Treat All versus targeted strategies to select HBV-infected people for antiviral therapy in The Gambia, west Africa: a cost-effectiveness analysis

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Summary

Background Global elimination of hepatitis B virus (HBV) requires expanded uptake of antiviral therapy, potentially by simplifying testing algorithms, especially in resource-limited countries. We evaluated the effectiveness, cost-effectiveness, and budget impact of three strategies that determine eligibility for anti-HBV treatment, as compared with the WHO 2015 treatment eligibility criteria, in The Gambia.

Methods We developed a microsimulation model of natural history using data from the Prevention of Liver Fibrosis and Cancer in Africa programme (known as PROLIFICA) in The Gambia, for an HBV-infected cohort of individuals aged 20 years. The algorithms included in the model were a conventional strategy using the European Association for the Study of the Liver (EASL) 2017 criteria, a simplified algorithm using hepatitis B e antigen and alanine aminotransferase (the Treatment Eligibility in Africa for the Hepatitis B Virus [TREAT-B] score), a Treat All approach for all HBV-infected individuals, and the WHO 2015 criteria. Outcomes to measure effectiveness were disability-adjusted life years (DALYs) and years of life saved (YLS), which were used to calculate incremental cost-effectiveness ratios (ICERs) with the WHO 2015 criteria as the base-case scenario. Costs were assessed from a modified social perspective. A budget impact analysis was also done. We tested the robustness of results with a range of sensitiviy analyses including probabilistic sensitivity analysis.

Findings Compared with the WHO criteria, TREAT-B resulted in 4877 DALYs averted and Treat All resulted in 9352 DALYs averted, whereas the EASL criteria led to an excess of 795 DALYs. TREAT-B was cost-saving, whereas the ICER for Treat All (US$2149 per DALY averted) was higher than the cost-effectiveness threshold for The Gambia (0·5 times the country's gross domestic product per capita: $352). These patterns did not change when YLS was the outcome. In a modelled cohort of 5000 adults (aged 20 years) with chronic HBV infection from The Gambia, the 5-year budget impact was $1·14 million for Treat All, $0·66 million for TREAT-B, $1·03 million for the WHO criteria, and $1·16 million for the EASL criteria. Probabilistic sensitivity analysis indicated that among the Treat All, EASL, and TREAT-B algorithms, Treat All would become the most preferred strategy only with a willingness-to-pay threshold exceeding approximately $72 000 per DALY averted or $110 000 per YLS.

Interpretation Although the Treat All strategy might be the most effective, it is unlikely to be cost-effective in The Gambia. A simplified strategy such as TREAT-B might be a cost-saving alternative.

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For the French translation of the abstract see **Online** for appendix 1

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Introduction

Hepatitis B virus (HBV) infection is a major global health issue. Worldwide in 2019, 296 million people had chronic HBV infection, and there were an estimated 820 000 deaths due to cirrhosis or hepatocellular carcinoma.[1] In 2016, a global strategy was endorsed to eliminate HBV infection as a public threat by 2030 and WHO set up ambitious service coverage goals to be reached by 2030 (diagnosing 90% of people infected with HBV and treating 80% of those eligible for treatment).[1] Given that less than 25% of HBV-infected people meet treatment eligibility criteria at a single timepoint assessment and current anti-HBV therapy is generally lifelong, evaluating treatment eligibility is a key step for the clinical management of chronic HBV infection.[2]

Screening for HBV infection is widely available via inexpensive rapid diagnostic tests that accurately detect hepatitis B surface antigen (HBsAg).[3] However, the assessment of anti-HBV treatment eligibility remains challenging, particularly in low-income and middle-income countries (LMICs).[3] Conventional eligibility criteria established by professional liver societies, including the European Association for the Study of the Liver (EASL) 2017 criteria, invariably require a nucleic acid test to quantify serum HBV DNA, an alanine aminotransferase (ALT) test, and liver fibrosis staging by

Research in context

Evidence before this study

To accelerate the momentum towards global elimination of hepatitis B virus (HBV), expanding testing and treatment services in resource-limited countries is crucial, especially in sub-Saharan Africa. However, current international guidelines for HBV treatment eligibility are complex and require tests that are not widely accessible in these settings. Consequently, simplifying the treatment eligibility criteria, with a Treat All strategy as the most drastic option, could serve as a practical alternative. Nonetheless, such simplification might have a substantial economic impact, particularly in resource-limited countries. We searched PubMed for articles published from database inception up to June 22, 2023, in any language, using the terms: "hepatitis B" AND "cost" AND ("treatment eligibility" OR "treat all"). We identified two articles that evaluated the cost-effectiveness of a Treat All strategy and two articles that assessed simplified eligibility criteria. Razavi-Shearer and colleagues (*J Viral Hepat* 2023; **30:** 718–26) found that in the USA, a Treat All intervention yielded an incremental cost-effectiveness ratio (ICER) of US$41 700 per disability-adjusted life year (DALY) averted (threshold: $65 850). Similarly, Sanai and colleagues (*J Infect Public Health* 2020; **13:** 1715–23) found that in Saudi Arabia, a Treat All intervention was cost-effective with an ICER of $22 050 per DALY averted (threshold: less than three times gross national income per capita—$66 150). In Korea, Lim and colleagues (*Aliment Pharmacol Ther* 2022; **56:** 519–28) showed that a simplified algorithm based on HBV DNA, without alanine aminotransferase or hepatitis B e antigen (HBeAg), was cost-effective, with an ICER of $2583 per DALY averted (threshold: $20 000). Crossan and colleagues (*J Viral Hepat* 2016; **23:** 139–49) found that in the UK, a Treat All strategy without any assessment of liver fibrosis was effective but not cost-effective (£28 137 per quality-adjusted life year, threshold: £20 000) in a subgroup of individuals with suspected fibrosis eligible for liver biopsy. However, we did not identify any studies assessing the cost-effectiveness of simplified testing algorithms or Treat All in low-income or middle-income countries.

Added value of this study

With use of a microsimulation model on a closed cohort, we evaluated the cost-effectiveness of three testing algorithms to select HBV-infected patients for antiviral therapy in The Gambia, compared with the WHO 2015 treatment criteria. These algorithms were a conventional strategy recommended by the European Association for the Study of the Liver (EASL 2017), simplified criteria based on alanine aminotransferase and HBeAg (the Treatment Eligibility in Africa for the Hepatitis B Virus [TREAT-B] score), and a Treat All approach for all HBV-infected individuals. We found that Treat All and TREAT-B might be more effective in reducing the HBV-related disease burden than the conventional criteria by EASL or WHO. However, implementing a Treat All approach in The Gambia might be associated with a substantial budget impact and was not deemed cost-effective.

