

**Universal Treatment *versus*  
Targeted Strategies:  
Optimal Approaches for Global  
Elimination of Hepatitis B**

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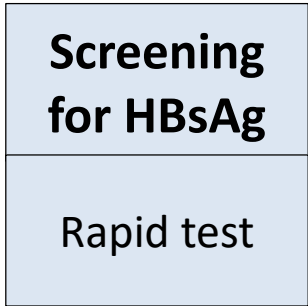


# TREATING PEOPLE WITH CHRONIC HBV INFECTION

**Screening  
for HBsAg**

Rapid test

US\$ <1



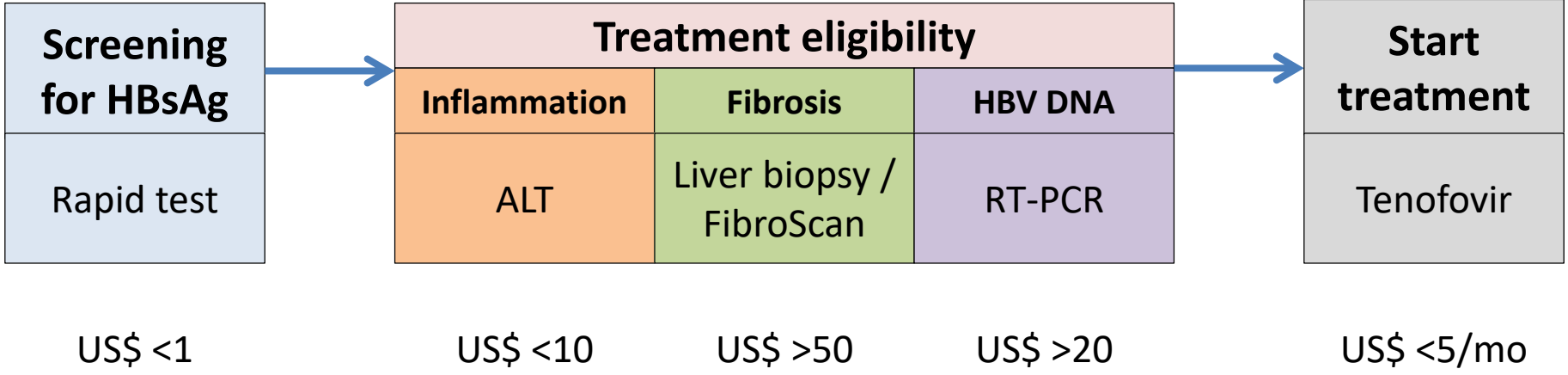
<b>Treatment eligibility</b>		
<b>Inflammation</b>	<b>Fibrosis</b>	<b>HBV DNA</b>
ALT	Liver biopsy / FibroScan	RT-PCR

