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# Global, regional and national burden of liver cancer 1990–2021: a systematic analysis of the global burden of disease study 2021

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## Abstract

**Background** Liver cancer is a growing global health issue, with significant geographical disparities in prevalence and mortality. Understanding these differences is key to developing effective prevention and treatment strategies.

**Methods** We analyzed liver cancer trends from 1990 to 2021 across 204 countries using data from the Global Burden of Disease (GBD) study. We modeled mortality from vital registration data and estimated non-fatal burden using primary studies, hospital discharges, and claims data. We calculated prevalence, mortality, YLLs, YLDs, and DALYs, adjusting for age and reporting rates per 100,000 population with 95% UI.

**Findings** In 2021, there were 739,299 (673114–821948) cases of liver cancer worldwide. The age-standardized prevalence rate increased from (7.75 [6.91–8.43] per 100,000 people) in 1990 to (8.68[7.90–9.67] per 100,000 people) in 2021, while the mortality rate slightly decreased from(4.48 [4.10–4.93] per 100,000 people) to (6.13 [5.58–6.84] per 100,000 people). High-income North America had the highest prevalence rate, and Southern Latin America had the lowest. Mongolia had the highest prevalence and mortality rates, while Morocco had the lowest. The total YLDs attributed to liver cancer nearly tripled from 1990 to 2021, and the age-standardized DALY rate decreased. In the frontier analysis, countries or regions with higher SDI have greater potential for burden improvement. In the frontier analysis of SDI and age-standardized liver cancer DALY rates in 2021, countries with higher SDI (> 0.85) and higher effective differences relative to their level of development include America, Canada, Germany, Netherlands, etc., while frontier countries with lower SDI (< 0.5) and lower effective differences include Somalia, Papua New Guinea, Yemen, Lao People's Democratic Republic, etc. Countries with larger effective differences include Togo, Gambia, Australia, Norway, etc.

**Conclusion** The global burden of liver cancer is decreasing, but the prevalence of liver cancer is increasing, with significant differences across regions worldwide. These findings can inform health policy and research to address this global challenge.

**Interpretation** From 1990 to 2021, the incidence of liver cancer in many regions has increased significantly, which is expected to impose a huge social and economic burden on governments and health systems in the coming years.

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Our research findings may assist policymakers in devising strategies to combat liver cancer, including educating professionals to address the burden of this complex disease.

**Keywords** Liver cancer, Socio-demographic index, Global health, Prevalence, DALYs, Frontier analysis

## Introduction

Liver cancer, is quietly spreading across the globe, with its incidence rate continuously climbing, posing a significant challenge in the field of global health [1]. Primary liver cancer is the sixth most diagnosed cancer globally and the fourth leading cause of cancer-related deaths. Histologically, it can be divided into two major categories: Hepatocellular carcinoma (accounting for 75% of all liver cancers) and Intrahepatic cholangiocarcinoma (accounting for 15% of all liver cancers) [2]. Primary liver cancer typically occurs in patients with liver disease or cirrhosis [3]. At present, over 90% of HCC cases occur in the context of chronic liver disease. Cirrhosis caused by any etiology is the strongest risk factor for HCC (Hepatocellular Carcinoma) [4]. The manifestations of liver cancer patients are typically characterized by pain in the liver area, gastrointestinal symptoms, fever, weight loss and fatigue, bleeding tendencies, lower limb edema, ascites, and other phenomena. The study underscores the need for targeted cancer prevention strategies and enhanced healthcare infrastructure in regions with the highest burden. The implications of these findings are crucial for shaping global health policy and directing research efforts towards addressing the rising challenge of liver cancer.

In previous studies, it has been found that the incidence of liver cancer and its main causes vary across different regions and countries. Hepatitis B virus (HBV) is the primary etiological agent in most parts of Asia (except Japan), South America, and Africa; Hepatitis C virus (HCV) is the main cause in Western Europe, North America, and Japan, while alcohol consumption is a causal factor in Central and Eastern Europe. Nonalcoholic steatohepatitis (NASH) is the leading cause in the "other" category and is a rapidly increasing risk factor, projected to become the main cause of liver cancer in high-income regions in the near future [5]. It is worth noting that the incidence and mortality rates of liver cancer remain significant public health issues globally. Although existing studies have covered predictions of liver cancer incidence and mortality rates [6–8]. statistical analyses of liver cancer in specific regions [1, 9], analyses of the correlation between liver cancer risk factors in different areas, as well as reports on the global disease burden of liver cancer from 1990 to 2019 [10, 11], the latest research reports on the global disease burden for 2021 are still insufficient. In previous research, there has been a notable absence of data analysis focusing on YLD, YLL, and DALY. This study leverages the latest Global Burden of Disease, Injuries, and Risk Factors Study GBD 2021 data to estimate the prevalence, mortality, YLD, YLL, and DALY for liver cancer. We present the findings on the burden of liver cancer across 204 countries and territories from 1990 to 2021.

## Methods

### Data source

The data of liver cancer analyzed in this study are derived from the GBD 2021, which provides the latest estimates of epidemiological data on the burden of 371 diseases and injuries across 21 GBD regions and 204 countries and territories from 1990 to 2021. All this data is accessible for free access through the Global Health Data Exchange (https://ghdx.healthdata.org/gbd-2021/sources) [12]. with detailed information on the data, methodologies, and statistical modelling available in previous reports [13]. The GBD study is currently the largest and most authoritative disease burden research conducted internationally, providing scientific and transparent evidence for the allocation of health resources in different countries around the world [14]. DisMod-MR 2.1 is a Bayesian meta-regression tool developed for the Global Burden of Disease (GBD) study, designed to estimate non-fatal health outcomes using sparse and heterogeneous epidemiological data. It generates internally consistent estimates of incidence, prevalence, remission, and mortality rates for various diseases and conditions. The tool is built on a Bayesian compartmental model framework, solving differential equations to modulate relationships between different epidemiological parameters, and uses a negative binomial rate model to handle overdispersion and zero-inflation in the data.

DisMod-MR 2.1 is a Bayesian meta-regression tool developed for the Global Burden of Disease (GBD) study. It is designed to estimate non-fatal health outcomes using sparse and heterogeneous epidemiological data. The tool is particularly useful for generating internally consistent estimates of incidence, prevalence, remission, and mortality rates for various diseases and conditions.

DisMod-MR 2.1 provides a comprehensive view of diseases. The tool extracts relevant epidemiological parameters such as incidence, prevalence, and mortality from published literature to form a baseline for global estimates. Household surveys, which typically include questions about health status, behaviors, and access to healthcare, provide population-representative data. Hospital admission data offers insights into the severity of diseases and the treatments received, while health insurance claims data provides detailed information on the utilization of healthcare services and associated costs. DisMod-MR 2.1 uses these data to estimate the economic burden of diseases, including direct medical costs and indirect costs. Vital registration systems provide accurate data on deaths and causes of death, and DisMod-MR 2.1 utilizes this data to estimate mortality rates for specific diseases, which is crucial for understanding the impact of diseases on population health. By analyzing death certificates, the tool can identify leading causes of death and track changes over time. Geospatial data helps to account for spatial variations in disease burden, and DisMod-MR 2.1 uses geographic information to identify areas with higher or lower prevalence rates. These data can include environmental factors, population density, and access to healthcare facilities. By integrating geospatial data, the tool can generate more accurate and localized estimates of disease burden. Time-series data provides information on how disease burden changes over time, and DisMod-MR 2.1 uses this data to track trends in incidence, prevalence, and mortality rates. These data help to identify emerging health issues and assess the impact of interventions. By analyzing time-series data, the tool can predict future disease burden and inform health policy decisions. The robustness of DisMod-MR 2.1 is validated through out-of-sample predictive validity, ensuring it provides the most accurate and reliable estimates [15]. All disease estimates in the GBD include a 95% UI, which is based on the 2.5th and 97.5th percentile values of the 500 draws from the posterior distribution [16].

#### Statistical analysis

To accurately measure the incidence trends of liver cancer, we employ the Age-Standardized Incidence Rate (ASR) and the Estimated Annual Percentage Change (EAPC). The age-standardized incidence refers to the incidence rate adjusted for the effects of age. It's important to note that the ASR for liver cancer does not directly represent the actual incidence of depression but is used to compare the incidence of depression across different countries, regions, or historical periods within the same region for easier data comparison. If there is a significant difference in the age structure of populations between two regions, comparing incidence rates alone may not accurately determine whether high incidence in a certain area is due to age composition differences or other influencing factors. Therefore, it is necessary to standardize the incidence rate by age.

The EAPC is a commonly used and significant measure of the trend in ASR over a specific time period [17]. We perform a linear regression analysis by plotting the natural logarithm of ASR against the calendar year, represented by the formula $y = \alpha + \beta x + \epsilon$, where y denotes ln (ASR) and x represents the calendar year. The EAPC is calculated as $100 \times (\exp(\beta) - 1)$, and its 95% confidence interval (CI) is derived from this linear regression model. If the EAPC and the upper limit of its 95% CI are both less than or equal to 0, we consider the ASR to be decreasing; if the EAPC and the lower limit of its 95% CI are both greater than or equal to 0, we consider the ASR to be increasing; in all other cases, the ASR is considered stable [18].

By calculating the gap between the actual Disability-Adjusted Life Years (DALY) rates and the frontier values for each nation or region, we arrive at what we term the "effective difference," reflecting the absolute distance from the health frontier. This metric serves as a benchmark to identify unrealized health potential at various stages of development and emphasizes the potential for optimization in policymaking and resource allocation to alleviate the burden of disease. Furthermore, by comparing the performance of different countries at similar Socio-demographic Index (SDI) levels, we can learn from the invaluable experiences of those at the forefront of health, informing the development of more effective and targeted disease prevention and control policies.

#### Frontier analysis

Frontier analysis constructs optimal boundary values to determine the best health indicators (such as the lowest age-standardized disease burden) that can be achieved at different levels of the Socio-demographic Index (SDI). The specific steps are as follows:

#### Selection of analysis method

The Free Disposal Hull (FDH) method combined with Data Envelopment Analysis (DEA) is employed to draw a non-linear frontier. The FDH method is a non-parametric approach that allows for the relaxation of convexity assumptions when defining the production possibility set, thereby providing more flexibility in handling data.

#### Data processing

Data from the Global Burden of Disease (GBD) database is utilized, and 500 bootstrap samples are used to calculate the average liver cancer Disability-Adjusted Life Year (DALY) rate for each SDI value. The bootstrap method effectively assesses data uncertainty and variability [19].

#### Smoothing of the frontier

Local polynomial regression (LOESS) is used to smooth the frontier, with a polynomial degree of 1 and a span of 0.2. LOESS is a non-parametric regression technique that can adapt to complex non-linear relationships and reduce noise through locally weighted regression. When drawing the frontier, countries with super-efficiency are excluded to avoid the impact of outliers on the results [20].

#### Generation of the frontier boundary

The smooth frontier boundary is generated through the above steps, representing the best health indicator levels that can be achieved at different SDI levels. Points on the frontier boundary indicate the theoretically achievable optimal health performance under given SDI conditions [21].

All statistical analyses in this study were conducted with precision using R software.