Implications of all the available evidence

Our findings suggest that although a Treat All strategy might appear highly attractive for The Gambia to reduce the burden of HBV-related disease, it might not be cost-effective. Instead, simplified approaches such as TREAT-B could be a cost-saving alternative to scale up HBV treatment coverage. Before widespread implementation of Treat All or other simplified testing algorithms in resource-limited countries, careful evaluation of economic, operational, and social feasibility is essential.

liver biopsy or transient elastography.[4] In contrast, in 2015, WHO adopted simplified criteria in which liver biopsy and transient elastography were replaced by serum biomarkers (aspartate aminotransferase-to-platelet ratio index [APRI]).[5] Further simplification with the exclusion of HBV DNA quantification has been proposed with the Treatment Eligibility in Africa for the Hepatitis B Virus (TREAT-B) score, which is based solely on ALT level and hepatitis B e antigen (HBeAg) serostatus.[6] The TREAT-B score, originally developed in The Gambia, has been evaluated in Africa, Asia, Australia, and Europe, and has shown moderate to high discrimination capability between individuals deemed eligible for treatment and those deemed ineligible according to the EASL 2017 criteria.[7–9] More recently, a Treat All strategy has been advocated to treat all people identified with chronic HBV infection, without assessing their HBV viral load, ALT level, or fibrosis stage.[10–12] Similar to a Treat All approach for HIV infection, the Treat All strategy for HBV infection could allow same-day initiation of antiviral treatment following a positive HBsAg screening test, without costly and complex clinical staging.[10] However, its feasibility and acceptability have not been tested in a real world setting.

Simplified testing algorithms could reduce the cost of initial assessment. However, as a trade-off, they might increase the risk of misclassification, resulting in patients at risk of liver complications being overlooked, or those with a minimal risk being unnecessarily given lifelong daily medication. Taking these factors into account, we assessed the effectiveness, cost-effectiveness, and budget impact of three different algorithms that determine eligibility for antiviral treatment (the Treat All, TREAT-B, and EASL criteria), as compared with a base-case scenario (WHO 2015 treatment criteria), in adults identified to carry HBsAg in The Gambia, west Africa.

Methods

Study setting

The Prevention of Liver Fibrosis and Cancer in Africa (PROLIFICA) study originally assessed the feasibility

and cost-effectiveness of a community-based and facility-based hepatitis B screen-and-treat intervention in The Gambia.[13,14] The PROLIFICA protocol was approved by The Gambia Government and UK Medical Research Council (MRC) Joint Ethics Committee, and is registered on ClinicalTrials.gov, NCT02129829. A cross-sectional dataset comprising 804 HBsAg-positive individuals with chronic HBV infection from the PROLIFICA study was used to parametrise the distribution of health states at baseline, to assess the probability of being eligible for treatment with tenofovir disoproxil fumarate (TDF) according to the EASL 2017 criteria (the gold standard reference criteria for the purposes of this study), and to determine the diagnostic sensitivity and specificity of alternative testing algorithms (WHO 2015, TREAT-B, and Treat All) to indicate EASL treatment eligibility (appendix 2 pp 3–14). This dataset of 804 individuals was used in original development of the TREAT-B score.[6]

The present study was reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards checklist.[15] Patient consent was not required for this secondary analysis.

Testing algorithms

Of four different testing algorithms evaluated in this study, the EASL 2017 criteria were considered to be the gold standard in terms of diagnostic accuracy, with 100% sensitivity and 100% specificity to indicate anti-HBV treatment eligibility, because the criteria are based on conventional reference tests (HBV DNA, ALT, and liver histopathology or transient elastography; appendix 2 pp 13–14). Nevertheless, the EASL criteria are not perfect for predicting the development of hepatocellular carcinoma, given that individuals who do not meet the EASL criteria still have a small risk of developing hepatocellular carcinoma.[16] The WHO 2015 criteria are currently recommended in The Gambia, and were therefore used as the base-case scenario. In these criteria, anti-HBV treatment is indicated in individuals with clinically diagnosed cirrhosis (ie, APRI >2·0) or in those aged 30 years or older with a viral load of at least 20 000 IU/mL and abnormal ALT (≥30 IU/L in men, ≥19 IU/L in women).[3] TREAT-B score is obtained by adding HBeAg serostatus (negative [±0] or positive [+1]), and ALT level (IU/L; <20 [±0], 20–39 [+1], 40–79 [+2], or ≥80 [+3]).[6] Finally, in the Treat All strategy, antiviral therapy would be initiated in all HBsAg-positive individuals immediately after entering the cohort.

Model structure

We developed a deterministic microsimulation using a closed cohort model of the natural history of chronic HBV infection, adapted from a previously published study,[14] with nine mutually exclusive health states: HBeAg-positive chronic infection, HBeAg-positive chronic hepatitis, HBeAg-negative chronic infection, HBeAg-negative chronic hepatitis, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, HBsAg-negative, and death. Because these health states are not exhaustive,[4] we introduced a novel state called HBeAg-negative grey zone within the present model. HBeAg-negative grey zone was defined according to HBV DNA and ALT concentrations (either HBV DNA <2000 IU/mL and ALT ≥40 U/L, or HBV DNA ≥2000 IU/mL and ALT <40 U/L; appendix 2 p 12). Within non-treated health states, we nested a decision tree, representing criteria for TDF treatment eligibility, onto the model structure to represent the effect of each strategy (appendix 2 pp 26–27). Given that the treatment eligibility criteria were primarily developed for adults[4] and 796 (99%) of the 804 participants in PROLIFICA were aged 20 years or older, the starting age of the modelled cohort was set at 20 years. Disease progression was simulated for annual cycles until the person died or reached age 90 years. In our simulation, all untreated patients were followed up annually with a set of diagnostic tests specific to each of the testing algorithms. Individuals initiated on TDF were monitored annually using the same tests (appendix 2 p 15). We incorporated 100 000 individuals with chronic HBV infection in our model, aiming for a balance between the real numbers of HBV-infected adults in The Gambia and ensuring sufficient numbers to minimise noise and stabilise the estimates. The model was built with Amua (version 0.3.0), an open-source software developed for decision modelling by the Center for Health Decision Science (Harvard University, Boston, MA, USA), and R Studio (version 2023.06.1+524; appendix 2 p 6). The model is publicly available.

See **Online** for appendix 2

For the **model** see https://dataverse.harvard.edu/dataset.xhtml?persistentId=doi:10.7910/DVN/LGMUP6

Input parameters

Transition probabilities between the different health states were obtained from previous literature (table 1). The health states do not fully overlap with the EASL 2017 treatment eligibility (eg, the HBeAg-positive chronic infection status is ineligible for individuals aged ≤30 years and eligible for those aged >30 years; appendix pp 12–14). Therefore, within each health state, the transition probabilities varied depending on whether or not the simulated individual met the EASL criteria: within each health state, the risk of hepatocellular carcinoma was 3·5 times higher in EASL-eligible than EASL-ineligible individuals;[41,58] and compensated cirrhosis could only occur in individuals with chronic hepatitis (HBeAg-positive chronic hepatitis or HBeAg-negative chronic hepatitis) who met the EASL criteria (appendix 2 pp 5–6). In addition, according to the result of an index testing algorithm, modelled patients who started tenofovir disoproxil fumarate (TDF) had 0·6 times the risk of compensated cirrhosis and 0·5 times the risk of hepatocellular carcinoma compared with patients not receiving antiviral therapy (ie, TDF; table 1).[54] Treatment failure secondary to treatment discontinuation was simulated, with a fixed rate (6·30%)

