

## Trends of Mortality in End-Stage Liver Disease — China, 2008–2020

Xiaoxiao Wang<sup>1,2,&</sup>; Huixin Liu<sup>3,&</sup>; Jinlei Qi<sup>4</sup>; Fangfang Zeng<sup>5,6,7</sup>; Lijun Wang<sup>4</sup>; Peng Yin<sup>4</sup>; Feng Liu<sup>1,2</sup>; Hongbo Li<sup>8</sup>; Yunning Liu<sup>4</sup>; Jiangmei Liu<sup>4</sup>; Lai Wei<sup>9</sup>; Xiaofeng Liang<sup>5,6,7</sup>; Yu Wang<sup>10</sup>; Huiying Rao<sup>1,2,#</sup>; Maigeng Zhou<sup>4,#</sup>

### ABSTRACT

**Introduction:** Liver cancer and cirrhosis represent the most prevalent forms of end-stage liver diseases (ESLDs). Notably, in China, deaths attributed to ESLDs contribute significantly to the global mortality rate of these disorders. Enhanced comprehension of the mortality profile associated with ESLDs in China could provide crucial insights into intervention prioritization, which could in turn help reduce the overall global burden of these diseases.

**Methods:** Data were obtained from China's Disease Surveillance Points system. The presentation includes both crude and age-standardized mortality rates, stratified by sex, residential location, and region. Using Joinpoint Regression, trends in annual mortality rates were estimated from the period of 2008 to 2020 and expressed as the average annual percentage change (AAPC).

**Results:** In 2020, the gross mortality rate of ESLD stood at 30.08 cases per 100,000 individuals. A higher age-standardized ESLD mortality rate was observed in males and rural populations in comparison to their female and urban counterparts, respectively. Noticeably, the highest mortality rates associated with liver cancer and cirrhosis were reported in South and Southwest China, respectively. A positive correlation was noticed between age-specific ESLD mortality rates and advancing age. Interestingly, an annual decrease in the ESLD mortality rate was observed from 2008 to 2020. In urban contexts, the AAPC of cirrhosis was noted to be higher than that of liver cancer.

**Conclusions:** The mortality rate associated with ESLDs in China decreased between 2008 and 2020. Nevertheless, the death burden attributable to ESLD continues to be alarmingly high. Future initiatives should prioritize the reduction of ESLD mortality in particular populations: males, elderly individuals, and those residing in rural regions of South and Southwest China. The emphasis of future interventions should be

placed on antiviral therapy for adults diagnosed with viral hepatitis, and on the prevention of hepatitis B virus (HBV) infection across all demographics.

### INTRODUCTION

End-stage liver disease (ESLD), a severe stage of chronic liver disease, represents a significant global public health challenge due to its high mortality rate (1–2). Notably, liver cancer and decompensated cirrhosis represent a substantial proportion of ESLD cases. In 2020, liver cancer was the second most common cause of cancer-related deaths in China, accounting for nearly half of liver cancer fatalities worldwide (3). Additionally, cirrhosis and other chronic liver disorders constitute approximately 14.9% of global mortality, further emphasizing the severe public health impact of these conditions in China (4).

The prevalence and mortality rates of ESLD can significantly differ among various regions in China. Hence, understanding the current state and pattern of ESLD mortality, as well as its temporal trends, within China as a whole and its individual regions is of utmost importance. Such information can guide the formulation of intervention priorities and help reduce the worldwide disease burden of ESLD. In this study, we have gathered data from the Disease Surveillance Points (DSPs) system administered by the Chinese Center for Disease Control and Prevention (CDC) to analyze the mortality profile of ESLD in 2020. Additionally, we have examined the fluctuations in the annual mortality rates from 2008 to 2020, considering factors such as gender, age group, residential location, regional differences, and per capita gross domestic product (GDP).

### METHODS

#### Data Source

Mortality data associated with ESLD, represented by

deaths stemming from liver function decompensation triggered by liver cancer and cirrhosis, were procured from the DSPs system. The DSPs system, initiated by the Chinese government in 1978, has progressively expanded its geographical reach over the past four decades. In 2013, the coverage of the DSPs system broadened from 161 to 605 data points, encapsulating more than 324 million citizens of China (accounting for 24.3% of the national populace). Deaths that transpire within these surveillance points are consistently reported, and the associated cause of death is codified as per the International Classification of Diseases-10th Revision (ICD-10) by professionally trained staff positioned in local hospitals or CDC branches.

This research classifies the root cause of mortality as ESLD, associated with specific ICD-10 codes: C22 signifies liver cancer, as well as K70.2–K70.4 and K74–K74.6, which refer to cirrhosis. This study received approval from the Ethics Committee of the National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention (No. 202219).

In our analysis, we took into consideration five key sociodemographic factors: year of occurrence, place of residence, gender, age bracket, and geographical location. To categorize age, we used 13 groups: under 30 years, 30–34 years, 35–39 years, 40–44 years, 45–49 years, 50–54 years, 55–59 years, 60–64 years, 65–69 years, 70–74 years, 75–79 years, 80–84 years, and over 85 years. Geographical locations were segmented into seven regions, in line with the divisions provided by the National Statistics Bureau. These divisions include: North China (Beijing Municipality, Tianjin Municipality, Hebei Province, Shanxi Province, and Inner Mongolia Autonomous Region); Northeast China (Heilongjiang Province, Jilin Province, and Liaoning Province); East China (Shanghai Municipality, Jiangsu Province, Zhejiang Province, Anhui Province, Jiangxi Province, Shandong Province, and Fujian Province); Central China (Henan Province, Hubei Province, and Hunan Province); South China (Guangdong Province, Guangxi Autonomous Region, and Hainan Province); Southwest China [Chongqing Municipality, Sichuan Province, Guizhou Province, Yunnan Province, and Xizang Autonomous Region (Tibet)]; and Northwest China (Shaanxi Province, Gansu Province, Qinghai Province, Ningxia Autonomous Region, and Xinjiang Autonomous Region). Data pertaining to per capita GDP was acquired from the National Bureau of

Statistics, with the information being accessed on January 8, 2022 (<https://data.stats.gov.cn/>).

## Statistical Analysis

Mortality rates are denoted as a count of deaths per 100,000 individuals. Using data derived from the 2010 Chinese census, the age-standardized mortality rate was computed (ASMRC) and aligned with Segi's world standard population (ASMRW). Using Joinpoint Regression software, the average annual percentage change (AAPC) and its 95% confidence interval (CI) were estimated to scrutinize the mortality rate trends from 2008 to 2020. Subsequently, a Gaussian process regression was applied to examine the correlation between ASMRC and per capita GDP.

Statistical analysis was conducted in the Joinpoint Regression Program (version 4.9.0.0, Statistical Research and Applications Branch, National Cancer Institute, Bethesda, MD, USA) and R (version 4.1.1, R Foundation for Statistical Computing, Vienna, Austria), and all testing was two-tailed with statistical significance set at 0.05.

## RESULTS

### ESLD Mortality in 2020

In 2020, the DSPs system reported a total of 102,067 ESLD-related deaths: 86,692 due to liver cancer and 15,375 attributed to cirrhosis. The average age at death for ESLD was 63.37 years, with liver cancer at 63.57 years and cirrhosis at 62.32 years. The crude mortality rate for ESLD was calculated at 30.08 deaths per 100,000 people, while liver cancer and cirrhosis had rates of 25.57 deaths and 4.51 deaths per 100,000 people, respectively.

Examining the data for each ESLD (liver cancer or cirrhosis), males consistently demonstrated higher age-standardized mortality rates (ASMRC and ASMRW) than females, especially in rural regions. Furthermore, individuals residing in rural locations recorded higher age-standardized mortality rates compared to their urban counterparts.

Upon stratification by region, consistent sex differences in ASMRC and ASMRW persisted due to ESLD, while differences due to residential location experienced slight variations. Specifically, ASMRC and ASMRW were observed to be higher in urban areas compared to rural regions in the North, Northeast, East, and Central regions of China (Supplementary Table S1, available in <http://weekly.chinacdc.cn/>).

