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GUIDELINES

APASL clinical practice guidelines on the management of chronic hepatitis B infection: a 2026 update

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Abstract

Globally, especially in the Asia Pacific region, chronic hepatitis B infection has led to an undesirable escalating morbidity and mortality with acute-on chronic liver failure, end-staged liver cirrhosis, and hepatocellular carcinoma. This has happened despite the past four decades of major scientific advances made in screening methods, vaccination strategies, highly effective low-cost anti-viral therapies, and surveillance strategies for early detection of hepatocellular carcinoma. To address this health threat, APASL has formed a Viral Elimination Taskforce to unite key opinion leaders from its member countries and regions. The ongoing shifts in hepatitis B epidemiology, socioeconomic changes, and advancements in technology are taken into consideration. With the conjoint efforts of all the members of the APASL Viral Elimination Taskforce, these clinical practice guidelines have been formulated aiming to facilitate healthcare professionals, policy-makers, and patients in making practical and cost-effective management decisions for chronic hepatitis B infection. Altogether, it provides recommendations in 13 major areas related to screening, vaccination, treatment, and HCC surveillance. The implementation of these clinical practice guidelines represents major APASL effort toward elimination of the disease burden due to chronic hepatitis B infection in Asia Pacific region.

Keywords Chronic hepatitis B · Prevention · Treatment · Hepatocellular carcinoma · Treat all · Guideline

Abbreviations

AI	Artificial intelligence
ALT	Alanine aminotransferase
AP	Asia Pacific
ALD	Alcohol-associated liver disease
CHB	Chronic hepatitis B
CPGs	Clinical Practice Guidelines
APASL	Asian Pacific Association for the Study of the Liver
AASLD	American Association for the Study of Liver Diseases
EASL	European Association for the Study of the Liver
DAA	Direct-acting antiviral
ETV	Entecavir
HBIG	Hepatitis B immunoglobulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B virus
HBVr	HBV reactivation
HCC	Hepatocellular carcinoma
HCP	Healthcare professionals
HIV	Human immunodeficiency virus
MAFLD	Metabolic dysfunction-associated fatty liver disease

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Extended author information available on the last page of the article

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MASLD	Metabolic dysfunction-associated steatotic liver disease
MASH	Metabolic dysfunction-associated steatohepatitis
MTCT	Mother-to-child transmission
NITs	Non-invasive tests
NUCs	Nucleos(t)ide analogs
Peg-IFN-α	Pegylated interferon alpha
qHBsAg	Quantitative HBsAg
TAF	Tenofovir alafenamide
TDF	Tenofovir disoproxil fumarate
VCTE	Vibration-controlled transient elastography
WHO	The World Health Organization

Introduction

Burden of diseases in Asia Pacific region

Hepatitis B virus (HBV) infection remains a major public health challenge in the Asia Pacific (AP) region, home to over two-thirds of the world's 260 million people with chronic HBV (CHB) infection [1]. Eight countries, i.e., China, India, Indonesia, Bangladesh, Vietnam, the Philippines, Pakistan, and Myanmar, collectively account for nearly 90% of HBV cases and related deaths in the AP region (Table 1). HBV prevalence among children under five in the AP region is lower than the global average, but the region's large pediatric population means an estimated 1.6–2.6 million being HBsAg-positive, representing 26–34% of the global burden in this age group [1]. The success of HBV control efforts in these countries will therefore largely determine the trajectory of disease burden reduction globally.

Despite the availability of universal vaccination, reliable diagnostics, and effective antiviral therapy, CHB diagnosis and treatment rates remain low in the AP region, often below 15% [2], severely hampering progress toward global elimination targets. Persistent barriers, such as insufficient linkage to care, unaffordable CHB treatment [3], constrained health budgets, low prioritization of HBV programs, stigma, fragmented health services, and weak integration of HBV care into primary health systems, continue to impede progress.

Evolving understanding of chronic hepatitis B natural history

Recent advances in HBV virology and immunopathology have reshaped our understanding of chronic hepatitis B (CHB). The traditionally defined "immune-tolerant" phase is now recognized as potentially progressive, with ongoing hepatic inflammation and hepatocellular carcinoma (HCC) risk even when alanine aminotransferase (ALT) levels are within so-called "references range" [4, 5]. Non-invasive fibrosis assessment and novel quantitative biomarkers, including quantitative HBsAg (qHBsAg), HBV RNA, and hepatitis B core-related antigen (HBcrAg), have transformed disease monitoring, risk stratification, and treatment decision-making [6].

In the AP region, most adults with CHB are now HBeAg-negative, while younger patients often present in the immune-tolerant phase with high viral loads but minimal biochemical abnormalities [7]. These evolving patterns underscore the need for earlier risk assessments and individualized treatment strategies.

Rationale for updated guidelines

Clinical practice guideline (CPG) development for CHB by regional professional associations, including Asian Pacific Association for the Study of the Liver (APASL) [10], American Association for the Study of Liver Diseases (AASLD) [8], and European Association for the Study of the Liver (EASL) [9], began more than two decades ago. These earlier CPGs by APASL were developed when many of today's diagnostic tools and treatment options were unavailable [10–12]. Eligibility criteria for antiviral therapy were based on studies conducted before the advance of novel biomarkers, such as qHBsAg, HBcrAg, HBV RNA, more precise HBV DNA quantification, and non-invasive fibrosis assessment technologies [10, 11, 13–17].

In recent years, the therapeutic landscape for CHB has evolved substantially. The reduced cost of established first-line antivirals with high-resistance barrier nucleos(t)ide analogs (NUCs) such as entecavir (ETV), tenofovir disoproxil fumarate (TDF), tenofovir alafenamide (TAF), and pegylated interferon-α has been proven to have long-term safety [18]. This together with emerging evidence supporting combination therapy [19, 20], early treatment initiation to reduce the risk of cirrhosis and liver cancer, and perhaps the development of new agents aiming for functional cure, are rapidly reshaping clinical management of CHB. Hence, simplified clinical algorithms are increasingly needed to improve diagnosis and treatment uptake amid persistently high HBV-related morbidity and mortality.

The rising prevalence of metabolic dysfunction-associated fatty liver disease (MAFLD, as defined and endorsed by APASL [21]) and alcohol-associated liver disease (ALD), further complicates CHB management. While the term metabolic dysfunction-associated steatotic liver disease (MASLD) has been proposed and adopted in some international consensus statements, MAFLD remains the recommended terminology within APASL guidelines and is widely used across the Asia Pacific region. In this guideline, MAFLD is therefore adopted in accordance with APASL recommendations, while MASLD is acknowledged when

Table 1 Overview of the HBV Burden, Globally, Asian-Pacific Region and Eight Countries of Main HBV Burden in Asian-Pacific Region

	Polaris 2024					GBD 2021					
	All ages			Age ≤ 5		All ages				Age 0–4	
	Population	HBV Prevalence	Annual Deaths	Population	HBV Prevalence	Population	HBV Prevalence	Deaths	DALYs	Population	HBV Prevalence
Global											
Number	8,161,972,573	244,945,114	1,133,629	781,374,019	4,688,244	7,891,353,301	291,232,478	649,184	21,465,451	658,171,689	10,172,957
Rate, per 100,000		3,001	14		600		3,691	8	272		1,546
Asian-Pacific Region											
Number	4,832,223,502	164,208,793	757,099	402,895,392	1,592,531	4,714,103,354	184,111,578	482,043	15,734,800	348,047,151	2,596,058
Rate, per 100,000		3,398	16		395		3,906	10	334		746
Percentage in Global	59%	67%	67%	52%	34%	60%	63%	74%	73%	53%	26%
Eight Countries of Main HBV Burden in Asian-Pacific Region											
Number	3,849,907,976	142,643,609	662,580	313,869,316	1,271,113	3,786,281,894	158,415,326	409,205	13,530,023	279,582,766	2,008,910
Rate, per 100,000		3,705	17		405		4,184	11	357		719
Percentage in AP region	80%	87%	88%	78%	80%	80%	86%	85%	86%	80%	77%
China Mainland											
Number	1,419,321,278	70,607,145	394,356	66,791,471	66,791	1,422,745,953	85,060,299	218,550	6,611,385	77,668,284	240,587
Rate, per 100,000		4,975	28		100		5,979	15	465		5,979
India											
Number	1,450,935,791	29,353,050	102,729	137,140,943	274,282	1,414,494,975	38,625,732	98,871	3,770,306	111,336,282	805,987
Rate, per 100,000		2,023	7		200		2,731	7	267		2,731
Indonesia											
Number	283,487,931	17,317,657	64,604	26,728,407	534,568	278,914,182	10,195,908	32,981	1,077,616	21,906,562	251,312
Rate, per 100,000		6,109	23		2,000		3,656	12	386		3,656
Bangladesh											
Number	173,562,364	7,250,456	30,632	19,876,222	79,505	164,636,116	4,037,533	13,910	444,181	14,364,063	44,655
Rate, per 100,000		4,177	18		400		2,452	8	270		2,452
Vietnam											
Number	100,987,687	6,234,315	30,296	8,515,171	85,152	100,267,854	6,607,677	14,494	465,477	8,141,786	92,046

Table 1 (continued)

	Polaris 2024					GBD 2021						
	All ages			Age ≤ 5		All ages				Age 0–4		
	Population	HBV Prevalence	Annual Deaths	Population	HBV Prevalence	Population	HBV Prevalence	Deaths	DALYs	Population	HBV Prevalence
Rate, per 100,000		6,173	30		1,000		6,590	14	464		6,590
Philippines											
Number	115,843,670	5,513,070	19,484	11,376,927	91,015	113,249,536	6,979,990	7,427	262,740	11,213,381	330,224
Rate, per 100,000		4,759	17		800		6,163	7	232		6,163
Pakistan											
Number	251,269,164	3,852,085	10,723	38,148,254	76,297	235,553,608	5,930,561	17,215	680,881	29,725,996	187,065
Rate, per 100,000		1,533	4		200		2,518	7	289		2,518
Myanmar											
Number	54,500,091	2,515,831	9,756	5,291,923	63,503	56,419,670	977,626	5,757	217,437	5,226,411	57,035
Rate, per 100,000		4,616	18		1,200		1,733	10	385		1,733

referring to international literature and broader consensus frameworks.

In addition, the rapid integration of artificial intelligence (AI) and big data analytics into clinical decision-making is anticipated to transform CHB management in future. Therefore, the updated APASL clinical practice guidelines are needed to provide evidence-based recommendations that reflect the evolving science, improve cost-effectiveness, and optimize care for CHB patients across the Asia Pacific region.

Methodology

The development of the current CPGs was initiated by the APASL Viral Elimination Taskforce established in 2022 as part of its mission to break the barriers to alleviate disease burden related to viral hepatitis in the AP region. The guideline development followed a rigorous, systematic, and evidence-based process to ensure validity, reliability, and clinical applicability of the recommendations. A panel comprising key opinion leaders from about 20 countries or special administrative regions across the AP region was convened to formulate the CPGs. The panel operated under the chairmanship of Drs. George Lau, Shiv Kumar Sarin, and Masao Omata. All members were selected based on their significant clinical experience and research contributions in the field of HBV infection and were required to comply with the APASL conflict of interest policy with full disclosure. Individuals whose research activities or publications were primarily sponsored by pharmaceutical companies were excluded to ensure unbiased recommendations and to uphold the best interests of patients and the public. The first face-to-face meeting was held during the 34th APASL Annual Meeting in Beijing, China, on 29th March 2025, where the workflow of the CPGs was discussed and agreed upon. The process began with the identification of key clinical questions related to the management of CHB, categorized according to clinical practice needs. Each panel member was assigned to address one or two questions, typically within their respective areas of expertise. A rigorous methodology was adopted, encompassing systematic literature reviews, evidence appraisal, consideration of patient values and preferences, cost-effectiveness, and feasibility. Comprehensive reviews of clinical trials, systematic reviews, meta-analyses, and other relevant studies were conducted by the panel members to inform the final recommendations. The quality of evidence and the strength of each recommendation were assessed using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (Table 2). On 20 September 2025, a hybrid meeting was conducted in Hong Kong SAR, China with 13 areas of recommendations presented by expert members and thoroughly

Table 2 GRADE system

Category	Grade / Symbol	Definition & Meaning	Typical Wording in Guidelines
Quality of Evidence	High (A)	We are very confident that the true effect lies close to the estimate of the effect. Further research is very unlikely to change our confidence in the estimate	"The evidence is of high quality…"
	Moderate (B)	We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate, but there is a possibility that it is substantially different. Further research may have an important impact	"The evidence is of moderate quality…"
	Low (C)	Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate. Further research is very likely to have an important impact	"The evidence is of low quality…"
	Very Low (D)	We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate. Any estimate is very uncertain	"The evidence is of very low quality…"
Strength of Recommendation	Strong (1)	The desirable effects of the intervention (benefits) clearly outweigh the undesirable effects (harms and burdens), or vice versa. Most informed patients would choose the recommended course of action	"We recommend…"
	Weak / Conditional (2)	The trade-offs are less certain: either the evidence is lower quality, or the benefits and harms are closely balanced. Different choices will be appropriate for different patients; shared decision-making is needed	"We suggest…" or "Conditionally recommend…"

discussed. Consensus on the final recommendations was achieved through structured discussions among the panel members with further multiple rounds of online and in-person meetings. The manuscript was subsequently drafted and received final approval from the APASL Steering Committee on 8 November 2025 at Washington DC, USA during the AASLD The Liver Meeting 2025.

Recommendations

The CHB CPG addresses key clinical questions in 13 areas, each accompanied by evidence-based recommendations (Table 3). The following sections present these recommendations along with their underlying clinical rationale.

I. Vaccination, screening, and testing

Vaccination

Hepatitis B vaccines, first developed as plasma-derived formulations in early 1980s and later as recombinant DNA vaccines, have dramatically reduced HBV transmission and liver disease burden worldwide. Universal immunization has led to marked declines in infection, chronic virus carriage, cirrhosis, and HCC [22]. A timely birth dose remains essential to prevent perinatal transmission [23]. For individuals who missed birth dose or childhood vaccination, catch-up and targeted vaccination remain essential particularly for high-risk populations, including immunocompromised individuals, patients at increased risk of severe hepatitis B, and those with a higher likelihood of occupational and non-occupational exposure [24].

In newborns, what is the optimal timing of the first dose of the hepatitis B vaccine to prevent perinatal transmission of HBV?

Timely administration of the hepatitis B birth dose is a highly effective intervention to prevent perinatal HBV transmission. Evidence demonstrates that vaccination within 24 h of birth provides substantial protection against infection, while delays significantly reduce effectiveness [25]. For infants born to HBsAg-positive mothers, early

Table 3 Summary of the CHB CPG

1	**Vaccination**
	In newborns, what is the optimal timing of the first dose of the hepatitis B vaccine to prevent perinatal transmission of HBV?
	In vaccinated individuals, is post-vaccination serologic testing necessary to confirm immunity?
	Should hepatitis B vaccination booster doses be given to individuals who have completed the primary vaccination series?
2	**Screening**
	Who should be screened for HBV infection?
	How to screen HBV infection?
3	**Assessment of liver fibrosis**
	How to assess liver fibrosis?
	How should liver fibrosis be assessed in resource-limited settings and what is the role of non-invasive tests?
	How to identify predominant driver of liver injury in patients with concurrent CHB and MAFLD non-invasively?
4	**Treatment goals**
	What are the goals of CHB therapy, and what are the surrogate endpoints for the treatment goals?
5	**Treatment Strategies**
	How effective are current therapies?
	What biomarkers should guide treatment?
	How should treatment decisions be guided by cost-effectiveness, long-term safety, and patient preferences?
	Should treatment be initiated in CHB patients at earlier fibrosis stages or specific groups that do not meet traditional treatment initiation criteria?
	Under what conditions can antiviral therapy be safely stopped, and how should relapse be monitored post-cessation?
6	**Special populations**
	How to manage HBV in pregnant women?
	How to manage HBV in population with metabolic comorbidities?
	How to manage HBV in patients with coinfections (HDV/HCV/HIV)?
	How to manage HBV in patients with alcohol-associated liver diseases?
	How to manage HBV in those with end-stage liver disease?
7	**Prevention of HBV reactivation related to the use of immunosuppressive therapy**
8	**HCC risk prediction**
	How do risk prediction models best guide HCC surveillance?
9	**HCC surveillance strategies**
	What surveillance strategies are needed for those with mPAGE-B $\geq$ 9?
	What surveillance strategies are needed for those with post-HBsAg clearance?
10	**Prevention of MTCT**
	In infants born to HBV-infected mothers, when should HBV testing be performed?
11	**Prevention of transmission in other populations**
	Should NUCs be used prophylactically to prevent HBV transmission in general populations and in HBV-infected healthcare professionals (HCP) performing exposure-prone procedures?
	In households or sexual contacts of individuals with chronic HBV infection, should family-based screening be implemented to identify undiagnosed infection and guide vaccination of susceptible persons?
12	**Service delivery models**
	How can stigma in occupational settings be addressed?
	What are optimal models of care to enhance access to screening and linkage to treatment?
13	**Functional cure**
	What is the role of functional cure as a therapeutic endpoint in the management of chronic hepatitis B?

vaccination within 12 h, in combination with hepatitis B immune globulin (HBIG), further reduces the risk of mother-to-child transmission to less than 5% [25]. Completion of the full hepatitis B vaccine series is recommended according to the standard schedule. For the conventional 3-dose regimen, vaccines should be administered at 0, 1, and 6 months, with the full series ideally completed within 6 months. When alternative accelerated schedules are used, doses should be given according to the approved product labeling. Completion of the full vaccine series ensures durable immunity and long-term protection.

Recommendations

1. The first dose of the hepatitis B vaccine should be administered to all clinically stable newborns within 24 h of birth. **(A1)**
2. For infants born to HBsAg-positive mothers, the vaccine should be administered within 12 h of birth, preferably together with hepatitis B immune globulin (HBIG). **(A1)**
3. Completion of the full vaccine series according to the standard schedule is necessary to ensure long-term protection. **(A1)**

In vaccinated individuals, is post-vaccination serologic testing necessary to confirm immunity?

Over 90% of healthy adults and over 95% of vaccinated infants achieve protective anti-HBs levels (≥ 10 mIU/mL) after the standard three-dose hepatitis B vaccination series [26]. Immune memory persists even as antibody levels decline, allowing rapid protection upon exposure [27]; thus, routine post-vaccination testing is clinically unnecessary and not cost-effective [28].

Testing is recommended only for high-risk groups. Early identification of non-responders through post-vaccination testing guides revaccination with higher or adjuvanted doses, optimizing individual and public health protection [29]. In immunocompromised populations, response rates are lower or wane faster [30]. Among individuals living with HIV, the response to vaccination is inversely correlated with CD4 count and HIV viral load control [31]. For healthcare workers, post-vaccination testing also serves as documentation for occupational safety [32]. Infants of HBsAg-positive mothers should be tested at 9–12 months as 5–10% may fail prophylaxis despite timely vaccination and HBIG [33]. Household contacts and sexual partners should complete vaccination and undergo post-vaccination serologic testing 1–2 months after the final dose to confirm protective immunity (anti-HBs ≥ 10 mIU/mL). These targeted approaches optimize individual and public health protection while avoiding unnecessary interventions in the general population.