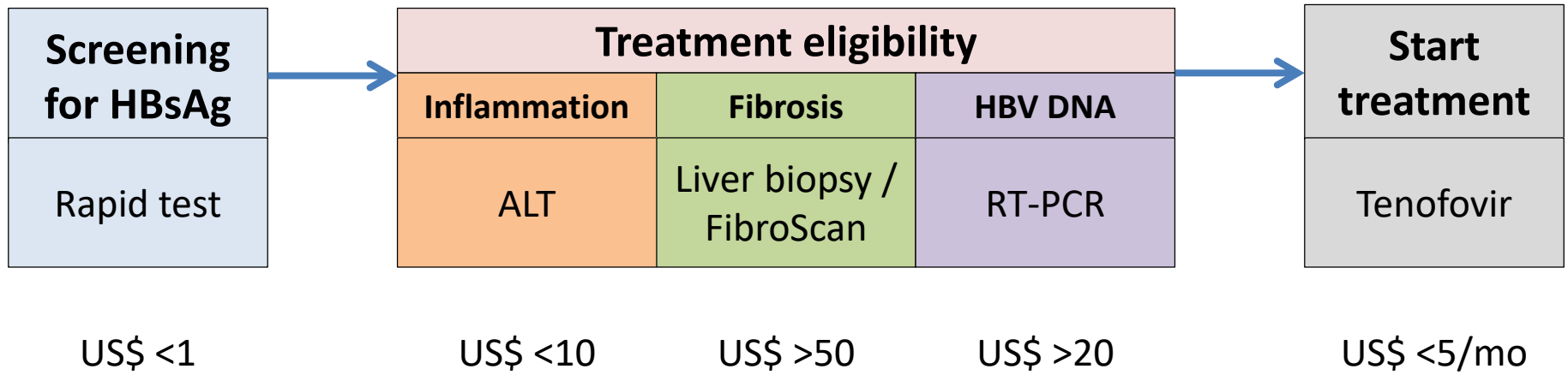
US\$ <1

US\$ <10

US\$ >50

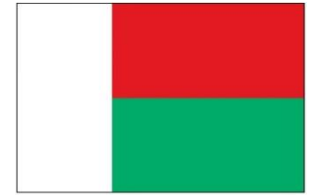
US\$ >20



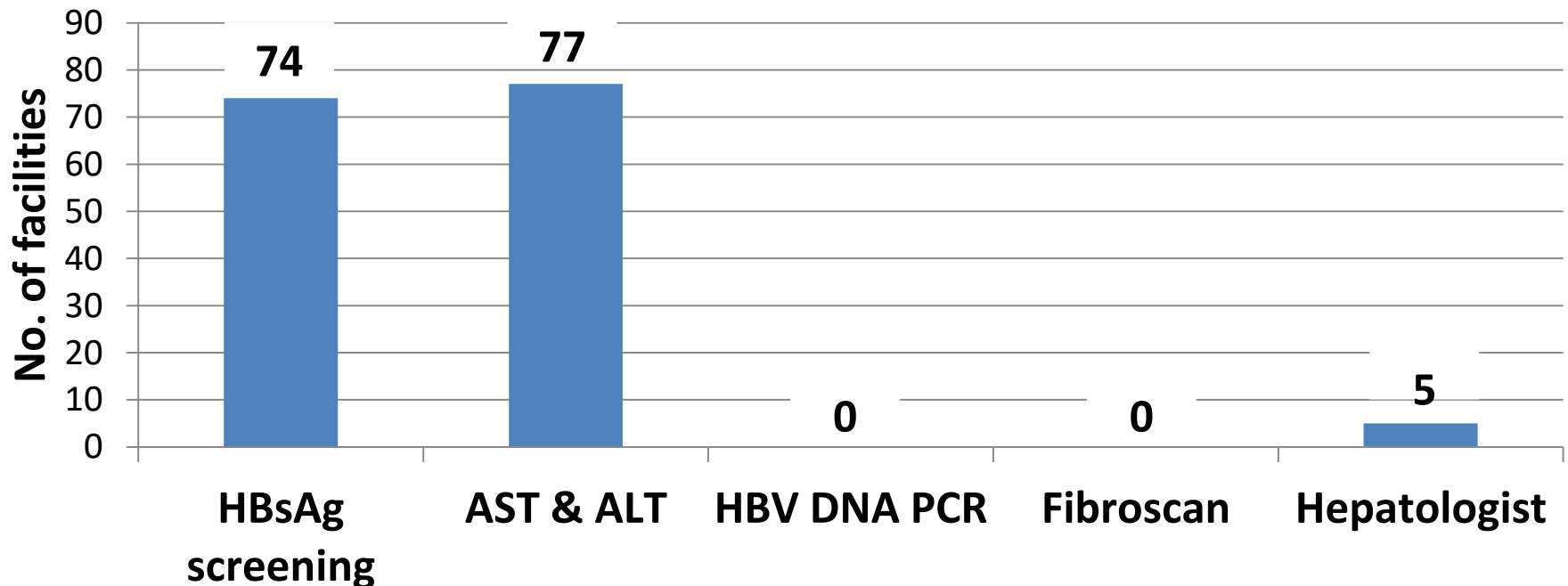


**10-30% meet the treatment eligibility criteria**

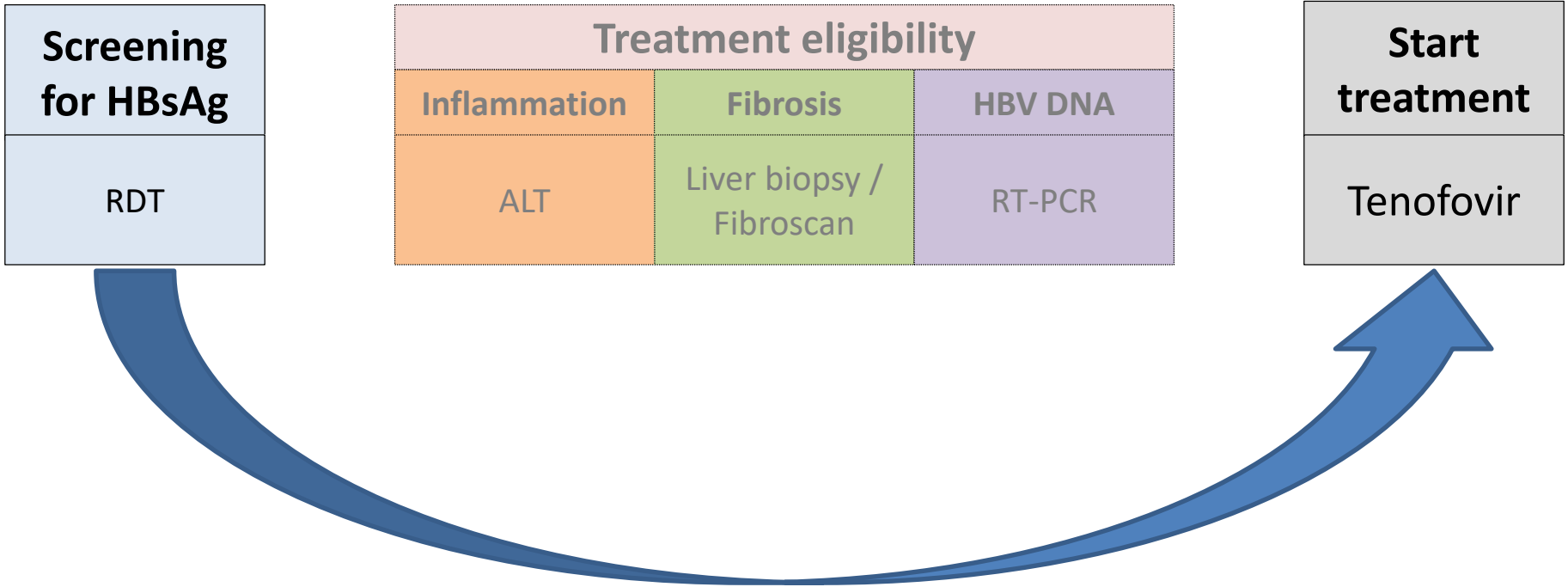
# Madagascar



- Population: 23.5 million
- Prevalence of HBsAg: 6.9%



# Treat All





# Treat All

## Pros

- Potentially improve treatment uptake by simplifying diagnosis
- People not meeting criteria may still develop liver diseases
- Cost-effective
- Tenofovir:
  - Not much adverse events
  - High barrier to resistance

## Cons

- Adherence to life-long treatment
