

Table 1 of the Supplement. Diagnostic Accuracy of Blood Tests vs. Liver Biopsy for Diagnosing Fibrosis or Cirrhosis in HCV-Infected Patients

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Adams, 2005 (34) Australia	Hepascore (bilirubin, g-glutamyltransferase, hyaluronic acid, a-2 macroglobulin, age, and sex) †† Fibrotest	Prospective	117 (development sample) 104 (validation sample)	Fibrosis (METAVIR F2-F4): 44% (development sample) and 57% (validation sample) Cirrhosis (METAVIR F4): 6% and 16% Biopsy quality: All ≥5 portal tracts; median 9 portal tracts and 13 mm	Development vs. validation sample Age: 40 vs. 41 years Female: 32% vs. 27% Genotype 1: 61% vs. 48%
Adler, 2008 (53) Belgium	Fibrotest FIB-4 Forns Index APRI Fibroindex	Unclear	152	Fibrosis (METAVIR F2-F4): 73% Cirrhosis (METAVIR F4): 12% Biopsy quality: Not reported	Not reported
Ahmad, 2011 (23) Pakistan	Fibrosis-cirrhosis index (alkaline phosphatase, bilirubin, albumin, platelet count)† AST/ALT ratio APRI FIB-4 Fibrosis Index Alkaline phosphatase Bilirubin Albumin Platelet count	Retrospective	157	Fibrosis (METAVIR F2-F4): 57% Cirrhosis (METAVIR F4): 13% Biopsy quality: Not reported	Age: 38 years Female: 27% Genotype 1: 14%

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Alsatie, 2007 (54) USA	5-item predictive index (DM, platelet count, INR, bilirubin, AST)†	Retrospective	190 (development sample) 94 (validation sample)	Fibrosis (METAVIR F2-F4): 41% Cirrhosis (METAVIR F4): 17%) Biopsy quality: All ≥15 mm	Reported for development and validation samples together Age: 45 years Female: 40% Genotype 1: 50%
Amorim, 2012 (55) Brazil	APRI FIB-4	Retrospective	119	Fibrosis (METAVIR-F2-F4): 34% Biopsy quality: Not reported	Age: 44 years Female: 38% Genotype 1: Not reported
Anderson, 2000 (56) Canada	AST/ALT ratio	Retrospective	133	Fibrosis or cirrhosis (method unclear): 82% Cirrhosis (method unclear): 46% Biopsy quality: Not reported	Age: 46 years Female: 30% Genotype 1: Not reported All had elevated ALT
Arabul, 2012 (57) Turkey	Platelet count Age-platelet Index AST/ALT ratio APRI	Retrospective	212	Fibrosis or cirrhosis (Ishak): Not reported Biopsy quality: Not reported	Not reported
Arain, 1011 (58) Pakistan	Hyaluronic acid	Unclear	98	Fibrosis (METAVIR F2-F4): 43% Biopsy quality: Not reported	Age: 43 years Female: 47% Genotype 1: Not reported
Attallah, 2013 (21) Egypt	Fibronectin Albumin APRI Fibronectin Discriminant Score†	Retrospective	145 (index development sample) 180 (validation sample)	Fibrosis (METAVIR F2-F4): 57% (development sample) and 51% (validation sample) Cirrhosis (METAVIR F4): 24% and 12% Biopsy quality: All >15 mm or >5 portal tracts	Development vs. validation samples Age: 42 vs. 40 years Female: 38% vs. 31% Genotype 1: Not reported

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Attallah, 2012 (27) Egypt	Age AST ALT Albumin Alkaline phosphatase Alpha fetoprotein Total bilirubin Platelet count AST/ALT ratio APRI FibroIndex FIB-4 Fibrosis-cirrhosis Index FibroQ Goteborg University Cirrhosis Index 4 Routine Laboratory Bloodtest Index Lok Index Fibrosis Routine Test (age, AST, platelet count, alpha fetoprotein, albumin)†	Prospective	2045 (index development sample) 3212 (validation sample)	Fibrosis (METAVIR F2-F4): 52% (development sample) and 32% (validation sample) Cirrhosis (METAVIR F4): 16% and 10% Biopsy quality: All >15 mm or >5 portal tracts	Development vs. validation samples Age: 44 vs. 42 years Female: 25% vs. 24% Genotype 1: Not reported
Attallah, 2011a (63) Egypt	Albumin Epithelial membrane antigen APRI Fibrosis Discriminant Score (AST, platelet count, epithelial membrane antigen, albumin)†	Prospective	154 (index development sample) 170 (validation sample)	Fibrosis (METAVIR F2-F4): 60% (development sample) and 59% (validation sample) Cirrhosis (METAVIR F4): 22% and 20% Biopsy quality: Not reported	Development vs. validation samples Age: 44 vs. 43 years Female: 40% vs. 22% Genotype 1: Not reported

