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Global and regional burden of alcohol-associated liver disease and alcohol use disorder in the elderly

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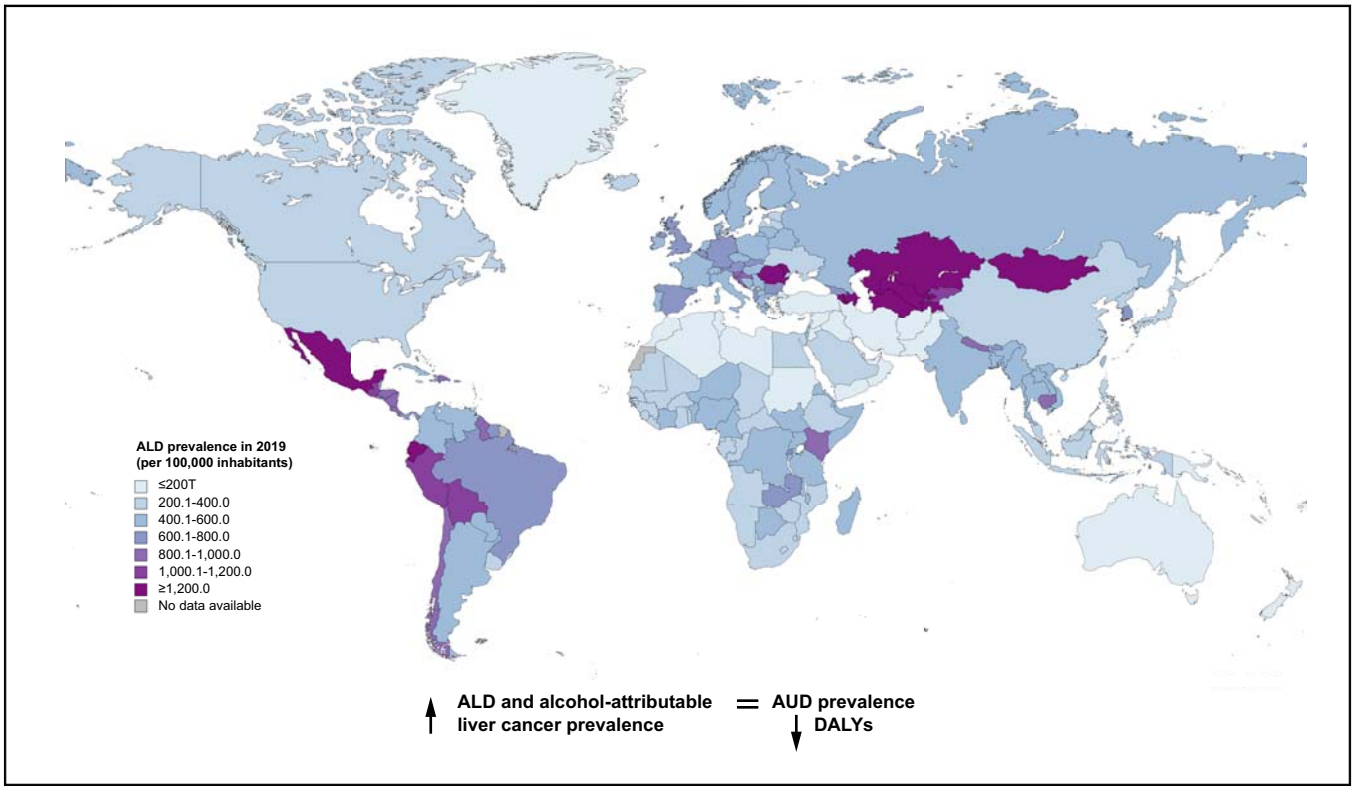
Graphical abstract



Highlights

- More than 9 million elderly people had AUD, over 3 million had cirrhosis, and nearly 70,000 had liver cancer due to alcohol.
- ALD was more common among the elderly than in the general population, whereas AUD was similar between the two groups.
- Nevertheless, AUD was less common in the elderly than in adolescents and young adults.
- The prevalence rates of ALD and AUD is increasing in many regions globally.

Impact and implications

The burden of alcohol-associated liver disease (ALD) and alcohol use disorder (AUD) is increasing. Advances in healthcare and education have resulted in a remarkable spike in life expectancy and a consequential population aging. Nevertheless, little is known about the epidemiology of ALD and AUD in the elderly. Our study indicates the increasing burden of ALD and AUD in the elderly population, necessitating early detection, intervention, and tailored care to the unique needs and complexities faced by older individuals grappling with these conditions.

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Research article

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Global and regional burden of alcohol-associated liver disease and alcohol use disorder in the elderly

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Background & Aims: Alcohol-associated liver diseases (ALDs) and alcohol use disorder (AUD) pose a global health risk. AUD is underrecognized in the elderly, and the burden of AUD complications, including ALD, may increase with aging populations and rising alcohol intake. However, there is a lack of epidemiological evidence on AUD and ALD in the elderly.

Methods: Using the Global Burden of Disease Study 2019, we analyzed the prevalence, mortality, disability-adjusted life years (DALYs), age-standardized rates (ASRs), and temporal change from 2000 to 2019 of ALD and AUD in the overall population and the elderly (65–89 years). The findings were categorized by sex, region, nation, and sociodemographic index.

Results: The prevalence rates of ALD in the elderly were higher than those in adolescents and young adults, whereas AUD levels were lower than those in adolescents and young adults. In 2019, there were 9.39 million cases (8.69% of cases in the overall population) of AUD, 3.23 million cases (21.8% of cases in the overall population) of alcohol-associated cirrhosis, and 68,468 cases (51.27% of cases in the overall population) of liver cancer from alcohol among the elderly. ASRs of the prevalence of ALD and AUD in the elderly increased in most regions; on the contrary, ASRs of death and DALYs decreased in most regions. Nevertheless, ASRs of death and DALYs from liver cancer from alcohol increased in many areas.

Conclusions: Our findings highlighted the increased prevalence of ALD in the elderly, with a burden of AUD comparable with that in the overall population. Public health strategies on ALD and AUD targeting the elderly are urgently needed.

Impact and implications: The burden of alcohol-associated liver disease (ALD) and alcohol use disorder (AUD) is increasing. Advances in healthcare and education have resulted in a remarkable spike in life expectancy and a consequential population aging. Nevertheless, little is known about the epidemiology of ALD and AUD in the elderly. Our study indicates the increasing burden of ALD and AUD in the elderly population, necessitating early detection, intervention, and tailored care to the unique needs and complexities faced by older individuals grappling with these conditions.

Keywords: Alcohol-associated cirrhosis; Public health; Geriatric; Epidemiology.
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Introduction

The global incidence of alcohol-associated liver diseases (ALD) – mainly cirrhosis and liver cancer – and alcohol use disorder (AUD) has been on the rise in recent decades.[1,2] Sequentially, the conditions exerted significant financial pressures on the health-care system. In the USA, for example, the government has incurred direct healthcare expenses, with costs projected to

exceed $355 billion, to mitigate the diseases' burdens.[3] Of all age groups, the elderly are at a particular risk.

Aging, a known risk factor for ALD, combined with the rising alcohol consumption exacerbated by the COVID-19 pandemic and the global surge in the aging population, intensifies health concerns.[4] Notably, despite similar alcohol consumption levels, elderly patients often experience worse outcomes than their younger counterparts. Regarding the aging process, with a reduction in alcohol-detoxifying enzymes as well as a decline in hepatic reserve and high comorbidities, the elderly become markedly vulnerable to alcohol toxicity and carcinogenicity. Regarding its effect on the liver, the elderly with chronic alcohol consumption are at a higher risk of developing advanced ALD including cirrhosis and, eventually, liver cancer.[5] Together, alcohol consumption in this aging population and its ALD consequences have been outgrowing.

However, despite the considerable strain of ALD and AUD on healthcare, large-scale epidemiological studies focusing on these conditions in the elderly remain scarce. In this study, we used the Global Burden of Disease 2019 (GBD 2019) study as a means to estimate the prevalence, mortality, and disability-adjusted life years (DALYs) of alcohol-associated cirrhosis, liver cancer from alcohol, and AUD. These demographics have been relatively understudied in this population.[6]

Materials and methods

Data source

This study used data from the GBD 2019 study, a comprehensive initiative aimed at quantifying the impact of 369 diseases and 87 risk factors across 204 countries and territories.[6] We extracted annual frequencies and age-standardized rates (ASRs) of alcohol-associated cirrhosis, liver cancer from alcohol, and AUD prevalence, mortality, DALYs, and their rates for participants in the overall population, in adolescents and young adults (AYA), and in those aged 65–89 years from 2000 to 2019. The data were differentiated by sex, age, region, and country. Access to these data was facilitated through the Global Health Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool), a regularly updated online resource maintained by a multinational collaboration and managed by the Institute for Health Metrics and Evaluation (IHME). The full methodology of GBD 2019 study and the estimation of alcohol consumption and burden are provided in Supplementary Materials 1 and 2.