- Question of feasibility
- HBV is different from HIV
  - Not all people with HBV develop liver diseases
  - Efficacy of treatment in people ineligible for treatment
  - No Global Fund, no subsidization

# Treat All

## Pros

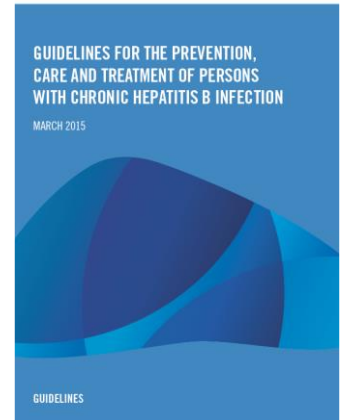
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# Updated WHO guidelines

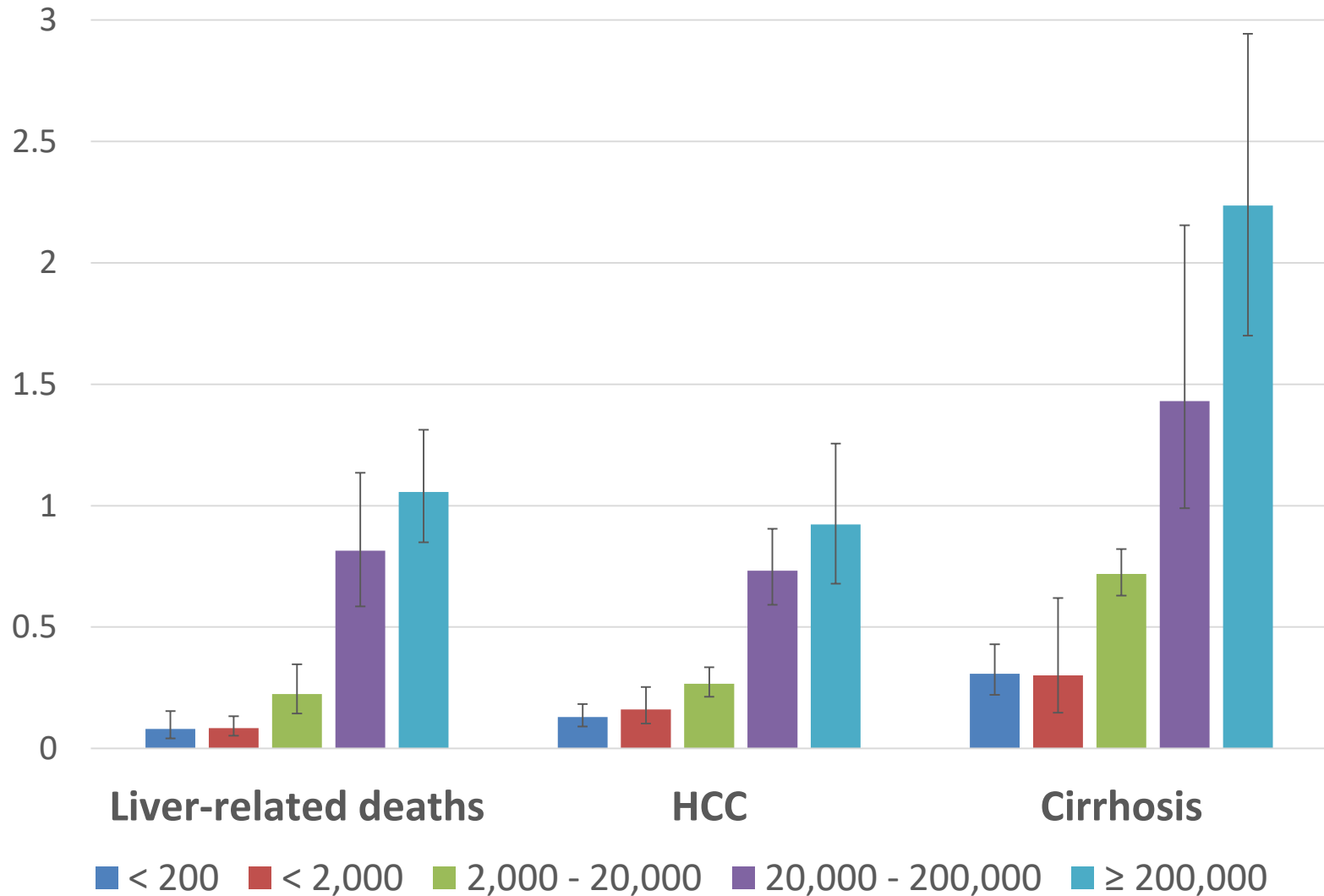
- First guidelines in 2015
    - Cirrhosis
  - OR
  - HBV DNA > 20 000 IU/mL & ALT > upper limit of normal
- 
- Revising the guidelines in 2023
    - Maintaining HBV DNA threshold?
    - Or lowering HBV DNA threshold?
    - Or « Treat All »?



