Journal of Clinical and Translational Hepatology **2025** vol. 13(7) | 599–604
DOI: 10.14218/JCTH.2025.00039

Review Article

Epidemiology, Achievements, and Challenges in the Elimination of Hepatitis B in China

You Deng[#], Tongtong Meng[#], Hong You, Jidong Jia[*] and Yu Wang[*]

Liver Research Center; The National Clinical Research Center for Digestive Diseases; State Key Laboratory of Digestive Health, Beijing Friendship Hospital, Capital Medical University, Beijing, China

Received: January 21, 2025 | **Revised:** April 04, 2025 | **Accepted:** April 29, 2025 | **Published online:** May 21, 2025

Abstract

China has made remarkable progress in controlling chronic hepatitis B virus (HBV) infection over the past three decades. The prevalence of hepatitis B surface antigen has declined from 9.72% in 1992 to 5.86% in 2020, with a striking reduction from 9.67% to 0.30% among children under five. Universal hepatitis B vaccination has been pivotal, preventing more than 40 million infections and seven million HBV-related deaths since 1992. Nevertheless, an estimated 75 million individuals are currently living with chronic HBV infection in China. Among them, only 59.78% are aware of their infection status, and about 30 million remain undiagnosed. Of those diagnosed, 38.25% (approximately 17 million) meet the criteria for antiviral treatment, yet only 17.33% (about three million) are receiving treatment. To accelerate progress toward the World Health Organization's elimination targets, China has updated its clinical guidelines to expand treatment eligibility and improve diagnosis and treatment coverage. Moreover, Chinese pharmaceutical companies and academic institutions are actively engaged in developing novel therapies with promising efficacy, aiming to achieve a functional cure. China's holistic approach, combining evidence-based public health interventions with active clinical management and innovative pharmaceutical development, provides valuable experience for global HBV elimination initiatives. This review aimed to summarize China's progress in HBV control, identify remaining gaps in diagnosis and treatment, and highlight strategic approaches, including public health interventions, clinical policy updates, and pharmaceutical innovation, toward achieving HBV elimination.

Citation of this article: Deng Y, Meng T, You H, Jia J, Wang Y. Epidemiology, Achievements, and Challenges in the Elimination of Hepatitis B in China. J Clin Transl Hepatol 2025; 13(7):599–604. doi: 10.14218/JCTH.2025.00039.

Keywords: Chronic hepatitis B; Prevalence; Prevention; Treatment; Functional cure; Management strategies; China.

[#]Contributed equally to this work.
[*]Correspondence to: Yu Wang and Jidong Jia, Liver Research Center, Beijing Friendship Hospital, Capital Medical University, No. 95, Yong'an Road, Xicheng District, Beijing 100050, China. ORCID: https://orcid.org/0000-0003-0057-9182 (YW) and https://orcid.org/0000-0002-4673-8890 (JJ). Tel: +86-10-63138435, E-mail: wangyuliver@ccmu.edu.cn (YW) and jia_jd@ccmu.edu.cn (JJ).

Introduction

In the early 1990s, China bore nearly one-third of the global hepatitis B virus (HBV) burden, with an alarming hepatitis B surface antigen (HBsAg) prevalence of 9.72%,[1] primarily due to mother-to-child transmission (MTCT). Remarkable progress has since been achieved through coordinated public health interventions, including universal infant hepatitis B (HepB) vaccination, comprehensive MTCT prevention programs, and expanded access to antiviral therapies. Despite these accomplishments, significant gaps remain in the diagnosis and treatment of people living with chronic hepatitis B (CHB). Therefore, innovative approaches are essential to meet the 2030 targets proposed by the World Health Organization (WHO), which aim for a 95% reduction in new infections and a 65% reduction in HBV-related mortality compared to 2015 levels.[2]

Epidemiological trends of chronic HBV infection in China

Over the past three decades, China has experienced profound changes in the epidemiology of HBV infection, as reflected in national seroepidemiological surveys. The seroprevalence of HBsAg in the general population declined from 9.72% in 1992 to 5.86% in 2020, representing a reduction of more than 39%.[1] This decline is even more pronounced among children aged one to four years, with HBsAg prevalence dropping from 9.67% in 1992 to 0.96% in 2006,[3] and further to 0.30% in 2020.[1] Modeling studies published in 2021 estimated that, if current prevention programs are maintained, China is projected to reach the target of less than 0.10% HBsAg prevalence among children aged one to four years by 2029.[4] A recent study published in 2023 suggests that the elimination target may be achieved even earlier, potentially by 2025, even under existing prevention measures.[5] These trends underscore the effectiveness of comprehensive public health strategies, particularly universal vaccination and MTCT prevention, in reducing HBV transmission and preventing new infections.

