APASL Viral Elimination Task Force

APASL CLINICAL PRACTICE GUIDELINES ON THE MANAGEMENT OF CHRONIC HEPATITIS B INFECTION: A 2026 UPDATE

Hong You*, Rakhi Maiwall*, Jing Chen*, Sang Hoon Ahn, Kadir Dokmeci, Xiaoguang Dou, Manal El-Sayed, Jian-Gao Fan, Rino Gani, Zhiliang Gao, Jacob George, Hasmik Ghazinian, George Goh, Saeed Hamid, Jinlin Hou, Shang-Chin Huang, Dong Ji, Jidong Jia, Tatsuo Kanda, Jia-Horng Kao, Yoon Jun Kim, Cosmas Rinaldi A. Lesmana, Rosmawati Mohamed, Qin Ning, Necati Ormeci, Motoyuki Otsuka, Diana Payawal, Pham Thanh Thuy, Keo Sailey, Manoj Kumar Sharma, Jose D Sollano, Jian Sun, Tawesak Tanwandee, Alexander Thompson, Fu-Sheng Wang, Guiqiang Wang, Lai Wei, Grace LH Wong, Vincent WS Wong, Eng Kiong Yeoh, Terry Cheuk-Fung Yip, Ming-Lung Yu, Wenhong Zhang, Hui Zhuang, Ching-Lung Lai, Masao Omata#, Shiv Kumar Sarin#, George Lau#

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APASL 2026

35TH ANNUAL MEETING OF THE ASIAN PACIFIC ASSOCIATION FOR THE STUDY OF THE LIVER

22-25 April 2026

İstanbul Lütfi Kırdar International Convention and Exhibition Centre

HBV Consensus: APASL CHB CPG GUIDELINES - A 2026 UPDATE

DATE: FRIDAY, 24 APRIL 2026 **TIME**:15:30 - 17:00 **VENUE**: Auditorium Room

MODERATORS: George LAU, Hong Kong;
SK Sarin, India

1. Opening Remarks (3 min)		
Necati ÖRMECİ, Türkiye		
SESSION 1 (18 min)		
Panelists: Masao OMATA, Japan / Hasmik GHAZINYAN, Armenia		
#	Topic	Speaker
2	Disease Burden, Methodology	Jing CHEN, Hong Kong
3	Vaccination	Diana PAYAWAL, Philippines
4	Screening	Ming-Lung YU, Taiwan
5	Assessment of Liver Fibrosis	Yoon Jun KIM, South Korea
SESSION 2A (30 min)		
Panelists: A. Kadir DÖKMECİ, Türkiye / Jidong JIA, China		
#	Topic	Speaker
6	Treatment Goals	Jia-Hong KAO, Taiwan ☐
7	Treatment Initiation Evaluation	Alexander THOMPSON, Australia
8	Current Strategies and Their Effectiveness (in Achieving Goals)	Hong YOU, China
9	Treatment Algorithm	Hong YOU, China
10	When to Stop	Hong YOU, China

SESSION 2B (15 min)		
Panelists: Jacob GEORGE, Australia / Jose SOLLANO, Philippines / Jian-Gao FAN, China		
#	Topic	Speaker
12	Special Groups 1 – MARLD	Shang-Chin Huang, Taiwan
13	Special Groups 2 – HIV/HIVD	Sun JIAN, China ☐
15	Special Groups 4 – Alcohol Drinkers	Tatsuo KANDA, Japan
16	Discussion	(All panelists)
SESSION 3 (7 min)		
Panelists: Jin-Lin HOU, China / Hong YOU, China		
#	Topic	Speaker
17	HCC Surveillance	Terry YIP, Hong Kong
18	Prevention of Transmission	FS Wang, China
SESSION 4 (15 min)		
Panelists: Tawesak Tanwande, Thailand / Jing CHEN, Hong Kong ☐		
#	Topic	Speaker
19	Future – Service Model	Saeed HAMID, Pakistan ☐
20	Future – Functional Cure	Lai WEI, China ☐
21	Future – Novel Diagnostic Markers	Rakhi MAIWALL, India
23. Conclusion and Closing Remarks		
George LAU, Hong Kong		

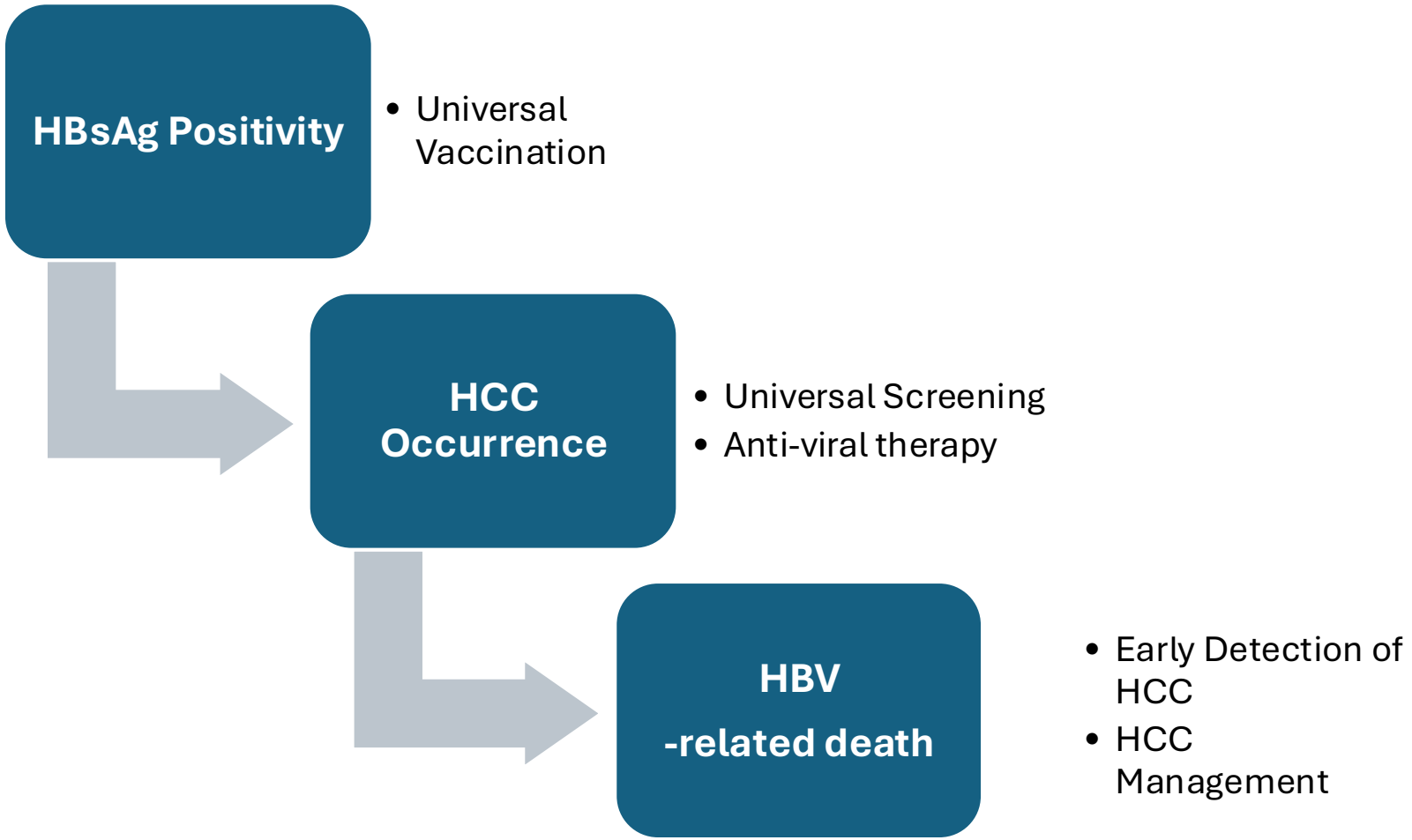
Challenges in Asia-Pacific region

WHO's 2030 global hepatitis elimination target and progress

Table 2.1. Progress towards global viral hepatitis targets, 2022

Indicator	Baseline – 2020	Progress – 2022	Targets – 2025	Targets – 2030
		Impact		
Number of new hepatitis B infections per year	1.5 million (1.11 million–2.09 million) 20 per 100 000 population	**1.23 million (0.81 million–1.53 million)** **16 per 100 000 population**	0.85 million (0.62 million–1.19 million) 11 per 100 000 population	170 000 (120 000–240 000) 2 per 100 000 population
Number of people dying from hepatitis B per year	0.82 million (0.56 million–1.23 million) 10 per 100 000 population	**1.10 million (0.88 million–1.74 million)** **14 per 100 000 population**	530 000 (360 000–800 000) 7 per 100 000 population	310 000 (210 000–470 000) 4 per 100 000 population

Measures to reduce the burden of disease



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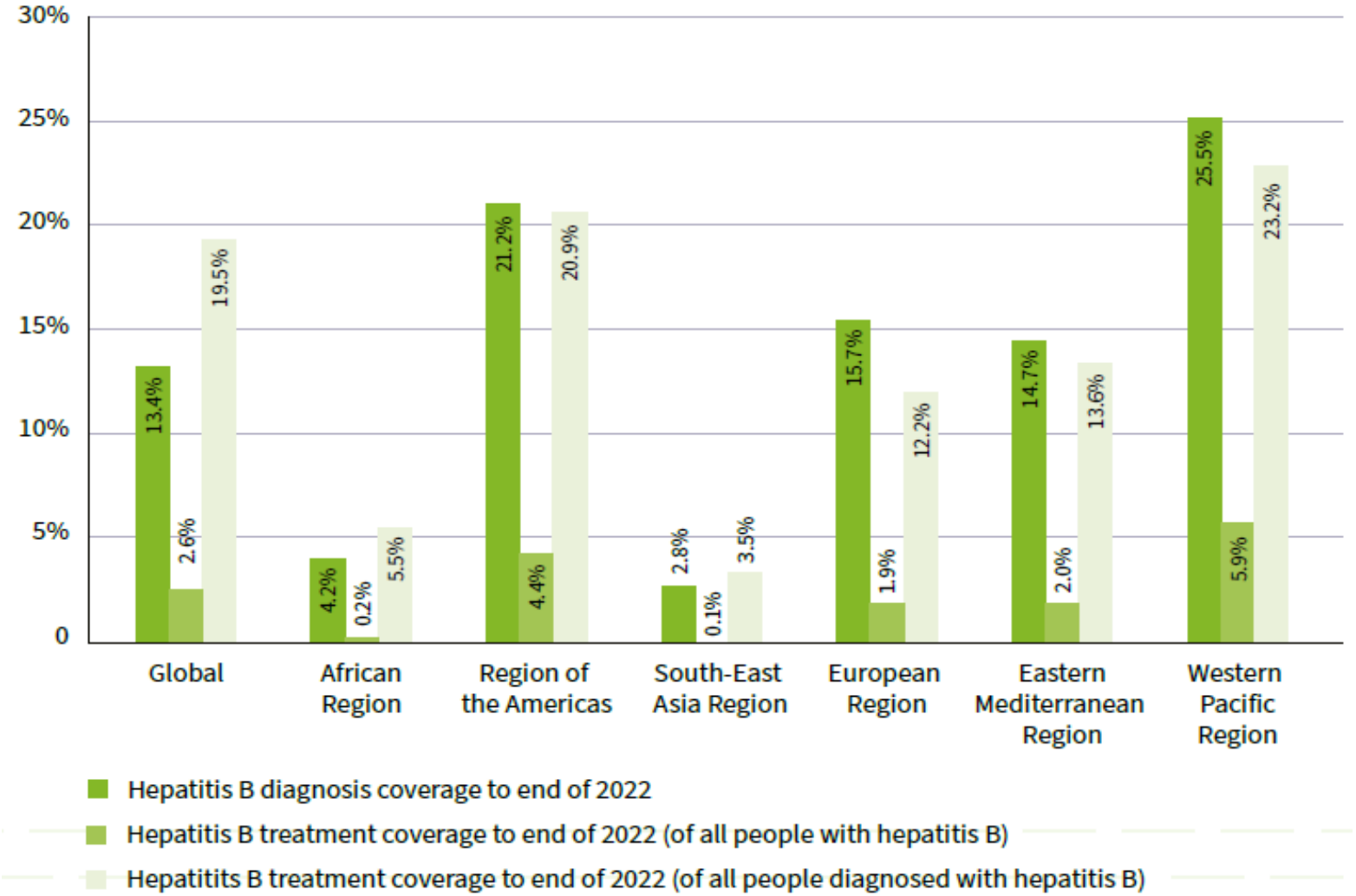
Challenge 1: Low Diagnosis and Treatment



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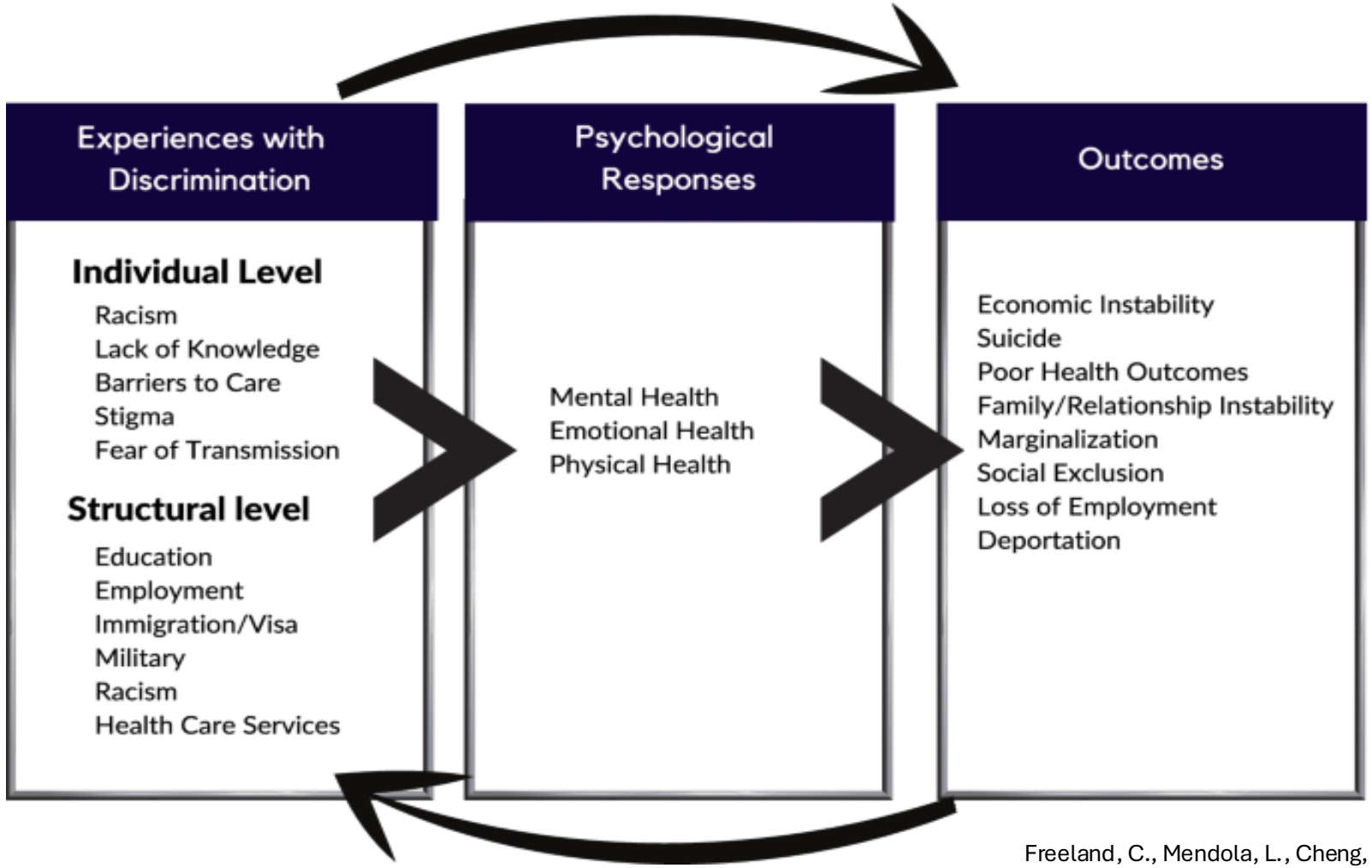
WHO 2024.

