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Trends in the disease burden of HBV and HCV infection in China from 1990-2019

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ABSTRACT

Objectives: This study aimed to reveal the 30-year dynamics of hepatitis B virus (HBV) and hepatitis C virus (HCV) disease burden in China from 1990-2019.
Methods: HBV/HCV data were retrieved from the Global Burden of Disease database. Joinpoint regression was used to examine temporal trends. Age-period-cohort models were applied to evaluate effects of patient age, period, and cohort on HBV/HCV-associated mortality and incidences.
Results: A dramatic decrease in the disease burden of HBV was found from 1990-2019, but the disease burden of HCV has remained stable since 2000. Patient age, period, and cohort exerted a significant effect on the diseases burden of HBV and HCV infection. Compared with women, men had a higher risk of HBV/HCV infections as well as HBV/HCV-associated mortality and liver cancer. Overweight, alcohol, tobacco, and drug use were important risk factors associated with HBV/HCV-associated liver cancer. The incidences of HBV- and HCV-associated liver cancer from 2019-2044 are expected to decrease by 39.4% and 33.3%, respectively.
Conclusion: The disease burden of HBV/HCV infection has decreased in China over the past 30 years, but HBV incidences remain high, especially in men. Effective management of HBV and HCV infections is still needed for high-risk populations.

Introduction

Hepatitis B virus (HBV) and hepatitis C virus (HCV) could cause acute/chronic hepatitis, cirrhosis, and eventually liver cancer (Fattovich, 2003; Ringelhan et al., 2017). At least 60% of liver cancers can be found in patients with HBV and/or HCV infection (de Martel et al., 2015). In the evaluation of global disease burden measured by the disability-adjusted life year (DALY), HBV and HCV accounted for the largest proportion of DALY in the category of chronic liver diseases (Paik et al., 2020). On the one hand, acute hepatitis B usually causes elevated transaminases and temporary jaundice, which are usually transient and self-limiting for most patients (Trépo et al., 2014). In contrast, patients with chronic HBV are more likely to progress to end-stage liver diseases and liver cancer, resulting in a high risk for mortality (Fattovich et al., 2008). On the other hand, compared with chronic HBV, chronic HCV often causes liver fibrosis and cirrhosis, which lead to a higher risk of liver cancer and mortality (Bruix et al., 2005; Westbrook and Dusheiko, 2014). Patients with acute hepatitis C are often asymptomatic (Grebely et al., 2011) and symptomatic patients usually have clinical symptoms, such as fatigue, nausea, jaundice, or ele-

Abbreviations: DALY, Disability-standardized life year; ASDR, Age-standardized DALY rate; ASIR, Age-standardized incident rate; ASMR, Age-standardized mortality rate; AAPC, Average annual percentage change; APC, Annual percentage change; GBD, Global Burden of Disease..

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vated aminotransferase, which are similar to those with acute hepatitis B.

A large population of patients infected with HBV and HCV have been reported in China, despite a great effort to control hepatitis diseases. China has invested heavily in basic research and vaccine and drug development to control the spread of HBV and HCV (Liu et al., 2016). Since the early 1990s, HCV screening (often before blood transfusion) and HBV immunization programs have been conducted mandatorily in China (Wang et al., 2014). Since 2005, the free HBV vaccination program has been implemented for newborns (Kane et al., 2013). These programs have consistently reduced the number of HBV and HCV infections to a large extent. Despite these efforts, the absolute number of HBV and HCV cases remains high in China due to its large population (Liu et al., 2019a).

As one of the most comprehensive global epidemiologic databases, the Global Burden of Disease (GBD) 2019 database includes information on the incidence, mortality, and DALYs (GBD 2019 Viewpoint Collaborators, 2019; GBD 2019 Diseases and Injuries Collaborators, 2020), but detailed analyses of HBV/HCV-associated disease burden in China have not been reported to date. On the basis of the GBD 2019 database, this study aimed to reveal the disease burden of HBV/HCV-associated liver diseases, explore the mortality-related risk factors of chronic HBV/HCV diseases, and evaluate the future trend of HBV/HCV-associated liver cancer in China.

Methods

Data source

We retrieved data from the GBD 2019 database (https://ghdx.healthdata.org/gbd-2019). The estimated population of China was retrieved from the United Nations World Population Prospects 2019 Revision (https://population.un.org/wpp/). The world standard population data were obtained from the World Standard (WHO 2000-2025) (https://seer.cancer.gov/stdpopulations/world.who.html).

Data collection

The incidences, mortality, DALY rates, sex, age, and main categories of diseases in China from 1990-2019 were extracted from the GBD 2019 database. HBV- and HCV-associated diseases include acute hepatitis, chronic hepatitis, cirrhosis, and liver cancer. Metric parameters included rates (per 100,000 population), percentages, and numbers. Risk factors attributable to deaths were also collected from the GBD 2019 database. A total of four factors were collected, including body mass index (BMI), alcohol use, drug use, and tobacco use. High BMI was defined as a value above 25 (kg/m^2). Alcohol use was defined as the average pure alcohol consumption $\geq$10g/day during the past 12 months. The consumption of pure alcohol (males: $\geq$60g, females: $\geq$48g) on a single occasion was defined as binge drinking. Drug use was defined as the regular use of opioids, cannabis, cocaine, amphetamines, and ever injected drugs (GBD 2016 Risk Factor Collaborators, 2017). Tobacco use included smoking, chewing tobacco, and secondhand smoke.

