«We don’t have data from Africa» -true or false?

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University of Oslo / HEPSANET

12 April 2024

HEPSANET
HEPATITIS B IN AFRICA
COLLABORATIVE NETWORK

World Health Organization

GUIDELINES FOR THE PREVENTI
CARE AND TREATMENT OF P
WITH CHRONIC HEPATITIS B

MARCH 2015

guide the future research agenda. Most of the evidence was based on st
in adults from Asia, North America and western Europe, and there is a st
lack of data to inform management from sub-Saharan Africa, and in childr

Research gaps

- Conduct longitudinal cohort studies especially in sub-Saharan Africa, but also in underresearched populations, such as children, young adults, and pregnant women with CHB to determine prognostic criteria and indications for initiating or deferring treatment.
- Conduct longitudinal studies to further evaluate different cut-offs for abnormal ALT in a range of settings and populations, as well as determine the prognostic significance of persistently normal ALT despite high HBV DNA levels in persons with CHB in sub-Saharan Africa and Asia.

Research gaps

- Assess the impact of antiviral therapy on CHB liver-associated and all-cause morbidity and mortality, especially in LMICs.
- Conduct treatment and cost–effectiveness studies on the use of tenofovir and entecavir in persons with CHB, especially in sub-Saharan Africa, and also among children in whom antiviral treatment is indicated.

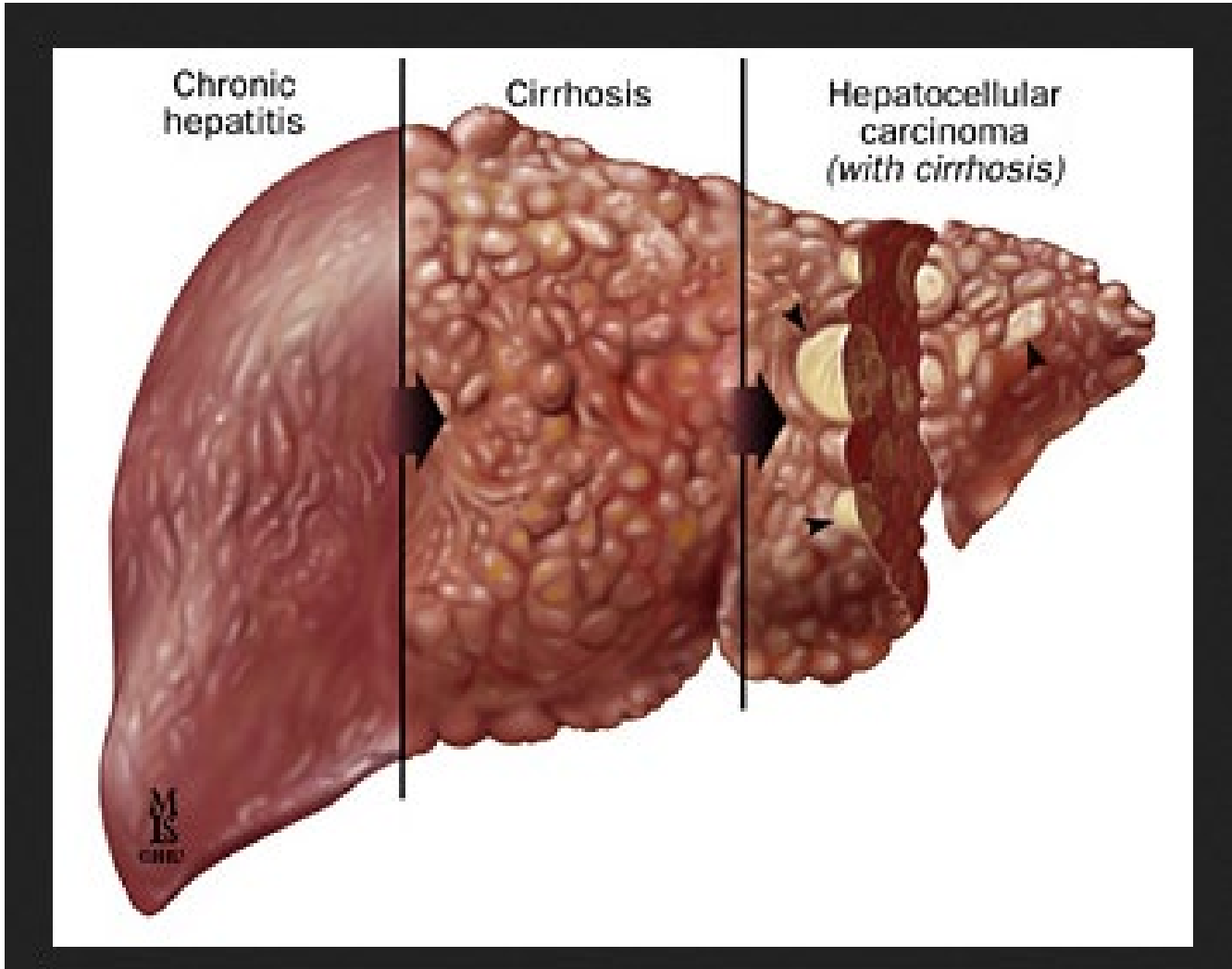
Research gaps

- Determine risk factors (including age) and thresholds for HCC and natural history in African populations through longitudinal cohort studies in sub-Saharan Africa.
- Conduct further RCTs of head-to-head comparisons between different HCC surveillance strategies, especially in sub-Saharan Africa.

