Towards Accelerating HBV Clinical Research in Africa

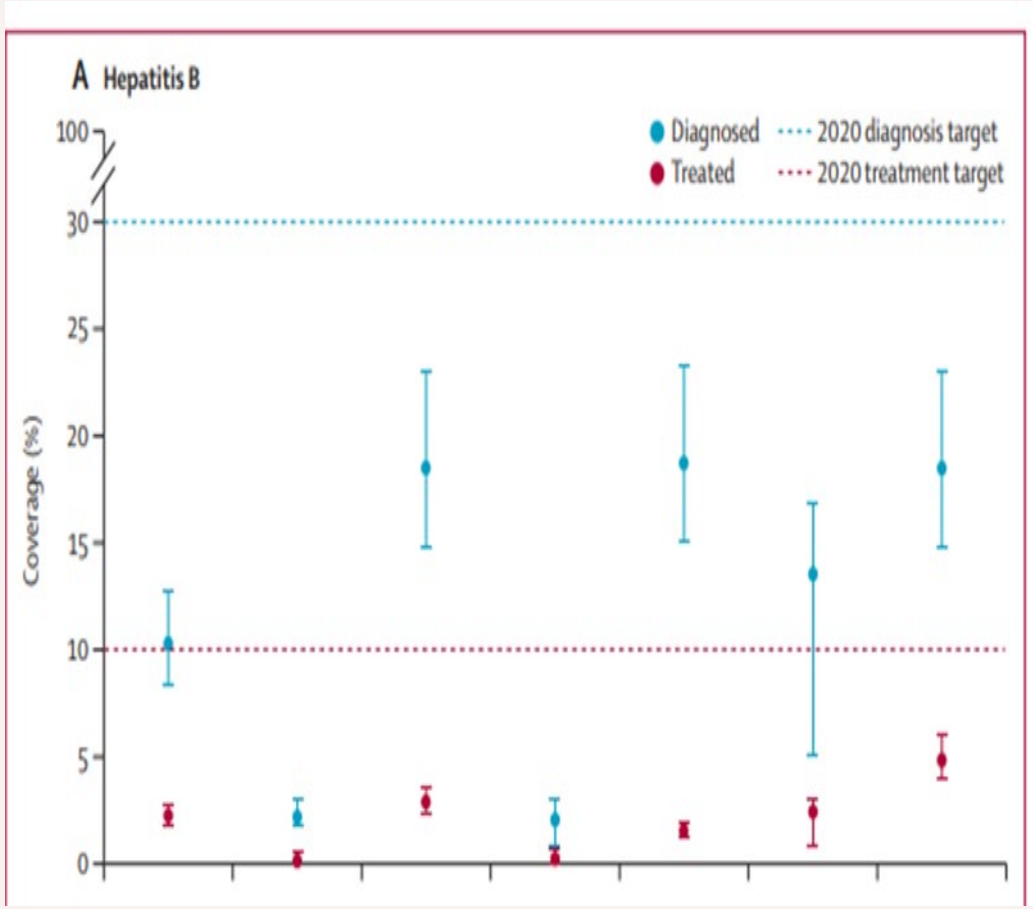
Friday, April 12, 2024

Culturgest Lisbon

COALITION FOR GLOBAL HEPATITIS ELIMINATION

THE TASK FORCE FOR GLOBAL HEALTH

Reaching Goals for Reductions in Hepatitis B related Mortality
Low HBV Diagnosis and Treatment Coverage B by Region, 2019



Region	Percent of persons living with HBV diagnosed	Percent of persons living with HBV on treatment (among those eligible)
Global	10%	2.1% (22% diagnosed)
WPRO	18.5%	18.5%
SEARO	2.1%	2.1%