Challenge 2: Stigma & Discrimination



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Freeland, C., Mendola, L., Cheng, V. *et al*. The unvirtuous cycle of discrimination affecting people with hepatitis B: a multi-country qualitative assessment of key-informant perspectives. *Int J Equity Health* **21**, 77 (2022). https://doi.org/10.1186/s12939-022-01677-6

Challenge 3: Specialist-Centered Care Dominates

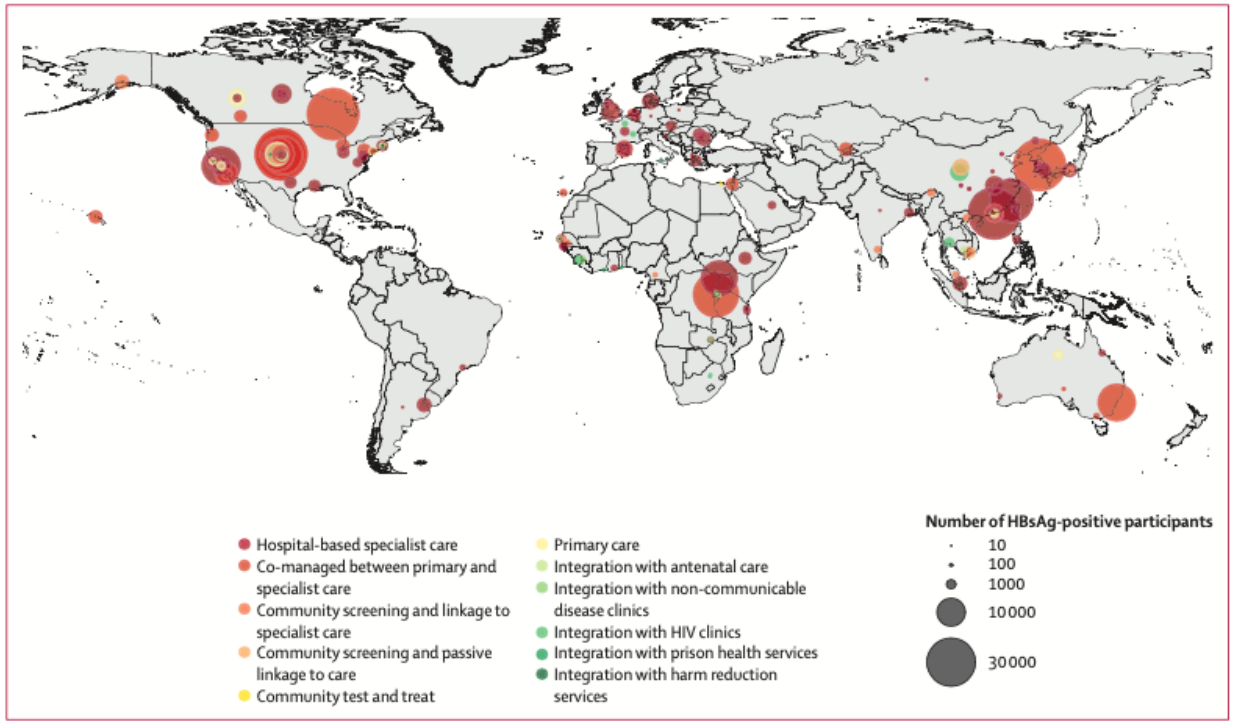
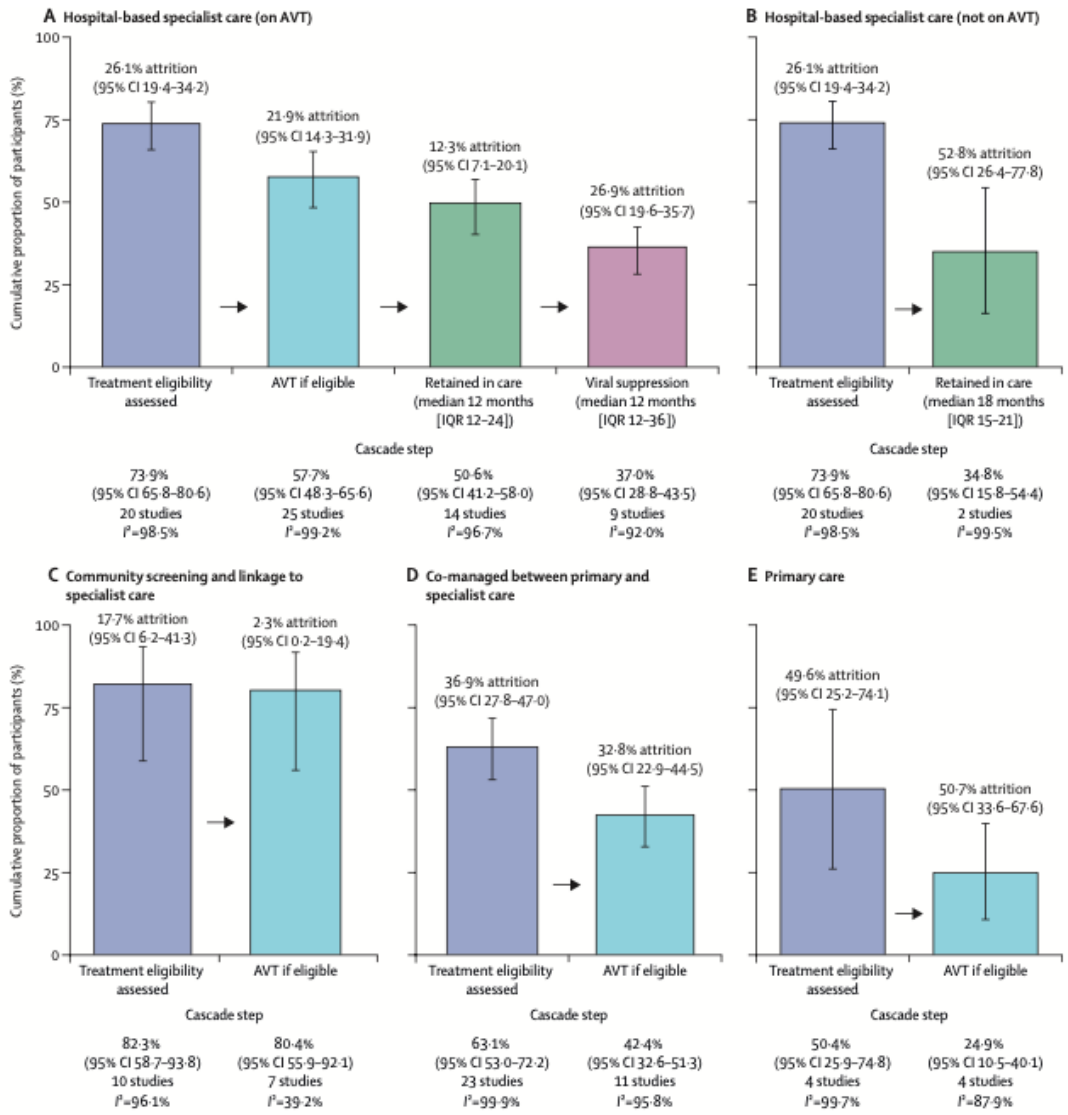


Figure 2: **Geographical distribution of 110 included cohorts (106 studies), with representation of study size**
The size of the points indicates the number of HBsAg-positive participants and colours indicate models of care. Point sizes are capped for cohorts with more than 30 000 participants (n=5) to facilitate visualisation (ie, these cohorts are represented at the same size as those with 30 000 participants).



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Lancet Gastroenterol Hepatol **2025** published **Online**
August 14, 2025 https://doi.org/10.1016/ S2468-1253(25)00163-3

Challenge 4: Limited Treatment Efficacy

Treatment Strategy	Study/Source	Population	HBsAg Loss Rate EOT	HBsAg Loss Rate EOF	Comments
PegIFN Add-On Therapy	Huang et al. (1)	Chinese		26.2% (21/80) at 96 weeks (48 weeks on-treatment + 24 weeks off-treatment)	Sustained HBsAg loss reported
PegIFN Add-On Therapy	PAS Study (2)	HBeAg- in Europe and Canada	10% (vs. 0% in NA monotherapy)		Significant improvement in HBsAg clearance rate ($p < 0.01$)
PegIFN Add-On Therapy	PARADISE Study (3)	At intermediate to high risk of HCC	22.7% at week 48 (vs. 0% NA)	16.7% at week 96 (vs. 0% NA)	Significant increase in HBsAg loss rates ($p < 0.05$)
PegIFN Add-On Therapy	Lim SG et al. RCT (4)	HBeAg- in Singapore		12.9% (vs. 0% in NA monotherapy)	Direct comparison with NA monotherapy and Switch strategy
Switch Therapy	Lim SG et al. RCT (4)	HBeAg- in Singapore		12.1% (vs. 0% in NA monotherapy)	Direct comparison with PegIFN add-on and NA monotherapy
Bepirovirsen Add-On Therapy	Yuen MF 2022 (5) – Group 1 (300 mg for 24 weeks)		26%	12%	Highest dose resulted in highest HBsAg loss
Discontinuation of NAs	Hall SAL, et al. 2022	HBeAg-negative CHB		1-8%	Caucasians had higher rate of HBsAg loss after discontinuation of NAs
NA Monotherapy	Multiple studies		<1%	<1%	Consistently low HBsAg loss rates

Challenge 4: Limited Treatment Efficacy

Hepatology International
https://doi.org/10.1007/s12072-025-10823-5

ORIGINAL ARTICLE

Functional cure with new antiviral therapy for hepatitis B virus: a systematic review and meta-analysis

Jing Chen[1] · Dong Ji[2] · Jidong Jia[3] · Hui Zhuang[4] · Xinxin Zhang[5] · Fu-Sheng Wang[6] · Wenhong Zhang[7] · Xiaoguang Dou[8] · Tawesak Tanwandee[9] · Shiv Kumar Sarin[10] · Rakhi Maiwall[10] · Manoj Kumar[10] · George Boon-Bee Goh[11] · Hasmik Ghazinyan[12] · Anuchit Chutaputti[13] · Pei-Jer Chen[14] · Hong You[15] · Ming-Lung Yu[16] · Jacob George[17] · Masao Omata[18] · Gui-qiang Wang[19,20] · George Lau[21,22] on behalf of APASL Viral Elimination Taskforce

Received: 26 September 2024 / Accepted: 8 March 2025

Abstract

Background Achieving a "functional" cure for chronic hepatitis B (HBV) is primary goal for novel antiviral treatments. We sought to evaluate efficacy and safety of these novel treatments and identified emerging barriers to achieving a functional cure.

Approach We systematically reviewed clinical trials from 2018 to 2023, identifying 244 trials from clinicaltrials.gov records on HBV. The primary outcome was functional cure rate at the end of follow-up (EOF). Secondary outcomes included changes in HBsAg levels, HBsAg loss rates, HBV DNA rebound, and adverse events. Meta-analysis was performed.

Results Our meta-analysis of 19 studies involving 1789 non-cirrhotic HBV patients found a minimal functional cure rate (0.0%, 95%CI 0.0–0.4%) and low HBsAg loss rates (0.9% at the end of treatment [EOT] and 0.1% at EOF). HBsAg levels declined at EOT (−0.41 log10 IU/mL, 95%CI −0.45 to −0.37, $p < 0.001$) but this reduction was not sustained to EOF. Virological relapse occurred in 20.5% of cases off-treatment. Although novel treatments were well-tolerated, they had higher adverse event rates (OR = 1.77, 95%CI 1.26–2.48). Challenges to achieving a functional cure include complex trial designs and unknown confounding factors.

Conclusion Novel antiviral treatments showed limited effectiveness in achieving HBsAg loss and reduction, highlighting

Effectiveness of novel antiviral treatment for CHB is limited

Our meta-analysis showed that the reported functional cure rate and HBsAg loss rate is minimum and not durable. The unknown confounding factors are identified.

Challenge 5: Financing Gaps

Affordability of annual HBV treatment (%)					
Country/Region	CHB	CC	HCC	Liver transplant	HCC surveillance
Armenia	26.88	26.88	NR	2240.14	10.75
Australia	1.39	3.31	220.58	1284.86	1.30
China mainland	8.12	21.56	121.68	1046.86	2.92
Egypt	20.89	25.53	63.45	2388.05	5.57
Hong Kong	39.20	65.34	522.69	2613.44	5.25
India	32.55	30.38	NR	5425.35	52.30
Indonesia	23.00	30.00	114.18	2778.12	11.84
Korea, Rep.	5.09	5.09	260.34	477.83	2.25
Malaysia	8.04	8.04	NR	NR	37.94
Mongolia	27.44	43.90	87.80	2194.90	7.74
Myanmar	78.60	94.93	940.34	9469.70	48.53
Pakistan	7.22	7.22	15.83	2500.00	8.58
Philippines	3.09	3.09	231.91	7730.37	41.20
Singapore	NR	2.16	159.03	1657.45	8.25
Taiwan	34.82	38.99	278.52	1392.60	3.98
Thailand	9.70	19.40	1940.24	727.59	12.61
Turkiye	7.15	11.18	40.24	1117.67	2.02

CHB: Chronic Hepatitis B; CC: compensated cirrhosis; HCC: hepatocellular carcinoma; NR: Not report.

Affordability was expressed as the percentage (%) of the annual treatment cost relative to the yearly minimum wage.

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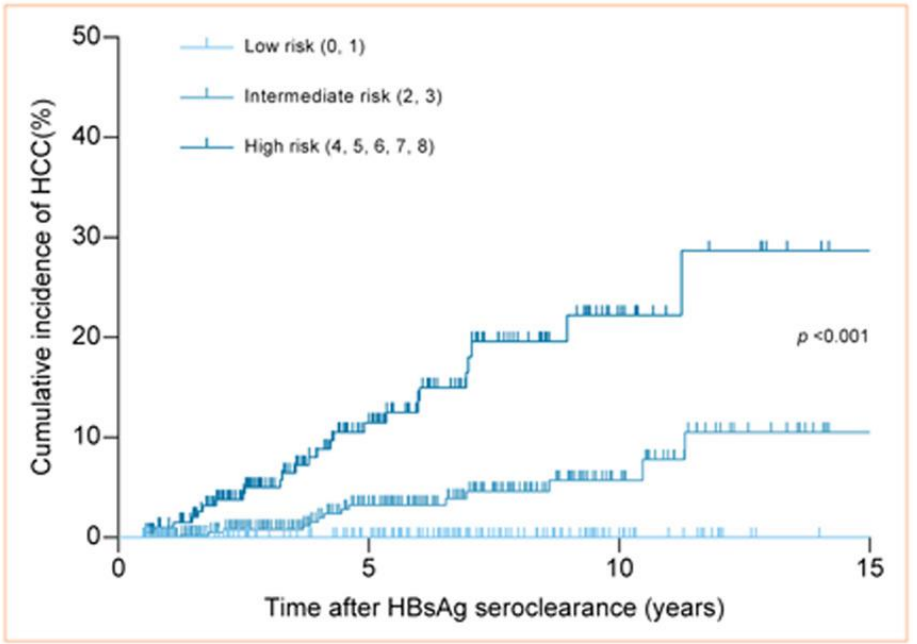
Chen J, Jidong Jia, Hui Zhuang, et al. Hepatology International https://doi.org/10.1007/s12072-024-10744-9

Challenge 6: Persistence risk of HCC after HBsAg clearance

	Risk score
Age (10-year increment)	
<40	0
≥40, <50	1
≥50, <60	2
≥60	3
Cirrhosis	
No	0
Yes	2
Family history of HCC	
No	0
Yes	1
More than moderate drinking	
No	0
Yes	2



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Yang H, Bae SH, Nam H, Lee HL, Lee SW, Yoo SH, Song MJ, Kwon JH, Nam SW, Choi JY, Yoon SK, Jang JW. A risk prediction model for hepatocellular carcinoma after hepatitis B surface antigen seroclearance. J Hepatol. 2022 Sep;77(3):632-641. doi: 10.1016/j.jhep.2022.03.032. Epub 2022 Apr 7.

Rationale for the updates

Speaker：Jing CHEN

Date：24 April, 2026

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You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

The Alarming Burden of HBV in the AP Region

KEY STATISTICS

- Global Epicenter: Over **66%** of the world's chronic HBV patients reside here.
- Case Concentration: **8 Countries** account for nearly **90%** of regional cases/deaths.

PERSISTENT CHALLENGES

- Diagnosis/Treatment rates remain critically low at **<15%**.

Barriers: Poor linkage to care | Unaffordable treatment | Social stigma | Inadequate infrastructure.

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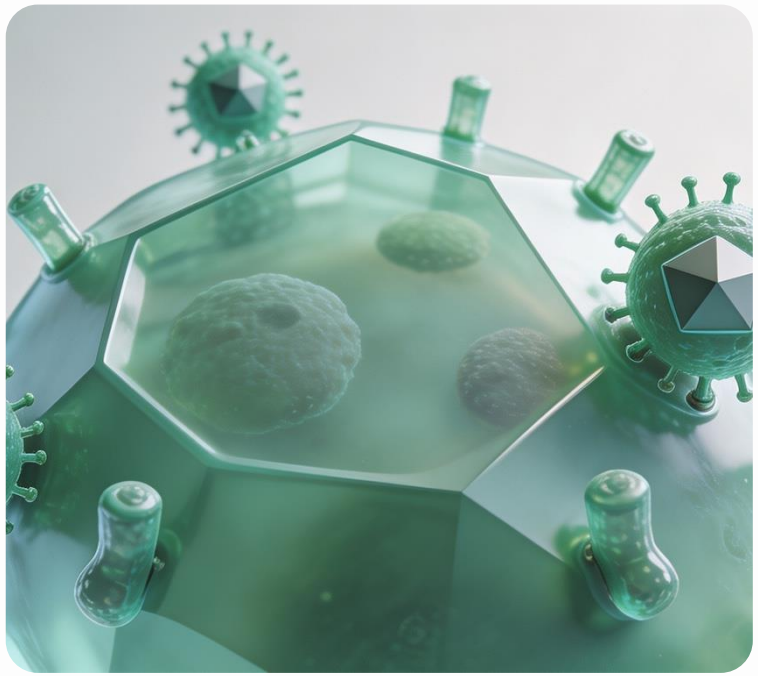
You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Paradigm Shifts in Understanding CHB



Re-evaluating the "Immune-Tolerant" Phase

• Challenged traditional view: Recognized as potentially progressive (even with normal ALT).
• Identified significant risk of Hepatocellular Carcinoma (HCC) in this phase.

The Rise of Novel Biomarkers

• Key markers: qHBsAg (response), HBV RNA (efficacy), HBcrAg (HCC risk).
• Reduced biopsy need via non-invasive fibrosis tools like FibroScan.

Changing Patient Profile

• A growing prevalence of HBeAg-negative adult patients.
• A significant cohort of younger patients presenting in the immune-tolerant phase.

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You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Rationale for Updated APASL Guidelines

Therapeutic Evolution

- **Safer & Effective:** High-barrier NUCs (ETV, TDF, TAF) are now standard.
- **Emerging Evidence:** Supports **combination therapy** & **earlier initiation** to prevent HCC.

Complex Patient Care

- **Co-existing Conditions:** The high prevalence of **MAFLD** and **ALD** significantly complicates the management of CHB patients.

Tech & AI Impact

- **Advanced Tools:** **AI and Big Data** offer powerful potential to improve risk stratification and enable personalized treatment plans.

THE IMPERATIVE FOR UPDATED GUIDELINES

To address the evolving landscape and complexities, there is a critical need for **simplified, evidence-based, and cost-effective** guidelines that can be applied across the diverse Asia-Pacific region.

