WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Department of HIV, Hepatitis and STIs Programme, WHO HQ, Geneva, Switzerland.

Date: Monday, 13 May 2024
Time: 14.30 – 16.00 (CET)
# WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Department of HIV, Hepatitis and STIs Programme, WHO HQ, Geneva, Switzerland.

<table>
<thead>
<tr>
<th>TIME (CET)</th>
<th>DATE (MONDAY, 13 MAY 2024)</th>
<th>SPEAKERS / CO-CHAIRS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Part 1: New hepatitis B guidelines – recommendations and rationale</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.30 – 14.35</td>
<td>Introductory remarks</td>
<td>Meg Doherty (WHO HQ)</td>
</tr>
<tr>
<td>14.35 – 15.00</td>
<td>New WHO hepatitis B guidance on expanded simplified treatment criteria, diagnostic innovations, service delivery recommendations, evidence base and rationale</td>
<td>Philippa Easterbrook (WHO HQ)</td>
</tr>
<tr>
<td>15.00 – 15.10</td>
<td>Q &amp; A</td>
<td>Niklas Luhmann, Philippa Easterbrook (WHO HQ)</td>
</tr>
<tr>
<td><strong>Part 2: New hepatitis B guidelines – perspectives and implementation considerations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.10 – 15.30</td>
<td>Access considerations</td>
<td>Oriel Fernandes (CHAI)</td>
</tr>
<tr>
<td></td>
<td>Perspective on new recommendations: Community and patients</td>
<td>Catherine Freeland (Hep B Foundation)</td>
</tr>
<tr>
<td></td>
<td>Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points</td>
<td>Polin Chan (SEARO), Kiyo Izumi (WPRO), Stela Bivol (EURO), Leandro Sereno (PAHO), Billy Aristide (AFRO), Ahmed Sabry (EMRO)</td>
</tr>
<tr>
<td>15.30 – 16.00</td>
<td>Q &amp; A and Discussion: Brief comments from countries on new guideline recommendations (China, Philippines, Malawi, Brazil, Cameroon)</td>
<td>Polin Chan (WHO SEARO), Niklas Luhmann (WHO HQ)</td>
</tr>
</tbody>
</table>

The webinar will be in English, French, Spanish, and Russian Language.

Please scan the QR code to download the full guidelines, policy brief, and related documents!
This session is being recorded and your attendance is consent to be recorded.
The PowerPoint slides and the recordings in 4 languages will be available on the WHO HBV Global Webinar Event Page.
A follow-up email with the event page link will be sent to registered participants.

Please rename your Zoom ID to identify yourself. (Full name & Country/Affiliation)
- (E.g. Sandi Min, MOH, Switzerland)
- (E.g. Sandi Min, WHO, Switzerland)

- Use the “Chat” or “Q&A” feature for questions and comments regarding the presentation.
- Use the “Raise Hand” feature if you want to talk during the Q&A session.
- The Host/Co-host of the webinar will unmute you during your turn.

Webinar is available in English, French, Spanish, and Russian languages.
Click on “interpretation” and choose the language that you would like to hear.
To hear the interpreted language only, click “mute Original Audio”

For Live Transcription (ENG), Click on “Show Captions” and the caption would appear on the screen. To close the caption, click “Hide Captions”

If you have any issues with audio or Zoom, Please send messages to the Host/Co-host of the webinar in the Zoom chat box.

WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery
<table>
<thead>
<tr>
<th>TIME</th>
<th>AGENDA TOPICS</th>
<th>SPEAKERS / CO-CHAIRS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Part 1: New hepatitis B guidelines – recommendations and rationale</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>14.30 – 14.35</td>
<td>Introductory remarks</td>
<td>Meg Doherty (WHO HQ)</td>
</tr>
<tr>
<td>14.35 – 15.00</td>
<td>New WHO hepatitis B guidance on expanded simplified treatment criteria, diagnostic innovations, service delivery recommendations, evidence base and rationale</td>
<td>Philippa Easterbrook (WHO HQ)</td>
</tr>
<tr>
<td>15.00 – 15.10</td>
<td>Q &amp; A</td>
<td>Niklas Luhmann, Philippa Easterbrook (WHO HQ)</td>
</tr>
<tr>
<td><strong>Part 2: New hepatitis B guidelines – perspectives and implementation considerations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15.10 – 15.30</td>
<td>Access considerations (7 min)</td>
<td>Oriel Fernandes (CHAI)</td>
</tr>
<tr>
<td></td>
<td>Perspective on new recommendations: Community and patients (5 min)</td>
<td>Catherine Freeland (Hep B Foundation)</td>
</tr>
<tr>
<td></td>
<td>Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points (13 min)</td>
<td>Polin Chan (SEARO), Kiyo Izumi (WPRO), Stela Bivol (EURO), Leandro Sereno (PAHO), Billy Aristide (AFRO), Ahmed Sabry (EMRO)</td>
</tr>
<tr>
<td>15.30 – 16.00</td>
<td>Q &amp; A and Discussion: Brief comments from countries on new guideline recommendations (2-3 min from each country) (China, Philippines, Malawi, Brazil, Cameroon)</td>
<td>Polin Chan (WHO SEARO), Niklas Luhmann (WHO HQ), Polin Chan (WHO SEARO)</td>
</tr>
</tbody>
</table>
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Part 1: New hepatitis B guidelines – recommendations and rationale
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Introductory Remark

Meg Doherty
Director
Department of Global HIV, Hepatitis and STIs Programmes
WHO HQ, Geneva, Switzerland.
Global Health Sector Strategy for HIV, VH and STIs

Global targets for elimination – including absolute targets for elimination

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Baseline - 2020</th>
<th>Targets - 2025</th>
<th>Targets - 2030</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B surface antigen (HBsAg) prevalence among children younger than 5 years old</td>
<td>0.94%</td>
<td>0.5%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Number of new hepatitis B infections per year</td>
<td>1.5 million new cases 20 per 100 000</td>
<td>850 000 new cases 11 per 100 000</td>
<td>170 000 new cases 2 per 100 000</td>
</tr>
<tr>
<td>Number of new hepatitis C infections per year</td>
<td>1.575 million new cases 20 per 100 000</td>
<td>1 million new cases 13 per 100 000</td>
<td>350 000 new cases 5 per 100 000</td>
</tr>
<tr>
<td>Number of new hepatitis C infections per year among people who inject drugs per year</td>
<td>8 per 100</td>
<td>3 per 100</td>
<td>2 per 100</td>
</tr>
<tr>
<td>Number of people dying from hepatitis B per year</td>
<td>820 000 deaths 10 per 100 000</td>
<td>530 000 deaths 7 per 100 000</td>
<td>310 000 deaths 4 per 100 000</td>
</tr>
<tr>
<td>Number of people dying from hepatitis C per year</td>
<td>290 000 deaths 5 per 100 000</td>
<td>240 000 deaths 3 per 100 000</td>
<td>140 000 deaths 2 per 100 000</td>
</tr>
<tr>
<td>Coverage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatitis B - percentage of people living with hepatitis B diagnosed / and treated</td>
<td>30%/30%</td>
<td>60%/50%</td>
<td>90%/80%</td>
</tr>
<tr>
<td>Hepatitis C - percentage of people living with hepatitis C diagnosed / and cured</td>
<td>30%/30%</td>
<td>60%/50%</td>
<td>90%/80%</td>
</tr>
</tbody>
</table>

**Coverage**

- Percentage of newborns who have benefited from a single birth dose of hepatitis vaccine and from other interventions to prevent the vertical (mother-to-child) transmission of hepatitis B virus:
  - 50% | 70% | 90%

- Hepatitis B vaccine coverage among children (third dose):
  - 90% | 90% | 90%

- Number of needles and syringes distributed per person who injects drugs:
  - 200 | 200 | 300

- Blood safety - proportion of blood units screened for bloodborne diseases:
  - 95% | 100% | 100%

- Safe injections - proportion of safe healthcare injections:
  - 95% | 100% | 100%

**Milestones**

- Planning - number of countries with control hepatitis elimination plans:
  - 780 | 30 | 90

- Surveillance - number of countries reporting burden and cascade annually:
  - 130 | 150 | 170

- Hepatitis C virus drug access - percentage average reduction in prices (in equivalent generic prices by 2025):
  - 20% | 50% | 60%

- Hepatitis B virus drug access - percentage average reduction in average prices (alignment with HIV drug prices by 2025):
  - 20% | 50% | 60%

- Elimination of vertical (mother-to-child) transmission - number of countries validated for the elimination of vertical transmission of either HIV, hepatitis B, or syphilis:
  - 15 | 50 | 100

- Elimination - number of countries validated for elimination of hepatitis C and/or hepatitis B:
  - 0 | 5 | 20

- Integration - proportion of people living with HIV who are treated for and cured from hepatitis C:
  - To be determined | 60%/50% | 90%/80%

---

1. Latest data as of 2020. Some targets use data from 2019 because of COVID-19 related service disruptions in the data reported for 2020. COVID-19 is not currently expected to affect the targets for 2020. All data will be disaggregated by age, sex and residence. The targets are specific to the disease.
2. Please note that the targets in this table are global targets and should be adjusted to set targets for countries in relation to the national context. For example, in some countries a target for hepatitis B is surface antigen prevalence among children younger than five years may be less than 0.1% or 0.2%, although the overall global target should be 0.1%.
3. Source: A comprehensive list of reduction strategies and actions are available in the report.

