QUADAS-2	Denoyel, 2004	Tashkandy, 2007	Benouda, 2009	Rao, 2009	Ol, 2009	Kosan, 2010	Park, 2012	Sommese, 2014	Arora, 2016
Study population	5,228 individuals: 5,015 random blood donors and 213 hospitalized patients	106 male blood donors	8,326 adults from the general population with unknown HCV serology underwent initial screening with ELISA v3.0	2,559 individuals: 2,082 blood donors (Beijing Red Cross Blood Center) and 477 patients (Peking University Hepatology Institute; including various HCV genotypes, non-C hepatitis, pregnant women, and lipidemia sera)	1,200 potential volunteer blood donors underwent screening with ELISA v4.0: 677 females, 523 males, mean age: 32.8 years, age range 18-52 year; sample stratified by two Cambodian provinces (600 each)	18,200 volunteer blood donors: 546 (3%) were women, 17,654 (97%) were men, 18,198 (99.9%) were first-time donors, mean age: 40 years, age range: 18-60 years	1,011 sera from individuals undergoing routine HCV screening	840 volunteer blood donors; Second University of Naples; January to June 2013	21,115 blood donors; blood bank; January 2013 to March 2014
Index test(s)	CLIA (ADVIA Centaur® HCV assay)	ELISA v3.0 (Abbott Murex anti-HCV)	ELISA V3.0 (Abbott Murex anti-HCV)	ELISA v4.0 (EIAgen, Adaltis)	ELISA v4.0 (Monolisa™, BioRad)	ELISA v3.0 (Innotest HCV Ab III, Innogenetics, Belgium)	CLIA (Vitros Anti-HCV assay, UK)	CMIA (Architect i200SR, Abbott, Germany)	ELISA v4.0 (Monolisa BioRad Ag-Ab Ultra)
Reference test(s)	MEIA (Abbott AxSYM® HCV v.3.0 assay)	LIA (INNo-LIA HCVAb III Update, INNOGENTICS, Belgium) and RT-PCR (High Pure Viral Nucleic Acid reagent set, Roche Molecular Biochemicals)	MEIA (Abbott AxSYM® HCV v.3.0 assay) and RT-PCR (Roche Amplicor HCV® v2.0)	ELISA v3.0 (Ortho HCV 3.0 ELISA)	CMIA (Abbott)	NAT (Procleix Ultrio kit, Chiron, USA)	ECLIA (Elecsys anti-HCV test, Roche, Germany)	ECLIA (Cobas e411, Roche, Germany)	NAT (Procleix Ultrio kit, Chiron, USA)
DOMAIN 1: PATIENT SELECTION									
Describe methods of patient selection:	Not described	All samples were collected at the Immunology and Serology Department at the Al-Noor Specialist Hospital, Makkah, Saudi Arabia. We excluded all samples from patients with diabetes or other endocrine diseases and autoimmune diseases.	8,326 adults from the general population with unknown HCV serology underwent initial screening with ELISA v3.0. Initial blood specimen collection took place in work settings, from December 2005 to April 2007 (16 months). A subset of 161 ELISA-positives and 100 ELISA-negatives were called back to undergo the reference standard (verification bias); 3/161 lost to follow-up.	2,559 individuals: 2,082 blood donors (Beijing Red Cross Blood Center) and 477 patients (Peking University Hepatology Institute; including various HCV genotypes, non-C hepatitis, pregnant women, and lipidemia sera)	1,200 potential volunteer blood donors underwent screening with ELISA. A subset of 80 ELISA-positive and 40 ELISA-negative were selected to undergo the reference test (verification bias)	Turkish Red Crescent Çapa Blood Centre of Istanbul; intermittently from February 2007 to March 2008; individuals underwent a mandatory physical exam (no exclusion criteria specified) prior to blood drawing;	Individuals undergoing "routine HCV screening"; sera collected between August 2009 and January 2011	"we selected a group of 840 samples from volunteer blood donors"	"we reviewed the donor screening data for anti-HCV from January 2013 to May 2014" Presumably, all donors during this time period are included.
