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Global Epidemiology of Alcohol-associated Liver Disease in Adolescents and Young Adults

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Abbreviations: ALD: alcohol-associated liver disease; APC: annual percent change; COD: Cause of Death; CODEm: Cause of Death Ensemble model; GBD: Global Burden of Disease; HBSC: Health Behaviour in School-aged Children; ICD-10: 10th revision of International Classification of Diseases; IHME: Institute for Health Metrics and Evaluation; MASLD: metabolic dysfunction-associated steatotic liver disease; MetALD: metabolic dysfunction-associated steatotic liver disease and increased alcohol intake; NHANES: National Health and Nutrition Examination Survey; SDI: sociodemographic index; UI: uncertainty interval; WHO: World Health Organization

Conflict of Interest

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, Bristol-Myers Squibb, 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.

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Data Availability

Information from the Global Burden of Disease (GBD) study 2019 is accessible through the Global Health Data Exchange (GHDx) query tool, managed by the Institute for Health Metrics and Evaluation (http://ghdx.healthdata.org/gbd-results-tool).

Institutional Review Board Approval

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The data utilized in this article were obtained from the publicly available GBD database and, thus, did not necessitate any institutional review board approval, ethics clearance, or consent from study subjects.

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Data curation – Pojsakorn Danpanichkul

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ABSTRACT

Background and Aims: The objective of the study was to analyze the prevalence, incidence, and death of alcohol-associated liver disease (ALD) among adolescents and young adults globally, continentally, and nationally, focusing on trends over time.

Methods: The study analyzed data from the Global Burden of Disease (GBD) study between 2000 and 2019. It examined ALD's prevalence, incidence, and death in adolescents and young adults aged 15–29, segmented by region, nation, and sociodemographic index. The analysis utilized Joinpoint regression modeling to calculate the annual percent change (APC) in the rate of these parameters over time.

Results: In 2019, there were 281,450 ALD prevalences, 18,930 incidences, and 3,190 deaths among adolescents and young adults globally. From 2000 to 2019, the age-adjusted prevalence rate per 100,000 increased in the 25–29 age group (APC: +0.6%, p=0.003), remained stable among ages 20–24 (p=0.302) and ages 15–19 (p=0.160). Prevalence increased significantly from age 15–19 to 20–24 (19-fold increase) and from age 20–24 to 25–29 (2.5-fold increase). ALD prevalence rates increased in all age groups in adolescents and young adults in Africa and the Eastern Mediterranean region. Around three-quarters of countries and territories experienced an increase in ALD incidence rates in young adults.

Conclusion: Over two decades, the burden of ALD among adolescents and young adults has increased globally. The study emphasizes the importance of public health policies aimed at reducing alcohol consumption and preventing ALD among younger populations.

Keywords: epidemiology; liver disease; adolescent; addiction

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INTRODUCTION

Adolescence is a crucial period marked by the adoption of various behaviors, including alcohol consumption. [1] The adolescent brain is sensitive to stimulation of the dopaminergic reward system, which can make alcohol consumption more appealing. [1-3] Adolescents are prone to taking risks as part of their developmental stage, which may lead to experimenting with alcohol and other substances. [1-3] According to the Health Behaviour in School-aged Children (HBSC) 2022 survey, 35% of adolescents acknowledged consuming alcohol at least once in their lifetime, while 20% reported alcohol consumption within the last 30 days. [4] The influence of peer groups plays a significant role in shaping adolescent decision-making, including decisions related to alcohol consumption. [1-3] Consuming alcohol during adolescence not only leads to immediate detrimental effects but also increases the likelihood of engaging in harmful alcohol use later in life. [5, 6] This suggests a potential gateway effect where early exposure to alcohol sets the stage for future alcohol-related problems. Harmful alcohol use is associated with several health problems, including alcohol-associated liver disease (ALD), psychiatric disorders, cardiovascular disease, and neoplasms, among others. [7-12] In addition, mortality from alcohol represented 12% of all unnatural mortality among adolescents and young adults.[13]

ALD encompasses a spectrum of conditions, ranging from steatosis to more severe forms like steatohepatitis, fibrosis, and cirrhosis. [12, 14] In addition, half of all deaths caused by cirrhosis are attributable to alcohol consumption. [15] While numerous studies in young individuals have been focused on liver diseases like metabolic dysfunction-associated steatotic liver disease (MASLD), there is scarce comprehensive data regarding ALD in this demographic. [16-18] This study addresses this gap by utilizing data from the Global Burden of Disease (GBD) Study 2019. The aim is to examine ALD's prevalence, incidence, and death among adolescents and young adults globally, across continents, and within individual nations. [19]

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METHODS

Data Source and Estimation Methods

The information on ALD prevalence, incidence, and death in this study was accessed from the GBD 2019 dataset.[19] This dataset, compiled by the Institute for Health Metrics and Evaluation (IHME) is a comprehensive repository of epidemiological data and is widely used for global health research and policy-making. [19] Prior publications have provided details of general methodologies for these estimations. [19-23] The detailed estimation methods are described in **Supplementary Material 1.** In this study, we integrated data from various sources using the GBD methodology to estimate the burden of ALD in adolescents and young adults (15-29 years). The International Classification of Diseases 10th revision (ICD-10) codes are utilized to identify chronic liver disease and cirrhosis from alcohol consumption. [23-25] Countries are grouped according to their developmental level using the Sociodemographic Index (SDI). The calculation of SDI is based on several indicators*,* such as the total fertility rate, average educational attainment, and income per capita (**Supplementary Table 1)**. The burden of ALD was stratified based on the World Health Organization (WHO) classification into six regions, including Africa, the Eastern Mediterranean, Europe, the Region of the Americas, Southeast Asia, and the Western Pacific.