The key knowledge gap: predictors of disease progression

- Can we predict who will die from hep B in Africa?
- Does cirrhosis and HCC occur at younger age in Africa?
- Are there unique risk factors for cirrhosis and HCC in Africa?

Who to treat?



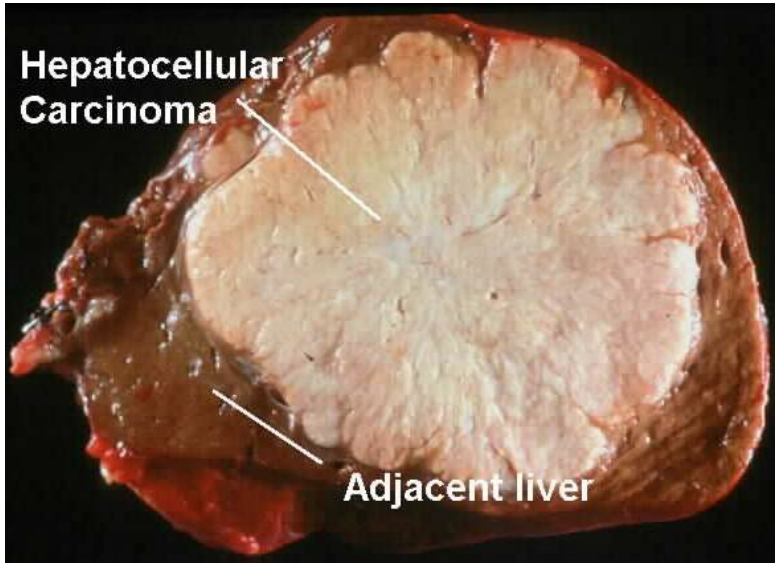
The key knowledge gap: predictors of disease progression

- Why can't we just rely on data from the REVEAL study?
- Disease progression depends on:
  - Host factors: age, sex, co-morbidities (obesity, T2DM), co-infections (HIV, HCV, HDV), lifestyle (alcohol, khat)
  - Viral factors: genotype
  - Environmental factors: aflatoxin, etc
  - Society: access to diagnosis and treat

All these factors are different in Africa compared to Taiwan!

What kind of study is needed to identify predictors of HCC / cirrhosis?

- We need a **large cohort study** with **>10 years follow-up** (like REVEAL)
- But we don't have time for that!
- And natural history studies are unethical in the era of antiviral therapy



Our work in Ethiopia

- Pilot study of 1303 HBV patients followed up since 2015
- 298 started TDF, can study treatment effect on:
  - Fibrosis regression
  - Normalization of ALT
  - HCC incidence
  - TDF toxicity
- 1005 untreated, can study disease progression:
  - Fibrosis progression
  - HCC / death

Aberra et al. BMC Infectious Diseases (2017) 17:438
DOI 10.1186/s12879-017-2549-8

BMC Infectious Diseases

RESEARCH ARTICLE Open Access

Early experiences from one of the first treatment programs for chronic hepatitis B in sub-Saharan Africa

Hanna Aberra[1], Hailemichael Desalegn[1], Nega Berhe[2,3], Girmay Medhin[2], Kathrine Stene-Johansen[4], Svein Gunnar Gundersen[5,6] and Asgeir Johannessen[3*]

Abstract

Contents lists available at ScienceDirect

Journal of Virological Methods

journal homepage: www.elsevier.com/locate/jviromet

...oint-of-care viral load test for hepatitis B in a ...etting

...nen Woldemedihn[a], Corina Silvia Rueegg[b], Hailemichael Des... ...Nega Berhe[d,e], Asgeir Johannessen[e,f,*]

Desalegn et al. BMC Gastroenterology (2019) 19:74
https://doi.org/10.1186/s12876-019-0993-1

BMC Gastroenterology

RESEARCH ARTICLE Open Access

Predictors of mortality in patients under treatment for chronic hepatitis B in Ethiopia: a prospective cohort study

Hailemichael Desalegn*, Hanna Aberra[1], Nega Berhe[2,3], Girmay Medhin[2], Bitsatab Mekasha[1], Svein Gunnar Gundersen[4,5] and Asgeir Johannessen[3,6]

PLOS ONE

vaccines MDPI

Article

Mother-to-Child Transmission of Hepatitis B Virus in Ethiopia

Desalegn et al. BMC Medicine (2023) 21:373
https://doi.org/10.1186/s12916-023-03082-4

BMC Medicine

RESEARCH ARTICLE Open Access

Five-year results of a treatment program for chronic hepatitis B in Ethiopia

Hailemichael Desalegn[1,2†], Stian Magnus Staurung Orllen[3,4†], Hanna Aberra[1], Eyerusalem Marno[1], Sine Grude[5], Kristina Hommersand[5], Nega Berhe[2,4,6], Svein Gunnar Gundersen[7] and Asgeir Johannessen[2,4,8*]

RESEARCH ARTICLE

Dry Blood Spots a Reliabl... Measurement of Hepatiti... Resource-Limited Setting...

