Management of HBV Infection in Primary Care Settings

Witsarut Manasirisuk, MD

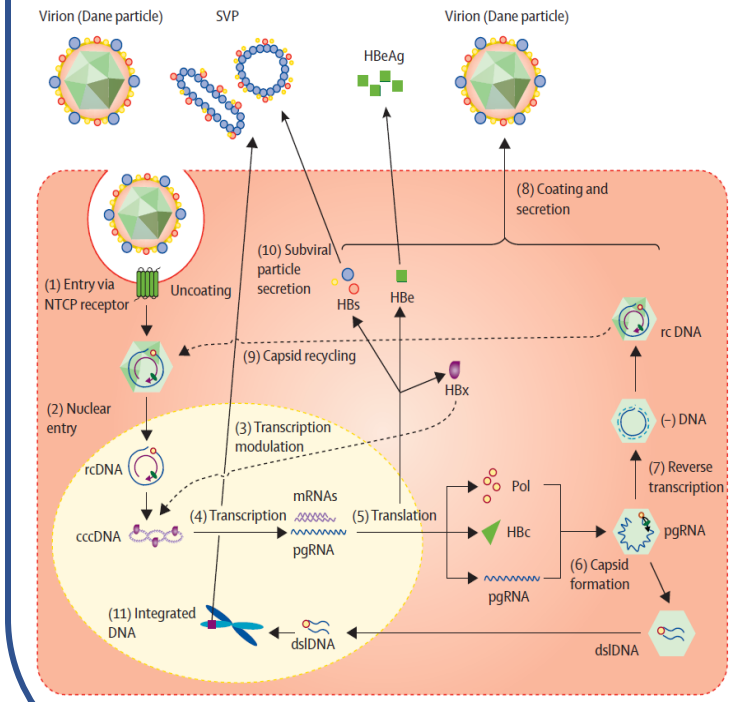
Division of Gastroenterology, Department of Medicine
Srinagarind Hospital, Faculty of Medicine, Khon Kaen University

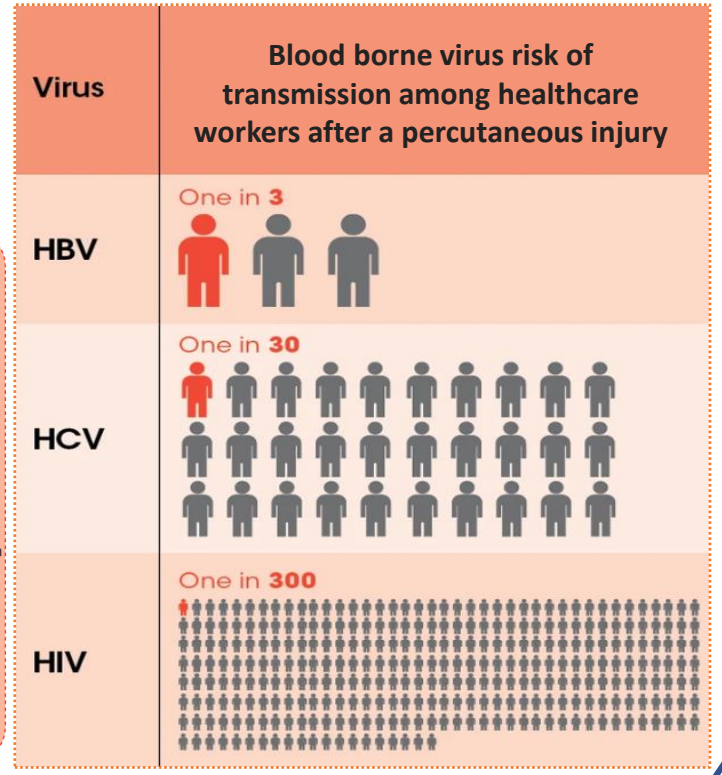
Outlines

- Introduction
- Epidemiology
- Screening and vaccination
- Management of chronic HBV infection

Introduction

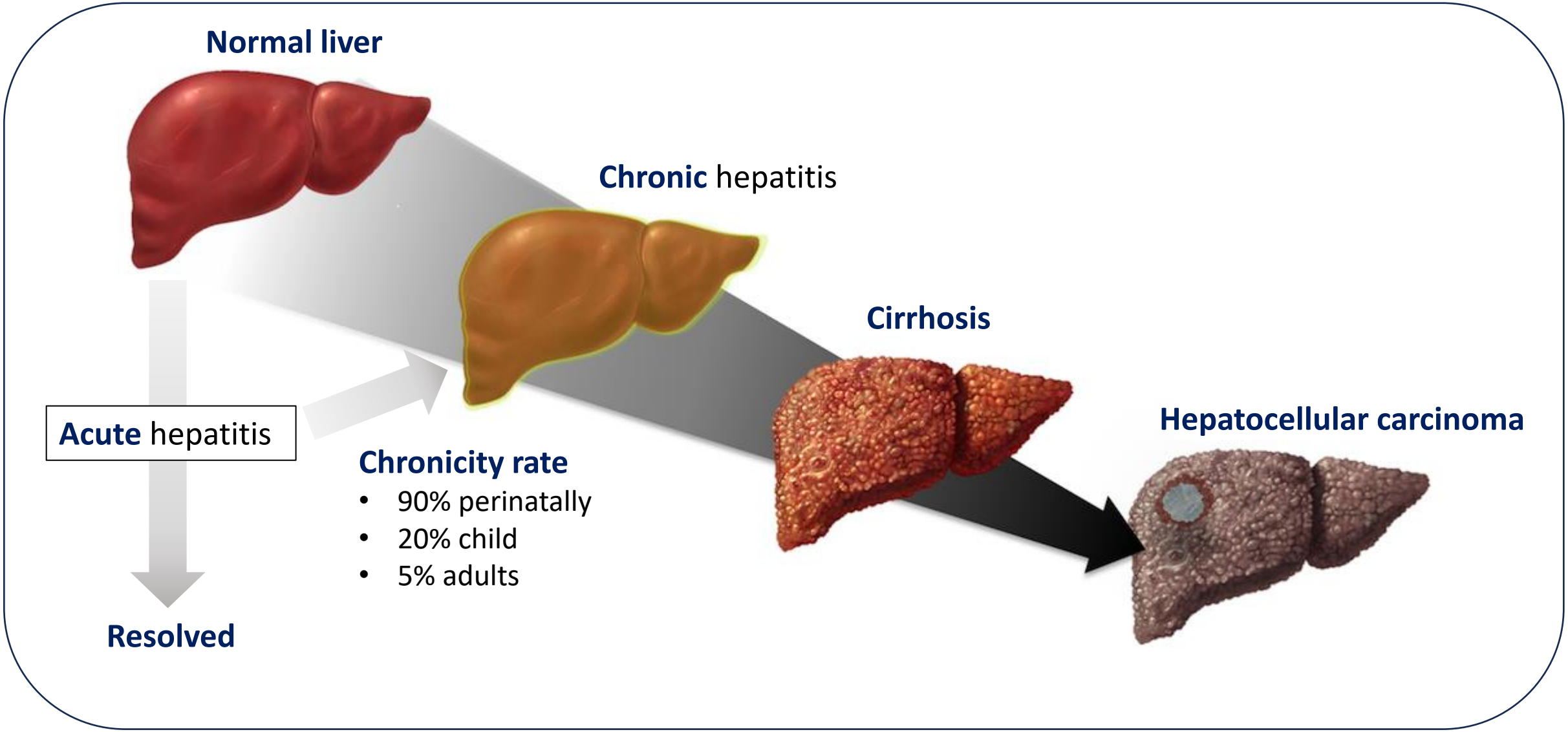
- Hepatitis B virus (HBV) is DNA virus
- Transmission via blood-to-blood contact
  - **Mother-to-child transmission (most common in Asian populations)**
  - Contaminated sharps/needles
  - Sexual activity



