**Name of Journal:** *World Journal of Hepatology*

**Manuscript NO:** 90659

**Manuscript Type:** EDITORIAL

**Changes in the etiology of liver cirrhosis and the corresponding management strategies**

Dai JJ *et al*. Changes and strategies of liver cirrhosis

Jin-Jin Dai, Yue-Ying Liu, Zhen-Hua Zhang

**Jin-Jin Dai,** Department of Infectious Diseases, Suzhou Hospital of Anhui Medical University, Suzhou 234000, Anhui Province, China

**Jin-Jin Dai, Yue-Ying Liu, Zhen-Hua Zhang,** Department of Infectious Diseases, The Second Affiliated Hospital of Anhui Medical University, Hefei 230601, Anhui Province, China

**Author contributions:** Dai JJ and Liu YY contributed to this paper; Zhang ZH designed the overall concept and outline of the manuscript; Liu YY contributed to the discussion and design of the manuscript; Dai JJ contributed to the writing, and editing the manuscript, illustrations, and review of literature.

**Supported by** Anhui Provincial Natural Science Foundation, No. 2108085MH298; University Scientific Research Project of Anhui Provincial Education Department, No. KJ2021A0323; Fund of Anhui Medical University, No. 2021xkj196; and Clinical Medicine Project of Anhui Medical University, No. 2021LCXK027.

**Corresponding author: Zhen-Hua Zhang, MD, PhD, Professor,** Department of Infectious Diseases, The Second Affiliated Hospital of Anhui Medical University, No. 678 Furong Road, Hefei 230601, Anhui Province, China. zzh1974cn@163.com

**Received:** December 10, 2023

**Revised:** January 16, 2024

**Accepted:** January 30, 2024

**Published online:**

**Abstract**

We read with interest the article by Xing Wang, which was published in the recent issue of the *World Journal of Hepatology* 2023; 15: 1294-1306. This article focuses particularly on the prevalence and trends in the etiology of liver cirrhosis (LC), prognosis for patients suffering from cirrhosis-related complications and hepatocellular carcinoma (HCC), and management strategies. The etiology of cirrhosis varies according to geographical, economic, and population factors. Viral hepatitis is the dominant cause in China. Vaccination and effective treatment have reduced the number of people with viral hepatitis, but the overall number is still large. Patients with viral hepatitis who progress over time to LC and HCC remain an important population to manage. The increased incidence of metabolic syndrome and alcohol consumption is likely to lead to a potential exponential increase in metabolic dysfunction-associated steatotic liver disease (MASLD)-associated LC and alcoholic liver disease in the future. Investigating the evolution of the etiology of LC is important for guiding the direction of future research and policy development. These changing trends indicate a need for greater emphasis on tackling obesity and diabetes, and implementing more effective measures to regulate alcohol consumption in order to reduce the occurrence of MASLD. In an effort to help cope with these changing trends, the authors further proposed countermeasures for healthcare authorities doctors, and patients.

**Key Words:** Liver cirrhosis; Etiology; Viral hepatitis; Alcoholic liver disease; Hepatocellular carcinoma; Metabolic dysfunction-associated steatotic liver disease

Dai JJ, Liu YY, Zhang ZH. Changes in the etiology of liver cirrhosis and the corresponding management strategies. *World J Hepatol* 2024; In press

**Core Tip:** China is aiming to eradicate viral hepatitis as a public health threat by 2030. It is expected that the prevalence of viral hepatitis will decrease in the coming years. The increasing prevalence of metabolic dysfunction-associated steatotic liver disease (MASLD) may emerge as a leading cause of liver cirrhosis. Additionally, excessive alcohol consumption is a significant risk factor. These shifting trends necessitate innovative management strategies. There is a need for sustained implementation of measures to eliminate viral hepatitis, as well as greater efforts to control obesity, diabetes and alcohol consumption to reduce the incidence of MASLD and Alcoholic liver disease.