For infants born to mothers who present in late pregnancy with high viral loads and have not had adequate maternal prophylaxis, administration of HBIG together with first dose of hepatitis B vaccine within 24 h of birth, followed by doses at 1 and 6 months, effectively prevents MTCT [34]. Maternal HBsAg may persist in infants for up to 7 months, potentially causing false-positive results, so testing should be delayed until after this period [35, 36]. Anti-HBs ≥ 10 mIU/mL indicates protective immunity, while < 10 mIU/mL requires a booster dose and retesting. Despite standard immunoprophylaxis, 5–10% of infants born to HBeAg-positive mothers with high HBV DNA (≥ 10^6 IU/mL) may still acquire HBV [37]. In such cases, early testing of HBsAg and HBV DNA 1–2 months after the second vaccine dose is recommended where feasible. Persistent dual positivity with rising HBV DNA confirms infection and warrants prompt referral for evaluation and management.

Recommendations

1. Routine post-vaccination serologic testing is *not* recommended for healthy individuals following hepatitis B or other standard vaccinations, given the high immunogenicity of current vaccines. **(A1)**
2. Testing is recommended for populations at risk of inadequate vaccine response or clinical consequences if unprotected:
    a. Immunocompromised patients: Test anti-HBs 1–2 months post-vaccination; repeat vaccination if < 10 mIU/mL. **(A1)**
    b. Healthcare workers: Test anti-HBs 1–2 months post-vaccination; repeat vaccination if < 10 mIU/mL, test HBsAg if persistently non-responsive. **(A1)**
    c. Infants of HBsAg-positive mothers: Combined testing of HBsAg and anti-HBs should be performed 1–2 months after completion of the full three-dose hepatitis B vaccine series (i.e., at 9-12 months of age) to assess the effectiveness of immunoprophylaxis. (**A1**)
    d. Household and sexual contacts of HBsAg-positive individuals: Test anti-HBs 1–2 months post-vaccination; repeat vaccination if < 10 mIU/mL. **(A2)**

Should hepatitis B vaccination booster doses be given to individuals who have completed the primary vaccination series?

Hepatitis B vaccination induces robust immune memory, providing long-lasting protection of at least 20 years in immunocompetent individuals, even as anti-HBs antibody levels decline [38]. Long-term follow-up studies show breakthrough infections and clinical disease are rare, supporting the recommendation against routine boosters in the general population. However, healthcare workers with ongoing exposures may be at increased risk, and immunocompromised individuals, such as dialysis patients or healthcare workers with ongoing exposure, may have weaker or waning immunity. In these groups, periodic anti-HBs monitoring can identify those who would benefit from a booster, ensuring targeted protection without unnecessary vaccination for most individuals. When anti-HBs concentration falls below 10 mIU/mL in high-risk or immunocompromised persons, booster dose may be considered.

Recommendations

1. Routine booster doses are *not* recommended for immunocompetent individuals who have completed the primary hepatitis B vaccination series and demonstrated an adequate immune response. **(A1).**
2. Booster doses should be considered for high-risk or immunocompromised individuals when anti-HBs concentration falls below 10 mIU/mL. In such individuals, post-vaccination serologic testing can guide the need for a booster dose. **(A1).**

Screening

Core principles of HBV screening

The World Health Organization (WHO) underscores the critical role of widespread screening, simplified diagnostic pathways, and vaccination in achieving global HBV elimination targets [2]. The HBV diagnosis rate remains low in the AP region. Undiagnosed infections perpetuate transmission and delay treatment, leading to advanced liver disease and death. Effective screening should combine universal and targeted strategies while ensuring equitable, patient-centered access to testing.

Who should be screened and tested for HBV infection?

Universal screening is highly cost-effective [39, 40], even at low prevalence (> 0.3%)[41]. In the AP region, where prevalence commonly exceeds 2%, universal one-time screening of adults is essential toward WHO's HBV elimination goals. Risk-based screening alone misses up to two-thirds of infections [42] because many individuals are asymptomatic or unaware of their exposure risk. In contrast, universal testing reduces undiagnosed cases, enables earlier intervention, and lowers morbidity, mortality, and transmission rates. Apart from clinical benefits, universal screening also helps to normalize testing, mitigate stigma, and ensure equitable access to care [43].

In addition to universal testing, targeted screening remains vital for specific high-risk groups. Individuals undergoing immunosuppressive or immunomodulatory therapy, such as tumor necrosis factor-alpha inhibitors, anti-CD20 agents, immune checkpoint inhibitors, tyrosine kinase inhibitors, CAR T cell therapy, or organ/bone marrow transplantation, are at elevated risk for HBV reactivation (HBVr) [44]. Screening before therapy is essential to identify those who should receive prophylactic antiviral treatment. Other priority populations include individuals with coinfections (e.g., HBV/HCV, HBV/HDV, HBV/HIV), existing other liver diseases, people who inject drugs, incarcerated individuals, and those with high-risk sexual, occupational and non-occupational exposures [45]. Early identification in these groups reduces the risk of transmission, reactivation, and severe liver outcomes. Universal maternal screening, ideally during the first trimester, is crucial to preventing mother-to-child transmission (MTCT). Timely initiation of antiviral therapy for mothers where indicated (referred to Sect. "Prevention of mother-to-child transmission") and appropriate newborn prophylaxis, hepatitis B vaccination with or without HBIG, are highly effective in blocking vertical transmission [46].

Screening strategies should be prioritized based on cost-effectiveness, integrating both universal and targeted approaches while optimizing factors, such as test cost, linkage to care, and timely implementation to maximize public health impact.

Recommendations

1. Universal HBV screening should be offered at population level at least once in adulthood in endemic regions (≥ 2% prevalence). **(B1)**
2. Risk-based screening should be performed in individuals at increased risk of HBV infection*, regardless of age or country of origins. **(B1)**

*Include: Persons with liver disease or with elevated ALT or levels of unknown origin; Individuals receiving immunosuppressive or immunomodulatory therapies, including cancer chemotherapy, immune checkpoint inhibitors, CAR T cell therapy, or organ/bone marrow transplantation; History or current Injection drug users (IDU); Inmates of correctional facilities; Recipients of unsafe injections; Men who have sex with men (MSM) or individuals with multiple sexual partners or a history of sexually transmitted infections; Family members, household contacts, and sexual partners of individuals with HBV; Patients on dialysis; Individuals with HBV-related extrahepatic manifestations; Persons co-infected with HCV or HIV; Pregnant women and infants born to HBV-infected mothers; Blood or organ donors; Healthcare workers; in low prevalence countries (<2%), recommend screening in people who were born in higher prevalence countries (>2%)

How to screen HBV infection?

HBsAg is the gold standard for diagnosing acute or chronic HBV infection. Standard immunoassays detect levels < 0.05 IU/mL, while ultrasensitive assays (< 0.005 IU/mL) may be needed for early infection, vaccine-escape mutants, or when HBV DNA testing is unavailable. In such cases, confirmatory HBV DNA or anti-HBc testing ensures diagnostic accuracy [47]. Anti-HBc antibodies indicate current or past infection and aid in staging and risk assessment [48]. IgM anti-HBc reflects acute or reactivated infection,

whereas IgG anti-HBc suggests chronic or resolved infection. Anti-HBs testing complements this by confirming immunity, vaccination status, or risk of relapse during immunosuppression. HBeAg, anti-HBe, ALT, and HBV DNA together help assess disease activity and treatment response.

HBV DNA quantification measures viral replication and guides treatment eligibility. Limited access remains a barrier; implementing reflex HBV DNA testing for HBsAg-positive samples can accelerate care and support elimination goals.

Recommendations

1. Initial HBV screening should include at least a screen panel comprising HBsAg and total anti-HBc. **(A1)**
2. Reflex testing, automatically initiating HBV DNA testing on HBsAg-positive specimens, may serve as an additional strategy to promote linkage-to-care and treatment. **(B2)**

Assessment of liver fibrosis

How to assess liver fibrosis?

Liver biopsy remains the gold standard for assessing inflammation, fibrosis, and concomitant conditions such as steatosis or iron overload in patients with CHB [49]. It accurately identifies disease phases and provides prognostic information, but its cost, invasiveness, risk, and sampling variability limit routine use. Importantly, advance fibrosis can occur even with normal ALT or low HBV DNA [50].

Non-invasive tests (NITs), including serum biomarkers and imaging techniques, are practical, safe, and reliable for detecting advanced fibrosis and cirrhosis, while allowing repeated monitoring of disease progression and treatment response. They are preferred as first-line assessment in most patients. Biopsy is reserved for selected situations, such as uncertain etiology, discordant NITs results, or concomitant conditions like MAFLD or HDV, where histology can clarify diagnosis, detect steatohepatitis, guide therapy, and refine prognosis.

Recommendations

1. Liver biopsy is the gold standard for diagnosing the extent and severity of inflammation and fibrosis in patients with CHB. **(A1)**
2. Non-invasive tests are preferred as first-line assessment for detection of severity of fibrosis in patients with CHB. **(B1)**
3. Liver biopsy should be individualized for patients with discordant non-invasive test results, or concomitant etiologies and/or metabolic comorbidities where the diagnosis may alter treatment decisions and prognosis. **(C2)**
4. Non-invasive tests using a combination of blood tests and imaging techniques are recommended over liver biopsy for determination of advance fibrosis and monitoring disease progression. **(B1)**

How should liver fibrosis be assessed in resource-limited settings and what is the role of non-invasive tests?

Simple blood-based scores like FIB-4 (age, AST, ALT, platelet count) and APRI (AST, platelet count) are inexpensive and widely validated. FIB-4 values > 1.3 indicate a higher probability of significant fibrosis (≥ F2), while > 2.67 strongly predicts advanced fibrosis or cirrhosis (F3–F4). For adults aged ≥ 65 years, age-adjusted thresholds (> 2.0 for significant fibrosis and > 3.25 for cirrhosis) improve accuracy. APRI cutoffs of 0.3–0.7 predict significant fibrosis (≥ F2) with 73% sensitivity and 65% specificity, while 0.8–1.2 predicts cirrhosis (F4) with 59% sensitivity and 74% specificity [51]. The WHO 2024 guidelines recommend initiating antiviral therapy in CHB patients with APRI > 0.5 or > 1 as indicative of significant fibrosis or cirrhosis respectively, regardless of HBV DNA or ALT levels [43].

Vibration-controlled transient elastography (VCTE) offers more accurate fibrosis assessment, with an optimal cutoff of 7.7 kPa for significant fibrosis (64% sensitivity, 83% specificity, HSROC 0.81) [52]. However, cost and infrastructure limit its availability, making serum-based tests the first-line approach, with VCTE as a supplementary tool when accessible.

Recommendations

1. Blood-based non-invasive tests (FIB-4 or APRI), should be used as the primary tools for liver fibrosis assessment in CHB patients in resource-limited settings. **(B1)**
2. Vibration-controlled transient elastography (VCTE) should be used as a complementary tool to improve diagnostic precision, particularly when treatment decisions remain uncertain after blood-based non-invasive assessment. **(B2).**

How to identify predominant driver of liver injury in patients with concurrent CHB and MAFLD non-invasively?

With population aging, more CHB patients present with cardiometabolic risk factors, such as obesity, diabetes, hypertension, and dyslipidemia [53]. Over one-third (35%) of CHB patients have hepatic steatosis [54], often linked to obesity, diabetes, hypertension, and lower HBV DNA levels [55]. Coexisting MAFLD increases the risks of cirrhosis, HCC [56], and liver-related mortality, in a dose-dependent manner

[57], while high BMI, and diabetes reduce the likelihood of cirrhosis regression during antiviral therapy [58].

In CHB patients, MAFLD contributes independently and synergistically to liver fibrosis, hepatocarcinogenesis, and mortality [59]. Even when viral replication is suppressed, metabolic liver injury persists, making metabolic risk assessment and intervention critical in comprehensive CHB management [60, 61].

In clinical practice, distinguishing HBV- from MAFLD-related liver injury can be challenging, as ALT elevations may reflect either condition or metabolic treatments. In phase 3 trials of metabolic dysfunction-associated steatohepatitis (MASH), mean baseline ALT typically ranges from 40 to 70 U/L and rarely exceeds 200 U/L [62–65], whereas CHB patients in the "indeterminate phase" exhibit higher fibrosis stages and greater HCC risk than those with low viraemic activity [66]. Antiviral therapy reduces the risk of HCC [67], decompensation, transplantation, and mortality in patients with moderate HBV DNA and ALT elevation, but benefits are less clear when ALT is elevated due to MAFLD or alcohol [68].

NITs including APRI, FIB-4, enhanced liver fibrosis, and VCTE remain useful [69–71] but may be influenced by inflammation, obesity, or necroinflammation [72, 73]. Although the underlying etiology may influence measurement thresholds, these tools cannot reliably distinguish HBV- from MAFLD-related injury. Emerging machine learning models and novel biomarkers show promise for differentiating disease activity, but further validation is required [74].

Recommendation

1. All CHB patients should be routinely evaluated for MAFLD, its components (obesity, diabetes, dyslipidemia, and hypertension), and the degree of hepatic fibrosis using non-invasive fibrosis assessment tools. **(B2)**
2. Patients with concurrent CHB and MAFLD should be monitored for liver disease progression and liver-related events, regardless of whether antiviral therapy has been started. **(B2)**
3. In patients with concurrent CHB and MAFLD, biomarkers of hepatic steatosis and fibrosis cannot be used to attribute the primary cause of liver injury to either HBV or MAFLD or both. **(C2)**

II. Treatment

Treatment goals

What are the goals of CHB therapy, and what are the surrogate endpoints for the treatment goals?

The overarching goal of CHB management is to reduce the global HBV disease burden through integrated strategies including vaccination, screening, anti-viral therapy, surveillance and prevention of transmission. At the individual level, therapy aims to prevent progression to cirrhosis, hepatic decompensation, and HCC, thereby improving long-term survival and quality of life (Fig. 1) [75].

CHB management follows a time-based, response-guided approach using validated markers, including HBV DNA, ALT, HBeAg status, and HBsAg level (qHBsAg), to guide treatment initiation, monitor response, and stratify risk. The choice of antiviral regimen, e.g., high-resistant barrier NUCs (long-term) or Pegylated interferon alpha (Peg-IFN-α) (finite), should be individualized according to the viral profile, fibrosis stage, comorbidities, adherence and patient preferences. Immune-modulatory therapy may be appropriate for selected patients depending on immune status and disease phase.

Sustained suppression of HBV DNA and ALT normalization, achievable with NUCs, is strongly associated with reduced risk of cirrhosis, HCC, and other liver-related complications [76]. Early ALT normalization within the first year of antiviral treatment further improves outcomes [77, 78]. In HBeAg-positive patients, anti-HBe seroconversion indicates effective viral control [79, 80], while in HBeAg-negative patients, maintaining low-level replication (HBV DNA < 2,000 IU/mL) and HBsAg < 1,000 IU/mL reduces HCC risk [81, 82].

The long-term goal is a functional cure defined as sustained HBsAg loss with undetectable HBV DNA after finite therapy [83]. Although uncommon with current therapies [84, 85], HBsAg loss remains the best surrogate marker of cure and is more likely in patients with low baseline HBsAg levels. A partial cure, defined as persistently low HBsAg (< 100 IU/mL) and normal ALT in non-cirrhotic, HBeAg-negative patients after finite therapy, is a practical surrogate associated with minimal HCC risk [86].

Recommendations Short-term goals

1. In both HBeAg-positive and HBeAg-negative patients receiving antiviral therapy, the primary short-term goal is to achieve sustained undetectable HBV DNA and normalization of ALT. **(A1)**

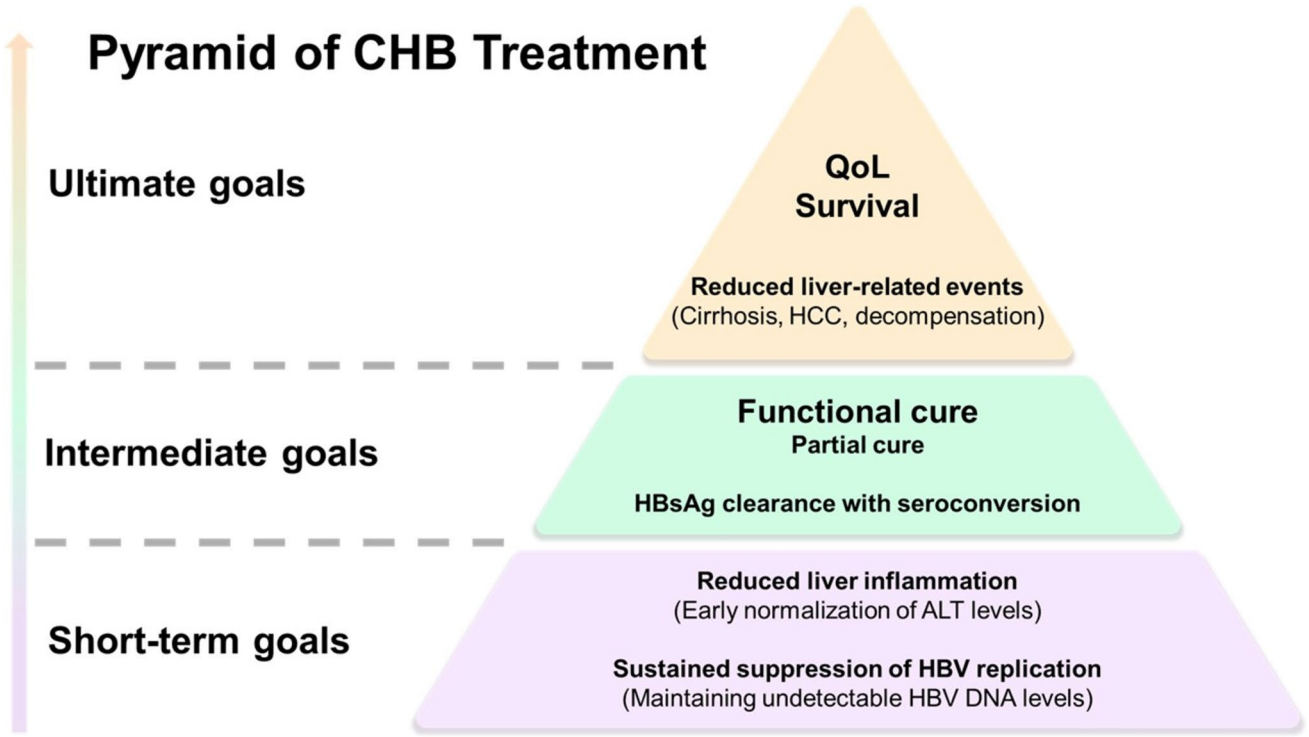


Fig. 1 Pyramid of CHB treatment

2. In HBeAg-positive patients, it is desirable to obtain HBeAg seroconversion as this reflects a favorable therapeutic response. **(A1)**
3. In HBeAg-negative patients, therapy should aim to maintain virologic suppression and persistently normal ALT. **(A1)**