	Base-case value	Probabilistic sensitivity analysis distribution	Probabilistic sensitivity analysis parameters*	References for base-case values
Annual disease transition rate†				
From HBeAg-positive chronic infection to:				
HBeAg-positive chronic hepatitis	0·0950 (0·0296–0·1813)	Beta	a=5·06; b=45·57	17–19
Hepatocellular carcinoma‡	0·0031 (0·0022–0·0041)	Beta	a=3·99; b=1324·35	20
From HBeAg-positive chronic hepatitis to:				
HBeAg-negative chronic infection	0·0740 (0·0630–0·0880)	Beta	a=142·00; b=1770·00	21
HBeAg-negative chronic hepatitis	0·0050 (0·0000–0·0488)	Beta	a=0·15; b=30·69	14
Compensated cirrhosis§	0·0277 (0·0100–0·0540)	Beta	a=6·14; b=215·45	22–28
Hepatocellular carcinoma‡	0·0065 (0·0027–0·0995)	Beta	a=12·60; b=1925·30	23–25,29–32
From HBeAg-negative chronic infection to:				
HBeAg-negative chronic hepatitis	0·0268 (0·0155–0·0471)	Beta	a=11·17; b=405·74	33–39
Hepatocellular carcinoma‡	0·0005 (0·0003–0·0008)	Beta	a=5·00; b=9995·00	20
HBsAg-negative	0·0100 (0·0080–0·0120)	Beta	a=17·15; b=1257·65	21
From HBeAg-negative chronic hepatitis to:				
HBeAg-negative chronic infection	0·0384 (0·0054–0·2731)	Beta	a=384·5; b=96116·5	40
Compensated cirrhosis§	0·0400 (0·0100–0·0520)	Beta	a=11·17; b=300·92	22–28,35,41,42
Hepatocellular carcinoma‡	0·0042 (0·0027–0·0056)	Beta	a=42·00; b=9958·00	20
From HBeAg-negative grey zone to:				
HBeAg-negative chronic infection	0·0659 (0·0509–0·0852)	Beta	a=51·93; b=736·06	43
HBeAg-negative chronic hepatitis	0·0148 (0·0086–0·0254)	Beta	a=10·82; b=720·52	43
Hepatocellular carcinoma‡	0·0011 (0·0002–0·0081)	Beta	a=0·21; b=192·63	43
From compensated cirrhosis to:				
Decompensated cirrhosis	0·0390 (0·0320–0·0460)	Beta	a=2·85; b=70·18	32,44–46
Hepatocellular carcinoma‡	0·0297 (0·0235–0·0359)	Beta	a=3·95; b=103·88	20
Death	0·0480 (0·0310–0·0660)	Beta	a=17·5; b=339·5	47
From decompensated cirrhosis to:				
Hepatocellular carcinoma	0·0376 (0·0230–0·0710)	Beta	a=9·41; b=240·88	46,48–53
Death	0·1880 (0·0430–0·3140)	Beta	a=3·58; b=7·83	47
From hepatocellular carcinoma to:				
Death	0·5450 (0·5450–1·000)	Beta	a=5·06; b=5·06	47
Treatment module				
Risk ratio of hepatocellular carcinoma, treated *vs* not treated	0·5 (0·4–0·7)	Log-normal	μ=0·69 ; σ=0·142	54
Risk ratio of compensated cirrhosis, treated *vs* not treated	0·6 (0·4–0·8)	Log-normal	μ=0·51; σ=0·177	54
Treatment adherence				
At year 1, %	93·70% (89·97–96·36)	NC	NC	55
At the end of the simulation (up to age 90 years or death), %	72·86% (57·78–87·95)	NC	NC	Adapted from 56
Disability weight				
Chronic hepatitis B virus infection without cirrhosis or hepatocellular carcinoma	0	NC	NA	57
Compensated cirrhosis	0	NC	NA	57
Decompensated cirrhosis	0·178 (0·123–0·250)	Beta	a=23·17; b=101·38	57
Hepatocellular carcinoma	0·288 (0·193–0·399)	Beta	a=54·76; b=762·70	57

(Table 1 continues on next page)

at 1 year, followed by an extrapolated constant rate thereafter, which was calibrated in the model to reach a cumulative rate of 27·14% at the end of the simulation (ie, end of follow-up; table 1).[55,56] Age-specific incidence rates of compensated cirrhosis and hepatocellular carcinoma in the absence of antiviral therapy were derived from the model and calibrated with epidemiological data for The Gambia from the Global Burden of Disease (GBD) 2019 database (appendix 2 p 8). GBD does not report the incidence rate

For the **GBD 2019 database** see https://www.healthdata.org/gbd/2019

	Base-case value	Probabilistic sensitivity analysis distribution	Probabilistic sensitivity analysis parameters*	References for base-case values
(Continued from previous page)				
Cost of each testing algorithm, US$ in 2020¶				
Treat All				
Start-up cost	0	NC	NA	..
Fixed cost	0	NC	NA	..
Variable cost, per patient per year‖				
Off treatment	NA	NC	NA	..
On treatment	$55·10	Gamma	20% range for each component part	..
TREAT-B				
Start-up cost	0	NC	NA	..
Fixed cost	0	NC	NA	..
Variable cost, per patient per year‖				
Off treatment				
HBeAg positive	$21·70	Gamma	20% range for each component part	..
HBeAg negative	$14·20	Gamma	20% range for each component part	..
On treatment	$55·10	Gamma	20% range for each component part	..
WHO 2015				
Start-up cost	NA	NA	NA	..
Fixed cost, per year	$58 072	NC	NA	..
Variable cost, per patient per year‖				
Off treatment				
HBeAg positive	$53·00	Gamma	20% range for each component part	..
HBeAg negative	$45·50	Gamma	20% range for each component part	..
On treatment	$55·10	Gamma	20% range for each component part	..
EASL 2017				
Start-up cost	$529 760	NC	NA	..
Fixed cost, per year	$59 752	NC	NA	..
Variable cost, per patient per year‖				
Off treatment				
HBeAg positive	$59·10	Gamma	20% range for each component part	..
HBeAg negative	$51·60	Gamma	20% range for each component part	..
On treatment	$55·10	Gamma	20% range for each component part	..
Hospital admission parameters				
Cost per hospital admission, US$ in 2020)	$83·70	Gamma	20% range for each component part	14
Number of hospital admissions per year for compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma, respectively	2, 3, and 3	Uniform	Low: 0 for all three; high: 4, 6, and 6	14

Values in parentheses are 95% CIs. Treatment refers to TDF medication. EASL=European Association for the Study of the Liver. HBeAg=hepatitis B e antigen. NA=not applicable. NC=not considered. TDF=tenofovir disoproxil fumarate. TREAT-B=Treatment Eligibility in Africa for the Hepatitis B Virus. *Estimation of parameters for probabilistic sensitivity analysis is described in appendix 2 (p 9); parameter "a" corresponds to the number of events, parameter "b" corresponds to the number of non-events. †In cases where multiple references contributed to a parameter, the base-case value was obtained from summary estimates presented in a systematic review by Lin and colleagues.[47] ‡Overall risk of hepatocellular carcinoma in each health state is presented. Within each health state, individuals eligible for treatment according to the EASL 2017 criteria were weighted for a 3·5 times higher risk of hepatocellular carcinoma than EASL-ineligible individuals. §Compensated cirrhosis could occur only in individuals who had chronic hepatitis (ie, HBeAg-positive chronic hepatitis or HBeAg-negative chronic hepatitis) and who met the EASL 2017 criteria. ¶Obtained as part of the current study (appendix 2 p 7). ‖Initial assessment visit includes routine blood tests, virology, ultrasound scan, transient elastography, and staff costs. Monitoring is done every 12 months both in those initiated on TDF and in those not receiving TDF.