Table 1 displays the geographical distribution of ASMRC of ESLD, inclusive of its individual components (liver cancer and cirrhosis) across China in 2020. While South China recorded the highest ASMRC of liver cancer (26.86 deaths per 100,000 people), the lowest observed ASMRC of liver cancer was in North China (16.44/13.29 deaths per 100,000 people). In contrast, Southwest China experienced the highest ASMRC of cirrhosis (7.14 deaths per 100,000 people). East China had the smallest occurrence, with an ASMRC of merely 2.11 deaths per 100,000 people.

TABLE 1. Geographic distribution of age-standardized mortality rates (ASMR) for end-stage liver disease in 2020 across seven regions in China.

Disease	Area	ASMR (per 100,000)
End-stage liver disease	North China	16.44
	Northeast China	27.43
	East China	20.21
	Central China	25.70
	South China	31.71
	Southwest China	28.34
	Northwest China	20.08
Liver cancer	North China	13.29
	Northeast China	22.80
	East China	18.10
	Central China	23.25
	South China	26.86
	Southwest China	21.20
	Northwest China	16.61
Cirrhosis	North China	3.15
	Northeast China	4.63
	East China	2.11
	Central China	2.45
	South China	4.85
	Southwest China	7.14
	Northwest China	3.46

Note: North China: Beijing Municipality, Tianjin Municipality, Hebei Province, Shanxi Province, and Inner Mongolia Autonomous Region; Northeast China: Heilongjiang Province, Jilin Province, and Liaoning Province; East China: Shanghai Municipality, Jiangsu Province, Zhejiang Province, Anhui Province, Jiangxi Province, Shandong Province, and Fujian Province; Central China: Henan Province, Hubei Province, and Hunan Province; South China: Guangdong Province, Guangxi Zhuang Autonomous Region, and Hainan Province; Southwest China: Chongqing Municipality, Sichuan Province, Guizhou Province, Yunnan Province, and Xizang Autonomous Region (Tibet); and Northwest China: Shaanxi Province, Gansu Province, Qinghai Province, Ningxia Hui Autonomous Region, and Xinjiang Uygur Autonomous Region.

## Age-Specific ESLD Mortality in 2008 and 2020

Both in 2008 and 2020, a consistent increase was observed in the age-specific ESLD mortality rates. However, the rate of increase in 2020 was less significant than that in 2008. This trend remained consistent even after accounting for variables such as residential location, sex, and region (Figure 1).

## Trends in ESLD Mortality from 2008 to 2020

In 2008, the mortality rate for ESLD in China was significantly high, with a crude rate of 35.92 deaths per 100,000 individuals. From 2008 to 2020, the general ASMRC for ESLD in China exhibited a downward trajectory. This decline remained consistent upon stratification by gender and location (Figure 2, Supplementary Table S2, available in <http://weekly.chinacdc.cn/>).

From 2008 to 2020, the AAPC in ASMRC of ESLD, stratified by gender or residential location, showed no variability. However, in urban regions, the AAPC in ASMRC of cirrhosis was higher than that linked to liver cancer (AAPC in ASMRC: AAPC=−5.2, 95% CI: −5.9, −4.4 versus AAPC=−3.3, 95% CI: −4.2, −2.5). This trend continued when data was stratified by gender, for both males and females (Supplementary Table S2).

Upon examining the data by region, there was a consistent decreasing trend in the ASMRC of ESLD from 2008 to 2020 (Figure 2). Throughout this time frame, liver cancer demonstrated a greater AAPC of ASMRC in Northern, Northeastern, Southern, and Southwestern China, while cirrhosis had a higher AAPC of ASMRC in Northeastern and Southwestern China. Additionally, when compared to liver cancer, cirrhosis exhibited a higher AAPC of ASMRC in Northeastern and Eastern China (Figure 2, Supplementary Table S3, available at <http://weekly.chinacdc.cn/>).

## Temporal Trends of Age Standardized ESLD Mortality with per Capita GDP

From 2008 to 2020, there was a noticeable downward trend in the ASMRC of ESLD, which corresponded with an increase in per capita GDP (Figure 3A–C). The lowest ASMRC of cirrhosis was observed when the per capita GDP exceeded 8,000 CNY, after which it appeared to stabilize (Figure 3C).

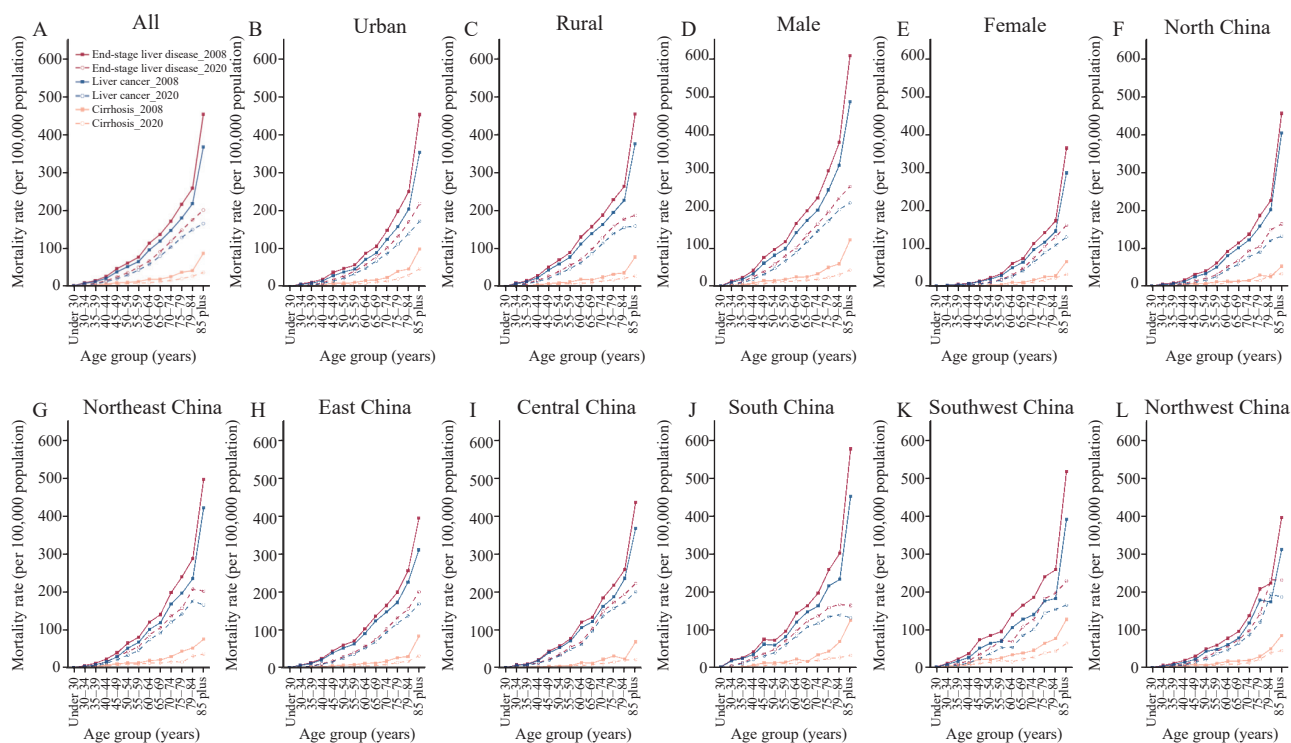


FIGURE 1. Trends in mortality rates for end-stage liver disease, liver cancer, and cirrhosis in 2008 and 2020. Among age groups based on all population (A) residential location (urban or rural, B–C), sex (male or female, D–E), and region (North, Northeast, East, Central, South, Southwest, or Northwest China (F–L).

Abbreviation: ASMRC=age-standardized mortality rates adjusted by the Chinese standard population.

When analyzed on a provincial-level administrative division (PLAD) basis, Guangdong — a province credited with a high per capita GDP — demonstrated the most significant reduction in the ASMRC of liver cancer. Conversely, the greatest decrease in the ASMRC of cirrhosis was recorded in Sichuan Province. Generally, the data insinuates that provinces with higher per capita GDP tend to manifest lower ASMRC of ESLD (Figure 3A–C).