Intermediate goals

1. Therapy should maintain virologic suppression and biochemical remission, which are validated surrogate markers of antiviral efficacy. **(A1)**
2. Where feasible, therapy may aim for functional cure, defined as sustained ($\geq$6 months) HBsAg loss with undetectable HBV DNA after completion of therapy. **(A1)**
3. When functional cure is unlikely, achieving a substantial decline in HBsAg levels (e.g., < 100 IU/mL) may be considered a partial cure and an appropriate therapeutic target. **(B1)**

Ultimate goals

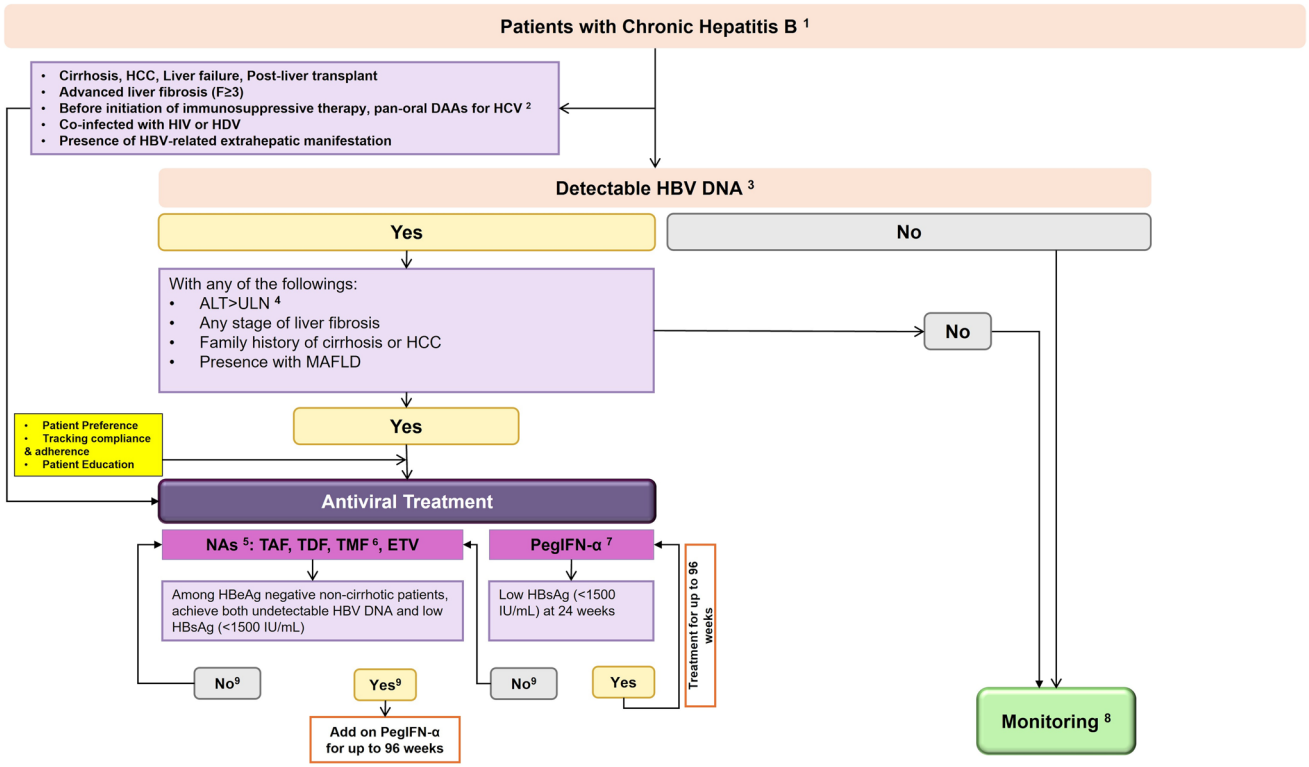
1. Public health efforts should aim to reduce the global HBV burden through vaccination, screening, timely antiviral treatment, and prevention of transmission. **(A1)**
2. Treatment should prevent liver-related complications and ultimately improve survival and quality of life. **(A1)**

Treatment strategies

The treatment strategies (Fig. 2) prioritize potent first-line NUCs (TAF, TDF, TMF, ETV) for their efficacy and safety, and protection against cirrhosis and HCC. Peg-IFN-α can serve as an alternative first-line option or as finite add-on therapy in NUC-suppressed patients with low HBsAg to pursue functional cure. Quantitative HBsAg and HBV DNA guide treatment initiation and decisions on finite Peg-IFN-α or NUCs discontinuation in non-cirrhotic patients. The approach incorporates cost-effectiveness, long-term safety, and patient preferences, supporting broader "treat-all" coverage, including early-stage and low-viremia groups. Treatment cessation is limited to non-cirrhotic patients achieving sustained HBsAg seroclearance or long-term suppression, with close monitoring, while cirrhotic patients should continue lifelong NUCs. Patient education and adherence support remain essential throughout care.

How effective are current therapies?

NUCs, including ETV, TDF and TAF, effectively suppress HBVDNA replication, resolve hepatic inflammation, and



1. HBsAg+ for 6 months
2. Refer to APASL reactivation management guideline 2022
3. Sensitive NAT assay (lower limit of detection <20 IU/L).
4. ULN: 40 IU/L
5. The selection of NAs should be individualized based on long-term safety and patient comorbidities. TAF and ETV are preferred in patients with or at risk of renal impairment or bone disease, while TDF or TAF is preferred in pregnant women, women of childbearing potential, and breastfeeding mothers.
6. TMF is only available in China
7. For those with contraindications to PegIFN-α, it is not suggested to initiate interferon-based therapy. Contraindications include decompensated liver disease (Child–Pugh B or C), severe psychiatric disorders, autoimmune diseases, uncontrolled thyroid disease, severe cardiac or renal impairment, uncontrolled seizures, pregnancy, or known hypersensitivity to interferon.
8. HBsAg-positive individuals not meeting treatment criteria require lifelong follow-up with regular ALT, HBV DNA, and fibrosis monitoring to detect disease reactivation or progression early.
9. NAs may be discontinued among those with sustained HBsAg seroclearance and Undetectable HBV DNA. To confirm sustained HBsAg seroclearance, HBsAg should be re-evaluated at least 6 months after initial loss to ensure durability of response.

Fig. 2 CHB treatment algorithm

prevent progression to cirrhosis, hepatic decompensation, and HCC (Table 4) [58, 67, 87–100]. Long-term NUCs therapy achieves undetectable HBV DNA in over 95% of HBeAg-negative patients, but HBsAg decline is slow [95], and annual HBsAg loss remains low [92], reflecting persistent antigen production from integrated HBV DNA. Tenofovir amibufenamide (TMF) shows antiviral efficacy and safety comparable to TAF [101]. In elderly patients with decompensated hepatitis B cirrhosis, TMF remains non-inferior to TAF with a similarly favorable safety profile [102]. However, its availability and use are currently limited in mainland China.

Peg-IFN-α is the only therapy capable of inducing HBsAg loss through both antiviral and immune-modulatory mechanisms [103]. Unlike NUCs, Peg-IFN-α is administered for a finite duration and consistently achieves higher HBsAg clearance, particularly in patients with genotypes A and B. A network meta-analysis of 47 randomized trials (13,826 patients) identified Peg-IFN-α-based regimens as the most effective approach for HBsAg loss across both HBeAg-positive and HBeAg-negative treatment-naïve populations [104]. Response to Peg-IFN-α strongly correlates with baseline HBsAg levels, with markedly higher functional cure rates seen in patients who initiate therapy with low pretreatment HBsAg [105].

While NUCs efficiently suppress viral replication and prevent disease progression [15], their effect on HBsAg loss is limited. Exploring strategies combining NUCs and PegIFN to enhance HBsAg loss rates, a meta-analysis of 49 studies assessed different antiviral treatment combinations [106]. The findings revealed that, compared to NUCs monotherapy, the initial combination of NUCs and IFN improved HBsAg seroclearance rates by 15 times (risk ratio 15.59, 95% CI 3.22–75.49), and IFN add-on NUCs also significantly improved HBsAg loss (RR: 4.52, 95% CI 1.95–10.47). These findings highlight the relevant role of interferon in achieving a functional cure for HBV. Combining long-term NUCs therapy with finite Peg-IFN-α-based regimens in selected patients offers the most promising

Table 4 Effectiveness of current CHB treatment strategies

Treatment Outcome	TDF	TAF	ETV	Peg-IFN	Combination (PegIFN add on NUCs)	Combination (NUC switch to PegIFN)
Short-term goals						
HBV DNA suppression(%)	1y: 67(e+) [8]; 93(e-) [7] 2 y [9]: 75(e+); 91(e-) 10y [15]: 98(e+); 100(e-)	1y: 64(e+)[8]; 94(e-)[7] 2y[9]: 73(e+); 90(e-) 8y[10]: 95(total)	1y: 67(e+)[1]; 90(e-)[2] 5y: 99(e+)[3]; 98(e-)[5]	1.5y: 14(e+)[12]; 19(e-)[13]	Compare with NUCs: Similar rate of HBV DNA suppression	
ALT normalization(%)	1y: 67(e+) [8]; 75(e-) [7] 2y [9]: 68(e+); 71(e-) 10y [15]: 78(e+); 83(e−)	1y: 72(e+) [9]; 83(e-) [7] 2y [9]: 75(e+); 81(e-) 8y [10]: 87(total)	1y: 68(e+) [9]; 78(e-) [2] 5y [10]: 95(total)	1.5y: 41(e+) [12]; 59(e-)[13]	Similar with NUCs	
Intermediate goals						
Necroinflammation resolution(%)	5y [11]: 87(total) 91(Ishak ≥ 3)		1y: 72(e+) [1]; 70(e−)[2]	1.5y: 49(e+) [12] (Reduced HAI) 55(e−) [13]		
Fibrosis regression(%)	5y [11]: 51(total) 74(Ishak ≥ 5)		1y: 39(e+) [1]; 36(e−)[2] 5y [6]: 80.4(total)	1.5y: 49(e+) [12] (Reduced HAI) 55(e−) [13]		
Long-term goals						
HBsAg loss (End of Follow-up)	annual: < 1% [19]	annual: < 1%	annual: < 1% [20]	3y: 11% (e+); 8–14% (e-) [21]	Compared to NUCs monotherapy, PegIFN add on improved HbsAg loss. RR:: 4.52, 95% CI 1.95–10.47 [22, 23]	Compared to NUCs monotherapy, NUCs switch-to IFN strategy improved HBsAg loss. RR: 12.15, 95% CI 3.99–37.01 [22]
HBV-related morbidity	TDF vs. treatment-naïve aHR [17]: HCC: 0.46; Decomp: 0.28	TAF vs. treatment-naive HR [16]: HCC: 0.27	ETV vs. treatment-naïve HR [14]: HCC: 0.55	Peg-IFN vs. ETV (e+)5y incidence [18]: Cirrhosis or HCC: 0% vs. 9.1%		
HBV-related mortality	LT or death: 0.06		LR death: 0.26; Death: 0.34			

e-: HBeAg-Negative; e+: HBeAg-positive

References: 1. Chang TT, et al. N Engl J Med. 2006;354:1001–10. 2. Lai CL, et al. N Engl J Med. 2006;354:1001–20. 3. Arends P, et al. Gut. 2015;64:1289–95. 4. Su TH, et al. Liver Int. 2016;36:1755–64. 5. Seto WK, et al. J Gastroenterol Hepatol. 2014;29:1028–34. 6. Chen S, et al. Hepatol Int. 2024;18:904–16. 7. Buti M, et al. Lancet Gastroenterol Hepatol. 2016;1:196–206. 8. Chan HL, et al. Lancet Gastroenterol Hepatol. 2016;1:185–95. 9. Agarwal K, et al. J Hepatol. 2018;68:672–81. 10. Buti M, et al. Aliment Pharmacol Ther. 2024;60:1573–86. 11. Marcellin P, et al. Lancet. 2013;381:468–75. 12. Lau GK, et al. N Engl J Med. 2005;352:2682–95. 13. Marcellin P, et al. N Engl J Med. 2004;351:1206–17. 14. Wong GL, et al. Hepatology. 2013;58:1537–47. 15. Marcellin P, et al. Liver Int. 2019;39:1868–75. 16. Lim YS, et al. Lancet Gastroenterol Hepatol. 2025;10:295–305. 17. Liu K, et al. Aliment Pharmacol Ther. 2019;50:1037–48. 18. Li SY, et al. J Viral Hepat. 2017;24:12–20. 19. Jian, W, et al. Virol J 22, 2025; 158. 20. Hsu YC, et al. J Infect Dis. 2021;224(11):1890–1899. 21. Jeng WJ, et al. Lancet 2023; 401: 1039–52. 22. Liu J, et al. Hepatol Int. 2020;14(6):958–972. 23. Matsumoto A, et al. J Gastroenterol. 2020; 55:977–89

approach to achieving functional cure, balancing efficacy, safety, and feasibility [107].

Patient education, regular monitoring, and adherence support are critical in CHB therapy. A formal, language-concordant HBV educational intervention significantly improved clinic follow-up, laboratory monitoring, and appropriate antiviral treatment [108]. Meta-analyses show that roughly 75% of patients adhere to NUCs, with limited understanding and forgetfulness among the main barriers [109]. Poor adherence is strongly linked to virologic breakthrough and drug resistance [110]. Health-education interventions more than double adherence for chronic communicable diseases [111].

Recommendations

1. TAF, TDF, TMF*, and ETV are the first-line NUCs treatment for CHB. **(A1)**
2. For those without contraindication# for immune therapy, Peg-IFN-α can be considered as a first-line treatment for CHB. **(A1)**
3. In NUCs-treated patients with sustained viral suppression (persistent undetectable HBV DNA) and low serum HBsAg levels (< 1500 IU/mL), the addition of Peg-IFN-α for a finite duration of up to 96 weeks may be considered in pursuit of functional cure, after evaluating patient willingness and clinical suitability. **(B1)**
4. Patients should receive structured education on the need of treatment, the importance of regular monitoring, and adherence to antiviral therapy to ensure optimal clinical outcomes. **(C1)**

* Available in China mainland.

Pegylated interferon alfa-2a is contraindicated in patients with [112]:

- Known hypersensitivity reactions, such as urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens–Johnson syndrome to alpha interferons, including PEGASYS, or any of its components.
- Autoimmune hepatitis
- Hepatic decompensation (Child–Pugh score greater than 6 [class B and C]) in cirrhotic patients before treatment
- Hepatic decompensation with Child–Pugh score greater than or equal to 6 in cirrhotic CHC patients coinfected with HIV before treatment
- Pegylated interferon alfa-2a is contraindicated in neonates and infants because it contains benzyl alcohol. Benzyl alcohol is associated with an increased incidence of neurologic and other complications which are sometimes fatal in neonates and infants.

What biomarkers should guide treatment?

Quantitative HBsAg reflects intrahepatic covalently closed circular DNA (cccDNA) activity [113] and integrated HBV DNA [114]. Declining HBsAg indicates reduced viral replication, and HBsAg loss sustained 24 weeks after treatment cessation represents functional cure. In HBeAg-negative CHB, HBV DNA < 2,000 IU/mL with HBsAg < 1,000 IU/mL suggests inactive infection, while HBsAg > 1,000 IU/mL predicts higher risk of reactivation and HCC. HBsAg < 10 IU/mL strongly predicts eventual HBsAg loss [82, 115–117].

Baseline HBV DNA is a key prognostic marker. Long-term cohort studies, including REVEAL-HBV [118], demonstrate a graded increase in cirrhosis and HCC risk with higher viral loads, independent of ALT and HBeAg status. This underscores the importance of integrating HBV DNA with HBsAg levels for treatment initiation.

HBsAg level can guide CHB therapy. Low end-of-treatment baseline levels predict sustained remission after NUCs discontinuation [119, 120], and on-treatment declines during Peg-IFN-α indicate higher response likelihood, whereas persistently high levels (> 20,000 IU/mL) suggest limited benefit from Peg-IFN-α treatment [121].

Emerging biomarkers, including HBV RNA, HBcrAg, and quantitative anti-HBc, offer additional insights into cccDNA activity, relapse risk, and HCC, but remain research tools until standardized [48, 122]. Quantitative HBsAg remains the most practical and validated biomarker for clinical decision-making.

Recommendations

1. HBV DNA with lower limit of quantification (< 10–20 IU/mL), by real-time quantitative polymerase chain reaction, should be tested before and during treatment. **(B1)**
2. Serum HBsAg levels should be tested at baseline and monitored during Peg-IFN-α and for discontinuation of long-term NUCs in non-cirrhotic patients. **(B1)**

How should treatment decisions be guided by cost-effectiveness, long-term safety, and patient preferences?

CHB management is shifting toward broader antiviral coverage. Economic models from China [123], Korea [124] and the US [125] show that treating lower-risk or "minimally active" patients are cost-effective in reducing HBV-related complications and mortality. A global review reports that early initiation of antiviral treatment is highly cost-effective in saving HBV-related mortality, reinforcing broader antiviral treatment strategies beyond Asia Pacific [126].

Collectively, these data support "treat-all" strategy that aligns with "WHO 2030" viral elimination goals.

High-resistance-barrier NUCs provide potent, persistent viral suppression with minimal resistance. The first-line NUCs are ETV, TDF, TAF, and TMF. However, long-term TDF use is associated with a higher fracture risk than ETV [127]. TAF offers similar efficacy to TDF with superior renal and bone safety, preferred in patients with renal disease, osteoporosis, or older age [128].

Shared decision-making improves adherence and addresses psychosocial burdens, such as stigma, fear of transmission, and treatment fatigue [129]. Achieving viral suppression can improve mental well-being. For instance, one study showed a 4.5-point increase in SF-36 mental component score after one year of ETV therapy [130]. While psychosocial improvement alone is not an indication for treatment initiation, these benefits underscore the broader value of antiviral therapy in enhancing patient-reported outcomes and quality of life.

Recommendations

1. Treatment should be prioritized for patients at highest risk of disease progression regardless of HBV DNA level or ALT. **(A1)**
2. Where resources allow, a "treat-all" approach should be adopted, initiating therapy for CHB patients beyond traditional high-risk criteria. **(B1)**
3. Therapy selection should consider long-term safety and presence of comorbidities. TAF or ETV are preferred over TDF in patients at risk for renal or bone disease. **(A1)**
4. Shared decision-making should be integrated into treatment planning, incorporating patient preferences, psychosocial factors, and willingness to commit to long-term therapy. **(B1)**

Should treatment be initiated in CHB patients at earlier fibrosis stages or specific groups that do not meet traditional treatment initiation criteria?

