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Diagnostic Performance of the HCV Core Antigen Test To Identify Hepatitis C in HIV-Infected Patients: a Systematic Review and Meta-Analysis

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ABSTRACT The standard algorithm for diagnosing hepatitis C virus (HCV) infection has two steps, an HCV antibody test for screening and a nucleic acid amplification test (NAAT) for confirmation. However, the HCV core antigen (HCVcAg) detection assay is an alternative for one-step diagnosis. We aimed to evaluate the diagnostic performance of the Abbott ARCHITECT HCV Ag assay to detect active hepatitis C in serum/plasma in people living with HIV/AIDS (PLWHA), through a systematic review and meta-analysis. PubMed, EMBASE, Scopus, Web of Science, and the Cochrane Library were searched until 20 September 2022 (PROSPERO, CRD42022348351). We included studies evaluating Abbott ARCHITECT HCV Ag assay (index assay) versus NAATs (reference test) in PLWHA coinfected with HCV who did not receive antiviral treatment for HCV. Meta-analysis was performed with the MIDAS module using Stata and random-effects models. The QUADAS-2 tool evaluated the risk of bias. The bivariate analysis was conducted on 11 studies with 2,407 samples. Pooled sensitivity was 0.95 (95% CI = 0.92 to 0.97), specificity 0.97 (95% CI = 0.93 to 0.99), positive likelihood ratio 37.76 (95% CI = 12.84 to 111.02), and negative likelihood ratio 0.06 (95% CI = 0.04 to 0.09). The area under the curve was 0.97 (95% CI = 0.20 to 1.00). For low prevalence (≤5%), the posttest probability that an individual with a positive test was a true positive ranged from 4% to 67%, whereas, at high prevalence (≥10%), the posttest probability was between 81% and 87%, indicating that a confirmatory test should be necessary, particularly with prevalence values of ≤1%. Regardless of prevalence, the probability that an individual with a negative test was a false negative was close to zero, indicating that the individual was not infected with HCV. In conclusion, the accuracy of the Abbott ARCHITECT HCV Ag assay was very good for HCV screening in serum/plasma samples from PLWHA. The clinical utility to confirm HCV infection was acceptable in high-prevalence settings (≥10%) but poor in low-prevalence settings (≤1%). Furthermore, it was excellent in excluding active HCV infection.

KEYWORDS core antigen, diagnostic accuracy, hepatitis C virus, people living with HIV, screening

Hepatitis C virus (HCV) infection can cause chronic hepatitis C (CHC), which, if not treated in time, can lead to fibrosis, cirrhosis, liver failure, hepatocellular carcinoma, and even death (1). HCV infection is a global health problem since about 58 million

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people worldwide have CHC, which causes almost 300,000 deaths yearly (2). The majority of cases are concentrated in developing countries, with a higher prevalence in high-risk populations such as men who have sex with men (MSM), female sex workers, people who inject drugs (PWID), and prisoners (3). Direct-acting antivirals (DAAs) against HCV have demonstrated high efficacy rates (>90%). However, HCV infection remains a serious social and public health problem because less than 20% of people infected with HCV are aware that they are infected, as CHC remains asymptomatic for a long time, progressively causing liver damage (2, 4). Therefore, the World Health Organization calls for eliminating viral hepatitis by 2030 by detecting 90% of patients with CHC and treating 80% of them (5).

HCV infection is common in people living with HIV/AIDS (PLWHA) since both viruses share transmission routes (6 to 8). There are around 2.9 million PLWHA coinfected with HCV (4). HCV/HIV coinfection negatively affects the transmission and natural history of HCV infection. HIV infection reduces the chance of HCV spontaneous clearance, increases chronic HCV infection rates, and accelerates the development of HCV-related liver diseases, such as liver cirrhosis, liver failure, and hepatocellular carcinoma (9, 10). Although combined antiretroviral therapy (cART) against HIV can improve these outcomes and decrease HCV-related mortality (11), the primary cause of morbi-mortality among HIV/HCV-coinfected individuals is related to liver diseases (12). As a result, HCV detection and effective treatment should be prioritized for this population.

Currently, the HCV diagnostic algorithm includes two steps: first, detection of antibodies against HCV (anti-HCV), and second, confirmation of active hepatitis C infection by detection of HCV-RNA (13). HCV-RNA detection in clinical practice is performed by a nucleic acid amplification test (NAAT), the gold standard confirmatory assay (14, 15). However, NAATs are time-consuming and involve qualified personnel and advanced equipment, which are expensive (15, 16). Furthermore, RNA is easily degraded, leading to false negative (FN) results (17). The HCV core antigen (HCVcAg) test is an alternative for active HCV infection diagnosis, which is easier, less expensive, and faster than NAATs (16, 18, 19). HCVcAg appears in blood before anti-HCV antibodies, correlates positively with HCV-RNA load, is more stable than HCV-RNA, and is detected within 12 to 15 days after HCV infection, anticipating the window period for diagnosis.