**INTRODUCTION**

Liver cirrhosis (LC) is the final stage of progressive liver fibrosis attributed to various etiologies. The etiology of LC varies according to geographical region, economy, lifestyle, and population. Globally, hepatitis B virus (HBV) and hepatitis C virus (HCV) are the leading causes of LC and liver-related mortalities. With the development of control of HBV and cure of HCV, the prevalence of viral hepatitis has decreased. Unfortunately, LC morbidity and mortality are increasing rather than declining. The prevalence of metabolic risk factor-associated liver disease has increased substantially due to the rising prevalence of metabolic syndrome (Mets) and obesity, coupled with increased alcohol consumption and aging. It is expected that metabolic dysfunction-associated steatotic liver disease (MASLD) will soon become the leading cause of LC worldwide[1].

LC and its complications are a major public health challenge worldwide, with a significant economic and health burden. China is ‘‘leader in liver diseases”[2]. In 2017, there were 10.6 million decompensated and 112 million compensated LC cases worldwide[3]. Approximately 2 million people worldwide die from liver disease each year[4]. According to the Global Burden of Disease project, LC caused about 1 million deaths in 2010 and 1.3 million in 2016[5]. Latin America and North Africa recorded the highest LC mortality rates, while the West Coast of the Pacific and Southeast Asia had the highest number of absolute deaths[6]. LC-related complications and hepatocellular carcinoma (HCC) are the main causes of death[7]. While HBV and HCV infections are significant acquired risk factors for HCC, excessive alcohol consumption and associated conditions such as Mets, type 2 diabetes mellitus, obesity, and MASLD have also emerged as important risk factors. Liver cancer morbidity and mortality are estimated to increase by more than 20% in the coming 50 years if the rate of incidence does not decrease by at least 3% per year[8]. In the recent issue of the *World Journal of Hepatology* 2023; 15: 1294-1306[9], that study addresses an important issue: the etiology of LC in China is also changing. Viral hepatitis cirrhosis is gradually decreasing, while non-viral hepatitis cirrhosis is gradually increasing, especially alcoholic liver disease (ALD) and MALSD.

The etiology of LC differs among regions and countries. From 1990 to 2016, China's provinces had very different epidemiological patterns[10]. China is a large and rapidly growing country with a vast population. Regional disparities in the burden of LC may be attributed not only to differences in economic development and healthcare, but also to variations in the distribution of risk factors. The burden of LC also changes over time, making it essential to conduct regionalization studies to analyze the evolution of disease burden and trends in different regions. Access to localized high-quality data is crucial for developing and refining cost-effective strategies for the prevention and treatment of LC, which is necessary to address the increasing burden of chronic liver disease. Wang found that HCC and acute-on-chronic liver failure (ACLF) were identified as the strongest risk factors for in-hospital mortality[9].

**Etiologies differences and temporal trends in burden of liver cirrhosis**

***Viral hepatitis***

Viral hepatitis continues to be the leading cause of LC. Recent studies have shown that approximately 56% of HCC cases are attributed to HBV, while 20% are due to HCV[11]. The lifetime risk of HCC for HBV carriers is estimated to be 10%-25%[12], with the incidence depending on active HBV infection and/or LC. In 2016, China had approximately 12 million LC patients, with 48.9% of cases caused by HBV infection[10]. China also has the largest population of HCV-infected individuals, estimated at 9.8 million[13]. On a global scale, it is projected that chronic HCV infection will not significantly change from 2020 to 2030, but long-term outcomes such as liver-related deaths, HCC, and decompensated LC are expected to increase by 14%-17% in adults[14].

China has implemented a comprehensive strategy to prevent HBV transmission, which includes immunization, interruption of mother-to-child transmission, safe injection practices, and ensuring the safety of blood donations. Hepatitis B vaccination is recognized as the most effective tool for preventing and eliminating HBV infection. China's Hepatitis B Virus prevention policy, launched in 1985, aims to increase neonatal immunization coverage. The use of the recombinant vaccine was approved nationwide in 1992, and the HBV-free vaccination program for children under 14 years was expanded in 2002[15]. Additionally, a catch-up HBV vaccination program for children aged 8-15 was implemented during 2009-2011[16]. The success of these programs in China has led to significant population-wide health benefits, with an estimated 120 million HBV infections and 28 million chronic infections averted.

The incidence of HCV has increased dramatically in China, almost ten folds from 2003 to 2017, due to improved testing technology and government focus[2]. Direct-acting antivirals (DAA) were approved in the United States in 2013, Europe in 2014, and in China in 2017, and have proven to be effective in treating HCV infection. However, of the 15.2 million people diagnosed with HCV worldwide from 2015-2019, only 9.4 million were receiving DAA medication[7]. It is important to establish and improve appropriate surveillance mechanisms to work towards eliminating HCV.