Table 1: **Input parameters for annual disease transition rates, disability weights, and costs**

of decompensated cirrhosis and thus the model was not calibrated for this outcome. All the calibration targets were prespecified before the model conception to ensure external validity.[59]

Costs

Costs were evaluated from a modified social perspective, encompassing expenses billed by health-care providers to either the health-care system or to the individuals

receiving care. Costs were obtained from the PROLIFICA study budget and from interviews with clinical managers of the MRC Clinic (Fajara, The Gambia) and the governmental teaching hospital (Edward Francis Small Teaching Hospital) in Banjul, The Gambia (appendix 2 p 7). We initially valued all costs in Gambian Dalasi and subsequently converted to US$ in 2020 using the mean annual exchange rate for 2020. Outpatient costs varied according to the testing algorithms. Inpatient costs were derived from our previous publication that used WHO-Choosing Interventions that are Cost-Effective (known as WHO-CHOICE) data[14] and adjusted for inflation from 2013 to 2020 in The Gambia. Intervention costs included start-up costs, fixed costs, and variable costs (table 1, appendix 2 p 15).

Outcomes

Clinical outcomes were presented for each testing algorithm and also for the natural history without any intervention. Clinical outcomes included cumulative incidence of becoming eligible for antiviral therapy and incidence of compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma. We also assessed cumulative incidence of being treated according to each algorithm in individuals who would have met the EASL 2017 criteria over a lifetime, and in those who would have never met the EASL 2017 criteria. Effectiveness was examined with use of disability-adjusted life years (DALYs) and years of life saved (YLS). We used life expectancy from the 2022 revision of the World Population Prospects to calculate years of life lost. We obtained disability weights for decompensated cirrhosis and hepatocellular carcinoma from the GBD 2019 (appendix 2 p 9). Disability weights were not available for compensated cirrhosis.

For the **World Population Prospects 2022** see https://population.un.org/wpp/

Cost-effectiveness analysis

The incremental cost-effectiveness ratio (ICER) between one algorithm and the next least expensive, non-dominated algorithm was calculated as the difference in the cost divided by the difference in DALYs or YLS. When ordering the strategies by increasing costs, a strategy was dominated if it was more expensive but less effective than the next least expensive strategy. An algorithm was deemed cost-effective if the ICER was less than 0·5 times the gross domestic product per capita in The Gambia ($704 in 2020, World Bank),[60] indicating a threshold at $352 per DALY averted or YLS.[61] A lifetime horizon was used.[62] Costs and health outcomes were discounted at 3% per year.[63] The budget impact analysis estimated the total undiscounted HBV-related costs after implementing each testing algorithm for the 20-year-old population in The Gambia in 2020. Adhering to guidelines of The Professional Society for Health Economics and Outcomes Research, we opted for a 5-year time horizon, as it could reflect an initial investment phase, harmonise with national health strategies, and remain generally unaffected by discounting effects.[64] The analysis assumed that of the 56 600 individuals aged 20 years in The Gambia (World Population Prospects 2022), 8·8% have chronic HBV infection,[13] which corresponds to 5000 adults (to the nearest thousand) with chronic HBV infection. The generic price of TDF in The Gambia was applied to the model ($40 per individual per year).

Six sets of one-way sensitivity analyses were done. First, disability weights for hepatocellular carcinoma according to the GBD 2019 varied from 0·288 (base-case value) to 0·540 (terminal stage, appendix 2 p 9). Second, although severe side-effects are rare for TDF,[4] we allocated disability weights (range: 0·000–0·050; corresponsing to the GBD health state of "generic uncomplicated disease: worry and daily medication"[57]) to individuals taking daily TDF medication to incorporate potential interference with daily activities.[65] Third, we set the risk of developing hepatocellular carcinoma among those non-eligible for EASL to zero. Fourth, the effectiveness (rate ratio) of TDF to prevent hepatocellular carcinoma was varied from 0·2 to 0·9 (base-case value: 0·5).[66] Fifth, the cumulative rate of treatment failure secondary to treatment discontinuation until the end of the simulation period was varied from 10·00% to 40·00%, per the confidence intervals for previously reported failure rate (base-case value: 27·14%).[56] Finally, we varied the discounting rate from 0% to 12%.[67] We also did multiway sensitivity analyses to simultaneously vary the cutoff scores of TREAT-B for treatment eligibility (≥1 to ≥3) and to identify sensitivity and specificity at the varying cutoffs compared against the EASL 2017 criteria for each health state (appendix 2 pp 16–17). Multivariate probabilistic sensitivity analyses were performed with 500 Monte Carlo simulations to evaluate second-order uncertainty by incorporating gamma distribution for costs and beta distributions for probabilities (table 1; appendix 2 pp 9, 23–25).[68] We ensured that all runs were within calibration targets. We reported the distribution of costs and effectiveness. Model uncertainty was accounted for in a cost-effectiveness acceptability curve for varying decision makers' willingness-to-pay thresholds per DALY averted or YLS.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

In our modelled cohort of 100 000 adults aged 20 years with chronic HBV infection in The Gambia, 9723 developed compensated cirrhosis and 13 170 developed hepatocellular carcinoma over $4·3\times10^6$ person-years without any antiviral therapy. Thus, the incidence rates derived from our model were 2·37 per 1000 person-years for compensated cirrhosis and 3·08 per 1000 person-