# Systematic review commissioned by the WHO

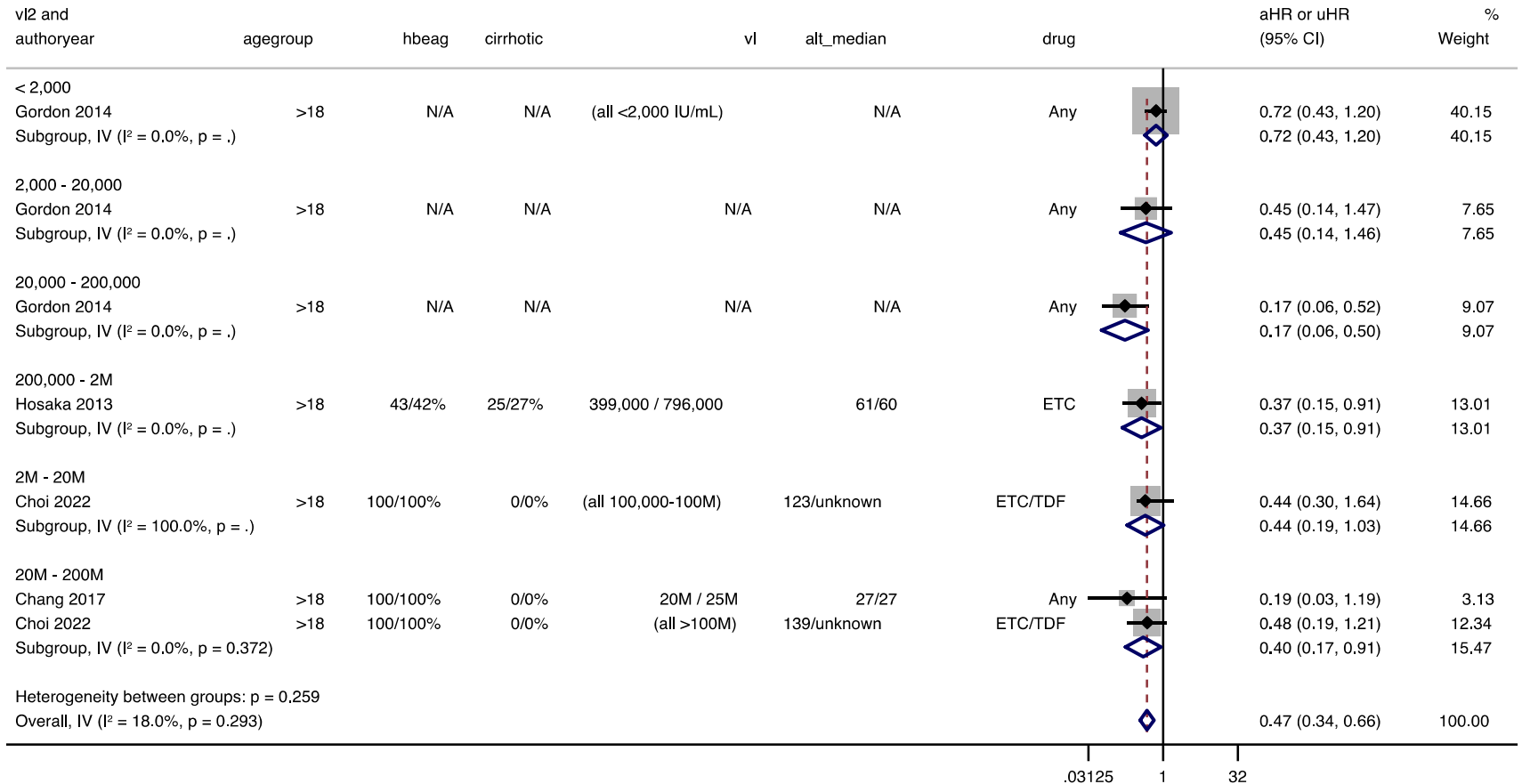
- To provide a summary estimate of:
  - The incidence rate of developing clinical outcomes without treatment in a group of HBV-infected people without cirrhosis
  - The efficacy of antiviral therapy at preventing clinical outcomes in a group of HBV-infected people without cirrhosis
  - Stratified by HBV DNA levels (IU/mL)
    - < 200
    - < 2000
    - 2000 – 20 000
    - 20 000 – 200 000
    - $\geq$  200 000