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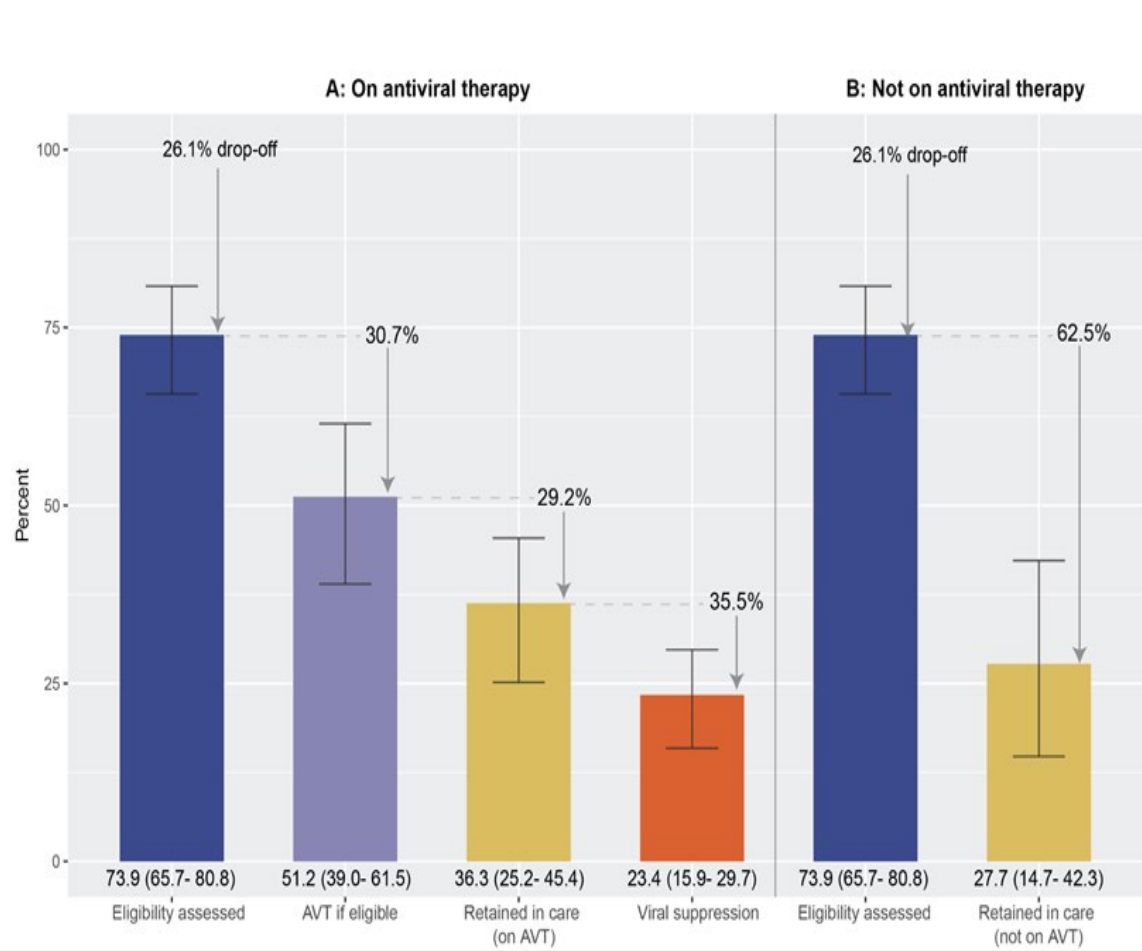
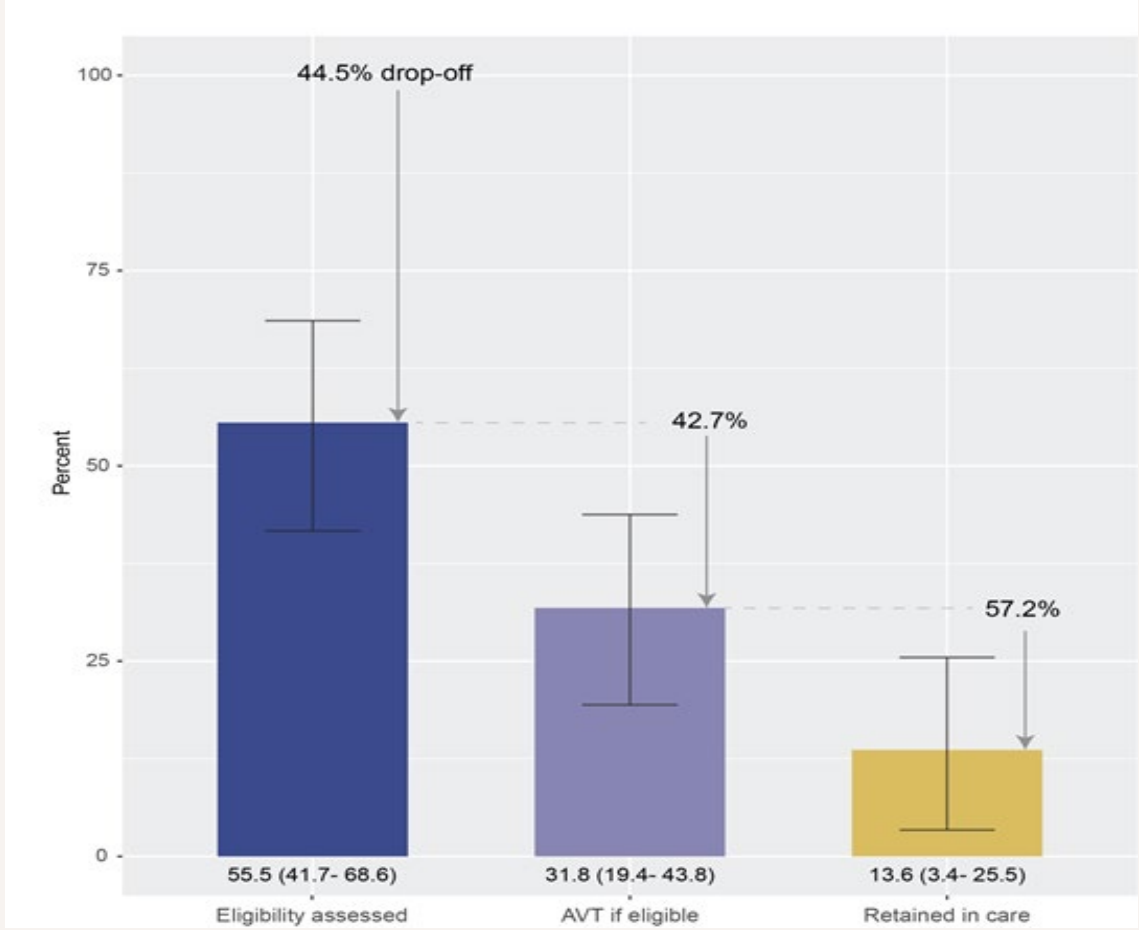
Lee KN, Clin Infect Dis. 2014 Jan;58(1):40-9; Abara WE, Ann Intern Med. 2017;167(11) Cui F et al 2023[:

Poor HBV Cascade of Care





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Priority 1: Simplify delivery models to assure decentralized, equitable access to hepatitis B testing and treatment

The research should answer key questions including:

- How can hepatitis B testing and treatment be effectively provided by non-specialists at different levels of the health system?
- What are effective models of hepatitis B service delivery for decentralized and non-specialized settings for resource-constrained settings?
- What are effective clinical practices to assess individuals with hepatitis B to determine their eligibility for treatment?
- What are effective models of care for migrants, refugees, and other key populations with limited access to care?
- How can the referral process to specialized care, when needed, be optimized?

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Table 1

Priority Research Area 1: Simplify models of care to assure decentralized and equitable access to hepatitis B testing and treatment

Design Options	Study Examples	Outcomes of Interest
Formative research including surveys, focus groups, and other behavioral science techniques **Timeline:** Short **Cost:** Low **Potential Impact:** Low	1. Provider perspectives on challenges in hepatitis B care delivery and preferences for simplified delivery of services 2. Provider and patient perspectives for optimizing communication and promoting acceptance of testing, initiation, and adherence to appropriate care and treatment	Inform priorities for studies to improve screening and care, motivations, preferences
Observational studies & implementation science **Timeline:** Medium **Cost:** Medium **Potential Impact:** High	1. Evaluate feasibility of implementing simplified models of testing, care, and treatment tailored for local context such as: — Modifications to expand capacity of current liver-care programs (including rapid diagnostics and ultrasonography) — Criteria for treatment initiation based on test availability or integration of hepatitis B care into HIV, primary, and other care services for populations, particularly with high hepatitis B prevalence (e.g. prisons) — Universal hepatitis B screening, reflex HBV DNA viral load testing, and peer navigation at facility entry points 2. Examine feasibility and effectiveness of simplified screening-entry and retention-in-care strategies (e.g., electronic or SMS reminders, peer counselors and groups, telehealth, financial incentives) 3. Modeling of cost-effectiveness of simplified hepatitis B testing and care strategies by care setting	**Care cascade:** testing, HBsAg positivity, linkage to care, treatment initiation, adherence, retention in care **Health outcomes:** HBV DNA suppression, ALT normalization, reversal of liver fibrosis, onset of cirrhosis, HCC, liver-related, mortality **Patient-reported outcomes:** acceptability, satisfaction, quality of life **Health system**: feasibility, cost effectiveness
Randomized controlled trials **Timeline:** Long **Cost:** High **Potential Impact:** High	1. Stepped-wedge cluster-randomized trial to evaluate the effectiveness of an intervention when implemented into a decentralized non-specialist model of care including simplified interventions (examples above) 2. Comparative trial to evaluate the effectiveness of differentiated care pathways for simplified hepatitis B service delivery within high-volume facilities 3. Modeling of cost-effectiveness of simplified hepatitis B testing and care strategies by care setting	**Care cascade:** testing, HBsAg positivity, linkage to care, treatment initiation, adherence, retention in care **Health outcomes:** HBV DNA suppression, ALT normalization, reversal of liver fibrosis; onset of cirrhosis, HCC, liver related mortality **Patient-reported outcomes:** acceptability, satisfaction, quality of life **Health system:** feasibility, cost effectiveness **Epidemiology:** Differences in outcomes by gender, age, and other factors

Timeline: Long: 3+ years; Medium: 1-3 years; Short: < 1 year
Cost: High: > USD 250,000 per year; Medium: USD 100-250,000 per year; Low: < USD 100,000 per year
Impact: Based on expert opinion