	Prevalence at baseline, n/N; % (95% CI)	Proportion eligible per EASL 2017, n/N; % (95% CI)	WHO 2015		TREAT-B*		Treat All	
			Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Total cohort								
Age <30 years (n=138)	NA	14/138; 10·1% (5·7–16·4)	7·1% (0·2–33·9)	100% (97·1–100)	85·7% (57·2–98·2)	79·8% (71·7–86·5)	100% (NA)	0% (NA)
Age ≥30 years (n=664)	NA†	51/664; 7·7% (5·8–10·0)	58·8% (44·2–72·4)	97·9% (96·4–98·9)	78·4% (64·7–88·7)	90·9% (88·3–93·0)	100% (NA)	0% (NA)
HBeAg-positive chronic infection								
Age <30 years	4/138; 2·9% (0·8–7·3)	1/4; 25·0% (0·6–80·6)	0% (0–97·5)	100% (29·2–100)	100% (2·5–100)	0% (0–70·8)	100% (NA)	0% (NA)
Age ≥30 years	NA†	12/15; 80·0% (51·9–95·7)	66·7% (34·9–90·1)	100% (29·2–100)	91·7% (61·5–99·8)	33·3% (0·8–90·6)	100% (NA)	0% (NA)
HBeAg-positive chronic hepatitis								
Age <30 years	9/138; 6·5% (3·0–12·0)	5/9; 55·6% (21·2–86·3)	0% (0–52·2)	100% (39·8–100)	100% (47·8–100)	0% (0–60·2)	100% (NA)	0% (NA)
Age ≥30 years	NA†	7/8; 87·5% (47·3–99·7)	100% (59·0–100)	100% (2·5–100)	100% (59·0–100)	0% (0–97·5)	100% (NA)	0% (NA)
HBeAg-negative chronic infection								
Age <30 years	96/138; 69·6% (61·2–77·1)	0/96; 0% (0–3·8)	NA‡	100% (96·2–100)	NA‡	100% (96·2–100)	NA‡	0% (NA)
Age ≥30 years	NA†	0/522; 0% (0–0·7)	NA‡	99·8% (98·9–100)	NA‡	100% (99·3–100)	NA‡	0% (NA)
HBeAg-negative chronic hepatitis								
Age <30 years	2/138; 1·4% (0·2–5·1)	2/2; 100% (15·8–100)	0% (0–84·2)	NA§	100% (15·8–100)	NA§	100% (NA)	0% (NA)
Age ≥30 years	NA†	11/18; 61·1% (35·7–82·7)	54·5% (23·4–83·3)	71·4% (29·0–96·3)	100% (71·5–100)	0% (0–41·0)	100% (NA)	0% (NA)
HBeAg-negative grey zone								
Age <30 years	23/138; 16·7% (10·9–24·0)	2/23; 8·7% (1·1–28·0)	0% (0–84·2)	100% (83·9–100)	0% (0–84·2)	14·3% (3·1–36·3)	100% (NA)	0% (NA)
Age ≥30 years	NA†	1/81; 1·2% (0·0–6·7)	0% (0·0–97·5)	87·5% (78·2–93·8)	0% (0·0–97·5)	42·5% (31·5–54·1)	100% (NA)	0% (NA)
Compensated cirrhosis								
Age <30 years	4/138; 2·9% (0·8–7·3)	4/4; 100% (39·8–100)	25·0% (0·6–80·6)	NA§	100% (39·8–100)	NA§	100% (NA)	NA§
Age ≥30 years	NA†	20/20; 100% (83·2–100)	45·0% (23·1–68·5)	NA§	55·0% (31·5–76·9)	NA§	100% (NA)	NA§

Input parameters were derived from a secondary analysis of the Prevention of Liver Fibrosis and Cancer in Africa study.[6] EASL=European Association for the Study of the Liver. HBeAg=hepatitis B e antigen. NA=not applicable. TREAT-B=Treatment Eligibility in Africa for the Hepatitis B Virus. *Cutoff score ≥2. †All simulated individuals aged 20 years at model initialisation. ‡None of the simulated individuals in this health state eligible per EASL 2017. §All simulated individuals in this health state eligible per EASL 2017.

Table 2: **Input parameters for the distribution of health states at baseline, proportion eligible for treatment per EASL criteria, and performance of alternative testing algorithms to indicate EASL 2017 treatment eligibility**

years for hepatocellular carcinoma, which fit well and were within the confidence intervals for incidence rates reported in the GBD 2019 in The Gambia (appendix 2 pp 28–29).

The cumulative incidence of becoming eligible for treatment with TDF according to EASL 2017 criteria was 14·2% (14 200 per 100 000 adults) during a lifetime horizon. Of the individuals who remained ineligible throughout their lifetime according to the EASL criteria (n=85 800), the number of individuals who would have been unnecessarily treated at some point in their life was 24 098 (28·1%) when applying the WHO 2015 algorithm, 38 938 (45·4%) when applying the TREAT-B algorithm, and 85 800 (100%) when applying the Treat All algorithm (appendix 2 p 18). By contrast, among individuals who fulfilled the EASL criteria during their lifetime (n=14 200), the number who would not have been treated was 6860 (48·3%) when using the WHO algorithm, 109 (0·8%) when using the TREAT-B algorithm, and 0 when using the Treat All algorithm.

The incidence rates of compensated cirrhosis did not vary according to the testing algorithms. The rates were 1·97 per 1000 person-years (WHO algorithm, base case),

	Cost		DALYs			YLS		
	Total cost (million US$)	Incremental cost* (million US$)	DALYs	Incremental DALYs averted†	ICER‡ (US$ per DALY averted)	YLS	Incremental YLS†	ICER‡ (US$ per YLS)
TREAT-B	$86·6	Less costly	359 938	4877	Cost-saving	4403	4403	Cost-saving
WHO 2015 (base case)	$114·5	0 (ref)	364 815	0 (ref)	NA	0 (ref)	0 (ref)	NA
EASL	$121·5	7·0	365 610	Less effective	Dominated§	−3495	Less effective	Dominated§
Treat All	$134·6	13·1	355 463	9352	$2149	7763	7763	$2589

Costs, DALYs averted, and YLS are for 100 000 adults over a lifetime starting from age 20 years and were discounted at 3% per year. DALYs=disability-adjusted life years. EASL=European Association for the Study of the Liver. ICER=incremental cost-effectiveness ratio. NA=not applicable. TREAT-B=Treatment Eligibility in Africa for the Hepatitis B Virus. YLS=years of life saved. *Relative to the next least costly strategy. †Relative to the next least effective strategy excluding strategies less costly than the base case. ‡ICER relative to the next least expensive, non-dominated algorithm was calculated as the ratio of the cost difference to the difference in DALYs averted or YLS. §Dominated indicates that the strategy is less effective compared with the base case (WHO criteria), therefore the ICER cannot be calculated.

Table 3: **Cost, effectiveness, and cost-effectiveness of the different testing algorithms for treatment eligibility in The Gambia**

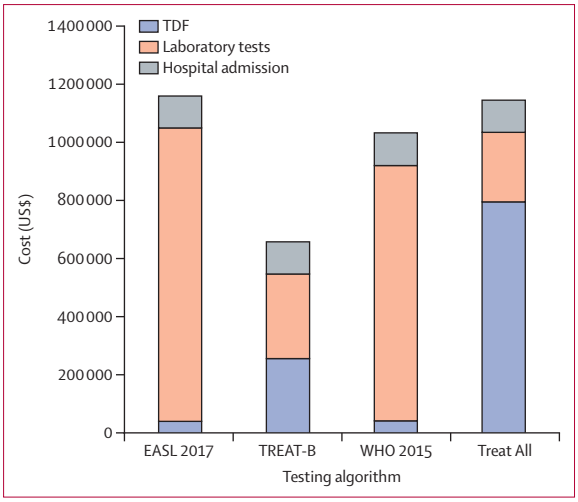

Figure 1: **5-year budget impact analysis of different testing algorithms in The Gambia**
Impact analysis for a cohort of 5000 individuals aged 20 years with chronic hepatitis B virus infection. TDF costs represent drug costs; laboratory tests include initial assessment and follow-up. Start-up costs are not represented because they are negligible. EASL=European Association for the Study of the Liver. TDF=tenofovir disoproxil fumarate. TREAT-B=Treatment Eligibility in Africa for the Hepatitis B Virus.

