The Burden of Liver Cirrhosis and Underlying Etiologies: Results from the Global Burden of Disease Study 2017

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Research

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Abstract

Background

Liver cirrhosis is a major health issue worldwide. Few studies have explored the prevalence trends caused by specific etiologies. This study was conducted to evaluate the pattern and prevalence trends.

Methods

We collected detailed data on liver cirrhosis based on GBD 2017 study. The ASR and EAPC were used to estimate the trends in prevalence by population, etiology and region.

Results

Globally, the number of prevalent cases increased 74.53% from 1990 to 2017. The worldwide ASR increased 0.75 per year. The increasing pattern was heterogeneous. The most pronounced increases were found in middle-high and high SDI regions, especially in the Caribbean, Andean Latin America and Southern Latin America. Among the etiologies, NASH-related liver cirrhosis accounted for 59.46% of the cases in 2017. The ASR increased 1.74 per year, and the increase was observed in all 5 SDI regions. In addition, the ASR of liver cirrhosis caused by alcohol use also increased in both sexes and all 5 SDI regions. In contrast, the ASR of liver cirrhosis caused by HBV and HCV decreased, especially in the middle and low-middle SDI regions.

Conclusions

By using vaccine and direct-acting antiviral therapy, the number of people suffering from HBV and HCV decreased, but liver cirrhosis was still a major threat to human health. Additionally, the number of people with cirrhosis caused by alcohol and NASH continued to grow. Thus, more targeted and specific strategies should be established in countries based on the etiology and prevalence trends for liver cirrhosis.

Background

Liver cirrhosis is a major health issue that afflicted more than 160 million people in 2017 worldwide [1]. Previous studies have documented that the incidence of liver cirrhosis varies, and chronic viral hepatitis is the most common cause, especially hepatitis B virus (HBV) and hepatitis C virus (HCV) [2, 3]. The highest incidence of liver cirrhosis was found in East Asia. In contrast, the incidence in Southern Latin America was the lowest, with a value of 12.1% [4]. Moreover, newly diagnosed cases have continued to increase globally in the last few decades, although many public health initiatives have been implemented.

The major causative agents of liver cirrhosis include hepatitis, alcohol, non-alcoholic steatohepatitis (NASH) and others [5]. The etiology of liver cirrhosis in each region or country varies based on the different risk factors. For instance, HBV is the main cause of liver cirrhosis in China [6]. In Mexico, Japan and the United States, liver cirrhosis is mainly caused by HCV. Moreover, the number of patients with cirrhosis caused by alcohol and NASH is continuously increasing. Thus, more targeted prevention strategies should be implemented based on the trends in liver cirrhosis.

The Global Burden of Disease (GBD) study provides estimates the liver cirrhosis burden in 195 countries and territories. By using the latest GBD 2017 study data, researchers can extensively investigate the trends and landscape of liver cirrhosis throughout the world. Bosetti *et al*. studied the worldwide mortality of cirrhosis in 2002, and de Carvalho *et al*. described the burden of liver cirrhosis in Brazil in 2017 [2, 5]. No study has been conducted to investigate the landscape of liver cirrhosis worldwide via the newest GBD data. In this study, we used GBD data to evaluate detailed information on liver cirrhosis. We also investigated the burden of liver cirrhosis by using the prevalence of various etiologies and overall liver cirrhosis prevalence.

Methods

Study data

Detailed information on liver cirrhosis was obtained from the GBD 2017 study. By using the sociodemographic index (SDI), the 195 countries and territories in the GBD 2017 study were divided into 5 groups. The 195 countries and territories were grouped into 21 regions according to their geographical location. The method of extracting data and the estimation method of liver cirrhosis disease burden were based on the Liu *et al* study [1]. Moreover, we collected and analyzed the human development index (HDI) and matched the HDI with the GBD data.

Statistical analysis

To study the trend in prevalence from 1990 to 2017, the age-standardized prevalence rate (ASR) and the estimated annual percentage change (EAPC) were used [1, 7]. By analyzing the ASR, we determine the prevalence of the disease and changes in etiology. Moreover, the ASR provided a theoretical basis for establishing targeted preventive strategies for public health departments [8]. In our study, EAPC was used to assess the trend in the ASR over a period of time [8, 9]. Additionally, a correlation analysis was conducted to study the influential factors for EAPC. All data were analyzed by R software (R 3.5.1 software, Institute for Statistics and Mathematics) and STATA (STATA 13.1, StataCorp LLC). A *p*-value less than 0.05 was considered statistically significant.

Results

Global liver cirrhosis burden

Globally, the number of prevalent cases increased 74.53%. China had the largest number of patients in 1990 (0.27 billion) and in 2017 (0.42 billion) (Fig. 1A-B, Table S6). Although China had the largest number of liver cirrhosis patients, the growth rate was only 54.88%. The United Arab Emirates had the highest increase with a growth rate of 837.26% (Fig. 1B, Table S6).

The worldwide ASR was 19640.0 per 100000 in 2017 and 15938.0 per 100000 in 1990 (Fig. 2A-B, Table 1). The highest ASR was found in Egypt, followed by Qatar and United Arab Emirates (Fig. 2A-B). The worldwide ASR increase 0.75 per year (95% CI 0.73–0.77) (Fig. 2C, Table 1). The largest increase was found in Oman, followed by Iran, Saint Vincent and the Grenadines (Fig. 2C). Forty of the 195 countries and territories demonstrated a decrease in ASR, and the largest decrease was observed in Mozambique (Fig. 2C).