Statistical analysis

The age-standardized rate was known to eliminate the differences in age structures. The methodology that calculates the age-standardized rate was reported previously (Liu et al., 2019b). To analyze the temporal trend of HBV and HCV infection per year, we used joinpoint regression models (https://surveillance.cancer.gov/joinpoint/) to calculate the annual percentage changes (APC), average annual percentage change (AAPC), as well as the trend test of them (Liu et al., 2021). The grid search method was used to determine the joinpoint, while permutation tests were used to select the optimal model. To evaluate the effects of age, period, and cohort on the incidence and mortality of HBV and HCV infection, we used the APC web tool (https://dceg.cancer.gov/tools/analysis/apc) to estimate the parameter of net drift, longitudinal age trend, age, period, and cohort deviations. The definition and function of these parameters have been discussed in previous studies (Gao et al., 2020). To predict the trends of incidence and mortality in HBV and HCV infection, we used the age-period-cohort model from the Nordpred package in R that takes into account the impact of population structures (Li et al., 2021; Saeaib et al., 2019; Valery et al., 2018). A *P*-value $<$0.05 was considered statistically significant. Statistical analyses were performed using the Joinpoint Regression Program v4.9, R x64 v4.1, and GraphPad prism v8.0.1.

Results

Temporal trend of the disease burden of HBV and HCV in China

On the basis of the extracted data from the GBD 2019 database, nearly 23,355,000 patients infected with HBV (approximately 29.0% of the global HBV infections) and nearly 625,000 patients infected with HCV (approximately 10.0% of the global HCV infections) occurred in China in 2019. Male patients accounted for a majority of HBV (64.6%) and HCV (53.5%) infections in 2019. Compared with the data in 1990, the number of HBV and HCV new infections in 2019 decreased by 30.1% and 38.0%, respectively. In 2019, the number of HBV-associated DALY cases and deaths was nearly 4,979,000 and 162,000, respectively (Table 1); the number of HCV-associated DALY cases and deaths was 2,035,000 and 78,000, respectively (s). Among HBV/HCV-associated diseases, liver cancer caused the highest mortality rate in 2019 (5.8 per 100,000 for HBV, 1.75 per 100,000 for HCV), followed by cirrhosis (2.2 per 100,000 for HBV, 2.3 per 100,000 for HCV), and acute hepatitis ($<$1 per 100,000 for HBV or HCV).

We used the age-standardized incident rate (ASIR), age-standardized DALY rate (ASDR), and age-standardized mortality rate (ASMR) to quantify the disease burden of HBV and HCV infections. All rates were reported per 100,000 person-years. The ASIR of HBV-associated diseases was much higher than that of HCV-associated diseases (Figure 1). The ASIR of HBV and HCV infection was consistently higher in men than in women, and so did the ASDR and ASMR (Figures S1 and S2). From 1990-2019, the ASIR of HBV (AAPC, -2.3[-2.4–2.1]) and HCV infection (AAPC, -1.5[-2.0–1.1]) was declining (Table S1). The difference was probably caused by the fact that the ASIR of HBV-associated diseases declined rapidly from 2000-2019, whereas the ASIR of HCV-associated diseases remained stable from 2000-2019. Incidences of cirrhosis and other chronic liver diseases significantly declined from 2010-2015 and remained stable from 2015-2019. The ASIRs and ASDRs of liver cancer also remained stable from 2010-2019.

Age-period-cohort analysis of incidence and mortality

From 1990 to 2019, the net drift of incidence was -2.3% (-2.4%–2.2%) per year for HBV-associated diseases and -1.8% (-2.2–1.4%) per year for HCV-associated diseases. A decrease in the overall annual percentage of HBV-associated diseases was nearly 1.3 times higher than that of HCV-associated diseases. The net drifts of mortality were -5.6% (-5.8–5.3%) per year for HBV-associated diseases and -4.8% (-5.2- -4.4%) per year for HCV-associated diseases (Figure 2A). Note that a high absolute value of net drifts of mortality indicates a fast decrease in mortality. An increase in HBV-associated mortality was found among patients aged $\leq$50 years and a decrease in patients aged $>$50 years (Figure 2B). The

Table 1
Changes in age-standardized rates and the incidences of HBV infections in China between 1990 and 2019.

Sex	Age-standardized incidence						Age-standardized mortality						Age-standardized DALY rates					
	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)
	No.×10^5	No.×10^5		ASIR/10^5	ASIR/10^5		No.×10^3	No.×10^3		ASMR/10^5	ASMR/10^5		No.×10^3	No.×10^3		ASDR/10^5	ASDR/10^5	
Total burden for HBV																		
All	334.3	233.6	-30.1	2726.0	1397.3	-48.7	228.7	162.1	-29.1	24.7	8.1	-67.2	80.3	49.8	-38.0	793.4	247.7	-68.8
Female	123.7	82.6	-33.2	2088.8	1008.5	-51.7	52.9	29.3	-44.7	11.8	2.9	-75.4	17.3	7.8	-54.7	355.8	77.3	-78.3
Male	210.6	151.0	-28.3	3327.4	1776.9	-46.6	175.8	132.8	-24.4	37.8	13.8	-63.5	63.0	42.0	-33.4	1211.7	419.7	-65.4
Acute hepatitis B																		
All	331.6	231.0	-30.3	2699.3	1384.0	-48.7	11.5	2.9	-74.8	1.2	0.2	-83.3	6.0	1.4	-76.2	54.6	8.3	-84.8
Female	123.0	81.9	-33.4	2074.6	1001.7	-51.7	4.4	0.8	-81.3	0.9	0.1	-88.9	2.3	0.4	-82.0	44.1	5.2	-88.2
Male	208.6	149.0	-28.5	3288.3	1756.8	-46.6	7.0	2.1	-70.7	1.4	0.2	-85.7	3.7	1.0	-72.5	64.5	11.4	-82.3
Cirrhosis and other chronic liver diseases due to HBV																		
All	1.2	1.3	8.6	10.2	6.7	-34.3	64.6	42.2	-34.7	7.3	2.2	-69.9	21.7	12.4	-42.9	218.2	61.7	-71.7
Female	0.4	0.5	16.3	8.3	5.1	-38.6	21.5	11.7	-45.5	5.0	1.2	-76.0	6.3	2.9	-54.2	134.5	28.0	-79.2
Male	0.7	0.8	2.7	12.0	8.3	-30.8	43.2	30.5	-29.4	9.6	3.3	-65.6	15.4	9.5	-38.2	297.7	95.8	-67.8
Cancer due to HBV																		
All	1.6	1.4	-14.6	16.5	6.6	-60.0	152.6	117.0	-23.3	16.2	5.8	-64.2	52.7	36.0	-31.7	520.6	177.7	-65.9
Female	0.3	0.2	-33.3	5.9	1.7	-71.2	27.0	16.7	-38.1	5.9	1.6	-72.9	8.6	4.5	-47.8	177.2	44.0	-75.2
Male	1.3	1.2	-10.7	27.1	11.8	-56.5	125.6	100.3	-20.2	26.8	10.2	-61.9	44.0	31.5	-28.5	849.5	312.5	-63.2