Statistical Analysis

The estimates for the prevalence, incidence, and death reported in this study are accompanied by 95% uncertainty intervals (UIs). UIs are determined by identifying the 2.5th and 97.5th ranked values across all 1,000 draws from the posterior distribution. This method accounts for the inherent uncertainty present in statistical modeling and provides a range of values for estimates. The GBD 2019 population estimate method was used to calculate the age-standardized rates. [19] Incidence rates were computed by dividing the number of new disease cases in a specific age group by the total population in that group, then multiplying by 100,000. Likewise, prevalence rates were determined by dividing the number of cases in a specific age group by the total population in that group, then multiplying by 100,000. Finally, death rates were determined by dividing the number of deaths in a particular age group by the corresponding population and multiplying by 100,000. We assessed the age-standardized rates, the weighted average of the age-specific rates. In this standardization, the weights are the proportions of a standard population in the corresponding age groups. Thus, the potential confounding effect of age was removed when comparing age-standardized rates computed using the same standard population, enabling comparisons across different populations without the effect of differences in age distributions. The annual percent change (APC) was calculated to evaluate changes in age-standardized rates over time. This analysis utilized the Joinpoint regression modeling version 4.9.1.0 of the Joinpoint regression program, which was developed by the Statistical Research and Applications Branch of the National Cancer Institute in Bethesda,

USA. The joinpoint regression is a set of linear statistical models that address the trends in disease burdens linked to disease over time. This model utilizes the least squares method to estimate the changing patterns of disease rates, offering a more objective analysis compared to traditional linear trend analyses. [10, 26, 27]

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RESULTS

Alcohol-associated liver disease burden among adolescents and young adults in 2019

In 2019, there were 281,450 prevalent cases, 18,930 incident cases, and 3,190 deaths of ALD in young adults globally (**Figure 1A-1C**). The ALD age-standardize rates of prevalence, incidence, and death (per 100,000) ranged from 0.7, 0.0, and 0.0 among ages 15–19 years to 13.1, 0.8, and 0.1 among ages 20–24 years to 32.8, 2.3, and 0.4 among ages 25–29 years, respectively (**Figure 1D-1F**). The age-standardized prevalence rate saw a 19-fold increase from ages 15–19 to 20–24 and a 2.5-fold rise from ages 20–24 to 25–29.

At the regional level, Southeast Asia reported the highest prevalence rate of ALD among the 15–19 age group (1.2 per 100,000) and 20–24 age group (24.1 per 100,000) (**Table 1**). In contrast, the highest ALD prevalence rates in the 25–29 age group were observed in the European region (64.5 per 100,000 population) (**Table 1**). According to socioeconomic status, low-middle SDI countries exhibited the highest prevalence rates in ages 15–19 (1.0 per 100,000), 20–24 (18.6 per 100,000), and 25–29 (45.8 per 100,000) compared to other SDI groups (**Table 1**).

Trends in alcohol-associated liver disease prevalence, incidence, and death rate from 2000 through 2019

From 2000 to 2019, the ALD age-standardized prevalence rate per 100,000 increased for those aged 25–29 years (APC=+0.6%, p=0.003); and remained stable among ages 20–24 years (p=0.302); and ages 15–19 years (p=0.16) (**Table 1**). The worsening trend (APC>0%) in ALD prevalent cases occurred in Africa and the Eastern Mediterranean in all stages of adolescence and young adults. In Africa, prevalence rates per 100,000 increased in those aged 25–29 (APC＝+1.5%, p<0.001), 20–24 (APC=+1.3%, p<0.001), 15–19 (APC=+0.6%, p<0.001) (**Figure 2A-2C**). In the Eastern Mediterranean region, prevalence rates per 100,000 also increased in those aged 25–29 (APC=+1.3%, p<0.001), 20–24 (APC=+1.2%, p<0.001), 15–19 (APC=+0.6%, p<0.001). The prevalence rates increased in those aged 25–29 (APC=+0.8%, p=0.026) in Southeast Asia. The prevalence rates also rose in those aged 25–29 (APC=+0.5%, p=0.001) and 20–24 (APC=+0.3%, p<0.001) in Europe. Among patients aged 15–19, prevalence rates remained stable in Europe (p=0.707) but decreased in the region of the Americas (APC=-0.5%, p<0.001), Southeast Asia (APC=-0.2%, p=0.009), and the Western Pacific region (APC=-1.0%, p<0.001) (**Table 1**). Regarding ages 20-24, prevalence rates per 100,000 population decreased in the region of the Americas (APC=-1.1%, p<0.001) and the Western Pacific region (APC=-0.6%, p<0.001) (**Table 1**). In people aged 25–29, prevalence rates also declined in the region of the Americas (APC=-1.3%, p<0.001) and remained stable in the Western Pacific region (p=0.204). Stratified by SDI, prevalence rates remained stable or declined in most SDI strata in adolescent and young adults, but increased in low (APC=0.6%, p=0.003), low-middle (APC=0.8%, p<0.001), and middle SDI (APC=0.8%, p<0.001) in people aged 25–29 (**Table 1**).