Table 1
The prevalence cases, age-standardized prevalence, and temporal trend of liver cirrhosis

Characteristics	1990		2017		1990–2017
	Prevalence cases No. ×10^3 (95% UI)	ASR per 100,000 No. (95% UI)	Prevalence cases No. ×10^3 (95% UI)	ASR per 100,000 No. (95% UI)	EAPC No. (95% CI)
Overall	859806.2(824380.7-897826.9)	15938.0(15281.3-16642.7)	1500585.1(1448741.6-556007.5)	19640.0(18961.4-20365.4)	0.75(0.73–0.77)
Sex					
Male	497119.5(475967.8-518679.3)	18293.1(17514.7-19086.4)	869833.4(840589.6-902125.6)	22684.3(21921.7-23526.5)	0.78(0.76–0.80)
Female	362686.7(347656.9-378963.6)	13547.3(12985.9-14155.3)	630751.7(608217.5-654309.0)	16572.8(15980.7-17191.7)	0.71(0.68–0.74)
Socio-demographic index					
Low	94685.8(88465.3-100505.6)	13575.0(12683.2-14409.4)	184884.8(173903.4-195232.8)	14333.2(13481.9-15135.4)	0.17(0.15–0.19)
Low-middle	162774.5(155126.4-171196.1)	15588.4(14856.0-16394.9)	306238.4(293912.5-318516.3)	17964.2(17241.1-18684.4)	0.47(0.44–0.50)
Middle	274254.4(261754.5-287477.2)	17681.1(16875.2-18533.5)	465401.9(450109.7-481764.9)	22265.4(21533.8-23048.2)	0.84(0.80–0.89)
Middle-high	204223.0(196299.4-212386.9)	18365.4(17652.8-19099.6)	348974.6(338232.4-360842.9)	25154.0(24379.7-26009.5)	1.13(1.09–1.18)
High	118729.6(115131.7-122453.7)	12291.3(11918.9-12676.9)	187162.1(181501.7-193274.6)	16420.4(15923.8-16956.7)	1.10(1.05–1.15)
Etiology					
Hepatitis B	333780.7(302793.8-363301.0)	6187.2(5612.8-6734.4)	431116.3(395729.0-468718.9)	5642.5(5179.4-6134.7)	-0.39(-0.46–0.34)
Hepatitis C	104466.6(92754.6-118648.8)	1936.5(1719.4-2199.4)	134493.9(118558.2-153823.8)	1760.3(1551.7-2013.3)	-0.39(-0.42–0.36)
Alcohol use	14608.3(13711.3-15577.7)	270.8(254.2-288.8)	26041.9(24252.8-28011.2)	340.8(317.4-366.6)	0.84(0.79–0.89)
NASH use	395517.8(379947.3-411747.6)	7331.6(7043.0-7632.4)	892322.8(858624.9-927954.4)	11678.9(11237.9-12145.3)	1.74(1.73–1.75)
other causes	11435.6(10525.0-12332.8)	212.0(195.1-228.6)	16616.0(15165.6-17954.6)	217.5(198.5–235.0)	0.04(-0.02-0.10)
Region					
Asia Pacific–high income	24927.2(24150.4-25743.5)	14362.3(13914.7-14832.6)	32679.1(31683.4-33789.1)	17472.2(16939.9-18065.7)	0.74(0.72–0.76)
Central Asia	13499.3(12852.9-14239.1)	19352.0(18425.3-20412.5)	18786.0(18042.2-19689.0)	20660.9(19842.9-21654.0)	0.19(0.16–0.22)
East Asia	282331.3(267461.8-296431.3)	22431.3(21249.9-23551.6)	437097.0(421139.9-454180.5)	29420.0(28346.0-30569.8)	0.95(0.87–1.02)
South Asia	117234.1(111749.9-122586.1)	10573.3(10078.7-11056.0)	227846.1(219321.8-237112.8)	12781.1(12302.9-13300.9)	0.73(0.68–0.78)
Southeast Asia	82056.6(78101.9-85947.5)	17580.1(16732.8-18413.7)	153712.2(148324.5-159319.1)	23272.7(22456.9-24121.6)	1.10(1.06–1.14)

Characteristics	1990		2017		1990–2017
	Prevalence cases No. ×10^3 (95% UI)	ASR per 100,000 No. (95% UI)	Prevalence cases No. ×10^3 (95% UI)	ASR per 100,000 No. (95% UI)	EAPC No. (95% CI)
Australasia	2175.9(2096.6-2260.3)	10734.0(10342.8-11150.3)	3984.6(3846.4-4125.6)	14034.5(13547.6-14531.3)	1.04(0.98–1.09)
Caribbean	3740.2(3587.6-3899.9)	10590.6(10158.5-11042.8)	7162.3(6855.5-7473.1)	15481.0(14817.9-16152.8)	1.51(1.48–1.54)
Central Europe	16411.8(15915.2-16928.1)	13221.7(12821.6-3637.7)	19332.0(18735.3-19909.0)	16839.2(16319.4-17341.8)	0.96(0.93–0.98)
Eastern Europe	34660.8(33341.6-36086.0)	15273.8(14692.5-15901.8)	40422.1(39099.0-41913.1)	19230.4(18600.9-19939.7)	0.90(0.87–0.94)
Western Europe	44535.2(43087.6-46012.2)	11547.2(11171.9-11930.2)	66697.6(64440.6-69061.5)	15404.7(14883.4-15950.6)	1.09(1.00-1.19)
Andean Latin America	4081.7(3930.9-4247.9)	10640.5(10247.5-11074.0)	9682.7(9385.1-9984.5)	15757.3(15273.1-16248.5)	1.48(1.46–1.49)
Central Latin America	22705.7(21807.9-23684.0)	13832.7(13285.8-14428.7)	50325.7(48670.7-52059.5)	19697.8(19050.0-20376.4)	1.31(1.24–1.39)
Southern Latin America	4206.2(4071.5-4346.8)	8488.9(8216.9-8772.5)	7920.9(7673.4–8183.0)	12072.9(11695.7-12472.4)	1.35(1.34–1.36)
Tropical Latin America	18969.0(18081.5-19864.1)	12361.5(11783.1-12944.8)	39332.2(37906.3-40869.9)	17980.9(17329.1-18683.9)	1.38(1.33–1.42)
North Africa and Middle East	65692.8(63184.7-68480.2)	19270.1(18534.4-20087.8)	154371.3(149104.3-159988.0)	25720.7(24843.2-26656.6)	1.08(1.03–1.14)
North America–high income	28629.0(27602.5-29744.1)	10198.5(9832.8-10595.7)	51926.9(50118.1-53900.2)	14388.8(13887.6-14935.6)	1.31(1.25–1.37)
Oceania	1474.4(1374.6-1569.5)	22833.1(21288.4-24306.7)	3149.2(2875.1-3345.6)	24988.0(22813.6-26546.2)	0.40(0.34–0.45)
Central Sub-Saharan Africa	11043.6(10010.8-11891.4)	20070.5(18193.6-21611.4)	21453.1(18431.5-23405.3)	17632.2(15148.7-19236.7)	-0.57(-0.68–0.46)
Eastern Sub-Saharan Africa	27284.0(25413.7-29317.5)	14242.8(13266.5-15304.4)	53083.1(49619.7-56551.1)	13501.0(12620.1-14383.0)	-0.29(-0.33–0.24)
Southern Sub-Saharan Africa	10896.7(10117.4-11680.6)	20763.0(19278.2-22256.6)	15345.9(14605.0-16118.5)	19833.4(18875.8-20831.9)	-0.08(-0.16-0.00)
Western Sub-Saharan Africa	43250.7(38022.3-46327.2)	22498.8(19779.0-24099.2)	86275.2(76873.3-91565.7)	19887.5(17720.2-21107.0)	-0.63(-0.72–0.55)