1·91 per 1000 person-years (EASL), 1·92 per 1000 person-years (TREAT-B), and 1·93 per 1000 person-years (Treat All; appendix 2 p 19). A similar pattern was observed for decompensated cirrhosis, with incidence rates of 0·79 per 1000 person-years (WHO), 0·75 per 1000 person-years (EASL), 0·75 per 1000 person-years (TREAT-B), and 0·77 per 1000 person-years (Treat All). By contrast, the incidence rates of hepatocellular carcinoma differed, at 2·03 per 1000 person-years (WHO), 2·45 per 1000 person-years (EASL), 2·02 per 1000 person-years (TREAT-B), and 1·98 per 1000 person-years (Treat All).

Using the PROLIFICA dataset, the sensitivity and specificity of the WHO criteria to indicate the EASL criteria were 7·1% (95% CI 0·2–33·9) and 100% (97·1–100), respectively, in individuals younger than 30 years, and 58·8% (44·2–72·4) and 97·9% (96·4–98·9), respectively, in those aged 30 years or older (table 2). By applying a cutoff of 2 or higher for TREAT-B total score, the sensitivity and specificity to indicate the EASL criteria were 85·7% (57·2–98·2) and 79·8% (71·7–86·5), respectively, in those younger than 30 years, and 78·4% (64·7–88·7) and 90·9% (88·3–93·0), respectively, in those aged 30 years or older. Finally, in the Treat All strategy, antiviral therapy would be initiated in all HBsAg-positive individuals immediately after entering the cohort, resulting in 100% sensitivity and 0% specificity (95% CIs not applicable) to indicate the EASL criteria. Sensitivity and specificity by health state and age group are summarised in table 2.

The projected health benefits of each testing algorithm in the cohort of 100 000 individuals over a lifetime are summarised in table 3. Compared with the WHO criteria (base case), TREAT-B reduced DALYs by 4877 and Treat All reduced DALYs by 9352; whereas, the EASL criteria increased DALYs by 795, indicating lower effectiveness. With use of YLS as an endpoint, TREAT-B and Treat All remained the most effective algorithms, with increases of 4403 YLS and 7763 YLS, respectively, compared with the WHO criteria. The EASL criteria were less effective than the WHO criteria (−3495 YLS). The discounted costs per person over a lifetime were $1145 (WHO), $1215 (EASL), $866 (TREAT-B), and $1346 (Treat All). Consequently, EASL was a dominated algorithm while TREAT-B was cost-saving compared with the base-case WHO criteria. Treat All was unlikely to be cost-effective, with ICERs of $2149 per DALY averted and $2589 per YLS, which are far above the cost-effectiveness threshold for The Gambia ($352).

Figure 1 presents the total undiscounted HBV-related costs incurred over a period of 5 years beginning from the implementation of each testing algorithm, for a cohort of 5000 adults aged 20 years with chronic HBV infection in The Gambia. Total costs were $1·03 million (WHO criteria), $1·16 million (EASL), $0·66 million (TREAT-B), and $1·14 million (Treat All). The costs of Treat All were mainly driven by treatment ($0·79 million

over 5 years) even when the generic (low) price of TDF in The Gambia was applied to the model ($40 per individual per year). For the other algorithms, the costs were mainly due to diagnostic tests.

In one-way sensitivity analyses, the overarching findings were unaffected by variations in the following factors within the limits specified: disability weights for hepatocellular carcinoma, TDF effectiveness, treatment failure rate secondary to treatment discontinuation, and discounting rate (appendix 2 p 30). Across all distinct scenarios for these factors, Treat All was more effective than the base-case WHO criteria, but the ICER consistently exceeded the cost-effectiveness threshold of $352. Relative to the WHO criteria, TREAT-B was consistently cost-saving and EASL was less effective with the same factor variations (data not shown). Conversely, the allocation of disability weights associated with a daily TDF therapy from 0·000 to 0·050 substantially impacted the effectiveness of each testing algorithm, exerting a greater effect on strategies that expanded treatment (figure 2). Treat All became much less effective than the base-case WHO criteria with an excess of 30 342 DALYs, whereas EASL became the best algorithm with 10 461 DALYs averted when applying a disability weight of 0·025. TREAT-B averted a similar amount of DALYs to the WHO criteria. Increasing the disability weight to 0·050 made EASL even more effective, and Treat All and TREAT-B even less effective compared with the WHO criteria. In a scenario in which the EASL criteria worked perfectly and EASL-ineligible individuals never developed hepatocellular carcinoma (appendix 2 p 20), the EASL criteria were more effective than the WHO criteria (2627 DALYs averted and 2117 YLS), but was not cost-effective in The Gambia (ICER: $2726 per DALY averted; $3382 per YLS). Treat All remained the most effective strategy in terms of DALYs and YLS, but the ICER was above the cost-effectiveness threshold (ICER: $11 484 per DALYs averted; $26 286 per YLS). TREAT-B was less effective than EASL (959 DALYs averted and 642 YLS), but cost-saving.

Multiway sensitivity analyses were done to vary the total score at which TREAT-B indicates TDF treatment eligibility (appendix 2 pp 16–17, 21–22). Applying a TREAT-B cutoff score of 1 (ie, ≥1) increased sensitivity and decreased specificity for indicating EASL treatment eligibility, and resulted in slightly higher effectiveness with regard to DALYs and YLS than a cutoff score of 2; however, compared with Treat All, a TREAT-B cutoff score of 1 was more costly and less effective. A TREAT-B score threshold of 3 decreased sensitivity and increased specificity for indicating EASL treatment eligibility, and resulted in lower effectiveness but lower cost than with a cutoff score of 2.

Using 500 Monte Carlo simulations for probabilistic sensitivity analyses, the mean effectiveness for Treat All was 3855 DALYs averted (95% CI –1545 to 9196) and 3181 YLS (–893 to 7296; appendix 2 pp 31–32). Regarding

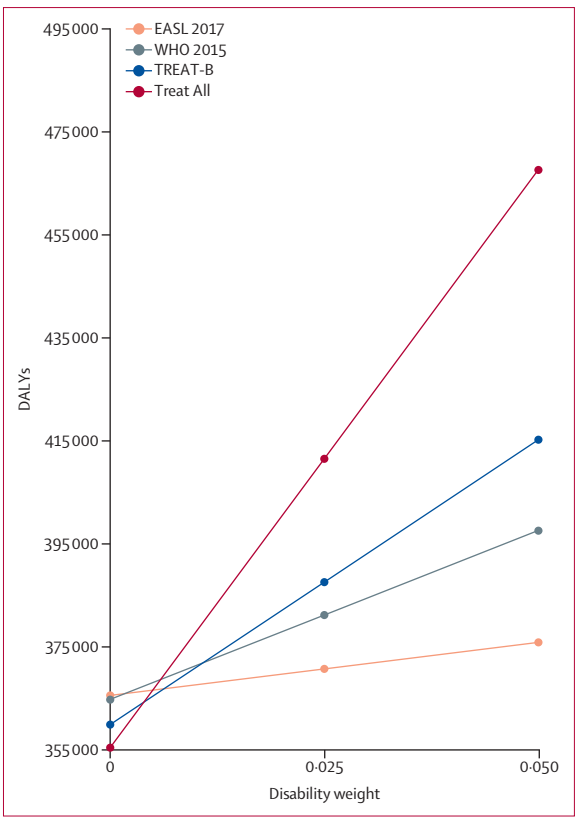

Figure 2: **Effectiveness of different testing algorithms for chronic hepatitis B virus infection in The Gambia according to disability weight of treatment**
Health outcome (DALYs) according to disability weight associated with daily treatment with tenofovir disoproxil fumarate for the four modelled testing algorithms. EASL=European Association for the Study of the Liver. DALYs=disability-adjusted life years. TREAT-B=Treatment Eligibility in Africa for the Hepatitis B Virus.