Definitions and measures

ALD comprises the pathology ranging from simple steatosis to cirrhosis and cancer. In the GBD 2019 study, the burden of ALD was available in the form of alcohol-associated cirrhosis and liver cancer from alcohol. Alcohol-associated cirrhosis in the elderly is defined as a diagnosis of this condition in patients aged 65–89 years, based on the relevant International Classification of Diseases Tenth Revision (ICD-10) codes K70–K70.3.[7] Similarly, liver cancer from alcohol is based on the ICD-10 code C22.[8] AUD in the same demographic age aligned with the ICD-10 codes F10.1 and F10.2.[9] This study aimed to estimate the global disease burden of ALD and AUD in the elderly, specifically stratified by the World Health Organization regions and sociodemographic index (SDI). SDI is a composite metric that integrates rankings of per capita incomes, educational achievement, and fertility rates of various countries (Table S1). Furthermore, to gain a more comprehensive understanding of the disease burden in the elderly, we analyzed the general population (all ages and its ASRs). The adopted methodology to ascertain the disease burden of alcohol-related complications from the GBD 2019 study has been outlined in a previous study.[10–13] In brief, the data used in this study were derived from population-based health registries, vital registration systems, or verbal autopsy studies. To ensure data accuracy, the GBD 2019 study assessed the data quality from each country or territory on a scale from 0 (lowest quality) to 5 (highest quality). Data quality ratings for the causes of death data from each country are available in Table S2. An array of statistical methods, including misclassification correction, garbage code redistribution, and noise reduction algorithms, was used to manage data heterogeneity. The annual prevalence of alcohol-associated cirrhosis, liver cancer from alcohol, and AUD was calculated using the following formula: Prevalence = Number of cases/Population size. Therefore, the term 'Number of cases' represents the count of each alcohol-related complication diagnosis confirmed by the conclusion of the given year. The burden of alcohol-related complications in this age group was also evaluated as DALYs, which is the sum of years of life lost (YLL) and years lived with disability (YLD). YLL is the number of deaths multiplied by the life expectancy at the death time. YLD is the prevalence of disease multiplied by disability weight, yielding the severity of the disease as a number between 0 (designated full health) and 1 (designated death).

Statistical analysis

Estimates for the frequency of cases, deaths, and disabilities were reported with 95% uncertainty intervals (UIs) as 2.5th and 97.5th ranked values across all 1,000 draws from a posterior distribution. ASRs were determined using the direct method applied to the GBD 2019 study population estimate.[6] For analyzing temporal changes in ASRs over time, we calculated the annual percentage change (APC) and 95% CI in ASRs using the Joinpoint regression program, version 4.6.1.0 (Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA). The APC designated in this study is the average APC, which provided the advantage of considering the trend transitions in the specific time frame.[14] When the APC and the lower limit of its 95% CI were both positive, this was interpreted as an increasing trend. In contrast, when the APC and the upper boundary were negative, this was interpreted as a decreasing trend.

Results

The global burden of ALD and AUD in the overall population and the elderly

In the elderly, the age-standardized prevalence rate (ASPR) was 461.66 (95% UI 344.34–596.83) for cirrhosis, 1,340.3 (95% UI 1,113.65–1,641.62) for AUD, and 9.77 (95% UI 7.62–12.31) for liver cancer (Tables 1–3). In the overall population, the ASPR was 176.27 (95% UI 143.99–214.28) for cirrhosis, 1,326.27 (95% UI 1,137.68–1,520.83) for AUD, and 1.61 (95% UI 1.3–1.95) for liver cancer per 100,000 population (Supplementary Material 3 and Tables S3–S5). In AYA, the ASPR was 54.08 (95% UI 36.61–73.72) for cirrhosis, 1,837.62 (95% UI 1,438.94–2,293.58) for AUD, and 0.11 (95% UI 0.08–0.16) for liver cancer per 100,000 population. The ASPR, age-standardized death rate (ASDR), and age-standardized DALYs (ASDALYs) in AYA are specified in Tables S6–S8.

Table 1. Summary of the global and regional burden of alcohol-associated cirrhosis prevalence, deaths, DALYs, age-standardized rates, and temporal progression from 2000 to 2019.

	Prevalence				Deaths				Disabilties			
	2019 cases (95% UI)	2019 ASPR, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*	2019 deaths (95% UI)	2019 ASDR, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*	2019 DALYs (95% UI)	2019 ASDALYs, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*
Overall	3,234,541.92 (2,412,519.54 –4,181,574.47)	461.66 (344.34–596.83)	0.26 (0.18–0.34)	<0.001	139,026.67 (10,8740.91 to 171,519.7)	19.84 (15.52 to 24.48)	-0.84 (-0.99 to -0.69)	<0.001	2,556,190.53 (1,980,714.7 to 3,182,600.33)	364.84 (282.71 to 454.25)	-1.01 (-1.23 to -0.8)	<0.001
Sex												
Female	1,225,636.68 (885,882.66 –1,627,469.51)	322.38 (233.02–428.08)	0.23 (0.13–0.33)	<0.001	44,623.92 (33,412.5 –58,097.9)	11.74 (8.79–15.28)	-0.88 (-1 to -0.77)	<0.001	792,505.61 (593,095.93 –1,044,905.76)	208.45 (156–274.84)	-1 (-1.1 to -0.89)	<0.001
Male	2,008,905.24 (1,509,540.21 –2,548,142.57)	626.91 (471.07–795.19)	0.21 (0.13–0.29)	<0.001	94,402.75 (74,227.71 –115,550.74)	29.46 (23.16–36.06)	-0.92 (-1.05 to -0.8)	<0.001	1,763,684.92 (1,381,007.23 –2,178,892.53)	550.38 (430.96–679.96)	-1.1 (-1.32 to -0.87)	<0.001
Region												
Africa	134,876.97 (87,441.78 –194,496.63)	397.45 (257.67–573.14)	1.16 (1–1.32)	<0.001	14,588.21 (10,262.42 –195,22.67)	42.99 (30.24–57.53)	-1.03 (-1.13 to -0.92)	<0.001	274,473.57 (188,562.43 –372,145.89)	808.82 (555.65–1096.64)	-1.09 (-1.21 to -0.97)	<0.001
Eastern Mediterranean	52,567.92 (31,823.2 –84,914.39)	179.08 (108.41–289.27)	1.15 (1.09–1.22)	<0.001	4,972.7 (2,949.9 –7,741.96)	16.94 (10.05–26.37)	-0.45 (-0.64 to -0.27)	<0.001	89,752.78 (51,485.29 –142,816.04)	305.75 (175.39–486.52)	-0.44 (-0.58 to -0.31)	<0.001
Europe	896,827.05 (696,905.85 –1,110,617.07)	612.2 (475.73–758.14)	-0.13 (-0.19 to -0.08)	<0.001	34,021.93 (27,248.76 –41,034.89)	23.22 (18.6–28.01)	-0.65 (-0.86 to -0.44)	<0.001	627,784.87 (503,131.6 –755,992.34)	428.54 (343.45–516.06)	-0.74 (-0.99 to -0.5)	<0.001
Americas	655,177.76 (493,941.75 –842,770.56)	586.8 (442.39–754.81)	0.53 (0.47–0.59)	<0.001	29,016.04 (23,262.72 –35,027.5)	25.99 (20.83–31.37)	0.15 (-0.09 to 0.39)	0.206	530,938.85 (424,693.65 –644,108.34)	475.53 (380.37–576.89)	0.15 (-0.15 to 0.44)	0.32
Southeast Asia	653,663.45 (459,983.48 –890,546.67)	479.75 (337.6–653.61)	1.38 (0.98–1.78)	<0.001	33,165.71 (25,187.04 –42,571.29)	24.34 (18.49–31.24)	-0.81 (-1.24 to -0.37)	<0.001	615,156.83 (457,227.02 –796,267.36)	451.49 (335.58–584.41)	-1.15 (-1.82 to -0.48)	0.001
Western Pacific	831,635.43 (596,351.77 –1,121,466.89)	345.95 (248.07–466.51)	0.41 (0.34–0.47)	<0.001	22,832.57 (17,471.71 –28,970.86)	9.5 (7.27–12.05)	-1.69 (-1.87 to -1.52)	<0.001	410,497.24 (311,180.57 –532,589.07)	170.76 (129.45–221.55)	-1.9 (-2.07 to -1.72)	<0.001
SDI												
Low	1,580,53.1 (106,987.18 –221,358.68)	424.16 (287.12–594.05)	1.43 (1.25–1.61)	<0.001	13,526.89 (9,473.6 –18,288.36)	36.3 (25.42–49.08)	-1.07 (-1.24 to -0.89)	<0.001	255,722.85 (175,329.42 –348,040.74)	686.27 (470.52–934.02)	-1.17 (-1.36 to -0.98)	<0.001
Low middle	519,187.87 (367,523.88 –697,656.47)	478.69 (338.86–643.24)	1.53 (0.94–2.13)	<0.001	29,336.1 (22,249.53 –37,187.87)	27.05 (20.51–34.29)	-0.67 (-1.09 to -0.25)	0.002	545,912.75 (405,224.83 –702,473.7)	503.34 (373.62–647.69)	-0.81 (-1.26 to -0.36)	<0.001
Middle	899,696.13 (646,673.24 –1,202,296.15)	445.57 (320.26–595.44)	0.93 (0.85 to 1.01)	<0.001	39,697.01 (30,849.76 –49,635.58)	19.66 (15.28–24.58)	-0.76 (-0.87 to -0.64)	<0.001	724,176.93 (559,127.02 –915,313.71)	358.65 (276.91–453.31)	-0.89 (-1.03 to -0.75)	<0.001
High middle	844,849.4 (639,200.9 –1,081,144.89)	469.83 (355.47–601.24)	-0.1 (-0.13 to -0.06)	<0.001	30,258.48 (24,527.34 –36,348.44)	16.83 (13.64–20.21)	-1.25 (-1.47 to -1.03)	<0.001	564,886.33 (454,079.23 –680,511.77)	314.14 (252.52–378.44)	-1.39 (-1.75 to -1.03)	<0.001
High	811,086.26 (612,093.67 –1,026,375.24)	469.32 (354.17–593.89)	-0.57 (-0.61 to -0.53)	<0.001	26,114.86 (20,673.59 –32,064.24)	15.11 (11.96–18.55)	-1.05 (-1.21 to -0.88)	<0.001	463,806.63 (365,007.98 –574,426.77)	268.37 (211.2–332.38)	-1.17 (-1.38 to -0.96)	<0.001

Joinpoint regression was used to analyze the progression from 2000 to 2019. p <0.05 signifies statistical significance. APC, annual percentage change; ASDALY, age-standardized disability-adjusted life year; ASDR, age-standardized death rate; ASPR, age-standardized prevalence rate; DALY, disability-adjusted life year; SDI, sociodemographic index; UI, uncertainty interval.