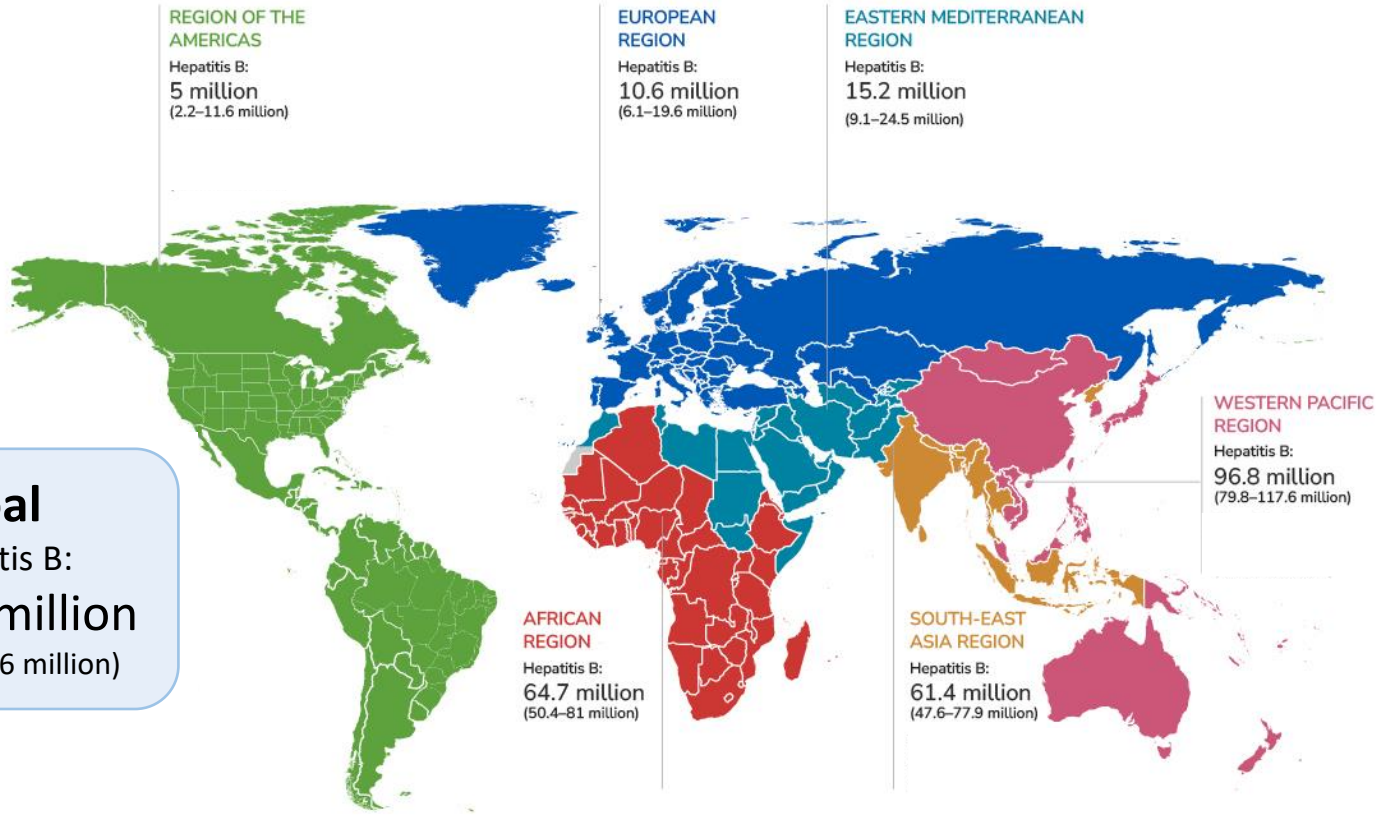


- Jeng WJ, et al. Lancet 2023.

Natural History of HBV Infection



Estimates of the Burden of Chronic HBV Infection



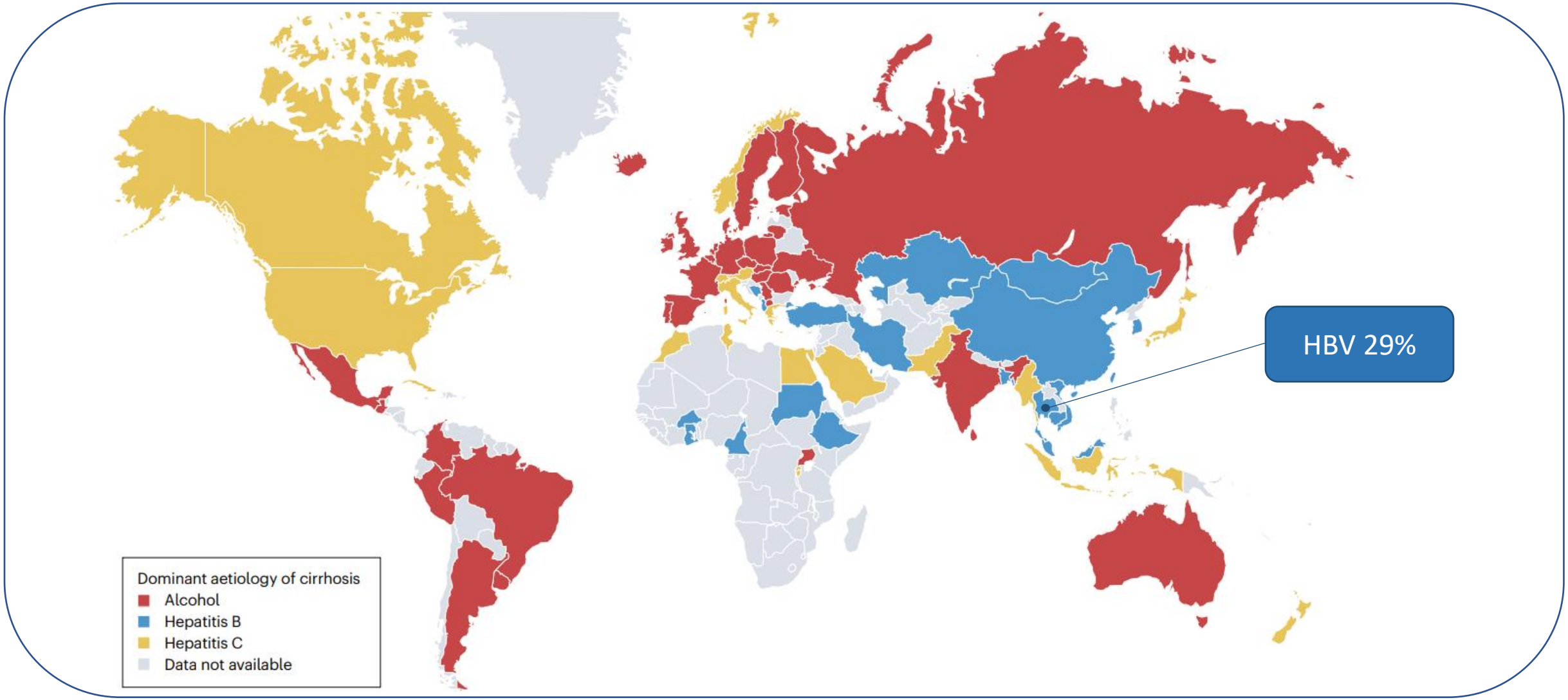
Global
Hepatitis B:
254 million
(225-286 million)

Thailand Hepatitis B:

- Prevalence of chronic HBV (HBsAg+): 2.56%
- HBV-related death rate (per 100,000): 18.1
- Proportion of persons living with HBV diagnosed: 12%
- Proportion of diagnosed persons receiving appropriate HBV treatment: 6%

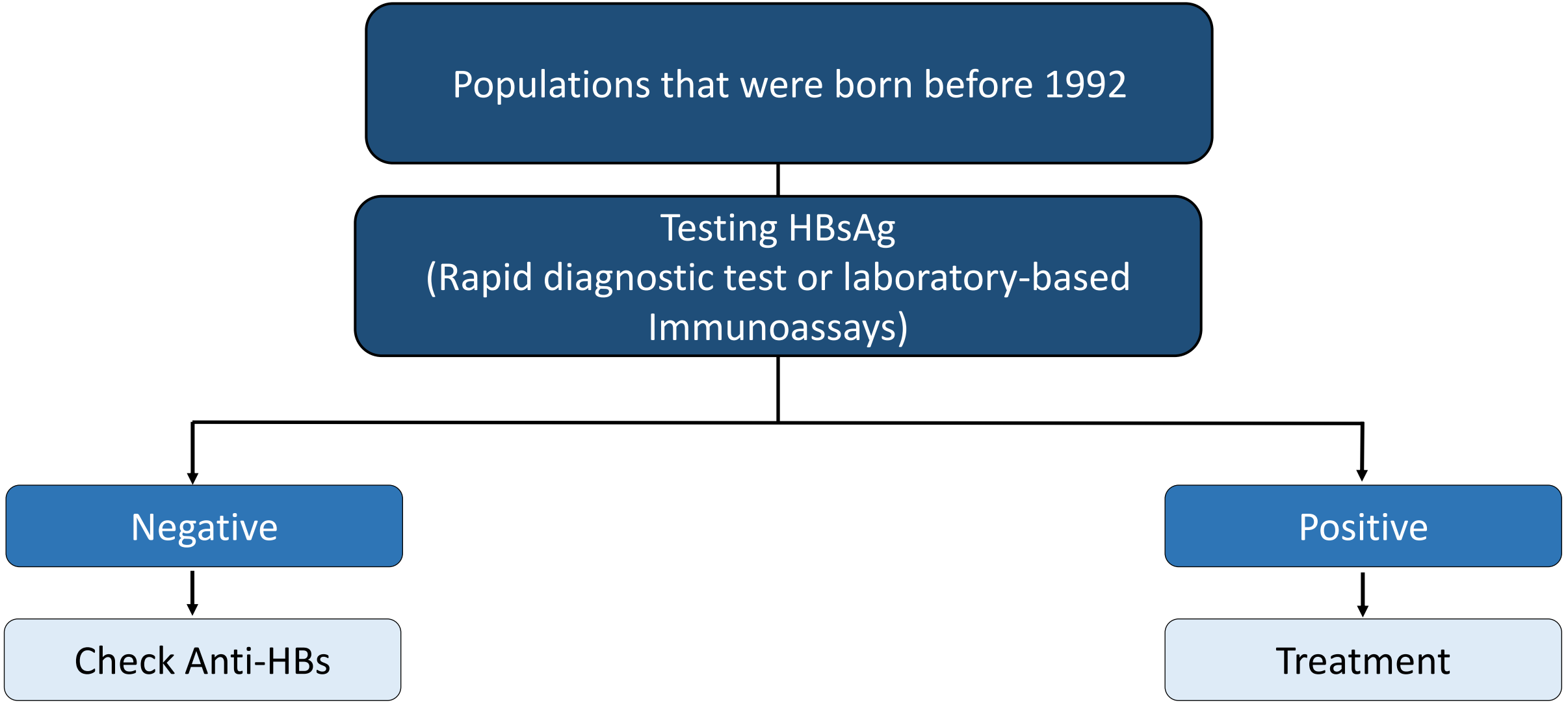
- WHO Global Health Observatory 2022
- Institute of Health Metrics and Evaluation (IHME). Global burden of Disease Study 2022 https://www.globalhep.org/country-progress/thailand

