Elimination of Mother-to-child transmission of Hepatitis B

Screening and Management of HBV during pregnancy

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Pan American Health Organization

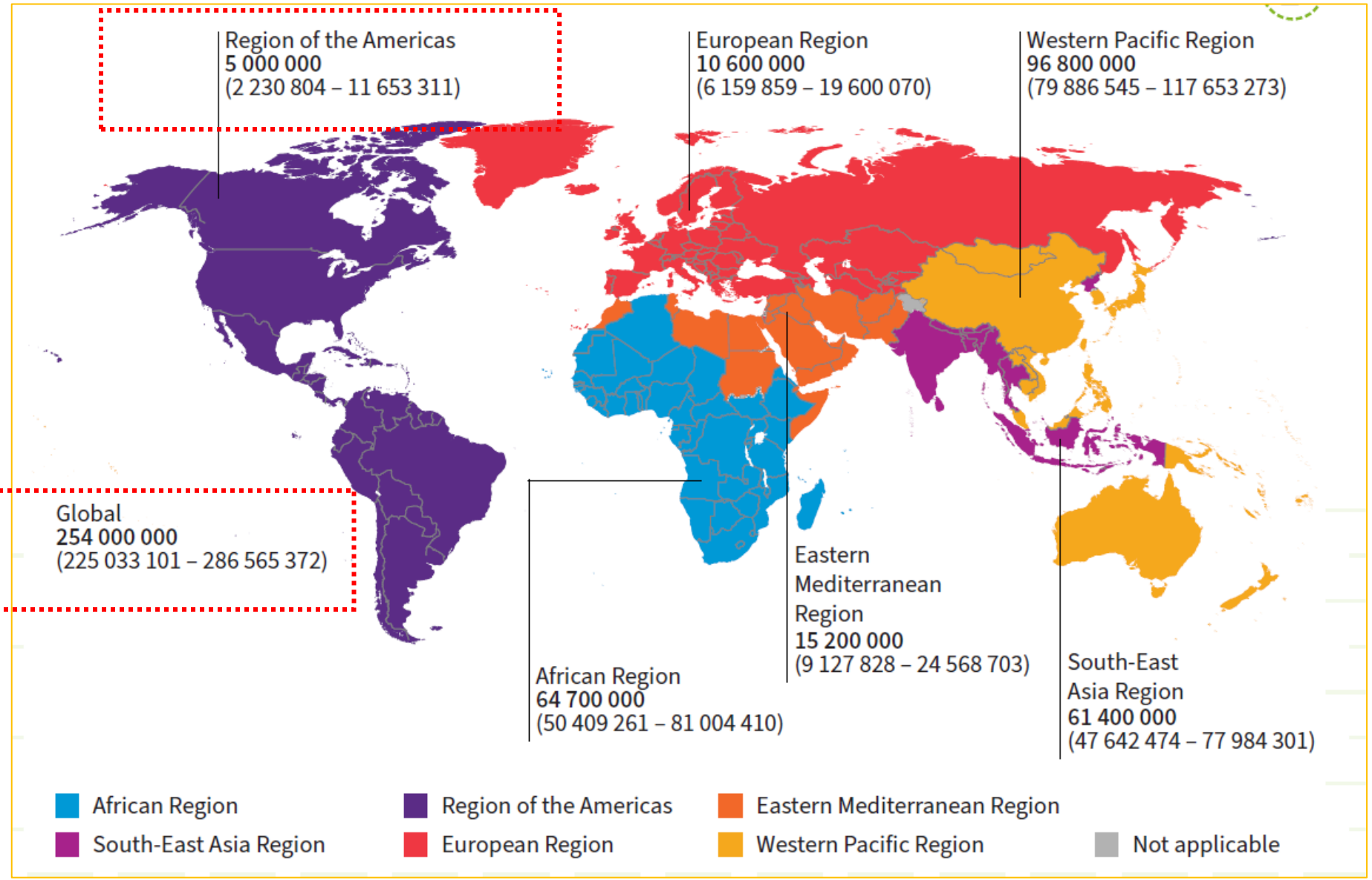
World Health Organization

Americas Region

Hepatitis B Prevalence by WHO Region, 2022

Global Viral Hepatitis Progress Report

an estimated **254 million people are living with hepatitis B**

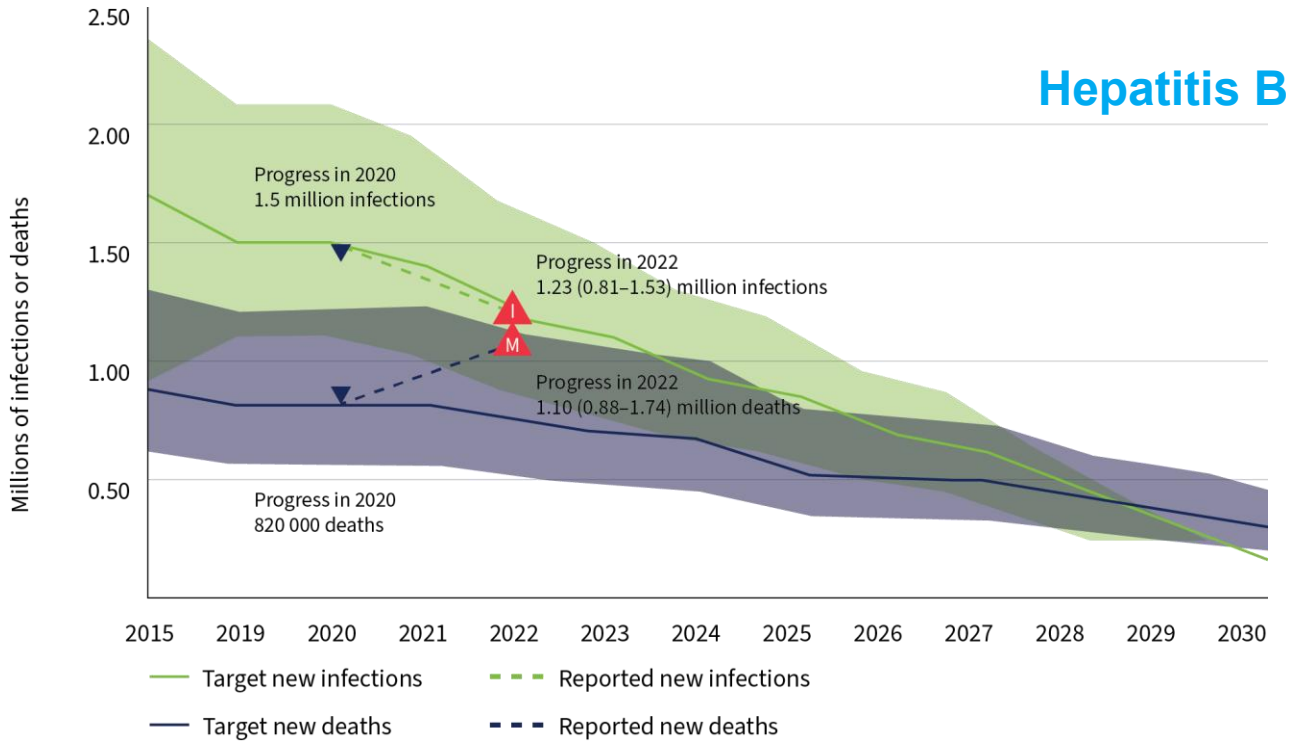


Source: WHO, Global hepatitis report 2024: action for access in low- and middle-income countries, 2024 https://www.who.int/publications/i/item/9789240027077 ;

Global Trends in Hepatitis B Incidence and Mortality, 2015-2030

- **Incidence:** The estimated number of people newly infected with hepatitis B decreased from 1.5 million in 2019 to 1.2 **million in 2022**

- **Increasing mortality** and a major cause of death from infectious diseases (along with TB and COVID).
- **HBV mortality increased** from an estimated 0.8 million deaths in 2019 to 1.1 million in 2022



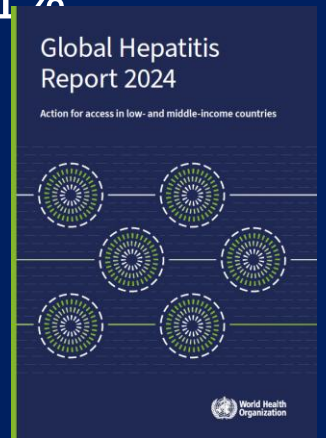
Trends in hepatitis B incidence and mortality, 2015–2030

Source: WHO, Global hepatitis report 2024: action for access in low- and middle-income countries, 2024 https://www.who.int/publications/i/item/9789240027077 ;

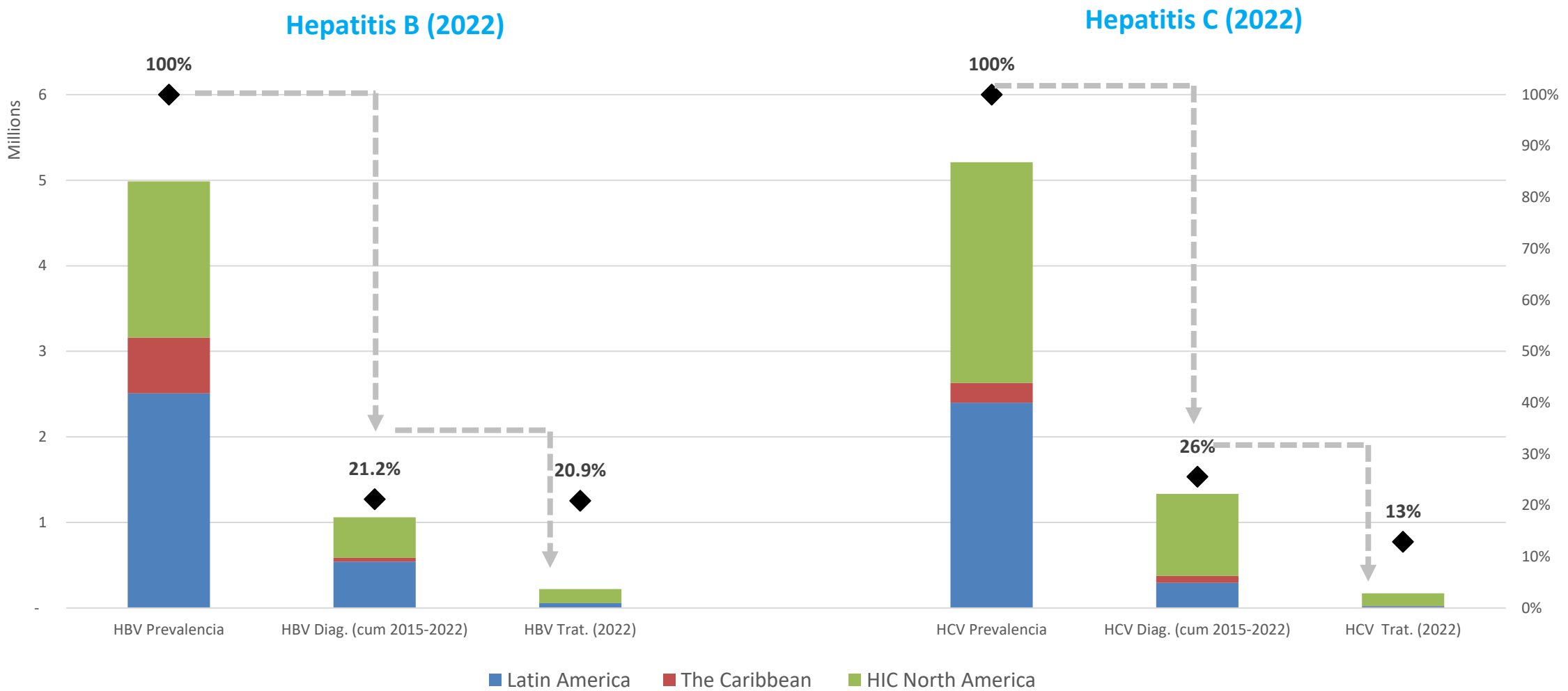
Hepatitis B in the Region of the Americas, 2022

Hepatitis B in the Americas, 2022

- **5.0 (0.5%) million people with chronic infection**
  - 2.5 million in Latin America
  - **720,000 in the Caribbean**
  - Prevalence in 5-year-olds: <0.1%
- 8,000 new infections
- 20,000 deaths

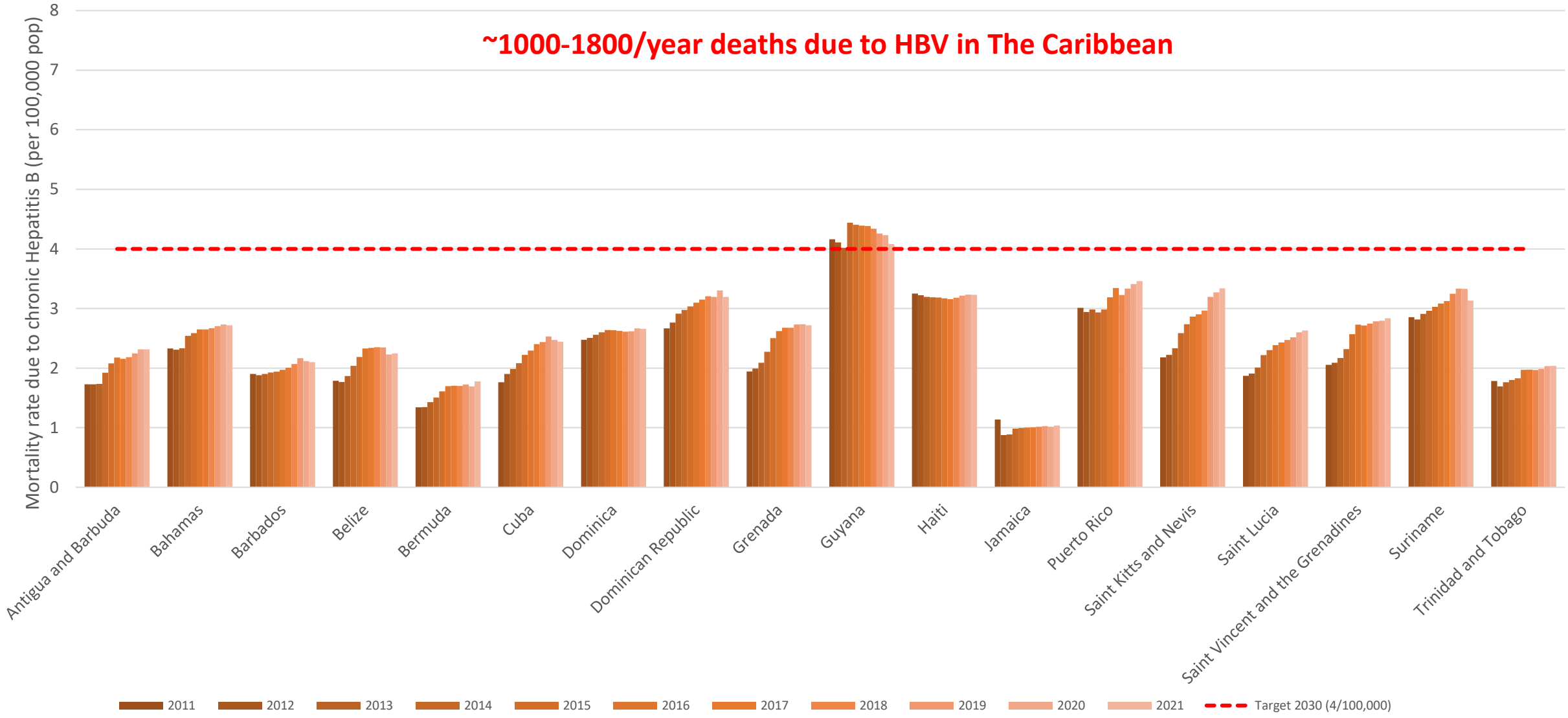


HBV and HCV Care Cascade in the Region of the Americas (2022)