The prevalence increased in all 5 SDI regions, especially in the middle-high SDI regions (Fig. 3, Table 1). For geographical regions, the number of prevalent cases increased in all 21 regions (Fig. 4A), and the largest number of liver cirrhosis cases was observed in East Asia, followed by South Asia and Southeast Asia (Fig. 4B). The highest ASR in 2017 was also found in East Asia (Fig. 4C, Table 1). Additionally, the greatest increase in ASR was found in the Caribbean (Table 1). In contrast, the greatest decrease in ASR was found in Western Sub-Saharan Africa, with an EAPC of -0.63 (95% CI -0.72–0.55) (Table 1).

For etiologies, NASH was the most important etiology for liver cirrhosis, with 0.89 billion prevalent patients (59.46% of liver cirrhosis cases). A total of 0.43 billion prevalence cases were infected with HBV (28.72%) (Fig. 5A, Table 1). Additionally, the greatest increase in

ASR was found in patients with NASH (EAPC = 1.74 95% CI 1.73–1.75). The ASR decreased in patients infected with HBV and HCV from 1990 to 2017 (Table 1).

The Influential Factors For EAPC

The ASR of liver cirrhosis could be considered the disease reservoir at baseline. Additionally, the HDI could be considered the level of available medical resources. The EAPC was negatively correlated with the ASR in 1990 (r=-0.548, p 0.001) (Fig. 5B). In contrast, the EAPC was positively correlated with the HDI in 2017 (r = 0.628, p 0.001) (Fig. 5B).

Liver Cirrhosis Due To NASH

Globally, approximately 59.46% of patients with liver cirrhosis had NASH in 2017 (Fig. 5A, Table 1). The number of prevalent cases increased 125.61% (Table S1). The country with the largest number of patients was China, and its growth rate was 117.89% (Fig S1A-B, Table S6). The highest ASR was observed in Qatar in 1990 and in United Arab Emirates in 2017 (Fig S2A-B). The ASR of liver cirrhosis caused by NASH increased 1.74 per year (95% CI 1.73–1.75) (Table S1). The highest increase in ASR was found in Oman (Fig S2C). Additionally, 193 countries demonstrated an increase in ASR; Afghanistan and Nigeria did not. The ASR also increased in all 5 SDI regions, especially in the middle and middle-high SDI regions (Table S1). For the geographical regions, the number of prevalent cases and the ASR both increased in all 21 regions (Fig S2C, Table S1). The highest increase in ASR was observed in Western Sub-Saharan Africa (Table S1).

Liver Cirrhosis Due To Hepatitis B

The number of prevalent cases of liver cirrhosis caused by hepatitis B increased 29.16% (Table S2). Globally, approximately 28.72% of patients with prevalent liver cirrhosis had HBV in 2017 (Fig. 5A). The largest number of patients in the world were in China (Fig S3A-B). Qatar had the highest increase in the number of hepatitis B patients with a growth rate of 568.30% (Fig S3B, Table S6). The highest ASR was found in Sierra Leone (Fig S4A-B). The ASR of liver cirrhosis caused by hepatitis B displayed a minor decrease with an EAPC of -0.39 (95% CI -0.46–0.34) (Table S2). The highest EAPC was found in Taiwan. In contrast, the lowest EAPC was observed in Mexico. Additionally, the ASR decreased in all 5 SDI regions, especially in the Middle SDI regions (Table S2). For the geographical regions, the ASR also decreased in all 21 regions (Fig S4C, Table S2).

Liver Cirrhosis Due To Hepatitis C

The prevalence of liver cirrhosis caused by hepatitis C increased 28.74% (Table S3). China also had the largest number of hepatitis C patients in the world (Fig S5A-B). The United Arab Emirates had the highest increase in hepatitis C patients (Fig S5B, Table S6). The highest ASR was observed in Egypt (Fig S6A-B). Similar to the liver cirrhosis caused by hepatitis B, the ASR for HCV-related liver cirrhosis displayed a decreasing trend with an EAPC of -0.39 (95% CI -0.42–0.36) (Table S3). The largest ASR increase was found in Iran, and the largest ASR decrease was found in Equatorial Guinea (Fig S6C). Additionally, the ASR also decreased in all 5 SDI regions. Amazing, the ASR increased in Eastern Europe and North America–high income regions (Fig S6C, Table S3).