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From 2000 through 2019, there was an annual increase in ALD incidence per 100,000 for the age group 15–19 years (APC=+0.5%, p<0.001), ages 20–24 years (APC=+0.2%, p=0.003), and ages 25–29 years (APC=+0.3%, p<0.001) (**Table 2**). The incidence rates of ALD varied across WHO regions, with three regions (Africa, Eastern Mediterranean, and Southeast Asia) showing a significant increase in incidence rates for ages 15–19 years; the same regions also experienced increases for ages 20–24 years, and four regions (Africa, Eastern Mediterranean, Southeast Asia, and Western Pacific) showed increases for ages 25–29. According to SDI, the ALD incidence rates rose in the low, low-middle, and middle SDI (except 25-29 years) categories, whereas there was a decrease in the high-middle and high SDI categories among adolescents and young adults (**Table 2**). When categorized by country, approximately 75% of nations/ territories show a rising trend in the incidence rates of ALD among young adults (**Figure 3A-B, Supplementary Table 2, and Supplementary Material 2**).

In contrast to the prevalence rate, the ALD death rate per 100,000 decreased in all age groups (ages 15–19 years [APC=-1.4%, p<0.001]; ages 20–24 years [APC=-1.1%, p<0.001]; and ages 25–29 years [APC=-0.6%, p=0.022]) globally (**Figure 2D-2F**). However, joinpoint analysis indicated an increasing trend in ALD death rate during 2000–2019 among ages 20–24 years (APC=+0.3%, p<0.001) and among ages 25–29 years (APC=+0.2%, p<0.001) in the Eastern Mediterranean region. Death rate also increased in people aged 25–29 in the European region (APC=+1.0%, p<0.001). Regarding SDI, age-adjusted death rates decreased in all SDI strata except remained stable in low SDI (p=0.054) and high-middle SDI in ages 25–29 (p=0.114) (**Table 3**).

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DISCUSSION

To the best of our knowledge, this is the most up-to-date study regarding the global epidemiology of ALD in adolescents and young adults. [28] Over 280,000 prevalent cases, 18,000 incident cases, and approximately 3,000 deaths were reported among individuals aged 15–29 years due to ALD. The prevalence of ALD increased significantly as individuals transitioned from the 15–19 to the 20–24 age group, with a nearly 19-fold increase. There was also a 2.5-fold increase in prevalence from the 20–24 to the 25–29 age group. The study noted a rising trend in prevalence rates across most geographical regions. Around 75% of countries experienced an increase in incidence rates of ALD among adolescents and young adults.

Southeast Asia bears the highest prevalence of ALD in adolescent and young adults, with over half of global prevalences occurring in this region. While Southeast Asia has the highest burden in younger age groups, Europe has the highest burden for the 25–29 age group. Prevalence rates are observed to be increasing across most regions, indicating a global trend of rising ALD burden among adolescents and young adults. The significant increase in prevalence rates from age 15–19 to 20–24 underscores the importance of early intervention and prevention strategies targeting harmful alcohol use among adolescents. The occurrence of MASLD and related metabolic factors among adolescents and young adults may exacerbate the progression of liver disease, adding to the burden of ALD. [16, 18, 24, 29] Additionally, the recent National Health and Nutrition Examination Survey (NHANES) study reported that mortality in people with MASLD who have increased alcohol intake (MetALD) and in those with ALD with metabolic dysfunction was higher than in those with MASLD alone. [30] These findings draw attention to alcohol consumption policies due to the poorer prognosis in these individuals. [30] However, many countries still have insufficient alcohol-related policies, emphasizing the need for more effective measures to address alcohol consumption among adolescents and young adults. [31, 32] Implementing comprehensive alcohol-related policies targeted at this population is crucial not only for mitigating the impact of ALD but also for addressing other medical conditions associated with alcohol consumption. [8, 33]

There is evidence of a rising incidence of ALD among adolescents and young adults in both the African and Eastern Mediterranean regions. This increase may be attributed to the growing influence of the alcohol industry in these areas and the adoption of Western norms regarding alcohol consumption. [34] Alcohol consumption in these regions is likely underreported, possibly due to religious factors in the Eastern Mediterranean and unrecorded alcohol consumption in Africa. [35-37] Underreporting may obscure the true burden of ALD and hinder effective policy development. [38, 39] There is a general decline in mortality rates across most WHO regions, except for increasing rates in the Eastern Mediterranean region among individuals aged 20–24 and 25–29. The GBD methodology involves an initial estimation of overall liver mortality, which is then divided into etiology-specific categories through a proportion model. [40] The decline in overall mortality, attributed to

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improved management of chronic hepatitis B and C, may obscure trends specifically related to ALD mortality. [40, 41] Limited data on etiological proportions and improvements in managing hepatitis B and C may lead to an underestimation of ALD mortality trends. [42] There is a need for more granular and comprehensive research to accurately examine patterns and impacts of ALD mortality, especially considering potential underestimation due to current methodologies. The harm of alcohol extends beyond ALD, including other medical conditions, self-harm, cancer, and interpersonal violence. Hence, the burden of alcohol in adolescents is substantial. [43, 44] In addition, since ALD increased by 19-fold from ages 15-19 to 20-24, detecting individuals at risk for cirrhosis early in life within the general population is essential for several reasons. Firstly, research indicates that cirrhosis typically develops after many years of alcohol exposure and remains asymptomatic until the disease reaches advanced stages, making it difficult to reverse. [14] Therefore, it is crucial to intervene before reaching the legal drinking age and developing ALD or alcohol-associated cirrhosis. Second, achieving remission of alcohol use disorder may be more difficult in younger individuals. [45] Thirdly, since ALD in adolescents is relatively understudied, A prospective study examining the impact of alcohol on liver outcomes should involve individuals from a very young age. [46, 47]