intervention costs, the TREAT-B, EASL, and Treat All algorithms were less costly than the WHO algorithm in 100%, 45·4%, and 15·2% of the 500 runs, respectively (appendix 2 p 33). For the subset of simulations in which the Treat All algorithm was more effective than the WHO algorithm (462 [92·4%] of 500), the mean ICER was $9740 per DALY averted (95% CI: cost saving to $54 609) and $51 191 per YLS (cost saving to $78 663; appendix 2 pp 34–35). Figure 3 presents the cost-effectiveness acceptability curve, illustrating the likelihood of a testing algorithm emerging as the most preferred option among the three alternatives, in terms of effectiveness and cost-effectiveness across varying decision makers' willingness-to-pay thresholds per DALY averted or YLS. Up to a willingness-to-pay threshold of $10 000 per DALYs averted, the probability of the TREAT-B algorithm being the most preferred strategy among the three algorithms would be 92·2%. This probability would decrease to 74·0% at a willingness-to-pay threshold of $20 000, and 61·2% at a threshold of $30 000. Results were similar for willingness-to-pay thresholds per YLS. Treat All would

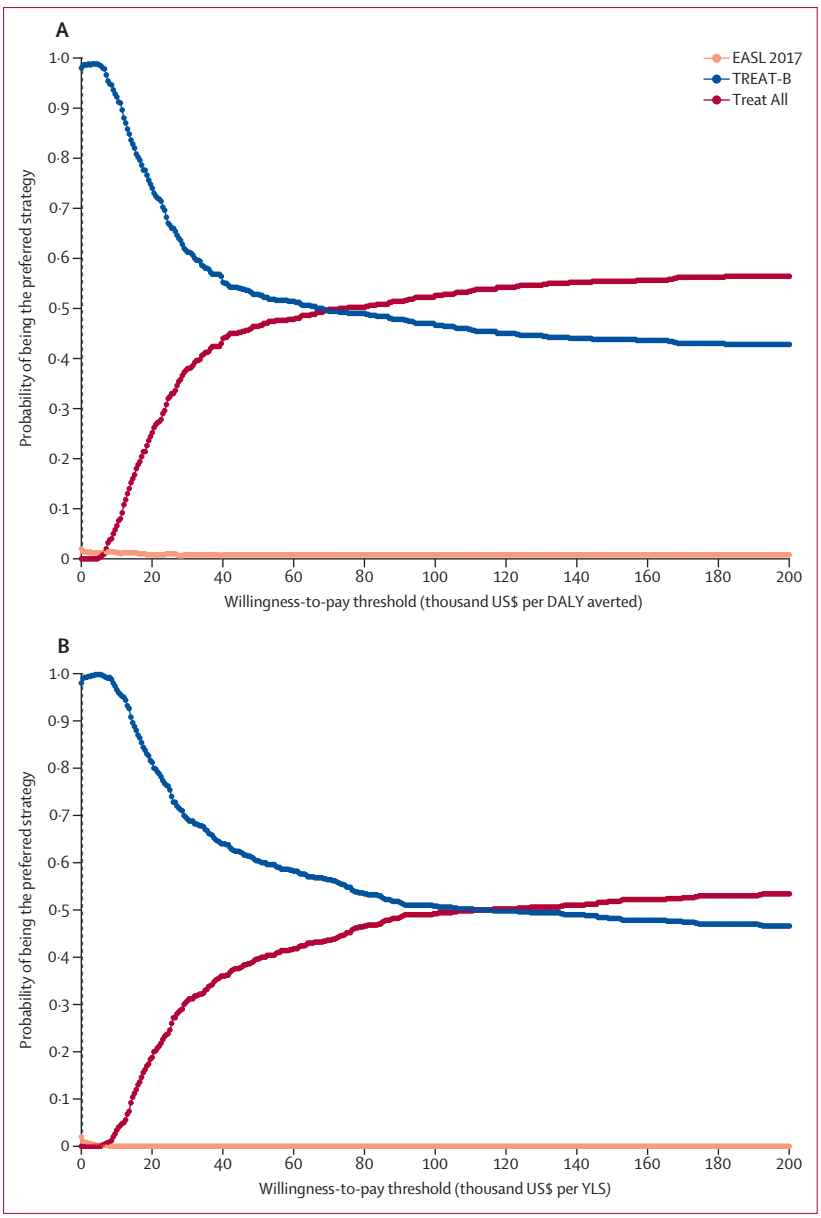

Figure 3: **Cost-effectiveness acceptability curve**
Curves indicate the probability of each strategy being the preferred strategy over a range of willingness-to-pay thresholds per DALY averted (A) or per YLS (B). The dashed line represents the willingness-to-pay threshold that can be applied to The Gambia (US$352, equivalent to 0·5 times the gross domestic product per capita of The Gambia). EASL=European Association for the Study of the Liver. DALYs=disability-adjusted life years. TREAT-B=Treatment Eligibility in Africa for the Hepatitis B Virus. YLS=years of life saved.

become the most preferred choice only if the willingness-to-pay threshold were to exceed approximately $72 000 per DALY averted or $110 000 per YLS, well above the cost-effectiveness threshold in The Gambia.

Discussion

Our study represents the first modelling analysis to estimate the effectiveness, costs, and cost-effectiveness of a Treat All strategy for hepatitis B in Africa. By comparing the Treat All strategy with targeted strategies that use either a comprehensive algorithm (EASL 2017 criteria) or simplified algorithm (TREAT-B and WHO 2015 criteria), the analysis yielded three principal findings. First, Treat All and TREAT-B might be more effective in reducing HBV-related disease burden in The Gambia than the EASL or WHO approaches, in which HBV-infected people are selected for treatment according to conventional criteria. Second, implementing a Treat All approach in The Gambia is unlikely to be cost-effective. Finally, the analysis suggested that a targeted, simplified algorithm, such as TREAT-B, might be cost-saving and have a lower budget impact than the Treat All strategy.