***Non-viral hepatitis***

43% of the world's population currently consumes alcohol, and the global prevalence of alcohol use disorders (AUD) is 5.1% (283 million individuals)[1]. Alcohol is the primary cause of LC worldwide, with nearly 60% of cirrhosis cases in Europe, North America, and Latin America attributable to alcohol[17]. AUD tends to be more common in high-income countries, while low-income countries are likely to underreport and underdiagnose. The highest prevalence of AUD is in European countries, but the absolute burden may be higher in Asia[1]. ALD has gradually become the second leading cause of advanced liver disease in the country due to increased alcohol consumption[13]. There is a clear tendency for the rate of ALD to increase among young people and women[7]. Most of the burden of ALD falls on the 15-44 age group, representing the young and vigorous years of life[18]. Women tolerate alcohol less well than men, tend to develop ALD after lower alcohol exposure, and are more likely to have progression of ALD[19]. The proportion of female drinkers is expected to rise as the proportion of working and single women in China continues to increase. Individuals with ALD are more likely to progress to cirrhosis than those with other causes of liver diseases, including non-alcoholic fatty liver disease (NAFLD). Obesity and Mets may also act synergistically to increase the severity of all stages of ALD. Alcohol abstinence reduces deaths[20]. Therefore, reducing alcohol consumption should be prioritized in public health efforts. The World Health Organization urges countries to develop preventive policies and actions to reduce alcohol consumption and harm. China has a long history of alcohol culture, and hazardous drinking behaviors are prevalent. Alcohol has become a major contributor to the overall burden of disease in China[21]. Despite the implementation of alcohol control strategies in China since 1990, including reforms to alcohol taxation policies, restrictions on alcohol advertising, bans on drink driving, alcohol restrictions for civil servants, and monitoring underage drinking, per capita alcohol consumption has increased dramatically over the past 30 years[22]. Based on available evidence, no level of alcohol consumption can be considered safe, and in order to minimize health effects, consumption should be zero. Challenges remain for China's alcohol control public health strategy.

NAFLD, now known as MASLD, affects a quarter of adults worldwide[23]. The prevalence of NAFLD is 24%-48% in North America[24], 23%-33% in Europe[24], and 28%-32.4% in Asia[25]. NAFLD is the second leading cause of liver transplants in the United States and Europe, and the primary cause of liver disease in females[26]. Approximately 20%-30% of individuals with NAFLD will develop non-alcoholic steatohepatitis (NASH), and 10%-20% of those with NASH will develop HCC[27]. However, NAFLD-associated cirrhosis is often under-recognized or referred to as 'cryptogenic cirrhosis'. Being overweight in late adolescence has been shown to be significantly associated with an increased risk of end-stage liver disease and liver-related mortality in adulthood[28]. Metabolic risk factors emerge as the greatest threat to the health of children and adolescents. As the population ages, MASLD-associated LC is expected to grow exponentially in the coming decades[29]. Despite MASLD being an urgent public health problem, no country has yet developed a national or local public health response[30].

The prevalence of autoimmune hepatitis (AIH)[31] and primary biliary cholangitis (PBC)[32] is increasing worldwide. Reports of PBC are increasing in eastern countries[33]. There is a high prevalence in females, while males appear to have a more aggressive disease and a poorer prognosis[34]. AIH is often detected in the later stages of the disease and is associated with higher mortality. Among individuals with AIH, those with LC were more likely to develop cancer, with a 29.18-fold increased risk of HCC, particularly with prolonged immunosuppressive treatment[35]. Therefore, early diagnosis and treatment could improve the outcome of AIH-related LC.

**Mortality and risk factors of liver cirrhosis**

Compensated cirrhosis is typically asymptomatic and often overlooked, but once decompensation occurs, mortality and morbidity significantly increase. The incidence of decompensation is 11% per year, but varies based on the underlying etiology[36]. ACLF is linked to organ failure and high short-term mortality in LC[37]. In the US, hospitalizations and costs related to ACLF have increased over the last decade[38]. The lowest incidence of ACLF but highest short-term mortality is observed in patients with HCV or MASLD[39]. HBV reactivation is a major predisposing factor for ACLF in China[40].