Link to GHSS: 9789240053779-eng.pdf
Worldwide, in 2022 estimated 304 million people are living with Hepatitis B (254 m) and Hepatitis C (50m)

2.2 M
# of new HBV & HCV infections/year

1.3 M
# deaths/year from HBV /HCV associated liver cirrhosis & Cancer

12M
Anti-HDV prevalence

https://www.who.int/publications/i/item/9789240091672
Progress towards hepatitis elimination by 2030 (2015 & 2022 WHA)

Absolute elimination targets defined and measurable

HBV incidence: HBsAg in children ≤5

<0.1%

Combined HBV & HCV mortality

<6/100,000 population

*95% reduction in HBV incidence and 65% reduction in mortality by 2030, compared with the 2015 baseline

Implications of HBV & HCV elimination

From 2.2 million new infections (in 2022) to 520,000 infections (by 2030)

From 1.3 M deaths (in 2022) to under 660,000 deaths (by 2030)
Achievements and gaps during Hepatitis B coverage

Huge gaps & regional disparity in diagnosis and treatment
Globally, only **13%** of 254 M with HBV diagnosed and **3%** treated

Scaling-up the hepatitis B responses has the potential to save over 8 million lives by 2030
Regional sections of report – Hepatitis B and C impact

63% of new HBV infections in Africa,

18% coverage birth dose in Africa, 48% globally

HCV incidence – improved data IDUs, unsafe medical injections, unsafe injections

<table>
<thead>
<tr>
<th>WHO region</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>New hepatitis B infections</td>
<td>New hepatitis C infections</td>
</tr>
<tr>
<td>African Region</td>
<td>771 000</td>
<td>172 000</td>
</tr>
<tr>
<td>Region of the Americas</td>
<td>8 000</td>
<td>176 000</td>
</tr>
<tr>
<td>South-East Asia Region</td>
<td>266 000</td>
<td>225 000</td>
</tr>
<tr>
<td>European Region</td>
<td>18 000</td>
<td>126 000</td>
</tr>
<tr>
<td>Eastern Mediterranean Region</td>
<td>86 000</td>
<td>183 000</td>
</tr>
<tr>
<td>Western Pacific Region</td>
<td>83 000</td>
<td>98 000</td>
</tr>
</tbody>
</table>

Table 2.4. Incidence and mortality of hepatitis B and C virus by WHO region, 2022
Together, these 38 countries represent nearly 80% of global viral hepatitis infections and deaths, and diverse contexts in terms of disease burden and response.
National testing plans and strategies are adopted but implementation is variable

National testing plans and strategies
• >70% national viral hepatitis testing approach.
• 60% costed national viral hepatitis testing plan
• ALL plans include a screening strategy for priority population groups.

Essential diagnostics lists
• <50% have added viral hepatitis diagnostics to their national EDLs.

Availability at primary health care level
• Primary care and community settings have limited use of rapid diagnostic testing.

Most countries rely on government funding or out-of-pocket funding for viral hepatitis testing.
## Access to hepatitis B and C medicines – overview

Access to medicines is yet to transition to a public health approach

<table>
<thead>
<tr>
<th>Countries have adopted WHO treatment guidelines</th>
<th>Essential Medicines List and registration</th>
<th>Product delivery at primary healthcare levels is limited.</th>
</tr>
</thead>
</table>
| • >80% of focus countries have included WHO-recommended treatment regimens in national treatment guidelines. | • 77% of countries have included hepatitis medicines in national essential medicines lists.  
• Product registration still varies and lags behind for medicines for children. | • 45% of reporting countries have TDF available for use in primary health care.  
• 30% have SOF and DAC available for use in primary healthcare  
• Most often treatments are available at tertiary levels and in specialized care only |
4.3 million children (<5 years) have chronic hepatitis B – despite global success of vaccination

70% of all new global infections in sub-Saharan Africa

Global achievement of childhood control (<1% HBsAg in children <5) and achievement of SDG targets (2020) except in SSA

2030 elimination is unachievable without interrupting perinatal infections in Africa

Major gaps in HBV vaccination interventions in regions of greatest prevalence

https://iris.who.int/bitstream/handle/10665/360348/9789240053779-eng.pdf?sequence=1
Out-of-pocket expenditure can be a barrier to access to birth dose and should be minimized to expand coverage of vaccination.

Fig. 3.33. Availability of hepatitis B vaccination free of charge in the public sector, WHO focus countries for the viral hepatitis response, 2023

BD: hepatitis B birth-dose vaccination; IV: hepatitis B infant vaccination.

100% WHO focus countries provided infant vaccination free of charge in the public sector, and 70% of countries provided hepatitis B birth-dose vaccination.
Updated Consolidated Guidelines on person-centred viral hepatitis strategic information (launch on 9 April 2024)
Call to Action to adopt a public health approach to make progress on HBV response

1. Linkage to testing, care, treatment and prevention

2. Long term adherence to antiviral treatment

3. Retention in care

4. Integration of hepatitis testing, care and treatment with other services

5. Simplified service delivery: Decentralization, Task sharing Differentiated care

6. Community engagement

Nationale mass screening for Viral hepatitis (Rwanda 2019)

Incorporating lessons learned from HIV, Covid 19 and HCV epidemics
Thank you

- Philippa Easterbrook
- Myat Sandi Min
- Diana Faini
- Catherine de Martel
- Francoise Renaud
- Daniel Low-Beer
- Funmi Lesi
- Niklas Luhman
- Yann Siegenthaler
- Laurent Poulain

- Hepatitis B GDG

For more information, please contact:
Global HIV, Hepatitis and Sexually Transmitted Infections Programmes
E-mail: hiv-aids@who.int
www.who.int/health-topics/hepatitis
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

New WHO hepatitis B guidance on expanded simplified treatment criteria, diagnostic innovations, service delivery recommendations, evidence base and rationale

Philippa Easterbrook
Department of Global HIV, Hepatitis and STIs Programmes
WHO HQ, Geneva, Switzerland.
2024 WHO HBV Guidelines for prevention, diagnosis, and treatment of people with chronic hepatitis B infection

Dr. Philippa Easterbrook, MD, FRCP, MPH
Global HIV, Hepatitis and STIs Programmes
WHO HQ, Geneva
Launch of WHO 2024 Hepatitis B Guidelines

Date: Saturday 30 March 2024, Time: 10.50-12.20
Place: Room 9 Annex A, Kyoto International Convention Centre, Kyoto, Japan.

Agenda

<table>
<thead>
<tr>
<th>Part 1: New hepatitis B guidelines</th>
<th>Speakers / Facilitators</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Introductory remarks</td>
<td>Meg Doherty (WHO HQ)</td>
</tr>
<tr>
<td>• New WHO hepatitis B guidance on expanded simplified treatment criteria, diagnostic innovations and service delivery recommendations, evidence-base and rationale</td>
<td>Philippa Easterbrook (WHO HQ)</td>
</tr>
<tr>
<td>• Community perspectives on implementation</td>
<td>Su Wang (Hepatitis B Foundation)</td>
</tr>
<tr>
<td>• Q&amp;A</td>
<td></td>
</tr>
</tbody>
</table>

Part 2: Implementation challenges and opportunities across the region

Regional overview of current HBV response in WPRO and SEARO

Panel Discussion: Perspectives from countries on new guidelines

<table>
<thead>
<tr>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>• China – Jin Lin Hou (Southern Medical University)</td>
</tr>
<tr>
<td>• Philippines – Janus Ong (University of the Philippines)</td>
</tr>
<tr>
<td>• India – Shu Sarle (Institute of Liver and Biliary studies)</td>
</tr>
<tr>
<td>• Vietnam – Cao Thi Thanh Thi (Hospital of Hanoi Medical University)</td>
</tr>
<tr>
<td>• Indonesia – Irian Hassan (University of Indonesia)</td>
</tr>
<tr>
<td>• Ethiopia – Halle Desalegn (St. Pauls Medical Centre, Addis Ababa)</td>
</tr>
</tbody>
</table>

Closing remarks by Co-chairs

Co-chairs: Saeed Hamid (Pakistan), Philippa Easterbrook (WHO)
WHO publishes new guidelines on hepatitis B

WHO has released new Guidelines on prevention, diagnosis and treatment of chronic hepatitis B (HBV) infection at the 2024 Asian Pacific Conference for the Study of Liver Disease (APASL) in Tokyo, Japan. These guidelines provide a substantial simplification and expansion of eligibility for treatment to overcome barriers in access to HBV testing and treatment.

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

The 2024 hepatitis B guidelines provide updated evidence-informed recommendations on key priority topics. They prioritize simplified treatment criteria for adults and adolescents and expanded eligibility for antiviral prophylaxis for pregnant women to prevent mother-to-child transmission of HBV.

www.who.int

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

This policy brief provides an overview and the summary of recommendations of the new 2024 Guidelines for the prevention, diagnosis, care and treatment for people with chronic hepatitis B infection.

www.who.int

WHO 2024 hepatitis B guidelines: an opportunity to transform care

Philippa J Easterbrook, Niklas Luhmann, Sahar Bajis, Myat Sandi Min, Mark Neuwirth, Olufunmilayo Ledé, et al.

https://www.thelancet.com/journals/langas/article/PIIS2468-1253(24)00089-X/abstract
HBV Guideline Recommendations (2015) and PMTCT update (2020)

**Algorithm of Who Recommendations on the Management of Persons with Chronic Hepatitis B Infection**

- **HBsAg positive**
  - **CIRRHOSIS**
    - **Clinical cirrhosis**
    - **NIPS (APRI score >2) in adults or FibroScan**
  - **ALT**
    - **Persistently abnormal**
    - **Intermittently abnormal**
    - **Persistently normal**
  - **HBV DNA**
    - >20,000 IU/mL
  - INITIATE NA THERAPY AND MONITOR
    - Nucleoside or nucleotide analogs
    - In adults aged 0-49 years
    - In children aged ≥12 years
    - In children aged 2-11 years
  - DEFER TREATMENT AND MONITOR
    - Every 6 months
  - DETECTION OF HCC
    - Genotyping with cirrhosis or HCC family history
    - Every 12 months
  - DISEASE PROGRESSION AND/OR TREATMENT RESPONSE IN ALL
    - ADHESION AT EACH END of treatment
    - ALT, HBV DNA and HBsAg
    - Clinical criteria and NIPS/APRI in adults or FibroScan
  - BASELINE AND TOXICITY MONITORING IN PERSONS ON TREATMENT
    - Renal function and risk factors for renal dysfunction
    - Every 6 months
  - CIRRHOSIS
    - Lifelong treatment
    - NO CIRRHOSIS
      - Anti-HBsAg/anti-HBc and seroconversion to anti-HBs and after completion of at least one additional year of treatment
      - Persistently normal ALT
      - Persistently undetectable HBV DNA

**Recommendation**

**TOPIC**

**Staging/ non-invasive test (NIT)**
- APRI preferred NIT to assess for the presence of cirrhosis

**Who to treat**
- Decompensated cirrhosis or cirrhosis (clinical criteria or APRI score >2), regardless of ALT levels, HBeAg, or HBV DNA.
- No cirrhosis but persistently abnormal ALT levels +/- ongoing HBV replication, (HBV DNA >20,000 IU/mL or HBeAg +ve).