Dominant Etiology of Cirrhosis



- Alberts CJ, et al. Lancet Gastroenterol Hepatol. 2022
- Huang DQ, et al. Nat Rev Gastroenterol Hepatol. 2023

Screening HBV Infection



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Vaccination of HBV

Born in 1992 or later

Measure Anti-HBs titers

- Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
- Anti-HBs titers <10 mIU/ml → Administer 1 dose of HepB vaccine and measure Anti-HBs titers (within 1-2 months after last dose)
  - Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
  - Anti-HBs titers <10 mIU/ml → Administer 2 doses of HepB vaccine and measure Anti-HBs titers (within 1-2 months after last dose)
    - Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
    - Anti-HBs titers <10 mIU/ml → Administer 3 doses of HepB vaccine and measure Anti-HBs titers
      - Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
      - Anti-HBs titers <10 mIU/ml → Nonresponder

Born before 1992

Standard adult HepB vaccination 3 doses (0, 1-, 6- month interval)

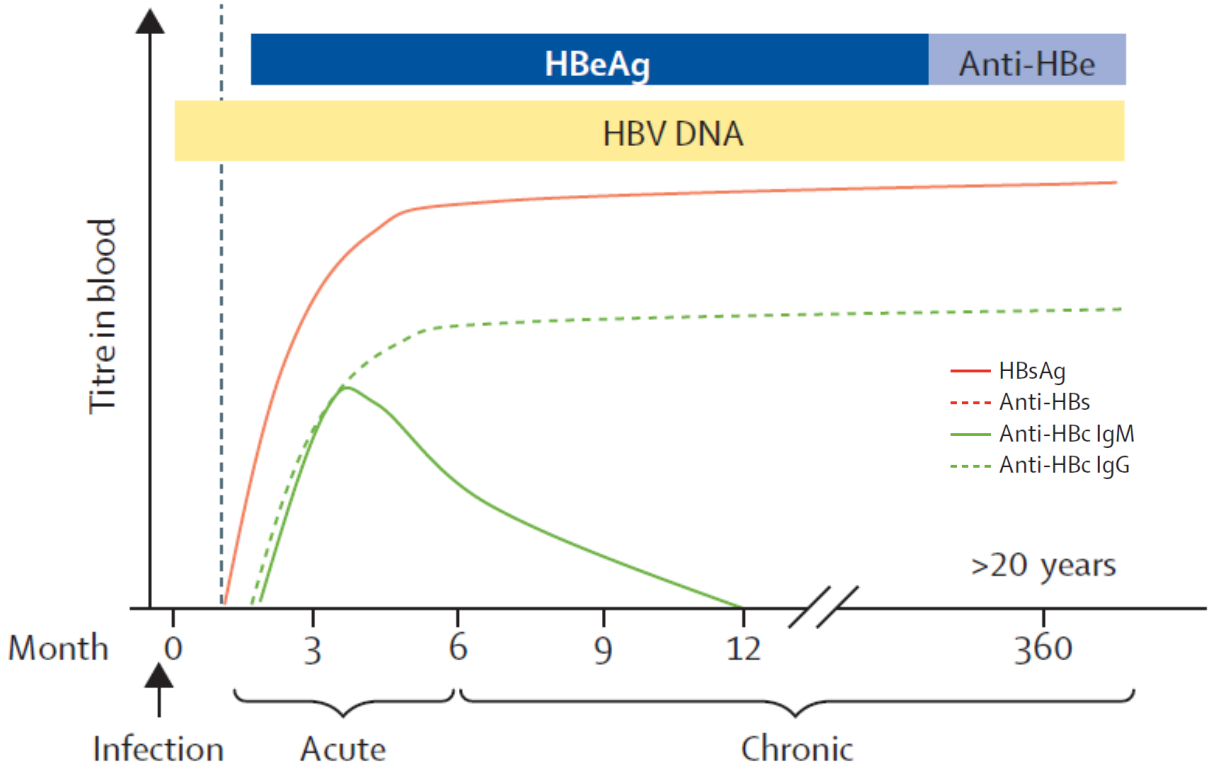
Measure Anti-HBs titers

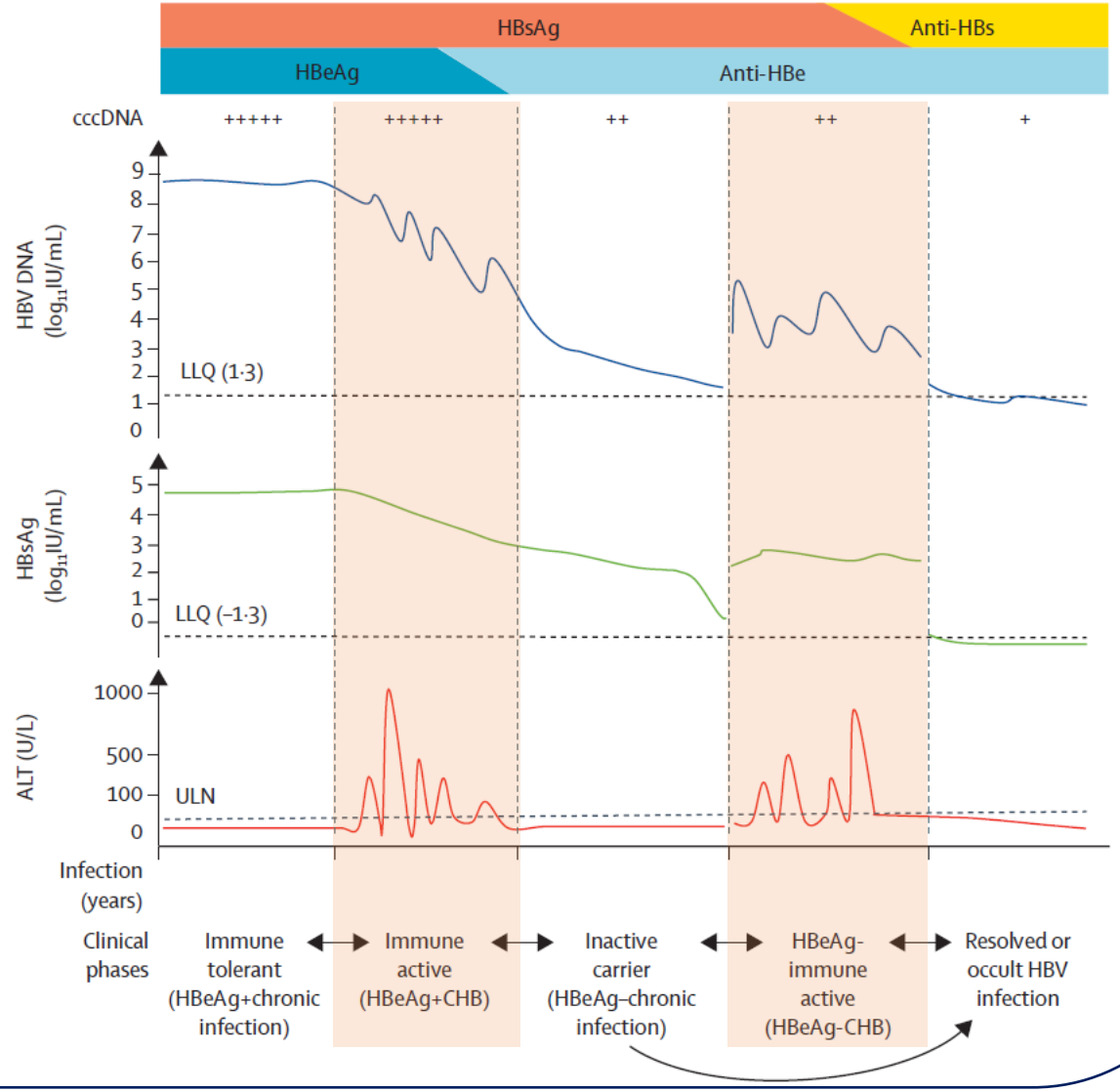
- Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
- Anti-HBs titers <10 mIU/ml → Administer 1 dose of HepB vaccine and measure Anti-HBs titers (within 1-2 months after last dose)
  - Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
  - Anti-HBs titers <10 mIU/ml → Administer 2 doses of HepB vaccine and measure Anti-HBs titers (within 1-2 months after last dose)
    - Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
    - Anti-HBs titers <10 mIU/ml → Administer 3 doses of HepB vaccine and measure Anti-HBs titers
      - Anti-HBs titers ≥10 mIU/ml → **Immunity to HBV**
      - Anti-HBs titers <10 mIU/ml → Nonresponder

