Supplementary Materials

Type of manuscript: Full-Length Text
Title: Diagnostic performance of HCV core antigen testing to identify hepatitis C in HIV-infected patients: a systematic review and meta-analysis
Running head: Diagnostic performance of HCVcAg test in PLWHA

Authors: Daniel SEPÚLVEDA-CRESPO [1,2,¥]; Ana TREVIÑO-NAKOURA [3,4,¥]; José M BELLON [5]; María A. JIMÉNEZ-SOUSA [1,2]; Pablo RYAN [2,6]; Isidoro MARTÍNEZ [1,2,¥]; Amanda FERNÁNDEZ-RODRÍGUEZ [1,2,¥]; Salvador RESINO [1,2,*,¥]
(¥), Both authors contributed equally to this study; (*), Corresponding author

Current affiliations:
(1) Unidad de Infección Viral e Inmunidad. Centro Nacional de Microbiología - Instituto de Salud Carlos III, Majadahonda, Spain.
(2) Centro de Investigación Biomédica en Red en Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain.
(3) Servicio de Medicina Preventiva y Salud Pública, Hospital Universitario Nuestra Señora de la Candelaria, Santa Cruz de Tenerife, Spain.
(4) Universidad Nacional de Educación a Distancia (UNED), Madrid, Spain
(5) Instituto de Investigación Sanitaria Gregorio Marañón (IiSGM), Madrid, Spain.
(6) Servicio de Medicina Interna, Hospital Universitario Infanta Leonor, Madrid, Spain.

Supplementary File 1: PRISMA-DTA Checklist and Abstracts Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	3-4
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	5
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5-6
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	Suppl. 5-12
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	Fig. 1
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5-6
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	5-6
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	6

Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	6-7
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	6-7
Section/topic	**#**	**PRISMA-DTA Checklist Item**	**Reported on page #**
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	6-7
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	8
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	Table 1
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	8-9
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	Fig. 2-4 and Suppl. Fig. 1-3
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	9
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	9-10
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	11
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	13

FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	14

Section/topic	#	PRISMA-DTA for Abstracts Checklist item	Reported on page #
TITLE and PURPOSE			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	2
Objectives	2	Indicate the research question, including components such as participants, index test, and target conditions.	2
METHODS			
Eligibility criteria	3	Include study characteristics used as criteria for eligibility.	2
Information sources	4	List the key databases searched and the search dates.	2
Risk of bias & applicability	5	Indicate the methods of assessing risk of bias and applicability.	2
Synthesis of results	A1	Indicate the methods for the data synthesis.	2
RESULTS			
Included studies	6	Indicate the number and type of included studies and the participants and relevant characteristics of the studies (including the reference standard).	2
Synthesis of results	7	Include the results for the analysis of diagnostic accuracy, preferably indicating the number of studies and participants. Describe test accuracy including variability; if meta-analysis was done, include summary results and confidence intervals.	2
DISCUSSION			
Strengths and limitations	9	Provide a brief summary of the strengths and limitations of the evidence	2
Interpretation	10	Provide a general interpretation of the results and the important implications.	2
OTHER			
Funding	11	Indicate the primary source of funding for the review.	14
Registration	12	Provide the registration number and the registry name	2

Supplementary File 2: Search strategy

Search strategy PubMed

("hepatitis c"[MeSH Terms] OR "hepacivirus"[MeSH Terms] OR ("hepatitis c"[Title/Abstract] OR "hepatitis c virus"[Title/Abstract] OR "hepatitis c viruses"[Title/Abstract] OR "hepatitis c like virus"[Title/Abstract] OR "hepatitis c like viruses"[Title/Abstract] OR "hepatitis virus type c"[Title/Abstract] OR "hcv"[Title/Abstract] OR "h c v"[Title/Abstract] OR "vhc"[Title/Abstract] OR "v h c"[Title/Abstract] OR "hepacivirus"[Title/Abstract] OR "hepaciviruses"[Title/Abstract] OR "hcv viral"[Title/Abstract] OR "hcv infected"[Title/Abstract] OR "hcv infection"[Title/Abstract] OR "hcv rna"[Title/Abstract] OR "hepatitis c virus rna"[Title/Abstract] OR "parenterally transmitted non a non"[Title/Abstract] OR "pt nanbh"[Title/Abstract])) AND ("diagnosis"[MeSH Terms] OR "diagnostic techniques and procedures"[MeSH Terms] OR "clinical laboratory techniques"[MeSH Terms] OR "mass screening"[MeSH Terms] OR "nucleic acid amplification techniques"[MeSH Terms] OR "rna"[MeSH Terms] OR "rna, viral/blood"[MeSH Terms] OR ("clinical laboratory diagnoses"[Title/Abstract] OR "clinical laboratory diagnostic"[Title/Abstract] OR "clinical laboratory techniques"[Title/Abstract] OR "clinical laboratory testing"[Title/Abstract] OR "diagnose"[Title/Abstract] OR "diagnoses"[Title/Abstract] OR "diagnosis of hcv"[Title/Abstract] OR "diagnosis"[Title/Abstract] OR "diagnostic techniques and procedures"[Title/Abstract]OR "diagnostic"[Title/Abstract] OR "hcv infection diagnosis"[Title/Abstract] OR "hcv testing"[Title/Abstract] OR "mass screening"[Title/Abstract] OR "mass screenings"[Title/Abstract] OR "molecular diagnostic techniques"[Title/Abstract] OR "screening approach"[Title/Abstract] OR "screening"[Title/Abstract] OR "testing diagnostic"[Title/Abstract] OR "plasma levels"[Title/Abstract] OR "sera"[Title/Abstract] OR "serum levels"[Title/Abstract] OR "dried blood filter" [Title/Abstract] OR "dried blood spot"[Title/Abstract] OR "dried blood" [Title/Abstract] OR "dried sample" [Title/Abstract] OR "filter paper" [Title/Abstract] OR "Whatman" [Title/Abstract] OR "DBS" [Title/Abstract] OR "assay kits"[Title/Abstract] OR "hcv assays"[Title/Abstract] OR "hcv pcr assay"[Title/Abstract] OR "hcv pcr method"[Title/Abstract] OR "hcv pcr"[Title/Abstract] OR "hcv rna levels"[Title/Abstract] OR "hcv rna quantification assays"[Title/Abstract] OR "hcv rna quantification"[Title/Abstract] OR "hepatitis c markers"[Title/Abstract] OR "hepatitis markers"[Title/Abstract] OR "immunoassay"[Title/Abstract] OR "quantitative assays"[Title/Abstract] OR "quantitative reverse transcription pcr"[Title/Abstract] OR "real time pcr"[Title/Abstract] OR "rna levels"[Title/Abstract] OR "roche cobas taqman assays"[Title/Abstract] OR "roche cobas taqman hcv"[Title/Abstract])) AND ("hepatitis c antigens"[MeSH Terms] OR ("antigens"[Title/Abstract] OR "core antigen assay"[Title/Abstract] OR "core antigen assays"[Title/Abstract] OR "core antigen test"[Title/Abstract] OR "core antigen"[Title/Abstract] OR "hcv ag assay"[Title/Abstract] OR "hcv ag detection"[Title/Abstract]OR "hcv ag"[Title/Abstract] OR "hcv antigen testing"[Title/Abstract] OR "hcv antigen"[Title/Abstract] OR "HCVcAg"[Title/Abstract] OR "hcv core antigen assay"[Title/Abstract] OR "hcv core antigen assays"[Title/Abstract] OR "hcv core antigen detection"[Title/Abstract] OR "hcv core antigen determination"[Title/Abstract] OR "hcv core antigen testing"[Title/Abstract] OR "hcv core antigen"[Title/Abstract] OR "hcv core protein"[Title/Abstract] OR "hcv core region"[Title/Abstract] OR "hcv cp"[Title/Abstract] OR "hcvcoreag"[Title/Abstract] OR "hepatitis c antigens"[Title/Abstract] OR "hepatitis c virus core antigen"[Title/Abstract] OR "hepatitis c virus core"[Title/Abstract] OR "hepatitis non a non b antigen"[Title/Abstract] OR "viral core proteins"[Title/Abstract])) AND ("accuracy"[Title/Abstract] OR "correlation"[Title/Abstract] OR "correlations"[Title/Abstract] OR

