Check for updates

Journal of Viral Hepatitis

WILEY

JOURNAL OF VIRAL HEPATITIS JVH

ORIGINAL ARTICLE OPEN ACCESS

Validation of a Point-Of-Care Ultrasound for Hepatitis Among Front-Line Healthcare Workers Managing Chronic Hepatitis B Virus Infection in Zambia

Costanza Bertoni[1,2] | Annie Kanunga[3,4] | Edford Sinkala[4,5] | Enock Syabbalo[4] | Helen Chitundu[4] | Alick Chikwezi[4] | Carolyn Chibundi[3] | Guy K. Muula[3] | Samuel Bosomprah[3,6] | Nicolò Capra[1] | Riccardo Lolatto[1] | Giulia Morsica[1] | Antonella Castagna[1,2] | Claudia Wallrauch[7,8] | Tom Heller[7,9] | Michael J. Vinikoor[3,5,10]

[1]Division of Infectious Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy | [2]Faculty of Medicine and Surgery, Vita-Salute San Raffaele University, Milan, Italy | [3]Centre for Infectious Disease Research in Zambia, Lusaka, Zambia | [4]University Teaching Hospital, Lusaka, Zambia | [5]Department of Medicine, University of Zambia, Lusaka, Zambia | [6]Department of Biostatistics, School of Public Health, University of Ghana, Accra, Ghana | [7]Lighthouse Clinic Trust, Lilongwe, Malawi | [8]Institute of Infectious Diseases and Tropical Medicine, LMU University Hospital, LMU Munich, Munich, Germany | [9]International Training and Education Center for Health, University of Washington, Seattle, Seattle, USA | [10]University of Alabama at Birmingham, Birmingham, USA

Correspondence: Michael J. Vinikoor (Michael.Vinikoor@cidrz.org)

Received: 15 November 2025 | **Revised:** 29 June 2026 | **Accepted:** 1 July 2026

Keywords: hepatitis B virus | hepatocellular carcinoma | liver cirrhosis | point-of-care ultrasound | resource limited settings

ABSTRACT

To close gaps in implementing care of people with hepatitis B virus (HBV) infection in resource-limited settings, we evaluated the accuracy of a novel liver point-of-care ultrasound (POCUS) protocol for hepatitis (PUSH) among front-line non-radiology health-care workers in Zambia. At University Teaching Hospital in Lusaka, Zambia, from March to June 2024, we trained four nurses and six physicians with experience in HBV management, but not in ultrasound (US), in the PUSH protocol, which includes visualizing the liver in three windows (epigastric, subcostal and right transcostal) to identify cirrhosis-suggestive features and liver lesions suspicious for hepatocellular carcinoma (HCC). Then, consecutive adult participants with chronic hepatitis B (PWHB) alone or HBV/HIV coinfection underwent PUSH with operators blinded to clinical data. We evaluated the accuracy of PUSH for significant fibrosis and cirrhosis using transient elastography (TE) as the reference standard test (RST) and for liver lesions that were possible HCC using a comprehensive abdominal ultrasound by an experienced radiographer as the RST. Nonparametric analysis of the receiver operating curve (ROC) for PUSH was adjusted for operator type (doctor vs. nurse), sex and HIV status. Among 197 PWHBs analysed, 69.5% were taking HBV antivirals and 27.9% had HBV/HIV. According to RSTs, 17.7% of PWHBs had significant fibrosis, 11.6% had cirrhosis and 3.5% had liver lesions. PUSH had low accuracy for significant fibrosis, with sensitivity of 8.3% (17.5–41.4), specificity of 100.0% (96.1–100) and an area under the curve (AUROC) of 0.54 (0.43–0.65), moderate accuracy for cirrhosis, with sensitivity of 60.9% (38.5–80.3), specificity of 97.7% (94.2–99.4) and AUROC of 0.79 (0.69–0.89), and higher accuracy for liver lesions, with 85.7% (42.1–99.6) sensitivity, 98.4% (95.5–99.7) specificity, AUROC of 0.92 (0.78–1.00). After an expedited training, front-line nurses and physicians treating HBV in Zambia were able to use PUSH to diagnose cirrhosis with moderate accuracy and liver lesions with high accuracy, although confidence intervals around performance estimates were wide. Liver POCUS including PUSH may be useful in HBV management when laboratory systems and TE are lacking.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2026 The Author(s). *Journal of Viral Hepatitis* published by John Wiley & Sons Ltd.

1 | Introduction

Hepatitis B is a leading cause of mortality worldwide, accounting for more estimated deaths than HIV [1, 2]. Acute and chronic HBV infections disproportionately affect Sub-Saharan Africa (SSA), which in 2022 had 65 million people with chronic infection and contributed to 63% of global incidence. In Africa, hepatitis B virus (HBV) infection is the leading cause of liver-related deaths and accounts for one-third of cirrhosis-related deaths [3, 4]. Alarmingly, fewer than 10% of people with chronic hepatitis B (CHB) in the region are diagnosed, and only 5% receive treatment according to WHO estimates [2]. Further gaps exist in delivering vaccination both to HBV-exposed newborns and adults at risk [5, 6].

1.1 | New WHO Guidelines and Challenges in Implementation

Implementing HBV clinical management programmes in low and middle-income countries (LMICs) such as many parts of Africa faces major challenges in determining eligibility for antiviral therapy. Eligibility requires demonstrating active viral replication, necroinflammatory activity and liver disease progression, but few patients have access to HBV DNA or hepatitis B e antigen (HBeAg) assays to assess viral activity or to transient elastography (TE) or biopsy to stage liver disease. Many individuals present with decompensated cirrhosis at diagnosis, when treatment is urgent and mortality is high, highlighting the need for earlier therapy initiation. To address implementation gaps, the World Health Organization (WHO) recommends determining eligibility using the AST to platelet ratio index (APRI), a proxy for significant fibrosis and cirrhosis, and persistent elevation of alanine aminotransferase (ALT) [7]. A low-cost score incorporating demographics, liver transaminases and platelet count was also developed by the Hepatitis B in Africa collaborative network [8]. Despite more inclusive guidelines, implementation remains challenging since many clinics cannot measure liver enzymes due to limited laboratory infrastructure, electricity, reagents and trained personnel.