## DISCUSSION

This study reveals a significant decrease in the mortality rates associated with liver cancer and cirrhosis between 2008 and 2020, likely due to the effective management of chronic viral hepatitis, inclusive of both hepatitis B and C. Since 1992, China has instituted a policy mandating neonatal hepatitis B vaccinations (5). Furthermore, in 2009, a nationwide “catch-up” hepatitis B vaccination initiative for children aged between 8 and 15 was commenced (6). These collective strategies resulted in a substantial decrease in the rate of hepatitis B surface antigen (HBsAg) positivity. Moreover, national guidelines

endorsed the use of first-line antiviral medicines, including pegylated interferon, entecavir, and tenofovir (7). Consequently, the proportion of chronic hepatitis B (CHB) patients receiving antiviral therapy increased from 13.5% in 2003 to 79.7% in 2016 (8). Concerning chronic hepatitis C (CHC), the implementation of direct-acting antiviral agents (DAAs) drastically lessened the burden of hepatitis C virus (HCV) infection in China. Specifically, the population with viremic HCV in China declined by around 536,000 from 2015 to 2020 (9). Collectively, these initiatives have reduced the mortality rates of liver cancer and cirrhosis associated with chronic viral hepatitis. A smaller decrease in mortality due to ESLD was observed in rural areas compared to urban areas — a correlation to the easier access in urban areas to timely treatment for chronic viral hepatitis, cirrhosis, and liver cancer (10).

From 2008 to 2020, decreases were observed in the mortality rates of ESLD, liver cancer, and cirrhosis concurrent with increases in per capita GDP. This trend aligns with prior research, which demonstrated a negative correlation between the Sociodemographic Index (SDI) values and the age-standardized mortality rates of cirrhosis and other chronic liver diseases (11).

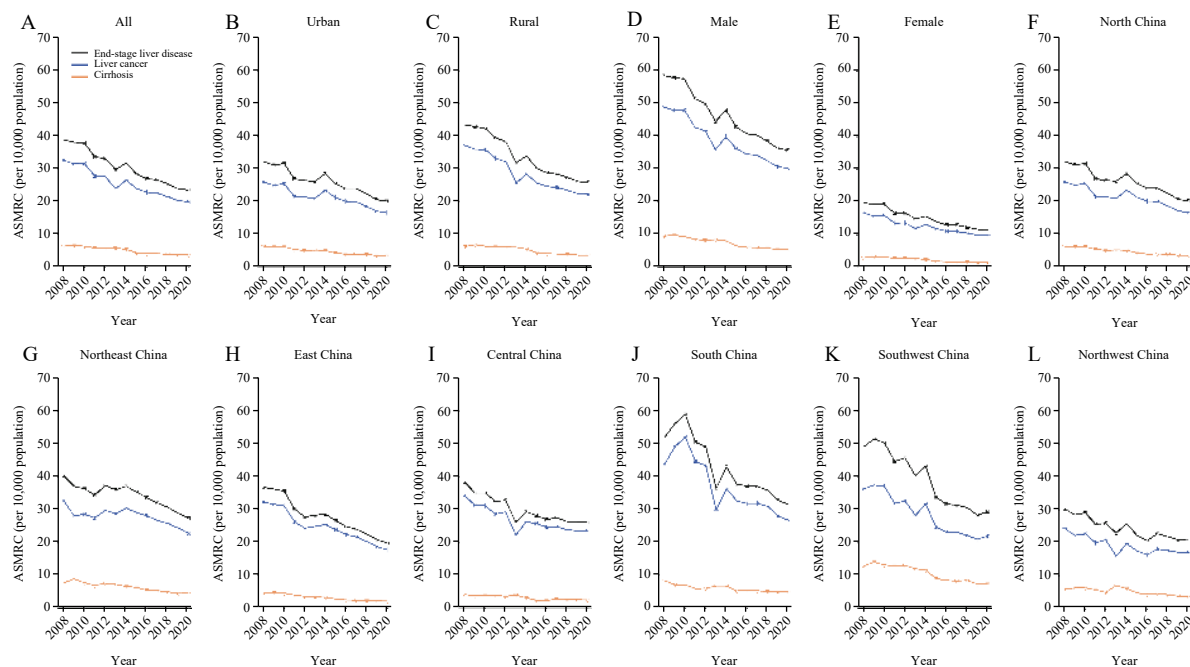


FIGURE 2. Trends in the ASMRC for end-stage liver disease, liver cancer, and cirrhosis from 2008 to 2020, broken down by all population (A), residential location (urban or rural, B–C), sex (male or female, D–E), and region (North, Northeast, East, Central, South, Southwest, or Northwest China, F–L).

ASMRC: age-standardized mortality rates, adjusted in accordance with the Chinese standard population

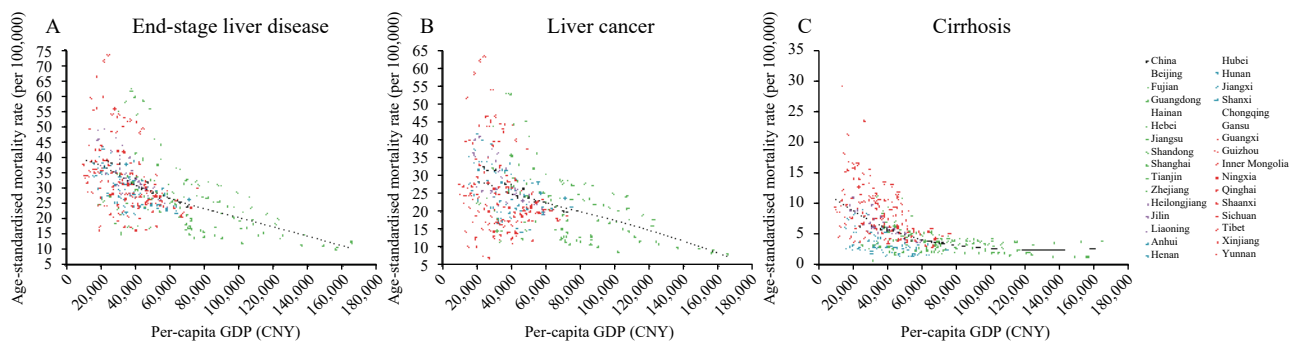


FIGURE 3. Age-standardized mortality rates for end-stage liver diseases stratified by per capita GDP in China from 2008 to 2020. (A) End-stage liver disease, (B) Liver cancer and (C) Cirrhosis.

Abbreviation: GDP=gross domestic product; CNY=Chinese Yuan.

It's possible that the decline in mortality rates could be attributed to improvements in sanitation, healthcare conditions, and the increased public awareness of medical treatment, all potentially facilitated by the rise in per capita GDP.

Hepatitis B virus (HBV) and HCV continue to be predominant contributors to cirrhosis and liver cancer mortality rates in China (12–13). As indicated by the GBD data of 2017, liver-related deaths (including liver cancer and cirrhosis) totalled 0.61 million in East Asia, 0.34 million in South Asia, 0.25 million in Southeast Asia, 0.12 million in Western Europe, and 0.1 million in the Middle East and North Africa (MENA) (14). In

2020, the death toll related to ESLD remained significantly high in China. This was consistent with the results from a data study on the burden of all cancers (15). First, despite the implementation of the neonatal hepatitis B vaccination program leading to a noticeable decline in HBV incidence and transmission, the prevalence of hepatitis B in China remains high due to an extensive population, approximately 84 million, living with CHB (8). Particularly in women of reproductive age, the prevalence of HBsAg persists between 5%–6% with the continuing risk being mother-to-child transmission. This poses a substantial challenge in advancing diagnostic coverage, eradicating

HBV infection, and lessening ESLD mortality resulting from CHB. Second, while DAA treatment has proven to achieve a higher curative rate in patients suffering from CHC (16), the actual diagnostic rate of Hepatitis C in China stands only at 2.1% (17). Owing to this low diagnostic rate, fewer CHC patients avail antiviral therapy, leading to higher incidences of HCV-related ESLD.

Our study faced several limitations. First, due to data unavailability in the DSPs system, we were unable to analyze morbidity and mortality data concerning specific etiologies of ESLD. Second, our study did not investigate fatalities resulting from other potential causes such as type 2 diabetes mellitus, which may have contributed to incompleteness in the report. Third, a significant challenge associated with the DSP data is the under-reporting of deaths, with higher rates observed in the west compared to the east and central regions, and rural areas more so than urban ones. This could potentially result in an underestimation of the overall mortality burden of ESLD, given that higher death rates were seen in rural areas and the west region. Despite these caveats, our study offers important insights into the mortality burden and shifting trends of ESLD, as well as disparities in mortality between liver cancer and cirrhosis. These findings enable the identification of high-risk populations and the development of preventive strategies, guiding future etiological studies on ESLD in China.