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You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Methods

Speaker: George LAU

Date：24 April, 2026

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APASL Viral Elimination Task Force

Mission	To reduce the burden and suffering caused by viral hepatitis through effective action and policy advocacy
Vision	”Hepatitis-free generation” in Asian-Pacific region
Goal	To bridge the gap between scientific advancements and public health implementation by providing pragmatic and cost-effective solutions
Value	Patient is our priority

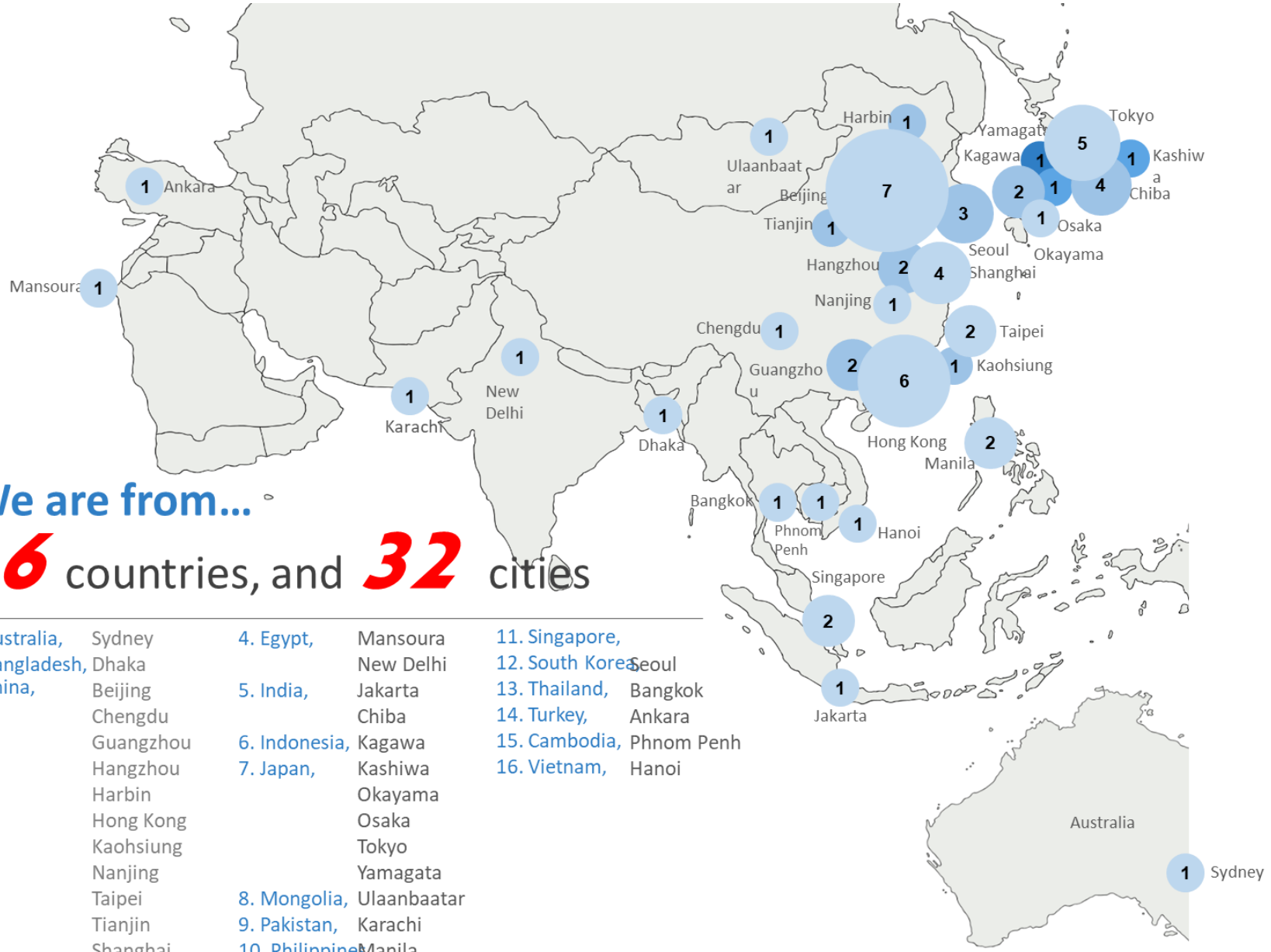
Expert Panel Formation

KOL

- Significant clinical experience and research contributions in the field of CHB
- 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

Chairmanship

- Drs. George Lau, Shiv Kumar Sarin, and Masao Omata



We are from…

16 countries, and **32** cities

1. Australia,	Sydney
2. Bangladesh,	Dhaka
3. China,	Beijing
	Chengdu
	Guangzhou
	Hangzhou
	Harbin
	Hong Kong
	Kaohsiung
	Nanjing
	Taipei
	Tianjin
	Shanghai
4. Egypt,	Mansoura
	New Delhi
5. India,	Jakarta
	Chiba
6. Indonesia,	Kagawa
7. Japan,	Kashiwa
	Okayama
	Osaka
	Tokyo
	Yamagata
8. Mongolia,	Ulaanbaatar
9. Pakistan,	Karachi
10. Philippines,	Manila
11. Singapore,	
12. South Korea,	Seoul
13. Thailand,	Bangkok
14. Turkey,	Ankara
15. Cambodia,	Phnom Penh
16. Vietnam,	Hanoi

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You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

APASL 2026 CHB CPG Panel Members

(In No particular order)

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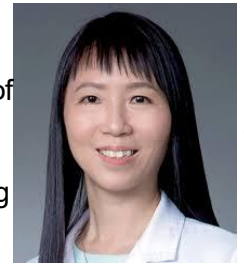

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St. Vincent's Hospital Melbourne and the University of Melbourne

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Manoj Kumar Sharma
Institute of Liver & Biliary Sciences, New Delhi, India

Initiation of APASL CHB CPG-2026 update
APASL Viral Elimination Taskforce Close-door Meeting

Date: March 29, 2025 **Time:** 11:00 - 13:00
Location: CNCC, Room 202, Level 2

From Right to Left: Anna Lok (US), Calvin Pan (US), George Goh Boon Bee (Singapore), Yoon Jun Kim (Korea), Ming-Lung Yu (Kaohsiung), Xiaoguang Dou (China), Hong You (China), Jian-Gao Fan (China), Diana A Payawal (Philippines), Tawesak Tanwandee (Thailand), Polin Chan (WHO), Masao Omata (Japan), George Lau (Chairman, Hong Kong China), John Ward (US), Rino A Gani (Indonesia), Terrault Norah (US), Alexander Thompson (Australia), Rosmawati Mohamed (Malaysia), Yu Wang (China), Terry Yip (Hong Kong, China), Shang-Chin Huang (Taipei), Saeed Hamid (Pakistan), Jing Chen (Hong Kong, China)
Participants not in the group photo: SK Sarin (India), Lai Wei (China)

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You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Identify Key Clinical Questions / Evidence review and synthesis

We had two online meetings to propose and discuss the key clinical questions

- Screening (2)
- Testing (3)
- Vaccination (3)
- Treatment (14)
- HCC Surveillance (2)
- Prevention and Reactivation (5)
- Open question and future direction (6)

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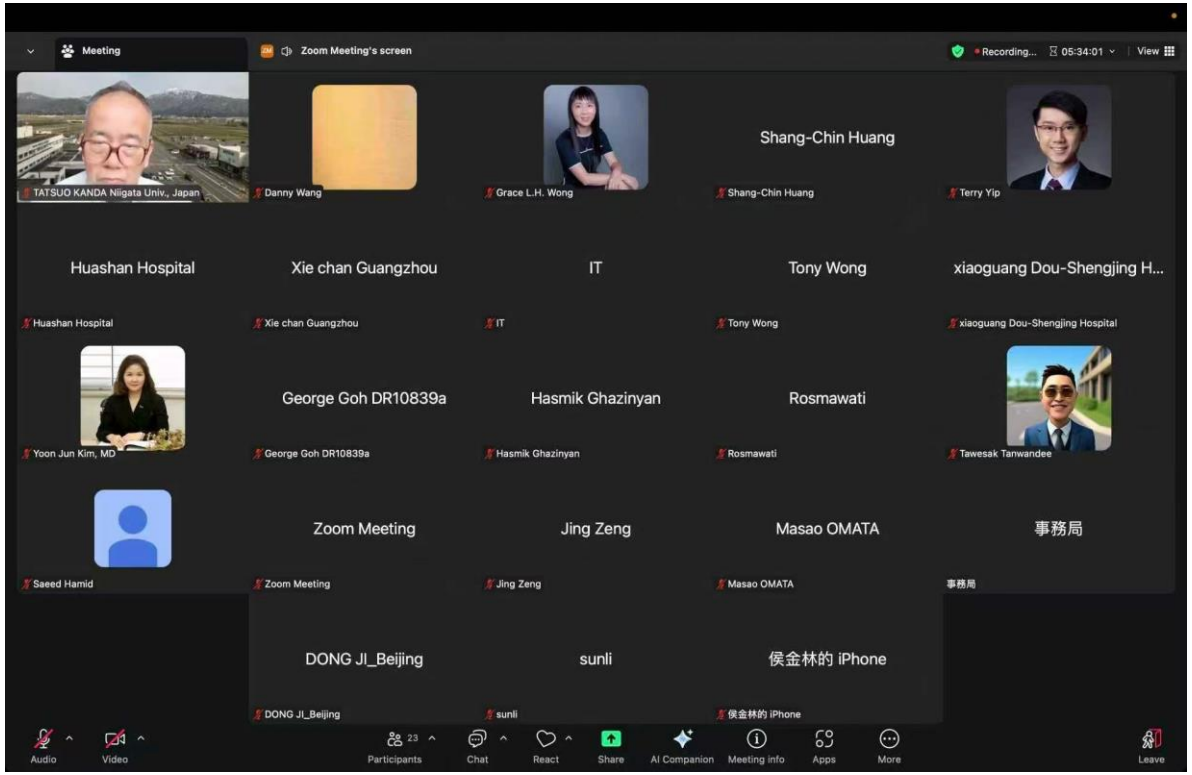
Evidence grading and formulation of recommendations

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..."

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Consensus on the final recommendations (hybrid)

Date: Sept 20, 2025 **Time:** 8:00 - 17:30 **Location:** EDINBURGH ROOM, 2/F, MANDARIN ORIENTAL HOTEL, 5 CONNAUGT ROAD CENTRAL, HONG KONG, CHINA SAR & Zoom



APASL
Viral Elimination
Task Force

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Important dates

Final Approval from Steering Committee of APASL	• 8th November 2025 at AASLD annual meeting , Washington DC, USA
Submitted to Hepatology and International (HI) and revision	• Nov 2025 - Feb 2026
Accepted by Hepatology and International (HI)	• Feb 22, 2026
Public announcement	• 24th April 2026 at 36th APASL annual meeting, Istanbul, Turkey

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APASL CHB CPG Recommendations

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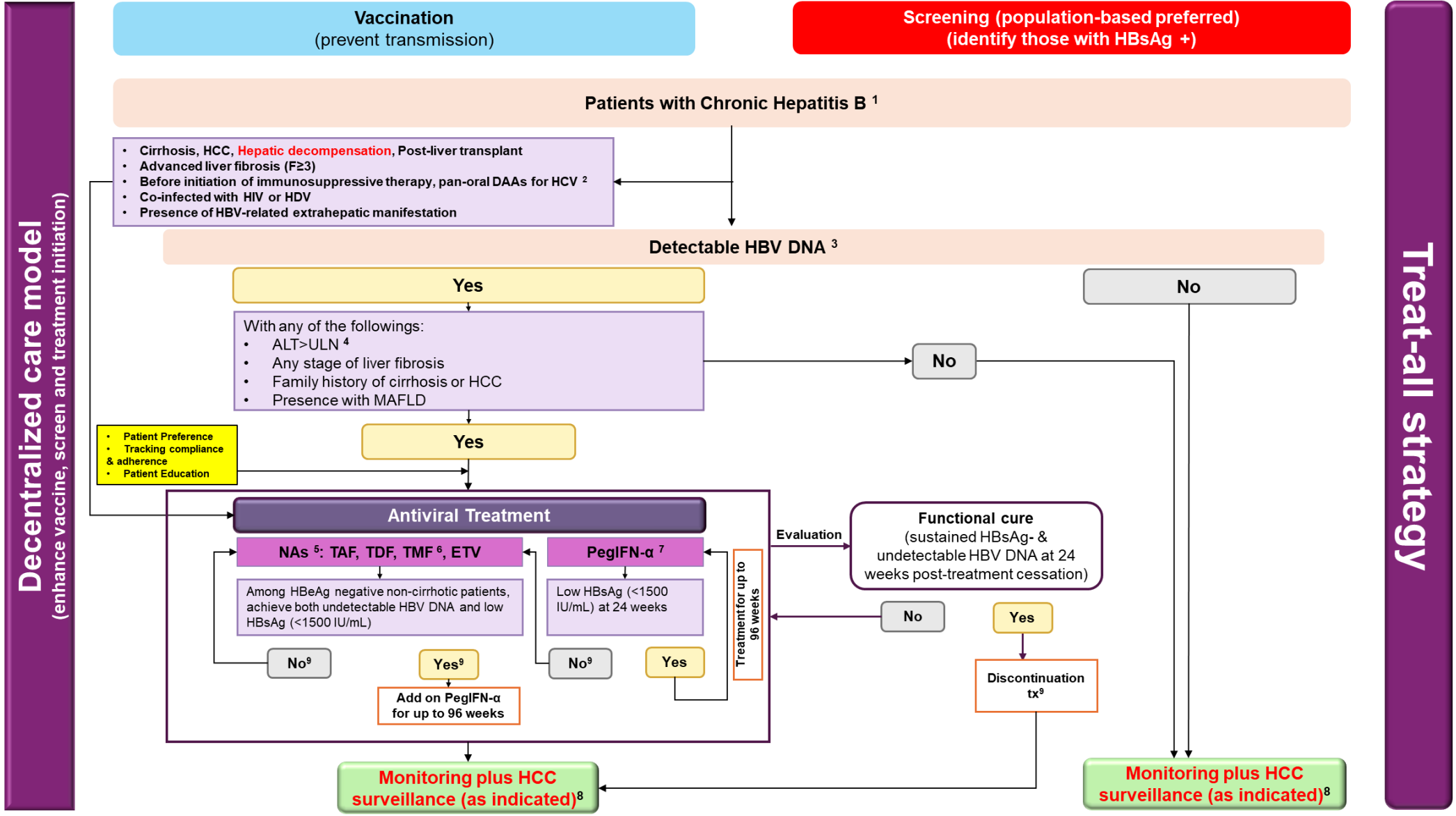

1. HBsAg+ for 6 months
2. Refer to APASL reactivation management guideline 2022
3. Sensitive NAT assay (lower limit of detection <20 IU/L).
4. ULN: 40 IU/L
5. The selection of NAs should be individualized based on long-term safety and patient comorbidities. TAF and ETV are preferred in patients with 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.

Section 1
Vaccination, Screening and Testing

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Vaccination

Speaker: Diana PAYAWAL

Date：24 April, 2026

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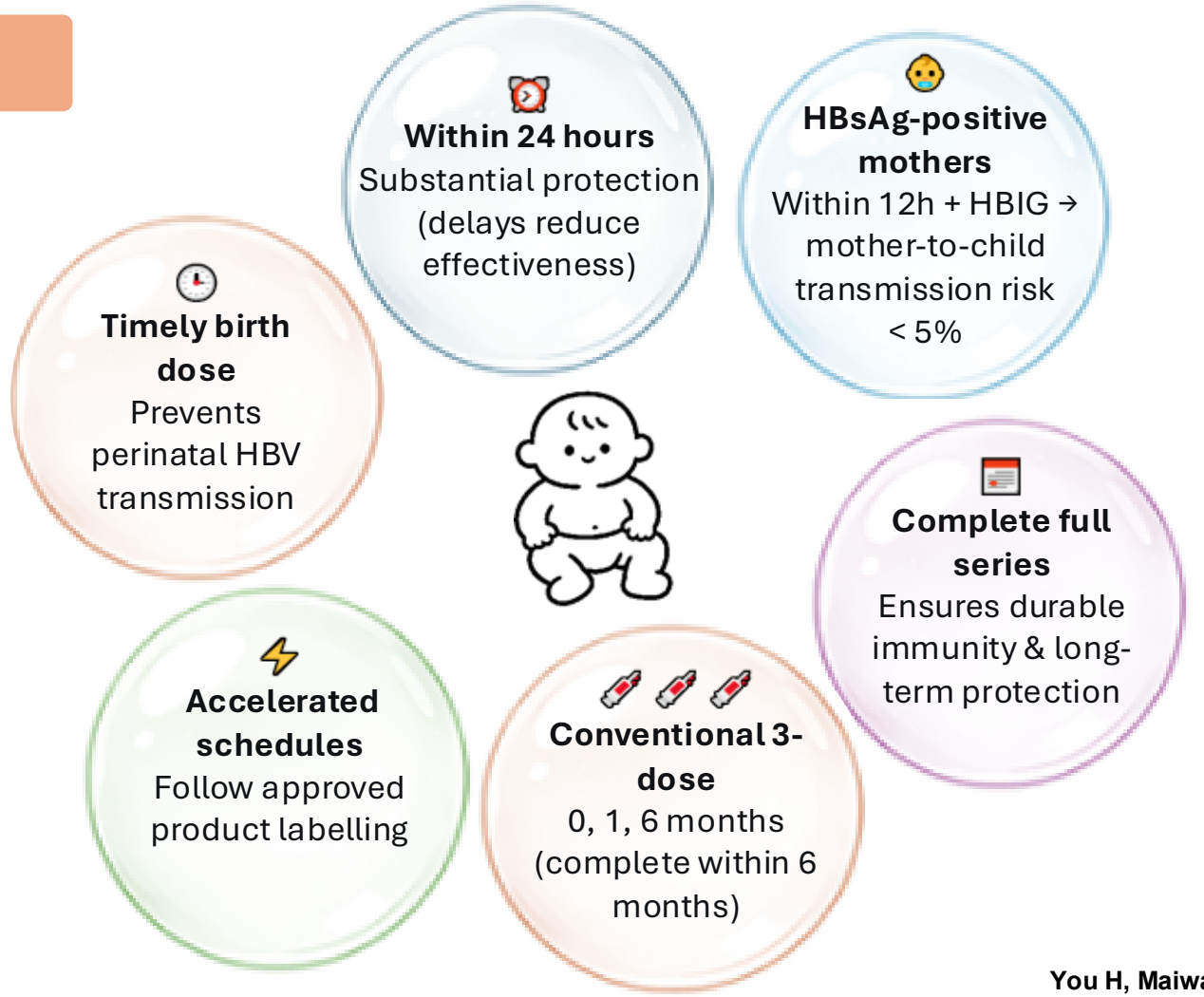
1. Vaccination