"negative predictive power"[Title/Abstract] OR "negative predictive value"[Title/Abstract] OR "negative predictive values"[Title/Abstract] OR "NPV"[Title/Abstract] OR "positive predictive power"[Title/Abstract] OR "positive predictive value"[Title/Abstract] OR "positive predictive values"[Title/Abstract] OR "PPV"[Title/Abstract] OR "receiver operating characteristics"[Title/Abstract] OR "regression analysis"[Title/Abstract] OR "ROC"[Title/Abstract] OR "sensitive"[Title/Abstract] OR "sensitivities"[Title/Abstract] OR "sensitivity"[Title/Abstract] OR "specific"[Title/Abstract] OR "specificity"[Title/Abstract] OR “Abbott ARCHITECT HCV Ag assay” OR “Abbott ARCHITECT HCV Ag test” OR “Abbott ARCHITECT i2000SR” OR “Abbott ARCHITECT test” OR “Abbott Diagnostics” OR “Abbott HCV core antigen” OR “Abbott Laboratories” OR “ARCHITECT” OR “ARCHITECT ci8200” OR “Architect core antigen” OR “Architect HCV Ag” OR “ARCHITECT HCV Core antigen” OR “ARCHITECT i2000SR” OR “ARCHITECT system” OR "cleia method" OR “chemiluminescence immunoassay”) NOT ("review"[Publication Type]) NOT ("meta-analysis"[Publication Type]) NOT ("systematic review"[Publication Type])

Search strategy Embase

#1 'hepatitis c'/exp OR 'hepacivirus'/exp OR 'hepatitis c virus':ti,ab,kw OR 'hepatitis c viruses':ti,ab,kw OR 'hepatitis c like viruses':ti,ab,kw OR 'hepatitis virus type c':ti,ab,kw OR hcv:ti,ab,kw OR 'h c v':ti,ab,kw OR vhc:ti,ab,kw OR 'v h c':ti,ab,kw OR hepacivirus:ti,ab,kw OR hepaciviruses:ti,ab,kw OR 'parenterally transmitted non a non':ti,ab,kw
#2 'diagnosis'/exp OR ('diagnostic techniques'/exp AND 'procedures'/exp) OR 'clinical laboratory techniques'/exp OR 'nucleic acid amplification techniques'/exp OR 'rna'/exp OR 'clinical laboratory diagnostic':ti,ab,kw OR 'clinical laboratory techniques':ti,ab,kw OR 'clinical laboratory testing':ti,ab,kw OR diagnose:ti,ab,kw OR diagnoses:ti,ab,kw OR 'diagnosis of hcv':ti,ab,kw OR diagnosis:ti,ab,kw OR ('diagnostic techniques':ti,ab,kw AND procedures:ti,ab,kw) OR diagnostic:ti,ab,kw OR 'hcv testing':ti,ab,kw OR 'mass screening':ti,ab,kw OR 'mass screenings':ti,ab,kw OR 'screening approach':ti,ab,kw OR screening:ti,ab,kw OR 'plasma levels':ti,ab,kw OR sera:ti,ab,kw OR 'serum levels':ti,ab,kw OR 'dried blood filter':ti,ab,kw OR 'dried blood spot':ti,ab,kw OR 'dried blood':ti,ab,kw OR 'dried sample':ti,ab,kw OR 'filter paper':ti,ab,kw OR whatman:ti,ab,kw OR dbs:ti,ab,kw OR 'assay kits':ti,ab,kw OR 'hcv assays':ti,ab,kw OR 'hcv pcr assay':ti,ab,kw OR 'hcv pcr':ti,ab,kw OR 'hcv rna levels':ti,ab,kw OR 'hcv rna quantification':ti,ab,kw OR 'hepatitis c markers':ti,ab,kw OR 'hepatitis markers':ti,ab,kw OR immunoassay:ti,ab,kw OR 'quantitative assays':ti,ab,kw OR 'quantitative reverse transcription pcr':ti,ab,kw OR 'real time pcr':ti,ab,kw OR 'rna levels':ti,ab,kw OR 'roche cobas taqman':ti,ab,kw
#3 'hepatitis c antigens'/exp OR antigens:ti,ab,kw OR 'cleia method':ti,ab,kw OR 'core antigen assay':ti,ab,kw OR 'core antigen assays':ti,ab,kw OR 'core antigen test':ti,ab,kw OR 'core antigen':ti,ab,kw OR 'hcv ag assay':ti,ab,kw OR 'hcv ag detection':ti,ab,kw OR 'hcv ag':ti,ab,kw OR 'hcv antigen testing':ti,ab,kw OR 'hcv antigen':ti,ab,kw OR hcvcoreag:ti,ab,kw OR hcvcag:ti,ab,kw OR 'hepatitis non a non b antigen':ti,ab,kw OR 'viral core proteins':ti,ab,kw
#4 'accuracy':ti,ab,kw OR 'correlation':ti,ab,kw OR 'correlations':ti,ab,kw OR 'negative predictive power':ti,ab,kw OR 'negative predictive value':ti,ab,kw OR 'negative predictive values':ti,ab,kw OR 'NPV':ti,ab,kw OR 'positive predictive power':ti,ab,kw OR 'positive predictive value':ti,ab,kw OR 'positive predictive values':ti,ab,kw OR 'PPV':ti,ab,kw OR 'receiver operating characteristics':ti,ab,kw OR 'regression analysis':ti,ab,kw OR 'ROC':ti,ab,kw OR 'sensitive':ti,ab,kw OR 'sensitivities':ti,ab,kw OR 'sensitivity':ti,ab,kw OR 'specific':ti,ab,kw OR 'specificity':ti,ab,kw OR 'Abbott ARCHITECT HCV Ag assay' OR ' Abbott ARCHITECT HCV Ag test' OR 'Abbott ARCHITECT i2000SR' OR 'Abbott ARCHITECT test' OR 'Abbott Diagnostics' OR 'Abbott HCV Ag' OR 'Abbott HCV core antigen' OR 'Abbott Laboratories' OR 'ARCHITECT' OR 'Architect core antigen' OR 'ARCHITECT i2000SR'
#5 #1 AND #2 AND #3 AND #4
#6 #5 AND ('Article'/it OR 'Article in Press'/it)

