REVIEW

Rapid Point-of-Care First-Line Screening Tests for Hepatitis B Infection: A Meta-Analysis of Diagnostic Accuracy (1980–2010)

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OBJECTIVES: **Three-hundred fifty million people worldwide are chronically infected with Hepatitis B, with four million acute infections annually. With infection concentrated in hard-to-reach populations and low resource settings, rapid point-of-care (POC) tests offer an efficient screening alternative to laboratory tests. We conducted a meta-analysis to evaluate accuracy of rapid POC tests screening for Hepatitis B.**

METHODS: **Two reviewers searched four databases, critiqued quality. A hierarchical Bayesian meta-analysis correcting for imperfect reference standards was used. Based on components of the antigen–antibody response, 17 studies were stratified into three subgroups: (i) Hepatitis B surface antigen (HBsAg) tests; (ii) anti-HBsAg tests, and (iii) HBs+eAg tests. Further, we pooled estimates on individual tests with sufficient data.**

RESULTS: **In subgroup 1, the pooled sensitivity (Sn) was 94.76% (95% credible interval (CrI): 90.08–98.23%) and specificity (Sp) was 99.54% (95% CrI: 99.03–99.95%). The Determine test reported a pooled Sn 98.2% (95% CrI: 94.7, 99.9) and Sp 99.9% (95% CrI: 99.3, 100); in subgroup 2, Sn 93.2% (95% CrI: 85.1, 98.5), Sp 93.1% (95% CrI: 81.9, 99.9); and in subgroup 3, the Binax test showed Sn 95.5% (95% CrI: 88.9, 99.4), Sp 99.8% (95% CrI: 99.3, 100).**

CONCLUSIONS: **HBsAg tests, including Determine, and the HBs+eAg test, Binax showed high accuracy. Improvements in sensitivity of antibody-based tests will enhance their potential for global first-line screening.**

SUPPLEMENTARY MATERIAL is linked to the online version of the paper at http://www.nature.com/ajg

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INTRODUCTION

The World Health Organization estimates that globally 350 million people are chronically infected with the Hepatitis B virus (HBV), with a further four million acute infections every year (1). Sub Saharan Africa, aboriginal Australia, the East Mediterranean, South East Asia, South America, the Pacific Islands, and the Inuit communities of Canada have high Hepatitis B prevalence (2). In United States, despite a policy of universal vaccination, the incidence of HBV infection remains high in marginalized populations—injection drug users, incarcerated populations, and MSM (men who have sex with men) (3). Finally, increases in travel and immigration impact the control of infection in countries with universal vaccination programs (4). Within this context, timely screening for HBV infection in marginalized populations in developed settings, and at-risk populations in endemic settings gain relevance for early detection, initiation of treatment and prevention of further transmission to infants, partners, and the community.

The Centers for Disease Control (CDC) recommend diagnosing Hepatitis B infection by detecting components of the antigen–antibody response, specifically by detection of the IgM antibody to the Hepatitis B core antigen (HBcAg), or the Hepatitis B surface antigen (HBsAg), and confirming that the patient is negative for IgM antibodies to the HBV to diagnose acute infection (5). Additionally, they recommend confirming chronic infection if an individual is negative for IgM antibodies to HBcAg, but positive for HBsAg and total anti-HBcAg (6). Use of the Hepatitis B e antigen

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(HBeAg) as a marker for active viral replication, and detection of HBV DNA in the blood by PCR is further recommended for staging of infection (7). Such detailed and expensive algorithms require sophisticated laboratories, technicians, with a continuous supply of electricity, and equipment to screen patients. Moreover, the time taken to run these tests, translates to delays in patient notification, referrals, and treatment, with associated losses-to-follow-up.

Rapid point-of-care (POC) tests screening for HBV circumvent these challenges, serving as an excellent tool for inexpensive first-line screening in global settings. In developed countries, as well, POC tests can aid in targeted screening of injection drug users, incarcerated populations, and MSM populations with high HBV prevalence. This untapped potential of POC tests has led to growing interest in this paradigm of decentralized testing. Before their widespread implementation, however, there is a need to ensure that these tests are reliable for first-line screening.