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

Rationale



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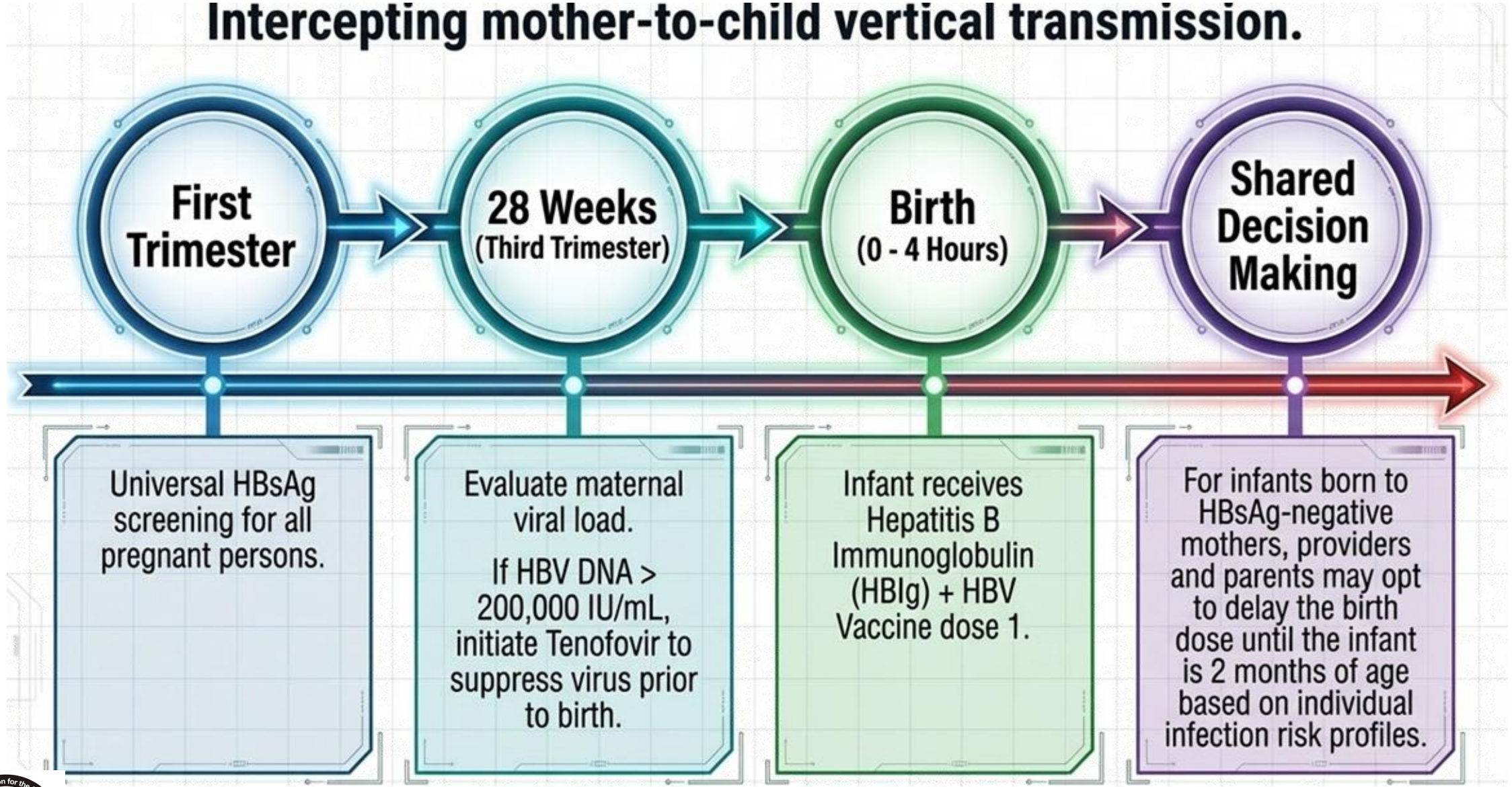
Rationale



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1. Vaccination

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

Recommendations

1.1.1 The **first dose** of the hepatitis B vaccine should be administered to **all clinically stable newborns** within **24 hours of birth**. **(A1)**

1.1.2 For infants born to **HBsAg-positive mothers**, the vaccine should be administered within **12 hours of birth**, preferably together with **hepatitis B immune globulin** (HBIG). **(A1)**

1.1.3 Completion of the **full vaccine series** according to the standard schedule is necessary to ensure **long-term protection**. **(A1)**

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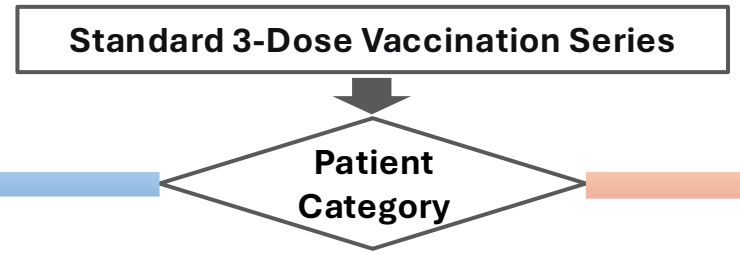
1. Vaccination

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

Rationale



Low Risk Groups

General Population & Infants (Standard Care)

- **High Efficacy:** >90% healthy adults & >95% vaccinated infants achieve protective anti-HBs (≥10 mIU/mL)
- **Immune Memory:** Persists despite antibody decline, ensuring rapid protection upon exposure

High-Risk Groups

High-Risk Groups & Non-Responders (Testing)

- **Immunocompromised:** Lower response rates & faster waning immunity.
- **HIV Population:** Response inversely correlates with CD4 count and viral load control.
- **Healthcare Workers:** Testing required for occupational safety documentation.
- **Household Contacts & Sexual Partners**
  - Complete vaccination series.
  - Test 1–2 months after final dose to confirm protective immunity (Anti-HBs ≥10 mIU/mL).
- **Infants of HBsAg-Positive Mothers**
  - Test at 9–12 months (delay to avoid false positives from maternal HBsAg lasting up to 7 months).
  - 5–10% may fail prophylaxis despite HBIG + vaccine.
  - Anti-HBs ≥10 mIU/mL: Protective immunity.
  - Anti-HBs <10 mIU/mL: Requires booster & retesting.
  - High Viral Load Cases (≥10^6 IU/mL): Consider early HBsAg & HBV DNA testing 1-2 months post-dose 2.

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1. Vaccination

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

Recommendations

1.2.1 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)

1.2.2 Testing is recommended for populations at risk of **inadequate vaccine response** or **clinical consequences** if unprotected:

- ***Immunocompromised patients***: Test anti-HBs 1–2 months post-vaccination; repeat vaccination if <10 mIU/mL. (A1)
- ***Healthcare workers***: Test anti-HBs 1–2 months post-vaccination; repeat vaccination if <10 mIU/mL, test HBsAg if persistently non-responsive. (A1)
- ***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)
- ***Household and sexual contacts of HBsAg-positive individuals***: Test anti-HBs 1–2 months post-vaccination; repeat vaccination if <10 mIU/mL. (A2)

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Hepatitis B Vaccination in Special Clinical Populations

Modified Dosing Strategies & Monitoring

Hemodialysis / CKD

- Double-dose recombinant (40 µg) at 0, 1, 2, 6 months
- 3-antigen vaccine (PreHevbrio): preferred (EASL 2024) — seroprotection 68% vs 50% standard
- Post-series anti-HBs q12 months; booster if <10 mIU/mL
- Vaccination before dialysis initiation is superior

HIV / Immunosuppression

- Initiate when CD4 >200/mm³ if possible (better response)
- HepB-CpG or 3-antigen preferred over standard vaccine
- Double-dose (40 µg) standard recombinant if others unavailable
- Post-vaccine anti-HBs monitoring at 4 weeks; revaccinate non-responders

Organ Transplant Candidates

- Vaccinate before listing — preferably before immunosuppression
- Accelerated schedule (0, 1, 2 m + booster at 6–12 m) if time-limited
- If already immunosuppressed: higher-dose or 3-antigen regimen
- Anti-HBc+/anti-HBs– recipients: monitor HBV DNA — risk of reactivation with IS

Chronic Liver Disease (non-HBV)

- All patients with CLD (MASLD, ALD, HCV, AIH, PBC) should be vaccinated
- HBV superinfection dramatically worsens outcomes and triggers decompensation
- Standard schedule; anti-HBs check after series — cirrhotic patients may respond poorly
- Revaccination with 3-antigen preferred in cirrhosis

Healthcare Workers

- Pre-employment HBV vaccination mandatory (OSHA; DOH Philippines Circular)
- Post-series anti-HBs within 1–2 months; document protective response
- Non-responders: repeat 3-dose series; if still <10 mIU/mL → determine HBsAg status
- Percutaneous/mucosal exposure: HBV-DNA source + PEP decision within 24 h

Diabetes Mellitus

- ACIP 2022: vaccinate all diabetics aged 19–59 years (any HepB formulation)
- Age ≥60: clinical judgment based on likelihood of infection / immune response
- Increased HBV transmission risk via shared glucose monitoring equipment
- HepB-CpG preferred: 2-dose, improved immunogenicity vs standard

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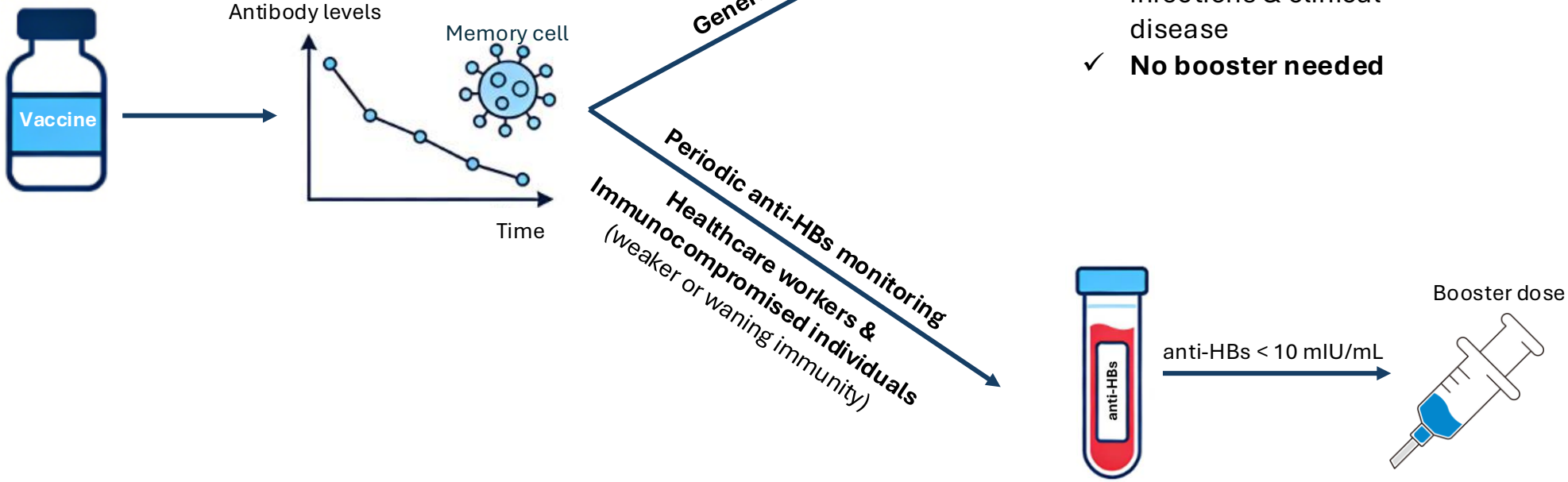
1. Vaccination

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

Rationale



- ✓ **Long-term** protection (≥20 yrs)
- ✓ **Rare** breakthrough infections & clinical disease
- ✓ **No booster needed**

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Do We Need Booster Doses? Waning Immunity Across the Life Course

Current Guideline Positions

CURRENT CONSENSUS: Routine booster doses are NOT recommended for immunocompetent individuals who achieved initial seroprotection (anti-HBs ≥10 mIU/mL). Immunologic memory persists for decades even after anti-HBs becomes undetectable.

Evidence for Immunologic Memory

- Anti-HBs may decline below 10 mIU/mL 10–20 yrs post-vaccination — this does NOT mean loss of protection
- Anamnestic (booster) response persists: rapid anti-HBs rise on exposure
- Long-term follow-up (>20 yrs) in vaccinated adults: no breakthrough infection when primed
- WHY: T-cell and B-cell memory maintained independently of circulating anti-HBs levels

When Boosters ARE Recommended

- Hemodialysis patients: annual anti-HBs; booster if <10 mIU/mL
- HIV/immunosuppressed: annual anti-HBs check; booster as needed
- Organ transplant recipients: post-transplant immunosuppression may ablate immunity — re-test and re-vaccinate
- Healthcare workers: initial post-vaccine anti-HBs; booster only if <10 mIU/mL (one-time recheck if high-risk)

Infant/Adolescent Cohorts in Asia

- WHO 2024: no booster needed for healthy vaccinated children through adolescence
- APASL: studies in Taiwan, China, South Korea confirm sustained protection >20 yrs post-infant series
- Exception: immunocompromised children (HIV, malignancy) — annual anti-HBs monitoring
- Philippines EPI: 3-dose infant series (6, 10, 14 wks) + birth dose = no additional booster

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1. Vaccination

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

Recommendations

1.3.1 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)

1.3.2 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)

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Screening

Speaker: Ming-Lung YU

Date：24 April, 2026

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2. Screening

2.1 Who should be screened and tested for HBV infection?

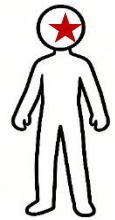
Rationale

Universal screening

- **Highly cost-effective**, even at low prevalence (>0.3%)
- **Essential in Asia-pacific** (prevalence >2%) to meet WHO elimination goals
- Risk-based screening **misses** up to **two-thirds** of infections
- **Benefits**:
  - ✓ Reduces undiagnosed cases, enables early intervention, lowers transmission
  - ✓ Normalizes testing, mitigates stigma, ensures equitable access

Targeted screening (High-risk groups)

- **Population**
  - Patients on immunosuppressive/ immunomodulatory therapy (HBVr)
  - Individuals with coinfections (HCV, HDV, HIV) or other liver diseases
  - People who inject drugs and incarcerated individuals
  - Those with high-risk exposures (sexual, occupational, non-occupational)
- **Benefits**: Enables prophylactic antiviral treatment, and reduces transmission and severe outcomes
- **Maternal screening**
  - Universal screening crucial, ideally in first trimester
  - Prevents mother-to-child transmission (MTCT)
  - Combine maternal antivirals (when indicated) with newborn prophylaxis (vaccine ± HBIG)



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2. Screening

2.1 Who should be screened and tested for HBV infection?

Recommendations

2.1.1 Universal HBV screening should be offered at population level **at least once** in adulthood in endemic regions (≥2% prevalence). (B1)

2.1.2 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%)

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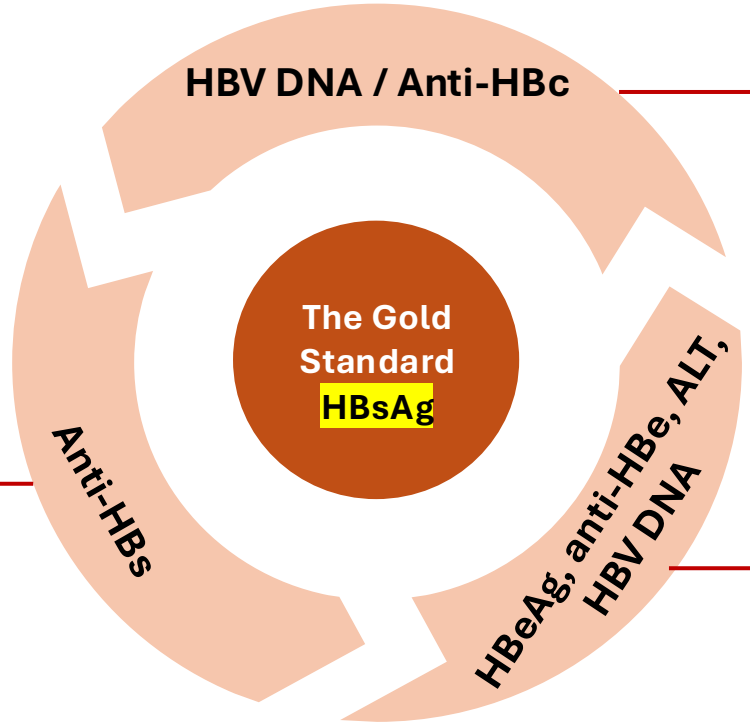
2. Screening

2.2 How to screen HBV infection?

Rationale



IgM: Acute or reactivated infection
IgG: Chronic or resolved infection

Confirm immunity, vaccination status, risk of relapse

Assess disease activity & treatment response

- HBV DNA Quantification: Measures viral replication & Guides treatment eligibility & Limited access
- Implement reflex testing (HBsAg+ → HBV DNA) to accelerate care

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2. Screening

2.2 How to screen HBV infection?

Recommendations

2.2.1 Initial HBV screening should include at least a **screen panel comprising HBsAg** and **total anti-HBc**. (A1)

2.2.2 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)

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Assessment of Liver Fibrosis

Speaker: Yoon Jun KIM

Date：24 April, 2026

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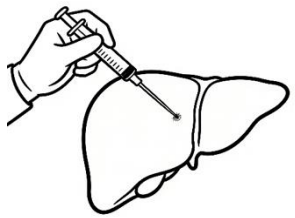
3. Assessment of Liver Fibrosis

3.1 How to assess liver fibrosis?

Rationale

Gold Standard (Biopsy)



- **Assesses inflammation, fibrosis, steatosis, iron overload**
- **Pros**: Accurate disease phase & prognostic information
- **Cons**: Invasive, costly, sampling variability, risk.
- **Advanced fibrosis** possible despite normal ALT / low HBV DNA

First-Line (Non-Invasive Tests)

- Serum biomarkers & Imaging techniques
- **Detects advanced fibrosis / cirrhosis**
- **Pros**: Practical, safe, reliable, repeatable (monitor progression / treatment).
- **Reserve biopsy for**: Uncertain aetiology, discordant NITs, concomitant conditions (e.g., MAFLD, HDV)

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3. Assessment of Liver Fibrosis

3.1 How to assess liver fibrosis?

Recommendations

3.1.1 Liver biopsy is the **gold standard** for diagnosing the extent and severity of **inflammation** and fibrosis in patients with CHB. (A1)

3.1.2 Non-invasive tests are preferred as first-line assessment for detection of severity of **fibrosis** in patients with CHB. (B1)

3.1.3 Liver biopsy should be **individualized** for patients with discordant non-invasive test results, or concomitant aetiologies and/or metabolic comorbidities where the diagnosis may alter treatment decisions and prognosis. (C2)

3.1.4 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)

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3. Assessment of Liver Fibrosis

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

Rationale

First-line: Simple blood-based scores (FIB-4 & APRI)

- **Pros**: Low cost, widely validated
- **FIB-4 cutoffs**:
  - ❑ >1.3: Indicates significant fibrosis (≥F2)
  - ❑ >2.67: Strongly predicts advanced fibrosis/cirrhosis (F3-F4)
  - ❑ Age-adjusted (≥65 yrs): Use >2.0 (significant) & >3.25 (cirrhosis)
- **APRI cutoffs**:
  - ❑ 0.3-0.7: Predicts significant fibrosis (≥F2)
  - ❑ 0.8-1.2: Predicts cirrhosis (F4)
- **WHO 2024 guideline (CHB):** Initiate antiviral therapy if APRI >0.5 (significant fibrosis) or >1 (cirrhosis), regardless of HBV DNA/ALT

