Health inequalities in the management of chronic hepatitis B in patients from Sub-Saharan Africa in high income countries

Tim Mitchell, Jeremy Nayagam, Geoff Dusheiko and Kosh Agarwal



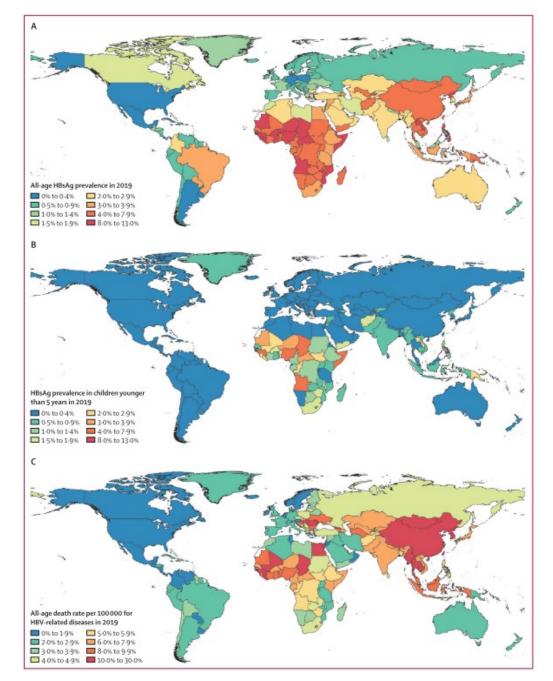
Hepatitis B and immigrants

- Western countries have become lands of immigration
 - From Africa, Eastern Europe Asia and Central America
- Asylum seekers refugees fleeing persecution, war and poverty
- Often destitute, or marginalised
- Conditions may not favour integration into host country
- Frequently poor, unemployed
- Continue cultural and religious traditions may not speak language host country
- May show "healthy migrant effect" harbour chronic hepatitis B or other BBV

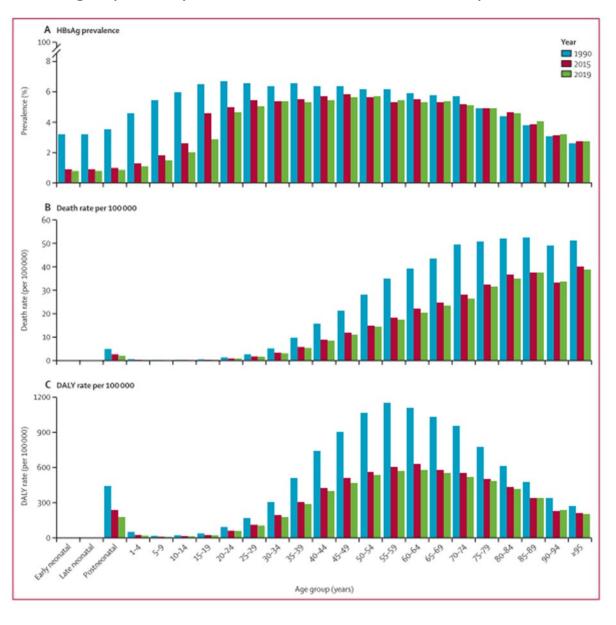
Hepatitis B sub-Saharan Africa

- Sub-Saharan Africa second highest prevalence HBV worldwide (6.5%)
- 80 million people living with chronic hepatitis B in the region
- Determined early childhood infection –residual mother to child transmission
- 90,000 people die per year from cirrhosis and hepatocellular carcinoma
- Low awareness diagnosis rates
- Impaired access to testing and access to antiviral treatment
- Coinfection HIV HBV, HBV HDV and HBV HCV