Was a consecutive or random sample of patients enrolled:	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes
Was a case-control design avoided?	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Did the study avoid inappropriate exclusions?	Yes	No	Yes	Yes	Yes	Yes	Yes	Unclear	Yes
Could the selection of patients have introduced bias?	Unclear risk	Unclear risk	High risk; due to verification bias, but easily correctable statistically	Low risk	High risk; due to verification bias, but easily correctable statistically	Low risk	Low risk	Low risk	Low risk
Describe included patients (prior testing, presentation, intended use of index test and setting):	5,015 random blood donors and 213 hospitalized patients; the 213 (4.1%) hospitalized patients do not reflect the setting or population of the review question.	106 male blood donors	8,326 adults from the general population with unknown HCV serology	477 / 2,559 (18.6%) patients did not meet our inclusion criteria in that they were sampled from a hepatology clinic and their HCV status was known at the outset	1,200 potential volunteer blood donors underwent screening with ELISA	18,200 volunteer blood donors: 546 (3%) were women, 17,654 (97%) were men, 18,198 (99.9%) were first-time donors, mean age: 40 years, age range: 18-60 years; individuals underwent a mandatory physical exam (no exclusion criteria specified) prior to blood drawing	1,011 sera from individuals undergoing routine HCV screening	840 volunteer blood donors: 275 (32.7%) were women, 564 (67.3%) men, mean age: 37.7 years (SD 12.5 years)	21,115 blood donors; presumably all consecutive blood donors during the study period
Is there concern that the included patients do not match the review question?	Low concern	Low concern	Low concern	High concern	Low concern	Low concern	Low concern	Low concern	Low concern
DOMAIN 2: INDEX TEST(S)									
Describe the index test and how it was conducted and interpreted:	CLIA (ADVIA Centaur® HCV assay); no further description	ELISA v3.0 (Abbott Murex anti-HCV)	ELISA v3.0 (Abbott Murex anti-HCV)	ELISA v4.0 (EIAgen, Adaltis)	ELISA v4.0 (Monolisa™, BioRad)	ELISA v3.0 (Innotest HCV Ab III, Innogenetics, Belgium); done "in parallel" with the reference test	CLIA (Vitros Anti-HCV assay, UK)	CMIA (Architect i200SR, Abbott, Germany)	ELISA v4.0 (Monolisa BioRad Ag-Ab Ultra)
Were the index test results interpreted without knowledge of the results of the reference standard?	Unclear	Unclear	Unclear	Yes; the EIAgen and Ortho tests were always run "side-by-side"	Yes	Unclear	Unclear	Unclear	Unclear
If a threshold was used, was it pre-specified?	Yes. "The presence or absence of antibodies to HCV is determined by comparing the sample index to the cut-off. Samples with an index value greater than 1.0 are considered to be reactive for anti-HCV."	Unclear; presumably used as per the kit manufacturer's instructions.	Unclear; presumably used as per the kit manufacturer's instructions.	Yes. "Both EIAs yield their final results as ratios of the specimen signal (in relative light units) to the cut-off value (signal-to-cut-off ratio, S/CO). S/CO ratios ≥1.0 were considered reactive for anti-HCV antibodies while those <1.0 were considered nonreactive. Specimen preparation and testing were carried out according to the manufacturers' instructions."	Yes. "The CMIA analysis of anti-HCV is based on the signal to cut-off ration (S/CO). An S/CO value less than 1.00 is classified as negative, and a value higher than 1.00 is classified as positive. Units with ratios in the range of 0.90-1.00 are classified as equivocal and re-analyzed twice."	Unclear; presumably used as per the kit manufacturer's instructions.	Yes. "A signal to cut-off ration (S/CO) greater than 1.0 was regarded as positive."	Yes. "For all assays, S/CO ratios ≥1 were considered as initial reactive (IR)."	Yes. "Samples with an S/CO ratio of ≥1.0 are defined by the manufacturer as positive."