In sum, the last decade has witnessed a substantial decline in ESLD mortality rates in China, which can be largely attributed to the implementation of the HBV vaccine and treatment for chronic viral hepatitis. Nevertheless, the mortality burden of ESLD remains substantial. As such, future research efforts and healthcare initiatives should prioritize the exploration of antiviral therapy for adults diagnosed with viral hepatitis and preventative measures against HBV infection across all demographics, with the goal of further reducing ESLD mortality.

**Conflicts of interest:** Prof. Rao HY has received speaking fees from Bristol-Myers Squibb, Gilead, and AbbVie. The other authors declared no conflicts of interest.

**Funding:** Supported by the Beijing Natural Science Foundation [No. 7232195], National Natural Science Foundation of China [No. 81870406, and No. 81602939], Capital's Funds for Health Improvement and Research [No. 2020-4-4087], Peking University Medicine Sailing Program for Young Scholars' Scientific & Technological Innovation [No.

BMU2023YFJHPY025] and Chinese foundation for hepatitis prevention and control-TianQing liver disease research fund subject [No. TQGB20210139].

doi: 10.46234/ccdcw2023.128

# Corresponding authors: Huiying Rao, rao.huiying@163.com; Maigeng Zhou, zhomaigeng@ncncd.chinacdc.cn.

<sup>1</sup> Peking University People's Hospital, Peking University Hepatology Institute, Beijing, China; <sup>2</sup> Beijing Key Laboratory of Hepatitis C and Immunotherapy for Liver Diseases, Beijing International Cooperation Base for Science and Technology on NAFLD Diagnosis, Beijing, China; <sup>3</sup> Peking University People's Hospital, Department of Clinical Epidemiology and Biostatistics, Beijing, China; <sup>4</sup> National Center for Chronic and Non-communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention, Beijing, China; <sup>5</sup> Department of Public Health and Preventive Medicine, School of Medicine, Jinan University, Guangzhou City, Guangdong Province, China; <sup>6</sup> Disease Control and Prevention Institute of Jinan University, Guangzhou City, Guangdong Province, China; <sup>7</sup> Jinan University-BioKangtai Vaccine Institute, Jinan University, Guangzhou City, Guangdong Province, China; <sup>8</sup> China Center for Economic Research, National School of Development, Peking University, Beijing, China; <sup>9</sup> Beijing Tsinghua Changgung Hospital, Tsinghua University, Beijing, China; <sup>10</sup> Chinese Foundation for Hepatitis Prevention and Control, Beijing, China.

<sup>&</sup> Joint first authors.

Submitted: May 16, 2023; Accepted: June 15, 2023

## REFERENCES

- Yu CS, Chen YD, Chang SS, Tang JH, Wu JL, Lin CH. Exploring and predicting mortality among patients with end-stage liver disease without cancer: a machine learning approach. *Eur J Gastroenterol Hepatol* 2021;33(8):1117 – 23. <http://dx.doi.org/10.1097/MEG.0000000000002169>.
- Tao YC, Chen EQ. Clinical application of stem cell in patients with end-stage liver disease: progress and challenges. *Ann Transl Med* 2020;8(8):564. <http://dx.doi.org/10.21037/atm.2020.03.153>.
- Cao W, Chen HD, Yu YW, Li N, Chen WQ. Changing profiles of cancer burden worldwide and in China: a secondary analysis of the global cancer statistics 2020. *Chin Med J (Engl)* 2021;134(7):783 – 91. <http://dx.doi.org/10.1097/CM9.0000000000001474>.
- GBD 2016 Disease and Injury Incidence and Prevalence Collaborators. Global, regional, and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2017;390(10100):1211 – 59. [http://dx.doi.org/10.1016/S0140-6736\(17\)32154-2](http://dx.doi.org/10.1016/S0140-6736(17)32154-2).
- Tang X, Allain JP, Wang H, Rong X, Chen J, Huang K, et al. Incidence of hepatitis B virus infection in young Chinese blood donors born after mandatory implementation of neonatal hepatitis B vaccination nationwide. *J Viral Hepat* 2018;25(9):1008 – 16. <http://dx.doi.org/10.1111/jvh.12901>.
- Liu ZQ, Mao XH, Jiang YF, Cai N, Jin L, Zhang TJ, et al. Changing trends in the disease burden of primary liver cancer caused by specific etiologies in China. *Cancer Med* 2019;8(12):5787 – 99. <http://dx.doi.org/10.1002/cam4.2477>.
- Chinese Society of Infectious Diseases, Chinese Medical Association, Chinese Society of Hepatology, Chinese Medical Association. The guidelines of prevention and treatment for chronic hepatitis B (2019 version). *Chin J Hepatol* 2019;27(12):938 – 61. <http://dx.doi.org/10.3760/cma.j.issn.1007-3418.2019.12.007>.
- Shan S, You H, Niu JQ, Shang J, Xie W, Zhang YX, et al. Baseline characteristics and treatment patterns of the patients recruited to the

- China registry of hepatitis B. *J Clin Transl Hepatol* 2019;7(4):322 – 8. <http://dx.doi.org/10.14218/JCTH.2019.00052>.
9. The Polaris Observatory HCV Collaborators. Global change in hepatitis C virus prevalence and cascade of care between 2015 and 2020: a modelling study. *Lancet Gastroenterol Hepatol* 2022;7(5):396 – 415. [http://dx.doi.org/10.1016/S2468-1253\(21\)00472-6](http://dx.doi.org/10.1016/S2468-1253(21)00472-6).
  10. Sun YY, Wang YH, Li MM, Cheng KL, Zhao XY, Zheng Y, et al. Long-term trends of liver cancer mortality by gender in urban and rural areas in China: an age-period-cohort analysis. *BMJ Open* 2018;8(2):e020490. <http://dx.doi.org/10.1136/bmjopen-2017-020490>.
  11. Li M, Wang ZQ, Zhang L, Zheng H, Liu DW, Zhou MG. Burden of cirrhosis and other chronic liver diseases caused by specific etiologies in China, 1990–2016: findings from the global burden of disease study 2016. *Biomed Environ Sci* 2020;33(1):1 – 10. <http://dx.doi.org/10.3967/bes2020.001>.
  12. Song C, Lv J, Liu Y, Chen JG, Ge ZJ, Zhu J, et al. Associations between hepatitis B virus infection and risk of all cancer types. *JAMA Netw Open* 2019;2(6):e195718. <http://dx.doi.org/10.1001/jamanetworkopen.2019.5718>.
  13. Wang MJ, Wang YT, Feng XS, Wang RJ, Wang YM, Zeng HM, et al. Contribution of hepatitis B virus and hepatitis C virus to liver cancer in China north areas: experience of the Chinese national cancer center. *Int J Infect Dis* 2017;65:15 – 21. <http://dx.doi.org/10.1016/j.ijid.2017.09.003>.
  14. Paik JM, Golabi P, Younossi Y, Mishra A, Younossi ZM. Changes in the global burden of chronic liver diseases from 2012 to 2017: the growing impact of NAFLD. *Hepatology* 2020;72(5):1605 – 16. <http://dx.doi.org/10.1002/hep.31173>.
  15. Fan XQ, Zhang B, He Y, Zhou XL, Zhang YY, Ma L, et al. Burden of disease due to cancer — China, 2000–2019. *China CDC Wkly* 2022;4(15):306 – 11. <http://dx.doi.org/10.46234/ccdcw2022.036>.
  16. Younossi ZM, Tanaka A, Eguchi Y, Lim YS, Yu ML, Kawada N, et al. The impact of hepatitis C virus outside the liver: evidence from Asia. *Liver Int* 2017;37(2):159 – 72. <http://dx.doi.org/10.1111/liv.13272>.
  17. Mei X, Lu HZ. Prevalence, diagnosis, and treatment of hepatitis C in mainland China. *Glob Health Med* 2021;3:270 – 5. <http://dx.doi.org/10.35772/ghm.2021.01080>.

