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MAJOR ARTICLE

Impact of Hepatitis B Virus Point-of-care DNA Viral Load Testing Compared With Laboratory-based Standard-of-care Approaches on Uptake of HBV Viral Load Testing, Treatment, and Turnaround Times: A Systematic Review and Meta-analysis

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Background. Point-of-care (PoC) hepatitis B virus (HBV) DNA viral load (VL) assays represent an alternative to laboratory-based standard-of-care (SoC) VL assays to accelerate diagnosis and treatment. We evaluated the impact of using PoC versus SoC approaches on the uptake of VL testing, treatment, and turnaround times from testing to treatment across the HBV care cascade.

Methods. We searched 5 databases, 6 conference websites, and contacted manufacturers for unpublished reports, for articles with or without a comparator (SoC VL testing), and had data on the uptake of VL testing, treatment, or turnaround times between hepatitis B surface antigen (HBsAg) testing, VL testing, and treatment in the cascade. We performed a random-effects meta-analysis on rates of VL testing and treatment initiation.

Results. Six studies, composing 9 arms, were included. Three PoC arms reported less than 1 day between screening for HBsAg positivity and VL testing, and the other one (2 arms) reported it between 7 and 11 days. Five arms reported the time to available VL test results (<1 day). Three studies reported 1–8 days between VL testing results and treatment initiation. Two studies reported the turnaround times between a positive HBsAg screening and treatment initiation (the same day and 27 days). Overall, 84.1% of those with HBsAg positivity were tested for DNA VL and 88.3% of eligible people initiated treatment.

Conclusions. HBV PoC DNA testing appears to be associated with a turnaround time of <1 day for receipt of VL results and appears associated with high rates of DNA testing and initiation of treatment among those eligible.

Clinical Trials Registration. PROSPERO CRD42023398440.

Keywords. hepatitis B virus; point-of-care; viral load; systematic review; meta-analysis.

Chronic hepatitis B virus (HBV) infection is a major global public health problem with significant morbidity and mortality [1–3]. According to the most recent estimate from the World Health Organization (WHO), there were 296 million people chronically infected with HBV in 2019, and approximately 800,000 deaths and 1.5 million new infections annually [4]. Efforts to eliminate viral hepatitis, particularly HBV, have gained momentum globally and at the national level. In China, with the expansion of the hepatitis B vaccine, the coverage of the 3 doses of the vaccine increased from 30% in 1992 to 99% in 2015 [5]. The prevalence of hepatitis B surface antigen (HBsAg) among the population younger than 30 years of age dropped from 10.1% in 1992 to 2.6% in 2014. The incidence of HBV infection in children younger than 5 years old decreased from 10% in the 1990s to 0.3% in 2014 [6]. The United States National Viral Hepatitis Action Plan aims at reducing new hepatitis infections and improving access to care and treatment for those living with viral hepatitis. However, there remains a major testing and treatment gap, with only

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10% of those with chronic HBV infection diagnosed and 2% treated globally [4], which overshadows the project of "the elimination of viral hepatitis as a global health threat by 2030" launched by WHO [7].

The primary diagnosis of chronic HBV is based on a positive HBsAg test. However, HBV DNA quantification is critical for determining eligibility for treatment, antiviral prophylaxis for prevention of mother-to-child transmission, and treatment monitoring [8, 9]. WHO guidelines [10] and other professional society guidelines [8, 11–14] recommend using a sensitive nucleic acid amplification test (NAAT) laboratory assay to quantify HBV DNA. However, in many low- and middle-income countries (LMICs), particularly in Africa, there is limited access to laboratory-based HBV DNA assays [15] because of high costs and requirements for specialized infrastructure, trained personnel, and a sample transport system. This has been a major barrier to more widespread uptake and initiation of HBV treatment. There is high-quality evidence of the clinical impact of point-of-care (PoC) assays for HIV viral load (VL) monitoring [16], HIV early infant diagnosis [17], tuberculosis diagnosis [18, 19], and hepatitis C virus (HCV) VL testing [20]. A systematic review of 45 studies found that PoC testing for HCV RNA VL was associated with reduced turnaround time from antibody test to treatment initiation and increased RNA testing and treatment uptake compared with laboratory-based RNA testing. PoC HCV VL assays also demonstrated excellent diagnostic performance relative to laboratory-based assays for both confirmations of viremia and as a test of cure and populations [21]. A high correlation between the laboratory-based Roche Cobas HBV VL tests and the PoC Xpert HBV VL Assay has been demonstrated, allowing for rapid, random access, and accurate assessment of HBV VL testing [22]. However, there are limited data and no previous systematic review on using PoC HBV DNA assays to promote access to HBV DNA quantification to determine treatment eligibility and uptake. This represents a particular opportunity with the increasing availability of these PoC platforms for use in HIV and tuberculosis care and during the COVID pandemic [23].