Prevalence and death rates hepatitis B



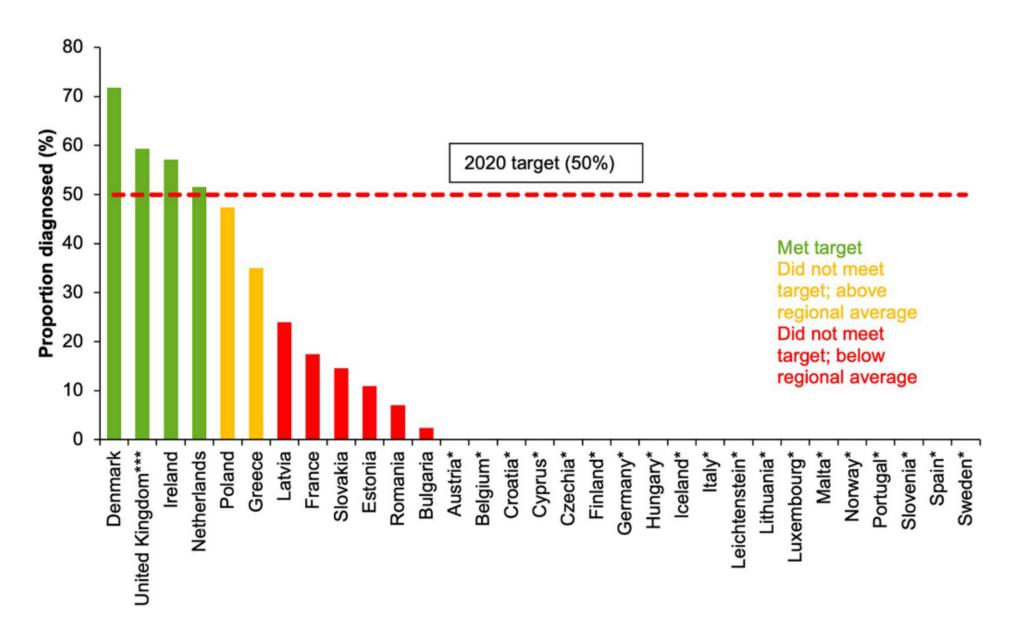
Age specific prevalence and death rates hepatitis B



Sheena, et al. (2022). "The Lancet Gastroenterology & Hepatology.

Effects in high income countries Europe

- Hepatitis B disproportionately affects migrant communities endemic regions
- United Kingdom:
 - Large African diaspora
 - Migrants contribute only 6% population72% chronic hepatitis B,
- Italy HBsAg seroprevalence sub-Saharans immigrants 7.4% to 13.9%
- Spain 8% and 15%
- Routine screening immigrants not performed
- Clinical guidelines and evidence base for treatment not based on SSA patients
- Participation in clinical trials in SSA rare (opposed to HIV)
- Challenges to engagement



Sharrock, K. C., et al. (2022). PLOS Glob Public Health 2(8): e0000841.

Clinical challenges

- Engagement challenging
- Stigma associated with diagnosis
- Absence of routine screening
- Complexities navigating health care system
- Language



In Europe and other high income areas:

Many not linked to care ----- but

Live in relatively resource rich countries

Ready access to antiviral therapy

WHO 2024 guidelines updated – expect expansion of treatment eligibility

Find those living with hepatitis B: Invest testing

Several feasible solutions for high resource settings

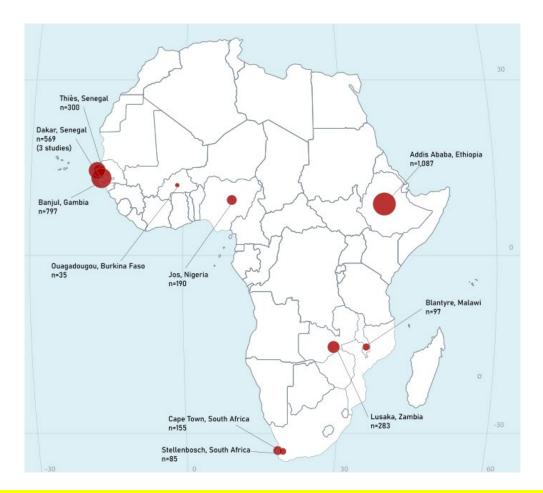
Rapid HBV esting in a low-cost, easy-to-use point-of-care (POC) test format

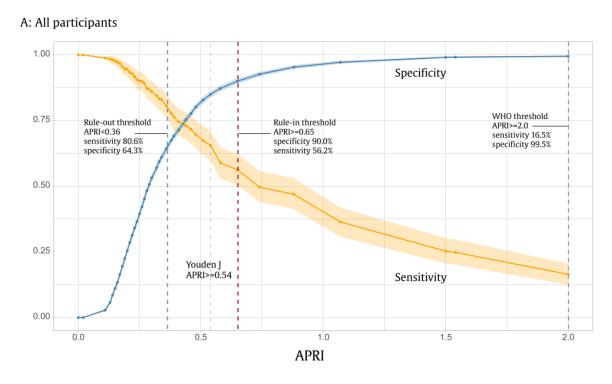
Dried blood spot facilitates centralized laboratory testing of HBV DNA

Nucleoside analogue treatment

- Guidelines framed by data from Western Pacific and Caucasian cohorts
- Detailed prospective studies not performed migrant SSA populations.
- Reasonable: Base indications on guidelines derived other populations
- Relatively low replicative state in anti-HBe-positive patients from SSA
- Questions in sub-Saharan Africans:
 - Staging of disease
 - Indications for treatment to prevent progression
 - Renal safety?
 - Bone safety?
 - Resistance?
 - HBV integrants and HBsAg expression
 - HCC surveillance
- Other markers serum pre-genomic RNA and hepatitis B core-related antigen
- Treat all strategy in high income countries?
- (Pegylated interferon: higher response rates in genotype A)

Relationship between sensitivity and specificity for APRI used to diagnose liver stiffness measurement >12.2 kPa (associated with cirrhosis).