Table 2. Summary of the global and regional burden of alcohol use disorder prevalence, death, DALYs, age-standardized rates, and temporal progression from 2000 to 2019.

	Prevalence				Deaths				Disabilties			
	2019 cases (95% UI)	2019 ASPR, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*	2019 deaths (95% UI)	2019 ASDR, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*	2019 DALYs (95% UI)	2019 ASDALYs, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*
Overall	9,390,531.56 (7,802,511.44 –11,501,656.11)	1,340.3 (1,113.65 –1,641.62)	0.07 (-0.04 to 0.17)	0.243	31,090.52 (27,094.02 –33,154.14)	4.44 (3.87–4.73)	-0.85 (-0.96 to -0.75)	<0.001	1,450,132.19 (1,167,502.23 –1,809,516.46)	206.98 (166.64 –258.27)	-0.41 (-0.48 to -0.34)	<0.001
Sex												
Female	2,320,174.56 (1,896,452.83 –2,891,494.5)	610.28 (498.83 –760.56)	0.24 (0.15 to 0.34)	<0.001	5,887.84 (5,397.46 –6,285.85)	1.55 (1.42–1.65)	-1.7 (-1.9 to -1.49)	<0.001	317,056.6 (25,1640.3 –405,164.06)	83.4 (66.19 –106.57)	-0.6 (-0.72 to -0.49)	<0.001
Male	7,070,357 (5,891,626.97 –8,629,208.93)	2,206.41 (1,838.57 –2,692.87)	-0.09 (-0.23 to 0.05)	0.211	25,202.68 (21,557.68 –27,023.65)	7.86 (6.73–8.43)	-0.77 (-0.89 to -0.65)	<0.001	1,133,075.59 (919,013.93 –139,9670.87)	353.59 (286.79 –436.79)	-0.46 (-0.54 to -0.37)	<0.001
Region												
Africa	400,180.67 (326,094.43 –494,122.11)	1,179.25 (960.93 –1,456.08)	-0.11 (-0.41 to 0.2)	0.488	1,506.08 (1,322.67 –1,720.79)	4.44 (3.9–5.07)	-0.42 (-0.53 to -0.31)	<0.001	62,077.69 (49,143.99 –77,679.62)	182.93 (144.82 –228.91)	-0.27 (-0.4 to -0.14)	<0.001
Eastern Mediterranean	171,989.51 (138,144.91 –218,907.33)	585.9 (470.6 –745.73)	0.1 (0.05 to 0.14)	<0.001	448.27 (291.38 –558.95)	1.53 (0.99–1.9)	-0.82 (-0.88 to -0.76)	<0.001	24,288.46 (18,592.13 –31,331.17)	82.74 (63.34 –106.73)	-0.25 (-0.29 to -0.21)	<0.001
Europe	2,670,257.68 (2,269,192.5 –3,150,860.78)	1,822.79 (1,549.02 –2,150.87)	-0.64 (-0.81 to -0.47)	<0.001	12,123.93 (10,977.71 –13,014.4)	8.28 (7.49–8.88)	-0.6 (-0.82 to -0.38)	<0.001	481,200.3 (398,464.7 –578,395.64)	328.48 (272 –394.83)	-0.71 (-0.89 to -0.53)	<0.001
Americas	1,931,408.08 (1,607,492.84 –2,343,184.13)	1,729.83 (1,439.72 –2,098.63)	0.48 (0.36 to 0.61)	<0.001	7,757.3 (7,266.17 –8,180.35)	6.95 (6.51–7.33)	-0.24 (-0.29 to -0.19)	<0.001	321,817.97 (267,340.41 –392,254.83)	288.23 (239.44 –351.32)	0.15 (0.11 to 0.2)	<0.001
Southeast Asia	1,882,716.08 (1,515,478.96 –2,378,910.35)	1381.8 (1112.27 –1745.97)	0.65 (0.56 to 0.74)	<0.001	4,547.43 (3,214.15 –5,503.69)	3.34 (2.36–4.04)	-1.08 (-1.83 to -0.32)	0.005	255,911.95 (193,904.02 –331,772.28)	187.82 (142.31 –243.5)	-0.03 (-0.23 to 0.16)	0.736
Western Pacific	2,311,165.54 (1,868,113.77 –2,910,879.66)	961.41 (777.11 –1,210.89)	1.4 (1.12 to 1.68)	<0.001	4,615.81 (3,231.51 –5,340.86)	1.92 (1.34–2.22)	0.08 (-0.02 to 0.17)	0.1	301,034.86 (227,051.79 –398,721.61)	125.23 (94.45 –165.86)	0.9 (0.5 to 1.29)	<0.001
SDI												
Low	556,028.12 (455,094.5 –689,913.09)	1492.18 (1,221.31 –1,851.48)	0.52 (0.47 –0.57)	<0.001	1,612.68 (1,385.28 –1,856.05)	4.33 (3.72–4.98)	-0.48 (-0.57 to -0.39)	<0.001	79,216.47 (61,847.3 –101,096.56)	212.59 (165.98 –271.31)	0.11 (0.05 to 0.17)	<0.001
Low middle	1,629,175.77 (1,327,595.31 –2,040,715.29)	1,502.11 (1,224.05 –1,881.55)	0.43 (0.34 to 0.52)	<0.001	5,561.01 (3,634.29 –6,362.7)	5.13 (3.35–5.87)	-0.38 (-0.52 to -0.23)	<0.001	253,003.17 (196,966.5 –319,198.54)	233.27 (181.6 –294.3)	0.04 (-0.12 to 0.19)	0.623
Middle	2,087,538.68 (1,682,851.28 –2,659,091.05)	1,033.85 (833.43 –1,316.91)	0.78 (0.6 to 0.95)	<0.001	5,529.56 (4,768.77 –6,206.45)	2.74 (2.36–3.07)	-0.9 (-0.96 to -0.83)	<0.001	295,640.37 (231,958.67 –379,063.46)	146.42 (114.88 –187.73)	0.11 (0 to 0.21)	0.044
High middle	2,769,785.03 (2,296,642.77 –3,386,159.2)	1,540.31 (1,277.19 –1,883.08)	-0.97 (-1.2 to -0.74)	<0.001	8,668.37 (7,822.88 –9,368.04)	4.82 (4.35–5.21)	-2.03 (-2.25 to -1.81)	<0.001	426,773.78 (339,303.08 –533,383.54)	237.33 (188.69 –296.62)	-1.51 (-1.68 to -1.35)	<0.001
High	2,344,305.5 (1,995,956.32 –2,773,807.95)	1,356.48 (1,154.91 –1,605)	0.86 (0.79 to 0.93)	<0.001	9,700.92 (9,032.4 –10,223.03)	5.61 (5.23–5.92)	0.32 (0.23 to 0.41)	<0.001	394,814.57 (327,706.33 –474,559.58)	228.45 (189.62 –274.59)	0.56 (0.49 to 0.63)	<0.001

Joinpoint regression was used to analyze the progression from 2000 to 2019. p <0.05 signifies statistical significance. APC, annual percentage change; ASDALY, age-standardized disability-adjusted life year; ASDR, ae-standardized death rate; ASPR, age-standardized prevalence rate; DALY, disability-adjusted life year; SDI, sociodemographic index; UI, uncertainty interval.

Table 3. Summary of the global and regional burden of liver cancer from alcohol prevalence, death, DALYs, age-standardized rates, and temporal progression from 2000 to 2019.