We undertook a systematic review and meta-analysis to evaluate the impact of using PoC HBV VL assays compared to laboratory-based standard-of-care (SoC) assays on HBV DNA testing and treatment uptake and turnaround times to DNA VL test and treatment initiation among HBsAg-positive people.

METHODS

The study was registered with PROSPERO, CRD42023398440, and it was conducted by following the guidelines of the Cochrane handbook.

Search Strategy and Selection Criteria

We searched PubMed, Scopus, Embase, WHO Global Index Medicus, and Global Health (EBSCOhost) and 3 China databases (CNKI, CQVIP, WANFANG DATA) for studies published before 10 January 2024 for observational (retrospective or prospective longitudinal cohorts or case series) and randomized controlled trials or single-arm nonrandomized controlled trials, that used PoC HBV DNA VL assays with or without a comparator laboratory-based SoC assay and contained data on outcomes across the HBV cascade of care and turnaround times. The reference lists of all retrieved articles were reviewed for additional relevant studies [24–29]. We also searched for conference abstracts (2020–2023) from six key hepatitis conferences (the American Association for the Study of Liver Diseases, Asian Pacific Association for the Study of the Liver, African Society of Laboratory Medicine, European Association for the Study of the Liver, and the International Network on Health and Hepatitis in Substance Users, and American Society For Microbiology conference). We also contacted people in the WHO Global Hepatitis Programme to solicit additional studies (completed and ongoing) on PoC HBV DNA assays, including manufacturers of PoC tests. The population, intervention, comparator, and outcome questions and search strategy are described in Supplementary Tables 1 and 2.

For the main search and studies identified through WHO partners, Y.D., C.F., F.L., and Y.T. conducted the search and independently evaluated articles (first the titles and abstracts and then the full texts of those selected from the title and abstract screening) for eligibility, and W.T. reviewed the final selection and arbitrated on differences between the primary reviews. Manuscript references were checked by Y.D. and C.F., with W.T. arbitrating selection differences.

The main intervention group used a PoC HBV DNA assay (PoC group), and the comparator group (if available) used a centralized, laboratory-based assay (non-PoC group). As in our prior PoC HCV RNA systematic review, the PoC HBV DNA viral load assay intervention was further categorized according to whether the PoC assay was used onsite (PoC onsite) or in a mobile unit (PoC mobile, defined as units that were not fixed to a particular site) or in a laboratory [20]. In addition, studies were further stratified into 4 models of care, according to whether HBV testing and treatment initiation were performed in the same or different sites and whether testing and treatment initiation were performed on the same or a different visit.

Data Analysis

For each study, data were extracted by C.F., Y.D., and F.L. using a standardized data extraction form and checked by S.G. and Y.T. Data extracted were country, setting, population type, population characteristics (mean or median age and percentage of female), study design, and publication type. Study authors

were contacted when necessary to clarify results or provide further information and data.

The outcomes were turnaround time in days from HBsAg test to HBV DNA VL test, HBV DNA VL sample collection to testing, HBV DNA VL test to results being made available to the patient, HBV DNA VL test to treatment initiation, and overall time from HBsAg test to treatment initiation.

Because of the lack of direct head-to-head comparative evidence, we focused on noncomparative data from people who underwent PoC VL testing. Y.D. and C.F. assessed the risk of bias for each study using a previously published tool [30] for observational studies that reported binary outcomes (Supplementary method and Supplementary Table 3). The certainty of evidence was assessed using the Grading of Recommendations Assessment, Development, and Evaluation framework, based on the risk of bias, consistency of results, directness of evidence, precision of estimates, and reporting bias [31]. The evidence for estimated turnaround times and rates of uptake began as low certainty for noncomparative outcomes. For imprecision, we downgraded 1 level if the difference between the upper and lower limits of the pooled confidence interval (CI) was greater than 10%; for reporting bias, we downgraded 1 level if reporting bias was suspected; for risk of bias, we downgraded 1 level if the evidence was assessed as having an overall moderate risk of bias; and we downgraded 2 levels for overall high risk of bias. For indirectness, we downgraded 1 level for indirectness in populations or outcomes. Based on our evaluations of these domains, we graded the certainty for each body of evidence as high, moderate, low, or very low. For the pooling of the results, we determined that there is heterogeneity across studies if $I^2 > 75\%$.