Previous reports have analyzed the diagnostic performance of the Abbott ARCHITECT HCV Ag assay for screening HCV infection in PLWHA (20 to 33), which is today's most widely used HCVcAg test for HCV screening (19). Freiman et al.'s meta-analysis (34) reported high accuracy of the Abbott ARCHITECT HCV Ag assay in the general population, but they did not report data on clinical applications and did not analyze data in PLWHA to diagnose active hepatitis C. To our knowledge, there is no meta-analysis on the diagnostic performance of the HCVcAg test to screen for hepatitis C in PLWHA, a high-risk population with particular characteristics (35).

This study aimed to evaluate the diagnostic performance of the Abbott ARCHITECT HCV Ag assay for detecting active hepatitis C in serum/plasma in PLWHA through a systematic review and meta-analysis of eligible studies published to date (20 September 2022).

MATERIALS AND METHODS

The systematic review was completed according to the Cochrane Handbook for Diagnostic Test Accuracy Reviews (36) and the Preferred Reporting Items for Systematic Reviews and Meta-Analysis of Diagnostic Test Accuracy (PRISMA-DTA) guidelines (37). A completed PRISMA-DTA checklist is available in Supplementary File 1 in the supplemental material.

Search strategy. Studies were identified using different search commands in Medline/PubMed, EMBASE, SCOPUS, Web of Science, and the Cochrane Library (see Supplementary File 2) between 1 January 1976 and 20 September 2022. This protocol was designed *a priori* and registered in the online database PROSPERO (CRD42022348351). The literature search was not restricted by language, publication time, study design, or geographic location. Reference lists of included studies were evaluated for further relevant records. Articles from other languages were translated into English with the help of Google Translate.

Study selection. Study inclusion was determined according to the following criteria: (i) evaluation of diagnostic accuracy in plasma/serum of PLWHA; (ii) comparison between the Abbott ARCHITECT HCV Ag assay and a NAAT (gold standard); and (iii) available data to formulate a 2 × 2 contingency table

(true positives [TP], false positives [FP], true negatives [TN], false negatives [FN]). The exclusion criteria were as follows: (i) no available data to estimate sensitivity or specificity (nor from the corresponding author upon reasonable request); (ii) a sample size of less than 10, to avoid bias in the random-effects model; (iii) nonhuman subjects, commercial samples, or off-market assays; (iv) data during and after HCV antiviral therapy; and (v) nonoriginal articles, unpublished data, or data published in case reports, comments, letters to the editor, conference abstracts, book chapters, and review articles. All studies were independently screened by two investigators (A.T.-N. and D.S.-C.), who carefully reviewed the full text of the selected papers to extract all data.

Data extraction. Diagnostic accuracy of the HCVcAg test and population characteristics were extracted by two investigators (D.S.-C. and A.T.-N.), who carefully reviewed the full text of the selected papers to extract all data and judged each study according to the previous criteria. Disagreement was resolved by consensus and/or consultations with the senior author (S.R.). One investigator (D.S.-C) contacted authors by e-mail for missing data up to three attempts, excluding those without a response.

Assessment of risk of bias. Study quality was evaluated using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool (38). The risk of bias and concerns over applicability were assessed by two reviewers (A.T.-N. and D.S.-C.). Discrepancies were resolved by a third reviewer (S.R.). The risk of bias was summarized in a table as "low," "unclear," or "high" for each domain, whereas the degree of applicability was rated as "low," "unclear," or "high" for the first three domains. The "unclear" category was used only when reported data were insufficient (see Supplementary File 3).

Statistical analysis. All statistical analyses were performed with the MIDAS package in STATA 15.0 (STATA Corp., College Station, TX, USA) (39, 40). Pooled sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), and the area under the curve of the summary receiver operating characteristic curve (AUC-SROC) were calculated using a bivariate model, with the studies that had $TP+FN > 0$ and $FP+TN > 0$. The bivariate analysis considers the size of the study and uses a random-effects approach to obtain heterogeneity beyond the methodological and clinical differences between studies. We also performed a univariate analysis with all studies, including those with $TP+FN = 0$ or $FP+TN = 0$.

The accuracy level was evaluated by plotting the SROC curve and calculating the AUC, considering very good (AUC = 0.90 to 1), good (0.80 to 0.90), fair (0.70 to 0.80), poor (0.60 to 0.70), and failed (0.50 to 0.60) (41). For clinical utility, a four-quadrant likelihood scatter matrix was used as follows (42): (i) left upper quadrant (LUQ; PLR >10, NLR <0.1): confirmation and exclusion; (ii) right upper quadrant (RUQ; PLR >10, NLR >0.1): confirmation only; (iii) left lower quadrant (LLQ; PLR <10, NLR <0.1): exclusion only; and (iv) right lower quadrant (RLQ; PLR <10, NLR >0.1): no confirmation or exclusion. The clinical or patient-relevant utility was also assessed with Fagan's nomogram, which gave the posttest prediction at the population level, taking into account the prevalence or pretest probability estimation (0.1%, 0.5%, 1%, 5%, 10%, and 15%) and the PLR and NLR values (43).