Since the 1990s, a number of rapid POC tests have been developed that primarily use blood samples to test for the HBsAg, HBs+eAg or antibodies to HBsAg (anti-HBsAg). These include tests such as Determine (Alere, Waltham, MA), Binax NOW (Binax, Portland, ME), Dainascreen (Inverness Medical, Waltham, MA), Serodia (Fujirebio, Tokyo, Japan), Hybritech (Hybritech, San Diego, CA), DRW (Diagnostics for the Real World, Cambridge, UK), Virucheck (Orchid Biomedical Systems, Goa, India), Cypress (Cypress Diagnostics, Langdorp, Belgium), Hexagon (Human Diagnostics Worldwide, Wiesbaden, Germany), Hepacard (J. Mitra & Co., New Delhi, India), Genedia (Green Cross, Yongin, S. Korea), Daewoong (Daewoong Biotech, Daejeon, S. Korea), SD (Standard Diagnostics, Daejeon, S. Korea), Asan (Asan Pharmaceutical, Seoul, S. Korea), One Check (Atlas Medical, Cambridge, UK), Accurate (Atlas Medical), Acon (Acon Laboratories, San Diego, CA), Atlas (Atlas Medical), Intec (Intec Products, Xiamen, China), Blue Cross (Blue Cross, Beijing, China), DIMA (Geseeschaft fur Diagnostika mbH, Gottingen, Germany), and Cortez (Cortez Diagnostics, Calabasas, CA). These tests can be used as a preliminary marker of infection, but further testing is required to stage disease and to determine clinical management.

In 2008, the first meta-analysis of diagnostic accuracy of rapid tests for HBV was published in the Korean language (8). Although the authors conducted a Standards for Reporting of Diagnostic Accuracy (STARD)-guided evaluation, they only focused on tests that detect HBsAg, ignoring other available antigen- and antibody-based tests, and used inaccurate statistical methods (i.e., assuming a perfect reference standard for comparison), limiting our understanding of their diagnostic performance. To fill this knowledge gap in global evidence, and given the interest in expanded screening for HBV, we systematically reviewed the existing global literature on the diagnostic performance of all (i.e., HBsAg based, Ab-HBsAg based, and HBs+ e Ag based) rapid POC tests used to screen for Hepatitis B in adults, while accounting for imperfect reference standards with Bayesian methods and critiquing the quality of studies.

METHODS

Search strategy

We followed Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines in the reporting of this review. The primary search was conducted in Medline (Pubmed), Biosis, Web of Science, and Embase (1980–2010). Bibliographies of included articles and reviews were manually searched for relevant citations, and experts in the field were contacted to ensure that the search strategy was complete.

Sample search string were ("Hepatitis B" OR "Hepatitis B Antibodies" OR "Hepatitis B Surface Antigens" OR "Hepatitis B Core Antigens" OR "Hepatitis B Antigens" OR "Hepatitis B e Antigens"), AND ("Point-of-Care Systems" OR "rapid test*" OR "diagnostic"), AND ("Sensitivity and Specificity" OR "diagnostic accuracy" OR "validity").

We included studies conducted only in adult populations, regardless of language, and using all study designs (cross-sectional, case–control). We included full-text articles, conference abstracts and letters, provided they contained enough information to calculate sensitivity and specificity.

Data abstraction and outcomes

Two independent reviewers (S.S. and Y.J.) conducted searches separately and pooled identified articles ($n=145$) for a preliminary screen. Of these, 55 articles were assessed by full-text review. Using our eligibility criteria, 17 studies were included in our meta-analysis. Details of this search are provided in **Figure 1**.