RESULTS

We identified 2490 deduplicated citations from the database search, 25 studies from searching reference lists and conference abstracts and querying manufacturers. After removing duplicates, there were 1390 citations. After title and abstract screening, 57 studies were assessed for eligibility. The majority of these studies (n = 50) were excluded, and most (n = 46) were excluded because they lacked PoC assay or no test for DNA viral load. Ultimately, 6 studies [24–29], composing 9 arms (N = 9029), were included (Figure 1).

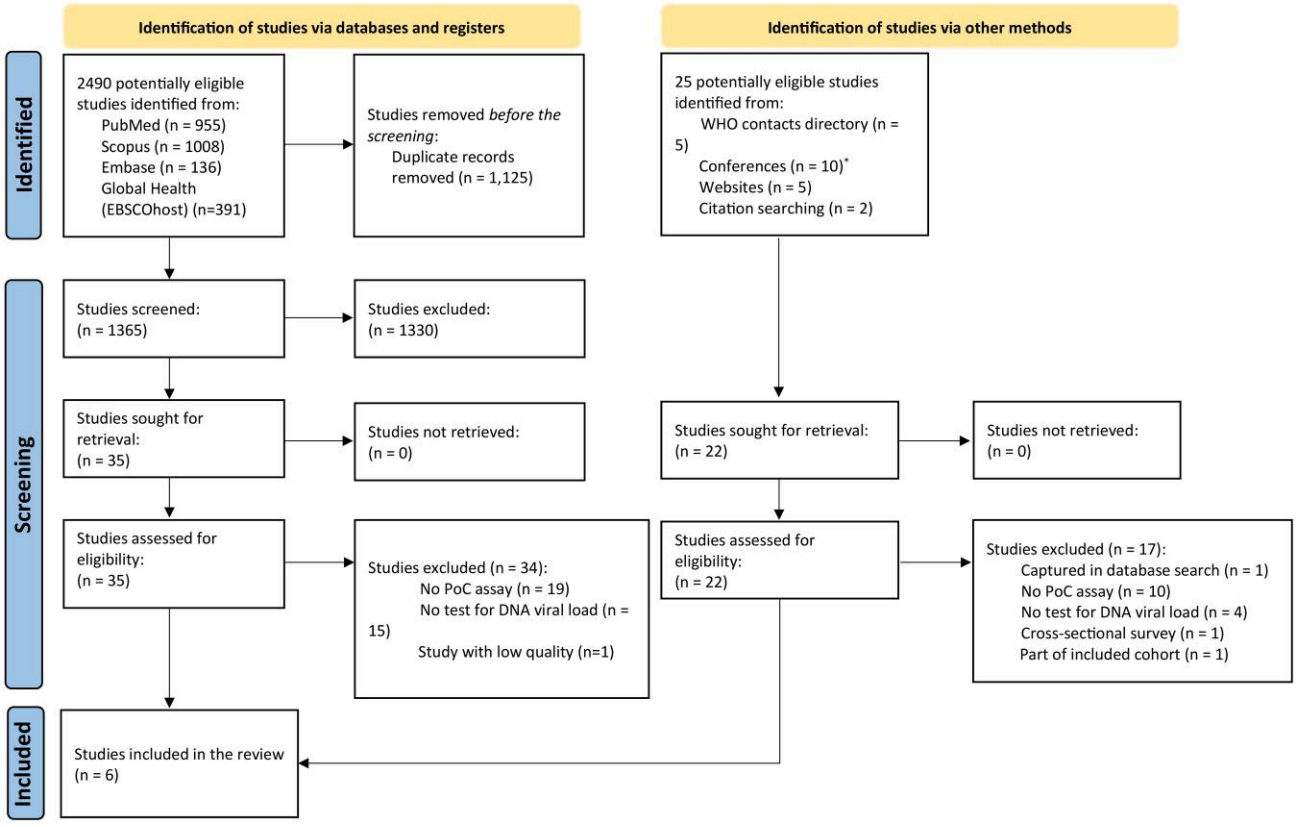

Figure 1. Flow diagram of study inclusion. *International Liver Conference 2020–2022, the International Network on Hepatitis in Substance Users symposia 2019, 2021, 2022, and the International Viral Hepatitis Elimination Meeting 2020–2022, American Association for the Study of Liver Diseases The Liver Meeting 2023, American Society for Microbiology 2020–2023.