Universal vaccination and MTCT prevention drive the epidemiological shifts

Universal infant hepatitis B vaccination has been the cornerstone of China's HBV control strategy. Since the launch of a nationwide immunization program in 1992,[3] timely birth dose administration within 24 h of birth, followed by two ad-

ditional doses at one and six months, has become standard practice. By 2002, the hepatitis B vaccine was integrated into the Expanded Program on Immunization, making it freely available to all newborns. In 2005, the government further strengthened this initiative by removing service-related fees, ensuring completely free HepB vaccination for infants.[6,7]

The impact of these policies has been profound. The prevalence of HBsAg among children under five declined from 9.67% in 1992 to 0.30% in 2020.[1] It is estimated that more than 40 million HBV infections and over seven million related deaths have been averted among individuals born after 1992. These achievements align with the WHO's target of reducing HBsAg prevalence among children to less than 1% by 2020.[8] Globally, however, significant disparities persist. By 2020, only 147 of 194 (76%) countries had achieved this target. While all countries in Europe and the Americas succeeded, only 15 of 47 (32%) countries in Africa met the goal.[9]

Equitable access to vaccination services has been pivotal to China's success. Special initiatives targeting hard-to-reach populations, particularly in rural and western provinces, included incentivizing facility-based deliveries, training healthcare workers, and providing free HepB vaccination.[10] As a result, the timely birth-dose coverage rate increased from 22.2% in 1992 to 95.6% in 2015, while three-dose coverage rose from 30% to 99.6%.[11,12] In contrast, the global birth-dose coverage in 2015 was only 38%.[13] In selected African countries, HepB-BD coverage ranged from 23% to 94%, and timely birth-dose coverage varied from 7% to 74%.[14]

MTCT has historically accounted for a significant proportion of chronic HBV cases in China, making its prevention a critical focus.[15] In response, China implemented a comprehensive strategy that encompasses several key measures: routine HBsAg screening for pregnant women;[16] maternal antiviral therapy during pregnancy for women with high viral loads;[17,18] combined immunoprophylaxis with HepB birth dose and hepatitis B immunoglobulin for exposed neonates;[19,20] and post-vaccination serological testing to evaluate the immune response.[21] The "Triple Elimination" program, launched in 2011, integrated efforts to combat HBV, HIV, and syphilis, further strengthening MTCT prevention by expanding outreach and resource allocation.[22,23] Real-world data confirm that when these measures are fully implemented, MTCT rates can be reduced to as low as 0.23%.[21]

However, challenges persist, particularly in rural and resource-limited settings. Reported barriers include unclear staff responsibilities for HepB-BD administration, lack of integration into routine newborn care, limited daily vaccination services, and insufficient healthcare worker training. Moreover, existing data tools often fail to capture vaccination timeliness.[14]

To address these challenges, the SHIELD program provides an integrated model for eliminating HBV MTCT. It standardizes clinical management based on international guidelines, incorporates digital health tools for follow-up and data collection, and follows a phased rollout strategy across pilot, implementation, and community scale-up stages. Real-world evidence shows that SHIELD achieved an overall MTCT rate of 0.23%, which declined to 0.16% in stage II and 0.03% in stage III among highly compliant populations.[21]

Notably, SHIELD demonstrated consistent MTCT outcomes across different geographic regions, socioeconomic strata, and hospital levels, underscoring its broad adaptability.[21,24] Its core components—affordable antivirals, standardized protocols, and mobile-based data systems—are readily transferable to low- and middle-income countries, particularly in underserved regions. Despite its success, SHIELD also encountered real-world barriers, including variability in antiviral adherence, incomplete post-vaccination serological testing, and unequal access to diagnostics. Although antiviral drugs are low-cost, the lack of universal reimbursement can limit treatment uptake. Nevertheless, SHIELD demonstrates that, with phased implementation, targeted training, and supportive digital tools, comprehensive MTCT prevention can be achieved at scale, even in under-resourced settings.

Disease burden and clinical management in HBV-infected individuals

The 2020 national serosurvey provided a comprehensive estimation of the clinical staging of CHB and the healthcare cascade in China. In addition to the overall decline in HBsAg prevalence, substantial differences remain across age groups. Among children aged one to four years, prevalence declined from 9.67% in 1992 to 0.30% in 2020. In the five-to-fourteen age group, it dropped from 10.74% to 0.38%; among individuals aged 15–29 years, from 9.76% to 2.62%; and among those aged ≥30 years, from 9.24% to 7.54%.[1] These trends reflect a strong cohort effect, whereby younger generations, benefiting from widespread infant vaccination, exhibit significantly lower HBsAg prevalence compared to older, unvaccinated cohorts.

According to the 2020 serosurvey, 78.03% of HBsAg-positive individuals aged 15 years and older were classified as chronic HBV carriers, followed by CHB patients (19.63%), cirrhosis (0.84%), and hepatocellular carcinoma (HCC) (0.15%).[1] However, data from the China Registry of Hepatitis B working group revealed a different pattern among individuals seeking healthcare: CHB patients constituted the largest proportion (71.4%), followed by chronic HBV carriers (16.8%), cirrhosis (11.8%), and HCC (1.58%).[25] This discrepancy reflects a selection bias, as individuals seeking care are more likely to have symptomatic or advanced disease. It also suggests that many people in the general population remain undiagnosed or untreated, increasing their risk of disease progression.