Could the conduct or interpretation of the index test have introduced bias?	Unclear risk	Unclear risk	Unclear risk	Low risk	Low risk	Unclear risk	Low risk	Low risk	Low risk
Is there concern that the index test, its conduct, or interpretation differ from the review question?	Low concern	Low concern	Low concern	Low concern	Low concern	Low concern	Low concern	Low concern	Low concern
DOMAIN 3: REFERENCE STANDARD(S)									
Describe the reference standard and how it was conducted and interpreted:	MEIA (Abbott AxSYM® HCV v.3.0 assay) -- detects antibodies only, cannot distinguish between acute, chronic or resolved (~15%) HCV infection	1) LIA (INNo-LIA HCVAb III Update, INNOGENTICS, Belgium) -- cannot differentiate between current and resolved infection; and 2) RT-PCR (High Pure Viral Nucleic Acid reagent set, Roche Molecular Biochemicals) -- can differentiate between current and resolved infection	1) MEIA (Abbott AxSYM® HCV v.3.0 assay) -- cannot differentiate between current and resolved infection; 2) RT-PCR (Roche Amplicor HCV® v2.0) -- able to differentiate between current and resolved infection	ELISA v3.0 (Ortho HCV 3.0 ELISA) -- Cannot differentiate between current and resolved infection	CMIA (Abbott)	NAT (Procleix Ultrio kit, Chiron, USA); done "in parallel" with the index test	ECLIA (Elecsys anti-HCV test, Roche, Germany)	ECLIA (Cobas e411, Roche, Germany)	NAT (Procleix Ultrio kit, Chiron, USA)
Is the reference standard likely to correctly classify the target condition (i.e., HCV infection)?	Yes; but unlike PCR/NAT this reference standard would fail to identify false-positives due to resolved infection	Yes (for PCR)	Yes (for PCR)	Yes; but unlike PCR/NAT this reference standard would fail to identify false-positives due to resolved infection	Yes; but unlike PCR/NAT this reference standard would fail to identify false-positives due to resolved infection	Yes	Yes; but unlike PCR/NAT this reference standard would fail to identify false-positives due to resolved infection	Yes; but unlike PCR/NAT this reference standard would fail to identify false-positives due to resolved infection	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?	Unclear	Unclear	Unclear	Yes; the EIAgen and Ortho tests were always run "side-by-side"	Yes; the subsample of blood units was "blindly re-analyzed" in Norway	Unclear	Unclear	Unclear	Unclear
Could the reference standard, its conduct, or its interpretation have introduced bias?	High risk	Unclear risk	Unclear risk	High risk	High risk	Low risk	High risk	High risk	Low risk
Is there concern that the target condition as defined by the reference standard does not match the review question?	Serious concern	Low concern (for PCR)	Low concern (for PCR)	Serious concern	Serious concern	Low concern	Serious concern	Serious concern	Low concern
DOMAIN 4: FLOW AND TIMING									
Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram):	2 patients with equivocal positive results were excluded from the authors' specificity calculation, but we will include them	All patients received ELISA, LIA, and RT-PCR.	A subset of 161 ELISA-positives and 100 ELISA-negatives were called back to undergo the reference standard (verification bias); 3/161 lost to follow-up	None	A subset of 80 ELISA-positive and 40 ELISA-negative were selected to undergo the reference test (verification bias)	None	None	None	None
Describe the time interval and any interventions between index test(s) and reference standard:	Not specified; presumably, both tests were applied to the same blood samples	All samples were aliquated into two portions; one was kept at 70°C until processing for RT-PCR and the other was subjected to HCV antibody detection by ELISA and LIA methods	time interval between tests not specified	The EIAgen and Ortho tests were always run "side-by-side"	Both tests were applied to the same blood samples	For each subject, two sets of blood samples were collected: one for serological testing and one for NAT testing	Not specified; presumably, all sera underwent both the index and reference test	Serum samples of the 840 blood donors were tested in parallel using the index and reference tests	All samples were screened with the index and reference tests in parallel; 3 pilot tube samples were collected with each donation - one was used for NAT, another for ELISA
Was there an appropriate interval between index test(s) and reference standard?	Yes	Yes	Unclear	Yes	Yes	Yes	Yes	Yes	Yes
Did all patients receive a reference standard?	Yes	Yes	No; verification bias is present	Yes	No; verification bias is present	Yes	Yes	Yes	Yes
Did patients receive the same reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all patients included in the analysis?	Yes	Yes	No; 3/161 lost to follow-up	Yes	Yes	Yes	Yes	Yes	Yes
Could the patient flow have introduced bias?	Low risk	Low risk	High risk; the differential sampling of 158/161 (98%) ELISA-positive and 100/8,165 (1%) ELISA-negative persons; Sn and Sp reported in the article are not adjusted for differential sampling leading to large verification bias; this is easily correctable statistically	Low risk	High risk; the differential sampling of 80/176 (45%) ELISA-positive and 40/1,024 (4%) ELISA-negative persons; Sn and Sp reported in the article are not adjusted for differential sampling leading to large verification bias; this is easily correctable statistically	Low risk	Low risk	Low risk	Low risk

Appendix to: Cadieux G, Campbell J, Dendukuri N. Systematic review of the accuracy of antibody tests used to screen asymptomatic adults for hepatitis C infection. *CMAJ Open* 2016. DOI:10.9778/cmajo.20160084.