Kathrine Stene-Johansen[1], Nadeem Yaqoob[1], Joa... Hailemichael Desalegn[2], Nega Berhe[3,4], Asgeir Joh...

1 Department of Virology, Norwegian Institute of Public Health,

...gn et al. BMC Medicine (2018) 16:234
...doi.org/10.1186/s12916-018-1229-x

CrossMark click for updates

OPEN ACCESS

RESEARCH ARTICLE

Treatment of chronic he... sub-Saharan Africa: 1-ye... pilot program in Ethiop...

Research Article
Viral Hepatitis

JOURNAL OF HEPATOLOGY

The WHO guidelines for chronic hepatitis B fail to detect half of the patients in need of treatment in Ethiopia

Hanna Aberra[1], Hailemichael Desalegn[1], Nega Berhe[2,3], Bitsatab Mekasha[1], Girmay Medhin[2], Svein Gunnar Gundersen[4,5], Asgeir Johannessen[3,6,*]

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See Editorial, pages 1043–1045

Liver INTERNATIONAL

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ORIGINAL ARTICLE

Hepatitis delta virus infection in a large cohort of chroni... hepatitis B patients in Ethiopia

Hanna Aberra, Emmanuel Gordien, Hailemichael Desalegn, Nega Berhe, Girmay Medhi... Bitsatab Mekasha, Svein G. Gundersen, Athenaïs Gerber, Kathrine Stene-Johansen, Joakim Øverbø, Asgeir Johannessen

First published: 20 October 2017 Full publication history

Open Forum Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America hivma hiv medicine association OXFORD

Renal Safety of Long-term Tenofovir Disoproxil Fumarate Treatment in Patients With Chronic Hepatitis B

ORIGINAL ARTICLE

WILEY Liver INTERNATIONAL

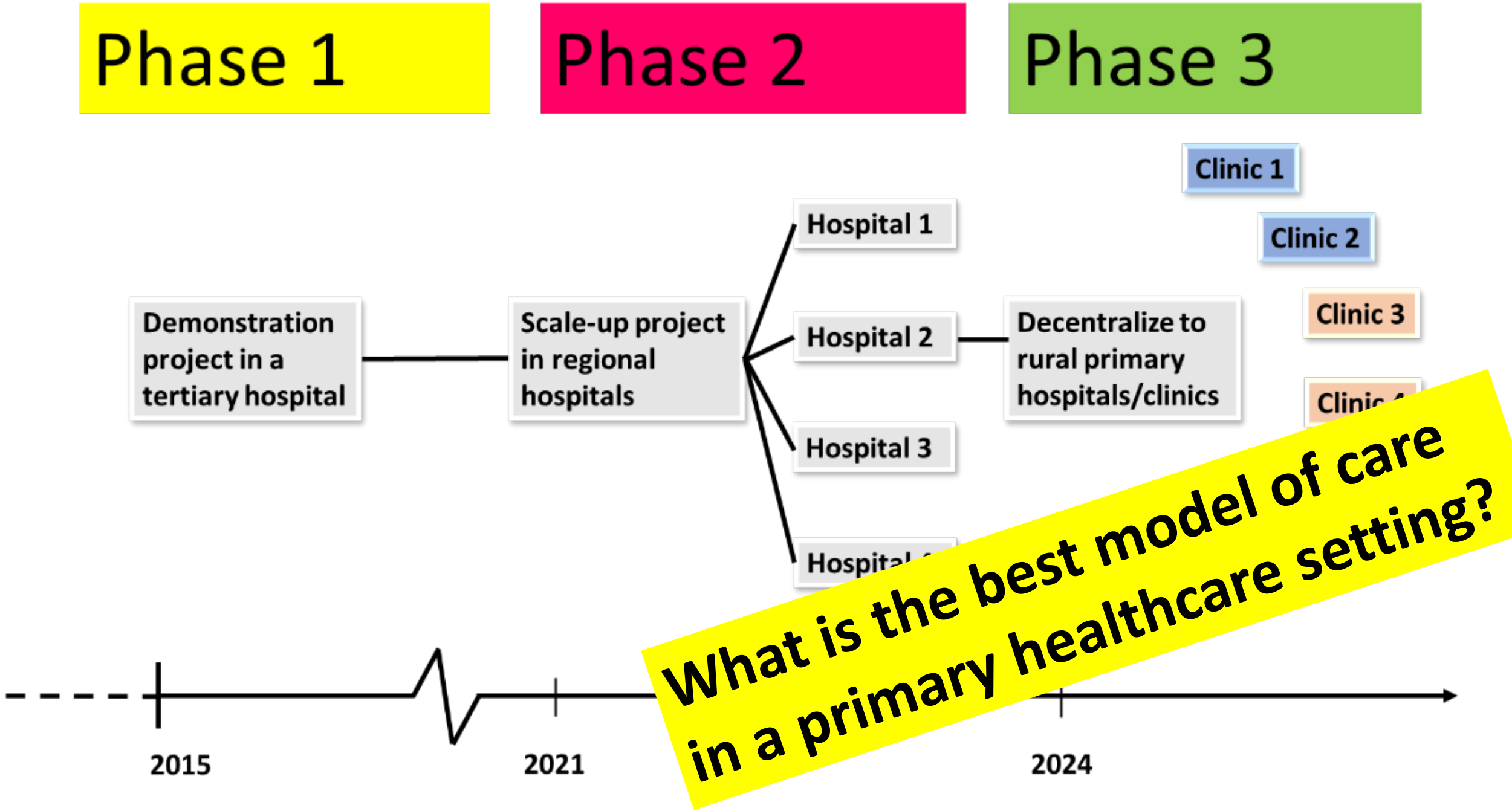
Are non-invasive fibrosis markers for chronic hepatitis B reliable in sub-Saharan Africa?