SUPPLEMENTARY TABLE S1. Mortality rates of end-stage liver disease in 2020, China

Region	location	Sex	ESLD			Liver cancer			Cirrhosis			LC/C ratio			
			Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )				
All	All	Both	102,067	30.08	23.50	17.89	86,692	25.57	19.92	15.18	4.51	3.59	2.71	5.55	
		Male	74,688	43.18	35.65	27.22	63,347	36.66	30.16	23.05	6.52	5.49	4.17	5.50	
		Female	27,365	16.45	11.69	8.79	23,335	14.03	9.99	7.53	2.42	1.70	1.27	5.87	
	Urban	Both	36,620	25.89	20.21	15.38	30,256	21.41	16.69	12.72	4.48	3.52	2.66	4.74	
		Male	26,455	36.57	30.25	23.17	21,990	30.43	25.13	19.26	6.14	5.12	3.91	4.91	
		Female	10,161	14.70	10.41	7.77	8,262	11.96	8.51	6.36	2.74	1.90	1.41	4.47	
	Rural	Both	65,447	33.08	25.91	19.71	56,437	28.55	22.26	16.96	4.53	3.65	2.76	6.10	
		Male	48,232	47.94	39.66	30.21	41,357	41.15	33.88	25.84	6.79	5.78	4.37	5.86	
		Female	17,205	17.69	12.60	9.52	15,072	15.51	11.04	8.35	2,132	1.56	1.17	7.07	
	North China	All	Both	9,102	21.29	16.44	12.56	7,406	17.32	13.29	10.17	3.97	3.15	2.39	4.22
			Male	6,369	29.07	23.69	18.20	5,189	23.69	19.22	14.76	5.39	4.47	3.44	4.30
			Female	2,733	13.11	9.35	7.04	2,217	10.63	7.58	5.74	2.48	1.76	1.30	4.30
		Urban	Both	3,557	17.90	13.71	10.50	2,635	13.25	10.10	7.74	4.65	3.61	2.75	2.80
			Male	2,457	23.98	19.46	15.09	1,857	18.13	14.72	11.38	5.86	4.74	3.72	3.10
			Female	1,100	11.43	8.02	5.96	778	8.07	5.67	4.25	3.36	2.35	1.71	2.41
Rural		Both	5,545	24.26	18.89	14.41	4,772	20.89	16.13	12.32	3.38	2.76	2.09	5.84	
		Male	3,912	33.58	27.56	21.03	3,332	28.62	23.28	17.80	4.97	4.28	3.23	5.44	
		Female	1,632	14.56	10.51	7.99	1,440	12.85	9.27	7.05	1.72	1.24	0.94	7.48	
Northeast China		All	Both	11,280	41.56	27.43	21.00	9,446	34.80	22.80	17.47	6.75	4.63	3.53	4.93
			Male	8,146	59.83	40.99	31.56	6,768	49.71	33.83	26.05	10.12	7.16	5.51	4.72
			Female	3,134	23.16	14.31	10.80	2,678	19.79	12.20	9.23	3.37	2.11	1.57	5.78
		Urban	Both	3,565	36.20	23.20	17.87	2,843	28.86	18.41	14.12	7.34	4.79	3.74	3.85
			Male	2,548	51.73	34.82	26.87	2,023	41.07	27.55	21.13	10.66	7.28	5.74	3.79
			Female	1,017	20.68	12.15	9.30	819	16.65	9.81	7.52	4.03	2.34	1.78	4.20
	Rural	Both	7,715	44.60	29.96	22.84	6,603	38.18	25.42	19.43	6.42	4.53	3.41	5.61	
		Male	5,598	64.40	44.56	34.23	4,744	54.59	37.47	28.85	9.81	7.09	5.38	5.28	
		Female	2,117	24.58	15.72	11.76	1,859	21.58	13.73	10.31	2.99	1.98	1.46	6.93	

Continued

Region	location	Sex	Death numbers	ESLD			Liver cancer			Cirrhosis			LC/C ratio
				Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	
East China	All	Both	28,287	27.63	20.21	15.37	25,337	24.74	18.10	13.78	2.11	1.59	8.59
		Male	20,457	39.29	30.66	23.39	18,424	35.38	27.57	21.04	3.09	2.35	8.91
		Female	7,832	15.57	10.16	7.62	6,915	13.74	9.02	6.78	1.14	0.84	7.90
	Urban	Both	10,630	24.33	17.80	13.55	9,323	21.33	15.64	11.92	2.16	1.63	7.23
		Male	7,491	33.36	26.20	20.03	6,652	29.62	23.24	17.78	2.96	2.25	7.86
		Female	3,140	14.79	9.55	7.14	2,671	12.58	8.20	6.15	1.35	0.99	6.08
	Rural	Both	17,657	30.09	21.99	16.71	16,014	27.28	19.92	15.15	2.07	1.56	9.64
		Male	12,967	43.78	34.04	25.93	11,772	39.74	30.84	23.51	3.20	2.42	9.63
		Female	4,693	16.13	10.59	7.95	4,244	14.59	9.60	7.22	0.99	0.73	9.69
Central China	All	Both	17,017	32.26	25.70	19.55	15,421	29.24	23.25	17.71	2.45	1.84	9.49
		Male	12,137	45.32	38.32	29.13	10,959	40.92	34.53	26.27	3.79	2.87	9.12
		Female	4,876	18.77	13.67	10.38	4,460	17.17	12.50	9.52	1.17	0.86	10.64
	Urban	Both	4,016	26.84	21.57	16.32	3,416	22.84	18.31	13.87	3.26	2.45	5.61
		Male	2,867	38.24	32.37	24.57	2,439	32.53	27.48	20.86	4.89	3.71	5.62
		Female	1,148	15.38	11.44	8.56	976	13.08	9.73	7.31	1.71	1.25	5.70
	Rural	Both	13,001	34.41	27.38	20.86	12,005	31.77	25.25	19.25	2.13	1.60	11.85
		Male	9,270	48.08	40.75	30.98	8,519	44.18	37.40	28.45	3.35	2.54	11.16
		Female	3,728	20.14	14.58	11.10	3,483	18.82	13.61	10.39	0.97	0.71	14.01
South China	All	Both	13,405	33.25	31.71	24.34	11,335	28.13	26.86	20.64	4.85	3.69	5.54
		Male	10,788	51.22	51.74	39.74	9,141	43.43	43.91	33.77	7.83	5.97	5.61
		Female	2,615	13.60	11.72	8.87	2,193	11.40	9.87	7.48	1.84	1.39	5.35
	Urban	Both	5,375	26.22	26.62	20.45	4,626	22.58	23.00	17.71	3.63	2.74	6.34
		Male	4,308	39.99	43.32	33.51	3,708	34.45	37.48	29.09	5.84	4.43	6.42
		Female	1,067	10.97	10.29	7.64	918	9.43	8.89	6.60	1.40	1.03	6.34
	Rural	Both	8,030	40.66	37.95	29.02	6,710	33.97	31.75	24.29	6.20	4.72	5.12
		Male	6,480	63.21	62.71	47.78	5,433	53.00	52.59	40.07	10.12	7.70	5.20
		Female	1,548	16.33	13.29	10.18	1,275	13.45	11.01	8.45	2.28	1.73	4.83

Continued																	
Region	location	Sex	ESLD						Liver cancer				Cirrhosis				LC/C ratio
			Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Death numbers	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )			
Southwest China	All	Both	17,500	35.87	28.34	21.47	13,201	27.06	21.20	16.09	4,298	8.81	7.14	5.38	2.97		
		Male	13,168	53.21	43.97	33.40	9,833	39.73	32.53	24.80	3,335	13.48	11.44	8.61	2.84		
		Female	4,322	17.97	12.95	9.68	3,362	13.97	10.09	7.53	960	3.99	2.86	2.16	3.53		
	Urban	Both	6,607	33.26	25.18	19.07	5,009	25.21	19.00	14.42	1,598	8.04	6.18	4.65	3.07		
		Male	4,908	49.09	38.71	29.49	3,716	37.17	29.08	22.27	1,192	11.92	9.63	7.22	3.02		
		Female	1,695	17.17	11.97	8.88	1,290	13.07	9.17	6.76	405	4.10	2.80	2.11	3.28		
	Rural	Both	10,893	37.66	30.62	23.20	8,192	28.32	22.80	17.30	2,700	9.34	7.82	5.90	2.92		
		Male	8,260	56.00	47.75	36.22	6,117	41.47	35.03	26.63	2,143	14.53	12.73	9.59	2.75		
		Female	2,627	18.52	13.64	10.25	2,071	14.61	10.75	8.07	555	3.91	2.90	2.18	3.71		
Northwest China	All	Both	5,477	22.13	20.08	15.05	4,545	18.36	16.61	12.45	932	3.76	3.46	2.59	4.80		
		Male	3,622	28.81	26.86	20.37	3,035	24.14	22.48	17.05	588	4.67	4.38	3.32	5.13		
		Female	1,853	15.21	13.38	9.81	1,509	12.39	10.88	7.97	344	2.82	2.51	1.84	4.34		
	Urban	Both	2,871	23.20	19.51	14.58	2,405	19.44	16.29	12.21	466	3.77	3.23	2.38	5.05		
		Male	1,877	29.93	26.18	19.84	1,595	25.43	22.20	16.85	282	4.50	3.98	2.99	5.58		
		Female	993	16.27	13.07	9.51	810	13.26	10.63	7.77	184	3.01	2.44	1.74	4.35		
	Rural	Both	2,606	21.06	20.61	15.49	2,141	17.29	16.91	12.68	466	3.76	3.70	2.81	4.57		
		Male	1,745	27.70	27.46	20.81	1,440	22.85	22.65	17.16	305	4.84	4.80	3.65	4.72		
		Female	860	14.15	13.68	10.12	700	11.51	11.14	8.19	161	2.64	2.55	1.93	4.37		