**First line treatment**
- Drugs with a high barrier to resistance (TAF vs. TDF or ETV).
- ETV in children aged 2-11 years.

**Treatment failure**
- Switch to TDF if evidence of resistance to 3TC, ETV, ADF, TBV.

**Treatment discontinuation**
- Never discontinue in persons with cirrhosis.
- If no cirrhosis, discontinuation on case-by-case basis (persistent HBeAg and/or HBsAg loss or undetectable HBV DNA)

**Monitoring (treatment response/toxicity)**
- On or pre-treatment: ALT + HBV DNA (HBSAg, HBeAg + APRI pre-treatment) annually. More frequent monitoring with cirrhosis.
- Assessment of baseline renal function prior to treatment initiation.
- Ultrasound + AFP every 6 months in persons with cirrhosis and/or family history of HCC.

**PMTCT antiviral prophylaxis (2020)**
- TDF prophylaxis in those with HBV DNA >200,000 IU/mL from 3rd trimester or HBeAg positive (if HBV DNA not available).
Why the need for updated WHO HBV guidelines?

- Still major gaps in testing and treatment uptake
  - Expanded and simplified treatment criteria
  - Progressive simplification

- Guidelines complex
  - High birth rate and high % of population < 20 yrs (25% of all HBsAg+ve in SSA)
  - Liver cancers at younger age in SSA
  - 75% HBsAg+ve HBV DNA < 2000 IU/mL in SSA

- Regional differences in demographics + epidemiology
  - Ongoing HBV DNA integration—oncogenicity
  - Significant rate of ongoing new infections through MTCT in SSA
  - More cohort data now available from SSA

- Emerging evidence
  - Limited access to HBV DNA in LMIC
  - Low uptake of Hep BD in SSA

- Access challenges

In 2022, 13% of 254 million people with chronic HBV infection were diagnosed + 3% treated
## Distinctive Features of WHO Guidelines

<table>
<thead>
<tr>
<th>Feature</th>
<th>WHO Guidelines</th>
<th>Other Guidelines</th>
</tr>
</thead>
</table>
| **Settings**                         | • Low- and middle-income countries  
• Generalised/concentrated epidemic settings | • High-income countries                |
| **Target audience**                  | • National Program Managers                                                  | • Treating clinicians                    |
| **Approach**                         | • The “public health approach”  
• Simplified and standardized approaches  
• Preferred regimens               | • Individualized treatment  
• Multiple treatment options        |
| **Formulating recommendations:**     | • GRADE - Feasibility, equity, end-user acceptability, resource use considered | • Variable use of evidence-based framework |
| Evidence-based approach              |                                                                                |                                          |
| **Guidelines Committee representation** | • 50% LMICs, programme managers, civil society                               | • Clinicians and researchers HICs        |
The WHO Guidelines process and GRADE

**PICO 1**
Can HCV care and treatment be delivered effectively and safely in lower level health facilities (decentralisation)?

**POPULATION:** Adults and adolescents (PWID, prisoners, PLHIV, general population).

**INTERVENTION:** HCV testing, care and treatment outside of hospital-based facilities (harm reduction sites, prisons, ART clinics, primary care).
- Full decentralisation (and integration) of testing and treatment at the same site.
- Partial decentralisation (and integration) of testing at decentralised site, and referral for treatment.

**COMPARISON:** HCV testing, care and treatment in hospital-based facilities (i.e. no decentralisation or integration).

**MAIN OUTCOMES:** Uptake of testing, viral load confirmation, linkage to care, treatment initiation, SVR12 cure assessment, SVR12.
- Patient satisfaction.
- Stratified according to population and setting.

**GRADE-ing recommendations**
- Strength of recommendation
  - Strong=do in most circumstances
  - Conditional=different choices may be appropriate under certain conditions
- Good practice statements: Can apply to recommendations that are “obvious” and for which certainty is high—even though this is difficult to prove directly

<table>
<thead>
<tr>
<th>Strength of Recommendation</th>
<th>Quality of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Very Low</td>
</tr>
<tr>
<td>Conditional</td>
<td>High</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Very Low</td>
</tr>
</tbody>
</table>

Commissioned reviews, modelling and surveys provided a key evidence base for the WHO HBV Guidelines update

1. Use of non-invasive tests
   - University College London

2a/2b. Who to treat
   - Natural history and treatment effectiveness according to VL and ALT
   - Institut Pasteur

3. MTCT rate
   - Imperial College, University of Liverpool

4. TAF and dual therapy (TDF/XTC)
   - University of Liverpool

5a/5b. POC HBV DNA (diagnostic performance and clinical impact)
   - University of North Carolina

6. Reflex HBV DNA viral load
   - University of North Carolina

7a/7b and 8. Delta testing: Who to test and how to test; Delta reflex testing
   - WHO and University of North Carolina

9. Simplified service delivery (HIV) (adherence, retention, refill and visit frequency)
   - Washington University in St. Louis

10 and 11. Simplified service delivery (models of care)
   - University of Liverpool/All India Institute/Harvard

15 Systematic reviews

Landscaping, access and costs

Acceptability, values and preferences
- 4 surveys and 3 literature reviews

Modelling

1. HBV diagnostics
   - CHAI

2. Delta serology and molecular tests
   - CHAI

3. TAF and dual therapy
   - CHAI

Health care worker – survey
   - ICE-HBV

Paediatricians – survey
   - PENTA

MOH Programme managers – survey
   - WHO

Community – survey
   - Hep B Foundation/WHA

Community – Literature review Africa
   - University of Ghana

Community – Literature review Asia
   - Burnet Institute, Melbourne

Community
   - Hep B Foundations

1. Proportion eligible and impact of expanded treatment eligibility
   - CDA

2. Antiviral prophylaxis for all HBsAg mothers
   - Imperial College

3. Numbers needed to treat – viral load threshold
   - Institut Pasteur
Guideline Development Group

- 30 to 40 experts
- All WHO regions
- Medical specialties
- Patients
- Unconflicted (financial and intellectual)
- Virtual meetings

WHO Steering Committee

Systematic Review and Modelling Teams

Guideline Dev. Group

WHO handbook for guideline development [https://apps.who.int/iris/handle/10665/145714]
Key topics of new Hepatitis B Guidelines across the cascade of prevention, diagnosis, treatment & care - WHO hepatitis B guidelines 2024

- Non invasive fibrosis assessment
- Who to treat
- First-line treatment
- PMTCT
- Simplifying diagnosis
- Simplifying service delivery

Recommendations
29
14 New (including updated)
RECOMMENDATIONS, EVIDENCE BASE, RATIONALE AND IMPLEMENTATION CONSIDERATIONS

7. Preventing mother-to-child transmission of hepatitis B using antiviral prophylaxis
   7.1 Recommendations
   7.2 Background
   7.3 Summary of the evidence
   7.4 Rationale for the recommendations
   7.5 Implementation considerations
   7.6 Research gaps
EXPANDED TREATMENT ELIGIBILITY

Chapter 4: Non-invasive assessment of liver disease stage
Chapter 5: Who to treat among people with CHB
Chapter 6: First-line antiviral therapies for CHB
Chapter 7: Preventing mother-to-child transmission of HBV using antiviral prophylaxis
Chapter 8: Who to treat and what antiviral drugs to use for adolescents and children
Chapter 9: Second-line antiviral therapies for managing treatment failure
RECOMMENDATIONS – Non-invasive tests for liver fibrosis

Updated recommendation:

• **APRI** (aspartate aminotransferase-to-platelet ratio index) is recommended as the preferred non-invasive test to assess for the presence of significant fibrosis or cirrhosis among adults in resource-limited settings.

• **Transient elastography** (FibroScan®) may be a preferable non-invasive test in settings where it is available and cost is not a major constraint.

*(strong recommendation, moderate-certainty evidence)*

New recommendation:

• **Evidence of significant fibrosis (≥F2)** should be based on an **APRI score of >0.5** or **transient elastography value of >7.0 kPa**, and **cirrhosis (F4)** should be based on clinical criteria (or an **APRI score of >1.0** or **transient elastography value of >12.5 kPa**).

*(adults: strong recommendation, moderate-certainty evidence; adolescents: strong recommendation, low-certainty evidence)*
RATIONALE for Recommendations on use of non-invasive tests

Systematic review of diagnostic accuracy of NITs (APRI/TE) ≥F2
- 219 studies compared diagnostic accuracy (sensitivity/specificity) for NITs vs liver biopsy for ≥F2
- Focus now on detection of significant fibrosis (≥F2) as well as cirrhosis for treatment – choice of low cut-off
- APRI lower cut-off >0.5: SENS 72% and SPEC 65%
- TE >7KPa: SENS 75% and SPEC 79%
- For cirrhosis F4: SENS (APRI 54%) and (TE 83%)

No of true and false positive, true and false negatives for ≥F2
- APRI lower cut-off >0.5: 183 TP, 263 FP, 68 FN and 488 TN
- TE >7KPa: Similar - 188 TP, 158 FP, 63 FN and 593 TN
RECOMMENDATIONS – Who to treat?