- คำแนะนำการให้วัคซีนป้องกันโรคสำหรับผู้ใหญ่และผู้สูงอายุ สมาคมโรคติดเชื้อแห่งประเทศไทย 2568

Chronic HBV Infection

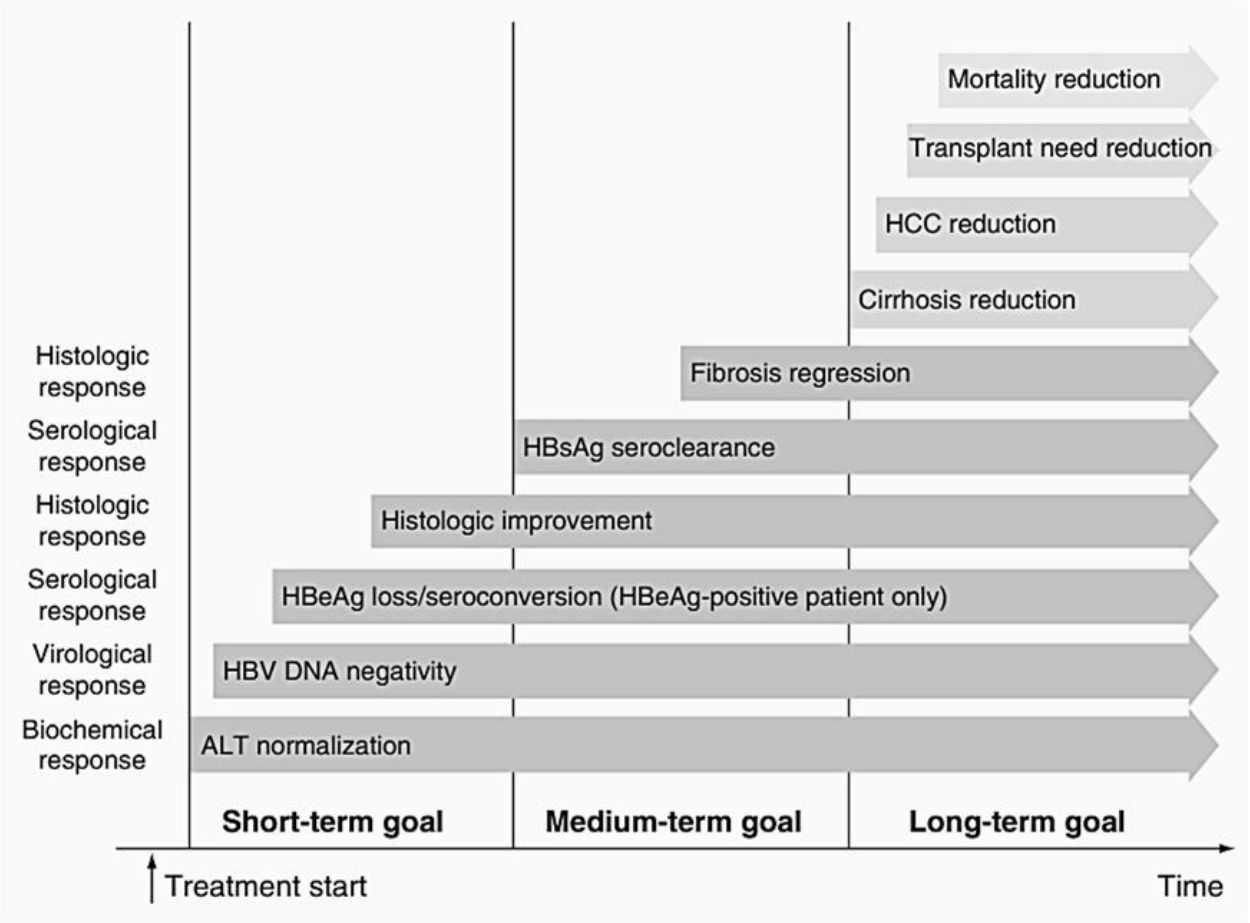
Serological Profiles During Chronic HBV Infection





- Jeng WJ, et al. Lancet 2023.

Clinical Goals of Chronic HBV Therapy



"Sustained virological response has been shown to decrease liver inflammation, decrease risk of cirrhosis and HCC, and reverse fibrosis even in patients with established cirrhosis"

- Su TH, et al. Expert Rev Gastroenterol Hepatol 2015.
- Jeng WJ, et al. Lancet 2023.

Goal of Treatment in Chronic HBV Infection

Intermediate goals

- **Biochemical response:** ALT normalization confirmed by ALT determination at least every 3 months for at least 1-year post-treatment
- **Virological response:** Undetectable HBV DNA
- **Serological response:** HBeAg to anti-HBe seroconversion in HBeAg-positive patients

Goal

- **Functional cure:** HBsAg loss with or without development of anti-HBs and undetectable HBV DNA at least 24 weeks after discontinuation of antiviral therapy

- **Complete functional cure:** complete clearance of cccDNA and virus serological markers

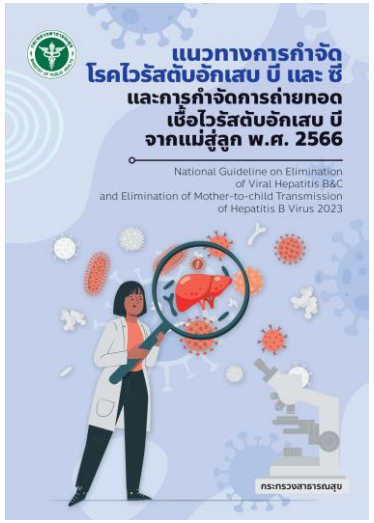
- EASL 2017 guideline
- WHO guideline 2024.

HBV Treatment Recommendation Based on Major Organization Guidelines

Risk Group	AASLD 2018	APASL 2015	EASL 2017	WHO 2024
Without cirrhosis	Treat if: - ALT ≥2x ULN[1], *or* - Significant histologic disease *and* - HBV DNA >2000 IU/mL if HBeAg-negative - HBV DNA >20,000 IU/mL if HBeAg-positive	Treat if: - ALT >2x ULN[2], or - Significant histologic disease *and* - HBV DNA >2000 IU/mL if HBeAg-negative - HBV DNA >20,000 IU/mL if HBeAg-positive	Treat if: - ALT >40 IU/L, HBV DNA >2,000 IU/mL, and biopsy evidence of at least moderate necroinflammation or fibrosis, *or* - HBV DNA >2,000 IU/mL and biopsy evidence of at least moderate fibrosis, *or* - HBV DNA >20,000 IU/mL and ALT > 2x ULN[2] regardless of degree of fibrosis	Treat if any: - HBV DNA >2000 IU/mL and an ALT > ULN[3] - Significant fibrosis[4] - Coinfection with HCV, HDV, or HIV - Family history of liver cancer or cirrhosis - Comorbidities (MASLD, T2D) - Immune suppression - Extrahepatic manifestations - Persistent abnormal ALT[3] (absence of access to an HBV DNA assay)
Compensated cirrhosis	HBV DNA detectable	Treat if: - HBV DNA >2,000 IU/mL, *or* - HBV detectable with ALT elevated[2]	HBV DNA detectable	Treat all
Decompensated cirrhosis	Treat all	HBV DNA detectable	Treat all	Treat all