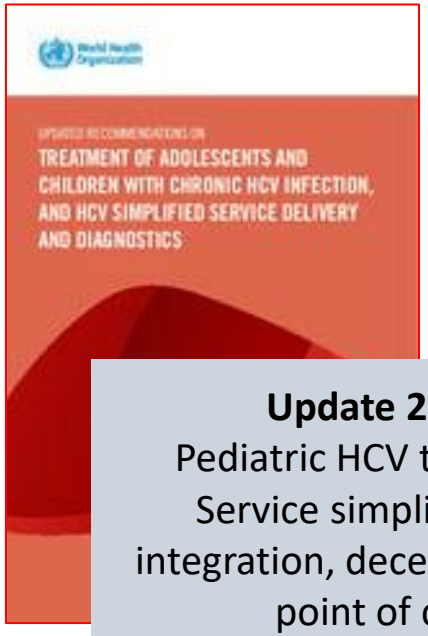
Source: WHO, Global Report on HIV, viral hepatitis and sexually transmitted infections, 2021 https://www.who.int/publications/i/item/9789240027077 ; Center for Disease Analysis Foundation/Polaris Observatory (http://www.polarisobservatory.com/); Hofmeister et al., 2019

Mortality rate due to liver cancer, cirrhosis and other chronic diseases caused by hepatitis B infection, 2011-2021 (per 100,000 pop)

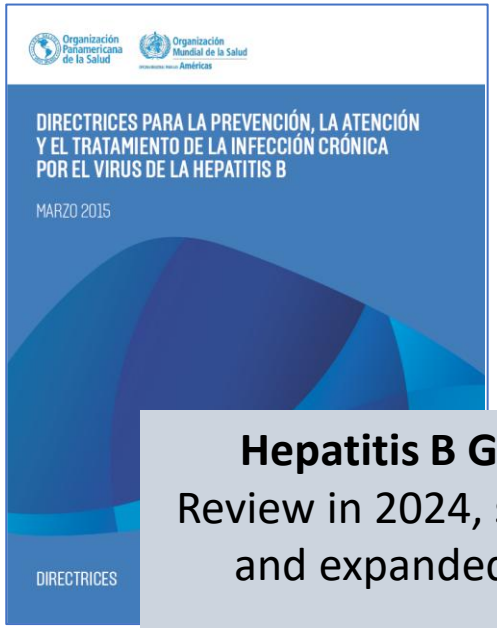


PAHO/WHO Guidelines and Recommendations

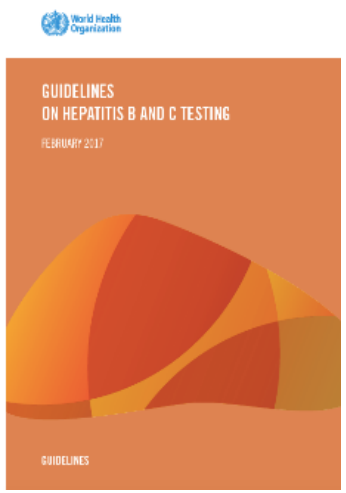
Hepatitis C Guidelines:
Simplified handling:
5 key steps

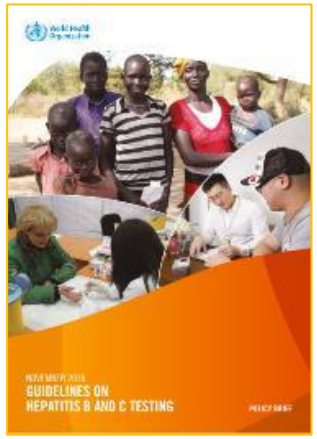


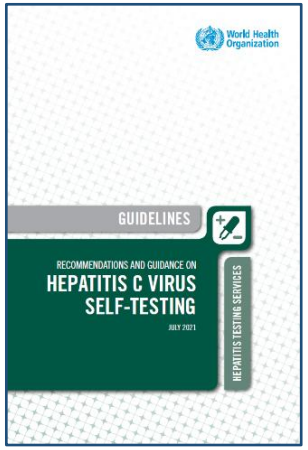
Update 2022;
Pediatric HCV treatment
Service simplification:
integration, decentralization,
point of care

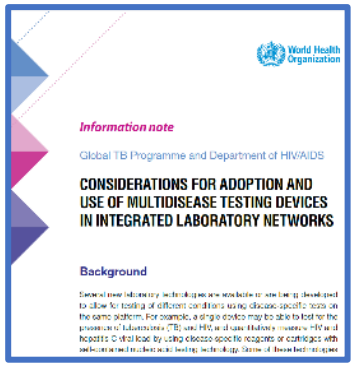


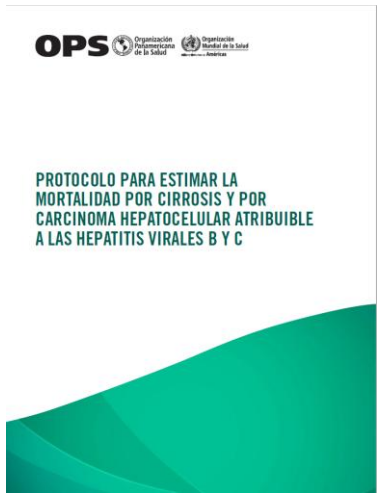
Hepatitis B Guidelines:
Review in 2024, simplification
and expanded eligibility











Classification of Viral Hepatitis

Pan American Health Organization

World Health Organization

Americas Region

Hepatitis

- A wide variety of causes/factors can lead to **liver inflammation**
- Most often caused by infection with a **hepatotropic virus**
- Other Causes
  - Alcohol
  - Drugs and medicines
  - Other infections (other viruses, parasites, bacteria)
  - Ischemia
  - Autoimmune disorders

Viral Hepatitis

- Hepatotropic viruses are viruses that selectively and preferentially infect and injure the liver
- At least five are currently known:

Virus	Type / Family	Genome	Envelope	Chronic?	Main Transmission Route(s)	Typical Settings / Risk Contexts
HAV	Picornavirus	RNA	No	No	Fecal–oral (contaminated food/water)	Poor sanitation, outbreaks, travelers
HBV	Hepadnavirus	DNA	Yes	Yes	Blood, sexual, perinatal	Health-care exposure, childbirth, MSM
HCV	Flavivirus	RNA	Yes	Yes	Blood (injection, transfusion)	Unsafe injections, PWID, unscreened blood
HDV	Defective RNA (requires HBV)	RNA	Yes	Yes	Co/super-infection with HBV	Endemic regions (Africa, Mediterranean, Amazon Basin)
HEV	Hepevirus	RNA	No	Rare (in immunosuppressed)	Fecal–oral (water/food)	Poor sanitation, outbreaks, pregnancy risk

Acute viral hepatitis

- Inflammation of the liver due to a **recent infection with a hepatotropic virus**.

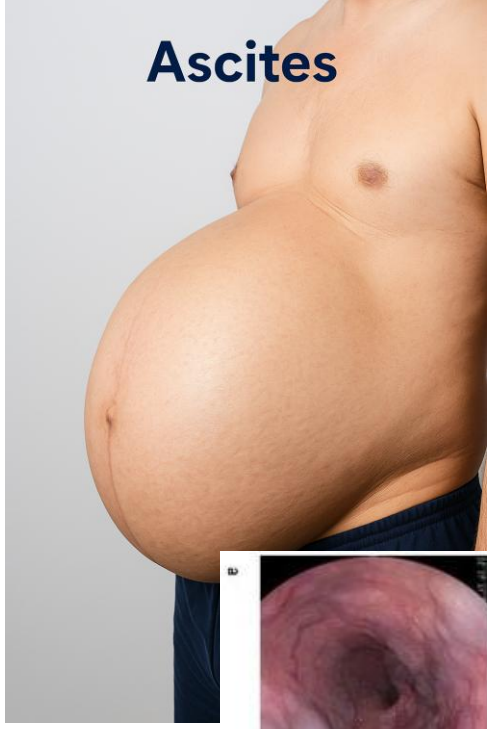
- **Short duration**: usually **days to weeks**.

- **Three clinical phases:**
  - **Prodrome:** malaise, fever, fatigue, nausea, vomiting, joint pain, rash **(few days)**
  - **Icteric phase:** jaundice, dark urine, pale stools, mild hepatomegaly **(days to weeks)**
  - **Convalescence:** gradual recovery of appetite and energy **(weeks)**

- **Investigation:**
  - **Liver function tests:** Bilirubin ↑, **AST/ALT ↑ (often >10× ULN)**, ALP moderately ↑, INR prolongation if severe.
  - **Imaging (Ultrasound):** To rule out biliary obstruction or other causes of jaundice
  - **Viral serology**: IgM anti-HAV; anti-HEV; HBsAg and IgM anti-HBc ; Anti-HCV and/or HCV RNA

- **Management:**
  - **Supportive care:** adequate hydration, rest as needed, control nausea and vomiting.
  - **No role** for antivirals, hepatoprotective drugs, or strict dietary restrictions.
  - **Red flags – Acute Liver Failure:** rapid jaundice progression, coagulopathy (INR > 1.5), confusion, or hepatic encephalopathy.

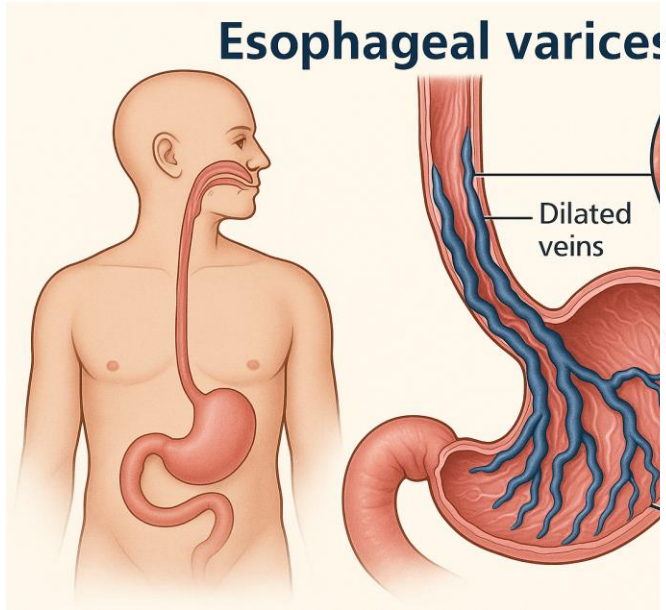
Chronic Viral Hepatitis

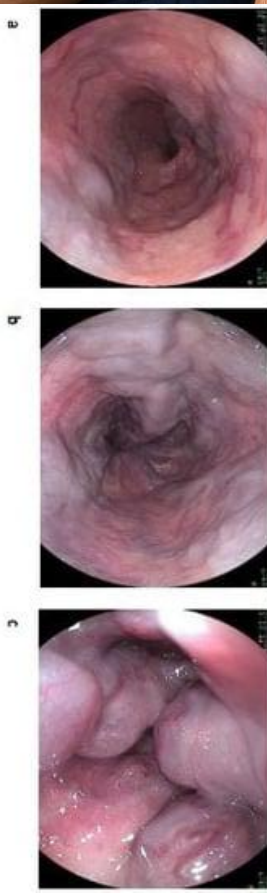


- Chronic inflammation of the liver lasting more than 6 months due to persistent infection with **HBV, HCV, or HDV.**
- Represents ongoing hepatocyte injury, with gradual healing through fibrosis formation.

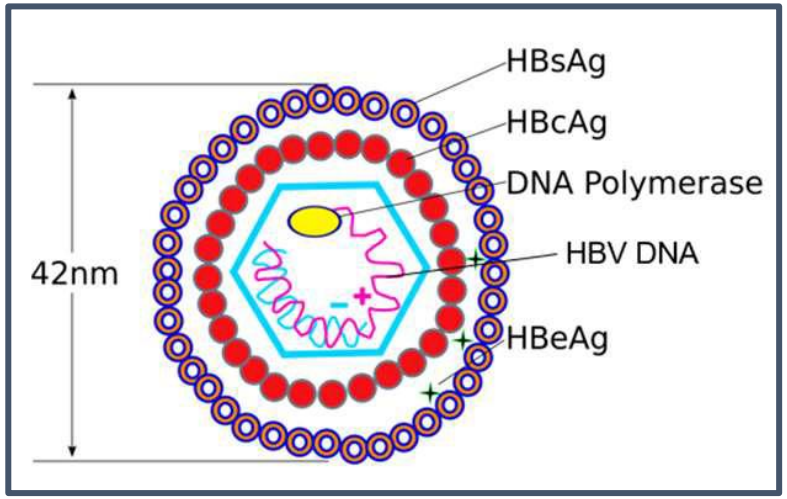
Clinical Characteristics:

- **Asymptomatic** or mildly symptomatic for years.
- **ALT/AST elevation**
- Progressive **fibrosis → cirrhosis → liver failure**.
  - signs of **liver failure**: jaundice, coagulopathy, encephalopathy
  - signs of **portal hypertension**: splenomegaly, Esophageal and gastric varices, ascites
  - fatigability, nausea, vomiting, weight loss, low-grade fever, abdominal fullness or pain.
  - **Other physical signs**: Palmar erythema, spider angiomas, dark skin pigmentation, gynecomastia, xanthomas, and subcutaneous bruising.