	Prevalence				Deaths				Disabilties			
	2019 cases (95% UI)	2019 ASPR, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*	2019 deaths (95% UI)	2019 ASDR, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*	2019 DALYs (95% UI)	2019 ASDALYs, per 100,000 people (95% UI)	2000–2019 APC (95% CI)	*p*
Overall	68,468.13 (53,359.86–86,281.67)	9.77 (7.62–12.31)	0.35 (0.2 to 0.5)	<0.001	54,627.46 (43,050.59–68,173.44)	7.8 (6.14–9.73)	-0.48 (-0.55 to -0.42)	<0.001	976543.9 (763189.35–1228121.32)	139.38 (108.93–175.29)	-0.68 (-0.77 to -0.6)	<0.001
Sex												
Female	13,843.77 (10,014.78–18,521.6)	3.64 (2.63–4.87)	-0.23 (-0.41 to -0.05)	0.012	12,221.6 (8,968.85–16,271.94)	3.21 (2.36–4.28)	-0.88 (-0.99 to -0.77)	<0.001	212,685.02 (154,166.73–287,393.79)	55.94 (40.55–75.59)	-1.07 (-1.19 to -0.95)	<0.001
Male	54,624.37 (43,095.78–67,801.15)	17.05 (13.45–21.16)	0.41 (0.28 to 0.54)	<0.001	42,405.85 (33,617.83–52,531.28)	13.23 (10.49–16.39)	-0.47 (-0.54 to -0.4)	<0.001	763,858.88 (603,362.37–951,481.18)	238.37 (188.29–296.92)	-0.7 (-0.83 to -0.58)	<0.001
Region												
Africa	1,793.57 (1,295.87–2,388.46)	5.29 (3.82–7.04)	-0.72 (-0.83 to -0.62)	<0.001	2,217.59 (1,625.48–2,928.14)	6.53 (4.79–8.63)	-0.83 (-0.89 to -0.77)	<0.001	40,961.91 (29,497.48–54,792.4)	120.71 (86.92–161.46)	-0.89 (-0.99 to -0.79)	<0.001
Eastern Mediterranean	1,207.32 (774.2–1,818.84)	4.11 (2.64–6.2)	0.95 (0.76 to 1.14)	<0.001	1,302.28 (844.53–1,952.62)	4.44 (2.88–6.65)	0.42 (0.05 to 0.79)	0.025	24,738.13 (15,707.34–38,061.33)	84.27 (53.51–129.66)	0.4 (0.01 to 0.79)	0.046
Europe	20,305.95 (15,870.01–25,283.18)	13.86 (10.83–17.26)	1.51 (1.41 to 1.62)	<0.001	15,221.13 (12,031.49–18,662.75)	10.39 (8.21–12.74)	0.68 (0.56 to 0.8)	<0.001	262,963.23 (206,534.68–324,771.63)	179.51 (140.99–221.7)	0.43 (0.31 to 0.56)	<0.001
Americas	10,749.54 (8,519.34–13,195.2)	9.63 (7.63–11.82)	2.58 (2.51 to 2.64)	<0.001	9,068.95 (7,372.11–10,747.26)	8.12 (6.6–9.63)	2.05 (1.98 to 2.12)	<0.001	162,287.27 (131,217.82–192,554.1)	145.35 (117.52–172.46)	2.11 (1.98 to 2.24)	<0.001
Southeast Asia	9,101.99 (6,624.52–11,991.93)	6.68 (4.86–8.8)	0.93 (0.84 to 1.02)	<0.001	10,505.39 (7,889.04–13689.55)	7.71 (5.79–10.05)	0.77 (0.51 to 1.03)	<0.001	192,226.29 (143,841–252,106.95)	141.08 (105.57–185.03)	0.6 (0.33 to 0.88)	<0.001
Western Pacific	25,140.61 (18,843.84–33,426.26)	10.46 (7.84–13.9)	-1.06 (-1.33 to -0.78)	<0.001	16,151.28 (12,091.36–21,242.82)	6.72 (5.03–8.84)	-2.77 (-3.05 to -2.49)	<0.001	290,517.58 (214,279.69–383,322.75)	120.85 (89.14–159.46)	-3.04 (-3.33 to -2.75)	<0.001
SDI												
Low	1,794 (1,295.78–2,397.95)	4.81 (3.48–6.44)	-0.23 (-0.24 to -0.22)	<0.001	2,208.98 (1,621.05–2,929.17)	5.93 (4.35–7.86)	-0.31 (-0.37 to -0.26)	<0.001	41,183.59 (29,788.64–54,989.27)	110.52 (79.94–147.57)	-0.4 (-0.45 to -0.35)	<0.001
Low middle	5,346.83 (4,056.35–6,946.76)	4.93 (3.74–6.4)	0.11 (-0.01 to 0.24)	0.073	6,484.79 (4,955.46–8,290.83)	5.98 (4.57–7.64)	0.04 (-0.14 to 0.21)	0.696	118,789.21 (89,722.92–154,527.52)	109.52 (82.73–142.48)	-0.21 (-0.44 to 0.02)	0.078
Middle	15,974.57 (11,707.52–21,471.56)	7.91 (5.8–10.63)	0.03 (-0.21 to 0.26)	0.812	16,230.64 (11,996.07–21,457.06)	8.04 (5.94–10.63)	-0.67 (-0.99 to -0.35)	<0.001	298,352 (217,769.06–396,289.96)	147.76 (107.85–196.26)	-0.81 (-0.99 to -0.63)	<0.001
Middle high	11,991.45 (9,231.44–15,185.96)	6.67 (5.13–8.45)	-1.1 (-1.25 to -0.95)	<0.001	11,178.17 (8,918.17–13,868.74)	6.22 (4.96–7.71)	-1.6 (-1.79 to -1.41)	<0.001	198,604.17 (157,364.77–248,563.4)	110.45 (87.51–138.23)	-1.88 (-2.04 to -1.73)	<0.001
High	33,326.8 (26,170.94–41,221.48)	19.28 (15.14–23.85)	1.62 (1.47 to 1.76)	<0.001	18,492.44 (14,885.66–22,487.45)	10.7 (8.61–13.01)	0.41 (0.32 to 0.5)	<0.001	319,041.63 (255,227.26–387,294.22)	184.61 (147.68–224.1)	0.18 (0.09 to 0.26)	<0.001

Joinpoint regression was used to analyze the progression from 2000 to 2019. p <0.05 signifies statistical significance. APC, annual percentage change; ASDALY, age-standardized disability-adjusted life year; ASDR, age-standardized death rate; ASPR, age-standardized prevalence rate; DALY, disability-adjusted life year; SDI, sociodemographic index; UI, uncertainty interval.

The global burden of ALD and AUD in the elderly

In 2019, among the elderly, alcohol-associated cirrhosis accounted for 21.8% of total cases across all age groups, with 3.23 million cases. Similarly, AUD in the elderly represented 8.69% of total AUD cases across all ages, amounting to 9.39 million cases. Lastly, liver cancer from alcohol in the elderly made up a substantial 51.27% of all such cases, with 68,468 cases, as detailed in Tables 1–3. From 2000 to 2019, the proportion of prevalence of elderly to the overall population with alcohol-associated cirrhosis (+2.1%), AUD (+2.79%), and liver cancer from alcohol (+3.93%) increased (Table S9). There were 139,027 deaths from alcohol-associated cirrhosis, 31,091 deaths from AUD, and 54,627 deaths from liver cancer from alcohol. In terms of DALYs, there were approximately 2.56 million, 1.45 million, and 976,544 DALYs related to alcohol-associated cirrhosis, AUD, and liver cancer from alcohol, respectively. The ASPRs of alcohol-associated cirrhosis, liver cancer from alcohol, and AUD were 461.66 (95% UI 344.34–596.83), 9.77 (95% UI 7.62–12.31), and 1,340.3 (95% UI 1,113.65–1,641.62) per 100,000 population, respectively. The ASDRs of these conditions were 19.84 (95% UI 15.52–24.48), 7.8 (95% UI 6.14–9.73), and 4.44 (95% UI 3.87–4.73) per 100,000 population. The ASDALYs were 364.84 (95% UI 282.71–454.25), 206.98 (95% UI 166.64–258.27), and 139.38 (95% UI 108.93–175.29) per 100,000 population for cirrhosis, AUD, and liver cancer from alcohol, respectively. An examination of trends from 2000 to 2019 indicated an annual rise in the ASPR for alcohol-associated cirrhosis (APC 0.26%, 95% CI 0.18–0.34%) and liver cancer from alcohol (APC 0.35%, 95% CI 0.2–0.5%), whereas AUD remained stable. The trend of ASDR revealed a reduction in deaths from alcohol-associated cirrhosis (APC -0.84%, 95% CI -0.99 to -0.69%), AUD (APC -0.85%, 95% CI -0.96 to -0.75%), and liver cancer from alcohol (APC -0.48%, 95% CI -0.55 to -0.42%). ASDALYs also declined in alcohol-associated cirrhosis (APC -1.01%, 95% CI -1.23 to -0.8%) liver cancer from alcohol (APC -0.68%, 95% CI -0.77 to -0.6%), and AUD (APC -0.41%, 95% CI -0.48 to -0.34%).

Alcohol-associated cirrhosis in the elderly

In 2019, the highest ASPR of alcohol-associated cirrhosis in the elderly was observed in Europe, with an ASPR of 612.2 (95% UI 475.73–758.14), whereas Africa exhibited the highest ASDR and ASDALYs at 42.99 (95% UI 30.24–57.53) and 808.82 (95% UI 555.65–1,096.64), respectively (Fig. 1A–C). The ASPR of alcohol-associated cirrhosis in the elderly demonstrated an upward trend in most regions from 2000 to 2019 (Table 1). The most notable change in ASPR was observed in Southeast Asia (APC 1.38%, 95% CI 0.98–1.78%), whereas it decreased in Europe (APC -0.13%, 95% CI -0.19 to -0.08%). In terms of SDI, low-middle SDI regions exhibited the highest ASPR with a value of 478.69 (95% UI 338.86–643.24), whereas low SDI regions exhibited the highest ASDR and ASDALYs with a value of 36.3 (95% UI 25.42 to 49.08) and 686.27 (95% UI 470.52 to 934.02) per 100,000 population (Fig. 1D–F). The uptrend in ASPR was observed across all SDI strata except for the high-middle SDI segment (APC -0.1%, 95% CI -0.13 to -0.06%) and high SDI segment (APC -0.57%, 95% CI -0.61 to -0.53%). The geographical variation in ASPRs of alcohol-associated cirrhosis in the elderly among different nations is illustrated in Fig. 2A, Table S10, and Supplementary Material 4.