Search strategy Web of Knowledge (WoS)

#1 ((((((((((((((((((TS=(hepatitis c)) OR TS=(hepatitis c virus)) OR TS=(hepatitis c viruses)) OR TS=(hepatitis c like virus)) OR TS=(hepatitis c like viruses)) OR TS=(hepatitis virus type c)) OR TS=(hcv)) OR TS=(h c v)) OR TS=(vhc)) OR TS=(v h c)) OR TS=(hepacivirus)) OR TS=(hepaciviruses)) OR TS=(hcv viral)) OR TS=(hcv infected)) OR TS=(hcv infection)) OR TS=(hcv rna)) OR TS=(hepatitis c virus rna)) OR TS=(parenterally transmitted non a non)) OR TS=(pt-nanbh)

#2 ((TS=(clinical laboratory diagnoses)) OR TS=(clinical laboratory diagnostic)) OR TS=(clinical laboratory techniques)) OR TS=(clinical laboratory testing)) OR TS=(diagnose)) OR TS=(diagnoses)) OR TS=(diagnosis of hcv)) OR TS=(diagnosis)) OR TS=(diagnostic techniques and procedures)) OR TS=(diagnostic)) OR TS=(hcv infection diagnosis)) OR TS=(hcv testing)) OR TS=(mass screening)) OR TS=(mass screenings)) OR TS=(molecular diagnostic techniques)) OR TS=(screening approach)) OR TS=(screening)) OR TS=(testing diagnostic)) OR TS=(plasma levels)) OR TS=(sera)) OR TS=(serum levels)) OR TS=(dried blood filter)) OR TS=(dried blood spot)) OR TS=(dried blood)) OR TS=(dried sample)) OR TS=(filter paper)) OR TS=(Whatman)) OR TS=(DBS)) OR TS=(assay kits)) OR TS=(hcv assays)) OR TS=(hcv pcr assay)) OR TS=(hcv pcr method)) OR TS=(hcv pcr)) OR TS=(hcv rna levels)) OR TS=(hcv rna quantification assays)) OR TS=(hcv rna quantification)) OR TS=(hepatitis c markers)) OR TS=(hepatitis markers)) OR TS=(immunoassay)) OR TS=(quantitative assays)) OR TS=(quantitative reverse transcription pcr)) OR TS=(real time pcr)) OR TS=(rna levels)) OR TS=(roche cobas taqman assays)) OR TS=(roche cobas taqman hcv)

#3 ((((((((((((((((((((((((TS=(antigens)) OR TS=(cleia method)) OR TS=(core antigen assay)) OR TS=(core antigen assays)) OR TS=(core antigen test)) OR TS=(core antigen)) OR TS=(hcv ag assay)) OR TS=(hcv ag detection)) OR TS=(hcv ag)) OR TS=(hcv antigen testing)) OR TS=(hcv antigen)) OR TS=(hcv core antigen assay)) OR TS=(hcv core antigen assays)) OR TS=(hcv core antigen detection)) OR TS=(hcv core antigen determination)) OR TS=(hcv core antigen testing)) OR TS=(hcv core antigen)) OR TS=(hcv core protein)) OR TS=(hcv core region)) OR TS=(hcv cp)) OR TS=(hcvcoreag)) OR TS=(hcvcag)) OR TS=(hepatitis c antigens)) OR TS=(hepatitis c virus core antigen)) OR TS=(hepatitis c virus core)) OR TS=(hepatitis non a non b antigen)) OR TS=(viral core proteins)

#4 ((TS=(accuracy)) OR TS=(correlation)) OR TS=(correlations)) OR TS=(negative predictive power)) OR TS=(negative predictive value)) OR TS=(negative predictive values)) OR TS=(NPV)) OR TS=(positive predictive power)) OR TS=(positive predictive value)) OR TS=(positive predictive values)) OR TS=(PPV)) OR TS=(receiver operating characteristics)) OR TS=(regression analysis)) OR TS=(ROC)) OR TS=(sensitive)) OR TS=(sensitivities)) OR TS=(sensitivity)) OR TS=(specific)) OR TS=(specificity)) OR TS=(Abbott ARCHITECT HCV Ag assay)) OR TS=(Abbott ARCHITECT HCV Ag test)) OR TS=(Abbott ARCHITECT HCV Antigen assay)) OR TS=(Abbott ARCHITECT i2000SR)) OR TS=(Abbott ARCHITECT test)) OR TS=(Abbott Diagnostics)) OR TS=(Abbott HCV Ag)) OR TS=(Abbott HCV core antigen)) OR TS=(Abbott Laboratories)) OR TS=(ARCHITECT)) OR TS=(ARCHITECT ci8200)) OR TS=(Architect core antigen)) OR TS=(Architect HCV Ag)) OR TS=(ARCHITECT HCV Core antigen)) OR TS=(ARCHITECT HCVAg)) OR TS=(ARCHITECT i2000SR)) OR TS=(ARCHITECT system)) OR TS=(ARCHITECTHCVAg)) OR TS=(ARCHITECT-i2000R)) OR TS=(cleia method)) OR TS=(chemiluminescence immunoassay)