## Incidence rates per 100 person-years



*Conde DY, Rakover A, Warsop Z, et al. unpublished data*

## HCC (observational studies) by baseline viral load



# The number needed to treat (NNT) for preventing one case of HCC

Viral load (IU/mL)	NNT
< 2000	149 people to treat after a median of 12 years
2000 – 19 999	45 people to treat after a median of 10 years
20 000 -199,999	11 people to treat after a median of 13 years

# Cost-effectiveness of Treat All

	Incremental cost-effectiveness ratio (ICER) per DALY averted	Threshold
Saudi Arabia	US\$ 22 050	US\$ 66 150
USA	US\$ 41 700	US\$ 65 850

Sanai FM et al., *J Infect Public Health*, 2020

Razavi-Shearer D et al., *J Viral Hepat*, 2023



# Cost-effectiveness of Treat All

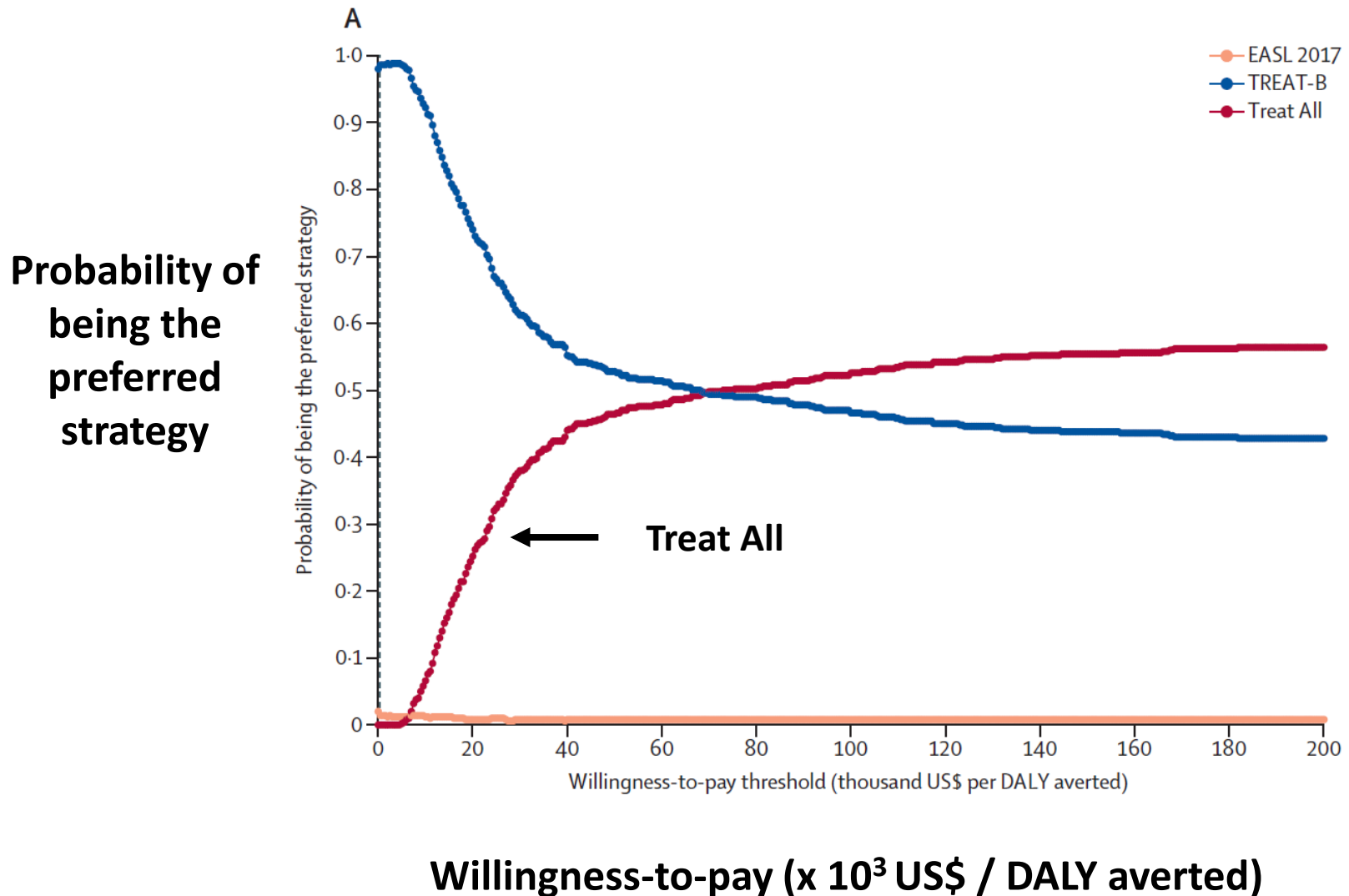
	Incremental cost-effectiveness ratio (ICER) per DALY averted	Threshold
Saudi Arabia	US\$ 22 050	US\$ 66 150
USA	US\$ 41 700	US\$ 65 850
The Gambia	US\$ 2 149	US\$ 352