Supplementary: Vibration-controlled transient elastography (VCTE)

- **Pro**: More accurate fibrosis assessment
- **Cutoff**: 7.7 kPa for significant fibrosis
- **Limitations**: Higher cost & Infrastructure requirements

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3. Assessment of Liver Fibrosis

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

Recommendations

3.2.1 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)

3.2.2 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)

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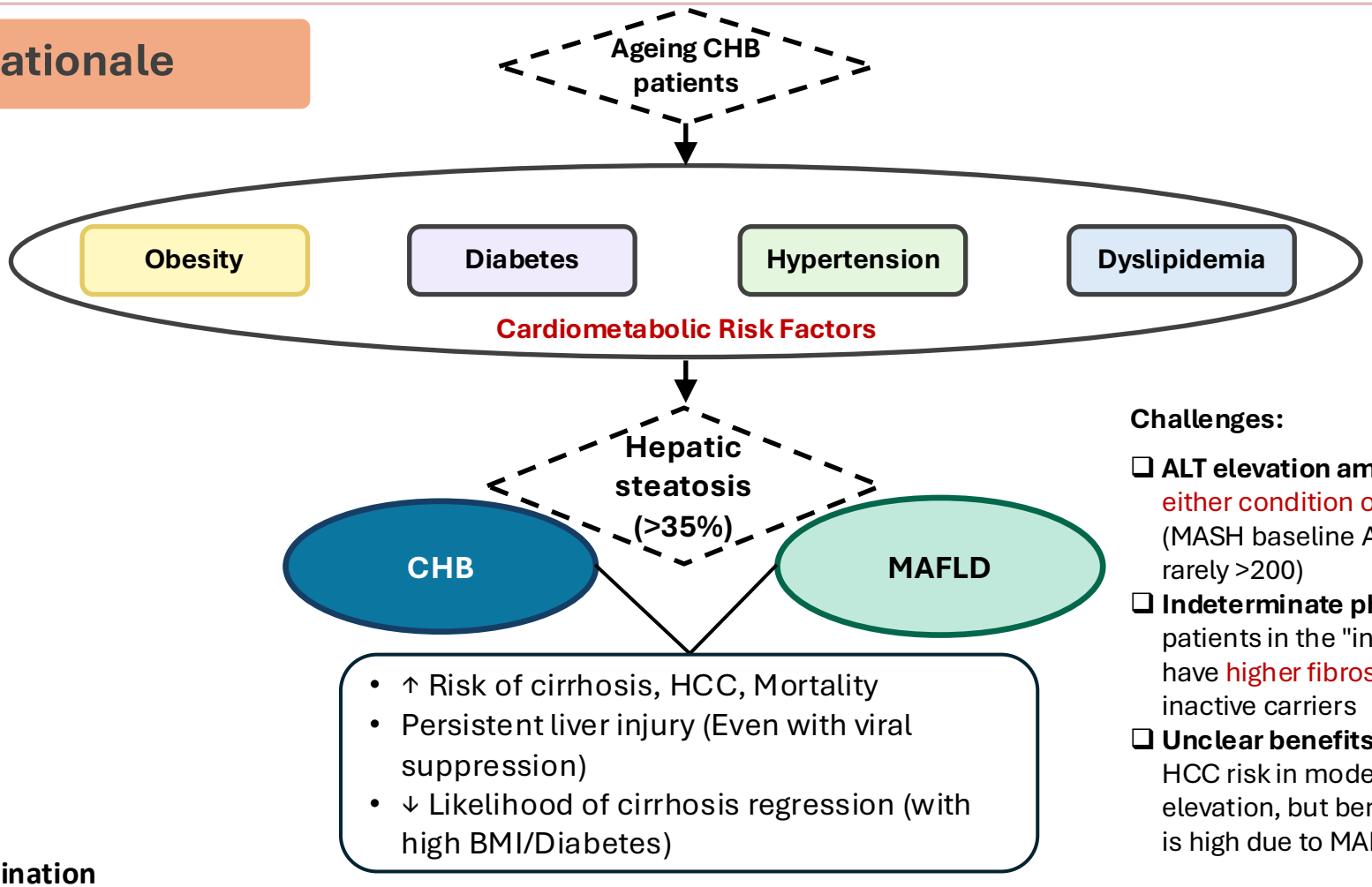
3. Assessment of Liver Fibrosis

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

Rationale



Challenges:

- ❑ **ALT elevation ambiguous**: Reflect either condition or metabolic treatments (MASH baseline ALT is often 40-70 U/L, rarely >200)
- ❑ **Indeterminate phase risk**: CHB patients in the "indeterminate phase" have higher fibrosis / HCC risk than inactive carriers
- ❑ **Unclear benefits**: Antivirals reduce HCC risk in moderate HBV DNA / ALT elevation, but benefits are unclear if ALT is high due to MAFLD / alcohol

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3. Assessment of Liver Fibrosis

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

Recommendations

3.3.1 All CHB patients should be routinely evaluated for **MAFLD**, **its components** (obesity, diabetes, dyslipidaemia, hypertension), and the **degree of hepatic fibrosis** using non-invasive fibrosis assessment tools. (B2)

3.3.2 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)

3.3.3 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)

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Section 2
Treatment

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Treatment Goal

Speaker: Jia-Hong KAO

Date：24 April, 2026

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4. Treatment goals

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

Rationale

Overarching goal
--Reduce global HBV burden

Management strategy
Validated markers (HBV DNA, ALT, HBeAg, qHBsAg)

Key therapeutic goals
Sustained HBV DNA suppression, ALT normalization, HBeAg seroconversion (+), low HBV DNA (<2000 IU/mL) and HBsAg (<1000 IU/mL) (-)

1

Choose regimen (Individualized)
High-resistance barrier NUCs (long-term) or Peg-IFN-α (finite)

2

3

Clinical outcomes
- NUC-induced viral suppression reduces risk (cirrhosis, HCC, complications)
- Early ALT normalization (within first year) improves outcomes

4

Long-term endpoints:
- ❖ **Functional cure**: Sustained HBsAg loss + undetectable HBV DNA (finite therapy)
- ❖ **Partial cure**: Persistently low HBsAg (<100 IU/mL) + normal ALT (non-cirrhotic, HBeAg-negative)

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4. Treatment goals

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

Recommendations

4.1.1 Short-term goals

4.1.1.1 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)

4.1.1.2 In **HBeAg-positive** patients, it is desirable to obtain **HBeAg seroconversion**, as this reflects a favourable therapeutic response. (A1)

4.1.1.3 In **HBeAg-negative** patients, therapy should aim to **maintain virologic suppression** and **persistently normal ALT**. (A1)

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4. Treatment goals

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

Recommendations

4.1.2 Intermediate goals

4.1.2.1 Therapy should **maintain virologic suppression** and **biochemical remission**, which are validated surrogate markers of antiviral efficacy. (A1)

4.1.2.2 Where feasible, therapy may aim for **functional cure**, defined as sustained (≥6 months) HBsAg loss with undetectable HBV DNA after completion of therapy. (A1)

4.1.2.3 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)

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4. Treatment goals

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

Recommendations

4.1.3 Ultimate goals

4.1.3.1 Public health efforts should aim to **reduce the global HBV burden** through vaccination, screening, timely antiviral treatment, and prevention of transmission. (A1)

4.1.3.2 Treatment should **prevent liver-related complications** and ultimately improve survival and quality of life. (A1)

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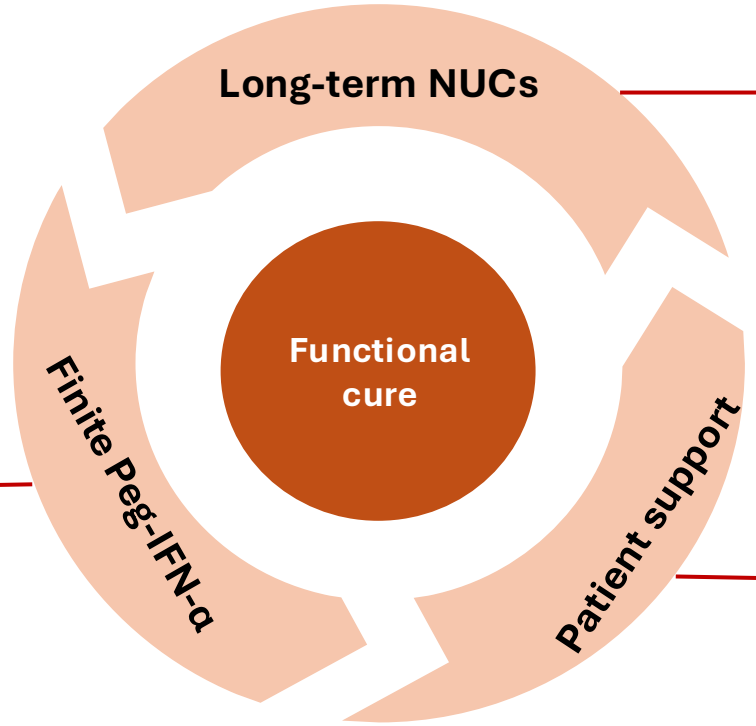
5. Treatment strategies

5.1 How effective are current therapies?

Rationale



NUCs (ETV, TDF, TAF)

- **Efficacy**: Suppress HBV replication, prevent progression
- **Virologic response**: >95% achieve undetectable HBV DNA (HBeAg-)
- **Limitation**: Low annual HBsAg loss
- **TMF**: Comparable efficacy/safety to TAF; effective in elderly decompensated cirrhosis, though limited availability in China

Peg-IFN-α therapy

- **Mechanism**: Only agent inducing HBsAg loss (antiviral & immune-modulatory)
- **Finite duration**: Higher HBsAg clearance (genotype A/B)
- **Predictor**: Response correlates with low baseline HBsAg

Patient management

- **Education**: Language-concordant programs improve monitoring & treatment uptake
- **Adherence**: ~75% adhere to NUCs; poor adherence linked to virologic breakthrough & drug resistance
- **Intervention**: Health education more than doubles adherence rates

Combination strategies (NUCs + Peg-IFN): *Crucial for functional cure*

- Initial combination: Improves HBsAg loss by 15x (RR 15.59)
- IFN Add-on: Improves HBsAg loss by 4.5x (RR 4.52)

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5. Treatment strategies

5.1 How effective are current therapies?

Recommendations

5.1.1 TAF, TDF, TMF*, and ETV are the **first-line** NUCs treatment for CHB. (A1)

5.1.2 For those **without contraindication**# for immune therapy, **Peg-IFN-α** can be considered as a first-line treatment for CHB. (A1)

5.1.3 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)

5.1.4 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: 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.

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Biomarkers guide treatment

Speaker: Alexander THOMPSON

Date：24 April, 2026

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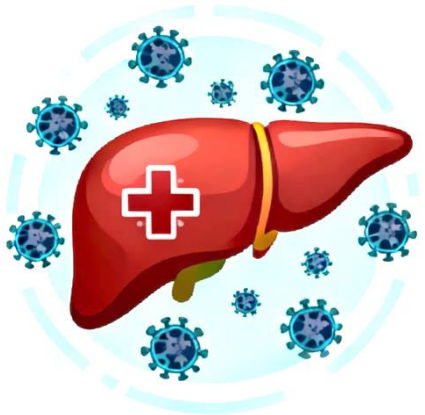
5. Treatment strategies

5.2 What biomarkers should guide treatment?

Rationale



❖ **HBV DNA**
- Key prognostic marker for long-term outcomes (cirrhosis & HCC risk):
  - Risk increases with higher viral load (independent of ALT/HBeAg status)
- ❖ <u>Guiding treatment:</u>
  - HBV DNA suppression is a key treatment end-point
  - HBV DNA rise > 1 log during NA treatment indicates antiviral resistance
  - Limited reduction in HBV DNA = PEGIFN stopping rule

❖ **HBsAg level**
- ❖ <u>Guiding treatment</u>
  - **Peg-IFN-α**: baseline / on-treatment HBsAg level predicts response
  - **NAs**: low end-of-treatment HBsAg level predicts sustained remission after NA-STOP
  - **NOVEL treatments:** low HBsAg level predicts higher response rate (easier to cure)

❖ **Emerging vs. Established biomarkers**
- **Emerging (research tools)**: HBV RNA, HBcrAg, quantitative anti-HBc

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5.2 What biomarkers should guide treatment?

Rationale

PEG-IFN: HBsAg levels can predict response

PEG-IFN monotherapy: On-treatment HBsAg levels

	HBeAg-positive		HBeAg-negative
	Genotype A or D	Genotype B or C	Genotype D
Week 12	No decline of HBsAg	HBsAg >20,000 IU/ml	No decline of HBsAg and HBV DNA decline <2 log
Week 24	HBsAg >20,000 IU/ml	HBsAg >20,000 IU/ml	

No decline / HBsAg > 20,000 = STOPPING rule

Sonneveld MJ, Hansen BE, Piratvisuth T, Jia JD, Zeuzem S, Gane E, et al. Hepatology 2013;58:872–880.
Rijckborst V, Hansen BE, Ferenci P, Brunetto MR, Tabak F, Cakaloglu Y, et al. J Hepatol 2012;56:1006–1011.
Pavlovic V, Yang L, Chan HLK, Hou J, et al. Antivir Ther. 019;24(2):133-140.

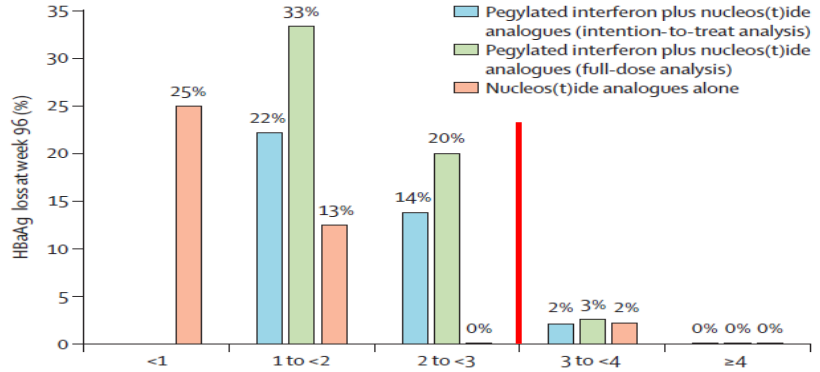
PEG-IFN add-on/switch (NA)

Asian: Baseline HBsAg < 1,500 → HBsAg loss

Baseline HBeAg status	Baseline HBsAg (IU/ml)	Wk 48 HBsAg loss	
		n/N (%)	*p* value†
HBeAg-negative	<1500	4/18 (22.2)	0.0133
	≥1500	0/32	
HBeAg-positive	<1500	2/12 (16.7)	n.s.
	≥1500	1/29 (3.5)	

PEG-IFN add-on (NA)

Caucasian/African: Baseline HBsAg < 1,000 → HBsAg loss



Ning Q, Han M, Sun Y, et al. (OSST trial) J Hepatol. 2014;61:777–784; Wu FP, Yang Y, Li M, et al. World J Gastroenterol. 2020;26:1525–1539; Bourlière M, Rabiega P, Ganne-Carrie N, et al. Lancet Gastroenterol Hepatol

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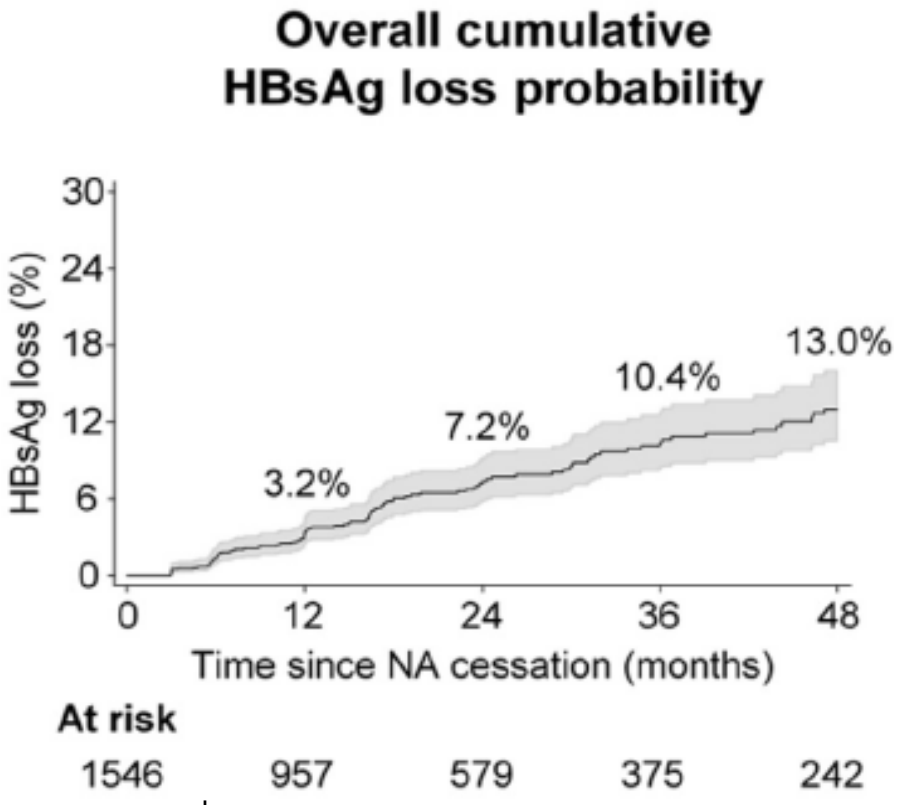
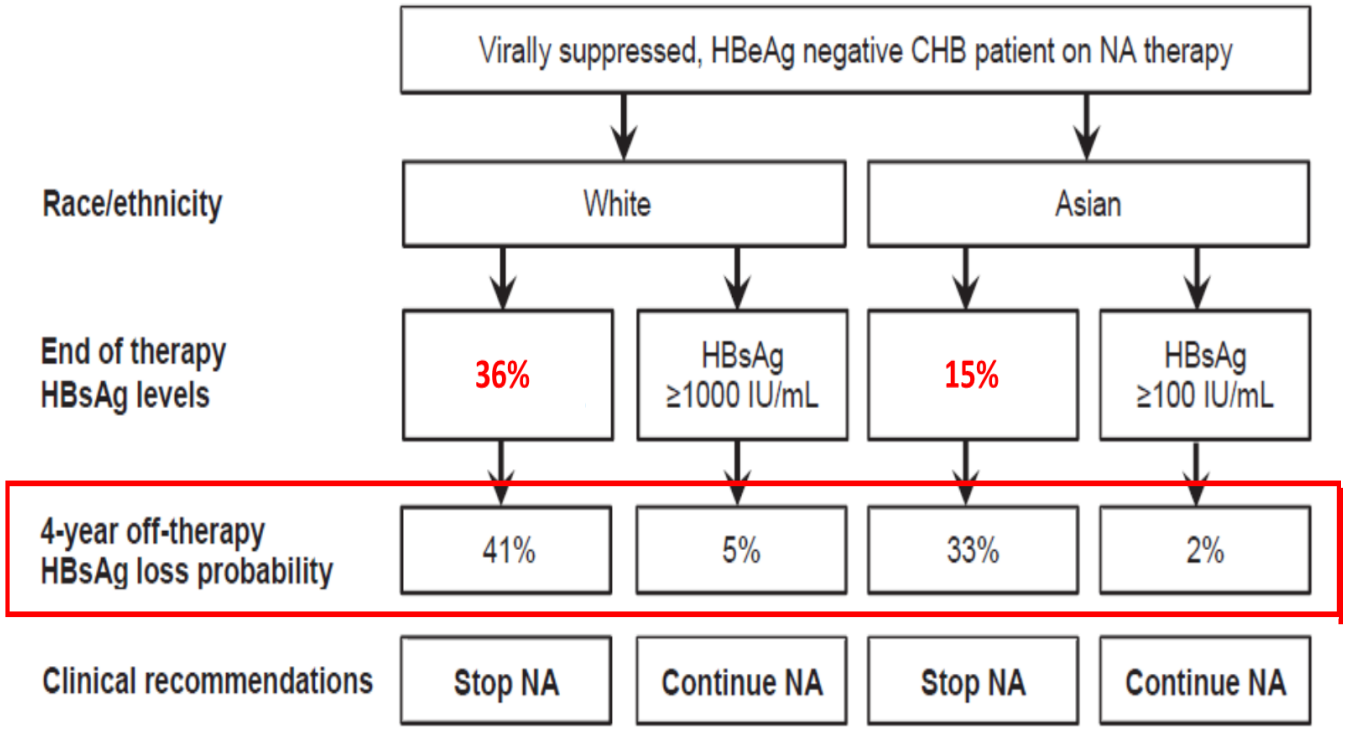
5.2 What biomarkers should guide treatment?