Sex-based disparities have also been observed. In the China Registry of Hepatitis B cohort, men accounted for 61.4% of CHB patients and 70.8% of cirrhosis patients.[25] Behavioral factors—such as higher rates of smoking and alcohol consumption among men—may contribute to this pattern. Smoking has been associated with impaired HBV-specific immune responses and accelerated liver disease progression,[26] while alcohol is a major risk factor for cirrhosis, with risk increasing exponentially with higher intake levels.[27]

Regional variations are notable as well. In a 2020 cohort of HBsAg-positive individuals aged ≥15 years, 40.0%, 26.1%, and 33.9% were from eastern, central, and western regions, respectively.[1] Among people who inject drugs, prevalence ranged from 15.9% in northern China to 25.3% in the south, with a national estimate of 19.6%.[28] These differences often reflect broader socioeconomic disparities. People in rural and western areas face reduced access to HBV care due to limited healthcare infrastructure, financial barriers, and lower awareness of the disease.[29,30] Gaps in insurance coverage and high out-of-pocket costs further contribute to delayed diagnosis and poor treatment adherence. Addressing these structural inequities is essential to advancing HBV elimination efforts.

Certain high-risk populations also face a disproportionate HBV burden. Among patients on hemodialysis in Asia, HBV prevalence is estimated at 7.44% (global: 7.32%),[31] while the China DOPPS study reported a notably higher prevalence

of 17.6%.[32] Among HIV-positive individuals, HBsAg positivity reached 11.0% in Shaanxi (n = 1,018)[33] and 6.9% in Ningxia (n = 1,008).[34] Among immunocompromised individuals, 41.2% of 980 patients with inflammatory bowel disease had current or past HBV infection.[35] These data highlight the need for micro-elimination strategies—targeted interventions within high-risk groups. Dialysis and HIV care settings can incorporate routine HBsAg screening and linkage to care. For immunocompromised patients, pre-treatment screening, vaccination, and antiviral prophylaxis should be integrated into clinical protocols. Such focused approaches are feasible and can accelerate progress toward HBV elimination.

The Polaris Observatory Collaboration estimated in 2022 that only 24% of people with CHB in China had been diagnosed, and just 15% were receiving treatment.[36] However, these figures likely underestimate the true burden, as many individuals tested through school- or workplace-based programs are not systematically linked to care. According to the 2020 serosurvey, 59.78% of HBsAg-positive individuals knew their status prior to the survey. Among those, 38.25% met the antiviral treatment criteria specified in the Guidelines for the Prevention and Treatment of Chronic Hepatitis B (2019 edition), and 17.33% were receiving treatment.[1] This gap between diagnosis and treatment may reflect barriers such as limited healthcare access, low public health awareness, and previously restrictive guidelines for initiating antiviral therapy.

In addition to structural barriers, systemic failures in linkage to care are critical contributors. Many individuals diagnosed with HBV are not effectively connected to services such as laboratory assessment, eligibility evaluation for antiviral therapy, or long-term clinical management. Suboptimal diagnostic processes—including passive case finding, fragmented referral systems, and underutilization of community-based screening—further hinder treatment uptake.

Socio-cultural factors also play a significant role. Hepatitis B-related stigma remains a major structural barrier to elimination in China. Discrimination in employment, education, and social relationships has been well documented and contributes to underreporting, delays in seeking care, and poor treatment adherence. A national survey found that among those aware of their infection, only 45.45% actively sought medical care. Reasons included the belief that the disease is mild or asymptomatic (79.91%), the perception that treatment is unnecessary (13.24%), and concerns about privacy or a preference for self-medication (6.86%).[37]

The implications of this gap are significant. While acute HBV incidence is projected to drop below two per 100,000 person-years by 2024, achieving the elimination target of a 90% incidence reduction, reducing HBV-related mortality remains a greater challenge.[5,38] A dynamic simulation model projected that under the status quo, HBV-related mortality targets would not be met until 2059, with an estimated 9.98 million deaths (95% CI: 9.27–10.70) by 2100.[5] In contrast, achieving 90% diagnostic coverage and 80% treatment coverage would accelerate HBV elimination by 8 years and potentially save 1.98 million lives (95% CI: 1.83–2.12).[5]

To bridge these gaps and meet elimination goals, future strategies must prioritize expanding treatment coverage, simplifying clinical guidelines, and addressing the socioeconomic barriers that hinder access to care in underserved areas. Strengthening community-based screening, implementing anti-stigma campaigns, and enhancing referral systems will be essential to improving diagnosis, treatment uptake, and long-term disease control. These efforts will be critical to achieving the WHO's 2030 target of reducing HBV-related mortality by 65% from the 2015 baseline.

Expanding treatment eligibility and improving diagnosis and treatment rates

To achieve the WHO's goal of "eliminating viral hepatitis as a major public health threat by 2030", China released updated guidelines in 2022. A key principle emphasized in the revised guidelines is the treatment of all individuals with quantifiable HBV DNA who are at risk of disease progression. These include individuals aged 30 years or older with any elevation in ALT, histological or non-invasive evidence of moderate necroinflammation or fibrosis, a family history of HBV-related cirrhosis or HCC, or extrahepatic manifestations.[39] This expanded treatment criterion aims to narrow the treatment gap in China.