Abbreviation: ESLD=End-stage liver disease; ASMRC=age-standardized mortality rate adjusted by the Chinese standard population; ASMRW=age-standardized mortality rate adjusted by the world standard population; LC=liver cancer; C=cirrhosis

Abbreviation: ESLD=End-stage liver disease; ASMRC=age-standardized mortality rate adjusted by the Chinese standard population; ASMRW=age-standardized mortality rate adjusted by the world standard population; LC=liver cancer; C=cirrhosis.

SUPPLEMENTARY TABLE S2. Crude rates, ASMRC, ASMRW and AAPC of ESLD and by residence and sex in China, 2008–2020.

	Year	All			Urban			Rural		
		Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )
ESLD	2008	35.92	38.89	29.79	32.44	32.28	24.55	38.03	43.56	33.49
	2020	30.11	23.53	17.91	25.86	20.19	15.36	33.15	25.97	19.76
	AAPC (95% CI)	-1.9	-4.4	-4.1	-2.1	-3.7	-3.6	-1.7	-4.8	-4.8
	2008–2020	(-2.5, -1.4)	(-4.9, -3.8)	(-4.8, -3.8)	(-2.9, -1.3)	(-4.4, -2.9)	(-4.4, -2.7)	(-2.5, -1.0)	(-5.5, -4.1)	(-5.4, -4.1)
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
ESLD	2008	52.17	58.43	44.67	47.06	48.18	36.64	55.21	65.59	50.25
	2020	43.19	35.67	27.23	36.51	30.2	23.13	48.01	39.73	30.26
	AAPC (95% CI)	-2.0	-4.3	-4.2	-2.3	-3.7	-3.5	-1.7	-4.7	-4.6
	2008–2020	(-2.5, -1.5)	(-4.9, -3.8)	(-4.8, -3.7)	(-3.1, -1.5)	(-4.5, -2.9)	(-4.4, -2.6)	(-2.5, -1.0)	(-5.4, -4.0)	(-5.3, -3.9)
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
ESLD	2008	18.98	19.96	15.29	17.46	16.96	12.86	19.91	22.13	17.04
	2020	16.48	11.72	8.81	14.69	10.41	7.92	17.75	12.64	9.55
	AAPC (95% CI)	-1.7	-4.7	-4.7	-1.7	-4.0	-4.0	-1.6	-5.2	-5.2
	2008–2020	(-2.3, -1.1)	(-5.2, -4.1)	(-5.3, -4.2)	(-2.5, -0.9)	(-4.6, -3.3)	(-4.6, -3.3)	(-2.3, -0.8)	(-5.8, -4.5)	(-5.8, -4.5)
	P-value	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	0.001	<0.001	<0.001
Liver cancer	2008	30.15	32.59	24.94	26.23	26.01	19.84	32.53	37.4	28.75
	2020	25.57	19.92	15.15	21.37	16.66	12.69	27.41	21.21	16.39
	AAPC (95% CI)	-1.7	-4.1	-4.1	-1.8	-3.3	-3.2	-1.5	-4.6	-4.6
	2008–2020	(-2.3, -1.1)	(-4.8, -3.5)	(-4.7, -3.4)	(-2.6, -1.0)	(-4.2, -2.5)	(-4.1, -2.3)	(-2.3, -0.7)	(-5.4, -3.8)	(-5.4, -3.8)
	P-value	<0.001	<0.001	<0.001	0.001	<0.001	<0.001	0.001	<0.001	<0.001
Liver cancer	2008	43.7	48.84	37.41	38.22	39.04	29.78	46.97	56.46	43.26
	2020	36.63	30.15	23.04	30.35	25.07	19.21	39.71	32.19	24.92
	AAPC (95% CI)	-1.8	-4.1	-4	-2.0	-3.4	-3.2	-1.6	-4.6	-4.5
	2008–2020	(-2.4, -1.2)	(-4.8, -3.5)	(-4.7, -3.4)	(-2.8, -1.2)	(-4.2, -2.5)	(-4.1, -2.3)	(-2.3, -0.7)	(-5.5, -3.7)	(-5.3, -3.6)
	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.001	<0.001	<0.001
Liver cancer	2008	16.02	16.83	12.89	13.94	13.5	10.25	17.3	19.22	14.8
	2020	14.05	10.01	7.54	11.95	8.5	6.35	15.55	11.07	8.37
	AAPC (95% CI)	-1.4	-4.3	-4.3	-1.3	-3.5	-3.5	-1.3	-4.9	-4.9
	2008–2020	(-2.0, -0.7)	(-5.0, -3.7)	(-5.0, -3.7)	(-2.2, -0.5)	(-4.3, -2.7)	(-4.4, -2.7)	(-2.1, -0.5)	(-5.6, -4.1)	(-5.7, -4.1)
	P-value	0.001	<0.001	<0.001	0.001	<0.001	<0.001	0.004	<0.001	<0.001

TABLE S2. (Continued)

	Year	All			Urban			Rural		
		Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )
Total	2008	5.77	6.3	4.79	6.21	6.26	4.71	5.50	6.33	4.83
	2020	4.54	3.61	2.73	4.49	3.53	2.67	4.56	3.68	2.78
	AAPC (95% CI)	-3.2	-5.5	-5.5	-3.6	-5.2	-5.1	-2.5	-5.7	-5.7
	2008-2020	(-4.3, -2.1)	(-6.4, -4.6)	(-6.4, -4.6)	(-4.6, -2.6)	(-5.9, -4.4)	(-5.9, -4.3)	(-4.9, 0.1)	(-6.9, -4.5)	(-6.9, -4.6)
Cirrhosis	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.055	<0.001	<0.001
	2008	8.47	9.59	7.26	8.84	9.14	6.86	8.25	9.9	7.53
	2020	6.56	5.52	4.19	6.16	5.14	3.92	6.84	5.82	4.41
	AAPC (95% CI)	-3.1	-5.3	-5.2	-3.7	-5.1	-4.9	-2.3	-5.4	-5.4
Female	2008-2020	(-4.1, -2.1)	(-6.1, -4.5)	(-6.0, -4.4)	(-4.7, -2.8)	(-5.9, -4.2)	(-5.8, -4.1)	(-4.6, 0.1)	(-6.5, -4.4)	(-6.4, -4.4)
	P-Value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.064	<0.001	<0.001
	2008	2.96	3.13	2.39	3.52	3.46	2.62	2.62	2.9	2.24
	2020	2.43	1.71	1.27	2.75	1.9	1.41	2.2	1.57	1.18
Male	AAPC (95% CI)	-3.4	-6.4	-6.5	-3.4	-5.8	-5.9	-2.8	-6.9	-7.0
	2008-2020	(-4.7, -1.9)	(-7.7, -5.2)	(-7.7, -5.3)	(-4.6, -2.2)	(-6.6, -4.9)	(-6.7, -5.0)	(-5.8, 0.3)	(-8.5, -5.3)	(-8.6, -5.4)
	P-Value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.072	<0.001	<0.001

Abbreviation: ESD=end-stage liver disease; ASMRC=age-standardized mortality rate adjusted by the Chinese standard population; ASMRW=age-standardized mortality rate adjusted by the world standard population; AAPC=average annual percentage change.