1.2 | The Role of Ultrasound

A valuable but underutilized tool in HBV management is B-mode ultrasound. Ultrasound is safe, widely available and relatively inexpensive, having evolved from bulky radiology equipment to portable, user-friendly devices used across medicine—including obstetrics, vascular evaluation and emergency care [9, 10]. Certain handheld systems now cost only a few thousand USD. In the African context, especially within maternity care, B-mode ultrasound (US) may be more reliably available than point-of-care (POC) blood tests, TE or laboratory testing. Although ultrasound is operator dependent and less sensitive than elastography or CT for diagnosing fibrosis or cirrhosis [11], it offers major advantages: no radiation, low cost, minimal maintenance, immediate results and suitability for diverse healthcare professionals. It enables real-time assessment of liver texture, tumours, parenchyma, blood vessels, ascites and splenic size—findings that can indicate cirrhosis and portal hypertension. Moreover, ultrasound plays a central role in hepatocellular carcinoma (HCC) screening in upper-income countries too, with 84% sensitivity at any stage and 63% at early stage when combined with α fetoprotein (AFP) and is recommended every 6 months for individuals with CHB and HCC risk [12]. Looking ahead, artificial intelligence (AI) may further enhance liver disease evaluation [13].

In this study, we validated a recently conceptualized liver POCUS protocol for hepatitis, termed 'PUSH,' in Zambia. While demonstrating proof of concept, the initial evaluation of PUSH in Malawi had limitations, including reliance on POCUS experts, access to clinical records, and absence of reference standards to estimate the accuracy for cirrhosis and HCC. To further the development of PUSH, we trained non-expert ultrasound users, front-line clinicians and nurses managing HBV, and conducted a blinded evaluation of PUSH performance for fibrosis, cirrhosis and HCC. Overall, this study sought to further validate PUSH as a practical tool to strengthen HBV care in LMICs.

2 | Methods

2.1 | Hepatitis B in Zambia

This study was performed at the largest hepatitis B clinic in Zambia, located at the University Teaching Hospital, Lusaka. In 2016, at a population level, Zambia was estimated to have chronic HBV prevalence of 6% in adults and 1% of children [14].

The first HBV clinical treatment guidelines in Zambia were issued by Ministry of Health in 2019, and provide guidance to clinicians on treatment initiation criteria based on WHO HBV management guidelines from 2015 as reference [15, 16]. HBV treatment is provided for free and entails combination tenofovir diproxil fumarate (TDF) or alafenamide (TAF) with lamivudine or emtricitabine as TDF/TAF monotherapy is not available locally. For people with HBV/HIV, regimens include a 3rd anti-HIV drug (i.e., usually an integrate strand inhibitor) [15].

2.2 | PUSH Origin and Protocol

The PUSH protocol was created in 2023 in Malawi to support Malawi's first HBV treatment guidelines [17]. It was inspired by FASH (Focused Assessment with Sonography for HIV-associated tuberculosis), another POCUS protocol focused on HIV-related tuberculosis, which has been widely used for TB diagnosis in Africa [18] when other diagnostic tests are lacking or have long turnaround times [19, 20].

The PUSH protocol entails viewing the liver in three sonographic windows: epigastric, subcostal, and right transcostal. While scanning the windows, trainees are taught to look for several signs of cirrhosis: enlarged caudate lobe (only with subcostal view), nodular liver surface, coarse echotexture and tortuous/reduced vascularity (Figure 1). Trainees are taught to report suspicion for cirrhosis if at least one of the four signs is detected. Additionally, while scanning in the 3 windows, operators are also taught to identify ascites and liver lesions that are suspicious for HCC. Lesions suspicious for HCC tend to be large mosaic lesions, have heterogeneous

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

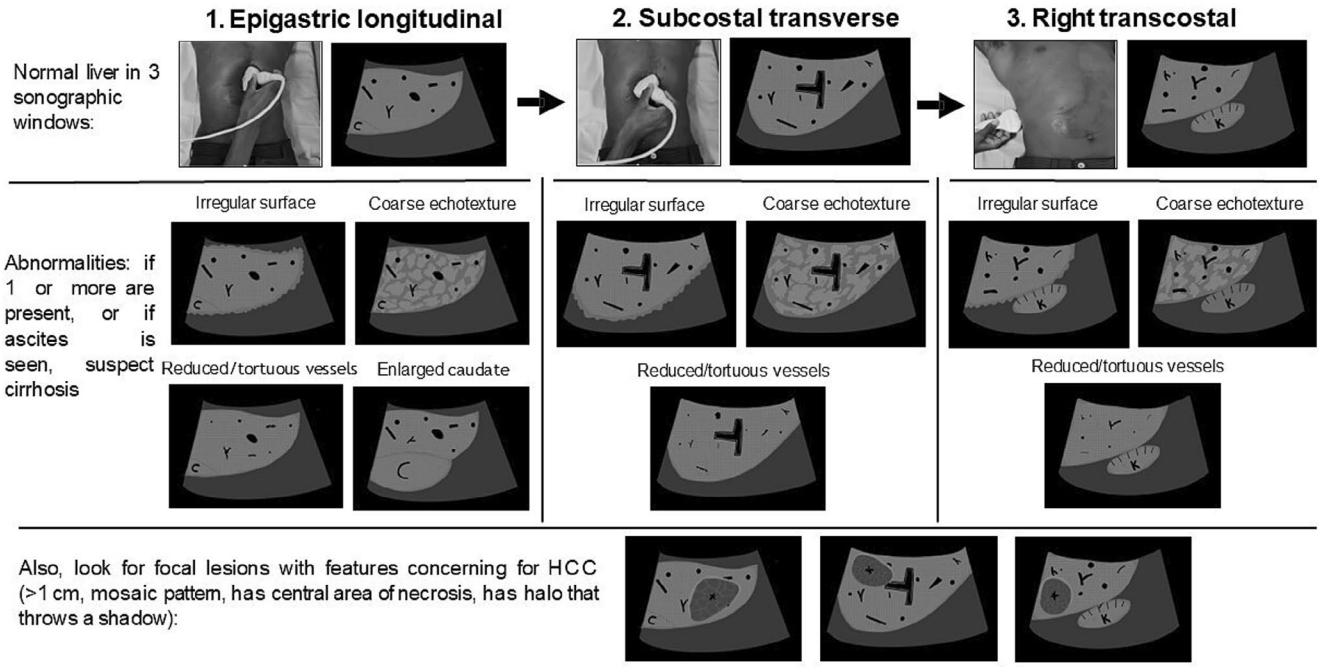


FIGURE 1 | Protocol for the Point-of-care Ultra Sound for Hepatitis (PUSH). Abbreviation: HCC, Hepatocellular carcinoma.

echotexture, fatty change, necrosis and calcification. A peripheral 'halo' of hypoechogenicity can often be seen too (Figure 1).