HBeAg-negative patients younger than 40 years old with low viral loads often appear clinically stable but may have ongoing necroinflammation or fibrosis, predisposing them to silent progression toward cirrhosis or HCC [131]. Evidence shows favorable antiviral responses in this group [132]; in a large Chinese cohort, Peg-IFN-α-based therapy achieved HBsAg loss in up to 35% of patients [133], supporting early intervention.

The conventional concept of the "inactive carrier" phase is increasingly questioned. Since 2015, this term has largely been replaced by "chronic HBV infection" to better reflect the persistent oncogenic potential despite low viral activity [12]. Patients with HBsAg ≥ 100 IU/mL, even with HBV DNA < 2,000 IU/mL, face higher HCC risk, up to 3.6-fold greater when HBsAg ≥ 1,000 IU/mL compared with < 100 IU/mL [86]. Moreover, patients with low-level viremia or HBsAg seroclearance remain at risk, with an annual HCC incidence of approximately 0.86%.[134].

As vaccination coverage expands and the CHB population ages, more patients fall into this "low-viraemia" category but retain residual oncogenic risk due to HBV integration and clonal hepatocyte expansion. With potent, safe, and affordable NUCs now widely available, expanding antiviral therapy to earlier fibrosis stages and low-viremia populations is both clinically justified and cost-effective [7]. This simplified "treat-all" approach addresses residual oncogenic risk, overcome the limitations of traditional phase-based classifications, and supports the broader goal of eliminating HBV-related morbidity and mortality by 2030 [135].

Recommendations

1. Antiviral therapy should be initiated for chronic HBV infection with detectable HBV DNA and ALT level over ULN (e.g. ≥ 40 IU/L), irrespective of fibrosis stage, or HBeAg status. This includes patients with minimal or no fibrosis (earlier fibrosis stages) and other specific subgroups at increased risk of disease progression, such as those with a family history of cirrhosis or hepatocellular carcinoma and those presenting with MAFLD. **(B1)**
2. Antiviral therapy should be prioritized for high-risk patients, irrespective of HBV DNA level. This includes patients with hepatocellular carcinoma, liver failure, advanced liver disease (cirrhosis or decompensation), HBV-related extrahepatic manifestations; patients underwent liver transplant, undergoing or planned for immunosuppressive or cytotoxic therapy, and co-infected with HIV/HCV/HDV. **(A1)**

Under what conditions can antiviral therapy be safely stopped, and how should relapse be monitored post-cessation?

Sustained HBsAg seroclearance (confirmed on two occasions ≥ 6 months apart), with or without anti-HBs seroconversion, is regarded as a criterion for discontinuing NUCs therapy in both HBeAg-positive and HBeAg-negative patients [136, 137]. The prognosis following both spontaneous [138] and NUCs-induced HBsAg seroclearance [139] are generally favorable.

Long-term evidence showed that structured NUCs discontinuation, even in patients with compensated cirrhosis, was associated with higher rates of HBsAg loss, lower HCC incidence, and improved overall survival compared with those maintained on continuous therapy [140]. But

discontinuation of NUCs carries a risk of virologic relapse, commonly defined as HBV DNA > 2,000 IU/mL, often followed by ALT flares, though rarely triggering severe exacerbations or death. Consolidation therapy reduces relapse risk, with ≥ 1 year after HBeAg loss in HBeAg-positive patients and ≥ 3 years after confirmed undetectable HBV DNA in HBeAg-negative patients [141].

Relapses typically occur within 6–24 weeks post-withdrawal [142], though late flares (> 1 year) can occur [143]. Given the dynamic patterns of virologic relapse and ALT flare, monitoring should include HBV DNA and ALT at least monthly for the first 6 months, quarterly during the first year, and biannual-to-annual thereafter. Patients with cirrhosis should continue lifelong NUCs therapy due to the risk of decompensation.

Emerging biomarkers, including HBV RNA and HBcrAg, show potential for relapse risk stratification prior to discontinuation of NUCs, but clinical application remains limited by availability, heterogeneous assays and lack of standardized cutoffs.

Recommendations

1. For both HBeAg-positive and HBeAg-negative non-cirrhotic patients, NUCs therapy can be discontinued upon achieving sustained HBsAg seroclearance* and undetectable HBV DNA regardless of anti-HBs seroconversion status. **(A1)**
2. For HBeAg-negative non-cirrhotic patients, upon achieving persistent undetectable HBV DNA for more than three years, NUCs therapy may be discontinued by experienced clinicians. Patients should be closely monitored with HBV DNA and ALT at least monthly for the first 6 months after discontinuation, and the monitoring interval may be extended thereafter based on clinical judgment. **(B2)**
3. For both HBeAg-positive and HBeAg-negative cirrhotic patients, discontinuation of NUCs therapy is *not* recommended. **(A2)**
4. HBsAg loss should be confirmed on two occasions ≥ 6 months apart to establish the durability of HBsAg loss. **(A1)**

* Sustained HBsAg seroclearance is defined as negative HBsAg for at least 6 months after treatment cessation.

In special populations

How to manage HBV in pregnant women?

All pregnant women should be screened for HBsAg early in pregnancy. Women who test positive should be assessed for antiviral therapy based on the same treatment indications as non-pregnant adults with chronic hepatitis B (HBV DNA level, ALT, HBeAg status, and fibrosis stage).

MTCT can occur in highly viremic mothers despite appropriate newborn active–passive vaccination, with risk increasing up to 30% as maternal HBV DNA exceeds 6–8 $\log_{10}$ IU/mL [144]. Reducing maternal viral load below 200,000 IU/mL with antiviral therapy effectively prevents perinatal transmission [145]. If HBV DNA is < 200,000 IU/mL and timely postpartum vaccination is ensured, antiviral therapy is not required [146].

HBeAg positivity is associated with high maternal HBV DNA levels, which significantly increase the risk of perinatal transmission. In pregnant CHB women, HBeAg status can be used as a surrogate marker of viral replication to guide the need for antiviral therapy.

Women identified as HBsAg-positive during pregnancy represent an important population for postpartum follow-up testing. Antenatal screening provides a critical opportunity to establish structured follow-up after delivery for women newly diagnosed with chronic HBV infection [147, 148]. Postpartum follow-up is essential to ensure long-term maternal health, prevent MTCT in future pregnancies, and guide ongoing clinical management. Postpartum assessment with HBsAg, HBV DNA, and ALT allows confirmation of infection status, evaluation of disease activity, and determination of the need for antiviral therapy [149]. Counseling and appropriate clinical management should be provided to reduce the risk of horizontal transmission to sexual partners and optimize outcomes in subsequent pregnancies.

Tenofovir (TDF or TAF) is preferred, with comparable efficacy in reducing the risk of HBV MTCT [150–152]. Initiation between 28–32 weeks of gestation is optimal. Recent trial showed that in pregnant women with high levels of viremia, TDF beginning at gestational week 16 combined with infant HBV vaccine is also effective to prevent MTCT where HBIG is not available [153]. Therapy may continue even after pregnancy if maternal indications exist; otherwise, it can be safely discontinued shortly after delivery or within 1–3 months postpartum with close monitoring. However, hepatitis flares have been reported in a substantial proportion of women following treatment cessation, most commonly within 24 weeks postpartum [154, 155], underscoring the need for enhanced postpartum monitoring. Currently, there are no safety concerns regarding tenofovir as HIV therapy or pre-exposure prophylaxis in breastfeeding women. Therefore, breastfeeding should not be discouraged if tenofovir (TDF, TAF) therapy is continued [156].

Recommendations

1. Screen all pregnant women for HBsAg early in pregnancy. **(A1)**

2. Pregnant women who test positive HBsAg should be assessed for antiviral therapy according to standard CHB indications. **(A1)**
3. In pregnant women with HBeAg-positive and/or HBV DNA ≥ 200,000 IU/mL, antiviral therapy with tenofovir (TDF or TAF) should be given during the third trimester of pregnancy for preventing mother-to-child transmission. **(A1)**
4. In women identified as HBsAg-positive during pregnancy, postpartum follow-up testing with HBsAg, HBV DNA, and ALT is recommended to confirm infection status, assess disease activity, and determine the need for antiviral therapy. Counseling and appropriate management should be provided to reduce the risk of transmission to sexual partners and in future pregnancies.**(B1)**
5. Breastfeeding is safe while the mother is on antiviral therapy with tenofovir (TDF or TAF). **(A1)**

How to manage HBV in patients with metabolic comorbidities?

The rising prevalence of fatty liver and metabolic comorbidities has added complexity to CHB management. The redefinition of MAFLD emphasizes both hepatic and systemic metabolic factors [157], with heterogeneous prognostic implications. Early studies linked MAFLD to accelerated fibrosis and increased HCC risk in CHB [158]. In contrast, while recent studies suggested simple hepatic steatosis may be protective, associated with lower liver-related mortality and higher HBsAg seroclearance [159–162], coexisting metabolic dysfunctions, including diabetes, obesity, and hypertension, drive dose-dependent increases in cirrhosis, HCC, and mortality, even during long-term NUCs therapy [163]. Diabetes is the strongest risk factor, particularly with poor glycemic control.

In children, MAFLD is increasingly common and primarily linked to metabolic risk factors rather than HBV [164–166]. HBV may increase necroinflammation but does not appear to accelerate fibrosis; higher HBsAg loss has been observed during antiviral therapy in children with MAFLD [167, 168]. Diagnostic criteria for metabolic syndrome, hepatic fibrosis (LSM), steatosis (CAP), and at-risk MAFLD (FAST) remain heterogeneous in pediatric populations [169].

Lifestyle intervention, encompassing dietary modification, physical activity, and behavioral change, remains the cornerstone of management in both adults and children with MAFLD. Low-carbohydrate or low-fat diets and combined diet–exercise programs improve liver and metabolic outcomes. Pharmacologic agents, such as metformin, incretin-based therapies (e.g., GLP-1 receptor agonists), and other emerging agents, may be adjunctive in children with prediabetes or type 2 diabetes though evidence for sustained ALT reduction is limited [170]. Early identification and management of metabolic comorbidities alongside antiviral therapy are essential to optimize long-term outcomes in CHB with MAFLD [171].

Recommendations

1. Optimal glycemic control should be offered in CHB patients with concurrent diabetes in collaboration with endocrinologists or primary care teams. **(A1)**
2. Lifestyle interventions are recommended for CHB patients with modifiable metabolic comorbidities. **(A1)**

How to manage HBV in patients with coinfections (HDV/HCV/HIV)?

In HIV coinfected patients In 2023, an estimated 39 million people were living with HIV [172], of whom 8.4% had HBV coinfection, rising to 9.8% in the Asia Pacific region [173]. Coinfected patients face increased risks of cirrhosis and HCC, supporting prompt initiation of antiretroviral therapy (ART) regardless of ALT, HBV DNA, or CD4 count, unless contraindicated.

ART regimens should include two anti-HBV agents, typically TAF or TDF plus lamivudine or emtricitabine. TAF is preferred in patients with renal or bone disease [174], while switching from TDF to TAF maintains viral suppression with reduced toxicity [175]. Lamivudine- or emtricitabine-only regimens should be avoided to prevent HBV resistance. When TDF/TAF are contraindicated, entecavir may be added to fully suppressive ART with close monitoring [176]. Peg-IFN-α is generally not recommended due to limited efficacy and tolerability.

Patients with low CD4 counts should be monitored for hepatic flares due to immune reconstitution inflammatory syndrome (IRIS), which may coincide with HBsAg loss [177]. Sustained HBV suppression through optimized ART adherence is crucial to prevent liver complications, including HCC.

Recommendations ART should be initiated promptly regardless of ALT levels, HBV DNA levels, or CD4 cell count, with ART regimens requiring two antiviral agents active against HBV. The NUCs backbone should include TDF or TAF plus lamivudine or emtricitabine. **(A1)**

In HDV co-infected patients HDV infects 12–60 million people globally, with 4.5–13% prevalence among HBsAg-positive individuals. Active infection is confirmed via HDV RNA; NITs including elastography, APRI, FIB-4 may assist, but liver biopsy is recommended if results are inconclusive or guide treatment [178].

For patients with HBV/HDV co-infection, Peg-IFN-α remains an established therapy, typically administered at Peg-IFN-α 180 µg weekly for up to 96 weeks, achieving 29% virological response at the end of 24-week post-treatment [179]. Week-96 phase III data show Bulevirtide (2–10 mg daily) provides consistent antiviral activity, with > 50% HDV RNA response, ALT normalization, and improving liver stiffness [180]. Responses increased with continued therapy, supporting long-term therapy due to frequent relapse after stopping. Despite its clinical efficacy, bulevirtide is currently associated with substantial cost and limited global availability, posing significant challenges for policy adoption and market access, particularly in low- and middle-income countries [181]. These considerations currently limit its widespread use outside selected settings. Combination BLV and Peg-IFN-α may enhance HDV RNA suppression and HBsAg decline, but evidence is still emerging and no finite stopping strategy exists.

There is no approved treatment for decompensated cirrhosis: Peg-IFN-α is contraindicated, and data for BLV in this population remain limited [182]. NUCs should be continued in all patients with active HBV replication or cirrhosis. Given the high relapse risk in HDV, close monitoring of HDV RNA, HBV DNA, ALT, synthetic function, and imaging is essential regardless of therapeutic strategy.

Recommendations

1. All patients with chronic HBV/HDV coinfection and compensated liver disease should be considered for anti-HDV treatment with Peg-IFN-α or bulevirtide. **(A1)**
2. Patients with decompensated cirrhosis should be evaluated for liver transplantation. **(A1)**

In HCV co-infected patients Patients with HBV/HCV coinfection have higher risks of liver-related death and HCC than monoinfected individuals [183]. Currently, direct-acting antiviral (DAA) therapy is recommended for all HBV/HCV-co-infected patients, with sustained virological response comparable to HCV monoinfection. However, HBV reactivation occurs in 5.9–24% during DAA therapy, and hepatitis flares in 1.9–9% [184, 185]. Prophylactic NUCs therapy reduces reactivation risk, especially in patients with cirrhosis [186, 187]. HBsAg-negative, anti-HBc-positive individuals are at low risk (< 2%[188]) but require ALT monitoring and NUCs initiation if clinically indicated.

Recommendations

1. Patients with HBV/HCV coinfection should receive anti-HCV treatment with DAAs. **(A1)**
2. For HBsAg-positive patients, prophylactic NUCs treatment is recommended before initiation of DAA treatment. **(A1)**
3. For HBsAg-negative but anti-HBc-positive patients, close monitoring of ALT, HBV DNA and HBsAg is required during DAA treatment. **(A1)**

How to manage HBV in patients with alcohol-associated liver diseases (ALD)?

CHB combined with excessive alcohol accelerates cirrhosis and HCC by increasing oxidative stress, liver injury, and reducing antiviral efficacy and adherence [189]. Complete abstinence is essential [190, 191], supported by psychosocial [192] and pharmacologic [193] interventions to maintain sobriety. Potent NUCs provide sustain viral suppression, whereas interferon is contraindicated. Long-term, often infinite NUCs therapy is recommended.

Regular monitoring of HBV DNA, liver and renal function, alcohol intake, and HCC surveillance is critical. Multidisciplinary care, including hepatology, addiction, nutrition, and psychosocial support, optimizes adherence, reinforces abstinence, and improves outcomes.

Recommendations

1. All patients with HBV and ALD should be strongly advised to abstain completely from alcohol. Pharmacological aids and structured psychosocial or addiction support should be offered to promote abstinence. **(A1)**
2. A multidisciplinary approach including hepatology, addiction medicine, nutrition, and mental health should be implemented, with structured patient education to reinforce abstinence, adherence to antiviral therapy, and recognition of decompensation. **(A1)**

How to manage HBV in those with end-stage liver disease?

Management of HBV-related end-stage liver disease (ESLD) focuses on antiviral therapy, complication control, and timely liver transplant evaluation.

Antiviral therapy with ETV, TAF, or TDF is safe and effective in decompensated cirrhosis, improving MELD and Child–Pugh scores [194], reducing HCC risk, and enabling hepatic recompensation (transplant-free survival > 80%[195]). TAF is preferred for renal and bone safety [196]. Lamivudine, adefovir, and pegylated interferon are not recommended [197, 198]. Therapy should continue indefinitely with renal dose adjustment.

Standard management of ascites, variceal bleeding, encephalopathy, and hepatorenal syndrome is essential, with HCC surveillance every six months. Patients with advanced disease, recurrent decompensation, or HBV-related HCC

should be evaluated for transplantation. Pre-transplant goals include HBV DNA suppression, nutrition optimization, and complication control. Post-transplant, antivirals should continue. HBIG plus NUCs should be used in high-risk patients, while monotherapy (TAF or ETV) may suffice in low-risk cases. HBcAb-positive donor livers can be used with prophylaxis in HBV-naive recipients.

Immunosuppressed and coinfected (HBV/HIV, HBV/HDV, HBV/HCV) patients require prophylactic or tailored antiviral therapy, with tenofovir-based regimens preferred in HBV/HIV.

Recommendations

1. Antiviral therapy should be initiated in all decompensated cirrhosis regardless of ALT or HBeAg status. **(A1)**
2. TAF, TDF, or ETV are first-line treatment, with preference for TAF over TDF due to better renal/bone safety. **(A1)**
3. Treatment must be continued infinitely in those with decompensation or prior HCC; discontinuation is *not* recommended. **(A1)**

Prevention of hepatitis B reactivation related to the use of immunosuppressive therapy

Recommendation

Please refer to APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy [44].

III. HCC surveillance

Risk prediction

How do risk prediction models best guide HCC surveillance?

Over the past two decades, multiple HCC risk models have been developed (Table 5). Age and cirrhosis (or surrogate markers) are the most consistent predictors, followed by sex. Early models, such as REACH-B, GAG-HCC, and CU-HCC, were derived from untreated cohorts and remain useful for identifying treatment-naïve patients who may benefit from antiviral therapy [199]. Among treated populations, PAGE-B and modified PAGE-B (mPAGE-B) are the most validated tools [200, 201]. These simple models, based on age, sex, and platelet count (± albumin), are practical for routine risk assessment. The mPAGE-B was adapted for Asian populations to improve accuracy [202].

HCC risk scores are particularly valuable for non-cirrhotic patients, refining surveillance beyond standard age thresholds (> 40 years in men, > 50 years in women). In a Hong Kong cohort of > 32,000 treated patients, PAGE-B and mPAGE-B effectively identified low-risk individuals who might safely forgo routine HCC surveillance [202]. The predictive accuracy of these scores may decline after 5 years of antiviral therapy as HCC risk decreases with sustained viral suppression [203–205]. Diabetes independently increases HCC risk [163], prompting newer models, such as CAMD and REAL-B, to incorporate metabolic factors for improved risk discrimination.