Sanai FM et al., *J Infect Public Health*, 2020

Razavi-Shearer D et al., *J Viral Hepat*, 2023

Luong Nguyen LB et al., *Lancet Glob Health* 2024

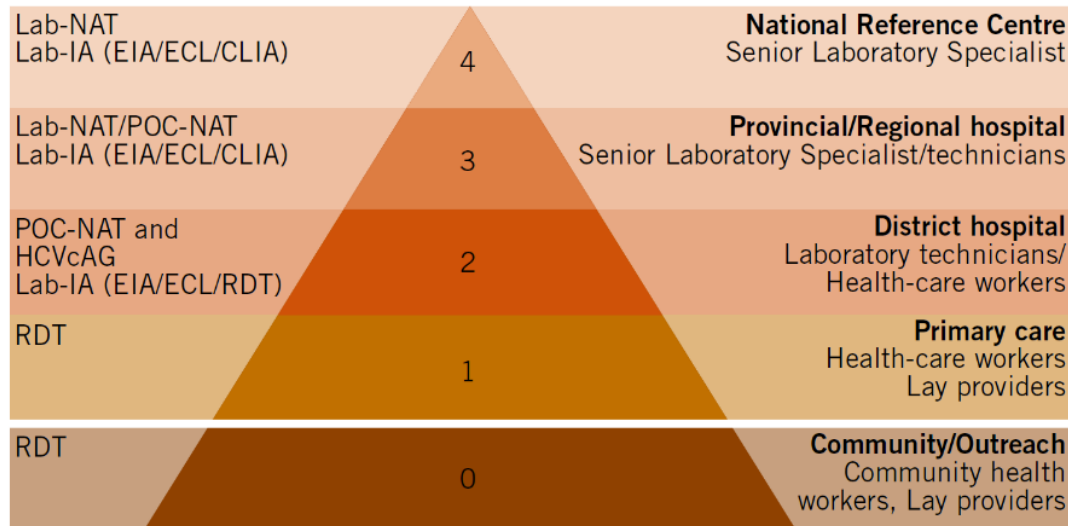
# Cost-effectiveness acceptability curve



- If not Treat All, then how can we best identify people in need of treatment?