#5 #1 AND #2 AND #3 AND #4

#6 #5 NOT (DT==("REVIEW" OR "MEETING ABSTRACT" OR "PROCEEDINGS PAPER" OR "NOTE" OR "BOOK CHAPTER" OR "EDITORIAL MATERIAL" OR "LETTER"))

Search strategy SCOPUS

(TITLE-ABS-KEY ("hepatitis c virus") OR TITLE-ABS-KEY ("hepatitis c like virus") OR TITLE-ABS-KEY ({hepatitis virus type c}) OR TITLE-ABS-KEY ({hcv}) OR TITLE-ABS-KEY ({h c v}) OR TITLE-ABS-KEY ({vhc}) OR TITLE-ABS-KEY ({v h c}) OR TITLE-ABS-KEY ("hepacivirus") OR TITLE-ABS-KEY ({hcv viral}) OR TITLE-ABS-KEY ({hcv infected}) OR TITLE-ABS-KEY ({hcv infection}) OR TITLE-ABS-KEY ("hcv rna") OR TITLE-ABS-KEY ({pt nanbh}) OR TITLE-ABS-KEY ({parenterally transmitted non a non})) AND (TITLE-ABS-KEY ({clinical laboratory diagnoses}) OR TITLE-ABS-KEY ({clinical laboratory techniques}) OR TITLE-ABS-KEY ({clinical laboratory testing}) OR TITLE-ABS-KEY ("diagnose") OR TITLE-ABS-KEY ({diagnostic techniques and procedures}) OR TITLE-ABS-KEY ({hcv infection diagnosis}) OR TITLE-ABS-KEY ({hcv testing}) OR TITLE-ABS-KEY ("mass screening") OR TITLE-ABS-KEY ({molecular diagnostic techniques}) OR TITLE-ABS-KEY ("screening*") OR TITLE-ABS-KEY ({testing diagnostic}) OR TITLE-ABS-KEY ({plasma levels}) OR TITLE-ABS-KEY ({sera}) OR TITLE-ABS-KEY ({serum levels}) OR TITLE-ABS-KEY ("dried blood*") OR TITLE-ABS-KEY ("dried sample*") OR TITLE-ABS-KEY ({DBS}) OR TITLE-ABS-KEY ({filter paper}) OR TITLE-ABS-KEY ({Whatman}) OR TITLE-ABS-KEY ({assay kits}) OR TITLE-ABS-KEY ("hcv assay") OR TITLE-ABS-KEY (hcv pcr*) OR TITLE-ABS-KEY ({hcv rna levels}) OR TITLE-ABS-KEY ("hcv rna quantification*") OR TITLE-ABS-KEY ("hepatitis C markers") OR TITLE-ABS-KEY ({immunoassay}) OR TITLE-ABS-KEY ("quantitative assay") OR TITLE-ABS-KEY ({quantitative reverse transcription pcr}) OR TITLE-ABS-KEY ({real time pcr}) OR TITLE-ABS-KEY ({rna levels}) OR TITLE-ABS-KEY ({roche cobas taqman})) AND (TITLE-ABS-KEY ({antigens}) OR TITLE-ABS-KEY ({cleia method}) OR TITLE-ABS-KEY ("core antigen*") OR TITLE-ABS-KEY ("hcv ag*") OR TITLE-ABS-KEY ("hcv antigen*") OR TITLE-ABS-KEY ("hcv core antigen*") OR TITLE-ABS-KEY ("hcv core*") OR TITLE-ABS-KEY ("hcv cp") OR TITLE-ABS-KEY ("hcvcag") OR TITLE-ABS-KEY ("hcvcoreag") OR TITLE-ABS-KEY ("hepatitis c antigen") OR TITLE-ABS-KEY ({viral core proteins})) AND (TITLE-ABS-KEY ({ accuracy }) OR TITLE-ABS-KEY ({ correlation }) OR TITLE-ABS-KEY ({ correlations }) OR TITLE-ABS-KEY ({ negative predictive power }) OR TITLE-ABS-KEY ({ negative predictive value }) OR TITLE-ABS-KEY ({ negative predictive values }) OR TITLE-ABS-KEY ({ NPV}) OR TITLE-ABS-KEY ({ positive predictive power }) OR TITLE-ABS-KEY ({ positive predictive value }) OR TITLE-ABS-KEY ({ positive predictive values }) OR TITLE-ABS-KEY ({ PPV}) OR TITLE-ABS-KEY ({ receiver operating characteristics }) OR TITLE-ABS-KEY ({ regression analysis }) OR TITLE-ABS-KEY ({ ROC }) OR TITLE-ABS-KEY ({ sensitive }) OR TITLE-ABS-KEY ({ sensitivities }) OR TITLE-ABS-KEY ({ sensitivity }) OR TITLE-ABS-KEY ({ specific }) OR TITLE-ABS-KEY ({ specificity }) OR ALL ({ Abbott ARCHITECT HCV Ag assay }) OR ALL ({ Abbott ARCHITECT HCV Ag test }) OR ALL ({ Abbott ARCHITECT HCV Antigen assay }) OR ALL ({ Abbott ARCHITECT i2000SR }) OR ALL ({ Abbott ARCHITECT test }) OR ALL ({ Abbott Diagnostics }) OR ALL ({ Abbott HCV Ag }) OR ALL ({ Abbott HCV core antigen }) OR ALL ({ Abbott Laboratories }) OR ALL ({ ARCHITECT }) OR ALL ({ ARCHITECT ci8200}) OR ALL ({ Architect core antigen }) OR ALL ({ Architect HCV Ag }) OR ALL ({ ARCHITECT HCV Core antigen }) OR ALL ({ ARCHITECT HCVAg }) OR ALL ({ ARCHITECT i2000SR }) OR ALL ({ ARCHITECT system }) OR ALL ({ ARCHITECTHCVAg }) OR ALL ({ ARCHITECT-i2000R })) AND (EXCLUDE (DOCTYPE , "re") OR EXCLUDE (DOCTYPE , "cp") OR EXCLUDE (DOCTYPE , "le") OR EXCLUDE (DOCTYPE , "sh")) AND (EXCLUDE (DOCTYPE , "no") OR EXCLUDE (DOCTYPE , "ed") OR EXCLUDE (DOCTYPE , "ch") OR EXCLUDE (DOCTYPE , "dp"))