Liver Cirrhosis Due To Alcohol Use

The prevalence of liver cirrhosis caused by alcohol use increased 78.27% (Table S4). China also had the largest number of patients related to alcohol use in the world (Fig S7A-B). The United Arab Emirates had the highest increase of cirrhosis patients caused by alcohol with a growth rate of 863.93% (Fig S7B, Table S6). Hungary had the highest ASR in 1990, and Slovakia had the highest ASR in 2017 (Fig S8A-B). Globally, the ASR increased 0.84 (95% CI 0.79–0.89) per year. With respect to the individual countries, the highest increase of ASR was observed in Vietnam (Fig S8C). Additionally, the ASR increased in all 5 SDI regions (Table S4). The ASR increased in all of the geographical regions except for Asia Pacific–high income, Western Sub-Saharan Africa and Southern Sub-Saharan Africa (Fig S8C, Table S4).

Liver Cirrhosis Due To Other Causes

The prevalence of liver cirrhosis caused by other causes increased 45.30% (Table S5). Although China also had the largest number of patients related to other causes, the growth rate was 4.10%. The highest growth rate was found in Qatar, with a value of 409.68%, and the lowest growth rate was found in Bosnia and Herzegovina (Fig S9A-B, Table S6). The highest ASR was observed in South Korea and Brunei (Fig S10A-B). The global ASR remained stable during this period with an EAPC of 0.04 (95% CI -0.02-0.10) (Fig S10C, Table S5). The ASR increased in the low and low-middle regions and decreased in the other three regions. Additionally, the ASR decreased in 7 regions, including Asia Pacific–high income, East Asia, Central Europe, etc. (Fig S10C, Table S5).

Discussion

The worldwide prevalence of liver cirrhosis continues increase with poor prognosis [10]. The heterogeneous pattern in risk factors causes the prevalence of liver cirrhosis to be different and makes the development of prevention policies complex [11, 12]. Although the incidence of HBV and HCV continuously decreases, the ever-increasing incidence of liver cirrhosis caused by alcohol and NASH remains a formidable threaten [13, 14].

In our study, we analyzed the trends in liver cirrhosis. In general, the prevalence of liver cirrhosis continuously increased. The trends were mainly dominated by an increase in NASH-induced liver cirrhosis, with a smaller contribution from alcohol use. In contrast, the prevalence of HBV and HCV increased during the period, but the ASR decreased [15]. The decreasing trends were mainly caused by the decrease in the number of patients with HBV- and HCV-related liver cirrhosis [16, 17]. In contrast to our view that hepatitis is the main cause of liver cirrhosis, liver cirrhosis caused by NASH occupied a major position in the prevalent cases [15]. Consequently, exploring the exact pattern of liver cirrhosis etiologies is important for developing specific preventive measures. In our study, the HDI and EAPC were found to be positively correlated. HDI was a summary measure indicative of a long and healthy life, being knowledgeable and having a decent standard of living. The HDI simplified and captured only part of human development details. Moreover, patients with liver cirrhosis had a long survival time. With the increase in the life expectancy index, the prevalence of patients with liver cirrhosis also increased. Thus, the dimensions of HDI might be positively correlated with EAPC. Moreover, a study conducted by Liu et al also indicated that the HDI and EAPC were positively correlated in patients with liver cancer [1]. In 1990 and 2017, 46% and 59% of liver cirrhosis patients, respectively, had NASH. The highest ASR increase in prevalent cases was also found in patients with NASH, which was different from the results found in other studies [1, 18]. Additionally, in contrast to other studies that used incidence as an indicator, we used prevalence as the indicator. Because patients with liver cirrhosis had a long survival time, it was more reasonable to use prevalence as the indicator. We further analyzed the reason why NASH accounts for the highest proportion in prevalent cases. We found that liver cirrhosis caused by hepatitis accounted for the highest proportion of deaths by analyzing the GBD data, while liver cirrhosis caused by NASH accounted for the lowest proportion of deaths. Therefore, more and more patients had cirrhosis caused by NASH over time, but fewer patients died, resulting in a higher proportion of prevalent cases. A study revealed that the annual percentage change of mortality of NASH-induced cirrhosis was 3-fold greater than that for alcohol-induced cirrhosis, and NASH surpassed alcohol and hepatitis to be the leading cause of liver cirrhosis in the United States [19]. This might be related to the obesity epidemic in the United States, and the burden of NASH-induced liver cirrhosis might increase over the next decade [20]. Thus, public policy, which focused on primary prevention, prompt diagnosis, and pre-emptive therapy should establish plans to raise awareness and decrease the disease burden of NASH.

HBV was an important risk factor for liver cirrhosis in some regions [21, 22]. Moreover, HBV infection contributed to half of the mortality associated with liver cancer [23]. In our study, we found that liver cirrhosis caused by HBV was more prevalent in the low-middle and middle SDI regions. Additionally, more than 50% of patients with liver cirrhosis in Africa were caused by HBV, and nearly 40% of the cases in East Asia, Central Asia and Oceania were also caused by HBV. By promoting HBV vaccination, the ASR of the 21 regions decreased over the last few decades. Although China had the largest number of HBV patients, the growth rate was only 10.21% from 1990 to 2017. This was mainly due to the promotion of HBV vaccines in China [24]. By implementing these measures, the number of patients suffering from HBV infection was significantly suppressed in the general population [25, 26]. Amazingly, although the ASR decreased during the period in all 5 SDI regions, the smallest decrease was found in high the SDI regions, such as North America–high income and South Asia. This finding indicates that more effective public measures to prevent HBV should be implemented in these countries [27]. Moreover, the development of anti-HBV drugs, such as entecavir and tenofovir, has further reduced the number of patients [28]. Thus, we can expect that the number of patients with liver cirrhosis caused by HBV will be significantly decreased in the future.

Similar to liver cirrhosis caused by HBV, the ASR of liver cirrhosis caused by HCV also decreased. Additionally, the ASR of liver cirrhosis caused by HCV also decreased in all 5 SDI regions. To our surprise, the ASR increased in Eastern Europe, Tropical Latin America and North America–high income, which was not the same as the results reported in the study conducted by The Polaris Observatory HCV Collaborators [29]. China also had the largest number of patients with HCV, but the growth rate was 34.01% [30]. This might be related to a lack of effective treatment measures before 2014. Subsequently, direct-acting antiviral therapy was introduced, and more than 90% of patients with all genotypes of HCV could be cured [31]. As a result, interventions should be introduced all over the world, such as promoting direct-acting antiviral therapy and reducing the therapy price.