AUD in the elderly

The highest burden of AUD in the elderly was observed in Europe, where the ASPR, ASDR, and ASDALYs were 1,822.79 (95% UI 1,549.02–2,150.87), 8.28 (95% UI 7.49–8.88), and 328.48 (95% UI 272 to 394.83) per 100,000 population, respectively (Fig. 3A–C). Although a decline in ASPR was observed across Europe (APC -0.64%, 95% CI -0.81 to -0.47%), ASPR was increased in other regions, with the most pronounced increase in the Western Pacific region (APC 1.4%, 95% CI 1.12–1.68%), yet it remained stable in Africa. Considering ASDR and ASDALYs, most regions exhibited a decrease in both measures, but ASDR remained stable in the Western Pacific region. When evaluated against the SDI, high-middle SDI regions exhibited the highest burden of AUD in the elderly, with ASPR and ASDALYs of 1,540.31 (95% UI

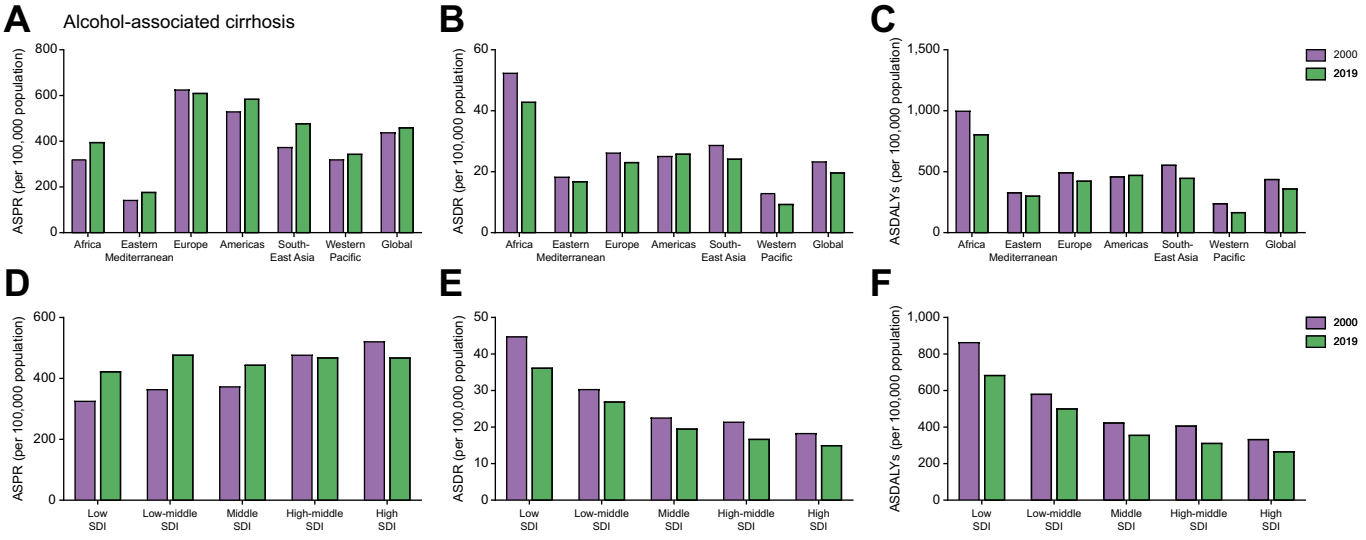

Fig. 1. ASPRs, ASDRs, and ASDLYs in patients aged 65–89 years with alcohol-associated cirrhosis in 2000 and 2019. (A, D) ASPRs, (B, E) ASDRs, and (C, F) ASDLYs, stratified by the World Health Organization region (A–C) and SDI (D–F). ASDLY, age-standardized disability-adjusted life year; ASDR, age-standardized death rate; ASPR, age-standardized prevalence rate; SDI, sociodemographic index.

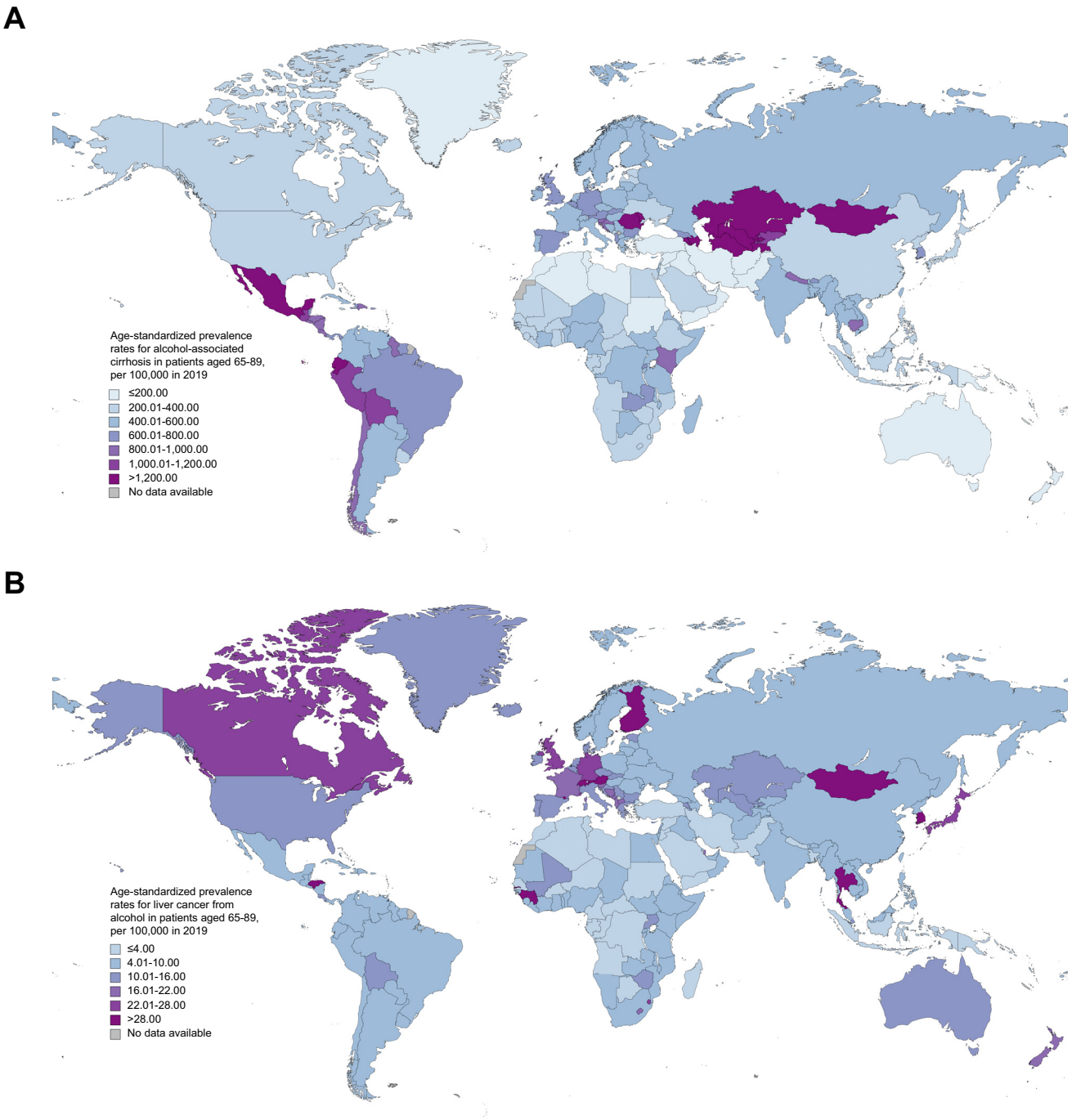

Fig. 2. Geographical variation in age-standardized prevalence rates of alcohol-associated cirrhosis in patients aged 65–89 years in 2019. (A) Alcohol-associated cirrhosis. (B) Liver cancer.

1,277.19–1,883.08) and 237.33 (95% UI 188.69–296.62) per 100,000 population, respectively (Fig. 3D–F). In contrast, ASDR was highest in high SDI regions with a value of 5.61 (95% UI 5.23–5.92). ASPR increased across most regions yet declined in high-middle SDI regions (APC -0.97%, 95% CI -1.2 to -0.74%). ASDR decreased in most SDI strata but increased in high SDI strata (APC 0.32%, 95% CI 0.23–0.41%).