[1]Upper limit of normal, defined as ALT 35 IU/L for men, 25 IU/L for women; [2]Defined as ALT 40 IU/L for both men and women; [3]Defined as greater than 19 IU/L for women and 39 IU/L for men
[4]APRI score of >0.5 or transient elastography value of >7 kPa

Management of Chronic HBV Infection



Persistence of **HBsAg for six months**

Evaluated:
- Severity of chronic liver disease: liver function test, CBC, and HBV DNA
- Evaluated co-disease: anti-HCV, and anti-HIV
- Ultrasonography upper abdomen

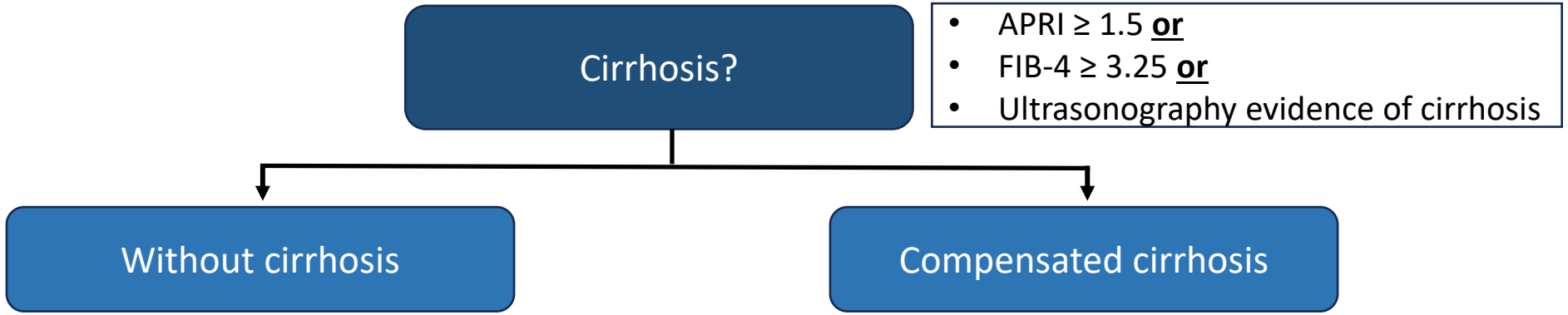
Clinical features of **decompensated cirrhosis**
- Jaundice (TB >2mg/dl), ascites, or hepatic encephalopathy

Suspected HCC

Suggesting start HBV treatment and expert referral

- แนวทางการตรวจคัดกรองและรักษาโรคไวรัสตับอักเสบ บี และ ซี สาหรับแพทย์เวชปฏิบัติทั่วไป พ.ศ. 2567

Management of Chronic HBV Infection



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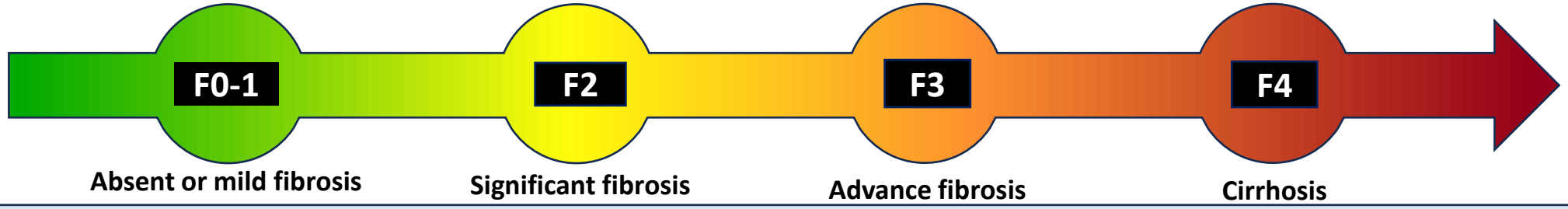
Non-invasive Scoring to Diagnosis Significant Fibrosis to Cirrhosis



- **APRI (AST to Platelet Ratio Index)**
  - APRI >1.5: Cirrhosis
  - APRI 0.5-1.5: Significant fibrosis
  - APRI <0.5: Rule out Significant fibrosis

$$\text{APRI} = \frac{(\text{AST in U/L}) / (\text{AST ULN in U/L}) \times 100}{(\text{Platelets in } 10^9\text{/L})}$$

- **FIB-4 (Fibrosis-4)**
  - FIB-4 >3.25: Cirrhosis
  - FIB-4 1.45 - 3.25: Significant fibrosis
  - FIB-4 <1.45: Rule out Significant fibrosis

$$\text{FIB-4} = \frac{(\text{Age* in years} \times \text{AST in U/L})}{(\text{Platelets in } 10^9\text{/L} \times \sqrt{(\text{ALT in IU/L})})}$$

**Use with caution in patients <35 or >65 years old, as the score has been shown to be less reliable in these patients*

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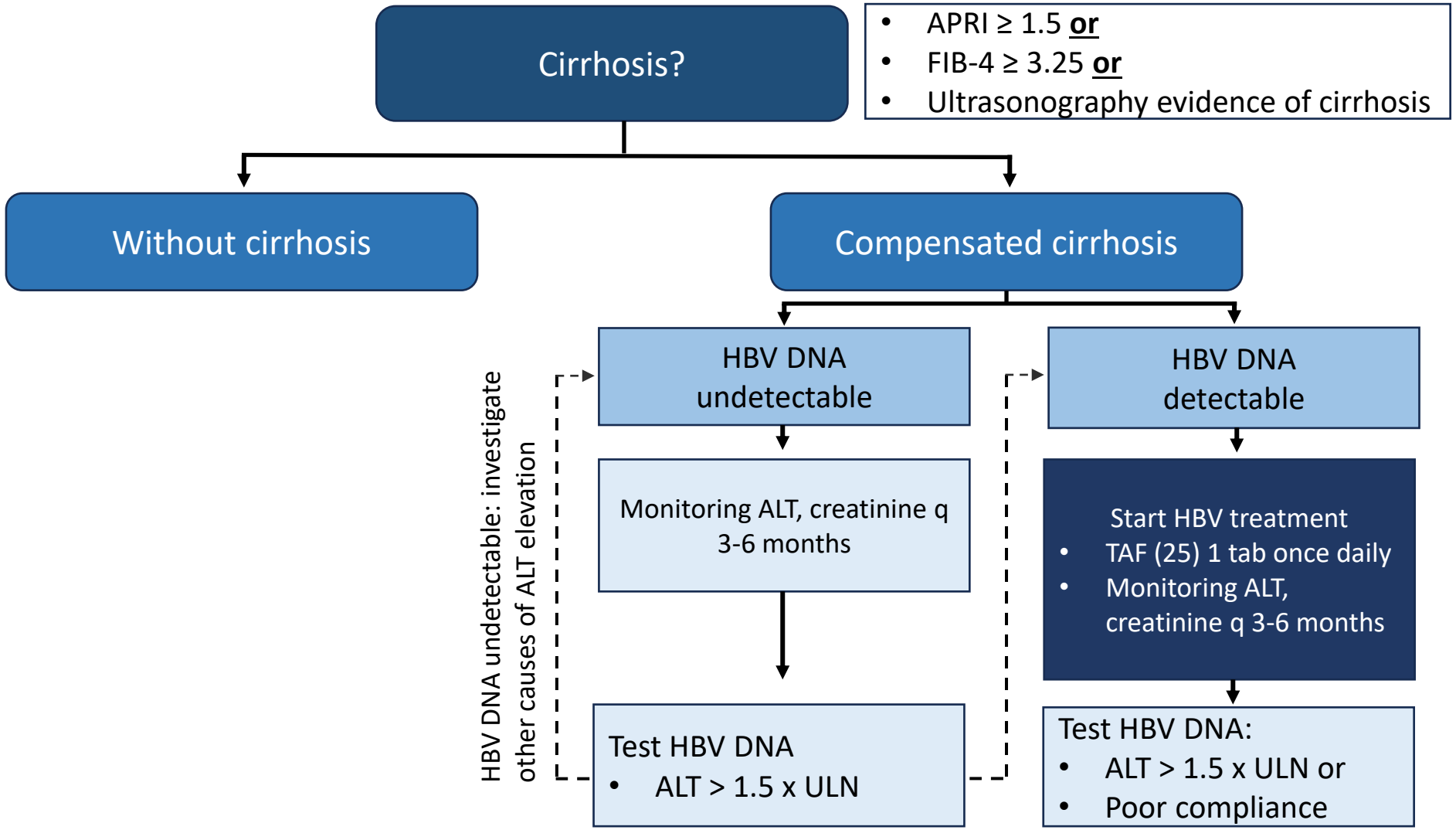