Recommendations

1. HCC risk scores which integrate age, fibrosis severity, and sex can identify at-risk patients on NUCs eligible for HCC surveillance. **(A1)**
2. Patients on NUCs with intermediate-to-high HCC risk (PAGE-B ≥ 10 and/or mPAGE-B ≥ 9) should receive HCC surveillance. **(B1)**
3. Interpretation of HCC risk scores should be approached with caution in patients with prolonged treatment duration (over 5 years) or those with diabetes. **(B2)**

Surveillance strategies

What surveillance strategies are needed for those with mPAGE-B ≥ 9?

Regular surveillance reduces HCC mortality by 37% [206], improving early detection (Relative Risk [RR] 1.86), curative treatment (RR 1.83), and survival (Hazard Ratio: 0.67) [207]. The mPAGE-B score effectively stratifies risk in Asian population, with ≥ 9 indicating high risk [202, 208].

Current guidelines recommend biannual ultrasound and AFP [209, 210], which are cost-effective [211] but have less than 50% sensitivity for early HCC [212], further reduced in cirrhosis or fatty liver [213].

Protein induced by vitamin K deficiency or antagonist II (PIVKA-II), a marker linked to tumor aggressiveness [214], enhances diagnostic accuracy when combined with AFP [215, 216], achieving > 90% sensitivity and detecting up to 43% more early HCC cases [217]. Thus, AFP + PIVKA-II + ultrasound is recommended for surveillance, especially in the Asia Pacific region.

Recommendations

1. AFP and ultrasound examinations are recommended every 6 months. **(A1)**
2. Combined testing with AFP, ultrasound, and PIVKA-II is recommended to improve early detection accuracy. **(B1)**

Table 5 Available HCC risk scores applicable to treatment-experienced patients with chronic hepatitis B based on large external validation studies and systematic review, and meta-analysis

Score (year of publication)	Parameters	Population for score development	Interpretation of HCC risk*
PAGED-B (2024)	Age, sex, platelets, HBV DNA (year 0), diabetes	Asian (South Korea) (0% cirrhosis, 100% HBeAg-positive)	Low: 0–6 High: 7–12
aMAP (2020)	Age, sex, platelets, albumin, bilirubin	Asian (China) (19% cirrhosis, 40% HBeAg-positive)	Low: 0–49.9 Intermediate: 50–59.9 High: 60–100
CAGE-B (2020)	Age (at year 5), cirrhosis (year 0), LSM (year 5)	Caucasian (Greece, Spain, Netherlands, Turkey) (27% cirrhosis; 18% HBeAg-positive)	Low: 0–5 Intermediate: 6–10 High: 11–16
SAGE-B (2020)	Age (at year 5), LSM (year 5)	Caucasian (Greece, Spain, Netherlands, Turkey) (27% cirrhosis; 18% HBeAg-positive)	Low: 0–5 Intermediate: 6–10 High: 11–15
REAL-B (2020)	Age, sex, cirrhosis, diabetes, platelets, AFP, alcohol use	Asia–Pacific (China, South Korea, Hong Kong, Taiwan, Japan, New Zealand) (20% cirrhosis, 37% HBeAg-positive)	Low: 0–3 Intermediate: 4–7 High: 8–13
AASL-HCC (2019)	Age, sex, cirrhosis, albumin	Asian (South Korea) (39% cirrhosis, 56% HBeAg-positive)	Low: 0–5 Intermediate: 6–19 High: 20–29
modified PAGE-B (2018)	Age, sex, platelets, albumin	Asian (South Korea) (20% cirrhosis, 34% HBeAg-positive)	Low: 0–8 Intermediate: 9–12 High: 13–21
CAMD (2018)	Age, sex, cirrhosis, diabetes	Asian (Taiwan) (26% cirrhosis)	Low: 0–7 Intermediate: 8–13 High: 14–23
HCC-RESCUE (2017)	Age, sex, cirrhosis	Asian (South Korea) (39% cirrhosis, 56% HBeAg-positive)	Low: 18–64 Intermediate: 65–84 High: ≥ 85
PAGE-B (2016)	Age, sex, platelets	Caucasian (Greece, Spain, Netherlands, Turkey) (21% cirrhosis; 16% HBeAg-positive)	Low: 0–9 Intermediate: 10–17 High: 18–25
modified REACH-B (2014)	Age, sex, HBeAg, ALT, LSM	Asian (South Korea) (18% cirrhosis, 52% HBeAg-positive)	Low: 0–9 High: 10–16

Scores were listed in reverse chronological order (newest to oldest) by publication date

*Risk stratification based on 3-year HCC risk for CAMD; and 5-year HCC risk for other scores

What surveillance strategies are needed for those post-HBsAg clearance?

Although functional cure significantly lowers HCC risk, residual risk persists due to cumulative liver injury, fibrosis, and metabolic or epigenetic factors [134, 218]. Patients with cirrhosis face an annual HCC incidence of 2–4%, justifying continued surveillance.

Recommendation Lifelong HCC surveillance with ultrasound and AFP is recommended for patients with advanced fibrosis and liver cirrhosis post-HBsAg clearance every 6 months. **(C1)**

IV. Prevention of transmission

Prevention of mother-to-child transmission

In infants born to HBV-infected mothers, when should HBV testing be performed?

Please refer to **recommendations for post-vaccination serologic testing**.

Prevention of transmission in other populations

Should NUCs be used prophylactically to prevent HBV transmission in general populations and in HBV-infected healthcare professionals (HCP) performing exposure-prone procedures?

While NUCs therapy also reduces the risk of HBV transmission, vaccination remains the primary and most effective strategy for preventing horizontal spread. In the general population, routine prophylactic NUCs therapy for transmission prevention is unnecessary as it offers minimal additional benefit over vaccination.

For HBV-infected HCPs performing exposure-prone procedures (EPPs), the risk of transmitting HBV to patients is low [219]. Evidence indicates that HCPs who are HBeAg-negative or have low HBV DNA levels present a reduced risk of transmission. Most expert and national guidelines, including those from the US CDC [220], recommend maintaining HBV DNA below 1,000 IU/mL for HCPs performing EPPs. Suppression of HBV DNA with NUCs therapy, ideally to undetectable levels, further minimizes this risk [221].

Recommendations

1. Routine prophylactic use of NUCs solely for preventing horizontal transmission is *not* recommended when hepatitis B vaccination is available. **(C2)**
2. Healthcare professionals (HCPs) with chronic HBV infection who perform exposure-prone procedures (EPPs) should receive NUCs therapy to maintain undetectable HBV DNA, thereby minimizing the already low risk of patient-to-patient transmission. **(A2)**

In households or sexual contacts of individuals with chronic HBV infection, should family-based screening be implemented to identify undiagnosed infection and guide vaccination of susceptible persons?

Household and sexual contacts of individuals with HBV are at increased risk of infection through close contact, sexual exposure, or perinatal transmission [222]. Family-based screening facilitates early detection of undiagnosed cases for monitoring or treatment and enables immediate vaccination of susceptible contacts, preventing further spread [43]. Observational and programmatic evidence consistently shows that contact-based screening increases case detection and vaccination uptake, thereby reducing household transmission, with moderate certainty of evidence supporting this approach.

Recommendations

1. Screening should be conducted for all household and sexual contacts of individuals with chronic HBV infection. **(B1)**
2. Screening should include HBsAg, anti-HBs, and anti-HBc to identify current infection, immunity, or susceptibility. **(B1)**

V. Open questions

Service delivery models

How can stigma in occupational settings be addressed?

Stigma against people living with HBV in occupational settings undermines workers' rights, contributes to discrimination, job loss, and psychological distress, and perpetuates public health inequities [223]. It is driven by misinformation about transmission [224], moral judgments linking HBV to "immoral" behaviors [225], fear of disease progression [226], and systemic or cultural legacies of discrimination. Workplace interventions are most effective when integrating clear policies, education, and legal safeguards. Confidentiality and employee support systems reduce fear and encourage disclosure in safe contexts. Education programs correct misconceptions, normalize discussion, and foster inclusive attitudes. Legal protections provide enforceable safeguards against discrimination and ensure fair treatment. Together, these measures create safe, inclusive work environments where employees are judged by performance rather than health status, promoting both individual well-being and organizational equity.

Management statements

1. Anti-discrimination policies explicitly covering HBV should be established and enforced, medical confidentiality ensured, and workplace practices aligned with national laws. Job restrictions should be evidence-based rather than stigma-driven.
2. Regular, evidence-based education should be provided to correct misconceptions about HBV and promote supportive workplace environments through awareness, peer support, and clear reporting mechanisms.
3. People living with hepatitis B should be given same status and rights as any other citizen of the world.

What are optimal models of care to enhance access to screening and linkage to treatment?

Achieving WHO 2030 HBV elimination targets requires accessible, safe, and efficient care models. Decentralized, primary care- and community-based approaches increase

testing uptake [227], reduce missed cases, and are cost-effective and scalable [228–230]. Point-of-care testing, reflex testing, mobile diagnostics, and simplified algorithms minimize delays, enable timely treatment initiation, and reduce loss to follow-up [231, 232]. Structured referral pathways ensure specialist oversight for complex cases [233]. Affordable antivirals and adherence strategies, including peer support and reminders, support long-term viral suppression. Integrating vaccination, MTCT prevention, blood safety, workforce planning, and community engagement promotes equity, reduces stigma, and sustains care, accelerating elimination without compromising outcomes.

Management statements

1. HBV testing, treatment, and monitoring can be decentralized to primary and community care providers, using point-of-care diagnostics and simplified algorithms, with clear referral pathways for complex cases.
2. Affordable access to tenofovir or entecavir should be ensured, adherence strengthened through patient-centered support, and HBV services embedded within national health frameworks to ensure equity and sustainability.

Functional cure

What is the role of functional cure as a therapeutic endpoint in the management of chronic hepatitis B?

Functional cure is now recognized as the primary therapeutic endpoint in CHB with sustained HBsAg loss as the hallmark, reflecting a durable restoration of host immune control over HBV replication [234, 235]. HBsAg loss is associated with regression of liver fibrosis [236] and a reduced risk of cirrhosis [237, 238], liver decompensation [139, 237], and liver transplantation [139]. Achieving HBsAg loss also contributes to reduce new infections [239] and improving patients' quality of life [240].

In the past few years, new investigational agents aiming to achieve functional cure have shown limited and often not sustained responses. Hence, the clinical significance of the reduction or loss of HBsAg related to these new investigational therapies might be different to those related to spontaneous or registered anti-HBV therapy, which is highly durable. In addition, there are also uncertainties in optimal dosing strategies, and potential confounding factors which need to be understood [84]. An understanding of the impact of these new therapies on the restoration of host immunity on viral replication is hence urgently required. Given these limitations, current evidence does not yet support broad clinical use of these novel agents outside well-controlled trials, emphasizing the need for cautious and evidence-based guideline recommendations.

For clinical trials, phase II trials should select endpoints based on the mechanism of the investigational drugs [241], whereas phase III trials should prioritize sustained HBsAg loss with undetectable HBV DNA at 24 weeks post-treatment [122] as the primary endpoint, supplemented by secondary virological, serological, and biochemical markers. Comprehensive safety monitoring, including immune-mediated flares and hepatic events, is essential, with follow-up tailored to the drug's mechanism to ensure an accurate assessment of benefit-risk profiles.

Finally, achieving functional cure in the Asia Pacific region remains challenging due to persistent gaps in prevention and diagnostics, variable access to treatments, financial constraints, limited public awareness, stigma, and fragmented health-system coordination. Multisectoral efforts are required to overcome these barriers and maximize the impact of functional cure strategies.

Management statements

1. Functional cure should be defined as sustained HBsAg loss (with or without anti-HBs seroconversion) accompanied by sustained undetectable HBV DNA at 24 weeks post-treatment cessation.
2. Functional cure should be considered a validated surrogate endpoint for improved clinical outcomes, and clinical trials should focus on immune-active HBeAg-positive and HBeAg-negative patients, with comprehensive safety monitoring tailored to each investigational agent.
3. Partial cure can be considered an intermediate therapeutic endpoint, defined as HBsAg < 100 IU/mL with undetectable HBV DNA.
4. Post-HBsAg clearance, close monitoring for virologic relapse should include HBV DNA and ALT every 3 months for the first year, then biannually and annually thereafter.
5. In the Asia Pacific region, achieving functional cure requires a multifaceted approach, including policies for prevention, early diagnosis, and affordable treatment, adequately trained healthcare providers, collaborative research funding, and patient and community education to reduce stigma and enhance engagement.

Discussion

Both AASLD [242] and EASL [243] updated CHB guidelines in 2025, reflecting converging principles but distinct operational approaches to whom, when, and how to treat, and when therapy may be stopped. Both recommend treatment

for all patients with cirrhosis and those with immune-active disease, but AASLD/IDSA applies stricter quantitative ALT and HBV DNA thresholds and explicitly incorporates shared decision-making for patients near treatment cut-offs or with uncertain disease activity. EASL adopts a broader, risk-based framework that integrates non-invasive fibrosis assessment and HCC risk factors, allowing treatment initiation even in selected patients with normal ALT. Treatment strategies are largely aligned, with both endorsing high-barrier NUCs as first-line therapy. But the guidelines differ sharply on when to stop. AASLD/IDSA generally advises continuing NUCs therapy until HBsAg loss, reserving deviations for shared decision-making, whereas EASL provides structured criteria for finite therapy in carefully selected non-cirrhotic, HBeAg-negative patients with the capacity for intensive post-cessation monitoring.

The current 2026 APASL guideline extends these discussions by offering context-specific recommendations tailored to Asia Pacific epidemiology and resource variability. APASL recommends treating non-cirrhotic patients with detectable HBV DNA, includes peg-IFN-α as first-line therapy in eligible patients, and supports peg-IFN-α add-on for NUC-treated, non-cirrhotic, HBeAg-negative individuals with undetectable HBV DNA and low HBsAg levels to increase the likelihood of functional cure. These criteria, supported by accumulating regional evidence, practical considerations and clinical experience, align with the growing international call [5] and national guidelines [244], for expanding treatment eligibility and leveraging immunomodulatory therapies to reduce long-term disease burden.

Looking ahead, CHB management is expected to shift toward increasingly personalized strategies driven by accessible viral and host biomarkers. Quantitative HBsAg, HBcrAg, and HBV RNA offer surrogates of intrahepatic cccDNA activity and may refine treatment initiation, on-treatment monitoring, and cessation decisions, provided they become affordable and widely available. Emerging immune-profiling and multi-omics approaches may further identify patients capable of achieving sustained off-treatment responses or benefiting from novel curative regimens.

Besides, effective management of CHB requires equitable access to screening, treatment and care. Decentralized care models that promote better coordination and integration of services across different levels of the healthcare systems is an essential pillar for substantially reducing the burden of HBV.

Finally, artificial intelligence and machine learning tools are poised to enhance CHB care by integrating clinical, imaging, and molecular data to improve fibrosis and HCC risk prediction [245, 246], guide treatment selection, and support safe treatment withdrawal [245–248]. Scalable AI-driven decision-support systems, particularly those using federated learning and explainable AI, may strengthen frontline care and support national hepatitis-elimination strategies [249, 250]. AI-driven models may also improve screening efficiency and case detection by identifying individuals at high likelihood of CHB using routinely collected clinical, laboratory, demographic, and health-system data. Together, these advances promise more precise, equitable, and data-driven CHB management, accelerating progress toward the "WHO 2030 plus" elimination targets.