## Results

#### Global level

Between 1990 and 2021, the number of patients with liver cancer increased from 345,912 (95% UI 299826–376632) to over 739,299 (673114–821948), and the global age-standardized prevalence rate of liver cancer increased from (7.75 [6.91–8.43] per 100,000 people) in 1990to (8.68[7.90–9.67] per 100,000 people) in 2021. The global map of age-standardized prevalence rates of liver cancer and the percentage change in age-standardized prevalence rates at the national level are shown in the following (Fig. 1). In all years from 1990 to 2021, the number of prevalent cases and the age-standardized prevalence rate of liver cancer were significantly higher in males than in females (Fig. 2). Overall, in 2021, there were nearly 218,700 (195,400–241,400) prevalent cases among females (29.59%) and nearly 520,500 (463,900–600,500) among males (70.41%). In 2021, the age-standardized prevalence rate for males was (127.6 [114.2-146.8] per 100,000 people), and for females it was (49.5 [44.3–54.5] per 100,000 people). The peak age-standardized prevalence rate of liver cancer for both males and females occurred in the 85–89 age group (Fig. 3).

#### Age and sex patterns

From 1990 to 2021, the total number of liver cancer-related deaths increased from 23,000 (20,000–27,000) to 483,800 (440,400–540,100) (Fig. 4). Despite the increase, the global age-standardized mortality rate decreased from (5.86 [5.37–6.45] per 100,000 people) in 1990 to (5.64 [5.12–6.29] per 100,000 people) in 2021, a rate that corresponds to a 3.75% (3.19–4.31) decrease in the age-standardized mortality rate over the study period. In 2021, the highest number of liver cancer deaths for both men and women occurred in the 65–69 age group, with the highest age-specific mortality rate for men in the 90–94 age group and for women in the age group above 95 years old. Liver cancer incidence (4.66[2.58–6.01] per 100,000 people) and patient numbers (30674[17025–39605]) are higher in children under the age of 5 compared to other adolescent age groups.

The total YLDs attributed to liver cancer almost doubled over the study period, increasing from 58,600 (UI 41,900–78,600) in 1990 to 126,500 (89,500–167,800) in 2021. However, the age-standardized YLD rate did not exhibit the same steep increase, from (1.38 UI [ 0.98–1.85] per 100,000 people) in 1990 to (1.47 [1.04–1.95 per] 100,000 people) in 2021. In 2021, the number of YLDs peaked in the 60–64 age group (80,000 [56,000–106,000]), and then declined in older age groups.

The total number of YLLs attributable to liver cancer was 7,495,000 (6,838,200–8,227,900) in 1990 and increased to 12,761,100 (11,560,500–14,332,200) in 2021. Over time, the age-standardized rate of YLLs for both sexes decreased, from (171.46 [156.33–188.74] per 100,000 people) in 1990 to (147.81[133.88–165.78] per 100,000 people) in 2021, for males and females combined. In 2021, the 65–69 age group had the highest number of YLLs (17,137 [15,642–18,997]), and similarly, the highest number of YLDs was also in the 65–69 age group (18,056.69 [UI 12,830.66–23,811.01]) (Fig. 5). In the age group<5 years old, the number of YLLs (26.90[20.96–34.06] per 100,000 people) and YLDs (0.30[0.18–0.46]), as well as the age-standardized incidence of YLDs (2015.95[1247.07-3079.96]) and YLLs (177091.50[138010.24-224177.61), are higher than those in other adolescent age groups.

The age-standardized rate of DALYs per 100,000 people decreased from 172.85 (157.83-190.16) in 1990 to 149.28 (135.23-167.48) in 2021. The total DALYs caused by liver cancer increased between1990(7.53 million [6.89–8.29 million]) and 2021 (12.88 million [11.67–14.47] million). In 2021, 99.01% of the total DALYs caused by liver cancer were due to YLL, and 0.99% were due to YLD.

#### Regional level

In 2021, among all super-regions, the high-income super-region had the highest age-standardized incidence rate (18.73 [17.69–19.76] per 100,000 population). Additionally, from 1990 to 2021, this region experienced the highest increase in age-standardized incidence rates. From 1990 to 2021, there was a significant decrease in age-standardized mortality rates in East Asia, South Asia, and Oceania (19.65%) (Fig. 6). In the high-income super-region, the total number of deaths caused by liver cancer increased from 59,929 (56,184 – 63,224) in 1990 to 121,117 (109,452 – 128,436) in 2021. The Latin America and Caribbean region had the fewest deaths among all super-regions, with 15,055 (13,882 – 16,175) deaths in 2021(Table 1). The number of female deaths was 6,916 (6,250-7,491), and the number of male deaths was 8,138 (7,469-8,811). This super-region also had the lowest age-standardized mortality rate among all GBD super-regions in 2021 (2.45 [2.26–2.64] per 100,000 people) (Fig. 6).

High-income Asia pacific was the region with the highest age-standardized prevalence rate for both sexes between 1990(26.40[24.27–28.29]) and 2021 (25.26[22.43–27.91]) per 100 000 population for both

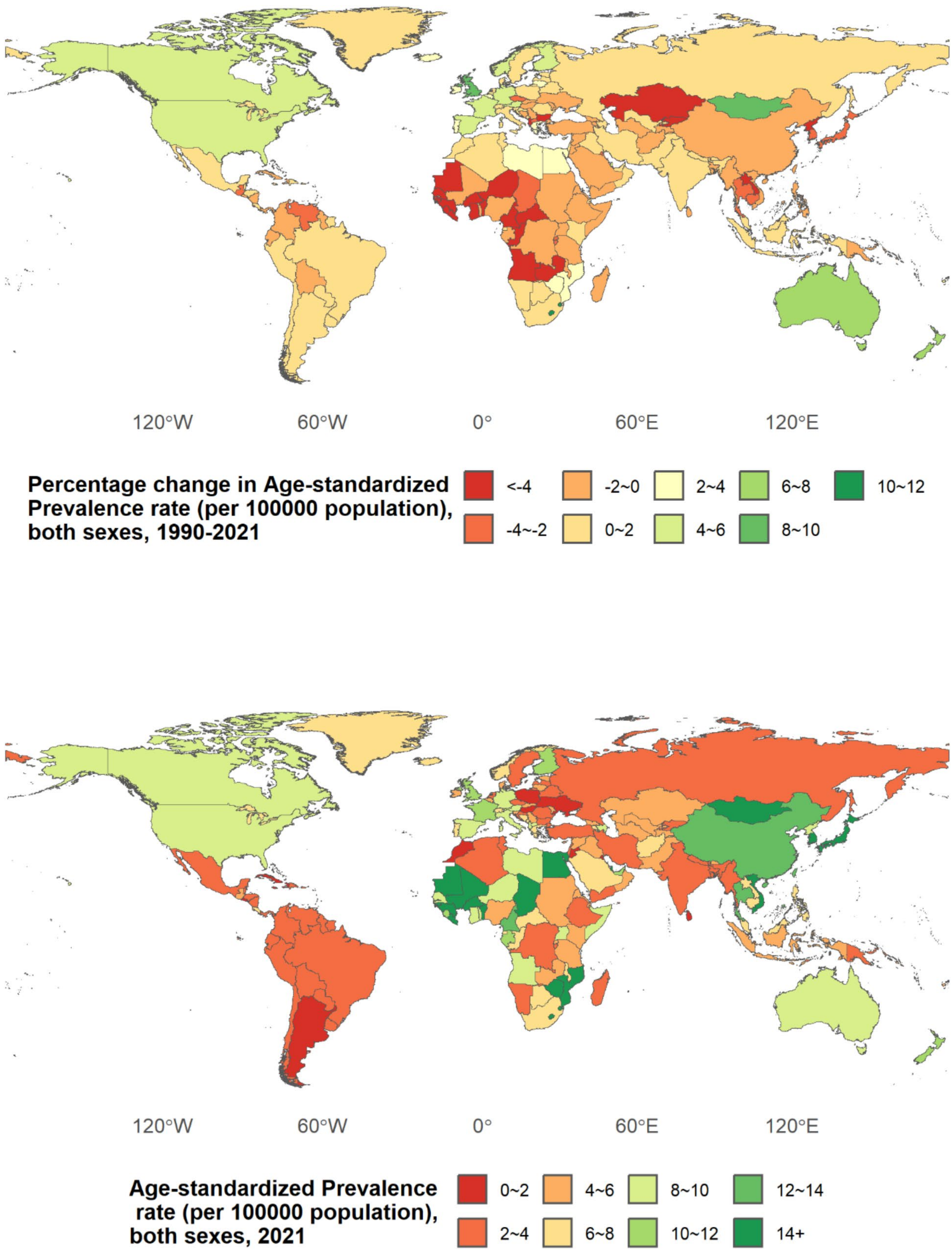


**Fig. 1** Percentage change in age-standardized prevalence rate (per 100 000 population) of liver cancer, both sexes, for 204 countries and territories, 1990–2021

Age-standardized prevalence rate (per 100 000 population) of liver cancer, both sexes, for 2024 countries and territories, 2021

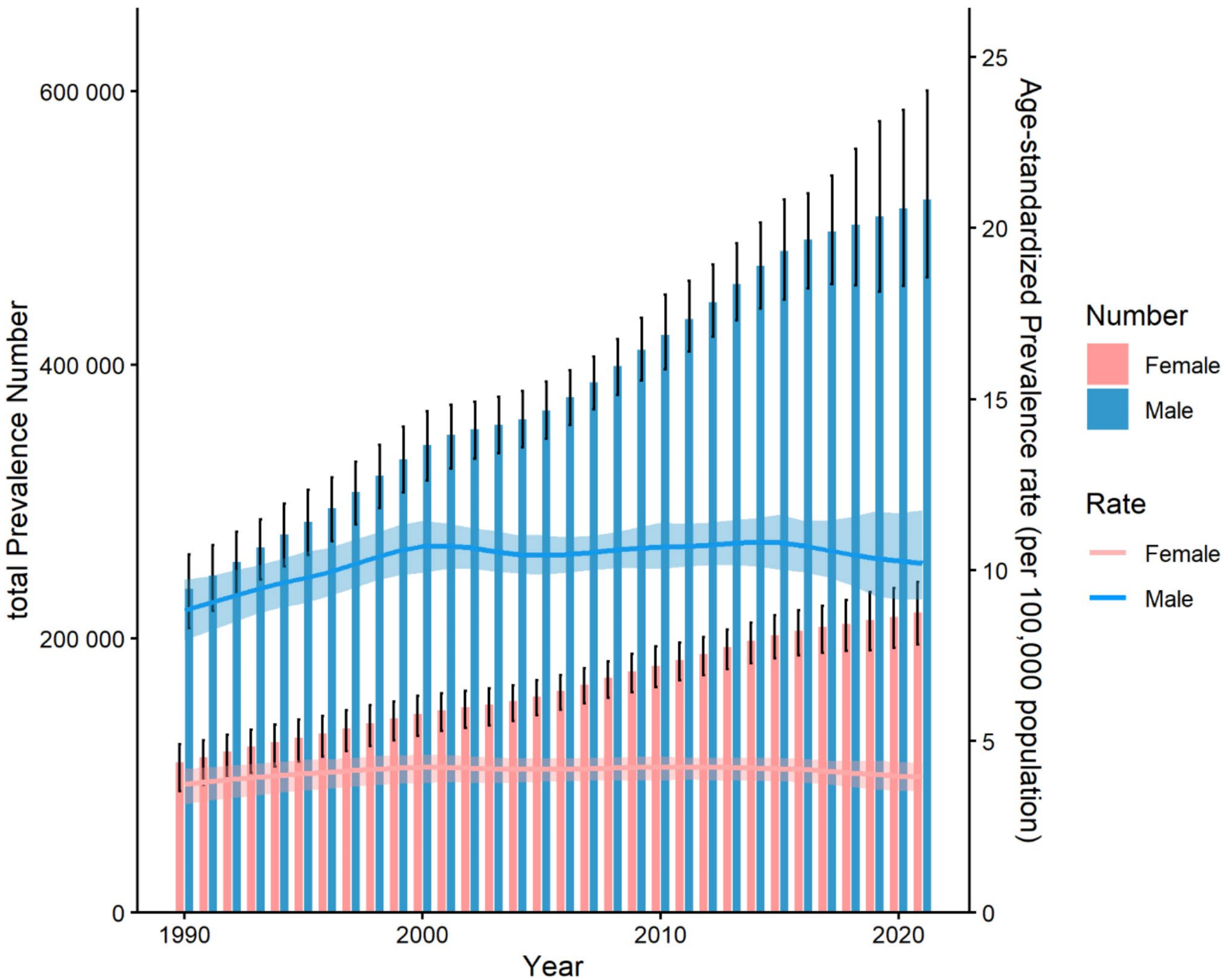


**Fig. 2** Trends from 1990 to 2021 in number and age-standardized prevalence rates of liver cancer at the global level
Error bars indicate the 95% UI for prevalent cases. Shading indicates the 95% UI for the age-standardized prevalence rate

sexes combined (Fig. 7). In 2021, Southern Latin America had the lowest age-standardized incidence rate (1.99 [1.79–2.19] per 100,000 people), followed by Tropical Latin America and the Caribbean regions.