Table 1. Characteristics of 6 Included Studies

Study	Study Population	Setting	City or Region, Country	Study Periods	Design	PoC Platform	Study Source	Number of Study Arms	Number of Populations	Study Group or Subgroup (Model of Care[b])	Risk of Bias[c]
Johannessen A et al (2023)[a]	General population	Hospital	Four sites outside Addis Ababa, Ethiopia (PoC)/ Addis Ababa, Ethiopia (non-PoC)	Non- PoC: 2015; PoC: 2021/12	Prospective	Xpert	WHO contacts directory	2	Non-PoC: 1303; PoC: 2794	Same site, different visit	Medium
Kachimanga C et al (2020)	Medical students	Separate venue away from the college campus	Freetown, Sierra Leone	2019/12	Prospective	Xpert	Additional search through Google website	1	203	Different site, different visit	Medium
Kawana W et al (2022)	Treatment-naïve patients with HBV	Public referral hospital's HIV clinic	Lusaka, Zambia	2021/9–2022/6	Prospective	Xpert	Conference abstract search	1	311	Same site, different visit	Low
Nyama ET et al (2023)	The general population (17 were pregnant)	Hospital HBV clinic	Kono District, Sierra Leone	2019/4–2021/4	Retrospective cohort	Xpert	WHO contacts directory	1	623	Different site, different visit	High
Shiha G et al (2020)	General population	Community (pop-up clinic)	Egypt	Site 1: 2018/10; site 2: 2018/12	Prospective	Xpert	Main database search	2	Site 1:475; Site 2: 3188	Same site, same visit	Low
Ndow G et al (2023)	General population	Hospital HBV clinic	Gambia	2023/3–2023/4	Prospective	Xpert	WHO contacts directory	2	Plasma: 90; DBS: 42	Same site, different visit	Medium

Abbreviations: HBV, hepatitis B virus; PoC, point of care.

Study source refers to how the study was identified: through the main database search strategy (PubMed, Scopus, Embase, WHO Global Index Medicus, and Global Health (EBSCOhost)), from the conference abstract search (the American Association for the Study of Liver Diseases (AASLD), Asian Pacific Association for the Study of the Liver (APASL), African Society of Laboratory Medicine (ASLM), European Association for the Study of the Liver (EASL), and the International Network on Health and Hepatitis in Substance Users (INHSU)), through the additional search on Google website, or contacts directory the WHO Global Hepatitis Programme.

[a]Marked as with a comparison arm.

[b]Same site, same visit refers to testing and treatment initiation at the same site and on the same visit; same site, different visit refers to testing and treatment initiation at the same site but treatment initiation on a different visit; different site, same visit refers to testing at one site with referral to another site for treatment initiation on the same visit; and different site, different visit refers to testing and treatment initiation at different sites and on different visits.

[c]Risk of bias was assessed for each study using a previously published and modified risk of bias tool used for observational studies that report binary outcomes based on tools by Hoy and colleagues and the ROBINS-I tool.

Table 2. Study Characteristics of the 6 Included Studies

Study Characteristics	Overall (n = 6)
Studies from LMICs (from World Bank 2021)[a]	6 (100.0%)
No. of studies with a non-PoC testing comparator arm[‡]	1 (16.7%)
Study Population	
General population, 4 (66.7%)	
Medical students, 1 (16.7%)	
Treatment-naïve patients with HBV, 1 (16.7%)	
WHO region	
Africa (Ethiopia, Sierra Leone [2], Zambia, Gambia)	5 (83.3%)
Eastern Mediterranean (Egypt)	1 (16.7%)
PoC studies by the model of care	
With VL testing and treatment in the same site on the same visit	1 (1)
With VL testing and treatment in the same site on the different visit	3 (3)
With VL testing and treatment in the different site on the same visit	0 (0)
With VL testing and treatment in the different site on the different visit	2 (2)
Location of PoC instrument	
Laboratory	4 (3)
Mobile	3 (2)
Clinic	1 (1)
Cascade outcomes available for the 10 HBV PoC assay arms	
HBsAg tested	3 (2)
HBV DNA tested	8 (6)
Linkage to care	2 (2)
Initiated treatment	8 (6)
Cascade turnaround time data available	
Time to DNA viral load test from screened HBsAg positive	5 (3)
Time between DNA test and result available	5 (3)
Time to treatment from DNA test results available	4 (3)
Time to treatment from screened HBsAg positive	3 (2)

Data are n (%).

HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; LMIC, low- and middle-income country; PoC, point-of-care; VL, viral load.

[a]LMIC as classified by the WorldBank in 2021; for this review, the LMICs where studies took place were Ethiopia, Sierra Leone, Zambia, Gambia, and Egypt.

Study Characteristics

Table 1 summarizes key study characteristics. Of the 6 included studies, 4 were in the general population [24, 27–29]; 1 study was among people with chronic hepatitis B infection and 1 was conducted among medical students. Five studies (83.3%) were based in Africa and 1 (16.7%) in the Middle East (Table 2). All studies were in LMICs. Five were prospective and 1 was retrospective. There was only 1 study with a non-PoC comparator arm [24]. Five studies had PoC assays on site, 2 mobile and 3 laboratory-based. The most common model of care for the 9 PoC (onsite and mobile) arms and the 1 laboratory-based SoC arm was at the same site for testing and treatment but at different visits (Table 3). Four studies (6 arms) reported turnaround times for at least 1 step of the HBV cascade, including uptake of viral load testing, treatment, or both.

Table 1 to 5 summarizes the different PoC and SoC groups, model-of-care category, and available outcome data for VL testing and treatment uptake and turnaround times for each study.

Turnaround Times Across Cascade of HBV Care (Tables 3 and 4)

Four studies reported the time across different steps of the HBV care cascade [24, 27, 28]. Three studies (5 arms) reported the time between screened HBsAg-positive and DNA VL tests [23–26]. Of these, 2 studies (3 arms) reported a turnaround time of less than 1 day [27, 28], and the other 1 (2 arms) reported a turnaround time between 7 and 11 days [29]. Of the 3 studies (5 arms) reporting data on PoC DNA VL testing, the time to available DNA VL test results was less than 1 day. Of the 3 studies reporting data on treatment initiation, the turnaround time from receipt of DNA testing results to treatment initiation ranged from 1 to 8 days. The overall turnaround time between a positive HBsAg test and treatment initiation was less than 1 day in 1 study

Table 3. Time Between key Steps in the HBV Cascade of Care for Each of the 7 HBV DNA PoC Testing Studies With Time Data Available

Study	Model of Care	City or Region, Country	Screened HBsAg Positive to DNA Viral Load Test	DNA Test to Results Made Available	DNA Test Results Available to Treatment Start	Screened HBsAg Positive to Treatment Start
Johannessen A et al (2023)	Same site, different visit	Four sites outside Addis Ababa, Ethiopia	…	1 d	1 d (IQR 0–7)	…
Nyama ET et al (2022)	Different site, different visit	Kono District, Sierra Leone	Same day	…	…	…
Shiha G et al (2020) (Site with GeneXpert 16 cartridge)	Same site, same visit	Dakahlia, Egypt	At the same time	105 min	40 min	Three h, 25 min
Shiha G et al (2020) (Site with GeneXpert 4 cartridge)	Same site, same visit	Cairo, Egypt	At the same time	105 min	1 d	…
Ndow G et al (2023) (Plasma)	Same site, different visit	Gambia	11 d (IQR: 4.5–19.3)	57 min (IQR: 56–57)	5–8 d	24–27 d
Ndow G et al (2023) (dried blood spots)	Same site, different visit	Gambia	7 d (IQR: 0–17)	57 min (IQR: 56–57)	5–8 d	24–27 d
Weighted median (IQR) of the median days between cascade steps		…	0 (0–0) d	0 (0–0) d	1 (1–1) d	25 (25–25) d

d, day; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; IQR, interquartile range; m, minute; PoC, point-of-care.

Table 4. Time Between key Steps in the HBV Cascade of Care for the one HBV DNA Non-PoC Testing Studies With Time Data Available

Study	Model of Care	City or Region, Country	Screened HbsAg Positive to DNA Viral Load Test	DNA Test to Results Made Available	DNA Test Results Available to Treatment Start	Screened HbsAg Positive to Treatment Start
Johannessen A, 2023	Same site, different visit	Addis Ababa, Ethiopia	N/A	2 wk to 2 mo	26 d (IQR 8–89)	N/A

HBV, hepatitis B virus; IQR, interquartile range; N/A, not available; PoC, point-of-care.

and 27 days in another study. Comparative information for non-PoC testing was limited. One study reported a turnaround time between 2 weeks and 2 months from the DNA VL test to available DNA VL test results and 26 days from receipt of DNA testing results to treatment initiation [24]. The quality of evidence was rated as very low (Supplementary Table 4).