A modeling study by Zhang *et al*.[40] evaluated various strategies for expanding antiviral treatment to achieve HBV elimination goals in China. Among these, lowering ALT initiation thresholds to 30 U/L for males and 19 U/L for females, with 80% coverage of individuals aged 18–80, demonstrated the potential to achieve a 65% reduction in HBV-related mortality by 2043. This strategy showed the greatest potential to reduce HBV-related complications and deaths, maximize quality-adjusted life years, and align with WHO's 2030 elimination targets, provided it is implemented with sufficient coverage.[41]

The "treat all" strategy goes a step further by recommending antiviral treatment for all HBV DNA-positive patients, regardless of ALT levels. This approach simplifies treatment criteria and ensures that even patients with "normal" ALT levels—often overlooked—can benefit from early intervention.[41] Notably, early treatment in specific populations, such as children under seven years of age[42] and HBeAg-positive patients with high viral loads ($>2\times10^7$ IU/mL),[43] has shown the potential to reduce long-term complications. However, initiating antiviral therapy during the HBeAg-positive chronic HBV infection phase remains controversial due to uncertainties regarding long-term benefits and concerns about persistent low-level viremia.[44,45]

While the "treat all" strategy demonstrates strong potential to meet WHO elimination targets, its implementation faces significant challenges. The overall cost and the need for extensive healthcare infrastructure raise concerns about feasibility, especially in resource-limited settings. Ensuring long-term adherence to therapy and addressing healthcare disparities between urban and rural populations are also critical barriers. Overcoming these challenges will require innovative solutions, such as leveraging digital health tools to improve patient compliance and optimizing resource allocation in underserved areas. However, improving compliance will require more than technological tools; systematic social research is needed to understand the perspectives of individuals living with hepatitis B and the barriers they face. Patient-centered education should also be integrated as part of a comprehensive strategy to enhance treatment adherence.

China's 2022 updated guidelines, which expanded treatment criteria to include most HBV DNA-positive individuals, represent a pivotal step toward bridging the gap between traditional ALT-based thresholds and the broader "treat all" approach. These national efforts are aligned with the WHO's 2024 guideline update, which emphasizes simplified algorithms and expanded treatment eligibility to support global elimination goals.[46] If effectively implemented, the updated guidelines could significantly improve treatment coverage, reduce HBV-related morbidity and mortality, and bring the country closer to achieving WHO's elimination targets.

Developing innovative therapies for a functional cure

A functional cure for CHB is defined as sustained HBsAg

loss and undetectable HBV DNA six months after cessation of therapy. It is associated with improved clinical outcomes and represents the optimal therapeutic goal. Novel therapies are being developed to achieve this, targeting three main mechanisms: inhibition of viral replication, reduction of viral antigen load, and restoration of HBV-specific immunity.[47] Interferon combined with nucleos(t)ide analogues (NAs) has shown promise in achieving HBsAg clearance in highly selected patients with favorable factors such as unquantifiable HBV DNA and low levels of HBsAg.[47] However, adverse effects limit the widespread use of interferon. Consequently, newer therapies aim to enhance HBsAg clearance with improved tolerability and broader applicability.

The biological basis of a functional cure involves durable suppression of HBV replication, typically through silencing of covalently closed circular DNA, the reservoir responsible for viral persistence. Immune exhaustion, partly driven by high levels of HBsAg originating from both covalently closed circular DNA and integrated HBV DNA, hampers host immune control and contributes to disease progression and oncogenesis.[48] Therefore, new therapies must both reduce antigen load and restore antiviral immune responses.

Several novel therapeutic agents for CHB are currently under clinical investigation, aiming to suppress viral replication, reduce antigen burden, and restore immune control. These include antiviral compounds such as NAs, capsid assembly modulators, and RNA-targeting agents like small interfering RNAs (e.g., VIR-2218, JNJ-3989) and antisense oligonucleotides (ASOs; e.g., bepirovirsen). Other agents, such as nucleic acid polymers, target HBsAg secretion. In parallel, immunomodulatory approaches are being explored to enhance HBV-specific immune responses. These include PEGylated interferon (PEG-IFN), toll-like receptor agonists (e.g., GS-9688), immune checkpoint inhibitors (e.g., nivolumab, cemiplimab), and a growing range of therapeutic vaccines (e.g., NASVAC, TG1050, VTP-300). While most of these agents are in early-phase trials, combination strategies—particularly those integrating agents with complementary mechanisms—are increasingly favored for their potential to improve functional cure rates.[47]

China's pharmaceutical and academic sectors have made substantial contributions to the advancement of HBV therapies. For instance, AHB-137, an ASO developed by AusperBio, significantly reduced HBsAg levels in Phase II trials. In the 300 mg treatment group, 62% of participants, and in the 225 mg group, 43% achieved HBsAg seroclearance within 12 weeks, with most clearance occurring in the first eight weeks (44% and 30%, respectively).[49] HH-003, a monoclonal antibody targeting the PreS1 region of HBV, and HH-006, a long-acting neutralizing antibody for subcutaneous administration developed by Huahui Health, have shown promise in managing HBV/HDV co-infections.[50] Meanwhile, Brii Biosciences has developed BRII-835 (VIR-2218), a GalNAc-conjugated RNAi-based therapy that demonstrated significant antigen-reducing effects and enhanced HBsAg clearance when combined with PEG-IFNα.[51]