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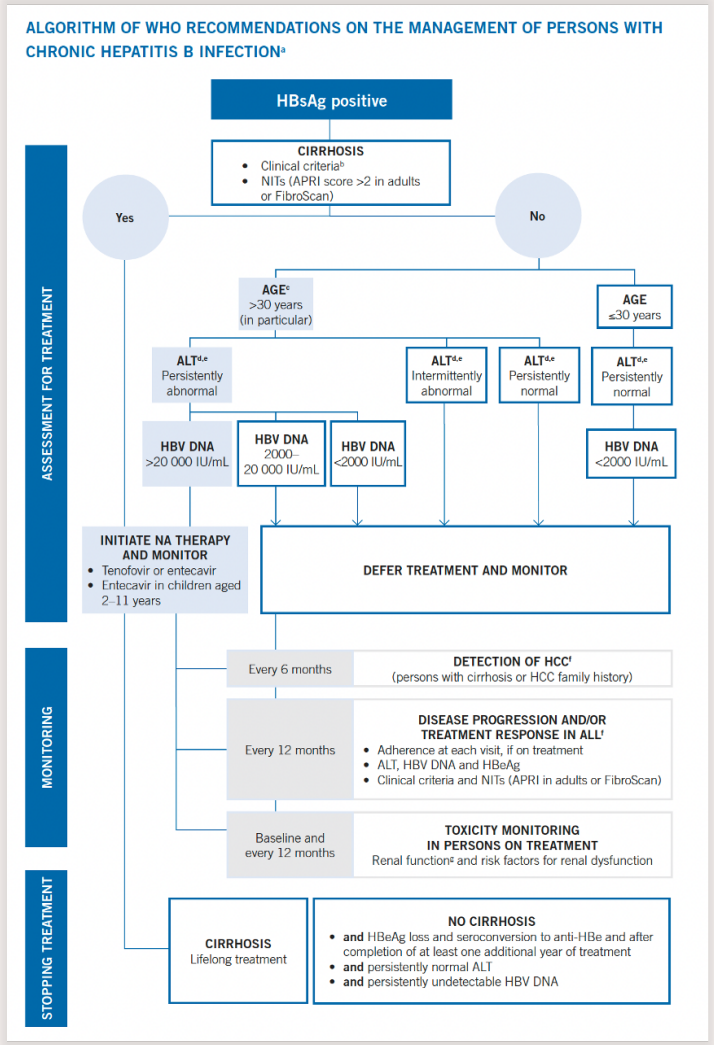
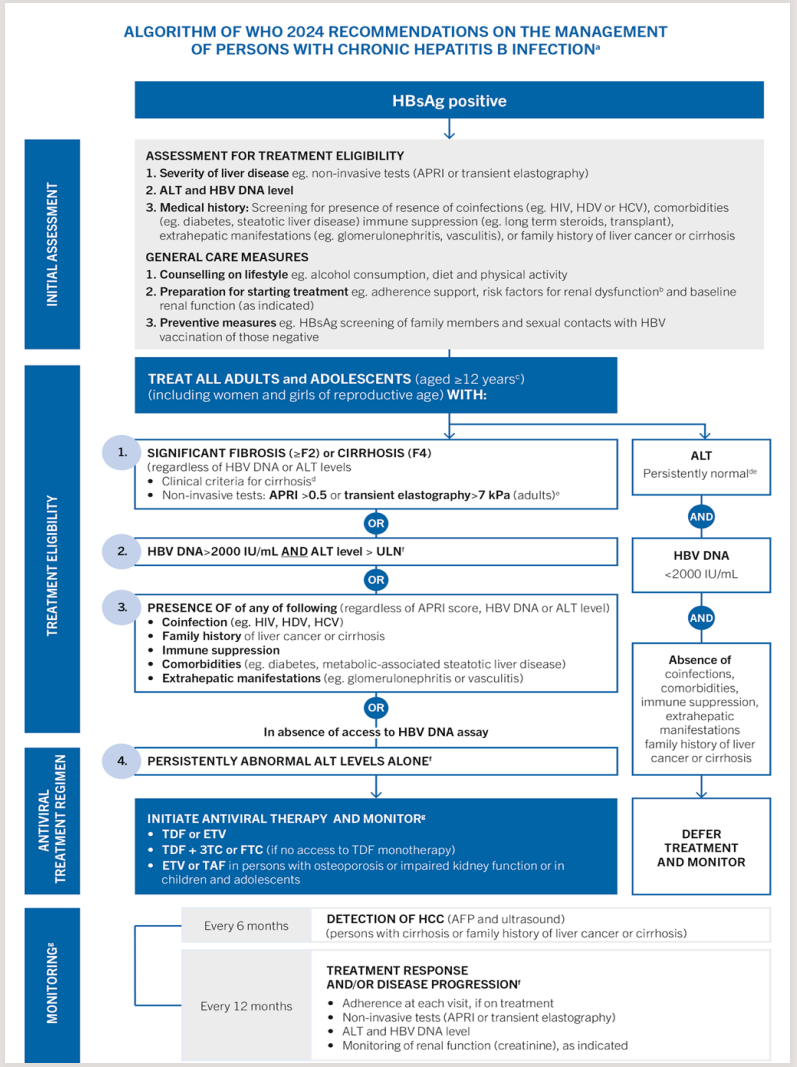
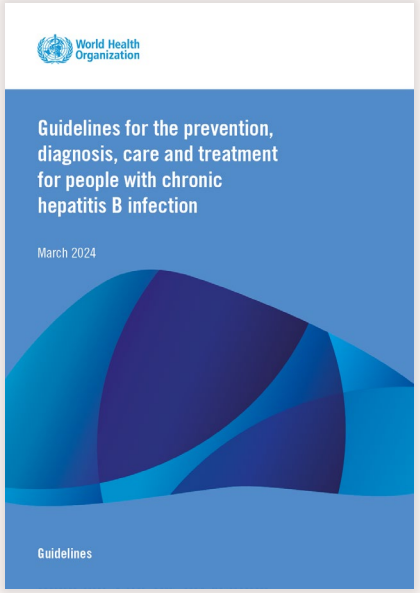
Simplify Eligibility Criteria for HBV Treatment