Alcohol was proven to be a major risk factor for liver cirrhosis. The ASR of liver cirrhosis caused by alcohol use increased from 1990 to 2017. The results obtained by Asrani et al also revealed that alcohol use and NASH have overtaken hepatitis as the primary causes of liver diseases in Western countries [32]. The increase in ASR was higher in females than in males, similar to the result obtained by Roerecke et al [33]. Additionally, alcohol was found to play an increasingly important role in chronic liver diseases [34]. Thus, polices to reduce alcohol consumption should be implemented to improve population health, and people with high alcohol consumption should receive interventions to reduce their intake [33].

Although the GBD data demonstrated the temporal trend in the prevalence of liver cirrhosis, several limitations should be noted. The accuracy of results obtained from GBD data depend on the quality and quantity of liver cirrhosis data. In some countries or regions, the liver cirrhosis data were incomplete or even missing. This may have led to an underestimation of the severity of liver cirrhosis. Additionally, we could only study the temporal trend in the prevalence of liver cirrhosis by each etiology, and the interaction between etiologies could not be studied via the GBD data.

In summary, liver cirrhosis poses a huge threat to people's health. Although the ASR of liver cirrhosis caused by hepatitis decreased with HBV vaccination and direct-acting antiviral therapy, the ASR of liver cirrhosis caused by alcohol and NASH continued to grow during the study period. Thus, public health priorities that target alcohol consumption and NASH should be implemented as soon as possible.

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Supplemental Figure Captions

Supplemental figure 1. The worldwide prevalence cases of liver cirrhosis caused by HBV in countries. (A) The worldwide prevalence cases of liver cirrhosis caused by HBV in 1990. (B) The worldwide prevalence cases of liver cirrhosis caused by HBV in 2017.

Supplemental figure 2. The global burden of liver cirrhosis caused by HBV in countries. (A) The ASR of liver cirrhosis caused by HBV in 1990. (B) The ASR of liver cirrhosis caused by HBV in 2017. (C) The EAPC of liver cirrhosis caused by HBV from 1990 to 2017.

Supplemental figure 3. The worldwide prevalence cases of liver cirrhosis caused by HCV in countries. (A) The worldwide prevalence cases of liver cirrhosis caused by HCV in 1990. (B) The worldwide prevalence cases of liver cirrhosis caused by HCV in 2017.

Supplemental figure 4. The global burden of liver cirrhosis caused by HCV in countries. (A) The ASR of liver cirrhosis caused by HCV in 1990. (B) The ASR of liver cirrhosis caused by HCV in 2017. (C) The EAPC of liver cirrhosis caused by HCV from 1990 to 2017.

Supplemental figure 5. The worldwide prevalence cases of liver cirrhosis caused by alcohol use in countries. (A) The worldwide prevalence cases of liver cirrhosis caused by alcohol use in 1990. (B) The worldwide prevalence cases of liver cirrhosis caused by alcohol use in 2017.

Supplemental figure 6. The global burden of liver cirrhosis caused by alcohol use in countries. (A) The ASR of liver cirrhosis caused by alcohol use in 1990. (B) The ASR of liver cirrhosis caused by alcohol use in 2017. (C) The EAPC of liver cirrhosis caused by alcohol use from 1990 to 2017.

Supplemental figure 7. The worldwide prevalence cases of liver cirrhosis caused by NASH in countries. (A) The worldwide prevalence cases of liver cirrhosis caused by NASH in 1990. (B) The worldwide prevalence cases of liver cirrhosis caused by NASH in 2017.

Supplemental figure 8. The global burden of liver cirrhosis caused by NASH in countries. (A) The ASR of liver cirrhosis caused by NASH in 1990. (B) The ASR of liver cirrhosis caused by NASH in 2017. (C) The EAPC of liver cirrhosis caused by NASH from 1990 to 2017.

Supplemental figure 9. The worldwide prevalence cases of liver cirrhosis caused by other causes in countries. (A) The worldwide prevalence cases of liver cirrhosis caused by other causes in 1990. (B) The worldwide prevalence cases of liver cirrhosis caused by other causes in 2017.

Supplemental figure 10. The global burden of liver cirrhosis caused by other causes in countries. (A) The ASR of liver cirrhosis caused by other causes in 1990. (B) The ASR of liver cirrhosis caused by other causes in 2017. (C) The EAPC of liver cirrhosis caused by other causes from 1990 to 2017.

Declarations

Ethical Approval and Consent to participate

Not applicable.

Consent for publication

All the author consent for publication

Availability of supporting data

Supporting data was shown in the supplemental figures and tables.

Competing interests

The authors declare no conflicts of interest.

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Authors' contributions

Study design: Zhai MM, Long JH, Li YM and Shu B. Data collection: Zhai MM, Long JH, Li YM and Shu B. Data analysis: Liu SS and Liu C. Figures: Li L. Manuscript writing: Long JH, Li L, Yang LP and Liu SS. Manuscript proofing: Long JH, Zhai MM, Li YM and Bo Shu.

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Not applicable.

Authors' information

Authors' information was shown in the title page.