Data abstraction and quality assessment using the QUADAS2 (Quality Assessment of Diagnostic Accuracy Studies) (9) and STARD (scored out of 25) (10) checklists were conducted separately by the two reviewers. Each item on the STARD checklist was weighted equally. The QUADAS2 checklist was domain based and assessed the level of bias in each study as high, low or unclear, with respect to patient selection, administration of index test, reference test, and patient flow (9). Inter-rater agreement was high (Cohen's Kappa of 0.89). In cases of disagreement, a third reviewer (N.P.P.) was contacted.

Data were abstracted for the following variables: study author; year and location of study; eligibility criteria; study design; biological specimen tested; reference test; sample size; raw cell numbers, i.e., true positives (tp), false negatives (fn), false positives (fp), true negatives(tn); sources of funding; and any reported conflict of interest. The principal outcome measures were pooled sensitivities and specificities.

Data synthesis and analysis

Subgroups for analysis. For the purposes of our analysis, we divided data into three subgroups, based on the component of the antigen–antibody response detected by the index test.

HBsAg-based tests. Within this group, the globally popular Determine test had sufficient data points to allow a separate pooling in a subanalysis, while all other HBsAg-based tests were pooled together (i.e., Dainascreen, Serodia, Hybritech, DRW, Virucheck, Hexagon, Cypress, Hepacard, Genedia, Daewoong, SD, Asan, One Check, Accurate, Acon, Atlas, Intec, Blue Cross, DIMA, and Cortez).

Anti-HBsAg-based tests. The tests examined in this subgroup included Genedia, Daewoong, Asan, and SD, but none had sufficient data points to be pooled separately.

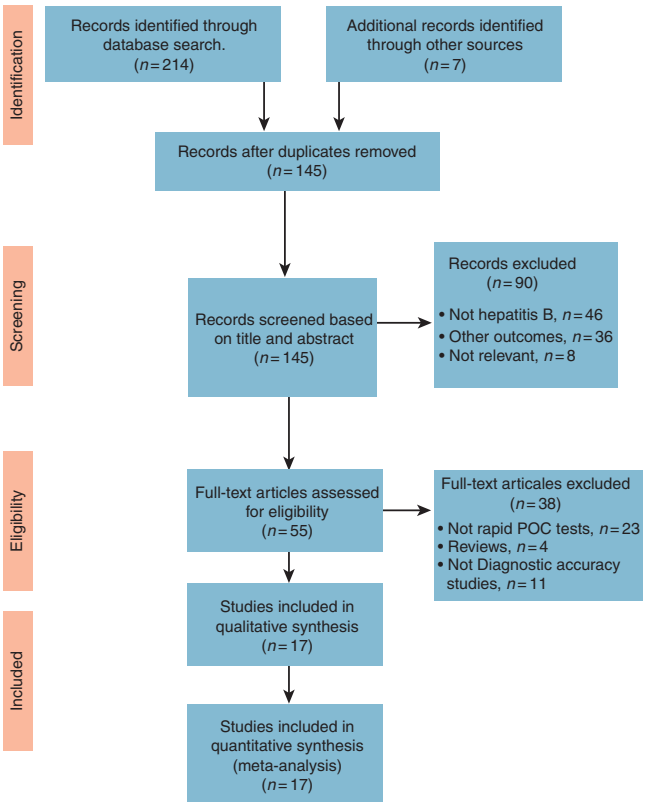

Figure 1. Flow chart of study inclusion methodology. POC, Point-of-Care.

HBs+eAg-based tests. The only test in this group, the Binax test simultaneously detects both the HBsAg and the HBeAg, and had sufficient data points for pooled accuracy.

Bayesian hierarchical summary receiver operating characteristic meta-analysis accounting for reference standard inaccuracy

CDC guidelines recommend confirming chronic infection if an individual is negative for IgM antibodies to HBcAg, but positive for HBsAg and total anti-HBcAg (6). However, none of the studies examining diagnostic accuracy of the rapid POC tests performed reference testing as per CDC standards. Therefore, we used a Bayesian hierarchical summary receiver operating characteristic model that estimates pooled sensitivity and specificity, taking into account the correlation between and within studies, and the fact that reference standards themselves do not perfectly classify true disease status (11). In order to be conservative, we assumed that each reference test had a range of sensitivity and specificity between 90% and 100%.