Table 2
Changes in age-standardized rates and the incidences of HCV infections in China between 1990 and 2019.

Sex	Age-standardized incidence						Age-standardized mortality						Age-standardized DALY rates					
	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)	1990	2019	Change (%)
	No.×10^5	No.×10^5		ASIR/10^5	ASIR/10^5		No.×10^3	No.×10^3		ASMR/10^5	ASMR/10^5		No.×10^3	No.×10^{-3}		ASDR/10^5	ASDR/10^5	
Total burden for HCV																		
All	9.96	6.25	-37.2	87.9	55	-37.4	80.0	78.04	-2.4	9.7	4.0	-58.8	23.98	20.36	-15.1	253.8	100.8	-60.3
Female	4.95	2.91	-41.2	91.1	54.6	-40.1	34.5	28.43	-17.6	8.4	2.8	-66.7	9.03	6.3	-30.2	199.2	60.3	-69.7
Male	5.01	3.35	-33.1	85.0	55.9	-34.2	45.5	49.61	9.0	11.0	5.5	-50.0	14.95	14.06	-6.0	304.2	142.4	-53.2
Acute hepatitis C																		
All	8.92	4.78	-46.4	77.3	47.1	-39.1	1.05	0.09	-91.4	0.1	0*	-	0.50	0.04	-92.0	4.6	0.2	-95.7
Female	4.51	2.32	-48.6	81.5	48.6	-40.4	0.48	0.03	-93.8	0.1	0	-	0.24	0.01	-95.8	4.4	0.2	-95.5
Male	4.41	2.47	-44.0	73.5	46.2	-37.1	0.57	0.06	-89.5	0.1	0	-	0.27	0.02	-92.6	4.8	0.3	-93.8
Cirrhosis and other chronic liver diseases due to HCV																		
All	0.69	1.13	63.8	6.1	6.1	0	41.79	44.87	7.4	4.6	2.3	-50.0	14.38	13.18	-8.3	143.3	65.5	-54.3
Female	0.24	0.42	75.0	4.6	4.3	-6.5	12.11	10.66	-12.0	2.8	1.0	-64.3	3.67	2.66	-27.5	77.4	25.7	-66.8
Male	0.46	0.71	54.3	7.5	7.9	5.3	29.68	34.21	15.3	6.5	3.7	-43.1	10.71	10.52	-1.8	206.1	106	-48.6
Cancer due to HCV																		
All	0.35	0.34	-2.9	4.5	1.8	-60.0	37.16	33.08	-11	5.0	1.8	-64	9.09	7.14	-21.5	105.9	35.1	-66.9
Female	0.21	0.18	-14.3	5.0	1.7	-66.0	21.92	17.74	-19.1	5.5	1.7	-69.1	5.13	3.64	-29.0	117.4	34.5	-70.6
Male	0.15	0.16	6.7	4.0	1.9	-52.5	15.24	15.34	0.7	4.3	1.8	-58.1	3.97	3.51	-11.6	93.3	36.1	-61.3