Uptake of HBV DNA Viral Load and Treatment Initiation (Table 5)

Among 3820 screened persons, the percentage HBsAg positive was 2.6% (95% CI, 0.3–6.8) in 2 studies (3 arms) [25, 28]. The percentage of those HBsAg positive (n = 3061) who had a PoC HBV DNA VL test was 84.1% (95% CI, 41.5–100.0) in 4 studies (5 arms) [24–26, 28]. The pooled percentage of people with a detectable HBV DNA VL among the 564 who had HBV DNA testing was 91.5% (95% CI, 71.9–100.0) in 4 studies (6 arms) [24–26, 28]. Among these patients, the viral load was <2000 IU/mL in 68.1% (384); 2000–20 000 IU/mL in 14.2% (80); and >20 000 IU/mL in 10.5% (59). The pooled estimate for the proportion of patients who were deemed eligible for treatment among those with detectable HBV DNA VL (n = 536) was 23.2% (95% CI, 7.0–43.9) in 4 studies (5 arms) [25, 27–29]. The percentage of people who initiated treatment among those assessed as eligible for treatment (n = 203) was 88.3% (95% CI, 65.8–100.0) in 5 studies (7 arms) [25–29]. The quality of evidence was rated as low (Supplementary Table 5). Overall, there was a high degree of heterogeneity across studies within each model-of-care category ($I^2 > 75\%$) for all outcomes and across all categories.

DISCUSSION

This is the first global systematic review and meta-analysis to examine the effectiveness of PoC HBV DNA viral load testing as a diagnostic alternative to centralized, laboratory-based viral load assays to confirm the presence of HBV DNA. Only 6 studies met the eligibility criteria. There were several key findings in our analysis. First, the time between a PoC HBV DNA test and the available results was short, ranging from 1 hour to 1 day. Second, studies indicate a high rate of HBV DNA VL testing among HBsAg-positive individuals and a high rate of treatment initiation among those who qualify for treatment. These findings suggest that despite the lack of comparative studies, HBV PoC DNA VL testing could facilitate the HBV cascade of care. The only 1 non-PoC study had a turnaround time ranging from 2 weeks to 2 months for obtaining DNA VL test results. There was a delay of 26 days from the receipt of DNA testing results to the initiation of treatment.

The analysis of HBV DNA testing and treatment outcomes from diverse populations reveals significant disparities based on regional factors and income levels [32]. Studies conducted predominantly in sub-Saharan Africa highlight urgent healthcare challenges in resource-limited settings [33]. The presence of onsite and mobile PoC assays significantly reduces turnaround times, ensuring timely interventions [34, 35]. In contrast, non-PoC methods lead to significant delays, emphasizing the importance of efficient diagnostic technologies [34]. Tailored interventions addressing population demographics and regional disparities are essential for equitable healthcare access. To optimize testing and treatment outcomes, efforts to bridge these gaps must prioritize the implementation of onsite and mobile PoC assays, particularly in LMICs [34, 35].

Recently, efforts to eliminate HBV on a global scale have gained momentum. Increasing vaccination coverage, expanding access to testing and treatment, and implementing comprehensive prevention programs effectively reduce new infection [36, 37]. National and international organizations collaborate to raise awareness, mobilize resources, and advocate for policy changes to address the challenges of HBV infection, particularly in high-burden regions [37, 38]. Despite progress, significant gaps remain in achieving universal access to prevention, testing, and treatment services. In a 2023 survey of national hepatitis program managers, based on 41 responses from 33 countries, there was reported limited access to laboratory-based HBV DNA assays but especially for PoC in sub-Saharan Africa, and approximately 50% of respondents reported no access to PoC HBV DNA assays. Although the availability and adoption of any PoC testing varies globally, they have been successfully used in clinical settings, particularly in LMICs in Africa [20, 39–43]. Integrating these PoC tests can contribute to the decentralization of HBV diagnosis, bringing testing capability closer to the PoC. Because the platform for PoC testing has increasingly been implemented for HIV and HCV, it's plausible and feasible to integrate HBV, HCV, and HIV PoC testing [44]. Integrating multiple PoC tests in a single platform offers multiple benefits, including streamlining the testing process, reducing time and cost, and identifying co-infections and comorbidities.