World Health Organization-recommended aspartate aminotransferase-to-platelet ratio index threshold is inappropriately high in sub-Saharan Africa; improved rule-in and rule-out thresholds can optimise treatment recommendations in this setting.

HCC surveillance

- Sparse data in patients from SSA:
- Guidelines highlight ethnicity as important factor in HCC development
- Society recommendations listed
- Specific risk factors (aflatoxin exposure)
- Locally validated risk scores required (burden of surveillance)

Society Recommendation

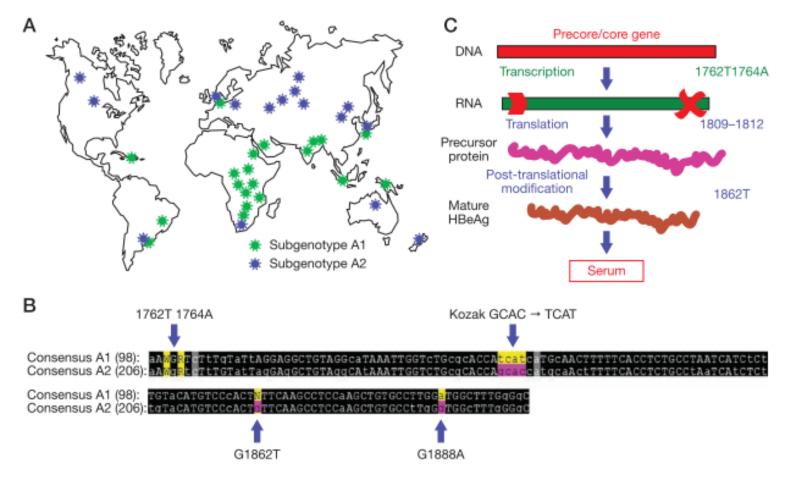
AASLD African males. 40 years

EASL No recommendation

APASL All African patients aged > 20 years

AASLD PRACTICE Person from Africa at earlier age

Migration and parameters of HBsAg subtype A1



Mutations in the BCP/PC region can lead to hepatitis B e antigen (HBeAg)-negativity in subgenotype A1.

HBeAg loss may imply genomic change rather than immunological control

Sequence variation position 1809-1812 (Kozak sequence) pre-core-core ORF of subgenotype A1 affects transcription

of pre-core mRNA, decreasing translation of HBeAg

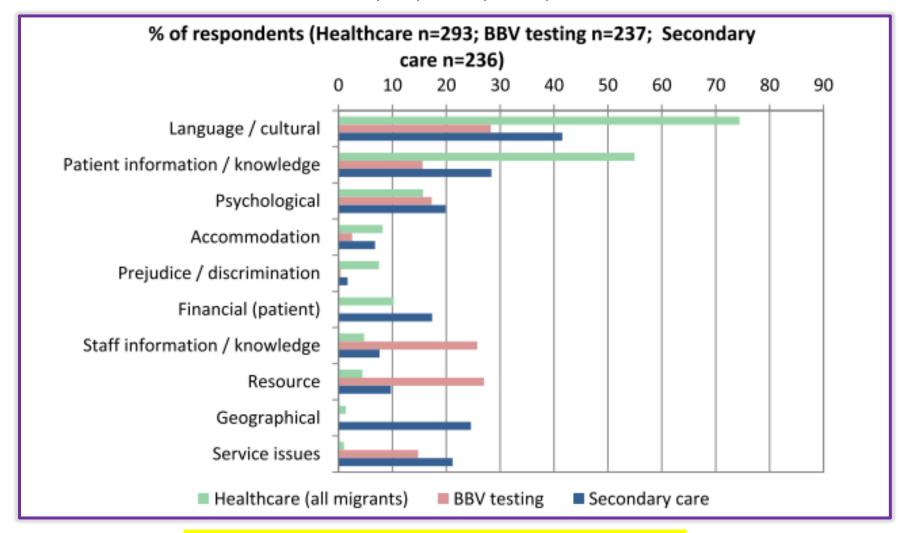
Variation by age and region may affect prevalence HBeAg