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References

1. WHO, Hepatitis B. 2024; https://www.who.int/news-room/fact-sheets/detail/hepatitis-b
2. World Health Organization. Global hepatitis report 2024: action for access in low- and middle-income countries. Geneva, 2024.
3. Chen J, Jia J, Zhuang H, Zhang W, Yang JM, Tanwandee T, et al. Assessing pricing and affordability of HBV treatment in Asia-Pacific region: a barrier to elimination. Hepatol Int. 2025;19(2):349–357
4. Duan M, Xiao H, Shi M, Xie Y, Zhao P, Li S, et al. Significant liver histological change is common in HBeAg-positive chronic hepatitis B with normal ALT. BMC Infect Dis. 2024;24(1):723
5. Kennedy PT, Allweiss L, Bertoletti A, Cornberg M, Gehring AJ, Guidotti LG, et al. Scientific and medical evidence informing expansion of hepatitis B treatment guidelines. Lancet Gastroenterol Hepatol. 2025;10(10):941–951
6. Gill US, Appleby VJ, Lens S. 'What is new in hepatitis B'. Frontline Gastroenterology 2026;17:161–171
7. Chen J, Lau G. HBV "Viral Elimination" in the Asia-Pacific region: current status and challenges. Clin Liver Dis (Hoboken). 2024;23(1): e0132
8. Lok AS, Heathcote EJ, Hoofnagle JH. Management of hepatitis B: 2000--summary of a workshop. Gastroenterology. 2001;120(7):1828–1853
9. de Franchis R, Hadengue A, Lau G, Lavanchy D, Lok A, McIntyre N, et al. EASL International on Hepatitis B. 13-14 September, 2002 Geneva, Switzerland. Switzerland Consensus statement (long version). J Hepatol. 2003;39(Suppl 1):S3–S25
10. Liaw YF, Leung N, Kao JH, Piratvisuth T, Gane E, Han KH, et al. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2008 update. Hepatol Int. 2008;2(3):263–83
11. Liaw YF, Kao JH, Piratvisuth T, Chan HL, Chien RN, Liu CJ, et al. Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2012 update. Hepatol Int. 2012;6(3):531–61
12. Sarin S, Kumar M, Lau GK, Abbas Z, Chan HL, Chen CJ, et al. Asian-Pacific clinical practice guidelines on the management of hepatitis B: a 2015 update. Hepatol Int. 2016;10(1):1–98
13. Liaw YF, Leung N, Guan R, Lau GK, Merican I, Asian-Pacific Consensus Working Parties on Hepatitis B. Asian-Pacific consensus statement on the management of chronic Hepatitis B: an update. J Gastroenterol Hepatol. 2003;18(3):239–245
14. Liaw YF, Leung N, Guan R, Lau GK, Merican I, McCaughan G, et al. Gane E Asian-Pacific consensus statement on the management of chronic hepatitis B: a 2005 update. Liver Int. 2005;25(3):472–89
15. Liaw YF, Sung JJ, Chow WC, Farrell G, Lee CZ, Yuen H, et al. Lamivudine for patients with chronic hepatitis B and advanced liver disease. N Engl J Med. 2004;351(15):1521–31
16. Lau G, Carman W, Locarnini S, Okuda K, Lu ZM, Williams R. Lam S Treatment of chronic hepatitis B virus infection: an Asia-Pacific perspective. J Gastroenterol Hepatol. 1999;14(1):3–12
17. Chen GF, Wang C, Lau G. Treatment of chronic hepatitis B infection-2017. Liver Int. 2017;37(Suppl 1):59–66
18. Roade L, Riveiro-Barciela M, Esteban R, Buti M. Long-term efficacy and safety of nucleos(t)ides analogues in patients with chronic hepatitis B. Ther Adv Infect Dis. 2021;8: 2049936120985954
19. 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):238–53
20. Sandmann L. Toward functional cure of hepatitis B: Is combination therapy the key? J Hepatol. 2025;83(1):271–272
21. Eslam M, Fan JG, Yu ML, Wong VW, Cua IH, Liu CJ, et al. The Asian Pacific association for the study of the liver clinical practice guidelines for the diagnosis and management of metabolic dysfunction-associated fatty liver disease. Hepatol Int. 2025;19(2):261–301
22. Wong GL, Hui VW, Yip TC, Liang LY, Zhang X, Tse YK, et al. Universal HBV vaccination dramatically reduces the prevalence of HBV infection and incidence of hepatocellular carcinoma. Aliment Pharmacol Ther. 2022;56(5):869–77
23. Lau GK, Lai CL, Wu PC. The natural history of chronic hepatitis B infection. Hong Kong Med J. 1997;3(3):283–288
24. Jeng WJ, Papatheodoridis GV, Lok ASF. Hepatitis B. Lancet. 2023;401(10381):1039–1052
25. World Health Organization. Hepatitis B vaccines: WHO position paper - July 2017. Wkly Epidemiol Rec. 2017;92(27):369–392
26. FitzSimons D, Hendrickx G, Vorsters A, Van Damme P. Hepatitis B vaccination: a completed schedule enough to control HBV lifelong? Vaccine. 2013;31(4):584–590 (**Milan, Italy, 17-18 November 2011.**)
27. Di Lello FA, Martinez AP, Flichman DM. Insights into induction of the immune response by the hepatitis B vaccine. World J Gastroenterol. 2022;28(31):4249–4262
28. McMahon BJ, Dentinger CM, Bruden D, Zanis C, Peters H, Hurlburt D, et al. Antibody levels and protection after hepatitis B vaccine: results of a 22-year follow-up study and response to a booster dose. J Infect Dis. 2009;200(9):1390–6
29. Bello N, Hudu SA, Alshrari AS, Imam MU, Jimoh AO. Overview of Hepatitis B vaccine non-response and associated B cell amnesia: a scoping review. Pathogens. 2024;13(7):554
30. Chancharoenthana W, Traitanon O, Leelahavanichkul A, Ronco C. Optimizing hepatitis B vaccination in chronic kidney disease: a comprehensive scoping review of strategies across CKD stages, dialysis, and transplant populations. Ren Fail. 2025;47(1): 2541873
31. Catherine FX, Piroth L. Hepatitis B virus vaccination in HIV-infected people: a review. Hum Vaccin Immunother. 2017;13(6):1–10
32. Beltrami EM, Williams IT, Shapiro CN, Chamberland ME. Risk and management of blood-borne infections in health care workers. Clin Microbiol Rev. 2000;13(3):385–407
33. Schillie S, Murphy TV, Fenlon N, Ko S, Ward JW. Update: shortened interval for postvaccination serologic testing of infants born to Hepatitis B-infected mothers. MMWR Morb Mortal Wkly Rep. 2015;64(39):1118–1120
34. Hou J, Cui F, Ding Y, Dou X, Duan Z, Han G, et al. Management algorithm for interrupting mother-to-child transmission of hepatitis B Virus. Clin Gastroenterol Hepatol. 2019;17(10):1929–36. e1
35. Nelson NP, Jamieson DJ, Murphy TV. Prevention of perinatal Hepatitis B virus transmission. J Pediatr Infect Dis Soc. 2014;3(Suppl 1(Suppl 1)):S7–S12
36. Zhang L, Gui XE, Wang B, Fan JY, Cao Q, Mullane K, et al. Serological pogvvsitive markers of hepatitis B virus in femoral venous blood or umbilical cord blood should not be evidence of in-utero infection among neonates. BMC Infect Dis. 2016;16(1):408
37. Lu Y, Zhu FC, Liu JX, Zhai XJ, Chang ZJ, Yan L, et al. The maternal viral threshold for antiviral prophylaxis of perinatal hepatitis B virus transmission in settings with limited resources:

A large prospective cohort study in China. Vaccine. 2017;35(48 Pt B):6627–33
38. Poorolajal J, Mahmoodi M, Majdzadeh R, Nasseri-Moghaddam S, Haghdoost A, Fotouhi A. Long-term protection provided by hepatitis B vaccine and need for booster dose: a meta-analysis. Vaccine. 2010;28(3):623–631
39. Toy M, Hutton D, Harris AM, Nelson N, Salomon JA, So S. Cost-effectiveness of 1-time universal screening for chronic hepatitis B infection in adults in the United States. Clin Infect Dis. 2022;74(2):210–217
40. Wong NS, Chan DP, Wong GL, Lee SS. Cost-effectiveness of universal screen-and-treat strategies for reducing morbidity and mortality of chronic Hepatitis B in a high-endemicity city. J Viral Hepat. 2025;32(5): e70027
41. Eckman MH, Kaiser TE, Sherman KE. The cost-effectiveness of screening for chronic Hepatitis B infection in the United States. Clin Infect Dis. 2011;52(11):1294–1306
42. Conners EE, Panagiotakopoulos L, Hofmeister MG, Spradling PR, Hagan LM, Harris AM, et al. Screening and testing for Hepatitis B virus infection CDC recommendations - United States. MMWR Recomm Rep. 2023;72(1):1–25
43. World Health Organization. Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection. Geneva, 2024.
44. Lau G, Yu ML, Wong G, Thompson A, Ghazinian H, Hou JL, et al. APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy. Hepatol Int. 2021;15(5):1031–48
45. Kanda T, Lau GK, Wei L, Moriyama M, Yu ML, Chuang WL, et al. APASL HCV guidelines of virus-eradicated patients by DAA on how to monitor HCC occurrence and HBV reactivation. Hepatol Int. 2019;13(6):649–61
46. Pan CQ, Zhu L, Yu AS, Zhao Y, Zhu B, Dai E. Tenofovir alafenamide versus tenofovir disoproxil fumarate for preventing vertical transmission in chronic Hepatitis B mothers: A systematic review and meta-analysis. Clin Infect Dis. 2024;79(4):953–964
47. Cornberg M, Wong VW, Locarnini S, Brunetto M, Janssen HLA, Chan HL. The role of quantitative Hepatitis B surface antigen revisited. J Hepatol. 2017;66(2):398–411
48. Kramvis A, Chang KM, Dandri M, Farci P, Glebe D, Hu J, et al. A roadmap for serum biomarkers for hepatitis B virus: current status and future outlook. Nat Rev Gastroenterol Hepatol. 2022;19(11):727–45
49. Mani H, Kleiner DE. Liver biopsy findings in chronic Hepatitis B. Hepatology. 2009;49(5 Suppl):S61-71
50. Tapper EB, Lok ASF. Use of liver imaging and biopsy in clinical practice. N Engl J Med. 2017;377(23):2296–2297
51. Liguori A, Zoncape M, Casazza G, Easterbrook P, Tsochatzis EA. Staging liver fibrosis and cirrhosis using non-invasive tests in people with chronic hepatitis B to inform WHO 2024 guidelines: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2025;10(4):332–349
52. Kim MN, An J, Kim EH, Kim HY, Lee HA, Yu JH, et al. Vibration-controlled transient elastography for significant fibrosis in treatment-naive chronic hepatitis B patients: A systematic review and meta-analysis. Clin Mol Hepatol. 2024;30(Suppl):S106–S16
53. Wong GL, Wong VW, Yuen BW, Tse YK, Luk HW, Yip TC, et al. An aging population of chronic hepatitis B with increasing comorbidities: a territory-wide study from 2000 to 2017. Hepatology. 2020;71(2):444–55
54. Jiang D, Chen C, Liu X, Huang C, Yan D, Zhang X, et al. Concurrence and impact of hepatic steatosis on chronic hepatitis B patients: a systematic review and meta-analysis. Ann Transl Med. 2021;9(23):1718
55. Peleg N, Issachar A, Arbib OS, Cohen-Naftaly M, Braun M, Leshno M, et al. Liver steatosis is a strong predictor of mortality and cancer in chronic hepatitis B regardless of viral load. JHEP Rep. 2019;1(1):9–16
56. Wong GL, Wong VW, Choi PC, Chan AW, Chim AM, Yiu KK, et al. Metabolic syndrome increases the risk of liver cirrhosis in chronic hepatitis B. Gut. 2009;58(1):111–7
57. Hong S, Hao Y, Sun L, Li P, Yang J, Zhang F, et al. Prevalence and risk factors of significant fibrosis in chronic hepatitis B patients with concurrent metabolic dysfunction-associated steatotic liver disease. Ann Hepatol. 2024;30(2):101589
58. Marcellin P, Gane E, Buti M, Afdhal N, Sievert W, Jacobson IM, et al. Regression of cirrhosis during treatment with tenofovir disoproxil fumarate for chronic hepatitis B: a 5-year open-label follow-up study. Lancet. 2013;381(9865):468–75
59. Zhou R, Yang L, Zhang B, Gu Y, Kong T, Zhang W, et al. Clinical impact of hepatic steatosis on chronic hepatitis B patients in Asia: A systematic review and meta-analysis. J Viral Hepat. 2023;30(10):793–802
60. Han E, Lee BW, Kang ES, Cha BS, Ahn SH, Lee YH, et al. Corrigendum to "Mortality in metabolic dysfunction-associated steatotic liver disease: A nationwide population-based cohort study" [Metabolism, Volume 152, March 2024, 155789]. Metabolism. 2024;154:155819
61. Han E, Lee BW, Kang ES, Cha BS, Ahn SH, Lee YH, et al. Mortality in metabolic dysfunction-associated steatotic liver disease: A nationwide population-based cohort study. Metabolism. 2024;152:155789
62. Anstee QM, Neuschwander-Tetri BA, Wong VW, Abdelmalek MF, Rodriguez-Araujo G, Landgren H, et al. Cenicriviroc Lacked Efficacy to Treat Liver Fibrosis in Nonalcoholic Steatohepatitis: AURORA Phase III Randomized Study. Clin Gastroenterol Hepatol. 2024;22(1):124–34 e1
63. Harrison SA, Bedossa P, Guy CD, Schattenberg JM, Loomba R, Taub R, et al. A Phase 3, Randomized, Controlled Trial of Resmetirom in NASH with Liver Fibrosis. N Engl J Med. 2024;390(6):497–509
64. Harrison SA, Wong VW, Okanoue T, Bzowej N, Vuppalanchi R, Younes Z, et al. Selonsertib for patients with bridging fibrosis or compensated cirrhosis due to NASH: Results from randomized phase III STELLAR trials. J Hepatol. 2020;73(1):26–39
65. Sanyal AJ, Newsome PN, Kliers I, Østergaard LH, Long MT, Kjær MS, et al. Phase 3 Trial of Semaglutide in Metabolic Dysfunction-Associated Steatohepatitis. N Engl J Med. 2025;392(21):2089–99
66. Lai JC, Wong GL, Tse YK, Hui VW, Lai MS, Chan HL, et al. Histological severity, clinical outcomes and impact of antiviral treatment in indeterminate phase of chronic hepatitis B: A systematic review and meta-analysis. J Hepatol. 2025;82(6):992–1003
67. Lim YS, Yu ML, Choi J, Chen CY, Choi WM, Kang W, et al. Early antiviral treatment with tenofovir alafenamide to prevent serious clinical adverse events in adults with chronic hepatitis B and moderate or high viraemia (ATTENTION): interim results from a randomised controlled trial. Lancet Gastroenterol Hepatol. 2025;10(4):295–305
68. Huang DQ, Tran A, Yeh ML, Yasuda S, Tsai PC, Huang CF, et al. Antiviral therapy substantially reduces HCC risk in patients with chronic hepatitis B infection in the indeterminate phase. Hepatology. 2023;78(5):1558–68
69. Lin KW, Kumar R, Shen F, Chan HL, Wong GL, Kumar R, et al. The utility of non-invasive tests to assess advanced fibrosis in Asian subjects with chronic hepatitis B and concomitant hepatic steatosis. Liver Int. 2023;43(5):1008–14
70. Liu Y, Huang Z, Lan X, Jia M, Zheng X, Hu M, et al. Diagnostic efficacy of vibration-controlled transient elastography in patients with metabolic dysfunction-associated liver disease and chronic hepatitis B. Gastroenterol Res Pract. 2024;2024:6722810

71. Wong VW, Adams LA, de Ledinghen V, Wong GL, Sookoian S. Noninvasive biomarkers in NAFLD and NASH - current progress and future promise. Nat Rev Gastroenterol Hepatol. 2018;15(8):461–478
72. Kim WR, Berg T, Asselah T, Flisiak R, Fung S, Gordon SC, et al. Evaluation of APRI and FIB-4 scoring systems for non-invasive assessment of hepatic fibrosis in chronic hepatitis B patients. J Hepatol. 2016;64(4):773–80
73. Wong VW, Irles M, Wong GL, Shili S, Chan AW, Merrouche W, et al. Unified interpretation of liver stiffness measurement by M and XL probes in non-alcoholic fatty liver disease. Gut. 2019;68(11):2057–64
74. Rui F, Yeo YH, Xu L, Zheng Q, Xu X, Ni W, et al. Development of a machine learning-based model to predict hepatic inflammation in chronic hepatitis B patients with concurrent hepatic steatosis: a cohort study. EClinicalMedicine. 2024;68:102419
75. Su TH, Kao JH. Improving clinical outcomes of chronic hepatitis B virus infection. Expert Rev Gastroenterol Hepatol. 2015;9(2):141–154
76. Lok AS, McMahon BJ, Brown RS Jr, Wong JB, Ahmed AT, Farah W, et al. Antiviral therapy for chronic hepatitis B viral infection in adults: A systematic review and meta-analysis. Hepatology. 2016;63(1):284–306
77. Choi J, Kim GA, Han S, Lim YS. Earlier alanine aminotransferase normalization during antiviral treatment is independently associated with lower risk of hepatocellular carcinoma in chronic hepatitis B. Am J Gastroenterol. 2020;115(3):406–414
78. Wong GL, Chan HL, Tse YK, Yip TC, Lam KL, Lui GC, et al. Normal on-treatment ALT during antiviral treatment is associated with a lower risk of hepatic events in patients with chronic hepatitis B. J Hepatol. 2018;69(4):793–802
79. Lin SM, Yu ML, Lee CM, Chien RN, Sheen IS, Chu CM, et al. Interferon therapy in HBeAg positive chronic hepatitis reduces progression to cirrhosis and hepatocellular carcinoma. J Hepatol. 2007;46(1):45–52
80. Niederau C, Heintges T, Lange S, Goldmann G, Niederau CM, Mohr L, et al. Long-term follow-up of HBeAg-positive patients treated with interferon alfa for chronic hepatitis B. N Engl J Med. 1996;334(22):1422–7
81. Chen CJ, Yang HI, Su JU, Jen CL, You SL, Lu SN, et al. Risk of hepatocellular carcinoma across a biological gradient of serum hepatitis B virus DNA level. JAMA. 2006;295(1):65–73
82. Tseng TC, Liu CJ, Yang HC, Su TH, Wang CC, Chen CL, et al. High levels of hepatitis B surface antigen increase risk of hepatocellular carcinoma in patients with low HBV load. Gastroenterology. 2012;142(5):1140–9 e3 (**quiz e13-4**)
83. Jeng WJ, Lok ASF. What will it take to cure hepatitis B? Hepatol Commun. 2023;7(4): e0084
84. Chen J, Ji D, Jia J, Zhuang H, Zhang X, Wang FS, et al. Functional cure with new antiviral therapy for hepatitis B virus: a systematic review and meta-analysis. Hepatol Int. 2025;19(4):773–95
85. Yeo YH, Ho HJ, Yang HI, Tseng TC, Hosaka T, Trinh HN, et al. Factors associated with rates of HBsAg seroclearance in adults with chronic HBV infection: a systematic review and meta-analysis. Gastroenterology. 2019;156(3):635–46.e9
86. Tseng TC, Huang SC, Pan MH, Liu CJ, Chen CJ, Yang WT, et al. Hepatitis B surface antigen level identifies patients with inactive chronic hepatitis B from Asia with HCC risk below surveillance threshold. Gut. 2025;74(11):1896–904
87. Marcellin P, Lau GK, Bonino F, Farci P, Hadziyannis S, Jin R, et al. Peginterferon alfa-2a alone, lamivudine alone, and the two in combination in patients with HBeAg-negative chronic hepatitis B. N Engl J Med. 2004;351(12):1206–17
88. Lau GK, Piratvisuth T, Luo KX, Marcellin P, Thongsawat S, Cooksley G, et al. Peginterferon Alfa-2a, lamivudine, and the combination for HBeAg-positive chronic hepatitis B. N Engl J Med. 2005;352(26):2682–95
89. Chang TT, Gish RG, De Man R, Gadano A, Sollano J, Chao YC, et al. A comparison of entecavir and lamivudine for HBeAg-positive chronic hepatitis B. N Engl J Med. 2006;354(10):1001–10
90. Lai CL, Shouval D, Lok AS, Chang TT, Cheinquer H, Goodman Z, et al. Entecavir versus lamivudine for patients with HBeAg-negative chronic hepatitis B. N Engl J Med. 2006;354(10):1011–20
91. Wong GL, Chan HL, Mak CW, Lee SK, Ip ZM, Lam AT, et al. Entecavir treatment reduces hepatic events and deaths in chronic hepatitis B patients with liver cirrhosis. Hepatology. 2013;58(5):1537–47
92. Seto WK, Lam YF, Fung J, Wong DK, Huang FY, Hung IF, et al. Changes of HBsAg and HBV DNA levels in Chinese chronic hepatitis B patients after 5 years of entecavir treatment. J Gastroenterol Hepatol. 2014;29(5):1028–34
93. Arends P, Sonneveld MJ, Zoutendijk R, Carey I, Brown A, Fasano M, et al. Entecavir treatment does not eliminate the risk of hepatocellular carcinoma in chronic hepatitis B: limited role for risk scores in Caucasians. Gut. 2015;64(8):1289–95
94. Buti M, Gane E, Seto WK, Chan HL, Chuang WL, Stepanova T, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of patients with HBeAg-negative chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet Gastroenterol Hepatol. 2016;1(3):196–206
95. Chan HL, Fung S, Seto WK, Chuang WL, Chen CY, Kim HJ, et al. Tenofovir alafenamide versus tenofovir disoproxil fumarate for the treatment of HBeAg-positive chronic hepatitis B virus infection: a randomised, double-blind, phase 3, non-inferiority trial. Lancet Gastroenterol Hepatol. 2016;1(3):185–95
96. Su TH, Hu TH, Chen CY, Huang YH, Chuang WL, Lin CC, et al. Four-year entecavir therapy reduces hepatocellular carcinoma, cirrhotic events and mortality in chronic hepatitis B patients. Liver Int. 2016;36(12):1755–64
97. Agarwal K, Brunetto M, Seto WK, Lim YS, Fung S, Marcellin P, et al. 96 weeks treatment of tenofovir alafenamide vs. tenofovir disoproxil fumarate for hepatitis B virus infection. J Hepatol. 2018;68(4):672–81
98. Liu K, Choi J, Le A, Yip TC, Wong VW, Chan SL, et al. Tenofovir disoproxil fumarate reduces hepatocellular carcinoma, decompensation and death in chronic hepatitis B patients with cirrhosis. Aliment Pharmacol Ther. 2019;50(9):1037–48
99. Marcellin P, Wong DK, Sievert W, Buggisch P, Petersen J, Flisiak R, et al. Ten-year efficacy and safety of tenofovir disoproxil fumarate treatment for chronic hepatitis B virus infection. Liver Int. 2019;39(10):1868–75
100. Buti M, Lim YS, Chan HL, Agarwal K, Marcellin P, Brunetto MR, et al. Eight-year efficacy and safety of tenofovir alafenamide for treatment of chronic hepatitis B virus infection: Final results from two randomised phase 3 trials. Aliment Pharmacol Ther. 2024;60(11–12):1573–86
101. Peng WT, Jiang C, Yang FL, Zhou NQ, Chen KY, Liu JQ, et al. Tenofovir amibufenamide vs tenofovir alafenamide for treating chronic hepatitis B: A real-world study. World J Gastroenterol. 2023;29(44):5907–18
102. Qiu X, Yin Y, Zhang S, Liu W. Effectiveness and safety of tenofovir amibufenamide and tenofovir alafenamide in treating elderly patients diagnosed with decompensated hepatitis B cirrhosis: a retrospective cohort study. Front Pharmacol. 2025;16: 1545108
103. Zhao Q, Liu H, Tang L, Wang F, Tolufashe G, Chang J, et al. Mechanism of interferon alpha therapy for chronic hepatitis B and potential approaches to improve its therapeutic efficacy. Antiviral Res. 2024;221:105782