Meta-analysis was conducted assuming perfect reference standards and imperfect reference standards as described above in R Version 2.11.1 (Lucent Technologies, Paris, France). Forest plots were generated using Meta-DiSc v.1.4 (Hospital Univeritario Ramon y Cajal, Madrid, Spain).

RESULTS

Characteristics of included studies

Please refer to **Table 1** for study characteristics and details.

The 17 final articles that examined various tests and different biological specimens contributed to 48 data points in all. Each data point refers to a set of tp, fp, fn, and tn for analysis. Studied populations ranged in risk from pregnant women (14) and healthy volunteers (12,13) to HIV-positive patients (25), incarcerated inmates (12,13), and confirmed HBV patients (12). Only two studies were conducted in field settings (13,17), the remaining were in well-controlled laboratory settings. A majority of the studies ($n=14$, 82%) were conducted in developing countries, while one study did not report the country of origin (15), the remainder were from developed countries. Two studies (11.76%) were reported in Korean, and translated, while all other studies were reported in English.

Results by subgroup

Forest plots of sensitivity and specificity for included studies are provided in **Figure 2a** and **b**.

Results of meta-analysis, stratified by subgroup and assuming both a perfect and an imperfect reference standard are presented in **Table 2**.

1. Subgroup 1: HBsAg-based tests
   (a) The Determine test showed the highest pooled sensitivity and specificity of all subgroups regardless of whether the reference standard was assumed to be perfect (Sn 97.6%; 95% credible interval (CrI): 96.3%, 98.6% and Sp 99.7%: 95% CrI: 99.2%, 99.9%), or imperfect (Sn 98.2%; 95% CrI: 94.7%, 99.9% and Sp 99.9%; 95% CrI: 99.3%, 100%).
   (b) The remaining HBsAg tests in this subgroup included Dainascreen, Serodia, Hybritech, DRW, Virucheck, Hexagon, Cypress, Hepacard, Genedia, Daewoong, SD, Asan, One Check, Accurate, Acon, Atlas, Intec, Blue Cross, DIMA, and Cortez. When results were pooled under the assumption of imperfect reference standards, the pooled sensitivity of this subgroup was 94.8% (95% CrI: 90.1, 98.2), and the pooled specificity was 99.5% (95% CrI: 99.1, 99.9).
2. Subgroup 2: Anti-HBsAG-based tests
   The tests examined in this subgroup included Genedia, Daewoong, Asan, and SD. The pooled sensitivity of this subgroup was 93.2% (95% CrI: 85.1, 98.5), while the pooled specificity was 93.1% (95% CrI: 81.9, 99.9).
3. Subgroup 3: HBsAg+HBeAg-based test
   The only test studied in this subgroup was the Binax test. Three studies reported on its accuracy (12,13,20), although one of them examined its accuracy in frozen sera, fresh sera, and whole blood (13), leading to a total of six data points. The Binax test showed a pooled sensitivity of 95.5% (95% CrI: 88.9%, 99.4%), and a pooled specificity of 99.8% (95% CrI: 99.3%, 100%).

Quality of studies. Please see **Appendix 1 online** for details on the study quality critique. With the updated QUADAS2 checklist, bias was assessed for each of the included studies. Of 17, 10 (59%) of the studies used a case–control design (12,16–18,21–24,26,27). Of all 17 studies, only 3 (18%) reported blinding of test readers