SUPPLEMENTARY TABLE S3. Crude rates, ASMRC, ASMRW and AAPC of ESLD by region in China, 2008–2020.

Region	Disease	Year	All			Urban			Rural		
			Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )
North China	ESLD	2008	28.06	30.19	23.13	26.07	24.99	18.91	29.88	36.08	27.89
		2020	20.99	16.21	12.38	17.54	13.45	10.29	24.01	18.69	14.26
		AAPC (95% CI) 2008–2020	-3.1 (-5.1, -1.0)	-5.7 (-6.7, -4.7)	-5.6 (-6.6, -4.6)	-4.2 (-5.6, -2.8)	-5.4 (-6.4, -4.5)	-5.2 (-6.2, -4.3)	-1.8 (-4.8, 1.2)	-6.2 (-7.5, -4.9)	-6.2 (-7.5, -5.0)
		P-value	0.004	<0.001	<0.001	<0.001	<0.001	<0.001	0.238	<0.001	<0.001
	Liver cancer	2008	23.78	25.67	19.73	20.87	20.17	15.30	26.46	31.99	24.79
		2020	17.08	13.10	10.03	13.00	9.91	7.59	20.66	15.95	12.19
		AAPC (95% CI) 2008–2020	-3.2 (-5.7, -0.7)	-5.9 (-7.1, -4.7)	-5.8 (-7.1, -4.6)	-4.6 (-6.1, -3.1)	-5.9 (-7.0, -4.8)	-5.7 (-6.8, -4.6)	-2.9 (-4.9, -0.9)	-6.7 (-8.5, -4.8)	-6.7 (-8.4, -4.9)
		P-value	0.012	<0.001	<0.001	<0.001	<0.001	<0.001	0.005	<0.001	<0.001
	Cirrhosis	2008	4.27	4.52	3.40	5.20	4.82	3.61	3.43	4.09	3.10
		2020	3.91	3.10	2.36	4.55	3.53	2.70	3.35	2.74	2.00
		AAPC (95% CI) 2008–2020	-2.4 (-3.7, -1.1)	-4.5 (-5.8, -3.3)	-4.5 (-5.7, -3.2)	-2.3 (-4.9, 0.3)	-3.8 (-5.0, -2.7)	-3.7 (-4.8, -2.5)	-1.2 (-4.4, 2.1)	-3.7 (-7.8, 0.6)	-3.6 (-7.7, 0.7)
		P-value	0.002	<0.001	<0.001	0.087	<0.001	<0.001	0.48	0.093	0.099
Northeast China	ESLD	2008	39.44	40.39	30.88	35.93	34.59	26.37	42.41	45.95	35.19
		2020	41.41	27.34	20.93	36.14	23.17	17.84	44.40	29.83	22.75
		AAPC (95% CI) 2008–2020	1.0 (-0.3, 2.3)	-2.7 (-3.9, -1.4)	-2.8 (-4.0, -1.5)	0.6 (-0.1, 1.3)	-2.8 (-4.2, -1.4)	-2.7 (-4.1, -1.2)	0.8 (-0.5, 2.1)	-3.2 (-4.2, -2.2)	-3.2 (-4.2, -2.2)
		P-value	0.126	<0.001	<0.001	0.092	<0.001	<0.001	0.236	<0.001	<0.001
	Liver cancer	2008	31.86	32.76	25.15	27.90	26.92	20.62	35.20	38.33	29.45
		2020	34.68	22.73	17.41	28.81	18.39	14.11	38.00	25.31	19.35
		AAPC (95% CI) 2008–2020	1.8 (0.7, 2.8)	-2.2 (-4.0, -0.4)	-2.1 (-3.9, -0.4)	1.1 (0.4, 1.9)	-2.2 (-2.9, -1.4)	-2.0 (-2.9, -1.1)	1.6 (-0.2, 3.5)	-2.6 (-4.2, -1.0)	-2.7 (-4.3, -1.1)
		P-value	0.003	0.015	0.019	0.006	<0.001	0.001	0.089	<0.001	0.001
	Cirrhosis	2008	7.58	7.62	5.73	8.03	7.67	5.75	7.21	7.62	5.74
		2020	6.73	4.61	3.52	7.33	4.78	3.74	6.40	4.52	3.40
		AAPC (95% CI) 2008–2020	-2.3 (-3.5, -1.1)	-5.2 (-6.3, -4.2)	-5.2 (-6.3, -4.1)	-1.4 (-3.2, 0.4)	-4.2 (-5.3, -3.0)	-4.0 (-5.2, -2.8)	-2.9 (-4.6, -1.2)	-6.1 (-7.6, -4.5)	-6.1 (-7.7, -4.5)
		P-value	0.003	<0.001	0.001	0.003	<0.001	0.001	0.003	<0.001	0.001

Continued

Region	Disease	Year	All			Urban			Rural		
			Crude rate (1/10 <sup>5</sup> )	ASMR (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMR (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMR (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )
East China	ESLD	2008	36.31	36.74	28.12	32.69	31.52	24.06	39.09	41.23	31.62
		2020	26.99	19.75	15.02	23.76	17.39	13.23	29.41	21.49	16.34
		AAPC (95% CI)	-2.6	-5.0	-4.9	-2.8	-4.7	-4.6	-2.7	-5.4	-5.4
		2008-2020	(-3.1, -2.2)	(-5.6, -4.4)	(-5.6, -4.2)	(-3.7, -1.8)	(-5.5, -3.9)	(-5.4, -3.7)	(-3.1, -2.2)	(-5.9, -4.9)	(-5.9, -4.8)
	Liver cancer	P-value	<0.001	<0.001	0.001	<0.001	<0.001	0.001	<0.001	<0.001	0.001
		2008	31.96	32.26	24.7	27.85	26.72	20.41	35.13	37.01	28.40
		2020	24.18	17.7	13.47	20.84	15.28	11.64	26.67	19.48	14.82
		AAPC (95% CI)	-2.3	-4.7	-4.6	-2.4	-4.3	-4.2	-2.5	-5.2	-5.2
		2008-2020	(-2.8, -1.8)	(-5.4, -4.0)	(-5.4, -3.8)	(-3.4, -1.3)	(-5.2, -3.4)	(-5.1, -3.2)	(-2.8, -2.1)	(-5.7, -4.7)	(-5.7, -4.6)
		P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
Central China	Cirrhosis	2008	4.35	4.49	3.42	4.85	4.81	3.65	3.97	4.22	3.22
		2020	2.82	2.05	1.55	2.92	2.11	1.59	2.74	2.02	1.52
		AAPC (95% CI)	-4.9	-7.3	-7.3	-5.2	-7.4	-7.3	-4.6	-7.3	-7.2
		2008-2020	(-5.8, -3.9)	(-8.1, -6.6)	(-8.0, -6.6)	(-6.5, -3.9)	(-8.2, -6.5)	(-8.2, -6.5)	(-5.8, -3.3)	(-8.2, -6.4)	(-8.1, -6.4)
	ESLD	P-value	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001
		2008	34.25	38.47	29.53	29.02	30.10	22.98	36.10	41.68	32.03
		2020	32.75	26.09	19.85	27.25	21.90	16.57	34.93	27.80	21.17
		AAPC (95% CI)	-0.4	-3.1	-3.1	-0.4	-2.1	-2.1	-0.4	-3.6	-3.4
		2008-2020	(-1.3, 0.6)	(-4.1, -2.2)	(-4.0, -2.1)	(-1.2, 0.5)	(-2.9, -1.2)	(-3.0, -1.2)	(-1.4, 0.7)	(-4.6, -2.7)	(-4.6, -2.2)
		P-value	0.402	<0.001	<0.001	0.360	<0.001	<0.001	0.487	<0.001	<0.001
Central China	Liver cancer	2008	30.66	34.35	26.35	23.74	24.33	18.64	33.11	38.20	29.30
		2020	29.68	23.60	17.98	23.18	18.59	14.08	32.26	25.63	19.55
		AAPC (95% CI)	-0.2	-2.9	-2.9	0	-1.7	-1.7	-0.2	-3.3	-3.2
		2008-2020	(-1.3, 1.0)	(-4.1, -1.8)	(-4.0, -1.7)	(-0.9, 0.9)	(-2.6, -0.7)	(-2.7, -0.7)	(-1.5, 1.2)	(-4.7, -1.8)	(-4.6, -1.8)
	Cirrhosis	P-value	0.762	<0.001	<0.001	0.974	0.003	0.004	0.774	<0.001	<0.001
		2008	3.58	4.12	3.18	5.28	5.78	4.33	2.98	3.48	2.73
		2020	3.07	2.49	1.87	4.07	3.31	2.49	2.68	2.16	1.63
		AAPC (95% CI)	-2.2	-4.9	-5.0	-2.1	-3.9	-4.0	-2.3	-5.2	-5.4
		2008-2020	(-3.9, -0.4)	(-6.5, -3.2)	(-6.6, -3.4)	(-3.2, -0.9)	(-5.1, -2.8)	(-5.0, -2.9)	(-4.9, 0.4)	(-7.7, -2.7)	(-7.8, -3.0)
		P-value	0.021	<0.001	<0.001	0.003	<0.001	<0.001	0.084	0.001	0.001