For this study, two PUSH developers (T.H. and C.W.) trained nurses and doctors in the protocol over a 3-day period. The trainees were 6 physicians (Bachelor of Medicine and Surgery with sub-specialization in internal medicine and/or gastroenterology or infectious diseases) and 4 nurses (Bachelors level) at the site hospital who routine care for people with HBV, but who had no/very limited prior experience performing US. Eight patients with known cirrhosis and/or HCC attended the training as volunteers to be scanned, so that trainees could gain experience with pathological liver imaging.

2.3 | Design of the Study

After the PUSH training we evaluated its performance in an observational study that ran from March to June 2024. The trainees performed PUSH on consecutive people with HBV (PWHB; based on being hepatitis B surface antigen [HBsAg] test positive) who attended the clinic if they were older than 18 years of age, were not currently/recently pregnant, did not have suspected/confirmed acute hepatitis B infection and did not have hepatitis C infection. While not a formal exclusion criterion, PWHB with clinically-apparent ascites were not included because of the requirement for valid TE results. Hepatitis delta coinfection was not an exclusion criterion, but it is very rare (~1%) among PWHB in Zambia [21].

For PWHB included in the study, we extracted medical records, and they underwent PUSH, a comprehensive abdominal ultrasound by a radiographer and TE on the same day or rarely on separate days. All PWHB were fasting at the time of ultrasound and TE.

Medical records included demographics, HBV treatment history, HIV status (based on HIV-1/2 antibodies), the use of tuberculosis medications or alcohol use, as well as the following lab results: platelets (PLTs), alanine aminotransferase (ALT) and alpha fetoprotein (AFP), HBV viral load and CD4 cells count (in case of HIV positivity). Extracted data were the most recent available within 6 months before PUSH.

A Mindray DP30 device was used for all PUSH and abdominal ultrasounds. Operators performing PUSH, abdominal ultrasound and TE were blinded to patient clinical information besides that the person had HBV infection. Using a standardized form, PUSH operators documented whether the PWHB had cirrhosis and whether they had lesions suspicious for HCC. To monitor fidelity to the PUSH protocol (i.e., three windows, etc.), ultrasound video clips were made periodically, and shared with the trainer for review, who then provided feedback.

Comprehensive ultrasounds were done by radiographers who were licensed by the Health Professionals Council of Zambia, and most were done by a single radiographer who is among the most experienced in the country. With a standardized form, radiographers documented the comprehensive ultrasound, including the presence of steatosis, based on hyperechoic appearance of liver versus right kidney parenchyma, and the LI-RADS (Liver Imaging Reporting And Data System) classification when a tumour/lesion was identified [22].

Liver fibrosis stage was based on median liver stiffness in kPa by TE (Fibroscan 402, Echosens, Paris, France) among 10 valid measures, with the measurement variability assessed by IQR/median ratio of less than 30%.

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

2.4 | Statistical Analysis

During analysis, we excluded any participant missing PUSH or TE data. We summarized the demographic and clinical characteristics of the PWHB, using median and interquartile range for continuous variables and frequencies and percentages for categorical variables. The Mann–Whitney test was used to assess differences between subjects with and without experience of treatment for continuous variables. For categorical data, the Chi-square test or Fisher's exact test was used. The prevalence of each condition (significant fibrosis, cirrhosis and focal liver lesions) was calculated as the proportion of participants confirmed positive by the reference standard, which was TE for significant fibrosis (≥7 kPa) and cirrhosis (>12.5 kPa), and abdominal ultrasound for HCC.

To evaluate PUSH's diagnostic performance, we compared its results with the reference standard using 2×2 tables. From these tables, we calculated sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV), along with exact Binomial 95% confidence intervals to account for the relatively rare occurrence of some conditions. Receiver operating characteristic (ROC) curves were generated, and the area under the ROC curve (AUROC) was used to evaluate the capacity of the test to discriminate between individuals with and without the condition. The AUROC was reported along with its corresponding 95% confidence interval. A multivariable logistic regression analysis was carried out to evaluate whether the PUSH protocol's capacity to predict cirrhosis and liver lesions could be improved by the inclusion of biological sex, HIV status and operator type (doctor or nurse). Comparisons between AUROCs were carried out using the DeLong test. In a subgroup analysis of HIV-negative treatment-naïve individuals, we explored whether PUSH could identify people who needed HBV antiviral therapy but were ineligible based on laboratory tests and TE. We described the proportion of participants eligible to start HBV antiviral therapy based on APRI >0.5, ALT elevation plus HBV DNA >2000 IU/mL or Fibroscan ≥7 kPa, and whether PUSH diagnosis of cirrhosis was made in anyone not meeting these criteria. We performed all analyses using SAS software, version 9.4 (SAS Institute, Cary, NC, USA). To ensure that our findings were robust, reliable and clinically relevant, we adhered to the Standards for Reporting of Diagnostic Accuracy Studies (STARD) guidelines.

3 | Results

3.1 | Characteristics of Participants

After excluding 7 who had missing/incomplete PUSH results and 12 with missing TE results, the analysis cohort comprised 197 PWHB, including 137 on and 60 naïve to antiviral treatment. Median age was 38.1 years (interquartile range, IQR: 34.2–46.1). Overall, age was higher among treatment experienced participants (39.7 years [IQR: 33.1–46.5] vs. untreated participants, 34.2 years [29.8–42.9]); $p=0.011$, and the majority of PWHB were men (111; 56.3%). Hepatitis B infection was diagnosed in a median of 1.8 years prior (IQR: 0.9–5.8 years). Most participants were HIV negative (142, 72.1%). In participants with HBV/HIV, the median CD4 T cell count was 456 cells/mm^3 (IQR: 349–632). ALT levels were available in 148 (75.1%) PWHB with a median ALT levels of 24.6 U/L (IQR: 19.3–33.3). Median ALT was higher in the treatment experienced versus naïve group (25.8 [IQR: 20; 37.8] vs. 22.3 [IQR: 17.4; 30.6]).