The Cochran-Q method and inconsistency index (I^2) quantified the heterogeneity between the studies, being significant with P of ≤ 0.10 and I^2 of ≥50%, respectively (44). Galbraith (radial) (45) and bivariate boxplots (bagplot) (46) were also used to analyze the heterogeneity. Furthermore, meta-regression was performed to define the impact of several factors on diagnostic accuracy measures ($P \leq 0.10$): year of publication (Yes: ≤2015; No: >2015), low- or middle-income countries (LMICs; Yes/No), all patients with positive anti-HCV (anti-HCV Ab +) (Yes/No), biological sample type (Yes: only serum; No: plasma or plasma/serum), frozen sample (Yes/No), large sample size (Yes: ≤100; No: >100), and HCV prevalence (≤50; No: >50). We used Deeks' funnel plot asymmetry test to evaluate publication bias, with a symmetric funnel shape when there is no publication bias ($P > 0.10$) (47).

Ethics approval and consent to participate. This study was approved by the Instituto de Salud Carlos III Ethics Committee (ref.: CEI PI 13_2021). This study involves clinical-epidemiological data of patients from published articles, so informed consent signed by patients was unnecessary.

Data availability. All relevant data are within the article and the supplemental material.

RESULTS

Search results. Figure 1A shows the flowchart summarizing the steps to identify the eligible studies. The initial search of electronic databases reported 9,368 articles covering the literature published between 1976 and 2022. Of these, 30% (n = 2,841) were duplicates, and the remaining 6,527 articles were reviewed. Based on the evaluation of titles and abstracts, together with a detailed evaluation, a total of 6,325 studies were filtered out. After evaluating the full texts of 202 studies, 14 were eligible for this meta-analysis because all reported the necessary information and met the inclusion criteria mentioned above (20 to 33).

Article characteristics. Table 1 summarizes the main characteristics of the 14 articles included in this meta-analysis. All studies were published between 2012 and 2022, had a cross-sectional design, included adults only, and were published in English, except one published in German (22). Three studies were carried out in LMICs (26, 28, 31). A total of 2,526 individuals were included, with 82.1% male and a mean age of 45. The HCV

