Pablo Arab^{13,14,16} | Karn Wijarnpreecha^{17,18,19} | Suthat Liangpunsakul^{20,21,22} 

Correspondence

Suthat Liangpunsakul, Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, IN, USA.
Email: sliangpu@iu.edu

Karn Wijarnpreecha, Division of Gastroenterology and Hepatology, Department of Medicine, University of Arizona College of Medicine, Phoenix, AZ, USA.
Email: dr.karn.wi@gmail.com

Abstract

Background: To investigate the trends in alcohol-associated liver disease (ALD), liver cancer from alcohol, and alcohol use disorder (AUD) burden among older adults in the United States (US).

Methods: We gathered the ALD, liver cancer from alcohol, and AUD prevalence, mortality, and age-standardized rates (ASRs) from the Global Burden of Disease (GBD) Study 2021 between 2010 and 2021. We estimated the annual percent change (APC) with confidence intervals (CIs) for the burden of ALD, liver cancer from alcohol, and AUD in older adults (>70 years) in the United States. The findings were contrasted with global estimates and categorized by sex and state.

Results: In 2021, there were approximately 512,340 cases of AUD, 56,990 cases of ALD, and 4490 cases of primary liver cancer from alcohol among older adults in the United States. In contrast to declining ASRs of prevalence and mortality in the global burden, these parameters were increased in older adults in the United States. From 2000 to 2021, prevalence from AUD (APC: 0.54%, 95% CI 0.43% to 0.65%), ALD (APC +0.54%, 95% CI 0.22% to 0.86%), and primary liver cancer from alcohol (APC 2.93%, 95% CI 2.76% to 3.11%) increased. Forty states in the United States exhibited a rise in the prevalence rates of ALD in older adults.

Conclusion: Our findings highlighted the increased prevalence and mortality of AUD, ALD, and primary liver cancer from alcohol among older adults in the United States, contrasting with the decline in global trends. Public health strategies on

Pojasorn Danpanichkul and Kwanjit Duangsonk are co-first authors.

For affiliations refer to page 376.

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ALD, AUD, and primary liver cancer from alcohol, which targets older adults, are urgently needed.

KEYWORDS

chronic liver disease, geriatric, public health, steatotic liver disease

INTRODUCTION

Alcohol consumption poses a significant public health burden in the United States (US), with over 4% of all mortality attributed to its effects (Shield et al., 2020). In recent years, alcohol-associated liver disease (ALD) has emerged as the leading cause of liver transplantation (Philip et al., 2022). This trend is reflected in the rising number of cirrhosis-related deaths, with approximately half of these deaths attributable to alcohol consumption (Mellinger, 2019). The economic impact of ALD is substantial, with estimates suggesting that between 2022 and 2040, the disease will incur a cost of \$880 billion (Julien et al., 2024). The annual incidence of liver cancer in patients with cirrhosis is reported to range from 0.32% to 5.6%, depending on the population studied (Jacob et al., 2023). Over the past two decades, apart from metabolic dysfunction-associated steatohepatitis, alcohol remains the only liver cancer etiology that has shown an increase (Danpanichkul, Suparan, Tothananarungroj, et al., 2024). Liver cancer from alcohol is linked to lower surveillance rates, more advanced Barcelona Clinic Liver Cancer (BCLC) stage at diagnosis, and poorer survival outcomes (Zeng et al., 2024).

Of particular concern is the aging population in the United States, with projections indicating a significant increase in the number of individuals aged 65 and over by the year 2040 (White et al., 2023). Aging is associated with a natural decline in alcohol metabolism and liver regeneration, which can escalate the risk of liver injuries and fibrosis (Kim et al., 2015; Lang et al., 2007; Ren et al., 2022). Unfortunately, older adults with ALD typically experience more adverse outcomes compared with younger individuals with the same condition (Meier & Seitz, 2008).

The combination of increasing alcohol consumption and an aging demographic presents a significant health challenge in the United States (Keyes, 2023; White et al., 2018). Moreover, it is crucial to recognize that ALD is not solely a standalone hepatic condition but is intricately linked with addiction diseases such as alcohol use disorder (AUD) (Diaz, Winder, et al., 2023; Han et al., 2017; Mellinger et al., 2023). Understanding this relationship is vital for adopting a more holistic approach to managing ALD. Despite the escalating trends in alcohol consumption and ALD, there remains a dearth of comprehensive research on the impact of AUD, ALD, and primary liver cancer from alcohol among older adults in the United States (Dawson et al., 2015). Our study aimed to address this gap by examining temporal shifts in the prevalence and mortality rates associated with ALD, AUD, and primary liver cancer from alcohol among older adults in the United States. We draw on insights from the Global

Burden of Disease (GBD) Study 2021 to achieve the aim (GBDCoD Collaborators, 2024).

METHODS

Data source

This investigation used the GBD Study 2021 dataset, a comprehensive project that assesses the impact of 369 diseases and 87 risk factors across 204 countries and territories. Focusing specifically on individuals aged over 70 years, we extracted annual frequencies and age-standardized rates (ASRs) of ALD, primary liver cancer due to alcohol, and AUD prevalence and mortality, spanning from 2000 to 2021 (GBDCoD Collaborators, 2024). To access this data, we utilized the Global Health Data Exchange query tool, an online platform regularly updated through international collaboration and overseen by the Institute for Health Metrics and Evaluation. The methodology of the GBD 2021 study and specific estimations related to alcohol consumption and its associated health burden are outlined in previous publications (GBDCoD Collaborators, 2024).