Structure of HBV viral particle and Serological Markers



Antigen-antibody		Nucleic acid
Antigen	Antibody	
HBsAg (Hepatitis B surface Antigen)	Anti-HBs (HB surface antibody)	HBV DNA (qualitative or quantitative)
HBcAg (Hepatitis B core Antigen) Does not appears in blood	IgM anti-HBc (HB core antibody IgM)	
	Total anti-HBc (IgM plus IgG)	
HBeAg (Hepatitis B e Antigen)	Anti-HBe (Hepatitis B e antibody)	

HBV Serological Markers

Test	Clinical Interpretation
HBsAg (hepatitis B surface antigen)	**Hallmark of infection.** Positive in the early phase of acute infection and persists in chronic infection. Quantification of HBsAg is a potential alternative marker of viraemia and is also used to monitor the response to antiviral treatment.
Anti-HBc IgM (hepatitis B core antibody)	IgM subclass of anti-HBc and observed during **acute infection** (used to differentiate between acute and chronic HBV infection). Might become positive during severe exacerbation of chronic infection.
Anti-HBc (total)	Develops around 3 months after infection (most constant marker of infection). Total anti-HBc (IgM, IgA, and IgG) indicates **resolved infection.**
HBeAg (hepatitis B e antigen)	Viral protein usually associated with **high viral load and high infectivity.**
Anti-HBe (hepatitis B e antibody)	Antibody to HBeAg usually indicates **decreasing HBV DNA.**
Anti-HBs (hepatitis B surface antibody)	Neutralizing antibody that confers **protection from infection.** Indicates recovery from acute infection (when with anti-HBc IgG) or **immunity from vaccination.**

Time course and interpretation of serological markers of HBV infection

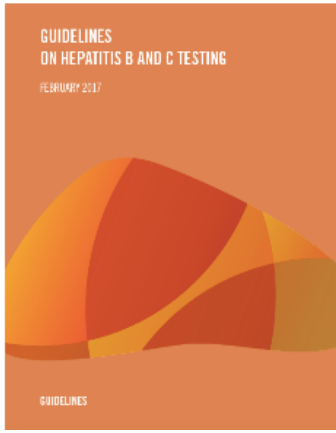


FIG. 4.2 Acute HBV infection with recovery

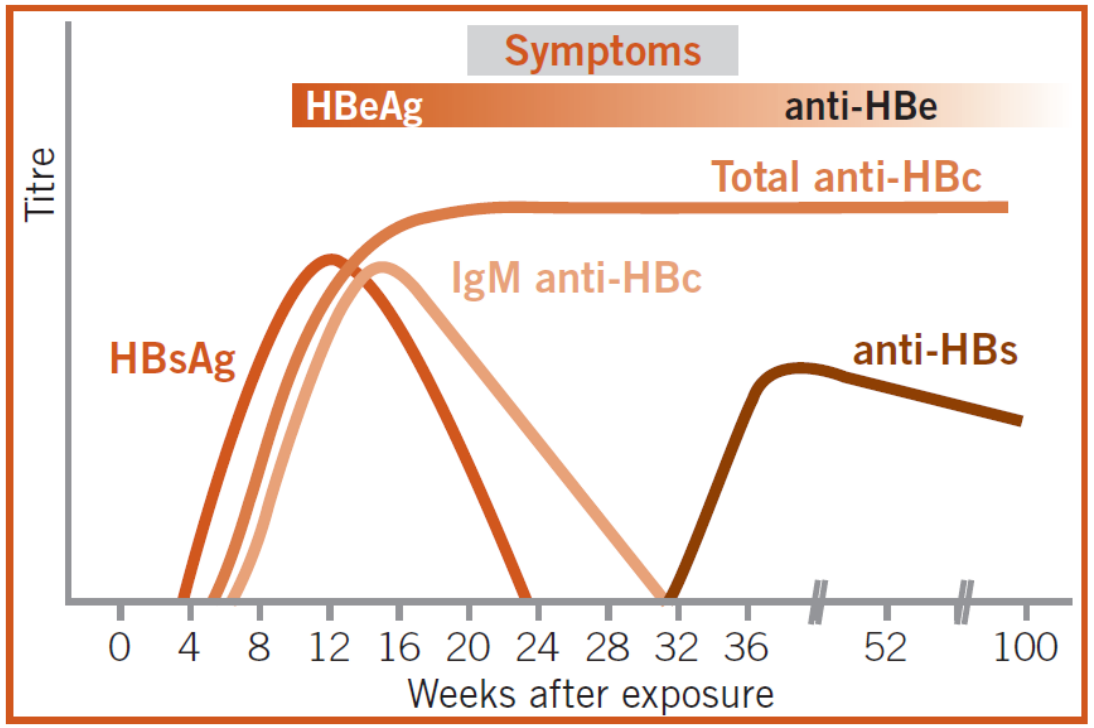
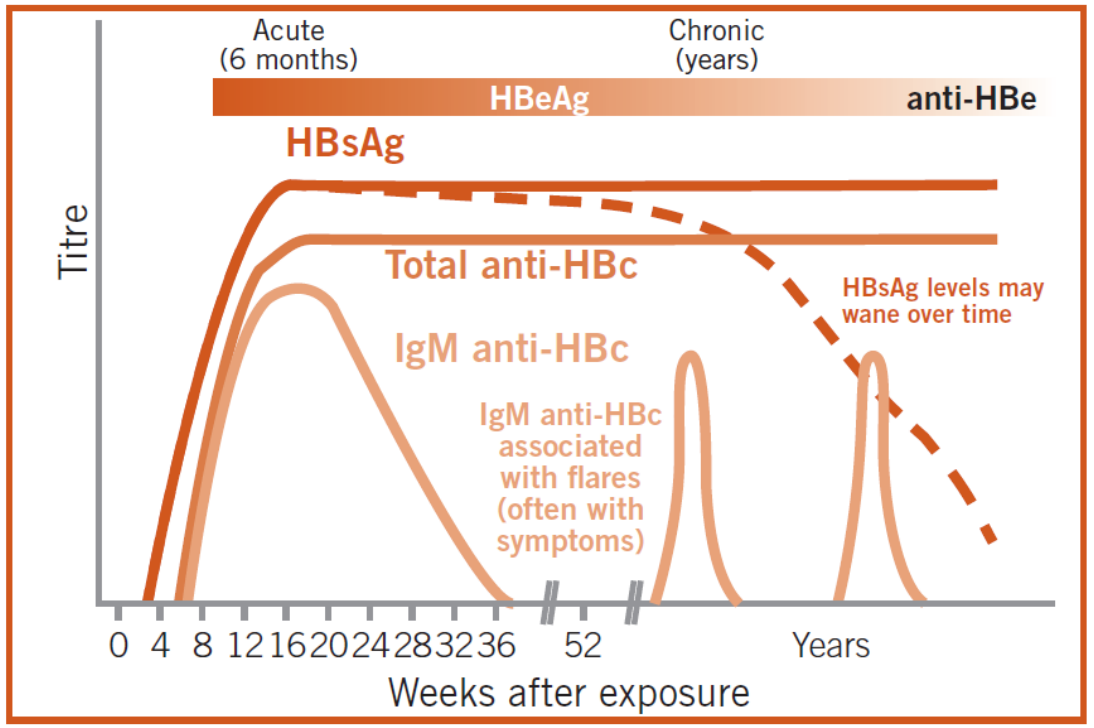


FIG. 4.3 Chronic HBV infection

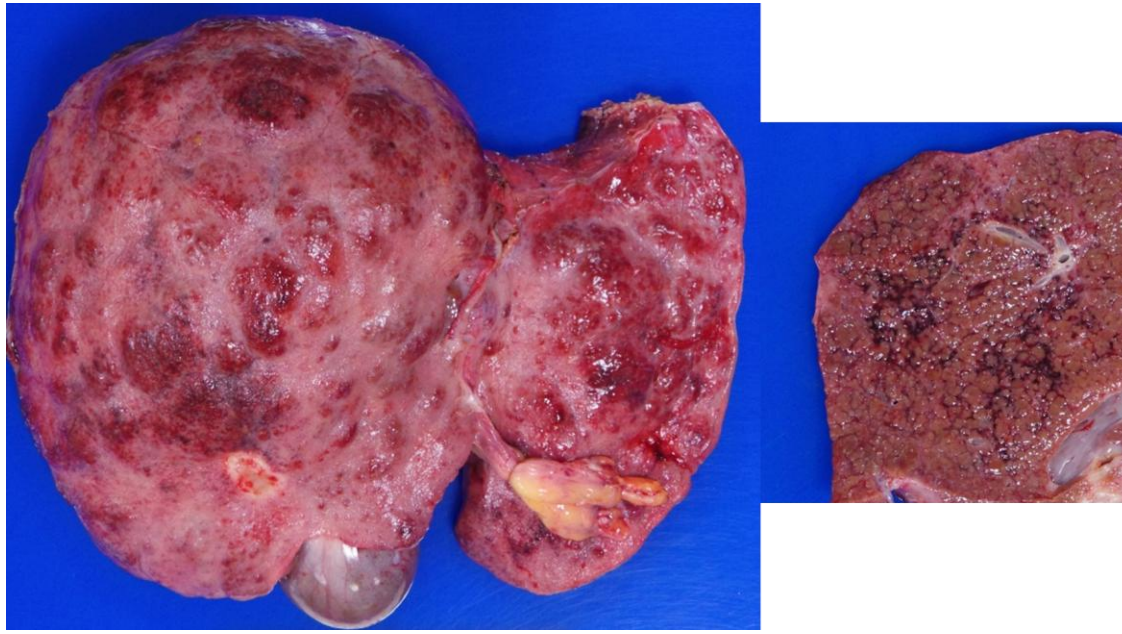


Interpretation of HBV serological markers

HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	Interpretation
−	−	−	−	Never exposed
−	+	−	+	Past natural infection, cleared – immunity achieved
−	+	−	−	Past natural infection, cleared – anti-HBs has waned over time or **false positive**
−	−	−	+	Immunity due to vaccination
−	+	+	+	Recent infection, recovered – immunity achieved
+	+	+	−	Acute infection, ongoing
+	+	−	−	Chronic infection (ongoing)

Progression of liver disease

METAVIR stage	F0	F1	F2	F3	F4
Definition	No fibrosis	Portal fibrosis without septa	Portal fibrosis with septa	Numerous septa without cirrhosis	Cirrhosis



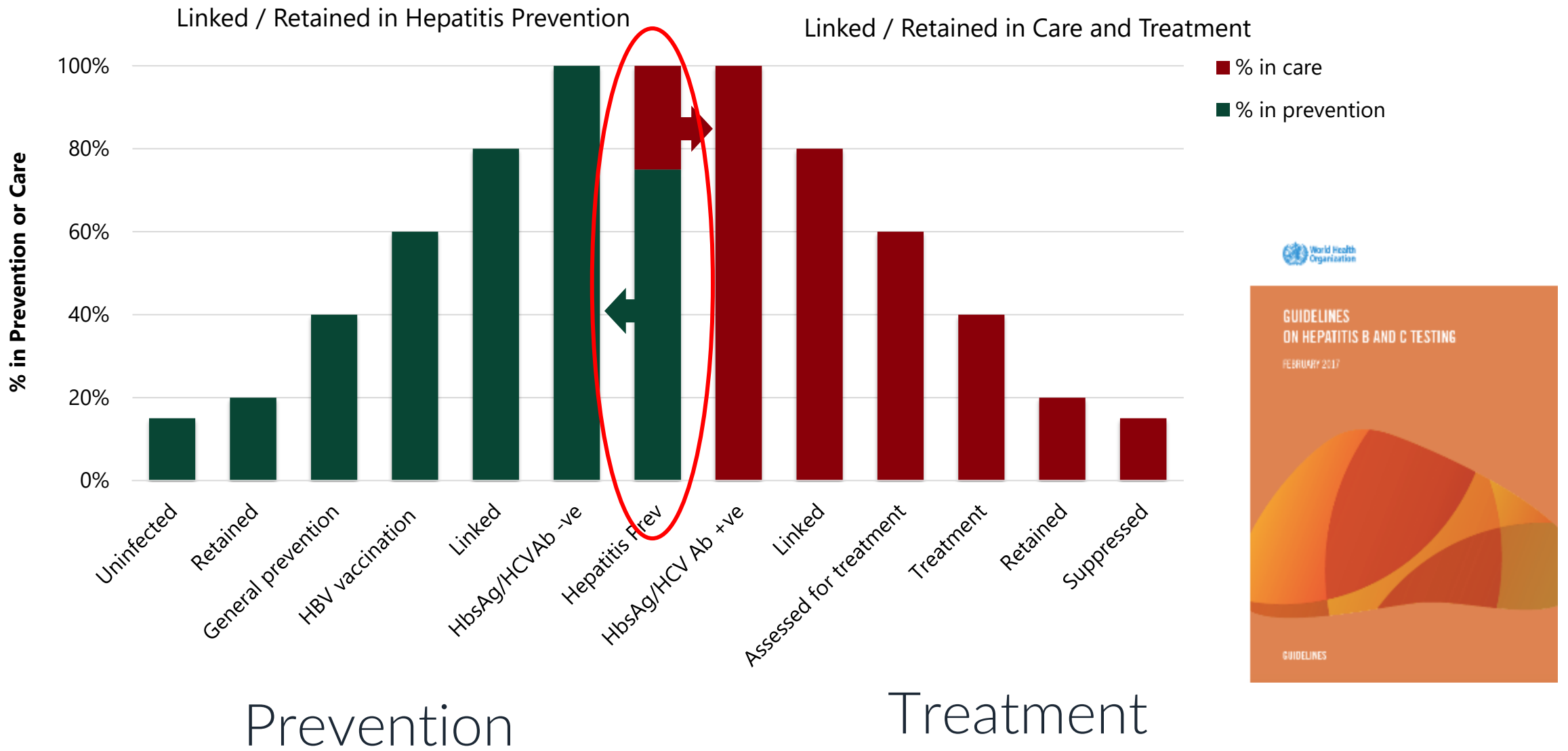
Hepatitis B Testing Strategies

Pan American Health Organization

World Health Organization

Americas Region

Viral hepatitis B testing is at core of entry to treatment and prevention cascade



Recommendations for the screening and diagnosis of hepatitis

How to test?

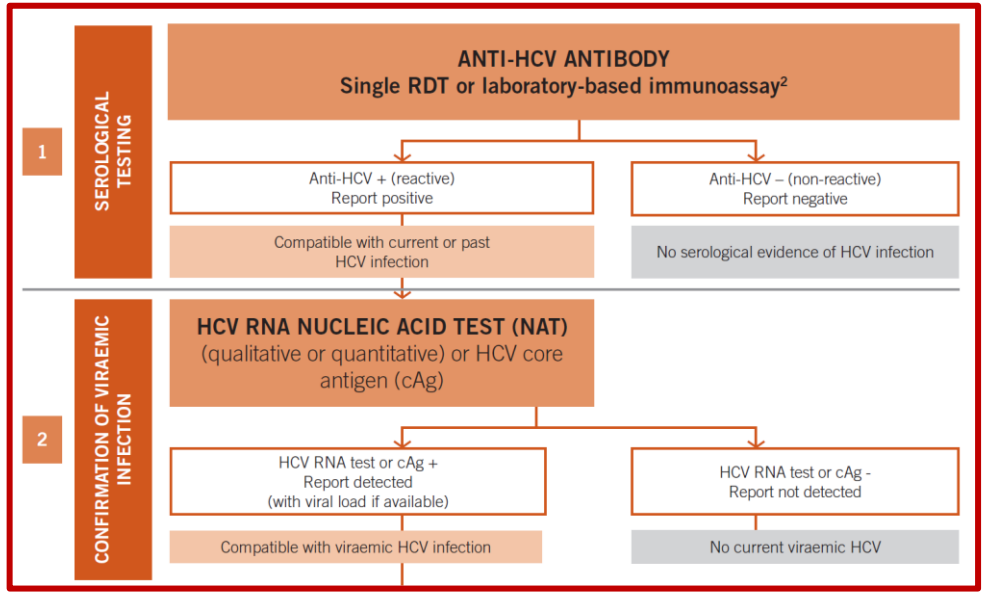
1. **A serological test HBsAG (EIA or RDT)**