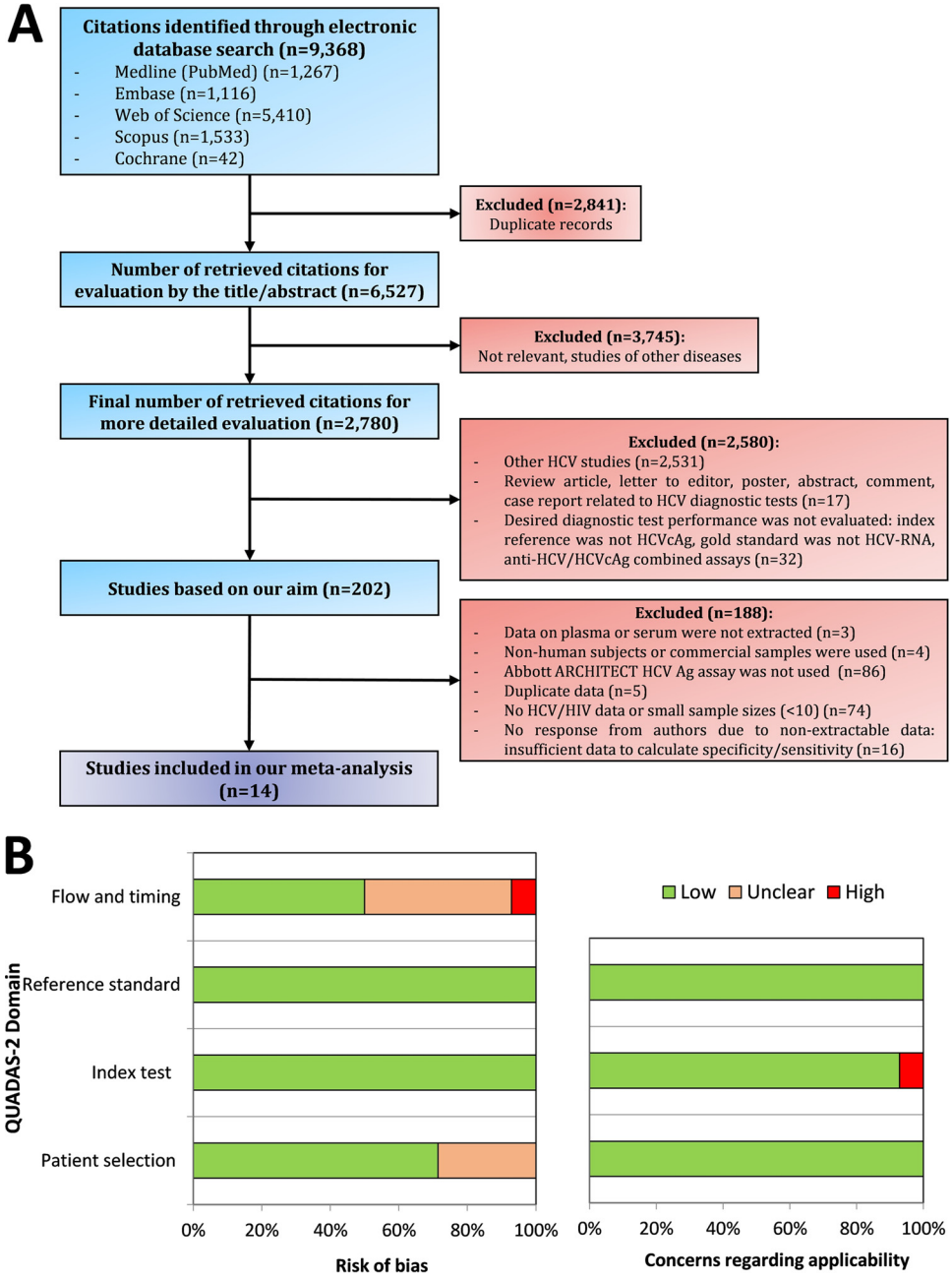

FIG 1 (A) Flowchart of the study searching process. (B) Quality assessment of eligible studies according to the QUADAS-2 tool. In panel B, green indicates a low risk, orange stands for unclear risk, and red indicates a high risk. cAg, core antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; QUADAS, quality assessment of diagnostic accuracy studies.

genotypes ranged from 1 to 6, and only four studies (21, 22, 30, 33) provided information on the HBV status, with a prevalence between 3.8 and 78.3%.

HCVcAg quantification was performed using the Abbott ARCHITECT HCV Ag assay, whose lower limit of detection (LLOD) was 3 fmol/L (0.06 pg/mL). The primary gold standard assay to detect HCV-RNA was the COBAS Ampliprep/COBAS TaqMan HCV Real-time PCR (Roche Diagnostics) (n = 9; LLOD: 12, 15, and 600 IU/mL) (20, 22, 25, 27 to 30, 32, 33), followed by the Abbott RealTime HCV Assay (Abbott Diagnostics) (n = 4; LLOD: 12 IU/mL) (21, 23, 26, 31) and the VERSANT HCV RNA Qualitative Assay (Siemens Healthcare Diagnostics) (n = 1; LLOD: 615 IU/mL) (24).

Assessment of risk of bias. QUADAS-2 (Fig. 1B and Supplementary File 3) showed that the risk of bias in the patient selection domain was unclear in four studies (21, 22,

TABLE 1 Summary of studies included in the meta-analysis detecting HCV core antigen with Abbott ARCHITECT HCVcAg assay in serum and/or plasma samples from PLWHA[a]

Author (yr) (reference)	Country	No.	Age (yrs)	Males (%)	HCV genotype	HBV (%)	Sample type	Sample condition	GS cutoff (IU/mL)
Mederacke et al. (2012) (20)	Germany	71	N/D	N/D	1, 3, 4	N/D	Serum/plasma	Frozen	15 and 600
Garbuglia et al. (2014) (21)	Italy	249	47	69.6	1, 3, 4	3.8	Plasma	Frozen	12
Van Helden et al. (2014) (22)	Germany	97	38.2	84.5	1, 2, 3	9.3	Serum	Frozen	15
Cresswell et al. (2015) (23)	UK	111	45.2	94.6	1, 3, 4	N/D	Serum	Frozen	N/D
Vanhommerig et al. (2015) (24)	Netherlands	91	N/D	100	1, 2, 3, 4	N/D	Serum	Unknown	615
Arboledas et al. (2017) (25)	Spain	68	49.8	80.5	1, 3, 4	N/D	Plasma	Frozen	15
Duchesne et al. (2017) (26)	Cameroon	78	46.3	43.5	1, 2, 4	N/D	Serum	Frozen	12
Hullegie et al. (2017) (27)	Netherlands	67	41	100	1	N/D	Serum/plasma	N/D	15 and 12
Mohamed et al. (2017) (28)	Tanzania	65	38	92.2	1, 4	N/D	Serum	Frozen	15
Talal et al. (2017) (29)	USA	19	53.8	59.6	1, 2, 3, 4	N/D	Serum	Frozen	15
Alonso et al. (2018) (30)	Spain	20	N/D	N/D	1, 2, 3	78.3	Serum	Frozen	15
Chayanupatkul et al. (2020) (31)	Thailand	36	41.4	83.3	1	N/D	Serum	Frozen	12
Rossetti et al. (2021) (32)	Italy	20	56	80	1, 2, 3, 4	N/D	Serum/plasma	Frozen	15 and 12
Sun et al. (2022) (33)	Taiwan	1534	40.5	97.6	1, 2, 6	10.3	Plasma	N/D	15

[a]GS, gold standard; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IU, international units; No., sample size; N/D, data not available; PLWHA, people living with HIV/AIDS; yrs = years.

26, 30) (28.6%) due to the lack of information on whether the study was consecutive, randomized, or neither. The patient sample to evaluate the diagnostic test accuracy was also not documented. Both flow bias and timing bias were unclear in six (42.9%) studies (20, 22, 25, 27, 28, 32) and high in one (7.1%) (33) because the delay between the reference test and the index test was not correctly reported.

All studies had a low risk of bias for the index and reference standard domains. Although the analytical sensitivity of the three NAATs used as a reference standard is different, overall, the tests were highly sensitive, and the variability was minimal. Besides, HCV-RNA loads measured by NAATs correlated well with HCVcAg levels, as is shown in most eligible studies (20 to 23, 26, 28 to 32). Moreover, even if the reference standard resulted in knowledge of the index test result, it is unlikely to introduce bias. The applicability of the included studies was low for all but one study (33), which showed significant concerns about the performance and interpretation of the HCVcAg test.