The Western Sub-Saharan Africa region had the highest age-standardized death rate in 2021 (9.37 [95% UI 7.84–10.98] per 100 000 population), followed by High-income Asia Pacific (9.19 [8.11–10.20] per 100 000 population). During the study period, Australasia (163.44%) and high-income North America (112.68%) experienced significant increases in age-standardized mortality rates. (Fig. 8). The age-standardized mortality rate in High-income Asia Pacific declined sharply (decreased by 40.44% from 1990 to 2021). Southern Latin America had the lowest age-standardized mortality rate among regions in 2021 (1.82 [1.64–2.00] per 100,000 people), followed by the Caribbean (1.89 [1.64–2.16] per 100,000 people) (Fig. 8).

### Burden of liver cancer by SDI

Higher SDI was associated with higher age-standardized prevalence rates of liver cancer, with values that were higher than the global rate in the two highest SDI quintiles, and lower than the global rate in the three lowest SDI quintiles (Fig. 9).

### National level

In 2021, the age-standardized incidence rate of liver cancer in China and India, the two most populous countries, was (13.28 [95% UI 10.74 to 16.41] per 100,000 people) and (3.16 [2.78 to 3.56] per 100,000 people), respectively. The age-standardized incidence rate of liver cancer was highest in Mongolia (76.56 [58.82 to 97.89] per 100,000 people), followed by the Republic of Korea (38.16 [31.50 to 46.61] per 100,000 people). At the national level, the greatest change in the age-standardized incidence rate of liver cancer between 1990 and 2021 occurred in the United Kingdom, where the rate increased by 296.53%,

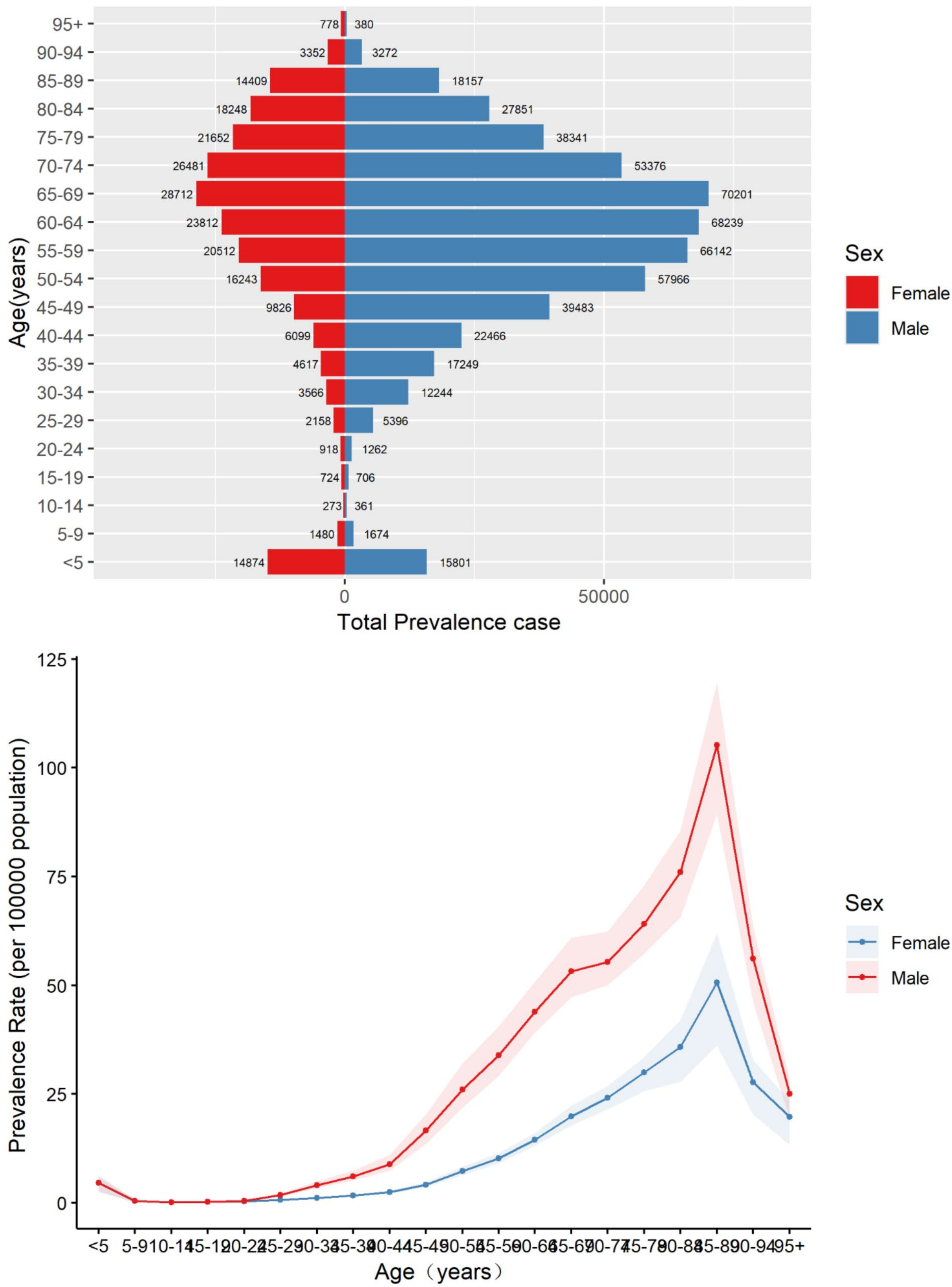


**Fig. 3** Age patterns by sex in 2021 of the total number of prevalent cases and age-specific prevalence rate of liver cancer at the global level

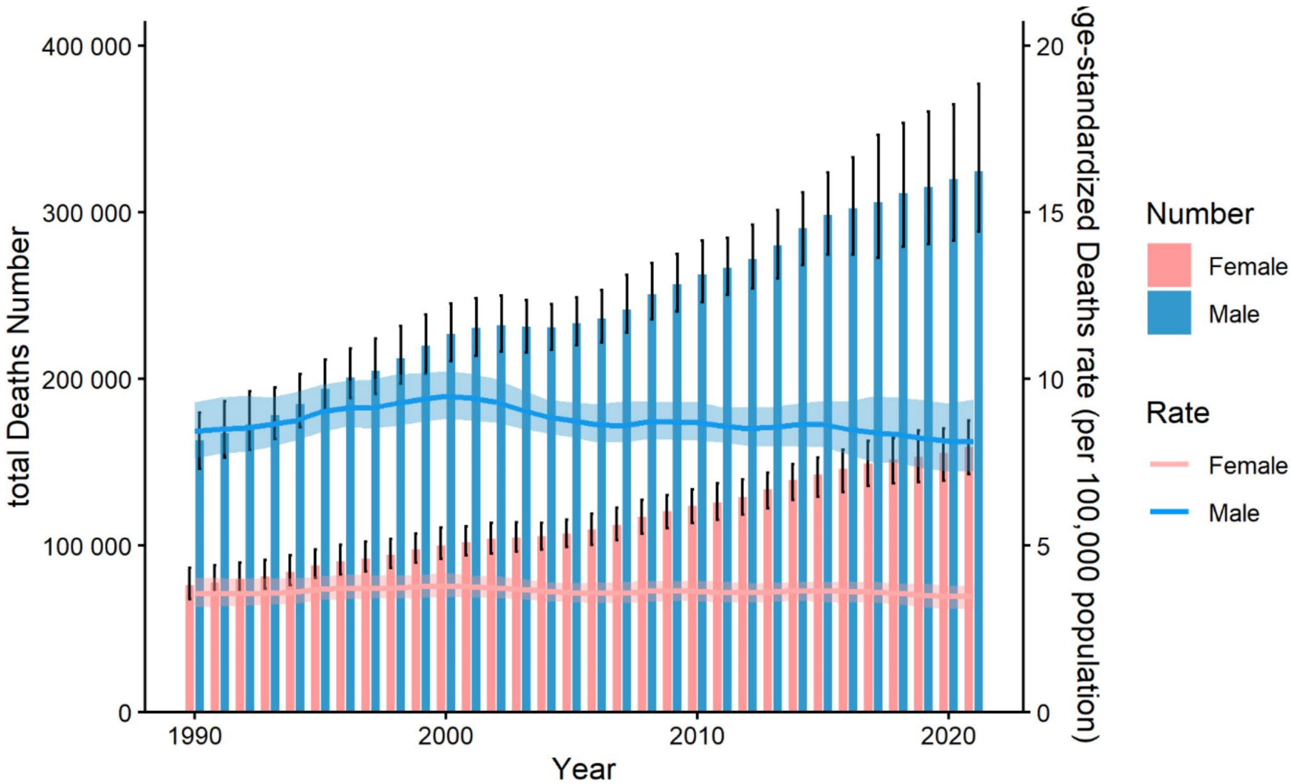


**Fig. 4** Trends from 1990 to 2021 in number and age-standardized death rates of liver cancer at the global level

followed by Australia, where the rate increased by 280.39%. The country with the largest decrease was Mauritius, with a decrease of 82.06% in its standardized incidence rate, followed by Kuwait with a decrease of 72.06%. In 1990, the age-standardized incidence rate of liver cancer in the United Kingdom was (2.86 [2.78 to 2.92] per 100,000 people), and by 2021, it had increased to (11.35 [10.81 to 11.78] per 100,000 people). In 1990, the age-standardized incidence rate of liver cancer in Mauritania was (4.47 [4.24 to 4.72] per 100,000 people), and by 2021, it had decreased to (0.80 [0.73 to 0.85] per 100,000 people).

In 2021, Mongolia had the highest age-standardized mortality rate (80.89 [62.08 to 102.56] per 100,000 people), while Morocco had the lowest (0.53 [0.38 to 0.68] per 100,000 people). At the national level, Poland experienced the largest increase in age-standardized mortality rate during the study period, rising from 1990(0.63 [0.59 to 0.68] per 100,000 population) to 2021(1.79 [1.62 to 1.96] per 100,000 population) — an increase of 183.02%. Mauritius saw the largest decrease in age-standardized mortality rate during the study period, with a drop of 83.94%. South Korea's age-standardized mortality rate decreased from 1990 (4.41 [4.18 to 4.67] per 100,000 people) to 2021 (0.70 [0.65 to 0.75] per 100,000 people) (Fig. 10).

**Frontier analysis**

The unrealized health gains from 1990 to 2021 across countries or regions with different levels of development are illustrated in the figure. As societal and demographic development occurs, the effective differences have generally widened, indicating that countries or regions with higher SDI have greater potential for burden improvement (Fig. 11).