Chinese researchers have also played a pivotal role in advancing global clinical studies on HBV cure strategies. Notably, China is a key participant in the Phase III clinical trials of bepirovirsen (GSK3228836), an ASO targeting all HBV mRNA transcripts. In Phase II trials, bepirovirsen demonstrated a 26% HBsAg clearance rate at the end of a 24-week treatment period, although post-treatment durability was limited to 9% at 24 weeks without rescue therapy.[52] The drug has received Breakthrough Therapy designation from China's National Medical Products Administration and Fast Track designation from the U.S. Food and Drug Administration, positioning it as a leading candidate for achieving a functional cure for CHB. Another notable example is xalnesiran, a small interfering RNA therapy targeting multiple HBV transcripts. Phase II trials led by Chinese investigators reported a 30% HBsAg clearance rate when combined with NAs and PEG-IFNα, with clearance rates rising to 47% among patients with baseline HBsAg levels below 1,000 IU/mL. These results suggest xalnesiran's potential as a cornerstone therapy, particularly for patients with low-antigen loads.[53] These contributions highlight China's multifaceted role in advancing HBV cure strategies. By leading key clinical trials and driving pharmaceutical innovation, China's pharmaceutical and hepatology sectors are shaping the global landscape of CHB management and pushing the boundaries of achieving a functional cure.

Despite these advances, several challenges remain. Optimizing the timing, sequencing, and duration of combination therapies is essential to maximize efficacy. The development of biomarkers for patient stratification and treatment response monitoring is also critical for improving treatment precision. Furthermore, the high cost of novel agents limits accessibility, particularly in resource-limited settings.[47,54] It is unlikely that a single cure strategy will suit all patients. Instead, individualized approaches—tailored to patients' virological and immunological profiles—will be key to achieving sustained functional cure.

Conclusions

China has achieved remarkable success in reducing HBV prevalence through evidence-based interventions, including universal infant HepB vaccination, MTCT prevention, and expanded healthcare access. Achieving the WHO's 2030 targets will require further strengthening of large-scale testing, early treatment, and long-term follow-up programs, as well as advancing innovative therapies and ensuring equitable healthcare delivery nationwide. With sustained investment and continued innovation, the elimination of hepatitis B as a public health threat is within reach, offering valuable insights and experience for global HBV control efforts.

Funding

This study was funded by the Capital's Funds for Health Improvement and Research (CFH 2022-2-1104).

Conflict of interest

JJ and YW received research grants, consulting fees, or speaker honoraria from BMS, Gilead, and GSK. HY has been an Editorial Board Member of *Journal of Clinical and Translational Hepatology* since 2021, JJ has been an Executive Associate Editor of *Journal of Clinical and Translational Hepatology* since 2013. The other authors have no conflict of interests related to this publication.

Author contributions

Literature screening and collection, and drafting of the initial manuscript (YD, TM). Conceptualization of the review framework, critical revision of core content, and final editing of the manuscript (JJ, YW, HY). All authors have approved the final version and publication of the manuscript.

References

[1] Hui Z, Yu W, Fuzhen W, Liping S, Guomin Z, Jianhua L, *et al*. New progress in HBV control and the cascade of health care for people living