Table 1. Studies included in meta-analysis

Study ID	Author	Country	Sample size	Study design	Index test	Reference standard	Population
1.	Clement (12)	Belgium	942	Case–control	Binax	MEIA	Patients with biopsy-proven HBV; healthy volunteers from a vaccine evaluation trial
2.	Lau (13)	United States	2,627	Cross-sectional	Binax	EIA	Incarcerated offenders; patients in Hepatology clinics; participants in a Chinese Community Health Fair; known HBV-positive patients
3.	Lien (14)	Vietnam	328	Cross-sectional	Determine Dainascreen Serodia	EIA	High-risk volunteers; pregnant women patients with other infectious diseases
4.	Nakata (15)	NR	300	Cross-sectional	Hybritech	Not specified	Prison inmates
5.	Ansari (16)	Iran	240	Case–Control	Acon Atlas Intec Blue Cross DIMA Cortez	PCR	Hospital patients
6.	Lin (17)	China, Guinea	1,250	Case–Control	DRW Determine	EIA	Hospital patients; blood donors
7.	Randrianirina (18)	Madagascar	200	Case–Control	Determine Virucheck Hexagon Cypress	EIA (HBsAg and anti-HBsAg)	Not specified
8.	Kaur (19)	India	2,754	Cross-sectional	Hepacard	EIA	Surgery patients; blood donors; patients ruling out HBV
9.	Akanmu (20)	Nigeria	238	Cross-sectional	Binax	ELISA	Blood donors
10.	Oh (21)	Korea	250 249	Case–Control	Genedia – HBsAg Genedia – anti-HBsAg	EIA	Not specified
11.	Whang (22)	Korea	200 200	Case–Control	Daewoong-HBsAg Genedia-HBsAg Daewoong – anti-HBsAg Genedia – anti-HBsAg	CLIA	Patients from Hospital Comprehensive Health Screening Center
12.	Cha (23)	Korea	40 40	Case–Control	SD – HBsAg Genedia – HBsAg Asan – HBsAg SD – anti-HBsAg Genedia – anti-HBsAg Asan – anti-HBsAg	MEIA	Volunteers from University Hospital
13.	Palmer (24)	Honduras, Dominican Republic, Trinidad, Jamaica	298	Case–Control	Determine	Not specified	Not specified
14.	Davies (25)	Malawi	75	Cross-sectional	Determine	EIA	HIV-positive adults
15.	Khan (26)	Pakistan	57	Case–Control	Onecheck Accurate	ELISA	Not specified
16.	Torane (27)	India	60	Case–Control	Hepacard	ELISA	Not specified
17.	Raj (28)	India	1,000	Cross-sectional	Hepacard	EIA or MEIA	Hospital laboratory samples

Anti-HBsAg, antibody to Hepatitis B surface antigen; CLIA, Chemiluminiscent Immunoassay; EIA: Enzyme Immunoassay; ELISA: Enzyme-linked Immunosorbent Assay; HBV, Hepatitis B virus; HBsAg, Hepatitis B surface antigen; MEIA, Microparticle Enzyme Immunoassay; NR, not reported; SD, standard diagnostics.