It is crucial to acknowledge the limitations outlined in our study, which may affect the interpretation and generalizability of our findings. The accuracy of GBD estimates is contingent upon the quality and completeness of vital registration systems across different countries. Variability in data quality may introduce bias and uncertainty into our analysis. [19] The GBD data used in our study predates the COVID-19 pandemic, which has had a significant impact on global alcohol consumption patterns. [48-50] The pandemic may have influenced alcohol consumption behaviors and the burden of ALD. In addition, prior research has revealed considerable underreporting of alcohol consumption among patients with MASLD, leading to an underestimated burden of ALD. [39, 51] For example, an HBSC report that focuses on adolescent substance use in Europe, Central Asia, and Canada found that substance use, including alcohol, in adolescents increased sharply in the 2021/ 2022 survey. [4] Lastly, the GBD 2019 study lacks detailed insights into specific types and patterns of alcohol consumption, including individual consumption levels and heavy episodic drinking among adolescents and young adults. This limitation may limit the depth of understanding of ALD trends. [52, 53] Despite limitations, our study provides valuable insights into the minimum global burden of ALD among adolescents and young adults. It highlights a notable surge in ALD as adolescents transition into young adulthood, corresponding to an increase in instances of drunkenness as this demographic ages. [4] This information is essential for informing policymakers and healthcare practitioners in their efforts to develop effective strategies for addressing ALD early in life.

In summary, our study underscores the pressing need for public policies and prevention programs aimed at curbing alcohol use among adolescents and young adults. Moving forward, efforts to improve data quality,

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incorporate pandemic-era trends, and gain a deeper understanding of alcohol consumption patterns will enhance the accuracy and relevance of future research in adolescents and young adults.

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FIGURE LEGEND

Figure 1

(A) The number of prevalences of ALD in patients aged 15–29 cases in 2000 and 2019; classified by World Health Organization Regions

(B) The number of incidences of ALD in patients aged 15–29 cases in 2000 and 2019; classified by World Health Organization Regions

(C) The number of deaths of ALD in patients aged 15–29 cases in 2000 and 2019; classified by World Health Organization Regions

(D) Age-standardized prevalence rates attributable to ALD in patients aged 15–29 from 2000 to 2019 by age group

(E) Age-standardized incidence rates attributable to ALD in patients aged 15–29 from 2000 to 2019 by age group

(F) Age-standardized death rates attributable to ALD in patients aged 15–29 from 2000 to 2019 by age group

Legend: ASDR: age-standardized death rates; ASIR: age-standardized incidence rates; ASPR: age-standardized prevalence rates

Figure 2

(A) Age-standardized prevalence rates attributable to ALD in patients aged 15–19 from 2000 to 2019 by the World Health Organization regions

(B) Age-standardized prevalence rates attributable to ALD in patients aged 20–24 from 2000 to 2019 by the World Health Organization regions

(C) Age-standardized prevalence rates attributable to ALD in patients aged 25–29 from 2000 to 2019 by the World Health Organization regions

(D) Age-standardized death rates attributable to ALD in patients aged 15–19 from 2000 to 2019 by the World Health Organization regions

(E) Age-standardized death rates attributable to ALD in patients aged 20–24 from 2000 to 2019 by the World Health Organization regions

(F) Age-standardized death rates attributable to ALD in patients aged 25–29 from 2000 to 2019 by the World Health Organization regions

Legend: ASDR: age-standardized death rate; ASPR: age-standardized prevalence rate

Figure 3

(A) Annual Percent Change of age-standardized incidence rates of ALD in patients aged 20–24 from 2000 to 2019 by country/ territory

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(B) Annual Percent Change of age-standardized incidence rates of ALD in patients aged 25–29 from 2000 to 2019 by country/ territory

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Table 1 Prevalence and age-standardized prevalence rate per 100,000 population of alcohol-associated liver disease in adolescents and young adults, stratified by sex, region, and sociodemographic index