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Attallah, 2011b (60)	Egypt	MMP-1	Unclear	129	Cirrhosis (METAVIR F4): 40% Biopsy quality: Not reported	Age: 38 years Female: 40% Genotype 1: Not reported
Attallah, 2007a (61)	Egypt	Albumin ALT Collagen III Collagen IV Fibrosis Discriminant Score (collagen III, collagen IV, albumin, and ALT)	Unclear	120 (derivation sample) 75 (validation sample)	Severe fibrosis (METAVIR F3-F4): 50% Biopsy quality: Not reported	Derivation and validation samples Age: Not reported Female: 42% and 43% Genotype 1: Not reported No habitual alcohol use
Attallah, 2007b (62)	Egypt	Fibronectin	Unclear	126	F1 to F3 Fibrosis (METAVIR): 90% (no F4) Biopsy quality: Not reported	Age: Not reported Female: 28% Genotype 1: Not reported Excluded for habitual alcohol use
Attallah, 2006a (59)	Egypt	Hyaluronic acid Hyaluronic acid-based Index (hyaluronic acid, N-acetyl- β -D-glucosaminidase, glucuronic acid, glucosamine, AST, ALT)†	Unclear	153 (index development sample) 100 (validation sample)	Fibrosis: Not reported Cirrhosis (method not reported): 37% (development sample) and not reported (validation sample) Biopsy quality: Not reported	Reported for validation sample only Age: Mean not reported, range 24-59 years Female: 25% Genotype 1: Not reported
Attallah, 2006b (60)	Egypt	Alkaline phosphatase Albumin Platelet count AST/ALT ratio 4 Routine Laboratory Bloodtest Index	Unclear	455 (derivation sample) 219 (validation sample)	Severe fibrosis (METAVIR F3-F4): 80% (derivation sample) and 46% (validation sample) Biopsy quality: Not reported	Derivation vs. validation samples Age: 47 vs. 46 years Female: 40% vs. 40% Genotype 1: Not reported All treatment-naïve

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i>*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Bain, 2004 (65) USA and Canada	Cirrhosis Discriminant Score	Prospective	81	Fibrosis (Hytiroglou F2-F4): 21% Biopsy quality: Not reported	Age: 43 years Female: 36% Genotype 1: Not reported
Becker, 2009(66) USA	Hepascore APRI FIB-4	Unclear	391	Fibrosis (METAVIR F2-F4): 50% Cirrhosis (METAVIR F4): 19% Biopsy quality: All ≥ 10 mm or ≥ 8 portal tracts; median 16 mm, 11% <10 mm	Age: 50 years Female: 30% Genotype 1: 75%
Bejarano, 2009 (67) Spain	Sabadell NIHCED index	Prospective	321	Severe fibrosis (Knodell 3-4): 59% (no patients had Knodell 2) Cirrhosis (Knodell 4): 20% Biopsy quality: Mean 11.6 mm and 12.2 portal tracts	Age: 48 years Female: 44% Genotype 1: Not reported
Ben Jazia, 2009 (68) Tunisia	AST/ALT ratio APRI Platelet count	Retrospective	35	Fibrosis (METAVIR F2-F4): 77% Cirrhosis (METAVIR F4): Not reported Biopsy quality: Not reported	Age: 49 years Female: 69% Genotype 1: 46%
Berg, 2004 (69) Germany	APRI	Retrospective	484	Fibrosis (Scheuer F2-F4): 52% Cirrhosis (Scheuer F4): 13% Biopsy quality: Not reported	Age: 46 years Female: 44% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Boeker, 2002 (70) Germany	TIMP-1 MMP-2 Hyaluronic acid AST ALT Alkaline phosphatase GGT Albumin	Unclear	78	Fibrosis (Ishak, grades not reported): 46% (27/59, excluding patient with cirrhosis) Cirrhosis (Ishak, grades not reported): 24% (19/78) Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported
Bonacini, 1997 (15) USA	Cirrhosis discriminant score (platelet count, AST/ALT ratio, prothrombin index, ascites, spider angiomas) [†] AST/ALT ratio	Retrospective	79	Fibrosis: Not reported Severe fibrosis (Knodell F3-F4): 35% Cirrhosis: Not reported Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported
Borroni, 2006 (71) Italy	AST/ALT ratio Cirrhosis Discriminant Score APRI Pohl's Index Age-platelet index	Retrospective	228	Severe fibrosis (Knodell F3-F4): 49% Cirrhosis (Knodell F4): 13% Biopsy quality: All ≥ 6 portal fields	Age: 42 years Female: 27% Genotype 1: 47% All elevated transaminases
Bota, 2011 (72) Romania	King's score Forns Index APRI	Retrospective	212	Fibrosis (METAVIR F2-F4): 91% Severe fibrosis (METAVIR F3-F4): 45% Cirrhosis (METAVIR F4) Biopsy quality: All ≥ 8 portal tracts; mean 34 mm	Age: 50 years Female: 67% Genotype 1: Not reported