Diagnostic validity. The bivariate analysis was conducted on 11 studies with 2,407 samples. Pooled sensitivity was 0.95 (95% CI = 0.92 to 0.97) (Fig. 2A), specificity was 0.97 (95% CI = 0.93 to 0.99) (Fig. 2B), PLR was 37.76 (95% CI = 12.84 to 111.02) (Fig. 2C), and NLR was 0.06 (95% CI = 0.04 to 0.09) (Fig. 2D). The AUC-SROC was 0.97 (95% CI = 0.20 to 1.00), suggesting that the overall diagnostic performance of HCVcAg in PLWHA was very good (Fig. S1 in the supplemental material). The univariate analysis (n = 14 articles) showed a pooled sensitivity of 0.96 (95% CI = 0.93 to 0.98), slightly higher than the bivariate analysis (Fig. S2).

Clinical application. Fagan's nomograms showed that for low prevalence (≤1%), the posttest probability that an individual with a positive test was a TP ranged from 4% to 28%, while, at high prevalence (≥10%), the posttest probability was between 81% and 87%, indicating that a confirmatory test should be necessary, particularly with prevalence values of ≤1% (Fig. 3). However, the probability that an individual with a negative test was an FN was close to zero, regardless of HCV prevalence (Fig. 3).

Exploration of heterogeneity. The heterogeneity tests showed I^2 = 40.6% (P = 0.08) for sensitivity (moderate heterogeneity), I^2 = 87.3% ($P < 0.001$) for specificity (considerable heterogeneity), I^2 = 78.8% ($P < 0.001$) for PLR (substantial heterogeneity), and no significant heterogeneity (I^2 = 37.0% [P = 0.10]) for NLR (Fig. 2). Three studies (22, 29, 30) in the Galbraith plot (Fig. 4A) and two studies (29, 30) in the bivariate box plot fell outside the 95% CI (Fig. 4B), suggesting a source of heterogeneity for these studies, especially for one common to both analyses (29). However, the heterogeneity did not change much after removing this article (29) from the analysis.

Meta-regression analysis showed that four factors (LMICs, biological sample type, sample size, and HCV prevalence) had a significant impact on heterogeneity ($P \leq 0.10$)