The APRI score was calculated for 117 (59.3%) PWHB. Overall, 39 participants had APRI score >0.5 (33.3%), suggestive of significant fibrosis, and 19 had score >1.0 (16.2%), a proxy for cirrhosis. HBV DNA viral loads were available for 104 PWHB. Viral load levels were equally distributed between participants on and not on treatment (Table 1).

3.2 | Reference Standard Measures of Liver Fibrosis and Lesions

The median liver stiffness level in the analysis cohort was 5.3 kPa (IQR: 4.3; 7.5). Among the analysis group, 23 (11.6%) PWHB had cirrhosis (i.e., TE >12.5 kPa) and 30 (17.7%) had significant fibrosis (i.e., ≥7 kPa). Among the comprehensive ultrasound scans done by the radiographer, 7 (3.5%) documented at least one suspicious liver lesion and 8 (4.0%) documented ascites. Among the 7 with lesions, 5 also had available AFP values, all of which were higher than 350 ng/L. Of note, all 7 possible cases of HCC were detected in the context of cirrhosis (i.e., liver stiffness >12.5 kPa). Additional details on the lesions such as diameter, number (single, multiple) and features were not systematically recorded for the purpose this study. Finally, per reference test, steatosis was documented in 21 of 164 (23.8%) ultrasounds.

3.3 | Diagnostic Accuracy of PUSH

PUSH classified 18 individuals with cirrhosis and 9 with liver lesions. For cirrhosis, the test correctly identified 60.9% of cases (sensitivity: 60.9%, 95% CI: 38.5–80.3). Its negative predictive value (NPV) was 95.0% (95% CI: 90.7–97.7; Table 2), and the AUROC for cirrhosis was 0.79 (95% CI: 0.69–0.89; Figure 2A). PUSH identified 85.7% of lesions correctly (sensitivity: 85.7%, 95% CI: 42.1–99.6) and was very reliable for those without lesions, with a NPV of 99.5% (95% CI: 97.1–100.0; Table 3). The AUROC was excellent at 0.92 (95% CI: 0.78–1.00; Figure 2B), indicating strong overall accuracy for detecting lesions. Including age, sex, HIV status, and operator type in the model alongside PUSH significantly improved the ability to predict cirrhosis, with an AUROC of 0.89 (95% CI: 0.79–0.98; $p=0.042$; Figure 3A). However, for liver lesions, the addition of these parameters did not lead to a statistically significant improvement in predictive performance (AUROC = 0.97, 95% CI: 0.91–1.00; $p=0.273$; Figure 3B).

Comparing PUSH findings of cirrhosis to significant fibrosis in LSM (>7.0 to ≤12.5 kPa), PUSH only detected 8.3% of cases (sensitivity: 8.3%, 95% CI: 1.86–23.68) and also had a reduced ability to rule out fibrosis, based on an NPV of 81.8% (95% CI: 75.1–87.3). The overall performance was poor for fibrosis, with an AUROC of 0.54 (95% CI: 0.49–0.59).

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

TABLE 1 | Characteristics of participants.

Characteristics	Total ($N=197$)	Treatment-naïve ($N=60$)	Treatment-experienced ($N=137$)	*p*
N (%)	197 (100.0%)	60 (30.5%)	137 (69.5%)	—
Age (IQR)	38.1 (31.5; 46.1)	34.2 (29.8; 42.9)	39.7 (33.1; 46.5)	0.011
Age group, years (%)				0.273
≤ 29	35 (17.8%)	14 (23.3%)	21 (15.3%)	
30–39	70 (35.5%)	23 (38.3%)	47 (34.3%)	
40–49	60 (30.5%)	17 (28.3%)	43 (31.4%)	
≥ 50	32 (16.2%)	6 (10%)	26 (19%)	
Sex (%)				0.801
F	86 (43.7%)	27 (45%)	59 (43.1%)	
M	111 (56.3%)	33 (55%)	78 (56.9%)	
HBV years (IQR), $n=190$	1.8 (0.9; 5.8)	0.9 (0.8; 1.9)	1.9 (0.9; 7.8)	0.003
Years since HBV diagnosis (%), $n=190$				0.015
< 1	29 (15.3%)	11 (19.6%)	18 (13.4%)	
1–5	110 (57.9%)	38 (67.9%)	72 (53.7%)	
> 5	51 (26.8%)	7 (12.5%)	44 (32.8%)	
HIV coinfection (%)				< 0.001
No	142 (72.1%)	60 (100%)	82 (59.9%)	
Yes	55 (27.9%)	0 (0%)	55 (40.1%)	
CD4, median (IQR) if HIV, $n=14$	456 (349; 632)	—	456 (349; 632)	—
ALT, median (IQR), $n=148$	24.6 (19.3; 33.3)	22.3 (17.4; 30.6)	25.8 (20; 37.8)	0.035
HBV DNA > 2000 U/L (%), $n=104$				0.756
No	72 (69.2%)	16 (66.7%)	56 (70%)	
Yes	32 (30.8%)	8 (33.3%)	24 (30%)	
APRI score, median (IQR), $n=117$	0.38 (0.27; 0.55)	0.35 (0.27; 0.45)	0.41 (0.30; 0.71)	0.070
Ascites by abdominal US				0.725
No	189 (95.9%)	58 (96.7%)	131 (95.6%)	
Yes	8 (4.1%)	2 (3.3%)	6 (4.3%)	

Abbreviations: APRI, AST to Platelet Ratio; IQR, interquartile range; N, number; U/L, unit/Litre; US, ultrasound.

TABLE 2 | PUSH performance for cirrhosis.

Cirrhosis reference	PUSH ultrasound test			Sensitivity (95% CI) [1]	Specificity (95% CI) [1]	PPV (95% CI) [2]	NPV (95% CI) [2]
	# Negative	# Positive	Total				
# Negative	170	4	174		97.7 (94.2, 99.4)		95.0 (90.7, 97.7)
# Positive	9	14	23	60.9 (38.5, 80.3)		77.8 (52.4, 93.6)	

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

Finally, in analysis of the subgroup of 60 PHWB who were HIV-negative and treatment naïve, we observed that 17 (28.3%) were treatment-eligible (WHO 2024 criteria) based on APRI score, TE or elevated ALT and HBV DNA > 2000 IU/mL. By PUSH, 2 of the 17 had cirrhosis. None of the 43 PWHBs who did not have clear indication for treatment had cirrhosis based on PUSH.