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Bourliere, 2008 (73) France	Hepascore Fibrotest	Prospective	467	Fibrosis (METAVIR F2-F4): 49% Cirrhosis (METAVIR F4): 7.5% Biopsy quality: Mean 20 mm and median 9 portal tracts; 59% \geq 15 mm and \geq 5 portal tracts	Age: 47 years Female: 41% Genotype 1: Not reported
Bourliere, 2006 (74) France	Fibrotest APRI Forns Index	Unclear	235	Fibrosis (METAVIR F2-F4): 42% Cirrhosis (METAVIR F4): 6.8% Biopsy quality: Mean 20 mm and median 9 portal tracts; 59% \geq 15 mm and \geq 5 portal tracts	Age: 46 years Female: 45% Genotype 1: Not reported
Boursier, 2012 (77) France	SAFE algorithm (based on APRI and Fibrotest)	Retrospective	1785	Fibrosis (METAVIR F2-F4): 55% Cirrhosis (METAVIR F4): 13% Biopsy quality: \geq 15 mm in 79%	Mean age: 48 years Female: 40% Genotype 1: Not reported
Boursier, 2011 (76) France	FibroMeter	Unclear	349 (sample 1) 380 (sample 2)	Sample 1 vs. sample 2 Fibrosis (METAVIR F2-F4): 68% vs. 49% Cirrhosis (METAVIR F4): 12% vs. 18% Biopsy quality: 94% \geq 15 mm and \geq 8 portal tracts	Sample 1 vs. sample 2 Age: 52 vs. 51 years Female: 40% vs. 38% Genotype 1: Not reported

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Boursier, 2009 (75)	France	FibroMeter Fibrotest Hepascore APRI Modified Fibrotest	Retrospective	1056	Fibrosis (METAVIR F2-F4): 52% Cirrhosis (METAVIR F4): 11% Biopsy quality: Not reported	Mean age: 46 years Female: 40% Genotype 1: Not reported
Burton, 2011 (78)	USA	APRI	Retrospective	268 (142 black, 117 white)	Fibrosis (Batts-Ludwig F2-F4): 49% Cirrhosis (Batts-Ludwig F4): 16% Biopsy quality: Not reported	Age: 52 years Female: 4.5% Genotype 1: 81%
Cales, 2010 (80)	France	FibroMeter FibroMeter 3G (hyaluronic acid replaced with GGT)† FibroTest Hepascore	Retrospective	1056 (index development sample) 458 (validation sample)	Fibrosis (METAVIR F2-F4): 52% and 48% Cirrhosis (METAVIR F4): 11% and 15% Biopsy quality: Not reported	Only reported for development sample Mean age: 46 years Female: 40% Genotype 1: Not reported
Cales, 2008 (79)	France	FibroMeter (sex added) Fibrotest Hepascore APRI FIB-4	Retrospective	1056	Fibrosis (METAVIR F2-F4): 52% Cirrhosis (METAVIR F4): 11% Biopsy quality: Not reported	Mean age: 46 years Female: 40% Genotype 1: Not reported
Cales, 2005 (20)	France	FibroMeter (platelet count, prothrombin index, AST, alpha-2-macroglobulin, hyaluronate, urea, age) APRI Fibrotest Forns' Index	Prospective	337 (derivation sample, HCV only) 120 (validation sample)	Fibrosis (METAVIR F2-F4): 56% (derivation sample) vs. 48% (validation sample) Cirrhosis (METAVIR F4): 16% vs. 12% Biopsy quality: Not reported for derivation sample, >=15 mm for validation sample	Derivation vs. validation samples Age: 44 vs. 44 years Female: 37% vs. 38% Genotype 1: Not reported