According to China Cancer Registry data, China's crude liver cancer death rate was 23.7 per 1 million in 2015[41]. Between 2020 and 2040, the number of new cases of HCC is expected to increase by 55.0%, with 1.3 million people estimated to die from HCC in 2040[8]. Effective treatment of HBV and HCV has an impact on the incidence of viral hepatitis-associated HCC. The HBV vaccination program is a key strategy to prevent HCC. A study in Taiwan reports more than 80% reduction in HCC incidence in adults vaccinated in infancy compared with the unvaccinated[42]. The annual incidence of HCC in patients with HCV-associated LC is 0.5%-10%[43]. A 70% reduction in the incidence of HCC following a sustained virological response was observed in a prospective study of French patients with HCV cirrhosis. This study suggests that DAA will play an important role in significantly reducing HCC rates in the future[44]. Increasing evidence suggests that HCC risk is increased by excessive alcohol consumption, Mets, atherosclerotic dyslipidemia, and consumption of aflatoxin-contaminated foods, all of which can be prevented[45]. The government can reduce the incidence of HCC by focusing on risk factor prevention and comprehensive HCC surveillance.

We generally agree with the views and conclusions presented in the text, which to some extent may also reflect the trend of etiological changes in hospitalized LC patients in southern China. Additionally, we find some interesting results in the text. Looking at the temporal trends in LC etiology, the overall incidence of hepatitis B-associated LC showed a decreasing trend but peaked significantly in 2011. The possible reason is that the author's hospital is one of the leading liver disease treatment centers in southern China, and over the years it has been actively developing new technologies and treatments for hepatitis B liver failure, attracting more hepatitis B patients to come to the clinic. This phenomenon peaked in 2011-2012. The total number of hepatitis B cases began to decline in 2013, in line with the overall downward trend. When considering the characteristics of the study population over 20 years, we found that the severity of the patients' conditions lessened, in addition to being associated with an increase in quality of care, was, in our opinion, due to the following reasons: (1) With economic development, improved health insurance policies, and more convenient transportation, the awareness and attention of patients to diseases has increased, leading to more hospital admissions for mild diseases; and (2) The authors' hospitals have evolved in their specialties, expanded their wards, and relaxed their indications for hospitalization, allowing them to provide medical care to a greater number of patients and have the capacity to admit and treat more patients with relatively minor illnesses.

**CLINICAL IMPLICATIONS**

LC and its complications continue to pose a significant public health burden, despite some improvements in HBV and HCV. The impact of targeting the elimination of viral hepatitis is just emerging, but an increase in other risk factors may add to the overall burden of LC. National health planning should be adapted to take these changes into account, including sustainable implementation of programs to eliminate viral hepatitis, expanding screening and treatment options for HBV/HCV, primary prevention of diabetes and obesity, as well as stronger measures for controlling alcohol. It is recommended that patients with chronic liver disease should have serum aminotransferase and alpha-fetoprotein tests, liver ultrasound and elasticity tests every six months, and those with LC or HCC every three months.

Investment in the prevention, detection, and treatment of liver disease has the potential to decrease the number of deaths caused by associated liver disease, lower the incidence of complications from advanced liver disease, and reduce the associated management costs. Tracking trends of LC is essential to identify effective strategies appropriate to the local disease burden and to implement cost-effective interventions.

**CONCLUSION**

We are at a crucial turning point in the recognition, prevention, and treatment of liver disease. Management strategies are needed not only at the national level, but also localized policies for various regions. Early detection and treatment of cirrhosis, with a focus on ALD and NASH, and continued implementation of strategies to eliminate viral hepatitis, must be given particular attention. Establishing well-functioning and comprehensive national health systems to achieve universal coverage is crucial. For hepatologists, it is critical to increase screening of high-risk groups, identify and eliminate disease-causing factors early, and improve monitoring and follow-up with LC and HCC. For patients, maintaining good lifestyle habits, making behavioral changes, and taking necessary precautions can reduce the risks.

**ACKNOWLEDGEMENTS**

We would like to express special thanks to Jun Zhang for their assistance with language polishing.