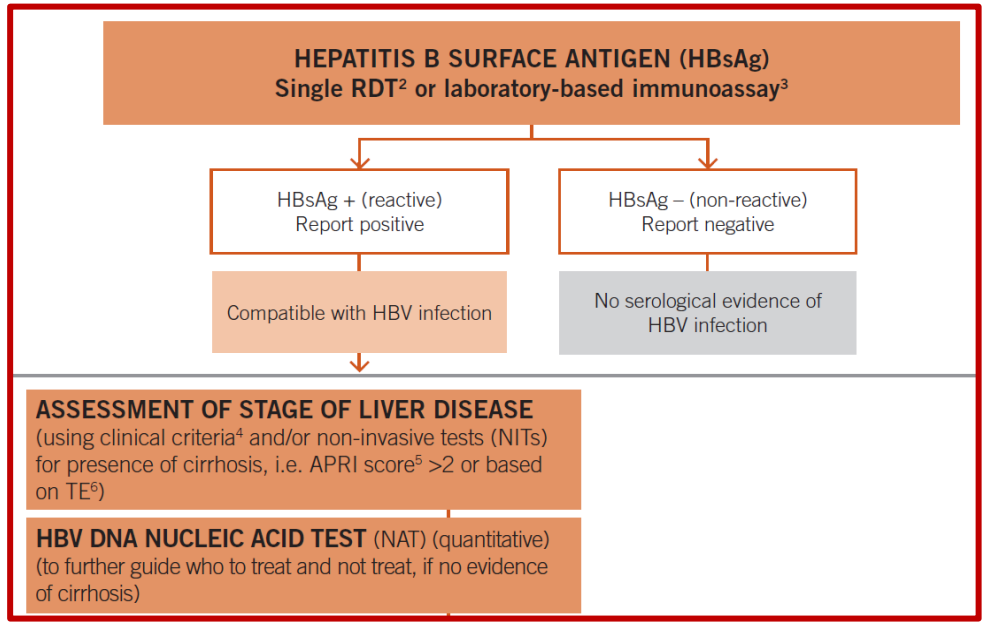
2. Followed by molecular testing (viral load)
   - **HBV DNA** to **guide treatment.**

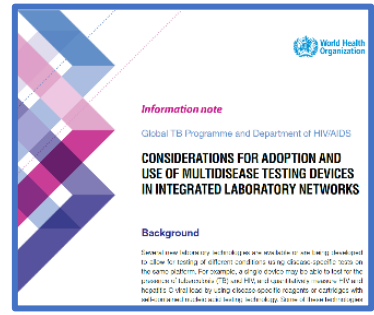
3. **Linkage to care**

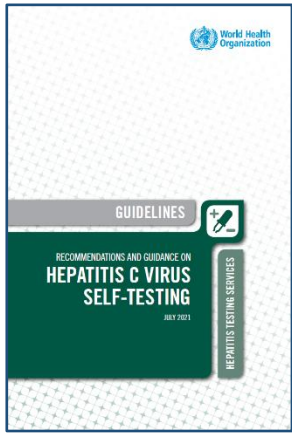
Considerations for Expanding Access

- **Rapid tests for point-of-care screening**
- Point-of-Care (PoC) Viral Load **- GeneXpert** and Other Multi-Diagnostic Platforms
- Using paper-based dried blood samples **(DBS)** for virology
- ***Reflex Viral load in laboratories***
- **Self Test**
- **Outreach activities**







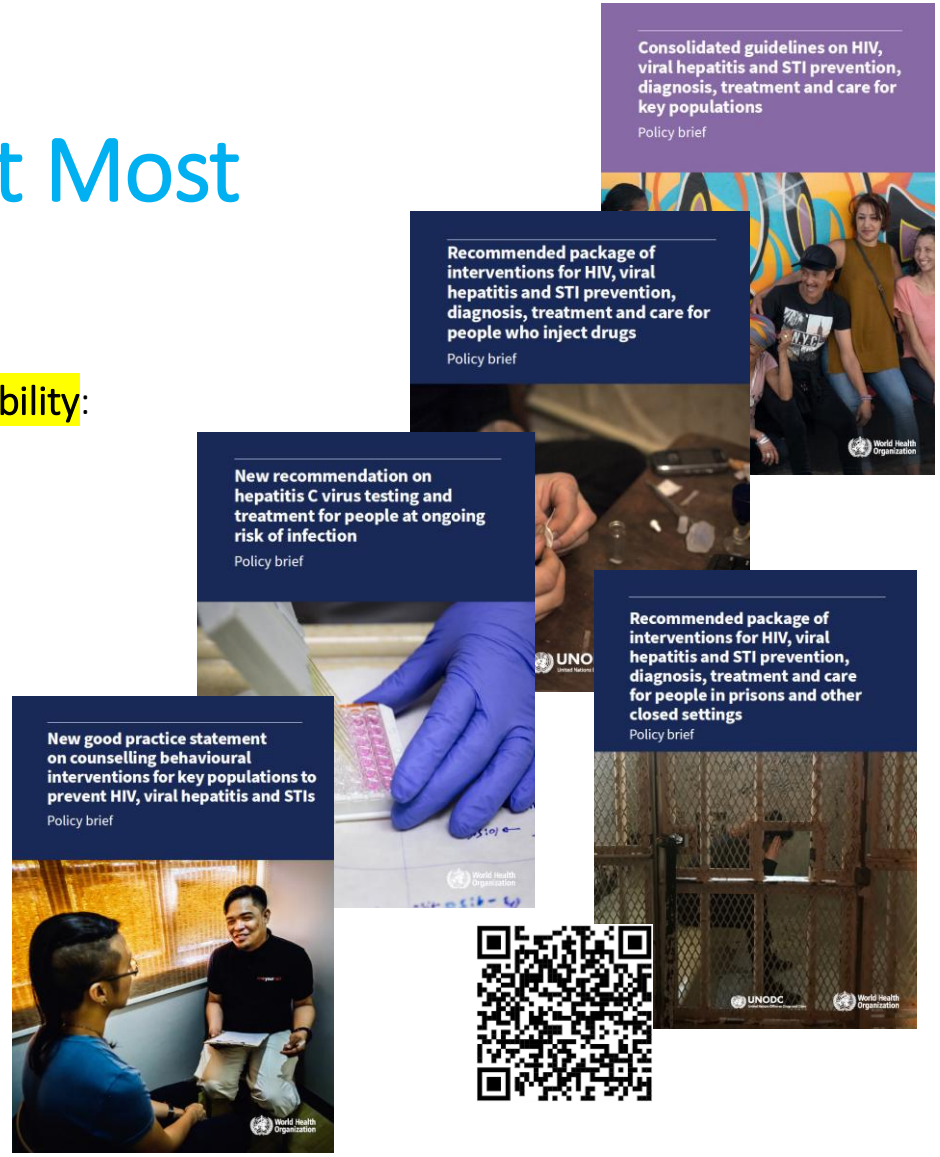


Ensuring Care for Those Who Need It Most

Offer testing to **all adults**; (in settings with **≥2% or ≥5%** HBsAg)

Certain Population Groups experience high incidence / prevalence, stigma or special vulnerability:

- Pregnant women (elimination of perinatal hepatitis B infection)
- Geographical areas
- Indigenous populations
- People on dialysis (other chronic care interventions)
- Health Professionals
- Exposure history: blood transfusions; tattoos, others
- Migrants
- People living with HIV
- People who inject drugs
- People in prisons or other closed settings
- Men who have sex with men
- Sex workers
- Other groups and populations identified in the local context…



Systematic review(Beard, 2024):

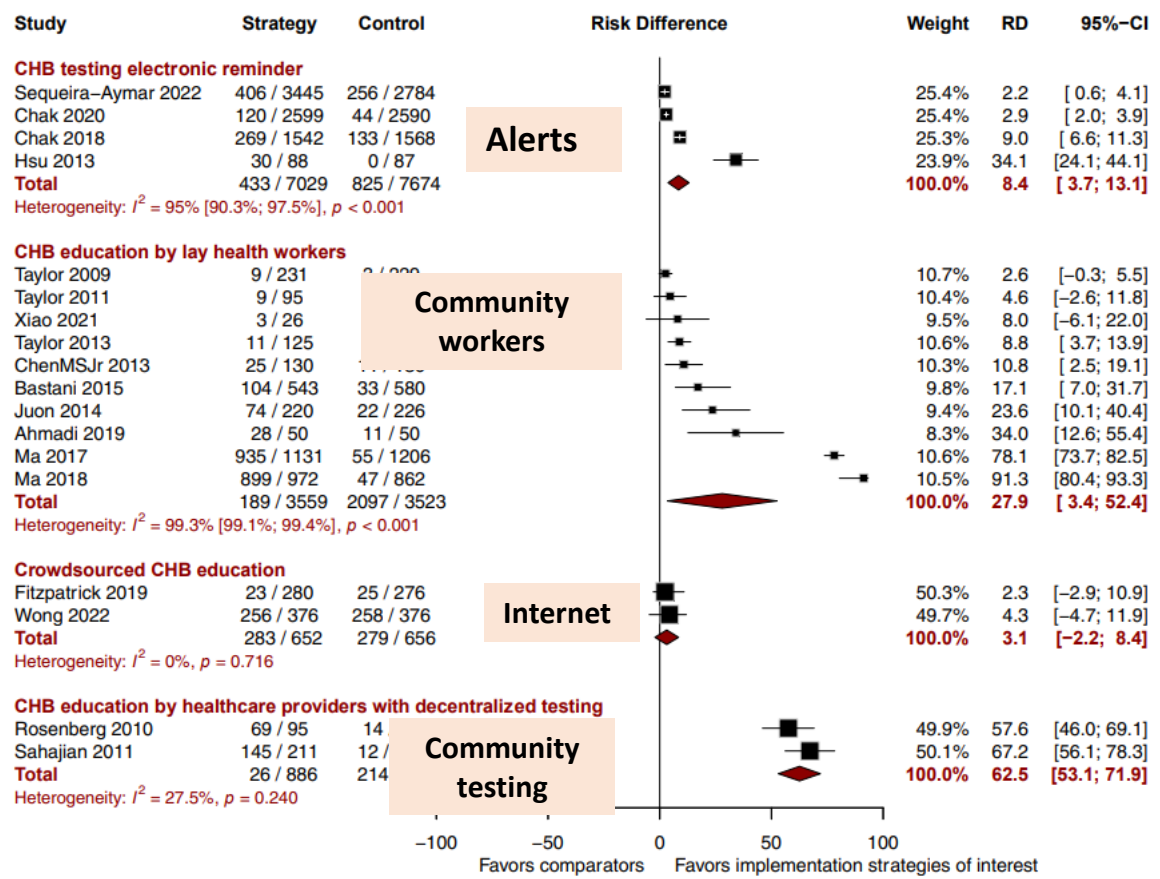
- *Integrated Test Implementation **HIV/HBV/HCV***
- *56 countries, **14 million individuals**.*
- *For every **3 people diagnosed with HIV**, another **4 with HBV** and **7 with HCV** were identified.*

Sub-Population	Number of studies	HIV positivity (%) [SD]	HBV positivity (%) [SD]	HCV positivity (%) [SD]	Total single BBV prevalence (%) [SD]
Blood Donors	43	1.01 [±1.70]	2.61 [±3.51]	1.07 [±1.42]	4.42 [±5.50]
Pregnant Women	16	1.92 [±3.17]	3.30 [±4.02]	1.23 [±1.71]	6.17 [±6.14]
Healthcare Attendees	34	2.02 [±5.04]	3.21 [±6.39]	3.51 [±8.12]	7.07 [±10.31]
Immigrants, Refugees and Asylum Seekers	35	1.30 [±1.76]	5.11 [±4.04]	2.05 [±2.27]	8.24 [±5.61]
General Population	11	2.45 [±4.28]	3.96 [±3.46]	3.95 [±3.88]	9.46 [±8.96]
Prisoners	15	2.05 [±2.03]	3.18 [±3.37]	7.90 [±6.82]	12.83 [±6.76]
Homeless Individuals	4	3.58 [±2.31]	1.72 [±0.70]	21.72 [±8.68]	27.02 [±10.86]
MSM	4	25.75 [±30.45]	2.54 [±2.56]	3.12 [±2.15]	30.54 [±32.03]
PWUD	13	14.03 [±13.27]	10.78 [±13.21]	50.26 [±20.62]	55.76 [±23.03]
Total		**3.12 [±7.71]**	**4.01 [±5.80]**	**6.70 [±14.64]**	**11.83 [16.86]**

Source: Beard et al Open Forum Infect Dis 2024

Systematic review and meta-analysis(Kim, 2024)

- Strategies to promote **hepatitis B testing**
- 130,598 individuals
- Communities; social networks; Primary Care



Source: Thanh Van Kim et al, eClinicalMedicine 2024

WHO Recommendations on Management of Hepatitis B

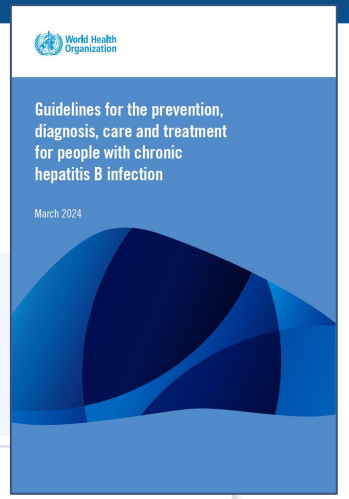
Pan American Health Organization

World Health Organization

Americas Region

Chronic Hepatitis B — Initial assessment

HBsAg positive



Assess treatment eligibility

Disease stage + labs + clinical context

1 Stage liver disease severity

Use **non-invasive assessment** (e.g., APRI or transient elastography) to estimate fibrosis/cirrhosis risk.

2 Check ALT/AST and HBV DNA

Interpret ALT relative to the lab ULN and review viral load to guide treatment decisions.

3 Medical history & risk modifiers

- Coinfections (HIV/HDV/HCV),
- Comorbidities,
- Immunosuppression,
- Extrahepatic disease,
- Family history of cirrhosis/liver cancer.

General care measures

Risk reduction + readiness + prevention

1 Lifestyle counselling

Address **alcohol** use, **diet** quality, and physical activity; tailor to metabolic and liver risk profile.

2 Prepare for treatment

Assess **adherence** support needs; evaluate renal risk factors and **baseline renal function** relevant.

3 Prevent transmission

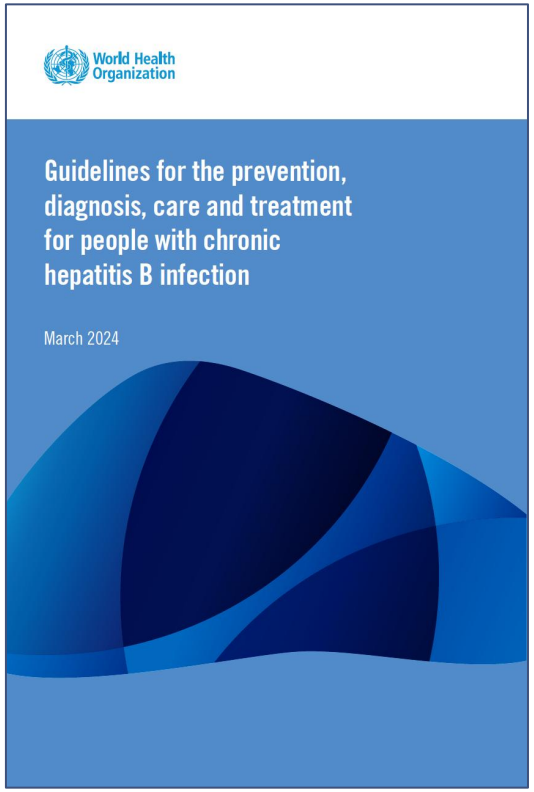
Screen **household/sexual contacts** (HBsAg) and **vaccinate** those who are HBV negative.