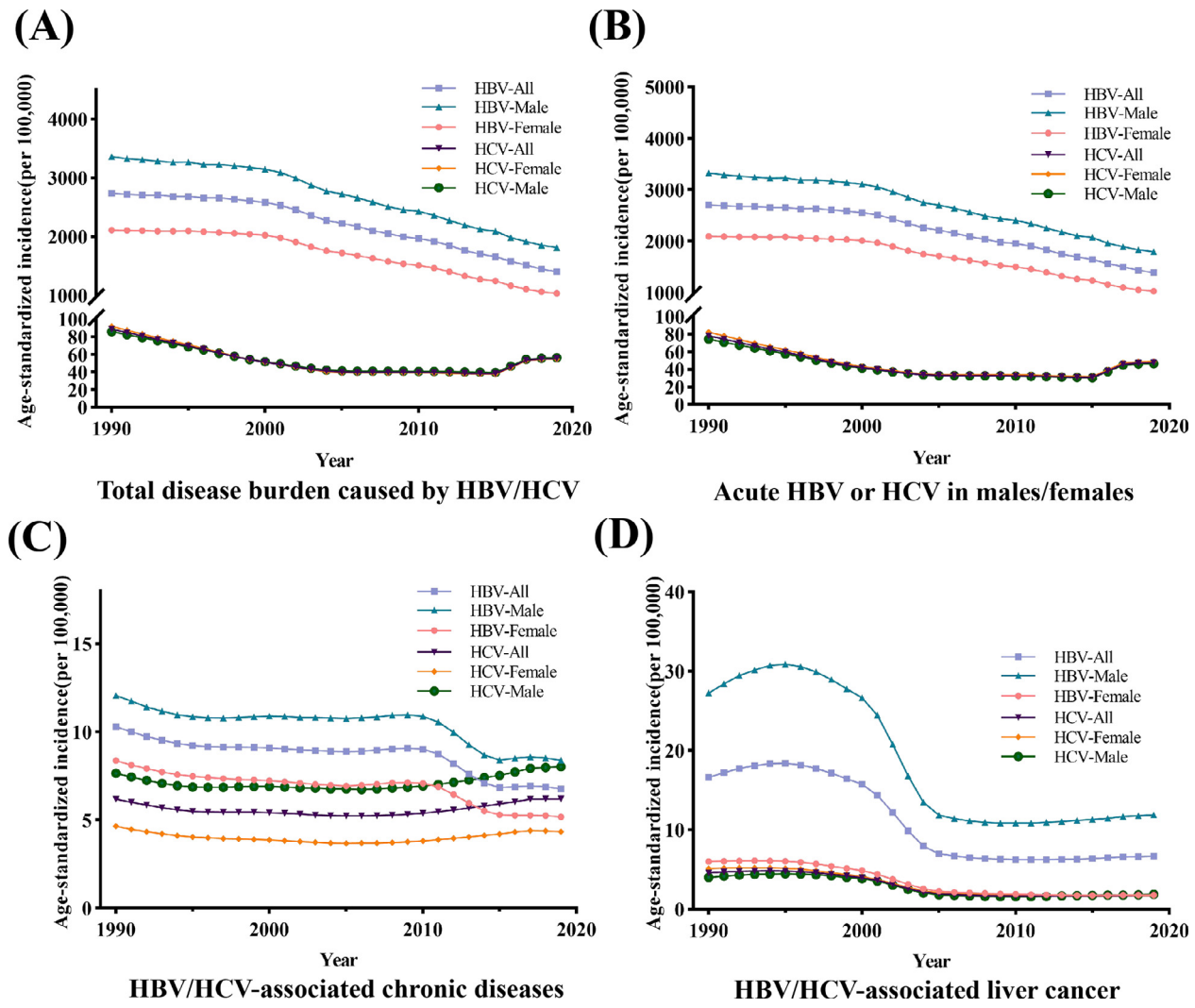

Figure 1. Temporal trend of age-standardized incidences for HBV- and HCV-associated diseases in China from 1990-2019. (A) Temporal trend of age-standardized incidences for total HBV/HCV-associated diseases; (B) Temporal trend of age-standardized incidences for acute hepatitis B and hepatitis C; (C) Temporal trend of age-standardized incidences for cirrhosis and other liver diseases associated with HBV/HCV; (D) Temporal trend of age-standardized incidences for HBV/HCV-associated liver cancer. Results of the age-standard DALY rate and age-standardized mortality are shown in Figure S1 and S2.

HCV-associated mortality was rising with age, and the mortality rate in patients aged >87 years was 14.1 per 100,000 (Figure 2B). The incidences of HCV-associated diseases were stable, whereas an increase in the incidences of HBV-associated diseases was observed in patients aged ≤30 years and a decrease in patients aged >30 years (Figure 2C). Compared with the period risk ratio from 2000-2004, there was a decrease in the period risk ratio of HBV-associated mortality (55%) and HCV-associated mortality (47%) from 2015-2019. The incidence of HBV- and HCV-associated diseases showed a similar decrease (Figure 2D). Cohort risk ratio of HBV- and HCV-associated diseases and mortality showed decreasing trends along with the birth age of patients (Figure 2E).

Risk factors for HBV/HCV-associated chronic diseases

Figure 3 shows the age distribution of HBV- and HCV-associated chronic diseases and liver cancer. The mortality risk was higher in patients with liver cancer than in those with cirrhosis or other chronic liver diseases (Figure 3). The number of deaths from HBV-associated liver cancer was highest in patients aged 65-69 years (15,654), whereas that of HCV-associated liver cancer was highest in patients aged 70-74 years (5374).

Since liver cancer, cirrhosis, and other chronic liver diseases are known for their high risk of mortality, we analyzed whether alcohol use, drug use, high BMI, or tobacco use could play a role in the risk factors of HBV/HCV-associated diseases. A large proportion (57.9%) of mortality among patients infected with HBV with cirrhosis and other chronic liver diseases could be attributable to alcohol use. In deaths of HCV-associated cirrhosis and other chronic liver diseases, alcohol use (60.2%) and drug use (81.5%) were attributed to a large proportion (Figure 4A). Tobacco use was the major death-associated factor in patients with HBV-associated liver cancer, especially those aged from 60- 69 years (25.4%). In contrast, drug use was the major death-associated factor in patients with HCV-associated liver cancer, especially in those aged from 35-59 years (88.5%) (Figure 4B).

Incidence and mortality of HBV/HCV-associated liver cancer

To predict the disease burden of HBV and HCV from 2019-2044, we used the Nordpred R package (see Methods) to evaluate the ASIR and ASMR of HBV/HCV-associated liver cancer, the number of cases, and deaths. Figure 5 shows the estimated number of HBV/HCV-infected new cases in men and women from 1990-2044.