Making the case

- National investment case, cost-effectiveness, disease impact modeling
- Vital catalyze political engagement public health National heath service
- Improve education and public familiarity with the disease
- Drive demand for testing and treatment
- Reduce discrimination enhance patient willingness to be tested.
- HCC surveillance and treatment within population context

Primary care staff knowledge and action for blood borne virus testing in migrant patients

National survey of primary care professionals

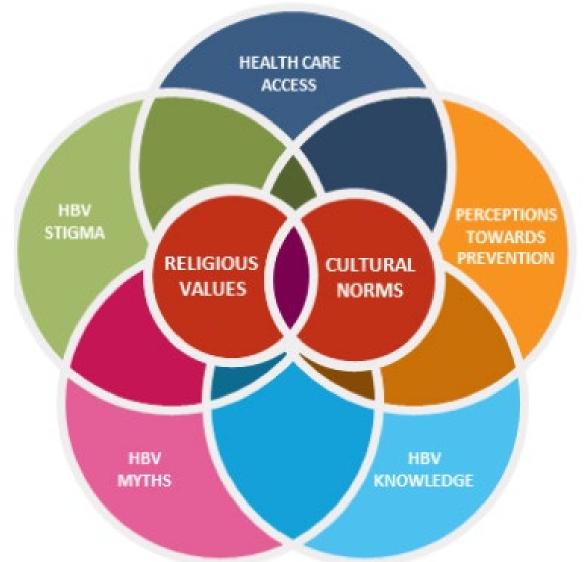


Perceived barriers for migrants to access healthcare

Roche R, et al. BMC public health 2021; 21(1): 336.

Interconnected nrohlems impair detection hepatitis B

- General lack o
- Lack of trust ir medical care
- Lower socioec
- Preference for
- Fear and misco
- Mistrust of the



y
ng their infection
unication with
ers
ties being missed.

Jones P et al Cancer Causes Control 2020; 31(12): 1079-91; Freeland e al Viruses 2020: 12(3)

Emphasis required to improve management

- Recognition of epidemiology
- Better data analysis
- Community health education: minority groups with educational focus
- Culturally relevant community interventions
- Assistance of social services, voluntary operations and cultural mediators
- Clinical psychological and legal management of vulnerable groups
- Should be a major objective of good Government
- Elimination targets will not be met in high-income countries
 - without an increase in awareness, diagnosis and treatment of migrant group

UKHSA report Hepatitis B in England 2023

- 95% of new chronic hepatitis B infections in the UK are in migrants
- NICE recommends HBV testing to anyone remaining at higher risk
- Vaccination to those testing negative to HBV.
- Migrants likely to maintain community links travel back to higher prevalence country
- Vulnerable migrants
 - Undocumented (those living in the UK with no legal status)
 - Asylum seekers and refugees
 - Unaccompanied minors
 - Low paid migrant workers
- Offered testing and vaccination commencing pre-departure or on arrival in England
- Culturally sensitive interventions to improve case-finding and retention in care of migrant
- Opt out testing emergency services

Future research opportunities: individuals from SSA chronic HBV living in high-income countries.

- Gather data on virological risk factors and the impact of biomarkers
- Identify demographic trends risk strarification in incident HCC and provide data.
- Validate surveillance for HCC in patients from SSA in high-income countries
- Collaborate with SSA centres to transfer skill sets and resources
- Using digital technologies improve multidisciplinary management of HCC
- Leverage the findings to assist improvements in home countries

Summary of Black ethnicity and genotype involvement in major chronic HBV trials.

| Study (first author, year) | Phase | Study population | Number | Black ethnicity | Genotype | Exclusion criteria |
|--|-------|--|--------|--|---|----------------------------------|
| Lai et al. 1998 ⁸⁶ | III | China (HK, Taiwan, mainland China) | 358 | 0 (0%) | Not specified | |
| Hadziyannis <i>et al.</i> 2003 ⁸⁷ | III | Canada, Greece, Israel, France, Italy, Australia, Taiwan, Singapore | 185 | 6 (3.2%) | Not specified | |
| Chang <i>et al.</i> 2006 ⁸⁸ | III | Europe (41 centres), North America (40), Asia (26), Australia (12), South America (18) | 715 | 16 (2.2%) | A – 27%, B – 20%, C – 27%, D – 12%, E – not mentioned, F – 4.5% | |
| Marcellin et al. 2008 ⁸⁹ | III | Europe (59%), North America (24%), Australia/NZ (17%) | 641 | 30 (4.7%) | A – 16%, B – 12%, C – 17%, D – 50%, E-H – 4% | |
| Buti <i>et al.</i> 2016 ⁹⁰ | III | Canada (11 sites), USA (14), UK (2), France (2), Italy (4), Poland (4), Romania (5), Russia (10), Spain (1), Turkey (5), Australia (5), NZ (1), India (10), Japan (11), HK (4), South Korea (10), Taiwan (5) | 425 | 8 (1.9%) | A – 5%, B – 24%, C – 38%, D – 31%, E – 2% | |
| Chan <i>et al.</i> 2016 ⁹¹ | III | East Asia (18% of patients), Europe (18%), North America (16%), Australia (2%), NZ (2%), India (13%) | 873 | 10 (1.1%) Nb. categorized as "other" | A – 7%, B – 17%, C – 52%, D – 23%, E – <1%, F – <1% | |
| Bazinet et al. 2020 ⁹² | II | Republic of Moldova | 40 | 0 (0%) | A – 3 (7.5%), D – 37 (92.5%) | ANC <1,500 cells/mm ³ |