Non-invasive tests for liver fibrosis

- **Liver biopsy** considered **impracticable** in low-income settings

- **APRI (aspartate aminotransferase-to-platelet ratio index)**
  - **>0.5** suggests significant fibrosis; **>1.0** suggests cirrhosis.
  - **recommended as the preferred non-invasive test**

$$\text{APRI} = \left(\frac{\text{AST (U/L)}}{\text{Upper Limit of Normal AST (U/L)}} \right) \div \text{Platelet count } (10^9/\text{L}) \times 100$$

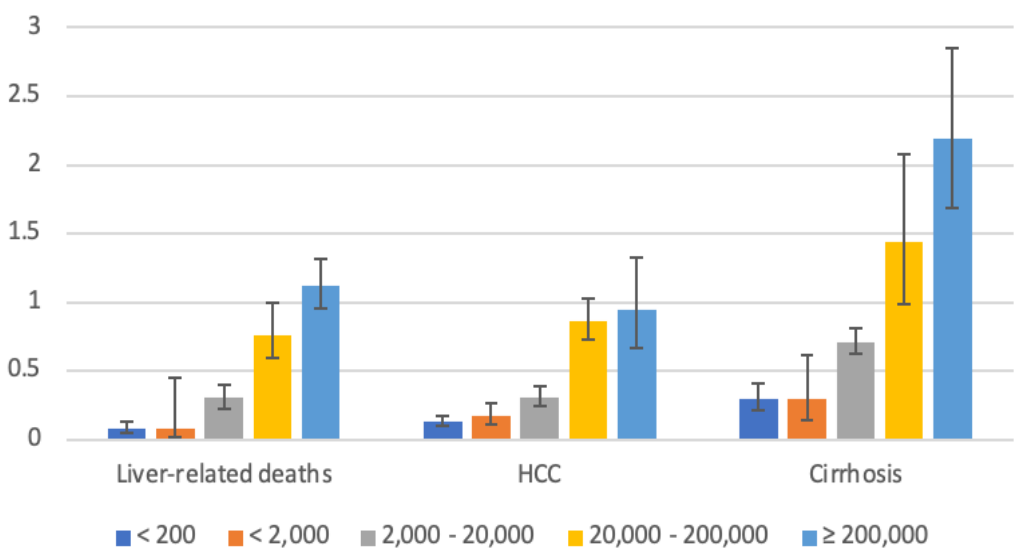


- **Transient Elastography (FibroScan®):**
  - Measures liver stiffness (kPa).
  - **>12 kPa** suggests cirrhosis.
  - Preferred in settings **where it is available and cost is not a major constraint**.

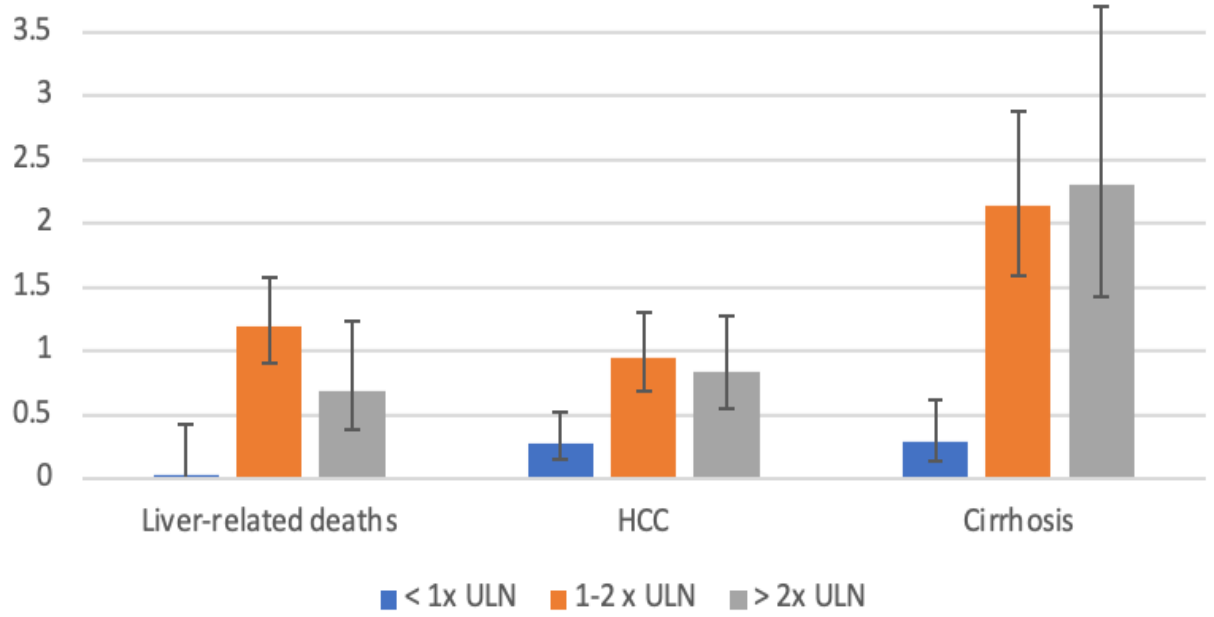
- **Others (specialized):**
  - FIB-4 Index; FibroTest, FibroSure, HepaScore, ELF test (combination of serological markers);
  - Shear-Wave or Acoustic Radiation Force Elastography (Ultrasound-based);
  - Magnetic Resonance Elastography (MRE).

Systematic review 1 – Natural history of CHB according to HBV DNA and ALT levels in adults

Pooled incidence rates according to single baseline HBV DNA



Pooled incidence rates according to single baseline ALT level



Evidence review

- 69 studies –65.2% from Western Pacific regions; 3 (4.3%) from Africa
- **VL:** Low incidence of HCC, cirrhosis and liver-related mortality in <200 and <2000 IU/ml strata. Dose-response increased incidence from above 2000 to >200,000 IU/ml
- **ALT:** low incidence in <ULN strata. Higher incidence in >1-2x ULN.

Systematic review 2 – Efficacy of antiviral treatment according to HBV DNA and ALT levels in adults

Variables		Number (Total n=80)	%
WHO regions	Western Pacific (WPR)	49	61.3%
	South East Asia (SEAR)	1	1.3%
	Eeastern Mediteranean (EMR)	3	3.8%
	Europe (EUR)	13	16.3%
	Africa (AFR)	3	3.8%
	Americas (AMR)	4	5%
	Combination	7	8,8%
Year of publication	Before 2015	40	50%
	After 2015 (including 2015)	38	47.5%
	Unpublished	2	2.5%
Study population	Adults	68	85%
	Children (<18 years)	10	12.5%
	Mixed	2	2.5%
Study included in the previous WHO systematic review	Yes	7	8.8%
	No	73	91.2%
Study design	RCT	6	11%
	Prospective cohort study	44	55%
	Retrospective cohort study	30	34%
Fibrosis assessment	Not reported	58	72.5%
	F0-1	3	3,8%
	F0-2	5	6,3%
	F0-3	14	17,5%
Duration of follow-up	< 5 years	31	38,8%
	≥ 5 years	49	61,3%

- 46 studies – 66% from Western Pacific region, 0 from AFRO or EMRO
- 33 RCTs and 13 observational studies;
- 63% in adults and 17 (46%) in <18 yrs
- **Outcomes:** 72% reported outcomes in >20,000, only 1 RCT and 6 observational studies in <20,000 IU/ml, and one RCT <2000

Summary estimates of efficacy of antiviral therapy at reducing outcomes in adults with CHB without cirrhosis, stratified by HBV DNA levels

Viral load stratum (IU/mL)	Outcome	No. of studies	Type of studies	RR/HR	95% CI	GRADE
<2,000	HCC	1	Cohort	aHR 0.72	0.43 - 1.20	Very low
	HBsAg seroconversion	1	RCT	RR 3.72	0.30 - 45.79	Very low
		4	Cohort	RR 36.21	8.74 - 149.39	Moderate
	HBsAg loss or reduction	6	Cohort	RR 5.88	1.37-33.01	Very low
2,000 - 20,000	HCC	1	Cohort	aHR 0.45	0.14 - 1.46	Very low
20,000 - 200,000	HCC	1	Cohort	aHR 0.17	0.06 - 0.52	Low
	Worsening of fibrosis	2	RCT	RR 0.56	0.25 - 1.15	Moderate
	Improvement of fibrosis	2	RCT	RR 1.23	0.48 - 8.12	Moderate
	Worsening of necroinflammation	2	RCT	RR 0.38	0.13 - 1.01	Low
	Improvement of necroinflammation	2	RCT	RR 1.42	0.76 - 4.41	Low
	ALT normalisation	1	RCT	RR 1.49	1.13 - 1.97	Moderate
	HBeAg loss	1	RCT	RR 0.40	0.05 - 3.13	Very low
	HBsAg loss or reduction	1	RCT	RR 0.34	0.01 - 8.16	Very low
	Undetectable viral load	2	RCT	RR 6.86	2.65 - 15.15	Moderate
200,000 - 2M	HCC	1	Cohort	aHR 0.37	0.15 - 0.91	Very low
	Improvement of necroinflammation	1	RCT	RR 0.86	0.40 - 1.82	Low
	ALT normalisation	1	RCT	RR 3.64	2.43 - 5.45	Low
	HBeAg loss	1	RCT	RR 6.88	0.38 - 124.52	Very low
	HBeAg seroconversion	2	RCT	RR 17.04	3.33 - 50.23	Moderate
	Undetectable viral load	3	RCT	RR 14.02	5.25 - 31.93	Moderate

HBV DNA level	Liver-related deaths	Cirrhosis	HCC
<2000	1190	137	210
2000-20,000	182	21	59
20,000-200,000	12	7	14

- **VL:** Higher treatment efficacy at higher baseline VL and ALT levels
- Very low to moderate quality evidence at VL<20,000 and low to high quality at >20,000
- **NNT:** to prevent one case of HCC was 210 at HBV DNA <2000, 59 at 2000-20,000, and 14 at >20,000 IU/ml

WHO Recommendations: When to treat **chronic hepatitis B**

Treat adults and adolescents (≥12 years) with chronic hepatitis B, including pregnant women, if ANY of the following apply

Quick rule

- Treat if there is evidence of **liver damage**, active **viral replication with liver inflammation**, or important **clinical risk factors.**

- If HBV DNA is not available, persistently abnormal ALT can support treatment.

1 **Significant fibrosis (≥ F2) or cirrhosis (F4)**

APRI >0.5 or elastography >7 kPa; treat **regardless of ALT or HBV DNA**.

2 **HBV DNA >2,000 IU/mL + ALT above Upper Limit of Normal: 30(M) and 19(F) U/L**

Adolescents: persistent ALT elevation rather than a single abnormal value (6-12 months)

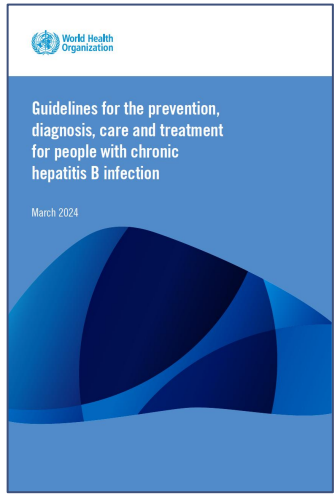
Raised ALT may normalize in pregnancy (reassess after delivery)

3 **Special situations**

Coinfection, family history of liver cancer/cirrhosis, immunosuppression, comorbidities, or extrahepatic manifestations.

4 **If HBV DNA is unavailable**

Persistently abnormal ALT levels alone can support treatment.



** **Children 2-11 Years:** treatment is generally offered on a case-by-case basis: cirrhosis or advancing liver fibrosis stage ≥F2, persistent HBV DNA >2000 IU/mL, comorbidities.

** **Children <2 Years:** Treatment not recommended

RECOMMENDATIONS– HOW TO TREAT

1. **Preferred regimens:**
   - Tenofovir disoproxil fumarate (TDF) or
   - Entecavir (ETV)

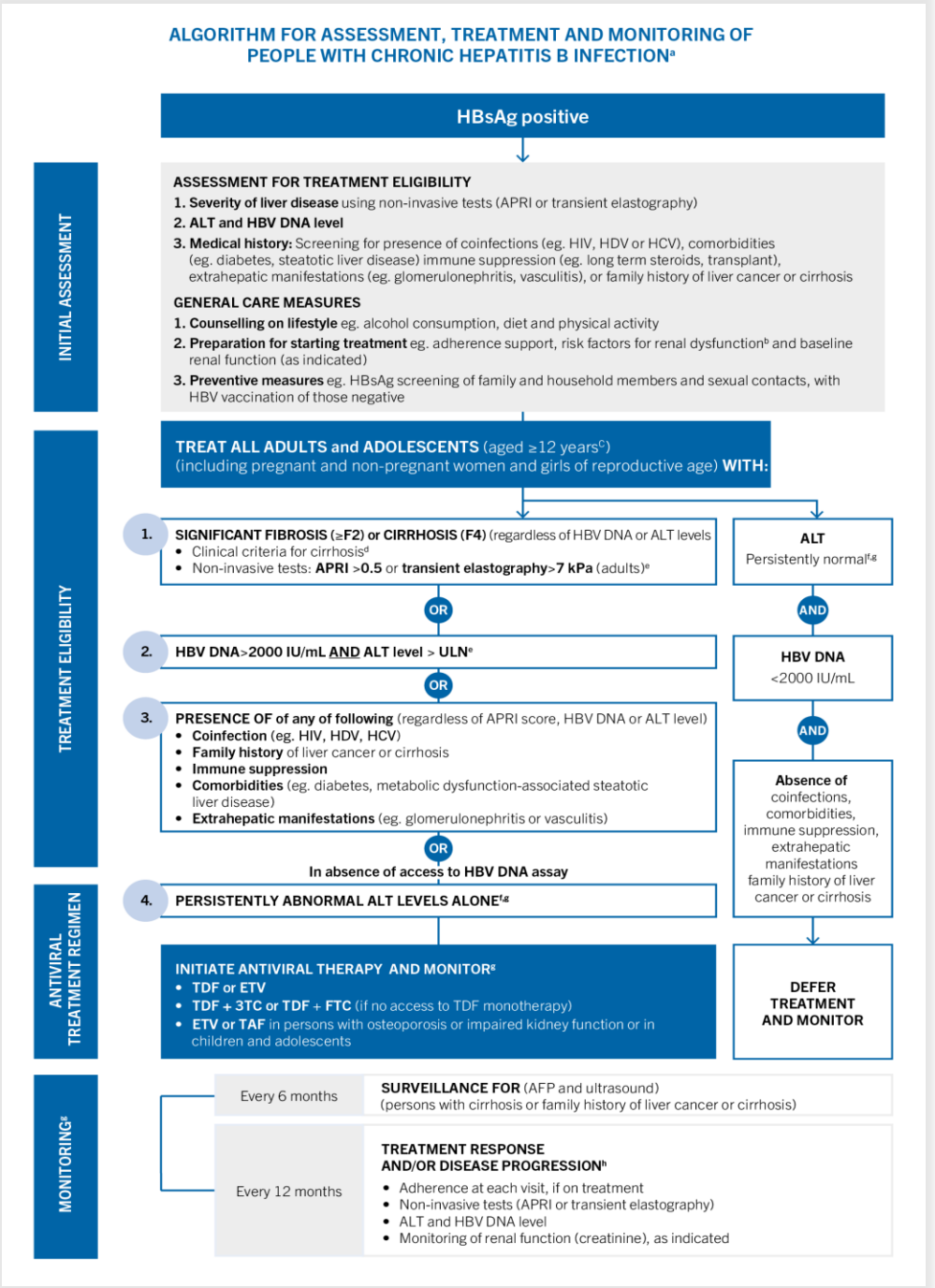
2. **Alternative regimens** (where TDF monotherapy is not available)
   - TDF + lamivudine (3TC)
   - TDF + emtricitabine (FTC)

