WHO Guidelines for HBV and HCV
Simplification and Scale up

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WHO Regional Office for Europe

Improving the Response of Global Public Health
in a Fast-changing World, Joint UNICEF-UNFPA-WHO meeting with manufacturers and suppliers, 2-4 December 2019
Global Health Sector Strategies, 2016–2021

The three organizing frameworks:

- Universal health coverage (UHC)
- Continuum of health services
- Public health approach
WHO Viral Hepatitis Elimination Targets: 2016

- 65% Reduction in Deaths from Chronic HBV and HCV
- New infections and Deaths ( Millions )
- New infections and Deaths ( Millions )

1.4 million deaths (in 2015) to under 500,000 deaths (by 2030)
6–10 million (in 2015) to 900,000 infections (by 2030)
95% decline in HBV infections
80% decline in HCV infections

Where are we now?
Progress on Global elimination service delivery 2030 targets

Global Hepatitis Report, WHO 2017
Bottlenecks

Planning
Financing
Infrastructure
Implementation
Prevention
Diagnosis
Treatment and Care
Monitoring and Evaluation
...

Complex tests
Invasiveness
Costs of Dx and Tx
Genotyping

Poor rate of success
Comorbidities
Coinfections
Transplantation
## Distinctive features of WHO guidelines

<table>
<thead>
<tr>
<th>Feature</th>
<th>WHO Guidelines</th>
<th>Other Guidelines</th>
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<tbody>
<tr>
<td><strong>TARGET AUDIENCE</strong></td>
<td>National Programme managers</td>
<td>Treating clinicians</td>
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<td><strong>SETTINGS</strong></td>
<td>• Low and middle income countries</td>
<td>High income countries</td>
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<td></td>
<td>• Generalised/Concentrated epidemic setting</td>
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<td></td>
<td>• Poor access to liver biopsy, and HBV DNA testing</td>
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<td><strong>EVIDENCE-BASED GRADE APPROACH</strong></td>
<td>Feasibility, equity, Resource use considered</td>
<td>Variable use of evidence-based framework</td>
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<tr>
<td><strong>APPROACH</strong></td>
<td>The “Public health approach”</td>
<td>Individualised treatment</td>
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</table>
WHO Guidelines on hepatitis B and C testing (2017)

Main recommendations on:

- Whom to test for chronic HBV and HCV infection?
- What tests to use for serology testing (RDTs or lab testing / one or two tests)
- Confirmation of chronic HCV infection
- Interventions to improve testing coverage and linkage to care and treatment

### Who to test for HBV and HCV?

<table>
<thead>
<tr>
<th>Testing Approaches</th>
<th>Recommendations</th>
</tr>
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</table>
| **FOCUSED TESTING FOR MOST AFFECTED POPULATIONS** | - In all epidemic settings, offer HBsAg or HCV Ab testing to adults and adolescents:  
  - From populations most affected by HBV or HCV infection (i.e. populations with high seroprevalence or history of risk exposure and/or behaviour);  
  - With a clinical suspicion of chronic viral hepatitis (i.e. symptoms, signs, laboratory markers)  
  - HBV: Sexual partners, children and other family members, and close household contacts of those with HBV infection;  
  - Health-care workers: in all settings, and offer HBV vaccination not vaccinated previously. |

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The document is from the World Health Organization (WHO) and provides guidelines on testing for hepatitis B virus (HBV) and hepatitis C virus (HCV). The recommendations focus on testing specific populations and settings where there is a higher risk of infection.
# Who to test for HBV and HCV?

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<tr>
<td><strong>GENERAL POPULATION TESTING</strong></td>
<td>• In settings with intermediate (&gt;2%) / high (&gt;5%) prevalence, offer all adults routine access to testing, with linkage to care and prevention services.</td>
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<td><strong>BIRTH COHORT TESTING (HCV)</strong></td>
<td>• Consider where specific identified birth cohorts of older persons at higher risk of HCV infection</td>
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<tr>
<td><strong>ROUTINE ANTENATAL CLINIC TESTING (HBV)</strong></td>
<td>• In settings with intermediate (&gt;2%) / high (&gt;5%) HBsAg prevalence, offer routine HBsAg testing to all pregnant women in antenatal clinic, with linkage to care and prevention services.</td>
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</table>
What assays to use: RDTs vs. EIA/CIAs?

- **HBV:** For diagnosis of hepatitis B infection in adults and children (>12 months of age), a single serological assay (EIA/CIA or RDT) that meets minimum performance standards is recommended.
  - **EIAs** are recommended as the preferred assay in settings where existing laboratory testing is available.
  - **RDTs** are recommended in settings where there is limited access to laboratory testing and/or in populations where access to rapid testing would facilitate linkage to care and treatment.