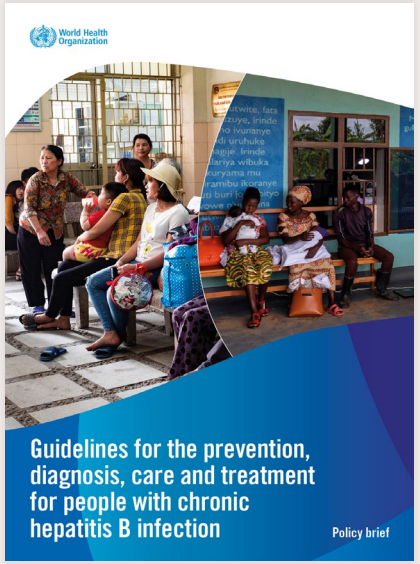
2015



2024 – NEW







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5.1 Recommendations

New recommendations – who to treat

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

1. Evidence of significant fibrosis (≥F2)[b] based on an APRI score of >0.5 or transient elastography[c] value of >7 kPa or evidence of cirrhosis (F4) (based on clinical criteria (or an APRI score of >1 or transient elastography value of >12.5 kPa[b]), regardless of HBV DNA or ALT levels.

(adults: strong recommendation, moderate-certainty evidence; adolescents: strong recommendation, low-certainty evidence)

OR

2. HBV DNA >2000 IU/mL and an ALT level above the 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.[d]

(adults: strong recommendation, high-certainty evidence [HBV DNA >20 000 IU/mL] and low-certainty evidence [HBV DNA 2000–20 000,]; adolescents: conditional recommendation, low-certainty evidence)

OR

3. Presence of **coinfections** (such as HIV, hepatitis D or hepatitis C); **family history** of liver cancer or cirrhosis; **immune suppression** (such as long-term steroids, solid organ or stem cell transplant); **comorbidities** (such as diabetes or metabolic dysfunction—associated steatotic liver disease); or **extrahepatic manifestations** (such as glomerulonephritis or vasculitis), regardless of the APRI score or HBV DNA or ALT levels.

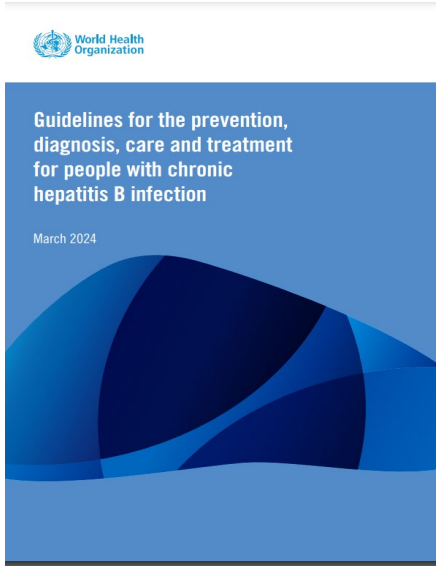
(adults: strong recommendation, moderate-certainty evidence; adolescents: conditional recommendation, low-certainty evidence)

OR

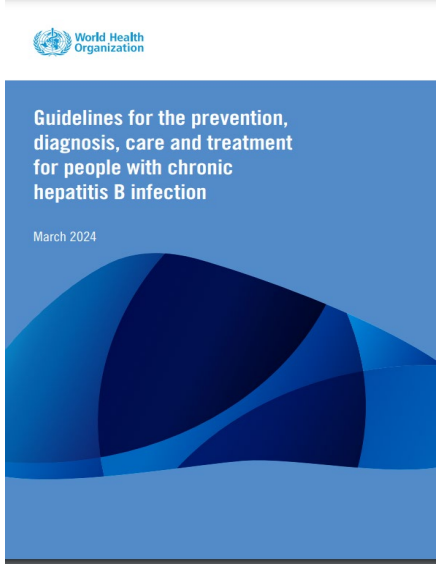
In the absence of access to an HBV DNA assay:

4. Persistently abnormal ALT levels (defined as two ALT values above the ULN at unspecified intervals during a 6- to 12-month period), regardless of APRI score.[e]

(adults and adolescents: conditional recommendation, very-low-certainty evidence)



8. Who to treat and what antiviral drugs to use for adolescents and children with CHB



8.1 Recommendations - Who to treat among adolescents (See Chapter 5)

New recommendations

Treatment is recommended for all adolescents (aged 12–17 years) with CHB[a] (including pregnant and non-pregnant adolescent girls of reproductive age) with:

1. Evidence of significant fibrosis (≥F2) based on clinical criteria[b] or an APRI score of >0.5 or transient elastography value of >7 kPa[c] or evidence of cirrhosis (F4) based on clinical criteria[c] (or an APRI score of >1 or transient elastography value of >12.5 kPa[d]), regardless of HBV DNA or ALT levels.

(adolescents: strong recommendation, low-certainty evidence)

OR

2. HBV DNA >2000 IU/mL and an ALT level above the ULN (30 U/L for boys and men and 19 U/L for girls and women). For adolescents, ALT>ULN at least twice in a 6- to 12-month period.[d]

(adolescents: conditional recommendation, low-certainty evidence)

OR

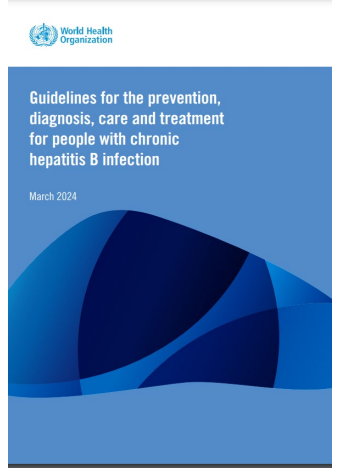
3. Presence of coinfections (such as HIV, HDV and HCV), family history of liver cancer or cirrhosis, immune suppression (such as long-term steroids, solid organ or stem cell transplant), comorbidities (such as diabetes, metabolic dysfunction–associated steatotic liver disease and iron overload secondary to treatment for disorders of the blood) or extrahepatic manifestations (such as glomerulonephritis or vasculitis), regardless of APRI score or HBV DNA or ALT level.

(adolescents: conditional recommendation, low-certainty evidence)

OR

4. Persistently abnormal ALT levels (in the absence of access to an HBV DNA assay), regardless of APRI score.[e]

(adolescents: conditional recommendation, very-low-certainty evidence)