3. **Osteoporosis and/or impaired kidney function:**
   - Entecavir (ETV) or
   - Tenofovir alafenamide fumarate (TAF)

4. **Children or adolescents**
   - aged ≥2 years: similar regimens (TDF, ETV, TDF+3TC, TDF+FTC)
   - TAF only for children aged ≥12 years
   - Ages <2 years: treatment not recommeded

(strong recommendation, moderate-certainty evidence)

World Health Organization



Chronic hepatitis B: treatment monitoring

FOLLOW-UP PLAN

1 HCC surveillance — EVERY 6 MONTHS

- Abdominal ultrasound + Apha-fetoprotein (AFP) for patients with
  - Cirrhosis
  - Family history of liver cancer or cirrhosis
  - age >40 years and HBV DNA >2,000 IU/mL without cirrhosis

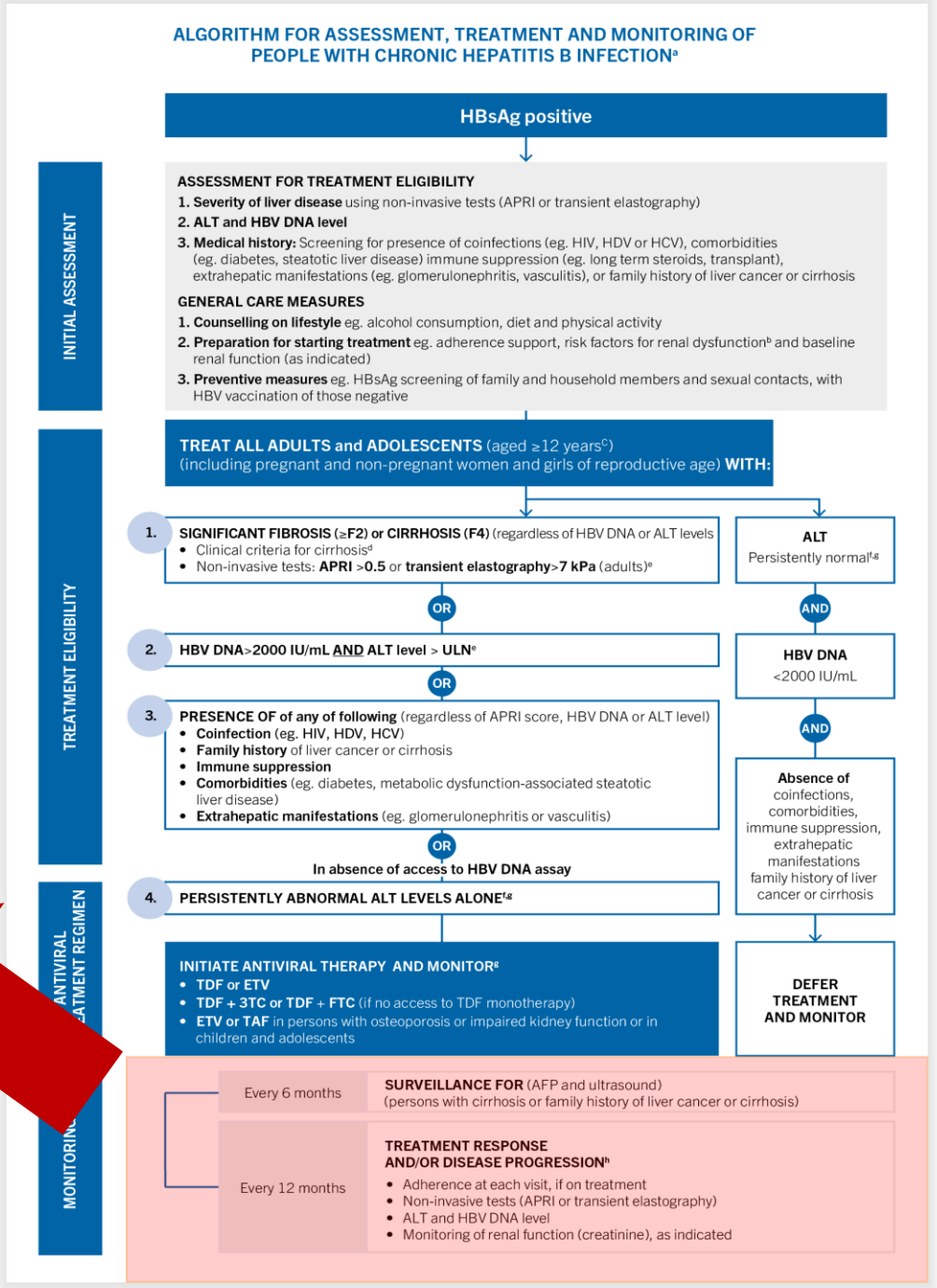
2 Monitor all patients — AT LEAST ANNUALLY

- **ALT** (and AST for APRI), HBsAg, HBeAg, **HBV DNA**
- **Non-invasive fibrosis assessment** if no cirrhosis at baseline
- Assess **adherence** at each visit if on treatment

3 Renal safety — BEFORE TREATMENT AND THEN ANNUALLY

- Baseline renal function and baseline risk assessment
- **Annual renal monitoring** on long-term tenofovir or entecavir

Use the right half of the slide for narrative, treatment pathway, or speaker notes visual.



ALGORITHM FOR ASSESSMENT, TREATMENT AND MONITORING OF PEOPLE WITH CHRONIC HEPATITIS B INFECTION[a]

HBsAg positive

INITIAL ASSESSMENT

ASSESSMENT FOR TREATMENT ELIGIBILITY

1. **Severity of liver disease** using non-invasive tests (APRI or transient elastography)
2. **ALT and HBV DNA level**
3. **Medical history:** Screening for presence of coinfections (eg. HIV, HDV or HCV), comorbidities (eg. diabetes, steatotic liver disease) immune suppression (eg. long term steroids, transplant), extrahepatic manifestations (eg. glomerulonephritis, vasculitis), or family history of liver cancer or cirrhosis

GENERAL CARE MEASURES

1. **Counselling on lifestyle** eg. alcohol consumption, diet and physical activity
2. **Preparation for starting treatment** eg. adherence support, risk factors for renal dysfunction[b] and baseline renal function (as indicated)
3. **Preventive measures** eg. HBsAg screening of family and household members and sexual contacts, with HBV vaccination of those negative

TREATMENT ELIGIBILITY

TREAT ALL ADULTS and ADOLESCENTS (aged ≥12 years[c]) (including pregnant and non-pregnant women and girls of reproductive age) **WITH:**

1. **SIGNIFICANT FIBROSIS (≥F2) or CIRRHOSIS (F4)** (regardless of HBV DNA or ALT levels
   - Clinical criteria for cirrhosis[d]
   - Non-invasive tests: **APRI >0.5** or **transient elastography>7 kPa** (adults)[e]

OR

2. **HBV DNA>2000 IU/mL AND ALT level > ULN**[e]

OR

3. **PRESENCE OF of any of following** (regardless of APRI score, HBV DNA or ALT level)
   - **Coinfection** (eg. HIV, HDV, HCV)
   - **Family history** of liver cancer or cirrhosis
   - **Immune suppression**
   - **Comorbidities** (eg. diabetes, metabolic dysfunction-associated steatotic liver disease)
   - **Extrahepatic manifestations** (eg. glomerulonephritis or vasculitis)

OR

In absence of access to HBV DNA assay

4. **PERSISTENTLY ABNORMAL ALT LEVELS ALONE**[f,g]

ALT
Persistently normal[f,g]

AND

HBV DNA
<2000 IU/mL

AND

Absence of
coinfections, comorbidities, immune suppression, extrahepatic manifestations family history of liver cancer or cirrhosis

ANTIVIRAL TREATMENT REGIMEN

INITIATE ANTIVIRAL THERAPY AND MONITOR[g]

- **TDF or ETV**
- **TDF + 3TC or TDF + FTC** (if no access to TDF monotherapy)
- **ETV or TAF** in persons with osteoporosis or impaired kidney function or in children and adolescents

DEFER TREATMENT AND MONITOR

MONITORING[g]

Every 6 months	**SURVEILLANCE FOR** (AFP and ultrasound) (persons with cirrhosis or family history of liver cancer or cirrhosis)
Every 12 months	**TREATMENT RESPONSE AND/OR DISEASE PROGRESSION**[h] • Adherence at each visit, if on treatment • Non-invasive tests (APRI or transient elastography) • ALT and HBV DNA level • Monitoring of renal function (creatinine), as indicated

World Health Organization

Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection

March 2024

ALGORITHM FOR ASSESSMENT, TREATMENT AND MONITORING OF PEOPLE WITH CHRONIC HEPATITIS B INFECTION[a]

HBsAg positive

INITIAL ASSESSMENT

ASSESSMENT FOR TREATMENT ELIGIBILITY

1. **Severity of liver disease** using non-invasive tests (APRI or transient elastography)
2. **ALT and HBV DNA level**
3. **Medical history:** Screening for presence of coinfections (eg. HIV, HDV or HCV), comorbidities (eg. diabetes, steatotic liver disease) immune suppression (eg. long term steroids, transplant), extrahepatic manifestations (eg. glomerulonephritis, vasculitis), or family history of liver cancer or cirrhosis

GENERAL CARE MEASURES

1. **Counselling on lifestyle** eg. alcohol consumption, diet and physical activity
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TREAT ALL ADULTS and ADOLESCENTS (aged ≥12 years[c]) (including pregnant and non-pregnant women and girls of reproductive age) **WITH:**

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   - Clinical criteria for cirrhosis[d]
   - Non-invasive tests: **APRI >0.5** or **transient elastography>7 kPa** (adults)[e]

OR

2. **HBV DNA>2000 IU/mL AND ALT level > ULN**[e]

OR

3. **PRESENCE OF of any of following** (regardless of APRI score, HBV DNA or ALT level)
   - **Coinfection** (eg. HIV, HDV, HCV)
   - **Family history** of liver cancer or cirrhosis
   - **Immune suppression**
   - **Comorbidities** (eg. diabetes, metabolic dysfunction-associated steatotic liver disease)
   - **Extrahepatic manifestations** (eg. glomerulonephritis or vasculitis)

OR

In absence of access to HBV DNA assay

4. **PERSISTENTLY ABNORMAL ALT LEVELS ALONE**[f,g]

ALT Persistently normal[f,g]

AND

HBV DNA <2000 IU/mL

AND

Absence of coinfections, comorbidities, immune suppression, extrahepatic manifestations family history of liver cancer or cirrhosis

DEFER TREATMENT AND MONITOR

ANTIVIRAL TREATMENT REGIMEN

INITIATE ANTIVIRAL THERAPY AND MONITOR[g]

- **TDF or ETV**
- **TDF + 3TC or TDF + FTC** (if no access to TDF monotherapy)
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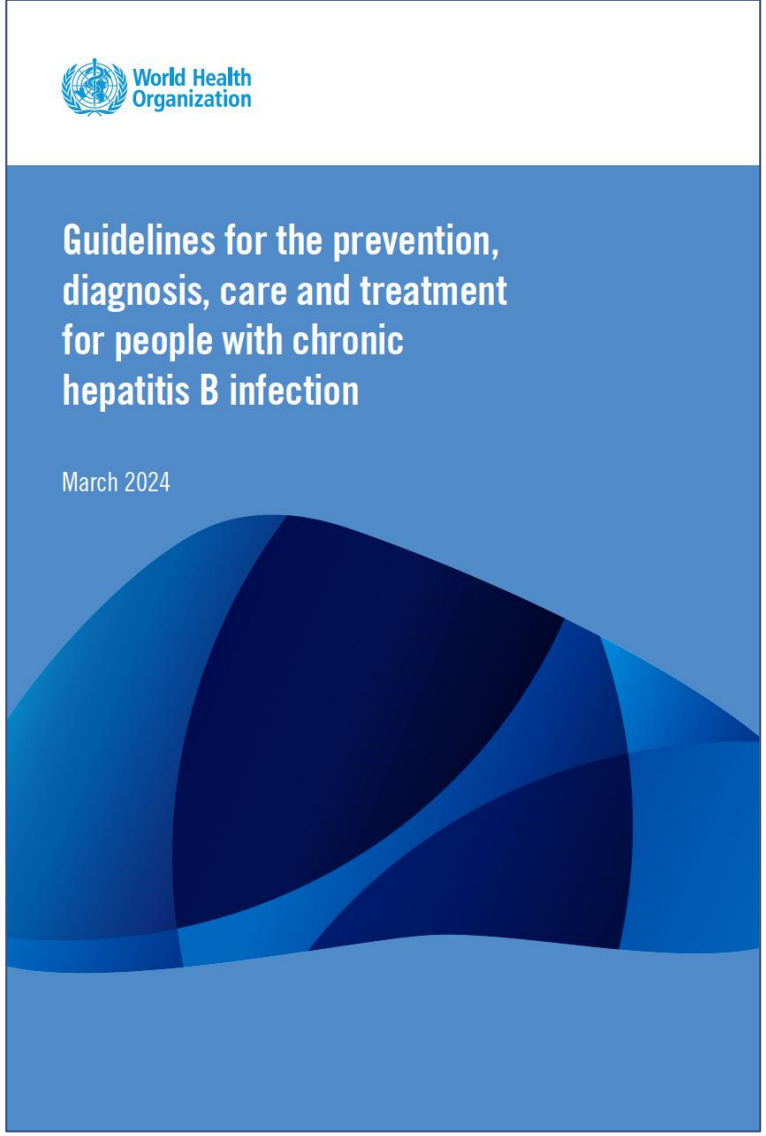


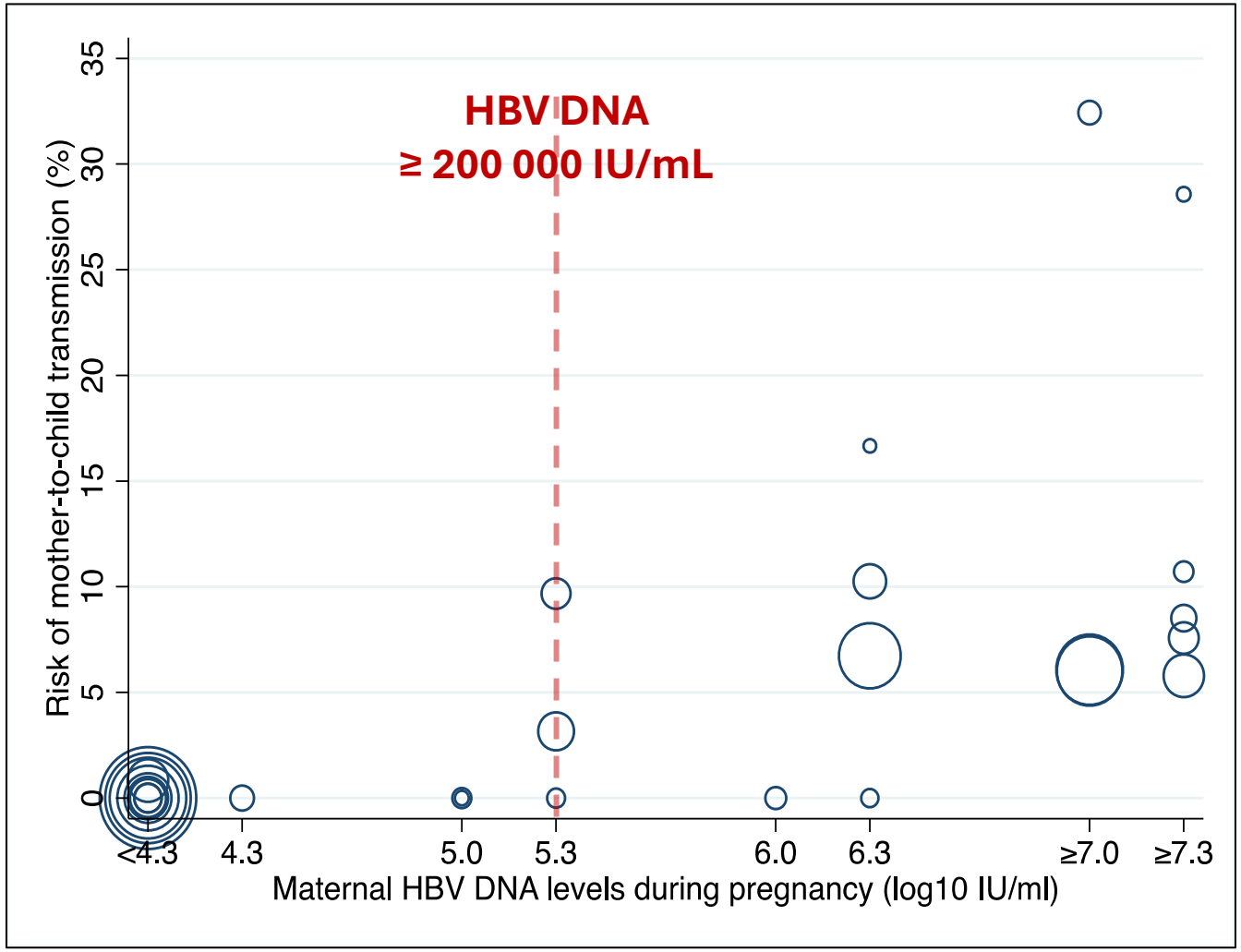
What to do when a pregnant is not eligible for treatment?