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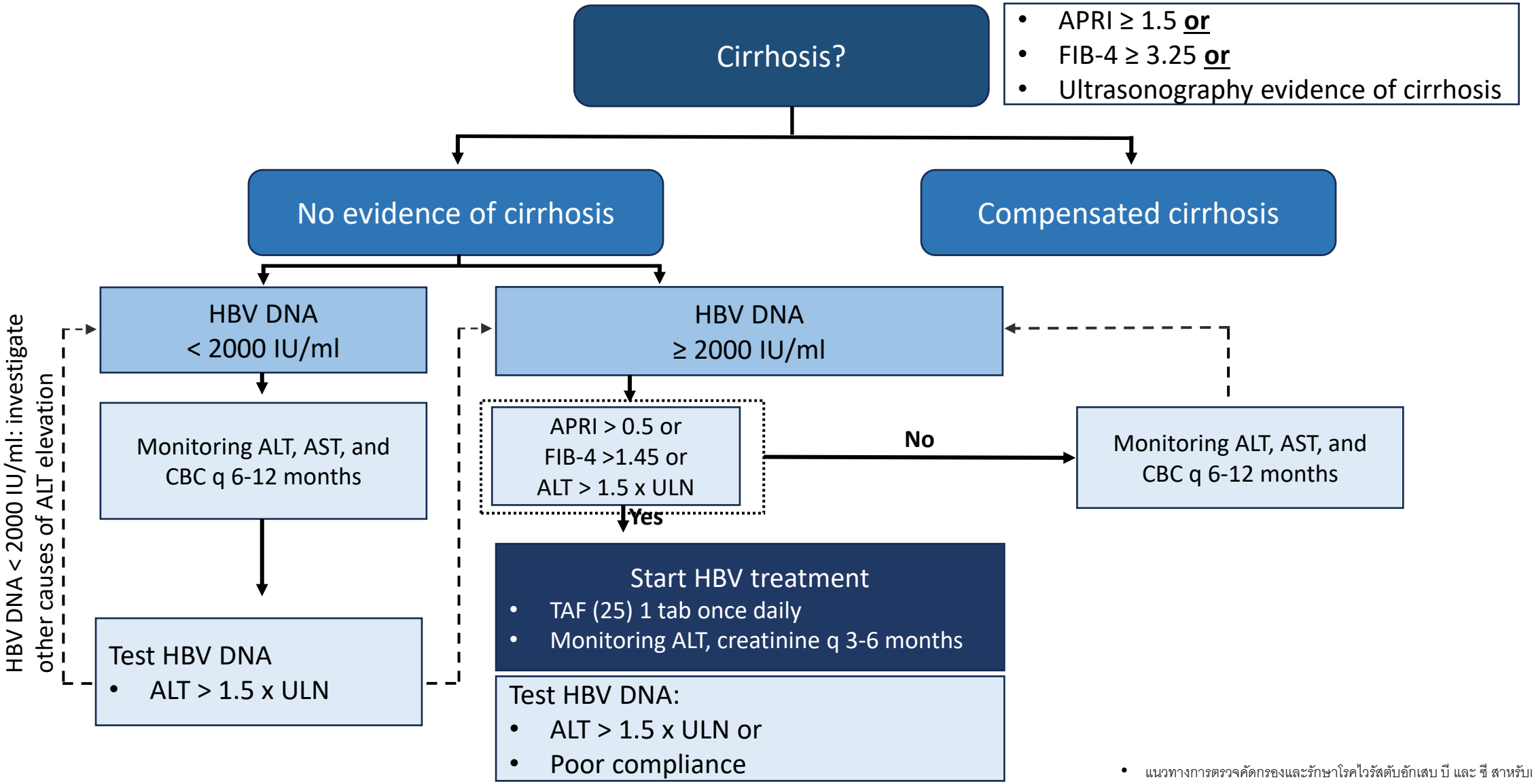

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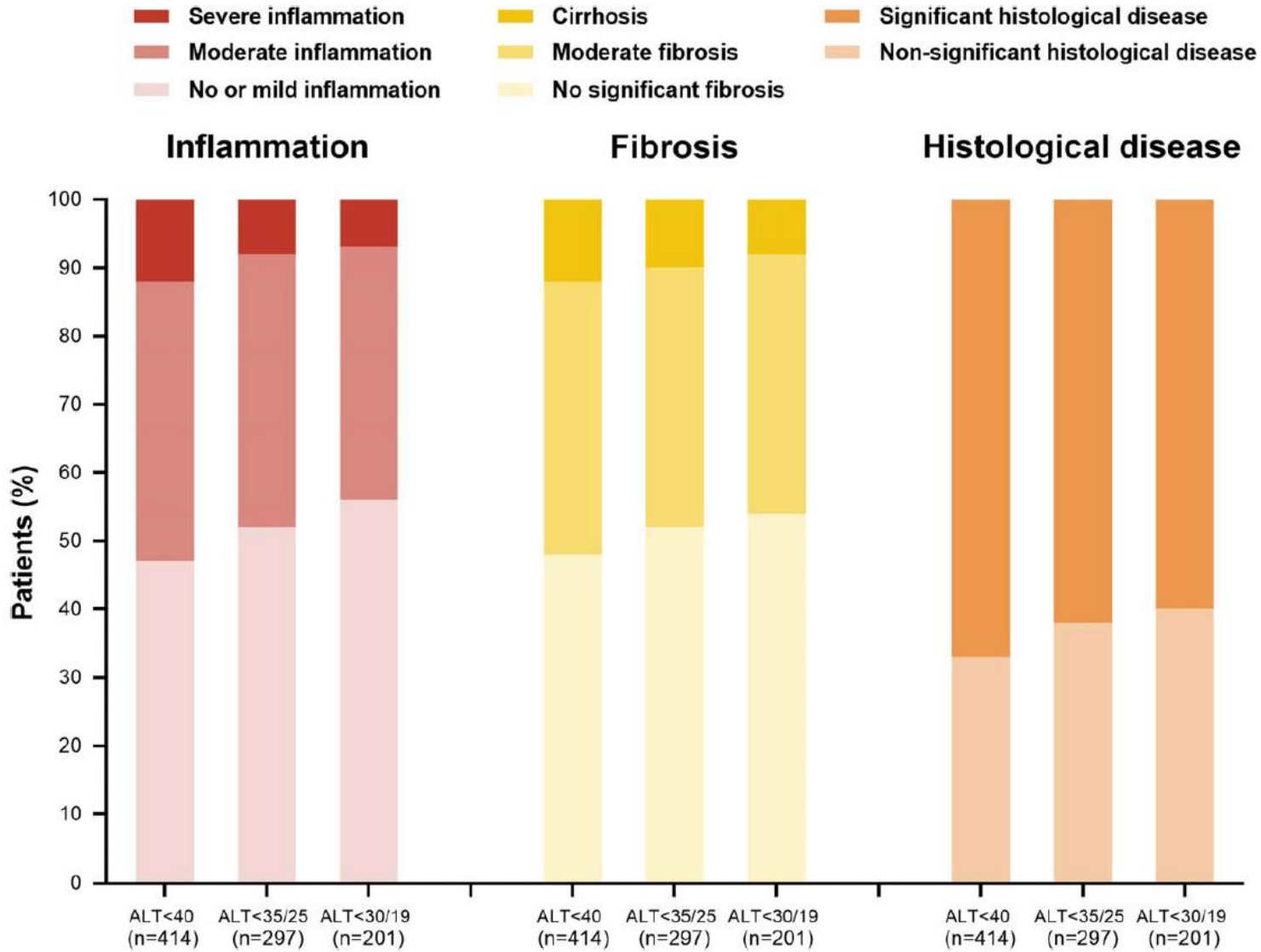
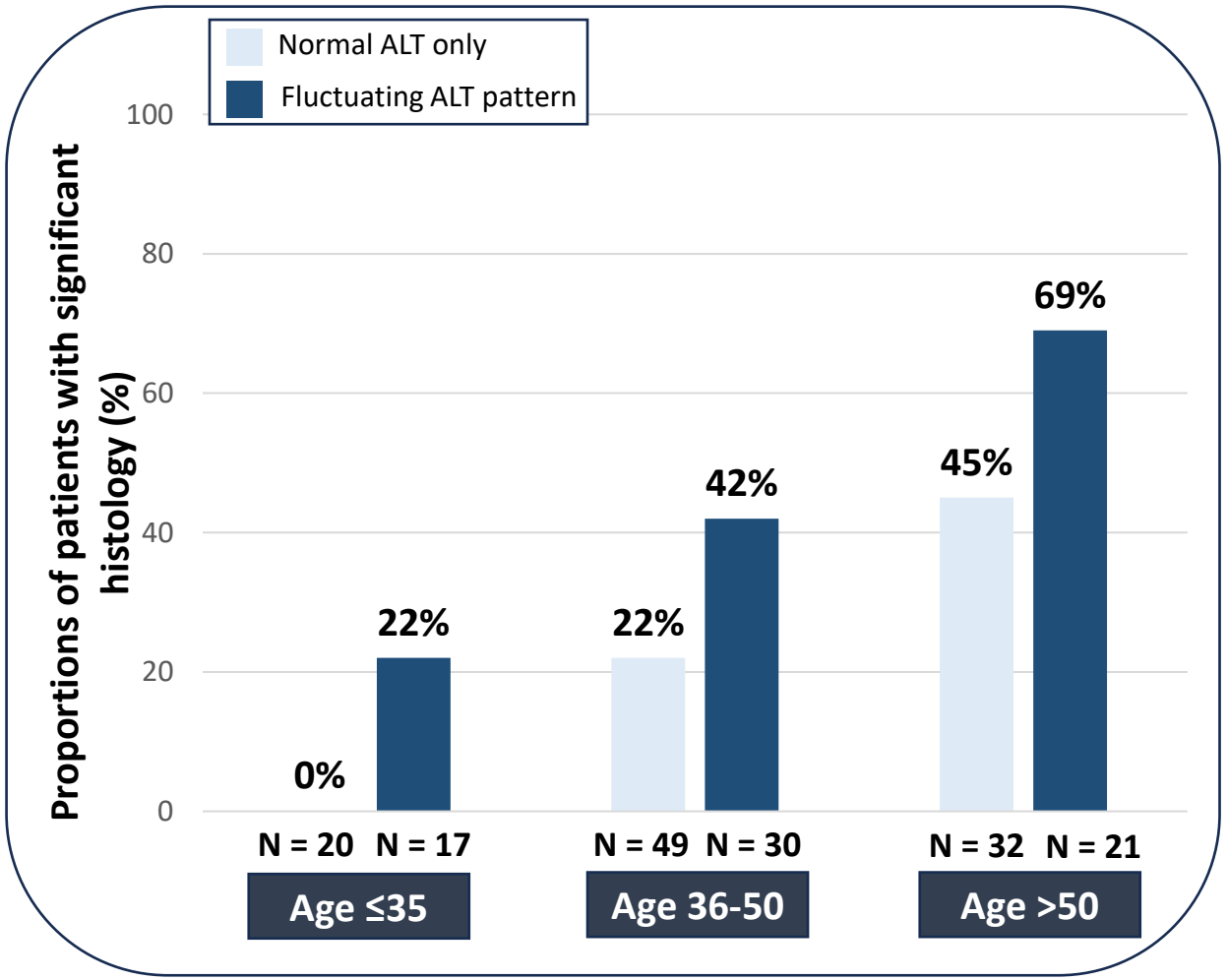
Histological Features of Chronic HBV Patients with Normal ALT