	15-19				20-24				25-29			
	2019 Prevalence (95% UI)	2019 Age standardized prevalence rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*	2019 Prevalence (95% UI)	2019 Age standardized prevalence rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*	2019 Prevalence (95% UI)	2019 Age standardized prevalence rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*
Overall	4,190 (1,010 to 9,540)	0.7 (0.2 to 1.5)	0.1 (0.0 to 0.2)	0.16	78,790 (42,910 to 136,630)	13.1 (7.1 to 22.8)	0.3 (-0.2 to 0.8)	0.302	198,470 (113,770 to 319,110)	32.8 (18.8 to 52.7)	0.6 (0.2 to 1.0)	0.003
Females	1,110 (250 to 2,610)	0.4 (0.1 to 0.9)	0.2 (0.1 to 0.2)	<0.001	20,320 (10,240 to 37,260)	6.9 (3.5 to 12.6)	0.4 (0.0 to 0.8)	0.054	51,340 (26,670 to 88,780)	17.1 (8.9 to 29.5)	0.5 (0.2 to 0.8)	0.002
Males	3,090 (760 to 6,950)	1.0 (0.2 to 2.2)	0.1 (-0.1 to 0.2)	0.391	58,460 (32,400 to 98,980)	19.2 (10.6 to 32.5)	0.2 (-0.2 to 0.7)	0.325	147,130 (85,990 to 232,610)	48.3 (28.2 to 76.3)	0.5 (0.2 to 0.8)	0.003
World Health Organization region												
Africa	710 (140 to 1,780)	0.6 (0.1 to 1.5)	0.6 (0.5 to 0.7)	<0.001	8,700 (4,090 to 16,580)	8.6 (4.1 to 16.5)	1.3 (1.0 to 1.5)	<0.001	17,890 (8,600 to 34,480)	20.8 (10.0 to 40.2)	1.5 (1.4 to 1.7)	<0.001
Eastern Mediterranean	300 (60 to 750)	0.4 (0.1 to 1.1)	0.6 (0.6 to 0.6)	<0.001	2,410 (1,180 to 4,540)	3.7 (1.8 to 7.1)	1.2 (0.9 to 1.5)	<0.001	4,500 (2,210 to 8,240)	7.5 (3.7 to 13.7)	1.3 (1.0 to 1.7)	<0.001
European Region	390 (90 to 960)	0.7 (0.2 to 1.8)	0.0 (-0.1 to 0.1)	0.707	11,310 (5,560 to 20,500)	20.6 (10.1 to 37.3)	0.3 (0.2 to 0.4)	<0.001	40,050 (22,360 to 66,350)	64.5 (36.0 to 106.9)	0.5 (0.2 to 0.8)	0.001
Region of the Americas	230 (60 to 540)	0.3 (0.1 to 0.7)	-0.5 (-0.6 to -0.4)	<0.001	6,690 (3,750 to 11,500)	8.6 (4.8 to 14.8)	-1.0 (-1.2 to -0.9)	<0.001	19,520 (11,590 to 30,660)	25.1 (14.9 to 39.5)	-1.3 (-1.5 to -1.2)	<0.001
South-East Asia	2,260 (610 to 4,940)	1.2 (0.3 to 2.6)	-0.2 (-0.4 to -0.1)	0.009	43,850 (24,380 to 73,890)	24.1 (13.4 to 40.6)	0.3 (0.1 to 0.5)	0.009	98,250 (56,910 to 154,460)	58.0 (33.6 to 91.2)	0.8 (0.1 to 1.5)	0.026
Western Pacific	300 (70 to 700)	0.3 (0.1 to 0.6)	-1.0 (-1.3 to -0.6)	<0.001	5,750 (3,140 to 9,990)	4.9 (2.6 to 8.4)	-0.5 (-0.8 to -0.3)	<0.001	18,060 (9,990 to 30,640)	12.1 (6.7 to 20.6)	-0.1 (-0.2 to 0.0)	0.204
Sociodemographic Index												
Low SDI	930 (210 to 2,180)	0.7 (0.2 to 1.8)	0.0 (-0.1 to 0.0)	0.087	12,840 (6,560 to 22,890)	12.4 (6.3 to 22.1)	0.2 (0.1 to 0.4)	0.003	25,480 (13,900 to 44,550)	29.8 (16.3 to 52.2)	0.6 (0.2 to 0.9)	0.003
Low-middle SDI	1,640 (410 to 3,670)	1.0 (0.2 to 2.1)	-0.1 (-0.2 to -0.1)	<0.001	30,050 (16,540 to 51,110)	18.6 (10.2 to 31.6)	0.3 (0.1 to 0.5)	<0.001	67,550 (38,920 to 107,170)	45.8 (26.4 to 72.6)	0.8 (0.5 to 1.2)	<0.001
Middle SDI	960 (240 to 2,140)	0.5 (0.1 to 1.2)	-0.1 (-0.3 to 0.1)	0.557	19,330 (10,660 to 33,110)	10.6 (5.8 to 18.2)	0.4 (-0.1 to 0.9)	0.079	50,910 (29,240 to 81,230)	26.1 (15.0 to 41.6)	0.8 (0.4 to 1.2)	<0.001
High-middle SDI	400 (100 to 920)	0.5 (0.1 to 1.1)	0.0 (-0.1 to 0.0)	0.136	9,850 (5,300 to 17,270)	10.9 (5.9 to 19.1)	-0.3 (-0.4 to -0.1)	<0.001	34,490 (19,730 to 55,850)	31.7 (18.1 to 51.3)	-0.2 (-0.3 to 0.0)	0.089
High SDI	260 (60 to 620)	0.4 (0.1 to 1.1)	-1.0 (-1.1 to -1.0)	<0.001	6,680 (3,520 to 11,610)	10.8 (5.7 to 18.8)	-0.6 (-0.7 to -0.5)	<0.001	19,980 (11,580 to 32,470)	29.4 (17.1 to 47.8)	-0.6 (-0.7 to -0.5)	<0.001

Abbreviation: CI: confidence interval; SDI: sociodemographic index; UI: uncertainty interval

Table 2 Incidence and age-standardized incidence rate per 100,000 population of alcohol-associated liver disease in adolescents and young adults, stratified by sex, region, and sociodemographic index