Definitions and measures

In the GBD 2021 study, the burden of ALD, primary liver cancer from alcohol, and AUD among older adults, defined as individuals aged over 70 years, was delineated using specific International Classification of Diseases Tenth Revision (ICD-10) codes. Specifically, ALD was classified using ICD-10 codes K70-K70.3, while primary liver cancer attributed to alcohol corresponded to ICD-10 code C22. AUD in this demographic was aligned with ICD-10 codes F10.1 and F10.2 (GBDCoD Collaborators, 2024). This study aimed to estimate the disease burden of ALD and AUD among older adults, focusing on the US population. The methodology employed in determining the burden of alcohol-related complications in the GBD 2021 study involved using data from various sources, including population-based health registries, vital registration systems, and verbal autopsy studies (GBDCoD Collaborators, 2024). Statistical methods such as misclassification correction, garbage code redistribution, and noise reduction algorithms were applied to address data heterogeneity and ensure accuracy. The annual prevalence of ALD, primary liver cancer attributed to alcohol, and AUD was calculated as follows: $\text{Prevalence} = \text{Number of cases} / \text{Population size}$. Here, the "number

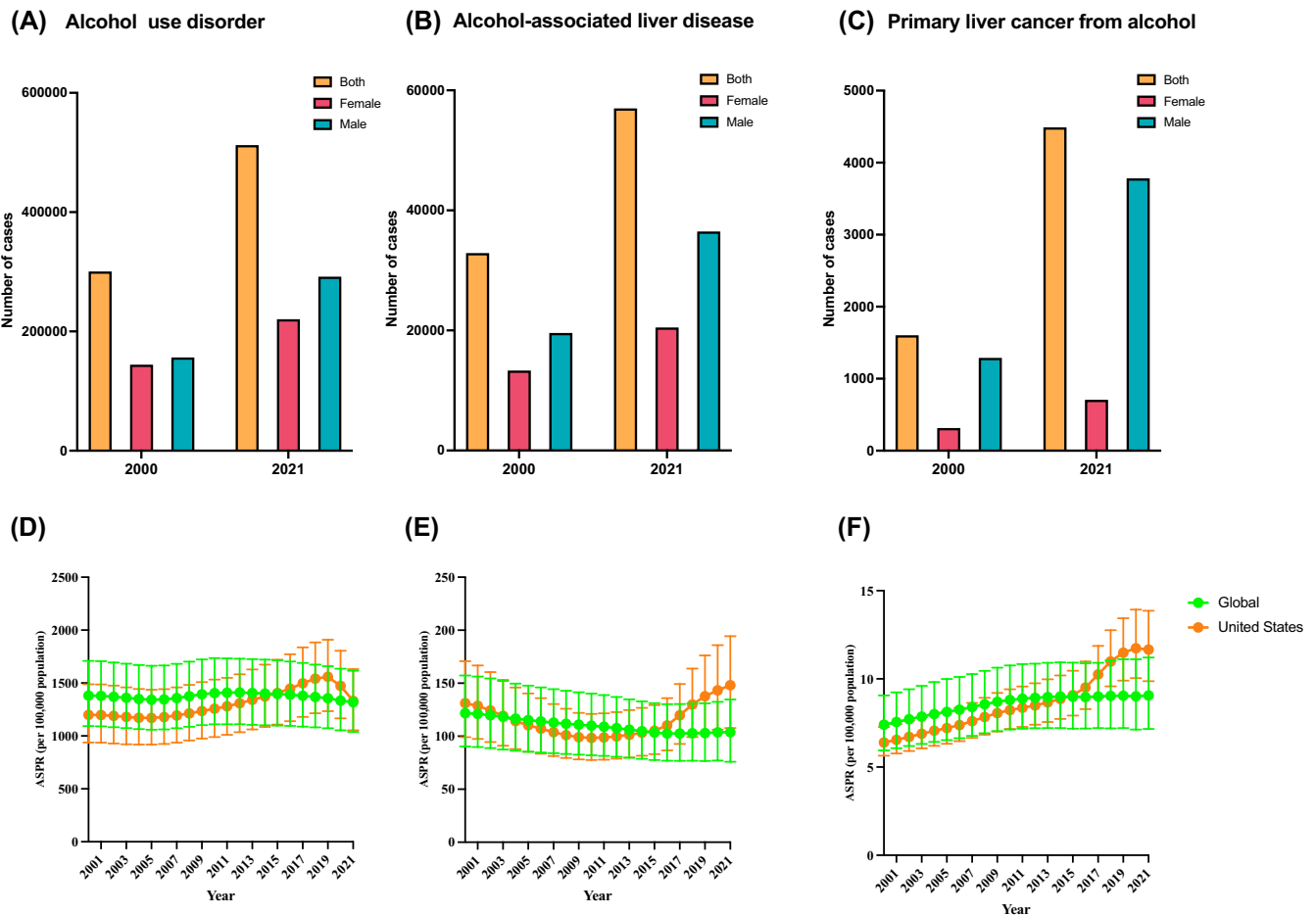


FIGURE 1 (A) Prevalence of patients aged over 70 with alcohol use disorder (AUD) in 2000 and 2021 in the United States, by sex. (B) Prevalence of patients aged over 70 with alcohol-associated liver disease (ALD) in 2000 and 2021 in the United States, by sex. (C) Prevalence of patients aged over 70 with primary liver cancer from alcohol in 2000 and 2021 in the United States, by sex. (D) Age-standardized prevalence rates (ASPRs) in patients aged over 70 with AUD from 2000 to 2021 in the United States and Global. (E) ASPRs in patients aged over 70 with ALD from 2000 to 2021 in the United States and Global. (F) ASPRs in patients aged over 70 with primary liver cancer from alcohol from 2000 to 2021 in the United States and Global ASPR, age-standardized prevalence rate.

of cases” refers to the count of diagnoses for each alcohol-related complication by the end of the respective year.