104. Sbarigia U, Vincken T, Wigfield P, Hashim M, Heeg B, Postma M. A comparative network meta-analysis of standard of care treatments in treatment-naive chronic hepatitis B patients. J Comp Eff Res. 2020;9(15):1051–1065
105. Song A, Lin X, Lu J, Ren S, Cao Z, Zheng S, et al. Pegylated Interferon Treatment for the Effective Clearance of Hepatitis B Surface Antigen in Inactive HBsAg Carriers: A Meta-Analysis. Front Immunol. 2021;12:779347
106. Liu J, Wang T, Zhang W, Cheng Y, He Q, Wang FS. Effect of combination treatment based on interferon and nucleos(t)ide analogues on functional cure of chronic Hepatitis B: a systematic review and meta-analysis. Hepatol Int. 2020;14(6):958–972
107. Huang D, Wu D, Wang P, Wang Y, Yuan W, Hu D, et al. End-of-treatment HBcrAg and HBsAb levels identify durable functional cure after Peg-IFN-based therapy in patients with CHB. J Hepatol. 2022;77(1):42–54
108. Wong RJ, Khalili M. A patient-centered Hepatitis B virus (HBV) educational intervention improves HBV care among underserved safety-net populations. J Clin Gastroenterol. 2020;54(7):642–647
109. Ford N, Scourse R, Lemoine M, Hutin Y, Bulterys M, Shubber Z, et al. Adherence to Nucleos(t)ide Analogue Therapies for Chronic Hepatitis B Infection: A Systematic Review and Meta-Analysis. Hepatol Commun. 2018;2(10):1160–7
110. Chotiyaputta W, Hongthanakorn C, Oberhelman K, Fontana RJ, Licari T, Lok AS. Adherence to nucleos(t)ide analogues for chronic Hepatitis B in clinical practice and correlation with virological breakthroughs. J Viral Hepat. 2012;19(3):205–212
111. Lutfian L, Wardika IJ, Mukminin MA, Zamroni AH, Rizanti AP, Chandra IN, et al. Effectiveness of health education in improving treatment adherence among patients with chronic communicable diseases: A systematic review and meta-analysis. Trop Med Int Health. 2025;30(7):598–612
112. U.S. Food and Drug Administration. Drugs@FDA: FDA-Approved Drugs. Dec, 11 ed; 2023.
113. Two research projects seek to improve immunization practices. *Bull Pan Am Health Organ* 1992; 26(1): 96-7
114. Imazeki F, Omata M, Yokosuka O, Okuda K. Integration of Hepatitis B virus DNA in hepatocellular carcinoma. Cancer. 1986;58(5):1055–1060
115. Brouwer WP, Chan HL, Brunetto MR, Martinot-Peignoux M, Arends P, Cornberg M, et al. Repeated measurements of hepatitis B Surface antigen identify carriers of inactive HBV During Long-term Follow-up. Clin Gastroenterol Hepatol. 2016;14(10):1481–9 e5
116. Liu J, Yang HI, Lee MH, Jen CL, Batrla-Utermann R, Lu SN, et al. Serum Levels of Hepatitis B Surface Antigen and DNA Can Predict Inactive Carriers With Low Risk of Disease Progression. Hepatology. 2016;64(2):381–9
117. Tseng TC, Liu CJ, Su TH, Wang CC, Chen CL, Chen PJ, et al. Serum hepatitis B surface antigen levels predict surface antigen loss in hepatitis B e antigen seroconverters. Gastroenterology. 2011;141(2):517–25
118. Iloeje UH, Yang HI, Su J, Jen CL, You SL, Chen CJ, et al. Predicting cirrhosis risk based on the level of circulating hepatitis B viral load. Gastroenterology. 2006;130(3):678–86
119. Hirode G, Choi HS, Chen CH, Su TH, Seto WK, Van Hees S, et al. Off-therapy response after nucleos(t)ide analogue withdrawal in patients with chronic hepatitis B: An International, Multicenter, Multiethnic Cohort (RETRACT-B Study). Gastroenterology. 2022;162(3):757–71.e4
120. van Bommel F, Berg T. Risks and benefits of discontinuation of nucleos(t)ide analogue treatment: a treatment concept for patients with HBeAg-negative chronic Hepatitis B. Hepatol Commun. 2021;5(10):1632–1648
121. Li F, Qu L, Liu Y, Wu X, Qi X, Wang J, et al. PegIFN alpha-2a reduces relapse in HBeAg-negative patients after nucleo(s)tide analogue cessation: A randomized-controlled trial. J Hepatol. 2025;82(2):211–21
122. Ghany MG, Buti M, Lampertico P, Lee HM, Faculty A-EH-HTEC. Guidance on treatment endpoints and study design for clinical trials aiming to achieve cure in chronic hepatitis B and D: report from the 2022 AASLD-EASL HBV-HDV Treatment Endpoints Conference. J Hepatol. 2023;79(5):1254–1269
123. 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
124. Lee H, Kim BK, Jang S, Ahn SH. Cost-effectiveness analysis of antiviral therapy for untreated minimally active chronic Hepatitis B to prevent liver disease progression. Clin Transl Gastroenterol. 2021;12(2): e00299
125. Razavi-Shearer D, Estes C, Gamkrelidze I, Razavi H. Cost-effectiveness of treating all Hepatitis B-positive individuals in the United States. J Viral Hepat. 2023;30(9):718–726
126. Lim YS, Kim WR, Dieterich D, Kao JH, Flaherty JF, Yee LJ, et al. Evidence for benefits of early treatment initiation for chronic hepatitis B. Viruses. 2023. https://doi.org/10.3390/v15040997
127. Yip TC, Lai JC, Yam TF, Tse YK, Hui VW, Lai MS, et al. Long-term use of tenofovir disoproxil fumarate increases fracture risk in elderly patients with chronic hepatitis B. J Hepatol. 2024;80(4):553–63
128. Chan HL, Buti M, Lim YS, Agarwal K, Marcellin P, Brunetto M, et al. Long-Term Treatment With Tenofovir Alafenamide for Chronic Hepatitis B Results in High Rates of Viral Suppression and Favorable Renal and Bone Safety. Am J Gastroenterol. 2024;119(3):486–96
129. Toumi M, Wallace J, Cohen C, Marshall C, Kitchen H, Macey J, et al. Experience and impact of stigma in people with chronic hepatitis B: a qualitative study in Asia, Europe, and the United States. BMC Public Health. 2024;24(1):611
130. Wu X, Hong J, Zhou J, Sun Y, Li L, Xie W, et al. Health-related quality of life improves after entecavir treatment in patients with compensated HBV cirrhosis. Hepatol Int. 2021;15(6):1318–27
131. Duan M, Chi X, Xiao H, Liu X, Zhuang H. High-normal alanine aminotransferase is an indicator for liver histopathology in HBeAg-negative chronic Hepatitis B. Hepatol Int. 2021;15(2):318–327
132. 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
133. Sheng Q, Wang N, Zhang C, Fan Y, Li Y, Han C, et al. HBeAg-negative patients with chronic hepatitis B virus infection and normal alanine aminotransferase: wait or treat? J Clin Transl Hepatol. 2022;10(5):972–8
134. Yang H, Bae SH, Nam H, Lee HL, Lee SW, Yoo SH, et al. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol. 2022;77(3):632–41
135. Chen J, You H, Lau G. Rethinking "inactive chronic Hepatitis B": should we treat patients with high HBsAg levels? Gut. 2025. https://doi.org/10.1136/gutjnl-2025-336373
136. Kao JH, Jeng WJ, Ning Q, Su TH, Tseng TC, Ueno Y, et al. APASL guidance on stopping nucleos(t)ide analogues in chronic hepatitis B patients. Hepatol Int. 2021;15(4):833–851
137. Wu D, Kao JH, Piratvisuth T, Wang X, Kennedy PT, Otsuka M, et al. Update on the treatment navigation for functional cure of chronic hepatitis B: Expert consensus 2.0. Clin Mol Hepatol. 2025;31(Suppl):S134–S64
138. Chen YC, Sheen IS, Chu CM, Liaw YF. Prognosis following spontaneous HBsAg seroclearance in chronic Hepatitis B

patients with or without concurrent infection. Gastroenterology. 2002;123(4):1084–1089
139. Anderson RT, Choi HS, Lenz O, Peters MG, Janssen HL, Mishra P, et al. Association between seroclearance of Hepatitis B surface antigen and long-term clinical outcomes of patients with chronic Hepatitis B virus infection: systematic review and meta-analysis. Clin Gastroenterol Hepatol. 2021;19(3):463–72
140. Jeng WJ, Chien RN, Chen YC, Lin CL, Wu CY, Liu YC, et al. Hepatocellular carcinoma reduced, HBsAg loss increased, and survival improved after finite therapy in hepatitis B patients with cirrhosis. Hepatology. 2024;79(3):690–703
141. Chi H, Hansen BE, Yim C, Arends P, Abu-Amara M, Van Der Eijk AA, et al. Reduced risk of relapse after long-term nucleos(t)ide analogue consolidation therapy for chronic hepatitis B. Aliment Pharmacol Ther. 2015;41(9):867–76
142. Höner zu Siederdissen C, Hui AJ, Sukeepaisarnjaroen W, Tangkijvanich P, Su WW, Nieto GE, et al. Contrasting timing of virological relapse after discontinuation of tenofovir or entecavir in Hepatitis B e Antigen-negative patients. J Infect Dis. 2018;218(9):1480–4
143. Dongelmans EJ, Hirode G, Hansen BE, Chen CH, Su TH, Seto WK, et al. Predictors of hepatic flares after nucleos(t)ide analogue cessation - Results of a global cohort study (RETRACT-B study). J Hepatol. 2025;82(3):446–55
144. Cheung KW, Seto MT, Lee CP. Mother-to-infant transmission of Hepatitis B virus infection: significance of maternal viral load and strategies for intervention. J Hepatol. 2013;59(2):400
145. 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):2324–34
146. Brown RS Jr, McMahon BJ, Lok AS, Wong JB, Ahmed AT, Mouchli MA, et al. Antiviral therapy in chronic hepatitis B viral infection during pregnancy: A systematic review and meta-analysis. Hepatology. 2016;63(1):319–33
147. Chang MS, Tuomala R, Rutherford AE, Mutinga ML, Andersson KL, Burman BE, et al. Postpartum care for mothers diagnosed with hepatitis B during pregnancy. Am J Obstet Gynecol. 2015;212(3):365.e1–7
148. Henderson JT, Webber EM, Bean SI. Screening for Hepatitis B infection in pregnant women: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. 2019;322(4):360–362
149. Pham TT, Maria N, Cheng V, Nguyen B, Toy M, Hutton D, et al. Gaps in prenatal Hepatitis B screening and management of HBsAg positive pregnant persons in the US, 2015–2020. Am J Prev Med. 2023;65(1):52–9
150. Funk AL, Lu Y, Yoshida K, Zhao T, Boucheron P, van Holten J, et al. Efficacy and safety of antiviral prophylaxis during pregnancy to prevent mother-to-child transmission of hepatitis B virus: a systematic review and meta-analysis. Lancet Infect Dis. 2021;21(1):70–84
151. Li B, Liu Z, Liu X, Liu D, Duan M, Gu Y, et al. Efficacy and safety of tenofovir disoproxil fumarate and tenofovir alafenamide fumarate in preventing HBV vertical transmission of high maternal viral load. Hepatol Int. 2021;15(5):1103–8
152. Zeng QL, Yu ZJ, Ji F, Li GM, Zhang GF, Xu JH, et al. Tenofovir alafenamide to prevent perinatal Hepatitis B transmission: a multicenter, prospective. Observational Study Clin Infect Dis. 2021;73(9):e3324–e32
153. Pan CQ, Dai E, Mo Z, Zhang H, Zheng TQ, Wang Y, et al. Tenofovir and Hepatitis B Virus Transmission During Pregnancy: A Randomized Clinical Trial. JAMA. 2025;333(5):390–9
154. Chang CY, Aziz N, Poongkunran M, Javaid A, Trinh HN, Lau DT, et al. Serum aminotransferase flares in pregnant and postpartum women with current or prior treatment for chronic Hepatitis B. J Clin Gastroenterol. 2018;52(3):255–61
155. Nguyen V, Tan PK, Greenup AJ, Glass A, Davison S, Samarasinghe D, et al. Anti-viral therapy for prevention of perinatal HBV transmission: extending therapy beyond birth does not protect against post-partum flare. Aliment Pharmacol Ther. 2014;39(10):1225–34
156. Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. AIDS. 2017;31(2):213–232
157. Eslam M, Newsome PN, Sarin SK, Anstee QM, Targher G, Romero-Gomez M, et al. A new definition for metabolic dysfunction-associated fatty liver disease: An international expert consensus statement. J Hepatol. 2020;73(1):202–9
158. Mao X, Cheung KS, Peng C, Mak LY, Cheng HM, Fung J, et al. Steatosis, HBV-related HCC, cirrhosis, and HBsAg seroclearance: A systematic review and meta-analysis. Hepatology. 2023;77(5):1735–45
159. Huang SC, Su TH, Tseng TC, Chen CL, Hsu SJ, Liao SH, et al. Distinct effects of hepatic steatosis and metabolic dysfunction on the risk of hepatocellular carcinoma in chronic hepatitis B. Hepatol Int. 2023;17(5):1139–49
160. Huang SC, Su TH, Tseng TC, Chen CL, Hsu SJ, Liu CH, et al. Metabolic dysfunction-associated steatotic liver disease facilitates Hepatitis B surface antigen seroclearance and seroconversion. Clin Gastroenterol Hepatol. 2024;22(3):581–90 e6
161. Huang SC, Su TH, Tseng TC, Hsu SJ, Hong CM, Lan TY, et al. All-cause and cause-specific mortality in patients with chronic hepatitis B and concurrent steatotic liver disease. J Hepatol. 2025;83(1):43–51
162. Huang SC, Su TH, Tseng TC, Liao SH, Hsu SJ, Hong CM, et al. Pre-existing and new-onset metabolic dysfunctions increase cirrhosis and its complication risks in chronic Hepatitis B. Am J Gastroenterol. 2025;120(2):401–9
163. Yip TC, Wong VW, Lai MS, Lai JC, Tse YK, Liang LY, et al. Diabetes mellitus impacts on the performance of hepatocellular carcinoma risk scores in chronic Hepatitis B patients. Clin Gastroenterol Hepatol. 2023;21(11):2864–75.e16
164. Schwimmer JB, Thai NQ, Noon SL, Ugalde-Nicalo P, Anderson SR, Chun LF, et al. Long-term mortality and extrahepatic outcomes in 1096 children with MASLD: A retrospective cohort study. Hepatology. 2025. https://doi.org/10.1097/hep.0000000000001357
165. Zeng J, Jin Q, Yang J, Yang RX, Zhang RN, Zhao J, et al. Prevalence and incidence of MAFLD and associated anthropometric parameters among prepubertal children of the Shanghai Birth Cohort. Hepatol Int. 2023;17(6):1416–28
166. Zou ZY, Zeng J, Ren TY, Huang LJ, Wang MY, Shi YW, et al. The burden and sexual dimorphism with nonalcoholic fatty liver disease in Asian children: A systematic review and meta-analysis. Liver Int. 2022;42(9):1969–80
167. Huang C, Lu Y, Wang Z, Jiang Q, Dong Y, Cao L, et al. Correlation between clinical indicators and liver pathology in children with chronic Hepatitis B. Biomedicines. 2024. https://doi.org/10.3390/biomedicines12122903
168. Wang L, Wang Y, Liu S, Zhai X, Zhou G, Lu F, et al. Nonalcoholic fatty liver disease is associated with lower hepatitis B viral load and antiviral response in pediatric population. J Gastroenterol. 2019;54(12):1096–105
169. Talebi Anaraki K, Heidari-Beni M, Arefian M, Kelishadi R. Managing pediatric metabolic syndrome: a systematic review of current approaches. BMC Pediatr. 2025;25(1):431
170. Katsagoni CN, Papachristou E, Sidossis A, Sidossis L. Effects of dietary and lifestyle interventions on liver, clinical and metabolic parameters in children and adolescents with Non-Alcoholic Fatty Liver Disease: a systematic review. Nutrients. 2020. https://doi.org/10.3390/nu12092864