Hailemichael Desalegn[1] | Hanna Aberra[1] | Nega Berhe[2] | Svein G. Gundersen[3,4] | Asgeir Johannessen[5]

Scale-up HBV program from 2021/22

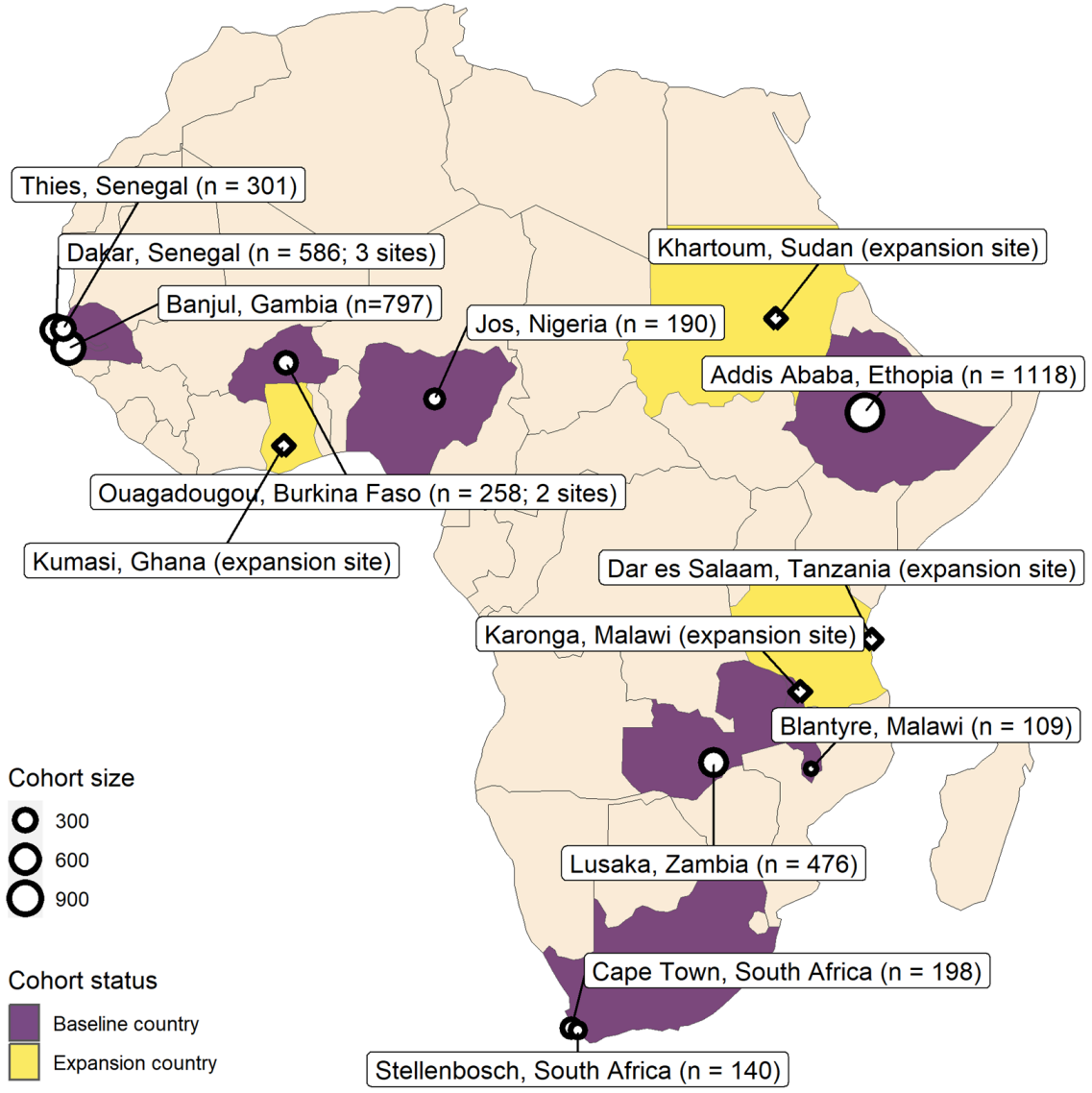
- Simpler, cheaper – and just as good?
- Decentralized to 4 regional hospitals
- Enrolled 6000 patients
- Integrated into local HIV or NCD clinics
- Used d… …ed …gorithm