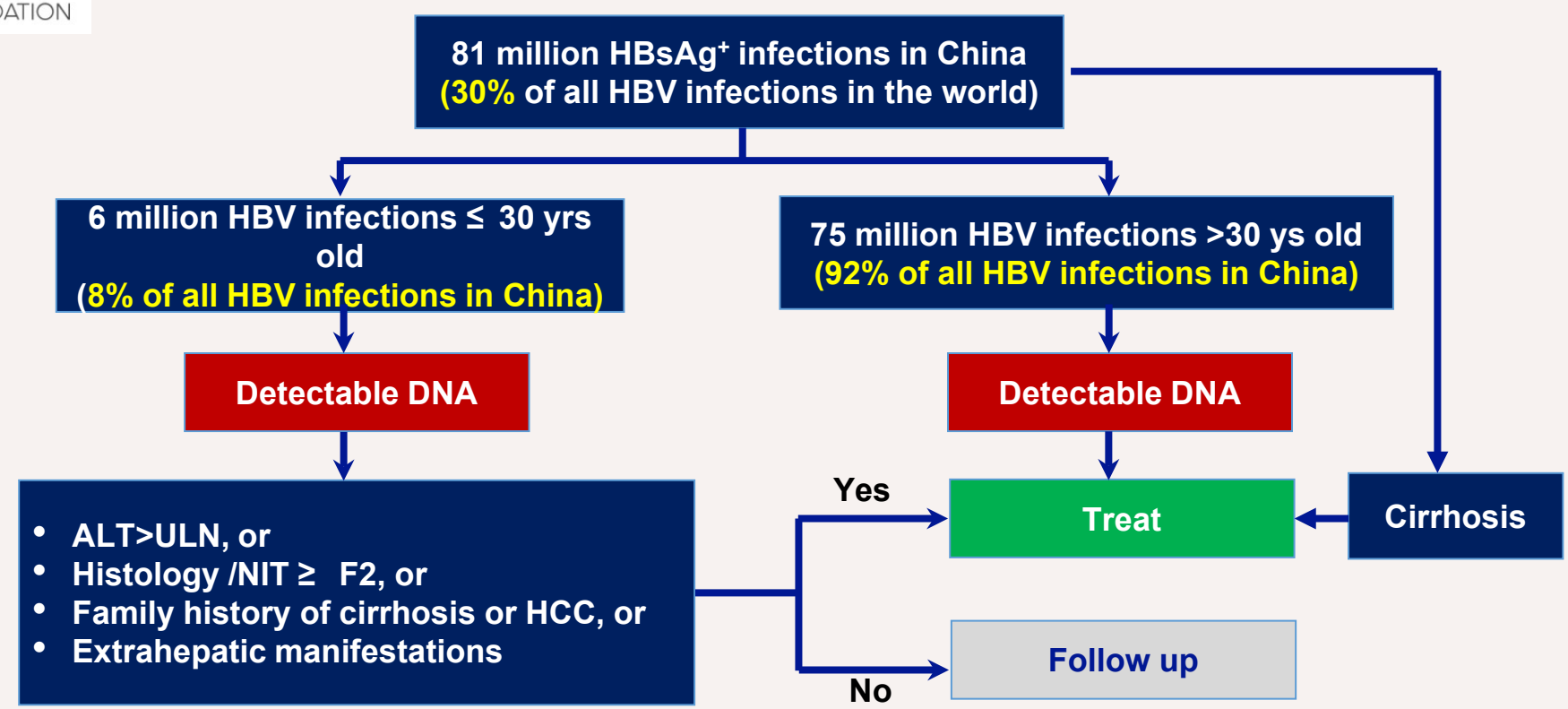


HBV Treatment for Children and Adolescents Research Needs

- Comparative trials and long-term follow-up studies of treatment effectiveness on disease progression, transmission and QoL
- Long-term prospective studies of potential adverse effects of long-term nucleos(t)ide analogue treatment
- Long-term follow-up studies to examine the rate of discontinuation of nucleos(t)ide analogue
- treatment and the optimal strategies to promote and maintain treatment • Data on the burden and routes of transmission of HBV among children and adolescents in
- Determining the population-based prevalence of liver fibrosis caused by hepatitis B andthe progression of fibrosis during childhood and further validating non-invasive tests of liver fibrosis for children and adolescents

China HBV Treatment Guidelines(2022)

-Test more, treat more, treat earlier and treat longer!



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Sample Research Questions

- What are studies to assess overall impact and effectiveness of updated and expanding treatment eligibility by WHO and national health ministries?
  - Treatment impact among people with low-level viraemia and early fibrosis stages in sub-Saharan Africa
  - Treatment impact among persons with certain co-morbidities (e.g.DM, HDV), social factors (e.g. migrants) or other factors (genotype)?

- What are studies to assess components of effective models of hepatitis B service delivery for decentralized and non-specialized settings for resource-constrained settings?
  - Health promotion
  - Community-based services
  - Service integration
  - Patient support for acceptance of testing, linkage to care and adherence to therapy
  - Technical tools to initiate and monitor response to therapy and disease progression

- What are studies to assess new technologies to facilitate clinical decisions regarding patient eligibility for treatment?
  - Non invasive tests for liver fibrosis
  - Virologic tests; DNA, crAg, quantitative HBsAg
  - Other

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Sample Research Questions

- ● What type of technical capacities and settings are needed to conduct research for decentralizing HBV care in Africa?
  - What type of settings?
  - What are the priority gaps in building this capacity?
- ● What is the role of communities in research to improve HBV care ?
  - Priority-setting;
  - Protocol development,
  - Study implementation
  - Date analysis and , presentation

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