With a shift in treatment perspectives toward broader eligibility criteria, particularly including individuals with chronic

Table 5. Summary of Outcomes Across HBV Cascade of Care for HBV DNA PoC Testing Studies

First Author	HbsAg Tested	HbsAg Positive	Percentage of HbsAg Positive Among People Who Have HbsAg Test	Linkage to Care	Percentage Of Linkage To Care Among People Who Were Hbsag Positive	HBV DNA Tested	Percentage of HBV DNA Tested Among People Who Were HbsAg Positive	HBV DNA Detectable	Percentage Of HBV DNA Detectable Among People Who Have HBV DNA Test	Meet Treatment Eligibility Criteria	Percentage of Meeting Treatment Eligibility Among That DNA Detectable	Initiated Treatment	Percentage of Initiating Treatment Among Those Who Met Treatment Eligibility
Johannessen A, 2023	…	2794	…	2794	2794/2794 (100.0%)	2794	2794/2794 (100.0%)	…	…	…	…	857[a]	…
Kachimanga C, 2020	157	16	16/157 (10.2%)	12	12/16 (75.0%)	11	11/16 (68.8%)	11[b]	11/11 (100.0%)	1[c]	1/11 (9.1%)	1	1/1 (100.0%)
Kawana W, 2022	…	220	…	…	…	128	128/220 (58.2%)	…	…	68[d]	…	35	35/68 (51.5%)
Nyama ET, 2022	…	…	…	…	…	399	…	399[e]	399/399 (100.0%)	113[f]	113/399 (28.3%)	74	74/113 (65.5%)
Shiha G, 2020 (Site with GeneXpert 16 cartridge)	475	4	4/475 (0.8%)	…	…	4	4/4 (100.0%)	3[g]	¾ (75.0%)	1[h]	1/3 (33.3%)	1	1/1 (100.0%)
Shiha G, 2020 (Site with GeneXpert 4 cartridge)	3188	27	27/3188 (0.8%)	…	…	18	18/27 (66.7%)	15[i]	15/18 (83.3%)	12[j]	12/15 (80.0%)	12	12/12 (100.0%)
Ndow G, 2023 (Plasma)	…	…	…	…	…	90	…	77[k]	77/90 (85.6%)	4	4/77 (5.2)	4	4/4 (100.0%)
Ndow G, 2023 (Dried blood spots)	…	…	…	…	…	42	…	31[l]	31/42 (73.8%)	4	4/31 (12.9)	4	4/4 (100.0%)
Pooled estimate (95% CI)	…	…	2.6% (0.3%–6.8%) ($I^2 = 94.0\%$)	…	N/A	…	84.1% (41.5%–100.0%) ($I^2 = 99.1\%$)	…	91.5% (71.9%–100.0%) ($I^2 = 93.9\%$)	…	23.2% (7.0%–43.9%) ($I^2 = 90.1\%$)	…	88.3% (65.8%–100.0%) ($I^2 = 74.8\%$)

ALT, alanine transaminase; CI, confidence interval; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCC, hepatocellular carcinoma; N/A, not available; PoC, point-of-care; TE, transient elastography.

[a]Treatment eligibility criteria: (1) decompensated cirrhosis; (2), compensated cirrhosis; (3) ALT > upper limit of normal and HBV viral load >2000 IU/mL; and (4) HCC in first-degree relative and HBV viral load >2000 IU/mL. Decompensated cirrhosis was defined as described previously. Aspartate aminotransferase to platelet ratio index ≥ 0.7 was used instead of liver stiffness measurements to define compensated cirrhosis.

[b]Median viral load: 871 (44–2440) IU/mL; viral load category: < 2000 IU/mL: 8; 2000–20 000 IU/mL: 2; > 20 000 IU/mL: 1.

[c]Treatment eligibility criteria: evidence of liver cirrhosis on the abdominal scan.

[d]Treatment indications: family history of liver cancer/cirrhosis, cirrhosis by TE, and ALT elevation with DNA >20 000 IU/mL.

[e]Viral load category: < 2000 IU/mL: 293; 2000–20 000 IU/mL: 56; > 20 000 IU/mL: 50.

[f]Treatment eligibility criteria: a diagnosis of cirrhosis; co-infection with either HIV or hepatitis C virus.