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Castera, 2010 (82) France	SAFE algorithm (based on APRI and Fibrotest)	Prospective	302	Fibrosis (METAVIR F2-F4): 76% Cirrhosis (METAVIR F4): 25% Biopsy quality: All ≥ 10 mm and ≥ 6 portal tracts; mean 20 mm and 15 portal tracts	Age: 52 years Female: 43% Genotype 1: Not reported All elevated ALT
Castera, 2009 (81) France	AST/ALT ratio APRI Prothrombin index Platelet count Fibrotest Lok Index	Prospective	298	Fibrosis (METAVIR F2-F4): 74% Cirrhosis (METAVIR F4): 23% Biopsy quality: All ≥ 10 mm and ≥ 6 portal tracts; mean 20 mm and 15 portal tracts	Age: 52 years Female: 43% Genotype 1: Not reported
Castera, 2005 (83) France	APRI Fibrotest	Prospective	193	Fibrosis (METAVIR F2-F4): 74% Cirrhosis (METAVIR F4): 25% Biopsy quality: Median 17 mm, median 2 fragments	Age: 51 years Female: 43% Genotype 1: Not reported
Cheong, 2011 (40) Korea	Significant Fibrosis Index (haptoglobin, a2MG, TIMP1, MMP2, GGT)† Zeng Index APRI Forns Index FIB-4 ELF index	Prospective	79 (index development sample) 27 (validation sample)	Fibrosis (METAVIR F2-F4): 79% (development sample) and 77% (validation sample) Cirrhosis (METAVIR F4): 13% and 28% Biopsy quality: Mean 12.6 mm and mean 13.2 portal tracts; 71% had ≥ 11 portal tracts	Development vs. validation samples Age: 42 vs. 42 years Female: 31% vs. 35% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Cheung, 2011 (26) Belgium	Fibrosis-protein Index (a-2 macroglobulin and hemopexin)† APRI	Unclear	62 (index development sample) 73 (validation sample)	Derivation and validation samples, respectively Fibrosis (METAVIR F2-F4): 50% and 71% Cirrhosis (METAVIR F4): 26% and 14% Biopsy quality: Median 1.6-2.0 cm and >8 portal tracts	Development vs. validation samples Age: 50 vs. 50 years Female: 48% vs/ 53% Genotype 1 or 4: 69% vs. 71%
Cheung, 2008 (84) USA	Platelet count Normalized AST/ALT ratio Pohl score APRI Lok Index	Prospective	490	Fibrosis (Batts-Ludwig F2-F4): 66% Cirrhosis (Batts-Ludwig F4): 14% Biopsy quality: Not reported	Age: 49 years Female: 2% Genotype 1: Not reported
Christensen, 2006 (85) USA	FIBROspect II	Retrospective	142	Fibrosis (Ishak ≥ 3): 38% Cirrhosis (Ishak 5 or 6): 18% Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported
Chrysanthos, 2006 (86) Greece	APRI	Unclear	284	Fibrosis (Ishak ≥ 3): 51% Cirrhosis (Ishak 5 or 6): 20% Biopsy quality: All >1.5 cm	Age: 49 years Female: 49% Genotype 1: Not reported
Cobbold, 2010 (87) UK	APRI ELF Index	Prospective	67	Fibrosis (Ishak ≥ 3): 55% Cirrhosis (Ishak 5 or 6): 21% Biopsy quality: All ≥ 10 mm, mean 24 mm	Age: 50 years Female: 34% Genotype 1: Not reported

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Colletta, 2005 (88)	Italy	Fibrotest	Unclear	40	Fibrosis (METAVIR F2-F4): 35% Cirrhosis (METAVIR F4): 0% Biopsy quality: Mean 20 mm, 7 portal tracts	Age: 44 years Female: 45% Genotype 1: 30% All had ALT \leq 1.2 times the upper limit of the reference range and Ishak score \leq 2
Colli, 2005 (89)	Italy	Cirrhosis Discriminant Score	Prospective	176	Severe fibrosis (METAVIR F3-F4): 38% Biopsy quality: Mean 41 mm	Age: 54 years Female: 45% Genotype 1: Not reported All had ALT \geq 1.5 times upper limit of normal
Crisan, 2012 (90)	Romania	APRI Forns Index FIB-4 Hepascore Fibrometer Fibrotest Combinations of APRI, Fibrometer, and Fibrotest	Prospective	446	Fibrosis (METAVIR F2-F4): 63% Severe fibrosis (METAVIR F3-F4): 27% Biopsy quality: Median 11 mm, mean 14 portal tracts, all $>$ 5 portal tracts	Age: 49 years Female: 62% Genotype 1: Not reported
Cross, 2010 (91)	UK	King's Score	Unclear	187	Fibrosis (Ishak \geq 3): 48% Cirrhosis (Ishak 5 or 6): 27% Biopsy quality: All \geq 10 mm or $>$ 10 portal tracts; mean 15 mm	Age: 49 years Female: 41% Genotype 1: 42%