Figures

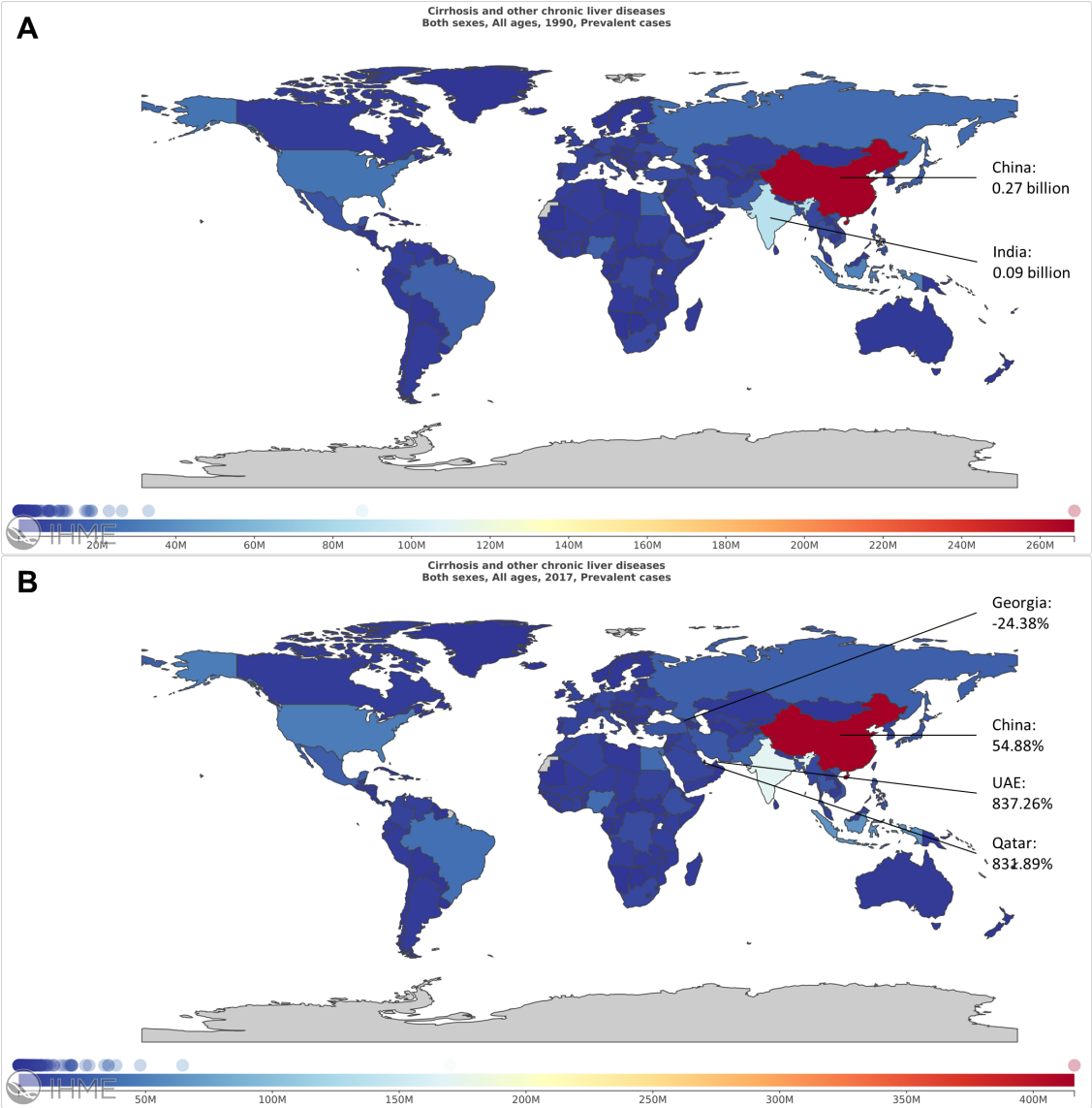

Figure 1

The worldwide prevalence cases of liver cirrhosis in 195 countries and territories. (A) The worldwide prevalence cases of liver cirrhosis in 1990. (B) The worldwide prevalence cases of liver cirrhosis in 2017. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