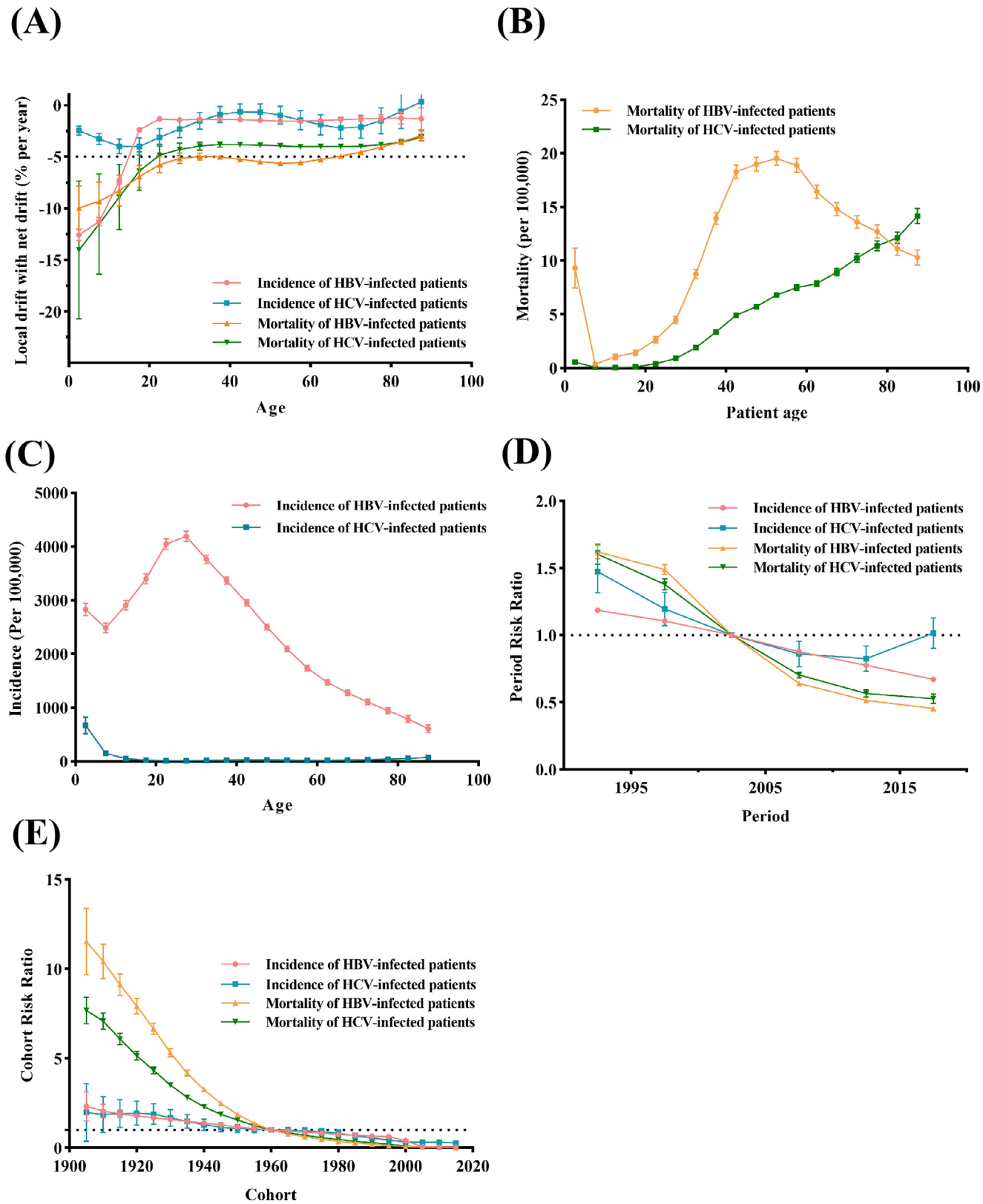

Figure 2. Age-period-cohort analysis of HBV- and HCV-associated diseases. (A) Local drift with net drift of incidence and mortality of HBV/HCV-associated diseases; (B) Age disparity of HBV- and HCV- associated mortality; (C) Age disparity of incidences of HBV/HCV–associated diseases; (D) Period risk ratio of HBV/HCV-associated incidences and mortality; (E) Cohort risk ratio of HBV/HCV-associated incidences and mortality.