4 | Discussion

4.1 | Summary of Key Findings

In a prospective cross-sectional assessment of 197 PWHB at a tertiary clinic in Zambia, 1 in 5 individuals had significant liver

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

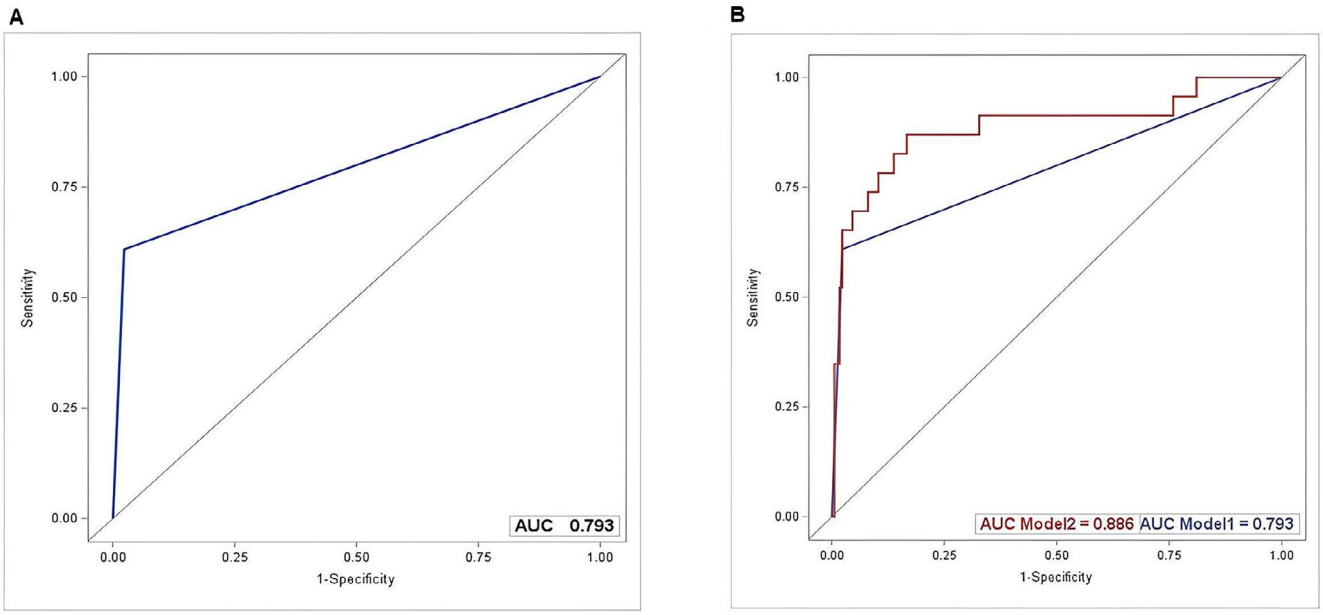


FIGURE 2 | (A) PUSH performance for cirrhosis by ROC curve. (B) PUSH performance for cirrhosis by ROC curve with and without consideration of participants' sex, age, HIV status and PUSH operator type. Model1: Standard accuracy; Model2: Accuracy considering sex, age, HIV status of participants and type of PUSH operator (physician vs. nurse). Abbreviations: AUC, Area under the curve.

TABLE 3 | PUSH performance for liver lesions.

Lesions reference	PUSH ultrasound test			Sensitivity (95% CI) [1]	Specificity (95% CI) [1]	PPV (95% CI) [2]	NPV (95% CI) [2]
	# Negative	# Positive	Total				
# Negative	187	3	190		98.4 (95.5, 99.7)		99.5 (97.1, 100)
# Positive	1	6	7	85.7 (42.1, 99.6)		66.7 (29.9, 92.5)	

Abbreviations: CI, confidence interval; NPV, negative predictive value; PPV, positive predictive value.

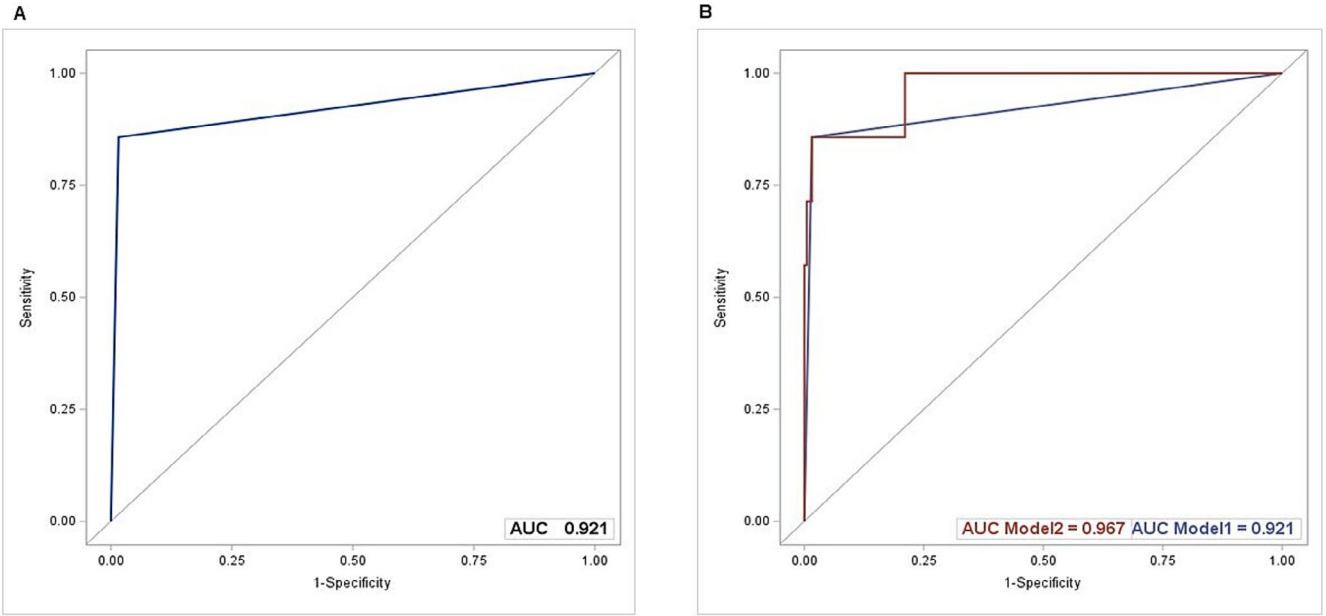


FIGURE 3 | (A) PUSH performance for liver lesions by ROC curve. (B) PUSH performance for liver lesions by ROC curve with and without consideration of participants' sex, age, HIV status and PUSH operator type. Model1: Standard accuracy; Model2: Accuracy considering sex, age, HIV status of participants, and type of PUSH operator (physician vs. nurse). Abbreviations. AUC, Area under the curve.