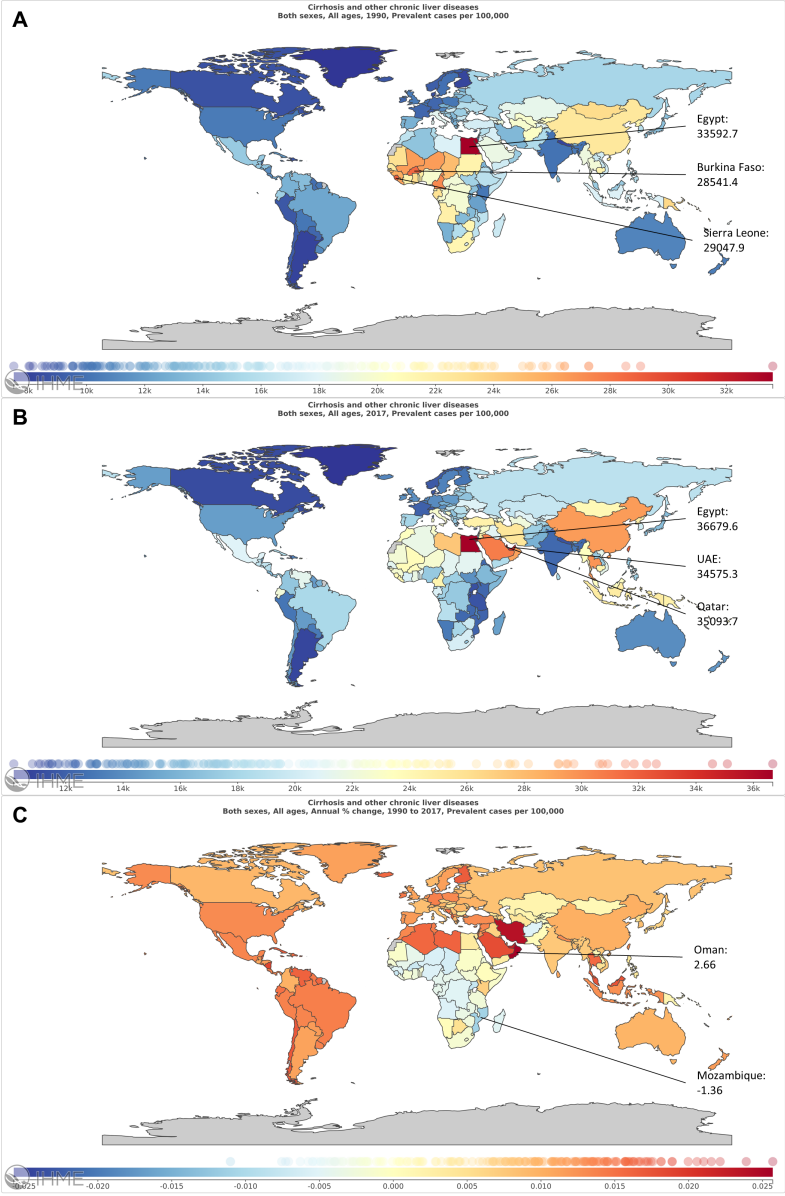

Figure 2

The global burden of liver cirrhosis in 195 countries and territories. (A) The ASR of liver cirrhosis in 1990. (B) The ASR of liver cirrhosis in 2017. (C) The EAPC of liver cirrhosis from 1990 to 2017. Note: The designations employed and the presentation of the material on this map do not imply the expression of any opinion whatsoever on the part of Research Square concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. This map has been provided by the authors.

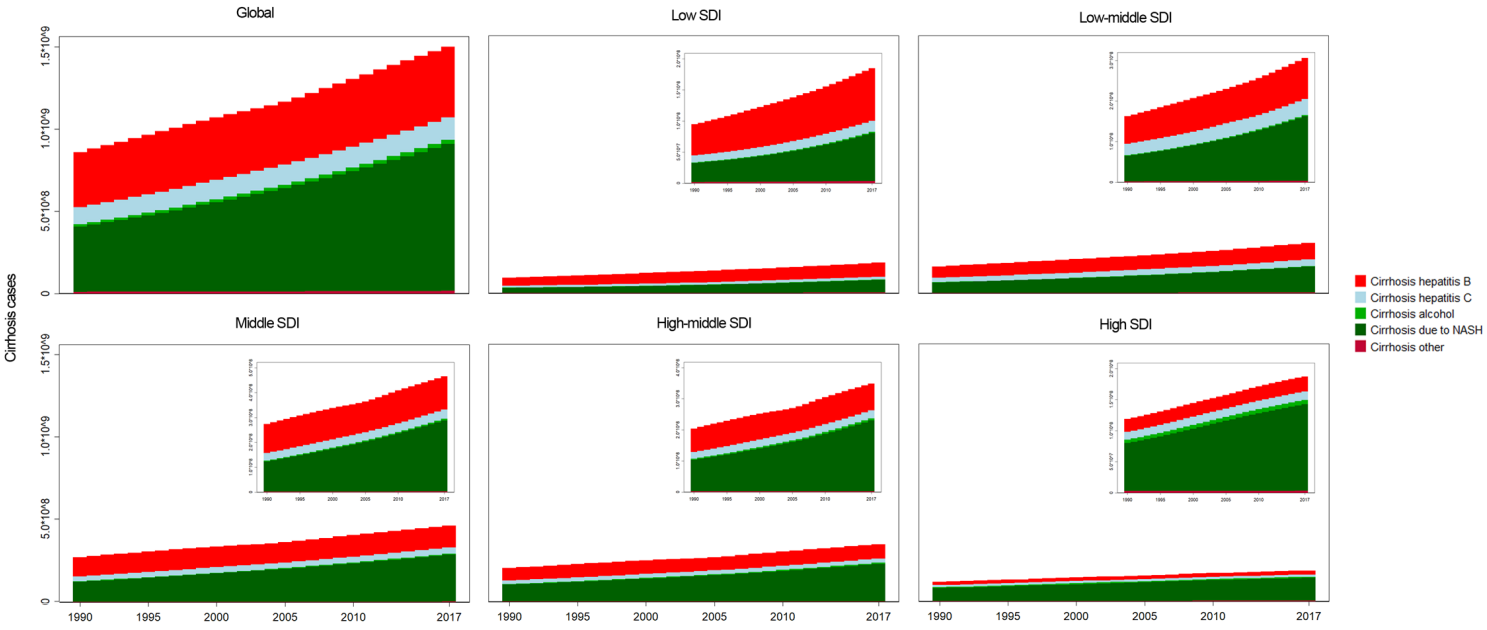

Figure 3

The analysis of liver cirrhosis and its etiologies. The liver cirrhosis cases caused by different etiologies, by SDI regions.