Statistical analysis

The findings of this study regarding the prevalence and mortality of alcohol-related conditions among older adults are accompanied by 95% uncertainty intervals (UIs). These UIs are derived from the 2.5th and 97.5th percentile values across a thousand simulations of the posterior distribution. Age-standardized rates were computed using the methodology outlined in the GBD 2021 study. To assess temporal trends in ASRs over time, the annual percent change (APC) was calculated. An APC with a positive lower bound of its 95% confidence interval (CI) indicates a rising trend, while a negative upper bound suggests a decline. The analysis was conducted using version 4.9.1.0 of the Joinpoint regression program from the National Cancer Institute's Statistical Research and Applications Branch in Bethesda, United States.

RESULTS

The burden of alcohol-associated liver disease, primary liver cancer from alcohol, and alcohol use disorder in older adults in the United States

Prevalence, death, age-standardized prevalence rate (ASPR), and age-standardized death rate (ASDR) are designated in [Figures 1A–F](#) and [2A–F](#). In 2021, older adults in the United States had 512,340 cases of AUD, 56,990 cases of ALD, and 4490 cases of primary liver cancer from alcohol ([Figure 1A–C](#)). Correspondingly, there were 2180 deaths attributable to AUD, 5930 deaths from ALD, and 3290 deaths due to primary liver cancer from alcohol ([Figure 2A–C](#)). The ASPRs of AUD, ALD, and primary liver cancer due to alcohol among older adults were 1331.25 (95% UI 1053.93 to 1630.82), 148.08 (95% UI 107.74 to 194.38), and 11.67 (95% UI 9.87 to 13.86) per 100,000 population, respectively ([Figure 1D–F](#)). The ASDRs of AUD, ALD, and primary liver cancer from alcohol among the older adults were 5.66 (95% UI 5.16 to 5.95), 15.41 (95% UI 12.40 to 18.40), and

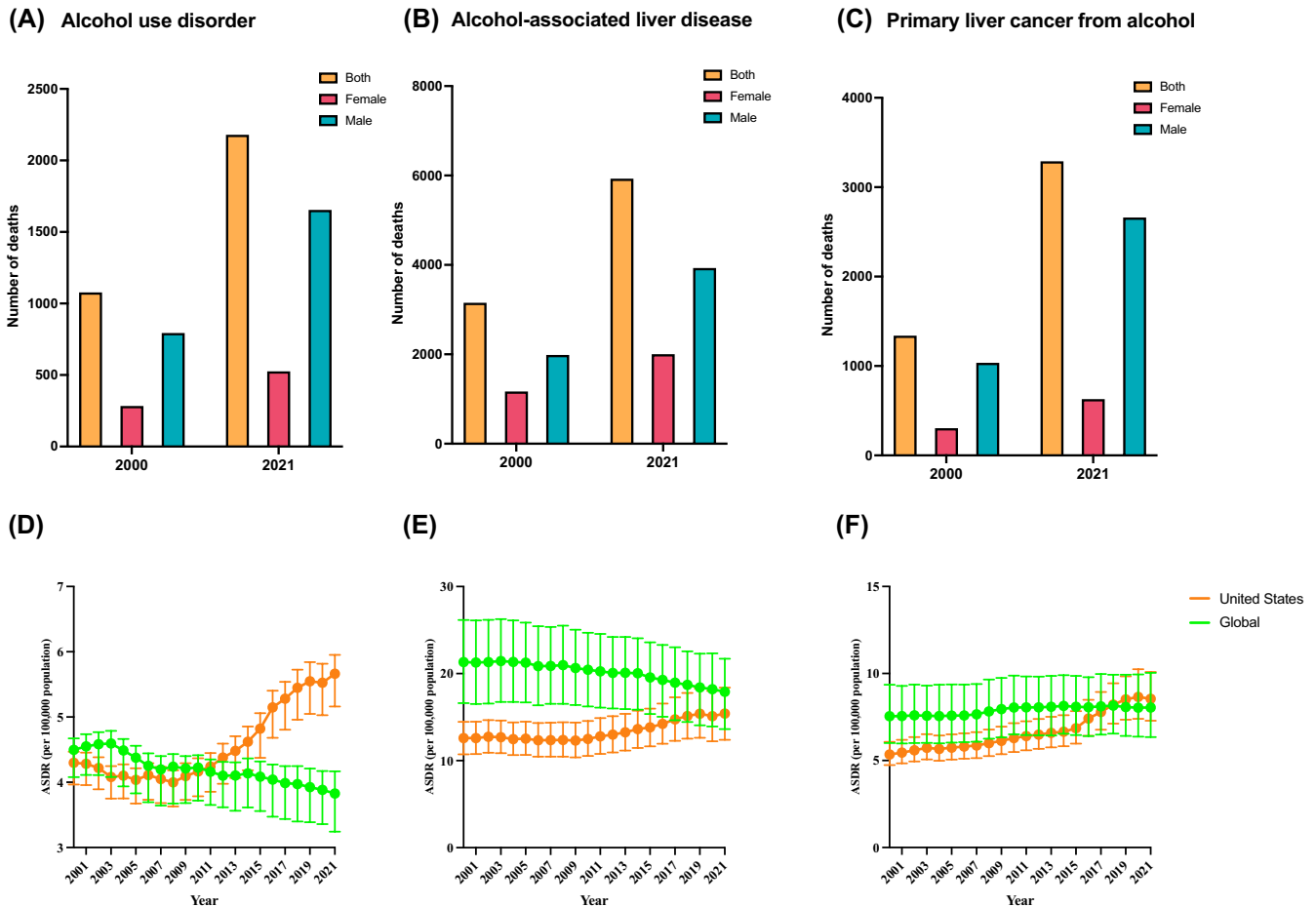


FIGURE 2 (A) Death from patients aged over 70 with alcohol use disorder (AUD) in 2000 and 2021 in the United States, by sex. (B) Death from patients aged over 70 with alcohol-associated liver disease (ALD) in 2000 and 2021 in the United States, by sex. (C) Death from patients aged over 70 with primary liver cancer from alcohol in 2000 and 2021 in the United States, by sex. (D) Age-standardized death rates (ASDRs) in patients aged over 70 with AUD from 2000 to 2021 in the United States and Global. (E) ASDRs in patients aged over 70 with ALD from 2000 to 2021 in the United States and Global. (F) ASDRs in patients aged over 70 with primary liver cancer from alcohol from 2000 to 2021 in the United States and Global ASPR, age-standardized prevalence rate.