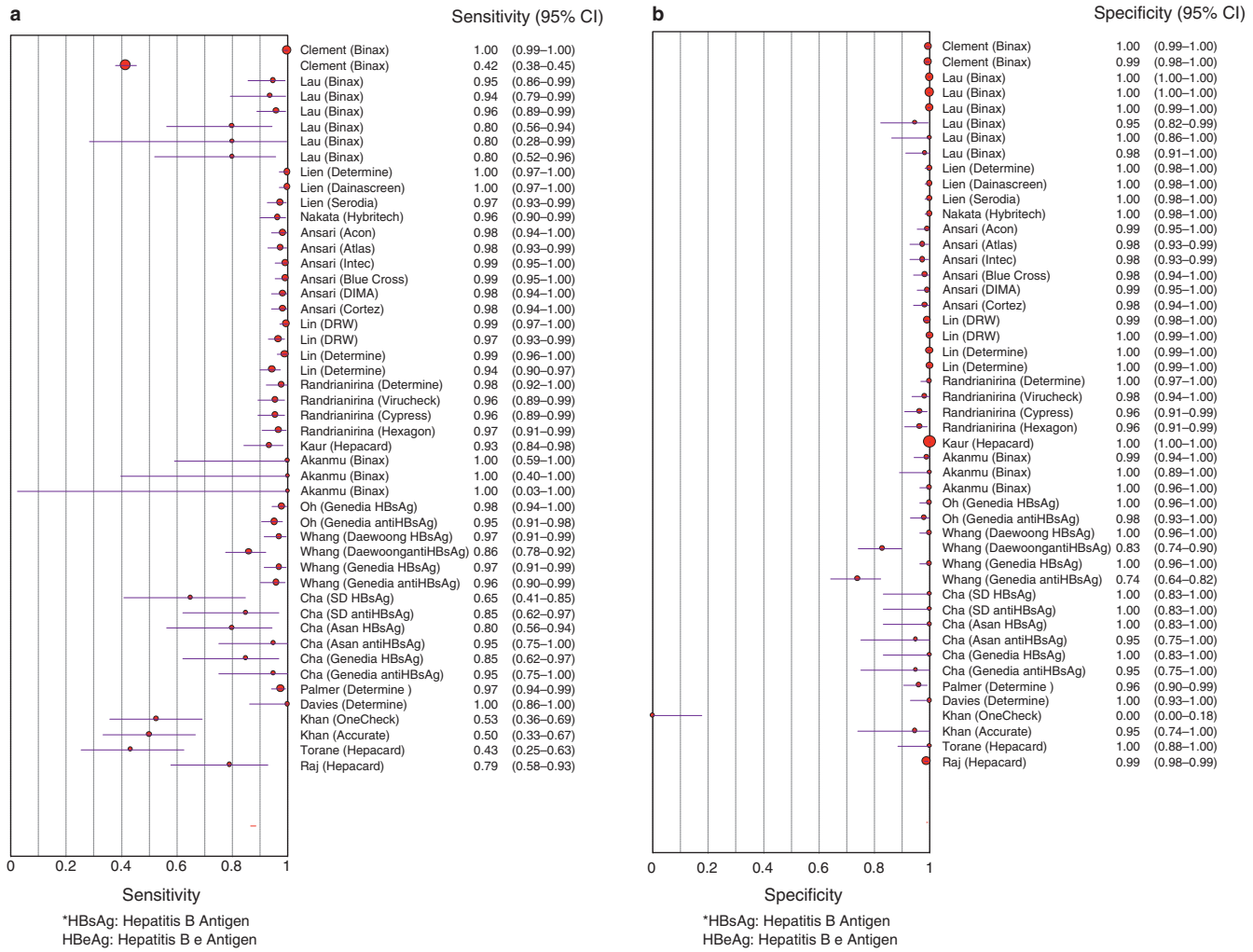

Figure 2. Forest plots of data from included studies. (**a**) Reported sensitivity of each study – forest plot. (**b**) Reported specificity of each study – forest plot. CI, confidence interval; DRW, Diagnostics for the Real World; SD, Standard Diagnostics.

(13,25,26). The reporting of articles as assessed by the STARD checklist was poor to medium (STARD score 7–13/25), with a number of required items missing from reporting of diagnostic accuracy. Finally, two studies (12%) reported either a financial or professional relationship with industry (14,17), while three studies explicitly reported no conflict of interest (13,18,25). The remaining 12 studies (65%) neglected to report on conflict of interest (12,15,16,19–24,26–28).

Table 2. Pooled sensitivity and specificity

	Assuming perfect reference standard		Assuming imperfect reference standard	
Subgroup	**Sensitivity (95% CrI)**	**Specificity (95% CrI)**	**Sensitivity (95% CrI)**	**Specificity (95% CrI)**
HBsAg tests	94.7% (93.7–95.6%)	99.4% (99.2–99.6%)	94.8% (90.1–98.2%)	99.5% (99.1–99.9%)
Determine – HbsAg	97.6% (96.3–98.6%)	99.7% (99.2–99.9%)	98.2% (94.7–99.9%)	99.96% (99.3–100%)
Binax – HBs/eAg	97% (95.6–98%)	99.7% (99.5–99.9%)	95.5% (88.9–99.4%)	99.8% (99.3–100%)
Anti-HBsAg tests	92.7% (89.7–95%)	87.4% (83.5–90.7%)	93.2% (85.1–98.5%)	93.1% (81.9–99.9%)

Anti-HbsAg, antibody to Hepatitis B surface antigen; CrI, credible interval; HBsAg, Hepatitis B surface antigen; HBeAg: Hepatitis B e Ag.