Treatment is recommended for all adults and adolescents (aged ≥12 years) with CHB (including pregnant women and girls and women of reproductive age) with:

1. **Evidence of significant fibrosis** (≥F2) based on **APRI score of >0.5 or transient elastography value of >7 kPa** or evidence of cirrhosis (F4) (based on clinical criteria or APRI score of >1 or transient elastography value of >12.5 kPa), **regardless of HBV DNA or ALT levels. (Adults: Strong/Mod, Adolescents Strong/Low)**

2. **HBV DNA >2000 IU/mL and an ALT level above upper limit of normal** (ULN) (30 U/L for men and boys and 19 U/L for women and girls). For adolescents, this should be based on ALT>ULN on at least two occasions in a 6- to 12-month period. **(Adults: Strong/high; [HBV DNA >20 000 IU/mL] & Low [HBV DNA 2000–20 000]; Adolescents: Conditional/Low)**

3. **Presence of coinfections** (such as HIV, hepatitis D or hepatitis C); **family history of liver cancer or cirrhosis; immune suppression; comorbidities** (such as metabolic-associated steatotic liver disease); or **extrahepatic manifestations, regardless of the APRI score or HBV DNA or ALT levels. (Adults: Strong/Mod; Adolescents: Conditional/Low)**

4. **In the absence of access to an HBV DNA assay:** **Persistently abnormal ALT levels** (defined as two ALT values >ULN at unspecified intervals during a 6- to 12-month period), **regardless of APRI score. (Adults and adolescents: Conditional/very Low)**
Expanded treatment eligibility - Key messages

- Recommendations now focus mainly on who to treat
- Inclusion of all age groups (adults and adolescents, including women of reproductive age (pregnant and non-pregnant)
  - Allows a common entry point for treatment, simplifying guidelines and implementation
  - Will mean many more pregnant and non-pregnant women will be on treatment for their own health. Complements expanded eligibility for antiviral prophylaxis – option for continuous treatment post-partum
- Four and/or options for meeting treatment eligibility
  - Will capture high proportion (≈ 50%) of all HBsAg vs. 8-15% previously.
  - Applicable to all settings – where there is ready or limited or no access to HBV DNA assays. Majority of HBsAg +ve will meet criteria for treatment without need for HBV DNA assay. Only 1 of 4 options requires access to HBV DNA.
  - Use of non-invasive tests (APRI/TE) (≥F2): greatest individual benefit in reducing liver cancer, cirrhosis and liver related mortality

Modelling: impact of changing age, HBV DNA and ALT levels eligibility for treatment

Proportion eligible according to different hypothetical treatment eligibility criteria

- Ethiopia - 2024
- Pakistan - 2024
EVIDENCE BASE AND RATIONALE for Recommendations on Who to treat

- Two systematic reviews and meta-analyses
  - Natural history of CHB according to baseline HBV DNA and ALT levels
  - The efficacy of antiviral therapy according to baseline HBV DNA and ALT levels
  - HBV DNA (<2000, 2000–20 000, 20 000–200 000 and ≥200 000 IU/mL) and ALT (<1, 1–2 and ≥2 times the ULN).

- Other systematic reviews and meta-analyses
  - Studies on treating cirrhosis and fibrosis
  - Studies on co-infection, co-morbidities, extra-hepatic manifestations

- Modelling: Proportion eligible for treatment and impact of expanded treatment eligibility (age, HBV DNA and ALT level)

- Number needed to treat (NNT) to prevent 1 case of HCC, liver-related mortality and cirrhosis, based on natural history studies and the efficacy of antiviral therapy from the systematic reviews

Acceptability, values and preferences surveys
- Three surveys among patients and affected community, health-care workers, MOH national programme managers
Systematic review 1 – Natural history of CHB according to HBV DNA and ALT levels in adults

**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

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

<table>
<thead>
<tr>
<th>VL (IU/ml)</th>
<th>Outcome</th>
<th>No. of studies</th>
<th>Type of studies</th>
<th>RR/HR</th>
<th>95% CI</th>
<th>GRADE</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2,000</td>
<td>HCC</td>
<td>1</td>
<td>Cohort</td>
<td>aHR 0.72</td>
<td>0.43 - 1.20</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>HBsAg seroconversion</td>
<td>1</td>
<td>RCT</td>
<td>RR 3.72</td>
<td>0.30 - 45.79</td>
<td>Very low</td>
</tr>
<tr>
<td>2,000 - 20,000</td>
<td>HCC</td>
<td>1</td>
<td>Cohort</td>
<td>aHR 0.45</td>
<td>0.14 - 1.46</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>HBsAg seroconversion</td>
<td>1</td>
<td>Cohort</td>
<td>aHR 0.17</td>
<td>0.06 - 0.52</td>
<td>Low</td>
</tr>
<tr>
<td>20,000 - 200,000</td>
<td>Worsening of fibrosis</td>
<td>2</td>
<td>RCT</td>
<td>RR 0.56</td>
<td>0.25 - 1.15</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Improvement of fibrosis</td>
<td>2</td>
<td>RCT</td>
<td>RR 1.23</td>
<td>0.48 - 8.12</td>
<td>Moderate</td>
</tr>
<tr>
<td>200,000 - 2M</td>
<td>Worsening of necroinflammation</td>
<td>2</td>
<td>RCT</td>
<td>RR 0.38</td>
<td>0.13 - 1.01</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>Improvement of necroinflammation</td>
<td>2</td>
<td>RCT</td>
<td>RR 1.42</td>
<td>0.76 - 4.41</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>ALT normalisation</td>
<td>1</td>
<td>RCT</td>
<td>RR 1.49</td>
<td>1.13 - 1.97</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>HBsAg loss</td>
<td>1</td>
<td>RCT</td>
<td>RR 0.40</td>
<td>0.05 - 3.13</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>HBsAg seroconversion</td>
<td>1</td>
<td>RCT</td>
<td>RR 0.34</td>
<td>0.01 - 8.16</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>Undetectable viral load</td>
<td>2</td>
<td>RCT</td>
<td>RR 6.86</td>
<td>2.65 - 15.15</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>HCC</td>
<td>1</td>
<td>Cohort</td>
<td>aHR 0.37</td>
<td>0.15 - 0.91</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>Improvement of necroinflammation</td>
<td>1</td>
<td>RCT</td>
<td>RR 0.86</td>
<td>0.40 - 1.82</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>ALT normalisation</td>
<td>1</td>
<td>RCT</td>
<td>RR 3.64</td>
<td>2.43 - 5.45</td>
<td>Low</td>
</tr>
<tr>
<td></td>
<td>HBsAg loss</td>
<td>1</td>
<td>RCT</td>
<td>RR 6.88</td>
<td>0.38 - 124.52</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>HBsAg seroconversion</td>
<td>2</td>
<td>RCT</td>
<td>RR 17.04</td>
<td>3.33 - 50.23</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Undetectable viral load</td>
<td>3</td>
<td>RCT</td>
<td>RR 14.02</td>
<td>5.25 - 31.93</td>
<td>Moderate</td>
</tr>
</tbody>
</table>

- **VL:** Higher treatment efficacy at higher baseline VL and ALT levels
- **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

- 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
Updated recommendation

- tenofovir disoproxil fumarate (TDF) or entecavir (ETV) – are recommended as preferred regimens and
- TDF + lamivudine (3TC) and TDF + emtricitabine (FTC) as alternative regimens (where TDF monotherapy is not available).

(strong recommendation, moderate-certainty evidence)

New recommendation:

- Entecavir (ETV) or tenofovir alafenamide fumarate (TAF) (if available) is recommended for people with established osteoporosis and/or impaired kidney function and
- for children or adolescents for whom antiviral therapy is indicated (ETV aged ≥ 3 years and TAF aged ≥12 years)

(strong recommendation, moderate-certainty evidence)

Evidence-base and Rationale

- Systematic review of 5 RCTs of TAF vs. TDF
  - Similar outcomes for undetectable HBV DNA.
  - No differences in adverse events- TAF less decline in renal function and BMD but changes small (1-3%)
  - Limited evidence on effects on clinical outcomes.

- Systematic review of 5 RCTs of dual therapy (TDF+FTC) vs. TDF monotherapy
  - Similar outcomes (HBV DNA suppression, ALT normalisation, HBsAg and eAg loss, and adverse events)

- Expanding access through dual therapy: In countries with limited availability of TDF monotherapy esp. LMICs/SSA - use of dual therapy available through HIV/ART programmes may expand treatment access
**RECOMMENDATIONS - Preventing mother to child transmission of HBV using antiviral prophylaxis**

**Updated recommendation**
In settings where HBV DNA or HBeAg testing is available, *prophylaxis with TDF is recommended for HBV-positive (HBsAg-positive) pregnant women with HBV DNA ≥200 000 IU/mL or positive HBeAg* (strong recommendation, moderate-certainty evidence)

**New 2024 recommendation**
In settings where neither HBV DNA nor HBeAg testing is available, *prophylaxis with TDF for all HBV-positive (HBsAg-positive) pregnant women may be considered* (conditional recommendation, low-certainty evidence)

*Preferably from the second trimester of pregnancy until at least delivery or completion of the infant HBV vaccination series), to prevent MTCT of HBV.*

All interventions should be given in addition to at least three doses of hepatitis B vaccination for all infants, including a timely birth dose.
EVIDENCE-BASE and RATIONALE - Preventing mother to child transmission of HBV using antiviral prophylaxis

- **2020 systematic review** showed protective effect of antiviral prophylaxis to prevent MTCT
  - TDF 300 mg: OR 0.16, 95% CI: 0.10–0.26.
  - No transmissions when HBV DNA<200,000 IU/ml.

- **Significant challenges remain in accessing HBV DNA or HBeAg testing** among HBsAg-positive pregnant women to determine eligibility for antiviral prophylaxis, especially in sub-Saharan Africa.

- **No studies have directly compared clinical impact and feasibility** of expanding antiviral prophylaxis access to all HBsAg-positive pregnant women versus HBV DNA-driven strategy.

- **Modelling analysis of “antiviral prophylaxis for all” strategy**
  - Universal BD remains the most cost-effective PMTCT intervention - 6.0 million (95% CI: 5.6–6.5) neonatal infections averted from 2024 to 2030.
  - Universal prophylaxis would be cost-effective in only 42 (40%) of 106 countries. The use of antiviral treatment would be five times higher vs. HBV–DNA driven strategy.
  - Relative cost–effectiveness of universal vs. HBV DNA–driven antiviral prophylaxis strategy depends highly on relative costs of treatment and diagnostic tests
IMPLEMENTATION CONSIDERATIONS – Antiviral prophylaxis for PMTCT

- **Increased coverage of HepBD vaccination should be priority**: Funding for introducing and scaling up hepatitis B birth-dose vaccination is now available through Gavi for eligible countries.

- **Universal testing for HBsAg, HIV and syphilis for pregnant women**: WHO recommends that all pregnant women are tested routinely for HIV, syphilis and HBsAg during pregnancy as part of a triple mother-to-child transmission elimination strategy.