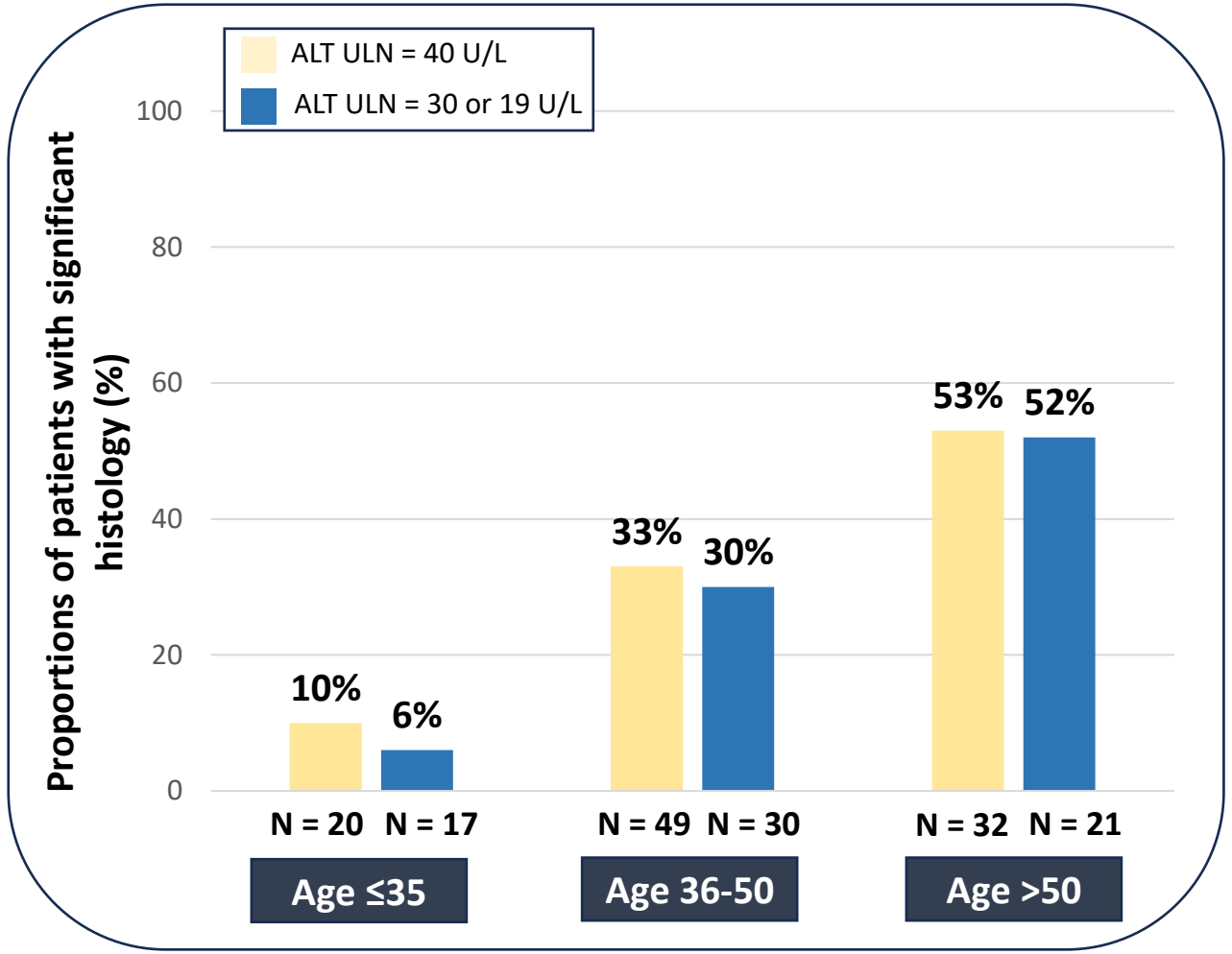
- Huang R, et al. Hepatol Commun 2024.

Significant Histology According to Age and ALT

Prevalence of significant histology by ALT patterns and ALT ULNs



Prevalence of significant histology by age and ALT ULNs



- Nguyen MH, et al. Am J Gastroenterol 2009.

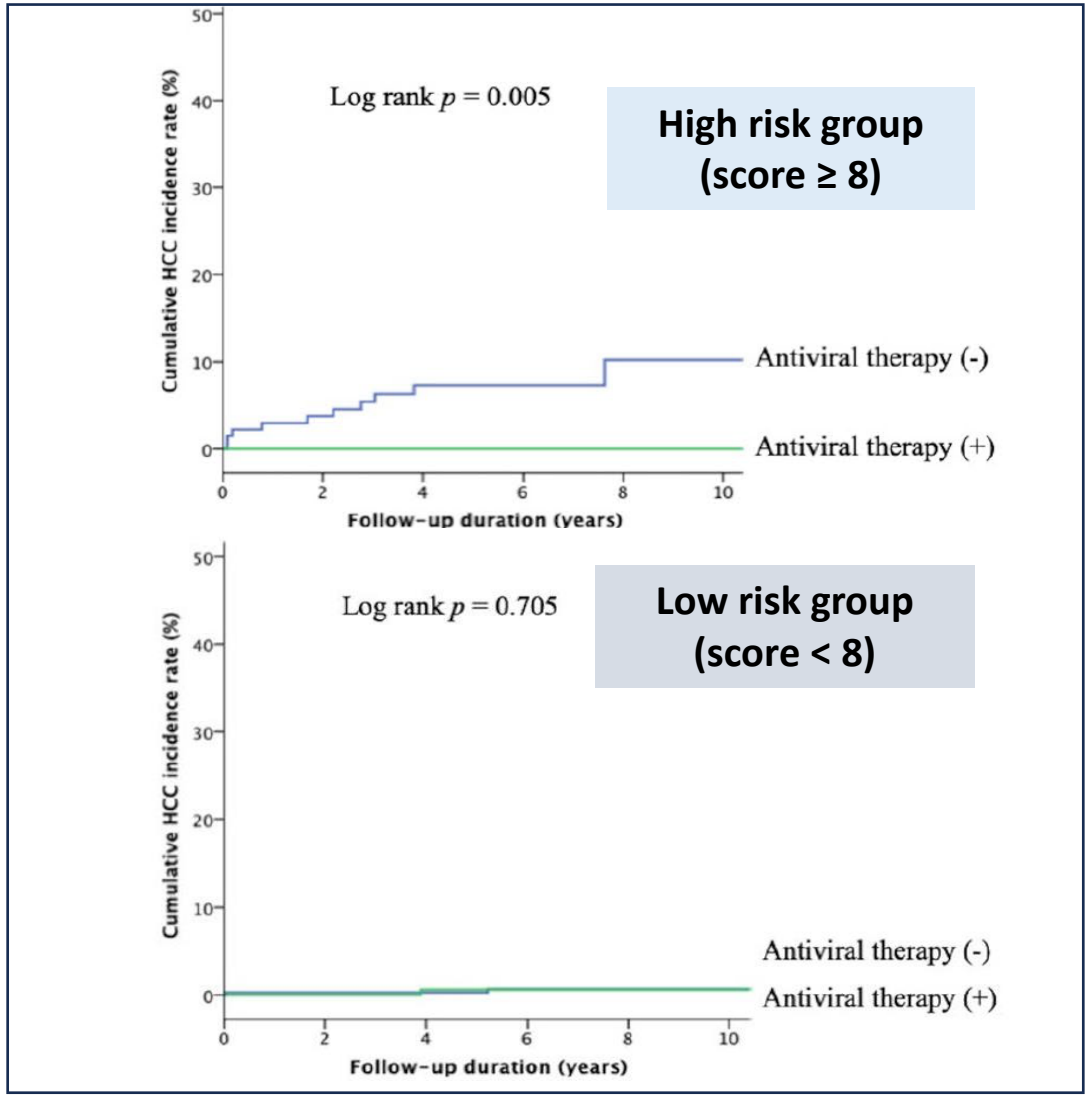
Antiviral Therapy for Chronic HBV Patients Decrease Risk of HCC