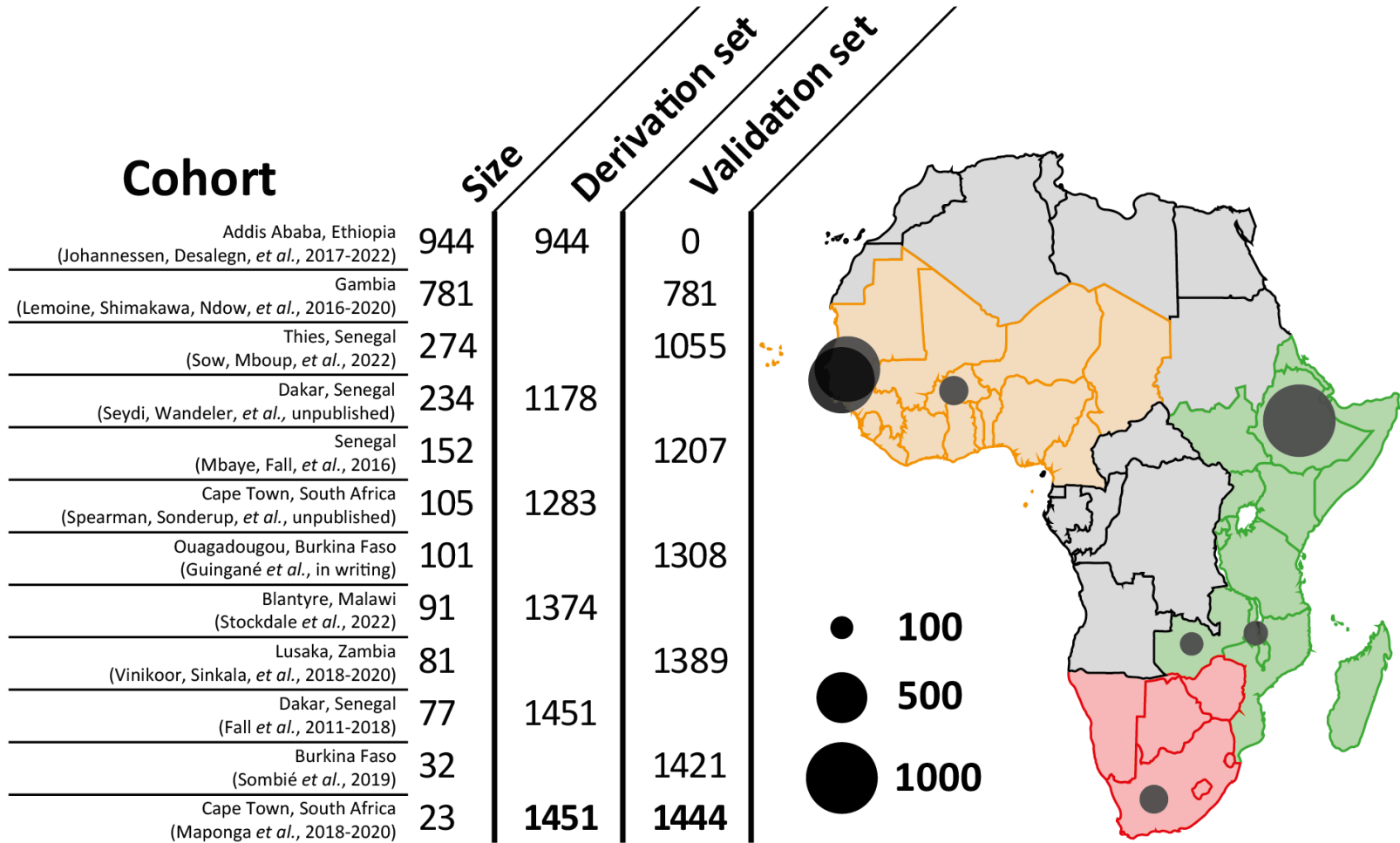
# HEPSANET score

- Develop and evaluate a score using tests available at lower-level facilities, to simplify the evaluation of antiviral therapy eligibility