- **Increased health-care worker capacity**: Increased number of trained health-care workers in antenatal clinic settings will be required to support expanded HepB antiviral prophylaxis and monitoring after treatment.

- **Simplified, integrated HIV, HBV and syphilis ANC testing and treatment pathways**, ideally in the context of triple elimination of MTCT, will be key to support implementation of HBV DNA or universal hepatitis B prophylaxis.
HBV AND HDV DIAGNOSTICS

Chapter 10: Measuring HBV DNA to guide treatment eligibility and monitor the response
Chapter 11: HBV DNA reflex testing
Chapter 6: Who to test for hepatitis Delta virus (HDV) infection
Chapter 7: How to test for HDV infection: testing strategy and choice of serological and NAT assays
Chapter 8: How to test for HDV infection: Laboratory-based reflex testing
RECOMMENDATIONS AND RATIONALE – HBV DNA testing and Reflex testing

New recommendations:

Point-of-care (POC) HBV DNA assays:

POC HBV DNA nucleic acid testing (NAT) assays may be used as an alternative approach to laboratory-based HBV DNA testing to assess HBV DNA level for treatment eligibility and to monitor treatment response.

(conditional recommendation, low-certainty evidence)

Reflex HBV DNA testing:

Reflex testing for those testing positive on HBsAg may be used as an additional strategy to promote linkage to care and treatment.

This can be achieved through either laboratory-based reflex HBV DNA testing using a sample already held in the laboratory or clinic-based reflex testing in a health-care facility through immediate sample collection following a positive HBsAg rapid diagnostic test (RDT).

(conditional recommendation, low-certainty evidence)

Three systematic reviews

- Diagnostic accuracy of POC assays review (15 studies): high sensitivity (96–98%) and specificity (98–99%)
- Clinical impact review of POC assays (7 studies) showed high uptake of testing (89% (95% CI 55–100%) and of treatment initiation (88% (95% CI 66–100%).
- Clinical impact review of Reflex HBV DNA testing (8 studies) showed high uptake of HBV DNA testing and treatment initiation.
RECOMMENDATIONS AND RATIONALE – HDV testing - Who to test?

New recommendations

Universal testing approach

Serological testing for anti-HDV antibodies may be performed for all individuals who are HBsAg positive, as the preferred approach to scale up access to HDV diagnosis and linkage to care (conditional recommendation, very-low-certainty evidence)

Priority population testing approach

In settings in which a universal anti-HDV antibody testing approach is not feasible because laboratory capacity or other resources are limited, testing for anti-HDV may be given priority in specific populations of HBsAg-positive individuals:

• people born in HDV-endemic countries, regions and areas;
• people with advanced liver disease, those receiving hepB treatment; and those with features suggesting HDV infection (such as low HBV DNA with high ALT levels); and
• people considered to have increased risk of HDV infection (haemodialysis recipients, people living with HCV or HIV, people who inject drugs, sex workers and men who have sex with men).

(conditional recommendation, very-low-certainty evidence)

Narrative review

• No studies directly evaluated impact and cost-effectiveness of different anti-HDV testing approaches.
• Observational studies from high income settings show poor testing uptake and case-finding based on risk-based approach, and marked increase with laboratory-based universal anti-HDV testing
• Effective case-finding crucial to implement preventative interventions eg. enhanced HCC surveillance, and access new treatment options
RECOMMENDATIONS – HDV testing

Diagnostic pathway
People with CHB (HBsAg positive) may be diagnosed with hepatitis D by using a serological assay to detect total anti-HDV followed by an NAT to detect HDV RNA and active (viraemic) infection among those who are anti-HDV positive.

Assays should meet minimum quality, safety and performance standards.

(conditional recommendation, low-certainty evidence)

Reflex testing
Reflex testing for anti-HDV antibody testing following a positive HBsAg test result and also for HDV RNA testing (where available) following a positive anti-HDV antibody test result, may be used as an additional strategy to promote diagnosis.

(conditional recommendation, low-certainty evidence)

How to test?

- Available commercial anti-HDV and molecular PCR assays have good diagnostic accuracy and correlate well with one another.
- Key limitation is lack of established gold standard assays and of an RDT for anti-HDV antibody.

Systematic review of reflex testing
- 11 studies of reflex anti-HDV Ab testing (3 had non-reflex comparator arm) in those HBsAg positive
- Increased uptake of serology testing (97% (95% CI: 92–100%) vs. 45% (95% CI: 0.3–98%) vs. non-reflex testing
- Very high uptake of reflex HDV RNA in those anti-HDV positive - 98% (95% CI: 77–100%) in 8 studies.
HBV DNA POC assays

- **Strategic choice - use of lab-based vs POC NAT platforms**: will depend on characteristics of testing site. eg. (storage facilities, infrastructure, level of staff skills) and costs.

- **Priority settings for placement of HBV DNA POC platforms**: eg. antenatal clinic sites for PMTCT antiviral prophylaxis, where fast-tracking confirmation of high HBV DNA can improve timely uptake of antiviral prophylaxis.

- **Optimal placement of a POC instrument is where testing and treatment are at the same site – a “one-stop shops”**

- **Opportunity for diagnostic integration across programmes using multi-disease testing platforms.** Countries with existing platforms for HIV or HCV viral load or TB testing, can consider collaboration and integration of HBV DNA testing.

---

HBV DNA Reflex and Delta serology and RNA testing

**Choice of laboratory-based reflex testing or clinic-based reflex HBV DNA testing for different country contexts**

- **Laboratory-based reflex testing approach** - settings with large testing volumes for HBsAg supported by extensive sample transport networks.

- **Clinic-based reflex specimen collection approach** - settings where RDTs used and limited access to lab services, and for populations such as PWID.

- **Train laboratory staff** - procedures for sample collection and processing for reflex testing (to minimize cross-contamination), and planning for additional costs
HBV SERVICE DELIVERY AND MONITORING

Chapter 15: Approaches to promote delivery of high-quality health services for CHB

Chapter 16: Monitoring for treatment response among people with CHB receiving treatment or not yet receiving treatment

Chapter 17: Monitoring the safety of nucleoside analogues

Chapter 18: Surveillance for hepatocellular carcinoma among people with CHB

Chapter 19: When to stop and restart antiviral therapy

Chapter 20: Management considerations for specific populations
EVIDENCE-BASE AND RATIONALE – HBV Service Delivery for a Public Health Response

• Lack of direct evidence to inform recommendations on service delivery with hepatitis B:
  • Few comparative studies of different models of care – mostly single arm observational studies
  • Few interventional studies, especially on adherence and retention
  • Heterogeneity of models and variations in outcome definitions
  • Limited outcome data across entire care cascade

• Approach:
  • Systematic review to identify different types of service delivery models for hepatitis B care and report key outcomes across the HBV care cascade
  • Use and adaptation of existing reviews from HIV literature – adherence, retention and tracking, frequency of treatment refills and clinic visits
## EVIDENCE-BASE AND RATIONALE – Range of observed HBV service delivery models

<table>
<thead>
<tr>
<th>MODEL CATEGORY</th>
<th>DEFINITION AND EXAMPLES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Community testing</td>
<td>Education and rapid POCT for general or targeted populations, with or without “linkage” to local care, sometimes vaccination for HbsAg negative</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>General populations</strong></td>
</tr>
<tr>
<td>Hospital-based</td>
<td>Inpatient or ambulatory care attached to a hospital, secondary/district and tertiary levels</td>
</tr>
<tr>
<td>Speciality clinic</td>
<td>Specialist care in ambulatory setting, including referral from testing camp or other community followed by visiting specialist or specialist clinic</td>
</tr>
<tr>
<td>Integrated</td>
<td>Hep B care delivered alongside other services, e.g., HIV, NCDs, harm reduction/OSA</td>
</tr>
<tr>
<td>Co-managed</td>
<td>Care led by non-specialist physicians/nurses/teams with input from or access to specialists via variety of platforms (e.g., virtual, case conference, visiting specialists)</td>
</tr>
<tr>
<td>Primary care</td>
<td>Care solely in primary care facilities by non-specialist physicians, nurses or teams</td>
</tr>
<tr>
<td>Outreach</td>
<td>Pop-up clinics, mobile clinics</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Key populations</strong></td>
</tr>
<tr>
<td></td>
<td>Pregnant/post-partum, PLHIV, migrants, Indigenous, PWID, prison populations</td>
</tr>
</tbody>
</table>
Quantitative studies (n=69): reporting of care cascade outcomes

Proportion reporting:

Early cascade (linkage & eligibility) = 33%
Late cascade (AVT + retention) = 6%
Complete cascade = 4%

- Eligibility assessed = 84%
- Meeting treatment eligibility = 39%
- Treatment initiation among eligible = 37%
- Viral suppression = 9%
- Retention = 16%
Overall cascade of care for general populations

Hospital/ specialist care models

A: On antiviral therapy

- Eligibility assessed: 73.9 (65.7-80.8)
- AVT if eligible: 51.2 (39.6-61.5)
- Retained in care (on AVT): 36.3 (25.2-45.4)
- Viral suppression: 23.4 (15.9-29.7)
- Eligibility assessed: 73.9 (65.7-80.8)
- Retained in care (not on AVT): 27.7 (14.7-42.3)

B: Not on antiviral therapy

- Eligibility assessed: 73.9 (65.7-80.8)
- AVT if eligible: 51.2 (39.6-61.5)
- Retained in care (on AVT): 36.3 (25.2-45.4)
- Viral suppression: 23.4 (15.9-29.7)
- Eligibility assessed: 73.9 (65.7-80.8)
- Retained in care (not on AVT): 27.7 (14.7-42.3)

Primary/mixed models

- Eligibility assessed: 55.5 (41.7-68.6)
- AVT if eligible: 31.8 (19.4-43.8)
- Retained in care: 13.8 (3.4-25.5)

44.5% drop-off

42.7% drop-off

57.2% drop-off
### Learning from HIV – WHO recommendations on service delivery (Adherence, multi-month prescriptions, frequency of clinical visits and retention)