	15-19				20-24				25-29			
	2019 Incidence (95% UI)	2019 Age standardized incidence rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*	2019 Incidence (95% UI)	2019 Age standardized incidence rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*	2019 Incidence (95% UI)	2019 Age standardized incidence rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*
Overall	190 (30 to 530)	0.0 (0.0 to 0.1)	0.5 (0.5 to 0.6)	<0.001	4,590 (1,760 to 9,450)	0.8 (0.3 to 1.6)	0.2 (0.1 to 0.4)	0.003	14,150 (5,280 to 25,750)	2.3 (0.9 to 4.3)	0.3 (0.2 to 0.4)	<0.001
Females	40 (10 to 110)	0.0 (0.0 to 0.0)	0.8 (0.7 to 0.9)	<0.001	770 (240 to 1,690)	0.3 (0.1 to 0.6)	0.3 (0.2 to 0.4)	<0.001	2,370 (790 to 4,550)	0.8 (0.3 to 1.5)	0.1 (-0.1 to 0.3)	0.167
Males	150 (30 to 410)	0.0 (0.0 to 0.1)	0.5 (0.4 to 0.5)	<0.001	3,830 (1,500 to 7,800)	1.3 (0.5 to 2.6)	0.2 (0.0 to 0.3)	0.049	11,790 (4,520 to 20,970)	3.9 (1.5 to 6.9)	0.4 (0.3 to 0.4)	<0.001
World Health Organization region												
Africa	30 (10 to 100)	0.0 (0.0 to 0.1)	1.2 (1.1 to 1.4)	<0.001	460 (150 to 1,000)	0.5 (0.2 to 1.0)	1.6 (1.5 to 1.7)	<0.001	930 (290 to 1,900)	1.1 (0.3 to 2.2)	1.9 (1.8 to 2.0)	<0.001
Eastern Mediterranean	10 (0 to 30)	0.0 (0.0 to 0.0)	1.5 (1.4 to 1.6)	<0.001	80 (20 to 190)	0.1 (0.0 to 0.3)	1.7 (1.4 to 2.0)	<0.001	160 (30 to 340)	0.3 (0.1 to 0.6)	1.7 (1.3 to 2.1)	<0.001

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European Region	20 (0 to 70)	0.0 (0.0 to 0.1)	0.2 (0.1 to 0.3)	<0.001	920 (380 to 1,800)	1.7 (0.7 to 3.3)	0.2 (0.0 to 0.4)	0.08	3,810 (1,640 to 6,600)	6.1 (2.6 to 10.6)	0.4 (-0.2 to 1.0)	0.152
Region of the Americas	10 (0 to 40)	0.0 (0.0 to 0.0)	-1.3 (-1.3 to -1.2)	<0.001	600 (260 to 1,160)	0.8 (0.3 to 1.5)	-2.1 (-2.3 to -2.0)	<0.001	2,200 (990 to 3,740)	2.8 (1.3 to 4.8)	-2.1 (-2.2 to -2.1)	<0.001
South-East Asia	90 (20 to 250)	0.0 (0.0 to 0.1)	0.8 (0.8 to 0.9)	<0.001	2,110 (760 to 4,380)	1.2 (0.4 to 2.4)	1.5 (1.3 to 1.7)	<0.001	5,340 (1,640 to 10,200)	3.2 (1.0 to 6.0)	2.3 (2.1 to 2.5)	<0.001
Western Pacific	20 (0 to 50)	0.0 (0.0 to 0.0)	-0.6 (-0.7 to -0.4)	<0.001	430 (170 to 850)	0.4 (0.1 to 0.7)	0.0 (-0.2 to 0.1)	0.435	1,700 (690 to 3,090)	1.1 (0.5 to 2.1)	0.3 (0.2 to 0.5)	<0.001
Sociodemographic Index												
Low SDI	40 (10 to 110)	0.0 (0.0 to 0.1)	0.9 (0.7 to 1.1)	<0.001	650 (220 to 1,380)	0.6 (0.2 to 1.3)	1.0 (0.9 to 1.2)	<0.001	1,370 (420 to 2,660)	1.6 (0.5 to 3.1)	1.5 (1.2 to 1.7)	<0.001
Low-middle SDI	70 (10 to 190)	0.0 (0.0 to 0.1)	0.9 (0.9 to 1.0)	<0.001	1,540 (570 to 3,190)	0.9 (0.4 to 2.0)	1.2 (1.0 to 1.4)	<0.001	4,000 (1,310 to 7,540)	2.7 (0.9 to 5.1)	1.8 (1.6 to 2.0)	<0.001
Middle SDI	50 (10 to 130)	0.0 (0.0 to 0.1)	0.4 (0.3 to 0.5)	<0.001	1,150 (450 to 2,350)	0.6 (0.2 to 1.3)	0.6 (0.2 to 0.9)	0.002	3,580 (1,370 to 6,560)	1.8 (0.7 to 3.4)	0.6 (0.4 to 0.9)	<0.001
High-middle SDI	20 (0 to 60)	0.0 (0.0 to 0.1)	-0.3 (-0.4 to -0.2)	<0.001	760 (300 to 1,510)	0.8 (0.3 to 1.7)	-0.8 (-1.1 to -0.5)	<0.001	3,270 (1,340 to 5,740)	3.0 (1.2 to 5.3)	-0.2 (-0.5 to 0.1)	0.161
High SDI	10 (0 to 40)	0.0 (0.0 to 0.1)	-1.1 (-1.2 to -1.0)	<0.001	500 (200 to 980)	0.8 (0.3 to 1.6)	-1.0 (-1.3 to -0.8)	<0.001	1,920 (900 to 3,230)	2.8 (1.3 to 4.8)	-1.1 (-1.2 to -1.0)	<0.001