Liver cancer from alcohol in the elderly

The regional variation of the ASPR of liver cancer from alcohol in the elderly across various nations is represented in Fig. 2B and Table S11. In 2019, the highest burden in terms of ASRs of liver cancer from alcohol in adults aged 65–89 years was observed in Europe, with ASPR, ASDR, and ASDALYs of 13.86 (95% UI 10.83–17.26), 10.39 (95% UI 8.21–12.74), and 179.51 (95% UI 140.99–221.7), respectively (Fig. 4A–C). The three countries with the highest ASPR per 100,000 population are Mongolia (183.28, 95% UI 114.66–269.18), the Republic of Korea (49.76, 95% UI 29.8–78.92), and Thailand (45.18, 95% UI 27.44–67.58). Similar to the prevalence rate of cirrhosis, the prevalence of liver cancer from alcohol demonstrated an upward trend in most regions from 2000 to 2019. The region of Americas experienced the most

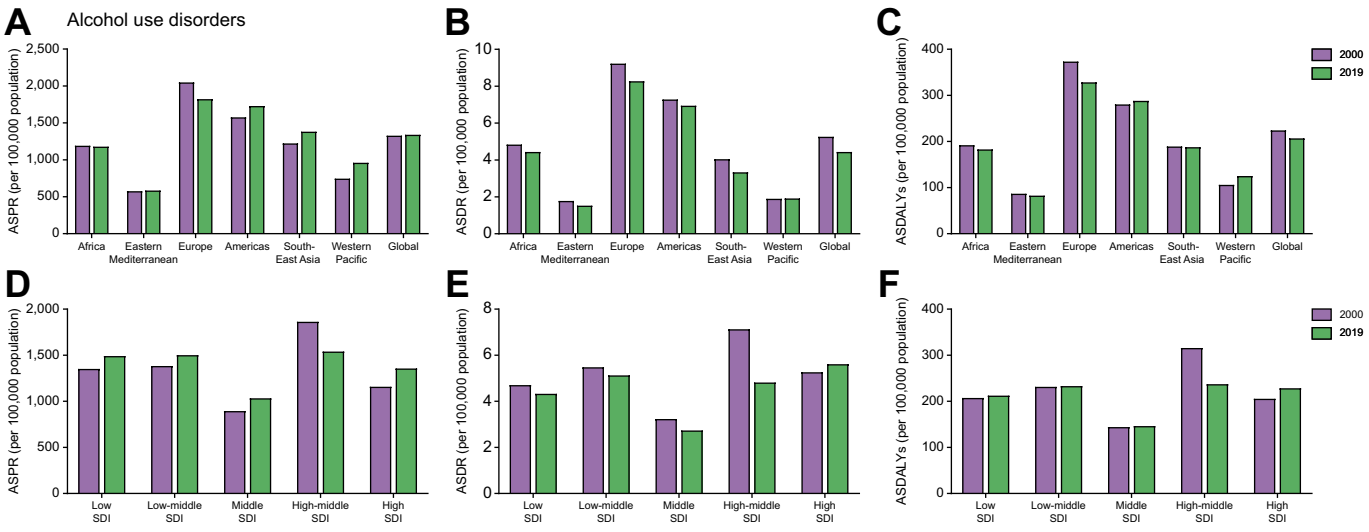

Fig. 3. ASPRs, ASDRs, and ASDLYs in patients aged 65–89 years with alcohol use disorder in 2000 and 2019. (A, D) ASPRs, (B, E) ASDRs, and (C, F) ASDLYs, stratified by the World Health Organization region (A–C) and SDI (D–F). ASDLY, age-standardized disability-adjusted life year; ASDR, age-standardized death rate; ASPR, age-standardized prevalence rate; SDI, sociodemographic index.

notable change (APC 2.58%, 95% CI 2.51–2.64%), whereas prevalence rates decreased in Africa (APC -0.72%, 95% CI -0.83 to -0.62%) and the Western Pacific region (APC -1.06%, 95% CI -1.33 to -0.78%) (Table 3). The change in mortality of liver cancer from alcohol varied across geographic regions. ASDR increased in most regions but decreased in Africa (APC -0.83%, 95% CI -0.89 to -0.77%) and the Western Pacific region (APC -2.77%, 95% CI -3.05 to -2.49%). ASDALYs also followed a similar pattern as ASDR, with an increase in most regions but a decrease in Africa (APC -0.89%, 95% CI -0.99 to -0.79%) and Western Pacific (APC -3.04, 95% CI -3.33 to -2.75%). In terms of SDI, high SDI countries exhibited the highest burden of ASPR, ASDR, and ASDALYs with values of 19.28 (95% UI 15.14–23.85), 10.7 (95% UI 8.61–13.01), and 184.61 (95% UI 147.68–224.1) per 100,000 population (Fig. 4D–F). The ASPR of liver cancer from alcohol increased in high SDI countries (APC 1.62%, 95% CI 1.47–1.76%) and decreased in low SDI countries (APC -0.23%,95% CI -0.24 to -0.22%) and high-middle SDI countries (APC -1.1%, 95% CI -1.25 to -0.95%). The ASDR of liver cancer from alcohol increased in high SDI countries (APC 0.41%, 95% CI 0.32–0.5%) and remained stable in low-middle SDI countries while decreasing in other strata. The ASDALYs from liver cancer from alcohol also increased in high SDI countries (APC 0.18%, 95% CI 0.09–0.26%) (Table 3).

Discussion

This study underscores the increasing prevalence of AUD and ALD as dual pathologies, affecting both the liver and addiction, in the elderly across diverse geographical regions and SDI segments. In 2019, there were over 3.2 million elderly adults with

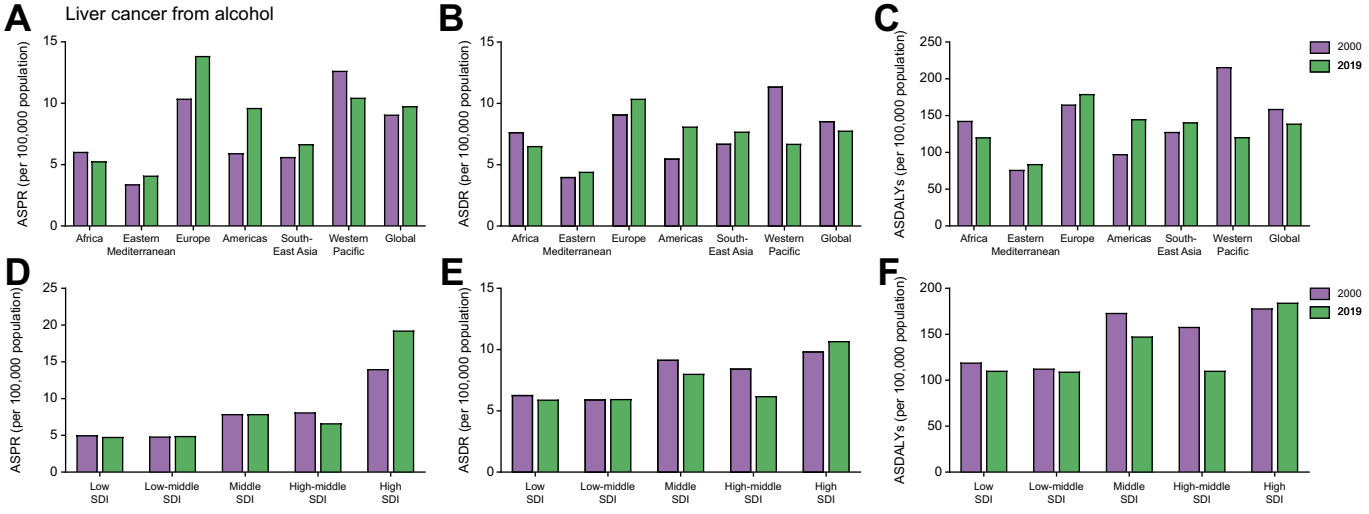

Fig. 4. ASPRs, ASDRs, and ASDLYs in patients aged 65–89 years with liver cancer from alcohol in 2000 and 2019. (A, D) ASPRs, (B, E) ASDRs, and (C, F) ASDLYs, stratified by the World Health Organization region (A–C) and SDI (D–F). ASDLY, age-standardized disability-adjusted life year; ASDR, age-standardized death rate; ASPR, age-standardized prevalence rate; SDI, sociodemographic index.

alcohol-associated cirrhosis, 68,000 with liver cancer from alcohol, and 9.4 million with AUD. The burden of AUD and ALD was higher in the elderly than in the general population. Interestingly, the elderly accounted for an increasing proportion of patients with AUD and ALD, with over half of patients with liver cancer being >65 years old. The prevalence rates of AUD and ALD in the elderly increased in most regions and SDI strata. Mortality and disability rates of alcohol-associated cirrhosis and AUD declined, but alcohol-associated liver cancer burden increased in the Eastern Mediterranean, Europe, the Americas, and Southeast Asia. As observed in the general population, elderly males had a higher burden of ALD and AUD than females.