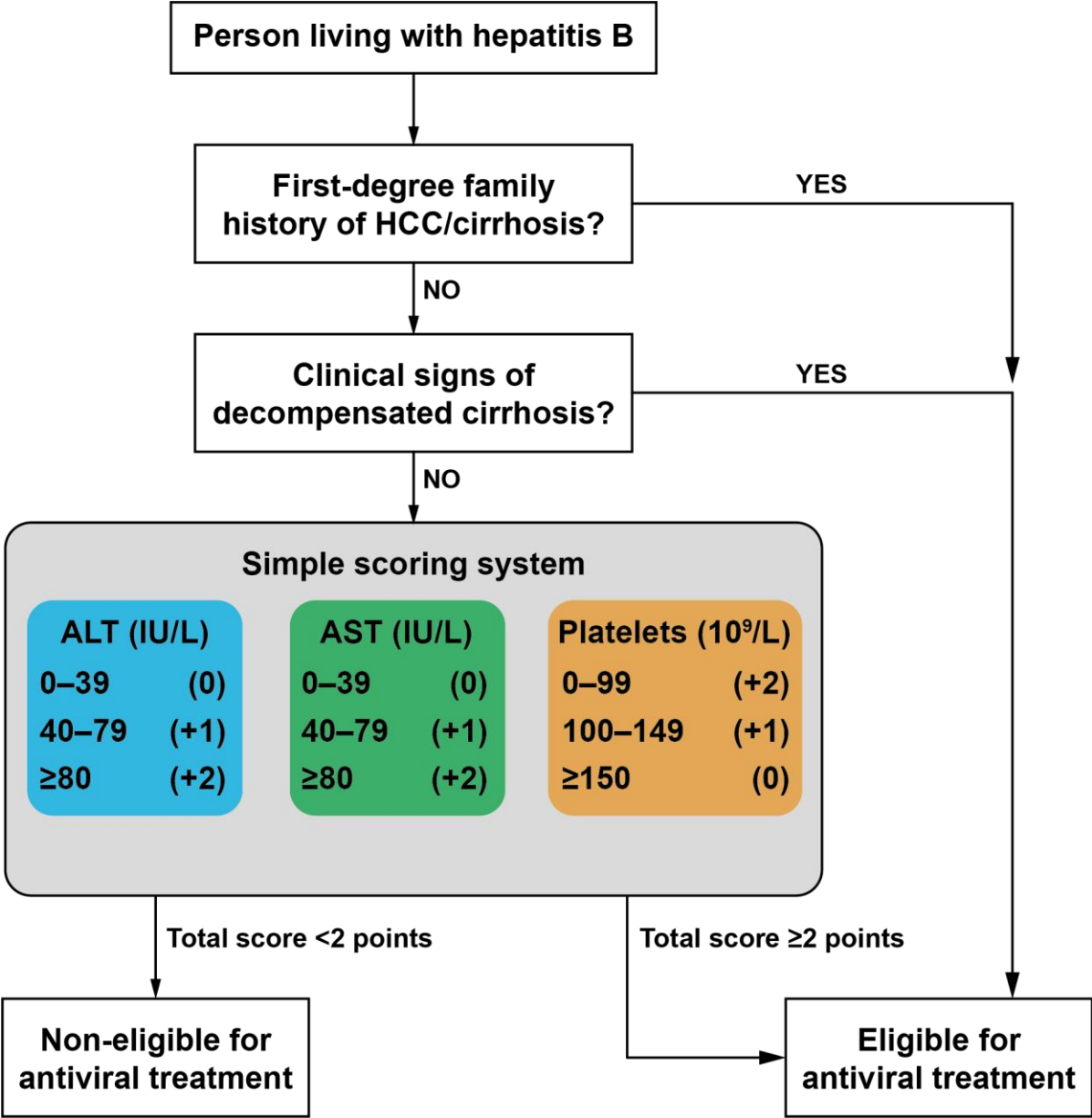


- Consider the EASL 2017 criteria as a reference

# HEPSANET



Parameters	Tiered level of healthcare facility*					Tier considered for analysis
	Tier0	Tier1	Tier2	Tier3	Tier4	
<b>Clinical parameters</b>						
Sex	100%	100%	100%	100%	100%	0/1
Age	100%	100%	100%	100%	100%	0/1
First-degree family history (HCC, cirrhosis)	73%	82%	100%	100%	100%	0/1
Clinical diagnosis of jaundice	73%	82%	100%	100%	100%	0/1
Clinical diagnosis of ascites	27%	45%	100%	100%	100%	2
Clinical diagnosis of hepatic encephalopathy	27%	36%	82%	100%	100%	2
Clinical diagnosing of variceal bleeding	18%	18%	55%	82%	100%	2
<b>Laboratory parameters</b>						
Full blood count (platelets)	9%	36%	100%	100%	100%	2
Alanine aminotransferase (ALT)	9%	36%	91%	91%	100%	2
Aspartate aminotransferase (AST)	9%	36%	91%	91%	100%	2
Gamma-glutamyl transferase (GGT)	0%	9%	55%	73%	100%	2
Bilirubin	0%	18%	64%	73%	100%	2
Prothrombin time (INR)	0%	18%	55%	64%	73%	2
HBeAg (Rapid diagnosis test)	9%	18%	36%	60%	55%	3
HBeAg (Laboratory-based immunoassays)	0%	0%	18%	45%	82%	3
HBV DNA (Xpert)	0%	0%	9%	55%	82%	3
HBV DNA (Conventional platform)	0%	0%	9%	27%	73%	4
Transient elastography (FibroScan)	0%	0%	0%	9%	82%	4
Liver biopsy	0%	0%	0%	9%	100%	4
Histopathology	0%	0%	0%	9%	82%	4

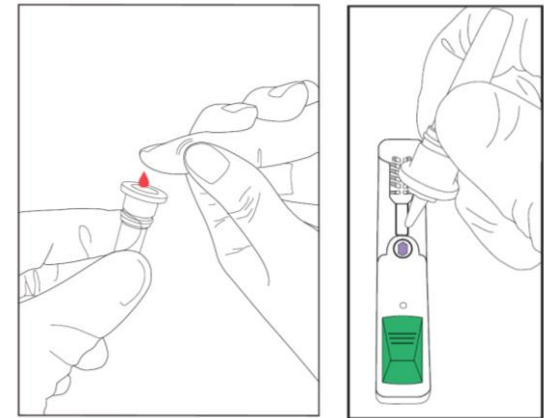


# Validation cohort (n = 1 444)

Test	AUROC [95% CI]	Sensitivity (%)	Specificity (%)
<b>HEPSANET score</b> (ALT, AST, platelet)	0.83 [0.80–0.86]	78	87
<b>WHO 2015</b> (HBV DNA, ALT, APRI)	0.68 [0.64–0.72]	38	98
<b>TREAT-B</b> (ALT, HBeAg)	0.88 [0.86–0.91]	91	85



- Rapid test to detect HBcrAg
- 284 HBV-infected adults in The Gambia
- Reference criteria: ALT, FibroScan, HBV DNA
- Index criteria: ALT, FibroScan, HBcrAg-RDT
  - Sensitivity 96.6%                      Specificity 86.3%



# Conclusions

- To achieve global elimination of hepatitis, it is essential to scale up screening & clinical staging for hepatitis B
- Treat All is attractive, but requires data on feasibility & acceptability
- This may be justified when HBV cure is possible
- Essential to develop a locally-adapted simplified model of care

# Thank you



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