Frontier analysis based on SDI and age-standardized liver cancer DALY rates in 2021. Boundaries are delineated with solid black lines; countries and regions are represented by points. The top 15 countries with the largest effective differences (the greatest gap between liver cancer DALYs and the boundary) are marked in black; frontier countries with lower SDI (< 0.5) and lower effective differences are marked in blue (e.g., Somalia, Papua New Guinea, Yemen, Lao People's Democratic Republic), and countries and regions with higher SDI (> 0.85) and higher effective differences relative to their level of development are marked in red (e.g., America, Canada, Germany, Netherlands). Red points indicate an increase in age-standardized liver cancer DALY rates from 1990 to 2021; blue points indicate a decrease in age-standardized liver cancer DALY rates from 1990 to 2021 (Fig. 12).

Between 1990 and 2021, the global burden of liver cancer increased significantly, with the number of cases rising from 345,912 to 739,299 and the age-standardized

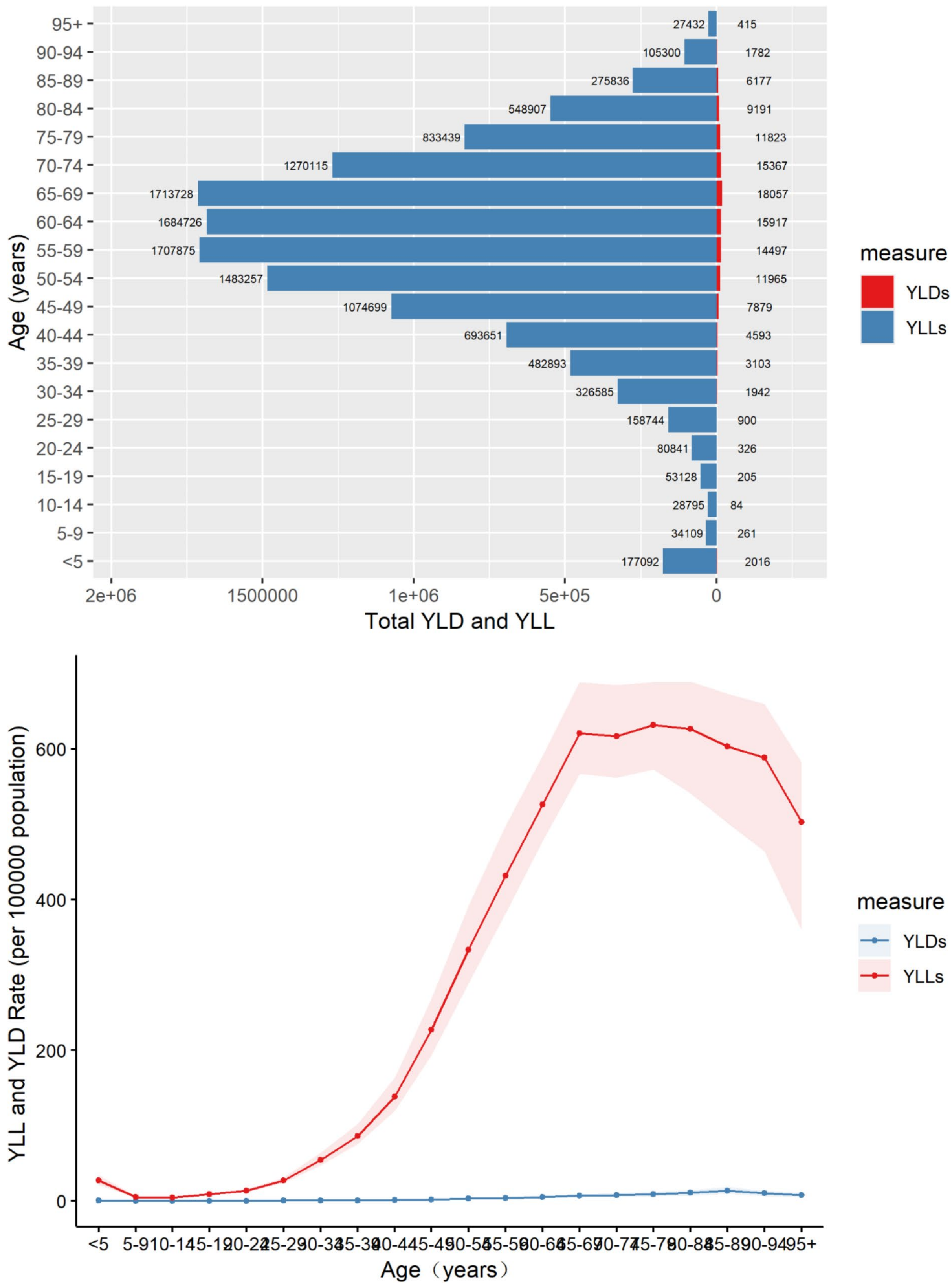


**Fig. 5** Global counts and age-specific rates of YLLs and YLDs due to liver cancer across age groups, 2021

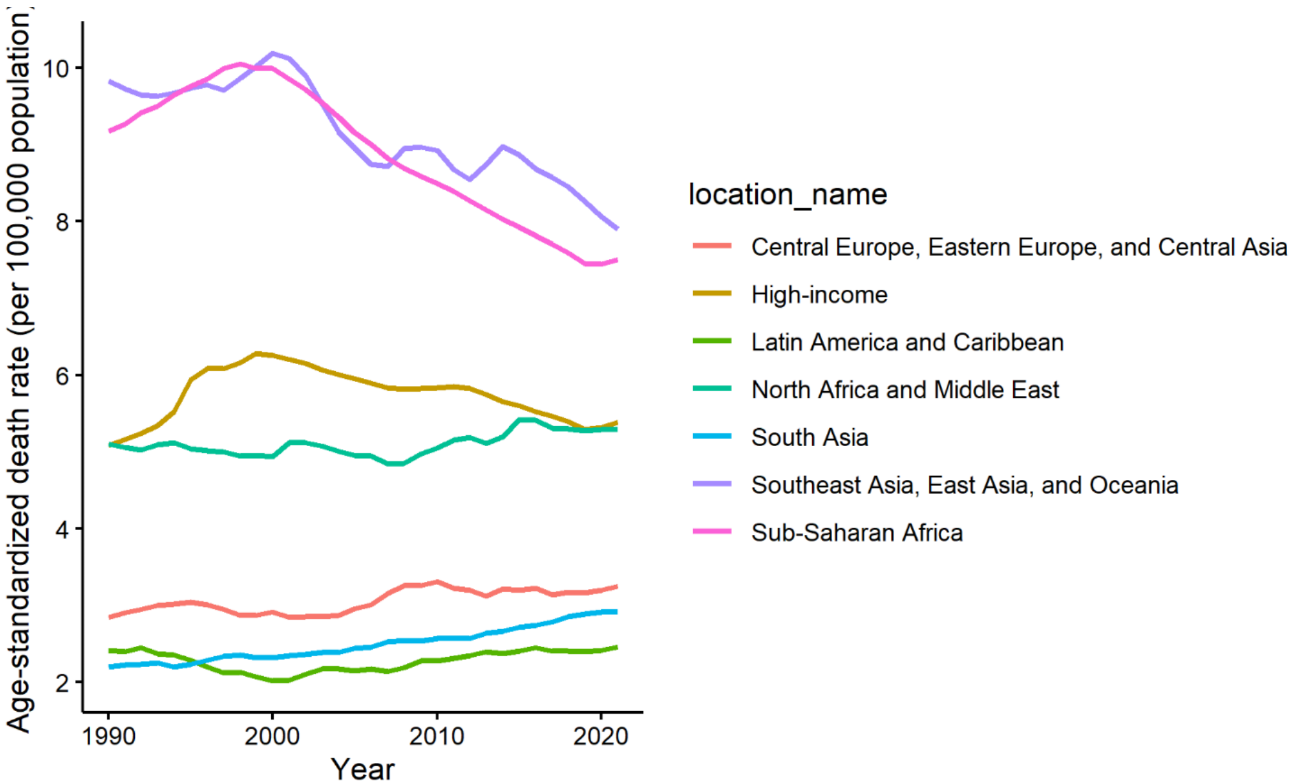


**Fig. 6** Trends from 1990 to 2021 in age-standardized death rate of liver cancer in seven GBD super-regions

prevalence rate increasing from 7.75 to 8.68 per 100,000. Despite a slight decrease in the global age-standardized mortality rate, the total number of deaths increased from 23,000 to 483,800. The total YLDs nearly doubled, and the total YLLs increased significantly, although the age-standardized rates of YLLs and DALYs decreased. Regionally, the high-income super-region had the highest incidence rate, while Southern Latin America had the lowest. Mongolia had the highest mortality rate, and Morocco had the lowest. The effective differences in health gains widened, indicating greater potential for burden improvement in countries with higher SDI.

## Discussion

In this study, we employed standardized methods to describe the burden of liver cancer at the global, super-regional, regional, and national levels. We report that currently, there are approximately 520,500 women and nearly 218,700 men worldwide suffering from liver cancer, with the number of cases on the rise. This is significant in the global context of treating liver cancer, as it has substantial implications for healthcare delivery systems and economies, given that the standard of care for these diseases, especially organ transplantation, is exceedingly costly [22].

China has the highest number of liver cancer patients in the world, and in 2021, nearly one-third of liver cancer patients lived in China, followed by Japan, indicating that the majority of liver cancer patients are concentrated in the Asian region. Similarly, in 2021, the country with the highest age-standardized incidence rate in the world was Mongolia, followed by South Korea, both of which are Asian countries. Previous reports indicated that China accounted for about half of the world's liver cancer patients, but this proportion has decreased to one-third in the current study, suggesting that effective prevention and treatment measures have been implemented in China [9]. In addition to the Asian region, many countries in Africa also have higher incidence rates than Europe and America. However, the incidence rate of liver cancer in Europe and the United States is also gradually increasing [23, 24].