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

fibrosis, 1 in 10 had cirrhosis and 1 in 20 had at least one liver lesion that was suggestive of HCC. In the hands of front-line physicians and nurses, the PUSH, a novel liver POCUS for people with viral hepatitis, showed varying levels of accuracy depending on the liver condition being assessed. Although limited by small sample size, it performed best for liver lesions suspicious for HCC, identifying 85.7% of cases and correctly ruling out 99.5% of non-cases with its specificity. For cirrhosis, PUSH had moderate accuracy compared to liver stiffness. In exploratory analyses, PUSH had poor accuracy for fibrosis. While not a preferred diagnostic test to make HBV treatment decisions, PUSH may have a role in clinical care where laboratory tests and TE are not routinely available. PUSH may allow clinics to streamline HCC screening.

Our main finding was that new liver POCUS called PUSH, designed for LMICs, was very feasible to use among physicians and nurses managing HBV in Zambia. The training course lasted just 3 days, followed by periodic supervision, which is relatively low cost and could be scaled up in other settings, as had been done for a POCUS to identify TB among people with HIV. In analysis of PUSH performance, there were no significant differences between nurses and physicians. This built on the initial PUSH study and some other studies on POCUS developed in different settings and medical fields such as emergency, neonatal intensive care unit, by nurses and frontline physicians [23–25].

We also demonstrated, using a rigorous study design, that PUSH had moderate performance in diagnosis of cirrhosis. While the prevalence of cirrhosis in the sample was relatively low, making confidence intervals wide, these data support future work on POCUS in the HBV field in many low-resource settings where laboratory services are often lacking and TE is rarely available [26]. B-mode ultrasound is known to be insensitive for cirrhosis (40%–55%) and the PUSH's accuracy aligned with other B-mode ultrasound data generated by experts [27]. That non-specialists could identify cirrhosis PUSH at a similar accuracy to experts may be due to their focus just on one organ system, unlikely what happens in a typical abdominal ultrasound. In the future, PUSH could perform even better, as in our evaluation the trainees had very light (and remote only) supervision after the initial training, limiting their 'learning curve'. We explored but confirmed that PUSH had poor ability to diagnosis significant fibrosis. This was expected as fibrosis has very subtle features on ultrasound. Although these data support PUSH for clinical care in resource-limited settings, in well-resourced sites, TE remains a preferred non-invasive diagnostic to stage liver disease.

We also demonstrated the high potential burden of HCC among people with HBV in Africa as 2.5% of unselected participants presenting to the HBV clinic had a suspicious liver lesion plus high AFP, which is highly suggestive of HCC in the context of chronic HBV infection. PUSH identified these lesions with nearly 90% accuracy, providing support to further exploration of this approach to support HBV programmes. Abdominal ultrasound is the imaging of choice for HCC screening in patients with chronic hepatitis B worldwide [28, 29], and it is proven to reduce HCC mortality in other regions when done every 6 months [30]. Our findings could be considered even more meaningful because data on HCC screening of people with HBV in Africa are scarce, and likely reflect the tiny fraction of people with HBV who are diagnosed and linked to care [31, 32]. In addition, because of gaps in surgical and interventional radiology-based approaches to treat HCC in Africa, early diagnosis is even more paramount.

In addition to demonstrating the feasibility and performance of PUSH for cirrhosis and HCC, we also explored its potential to identify people who need to initiate HBV antiviral therapy under expanded guidelines that were proposed by WHO in 2024. In the limited sample of 60 treatment-naïve individuals with HBV monoinfection, of whom ~20% met treatment criteria per new WHO guidelines, only two had cirrhosis per PUSH. This suggested that PUSH may not be able to substitute for the 2024 criteria, likely because they focus on fibrosis, and as mentioned, B-mode ultrasound is not reliable to detect liver fibrosis [33, 34]. However, in a setting where neither lab nor elastography were available, which occurs often in resource-constrained settings, PUSH alone could classify some individuals as needing immediate therapy, and often compensated cirrhosis can be subtle to detect.

These data are important for several reasons. First, there are major gaps in classifying treatment eligibility in the HBV field overall, particularly in LMICs, and novel approaches such as POCUS are needed. There is also a need to improve HCC screening and ascertainment globally but particularly in Africa, where HCC is the first cause of cancer death among men and yet data are severely lacking when compared to other cancers. With a POCUS protocol, a clinic could both assess treatment eligibility for treatment and do HCC screening, without the need to refer people to other departments or health facilities for initial detection. PUSH could, for example, bring HCC screening to rural areas, where the cancer risk may be even higher than urban ones. Diagnosis of HCC is important even if treatment options are generally limited in Africa compared to high income countries [35] because African countries are increasingly offering treatments [36], and capacity in hepatobiliary surgery and interventional radiology is rapidly growing. Also, screening and follow-up could bring more accurate estimates of the prevalence of this cancer, which are lacking, and give to some patients access to medical counselling and better palliative care, even if not receiving curative treatment. In general, the use of the PUSH protocol could be tailored to the characteristics and needs of each specific low-income setting, and all these implementation advantages may offset the diagnostic limitations of POCUS compared to gold standard tests. Finally, the moderate-good accuracy of the liver POCUS in a low-income setting, using newly and minimally trained nurses and doctors, is very encouraging for this field.

4.2 | Strengths and Limitations

This study had several notable strengths. Importantly, we blinded PUSH operators to participants' clinical information, providing an unbiased evaluation. We also included both nurses and physicians (40% and 60% of the operators respectively) without past ultrasound experience as PUSH operators and a representative sample of people with HBV, treated and untreated and with and without HIV, a major coinfection that accelerates liver disease. Moreover, we exclusively used facilities and devices which were already available in our setting and time dedicated to training was short and effective, so that the implementation

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

of PUSH did not negatively impact the usual workflow at the clinic. Because of these reasons, in our study setting we can consider PUSH as a cost-effective and acceptable add to the normal clinical practice in public hospitals in Africa.