**REFERENCES**

1 **Meza V**, Arnold J, Díaz LA, Ayala Valverde M, Idalsoaga F, Ayares G, Devuni D, Arab JP. Alcohol Consumption: Medical Implications, the Liver and Beyond. *Alcohol Alcohol* 2022; **57**: 283-291 [PMID: 35333295 DOI: 10.1093/alcalc/agac013]

2 **Xiao J**, Wang F, Wong NK, He J, Zhang R, Sun R, Xu Y, Liu Y, Li W, Koike K, He W, You H, Miao Y, Liu X, Meng M, Gao B, Wang H, Li C. Global liver disease burdens and research trends: Analysis from a Chinese perspective. *J Hepatol* 2019; **71**: 212-221 [PMID: 30871980 DOI: 10.1016/j.jhep.2019.03.004]

3 **GBD 2017 Cirrhosis Collaborators**. The global, regional, and national burden of cirrhosis by cause in 195 countries and territories, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. *Lancet Gastroenterol Hepatol* 2020; **5**: 245-266 [PMID: 31981519 DOI: 10.1016/S2468-1253(19)30349-8]

4 **Asrani SK**, Devarbhavi H, Eaton J, Kamath PS. Burden of liver diseases in the world. *J Hepatol* 2019; **70**: 151-171 [PMID: 30266282 DOI: 10.1016/j.jhep.2018.09.014]

5 **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**: 1211-1259 [PMID: 28919117 DOI: 10.1016/S0140-6736(17)32154-2]

6 **Mokdad AA**, Lopez AD, Shahraz S, Lozano R, Mokdad AH, Stanaway J, Murray CJ, Naghavi M. Liver cirrhosis mortality in 187 countries between 1980 and 2010: a systematic analysis. *BMC Med* 2014; **12**: 145 [PMID: 25242656 DOI: 10.1186/s12916-014-0145-y]

7 **Devarbhavi H**, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. *J Hepatol* 2023; **79**: 516-537 [PMID: 36990226 DOI: 10.1016/j.jhep.2023.03.017]

8 **Rumgay H**, Arnold M, Ferlay J, Lesi O, Cabasag CJ, Vignat J, Laversanne M, McGlynn KA, Soerjomataram I. Global burden of primary liver cancer in 2020 and predictions to 2040. *J Hepatol* 2022; **77**: 1598-1606 [PMID: 36208844 DOI: 10.1016/j.jhep.2022.08.021]

9 **Wang X**, Luo JN, Wu XY, Zhang QX, Wu B. Study of liver cirrhosis over twenty consecutive years in adults in Southern China. *World J Hepatol* 2023; **15**: 1294-1306 [PMID: 38223413 DOI: 10.4254/wjh.v15.i12.1294]

10 **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**: 1-10 [PMID: 32029053 DOI: 10.3967/bes2020.001]

11 **Maucort-Boulch D**, de Martel C, Franceschi S, Plummer M. Fraction and incidence of liver cancer attributable to hepatitis B and C viruses worldwide. *Int J Cancer* 2018; **142**: 2471-2477 [PMID: 29388206 DOI: 10.1002/ijc.31280]

12 **McGlynn KA**, Petrick JL, London WT. Global epidemiology of hepatocellular carcinoma: an emphasis on demographic and regional variability. *Clin Liver Dis* 2015; **19**: 223-238 [PMID: 25921660 DOI: 10.1016/j.cld.2015.01.001]

13 **Wang WJ**, Xiao P, Xu HQ, Niu JQ, Gao YH. Growing burden of alcoholic liver disease in China: A review. *World J Gastroenterol* 2019; **25**: 1445-1456 [PMID: 30948908 DOI: 10.3748/wjg.v25.i12.1445]

14 **GBD 2019 Europe Hepatitis B & C Collaborators**. Hepatitis B and C in Europe: an update from the Global Burden of Disease Study 2019. *Lancet Public Health* 2023; **8**: e701-e716 [PMID: 37633679 DOI: 10.1016/S2468-2667(23)00149-4]

15 **Cui F**, Shen L, Li L, Wang H, Wang F, Bi S, Liu J, Zhang G, Wang F, Zheng H, Sun X, Miao N, Yin Z, Feng Z, Liang X, Wang Y. Prevention of Chronic Hepatitis B after 3 Decades of Escalating Vaccination Policy, China. *Emerg Infect Dis* 2017; **23**: 765-772 [PMID: 28418296 DOI: 10.3201/eid2305.161477]