We have also observed a clear trend in liver cancer mortality rates from the lowest to the highest quintile of the SDI, with higher incidence rates in countries with a higher SDI. This pattern has been retained over time, indicating that the burden of liver cancer remains relatively high in countries with a higher Development Index, such as the United Kingdom, the United States, Canada, and Australia. Many studies suggest that this correlation may indicate the presence of common environmental pressures in these regions [25, 26, 27], which are significant risk factors for liver cancer. For instance, some studies have reported that a high Western diet

**Table 1** The number of death and dalys due to liver cancer and ASR (per 100000 population) 95% UI in 2021

| | Mortality | | | | | | Disability-adjusted life years (DALYs) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Both sexes | | Female | | Male | | Both sexes | | Female | | Male | |
| Regions | ASR | Number | ASR | Number | ASR | Number | ASR | Number | ASR | Number | ASR | Number |
| Global | 5.65 (5.12–6.29) | 483,875 (440400–540177) | 3.46 (3.11–3.80) | 159,179 (142936–175020) | 8.10 (7.23–9.37) | 324,696 (288483–376834) | 149.29 (135.23-167.49) | 12,887,652 (11673535–14472228) | 85.06 (77.25–93.70) | 3,811,476 (3455663–4199822) | 217.65 (191.58-255.35) | 9,076,177 (7970743–10670814) |
| Central Asia | 7.26 (6.18–8.45) | 5902 (5013–6903) | 5.53 (4.73–6.42) | 2468 (2116–2866) | 9.47 (8.04–11.19) | 3434 (2888–4083) | 188.77 (160.02-221.65) | 167,974 (142229–197862) | 138.48 (118.53-161.11) | 65,974 (56557–77146) | 249.38 (209.47-296.81) | 102,001 (85226–121967) |
| East Asia | 8.36 (6.84–10.22) | 178,495 (145380–218906) | 4.60 (3.63–5.74) | 51,886 (40854–64945) | 12.38 (9.54–16.41) | 126,609 (97173–168205) | 239.81 (193.34-296.83) | 5,063,800 (4074239–6285122) | 112.68 (88.36-141.59) | 1,240,658 (970561–1565435) | 367.40 (282.43-485.31) | 3,823,142 (29256628 – 5101718) |
| South Asia | 2.92 (2.64–3.22) | 43,495 (39277–47982) | 2.01 (1.77–2.26) | 14,987 (13237–16930) | 3.87 (3.39–4.40) | 28,508 (24834–32422)’ | 79.69 (71.78–88.03) | 1,274,599 (1146363–1411897) | 53.72 (47.52–60.87) | 429,124 (378902–486470) | 106.14 (92.16-120.84) | 845,475 (734893–963960) |
| Southeast Asia | 6.66 (5.23–8.57) | 43,943 (34596–56935) | 3.75 (2.51–4.81) | 12,636 (8413–16233) | 9.98 (8.03–13.41) | 31,307 (24978–42490) | 179.67 (141.22-234.26) | 1,287,277 (1007129–1686531) | 91.37 (60.46–118.00) | 329,883 (216738–428024) | 275.82 (220.49-376.31) | 957,394 (763959-13053589) |
| An-dean Latin America | 2.72 (2.09–3.40) | 1584 (1221–1983) | 2.67 (2.06–3.39) | 842 (641–1067) | 2.75 (2.09–3.48) | 743 (571–940) | 65.79 (50.56–82.92) | 39,834 (30596–50172) | 65.09 (49.60-82.29) | 20,353 (15527–25717) | 66.35 (50.05–83.98) | 19,482 (14689–24625) |
| Central Latin America | 3.09 (2.80–3.39) | 7565 (6867–8321) | 2.76 (2.46–3.06) | 3681 (3275–4073) | 3.47 (3.08–3.89) | 3884 (3442–4347) | 73.57 (66.47–81.22) | 185,646 (167689–204994) | 65.10 (57.74–72.59) | 88,016 (77917–98101) | 83.29 (73.59–93.65) | 97,630 (86240–109769) |
| Southern Latin America | 1.83 (1.64-2.00) | 1605 (1443–1761) | 1.21 (1.09–1.31) | 601 (540–656) | 2.61 (2.28–2.94) | 1004 (879–1134) | 44.05 (39.68–48.34) | 37,431 (33709–41091) | 28.65 (26.33–30.89) | 13,321 (12157–14415) | 62.41 (54.100-70.84) | 24,111 (20891–27369) |
| Tropi-cal Latin America | 1.91 (1.78–2.02) | 4889 (4567–5144) | 1.39 (1.25–1.48) | 1968 (1775–2091) | 2.55 (2.37–2.71) | 2921 (2723–3110) | 48.62 (46.03–50.99) | 125,606 (119005–131666) | 34.34 (31.95–36.11) | 47,736 (44344–50202) | 65.24 (60.76–69.26) | 77,870 (72571–82564) |
| Caribbean | 1.89 (1.64–2.16) | 1017 (884–1162) | 1.48 (1.27–1.74) | 426 (366–503) | 2.35 (2.01–2.71) | 591 (506–680) | 48.38 (41.47–55.88) | 25,729 (22107–29711) | 37.04 (31.59–44.22) | 10,297 (8816–12303) | 60.75 (51.45–70.63) | 15,432 (13061–17929) |
| Central Europe | 3.01 (2.71–3.35) | 6692 (6026–7442) | 1.80 (1.61-2.00) | 2371 (2116–2644) | 4.55 (4.10- | 4322 (3891–4808) | 73.70 (65.97–82.12) | 152,064 (136011–169479) | 41.75 (37.50-46.62) | 48,663 (43666–54330) | 111.41 (100.12-124.27) | 103,401 (92885–115398) |
| Eastern Europe | 2.41 (2.24–2.60) | 8332 (7734–8973) | 1.51 (1.37–1.66) | 3334 (3017–3646) | 3.78 (3.42–4.15) | 4998 (4506–5507) | 64.40 (59.67–69.67) | 208,185 (192395–225656) | 38.22 (34.74–41.92) | 73,113 (66069–80371) | 100.58 (90.54-110.59) | 135,072 (121338–149208) |
| Western Europe | 4.58 (4.22–4.84) | 43,610 (39596–46256) | 2.63 (2.32–2.81) | 14,716 (12589–15988) | 6.85 (6.38–7.30) | 28,894 (26739–30913) | 106.07 (99.82-111.42) | 881,874 (819766–929896) | 58.27 (53.43–61.19) | 267,041 (237764–284311) | 158.78 (148.89-168.11) | 614,833 (575073–652253) |

**Table 1** (continued)

| | Mortality | | | | | | Disability-adjusted life years (DALYs) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Both sexes | | Female | | Male | | Both sexes | | Female | | Male | |
| Regions | ASR | Number | ASR | Number | ASR | Number | ASR | Number | ASR | Number | ASR | Number |
| North Africa and Middle East | 5.29 (4.51–6.11) | 23,679 (20090–27462) | 3.68 (3.15–4.20) | 8067 (6826–9279) | 6.87 (5.78–8.13) | 15,612 (13024–18659) | 134.79 (114.08-156.58) | 673,287 (567574–783681) | 93.77 (79.50-108.32) | 230,277 (194892–267067) | 174.42 (145.74-208.21) | 443,010 (369326–530227) |
| Southern Africa | 9.54 (7.60-11.97) | 9064 (7089–11617) | 6.83 (5.76–8.10) | 3548 (2979–4201) | 13.17 (9.68–18.35) | 5516 (3996–7758) | 250.56 (194.54-322.96) | 283,601 (216687–371273) | 169.47 (141.67-202.15) | 103,335 (85300–125357) | 350.67 (254.27-493.07) | 180,266 (129249–253778) |
| Central Sub-Saharan Africa | 5.50 (2.60-11.61) | 3031 (1465–6263) | 4.65 (2.07–10.95) | 1360 (620–3195) | 6.53 (3.01–15.80) | 1671 (766–3945) | 143.53 (69.14-297.61) | 99,409 (47598–209360) | 118.89 (54.25-277.83) | 43,206 (19877–99143) | 171.87 (78.98-408.05) | 56,203 (25176–132731) |
| Eastern Sub-Saharan Africa | 5.76 (4.46–7.53) | 9930 (7532–13067) | 5.64 (4.59–6.79) | 4921 (3945–5975) | 5.80 (4.07–8.89) | 5009 (3474–7655) | 150.42 (113.96-198.62) | 325,428 (242048–438427) | 140.01 (112.59-170.29) | 156,124 (123614–195571) | 160.35 (111.17-245.59) | 169,305 (114884–254939) |
| Southern Sub-Saharan Africa | 8.02 (6.87–9.34) | 4645 (3967–5443) | 6.01 (5.00-7.10) | 1971 (1625–2340) | 10.88 (8.84–13.40) | 2674 (2148–3298) | 218.19 (185.23-257.19) | 144,312 (121227–170751) | 158.09 (129.94-190.56) | 56,963 (46574–69190) | 294.75 (234.45-364.86) | 87,349 (69245–109637) |
| Western Sub-Saharan Africa | 9.37 (7.84–10.98) | 19,287 (15820–22935) | 7.68 (6.25–9.25) | 7842 (6317–9630) | 11.27 (9.42–13.35) | 11,445 (9371–13723) | 249.93 (204.22-298.73) | 641,819 (515896–773751) | 190.15 (152.73-234.02) | 244,124 (191971–303900) | 316.32 (258.28-379.12) | 397,695 (319254–480232) |
| Oceania | 3.46 (2.32–6.12) | 271 (179–492) | 2.39 (1.68–3.66) | 87 (60–136) | 4.45 (2.84–9.20) | 184 (115–382) | 96.37 (63.69-175.12) | 8992 (5879–16559) | 64.31 (44.60-100.24) | 2857 (1933–4515) | 126.16 (78.95-262.13) | 6135 (3768–12818) |
| Australasia | 4.90 (4.38–5.44) | 2593 (2303–2889) | 2.89 (2.45–3.29) | 833 (695–961) | 7.11 (6.27–8.11) | 1760 (1547–2017) | 121.99 (109.82-135.46) | 58,668 (52504–65203) | 69.34 (61.23–74.45) | 17,494 (15187–19781) | 178.33 (156.93-202.51) | 41,174 (36398–46839) |
| High SDI | 5.51 (5.05–5.83) | 117,889 (106689–125242) | 3.13 (2.73–3.36) | 39,208 (33001–42742) | 8.26 (7.74–8.70) | 78,681 (73488–82878) | 127.92 (120.57-134.41) | 2,453,150 (2289462–2587416) | 68.25 (62.22–71.98) | 719,953 (636982–768555) | 192.82 (183.10-202.84) | 1,733,197 (1643589–1821466) |
| High-middle SDI | 5.53 (4.77–6.44) | 107,715 (93068–125153) | 3.01 (5.54–3.53) | 32,971 (27744–38652) | 8.43 (7.00-10.41) | 74,744 (61994–92626) | 152.60 (129.49-181.81) | 2,877,560 (2446560–3427883) | 72.99 (61.19–86.96) | 748,278 (626071–895447) | 237.73 (194.37-298.03) | 2,129,282 (1738602–2673350) |
| Middle SDI | 6.21 (5.43–7.26) | 166,730 (145739–196163) | 3.68 (3.14–4.33) | 50,911 (43477–59907) | 8.97(7.50-11.08) | 115,819 (96600–144017) | 169.71 (147.41-200.85) | 4,746,028 (1407709–5643717) | 89.63 (77.51-104.64) | 1,270,194 (1095521–1485064) | 253.40 (233.31-316.07) | 3,475,834 (2890565–4335402) |
| Low-middle SDI | 4.26 (3.88–4.70) | 61,938 (56193–68549) | 3.15 (2.83–3.47) | 23,382 (21016–25935) | 5.46 (4.83–6.26) | 38,556 (33917–44388) | 116.37 (104.91-128.97) | 1,839,382 (1651208–2045499) | 83.11 (74.57–92.09) | 668,163 (600497–740408) | 151.35 (132.39-174.69) | 1,171,219 (1019886–13522238) |
| Low SDI | 5.60 (4.62–7.02) | 29,329 (23875–37216) | 4.87 (3.98–6.07) | 12,613 (10219–15854) | 6.35 (5.11–8.18) | 16,716 (13365–21724) | 151.07 (122.38-192.78) | 964,542 (772939–1243934) | 125.12 (101.05-157.96) | 402,650 (321939–514583) | 177.46 (141.62-231.14) | 561,891 (442820–738136) |