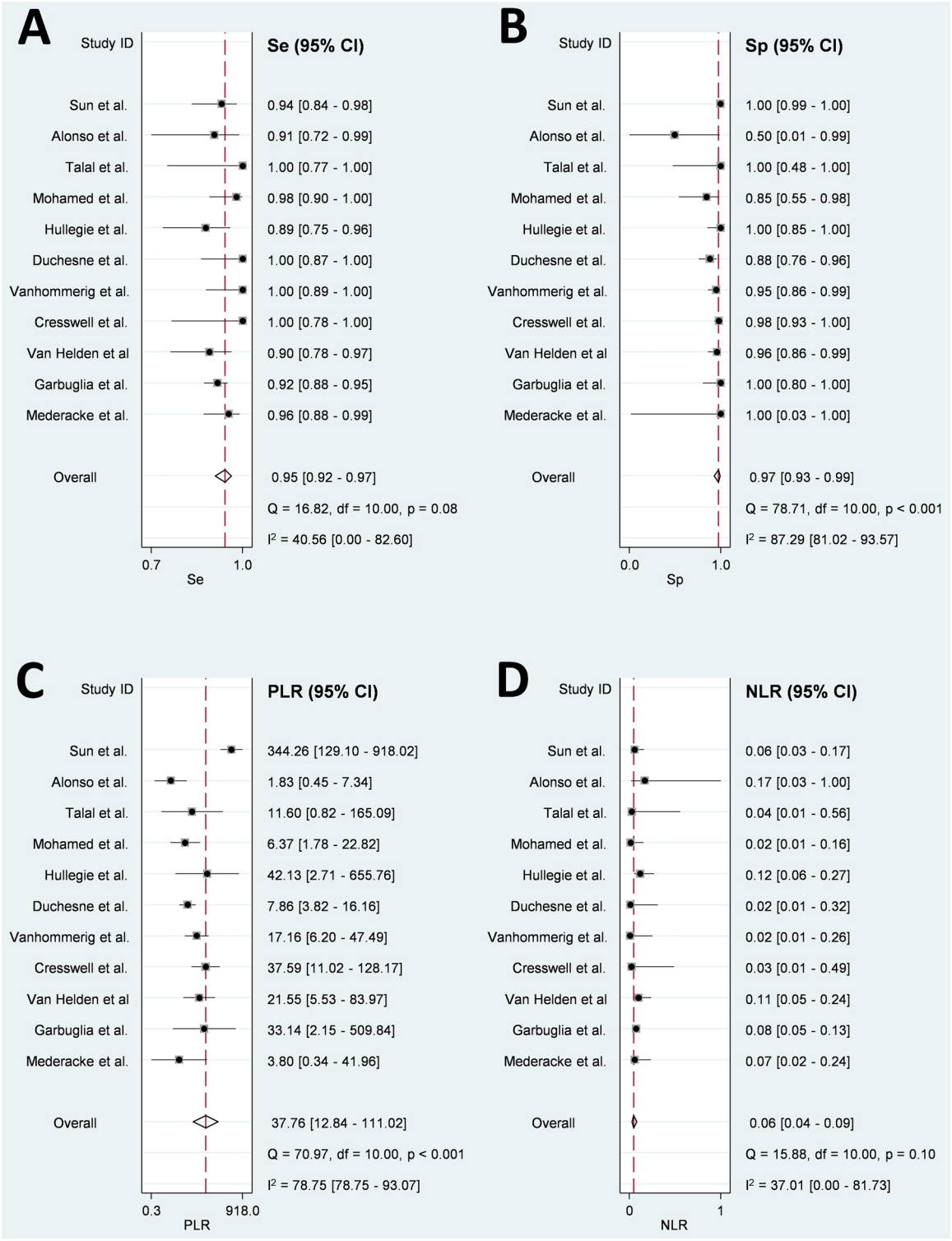

FIG 2 Forest plots of pooled Se (A), Sp (B), PLR (C), and NLR (D) for all studies included in the bivariate analysis for detecting active HCV infection with Abbott ARCHITECT HCV Ag assay in PLWHA compared with a confirmatory nucleic acid test. 95% CI, 95% confidence interval; HCV, hepatitis C virus; I^2, inconsistency index; NLR, negative likelihood ratio; PLR, positive likelihood ratio; PLWHA, people living with HIV/AIDS; Se, sensitivity; Sp, specificity.

(Table S1). Moreover, year of publication, LMIC, all patients with anti-HCV Ab +, biological sample type, frozen sample, gold standard cutoff, and sample size had a significant effect on sensitivity ($P \leq 0.10$), but only LMIC, biological sample type, frozen sample, and sample size had a significant impact on specificity ($P \leq 0.10$) (Table S2). However,