16 **Hutton DW**, So SK, Brandeau ML. Cost-effectiveness of nationwide hepatitis B catch-up vaccination among children and adolescents in China. *Hepatology* 2010; **51**: 405-414 [PMID: 19839061 DOI: 10.1002/hep.23310]

17 **Avila MA**, Dufour JF, Gerbes AL, Zoulim F, Bataller R, Burra P, Cortez-Pinto H, Gao B, Gilmore I, Mathurin P, Moreno C, Poznyak V, Schnabl B, Szabo G, Thiele M, Thursz MR. Recent advances in alcohol-related liver disease (ALD): summary of a Gut round table meeting. *Gut* 2020; **69**: 764-780 [PMID: 31879281 DOI: 10.1136/gutjnl-2019-319720]

18 **GBD 2016 Alcohol Collaborators**. Alcohol use and burden for 195 countries and territories, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet* 2018; **392**: 1015-1035 [PMID: 30146330 DOI: 10.1016/S0140-6736(18)31310-2]

19 **Buzzetti E**, Parikh PM, Gerussi A, Tsochatzis E. Gender differences in liver disease and the drug-dose gender gap. *Pharmacol Res* 2017; **120**: 97-108 [PMID: 28336373 DOI: 10.1016/j.phrs.2017.03.014]

20 **Arab JP**, Roblero JP, Altamirano J, Bessone F, Chaves Araujo R, Higuera-De la Tijera F, Restrepo JC, Torre A, Urzua A, Simonetto DA, Abraldes JG, Méndez-Sánchez N, Contreras F, Lucey MR, Shah VH, Cortez-Pinto H, Bataller R. Alcohol-related liver disease: Clinical practice guidelines by the Latin American Association for the Study of the Liver (ALEH). *Ann Hepatol* 2019; **18**: 518-535 [PMID: 31053546 DOI: 10.1016/j.aohep.2019.04.005]

21 **GBD 2019 Risk Factors Collaborators**. Global burden of 87 risk factors in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet* 2020; **396**: 1223-1249 [PMID: 33069327 DOI: 10.1016/S0140-6736(20)30752-2]

22 **Hu A**, Jiang H, Dowling R, Guo L, Zhao X, Hao W, Xiang X. The transition of alcohol control in China 1990-2019: Impacts and recommendations. *Int J Drug Policy* 2022; **105**: 103698 [PMID: 35483250 DOI: 10.1016/j.drugpo.2022.103698]

23 **Dai JJ**, Zhang YF, Zhang ZH. Global trends and hotspots of treatment for nonalcoholic fatty liver disease: A bibliometric and visualization analysis (2010-2023). *World J Gastroenterol* 2023; **29**: 5339-5360 [PMID: 37899789 DOI: 10.3748/wjg.v29.i37.5339]

24 **Riazi K**, Azhari H, Charette JH, Underwood FE, King JA, Afshar EE, Swain MG, Congly SE, Kaplan GG, Shaheen AA. The prevalence and incidence of NAFLD worldwide: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2022; **7**: 851-861 [PMID: 35798021 DOI: 10.1016/S2468-1253(22)00165-0]

25 **Li J**, Zou B, Yeo YH, Feng Y, Xie X, Lee DH, Fujii H, Wu Y, Kam LY, Ji F, Li X, Chien N, Wei M, Ogawa E, Zhao C, Wu X, Stave CD, Henry L, Barnett S, Takahashi H, Furusyo N, Eguchi Y, Hsu YC, Lee TY, Ren W, Qin C, Jun DW, Toyoda H, Wong VW, Cheung R, Zhu Q, Nguyen MH. Prevalence, incidence, and outcome of non-alcoholic fatty liver disease in Asia, 1999-2019: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol* 2019; **4**: 389-398 [PMID: 30902670 DOI: 10.1016/S2468-1253(19)30039-1]

26 **Cotter TG**, Charlton M. Nonalcoholic Steatohepatitis After Liver Transplantation. *Liver Transpl* 2020; **26**: 141-159 [PMID: 31610081 DOI: 10.1002/lt.25657]