Rationale

Stopping NA in HBeAg-negative patients: End-of-treatment HBsAg levels predict HBsAg loss



*n=231 HBeAg-positive at the time NUC therapy started



Thresholds chosen based on a target for HBsAg loss of > 30%

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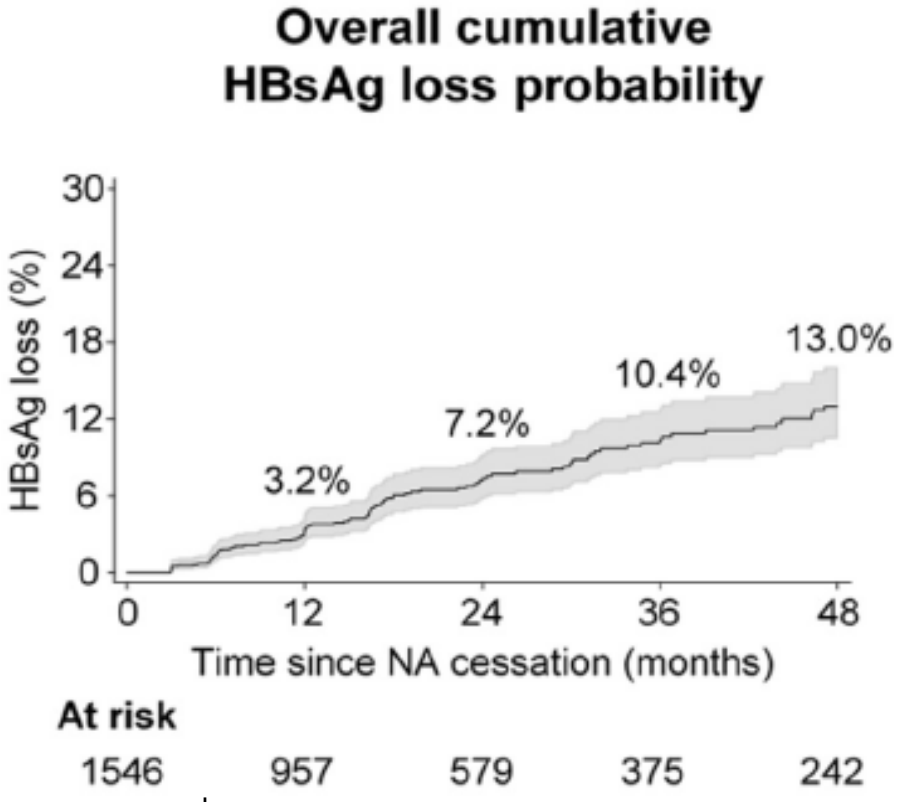
Hirode G (RETRACT-B), Gastro, 2022

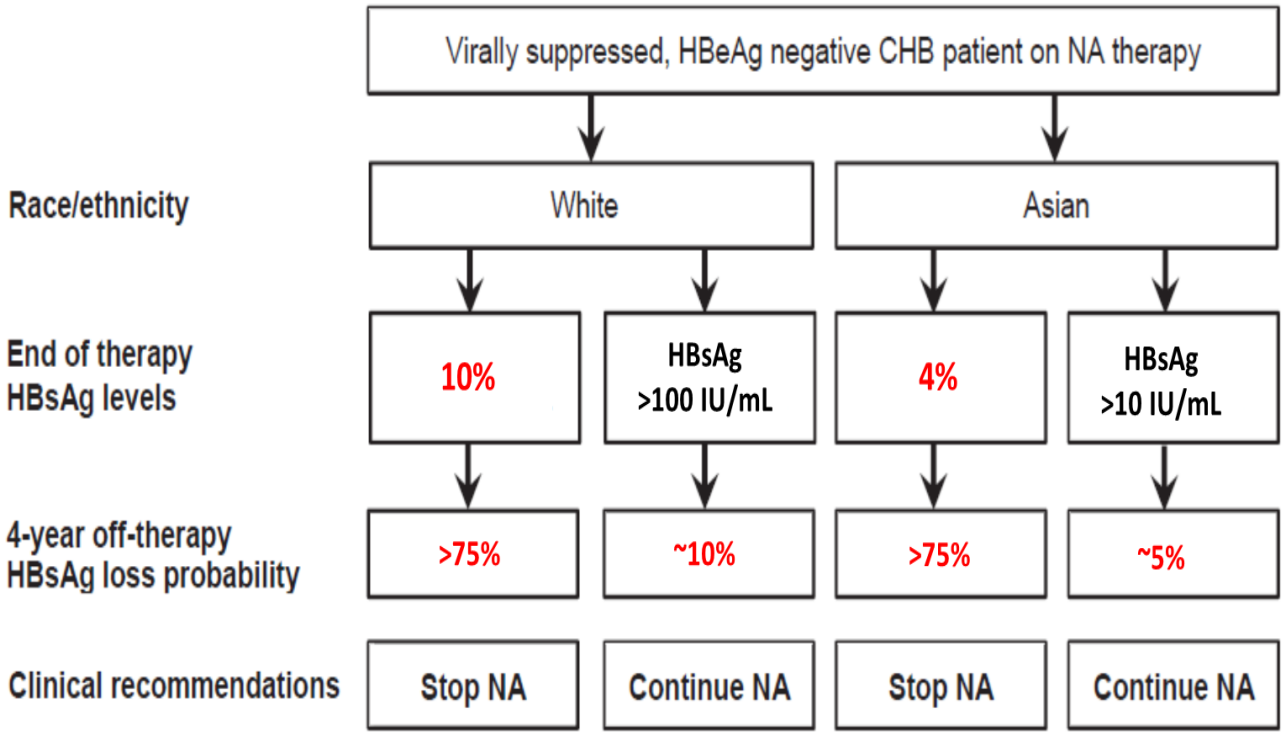
5.2 What biomarkers should guide treatment?

Rationale

Stopping NA in HBeAg-negative patients: End-of-treatment HBsAg levels predict HBsAg loss



*n=231 HBeAg-positive at the time NUC therapy started



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Hirode G (RETRACT-B), Gastro, 2022

5. Treatment strategies

5.2 What biomarkers should guide treatment?

Recommendations

5.2.1 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)

5.2.2 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)

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

5. Treatment strategies

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

Rationale

💰 Economic evidence for "Treat-All"

- Aligns w **WHO 2030 viral elimination goals**
- **Shift toward broader antiviral coverage**
  - E.g. China, Korea, WHO
- Early treatment initiation **reduces HBV-related deaths**
  - Treating lower-risk / minimally active patients is cost-effective in reducing mortality.
  - Treatment reduces transmission (MTCT, horizontal)
- NA treatment may be cheaper than monitoring

➕ Optimal NUC therapy

- **High resistance barrier** NUCs (ETV, TDF, TAF, TMF) provide potent, persistent viral suppression.
- **TDF caution**: Long-term use linked to higher fracture risk vs. ETV
- **TAF advantage**: Similar efficacy to TDF, but superior renal and bone safety → preferred in patients with renal disease, osteoporosis, or older age.

☁ Patient-centered care

- **Shared decision-making** improves adherence, reduces psychosocial burdens.
- Viral suppression can enhance mental well-being:
  - e.g., **SF-36 mental score ↑4.5 points** after 1 year of ETV.
  - Psychosocial improvement alone is not a treatment indication, but it underscores the **broader value of therapy** in improving quality of life and patient-reported outcomes.

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5. Treatment strategies

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

Recommendations

5.3.1 Treatment should be **prioritized** for patients at **highest risk** of disease progression regardless of HBV DNA level or ALT. (A1)

5.3.2 Where resources allow, a **"treat-all" approach** should be adopted, initiating therapy for CHB patients beyond traditional high-risk criteria. (B1)

5.3.3 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)

5.3.4 Shared decision-making should be integrated into treatment planning, incorporating patient preferences, psychosocial factors, and willingness to commit to long-term therapy. (B1)

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Treatment initiation, strategies and cessation

Speaker: Hong YOU

Date：24 April, 2026

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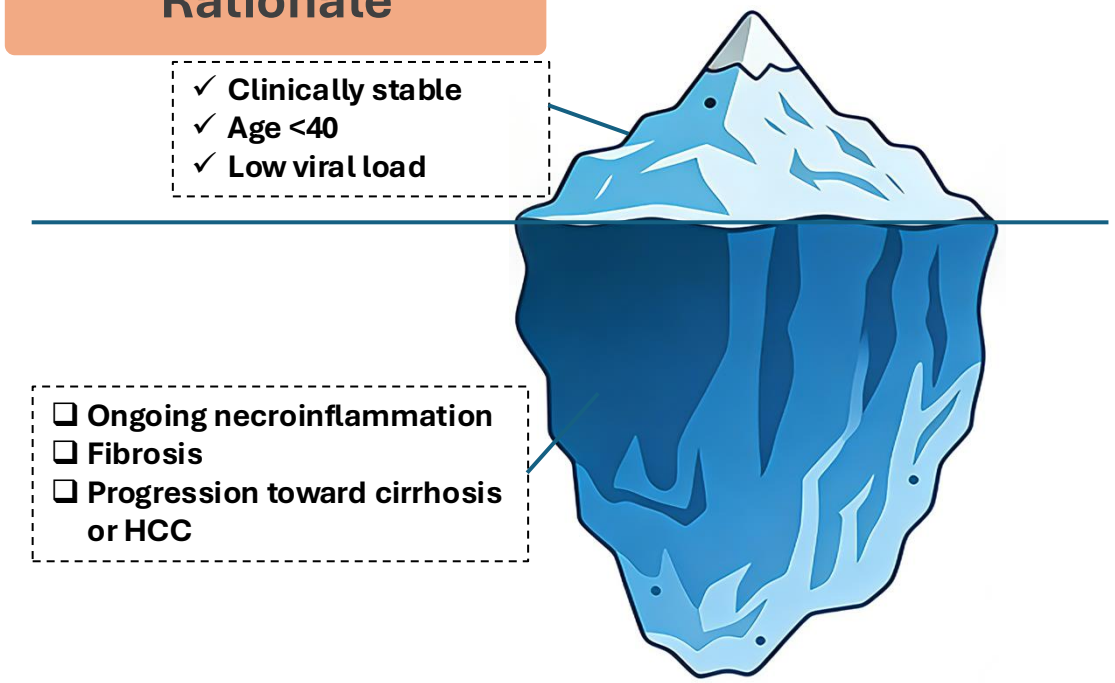
5. Treatment strategies

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

Rationale

- ✓ **Clinically stable**
- ✓ **Age <40**
- ✓ **Low viral load**



- ❑ **Ongoing necroinflammation**
- ❑ **Fibrosis**
- ❑ **Progression toward cirrhosis or HCC**

Why intervene?

- Antiviral response is strong - **early intervention works**
- Peg-IFN-α Therapy: up to 35% HBsAg loss (large Chinese cohort).

Patients with CHB

- HBsAg ≥100 IU/mL (even with DNA <2000) = Higher HCC risk
- HBsAg ≥1000 IU/mL = 3.6-fold greater HCC risk vs. <100 IU/mL
- Low-level viraemia / HBsAg loss: remain at risk (annual HCC ~0.86%)

Solution: "Treat-all"

- NUCs now potent, safe, affordable, and widely available
- **Clinically justified & cost-effective** to treat earlier fibrosis and low viraemia
- **2030 Goal**

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5. Treatment strategies

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

Recommendations

5.4.1 Antiviral therapy should be initiated for chronic HBV infection with **detectable HBV DNA** and **ALT level over ULN (≥ 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)

5.4.2 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)

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5. Treatment strategies

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

Rationale

Sustained HBsAg seroclearance (two occasions ≥6 months apart)

Consider discontinuation (+ & -)

- ❑ **Benefit**: higher HBsAg loss, lower HCC incidence, improved survival
- ❑ **Risk**: virologic relapse (HBV DNA >2000 IU/mL) & ALT flares (rare severe events)

Biomarkers (HBV RNA & HBcrAg) relapse risk stratification prior to discontinuation of NUCs (limited clinical application)

Relapse prevention & Monitoring

Relapse: often within 6-24 weeks post-withdrawal

Consolidation Therapy: Crucial to reduce risk (≥1 yr after HBeAg loss in HBeAg+; ≥3 yrs after undetectable DNA in HBeAg-)

Monitoring: HBV DNA and ALT monthly for 6 months, then quarterly, then biannually

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5. Treatment strategies

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

Recommendations

5.5.1 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)

5.5.2 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)

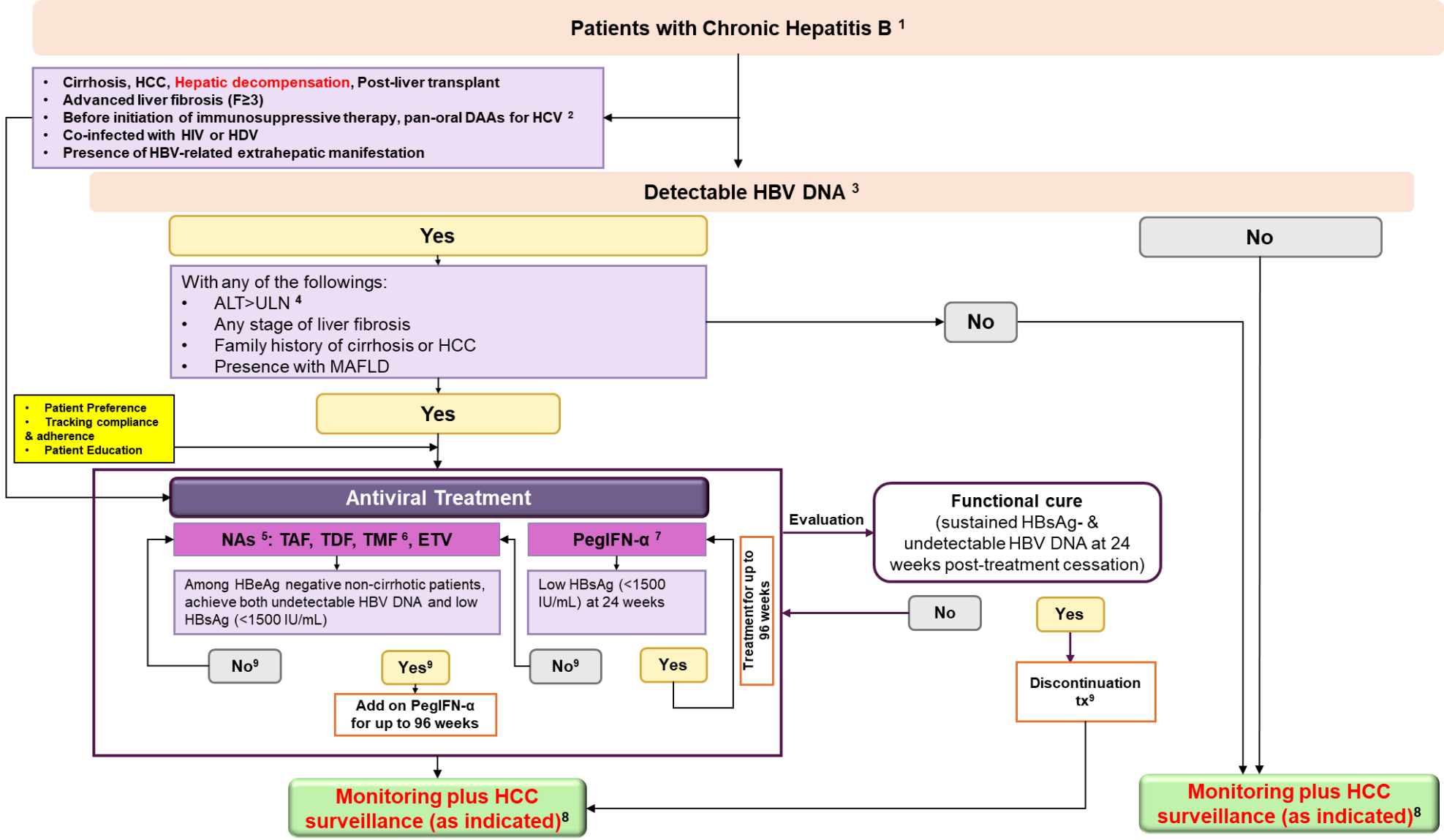
5.5.3 For both **HBeAg-positive and HBeAg-negative cirrhotic** patients, discontinuation of NUCs therapy is **not** recommended. (A2)