Will assess a simplified approach to HBV treatment


Phase 1
Phase 2
Phase 3
Demonstration project in a tertiary hospital
Scale-up project in regional hospitals
Hospital 1
Hospital 2
Hospital 3
Decentralize to rural primary hospitals/clinics
Clinic 1
Clinic 2
Clinic 3
2015
2021
2024
What is the best model of care in a primary healthcare setting?

HEPSANET (Hepatitis B in Africa collaborative network)

- Merged data from multiple cohorts in Africa
- **Will generate large conclusive studies** – rather than many small (inconclusive) studies
- First phase: cross-sectional data – easy but limited value
- Second phase: longitudinal data – harder but more interesting!
  - Will include >10,000 patients with >1 year follow-up



nature communications

Article

https://doi.org/10.1038/s41467-022-35729-w

Systematic review and individual-patient-data meta-analysis of non-invasive fibrosis markers for chronic hepatitis B in Africa

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Check for updates

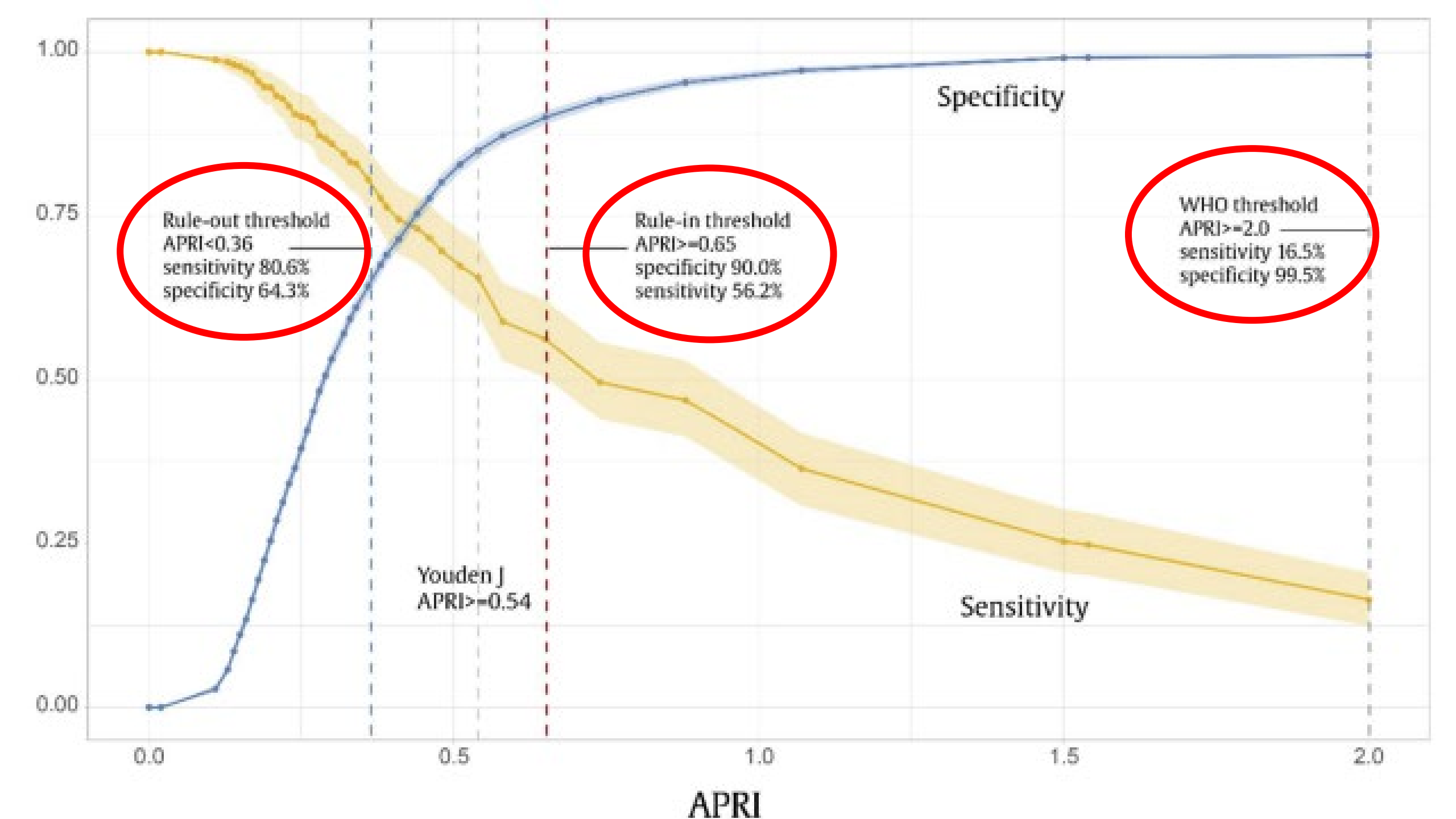
Asgeir Johannessen[1,2,23] ✉, Alexander J. Stockdale[3,4,23], Marc Y. R. Henrion[4,5,23], Edith Okeke[6], Moussa Seydi[7], Gilles Wandeler[8], Mark Sonderup[9], C. Wendy Spearman[9], Michael Vinikoor[10,11], Edford Sinkala[10], Hailemichael Desalegn[1,12], Fatou Fall[13], Nicholas Riches[5], Pantong Davwar[6], Mary Duguru[6], Tongai Maponga[14], Jantjie Taljaard[15], Philippa C. Matthews[16,17,18], Monique Andersson[14,16], Souleyman Mboup[19], Roger Sombie[20], Yusuke Shimakawa[21,24] & Maud Lemoine[22,24]