8.55 (95% UI 7.28 to 10.09) per 100,000 US population, respectively (Figure 2D-F).

Between 2000 and 2021, the US older adults experienced an upward trend in the ASPRs for AUD (APC 0.54%, 95% CI 0.43% to 0.65%), ALD (APC: 0.54%, 95% CI 0.22% to 0.86%), and primary liver cancer attributable to alcohol (APC: 2.93%, 95% CI 2.76% to 3.11%) (Tables 1-3).

The burden of AUD, ALD, and liver cancer from alcohol in the global older adult population is designated in Figures 1D-F and 2D-F. Globally, the trends were slightly different compared with the US population, showing a decrease in ASPR from ALD (APC -0.76%, 95% CI: -0.83% to -0.70%) and AUD (APC: -0.22%, 95% CI -0.33% to -0.12%), while the ASPR of primary liver cancer from alcohol increased (APC: 0.94%, 95% CI 0.85% to 1.04%) (Tables 1-3). In terms of the ASDRs, global trends indicated a decline in ASDR from AUD (APC: -0.76%, 95% CI -1.05% to -0.47%) and ALD (APC: -0.83%, 95% CI -0.94% to -0.72%) (Tables 1 and 2). However, an increase was observed in primary liver cancer from alcohol (APC: 0.29%, 95% CI 0.17% to 0.41%) (Table 3). Contrarily, in the United States, the ASDR

showed an increase across all three categories: AUD (APC: 1.34%, 95% CI 0.78% to 1.90%), ALD (APC 0.96%, 95% CI 0.55% to 1.36%), and primary liver cancer from alcohol (APC: 2.32%, 95% CI 1.87% to 2.77%) (Tables 1-3).

The burden of alcohol-associated liver disease, primary liver cancer from alcohol, and alcohol use disorder in older adults in the United States by sex

Prevalence and deaths from AUD, ALD, and primary liver cancer due to alcohol are designated in Figures 1A-C and 2A-C. The ASPRs of AUD, ALD, and primary liver cancer due to alcohol among the older adult females were 1016.8 (95% UI 807.42 to 1237.54), 94.52 (95% UI 66.17 to 128.42), and 3.26 (95% UI 2.59 to 4.11) per 100,000 population, respectively (Tables 1-3). For males, the ASPRs were 1737.36 (95% UI 1364.43 to 2146.37) for AUD, 217.25 (95% UI 162.07 to 281.61) for ALD, and 22.52 (95% UI 19.14 to 26.58) for primary liver cancer from alcohol per 100,000 population in 2021 (Tables 1-3).

TABLE 1 Prevalence, death, and their age-standardized rates and annual percent change of alcohol use disorder in patients aged over 70 from 2000 to 2021.

	2021, prevalence (95% UI)	2021, age-standardized prevalence rates per 100,000 (95% UI)	Annual percent change from 2000 to 2021 (95% CI)	p	2021, death (95% UI)	2021, age-standardized death rates per 100,000 (95% UI)	Annual percent change from 2000 to 2021 (95% CI)	p
Overall	512,340 (405,610 to 627,640)	1331.25 (1053.93 to 1630.82)	0.54 (0.43 to 0.65)	<0.001	2180 (1990 to 2290)	5.66 (5.16 to 5.95)	1.34 (0.78 to 1.9)	<0.001
Female	220,550 (175,130 to 268,430)	1016.8 (807.42 to 1237.54)	0.35 (0.3 to 0.4)	<0.001	530 (450 to 560)	2.42 (2.08 to 2.6)	1.16 (0.48 to 1.84)	0.001
Male	291,800 (229,160 to 360,490)	1737.36 (1364.43 to 2146.37)	0.49 (0.34 to 0.64)	<0.001	1650 (1530 to 1730)	9.85 (9.08 to 10.3)	0.99 (0.58 to 1.39)	<0.001
Global	6.52 million (5.13 million to 7.99 million)	1319.13 (1038.48 to 1615.37)	-0.22 (-0.33 to -0.12)	<0.001	18,920 (16,040 to 20,600)	3.83 (3.24 to 4.17)	-0.76 (-1.05 to -0.47)	<0.001

Abbreviations: CI, confidence interval; UI, uncertainty interval.

TABLE 2 Prevalence, death, and their age-standardized rates and annual percent change of alcohol-associated liver disease in patients aged over 70 from 2000 to 2021.

	2021, prevalence (95% UI)	2021, age-standardized prevalence rates per 100,000 (95% UI)	Annual percent change from 2000 to 2021 (95% CI)	p	2021, death (95% UI)	2021, age-standardized death rates per 100,000 (95% UI)	Annual percent change from 2000 to 2021 (95% CI)	p
Overall	56,990 (41,470 to 74,810)	148.08 (107.74 to 194.38)	0.54 (0.22 to 0.86)	0.001	5930 (4770 to 7080)	15.41 (12.4 to 18.4)	0.96 (0.55 to 1.36)	<0.001
Female	20,500 (14,350 to 27,860)	94.52 (66.17 to 128.42)	0.29 (-0.15 to 0.73)	0.197	2000 (1510 to 2480)	9.22 (6.94 to 11.43)	0.83 (0.65 to 1.01)	<0.001
Male	36,490 (27,220 to 47,300)	217.25 (162.07 to 281.61)	0.4 (0.13 to 0.67)	0.004	3930 (3240 to 4610)	23.4 (19.28 to 27.46)	0.69 (0.25 to 1.13)	0.002
Global	513,440 (374,930 to 665,730)	103.86 (75.84 to 134.66)	-0.76 (-0.83 to -0.7)	<0.001	88,540 (67,380 to 107,310)	17.91 (13.63 to 21.71)	-0.83 (-0.94 to -0.72)	<0.001

Abbreviations: CI, confidence interval; UI, uncertainty interval.