[g]Viral load category: ≤ 2000 IU/mL: 2; > 2000 IU/mL: 1.

[h]Treatment eligibility criteria: HBV viral load >2000 IU/mL.

[i]Viral load category: ≤ 2000 IU/mL: 3; > 2000 IU/mL: 12.

[j]Treatment eligibility criteria: HBV viral load >2000 IU/mL.

[k]Median viral load: 1195 (305–3640) IU/mL; viral load category: < 2000 IU/mL: 50; 2000–20 000 IU/mL: 20; > 20 000 IU/mL: 7.

[l]Median viral load: 33 (19–68.5) IU/mL; viral load category: < 2000 IU/mL: 28; 2000–20 000 IU/mL: 2; > 20 000 IU/mL: 1.

viral replication, PoC testing becomes increasingly relevant. PoC testing offers a valuable opportunity for rapidly identifying individuals with chronic replication, enabling prompt treatment initiation and potentially mitigating long-term liver-related complications. The potential reduction in the long-term risk of hepatocellular carcinoma associated with decreased HBV replication underscores the importance of timely identification and management of individuals with chronic HBV infection [45, 46]. In resource-rich settings, PoC testing can streamline patient management pathways, allowing for more efficient identification and treatment of individuals with chronic HBV infection. Additionally, in resource-limited LMICs, PoC testing is a practical solution to overcome diagnostic barriers and improve patient care [34, 47, 48].

This review had several key strengths. First, we categorized the PoC studies based on the assay location (clinic, mobile unit, or laboratory) and the models of care (same/different site, same/different visit) used for HBV testing and treatment initiation to assess how the factors might impact PoC testing. However, findings were limited by the small number of studies and lack of comparative data. Second, 6 of 7 studies were from LMICs. Third, the review presents key outcomes related to turnaround times in different steps of the HBV care cascade and the uptake of HBV DNA VL testing and treatment.

This study also has several limitations. First, only 6 studies were included in this systematic review and meta-analysis. However, we did identify original studies from LMICs with a high burden of HBV. Second, only 1 study had a comparator group. This limits the inferences that can be made based on these data. At the same time, GRADE allows us to provide detailed information about the certainty of evidence. One of the included researches focused on patients co-infected with HIV and HBV. Treatment initiation is necessary on detection of HBV positivity, differing from the criteria for initiating treatment in sole HBV infection. This variation can influence the time assessment from DNA test to treatment. However, because of the limited availability of studies that meet our research criteria, we also included them in our analysis. Moreover, in clinical practice, physicians assess the need for treatment based on various test results (ie, HBV-related or liver enzyme parameters). However, the patient hesitates to initiate treatment in the real world because of the long-term treatment with nucleos(t)ide analogs without any clear cessation criteria in the current guideline or the expensive interferon therapy with intimidating side effects. Consequently, patients may require additional time to evaluate whether to commence treatment. The time to treatment may not accurately reflect the time to obtain assay results.

This systematic review has potential policy and clinical management implications. Despite the lack of comparative studies, HBV PoC DNA VL testing may potentially improve the management and monitoring of HBV infection. A complementary systematic review found that HBV PoC assay is associated with excellent performance (sensitivity and specificity) and reliability for HBV DNA quantification [36]. Although our research has been primarily on HBV VL testing, it is worth noting the potential utility of PoC for HBeAg testing in identifying individuals with high viral replication. Integrating PoC HBeAg testing alongside HBV VL testing may offer a more comprehensive understanding of available diagnostic options, providing clinicians with valuable insights into managing HBV infection.

CONCLUSION

HBV PoC DNA testing appears to be associated with a turnaround time of <1 day for receipt of VL results and appears associated with high rates of DNA testing and initiation of treatment among those eligible. More studies are needed to establish the effects of PoC HBV DNA testing versus non-PoC testing on the HBV cascade of care.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Author contributions. P.E. and W.T. conceptualized the study. P.E., W.T., and Y.T. designed the study. Y.D., C.F., and F.L. reviewed and assessed the studies for inclusion. Y.D., C.F., F.L., S.G., W.T., and Y.T. extracted data. Y.D. and C.F. performed the risk of bias assessment. W.T. and R.C. contributed to the GRADE analysis. Y.T. and W.T. carried out analyses. W.T., S.G., and Y.T. produced the first draft of the manuscript. All authors contributed to interpreting data and revising the manuscript critically for important intellectual content.

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