Abbreviation: CI: confidence interval; SDI: sociodemographic index; UI: uncertainty interval

Table 3 Death and age-standardized death rate per 100,000 population of alcohol-associated liver disease in adolescents and young adults, stratified by sex, region, and sociodemographic index

Death	**15-19**				**20-24**				**25-29**			
	2019 Death (95% UI)	2019 Age standardized death rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*	2019 Death (95% UI)	2019 Age standardized death rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*	2019 Death (95% UI)	2019 Age standardized death rate per 100,000 (95% UI)	2000 to 2019 annual percent change (95% CI)	*p*
Overall	40 (10 to 90)	0.0 (0.0 to 0.0)	-1.4 (-1.6 to -1.1)	<0.001	730 (400 to 1,240)	0.1 (0.1 to 0.2)	-1.1 (-1.4 to -0.7)	<0.001	2,420 (1,450 to 3,840)	0.4 (0.2 to 0.6)	-0.6 (-1.2 to -0.1)	0.022
Females	10 (0 to 20)	0.0 (0.0 to 0.0)	-1.5 (-1.8 to -1.2)	<0.001	170 (90 to 300)	0.1 (0.0 to 0.1)	-1.3 (-1.6 to -0.9)	<0.001	470 (270 to 790)	0.2 (0.1 to 0.3)	-0.9 (-1.2 to -0.6)	<0.001
Males	30 (10 to 70)	0.0 (0.0 to 0.0)	-1.3 (-1.6 to -1.0)	<0.001	560 (310 to 950)	0.2 (0.1 to 0.3)	-1.0 (-1.4 to -0.6)	<0.001	1,950 (1,180 to 3,030)	0.6 (0.4 to 1.0)	-0.6 (-1.1 to 0.0)	0.045
World Health Organization region												
Africa	10 (0 to 30)	0.0 (0.0 to 0.0)	-1.1 (-1.3 to -1.0)	<0.001	140 (70 to 260)	0.1 (0.1 to 0.3)	-0.2 (-0.4 to 0.0)	0.021	360 (180 to 670)	0.4 (0.2 to 0.8)	0.0 (-0.2 to 0.1)	0.876
Eastern Mediterranean	0 (0 to 10)	0.0 (0.0 to 0.0)	-0.4 (-0.5 to -0.2)	<0.001	40 (20 to 80)	0.1 (0.0 to 0.1)	0.3 (0.2 to 0.3)	<0.001	90 (40 to 160)	0.2 (0.1 to 0.3)	0.2 (0.1 to 0.3)	<0.001
European Region	0 (0 to 10)	0.0 (0.0 to 0.0)	-3.4 (-4.0 to -2.8)	<0.001	80 (40 to 140)	0.1 (0.1 to 0.3)	-1.4 (-1.9 to -0.9)	<0.001	460 (280 to 730)	0.7 (0.4 to 1.2)	1.0 (0.5 to 1.5)	<0.001
Region of the Americas	0 (0 to 0)	0.0 (0.0 to 0.0)	-1.7 (-1.9 to -1.4)	<0.001	80 (40 to 120)	0.1 (0.1 to 0.2)	-1.9 (-2.7 to -1.2)	<0.001	310 (200 to 450)	0.4 (0.3 to 0.6)	-1.7 (-2.2 to -1.2)	<0.001
South-East Asia	20 (10 to 40)	0.0 (0.0 to 0.0)	-2.3 (-3.5 to -1.2)	<0.001	360 (200 to 590)	0.2 (0.1 to 0.3)	-1.6 (-2.4 to -0.8)	<0.001	1,060 (640 to 1,640)	0.6 (0.4 to 1.0)	-1.4 (-2.2 to -0.6)	<0.001
Western Pacific	0 (0 to 0)	0.0 (0.0 to 0.0)	-2.4 (-2.6 to -2.1)	<0.001	40 (20 to 70)	0.0 (0.0 to 0.1)	-1.7 (-2.0 to -1.4)	<0.001	150 (80 to 250)	0.1 (0.1 to 0.2)	-1.9 (-2.4 to -1.4)	<0.001
Sociodemographic Index												
Low SDI	10 (0 to 30)	0.0 (0.0 to 0.0)	-1.8 (-2.4 to -1.3)	<0.001	150 (70 to 270)	0.1 (0.1 to 0.3)	-1.0 (-1.5 to -0.6)	<0.001	380 (200 to 680)	0.4 (0.2 to 0.8)	-0.8 (-1.6 to 0.0)	0.054
Low-middle SDI	10 (0 to 30)	0.0 (0.0 to 0.0)	-2.0 (-2.7 to -1.3)	<0.001	290 (150 to 500)	0.2 (0.1 to 0.3)	-1.2 (-1.7 to -0.6)	<0.001	880 (510 to 1,410)	0.6 (0.3 to 1.0)	-0.8 (-1.6 to -0.1)	0.03
Middle SDI	10 (0 to 20)	0.0 (0.0 to 0.0)	-1.7 (-2.2 to -1.2)	<0.001	200 (110 to 340)	0.1 (0.1 to 0.2)	-1.2 (-1.5 to -0.9)	<0.001	660 (390 to 1,010)	0.3 (0.2 to 0.5)	-0.9 (-1.3 to -0.4)	<0.001