TABLE 3 Prevalence, death, and their age-standardized rates and annual percent change of primary liver cancer from alcohol in patients aged over 70 from 2010 to 2021.

	2021, prevalence (95% UI)	2021, age-standardized prevalence rates per 100,000 (95% UI)	Annual percent change from 2000 to 2021 (95% CI)	p	2021, death (95% UI)	2021, age-standardized death rates per 100,000 (95% UI)	Annual percent change from 2000 to 2021 (95% CI)	p
Overall	4490 (3800 to 5340)	11.67 (9.87 to 13.86)	2.93 (2.76 to 3.11)	<0.001	3290 (2800 to 3880)	8.55 (7.28 to 10.09)	2.32 (1.87 to 2.77)	<0.001
Female	710 (560 to 890)	3.26 (2.59 to 4.11)	2.18 (2.03 to 2.34)	<0.001	630 (500 to 790)	2.9 (2.29 to 3.62)	1.78 (1.37 to 2.2)	<0.001
Male	3780 (3210 to 4460)	22.52 (19.14 to 26.58)	2.67 (2.5 to 2.85)	<0.001	2660 (2280 to 3110)	15.84 (13.59 to 18.5)	2.05 (1.6 to 2.51)	<0.001
Global	44,780 (35,410 to 55,450)	9.06 (7.16 to 11.22)	0.94 (0.85 to 1.04)	<0.001	39,790 (31,380 to 49,640)	8.05 (6.35 to 10.04)	0.29 (0.17 to 0.41)	<0.001

Abbreviations: CI, confidence interval; UI, uncertainty interval.

The ASDRs of AUD, ALD, and primary liver cancer from alcohol among females were 2.42 (95% UI 2.08 to 2.60), 9.22 (95% UI 6.94 to 11.43), and 2.90 (95% UI 2.29 to 3.62), respectively (Tables 1–3). The ASDRs of AUD, ALD, and primary liver cancer from alcohol for males were 9.85 (95% UI 9.08 to 10.30), 23.40 (95% UI 19.28 to 27.46), and 15.84 (95% UI 13.59 to 18.50), respectively (Tables 1–3).

The burden of alcohol-associated liver disease, primary liver cancer from alcohol, and alcohol use disorder by state

In 2021, Alaska had the highest ASPR from AUD in older adults, with a value of 2025.63 (95% UI 1592.51 to 2542.83). The District of Columbia and New Mexico followed, with ASPRs of 1977.46 (95% UI 1580.70 to 2402.49) and 1923.35 (95% UI 1516.62 to 2377.12), respectively (Figure 3A). From 2000 to 2021, ASPR for AUD increased in all states, with the highest uptrend observed in West Virginia (APC: 0.72%, 95% CI 0.60% to 0.84%), Mississippi (APC: 0.66%, 95% CI 0.55% to 0.76%), and Kentucky (APC: 0.65%, 95% CI 0.54% to 0.76%) (Table S1).

Regarding ALD, New Mexico had the highest ASPR among older adults, with a value of 183.41 (95% UI 133.41 to 239.33), followed by Massachusetts and Nevada, with values of 176.95 (95% UI 131.94 to 233.68) and 171.51 (95% UI 125.46 to 224.37), respectively (Figure 3B). From 2000 to 2021, ASPR from ALD increased in 39 states, with the highest increase observed in Iowa (APC: 1.15%, 95% CI 0.91% to 1.39%), Indiana (APC: 1.07%, 95% CI 0.71% to 1.42%), and North Carolina (APC: 1.02%, 95% CI 0.80% to 1.24%) (Table S2).

In 2021, Hawaii had the highest ASPR of primary liver cancer from alcohol in older adults, with a value of 24.58 (95% UI 17.87 to 31.86); this is followed by Massachusetts and Connecticut, with a value of 18.29 (95% UI 13.33 to 24.4) and 17.83 (95% UI 13.14 to 23.67), respectively (Figure 3C). From 2000 to 2021, ASPR from primary liver cancer in older adults increased in all states, with the highest rise observed in Oregon (APC: 3.96%, 95% CI 3.87% to 4.05%), Arizona (APC: 3.83%, 95% CI 3.59% to 4.07%), and Kansas (APC: 3.71%, 95% CI 3.51% to 3.91%) (Table S3).

The burden of alcohol-associated liver disease, primary liver cancer from alcohol, and alcohol use disorder by age group

ASDR of AUD is highest in the 55–59 age group with ASDR of 12.94 (95% UI 12.48 to 13.39), while older adults ranked as the seventh rank, after 55–59, 60–64, 50–54, 65–69, 45–49, and 40–44. For ALD, the highest ASDR with an ASDR of 18.66 (95% UI 14.05 to 23.08) per 100,000 population is observed in the 60–64 age group, with older adults ranked as the fourth rank, after 60–64, 65–69, and 55–59, respectively. Regarding primary liver cancer from alcohol, the highest ASDR in 2021 is observed in