<table>
<thead>
<tr>
<th><strong>Adherence support interventions</strong> should be provided to people receiving ART</th>
<th>Strong</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical visits</strong> every 3-6 months, preferably 6 months if feasible*</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>ART dispensing/refills</strong> every 3-6 months, preferably 6 months if feasible*</td>
<td>Strong</td>
</tr>
<tr>
<td><strong>Tracing</strong> and support for people who have disengaged</td>
<td>Strong</td>
</tr>
<tr>
<td>ART initiation may be offered outside the health facility</td>
<td>Conditional</td>
</tr>
<tr>
<td>SRH services, including contraception, may be integrated with HIV services</td>
<td>Conditional</td>
</tr>
<tr>
<td>Diabetes and hypertension care may be integrated with HIV services</td>
<td>Conditional</td>
</tr>
<tr>
<td>Psychosocial interventions should be provided to all adolescents and young adults living with HIV</td>
<td>Strong</td>
</tr>
<tr>
<td>Task sharing of specimen collection and point-of-care testing with non-lab personnel when professional capacity is limited</td>
<td>Strong</td>
</tr>
</tbody>
</table>

#### Good Practice Statements

- **Health systems should invest in people-centred practices**
- **Same day ART initiation should include approaches to improve uptake, adherence and retention**
- **Non-judgmental, tailored approaches to assessing adherence**

Adherence support interventions should be provided to people receiving ART

- peer counsellors
- mobile phone text messages
- reminder devices
- cognitive behavioural therapy
- behavioural skills and medication adherence training
- fixed-dose combinations and once-daily regimens
8 KEY APPROACHES — Service Delivery for a Public Health Response

1. **Strategies to strengthen LINKAGE from testing to care, treatment and prevention**: e.g. peer support, use of dried blood spots to facilitate testing (WHO 2017 testing guidelines)

2. **Strategies to promote and sustain LONG-TERM ADHERENCE to antiviral treatment**: e.g. use of peer counsellors, text reminders, cognitive behavioural therapy, adherence clubs

3. **Strategies to promote RETENTION IN CARE and trace and re-engage those disengaged from care**: e.g. counselling, peer and family support, patient trackers

4. **INTEGRATION of hepatitis testing, care and treatment** with other services (e.g. HIV services and primary care) to increase efficiency and reach of hepatitis services

5. **DE-CENTRALISED** testing and treatment services at primary health facilities or HIV/ART clinics to promote access to care (facilitated by task-sharing/differentiated care approach).

6. **TASK-SHARING**, supported by training and mentoring of health-care workers and peer workers

7. **DIFFERENTIATED CARE** with assessment of level-of-care needs, and specialist referral as appropriate for those with complex problems

8. **COMMUNITY ENGAGEMENT** and peer support to promote access to services and linkage to the continuum of care, which includes addressing stigma and discrimination
Implementation priorities

I  
Scale-up of testing and case-finding

II  
Updating of national Guidelines with adoption of recommendations informed by local context* and implementation considerations

III  
Widespread education and awareness raising campaigns among community and healthcare workers

IV  
Promote wide access to training and capacity building of healthcare workers to provide adherence support and retention

V  
Opportunities for cost reductions for HBV meds and diagnostics

*Local context including national HBV epidemiology, health systems and laboratory capacity, supply systems for drugs and other commodities, availability of financial resources, the organization and capacity of the health system and the anticipated cost–effectiveness of the various interventions
RESEARCH AGENDA AND IMPLEMENTATION CONSIDERATIONS

- Surveillance for HCC
- Use of non-invasive tests
- Who to treat
- First-line antiviral regimens
- Use of antiviral prophylaxis for PMTCT
- Treatment of adolescents and children
- Simplified service delivery
- Delta testing: Who to test and how to test
- Reflex HBV DNA testing
- Point-of-care HBV DNA testing
Acknowledgments
Guidelines Development Group and WHO Steering Committee

Co-chairs: Saeed Sadiq Hamid (The Aga Khan University, Pakistan), Wendy Spearman (University CapeTown, South Africa) and GRADE methodologist: Roger Chou (Oregon Health and Science University, Portland, USA).

GDD: Danjuma Adda (World Hepatitis Alliance), Suna Balkan (Médecins Sans Frontièrres, France), Ajeet Singh Bhadoria (All India Institute of Medical Sciences, Rishikesh, India), Yap Boun (Pasteur Institute of Bangui, Cameroun), Maria Buti (Hospital Universitario Valle Hebron, Spain), Vladimir Chulanov (National Medical Research Centre for TB and Infectious Diseases, Russian Federation), Chari Cohen (Hepatitis B Foundation), Naranjargal Dashdorj (Onom Foundation, Mongolia), Hailiemichael Desalegn Mekonnen (St Paul's Hospital Millennium Medical College, Ethiopia), Manal Hamdy El-Sayed (Ain Shams University, Egypt), Jordan Feld (Toronto General Hospital, University of Toronto), Jin-Lin Hou (Southern Medical University, China), Saleem Kamili (Centers for Disease Control and Prevention, United States), Patrick Kennedy (Queen Mary’s University, UK), Giten Khwairakpam (WREAT Asia, Thailand), David Muljono (Eijkman Institute for Molecular Biology, Indonesia), Wongani Mzumara (Ministry of Health, Malawi), Edith Okeke (Jos University Teaching Hospital, Nigeria), Janus Öng (University of the Philippines, Philippines), Christian B. Ramers (Clintons Health Access Initiative, USA), Tânia Reuter (Federal University of Espírito Santo, Brazil), Cielo Yaneth Rios-Hincapie (Ministry of Health and Social Protection, Colombia), Lewis Roberts (Mayo Clinic, United States), Cao Thi Thanh Thuy (Clintons Health Access Initiative, Vietnam), Su Wang (Center for Asian Health and Viral Hepatitis, United States).

Paediatrics sub-group: Alasdair Bamford (Great Ormond Street Institute of Child Health, UK), Mei Hwei Chang (College of Medicine National Taiwan University and Children Hospital, Taiwan (China), Geoffrey Dusheiko (King’s College Hospital, United Kingdom), Giuseppe Indolfi (Anna Meyer Children’s University-Hospital of Florence, Italy), Simon Ling (The Hospital For Sick Children, Canada), Fatima Mir (Department of Pediatrics and Child Health, Aga Khan University, Pakistan), Tammy Meyers (School of Women’s and Children's Health, UNSW, Sydney, Australia).

Delta co-infection sub-group: Segolene Briclher (French National Reference Centre for Hepatitis B, C and Delta, France), You Hong (Capital Medical University, China), Will Irving (University of Nottingham, UK), Francesco Negro (University of Geneva, Switzerland), Cirley Maria de Oliveira Lobato (Faculdade de Medicina da Universidade Federal do Acre, Brazil), Cihan Yurdaydin (University of Ankara, Turkey).

WHO Steering Committee
WHO headquarters staff: (GHP) Philippa Easterbrook, Olufunmilayo Lesi, Niklas Luhmann, Myat Sandi Min, Catherine de Martel; and Meg Doherty, Nathan Ford, Morkor Newman, Marco Vitoria, Lara Vojnov.
WHO regional office staff: Kiyohiko Izumi (WPRO), Casimir Mingiedi Mazengo (AFRO), Joumana Hermez (EMRO), Marcelo Naveira (EURO), Bharat Bhushan Rewari (SEARO), Leandro Soares Sereno (PAHO).
New WHO hepatitis B guidance on expanded simplified treatment criteria, diagnostic innovations, service delivery recommendations, evidence base and rationale

Q & A
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Part 2:
New hepatitis B guidelines – perspectives and implementation considerations
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Access considerations

Oriel Fernandes
Clinton Health Access Initiative (CHAI)
HEPATITIS B MARKET ACCESS CONSIDERATIONS

WHO Global Webinar on 2024 WHO Hepatitis B Guidelines

Oriel Fernandes, Senior Director, Clinton Health Access Initiative
Based in Kigali, Rwanda
May 2024
1. **Hepatitis B Diagnostics**
   - HBV RDT: Supplier Landscape and Pricing
   - HBV DNA: Supplier Landscape and Pricing

2. **Hepatitis B Treatment**
   - Pricing snapshots of TDF, TDF/XTC and TAF
   - Global Access Pricing for TDF
The global prices for HBsAg RDTs are generally comparable with those of RDTs across other disease areas. Of multiple high-burden LMIC surveyed, most procuring the test around 1 USD. Prices range from typically 0.58 – 1.22 USD, with exceptions like India (0.09 USD) and Nigeria (up to 2.40 USD).

Four HBsAg products have WHO prequalification -- two rapid diagnostics tests (RDTs) and two lab-based immunoassays. Several countries use RDT tests for point-of-care diagnosis, with less infrastructure and training required. Additionally, multiple manufacturers have SRA-approved products and several qualified for procurement by global stakeholders such as the Global Fund.

Integrating screening services could facilitate access and uptake of testing across diseases for person-centered, comprehensive care. Using the antenatal care platform for screening HIV, HBV, and syphilis in one visit can support triple elimination goals. Multiple manufacturers have developed combination RDT that can screen for HBV, HCV, HIV, and syphilis (combinations vary).