Search strategy Cochrane

#1 MeSH descriptor: [Hepatitis C] explode all trees
#2 MeSH descriptor: [Hepacivirus] explode all trees
#3 ("hepatitis c"):ti,ab,kw
#4 ("hepatitis c virus"):ti,ab,kw
#5 ("hepatitis c viruses"):ti,ab,kw
#6 ("hcv"):ti,ab,kw
#7 ("h c v"):ti,ab,kw
#8 ("vhc"):ti,ab,kw
#9 ("hepacivirus"):ti,ab,kw
#10 ("hcv viral"):ti,ab,kw
#11 ("hcv infected"):ti,ab,kw
#12 ("hcv infection"):ti,ab,kw
#13 ("hcv rna"):ti,ab,kw
#14 ("hepatitis c virus rna"):ti,ab,kw
#15 #1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14
#16 MeSH descriptor: [Diagnosis] explode all trees
#17 MeSH descriptor: [Diagnostic Techniques and Procedures] explode all trees
#18 MeSH descriptor: [Clinical Laboratory Techniques] explode all trees
#19 MeSH descriptor: [Mass Screening] explode all trees
#20 MeSH descriptor: [Nucleic Acid Amplification Techniques] explode all trees
#21 MeSH descriptor: [RNA] explode all trees
#22 ("clinical laboratory diagnoses"):ti,ab,kw
#23 ("clinical laboratory diagnostic"):ti,ab,kw
#24 ("clinical laboratory techniques"):ti,ab,kw
#25 ("clinical laboratory testing"):ti,ab,kw
#26 ("diagnose"):ti,ab,kw
#27 ("diagnoses"):ti,ab,kw
#28 ("diagnosis of hcv"):ti,ab,kw
#29 ("diagnosis"):ti,ab,kw
#30 ("diagnostic techniques and procedures"):ti,ab,kw
#31 ("diagnostic"):ti,ab,kw
#32 ("hcv infection diagnosis"):ti,ab,kw
#33 ("hcv testing"):ti,ab,kw
#34 ("mass screening"):ti,ab,kw
#35 ("mass screenings"):ti,ab,kw
#36 ("molecular diagnostic techniques"):ti,ab,kw
#37 ("screening approach"):ti,ab,kw
#38 ("screening"):ti,ab,kw
#39 ("testing diagnostic"):ti,ab,kw
#40 ("plasma levels"):ti,ab,kw
#41 ("sera"):ti,ab,kw
#42 ("serum levels"):ti,ab,kw
#43 ("dried blood"):ti,ab,kw
#44 ("dried sample"):ti,ab,kw
#45 ("filter paper"):ti,ab,kw
#46 ("Whatman"):ti,ab,kw
#47 ("DBS"):ti,ab,kw
#48 ("assay kits"):ti,ab,kw
#49 ("hcv assays"):ti,ab,kw

#50 ("hcv pcr"):ti,ab,kw
#51 ("hcv rna levels"):ti,ab,kw
#52 ("hcv rna quantification"):ti,ab,kw
#53 ("hepatitis markers"):ti,ab,kw
#54 ("immunoassay"):ti,ab,kw
#55 ("quantitative assays"):ti,ab,kw
#56 ("quantitative reverse transcription pcr"):ti,ab,kw
#57 ("real time pcr"):ti,ab,kw
#58 ("rna levels"):ti,ab,kw
#59 ("roche cobas taqman"):ti,ab,kw
#60 #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 or #32 or #33 or #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 or #46 or #47 or #48 or #49 or #50 or #51 or #52 or #53 or #54 or #55 or #56 or #57 or #58 or #59
#61 MeSH descriptor: [Hepatitis C Antigens] explode all trees
#62 ("antigens"):ti,ab,kw
#63 ("cleia method"):ti,ab,kw
#64 ("core antigen assays"):ti,ab,kw
#65 ("core antigen"):ti,ab,kw
#66 ("hcv ag"):ti,ab,kw
#67 ("hcvcAg"):ti,ab,kw
#68 ("hcv antigen"):ti,ab,kw
#69 ("hcv core antigen"):ti,ab,kw
#70 ("hcv core protein"):ti,ab,kw
#71 ("hcv core region"):ti,ab,kw
#72 ("hepatitis c antigens"):ti,ab,kw
#73 ("hepatitis c virus core antigen"):ti,ab,kw
#74 ("hepatitis c virus core"):ti,ab,kw
#75 ("viral core proteins"):ti,ab,kw
#76 #61 or #62 or #63 or #64 or #65 or #66 or #67 or #68 or #69 or #70 or #71 or #72 or #73 or #74 or #75
#77 ("accuracy"):ti,ab,kw
#78 ("correlation"):ti,ab,kw
#79 ("correlations"):ti,ab,kw
#80 ("negative predictive power"):ti,ab,kw
#81 ("negative predictive value"):ti,ab,kw
#82 ("negative predictive values"):ti,ab,kw
#83 ("NPV"):ti,ab,kw
#84 ("positive predictive power"):ti,ab,kw
#85 ("positive predictive value"):ti,ab,kw
#86 ("positive predictive values"):ti,ab,kw
#87 ("PPV"):ti,ab,kw
#88 ("receiver operating characteristics"):ti,ab,kw
#89 ("regression analysis"):ti,ab,kw
#90 ("ROC"):ti,ab,kw
#91 ("sensitive"):ti,ab,kw
#92 ("sensitivities"):ti,ab,kw
#93 ("sensitivity"):ti,ab,kw
#94 ("specific"):ti,ab,kw
#95 ("specificity"):ti,ab,kw

#96 "Abbott ARCHITECT i2000SR"
#97 "Abbott Diagnostics"
#98 "Abbott Laboratories"
#99 "ARCHITECT"
#100 "ARCHITECT ci8200"
#101 "ARCHITECT i2000SR"
#102 "ARCHITECT system"
#103 "cleia method"
#104 "chemiluminescence immunoassay"
#105 #77 or #78 or #79 or #80 or #81 or #82 or #83 or #84 or #85 or #86 or #87 or #88 or #89 or #90 or #91 or #92 or #93 or #94 or #95 or #96 or #97 or #98 or #99 or #100 or #101 or #102 or #103 or #104
#106 #15 and #60 and #76 and #105

Supplementary File 3: Risk of bias assessment adapted from QUADAS-2

Domain 1: Patient Selection

1.1 Risk of Bias: Could the selection of patients have introduced bias?

Signaling questions and answer guidelines

Signaling question 1: Was a consecutive or random sample of patients or specimens enrolled?