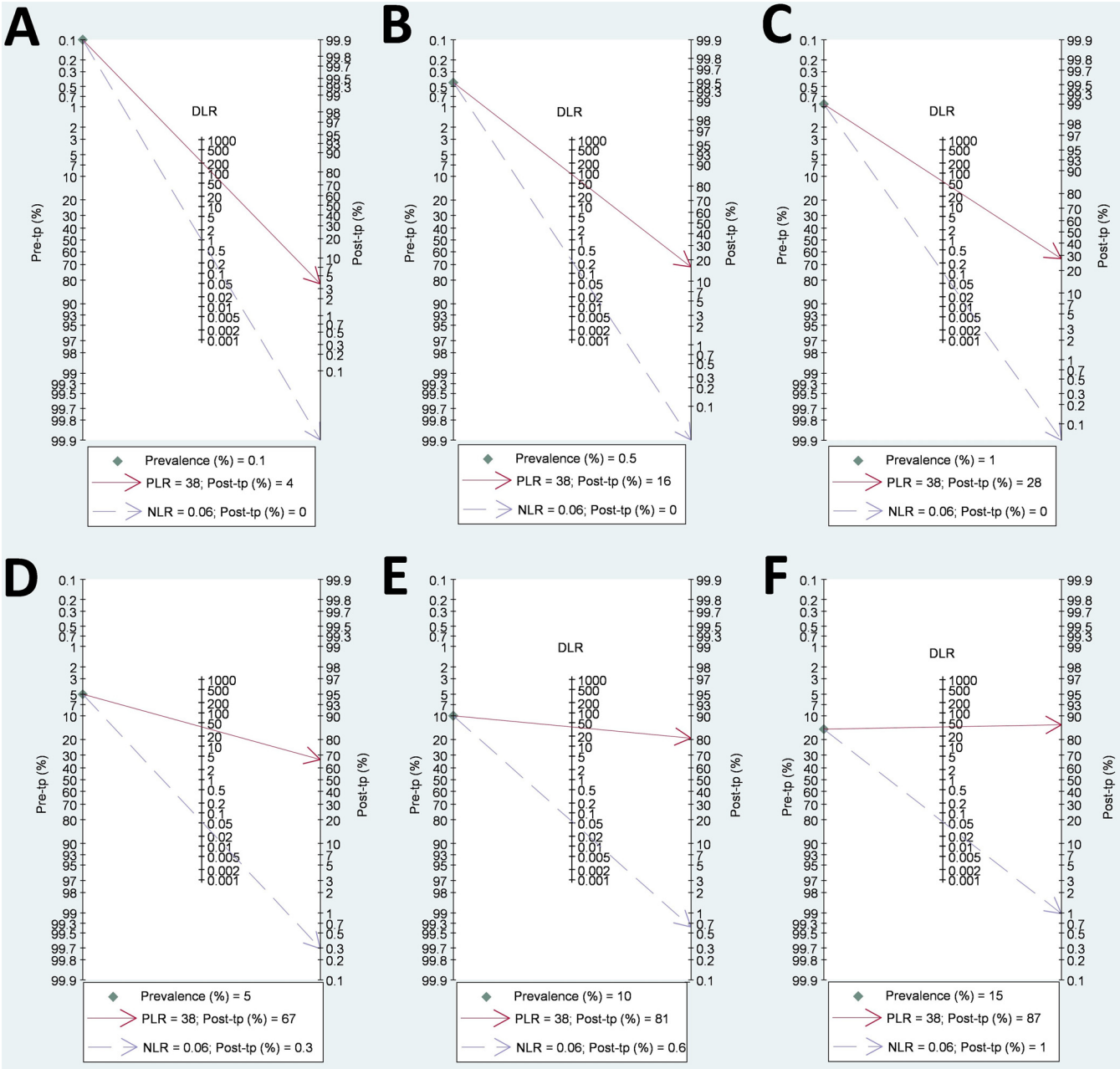

FIG 3 Fagan's plot of PLR and NLR to evaluate the clinical utility of detecting active HCV infection in PLWHA with Abbott ARCHITECT HCV Ag assay compared with a confirmatory nucleic acid test at different HCV prevalence percentages: 0.1% (A), 0.5% (B), 1% (C), 5% (D), 10% (E), and 15% (F). DLR, diagnostic likelihood ratio; HCV, hepatitis C virus; NLR, negative likelihood ratio; PLR, positive likelihood ratio; PLWHA, people living with HIV/AIDS; Post-tp, posttest probability; Pre-tp, pretest probability.

these significant differences in sensitivity and specificity were minor, with very close values between the groups, and in practice, they were not very relevant.

Based on Deeks' funnel plot, publication bias was observed ($P = 0.01$), indicating a potential impact on heterogeneity (Fig. S3).

DISCUSSION

In this bivariate meta-analysis, we found two main findings. (i) The diagnostic validity (accuracy) of the Abbott ARCHITECT HCV Ag assay to diagnose active HCV infection in serum/plasma samples from PLWHA was very high, where the sensitivity, specificity, and AUC-SROC values were very good. (ii) The HCVcAg assay showed limited clinical utility to

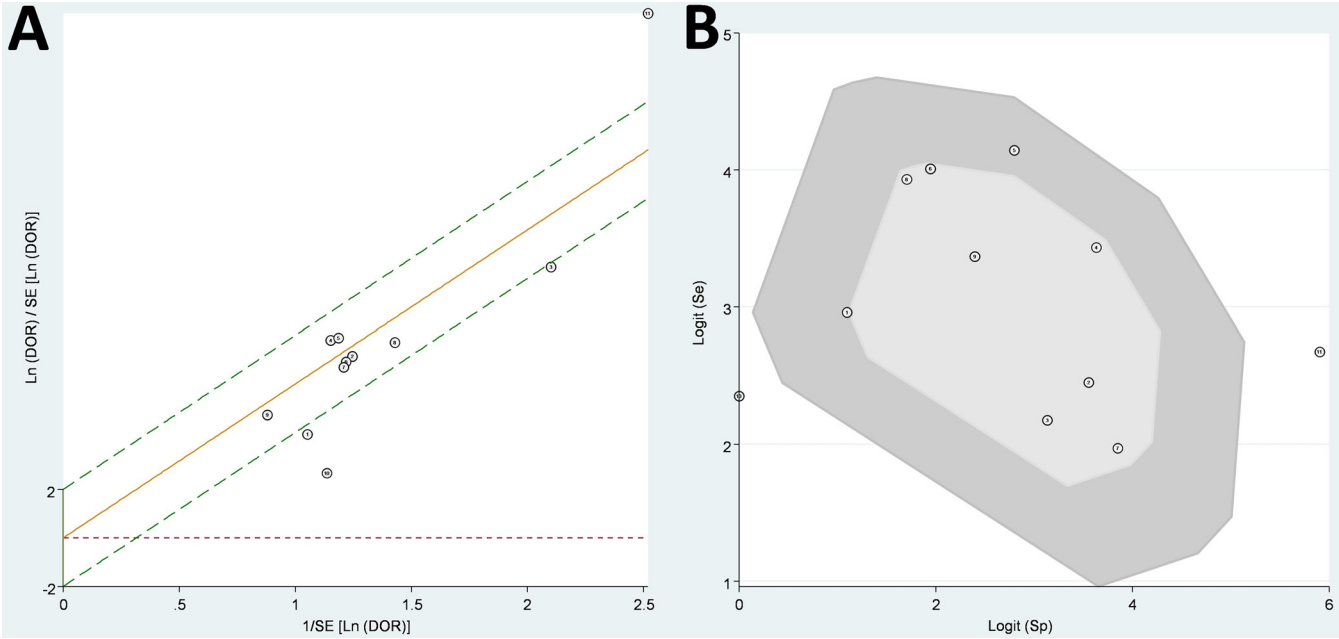

FIG 4 Galbraith plot (A) and bagplot (B) to assess heterogeneity of the bivariate meta-analysis. DOR, diagnostic odds ratio; Se, sensitivity; SE, standard error; Sp, specificity.

confirm active HCV infection, mainly in low-prevalence settings (≤1%). Still, it was excellent because the HCVcAg assay excluded active HCV infection regardless of prevalence.