DISCUSSION

Our meta-analysis suggests that rapid POC HBsAg-based tests, including the Determine test and the HBs + eAg-based Binax test have high diagnostic accuracy, while antibody-based tests require improvements in their accuracy parameters before they can safely be recommended for first-line screening.

Interestingly, the Korean meta-analysis by Hwang *et al.* (8) also reported high accuracy a pooled sensitivity of 98.1% (95% CrI: 97.7, 98.5), and a pooled specificity of 99.6% (95% CrI: 99.2, 99.9) for HBsAg-based tests, reinforcing the high performance of most rapid POC tests used to screen for Hepatitis B. However, lack of complete global data, and imperfect adjustment of reference standards limited the interpretation of these results. In our meta-analysis, adjustment with Bayesian methods, allowed for an accurate estimation of performance for the three subgroups.

Implications

The high accuracy of tests such as Determine and Binax is very encouraging. Although not yet approved in North America, these tests could safely be approved and integrated for public health screening of at-risk populations identified by the CDC, such as those born in areas of high prevalence (≥2%), MSMs, injection drug users, those infected with HIV, household contacts or sex partners of infected persons (29).

However, other antibody-based tests require improvements in their accuracy parameters, which will not only help clinicians to improve their post-test probability of diagnosis but also serve as a gateway to actively stage Hepatitis B, and offer prophylaxis, or treatment. In terms of their global uptake, it is also important to lower the costs of these screening tests, in line with inexpensive HIV tests, for them to be useful to screen the majority of patients worldwide who cannot currently afford laboratory-based HBV screening tests. Evidence from included studies shows that biomarker-based Hepatitis B POC tests offer the benefits of cheap and rapid diagnosis, along with convenience, easy storage (12,13,16), small blood samples for testing (13), minimal training of professionals for testing (12,13,16,21,22), and minimal expensive equipment (22,23). The main limitation of these tests, as with other biomarker-based tests (e.g., HIV and Hepatitis C), is their inability to stage infection. However, their utility with respect to expedited screening cannot be disregarded.

Furthermore, in future, with rapid development of more advanced biomarker-based and DNA/RNA-based multiplex POC testing platforms that detect HIV, HBV, and Hepatitis C Virus simultaneously (e.g., Multiplo Medmira Laboratories, Halifax, NS, Canada), the need to improve the performance of HBV tests will be critical to paving the way for greater integration of biomarker-based rapid tests in integrated sexually transmitted infection/HIV global screening initiatives.

Strengths and limitations

This meta-analysis had a number of strengths, namely, it was a global evidence synthesis, used a Bayesian hierarchical model, adjusted for imperfect reference standards, used a pre-specified protocol, included an exhaustive search of the major scientific databases, and reference lists of reviews and articles. We also included studies of all languages, avoiding publication (language) bias. Other biases in diagnostic meta-analyses were unlikely, namely, incorporation bias was not likely to be present since all participants received both index tests and confirmatory tests independently. Also, since all studies administered the same reference standard to all patients, partial or differential verification bias was avoided. Moreover, two independent reviewers abstracted data and critiqued the quality of included studies using the validated QUADAS2 and STARD checklists. Despite all these measures, however, it is possible that we may have missed some relevant articles, especially since this is a relatively new and expanding field of research.