27 **Ahmed A**, Wong RJ, Harrison SA. Nonalcoholic Fatty Liver Disease Review: Diagnosis, Treatment, and Outcomes. *Clin Gastroenterol Hepatol* 2015; **13**: 2062-2070 [PMID: 26226097 DOI: 10.1016/j.cgh.2015.07.029]

28 **Hagström H**, Stål P, Hultcrantz R, Hemmingsson T, Andreasson A. Overweight in late adolescence predicts development of severe liver disease later in life: A 39years follow-up study. *J Hepatol* 2016; **65**: 363-368 [PMID: 27321729 DOI: 10.1016/j.jhep.2016.03.019]

29 **Estes C**, Anstee QM, Arias-Loste MT, Bantel H, Bellentani S, Caballeria J, Colombo M, Craxi A, Crespo J, Day CP, Eguchi Y, Geier A, Kondili LA, Kroy DC, Lazarus JV, Loomba R, Manns MP, Marchesini G, Nakajima A, Negro F, Petta S, Ratziu V, Romero-Gomez M, Sanyal A, Schattenberg JM, Tacke F, Tanaka J, Trautwein C, Wei L, Zeuzem S, Razavi H. Modeling NAFLD disease burden in China, France, Germany, Italy, Japan, Spain, United Kingdom, and United States for the period 2016-2030. *J Hepatol* 2018; **69**: 896-904 [PMID: 29886156 DOI: 10.1016/j.jhep.2018.05.036]

30 **Lazarus JV**, Mark HE, Villota-Rivas M, Palayew A, Carrieri P, Colombo M, Ekstedt M, Esmat G, George J, Marchesini G, Novak K, Ocama P, Ratziu V, Razavi H, Romero-Gómez M, Silva M, Spearman CW, Tacke F, Tsochatzis EA, Yilmaz Y, Younossi ZM, Wong VW, Zelber-Sagi S, Cortez-Pinto H, Anstee QM; NAFLD policy review collaborators. The global NAFLD policy review and preparedness index: Are countries ready to address this silent public health challenge? *J Hepatol* 2022; **76**: 771-780 [PMID: 34895743 DOI: 10.1016/j.jhep.2021.10.025]

31 **Katsumi T**, Ueno Y. Epidemiology and surveillance of autoimmune hepatitis in Asia. *Liver Int* 2022; **42**: 2015-2022 [PMID: 34990076 DOI: 10.1111/liv.15155]

32 **Colapietro F**, Bertazzoni A, Lleo A. Contemporary Epidemiology of Primary Biliary Cholangitis. *Clin Liver Dis* 2022; **26**: 555-570 [PMID: 36270716 DOI: 10.1016/j.cld.2022.06.001]

33 **Boonstra K**, Kunst AE, Stadhouders PH, Tuynman HA, Poen AC, van Nieuwkerk KM, Witteman EM, Hamann D, Witteman BJ, Beuers U, Ponsioen CY; Epi PSC PBC study group. Rising incidence and prevalence of primary biliary cirrhosis: a large population-based study. *Liver Int* 2014; **34**: e31-e38 [PMID: 24387641 DOI: 10.1111/liv.12434]

34 **Shiffman ML**. Autoimmune Hepatitis: Epidemiology, Subtypes, and Presentation. *Clin Liver Dis* 2024; **28**: 1-14 [PMID: 37945151 DOI: 10.1016/j.cld.2023.06.002]

35 **Sharma R**, Verna EC, Simon TG, Söderling J, Hagström H, Green PHR, Ludvigsson JF. Cancer Risk in Patients With Autoimmune Hepatitis: A Nationwide Population-Based Cohort Study With Histopathology. *Am J Epidemiol* 2022; **191**: 298-319 [PMID: 33913487 DOI: 10.1093/aje/kwab119]

36 **Fleming KM**, Aithal GP, Card TR, West J. The rate of decompensation and clinical progression of disease in people with cirrhosis: a cohort study. *Aliment Pharmacol Ther* 2010; **32**: 1343-1350 [PMID: 21050236 DOI: 10.1111/j.1365-2036.2010.04473.x]

37 **Serper M**, Kaplan DE, Shults J, Reese PP, Beste LA, Taddei TH, Werner RM. Quality Measures, All-Cause Mortality, and Health Care Use in a National Cohort of Veterans With Cirrhosis. *Hepatology* 2019; **70**: 2062-2074 [PMID: 31107967 DOI: 10.1002/hep.30779]