The Abbott ARCHITECT HCV Ag assay is an inexpensive, rapid (~40 min), and easy-to-perform assay with high analytical sensitivity for HCV RNA loads above 10,000 IU/mL, although slightly lower for viral values below this cutoff (17, 48). To our knowledge, this meta-analysis is the first to show the diagnostic performance of the Abbott ARCHITECT HCV Ag assay to diagnose active HCV infection in PLWHA. Freiman et al. (34) published an outstanding meta-analysis that evaluated the Abbott ARCHITECT HCV Ag assay to detect active HCV infection. However, they did not perform a meta-analysis on a subgroup of PLWHA due to the lack of necessary studies. Now, we evaluated the diagnostic performance of the Abbott ARCHITECT HCV Ag assay in PLWHA, collecting data from 14 studies (n = 2,526 individuals), a sample size large enough to extract conclusive results. Our meta-analysis and that of Freiman et al. (34) achieved very similar results in sensitivity (95.0% versus 93.4%), specificity (97.0% versus 98.8%), NLR (both 0.06), and AUC-SROC (both >97%). However, the overall PLR value from our meta-analysis was lower than that of Freiman et al. (34) (37.76 versus 80.6). Despite the latter, both meta-analyses showed an excellent and similar diagnostic validity (accuracy) of the HCVcAg assay for HCV detection. Moreover, Freiman et al. (34) did not show data on clinical application and only highlighted the possible replacement of NAAT by HCVcAg tests in scenarios with a high HCV prevalence. Our meta-analysis found solid evidence to accept or rule out active HCV infection. Fagan's nomogram showed that the clinical utility of the HCVcAg assay was small in low-prevalence (≤1%) and limited in high-prevalence (≥10%) settings. Thus, NAAT should be necessary to confirm a positive result of the HCVcAg assay. In the best case, the Abbott ARCHITECT HCV Ag test could be an alternative to NAAT in high-prevalence settings (≥10%) where the probability of active HCV infection is greater than 80%. The high prevalence of hepatitis C is usually found in high-risk populations (prisoners, PWID, MSM, or sex workers), where HIV/HCV coinfection is generally high because HCV and HIV share common transmission routes (6). Besides, these risk populations have a higher chance of HCV reinfection after being cured with DAA treatment because they have high-risk behaviors that lead to HCV transmission (49).

The quality of a meta-analysis depends on the quality of the included studies. In our meta-analysis, the overall quality was medium-high because many elements

related to the risk of bias were unclear or missing. Some studies did not show information on the use of consecutive or random samples, the design of the studies resembled that of case-control studies, and little information was provided on the flow of patients and time in the study.

Heterogeneity is another factor to consider when assessing a meta-analysis. Our meta-analysis showed moderate-substantial heterogeneity, which is common in meta-analyses of diagnostic tests because all potential confounders are difficult to control. The meta-regression showed that LMIC, biological sample type, sample size, and HCV prevalence significantly impacted heterogeneity. It may also be due to other factors not being analyzed due to insufficient raw data from HCV viral load, HCV subtype, HBV coinfection, or RNA extraction methods. Therefore, a random effects analysis should be used as there is significant heterogeneity between studies, assuming that all studies measure different parameters (50). Furthermore, all analyzed confounders, except HCV prevalence, impacted sensitivity and/or specificity, but their effect was clinically irrelevant.

Limitations. Finally, some limitations must be considered to interpret our data correctly. (i) We found publication bias in favor of a greater tendency to publish studies with favorable results. Probably, some studies with unfavorable data have not been published. (ii) There was a lack of essential data in some articles. In several works, plasma and serum samples were used in the same study, and the frozen condition of the sample was unknown. Furthermore, as discussed above, we could not analyze by meta-regression the impact of several relevant factors (HCV viral load, HCV subtype, and HBV coinfection, among others) due to the lack of raw data in many articles. (iii) We could not test at what concentration of HCV Ag the RNA is always positive because the ARCHITECT HCV Ag assay uses a cutoff point set by the manufacturer. Besides, we have only aggregated data from each study, not data from the individuals included in these studies. (iv) The same protocols were not applied to extract and determine HCV-RNA, which could affect the results. Additional studies are needed to improve the evaluation of the diagnostic performance of the Abbott ARCHITECT HCV Ag assay in PLWHA.

Conclusions. In conclusion, the accuracy of the Abbott ARCHITECT HCV Ag assay was very good for HCV screening in serum/plasma samples from PLWHA. The clinical utility to confirm HCV infection was acceptable in high-prevalence settings ($\geq$10%), but poor in low-prevalence settings ($\leq$1%) and excellent in excluding active HCV infection. This HCVcAg assay could help implement HCV screening programs in PLWHA in high-risk populations with difficult access to the health system (PWID, MSM).

SUPPLEMENTAL MATERIAL

Supplemental material is available online only.

SUPPLEMENTAL FILE 1, PDF file, 1 MB.

ACKNOWLEDGMENTS

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The authors declare no competing interests.

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Daniel Sepúlveda-Crespo, investigation, resources, writing – original draft; Ana Treviño-Nakoura, investigation, resources, writing – review, and editing; José M. Bellón, investigation, methodology, formal analysis, writing – review, and editing; María A. Jiménez-Sousa, writing – review, and editing; Pablo Ryan, writing – review, and editing. Isidoro Martínez, methodology,

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