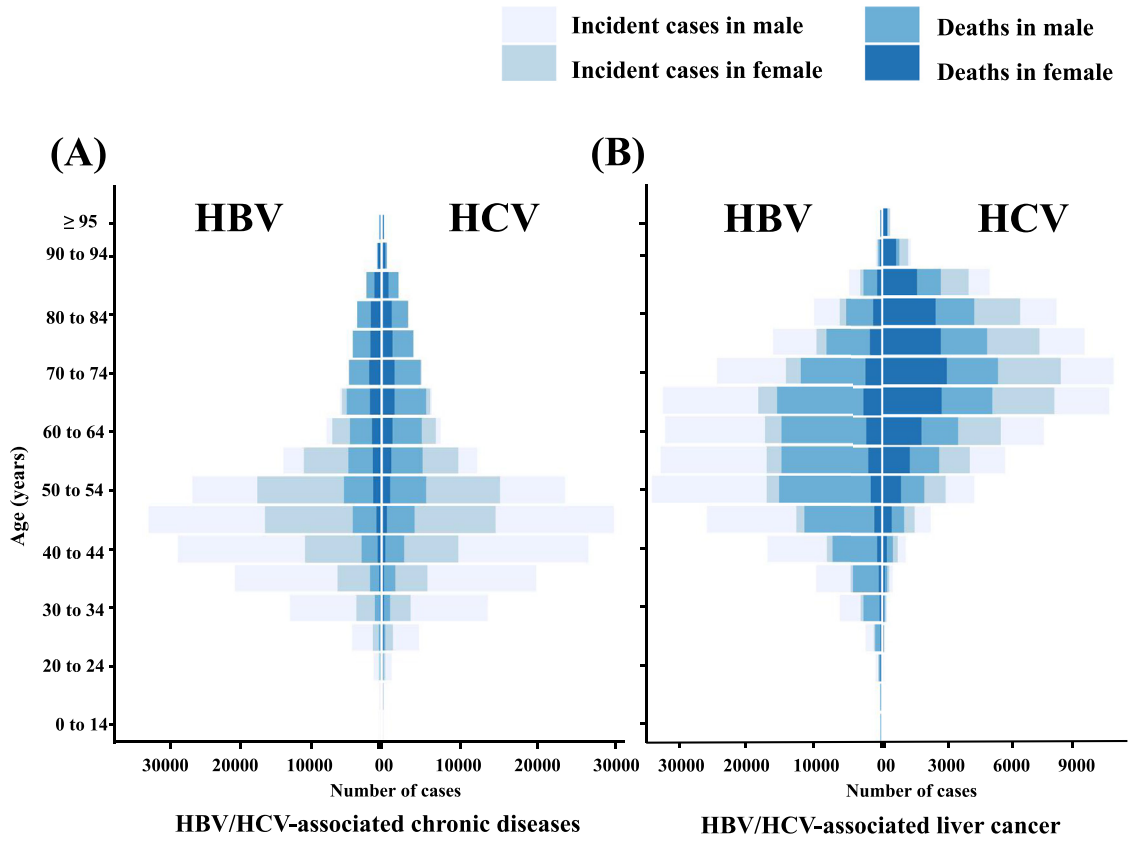

Figure 3. Age distribution of HBV- and HCV-associated chronic diseases and liver cancer in 2019. (A) Age distribution of HBV- and HCV-associated cirrhosis and other chronic liver diseases; (B) Age distribution of HBV- and HCV-associated liver cancer.

The overall incidence and mortality of HBV- and HCV-associated liver cancer is expected to steadily decline till 2034 and to remain stable thereafter. The ASIR of HBV-related liver cancer in 2019 was 6.6 per 100,000 population, which will likely fall to 4.0 per 100,000 population by 2044. If the ASIR increased 1% per year on the basis of the reference data of 2019, the number of liver cancer new cases would increase by approximately 85.9% in 2044. The difference between the upper and lower limits was 70.9% (Figure 5B). The incidences of HBV-associated liver cancer will decrease by approximately 21.0% from 2019-2044 and the decrease will be 15.4% and 28.0% among men and women, respectively.

Age-standardized mortality rates and age-standardized incidence rates shared similar patterns in patients infected with HBV with liver cancer (Figure 5A and 5C), so did the number of HBV-associated new cases and deaths (Figure 5B and 5D). There is a small decline in age-standardized incidence rates in HCV-associated liver cancer (from 1.8 per 100,000 in 2019 to 1.2 per 100,000 in 2044), with a small difference between men and women (Figure 5E and 5G). In 2019, there were 31,128 new cases of HCV-associated liver cancer, which will probably rise to 40,237 (22.6% increase) in 2044. The increase in the total incidence of HCV-associated liver cancer was 26.6% and 23.7% for men and women, respectively (Figure 5F). Compared with results in 2019, the total incidence of HCV-associated liver cancer in 2044 will increase by 34.2% (men: 25.3%, women: 30.1%) (Figure 5H).

Discussion

We analyzed the disease burden of HBV and HCV infections in China in the past 30 years. The overall HBV- and HCV-associated disease burden has been decreasing in China. The total burden of HCV infection and the burden of HCV-associated diseases also decreased globally (Ginzberg et al., 2018; Ott et al., 2017; Thrift et al., 2017). The incidence of acute hepatitis B decreased significantly over time but that of HBV-related chronic diseases remained stable in recent years. In contrast, the ASMR and ASDR of acute and chronic HBV and HCV exhibited a decreasing trend in recent years.

We used an age-period-cohort model to analyze the effect of age, period, and cohort on the incidences and mortality of HBV and HCV infection. Age effects reflect the change of incidence/mortality along with patient age. Period effects refer to the change of incidence/mortality in different time periods due to many factors, such as different screening strategies, disease diagnosis technology, changes in disease definitions and registration, and improvement in treatment. Cohort effects cover the changes of incidence/mortality due to different levels of exposure to risk factors in different generations (Robertson et al., 1999). Our results suggest that the age and period effects on the HBV- and HCV-associated incidences and mortality were statistically significant, and the risk of incidence and mortality decreased over time. Of interest, patients born after 2000 had a lower mortality risk than those born before 2000, probably due to the improvement of medical care levels and the application of antiviral drugs (Jing et al., 2020; Shi et al., 2021; Wang et al., 2014). After controlling period and cohort effects, we observed that the risk of HCV-associated mortality increased with age, whereas the risk of incidence was similar across different age groups, except for those patients aged ≤5 years. The high incidences of HCV in patients aged ≤5 years might be associated with mother-to-child transmission (Dugan et al., 2021; Gentile et al., 2014).

Since HBV- and HCV-associated deaths are mainly due to chronic liver diseases, such as cirrhosis and liver cancer, we analyzed the mortality-associated risk factors in patients with chronic hepatitis infections. It is known that many risk factors are asso-