In sub-Saharan Africa, simple biomarkers of liver fibrosis are needed to scale-up hepatitis B treatment. We conducted an individual participant data meta-analysis of 3,548 chronic hepatitis B patients living in eight sub-Saharan African

APRI – WHO2015 recommended thresholds

	Significant fibrosis (<7.9 kPa)	Cirrhosis (>12.2 kPa)
APRI		
Cut-off value	1.5	2.0
Sensitivity (95% CI)	11.8% (9.4-14.2)	16.5% (12.5-20.5)
Specificity (95% CI)	99.2% (98.9-99.5)	99.5% (99.2-99.7)

Useless in clinical practise!


1.00
0.75
0.50
0.25
0.00
0.0
0.5
1.0
1.5
2.0
APRI
Specificity
Sensitivity
Rule-out threshold
APRI<0.36
sensitivity 80.6%
specificity 64.3%
Rule-in threshold
APRI>=0.65
specificity 90.0%
sensitivity 56.2%
WHO threshold
APRI>=2.0
sensitivity 16.5%
specificity 99.5%
Youden J
APRI>=0.54

Development and evaluation of a simple treatment eligibility score (HEPSANET) to decentralise hepatitis B care in Africa: a cross-sectional study

Nicolas Minier, Alice Nanelin Guingané, Edith Okeke, Edford Sinkala, Asgeir Johannessen, Monique I Andersson, Pantong Davwar, Hailemichael Desalegn, Mary Duguru, Fatou Fall, Souleyman Mboup, Tongai Maponga, Philippa C Matthews, Adrià Ramírez Mena, Gibril Ndow, Stian M S Orlien, Nicholas Riches, Moussa Seydi, Mark Sonderup, C Wendy Spearman, Alexander J Stockdale, Jantjie Taljaard, Michael Vinikoor, Gilles Wandeler, Maud Lemoine, Yusuke Shimakawa*, Roger Sombié**

Lancet Gastroenterol Hepatol 2024

Published Online February 14, 2024

Summary

Background Hepatitis B virus (HBV) elimination requires expanding and decentralising HBV care services. However, peripheral health facilities lack access to diagnostic tools to assess eligibility for antiviral therapy. Through the Hepatitis B in Africa Collaborative Network (HEPSANET), we aimed to develop and evaluate a score using tests

	N	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Validation dataset	1444	..	..	..
Tier-specific algorithms*				
Tier 0/1	1444	0·62 (0·59–0·65)	87% (81–92)	37% (35–40)
Tier 2 (HEPSANET score)	1444	0·83 (0·80–0·86)	78% (71–85)	87% (86–89)
Tier 3 (complete case analysis)	1430	0·88 (0·86–0·91)	91% (85–95)	85% (83–87)
Tier 3 (single imputation)†	1444	0·88 (0·85–0·90)	91% (86–95)	84% (82–86)
WHO 2015 guidelines	1444	0·68 (0·64–0·72)	38% (31–46)	98% (97–98)