38 **Allen AM**, Kim WR, Moriarty JP, Shah ND, Larson JJ, Kamath PS. Time trends in the health care burden and mortality of acute on chronic liver failure in the United States. *Hepatology* 2016; **64**: 2165-2172 [PMID: 27696493 DOI: 10.1002/hep.28812]

39 **Mahmud N**, Kaplan DE, Taddei TH, Goldberg DS. Incidence and Mortality of Acute-on-Chronic Liver Failure Using Two Definitions in Patients with Compensated Cirrhosis. *Hepatology* 2019; **69**: 2150-2163 [PMID: 30615211 DOI: 10.1002/hep.30494]

40 **Qin G**, Shao JG, Zhu YC, Xu AD, Yao JH, Wang XL, Qian YK, Wang HY, Shen Y, Lu P, Wang LJ. Population-representative Incidence of Acute-On-Chronic Liver Failure: A Prospective Cross-Sectional Study. *J Clin Gastroenterol* 2016; **50**: 670-675 [PMID: 27136963 DOI: 10.1097/MCG.0000000000000538]

41 **Wang Y**, Yan Q, Fan C, Mo Y, Wang Y, Li X, Liao Q, Guo C, Li G, Zeng Z, Xiong W, Huang H. Overview and countermeasures of cancer burden in China. *Sci China Life Sci* 2023; **66**: 2515-2526 [PMID: 37071289 DOI: 10.1007/s11427-022-2240-6]

42 **Chiang CJ**, Yang YW, You SL, Lai MS, Chen CJ. Thirty-year outcomes of the national hepatitis B immunization program in Taiwan. *JAMA* 2013; **310**: 974-976 [PMID: 24002285 DOI: 10.1001/jama.2013.276701]

43 **El-Serag HB**, Kanwal F. Epidemiology of hepatocellular carcinoma in the United States: where are we? Where do we go? *Hepatology* 2014; **60**: 1767-1775 [PMID: 24839253 DOI: 10.1002/hep.27222]

44 **Nahon P**, Bourcier V, Layese R, Audureau E, Cagnot C, Marcellin P, Guyader D, Fontaine H, Larrey D, De Lédinghen V, Ouzan D, Zoulim F, Roulot D, Tran A, Bronowicki JP, Zarski JP, Leroy V, Riachi G, Calès P, Péron JM, Alric L, Bourlière M, Mathurin P, Dharancy S, Blanc JF, Abergel A, Serfaty L, Mallat A, Grangé JD, Attali P, Bacq Y, Wartelle C, Dao T, Benhamou Y, Pilette C, Silvain C, Christidis C, Capron D, Bernard-Chabert B, Zucman D, Di Martino V, Thibaut V, Salmon D, Ziol M, Sutton A, Pol S, Roudot-Thoraval F; ANRS CO12 CirVir Group. Eradication of Hepatitis C Virus Infection in Patients With Cirrhosis Reduces Risk of Liver and Non-Liver Complications. *Gastroenterology* 2017; **152**: 142-156.e2 [PMID: 27641509 DOI: 10.1053/j.gastro.2016.09.009]

45 **Jinjuvadia R**, Patel S, Liangpunsakul S. The association between metabolic syndrome and hepatocellular carcinoma: systemic review and meta-analysis. *J Clin Gastroenterol* 2014; **48**: 172-177 [PMID: 24402120 DOI: 10.1097/MCG.0b013e3182a030c4]

**Footnotes**

**Conflict-of-interest statement:** The authors declare that they have no conflicts of interest.

**Open-Access:** This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/

**Provenance and peer review:** Invited article; Externally peer reviewed.

**Peer-review model:** Single blind

**Peer-review started:** December 10, 2023

**First decision:** January 15, 2024

**Article in press:**

**Specialty type:** Gastroenterology & hepatology

**Country/Territory of origin:** China

**Peer-review report’s scientific quality classification**

Grade A (Excellent): 0

Grade B (Very good): B

Grade C (Good): 0

Grade D (Fair): 0

Grade E (Poor): 0

**P-Reviewer:** Sintusek P, Thailand **S-Editor:** Gong ZM **L-Editor:** A **P-Editor:**