- Yes: the study enrolled a consecutive or random sample of eligible patients
- No: the study selected patients by selection or convenience
- Unclear: the study did not report how the patient selection was

Signaling question 2: Was a case-control design avoided?

- Yes: the study is not a case-control design
- No: the study is a case-control design
- Unclear: the study design was not reported, or we were unable to identify from the text

Signaling question 3: Did the study avoid inappropriate exclusions?

- Yes: the study enrolled consecutive or random samples of eligible patients
- No: the study excluded samples based on their prior testing, as these exclusions significantly reduce the generalizability of a study's findings
- Unclear: the study did not report exclusion criteria, or we were unable to identify from the text

Risk of Bias was evaluated as 'low risk' if studies scored 'yes' on all the questions or two questions were answered with 'yes' and one with 'unclear'; 'high risk' if two or more questions were answered with 'no' or one question was answered with 'no' and two with 'unclear'; and 'unclear risk' if studies scored 'unclear' on all the questions, two questions are answered with 'unclear' and one with 'yes', two questions were answered with 'yes' and one with 'no', or each question was answered with 'yes', 'no' and 'unclear'

1.2 Applicability: Are there concerns that the included patients and setting do not match the review question?

- Low concern: the study enrolled a broad study population in any setting
- High concern: the study inappropriately included healthy or blood donors only
- Unclear concern: the population was not well characterized, or we could not identify if a study's patients did not match our review question.

Domain 2: Index Test

2.1 Risk of Bias: Could the conduct or interpretation of the index test have introduced bias?

Signaling question 1: Were the index test results interpreted without knowing the reference standard results?

- Yes: results of the reference standard (HCV-RNA) test were blinded. Studies where the HCVcAg test was reported blinded to the HCV-RNA test or if it was clear that the HCVcAg test was reported before the results of the HCV-RNA test were available
- No: results of reference standard were unblended. The results of the HCVcAg test were reported on previous knowledge of the HCV-RNA test
- Unclear: we were unable to identify whether stored samples were tested or the HCVcAg test results were interpreted without knowledge of the HCV-RNA test results

Signaling question 2: If a threshold was used, was it pre-specified?

- Yes: the limit of detection for commercially available HCVcAg tests was pre-specified by the manufacturer
- No: the threshold of the HCVcAg test was personally selected to optimize sensitivity and specificity, leading to over-optimistic estimates of test performance
- Unclear: we could not determine whether the threshold of the HCVcAg test was pre-specified or not

Risk of Bias was evaluated as 'low risk' if studies scored 'yes' on all the questions, or one question was answered with 'yes' and the other one with 'unclear'; 'high risk' if studies scored 'no' on all the questions, or one question was answered with 'no' and another one with 'unclear'; and 'unclear risk' if studies scored 'unclear' on all the questions; or questions were answered with 'yes' and 'no'

2.2 Applicability: Are there concerns that the index test, its conduct, or interpretation differ from the review question?

- Low concern: the HCVcAg test was performed according to the manufacturer's recommendations
- High concern: the HCVcAg test procedure was inconsistent with the manufacturer recommendations (i.e., additional processing steps were added), or there was a delayed assessment of samples to perform the HCVcAg test
- Unclear concern: the HCVcAg test was not discussed in the study, or we were unable to determine how the HCVcAg test was conducted or interpreted

<u>Domain 3: Reference standard</u>

3.1 Risk of Bias: Could the reference standard, its conduct, or its interpretation have introduced bias?

Signaling question 1: Is the reference standard likely to classify the target condition correctly?

- Yes: the reference standard for HCV-RNA testing was a nucleic acid amplification test
- No: the reference standard for HCV-RNA testing was not a nucleic acid amplification test, or a combination of different nucleic acid amplification tests was used
- Unclear: there is insufficient information about which was reference standard for HCV-RNA testing used, or we were unable to identify from the text

Signaling question 2: Were the reference standard results interpreted without knowing the index test results?

- Yes: studies where the HCV-RNA test was interpreted blindly to the results of the HCVcAg test
- No: studies where the HCV-RNA test was not interpreted blindly to the results of the HCVcAg test
- Unclear: we were unable to identify whether stored samples were tested or if the HCV-RNA test results were interpreted without knowledge of the HCVcAg test results

3.2 Applicability: Are there concerns that the target condition as defined by the reference standard does not match the question?

- Low concern: the HCV-RNA test was performed according to the manufacturer's recommendations
- High concern: the HCV-RNA test procedure was inconsistent with the manufacturer recommendations, or there was a delayed assessment of samples to perform the HCV-RNA test
- Unclear concern: the HCV-RNA test was not discussed in the study, or we were unable to determine how the HCV-RNA test was conducted or interpreted

Domain 4: Flow and timing

4.1 Risk of Bias: Could the patient flow have introduced bias?

Signaling question 1: Was there an appropriate interval between the index test and reference standard?

- Yes: samples for HCVcAg and reference standards tests did obtain at the same time
- No: samples for HCVcAg and reference standards tests did not obtain at the same time
- Unclear: it was not discussed in the study, or we were unable to determine when HCVcAg and reference standards tests test were conducted or interpreted

Signaling question 2: Did all patients in the study receive the same reference standard?

- Yes: the study used the same rt-PCR for all samples
- No: the study used different types of rt-PCR to analyze all samples
- Unclear: it was not defined in the study, or we were unable to interpret the used rt-PCR

Signaling question 3: Were all patients included in the analysis?