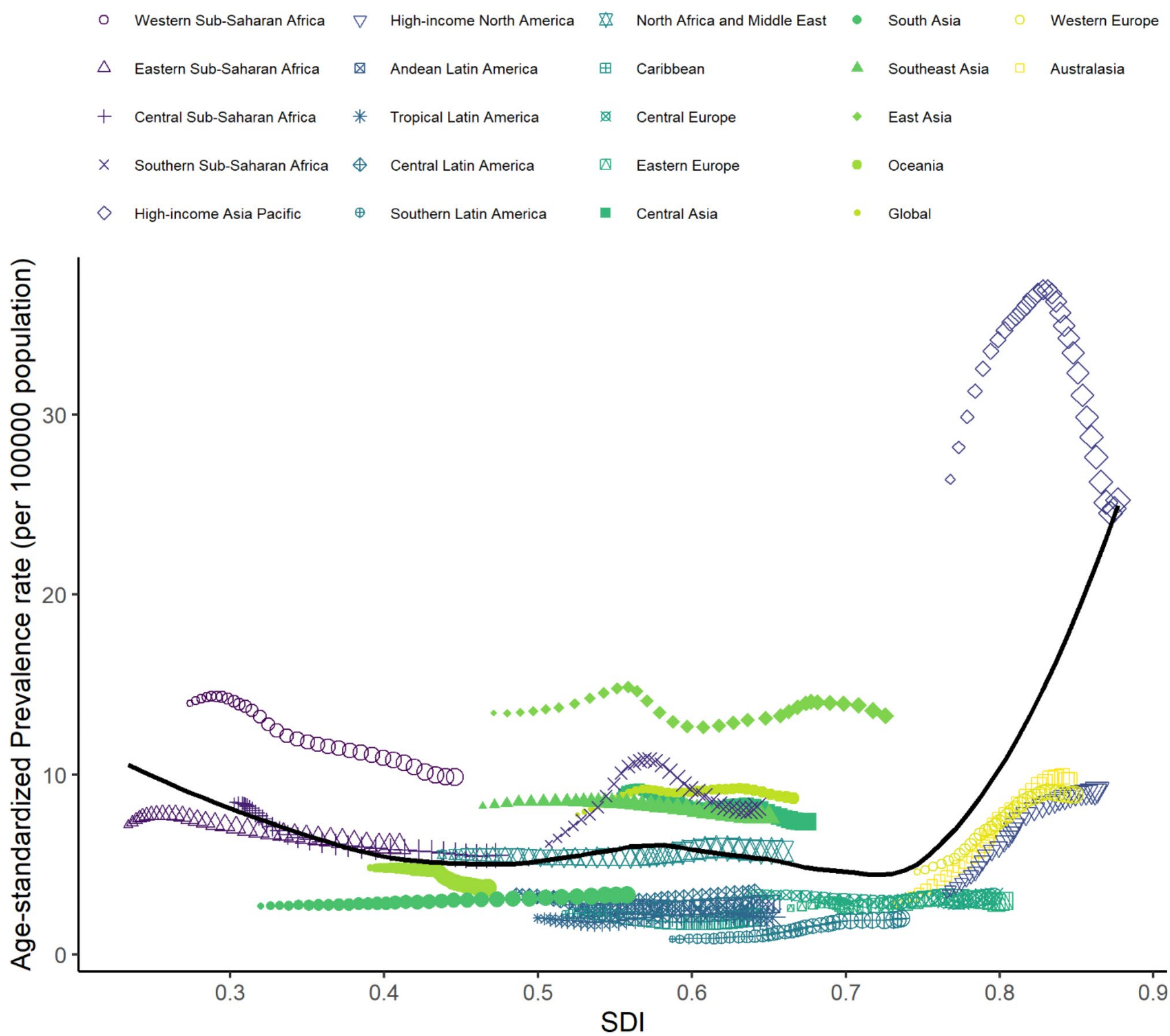


**Fig. 7** Age-standardized prevalence rate of liver cancer globally and for 21 GBD regions by SDI, 1990–2021

pattern increases the incidence of liver cancer by 24% [5], and the intake of fruits, grains, tea, and dietary fiber is significantly associated with liver cancer. Similarly, controlling smoking, alcohol consumption, and drug use contributes to the decline in liver cancer-related mortality in most SDI regions [28, 29]. Although this study did not assess the role of potential risk factors in liver cancer incidence, these risk factors may include urbanization, a cleaner environment [8, 30]. diets low in fiber and high in meat, and chronic infections such as hepatitis B and C, all of which are risk factors for liver cancer.

The diagnosis and treatment of liver cancer exhibit significant regional disparities, which may stem from the uneven distribution of medical resources, the varying capabilities of healthcare systems, and the financial status of patients. In countries with higher incomes, the survival rates of liver cancer patients have seen a notable improvement due to ongoing advancements in medical technology and the relative abundance of healthcare resources. However, in low-income and middle-income countries, the limited availability of medical resources often leads to greater challenges in the early detection and effective treatment of liver cancer.

Additionally, we have observed that in the pediatric age groups, the under-5 age group exhibits higher numbers of liver cancer patients, as well as higher age-standardized incidence rates YLDs and YLLs due to the disease, compared to other pediatric age groups. This indicates that the disease burden of liver cancer is relatively heavier at this age, necessitating special attention and the implementation of appropriate preventive and treatment measures. Although liver tumors are rare in children, they are

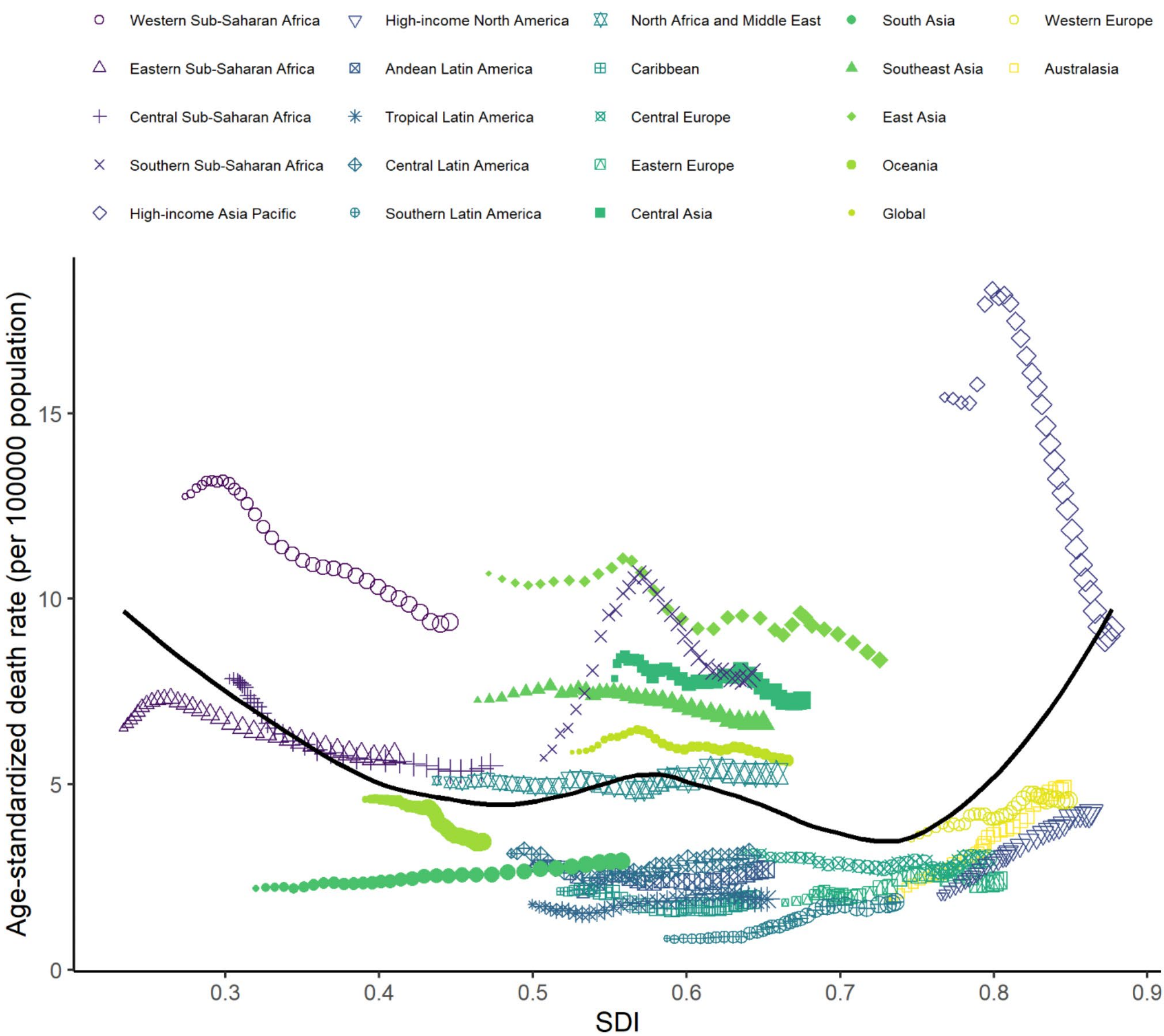


**Fig. 8** Age-standardized death rate of liver cancer globally and for 21 GBD regions by SDI, 1990–2021
The expected age-standardized death rate in 2021 based solely on SDI is represented by the black line. For each region, points from left to right depict estimates from each year from 1990 to 2021

relatively common in children with certain specific risk factors, thus warranting increased vigilance and, in some cases, screening [31].

In areas with higher SDI, the higher incidence of liver cancer may indicate that individuals with higher socioeconomic status are at greater risk of developing liver cancer, possibly due to their lifestyle, dietary habits, or other health-related behaviors. Therefore, it may be necessary to strengthen health education and regular health check-ups among these populations to facilitate early detection and treatment of liver cancer. At the same time, the high diagnosis rate of liver cancer in these areas may also be related to the abundance of medical resources, such as easier access to advanced diagnostic tools and medical services, which helps to improve the early diagnosis rate of liver cancer. This difference reflects the inequality in the distribution of medical resources and the disparities in access to health services between different socioeconomic groups.

Our report indicates an increase in age-standardized prevalence of liver cancer in regions that previously had lower incidence rates, including East and South Asia, Oceania, and sub-Saharan Africa. A combination of factors, such as improvements in socioeconomic status in emerging industrialized nations, changes in diet and other lifestyle factors, advancements in sanitary conditions, alterations in microbiota, and environmental factors, may contribute to an elevated risk of developing