with HBV in China: evidence from the fourth national serological survey, 2020. Lancet Reg Health West Pac 2024;51:101193. doi:10.1016/j.lanwpc.2024.101193, PMID:39315090.
[2] Zhou H, Yan M, Che D, Wu B. Trends in Mortality Related to Hepatitis B and C from 1990 to 2019 in the Western Pacific Region. Gut Liver 2024;18(3):539–549. doi:10.5009/gnl230023, PMID:38638100.
[3] Cui F, Shen L, Li L, Wang H, Wang F, Bi S, *et al*. Prevention of Chronic Hepatitis B after 3 Decades of Escalating Vaccination Policy, China. Emerg Infect Dis 2017;23(5):765–772. doi:10.3201/eid2305.161477, PMID:28418296.
[4] Hui Z, Nayagam S, Chan P, Fuzhen W, Thursz M, Zundong Y, *et al*. Progress towards elimination of mother-to-child transmission of hepatitis B virus infection in China: a modelling analysis. Bull World Health Organ 2021;99(1):10–18. doi:10.2471/BLT.19.248146, PMID:33658732.
[5] Li R, Shen M, Ong JJ, Cui F, Hu W, Chan P, *et al*. Blueprint to hepatitis B elimination in China: A modelling analysis of clinical strategies. JHEP Rep 2023;5(10):100833. doi:10.1016/j.jhepr.2023.100833, PMID:37675271.
[6] Kane MA, Hadler SC, Lee L, Shapiro CN, Cui F, Wang X, *et al*. The inception, achievements, and implications of the China GAVI Alliance Project on Hepatitis B Immunization. Vaccine 2013;31(Suppl 9):J15–J20. doi:10.1016/j.vaccine.2013.03.045, PMID:24331015.
[7] Liang X, Bi S, Yang W, Wang L, Cui G, Cui F, *et al*. Epidemiological serosurvey of hepatitis B in China—declining HBV prevalence due to hepatitis B vaccination. Vaccine 2009;27(47):6550–7. doi:10.1016/j.vaccine.2009.08.048, PMID:19729084.
[8] Breakwell L, Anga J, Cooley G, Ropiti L, Gwyn S, Wannemuehler K, *et al*. Seroprevalence of chronic hepatitis B virus infection and immunity to measles, rubella, tetanus and diphtheria among schoolchildren aged 6-7 years old in the Solomon Islands, 2016. Vaccine 2020;38(30):4679–4686. doi:10.1016/j.vaccine.2020.05.029, PMID:32473876.
[9] GBD 2019 Hepatitis B Collaborators. Global, regional, and national burden of hepatitis B, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Gastroenterol Hepatol 2022□ doi:10.1016/S2468-1253(22)00124-8, PMID:35738290.
[10] Hutin Y, Hennessey K, Cairns L, Zhang Y, Li H, Zhao L, *et al*. Improving hepatitis B vaccine timely birth dose coverage: lessons from five demonstration projects in China, 2005-2009. Vaccine 2013;31(Suppl 9):J49–J55. doi:10.1016/j.vaccine.2013.03.025, PMID:24331021.
[11] Liu J, Liang W, Jing W, Liu M. Countdown to 2030: eliminating hepatitis B disease, China. Bull World Health Organ 2019;97(3):230–238. doi:10.2471/BLT.18.219469, PMID:30992636.
[12] Chen S, Mao W, Guo L, Zhang J, Tang S. Combating hepatitis B and C by 2030: achievements, gaps, and options for actions in China. BMJ Glob Health 2020;5(6):e002306. doi:10.1136/bmjgh-2020-002306, PMID:32605935.
[13] WHO. Global Health Sector Strategy on Viral Hepatitis 2016-2021. Available from: https://iris.who.int/bitstream/handle/10665/246177/WHO-HIV-2016.06-eng.pdf.
[14] Moturi E, Tevi-Benissan C, Hagan JE, Shendale S, Mayenga D, Murokora D, *et al*. Implementing a Birth Dose of Hepatitis B Vaccine in Africa: Findings from Assessments in 5 Countries. J Immunol Sci 2018;Suppl(5):31–40. PMID:30931434.
[15] Liu J, Zeng Q, Ji F, Ren H, Zhang W, Li L, *et al*. Chinese Clinical Practice Guidelines for the Prevention and Treatment of Mother-to-child Transmission of Hepatitis B Virus (Version 2024). J Clin Transl Hepatol 2024;12(11):975–983. doi:10.14218/JCTH.2024.00258, PMID:39544248.
[16] Chen HL, Lin LH, Hu FC, Lee JT, Lin WT, Yang YJ, *et al*. Effects of maternal screening and universal immunization to prevent mother-to-infant transmission of HBV. Gastroenterology 2012;142(4):773–781.e2. doi:10.1053/j.gastro.2011.12.035, PMID:22198276.
[17] Chen HL, Lee CN, Chang CH, Ni YH, Shyu MK, Chen SM, *et al*. Efficacy of maternal tenofovir disoproxil fumarate in interrupting mother-to-infant transmission of hepatitis B virus. Hepatology 2015;62(2):375–386. doi:10.1002/hep.27837, PMID:25851052.
[18] Pan CQ, Duan Z, Dai E, Zhang S, Han G, Wang Y, *et al*. Tenofovir to Prevent Hepatitis B Transmission in Mothers with High Viral Load. N Engl J Med 2016;374(24):2324–2334. doi:10.1056/NEJMoa1508660, PMID:27305192.
[19] de Villiers MJ, Nayagam S, Hallett TB. The impact of the timely birth dose vaccine on the global elimination of hepatitis B. Nat Commun 2021;12(1):6223. doi:10.1038/s41467-021-26475-6, PMID:34711822.
[20] Su WJ, Chen SF, Yang CH, Chuang PH, Chang HF, Chang MH. The Impact of Universal Infant Hepatitis B Immunization on Reducing the Hepatitis B Carrier Rate in Pregnant Women. J Infect Dis 2019;220(7):1118–1126. doi:10.1093/infdis/jiy706, PMID:30576506.
[21] Yin X, Wang W, Chen H, Mao Q, Han G, Yao L, *et al*. Real-world implementation of a multilevel interventions program to prevent mother-to-child transmission of HBV in China. Nat Med 2024;30(2):455–462. doi:10.1038/s41591-023-02782-x, PMID:38297093.
[22] Shan S, Jia J. Prevention of Mother-to-Child Transmission of Hepatitis B Virus in the Western Pacific Region. Clin Liver Dis (Hoboken) 2021;18(1):18–21. doi:10.1002/cld.1096, PMID:34484699.
[23] Wang AL, Qiao YP, Wang LH, Fang LW, Wang F, Jin X, *et al*. Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China. Bull World Health Organ 2015;93(1):52–56. doi:10.2471/BLT.14.139626, PMID:25558108.
[24] Yin X, Han G, Zhang H, Wang M, Zhang W, Gao Y, *et al*. A Real-world Prospective Study of Mother-to-child Transmission of HBV in China Using a Mobile Health Application (Shield 01). J Clin Transl Hepatol 2020;8(1):1–8. doi:10.14218/JCTH.2019.00057, PMID:32274339.