Risk of Hepatitis B mother-to-child transmission and protective effect of recommended interventions

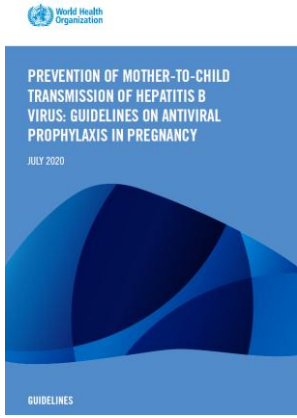
Interventions	Women with high viral load	Women with high viral loads, receiving antiviral treatment
No vaccination	100% (90.3 – 100)	5.6% (4.5 – 5.6)
Vaccine – 24h dose only	90% (81.3 – 100)	5.1% (4.1 – 5.6)
Complete vaccination, without the 24-hour dose.	32.7% (29 – 35)	1.6% (1.5 – 1.8)
Full vaccination without HBIG	13.8% (9.6 – 41.3)	0.7% (0.5 – 2.1)
Full vaccination with HBIG	7.7% (1.5 – 20.7)	0.4% (0.1 – 1.0)

Results of the DNA viral load threshold assessment for vertical transmission

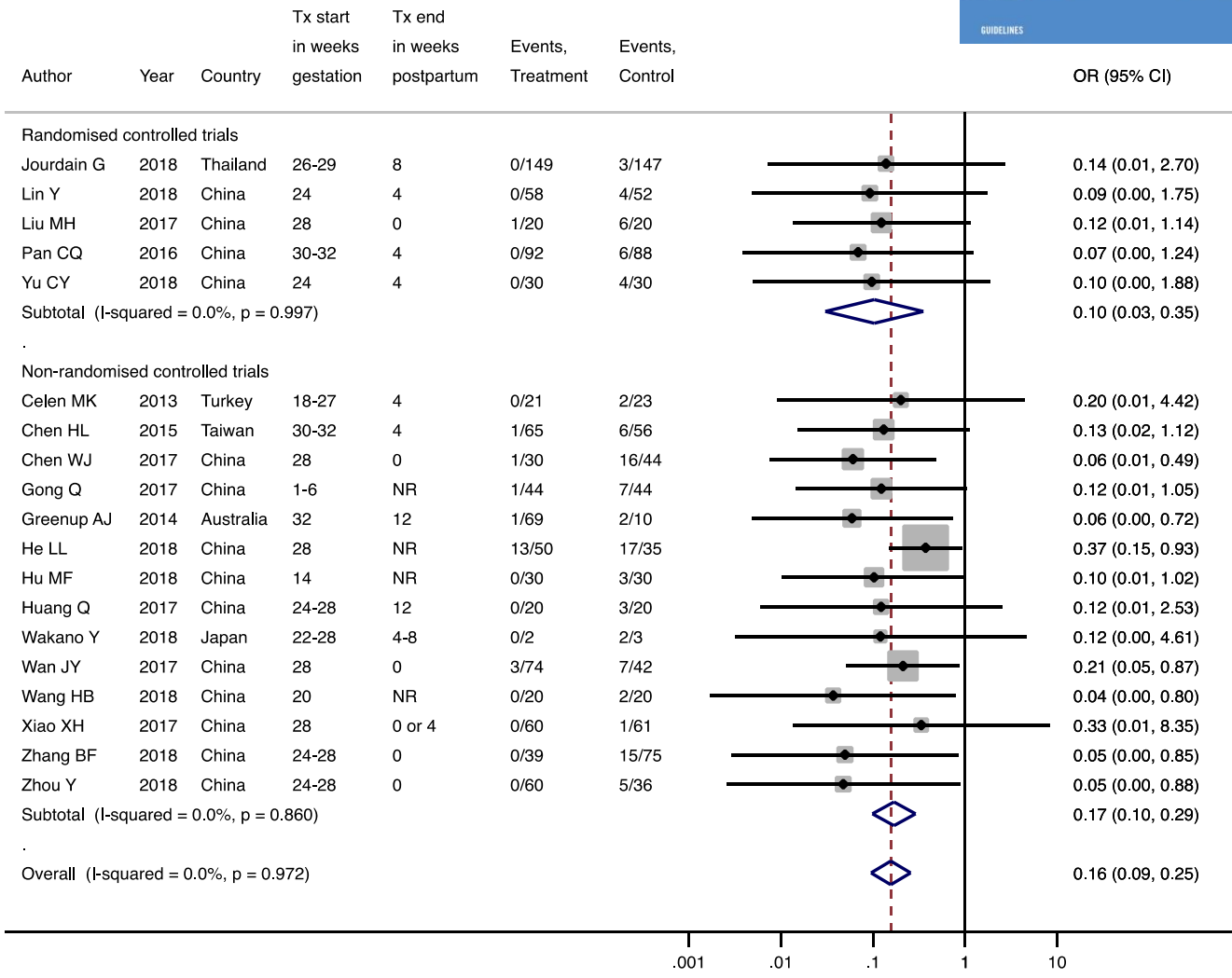
- When the timely dose of vaccine and immunoglobulin is used, no breakthrough infection was reported when maternal HBV DNA viral load was less than **5.3 log IU/mL (200,000 IU/mL)**



Efficacy of TDF for the prophylaxis of mother-to-child transmission of HBV



- 19 studies included
- Recruitment: 2007 - 2018
- Countries:
  - China (Mainland, n=14 & Taiwan, n=1)
  - Japan (n=1)
  - Australia (n=1)
  - Thailand (n=1)
  - Turkey (n=1)
- Meta-analysis:
  - **TDF 300mg: OR 0.16 (95% CI: 0.10-0.26)**

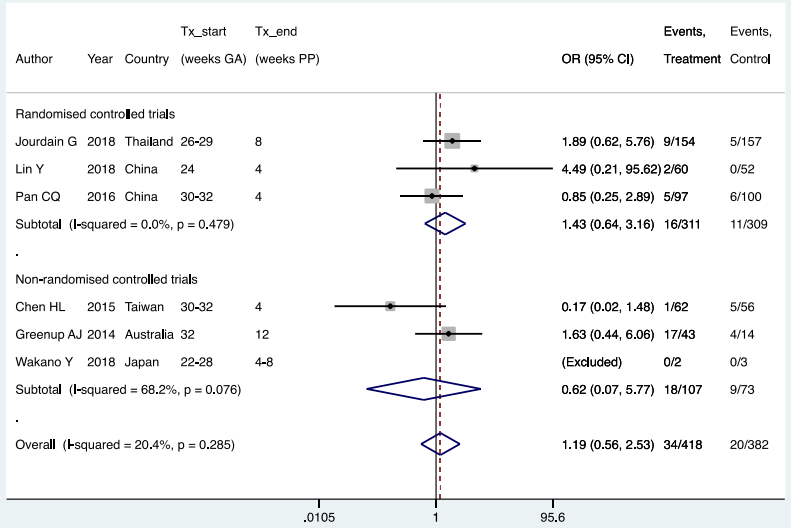


TDF Safety Results

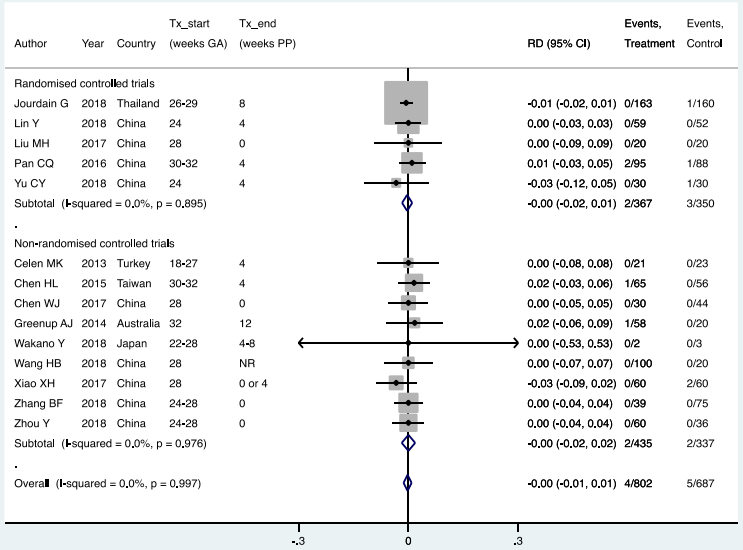
- TDF Drug of Choice, as it has a high barrier against drug resistance and is recommended by the WHO as a treatment for HBV infection

- **No harmful maternal or infant effects of TDF were observed:**

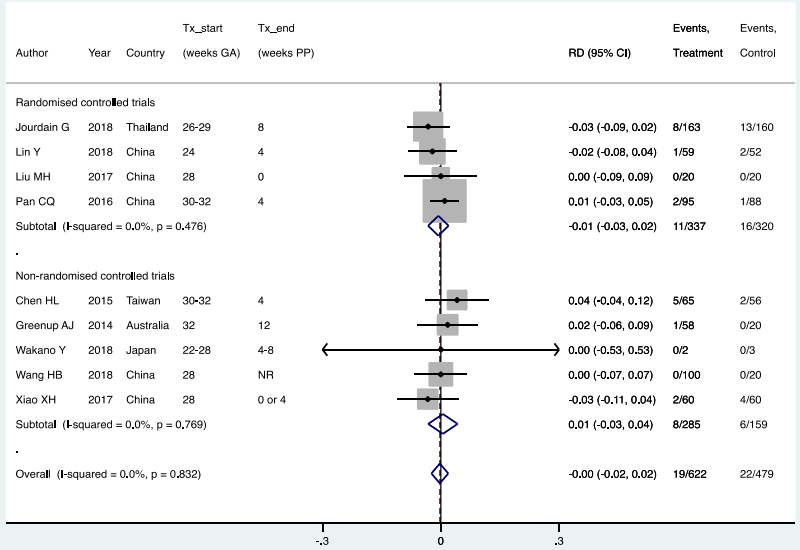
TDF 300mg, HBV flare odds ratio



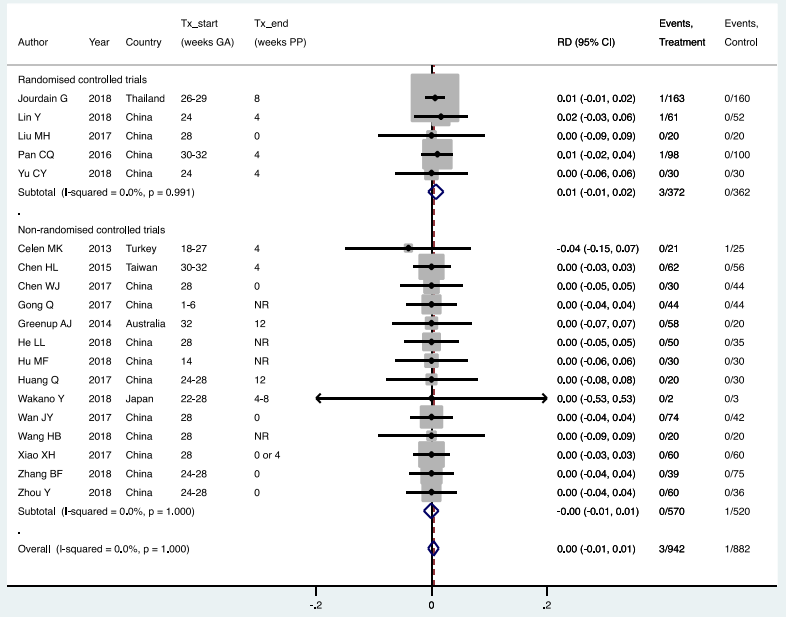
TDF 300mg, Congenital abnormalities risk difference