- **HCV:** To test for exposure to hepatitis C infection in adults and children (>18 months of age), a single serological assay (antibody or antibody/antigen combination) (either RDTs or EIA/CIA) that meets minimum performance standards* is recommended.
  - **RDTs** are recommended in settings where there is limited access to laboratory testing and/or in populations where access to rapid testing would facilitate linkage to care and treatment.
Confirmation of HCV infection / treatment response assessment

- Directly following a positive HCV antibody serological test, the use of a nucleic acid testing (NAT) (either quantitative or qualitative RNA) is recommended as the preferred strategy to diagnose viraemic HCV infection.

- A core HCV antigen assay, that has comparable clinical sensitivity, is an alternative to NAT to diagnose viraemic infection.

- Confirmation of cure – 12 or 24 weeks after the antiviral treatment через 12 (i.e. sustainable virologic response – SVR12 or SVR24) qualitative or quantitative HCV RNA testing should be performed.
Promoting uptake and linkage

- Use of DBS specimens for virology ± serology
- **On-site or immediate RDT testing** with same day results
- Trained peer and lay health workers
- **Clinician reminders** to prompt provider initiated, facility-based testing
- **Testing as part of integrated services** at a single facility
Why WHO hepatitis B treatment guidelines?

- **Existing HBV Guidelines**
  - EASL 2017, NICE 2013, PCDT 2015, MSF 2018
- **Similarities and differences**
  - Indications for treatment
  - Choice for antiviral treatment
  - HCC surveillance
- **Local context**
  - high income, variable access to testing, elimination as goal, HDV, models of care…
### WHO recommendations (2015)

<table>
<thead>
<tr>
<th>TOPIC</th>
<th>RECOMMENDATION</th>
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<td>Staging/ non-invasive test (NIT)</td>
<td>APRI preferred NIT is a preferred non-invasive test.</td>
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</table>
| Who?                                       | 1) Decompensated cirrhosis  
2) Cirrhosis (clinical criteria or APRI score >2), regardless of ALT levels, HBeAg, or HBV DNA.  
3) No cirrhosis but persistently abnormal ALT levels +/- ongoing HBV replication, (HBV DNA >20,000 IU/mL or HBeAg +ve). |
| How? First line treatment                   | Antivirals with high barrier to resistance (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. |
| Monitoring for HCC                         | Ultrasound + AFP every 6 months in persons with cirrhosis and/or family history of HCC. |

### NEW DIRECTIONS/PRIORITIES (2019/2020):

1. PMTCT – antivirals (Tenofovir)  
Criteria for treatment
2. TAF vs. TDF  
3. ‘Functional cure’ agenda

Main recommendations on:

• Who, when and how to treat?
• Simplified service delivery
• Developments:
  • Price reductions and wider availability of generics
  • WHO Progress Report on Access to HCV treatment, ’18
  • New pan-genotypic DAA regimens approved
  • Accumulated evidence on safety and effectiveness
Who, when?

- Those infected above 12 years of age (except: pregnant women)
  - **DAAs:** high rates of cure/Sustained Virological Response (SVR)
  - **SVR:** reduced all-cause mortality, liver-related mortality, incidence of HCC (based primarily on IFN data), improvement of comorbidities (diabetes, depression and chronic kidney disease)

- Treatment of adolescents is effective and well tolerated
What treatment to use?

WHO recommends pan-genotypic DAA regimens for treatment of persons with chronic hepatitis C infection aged 18 years and above

- Sofosbuvir/Velpatasvir
- Glecaprevir/Pibrentasvir
- Daclatasvir/Sofosbuvir*

*(based on real-world observational studies, including MSF data for genotypes 5 and 6)
1. Comprehensive national planning for the elimination of HCV infection
2. Simple and standardized algorithms across the continuum of care
3. Integration of hepatitis testing, care and treatment with other services
4. Strategies to strengthen linkage from testing to care, treatment and prevention
5. Decentralized services, supported by task-sharing
6. Community engagement and peer support
7. Efficient procurement and supply management of medicines and diagnostics
8. Data systems to monitor the quality of individual care and the cascade of care
- RDT
- ELISA

- Qualitative PCR
- Quantitative PCR
- HCVcAg

- APRI
- FibroScan

- HIV
- HBsAg, HBeAg, HBV VL
- Genotyping
- Pregnancy
- Liver/kidney tests

- Qualitative PCR
- Quantitative PCR
Summary

• **Simplification** and **scale-up** for both testing and treatment (especially for HCV)
• ‘**Treat all**’ for HCV (exceptions: pregnant women and children under age 12)
• Genotyping remains a barrier - **pan-genotypic DAA regimens for HCV**
• Dynamic scenarios for DAAs and regimens; **registration** remains a barrier and stands as priority
• **Equity** in access to DAAs is a critical guiding principle – **UHC**
• **Need to address HBV and HDV**
Acknowledgement

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