Continued

Region	Disease	Year	All			Urban			Rural		
			Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )
South China	ESLD	2008	44.96	51.91	39.77	38.52	41.22	31.53	48.11	58.71	45.04
		2020	32.93	31.42	24.11	25.74	26.13	20.07	40.51	37.84	28.93
		AAPC (95% CI)	-3.9	-4.9	-4.8	-3.5	-2.9	-2.7	-3.2	-5.2	-5.2
		2008-2020	(-5.5, -2.3)	(-6.2, -3.6)	(-6.1, -3.5)	(-5.2, -1.9)	(-4.8, -1.0)	(-4.8, -0.6)	(-5.4, -0.9)	(-7.4, -3.0)	(-7.3, -2.9)
	Liver cancer	P-value	<0.001	<0.001	<0.001	0.001	0.007	0.016	0.011	<0.001	<0.001
		2008	37.91	43.67	33.56	30.71	32.76	25.19	41.42	50.53	38.84
		2020	27.85	26.60	20.44	22.15	22.56	17.37	33.85	31.66	24.22
		AAPC (95% CI)	-4.1	-5.0	-4.9	-3.2	-2.5	-2.4	-3.5	-5.6	-5.5
		2008-2020	(-6.0, -2.2)	(-6.6, -3.4)	(-6.5, -3.3)	(-4.9, -1.5)	(-4.4, -0.6)	(-4.4, -0.3)	(-6.0, -0.9)	(-8.1, -3.0)	(-8.0, -2.9)
		P-value	0.001	<0.001	<0.001	0.002	0.014	0.030	0.013	0.001	0.001
Southwest China	Cirrhosis	2008	7.05	8.24	6.21	7.81	8.46	6.34	6.68	8.18	6.20
		2020	5.08	4.82	3.67	3.59	3.57	2.70	6.66	6.18	4.71
		AAPC (95% CI)	-2.8	-3.9	-3.8	-5.1	-4.8	-4.6	-0.8	-2.9	-2.8
		2008-2020	(-4.1, -1.6)	(-5.2, -2.7)	(-5.0, -2.5)	(-7.2, -3.0)	(-7.4, -2.1)	(-7.2, -1.9)	(-2.4, 0.9)	(-4.3, -1.6)	(-4.1, -1.6)
	ESLD	P-value	<0.001	<0.001	<0.001	<0.001	0.002	0.003	0.319	0.001	<0.001
		2008	43.79	49.08	37.75	39.93	41.75	31.61	45.58	53.01	41.03
		2020	37.18	29.38	22.25	34.47	26.10	19.77	39.04	31.74	24.05
		AAPC (95% CI)	-2.7	-5.4	-5.3	-2.3	-4.5	-4.4	-2.8	-5.6	-5.6
		2008-2020	(-4.0, -1.5)	(-6.4, -4.3)	(-6.3, -4.4)	(-3.8, -0.7)	(-5.9, -3.1)	(-5.8, -3.0)	(-4.2, -1.4)	(-6.9, -4.4)	(-6.7, -4.5)
		P-value	0.001	<0.001	<0.001	0.008	<0.001	<0.001	0.001	<0.001	<0.001
Southwest China	Liver cancer	2008	32.49	36.26	28.02	29.71	31.04	23.59	33.78	39.08	30.41
		2020	28.05	21.98	16.68	26.13	19.69	14.95	29.36	23.63	17.93
		AAPC (95% CI)	-2.6	-5.2	-5.2	-1.7	-3.9	-3.8	-2.9	-5.7	-5.7
		2008-2020	(-3.8, -1.3)	(-6.2, -4.2)	(-6.1, -4.2)	(-3.5, 0.1)	(-5.6, -2.2)	(-5.5, -2.1)	(-4.4, -1.3)	(-7.2, -4.3)	(-7.1, -4.3)
	Cirrhosis	P-value	0.001	<0.001	<0.001	0.064	<0.001	0.001	0.002	<0.001	<0.001
		2008	11.30	12.82	9.73	10.23	10.70	8.02	11.80	13.93	10.62
		2020	9.13	7.40	5.57	8.34	6.41	4.82	9.63	8.11	6.11
		AAPC (95% CI)	-2.8	-5.8	-5.7	-4.0	-6.3	-6.2	-2.0	-4.8	-4.9
		2008-2020	(-5.4, -0.1)	(-7.0, -4.5)	(-7.0, -4.5)	(-6.0, -2.1)	(-8.0, -4.5)	(-7.9, -4.4)	(-4.0, 0.1)	(-6.7, -3.0)	(-6.6, -3.1)
		P-value	0.042	<0.001	<0.001	0.001	<0.001	<0.001	0.067	<0.001	<0.001

Continued

Region	Disease	Year	All			Urban			Rural		
			Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )	Crude rate (1/10 <sup>5</sup> )	ASMRC (1/10 <sup>5</sup> )	ASMRW (1/10 <sup>5</sup> )
Northwest China	ESLD	2008	23.46	30.46	23.02	27.20	30.93	23.10	21.78	30.25	23.06
		2020	22.94	20.81	15.60	24.05	20.22	15.12	21.83	21.36	16.06
		AAPC (95% CI)	-0.3	-3.1	-3.2	-1.3	-2.8	-2.8	-0.4	-3.0	-3.1
		2008–2020	(-1.3, 0.6)	(-4.0, -2.3)	(-4.0, -2.4)	(-4.2, 1.7)	(-4.2, -1.4)	(-4.2, -1.4)	(-1.4, 0.5)	(-4.5, -1.5)	(-4.5, -1.7)
		P-value	0.485	<0.001	<0.001	0.383	0.001	0.001	0.344	<0.001	<0.001
Northwest China	Liver cancer	2008	18.87	24.48	18.51	22.58	25.49	19.04	17.20	23.94	18.27
		2020	19.04	17.22	12.91	20.15	16.88	12.66	12.92	17.53	13.14
		AAPC (95% CI)	0.1	-2.8	-2.8	-1.3	-3.0	-2.9	0.2	-2.6	-2.7
		2008–2020	(-1.3, 1.5)	(-4.1, -1.4)	(-4.1, -1.5)	(-4.2, 1.8)	(-4.4, -1.6)	(-4.3, -1.5)	(-1.4, 1.9)	(-4.3, -0.9)	(-4.4, -1.0)
		P-Value	0.889	0.001	0.001	0.406	0.001	0.001	0.748	0.006	0.005
Northwest China	Cirrhosis	2008	4.59	5.97	4.51	4.62	5.44	4.06	4.57	6.31	4.79
		2020	3.90	3.59	2.69	3.90	3.34	2.46	3.90	3.84	2.92
		AAPC (95% CI)	-1.9	-4.5	-4.6	0.2	-2.2	-2.3	-2.4	-5.5	-5.1
		2008–2020	(-3.9, 0.2)	(-6.4, -2.7)	(-6.5, -2.7)	(-2.5, 2.9)	(-4.9, 0.6)	(-5.1, 0.7)	(-5.8, 1.2)	(-8.0, -2.9)	(-8.0, -2.1)
		P-value	0.07	<0.001	<0.001	0.889	0.113	0.115	0.191	0.001	0.001

Abbreviation: ESLD=end-stage liver disease; ASMRC=age-standardized mortality rate adjusted by the Chinese standard population; ASMRW=age-standardized mortality rate adjusted by the world standard population; AAPC=average annual percentage change.