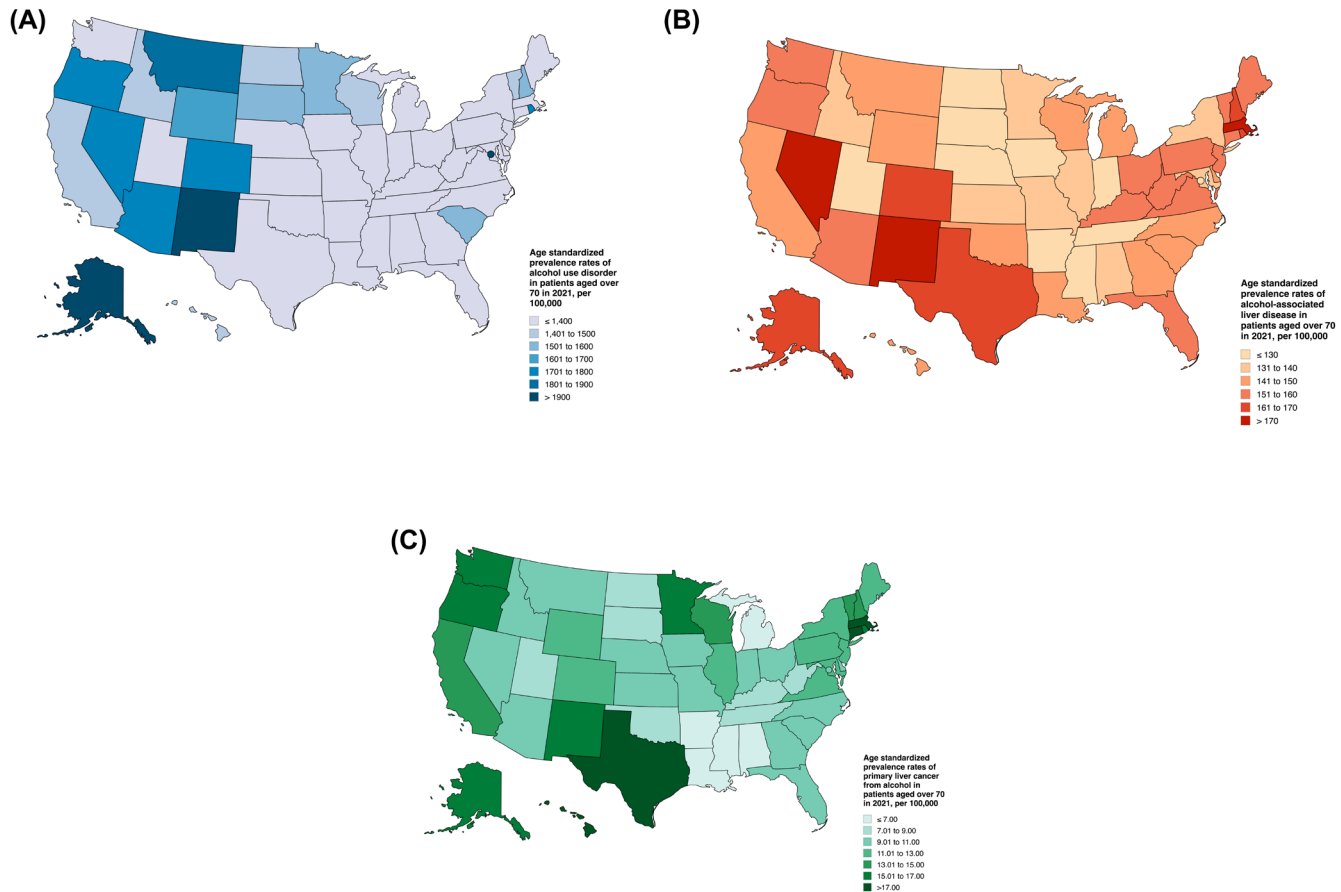


FIGURE 3 (A) Age-standardized prevalence rates (ASPRs) in patients aged over 70 with alcohol use disorder per 10,000 in the United States in 2021, stratified by states. (B) ASPRs in patients aged over 70 with alcohol-associated liver disease per 10,000 in the United States in 2021, stratified by states. (C) ASPRs in patients aged over 70 with primary liver cancer from alcohol per 10,000 in the United States in 2021, stratified by states.

the older adult group, with an ASDR of 8.55 (95% UI 7.28 to 10.09) per 100,000 population (Table S4).

DISCUSSION

This study provides a comprehensive perspective into the epidemiological trends of AUD, ALD, and primary liver cancer from alcohol among older adults (>70 years old) in the United States. Our findings reveal an increase in both the prevalence and mortality rates of these conditions in older adults. In 2021, our study estimates that there were over 512,340 older adults in the US living with AUD, accompanied by 56,990 cases of ALD and 4490 cases of primary liver cancer attributed to alcohol. These figures underscore the substantial burden of alcohol-related conditions among older adults in the country. Contrary to the global trend where mortality rates from ALD and AUD are declining, our study reveals that mortality rates in the United States have risen in the past two decades. This alarming trend underscores the urgent need for targeted interventions and healthcare strategies aimed at addressing the growing burden of ALD and AUD among older adults. Moreover, our analysis indicates that prevalence rates of AUD and ALD among older adults increased

in the majority of states, with prevalence rates from ALD rising in 40 states across the United States. Given the interconnectedness of AUD and ALD, the disparities observed in states like Ohio, West Virginia, Massachusetts, and Texas, where there is a higher burden of ALD but a lower prevalence of AUD, suggest that the estimates of AUD presented in this paper may be conservative.

Our research underscores the persistent and escalating concern of AUD among older adults, highlighting the critical need for effective management strategies. This finding is particularly significant as harmful alcohol use can interact with other risk factors such as obesity, type 2 diabetes mellitus, and hepatitis B and C viruses, increasing the risk of chronic liver disease commonly attributable to different conditions (Diaz, Arab, et al., 2023). In older adults, alcohol can also increase the risk of mortality from falls, carcinogenesis, and cardiovascular complications (Meza et al., 2022; White et al., 2023). However, there remains a substantial gap in understanding the optimal management of harmful alcohol consumption and AUD in older adults, especially among those with multiple comorbidities (Fenollal-Maldonado et al., 2022). Recognizing the critical role of age and comorbidities within the context of ALD can provide a foundation for developing enhanced healthcare approaches tailored to the needs of older adults (Khan & Roberts, 2018; Rigler, 2000).