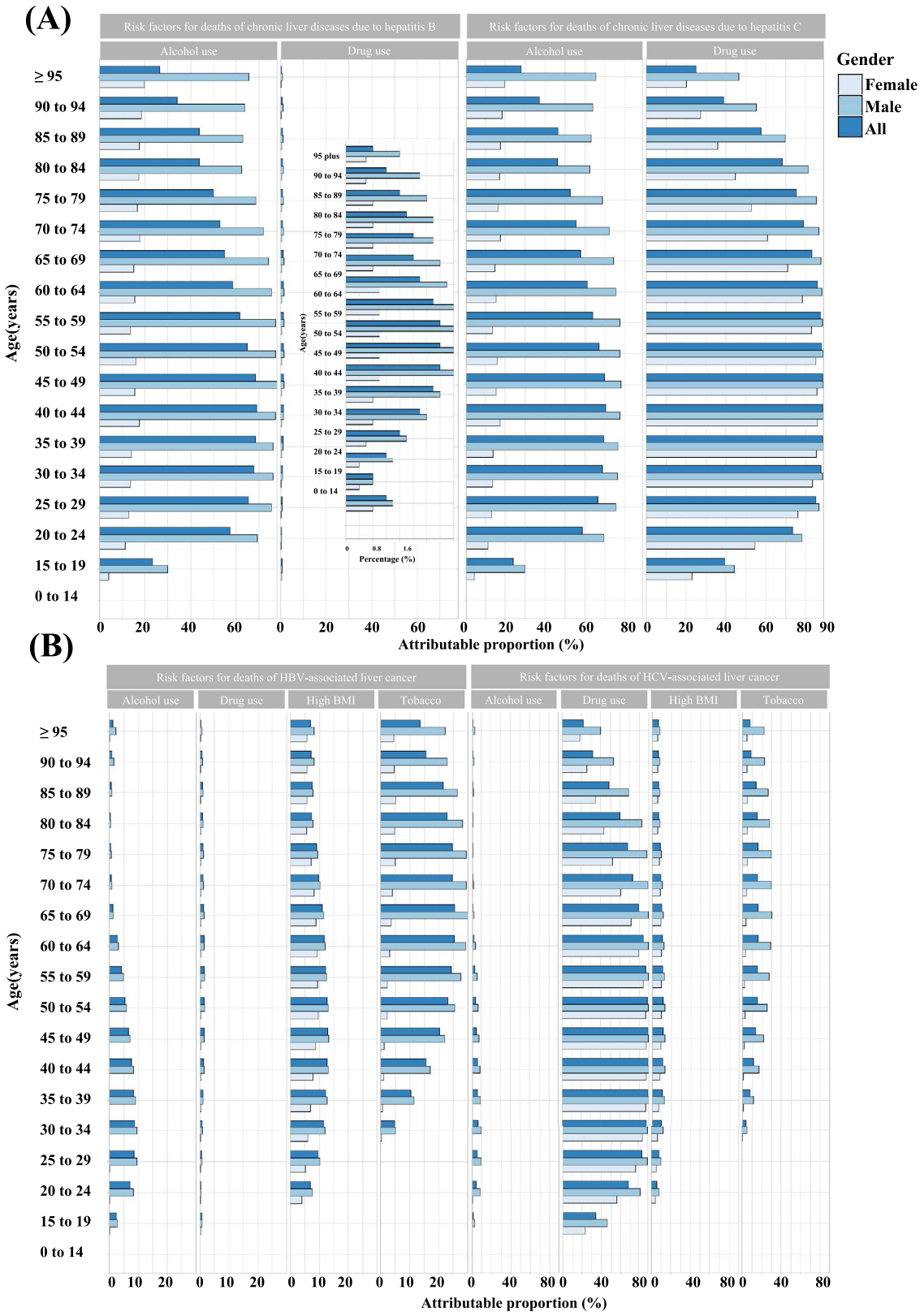

Figure 4. Four risk factors (alcohol use, drug use, high BMI, tobacco use) attributable to deaths among HBV/HCV-infected patients with chronic liver diseases (A) and liver cancer (B).