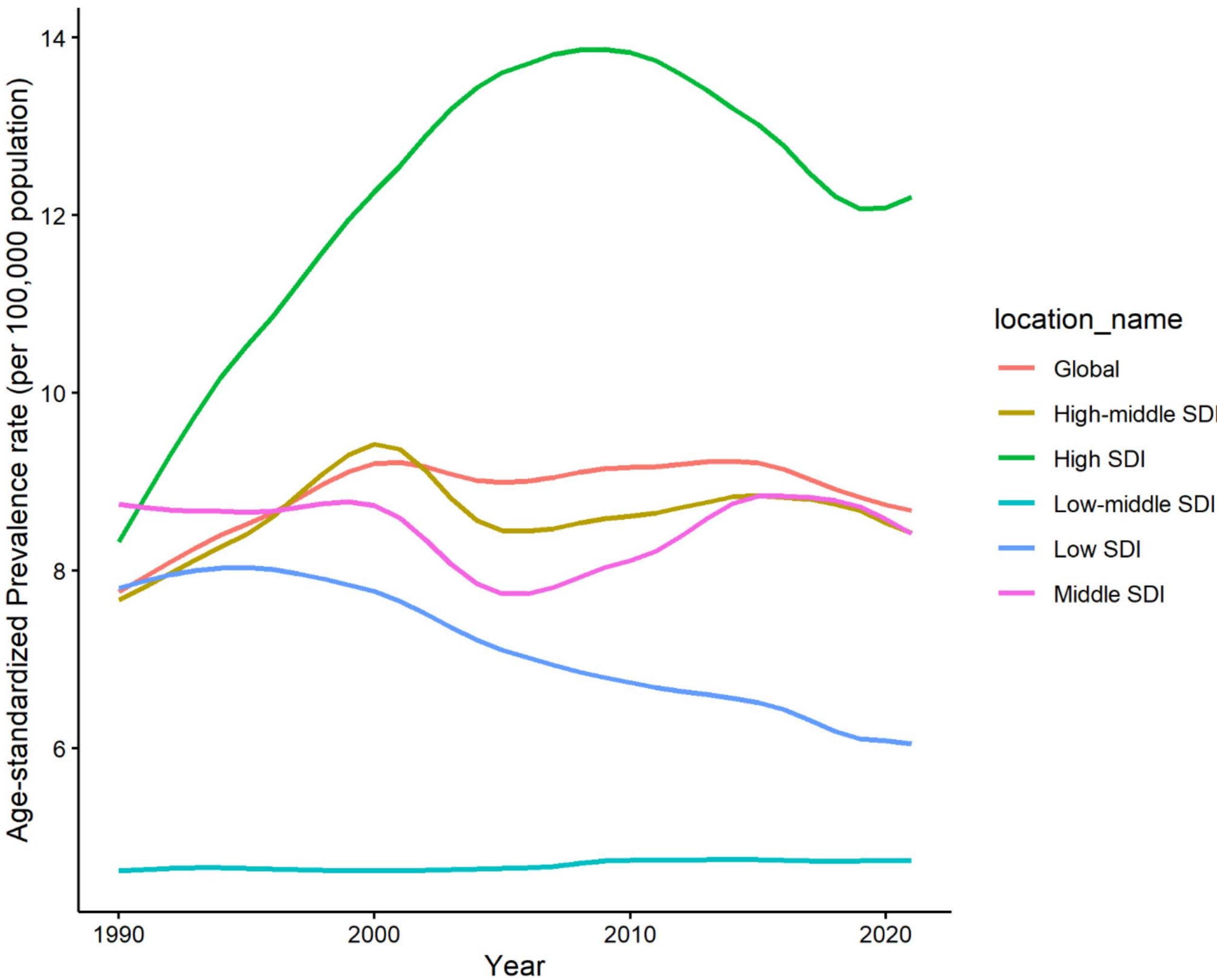


**Fig. 9** Trends from 1990 to 2021 in age-standardized prevalence rates of liver cancer by SDI quintile

liver cancer. Behavioral and environmental factors are likely playing an increasingly significant role in the progression of liver cancer. Various factors that can increase the risk of liver cancer include smoking, lifestyle choices, dietary habits, intestinal infections, and air pollution.

With the continuous improvement of the healthcare system, we have not only expanded the application range of diagnostic tools but also enhanced the awareness of patients and healthcare providers, which contributes to an increased diagnostic rate [32]. In regions where the incidence of liver cancer was previously low, the current upward trend in incidence poses new challenges to healthcare providers and policymakers, requiring them to thoughtfully plan and adjust existing healthcare strategies. Nearly three-quarters of the population about 3–5 billion people live in developing countries. Nearly 2.7 billion people live in India and China. In the context of a vast population base, the number of people affected by diseases naturally increases, and the number of liver cancer patients is no exception. Even if the mortality rate declines, the rise in disability rates could have a severe socio-economic impact on developing countries in the coming years. This impact may intensify the pressure on these countries in terms of medical resource allocation, disease prevention, and treatment strategies, thereby posing challenges to public health systems. Especially in low- and middle-income countries, limited medical resources may make the diagnosis and treatment of liver cancer more difficult, which not only affects the quality of life of patients but also increases the overall burden on society. Therefore, strengthening the prevention of liver cancer, early diagnosis and treatment, and raising public awareness of healthy lifestyles are crucial for mitigating the socio-economic impacts of liver cancer in the future. It is worth noting that the economic impact of liver cancer is not limited to its burden on the healthcare system. A study report from the United States estimates that, in the relevant calculations, a loss of annual income

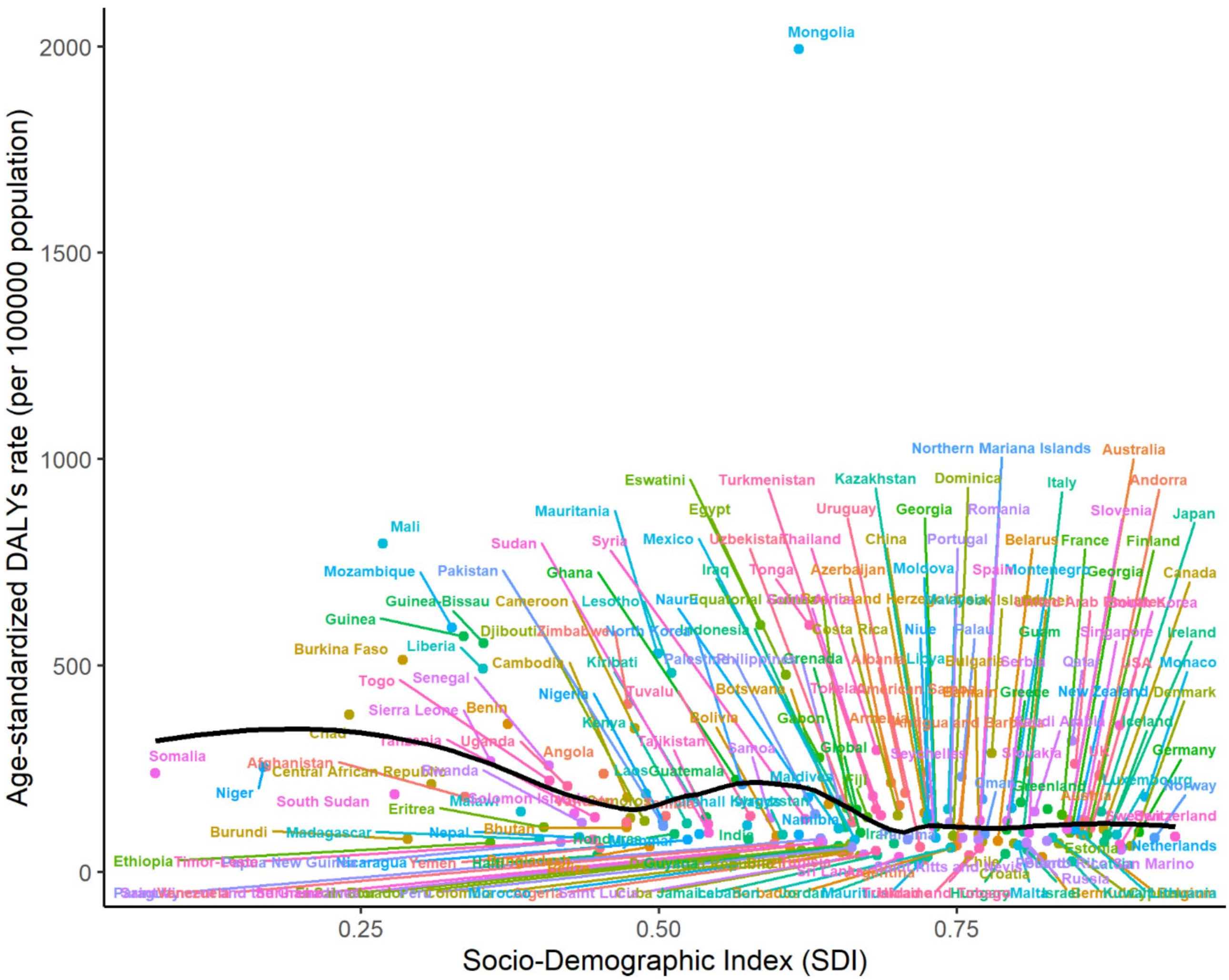


**Fig. 10** Age-standardized DALYs rates from liver cancer by SDI for 195 countries and territories in 2021
The black line represents the expected age standardized DALYS rate of liver cancer based solely on SDI

of 94.4 billion US dollars is related to cancer mortality [33]. Therefore, liver cancer poses an increasing burden not only on the healthcare system but also on the entire economy.

We report that from 1990 to 2021, there has been a decline in age-specific mortality rates at the global and regional levels. The general decline in mortality rates may reflect an increase in the survival rates of liver cancer patients, thanks to the combined effects of various factors. The widespread use of immunomodulators, the early introduction of biologic agents, continuous improvements in surgical techniques, and the growing awareness of the importance of early detection and treatment of liver cancer have all played a positive role in increasing patients' chances of survival. These advancements have not only reduced the mortality rate of liver cancer but also improved patients' quality of life, although they may be accompanied by a relative increase in disability rates. In the coming years, these changes may have a profound impact on the healthcare systems and socio-economic landscapes of developing countries [34, 35].

In countries with lower SDI, the incidence of liver cancer is relatively lower, which may imply that the age-standardized mortality rates are also lower in these areas. However, this lower reported mortality could also be due to the poor quality of death registration systems in these countries, leading to underreporting of liver cancer-related deaths. Moreover, the medical technology and diagnostic capabilities in countries with low SDI may be limited, which could result in a lower detection rate of liver cancer, thereby affecting the reporting of liver cancer cases. In these regions, the underreporting of incidence and mortality rates of liver cancer may be partly due to insufficient detection of liver cancer-related deaths. Therefore, improving medical technology and diagnostic capabilities in these countries, as well as enhancing death registration systems, is crucial for more accurately assessing the disease burden of liver cancer.

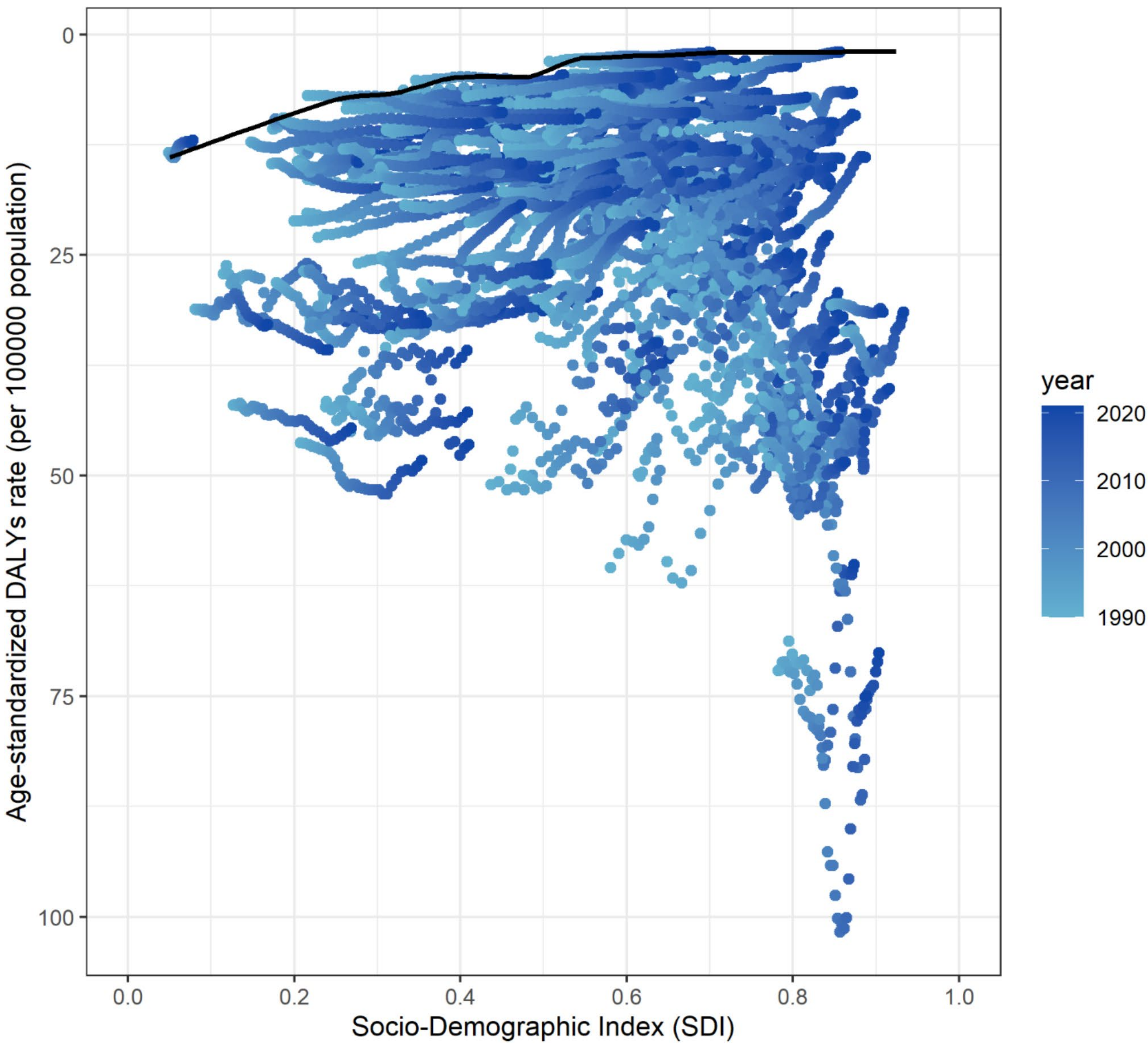


**Fig. 11** Frontier analysis of SDI and age-standardized liver cancer DALY rates from 1990 to 2021. Boundaries are delineated with solid black lines; countries and regions are represented by points. The changes in SDI and age-standardized DALY rates for each country or region are presented in a blue gradient