171. Chang XJ, Shi YW, Wang J, Liu HB, Chen Y, Zhu XN, et al. Influence of weight management on the prognosis of steatohepatitis in chronic hepatitis B patients during antiviral treatment. Hepatobiliary Pancreat Dis Int. 2021;20(5):416–25
172. UNAIDS. Global HIV & AIDS statistics — Fact sheet. 2025. https://www.unaids.org/en/resources/fact-sheet (accessed 24 Oct 2025).
173. Leumi S, Bigna JJ, Amougou MA, Ngouo A, Nyaga UF, Noubiap JJ. Global burden of Hepatitis B infection in people living with Human Immunodeficiency Virus: A systematic review and meta-analysis. Clin Infect Dis. 2020;71(11):2799–2806
174. Yoshikawa S, Yoshio S, Yoshida Y, Tsutsui Y, Kawai H, Yamazoe T, et al. Impact of immune reconstitution-induced hepatic flare on Hepatitis B surface antigen loss in Hepatitis B virus/human immunodeficiency virus-1 coinfected patients. J Infect Dis. 2021;223(12):2080–9
175. Huang YS, Cheng CY, Sun HY, Cheng SH, Lu PL, Lee CH, et al. Week 96 Results of Switching from Tenofovir Disoproxil Fumarate-Based Antiretroviral Therapy to Coformulated Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide among HIV/Hepatitis B Virus-Coinfected Patients. Microbiol Spectr. 2023;11(3): e0512522
176. McMahon MA, Jilek BL, Brennan TP, Shen L, Zhou Y, Wind-Rotolo M, et al. The HBV drug entecavir - effects on HIV-1 replication and resistance. N Engl J Med. 2007;356(25):2614–21
177. Iannetta M, Crea AM, Di Lorenzo A, Campogiani L, Teti E, Malagnino V, et al. Hepatitis B-Related Hepatic Flare During Immune Reconstitution Syndrome After Antiretroviral Treatment Initiation in an HBV Surface Antigen-Positive Patient With HIV: Viroimmunological and Histological Characterization. Open Forum Infect Dis. 2022;9(9):ofac451
178. Buti M, Esteban R, Jardi R, Esteban JI, Guardia J. Serological diagnosis of acute Delta hepatitis. J Med Virol. 1986;18(1):81–85
179. Abdrakhman A, Ashimkhanova A, Almawi WY. Effectiveness of pegylated interferon monotherapy in the treatment of chronic Hepatitis D virus infection: A meta-analysis. Antiviral Res. 2021;185: 104995
180. Wedemeyer H, Aleman S, Brunetto M, Blank A, Andreone P, Bogomolov P, et al. Bulevirtide monotherapy in patients with chronic HDV: Efficacy and safety results through week 96 from a phase III randomized trial. J Hepatol. 2024;81(4):621–9
181. Foundation; HB. Drug Profile: Three Hepatitis Delta Therapies That We Hope to See Widely Available Soon. 2023. https://www.hepb.org/blog/drug-profile-three-hepatitis-delta-therapies-hope-see-widely-available-soon/ (accessed 15 Jan 2026).
182. Martini S, Tandoi F, Romagnoli R, Rizzetto M. Liver transplantation in Hepatitis B/Hepatitis D (Delta) virus coinfected recipients. Transplantation. 2022;106(10):1935–1939
183. Amin J, Law MG, Bartlett M, Kaldor JM, Dore GJ. Causes of death after diagnosis of Hepatitis B or Hepatitis C infection: A large community-based linkage study. Lancet. 2006;368(9539):938–945
184. Chen G, Wang C, Chen J, Ji D, Wang Y, Wu V, et al. Hepatitis B reactivation in hepatitis B and C coinfected patients treated with antiviral agents: A systematic review and meta-analysis. Hepatology. 2017;66(1):13–26
185. Mücke MM, Backus LI, Muecke VT, Coppola N, Preda CM, Yeh ML, et al. Hepatitis B virus reactivation during direct-acting antiviral therapy for hepatitis C: a systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2018;3(3):172–80
186. Cheng PN, Liu CJ, Chen CY, Tseng KC, Lo CC, Peng CY, et al. Entecavir Prevents HBV Reactivation During Direct Acting Antivirals for HCV/HBV Dual Infection: A Randomized Trial. Clin Gastroenterol Hepatol. 2022;20(12):2800–8
187. Yeh ML, Huang CF, Huang CI, Holmes JA, Hsieh MH, Tsai YS, et al. Hepatitis B-related outcomes following direct-acting antiviral therapy in Taiwanese patients with chronic HBV/HCV co-infection. J Hepatol. 2020;73(1):62–71
188. Oh JH, Park DA, Ko MJ, Yoo JJ, Yim SY, Ahn JH, et al. Direct-Acting Antivirals and the Risk of Hepatitis B Reactivation in Hepatitis B and C Co-Infected Patients: A Systematic Review and Meta-Analysis. J Pers Med. 2022. https://doi.org/10.3390/jpm12121957
189. Devarbhavi H, Asrani SK, Arab JP, Nartey YA, Pose E, Kamath PS. Global burden of liver disease: 2023 update. J Hepatol. 2023;79(2):516–537
190. Gratacós-Ginès J, Bruguera P, Pérez-Guasch M, López-Lazcano A, Borràs R, Hernández-Évole H, et al. Medications for alcohol use disorder promote abstinence in alcohol-associated cirrhosis: Results from a systematic review and meta-analysis. Hepatology. 2024;79(2):368–79
191. Oldroyd C, Greenham O, Martin G, Allison M, Notley C. Systematic review: interventions for alcohol use disorder in patients with cirrhosis or alcohol-associated hepatitis. Aliment Pharmacol Ther. 2023;58(8):763–773
192. Tyson LD, Cheng A, Kelleher C, Strathie K, Lovendoski J, Habtemariam Z, et al. Acamprosate may be safer than baclofen for the treatment of alcohol use disorder in patients with cirrhosis: a first description of use in real-world clinical practice. Eur J Gastroenterol Hepatol. 2022;34(5):567–75
193. Singal AK, Mathurin P. Diagnosis and treatment of alcohol-associated liver disease: a review. JAMA. 2021;326(2):165–176
194. Jang JW, Choi JY, Kim YS, Woo HY, Choi SK, Lee CH, et al. Long-term effect of antiviral therapy on disease course after decompensation in patients with hepatitis B virus-related cirrhosis. Hepatology. 2015;61(6):1809–20
195. Singal AK, Salameh H, Kuo YF, Fontana RJ. Meta-analysis: the impact of oral anti-viral agents on the incidence of hepatocellular carcinoma in chronic hepatitis B. Aliment Pharmacol Ther. 2013;38(2):98–106
196. Shim JH, Lee HC, Kim KM, Lim YS, Chung YH, Lee YS, et al. Efficacy of entecavir in treatment-naive patients with hepatitis B virus-related decompensated cirrhosis. J Hepatol. 2010;52(2):176–82
197. Chan HL, Chen YC, Gane EJ, Sarin SK, Suh DJ, Piratvisuth T, et al. Randomized clinical trial: efficacy and safety of telbivudine and lamivudine in treatment-naive patients with HBV-related decompensated cirrhosis. J Viral Hepat. 2012;19(10):732–43
198. Liaw YF, Raptopoulou-Gigi M, Cheinquer H, Sarin SK, Tanwandee T, Leung N, et al. Efficacy and safety of entecavir versus adefovir in chronic hepatitis B patients with hepatic decompensation: a randomized, open-label study. Hepatology. 2011;54(1):91–100
199. Huang L, Feng L, Lu Y, Hu B, Liang H, Ren A, et al. Evaluating the predictive value of clinical models for HBV-related hepatocellular carcinoma: A meta-analysis. Front Med (Lausanne). 2025;12:1529201
200. Wu S, Zhou J, Wu X, Sun Y, Wang B, Kong Y, et al. Comparative Performance of 14 HCC Prediction Models in CHB: A Dynamic Validation at Serial On-Treatment Timepoints. Am J Gastroenterol. 2022;117(9):1444–53
201. Xu X, Jiang L, Zeng Y, Pan L, Lou Z, Ruan B. HCC prediction models in chronic hepatitis B patients receiving entecavir or tenofovir: a systematic review and meta-analysis. Virol J. 2023;20(1): 180
202. Yip TC, Wong GL, Wong VW, Tse YK, Liang LY, Hui VW, et al. Reassessing the accuracy of PAGE-B-related scores to predict hepatocellular carcinoma development in patients with chronic hepatitis B. J Hepatol. 2020;72(5):847–54
203. Chon HY, Lee HA, Park SY, Seo YS, Kim SG, Lee CH, et al. CAGE-B and SAGE-B models better predict the hepatitis B

virus-related hepatocellular carcinoma after 5-year entecavir treatment than PAGE-B. J Dig Dis. 2023;24(2):113–21
204. Kim BG, Park NH, Lee SB, Jeon S, Park JH, Jung SW, et al. The risk of hepatocellular carcinoma within and beyond the first 5 years of entecavir in Korean patients with chronic hepatitis B. Liver Int. 2018;38(12):2269–76
205. Papatheodoridis GV, Idilman R, Dalekos GN, Buti M, Chi H, van Boemmel F, et al. The risk of hepatocellular carcinoma decreases after the first 5 years of entecavir or tenofovir in Caucasians with chronic hepatitis B. Hepatology. 2017;66(5):1444–53
206. Zhang BH, Yang BH, Tang ZY. Randomized controlled trial of screening for hepatocellular carcinoma. J Cancer Res Clin Oncol. 2004;130(7):417–422
207. Singal AG, Zhang E, Narasimman M, Rich NE, Waljee AK, Hoshida Y, et al. HCC surveillance improves early detection, curative treatment receipt, and survival in patients with cirrhosis: A meta-analysis. J Hepatol. 2022;77(1):128–39
208. Tourkochristou E, Kalafateli M, Triantos C, Aggeletopoulou I. Evaluation of PAGE-B score for hepatocellular carcinoma development in chronic hepatitis b patients: reliability, validity, and responsiveness. Biomedicines. 2024;12(6):1260
209. Kanwal F, Singal AG. Surveillance for hepatocellular carcinoma: current best practice and future direction. Gastroenterology. 2019;157(1):54–64
210. Singal AG, Kanwal F, Llovet JM. Global trends in hepatocellular carcinoma epidemiology: implications for screening, prevention and therapy. Nat Rev Clin Oncol. 2023;20(12):864–884
211. Santi V, Trevisani F, Gramenzi A, Grignaschi A, Mirici-Cappa F, Del Poggio P, et al. Semiannual surveillance is superior to annual surveillance for the detection of early hepatocellular carcinoma and patient survival. J Hepatol. 2010;53(2):291–7
212. Tzartzeva K, Obi J, Rich NE, Parikh ND, Marrero JA, Yopp A, et al. Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients With Cirrhosis: A Meta-analysis. Gastroenterology. 2018;154(6):1706–18 e1
213. Sherman M. Limitations of screening for hepatocellular carcinoma. Hepat Oncol. 2014;1(2):161–163
214. Feng H, Li B, Li Z, Wei Q, Ren L. PIVKA-II serves as a potential biomarker that complements AFP for the diagnosis of hepatocellular carcinoma. BMC Cancer. 2021;21(1):401
215. Chan HL, Vogel A, Berg T, De Toni EN, Kudo M, Trojan J, et al. Performance evaluation of the Elecsys PIVKA-II and Elecsys AFP assays for hepatocellular carcinoma diagnosis. JGH Open. 2022;6(5):292–300
216. Toan BN, Tan CK, Hasan I, Setiawan L, Yu ML, Izumi N, et al. Utility of combining PIVKA-II and AFP in the surveillance and monitoring of hepatocellular carcinoma in the Asia-Pacific region. Clin Mol Hepatol. 2023;29(2):277–92
217. Ricco G, Cavallone D, Cosma C, Caviglia GP, Oliveri F, Biasiolo A, et al. Impact of etiology of chronic liver disease on hepatocellular carcinoma biomarkers. Cancer Biomark. 2018;21(3):603–12
218. Yip TC, Wong VW, Lai MS, Lai JC, Hui VW, Liang LY, et al. Risk of hepatic decompensation but not hepatocellular carcinoma decreases over time in patients with hepatitis B surface antigen loss. J Hepatol. 2023;78(3):524–33
219. Diel R, Nienhaus A. Risk of Hepatitis B transmission by healthcare workers - a systematic review. GMS Hyg Infect Control. 2025;20: Doc43
220. Centers for Disease C, Prevention. Updated CDC recommendations for the management of Hepatitis B virus-infected health-care providers and students. MMWR Recomm Rep. 2012;61(RR-3):1–12
221. Gerlich WH. Reduction of infectivity in chronic hepatitis B virus carriers among healthcare providers and pregnant women by antiviral therapy. Intervirology. 2014;57(3–4):202–211
222. Sabeena S, Ravishankar N. Horizontal modes of transmission of hepatitis B virus (HBV): a systematic review and meta-analysis. Iran J Public Health. 2022;51(10):2181–2193
223. European Centre for Disease Prevention and Control. A pilot survey of stigma related to infection with hepatitis B and C. Stockholm: ECDC; 2025
224. Zimmermann BM, Willem T, Rost M, Matthes N, Buyx A. Perceptions of stigma among patients with hepatitis B in Germany: cross-sectional survey. JMIR Form Res. 2025;9: e66379
225. Yozgat A, Can G, Can H, Ekmen N, Akyol T, Kasapoglu B, et al. Social stigmatization in Turkish patients with chronic hepatitis B and C. Gastroenterol Hepatol. 2021;44(5):330–6
226. Katcher JG, Klassen AC, Hann HW, Chang M, Juon HS. Racial discrimination, knowledge, and health outcomes: the mediating role of hepatitis B-related stigma among patients with chronic hepatitis B. J Viral Hepat. 2024;31(5):248–254
227. Van Kim T, Pham TN, Phan P, Le MH, Le Q, Nguyen PT, et al. Effectiveness and implementation of decentralized, community- and primary care-based strategies in promoting hepatitis B testing uptake: a systematic review and meta-analysis. EClinicalMedicine. 2024;76:102818
228. Hosking K, Binks P, De Santis T, Wilson PM, Gurruwiwi GG, Bukulatjpi SM, et al. Evaluating a novel model of hepatitis B care, Hep B PAST, in the Northern Territory of Australia: results from a prospective, population-based study. Lancet Reg Health West Pac. 2024;48:101116
229. Muniyandi M, Tyagi K, Singh M, Prakash V, Karikalan N, Senthilkumar S, et al. Economic evaluation of implementing a decentralised Hepatitis B virus diagnostic intervention under National Viral Hepatitis Control Programme in Tamil Nadu. South India Trop Med Int Health. 2021;26(3):374–84
230. Zhang L, Liu H, Zou Z, Su S, Ong JJ, Ji F, et al. Shared-care models are highly effective and cost-effective for managing chronic hepatitis B in China: reinterpreting the primary care and specialty divide. Lancet Reg Health West Pac. 2023;35:100737
231. Cooke GS, Andrieux-Meyer I, Applegate TL, Atun R, Burry JR, Cheinquer H, et al. Accelerating the elimination of viral hepatitis: a Lancet Gastroenterology & Hepatology Commission. Lancet Gastroenterol Hepatol. 2019;4(2):135–84
232. Stockdale AJ, Holt B, Bhadoria AS, Sadasivan A, Ikeda D, Pollack T, et al. Service delivery models and care cascade outcomes for people living with chronic hepatitis B: a global systematic review and meta-analysis. Lancet Gastroenterol Hepatol. 2025;10(11):1013–27
233. O'Leary DA, Cropp E, Isaac D, Desmond PV, Bell S, Nguyen T, et al. "B in IT" - a community-based model for the management of hepatitis B patients in primary care clinics using a novel web-based clinical tool. Hepatol Med Policy. 2018;3:1
234. Lau GK, Suri D, Liang R, Rigopoulou EI, Thomas MG, Mullerova I, et al. Resolution of chronic hepatitis B and anti-HBs seroconversion in humans by adoptive transfer of immunity to hepatitis B core antigen. Gastroenterology. 2002;122(3):614–24
235. Narmada BC, Khakpoor A, Shirgaonkar N, Narayanan S, Aw PP, Singh M, et al. Single-cell landscape of functionally cured chronic hepatitis B patients reveals activation of innate and altered CD4-CTL-driven adaptive immunity. J Hepatol. 2024;81(1):42–61
236. Mak LY, Hui RW, Chung MS, Wong DK, Fung J, Seto WK, et al. Regression of liver fibrosis after HBsAg loss: A prospective matched case-control evaluation using transient elastography and serum enhanced liver fibrosis test. J Gastroenterol Hepatol. 2024;39(12):2826–34
237. Morais E, Mason L, Dever J, Martin P, Chen JV, Felton L, et al. Clinical Consequences of Hepatitis B Surface Antigen Loss in Chronic Hepatitis B Infection: A Systematic Literature Review and Meta-Analysis. Gastro Hep Adv. 2023;2(7):992–1004

238. Vittal A, Sharma D, Hu A, Majeed NA, Terry N, Auh S, et al. Systematic review with meta-analysis: the impact of functional cure on clinical outcomes in patients with chronic hepatitis B. Aliment Pharmacol Ther. 2022;55(1):8–25
239. Sheng Q, Ding Y, Li B, Han C, Li Y, Zhang C, et al. Efficacy and safety of nucleos(t)ide analogues to prevent hepatitis B virus mother-to-child transmission in pregnant women with high viremia: real life practice from China. Int J Med Sci. 2018;15(8):796–801
240. Ghany MG, Pan CQ, Lok AS, Feld JJ, Lim JK, Wang SH, et al. Effects of Treatment of Chronic Hepatitis B Virus Infection on Patient-Reported Outcomes. Clin Gastroenterol Hepatol. 2018;16(10):1641–9 e6
241. Author Group of Expert O. [Expert opinions on the technical guiding principles for clinical trials of drugs in the treatment of chronic hepatitis B virus infection]. Zhonghua Gan Zang Bing Za Zhi. 2025;33(6):534–544
242. Ghany MG, Pan CQ, Lok AS, Feld JJ, Lim JK, Wang SH, et al. AASLD/IDSA Practice Guideline on treatment of chronic hepatitis B. Hepatology. 2025;83(4):974–997
243. European Association for the Study of the L. EASL clinical practice guidelines on the management of hepatitis B virus infection. J Hepatol. 2025;83(2):502–583
244. You H, Wang FS, 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):1425–42
245. Dana J, Meyer A, Paisant A, Rode A, Sartoris R, Séror O, et al. Improving risk stratification and detection of early HCC using ultrasound-based deep learning models. JHEP Rep. 2025;7(10):101510
246. Feng S, Wang J, Wang L, Qiu Q, Chen D, Su H, et al. Current Status and Analysis of Machine Learning in Hepatocellular Carcinoma. J Clin Transl Hepatol. 2023;11(5):1184–91
247. Spann A, Strauss AT, Davis SE, Bhat M. The role of artificial intelligence in chronic liver diseases and liver transplantation. Gastroenterology. 2025;169(3):456–470
248. Wong GL, Hui VW, Tan Q, Xu J, Lee HW, Yip TC, et al. Novel machine learning models outperform risk scores in predicting hepatocellular carcinoma in patients with chronic viral hepatitis. JHEP Rep. 2022;4(3):100441
249. Dong W, Da Roza CC, Cheng D, Zhang D, Xiang Y, Seto WK, et al. Development and validation of HBV surveillance models using big data and machine learning. Ann Med. 2024;56(1):2314237
250. Elhaddad M, Hamam S. AI-driven clinical decision support systems: an ongoing pursuit of potential. Cureus. 2024;16(4):e57728

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