Our study also had some limitations. First, by pooling tests with limited evidence into one subgroup, while separately analyzing tests with sufficient evidence (i.e., Determine and Binax), we may have obscured the high accuracy of some tests. For instance, Lin *et al.* (17) reported higher estimates of accuracy for the DRW test compared with Determine in a head-to-head comparison. Other tests namely, the DRW test, Virucheck, Dainascreen, Serodia, Hybritech, Hexagon, Cypress, Daewoong, Acon, Atlas, Intec, Blue Cross, DIMA, Cortez, and Genedia showed sensitivity and specificity estimates of >95%. However, these tests had too few studies that validated their accuracy. Second, we were unable to explore the variability in accuracy depending on the stage of infection (in acute vs. chronic); and, with presence of co-infections. This was due to a lack of information in the studies and lack of adequate data. Future studies that stratify data based on the stage of infection, or by co-infection with HIV, Hepatitis C, or syphilis could explore this issue in different populations. Third, although we accounted for imperfect reference standards using statistical techniques, we could not completely eliminate errors in classifying true disease status, with use of incomplete reference standards, that may have persisted across studies. There is a need for standardization of reference standards used in this field. Fourth, the conservative ranges of sensitivity and specificity that we assumed as priors (90–100%) for the reference standards may have resulted in a widening of confidence intervals than if narrower ranges had been used in analysis, and although we explored the variability in the test positivity threshold across studies, we could not adjust for variability between index tests, and among test readers. Fifth, a majority (60%) of studies utilized case–control study designs that are known to overestimate accuracy, with a potential for spectrum bias. Finally, the implementation research in diagnostics on Hepatitis B has, so far, only focused on evaluating test accuracy. With two tests reaching acceptable levels of accuracy of 98–99%, it is time to move forward beyond accuracy, toward evaluation of patient centered outcomes, i.e., impact of use at POC, impact on turnaround times, increase in uptake of tests, impact on management of co-infections, variability in accuracy with variable prevalence in different populations and settings, and feasibility of use at various settings, besides, convenience, cost preferences, and cost effectiveness. These outcomes are key in shaping global policy in diagnostics as it becomes more patient centered in the future.

CONCLUSION

It is of no surprise that the World Health Organization recently labeled prevention and control efforts for Hepatitis B as "fragmented" compared with HIV, and has predicted its rising role as a cause of death in the coming decades, emphasizing the need for timely prevention and screening strategies (30). The CDC has already formulated new guidelines to expedite screening in at-risk populations (29).

This meta-analysis suggests that HBsAg and HBs+eAg-based rapid POC tests used to screen for Hepatitis B have high accuracy while the accuracy of antibody-based tests requires refinement. Of note, Determine and Binax emerged as tests with high sensitivity and specificity. The result of this meta-analysis suggests that these tests could be potentially used in first-line screening initiatives for marginalized populations, and for resource limited settings.

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CONFLICT OF INTEREST

Guarantor of the article: Nitika Pant Pai, MD, MPH, PhD.
Specific author contributions: Conception and design: Nitika Pant Pai, Sushmita Shivkumar, and Rosanna Peeling; data abstraction: Sushmita Shivkumar, Yalda Jafari, and Nitika Pant Pai; data analyses and interpretation: Sushmita Shivkumar, Lawrence Joseph, and Nitika Pant Pai; writing of the manuscript: Sushmita Shivkumar, Yalda Jafari, Lawrence Joseph, Rosanna Peeling, and Nitika Pant Pai.
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Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ The global prevalence of Hepatitis B, especially in the context of co-infection with HIV and Hepatitis C is high.
- ✓ Screening with point-of-care tests offers a convenient, rapid, and cheap option for detection in marginalized populations and low resource settings.
- ✓ Before their adoption in screening programs, there is a need to validate their diagnostic accuracy.

WHAT IS NEW HERE

- ✓ In this first meta-analysis of global evidence, the specificity of blood-based point-of-care tests has been found to be high.
- ✓ The sensitivity and specificity of the Determine test is close to 100%. However, the sensitivity of other tests needs improvement before their widespread use.

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