Although the fatal burden of liver cancer has decreased, the non-fatal health burden continues to rise. liver cancer severely impacts patients' lives across physical, psychological, familial, and social dimensions. Consequently, the secondary effects of liver cancer can be observed through the increased incidence of anxiety, depression, and other emotional issues. These emotional problems not only affect patients' mental health but can also impact their treatment adherence and quality of life. Therefore, for liver cancer patients, providing comprehensive support, including psychological and social assistance, is crucial. A study from 2023 has indicated that patients with liver cancer often bear a significant disease burden, and they experience notable levels of anxiety and depression after liver resection surgery. However, the Global Burden of Disease (GBD) disability weights only consider the specific symptoms of liver cancer, not the social stigma, depression, anxiety, and other inflammatory conditions that may accompany the disease. This suggests that while the fatal burden of liver cancer has seen a decline, the non-fatal burden, including the psychological and social impacts, continues to increase. It is important to recognize and address these aspects of the disease to provide comprehensive care for patients [36].

Although there is no clear research report indicating a direct correlation between gender and the incidence of liver cancer, past research reports and this study show that the incidence and number of male patients with liver

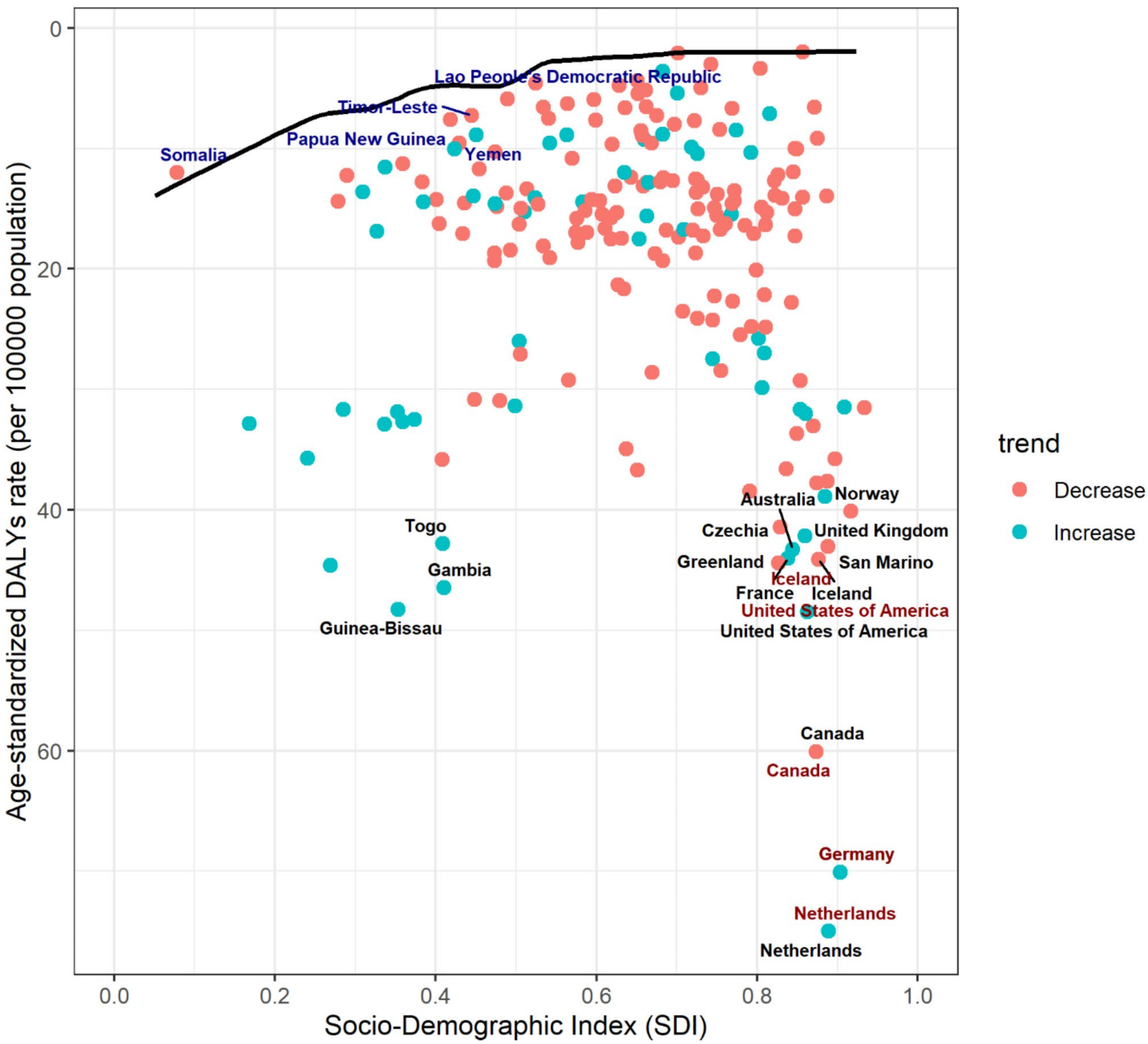


**Fig. 12** Frontier analysis of SDI and age-standardized liver cancer DALY rates in 2021

cancer are both higher than those of females [37]. The differences in biological, social, and economic exposures between males and females may account for this disparity. Similarly, reported that in China many liver cancer-related deaths can be attributed to four risk factors: smoking (20%), drug use (13.6%), alcohol consumption (11.7%), and high body mass index (10.1%) [38]. These high-risk factors are often more prevalent in males than in females, which may also be one of the reasons for the higher incidence and mortality rates in males. Some studies have indicated that there is a connection between the gut microbiota and liver cancer, a connection that may be associated with differences among various ethnicities and genders. However, the complex pathophysiological mechanisms behind this link are not yet fully understood and require further exploration through extensive data and experimental research. Additionally, the diversity and composition of the gut microbiota may vary among different genders and age groups, and these differences could be related to changes in the risk of liver cancer. Therefore, delving deeper into the relationship between the gut microbiota and liver cancer is of significant importance for early diagnosis and treatment [39, 40].

The natural course of liver cancer is characterized by high mortality rates and low survival rates. However, due to the persistently high incidence of the disease, the number of people affected has continued to grow annually from 1990 to 2021. Although there has been a decline in incidence rates in some middle and high-income regions, the rates in low-income areas are increasing year by year, with a projected continued increase in the future. The rise in incidence rates, coupled with an increase in rates in areas that historically had low incidence, will have significant impacts on health and the economy. Our research findings may assist health service planners and policymakers in justifying and prioritizing resource allocation to address the growing number of liver cancer patients. This study will encourage health planners to develop cost-effective and simple community-based interventions for primary health care professionals to implement. This is necessary because liver cancer can persist for many years, with a possibility of recurrence, and the aging population is on the rise. The study underscores the need for targeted cancer prevention strategies and enhanced healthcare infrastructure in regions with the highest burden.

Although this study provides valuable insights into the global burden of liver cancer, it also has some limitations. In terms of data quality and availability, there is a lack of data on liver cancer incidence and mortality in some countries and regions, especially in low-income and conflict-affected areas, which may lead to inaccurate burden estimates. The quality and completeness of data from different sources vary, and there may be reporting biases. Methodologically, the statistical models used involve several assumptions that may affect the robustness of the estimates, and the analysis is limited to a specific time range, making it difficult to extrapolate future trends. Regarding population representativeness, the study may not fully represent all subpopulations, especially in areas with limited data. The scope of risk factor analysis is limited, and correlation does not imply causation. Geographically and socioeconomically, there are significant regional differences in the burden of liver cancer, and the Socio-Demographic Index (SDI) as a proxy for development may oversimplify complex factors. In terms of diagnostic and treatment practices, there are significant differences in diagnostic criteria and the availability and quality of treatments across countries, which affect the accuracy of the results. Future research needs to improve data collection, refine modeling techniques, and conduct more detailed risk factor analyses to enhance the accuracy and applicability of the findings and provide more effective information for liver cancer prevention and treatment.

## Conclusion

This study provides a comprehensive analysis of the global, regional, and national burden of liver cancer from 1990 to 2021, utilizing data from the Global Burden of Disease (GBD) study. The findings reveal a significant increase in the number of liver cancer cases and a rising burden, particularly in regions with higher Socio-demographic Index (SDI) values. Despite a slight decrease in the global age-standardized mortality rate, the overall burden of liver cancer continues to grow, posing substantial challenges to healthcare systems and economies worldwide.

The study highlights significant regional disparities in liver cancer incidence and mortality, with the highest burden observed in high-income North America and the lowest in Southern Latin America. Notably, Mongolia had the highest prevalence and mortality rates, while Morocco had the lowest. The increasing trend in liver cancer cases in regions with previously lower incidence rates, such as East and South Asia, Oceania, and sub-Saharan Africa, underscores the need for targeted prevention and treatment strategies.

The research also underscores the importance of understanding the underlying risk factors and the potential for health gains in regions with higher SDI. The findings suggest that countries with higher SDI have greater potential for burden improvement, indicating the need for enhanced healthcare infrastructure and resource allocation to address the growing number of liver cancer patients.

In conclusion, the global burden of liver cancer is increasing, with stark regional differences. These findings can inform health policy and research to address this global challenge. Future efforts should focus on improving data collection, refining modeling techniques, and conducting more detailed risk factor analyses to enhance the accuracy and applicability of the findings. This will help in developing more effective strategies for liver cancer prevention and treatment, ultimately reducing the socio-economic impact of this disease.

## Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12889-025-22026-6 .

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

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**Author contributions**

ZC. J and GQ. Z wrote the main manuscript text and HJ. D and YH.B prepared Figs. 1, 2, 3, 4 and 5, LB.W and W.C prepared Figs. 5, 6, 7, 8, 9 and 10. All authors reviewed the manuscript.

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**Data availability**

The datasets generated and/or analyzed during the current study are available in the GBD 2021. Publicly available datasets were analyzed in the current study. The data can be found here: http://ghdx.healthdata.org/gbd-resul ts-tool. The analyzed data will be shared upon reasonable request to the corresponding author.

## Declarations

### Ethics approval and consent to participate
Not applicable.

### Consent for publication
Not applicable.

### Competing interests
The authors declare no competing interests.

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