Source: Clinton Health Access Initiative (CHAI) Hepatitis B Market Report 2022; publication expected December 2022
## HBV DIAGNOSTICS: RDT SUPPLY AND PRICING LANDSCAPE

<table>
<thead>
<tr>
<th>Product</th>
<th>Supplier</th>
<th>Reported Sensitivity</th>
<th>Reported Specificity</th>
<th>Regulatory Approval</th>
<th>Analytical Sensitivity</th>
<th>Specimen Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determine HBsAg 2</td>
<td>Abbott</td>
<td>100%²</td>
<td>100%²</td>
<td>WHO PQ</td>
<td>0.1 IU/mL</td>
<td>Serum, plasma, capillary, and venous whole blood</td>
</tr>
<tr>
<td>Bioline HBsAg</td>
<td>Abbott</td>
<td>100%³</td>
<td>99%³</td>
<td>WHO PQ</td>
<td>2.06 IU/ml</td>
<td>Serum, plasma, venous whole blood</td>
</tr>
<tr>
<td>First Response HBsAg Card Test</td>
<td>Premier Medical Corporation</td>
<td>98.98%⁴</td>
<td>100%⁴</td>
<td>CE Mark</td>
<td>N/A</td>
<td>Serum, plasma, capillary and venous whole blood</td>
</tr>
<tr>
<td>Vickia HBsAg</td>
<td>biomeriux</td>
<td>98.9%⁵</td>
<td>98.9%⁵</td>
<td>CE Mark (PQ not maintained)</td>
<td>N/A</td>
<td>Serum, plasma, Whole blood</td>
</tr>
<tr>
<td>STANDARD Q HBsAg Test</td>
<td>SD Biosensor</td>
<td>100%⁵</td>
<td>100%⁵</td>
<td>ERPD until November 2022</td>
<td>N/A</td>
<td>Serum, plasma</td>
</tr>
</tbody>
</table>

### Multiple manufacturers with HBsAg RDT without known Stringent Regulatory Authority approvals (nonexhaustive):
- Accubio/OrientGene
- Beijing Wantai
- Biosynex
- CTK Biotech
- Wondfo
- Intec Products
- Shandong Kanghua
- Shanghai Kehua

2. Determine HBsAg 2 (Abbott) – [WHO Prequalification Report](https://www.who.int/health-topics/sha hepatitisc/topics/diagnostics#tab=tab-1)
3. Bioline HBsAg (Abbott) - [WHO Prequalification Report](https://www.who.int/health-topics/sha hepatitisc/topics/diagnostics#tab=tab-1)
4. First Response HBsAg Card Test (PMC) – [Instructions for Use](https://www.who.int/health-topics/sha hepatitisc/topics/diagnostics#tab=tab-1)
5. Biomeriux Vickia HBsAG [here](https://www.who.int/health-topics/sha hepatitisc/topics/diagnostics#tab=tab-1)
6. STANDARD Q HBsAg Test (SD Biosensor) – [Instructions for Use](https://www.who.int/health-topics/sha hepatitisc/topics/diagnostics#tab=tab-1)
Most major suppliers offer global access pricing (GAP) for LMIC ranging from 9-15 USD with variable terms, conditions, and country inclusion.

Final cost paid by countries for HBV VL varies across countries.

A collection of sample countries showed range from 9.30 USD (Rwanda) to 62 USD on the high-end (Vietnam).

Several manufacturers have HBV VL products with SRA approvals.

Most manufacturers with HIV and HCV molecular tests also have HBV DNA.

Data requested from major HBV VL suppliers demonstrated a 70% increase in procurement volumes from 2016 – 2019.

Nonexhaustive data from participating suppliers shows at least 400,000 tests procured for LMIC market in 2021, far below expected need.

Despite a decline in growth in 2020 due to the COVID-19 pandemic, sale volumes are forecasted to increase growing forward.

1. **Demand Generation**: limited visibility quantifying and forecasting demand in-country, particularly with limited public programming

2. **Limited access**: HBV VL often performed at centralized lab facilities; integrating with other disease platform (HIV, COVID, TB) can improve testing access

3. **Affordability**: Prices for HBV VL remain a significant cost and often a cited barrier

Source: Clinton Health Access Initiative (CHAI) Hepatitis B Market Report 2022; publication expected December 2022
# HBV DIAGNOSTICS: VIRAL LOAD SUPPLY AND PRICING LANDSCAPE

- Multiple manufacturers have HBV VL products with CE mark
- WHO prequalification application open for HBV DNA suppliers to submit for approvals in December 2022
- Most major suppliers offer global access pricing (GAP) for LMICs ranging from US $9-15 with variable terms, conditions, and country inclusion

<table>
<thead>
<tr>
<th>Manufacturer/Product</th>
<th>Regulatory Approval</th>
<th>Platform</th>
<th>Global Access Price ($US)</th>
<th>Sample Type</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Whole Blood</td>
</tr>
<tr>
<td><strong>Near POC</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cepheid Xpert HBV Viral Load</td>
<td>CE Mark</td>
<td>GeneXpert Instruments</td>
<td>14.90</td>
<td>✓</td>
</tr>
<tr>
<td>Molbio Truenat HBV</td>
<td>None</td>
<td>Trulab Real Time micro-PCR Platform</td>
<td>12.00</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Conventional</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abbott Alinity m HBV</td>
<td>CE Mark</td>
<td>Alinity m System</td>
<td>N/A</td>
<td>✓</td>
</tr>
<tr>
<td>Abbott HBV VL Assay</td>
<td>CE Mark</td>
<td>m2000</td>
<td>9.60 – 15.55 FCA</td>
<td>✓</td>
</tr>
<tr>
<td>Qiagen artus HBV RG RT-PCR Kit / artus HBV QS-RGQ Kit</td>
<td>CE Mark</td>
<td>Rotor-Gene Q/Rotor Gene Instrument</td>
<td>N/A</td>
<td></td>
</tr>
<tr>
<td>Roche Cobas HBV Test</td>
<td>CE Mark, US FDA</td>
<td>CAP/CTM, cobas 4800/5800/6800/8800 systems</td>
<td>8.90 CPT</td>
<td>✓</td>
</tr>
<tr>
<td>Hologic Aptima HBV Quant Assay</td>
<td>CE Mark, US FDA</td>
<td>Panther System</td>
<td>11.28 DAP</td>
<td>✓</td>
</tr>
</tbody>
</table>

Source: CHAI HBV Market Report 2022 and supplier communication
HBV TREATMENT: PRICE VARIES ACROSS LMICS

- Price of TDF varies across countries, especially between HBV programs and HIV programs.
- TDF is a lifelong drug, making affordable access is key for HBV programs and patients.
CHAI and Hepatitis Fund signed a global access pricing agreements for hepatitis treatment in 2023

- TDF 300mg at or below US$ 2.4 for 30-tablet (US$28.8 per patient per year) from Viatris and Hetero
- All products offered would be either US-FDA approved or WHO pre-qualified
- Who can access these agreements? - Any organization or entity that is purchasing these medicines on behalf of public sector patients in the territory as per the licensing agreement of generic manufacturers with innovators.

To translate global access price to low in-country price, it is critical that countries/programs:

1. Amplify communication on these pricing agreements to all stakeholders particularly procurement divisions

2. Optimize in-country markups by seeking clarity on components of additional costs and find opportunities to streamline them

3. Accelerate scale-up of hepatitis services and drive demand for services by engaging with community groups

To learn more about the pricing deal for generic viral hepatitis medicines, scan the QR code.
HBV TREATMENT REGIMEN: ACCESS CONSIDERATIONS

Benchmark price of HBV treatment regimen

- TDF/FTC costs ~1.5 times TDF price. TDF/3TC is 15-20% cheaper than TDF/FTC and 30-40% costlier than TDF
- TAF is not available under Global Fund PPM or USAID, but TAF/FTC/DTG is available at $5 per pack – costlier due to added drug component.
  - Under the viral hepatitis program of India, the price of TAF is ~1.5 times TDF procurement price
  - Export data analysis of TAF and TDF by Indian generics, TAF is estimated to be ~1.2-1.4 times TDF price

<table>
<thead>
<tr>
<th>Product</th>
<th>TDF 300 mg</th>
<th>TDF/FTC 300/200mg</th>
<th>TDF/3TC 300/300 mg</th>
<th>TAF/FTC/DTG 25/200/50 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pack Size</td>
<td>30 tablets</td>
<td>30 tablets</td>
<td>30 tablets</td>
<td>30 tablets</td>
</tr>
<tr>
<td>CHAI Negotiated Access Price</td>
<td>$2.4</td>
<td>$2.4</td>
<td>$2.4</td>
<td>$2.4</td>
</tr>
<tr>
<td>Global Fund PPM Price (Oct 2022)</td>
<td>$2.4</td>
<td>$3.97</td>
<td>$3.37</td>
<td>$5.00</td>
</tr>
</tbody>
</table>

Market outlook

Both TDF/FTC and TAF can be cost-effective therapy as the prices are likely to decline with inclusion in viral hepatitis guidelines across LMICs and subsequent increase in demand.

**TDF/XTC (TDF/3TC or TDF/FTC)**

1. Marginally costlier due to an added drug component
2. Inclusion in the HBV guidelines allows demand consolidation of both HIV PrEP as well as HBV patients. This will help manufacturers benefit from economies of scale and an opportunity to optimize cost. Both PrEP and HBV programs would benefit from this reduction of cost

**TAF**

1. Currently, procurement of TAF by programs in LMICs is ~1.5 times costlier than TDF
2. Difference in price can be attributed to the overall low market share of TAF (~12% of HBV treatment market across LMICs) as demand is limited to use for patients with renal impairment in public programs and private sector
3. TAF price likely to come down as more countries include TAF in HBV guidelines
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Perspective on new recommendations: Community and patients

Catherine Freeland
Hep B Foundation
Community Involvement and Next Steps in Disseminating Updated Hepatitis B World Health Organization Guidelines

Catherine Freeland, PhD, MPH
Hepatitis B Foundation
Catherine.Freeland@hepb.org
Community Values and Preferences Working Group

Working Group: Catherine Freeland (Hepatitis B Foundation), Chari Cohen (Hepatitis B Foundation), Jack Wallace (Burnet Institute), Camila Picchio (ICE-HBV and ISGlobal), Capucine Penicaud (The Hepatitis Fund), Noemi Toussignant, Hailemichael Desalegn (St. Paul's Hospital, Ethiopia), Charles Ampong Adjei (University of Ghana), Jessica Hicks (World Hepatitis Alliance), Cary James (World Hepatitis Alliance), Danjuma Adda (World Hepatitis Alliance), Su Wang (World Hepatitis Alliance and Hepatitis B Foundation)
2023 Survey Methods:
The survey was organized into three main sections: 
1. eligibility and demographic section (five questions); 
2. current clinical management including treatment experiences (seven questions), and 
3. preferences for treatment, management, and provider interactions (15 questions).

Stigma and discrimination was also assessed through the Hepatitis B Foundation Discrimination Registry

Assessment of Provider Preferences and Values
Provider Preferences for treatment and management, access to testing and treatment
Key Findings: Barriers

• A sample of 560 from 76 countries responded to the survey. To inform guidelines past research and literature were assessed.

Hepatitis B Medical Care

Less than half (49%, N = 268) of respondents reported visiting a doctor to check the health of their liver regularly (every 6–12 months)

“The price for the necessary testing such as Hep B DNA, liver function test, etc. must be affordable to enable Hep B patients [to] get access to treatments.”