Contrary to the global trend of decreasing mortality rates from ALD and AUD, our study underscores a concerning uptrend in these mortality rates among US older adults (Danpanichkul et al., 2024; Danpanichkul, Ng, Muthiah, et al., 2024; Danpanichkul, Suparan, Ng, et al., 2024). This worrisome pattern aligns with findings from a multicenter research utilizing data from the Centers for Disease Control and Prevention, which encompasses the general population (Ilyas et al., 2023; Moon et al., 2020). Several factors contribute to the rising burden of ALD and AUD in the United States. Firstly, more comprehensive documentation of these conditions in the United States than global data may contribute to the observed uptrend, as higher data quality ratings indicate (Diseases & Injuries, 2020). Additionally, this rise is further explained by the increasing prevalence of alcohol consumption, coupled with the interplay of confounding risk factors such as metabolic syndrome, metabolic dysfunction-associated steatotic liver disease (MASLD), and metabolic dysfunction and alcohol-associated liver disease (MetALD), which are highly prevalent in the United States (Aboona et al., 2024; Breslow et al., 2017; Danpanichkul et al., 2023; Diaz, Lazarus, et al., 2024; Mahli & Hellerbrand, 2016; Wang et al., 2020). With the United States facing an aging population predicted to reach 72.1 million older adults by 2030, there is an urgent need for more comprehensive research into ALD and AUD among older adults (Blow & Barry, 2012).

To address the rising mortality linked to ALD, policies that reduce alcohol consumption and encourage abstinence, particularly among younger adults, are essential in mitigating future risks. In 2018, the World Health Organization (WHO) introduced the SAFER framework to lower alcohol intake and its health impacts, reinforced by the global alcohol action plan 2022–2030 (Jernigan & Trangenstein, 2020). Since alcohol is especially harmful in those with advanced liver disease, older adults would also benefit from policies to lower alcohol intake. A recent study highlighted the strong link between public health policies and reductions in AUD, ALD, and liver cancer (Diaz, Fuentes-Lopez, et al., 2024). Effective strategies include stricter alcohol availability controls, enforcing drink-driving measures, enhancing access to screening and treatment, and raising alcohol prices through excise taxes to lower the liver disease burden, particularly in older adults (Ayares et al., 2022; Diaz et al., 2021).

While ALD and AUD are commonly considered interrelated pathology of liver and addiction disease, our study found a disagreement between the burden of ALD and AUD in each state. Several factors, including the pattern of alcohol consumption, which does not reach the diagnosis of AUD, the reporting system, or racial disparities, may influence the variation in ALD and AUD burden between states (Anouti et al., 2024; Spillane et al., 2020). Previous investigations utilizing the CDC WONDER database have revealed that older American Indian/Alaska Native adults experience higher alcohol-related mortality rates compared with other ethnic groups (Karaye et al., 2023). This disparity is particularly evident in states with significant populations of American Indian/Alaska Natives, such as New Mexico, Arizona, and Alaska.

However, it is essential to acknowledge that poverty and health-care accessibility may also contribute to this issue. Further studies incorporating these social health determinants are warranted to better understand the impact of ALD and AUD within this demographic (Askgaard et al., 2021). Regarding sex differences, our study observed a lower overall burden of ALD in females than in males and a less pronounced temporal change in both prevalence and mortality. This difference can be partly attributed to lower alcohol consumption and reduced levels of dehydrogenase enzymes among females (McCaul et al., 2019). However, women in old age are typically less likely to seek assistance compared with their male counterparts, which may result in healthcare providers under-recognizing the risks of excessive drinking and the potential for ALD in this demographic. Additionally, societal norms regarding alcohol consumption are shifting, and women tend to increase their alcohol consumption at postmenopausal ages (Peltier et al., 2020).

Our study, using the GBD 2021 database, is not without limitations. First, interpreting mortality data, especially on a global scale, requires caution. The GBD approach estimates overall liver-related mortality and categorizes it into distinct causes (GBDCoD Collaborators, 2024; Paik et al., 2023). Therefore, a decrease in deaths attributable to viral hepatitis may obscure the actual impact of ALD in the global mortality data (Danpanichkul et al., 2023; Diseases & Injuries, 2020; Paik et al., 2023). Second, the GBD 2021 data did not provide differences in racial or ethnicity, an essential factor influencing ALD outcomes (Anouti et al., 2024; Tapper & Parikh, 2018). Third, comparing global and US data may introduce bias due to varying data quality across countries. The trends should be interpreted with caution, as discrepancies exist. For instance, GBD 2019 data showed a rise in liver cancer incidence in the United States while a decline was seen globally. Further studies are needed to confirm the reliability of US data on AUD, ALD, and alcohol-associated liver cancer (Al Ta'ani et al., 2024; Cao et al., 2023; Danpanichkul, Aboona, Sukphutanan, et al., 2024). Fifth, we could not estimate the overlap prevalence of ALD and AUD due to the inherent limitation of the database. A significant challenge in studying ALD epidemiology is the lack of definitive biomarkers for diagnosis and the absence of extensive, population-specific datasets for ALD, unlike those available for hepatitis C or hepatitis B (Arnts et al., 2021; Israelsen et al., 2024; Rogal et al., 2020). Hence, it is imperative to establish public health policies focused on reducing alcohol consumption and to actively pursue the development of new therapeutic interventions. These efforts are essential to address the silent epidemic of ALD and AUD, particularly among the elderly, a demographic that has not been extensively studied in this context (Milic et al., 2018). This approach is crucial for addressing the rising challenges posed by AUD, ALD, and primary liver cancer from alcohol and promoting the well-being of older populations, projected to constitute 20% of the US population by 2040 (Gamble et al., 2013).