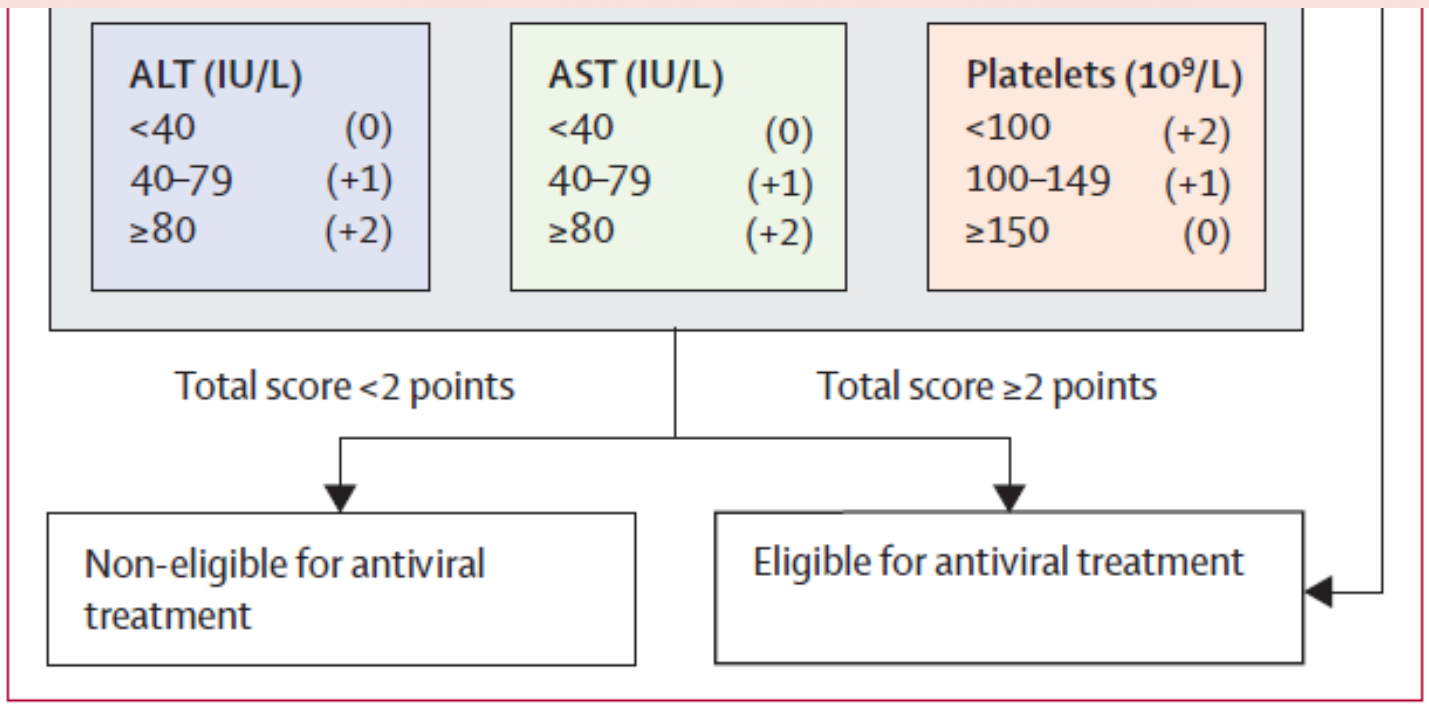
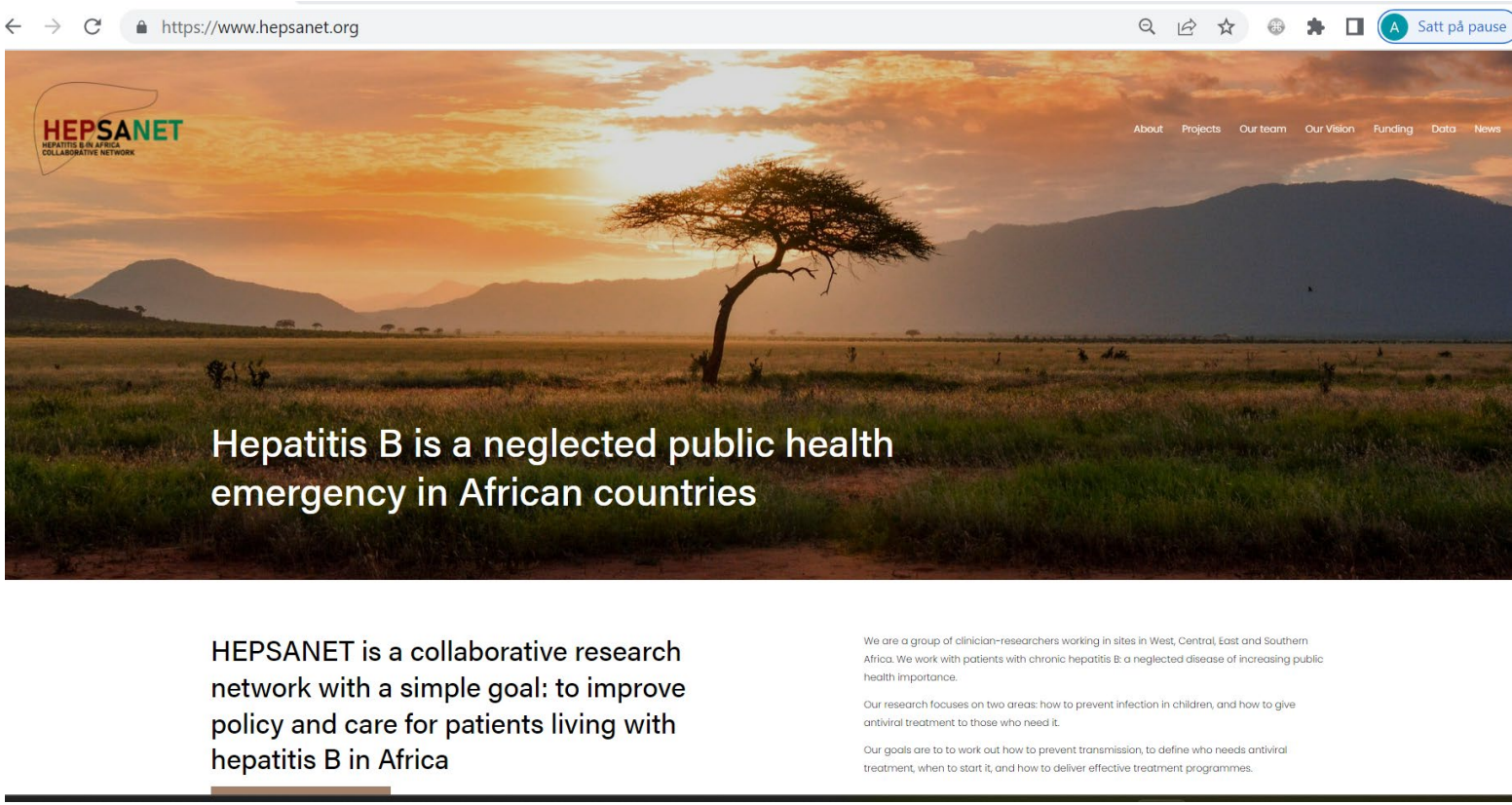