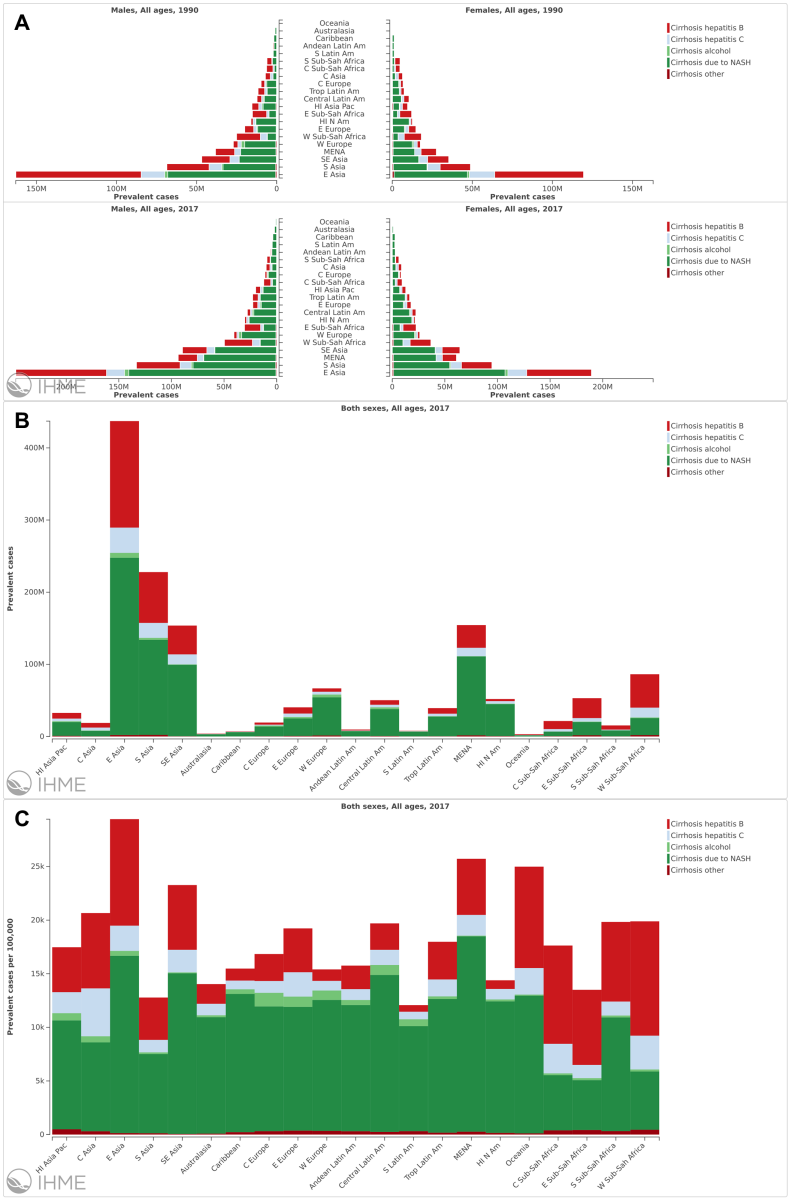

Figure 4

The analysis of liver cirrhosis at a regional level. (A) The prevalence cases of liver cirrhosis caused by different etiologies in different region and sex. (B) The prevalence cases of liver cirrhosis in different regions. (C) The ASR of liver cirrhosis in different regions.

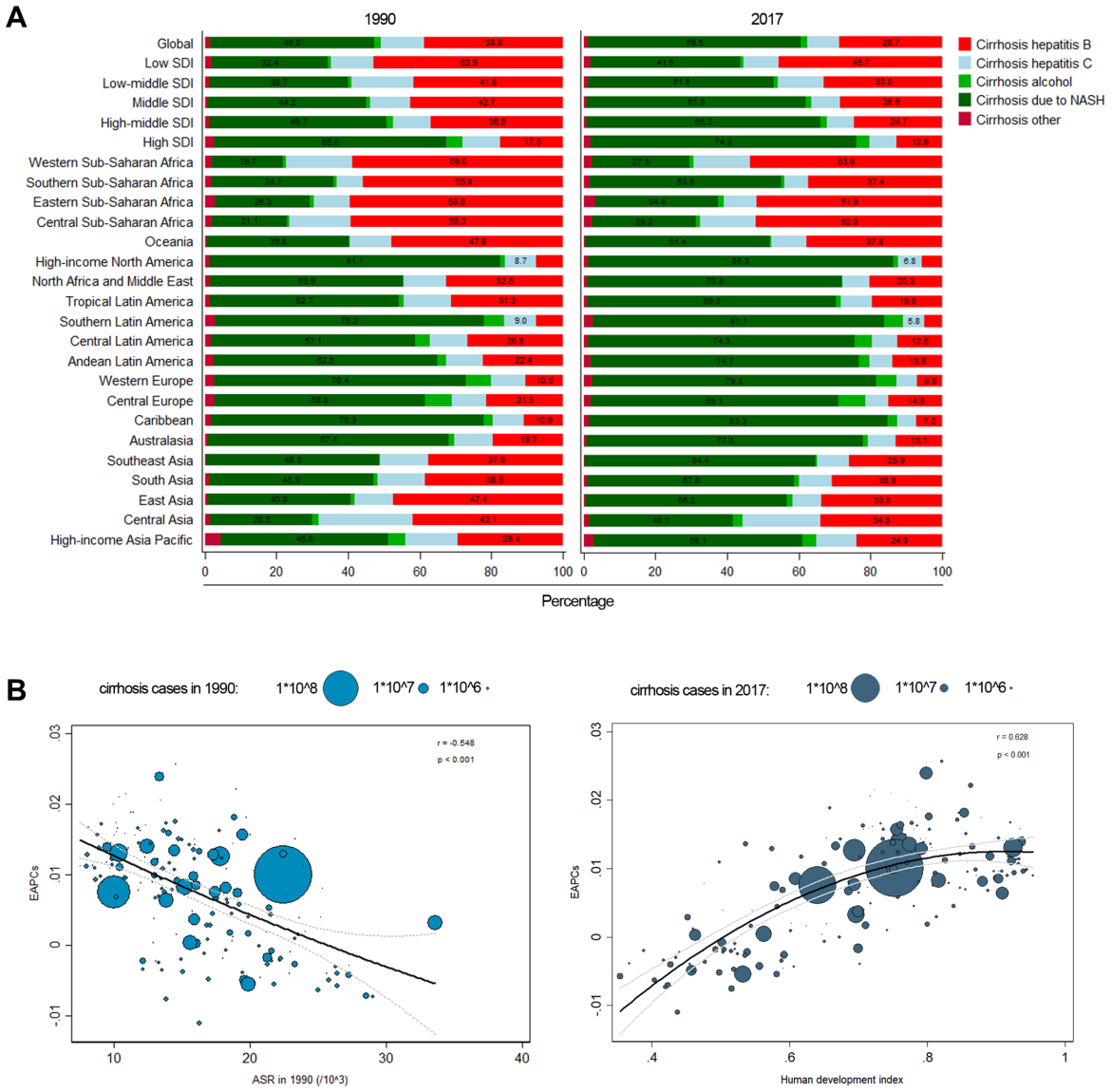

Figure 5

(A) Composition ratio of each etiology in prevalence cases of liver cirrhosis in 1990 and 2017. (B) The correlation between EAPC and ASR in 1990, HDI in 2017.

Supplementary Files

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