5.5.4 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

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

Treatment Algorithm

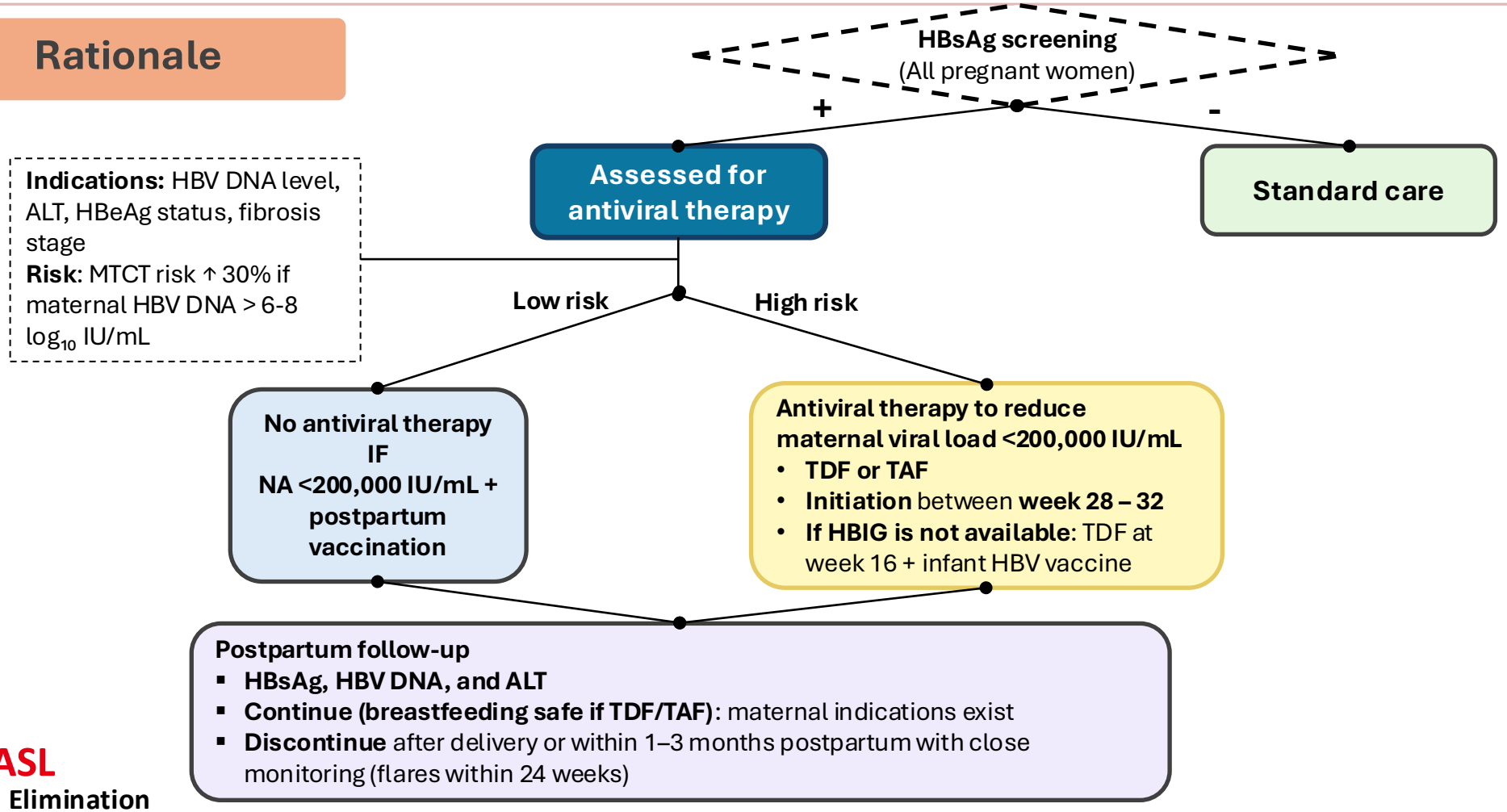


1. HBsAg+ for 6 months
2. Refer to APASL reactivation management guideline 2022
3. Sensitive NAT assay (lower limit of detection <20 IU/L).
4. ULN: 40 IU/L
5. The selection of NAs should be individualized based on long-term safety and patient comorbidities. TAF and ETV are preferred in patients with 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.

6. In special populations

6.1 How to manage HBV in pregnant women?

Rationale



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6. In special populations

6.1 How to manage HBV in pregnant women?

Recommendations

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

6.1.2 Pregnant women who test **positive HBsAg** should be assessed for **antiviral therapy** according to standard CHB indications. (A1)

6.1.3 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)

6.1.4 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. Counselling and appropriate management should be provided to reduce the risk of transmission to sexual partners and in future pregnancies.(B1)

6.1.5 Breastfeeding is **safe** while the mother is on antiviral therapy with tenofovir (TDF or TAF). (A1)

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In MAFLD population

Speaker: Shang-Chin Huang

Date：24 April, 2026

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6. In special populations

6.2 How to manage HBV in patients with metabolic comorbidities?

Rationale

Impact of MAFLD on CHB

Early studies:

MAFLD → accelerated fibrosis & HCC

Recent studies:

Simple steatosis may be protective (HBsAg seroclearance ↑)

Metabolic dysfunctions (Diabetes, Obesity, Hypertension) → dose-dependent increases (cirrhosis, HCC, mortality)

Diabetes (poor glycemic control) is the strongest risk

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6. In special populations

6.2 How to manage HBV in patients with metabolic comorbidities?

Rationale

Children

- **MAFLD is increasingly common**
- **MAFLD is primarily linked to metabolic risk factors**
- **Higher HBsAg loss** during therapy in MAFLD kids

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6. In special populations

6.2 How to manage HBV in patients with metabolic comorbidities?

Rationale

Management

Cornerstone: lifestyle intervention (diet & exercise)

Adjuncts for those with diabetes: pharmacologic agents

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6. In special populations

6.2 How to manage HBV in patients with metabolic comorbidities?

Recommendations

6.2.1 Optimal glycemic control should be offered in CHB patients with **concurrent diabetes** in collaboration with endocrinologists or primary care teams. (A1)

6.2.2 Lifestyle interventions are recommended for CHB patients with **modifiable metabolic comorbidities**. (A1)

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In coinfection population

Speaker: Jian SUN

Date：24 April, 2026

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6. In special populations

6.3 How to manage HBV in patients with coinfections (HDV/HCV/HIV)? -- In HIV coinfected patients

Rationale

Epidemiology:
- 39 million people living with HIV in 2023.
- 8.4% HBV coinfection globally; 9.8% in Asia-Pacific.
- Increased risks of cirrhosis and HCC → prompt ART initiation unless contraindicated, regardless of ALT, HBV DNA, CD4

Peg-IFN-α not recommended (limited efficacy/tolerability)

Treatment:
- **Must include** two anti-HBV agents: **TAF/TDF + lamivudine/emtricitabine**
- **TAF** preferred in **renal/bone disease:** Switching from TDF to TAF maintains suppression with reduced toxicity
- **Avoid lamivudine/emtricitabine-only regimens** (risk of HBV resistance).
- If TDF/TAF contraindicated, add **entecavir** to fully suppressive ART with close monitoring.

Monitoring:
- Monitor for **hepatic flares** due to IRIS in low CD4 patients; may coincide with HBsAg loss
- **Sustained HBV suppression** via optimized ART adherence crucial to prevent liver complications (including HCC)

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6. In special populations

6.3 How to manage HBV in patients with coinfections (HDV/HCV/HIV)?
-- In HIV coinfected patients

Recommendations

6.3.1 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)

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6. In special populations

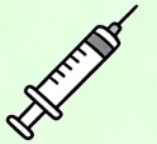
6.3 How to manage HBV in patients with coinfections (HDV/HCV/HIV)?
-- In HDV coinfected patients

Rationale

Epidemiology & diagnosis

Global burden: 12–60 million infected
Prevalence: 4.5–13% in HBsAg+ individuals
Active infection: Confirmed by HDV RNA
NITs: Elastography, APRI, FIB-4 (supportive)
Liver biopsy: If NITs inconclusive or to guide treatment

Established therapy (Peg-IFN-α)



Established therapy: Peg-IFN-α 180 μg (up to 96 weeks)
Response: 29% virological response (24-week post-treatment)

Emerging therapy (Bulevirtide)

Dose: 2–10 mg daily
Week-96 outcomes: 50% HDV RNA response; ALT normalization; improved liver stiffness
Long-term therapy: Needed (high relapse risk after stopping)
Challenges: High cost, limited global availability (especially LMICs)
Combination with Peg-IFN-α: Enhanced suppression (emerging evidence, no finite stopping strategy)

Special Populations & Monitoring

Decompensated cirrhosis:
- No approved treatment
- Peg-IFN-α contraindicated
- BLV data limited

NUCs: Continue in HBV replication or cirrhosis
Monitoring essentials (regardless of therapy): HDV RNA, HBV DNA, ALT synthetic function, imaging

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6. In special populations

6.3 How to manage HBV in patients with coinfections (HDV/HCV/HIV)?
-- In HDV coinfected patients

Recommendations

6.3.2 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)

6.3.3 Patients with **decompensated cirrhosis** should be evaluated for **liver transplantation**. (A1)

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6. In special populations

6.3 How to manage HBV in patients with coinfections (HDV/HCV/HIV)?
-- In HCV coinfected patients

Rationale

- **Higher risks**: Coinfected patients have increased risks of liver-related death and HCC vs. monoinfection.
- **DAA therapy**: Recommended for all HBV/HCV coinfected patients; efficacy similar to HCV monoinfection.
- **HBV reactivation**: Occurs in 5.9–24% during DAA treatment (hepatitis flares in 1.9–9%).
- **Prophylactic NUCs**: Reduces reactivation risk, especially in cirrhosis.
- **Low-risk group** ($HBsAg^-$/anti-HBc^+): Reactivation risk <2%; monitor ALT, start NUCs if clinically indicated.

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6. In special populations

6.3 How to manage HBV in patients with coinfections (HDV/HCV/HIV)?
-- In HCV coinfected patients

Recommendations

6.3.4 Patients with **HBV/HCV coinfection** should receive **anti-HCV treatment with DAAs**. (A1)

6.3.5 For **HBsAg-positive** patients, **prophylactic NUCs treatment** is recommended before initiation of DAA treatment. (A1)

6.3.6 For **HBsAg-negative but anti-HBc-positive** patients, **close monitoring** of ALT, HBV DNA and HBsAg is required during DAA treatment. (A1)

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In ALD population

Speaker: Tatsuo KANDA

Date：24 April, 2026

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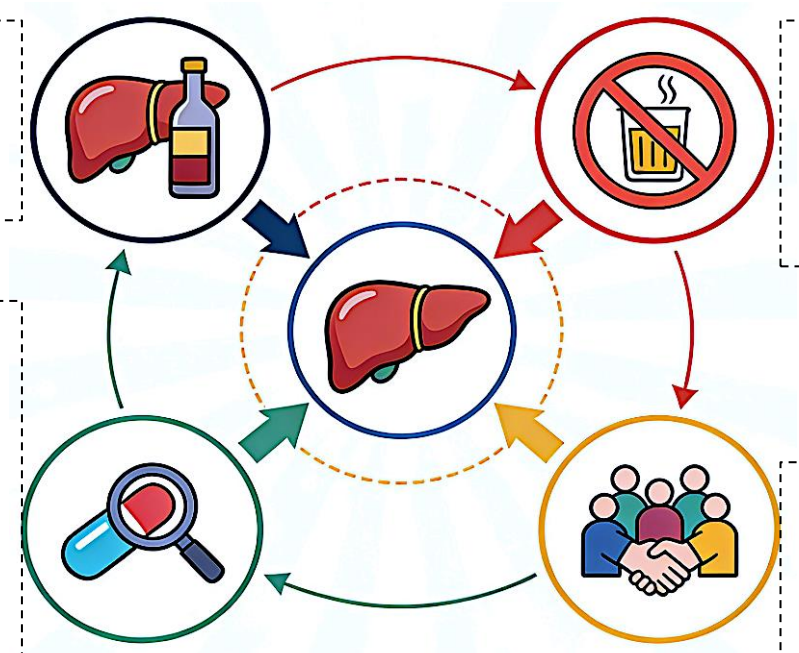
6. In special populations

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

Rationale

- **CHB + excess alcohol →** accelerates cirrhosis & HCC
- **↑ oxidative stress, liver injury**
- **↓ antiviral efficacy & adherence**



- **Complete abstinence**
- **Supported by:**
  - · Psychosocial interventions
  - · Pharmacologic interventions (to maintain sobriety)

- **Antiviral therapy**
  - · Potent NUCs → sustained viral suppression
  - · Interferon is contraindicated
  - · Long-term (often infinite) NUCs therapy recommended
- **Monitoring:** HBV DNA, liver & renal function, alcohol intake, HCC surveillance

- **Multidisciplinary care:** hepatology, addiction, nutrition, psychosocial support
- **Goals:** optimize adherence; reinforce abstinence; improve outcomes

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

Rationale

Complete abstinence is essential, supported by psychosocial and pharmacologic interventions to maintain sobriety.

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You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

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

Rationale Alcohol seems to enhance HBV replication

- Heavy alcohol drinking prolongs seroconversion from HBeAg. The prevalence curves tended to be higher and decrease more slowly in heavy drinkers than in the nondrinkers (Nomura H, et al. Fukuoka Igaku Zasshi. 1996).
- A single one-week period of social drinking in patients with chronic HBV infection does not cause enhanced viral replication (Novick DM, et al. Alcohol Clin Exp Res. 1987).
- Exposure of HepG2.2.15 cells to an acetaldehyde-generating system (AGS) increased HBV RNA, HBV DNA, and cccDNA expressions and suppressed the activation of ISGs, APOBEC3G, ISG15, and OAS1. Ethanol disrupts the protective crosstalk between macrophages and HBV-infected hepatocytes (Ganesan M,et al. Biomolecules. 2025)
- Ethanol enhances transcriptional activity of HBV promoters in human hepatoma cells in an oxidative stress-independent manner; and CYP2E1-mediated oxidative stress potentiates the ethanol-induced transactivation of HBV (Min BY, et al. Biochem Biophys Res Commun. 2013).

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

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

Rationale

Excess intake of alcohol seems to enhance liver fibrosis and HCC

- Ethanol intake >30 g/day is the most important and evitable risk factor for cirrhosis and death in patients with chronic HBV infection (Bellentani S, et al. Dig Dis. 2010).
- The proportions of patients with Child Pugh grade C (28.0% vs 18.8%, P < 0.001) or MELD greater than 18 (24.1% vs 18.5%, P < 0.001) in the ALD + HBV group exceeded significantly those in the HBV group (Abassa KK, et al. BMC Gastroenterol. 2022).
- Heavy alcohol intake and ALDH2 rs671 polymorphism are associated with significantly increased risk of HCC development and mortality in patients with HBV-related cirrhosis (Tsai MC, et al. JAMA Netw Open. 2022).
- The significant synergy between heavy alcohol consumption, hepatitis virus infection, and diabetes mellitus may suggest a common pathway for hepatocarcinogenesis (Hassan MM, et al. Hepatology. 2002).

You H, Maiwall R, Chen J et al. Hepatology International 2026 (in press)

6. In special populations

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

Recommendations

6.4.1 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)

6.4.2 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)

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6. In special populations

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

Rationale

Antiviral therapy (foundation)

Preferred (safe & effective): ETV, TAF (renal/bone safety), TDF.
Benefits: Improves MELD & child-Pugh scores, reduces HCC risk, enables recompensation (>80% transplant-free survival)
NOT Recommended: Lamivudine, Adefovir, Peg-IFN
Rule: Indefinite therapy; adjust dose for renal function

Supportive care & Monitoring

Standard management: Ascites, variceal bleeding, encephalopathy, hepatorenal syndrome
Surveillance: HCC screening every 6 months

Transplantation

Pre-transplant: HBV DNA suppression, nutrition optimization, complication
Post-transplant:
High risk: HBIG + NUCs.
Low risk: monotherapy (TAF / ETV)
HBcAb+ donor: prophylaxis (naïve)

Immunosuppressed / Coinfections (HIV, HDV, HCV):
- ☐ **Require prophylactic or tailored therapy**
- ☐ **HBV/HIV: Tenofovir-based regimens preferred**

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6. In special populations

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

Recommendations

6.5.1 Antiviral therapy should be initiated in **all decompensated cirrhosis** regardless of ALT or HBeAg status. (A1)

6.5.2 TAF, TDF, or ETV are first-line treatment, with preference for **TAF** over TDF due to **better renal/bone safety**. (A1)

6.5.3 Treatment must be continued **infinitely** in those with **decompensation or prior HCC**; discontinuation is not recommended. (A1)

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7. Prevention of Hepatitis B Reactivation related to the use of immunosuppressive therapy

Recommendations

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

Lau G, Yu ML, Wong G, et al. APASL clinical practice guideline on hepatitis B reactivation related to the use of immunosuppressive therapy. *Hepatol Int* 2021; **15**(5): 1031-48.

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Section 3
HCC Surveillance

Speaker: Terry YIP

Date：24 April, 2026

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8. Risk prediction

8.1 How do risk prediction models best guide HCC surveillance?

Rationale

01 Early models

- REACH-B, GAG-HCC, CU-HCC (untreated cohorts)
- Useful for identifying **treatment-naïve** patients who may benefit from **antiviral therapy**.

02 Treated population

- **Most validated**: PAGE-B, mPAGE-B (for Asians)
- Based on **age, sex, platelet count** (±albumin)
- REACH-B, GAG-HCC, CU-HCC (untreated cohorts)
- Useful for identifying at-risk **treated** patients who may benefit from **HCC surveillance**.