Nevertheless, the study had several limitations as well. First, fibrosis, cirrhosis and lesions were relatively uncommon; this inevitably led to larger confidence intervals for performance tests. Second, the reference standards we used had limitations of their own. For cirrhosis, liver biopsy is the gold standard, not elastography; however, it was not possible to have biopsies because of the cost and clinical indication. While the radiographer's ultrasounds can be considered the gold standard to detect liver lesions in this geographical area, the international gold standard would be a CT scan. Another limitation was that we did not systematically document the size and characteristics of lesions seen on PUSH or standard ultrasound. Anecdotally, lesions were large; therefore, whether PUSH can identify lesions that are small and more amenable to treatment was not established. Lesions suspicious for HCC were not confirmed to be HCC using multiphase CT or MRI, which limits our confidence in this aspect of PUSH. Finally, most participants were already on treatment and had been in care for several years, and this factor influenced partially the accuracy of TE evaluations. Those not on treatment had minimal cirrhosis. Therefore, we could not comment on using PUSH alone versus or in combination with laboratory tests to determine treatment eligibility.

4.3 | Implications—For Further Research, Practice, and/or Policy

In the future, liver POCUS protocols for HBV care should be further improved and developed. For example, the development of the protocol could be advanced by studying its performance in different settings, especially with lower resources than those we had in Zambia's capital city, and on populations with different environmental risk factors. In order to improve PUSH, an analysis of the pathological characteristics of the liver which are most difficult to recognize for operators could lead to adjustments in the training phase and/or to effective modifications of the form questions. Also, access to clinical information could be allowed during routine examinations and could improve performance. We also have to consider that AI is spreading across the world in every field of knowledge and is also reaching Africa [37]. It could further improve POCUS like the PUSH, and simple POCUS protocols could soon be performed by operators with little experience in ultrasound, just like in our study, but supported with AI technology to diagnose any kind of liver lesion and effectively recognize cirrhosis. This could implement HBV care and healthcare in general in Africa's rural areas where physicians are few [38]. Finally, PUSH could hopefully be part of a management algorithm for chronic hepatitis B patients, as it already represents a valuable chance for screening and decision for treatment in Sub Saharan Africa and other resource-limited countries.

5 | Conclusion

Nurses and physicians working at a hepatitis clinic in Zambia were trained on a new point-of-care ultrasound protocol for hepatitis, called PUSH. Thereafter, in a blinded evaluation, they were able to identify cirrhosis and liver lesions suspicious for HCC with moderate and high accuracy, respectively, supporting the need to further develop liver POCUS for the management of HBV, particularly in LMICs and challenging settings within rich countries too.

Funding

This study was funded by the U.S. National Institutes of Health via grants R01AI147727 and R37AI179640.

Ethics Statement

The study was approved by the University of Zambia Biomedical Research Ethics Committee. A waiver of informed consent was obtained for analysis of the data, which were collected as part of routine care.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

References

1. World Health Organization, "HIV Statistics, Globally and by WHO Region," (2023), https://cdn.who.int/media/docs/default-source/hq-hiv-hepatitis-and-stis-library/j0294-who-hiv-epi-factsheet-v7.pdf.

2. World Health Organization, "WHO Global Hepatitis Report 2024," (2024), https://www.who.int/publications/i/item/9789240091672.

3. C. W. Spearman, M. I. Andersson, B. Bright, et al., "A New Approach to Prevent, Diagnose, and Treat Hepatitis B in Africa," *BMC Global and Public Health* 1 (2023): 24.

4. B. Surial, D. Wyser, C. Béguelin, A. Ramírez-Mena, A. Rauch, and G. Wandeler, "Prevalence of Liver Cirrhosis in Individuals With Hepatitis B Virus Infection in Sub-Saharan Africa: Systematic Review and Meta-Analysis," *Liver International* 41 (2021): 710–719.

5. S. O. Aremu, A. I. Adamu, B. Fatoke, et al., "Challenges to Implementing Mandatory Hepatitis B Vaccination: Bridging Immunization Gaps Among Health Workers in Sub-Saharan Africa," *Tropical Medicine and Health* 53, no. 1 (2025): 35.

6. N. Riches, M. Y. R. Henrion, P. MacPherson, et al., "Vertical Transmission of Hepatitis B Virus in the WHO African Region: A Systematic Review and Meta-Analysis," *Lancet Global Health* 13, no. 3 (2025): e447–e458.

7. World Health Organization, "Guidelines for the Prevention, Diagnosis, Care and Treatment for People With Chronic Hepatitis B Infection," (2024).

8. N. Minier, A. N. Guingané, E. Okeke, et al., "Development and Evaluation of a Simple Treatment Eligibility Score (HEPSANET) to Decentralise Hepatitis B Care in Africa: A Cross-Sectional Study," *Lancet Gastroenterology & Hepatology* 9, no. 4 (2024): 323–332.

9. P. G. Newman and G. S. Rozycki, "The History of Ultrasound," *Surgical Clinics of North America* 78, no. 2 (1998): 179–195.

10. S. R. Wilson, "Ultrasound: Novel Techniques," *Abdominal Radiology* 43 (2018): 761.

11. S. Sharma, K. Khalili, and G. C. Nguyen, "Non-Invasive Diagnosis of Advanced Fibrosis and Cirrhosis," *World Journal of Gastroenterology* 20, no. 45 (2014): 16820–16830.

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License

12. K. Tzartzeva, J. Obi, N. E. Rich, et al., "Surveillance Imaging and Alpha Fetoprotein for Early Detection of Hepatocellular Carcinoma in Patients With Cirrhosis: A Meta-Analysis," *Gastroenterology* 154, no. 6 (2018): 1706–1718.

13. D. Ruan, Y. Shi, L. Jin, et al., "An Ultrasound Image-Based Deep Multi-Scale Texture Network for Liver Fibrosis Grading in Patients With Chronic HBV Infection," *Liver International* 41 (2021): 2440–2454.

14. Zambia. Ministry of Health, "Zambia Population-Based HIV Impact Assessment: ZAMPHIA 2016—Summary Sheet," (2019).

15. Zambian Ministry of Health, "Implementation Framework & Clinical Guidance for Viral Hepatitis Prevention & Treatment," (2019).