- Yes: the whole population recruited into the study was included in the analysis, or any exclusion was adequately described
- No: participants were missing, or the study excluded samples without a given reason
- Unclear: not enough information was given to assess why participants were excluded from the analysis, or we were unable to find an explanation for the exclusion of samples

Risk of Bias was evaluated as 'low risk' if studies scored 'yes' on all the questions or two questions were answered with 'yes' and one with 'unclear'; 'high risk' if two or more questions were answered with 'no' or one question was answered with 'no' and two with 'unclear'; and 'unclear risk' if studies scored 'unclear' on all the questions, two questions are answered with 'unclear' and one with 'yes', two questions were answered with 'yes' and one with 'no', or each question was answered with 'yes', 'no' and 'unclear'

Summary of the quality assessment by using QUADAS-2

	Risk of bias				Concerns regarding applicability		
Author (year)	**Patient selection**	**Index test**	**Ref. standard**	**Flow and timing**	**Patient selection**	**Index test**	**Ref. standard**
Mederacke et al. (2012)	L	L	L	UC	L	L	L
Garbuglia et al. (2014)	UC	L	L	L	L	L	L
Van Helden et al. (2014)	UC	L	L	UC	L	L	L
Cresswell et al. (2015)	L	L	L	L	L	L	L
Vanhommerig et al. (2015)	L	L	L	L	L	L	L
Alados-Arboledas et al. (2017)	L	L	L	UC	L	L	L
Duchesne et al. (2017)	UC	L	L	L	L	L	L
Hullegie et al. (2017)	L	L	L	UC	L	L	L
Mohamed et al. (2017)	L	L	L	UC	L	L	L
Talal et al. (2017)	L	L	L	L	L	L	L
Alonso et al. (2018)	UC	L	L	L	L	L	L
Chayanupatkul et al. (2020)	L	L	L	L	L	L	L
Rossetti et al. (2021)	L	L	L	UC	L	L	L
Sun et al. (2022)	L	L	L	H	L	H	L

H= high; L= low; Ref = reference; UC = unclear

Supplementary Tables

Supplementary Table 1. Results of bivariate meta-regression (inconsistency index) in subgroup analysis for detecting active HCV infection in PLWHA with Abbott ARCHITECT HCVcAg assay compared with a confirmatory nucleic acid test.

Parameter	Category	I^2 [95%CI]	X^2	*p*-value
Year of publication	Yes: ≤2015 No: >2015	0 [0-100]	0.27	0.87
LMIC	Yes No	73 [39-100]	7.31	**0.03**
All patients with anti-HCV Ab +	Yes No	0 [0-100]	1.87	0.39
Biological sample type	Yes: only serum No: plasma or plasma/serum	84 [67-100]	12.63	**0.001**
Frozen sample	Yes No	53 [0-100]	4.22	0.12
Gold standard cutoff	≤15 IU/mL >15 IU/mL	31 [0-100]	2.90	0.23
Sample size	Yes: ≤100 No: >100	75 [44-100]	7.85	**0.02**
HCV prevalence	≤50% >50%	62 [15-100]	5.27	**0.07**

95%CI = 95% confidence interval; Anti-HCV Ab + = positive anti-HCV; cAg = core antigen; HCV = hepatitis C virus; IU = international units; I^2 = inconsistency index; IU = international units; LMIC = low- or middle-income country; PLWHA = people living with HIV/AIDS; X^2 = Pearson's chi-squared test.

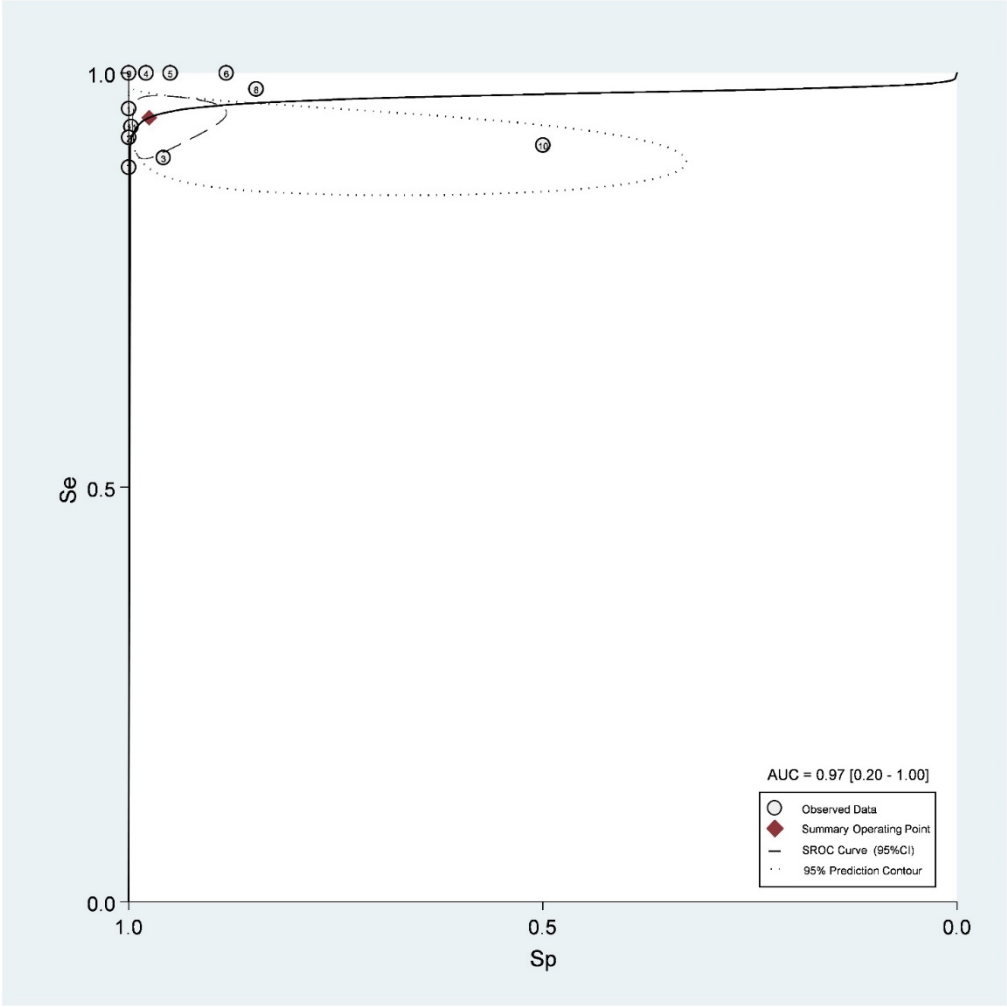
Supplementary Table 2. Results of bivariate meta-regression (sensitivity and specificity) and subgroup analysis in detecting active HCV infection in PLWHA with Abbott ARCHITECT HCVcAg assay compared with a confirmatory nucleic acid test.