03 New models

- **Value for non-cirrhotic patients**: refine surveillance beyond standard age thresholds (>40 yrs in men, >50 yrs in women)
- **Newer models** (CAMD, REAL-B) incorporate **metabolic factors** for improved risk discrimination
- **Challenge**: ↓ Accuracy after 5 years of antiviral therapy

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8. Risk prediction

8.1 How do risk prediction models best guide HCC surveillance?

Recommendations

8.1.1 HCC risk scores which integrate age, fibrosis severity, and sex can identify at-risk patients on NUCs eligible for HCC surveillance. (A1)

8.1.2 Patients on NUCs with **intermediate-to-high HCC risk** (PAGE-B ≥10 and/or mPAGE-B ≥9) should receive HCC surveillance. (B1)

8.1.3 Interpretation of HCC risk scores should be approached with caution in patients with **prolonged treatment duration** (over 5 years) or those with **diabetes**. (B2)

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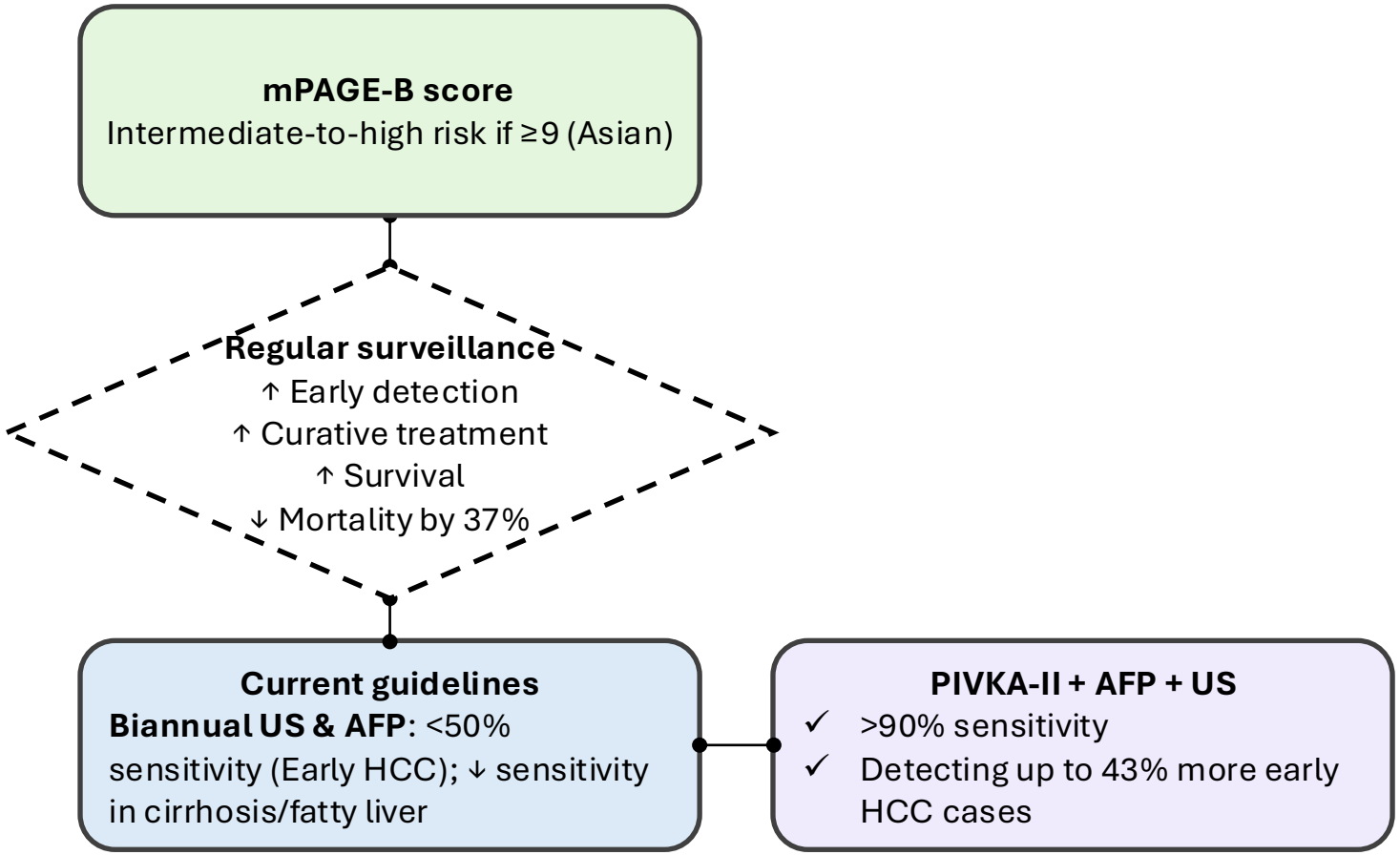
9. Surveillance strategies

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

Rationale



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9. Surveillance strategies

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

Recommendations

9.1.1 AFP and US examinations are recommended **every 6 months**. (A1)

9.1.2 Combined testing with AFP, US and PIVKA-II is recommended to improve early detection accuracy. (B1)

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9. Surveillance strategies

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

Rationale

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

Recommendations

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

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Section 4
Prevention of Transmission

Speaker: Fu-Sheng WANG

Date：24 April, 2026

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10. Prevention of Mother-to-Child-Transmission

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

Please refer to recommendation 1.2.2.

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11. Prevention of transmission in other populations

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

Rationale

Category

General population

- Vaccination is the **primary and most effective** strategy for preventing horizontal HBV transmission.
- NUCs therapy can reduce transmission risk but offers **minimal additional benefit** over vaccination.
- **Routine prophylactic NUCs** for transmission prevention in general population is **unnecessary**.

HBV-infected HCPs performing EPPs

- **Risk** of transmitting HBV to patients during EPPs is **low**.
- **Lower risk** if HCP is **HBeAg-negative** or has **low HBV DNA**.
- Guidelines (CDC) recommend **HBV DNA <1000 IU/mL** for HCPs performing EPPs.
- **NUCs suppression** (to undetectable levels) further minimizes transmission risk.

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

Recommendations

11.1.1 Routine prophylactic use of NUCs **solely** for preventing horizontal transmission is **not recommended** when hepatitis B vaccination is available. (C2)

11.1.2 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)

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11. Prevention of transmission in other populations

11.2 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?

Rationale

Family-based HBV screening

High-risk groups & transmission

- ✓ Close contact
- ✓ Sexual exposure
- ✓ Perinatal transmission

Proven impact

- Increases case detection & vaccination uptake
- Reduces household transmission
- Evidence certainty: Moderate

1

2

3

Why screen families?

- **Early detection**: Find undiagnosed cases for monitoring/treatment
- **Immediate protection**: Vaccinate susceptible contacts to block further spread

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11. Prevention of transmission in other populations

11.2 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?

Recommendations

11.2.1 Screening should be conducted for **all household and sexual contacts** of individuals with chronic HBV infection. (B1)

11.2.2 Screening should include **HBsAg, anti-HBs, and anti-HBc** to identify current infection, immunity, or susceptibility. (B1)

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Section 5
Open Questions

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12. Service Delivery Model

Speaker: Saeed HAMID

Date：24 April, 2026

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12.1 How can stigma in occupational settings be addressed?

Causes of stigma

(1) **Misinformation** about transmission
(2) **Moral judgments** linking HBV to "immoral" behaviors
(3) **Fear** of disease progression
(4) **Systemic/cultural** discrimination legacies

Impact of stigma

- **Undermines** workers' **rights**
- Leads to **discrimination**, **job loss**, and **psychological distress**
- Perpetuates public health **inequities**

Workplace interventions

- Clear **policies**, **education**, and **legal safeguards**
- Confidentiality and employee **support systems** to reduce fear
- **Education programs** to correct misconceptions and foster inclusion
- **Legal protections** to ensure fair treatment and prevent discrimination

Outcome

- Safe, inclusive **work environments**
- Employees judged by **performance**, not health status
- Promotes **individual well-being** and organizational **equity**

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12.1 How can stigma in occupational settings be addressed?

Management statement

12.1.1 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.

12.1.2 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.

12.1.3 People living with hepatitis B should be given same status and rights as any other citizen of the world.

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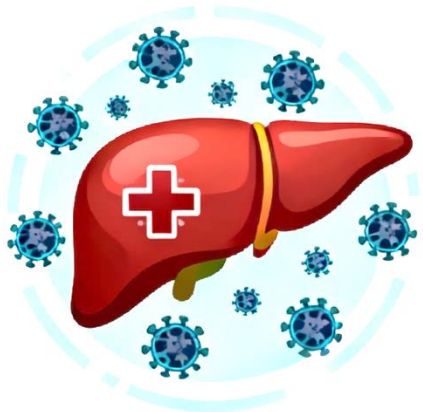
12.2 What are optimal models of care to enhance access to screening and linkage to treatment?



- **Decentralized care models:** Primary care & community-based approaches increase testing, reduce missed cases, and are cost-effective.
- **Simplified diagnostics:** Point-of-care testing, reflex testing, and mobile tools reduce delays and follow-up losses.
- **Structured referral pathways:** Ensure specialist oversight for complex cases.
- **Affordable treatment & adherence:** Use of low-cost antivirals, peer support, and reminders for long-term viral suppression.
- **Integrated strategies:** Combine vaccination, MTCT prevention, blood safety, workforce training, and community engagement.
- **Equity & stigma reduction:** Community involvement promotes fairness and reduces discrimination.
- **Goal:** Accelerate HBV elimination by 2030 without compromising care outcomes.

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

Management statement

12.2.1 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.

12.2.2 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.

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13. Functional Cure

Speaker: Lai WEI

Date：24 April, 2026

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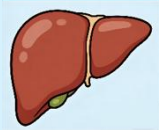
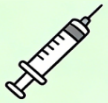
13.1 What is the role of functional cure as a therapeutic endpoint in the management of chronic hepatitis B?

The Goal: functional cure



Definition: Functional cure is the primary therapeutic endpoint in CHB.
Hallmark: HBsAg loss (durable restoration of immune control)
Clinical benefits:

- Regression of liver fibrosis
- Reduced risk of cirrhosis, decompensation, and transplantation
- Reduces new infections & improves patients' quality of life



The reality: limitations of novel agents

Current outcomes: New investigational agents show limited & not sustained responses.
Key uncertainties:

- Durability differs from spontaneous/traditional therapy.
- Unknown optimal dosing & host immunity restoration.

Guidance for use: Not ready for broad clinical use (only in well-controlled trials)
Clinical trial design:

- Phase II: Endpoints based on drug mechanism
- Phase III: Primary endpoint: Sustained HBsAg loss + undetectable HBV DNA (24 weeks post-treatment)
- Safety: Monitor immune flares & hepatic events

Regional focus: barriers in asia-pacific

Persistent gaps:

- Prevention & Diagnostics
- Variable access to treatments
- Financial constraints

Social barriers:

- Limited public awareness
- Stigma
- Fragmented health-system coordination

Solution: Multisectoral efforts required to maximize impact of cure strategies.

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

Management statement

13.1.1 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**.

13.1.2 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.

13.1.3 Partial cure can be considered an **intermediate therapeutic endpoint**, defined as HBsAg <100 IU/mL with undetectable HBV DNA.

13.1.4 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.

13.1.5 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.

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14. Future directions

Speaker: Rakhi MAIWALL

Date：24 April, 2026

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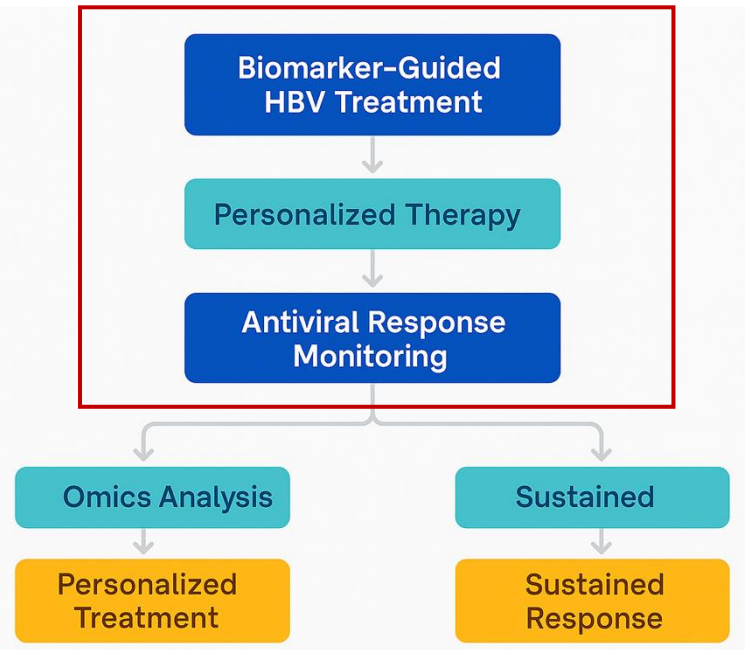
Biomarker-Guided HBV Management

Toward Personalized Treatment

- Future HBV management will emphasize **personalized therapy** guided by viral and host biomarkers.
- Key viral markers: **HBV RNA, HBcrAg, quantitative HBsAg**
  - Reflect **intrahepatic cccDNA activity**
  - Enable **precise monitoring** of antiviral response
- **Equitable access** to biomarker testing is crucial, especially in low- and middle-income countries.



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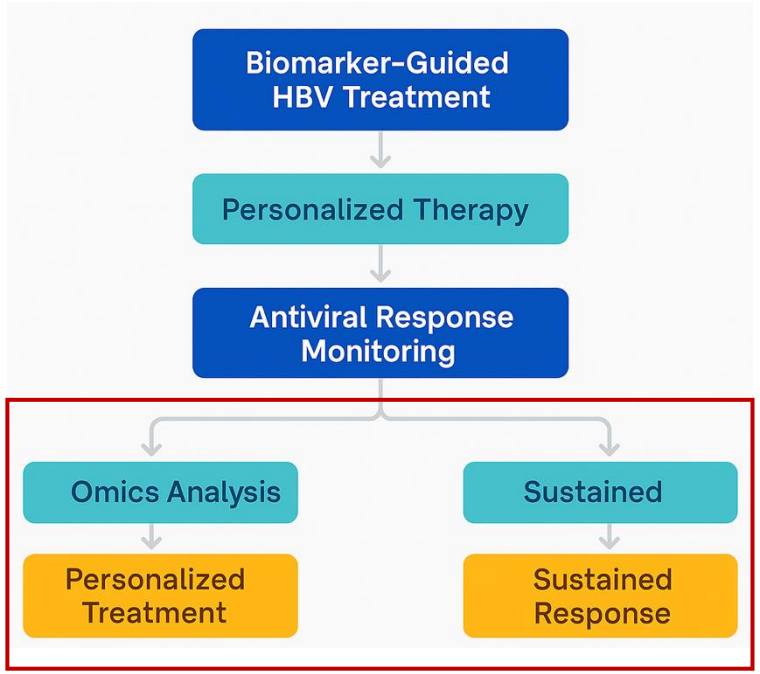
Biomarker-Guided HBV Management

Integrated Viral–Host Biomarkers

- Emerging immunological and molecular markers may predict **sustained off-treatment responses**.
- Assessment of HBV-specific $CD4^+$/$CD8^+$ T-cell activity and immune profiles (**peripheral vs intrahepatic**).
- Advanced **omics** (cytokine profiling, proteomics, metabolomics):
  - **Predict response** to NAs or interferon
  - Identify candidates for **curative regimens** targeting HBsAg clearance and HCC prevention.



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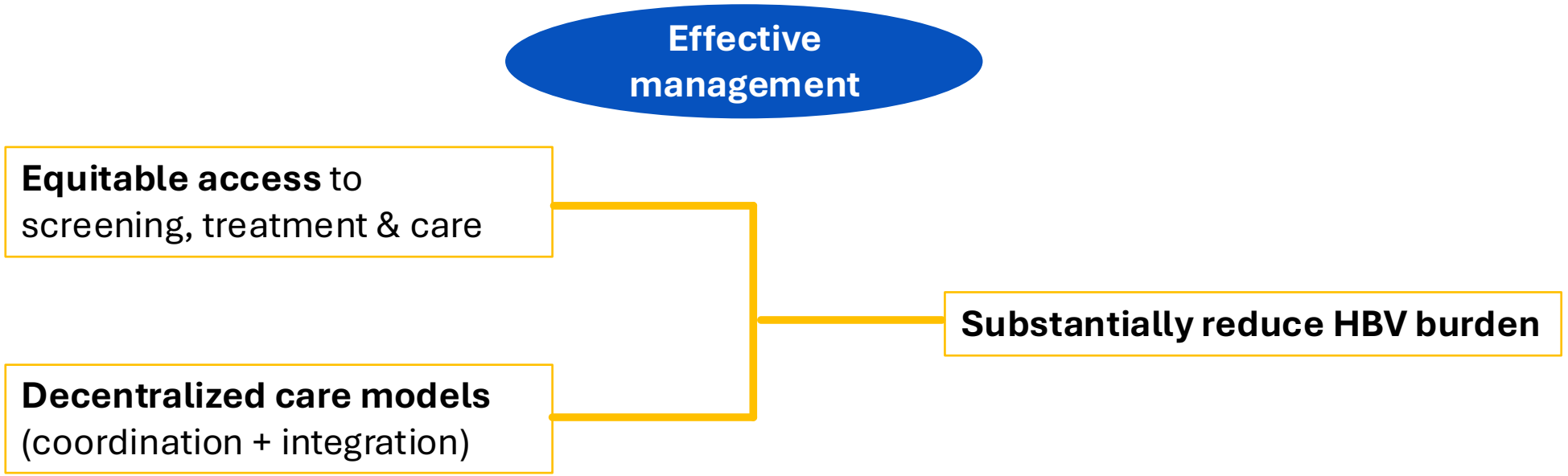
Biomarker-Guided HBV Management



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Future directions

Transformative Role of AI

1 Transformative Role of AI

- AI (ML, DL, predictive analytics enances diagnosis, prognosis, and treatment opfirimization in CHB.
- Enables **individualized care** by integrating large-scale, miмidimensional data

2 Clinical Applications

Prediction

ML/DL models outperform PAGE-8 and REACH-B to fibrosis, cirrhosis, and HCC

Risk Stratification

AI algorithms **identıfty rapid progressors**, guide **surveillancnce intervals**, and optimize treatment timing

3 Molecular & Population-Level Insights

- **Molecular integration:** Multi-omics (genomic, transcriptomic, proteomic) +viral markers (HBsAg, HBy RNA. HBcrAg) to predict **treatment response** and **functional cure potentra**.
- **Population analytics:** EHRs, surveillance systems, and registries +enable **real-world** evaluation of care cascades, adherence, and resource allocation

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Future directions

Transformative Role of AI

4 AI-Driven Decision Support

- **Clinical Decision-Support Systems** (CDSS): Assist in treatment initiation, fibrosis estimation, drug interaction alerts, and linkage to care.
- **Federated learning:** Supports global model development while preserving patient privacy.

5 Future Directions

- **Explainable AI (XAI)** to bulid clinician trust
- **Integration of multi-modal biomarkers** for predicting off-treatment responses
- **Continuous learning systems** using real-world data for adaptive

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APASL 2026

35TH ANNUAL MEETING OF THE ASIAN PACIFIC ASSOCIATION FOR THE STUDY OF THE LIVER

22-25 April 2026

İstanbul Lütfi Kırdar International Convention and Exhibition Centre

HBV Consensus: APASL CHB CPG GUIDELINES - A 2026 UPDATE

DATE: FRIDAY, 24 APRIL 2026

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