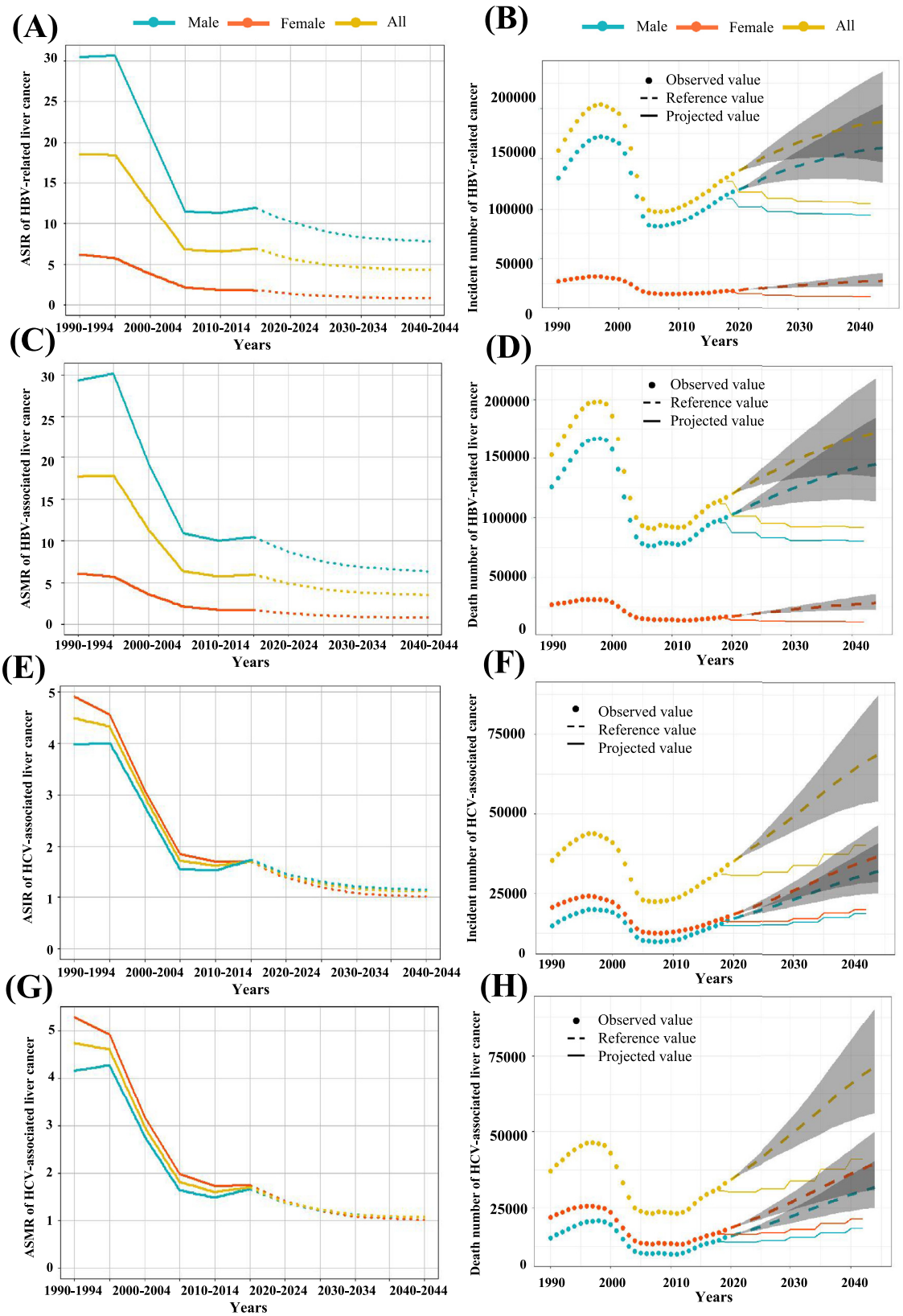

Figure 5. Projection of HBV/HCV-associated liver cancer. (A) Projection of ASIR of HBV-associated liver cancer. The solid lines are the observed value and the dotted lines are the predicted value; (B) Projection on the incident number of HBV-associated liver cancer cases. The gray curved areas are references on the basis of a 1% increase or decrease in the ASIR of 2019, while the dotted line in the middle of the curved area is calculated on the basis of the ASIR of 2019. Dots lines and solid lines represent the observed and predicted values, respectively; (C) Projection of ASMR of HBV-associated liver cancer; (D) Projection of deaths of HBV-associated liver cancer cases, by sex; (E) Projection of ASIR of HCV-associated liver cancer; (F) Projection on incident number of HCV-associated liver cancer cases; (G) Projection of ASMR of HCV-associated liver cancer; (H) Projection on the deaths of HCV-associated liver cancer. ASIR, age-standardize incidence rate; ASDR, age-standardized DALY rate; ASMR, age-standardized mortality rate.

ciated with chronic HBV, including male sex (Si et al., 2019), advanced age, low BMI (Desalegn et al., 2019), alcohol use, high alanine aminotransferase (Zhou et al., 2020a), and decompensated cirrhosis (Desalegn et al., 2019). HCV-associated factors include male sex, advanced age, and lifestyle, such as smoking and drinking (Nguyen et al., 2009). We found that alcohol use was associated with the deaths of HBV- and HCV-related cirrhosis and other chronic liver diseases. Alcohol is known as a liver toxin and alcohol use is recognized among the top 10 risk factors for deaths and the GBD and injury. A synergistic effect between alcohol use and liver damage is known to cause chronic liver diseases and to increase the risk of cirrhosis and hepatocellular carcinoma (Hsu and Kowdley, 2016; Im et al., 2021). Furthermore, alcohol consumption increases the risk of adverse outcomes for HBV/HCV-associated liver diseases (Fuster and Samet, 2018). In our analysis of deaths, smoking incidences were higher among men than women. Previous studies suggested that smoking is an independent risk factor for liver fibrosis, and tobacco-related chemicals cause a variety of body damage, including liver damage (Premkumar and Anand, 2021). In addition to alcohol use, tobacco use, smoking, opioid abuse, and drug use are also important factors associated with HBV and HCV infections (Shi et al., 2021).

To understand the long-term burden of HBV- and HCV-associated liver cancer, we predicted their future incidence and mortality in China. Our results suggested that the ASIR and ASMR of HBV-related liver cancer would likely decrease in the future. On the basis of the ASIR and ASMR of 2019, we made a reference trend forecast for the number of HBV- and HCV-associated liver cancer cases and deaths. Our results show that a 1% annual increase or decrease from the 2019 reference data will result in a difference of 70.9% (1% annual decrease: 15.0%, 1% annual increase: 85.9%) of the projected number in 2044, whereas the difference in HCV-related liver cancer is 107.1% (1% annual decrease: 73.9%, 1% annual increase: 181.0%). Therefore, controlling viral infection is important to prevent liver cancer. From the perspective of sex, the ASIR and ASMR of HBV-associated liver cancer in men were higher than that in women. Our results indicate that male patients are at higher risk for HBV-associated liver cancer, which should be the focus of future prevention and control. Moreover, the COVID-19 pandemic that causes severe morbidity and mortality (Jing et al., 2022, Jiang et al., 2020; Li and De Clercq, 2020; Li et al., 2020, 2022; Miao et al., 2021; Zhou et al., 2020b) exerts an impact on the HBV/HCV screening and management (Mandel et al., 2022). Future studies need to estimate HBV/HCV disease burden with detailed data of other social, economic, and pandemic factors.

Our study has several limitations. First, our study analyzed the HBV/HCV-associated disease burden in China using the GBD 2019 database (Liu et al., 2022), but missing data and model deviations might affect the results (Wang et al., 2022). Second, our study could not report the spatial distribution of HBV and HCV infection in China because there is a lack of provincial data in the GBD database. Third, risk factors were analyzed but the impact of HCV/HBV treatment interventions (De Clercq and Li, 2016; Li and De Clercq, 2022; Li et al., 2021a, 2021b) was not analyzed in our study. Future studies are still needed to address the role of risk factors in the control of HBV and HCV infections.

Conclusions

The HBV- and HCV-associated disease burden has decreased in China over the past 30 years. The disease burden of HBV is much higher than that of HCV, especially among men. Mortality rates are much lower in patients with acute hepatitis infection than in those with other HBV/HCV-associated liver diseases. Alcohol, tobacco, and drug use are important risk factors for HBV- and HCV-associated chronic liver diseases. The incidences of HBV- and HCV-associated liver cancer are expected to decline in China. Effective management of HBV and HCV infections is still needed for high-risk populations.

Authors contributions

TY performed statistical analyses and drafted the manuscript; QZ, TC, and MX contributed with data interpretation; HZ, MRP, and EDC contributed with the discussions of the manuscript. GL obtained funding and revised the manuscript. All authors contributed to the final article.

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Ethical approval statement

Ethical approval and statement from an ethics committee were not required because this study disclosed no patient information and used publicly available data freely shared by the GBD2019 database (https://www.healthdata.org/about/data).

Declaration of competing interest

The authors have no competing interests to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.06.017.

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