Figure 2: Tier 2 algorithm (HEPSANET score)

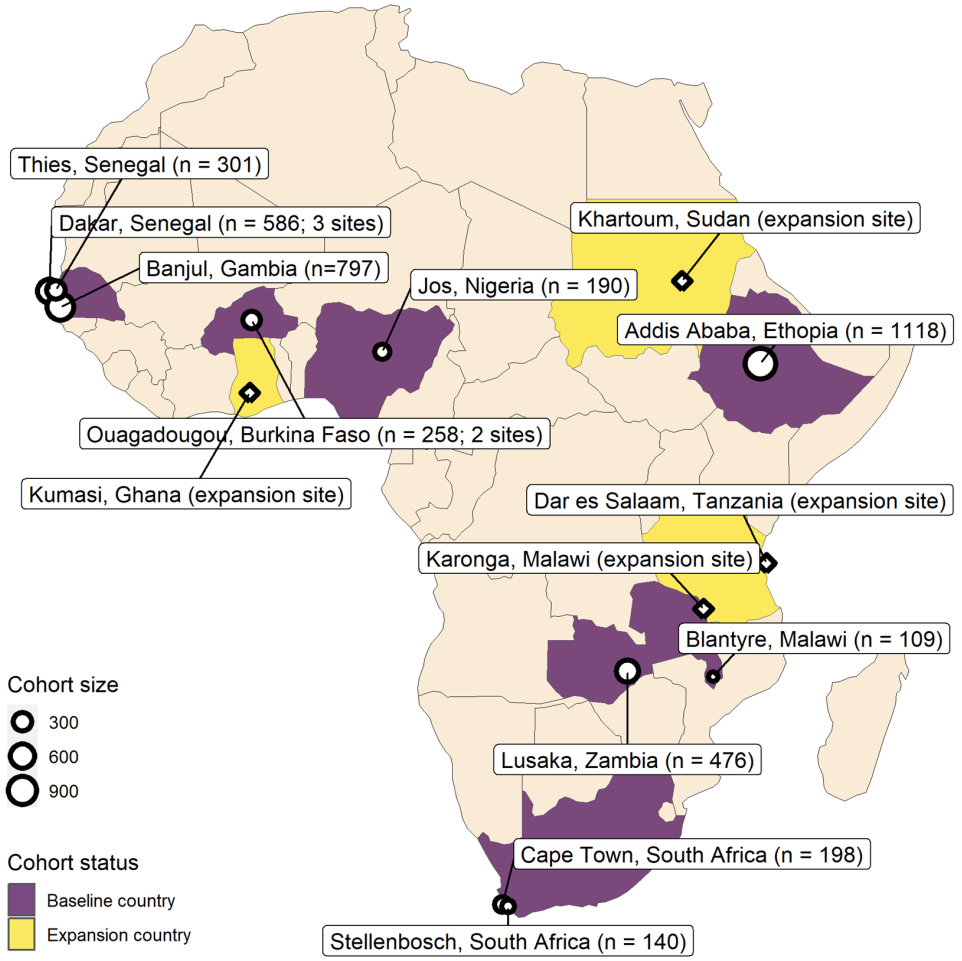
HEPSANET – status 12 April 2024

- 12 countries on board
- All site personnel have been trained in GCP and HBV management
- eCRF is up and running
- Published 4 articles
- Website active
- Employed data managers to oversee data quality
- Funded by EASL and John C Martin Foundation



Vision of HEPSANET

- Generate **conclusive studies** from Africa
- **Develop African HBV guidelines** in collaboration with Africa CDC
- **Strengthen research capacity** of its partners
- A **platform** for future research ideas (biomarkers, health economics, social sciences, new diagnostics, new drugs, HDV studies, etc)



«We don’t have data from Africa»

-true or false?


HEPSANET
HEPATITIS B IN AFRICA
COLLABORATIVE NETWORK