16. World Health Organization, "Guidelines for the Prevention, Diagnosis, Care and Treatment for People With Chronic Hepatitis B Infection," (2015).

17. T. Heller, V. Phiri, T. Kumwenda, et al., "Point-Of-Care Ultrasound to Inform Antiviral Treatment Initiation in Chronic Hepatitis B Virus Infection in Low-Resource Settings - The PUSH Protocol," *Ultrasound Journal* 16, no. 1 (2024): 18.

18. S. Belard, F. Taccari, T. Kumwenda, M. A. M. Huson, C. Wallrauch, and T. Heller, "Point-Of-Care Ultrasound for Tuberculosis and HIV-Revisiting the Focused Assessment With Sonography for HIV-Associated Tuberculosis (FASH) Protocol and Its Differential Diagnoses," *Clinical Microbiology and Infection* 30, no. 3 (2024): 320–327.

19. T. Heller, C. Wallrauch, R. Lessells, S. Goblirsch, and E. Brunetti, "Short Report: Short Course for Focused Assessment With Sonography for Human Immunodeficiency Virus/Tuberculosis: Preliminary Results in a Rural Setting in South Africa With High Prevalence of Human Immunodeficiency Virus and Tuberculosis," *American Journal of Tropical Medicine and Hygiene* 82 (2010): 512–515.

20. T. Heller, C. Wallrauch, S. Goblirsch, and E. Brunetti, "Focused Assessment With Sonography for HIV-Associated Tuberculosis (FASH): A Short Protocol and a Pictorial Review," *Critical Ultrasound Journal* 4, no. 1 (2012): 21.

21. M. P. Manns, "Hepatitis D Virus in Africa: Several Unmet Needs," *Lancet Global Health* 5, no. 10 (2017): 953–954.

22. C. Riebensahm, H. Chitundu, G. Muula, et al., "Screening for Hepatocellular Carcinoma Among Adults With HIV/HBV Co-Infection in Zambia: A Pilot Study," (2022).

23. S. Kalam, N. Selden, K. Haycock, T. Lowe, H. Skaggs, and V. A. Dinh, "Evaluating the Effect of Nursing-Performed Point-Of-Care Ultrasound on Septic Emergency Department Patients," *Cureus* 15, no. 6 (2023): e40519.

24. J. H. Tong, C. Manipon, S. Vallandingham-Lee, R. Dasani, A. S. Davis, and S. Bhombal, "The Role of Neonatal Nurse Practitioners in the Implementation of a Bedside Point-Of-Care Ultrasound Program," *Advances in Neonatal Care* 24, no. 6 (2024): 536–543.

25. L. Shaddock and T. Smith, "Potential for Use of Portable Ultrasound Devices in Rural and Remote Settings in Australia and Other Developed Countries: A Systematic Review," *Journal of Multidisciplinary Healthcare* 15 (2022): 605–625.

26. M. W. Sonderup, P. S. Kamath, Y. A. Awuku, et al., "Managing Cirrhosis With Limited Resources: Perspectives From Sub-Saharan Africa," *Lancet Gastroenterology & Hepatology* 9, no. 2 (2024): 170–184.

27. A. Smith, K. Baumgartner, and C. Bositis, "Cirrhosis: Diagnosis and Management," *American Family Physician* 100, no. 12 (2019): 759–770.

28. H. B. El-Serag and J. A. Davila, "Surveillance for Hepatocellular Carcinoma: In Whom and How?," *Therapeutic Advances in Gastroenterology* 4, no. 1 (2011): 5–10.

29. Q. Wan, C. Anugwom, H. Desalegn, and J. D. Debes, "Hepatocellular Carcinoma in Hepatitis B and Human Immunodeficiency Virus Coinfection in Africa: A Focus on Surveillance," *Hepatoma Research* 8 (2022): 39.

30. B. H. Zhang, B. H. Yang, and Z. Y. Tang, "Randomized Controlled Trial of Screening for Hepatocellular Carcinoma," *Journal of Cancer Research and Clinical Oncology* 130, no. 7 (2004): 417–422.

31. J. S. Ford, J. Kayandabila, J. C. Morrison, et al., "Combined Hepatitis B Virus and Hepatocellular Carcinoma Screening Using Point-Of-Care Testing and Ultrasound in a Tanzanian Emergency Department," *American Journal of Tropical Medicine and Hygiene* 110, no. 2 (2024): 399–403.

32. N. Shankar, L. Kuo, N. K. Cleveland, et al., "Point-Of-Care Ultrasound in Gastroenterology and Hepatology," *Clinical Gastroenterology and Hepatology* 23 (2025): 1277–1290.

33. M. Virarkar, A. C. Morani, M. W. Taggart, and P. Bhosale, "Liver Fibrosis Assessment," *Seminars in Ultrasound, CT, and MR* 42, no. 4 (2021): 381–389.

34. R. N. Karanjia, M. M. Crossey, I. J. Cox, et al., "Hepatic Steatosis and Fibrosis: Non-Invasive Assessment," *World Journal of Gastroenterology* 22, no. 45 (2016): 9880–9897.

35. S. Sobnach, U. Kotze, C. W. Spearman, et al., "The Management and Outcomes of Hepatocellular Carcinoma in Sub-Saharan Africa: A Systematic Review," *HPB* 26 (2024): 21–33. ISSN 1365-182X.

36. G. K. Abou-Alfa, M. Afihene, M. Capanu, et al., "Africa Guidelines for Hepatocellular Carcinoma Buildup Process," *JCO Global Oncology* 9 (2023): e2300159.

37. R. Nuwer, "Why AI Might Be a Game-Changer for Africa," *Nature* 633, no. 8030 (2024): S12–S14.

38. S. Kazemzadeh, J. Yu, S. Jamshy, et al., "Deep Learning Detection of Active Pulmonary Tuberculosis at Chest Radiography Matched the Clinical Performance of Radiologists," *Radiology* 306, no. 1 (2023): 124–137.

13652893, 2026, 9, Downloaded from https://onlinelibrary.wiley.com/doi/10.1111/jvh.70216 by University of Ghana - Accra, Wiley Online Library on [01/09/2026]. See the Terms and Conditions (https://onlinelibrary.wiley.com/terms-and-conditions) on Wiley Online Library for rules of use; OA articles are governed by the applicable Creative Commons License