Parameter	Category	No.	Se [95%CI]	*p*-value	Sp [95%CI]	*p*-value
Year of publication	Yes: ≤2015	5	0.94 [0.91-0.97]	**<0.001**	0.98 [0.94-1.00]	0.55
	No: >2015	6	0.95 [0.92-0.98]		0.97 [0.93-1.00]	
LMIC	Yes	2	0.99 [0.96-1.00]	**0.07**	0.88 [0.72-1.00]	**0.01**
	No	9	0.93 [0.91-0.95]		0.98 [0.97-1.00]	
All patients with anti-HCV Ab +	Yes	4	0.95 [0.92-0.98]	**<0.001**	0.92 [0.77-1.00]	0.29
	No	7	0.95 [0.92-0.98]		0.98 [0.96-1.00]	
Biological sample type	Yes: only serum	7	0.96 [0.94-0.99]	**<0.001**	0.94 [0.91-0.97]	**<0.001**
	No: plasma or plasma/serum	4	0.93 [0.90-0.95]		1.00 [0.99-1.00]	
Frozen sample	Yes	8	0.95 [0.92-0.98]	**0.03**	0.95 [0.90-1.00]	**0.01**
	No	3	0.94 [0.90-0.99]		0.99 [0.98-1.00]	
Gold standard cutoff	≤15 IU/mL	8	0.94 [0.91-0.96]	**<0.001**	0.97 [0.94-1.00]	0.49
	>15 IU/mL	3	0.97 [0.95-1.00]		0.98 [0.93-1.00]	
Sample size	Yes: ≤100	8	0.95 [0.92-0.98]	**0.03**	0.94 [0.89-0.98]	**<0.001**
	No: >100	3	0.94 [0.89-0.99]		1.00 [0.99-1.00]	
HCV prevalence	≤50%	4	0.98 [0.95-1.00]	0.81	0.98 [0.95-1.00]	0.55
	>50%	7	0.94 [0.91-0.97]		0.96 [0.90-1.00]	

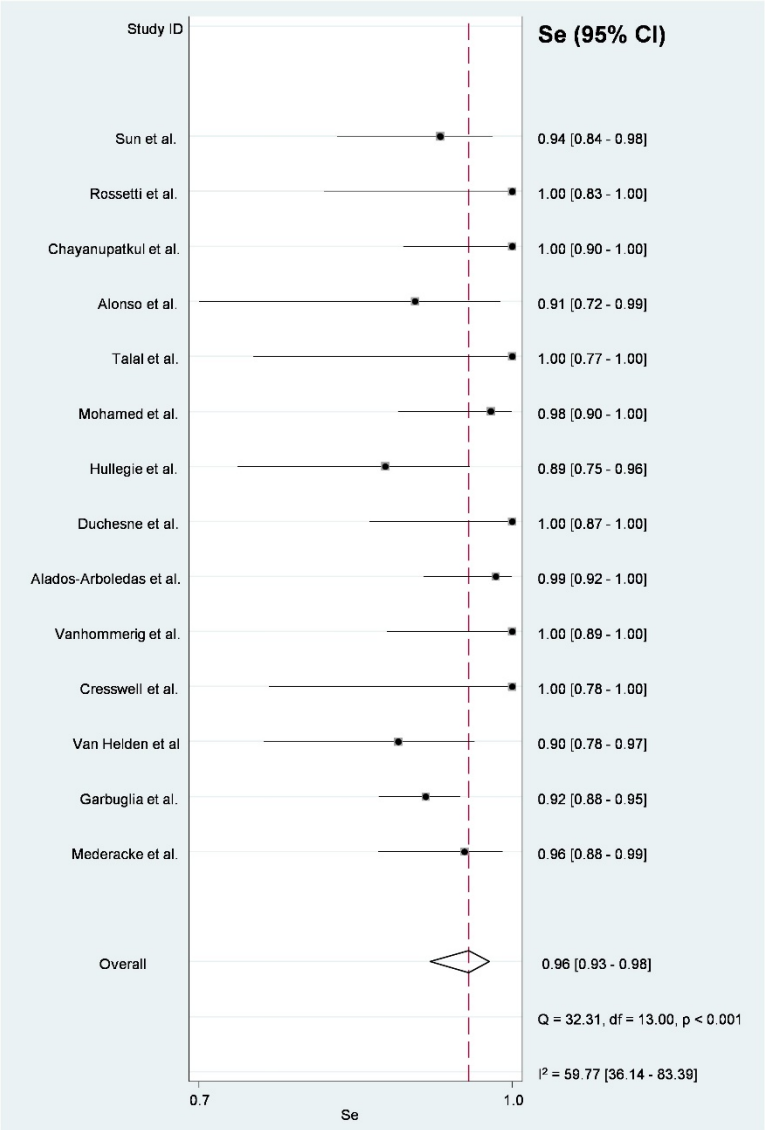
95%CI = 95% confidence interval; Anti-HCV Ab + = positive anti-HCV; cAg = core antigen; HCV= hepatitis C virus; IU= international units; LMIC= low- or middle-income country; No.= number of articles; PLWHA = people living with HIV/AIDS; Se= sensitivity; Sp= specificity.

Supplementary Figures

Supplementary Figure 1. Hierarchical SROC curve plot in detecting active HCV infection in PLWHA with Abbott ARCHITECT HCV Ag assay compared with a confirmatory nucleic acid test. **Abbreviations**: 95%CI = 95% confidence interval; AUC = area under the curve; HCV = hepatitis C virus; PLWHA = people living with HIV/AIDS; Se = sensitivity; Sp = specificity; SROC = summary receiver operating characteristic.



Supplementary Figure 2. Forest plots of pooled sensitivity for all studies included in the univariate analysis in detecting active HCV infection in PLWHA with Abbott ARCHITECT HCV Ag assay compared with a confirmatory nucleic acid test. **Abbreviations**: 95% CI = 95% confidence interval; HCV = hepatitis C virus; I^2 = inconsistency index; PLWHA = people living with HIV/AIDS; Q = Cochran's Q test; Se = sensitivity



Supplementary Figure 3. Deeks's funnel plot asymmetry test for publication bias in detecting active HCV infection in PLWHA with Abbott ARCHITECT HCV Ag assay compared with a confirmatory nucleic acid test. **Abbreviations**: DOR = diagnostic odds ratio; ESS = single effective size; HCV = hepatitis C virus; PLWHA = people living with HIV/AIDS.