[25] Xu XQ, Wang H, Shan S, You H, Nan YM, Xu XY, *et al*. Ten-year changes in clinical characteristics and antiviral treatment patterns of chronic hepatitis B in China: a CR-HepB-based real-world study. Zhonghua Gan Zang Bing Za Zhi 2023;31(7):698–704. doi:10.3760/cma.j.cn501113-20230518-00226, PMID:37580251.
[26] Rutledge SM, Asgharpour A. Smoking and Liver Disease. Gastroenterol Hepatol (N Y) 2020;16(12):617–625. PMID:34035697.
[27] Roerecke M, Vafaei A, Hasan OSM, Chrystoja BR, Cruz M, Lee R, *et al*. Alcohol Consumption and Risk of Liver Cirrhosis: A Systematic Review and Meta-Analysis. Am J Gastroenterol 2019;114(10):1574–1586. doi:10.14309/ajg.0000000000000340, PMID:31464740.
[28] Shan S, Zhao X, Jia J. Comprehensive approach to controlling chronic hepatitis B in China. Clin Mol Hepatol 2024;30(2):135–143. doi:10.3350/cmh.2023.0412, PMID:38176692.
[29] Wang X, Liu J, Wang Q, Qiao Y, Jin X, Li Z, *et al*. Economic-related inequalities in hepatitis B virus infection among 115.8 million pregnant women in China from 2013 to 2020. EClinicalMedicine 2022;49:101465. doi:10.1016/j.eclinm.2022.101465, PMID:35747197.
[30] Han Z, Yin Y, Zhang Y, Ehrhardt S, Thio CL, Nelson KE, *et al*. Knowledge of and attitudes towards hepatitis B and its transmission from mother to child among pregnant women in Guangdong Province, China. PLoS One 2017;12(6):e0178671. doi:10.1371/journal.pone.0178671, PMID:28575040.
[31] Khalesi Z, Razizadeh MH, Javadi M, Bahavar A, Keyvanlou Z, Saadati H, *et al*. Global epidemiology of HBV infection among hemodialysis patients: A systematic review and meta-analysis. Microb Pathog 2023;179:106080. doi:10.1016/j.micpath.2023.106080, PMID:36948364.
[32] Zhao X, Niu Q, Gan L, Hou FF, Liang X, Ni Z, *et al*. Baseline data report of the China Dialysis Outcomes and Practice Patterns Study (DOPPS). Sci Rep 2021;11(1):873. doi:10.1038/s41598-020-79531-4, PMID:33441625.
[33] Zhang C, Ren Q, Chang W. Epidemiological Features and Risk Factors for Acquiring Hepatitis B, Hepatitis C, and Syphilis in HIV-Infected Patients in Shaanxi Province, Northwest China. Int J Environ Res Public Health 2020;17(6):1990. doi:10.3390/ijerph17061990, PMID:32197326.
[34] Li L, Yang D, Chen X, Kuai W, Ma X. The prevalence of hepatitis B virus infection among HIV-infected patients in the Ningxia Hui Autonomous Region, China, November 2002 to July 2023. Diagn Microbiol Infect Dis 2024;110(1):116417. doi:10.1016/j.diagmicrobio.2024.116417, PMID:38954861.
[35] Chen D, Luo S, Ben Q, Lu L, Wan X, Wu J. Prevalence of hepatitis B and C and factors for infection and nonimmune in inflammatory bowel disease patients in China. Eur J Gastroenterol Hepatol 2017;29(5):509–515. doi:10.1097/MEG.0000000000000838, PMID:28350740.
[36] Polaris Observatory Collaborators. Global prevalence, cascade of care, and prophylaxis coverage of hepatitis B in 2022: a modelling study. Lancet Gastroenterol Hepatol 2023;8(10):879–907. doi:10.1016/S2468-1253(23)00197-8, PMID:37517414.
[37] Meng TT, Miao N, Zheng H, Wang FZ, Yin ZD, Shen LP, *et al*. Self-awareness rate and its influencing factors of their infection status among hepatitis B surface antigen-positive persons aged 15-69 years in China. Zhonghua Gan Zang Bing Za Zhi 2022;30(5):534–540. doi:10.3760/cma.j.cn501113-20220303-00097, PMID:35764546.
[38] Nayagam S, Chan P, Zhao K, Sicuri E, Wang X, Jia J, *et al*. Investment Case for a Comprehensive Package of Interventions Against Hepatitis B in China: Applied Modeling to Help National Strategy Planning. Clin Infect Dis 2021;72(5):743–752. doi:10.1093/cid/ciaa134, PMID:32255486.
[39] You H, Wang F, Li T, Xu X, Sun Y, Nan Y, *et al*. Guidelines for the Prevention and Treatment of Chronic Hepatitis B (version 2022). J Clin Transl Hepatol 2023;11(6):1425–1442. doi:10.14218/JCTH.2023.00320, PMID:37719965.
[40] Zhang S, Wang C, Liu B, Lu QB, Shang J, Zhou Y, *et al*. Cost-effectiveness of expanded antiviral treatment for chronic hepatitis B virus infection in China: an economic evaluation. Lancet Reg Health West Pac 2023;35:100738. doi:10.1016/j.lanwpc.2023.100738, PMID:37424693.
[41] Zhang M, Kong Y, Xu X, Sun Y, Jia J, You H. "Treat-all" Strategy for Patients with Chronic Hepatitis B Virus Infection in China: Are We There Yet? J Clin Transl Hepatol 2024;12(6):589–593. doi:10.14218/JCTH.2024.00091, PMID:38974957.
[42] Zhu SS, Dong Y, Zhang HF, Wang LM, Xu ZQ, Zhang M, *et al*. A randomized controlled study on factors influencing the curative effect of sequential combined interferon and lamivudine therapy in children with immune-tolerant phase chronic hepatitis B. Zhonghua Gan Zang Bing Za Zhi 2019;27(8):604–609. doi:10.3760/cma.j.issn.1007-3418.2019.08.004, PMID:31594077.
[43] Choi GH, Kim GA, Choi J, Han S, Lim YS. High risk of clinical events in untreated HBeAg-negative chronic hepatitis B patients with high viral load and no significant ALT elevation. Aliment Pharmacol Ther 2019;50(2):215–226. doi:10.1111/apt.15311, PMID:31135074.
[44] Zhou J, Wang F, Li L, Chen E. Expanding antiviral therapy indications for HBeAg-negative chronic hepatitis B patients with normal ALT and positive HBV DNA. Precis Clin Med 2022;5(4):pbac030. doi:10.1093/pcmedi/pbac030, PMID:36519139.
[45] Oliveri F, Surace L, Cavallone D, Colombatto P, Ricco G, Salvati N, *et al*. Long-term outcome of inactive and active, low viraemic HBeAg-negative-hepatitis B virus infection: Benign course towards HBsAg clearance. Liver Int 2017;37(11):1622–1631. doi:10.1111/liv.13416, PMID:28296013.
[46] WHO. Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection. Available from: https://iris.who.int/bitstream/handle/10665/376353/9789240090903-eng.pdf.
[47] Lim SG, Baumert TF, Boni C, Gane E, Levrero M, Lok AS, *et al*. The scientific basis of combination therapy for chronic hepatitis B functional cure. Nat Rev Gastroenterol Hepatol 2023;20(4):238–253. doi:10.1038/s41575-022-00724-5, PMID:36631717.