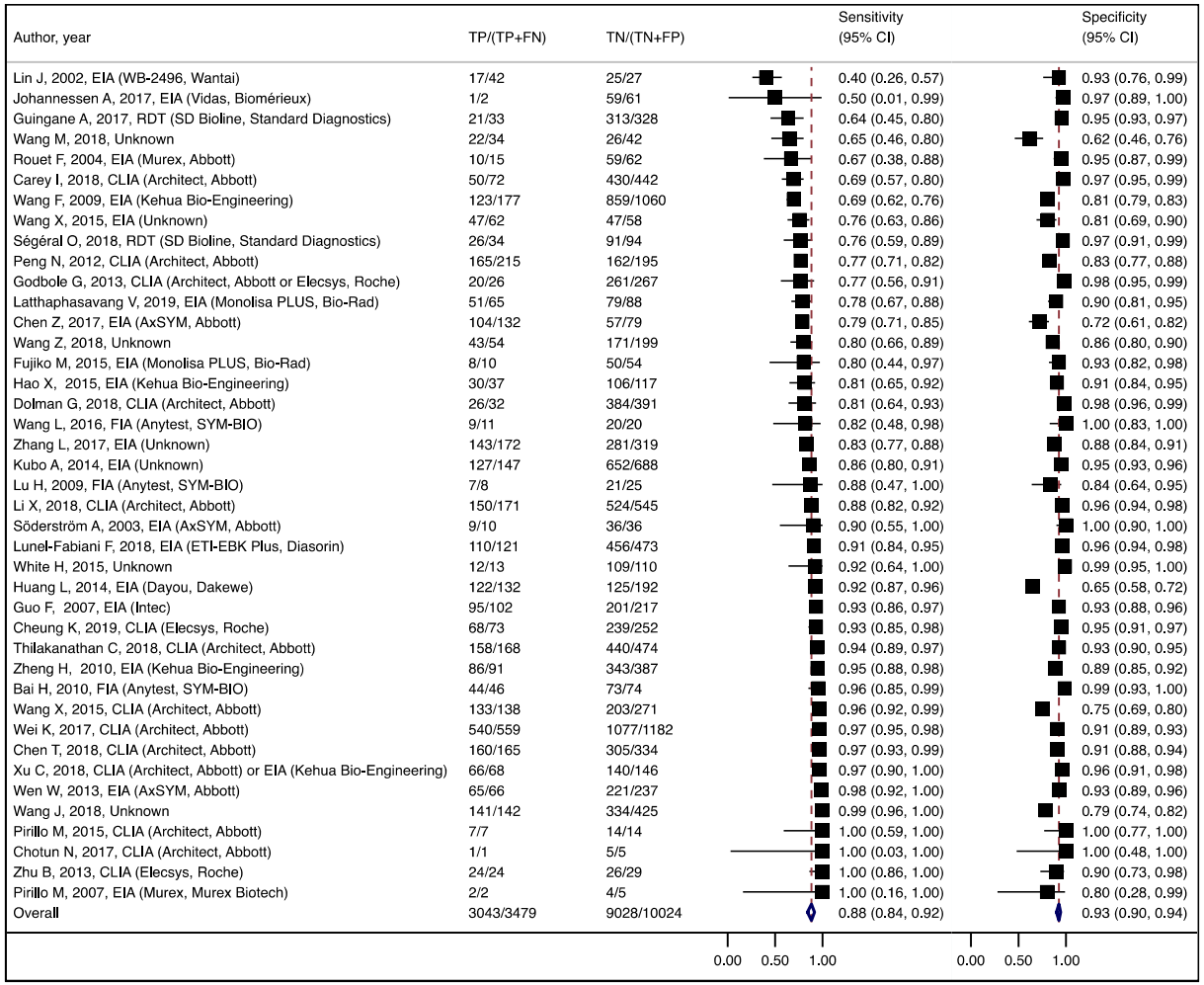
TDF 300mg, Prematurity risk difference



TDF 300mg, fetal demise risk difference



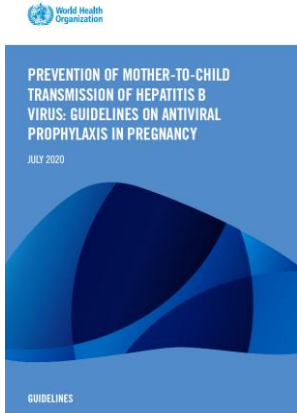
Performance of HBeAg to diagnose HBV DNA ≥ 200 000 IU/mL



Author, year	TP/(TP+FN)	TN/(TN+FP)	Sensitivity (95% CI)	Specificity (95% CI)
Lin J, 2002, EIA (WB-2496, Wantai)	17/42	25/27	0.40 (0.26, 0.57)	0.93 (0.76, 0.99)
Johannessen A, 2017, EIA (Vidas, Biomérieux)	1/2	59/61	0.50 (0.01, 0.99)	0.97 (0.89, 1.00)
Guingane A, 2017, RDT (SD Bioline, Standard Diagnostics)	21/33	313/328	0.64 (0.45, 0.80)	0.95 (0.93, 0.97)
Wang M, 2018, Unknown	22/34	26/42	0.65 (0.46, 0.80)	0.62 (0.46, 0.76)
Rouet F, 2004, EIA (Murex, Abbott)	10/15	59/62	0.67 (0.38, 0.88)	0.95 (0.87, 0.99)
Carey I, 2018, CLIA (Architect, Abbott)	50/72	430/442	0.69 (0.57, 0.80)	0.97 (0.95, 0.99)
Wang F, 2009, EIA (Kehua Bio-Engineering)	123/177	859/1060	0.69 (0.62, 0.76)	0.81 (0.79, 0.83)
Wang X, 2015, EIA (Unknown)	47/62	47/58	0.76 (0.63, 0.86)	0.81 (0.69, 0.90)
Ségéral O, 2018, RDT (SD Bioline, Standard Diagnostics)	26/34	91/94	0.76 (0.59, 0.89)	0.97 (0.91, 0.99)
Peng N, 2012, CLIA (Architect, Abbott)	165/215	162/195	0.77 (0.71, 0.82)	0.83 (0.77, 0.88)
Godbole G, 2013, CLIA (Architect, Abbott or Elecsys, Roche)	20/26	261/267	0.77 (0.56, 0.91)	0.98 (0.95, 0.99)
Latthaphasavang V, 2019, EIA (Monolisa PLUS, Bio-Rad)	51/65	79/88	0.78 (0.67, 0.88)	0.90 (0.81, 0.95)
Chen Z, 2017, EIA (AxSYM, Abbott)	104/132	57/79	0.79 (0.71, 0.85)	0.72 (0.61, 0.82)
Wang Z, 2018, Unknown	43/54	171/199	0.80 (0.66, 0.89)	0.86 (0.80, 0.90)
Fujiko M, 2015, EIA (Monolisa PLUS, Bio-Rad)	8/10	50/54	0.80 (0.44, 0.97)	0.93 (0.82, 0.98)
Hao X, 2015, EIA (Kehua Bio-Engineering)	30/37	106/117	0.81 (0.65, 0.92)	0.91 (0.84, 0.95)
Dolman G, 2018, CLIA (Architect, Abbott)	26/32	384/391	0.81 (0.64, 0.93)	0.98 (0.96, 0.99)
Wang L, 2016, FIA (Anytest, SYM-BIO)	9/11	20/20	0.82 (0.48, 0.98)	1.00 (0.83, 1.00)
Zhang L, 2017, EIA (Unknown)	143/172	281/319	0.83 (0.77, 0.88)	0.88 (0.84, 0.91)
Kubo A, 2014, EIA (Unknown)	127/147	652/688	0.86 (0.80, 0.91)	0.95 (0.93, 0.96)
Lu H, 2009, FIA (Anytest, SYM-BIO)	7/8	21/25	0.88 (0.47, 1.00)	0.84 (0.64, 0.95)
Li X, 2018, CLIA (Architect, Abbott)	150/171	524/545	0.88 (0.82, 0.92)	0.96 (0.94, 0.98)
Söderström A, 2003, EIA (AxSYM, Abbott)	9/10	36/36	0.90 (0.55, 1.00)	1.00 (0.90, 1.00)
Lunel-Fabiani F, 2018, EIA (ETI-EBK Plus, Diasorin)	110/121	456/473	0.91 (0.84, 0.95)	0.96 (0.94, 0.98)
White H, 2015, Unknown	12/13	109/110	0.92 (0.64, 1.00)	0.99 (0.95, 1.00)
Huang L, 2014, EIA (Dayou, Dakewe)	122/132	125/192	0.92 (0.87, 0.96)	0.65 (0.58, 0.72)
Guo F, 2007, EIA (Intec)	95/102	201/217	0.93 (0.86, 0.97)	0.93 (0.88, 0.96)
Cheung K, 2019, CLIA (Elecsys, Roche)	68/73	239/252	0.93 (0.85, 0.98)	0.95 (0.91, 0.97)
Thilakanathan C, 2018, CLIA (Architect, Abbott)	158/168	440/474	0.94 (0.89, 0.97)	0.93 (0.90, 0.95)
Zheng H, 2010, EIA (Kehua Bio-Engineering)	86/91	343/387	0.95 (0.88, 0.98)	0.89 (0.85, 0.92)
Bai H, 2010, FIA (Anytest, SYM-BIO)	44/46	73/74	0.96 (0.85, 0.99)	0.99 (0.93, 1.00)
Wang X, 2015, CLIA (Architect, Abbott)	133/138	203/271	0.96 (0.92, 0.99)	0.75 (0.69, 0.80)
Wei K, 2017, CLIA (Architect, Abbott)	540/559	1077/1182	0.97 (0.95, 0.98)	0.91 (0.89, 0.93)
Chen T, 2018, CLIA (Architect, Abbott)	160/165	305/334	0.97 (0.93, 0.99)	0.91 (0.88, 0.94)
Xu C, 2018, CLIA (Architect, Abbott) or EIA (Kehua Bio-Engineering)	66/68	140/146	0.97 (0.90, 1.00)	0.96 (0.91, 0.98)
Wen W, 2013, EIA (AxSYM, Abbott)	65/66	221/237	0.98 (0.92, 1.00)	0.93 (0.89, 0.96)
Wang J, 2018, Unknown	141/142	334/425	0.99 (0.96, 1.00)	0.79 (0.74, 0.82)
Pirillo M, 2015, CLIA (Architect, Abbott)	7/7	14/14	1.00 (0.59, 1.00)	1.00 (0.77, 1.00)
Chotun N, 2017, CLIA (Architect, Abbott)	1/1	5/5	1.00 (0.03, 1.00)	1.00 (0.48, 1.00)
Zhu B, 2013, CLIA (Elecsys, Roche)	24/24	26/29	1.00 (0.86, 1.00)	0.90 (0.73, 0.98)
Pirillo M, 2007, EIA (Murex, Murex Biotech)	2/2	4/5	1.00 (0.16, 1.00)	0.80 (0.28, 0.99)
Overall	3043/3479	9028/10024	0.88 (0.84, 0.92)	0.93 (0.90, 0.94)

Sensitivity: 88% (IC95%: 84-92%)

Specificity 93% (IC95%: 90-94%)



Prevention of mother-to-child transmission of HBV through **antiviral prophylaxis**

1) In settings where HBV DNA or HBeAg testing is available:

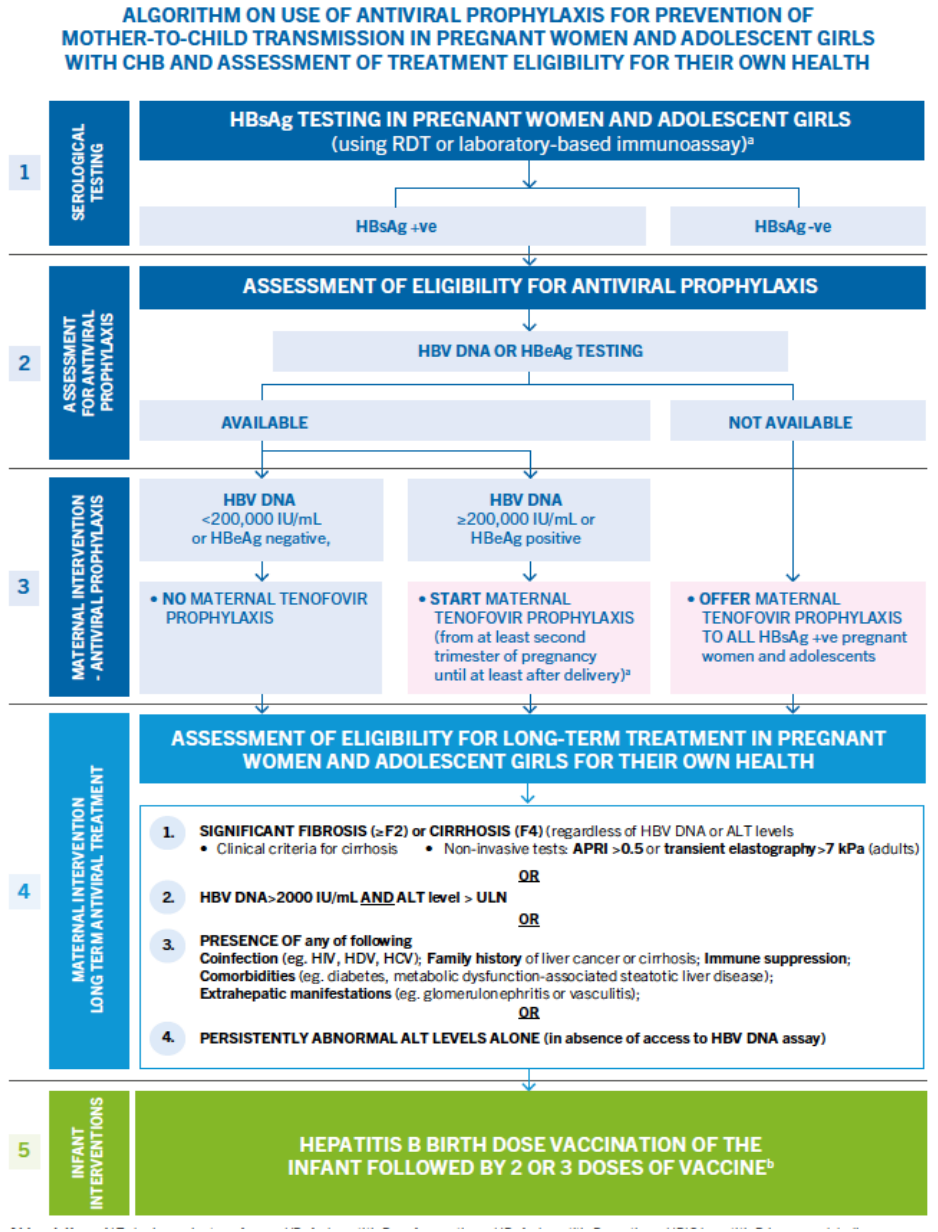
TDF prophylaxis is recommended for HBsAg-positive pregnant women with

- **HBV DNA ≥200,000 IU/mL or**
- **HBeAg-positive**

2) In settings where HBV and HBeAg DNA testing are not available:

TDF prophylaxis may be considered for **all HBsAg-positive** pregnant women

3) Prophylaxis preferably **from the second trimester** of pregnancy until at least delivery or completion of the HBV childhood vaccination series.



Integrated ANC HBV pathway

Screen all pregnant women

HBsAg test (RDT or laboratory assay)

HBsAg negative

Prevention package

- Risk-reduction counselling
- Vaccinate mother and susceptible contacts (if indicated)
- Plan for timely birth dose

HBsAg positive

Assess maternal treatment eligibility

- Fibrosis/cirrhosis (APRI or elastography)
- ALT and HBV DNA when available
- Coinfection, immunosuppression, family history, comorbidities

Treatment eligible

- **Start treatment**
- Monitor ALT/HBV DNA
- Monitor renal function
- HCC surveillance if indicated

Not treatment eligible

Consider prophylaxis:

- HBV DNA ≥200,000 IU/mL or
- HBeAg+ or
- HBsAg+ (all)

maternal TDF from 2nd trimester through delivery/postpartum

Exposed Infant:

- **Immunoglobulin (HBIG),**
- **hepatitis B birth dose (preferably ≤24h) + complete vaccine series +**
- **HBsAg testing at 9-12 months**

All Infants: hepatitis B birth dose (preferably ≤24h) + complete vaccine series

Recommendations for the Caribbean to accelerate progress towards viral hepatitis elimination

Verticality of programs

EMTCT Plus requires **inter-programmatic work** focused on strengthening MCH and PHC and **leveraging national political commitment**.

Expand birth dose coverage

- Ensure timely administration in the first 24 hours
- Availability in public and private delivery wards
- Raise awareness among pregnant women, families, and the community
- Exposed infants: complete vaccine series and HBIG when indicated

Expand ANC hepatitis B services

- Universal HBsAg screening early in pregnancy
- Use of point-of-care rapid tests
- Service integration and linkage to care and treatment/prophylaxis of HBsAg-positive persons

Demonstrate impact

Strengthen data reporting systems for

- vaccine and HBIG coverage
- testing and treatment among pregnant women
- post-vaccination testing of exposed infants.

Conclusions

Pan American Health Organization

World Health Organization

Americas Region