Consistent with prior research, this study identified a higher burden of ALD in the elderly than in the general population.[15] Nevertheless, many current international clinical practice guidelines issued by various organizations, such as the AASLD[16] and EASL,[17] lack specific recommendations for managing ALD in older adults. Recognizing age as a significant factor in ALD could potentially lead to improving care in our aging society, particularly given the increasing proportion of ALD-related complications occurring in elderly populations. In contrast to ALD, the elderly population is likely to experience AUD similar to the overall population. General alcohol intake limits may not apply to the elderly, considering their reduced alcohol metabolism and higher comorbidities. Furthermore, the characteristics of AUD identified by conventional screening tools such as CAGE, AUDIT, or mean corpuscular volume may not be entirely generalizable to older individuals.[18–22] Hence, there is a need for screening methods specifically tailored to the elderly population that can effectively identify AUD in this demographics. As previous studies have suggested, treatment for AUD can be advantageous for older individuals, similar to their younger counterparts. Therefore, clinicians should not overlook the importance of screening elderly patients for AUD and ALD.[20]

Regionally, the burden of ALD and AUD was highest in Europe and the region of the Americas in parallel to societal norms of alcohol consumption in these regions.[23] Nevertheless, despite historically low burdens of ALD and AUD, the Eastern Mediterranean witnessed an increase in both burdens, potentially reflecting the cultural shift toward normalizing alcohol consumption.[24] Interestingly, although the burden of alcohol-associated cirrhosis, AUD, and liver cancer from alcohol were probably correlated with each other, our study pointed out that the increasing prevalence rates of each condition differ. For example, even though Europe experienced a decline in alcohol-associated cirrhosis and AUD, the prevalence rates of liver cancer attributed to alcohol were rising in these regions. For alcohol-associated cirrhosis, the countries with the highest prevalence rates in the elderly were Mongolia, Uzbekistan, and Kazakstan. In contrast, prevalence rates of liver cancer from alcohol were highest in Mongolia, the Republic of Korea, and Thailand. This disparity suggests that factors beyond alcohol consumption alone may contribute to the development of these two distinct alcohol-related liver conditions. Although alcohol consumption undoubtedly plays a central role, additional elements such as genetic predispositions and healthcare access could also influence the prevalence rates. The different burdens of ALD and AUD could be as a result of differing patterns of drinking that do not fit with the criteria of diagnosis AUD, such as binge drinking and moderate drinking. In terms of the discordance between cirrhosis and cancer burdens, this study, aligning with previous literature, pointed out that lower SDI countries were likely to have higher burdens of cirrhosis, whereas higher SDI countries showed the opposite trend.[12] In contrast, higher-SDI countries were inclined to incur a higher burden of liver cancer than lower-SDI countries.[12] This could be attributed to the increasing capacity for diagnosis and registration of cancer cases and deaths in higher SDI strata. However, the exact factor related to SDI needs to be further investigated. Apart from socioeconomic inequality in accessing medical care and having heavy regular or heavy episodic alcohol consumption, individuals with low socioeconomic status, for example, were found to experience higher alcohol-associated mortality.[25] Furthermore, in a population with low socioeconomic status, other chronic liver diseases, such as chronic viral hepatitis and metabolic dysfunction associated steatotic liver disease (MASLD), may serve as co-factors that concurrently worsen liver injury caused by alcohol. Nevertheless, a further study addressing how different SDIs preferentially influence the burden of cirrhosis and liver cancer is needed.

In terms of SDI, this study found that the prevalence of ALD and AUD was highest in high SDI countries, which aligned with previous studies in overall populations.[26,27] High SDI countries underwent a decline in mortality and disability of AUD and ALD, whereas low and low-middle SDI countries underwent an increase in these parameters of AUD and ALD, possibly reflecting alcohol industry strategies targeting these segments herein, by passing stricter regulation and public health campaigns in high SDI countries.[28] This discrepancy can be attributed to factors such as higher access to healthcare, increased health literacy, and fewer adjunctive risk factors for ALD and AUD. Hence, policymakers, particularly those in low SDI countries, should contemplate customizing policies related to ALD and AUD, considering the significant mortality and morbidity in these regions. However, it is crucial not to overlook the lower burden observed in higher SDI countries. Multiple sources of evidence have highlighted the relatively limited adoption of AUD screening practices.[29,30] Even in countries with higher rates of AUD screening, there is still a low level of AUD pharmacotherapy and low adherence to established guidelines.[31,32] In terms of ALD, which is usually clinically silent for a long time in the early stage, there are currently no existing screening guidelines.[33] Henceforth, reliable non-invasive screening methods must be implemented for populations at risk of developing advanced ALD. For healthcare providers, understanding AUD and receiving proper training are necessary to enable better detection of the problem.

In terms of sex, multiple studies have pointed out the increasing burden of ALD and AUD to a greater extent in females than in males.[34–36] In contrast, some studies found that the burden of ALD and AUD were lower in women, possibly owing to substantially lower levels of alcohol consumption.[37–39] The differences could be attributed to variations in the population of the studies, with some mainly involving younger adults or overall populations, whereas this study focused on the elderly. In addition, the GBD employs a modeling strategy rather than a cohort study design, using various estimation methods to determine disease burdens and associated risk factors, possibly explaining the discrepancies in the results.[6] Stigma and unequal healthcare access resulting in reporting biases in females, particularly in the elderly, could also lead to underestimation of the true ALD and AUD burden among women, potentially

overshadowing a high and rising burden among this demographic.[40–42] In addition, alcohol screening tools exhibited less specificity for women, and there are often missed opportunities for diagnosis and further management.[43] Furthermore, females also exhibited lower access to liver transplantation and higher mortality once cirrhosis was established.[44,45] It is therefore critical to address these disparities, ensuring equal access to healthcare resources and refining our understanding of the differential gender impacts of ALD. A comprehensive approach that considers the interaction between biological sex, social gender roles, and alcohol consumption may provide a more nuanced understanding of the burden of ALD and AUD and inform tailored interventions for preventing and managing the diseases.

Drawing upon the GBD 2019 data, first, this study acknowledged the inherent limitations tied to the unavailability of MASLD with increased alcohol intake, the attribution of only one etiology for cirrhosis and cancer, and possible confounders that could affect the burden of ALD.[6,46–49] Second, it is critical to recognize that the data from the GBD 2019 preceded the onset of the COVID-19 pandemic, which has been associated with a rise in alcohol consumption worldwide.[50–52] Third, the interpretation of decline in mortality should be considered, as GBD initially calculates total liver mortality and then divides these into five specific causes. Therefore, the decline in mortality from viral hepatitis outcomes could potentially obscure ALD-related mortality.[6,53] Fourth, this study might have underestimated the burden on the elderly owing to underdetection, as it included the population aged 65–89 years and did not assess the burden of people aged over 90 years.[18] Fifth, the GBD 2019 study could not assess the pattern of alcohol consumption and also lacked data regarding individual levels, which could affect the disease outcomes.[54] Nevertheless, this study elucidated the lowest level of burden of ALD and AUD exerted on the global healthcare system. Therefore, the insights from this study highlight the urgent need for strategies to tackle the issue of ALD and AUD, which are commonly found coexisting, including in the elderly.[55] Essentially, there is a shortage of treatments for AUD and ALD, unlike for MASLD, another common cause of chronic liver disease. Therefore, a public health policy aimed at reducing alcohol consumption and efforts to develop new therapeutic approaches to curb this silent epidemic of ALD and AUD, particularly in a relatively understudied population – the elderly – is necessary.

Conclusion

The worldwide impact of ALD and AUD is significant, with a notable burden already presenting in Europe and the region of the Americas while increasing in other areas. The burden of ALD is greater in the elderly population, whereas the burden of AUD is comparable with that in the general population. The study results emphasize the need for targeted public health interventions, including specialized screening and treatment approaches for the elderly.

Abbreviations

ALD, alcohol-associated liver disease; APC, annual percent change; ASDALY, age-standardized disability-adjusted life year; ASDR, age-standardized death rate; ASPR, age-standardized prevalence rate; ASR, age-standardized rate; AUD, alcohol use disorder; AYA, adolescents and young adults; DALY, disability-adjusted life year; GBD 2019, Global Burden of Disease 2019; GHDx, Global Health Data Exchange; ICD-10, International Classification of Diseases Tenth Revision; IHME, Institute for Health Metrics and Evaluation; MASLD, metabolic dysfunction associated steatotic liver disease; SDI, sociodemographic index; UI, uncertainty interval; YLD, years lived with disability; YLL, years of life lost.

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Conflicts of interest

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Please refer to the accompanying ICMJE disclosure forms for further details.

Authors' contributions

Conceptualization: PD, KW, DQH. Data curation: PD, NP. Formal analysis: PD, CHN. Investigation: PD, DD, MDM. Methodology: PD, SK, NC. Project administration: PD, KW, NP. Supervision: KW, NP, DQH, MN. Validation: PD, DD, SK. Visualization: PD, MDM. Writing – original draft: PD, KS, CHN, DQH, LAD. Writing – review and editing: KW, VLC, NC, MN, JPA. Have read and approved the final version of the manuscript for submission: all authors.

Data availability statement

Data from the Global Burden of Disease Study in 2019 can be retrieved using the GlobalHealth Data Exchange (GHDx) query tool (http://ghdx.healthdata.org/gbd-results-tool) which is maintained by the Institute for Health Metrics and Evaluation (IHME).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.jhepr.2024.101020.

References

Author names in bold designate shared co-first authorship

[1] Grucza RA, Sher KJ, Kerr WC, et al. Trends in adult alcohol use and binge drinking in the early 21st-century United States: a meta-analysis of 6 national survey series. Alcohol Clin Exp Res 2018;42:1939–1950.
[2] Mellinger JL, Shedden K, Winder GS, et al. The high burden of alcoholic cirrhosis in privately insured persons in the United States. Hepatology 2018;68:872–882.
[3] Julien J, Ayer T, Tapper EB, et al. The rising costs of alcohol-associated liver disease in the United States. Am J Gastroenterol 2024;119:270–277.
[4] Julien J, Ayer T, Tapper EB, et al. Effect of increased alcohol consumption during COVID-19 pandemic on alcohol-associated liver disease: a modeling study. Hepatology 2022;75:1480–1490.
[5] Meier P, Seitz HK. Age, alcohol metabolism and liver disease. Curr Opin Clin Nutr Metab Care 2008;11:21–26.
[6] GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet 2020;396:1204–1222.