In 2016, WHO recommended that all people living with HIV should receive lifelong antiretroviral therapy irrespective of clinical status or CD4 cell count.[69] Since then, treating all people living with HBV has become a subject of debate. Indeed, previous modelling studies in high-income countries supported Treat All as a cost-effective strategy to accelerate HBV elimination.[11,70] Patients with chronic HBV infection who are ineligible for antiviral therapy according to conventional criteria that are based on reference tests might still carry a small risk of liver complications,[16] and therefore Treat All resulted in the highest DALYs averted compared with the targeted strategies in previous studies[11,70] and the present study. However, two reasons might explain why Treat All was not cost-effective in our analysis. First, the cost-effectiveness threshold in The Gambia ($352) is considerably lower than those applied in Saudi Arabia and the USA (exceeding $60 000).[11,70] Second, our analysis found a lower reduction in hepatocellular carcinoma incidence with Treat All (2·5%; incidence rate of 1·98 per 1000 person-years with Treat All *vs* 2·03 per 1000 person-years with the WHO criteria) compared with the study in Saudi Arabia (50%).[11] This discrepancy in effectiveness can be attributed to differences in model structure (our model does not account for the benefits of treatment in preventing transmission), input data (treatment effectiveness for hepatocellular carcinoma: 50% in our study versus 90% in the Saudi Arabian study), and base-case scenarios. Importantly, limited research on individuals currently designated as ineligible for treatment suggests uncertain effectiveness of antiviral therapy in preventing important clinical outcomes.[71]

Our finding that Treat All is unlikely to be cost-effective remained constant after performing sensitivity analyses on model parameters. Notably, our budget analysis found that even with the low generic cost of TDF in The Gambia ($40 per year), the Treat All cost $1·14 million over 5 years, mainly due to drug costs (figure 1). Our results highlight the importance of considering the economic feasibility of public health interventions, even when they might provide clinical benefits. Advanced economic assessment, including value of information analysis, might provide useful insights into the potential benefits of addressing

knowledge gaps associated with Treat All.

The acceptability of Treat All is also questionable, as it requires lifelong treatment even for individuals who might not develop chronic liver disease. Although nucleos(t)ide analogues such as TDF are generally well tolerated, adherence might be suboptimal,[56] especially in the presence of stigma associated with hepatitis B infection.[72] Additionally, treatment interruptions carry a 1–2% risk of severe hepatic flare with liver decompensation.[73] Furthermore, the burden of treatment, including daily medication intake that might interfere with daily activities or lifestyle, cannot be overlooked.[65] In our sensitivity analysis, we assigned a small disability weight (0·025–0·050)[57] to individuals undergoing antiviral therapy, and found that Treat All became the least effective intervention among the four assessed. Evaluating the impact of treatment on health is challenging; studies have shown improvement in patient-reported outcomes for HBV-infected individuals receiving anti-HBV therapy,[74] but these studies did not consider individuals who are ineligible for treatment according to established guidelines.

Operational feasibility is another concern for implementing Treat All. HBV affects 7-times more individuals worldwide than HIV,[1] and unlike HIV, it does not inevitably result in premature death for all those infected. As more than 95% of people with chronic HBV infection live in LMICs,[75] the widespread adoption of Treat All might present substantial logistical and financial challenges, particularly by increasing total drug costs. Nevertheless, several similarities exist between HBV and HIV. Both are endemic in sub-Saharan Africa, and antiviral drugs used for HIV are also effective against HBV. Successful treatment of co-infected individuals has been shown in extensive HIV Treat All rollout programmes.[76] These findings highlight the importance of directing additional treatment efforts toward HBV monoinfected individuals and emphasise the urgency of donor support, such as from the Global Fund, for investments in HBV treatment.

The Treat All strategy did not appear to be the optimal testing algorithm for The Gambia, and our model suggested that a targeted simplified strategy, such as TREAT-B, might be better adapted. TREAT-B could lead to a similar reduction in compensated cirrhosis, decompensated cirrhosis, and hepatocellular carcinoma cases as a Treat All approach, while being cost-saving, with a 5-year budget that was almost half the expense of the Treat All budget ($0·66 million *vs* $1·14 million). Further investigation is warranted to determine the potential utility of the TREAT-B algorithm in different settings. Our model confirms that the EASL guidelines might be too conservative, as indicated by the higher number of hepatocellular carcinoma cases reported with the EASL treatment criteria versus the other criteria. Furthermore, tests required to assess EASL criteria (ie, transient elastography and HBV DNA) are not widely accessible particularly in local clinical settings in LMICs.

Our study has limitations. Although we primarily applied real-life country-specific data to parametrise our model, including health state distributions, performance of testing algorithms, and costs, we also drew upon non-African natural history data involving different viral genotypes. Similarly, considering variations in cultural, environmental, and demographic contexts that influence the rating of health state severity, the relevance of disability weights from the GBD 2019 study for the Gambian population might warrant scrutiny.[77] Another limitation was that the PROLIFICA data used to derive the performance of TREAT-B were cross-sectional. As such, we used a time-dependent variable to model eligibility over time, and the cumulative proportion of becoming treatment eligible was consistent with the literature.[2] Our primary analysis employed a deterministic Monte Carlo simulation methodology. This approach entails addressing first-order uncertainty, arising from interindividual variability, through individualised simulations designed to assess various disease outcomes. Although second-order uncertainty was not assessed in our main analysis, it was tested by the probabilistic sensitivity analyses, which confirmed our primary analysis results. Our model does not encompass the complexity of health-care delivery by omitting distinct care cascades aligned with each strategy. We solely accounted for treatment failure due to treatment discontinuation before and after 1 year to address instances of loss to follow-up. Our model focused on individual health benefits and did not consider HBV transmission, in particular prevention of HBV mother-to-child transmission, as another important component of HBV elimination. Finally, our model did not assess the time interval between treatment decisions being made and treatment initiation, which is a major problem in many LMICs.

In summary, our analysis shows that although Treat All is an appealing approach for minimising the burden of HBV in The Gambia, it is currently unlikely to be cost-effective in this setting. Our findings suggest that a simplified targeted testing algorithm, such as TREAT-B, might be a better strategy to reduce HBV-related morbidity and mortality in a cost-saving way. Further evaluation is needed to establish whether our findings are generalisable to other resource-limited settings.

Contributors

LBLN, ML, SN, and YS formulated the research questions. ML, GN, ZJW, SN, and YS collected the original data. TBH, UD'A, and MT supervised the work. LBLN and YS analysed the data. LBLN, ML, and YS wrote the manuscript. All authors reviewed and approved the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication. LBLN and YS have directly accessed and verified the underlying data reported in the manuscript.

Equitable partnership declaration

The authors of this paper have submitted an equitable partnership declaration (appendix 3). This statement allows researchers to describe how their work engages with researchers, communities, and

See Online for appendix 3

environments in the countries of study. This statement is part of *The Lancet Global Health*'s broader goal to decolonise global health.

Declaration of interests

LBLN has received personal fees from Sanofi and Pfizer for speaker or consultant roles. ML has received research grants from Gilead Sciences and Abbott Laboratories. YS has received consulting fees from WHO, research grants from Gilead Sciences, and research materials from Abbott Laboratories and Fujirebio. SN has received a research grant from Gavi and consulting fees from WHO. All other authors declare no competing interests.

Data sharing

De-identified participant data, used to inform the model's parameters, can be made available upon reasonable request, subject to approval by the scientific committee of the PROLIFICA project. Requests should be made online at https://www.prolifica.africa/. All aggregated data utilised for model parameterisation and the code for simulating the model with these data are accessible online (https://dataverse.harvard.edu/dataset.xhtml?persistentId=doi:10.7910/DVN/LGMUP6).

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