In conclusion, our study highlights the concerning upward trends in both the prevalence and mortality rates of AUD, ALD, and primary liver cancer from alcohol in the United States. It is imperative

to implement specialized screening and treatment protocols to effectively address the increasing impact of AUD, ALD, and primary liver cancer from alcohol, particularly among the elderly population. These interventions should be designed to identify and support individuals at risk for or already affected by these conditions, focusing on early detection, intervention, and management. These targeted strategies are essential in mitigating the growing health burden posed by AUD, ALD, and primary liver cancer from alcohol, especially in the context of an aging population.

AUTHOR CONTRIBUTIONS

Conceptualization: Pojsakorn Danpanichkul, Karn Wijarnpreecha, and Juan Pablo Arab. Data curation: Pojsakorn Danpanichkul and Kwanjit Duangsonk. Formal analysis: Pojsakorn Danpanichkul, Kwanjit Duangsonk, Ethan Kai Jun Tham, and Vitchapong Prasitsumrit. Investigation: Pojsakorn Danpanichkul, Daniel Tung, and Ethan Kai Jun Tham. Methodology: Pojsakorn Danpanichkul, Kwanjit Duangsonk, and Ethan Kai Jun Tham. Project Administration: Pojsakorn Danpanichkul, Karn Wijarnpreecha, Suthat Liangpunsakul, and Mazen Noureddin. Supervision: Karn Wijarnpreecha, Mazen Noureddin, Juan Pablo Arab, and Suthat Liangpunsakul. Validation: Pojsakorn Danpanichkul, Primrose Tothananarungroj, Thanida Auttapracha, and Vitchapong Prasitsumrit. Visualization: Pojsakorn Danpanichkul, Benedix Sim, and Primrose Tothananarungroj. Writing—original draft: Pojsakorn Danpanichkul, Primrose Tothananarungroj, Luis Antonio Díaz, and Romelia Barba. Writing—review and editing: Karn Wijarnpreecha, Vincent L. Chen, Lorenzo Leggio, Mazen Noureddin, Ju Dong Yang, Juan Pablo Arab, Luis Antonio Díaz, Robert J. Wong, and Suthat Liangpunsakul.

AFFILIATIONS

¹Department of Internal Medicine, Texas Tech University Health Sciences Center, Lubbock, Texas, USA

²Department of Microbiology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

³Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

⁴Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

⁵Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

⁶Division of Gastroenterology and Hepatology, Department of Medicine, National University Health System, Singapore, Singapore

⁷Gastroenterology Section, Veterans Affairs Palo Alto Healthcare System, Palo Alto, California, USA

⁸Division of Gastroenterology and Hepatology, Stanford University School of Medicine, Palo Alto, California, USA

⁹Clinical Psychoneuroendocrinology and Neuropsychopharmacology Section, Translational Addiction Medicine Branch, National Institute on Drug Abuse Intramural Research Program (NIDA IRP) and National Institute on Alcohol Abuse and Alcoholism Division of Intramural Clinical and Biological Research (NIAAA DICBR), NIH, Baltimore and Bethesda, Maryland, USA

¹⁰Karsh Division of Gastroenterology and Hepatology, Comprehensive Transplant Center, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, California, USA

¹¹Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of Michigan, Ann Arbor, Michigan, USA

¹²Houston Research Institute and Houston Methodist Hospital, Houston, Texas, USA

¹³Departamento de Gastroenterología, Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile

¹⁴Observatorio Multicéntrico de Enfermedades Gastrointestinales (OMEGA), Santiago, Chile

¹⁵Division of Gastroenterology, MASLD Research Center, University of California at San Diego, La Jolla, California, USA

¹⁶Division of Gastroenterology, Hepatology, and Nutrition, Department of Internal Medicine, Virginia Commonwealth University School of Medicine, Richmond, Virginia, USA

¹⁷Division of Gastroenterology and Hepatology, Department of Medicine, University of Arizona College of Medicine, Phoenix, Arizona, USA

¹⁸Department of Internal Medicine, Banner University Medical Center, Phoenix, Arizona, USA

¹⁹BIO5 Institute, University of Arizona College of Medicine-Phoenix, Phoenix, Arizona, USA

²⁰Division of Gastroenterology and Hepatology, Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana, USA

²¹Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, Indiana, USA

²²Roudebush Veterans' Administration Medical Center, Indianapolis, Indiana, USA

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The figures of the map of the United States were created by using mapchart.net.

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CONFLICT OF INTEREST STATEMENT

Suthat Liangpunsakul has served as a consultant for Durect and Surrozen. **Mazen Noureddin** has been on the advisory board for 89BIO, Gilead, Intercept, Pfizer, Novo Nordisk, Blade, EchoSens, Fractyl, Terns, Siemens, and Roche diagnostics; has received research support from Allergan, BMS, Gilead, Galmed, Galectin, Genfit, Conatus, Enanta, Madrigal, Novartis, Pfizer, Shire, Viking and Zydus; and is a minor shareholder or has stocks in Anaetos, Rivus Pharma, and Viking. **Vincent Chen's** institution has received research grants from KOWA and AstraZeneca. **Robert J Wong** has research grants (to his institution) from Gilead Sciences, Exact Sciences, Durect Corporation, and Theratechnologies. He also consulted (without compensation) for Gilead Sciences, Salix, and Mallinckrodt.

DATA AVAILABILITY STATEMENT

Data from the Global Burden of Disease (GBD) study in 2021 can be retrieved using the Global Health Data Exchange query tool (<http://ghdx.healthdata.org/gbd-results-tool>), which the Institute for Health Metrics and Evaluation maintains.

ORCID

Pojsakorn Danpanichkul  <https://orcid.org/0000-0002-9121-165X>

Lorenzo Leggio  <https://orcid.org/0000-0001-7284-8754>

Suthat Liangpunsakul  <https://orcid.org/0000-0002-6504-8123>

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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