Access to Medication

Many individuals reported facing challenges accessing affordable medication consistently

“I think most at times, some clients are told per their test results, they don’t need treatment which I was thinking why not starting treatment to rather prevent the stage where the case is now serious”

Health Care Worker Knowledge

Many reported not having access to a knowledgable provider

“Knowledgeable Health care worker who understands the disease, that I have a doctor that actually cares about me and my hepatitis B.”
Key Findings: Preferences & Values

Priorities for testing, management & treatment:
- **Convenience of care setting**, knowledge of care team, availability of counseling, confidentiality, and **cost**
- Respondents requested **simplified guidelines**
- **Increased accessibility** and **affordability of medical care (tests) and treatment**
- Respondents request **point-of-care testing** with the ability to have test and treat models, especially to **reduce transmission to family**
- Individuals with lived experience want to be **involved in treatment options** and decision-making

Stigma and discrimination play a major role
- Discrimination reported in **employment, health care settings, and immigration**
- Can impact care-seeking and adherence
Ongoing dissemination and advocacy is required from civil society to ensure that the guidelines are adopted and implemented widely.
Thank You

Email: Catherine.Freeland@hepb.org

www.hepb.org
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points

Polin Chan
WHO SEARO
### WHO South-East Asia Region

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Hepatitis B virus</th>
<th>Hepatitis C virus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of people living with <em>hepatitis infection</em></strong></td>
<td>61 400 000</td>
<td>9 100 000</td>
</tr>
<tr>
<td><strong>Hepatitis B surface antigen (HBsAg) prevalence</strong> among children younger than 5 years old</td>
<td>0.4%</td>
<td></td>
</tr>
<tr>
<td><strong>Number of new hepatitis infections per year</strong></td>
<td>266 000</td>
<td>225 000</td>
</tr>
<tr>
<td><strong>Number of deaths caused by hepatitis virus infection per year</strong></td>
<td>218 000</td>
<td>42 000</td>
</tr>
<tr>
<td><strong>Percentage of people living with hepatitis virus who are diagnosed</strong></td>
<td>2.8%</td>
<td>26%</td>
</tr>
<tr>
<td><strong>Percentage of people living with hepatitis virus who receive treatment</strong></td>
<td>3.5%</td>
<td>14%</td>
</tr>
</tbody>
</table>

11 countries and home to 2 billion people
Regional challenges and priorities

Access to test and treatment:
- Several SEAR countries manufacture generic hepatitis B and C medications.
- The cost varies significantly: the reported price of generic for a 28-day supply in public sector
  - TDF ranges from US$ 1.2 in India and US$ 4.8 in Indonesia per bottle
  - Entecavir use remains limited
- HBV testing among ANC: rapidly being scaled up
- HBV DNA access: remains limited, POC scaling up
- Models of services: scaling up beyond tertiary centers is being piloted, need to co-opt private sector services
- Hepatitis delta: unknown epidemiology in SEAR

Regional Priorities:
- Advocacy for greater political commitment and resource allocation at the national level
- Expanding access to testing and treatment beyond larger hospitals and referral centres
- Addressing price variability and cost barriers to accessing services
- Update guidelines and retrain HCWs
- Strengthen data systems
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points

Kiyo Izumi
WHO WPRO
WHO Western-Pacific Region

Prevalent Cases of **Chronic Hepatitis B**

Global: 254 millions

**Western Pacific Region**

- 97 millions (38%)

**China** 80 mil

**Viet Nam** 6.5 mil

**Philippines** 7.7 mil

**Other countries**
Regional Priorities:

1. **Enhance prevention efforts** including vaccination, PMTCT, and blood safety
2. **Expand testing and treatment** to reduce morbidity and mortality
3. **Strengthen strategic information** to enhance advocacy, resource mobilization, and M&E

Guideline Updates

- **Adopted new recommendations:** CHN, PHL
- **Updates underway:** VNM, KHM, LAO, (PHL)
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points

Stela Bivol
WHO EURO
Hepatitis B WHO European Region 2024

10.6 million people are living with HBV
New infections: 18 000
Deaths: 32 000
Diagnosed: 16%
Treated: 12%

>80% of HBV chronic infections are attributed to 13 MS
(absolute numbers)
- Uzbekistan
- Türkiye
- Russian Federation
- Italy
- Romania
- Ukraine
- United Kingdom
- Kazakhstan
- Kyrgyzstan
- Spain
- Azerbaijan
- Poland
- Tajikistan

• 53 member states
• 17 time zones
• Approximately 900 million people
WHO EURO Regional Priorities

#### VALIDATION OF CONTROL AND ELIMINATION

- Support the application for hepatitis B control targets
  - 50/53 MS have HBV in their universal childhood vaccination programs
  - 9 MS validated for having achieved Hep B control targets
- Support the application of MS for validation of elimination
- Triple EMTCT Initiative
- Showcase achievements in incidence and mortality targets

#### PROGRAMS SCALE UP

- Political commitment, national programs with ambition to eliminate
- Screening strategies, expand testing and treatment
- Adopt and implement decentralised and simplified models of HBV care
- Capacity building at non-specialized level
- Support discussions on access to diagnosis and treatment

#### GUIDANCE AND DATA

- Prepare regional estimates and assess challenges and gaps towards interim 2025 targets
- Disseminate person-centred viral hepatitis strategic information guidance
- Translate and disseminate new hepatitis B recommendations
- Support countries in uptake of HBV guidelines
  - Key countries expressing interest: Georgia, Ukraine, Uzbekistan, Turkmenistan

#### Collaborate and further integrate viral hepatitis in programmes and services

- people living in prisons -- migrants and refugees -- microelimination
- cancer prevention and awareness -- multidisease elimination
- Interinstitutional approach
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points

Ahmed Sabry
WHO EMRO
HBV burden in the Eastern Mediterranean Region 2022

Number of HBV infections: 15 millions

| Incidence (number of new HBV cases) | 86,000 |
| Number of deaths attributed to HBV | 41,000 |
Countries planning HBV guidelines update

- Afghanistan (already started)
- Morocco and Egypt (early discussions)
- Iran, Iraq, Pakistan, Syria, Somalia, Sudan and Yemen (already prioritised)
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points

Billy Aristide
WHO AFRO
Hepatitis B WHO Africa Region 2024

- **65 million** people are living with HBV
- New infections per year: **771 000**
- Deaths: **272 000**
- Diagnosed: **4.2%**
- Treated among those diagnosed: **5.5%**
- Treated among all people with Hep B: **0.2%**

- 47 member states regrouped in two sub regions
  - 26 countries in WCA
  - 21 countries in ESA
- Approximately 1 billion people
Regional landscape

Achievements/Challenges

- **National treatment guidelines** have been updated in accordance with WHO recommendations
  - Guideline Update plan for Zambia-Kenya-Uganda-Botswana
  - Done for Malawi and Sierra Leone
- In process of the development of NSP for Viral Hepatitis: Côte d'Ivoire- Ghana-
- **Product availability** in primary health care is limited.
- **Lowest reported price** of the last public sector procurement of TDF varies between US$ 2.20 in South Africa and US$ 26.70 in the Democratic Republic of the Congo for a generic 30-tablet supply of TDF.
- African Region has the **lowest coverage of the hepatitis B birth-dose vaccination**, at 18%.
- **Availability of IVDs** in the African Region is relatively limited.

Regional priorities:

- Leveraging HIV, primary health care and maternal and child health care services,
- Expanding access to IVDs as an entry point to expand access to treatment and care,
- Addressing the variability in prices paid for health products in the Region
- Continuing to advocate for increased domestic funding.
- Develop a Viral Hepatitis investment framework in the region
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Spotlight from six WHO regions by WHO Hepatitis Regional Focal Points

Leandro Sereno
PAHO
Viral Hepatitis B in the Americas

52 Countries and Territories – 1 billion population

Hepatitis B (2022)
• 5.1 million (0.5%) people with chronic infection
  • 2.5 million in Latin America
  • 650,000 in the Caribbean
• Prevalence in children aged 5 years: 0.07%
• 8,000 new chronic infections
• 18,000-23,000 hepatitis B deaths
Viral Hepatitis B in the Americas

Vaccination Coverage

Hepatitis B vaccine coverage in the Americas (%)

- Birth dose (24 hours)
- Third dose (1 year)

Cascade of Care

- HBV Prevalence
- HBV Diag.
- HBV Treat.

Regional Coverage of Services (%)

Number of cases (n)

- Latin America
- The Caribbean
- HIC North America

#UniversalHealth
Key progresses and challenges
Region of the Americas

• EMTCT
  - All countries and territories have introduced hepatitis B vaccination into their routine immunization schedules for infants
  - 33 countries and territories have introduced universal birth dose.
  - 15 countries have set goals to eliminate mother-to-child transmission of hepatitis B

• National Guidelines: 17 Countries with HBV guidelines developed
  - Countries in The Caribbean currently developing their guidelines
  - Key countries expressing interest in updating current guidelines: Mexico, Colombia and Brazil.

• Service Delivery:
  - Most countries (24) report HBV DNA capacity but primarily centralized in reference labs.
  - More countries adopting HBsAg POC RDT and integration of testing in Primary Health Care.
  - Treatment and care at reference hospitals.

• Priorities and Challenges
  - Greater public awareness on viral hepatitis B and C is needed (community and civil society)
  - Political commitment to scale up national responses (increased financial resources allocated)
  - Expanding availability of services: screening strategies and service integration
  - Further expand vaccination coverages (HepBD), and scale up screening and prophylaxis during pregnancy
  - Address the costs of viral hepatitis diagnostics and treatments (PAHO Strategic Fund)
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Brief comments from countries on new guideline recommendations

• Wongani Mzumara (MOH, Malawi)
• Mário Peribanez Gonzalez (MOH, Brazil)
• Rose Armelle ADA (MOH, Cameroon)
• Janus Ong (The University of Philippines, Philippines)
• Jidong Jia (Capital Medical University, China)
WHO Global Webinar: Technical Briefing on 2024 WHO Hepatitis B Guidelines on Diagnosis, Treatment, and Service Delivery

Thank you for your attention!

Please scan the QR code to download the full guidelines, policy brief, and related documents!