[48] Fanning GC, Zoulim F, Hou J, Bertoletti A. Therapeutic strategies for hepatitis B virus infection: towards a cure. Nat Rev Drug Discov 2019;18(11):827–844. doi:10.1038/s41573-019-0037-0, PMID:31455905.
[49] Ding Y, Yu X, Liang X, Ren H, Xu C, Wang W, *et al*. HBsAg loss and seroconversion in HBeAg-negative chronic hepatitis B subjects on NA therapy after AHB-137 treatment: preliminary data from an ongoing multicenter, randomized, open-label phase IIA study. Proceedings of the AASLD 2024; Nov 15-19, 2024; San Diego, CA, USA.
[50] Wang X, Chi X, Zhang Y, Gu Y, Xiao L, Qi Y, *et al*. Safety and efficacy of anti-pre-S1 domain monoclonal antibody (HH-003) treatment in patients with co-infection of chronic hepatitis B virus and hepatitis D virus. Proceedings of the EASL Congress 2023; 21-24 June 2023; Vienna, Austria.
[51] Jia J, Lin B, Hu P, Xie Q, Douglas M, Lv F. Efficacy and safety of elebsiran (BRII-835) and pegylated interferon alfa-2a (PEG-IFN-α) combination therapy vs pegifn in virologically suppressed participants with chronic hepatitis b virus (HBV) infection: preliminary results from an ongoing phase 2, randomized, open-label study (ensure). Proceedings of the AASLD 2024; Nov 15-19, 2024; San Diego, CA, USA.
[52] Yuen MF, Lim SG, Plesniak R, Tsuji K, Janssen HLA, Pojoga C, *et al*. Efficacy and Safety of Bepirovirsen in Chronic Hepatitis B Infection. N Engl J Med 2022;387(21):1957–1968. doi:10.1056/NEJMoa2210027, PMID:36346079.
[53] Hou J, Zhang W, Xie Q, Hua R, Tang H, Morano Amado LE, *et al*. Xalnesiran with or without an Immunomodulator in Chronic Hepatitis B. N Engl J Med 2024;391(22):2098–2109. doi:10.1056/NEJMoa2405485, PMID:39774313.
[54] Fung S, Choi HSJ, Gehring A, Janssen HLA. Getting to HBV cure: The promising paths forward. Hepatology 2022;76(1):233–250. doi:10.1002/hep.32314, PMID:34990029.