Retrospective study of 749 chronic hepatitis B patients persistent serum ALT < 2 x ULN or HBV-DNA < 2000 IU/ml

High risk HCC patients (score ≥8)

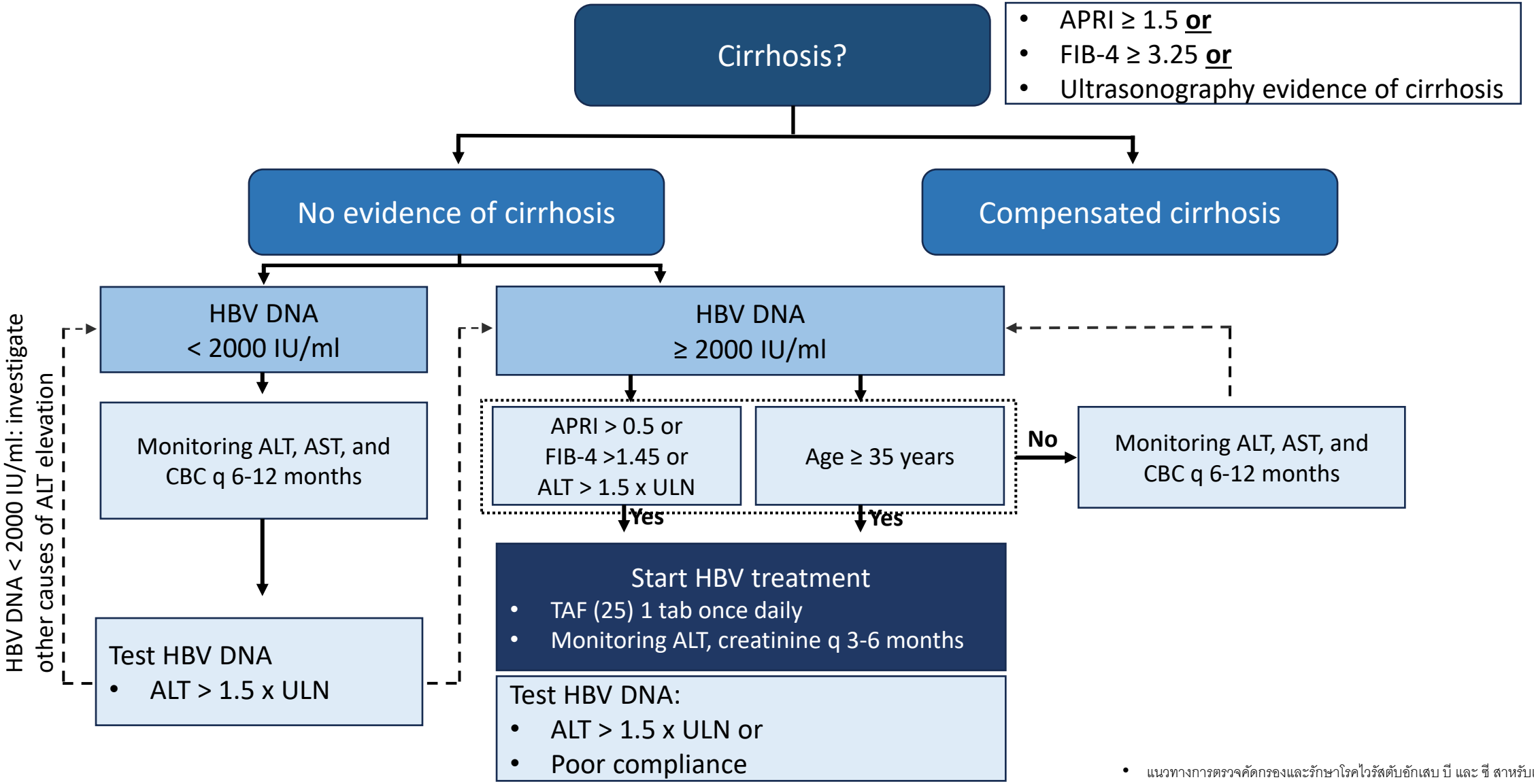
1. Age 40-49 (1 point), ≥50 (5 points)
2. Male (3 points)
3. Family history of HCC (5 points)
4. HBV DNA ≥ 2000 IU/ml (1 point)

The effects of reduction of HCC by antiviral therapy



- Teng W, et al. Hepatol Int 2021.

Management of Chronic HBV Infection



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Recommend Therapy in Thailand

Tenofovir alafenamide (TAF)

- First-line therapy; switch therapy from lamivudine, entecavir, tenofovir disoproxil fumarate (TDF); compensated or decompensated cirrhosis with detectable HBV DNA ; or prophylaxis therapy in immunosuppressed patients
- Dosage: 25 mg taken orally once daily with food
- Not recommended in patients with eGFR below 15 mL/min who are not receiving renal replacement therapy

Tenofovir disoproxil fumarate (TDF)

- Pregnancy
- Patients with eGFR below 15 mL/min who are not receiving renal replacement therapy

Entecavir (ETV)

- Alternative first-line therapy in renal impaired (Cr > 1.5 mg/dL, eGFR ≤ 50 mL/min or proximal tubular dysfunction including hypokalemia, hypophosphatemia, glucosuria, proteinuria ≥ 1 g/day), or osteopenia/osteoporosis

- ประกาศคณะกรรมการพัฒนาระบบยาแห่งชาติ พ.ศ. 2565

Renal Dose Adjustments

- **Tenofovir disoproxil fumarate (TDF)**

eGFR (ml/min)	Dose
≥ 50	300 mg orally once a day
30-49	300 mg orally every 48 hours
10-29	300 mg orally every 72-96 hours
Hemodialysis	300 mg orally every 7 days

- **Entecavir (ETV)**

eGFR (ml/min)	Dose
≥ 50	0.5 mg orally once a day
30-49	0.5 mg orally every 48 hours
10-29	0.5 mg orally every 72 hours
<10	0.5 mg orally every 7 days
Hemodialysis or CAPD	0.5 mg orally every 7 days

HCC Screening

- Males ≥ 40 years **or**
- Females ≥ 50 years **or**
- First-degree relative of HCC

Ultrasound upper abdomen with AFP every 6-12 months

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Conclusion and Key Messages

- **Chronic hepatitis B** is the common cause of cirrhosis in Thailand
- **Vertical transmission** is the primary route of infection
- **Achieving optimal outcomes** requires appropriate HBV treatment
- **Indication for treatment** in chronic hepatitis B
  - **Non-cirrhosis:** HBV DNA ≥ 2000 IU/mL plus one of the following: ALT > 1.5xULN or at least F2 fibrosis
  - **Cirrhosis:** detectable HBV DNA (except decompensated cirrhosis)
- **Tenofovir alafenamide (TAF)** is the first-line therapy
- **HCC surveillance:**
  - Males ≥ 40 years or females ≥ 50 years or first-degree relative of HCC
  - Recommended: ultrasound and AFP every 6-12 months
- **Screening and vaccination** are keys strategies for HBV elimination