Mitchell T, JHEP Reports. 2022;doi:10.1016/j.jhepr.2022.100623

Adding the patients' voice



nminatory laws and practices.

We want whole person care, not care that is focused only our

iver. We want our doctors to consider the overall impact of hepatitis B

We want our doctors to consider the overall impact of nepatitis B on our whole lives and consider outcomes which are important to us.

d diagnostic testing is not accessible.

on our whole lives and consider outcomes which are important to us.

We want to not worry about developing liver cancer or spreading

the intection because of our inability to access care and treatment.

We want flexibility in the treatment recommendations, so that

We want nexibility in the treatment recommendations, 50 that we are resource limited we can receive care and treatment even if we are resource limited.

out waring to live accessions.

complified treatment strategies, so that care is available

deninion making for our care wh

We want to not worry about developing liver cancer or spreading the infection because of our inability to access care and treatment.

our lives may be cut short.

criminatory laws and practices.



Urgent need for lived experience in hepatitis B guide

Published Online Globally, nearly 300 million people live with https://doi.org/10.1016/ Hepatitis D VIII S (FIDV), Hawing It the Host Connicul S2468-1253(23)00455-7 chronic infection, Although mortality rates have https://doi.org/10.1016/ hepatitis B virus (HBV), making it the most common a core part of current treatment eligibility this thick tack is inarraceible for many 1 remained stable for the past 20 years, two people die from HBV every minute. WHO has called for the elimination of hepatitis B as a public health threat by 2030, setting goals to prevent new infections through birth-dose vaccination and to prevent illness and death by improving testing, clinical management, and treatment However,

progress towards elimination has stalled 5.6 Professional medical societies and WHO developed guidelines to help facilitate the management and treatment of HBV. Currently, updates to these guidelines are in development for many societies, including the European Association for the Study of the Liver and the American Association for the Study of Liver Diseases. This is a pivotal opportunity to consider treatment expansion and align and harmonise recommendations globally. Although the goal of elimination is to treat 80% of eligible individuals by 2030,

but this test is inaccessible for many. T of people with HBV have no access to spe simplification of guidelines is essential to e non-specialists can care for people with I 2022-30 Global Health Sector Strategy calls for centred care, health equity, and community enga as core elements of disease elimination with a fc primary care and care integration. These consider should be implemented within HBV guidelines,

the involvement of people with HBV in guid People with HBV know the direct impacts a challenges of accessing care. Research shows peop with HBV face considerable stigma and discrimination and HBV is also associated with physical, psychological, emotional, social, and professional impacts. The Many aspects of HBV management require shared decision making and both sides of this sharing process must

www.thelancet.com/gastrohep Vol 9 April 2024

Comment

be represented for guidelines to meaningfully reflect optimal care. It is crucial to consider the impacts, and patient preferences, to develop practical treatment guidelines that are relevant, applicable, and realistic to

282

ment are too

We are

of you

Me are

15-40% of people with HBV will develop liver cirrhosis, 15-40% of people with HBV will develop liver cirrhosis, liver cancer, or liver failure. Appropriate management and treatment can reduce this rick. However there are initially involved in the antire development. are barriers to accessing the entire care continuum of HBV. Elimination requires public health approaches to prevent morbidity and mortality. Many people could benefit from antiviral therapy, which can substantially reduce the risk of liver damage and liver

and often, medical experts will make assumptions about patient values. Such assessments must come from people with lived experience and should be formalised. 2 To ensure that updated treatment guidelines can be adopted widely and have an impact on the people who

guideline committees through the entire development process; 2) integration of patient values and parent in guideline development 31 a ball HBV as not just a live