[7] Hayward KL, Johnson AL, McKillen BJ, et al. ICD-10-AM codes for cirrhosis and related complications: key performance considerations for population and healthcare studies. BMJ Open Gastroenterol 2020;7:e000485.
[8] Rumgay H, Shield K, Charvat H, et al. Global burden of cancer in 2020 attributable to alcohol consumption: a population-based study. Lancet Oncol 2021;22:1071–1080.
[9] Grant BF. ICD-10 harmful use of alcohol and the alcohol dependence syndrome: prevalence and implications. Addiction 1993;88:413–420.
[10] Ye F, Zhai M, Long J, et al. The burden of liver cirrhosis in mortality: results from the Global Burden of Disease Study. Front Public Health 2022;10:909455.
[11] GBD 2016 Alcohol and Drug Use Collaborators. The global burden of disease attributable to alcohol and drug use in 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet Psychiatry 2018;5:987–1012.
[12] Liu Y, Sun Z, Wang Q, et al. Contribution of alcohol use to the global burden of cirrhosis and liver cancer from 1990 to 2019 and projections to 2044. Hepatol Int 2023;17:1028–1044.
[13] Danpanichkul P, Ng CH, Muthiah M, et al. From shadows to spotlight: exploring the escalating burden of alcohol-associated liver disease and alcohol use disorder in young women. Am J Gastroenterol 2024. https://doi.org/10.14309/ajg.0000000000002642.
[14] Clegg LX, Hankey BF, Tiwari R, et al. Estimating average annual per cent change in trend analysis. Stat Med 2009;28:3670–3682.
[15] Abu-Freha N, Estis-Deaton A, Aasla M, et al. Liver cirrhosis in elderly patients: clinical characteristics, complications, and survival-analyses from a large retrospective study. Aging Clin Exp Res 2022;34:2217–2223.
[16] Crabb DW, Im GY, Szabo G, et al. Diagnosis and treatment of alcohol-associated liver diseases: 2019 practice guidance from the American Association for the Study of Liver Diseases. Hepatology 2020;71:306–333.
[17] European Association for the Study of the Liver. EASL Clinical Practice Guidelines: management of alcohol-related liver disease. J Hepatol 2018;69:154–181.
[18] O'Connell H, Chin AV, Cunningham C, et al. Alcohol use disorders in elderly people – redefining an age old problem in old age. BMJ 2003;327:664–667.
[19] Bernadt MW, Mumford J, Taylor C, et al. Comparison of questionnaire and laboratory tests in the detection of excessive drinking and alcoholism. Lancet 1982;1:325–328.
[20] Curtis JR, Geller G, Stokes EJ, et al. Characteristics, diagnosis, and treatment of alcoholism in elderly patients. J Am Geriatr Soc 1989;37:310–316.
[21] Joshi P, Duong KT, Trevisan LA, et al. Evaluation and management of alcohol use disorder among older adults. Curr Geriatr Rep 2021;10:82–90.
[22] Gamaldo AA, Ferrucci L, Rifkind JM, et al. Age-related changes in mean corpuscular volume in adult whites and African Americans. J Am Geriatr Soc 2011;59:1763–1764.
[23] GBD 2016 Alcohol Collaborators. Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. Lancet 2018;392:1015–1035.
[24] Safiri S, Nejadghaderi SA, Noori M, et al. Burden of diseases and injuries attributable to alcohol consumption in the Middle East and North Africa region, 1990–2019. Sci Rep 2022;12:19301.
[25] Probst C, Lange S, Kilian C, et al. The dose–response relationship between socioeconomic deprivation and alcohol-attributable mortality risk – a systematic review and meta-analysis. BMC Med 2021;19:268.
[26] Zhang N, Xue F, Wu XN, et al. The global burden of alcoholic liver disease: a systematic analysis of the Global Burden of Disease Study 2019. Alcohol Alcohol 2023;58:485–496.
[27] Xie C, Singal AK. Global burden of cirrhosis and liver cancer due to alcohol: the past, present, and the future. Hepatol Int 2023;17:830–832.
[28] Walls H, Cook S, Matzopoulos R, et al. Advancing alcohol research in low-income and middle-income countries: a global alcohol environment framework. BMJ Glob Health 2020;5:e001958.
[29] Mushi D, Moshiro C, Hanlon C, et al. Missed opportunity for alcohol use disorder screening and management in primary health care facilities in northern rural Tanzania: a cross-sectional survey. Subst Abuse Treat Prev Pol 2022;17:50.
[30] AlShamlan NA. Screening and management of tobacco, alcohol, and unhealthy drug use in Saudi Arabia: uptake and practices from primary care physicians' perspective. Fam Pract 2022;39:1031–1040.
[31] Mushi D, Francis JM, Moshiro C, et al. Integration of alcohol use disorder interventions in general health care settings in Sub-Saharan Africa: a scoping review. Front Psychiatry 2022;13:822791.
[32] Rathod SD, De Silva MJ, Ssebunnya J, et al. Treatment contact coverage for probable depressive and probable alcohol use disorders in four low- and middle-income country districts: the PRIME cross-sectional community surveys. PLoS One 2016;11:e0162038.
[33] Asphaug L, Thiele M, Krag A, et al. Cost-effectiveness of noninvasive screening for alcohol-related liver fibrosis. Hepatology 2020;71:2093–2104.
[34] Ilyas F, Ali H, Patel P, et al. Rising alcohol-associated liver disease-related mortality rates in the United States from 1999 to 2022. Hepatol Commun 2023;7:e00180.
[35] Anouti A, Mellinger JL. The changing epidemiology of alcohol-associated liver disease: gender, race, and risk factors. Semin Liver Dis 2023;43:50–59.
[36] Bertha M, Shedden K, Mellinger J. Trends in the inpatient burden of alcohol-related liver disease among women hospitalized in the United States. Liver Int 2022;42:1557–1561.
[37] White AM. Gender differences in the epidemiology of alcohol use and related harms in the United States. Alcohol Res 2020;40:1.
[38] Huang DQ, Mathurin P, Cortez-Pinto H, et al. Global epidemiology of alcohol-associated cirrhosis and HCC: trends, projections and risk factors. Nat Rev Gastroenterol Hepatol 2023;20:37–49.
[39] Tan DJH, Setiawan VW, Ng CH, et al. Global burden of liver cancer in males and females: changing etiological basis and the growing contribution of NASH. Hepatology 2023;77:1150–1163.
[40] Pinedo M, Zemore S, Beltran-Giron J, et al. Women's barriers to specialty substance abuse treatment: a qualitative exploration of racial/ethnic differences. J Immigr Minor Health 2020;22:653–660.
[41] Milic J, Glisic M, Voortman T, et al. Menopause, ageing, and alcohol use disorders in women. Maturitas 2018;111:100–109.
[42] Griffin SM, Karia FP, Zimmerman A, et al. A mixed-methods study: sex differences in experiences of stigma associated with alcoholism and alcohol use disorders among injury patients in Tanzania. Alcohol Clin Exp Res 2020;44:1700–1707.
[43] Bradley KA, Boyd-Wickizer J, Powell SH, et al. Alcohol screening questionnaires in women: a critical review. JAMA 1998;280:166–171.
[44] Keyes KM, Li G, Hasin DS. Birth cohort effects and gender differences in alcohol epidemiology: a review and synthesis. Alcohol Clin Exp Res 2011;35:2101–2112.
[45] **Kaplan A**, **Wahid N**, Fortune BE, et al. Black patients and women have reduced access to liver transplantation for alcohol-associated liver disease. Liver Transpl 2023;29:259–267.
[46] Danpanichkul P, Ng CH, Muthiah MD, et al. The silent burden of non-alcoholic fatty liver disease in the elderly: a global burden of disease analysis. Aliment Pharmacol Ther 2023;58:1062–1074.
[47] Tan DJH, Ng CH, Muthiah M, et al. Rising global burden of cancer attributable to high BMI from 2010 to 2019. Metabolism 2023;152:155744.
[48] Diaz LA, Arab JP, Louvet A, et al. The intersection between alcohol-related liver disease and nonalcoholic fatty liver disease. Nat Rev Gastroenterol Hepatol 2023;20:764–783.
[49] **Danpanichkul P**, **Suparan K**, Kim D, et al. What is new in metabolic dysfunction-associated steatotic liver disease in lean individuals: from bench to bedside. J Clin Med 2024;13:278.
[50] Toyoda H, Huang DQ, Le MH, et al. Liver care and surveillance: the global impact of the COVID-19 pandemic. Hepatol Commun 2020;4:1751–1757.
[51] Bittermann T, Mahmud N, Abt P. Trends in liver transplantation for acute alcohol-associated hepatitis during the COVID-19 pandemic in the US. JAMA Netw Open 2021;4:e2118713.
[52] Da BL, Im GY, Schiano TD. Coronavirus disease 2019 hangover: a rising tide of alcohol use disorder and alcohol-associated liver disease. Hepatology 2020;72:1102–1108.
[53] Paik JM, Henry L, Younossi ZM. Nonalcoholic fatty liver disease mortality may not be decreasing: a need for careful interpretation of GBD 2019 estimates of liver deaths. Cell Metab 2023;35:1087–1088.
[54] DiMartini A, Day N, Dew MA, et al. Alcohol consumption patterns and predictors of use following liver transplantation for alcoholic liver disease. Liver Transpl 2006;12:813–820.
[55] Rogal S, Youk A, Zhang H, et al. Impact of alcohol use disorder treatment on clinical outcomes among patients with cirrhosis. Hepatology 2020;71:2080–2092.