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High-middle SDI	0 (0 to 10)	0.0 (0.0 to 0.0)	-1.9 (-3.4 to -0.4)	0.014	80 (40 to 120)	0.1 (0.0 to 0.1)	-2.2 (-2.8 to -1.7)	<0.001	410 (270 to 600)
High SDI	0 (0 to 0)	0.0 (0.0 to 0.0)	-3.9 (-4.2 to -3.6)	<0.001	20 (10 to 30)	0.0 (0.0 to 0.0)	-2.8 (-2.9 to -2.6)	<0.001	100 (60 to 150)

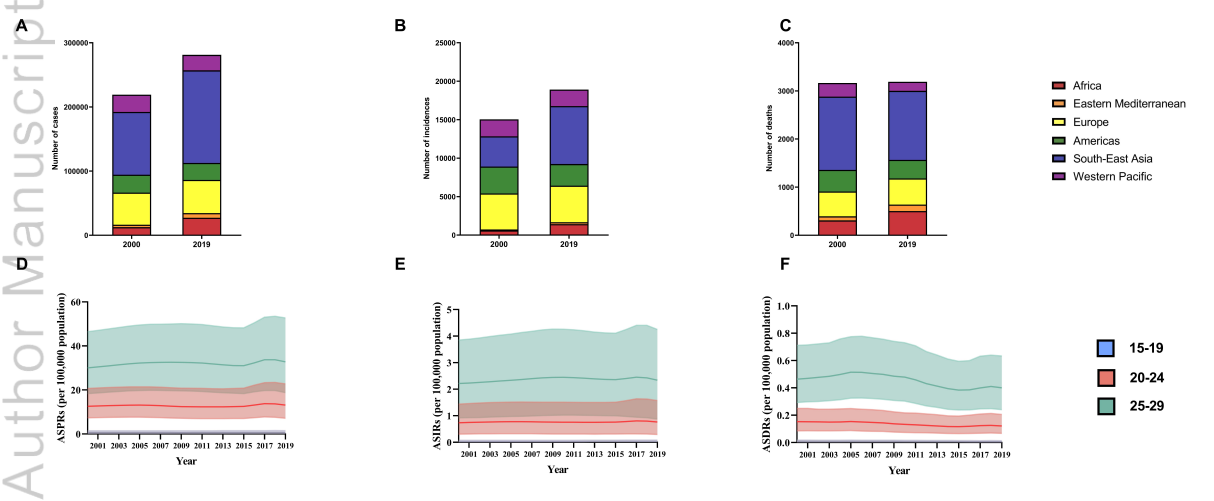
Abbreviation: CI: confidence interval; SDI: sociodemographic index; UI: uncertainty interval

Graphial abstract text

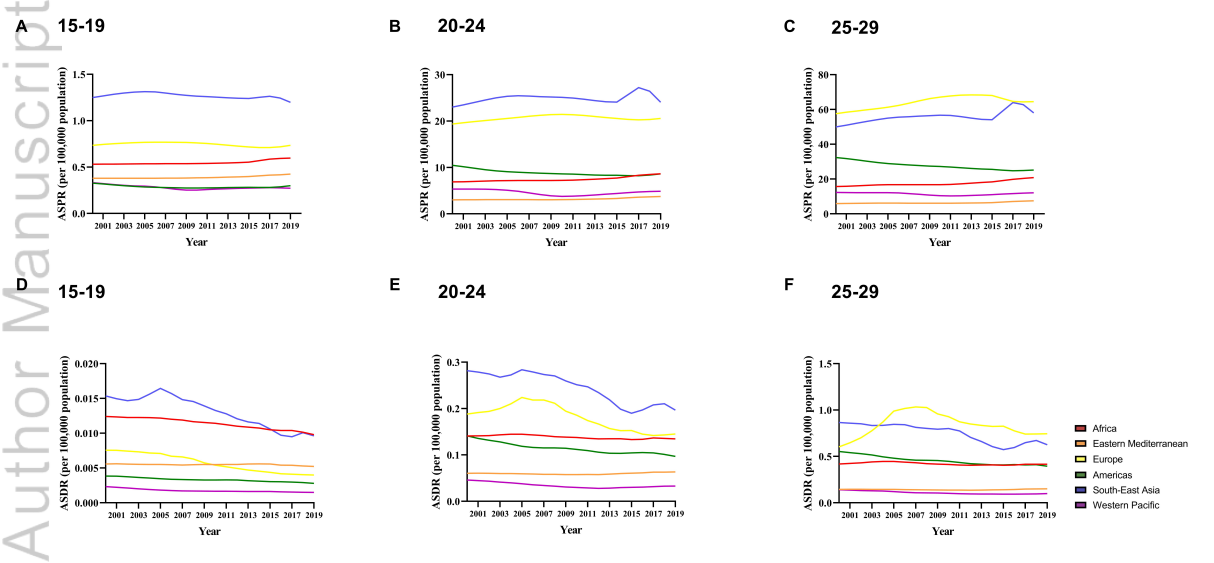
In 2019, there were over 281,000 cases of ALD in adolescent and young adults. Prevalence increased significantly from age 15–19 to 20–24 (19-fold increase) and from age 20–24 to 25–29 (2.5-fold increase). ALD has become more common, especially in Africa and the Eastern Mediterranean.

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