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Cross, 2009 (35) UK	King's Score (age, AST, INR, platelets)† AST/ALT ratio AST APRI Age-platelet index Cirrhosis Discriminant Score FIB-4 index Pohl index (AAR≥1 and platelets <150)	Retrospective	602 (index development sample) 105 (validation sample)	Fibrosis (Ishak ≥3): 45% (development sample) vs. 48% (validation sample) Cirrhosis (Ishak 5 or 6): 22% vs. 14% Biopsy quality: All >10 mm and >10 portal tracts	Development vs. validation samples Age: median 43 vs. 43 years Female: 35% vs. 30% Genotype 1: 55% vs. not reported
Deghady, 2012 (92) Egypt	AST/ALT ratio APRI	Unclear	79	Severe fibrosis (METAVIR F3- F4): 42% Cirrhosis (METAVIR F4): 13% Biopsy quality: Not reported	Age: 55 years Female: Not reported Genotype 1: Not reported
Dinesen, 2008 (93) Germany	APRI AST/ALT ratio FibroIndex	Unclear	96	Cirrhosis (Batts-Ludwig F4): 28% Biopsy quality: Not reported	Age: 48 years Female: 41% Genotype 1: Not reported
Ehsan, 2008 (94) Egypt	Age-platelet index Lok Index Cirrhosis discriminant score Goteborg University Cirrhosis Index APRI Pohl Index AST/ALT ratio	Unclear	116	Fibrosis: Not reported Cirrhosis (Ishak 5-6): 30% Biopsy quality: Mean 12 mm	Age: 39 years Female: 16% Genotype 1: Not reported
El-Gindy, 2003 (95) Egypt	MMP-2 TIMP-1	Unclear	41	Fibrosis (Ishak 1-6): 71% Cirrhosis (Ishak 5-6):34% Biopsy quality: Not reported	Age: 48 years Female: 41% Genotype 1: Not reported

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
El-mezayen, 2013 (96)	Egypt	Ferritin Hyaluronic acid AST/ALT ratio Fibrosis Discriminant Score (hyaluronic acid, beta-glucuronidase, glucosamine, ferritin, AST, ALT)	Unclear	210	Fibrosis (METAVIR F1-F2): 57% (other 43% had F3 fibrosis, no F0 or F4) Biopsy quality: Not reported	Age: 39 years Female: 21% Genotype 1: Not reported All treatment-naïve No habitual alcohol use
El-Sayed, 2011 (97)	Egypt	APRI AST/ALT ratio AST	Unclear	37	Severe fibrosis (METAVIR F3-F4): 68% Biopsy quality: All ≥ 10 mm and ≥ 5 portal tracts	Age: 41 years Female: 14% Genotype 1: Not reported
El-Shorbagy, 2004 (98)	Egypt	7-item predictive index (platelet count, MMP-9, portal vein diameter, spleen diameter, ALT, AST, viral load)†	Unclear	109	Fibrosis (G2S2 or G3S3): 80% Cirrhosis (G3S3): 18% Biopsy quality: Not reported	Age: 46 years Female: 29% Genotype 1: Not reported
Fabris, 2008 (99)	Italy	APRI AST/ALT ratio Age-platelet index Cirrhosis Discriminant Score Forns Index Fibro Index	Retrospective	167	Fibrosis (METAVIR F2-F4): 41% Cirrhosis (METAVIR F4): 11% Biopsy quality: Average 19 mm and median 7 portal tracts	Age: 49 years Female: 50% Genotype 1 + 4: 50%
Ferraioli, 2012(100)	Italy	APRI	Prospective	130	Fibrosis (METAVIR F2-F4): 46% Cirrhosis (METAVIR F4): 18% Biopsy quality: Median 25 mm	Age: 46 years Female: 30% Genotype 1: Not reported

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Fontana, 2008 (33) USA	HALT-C model (platelet count, TIMP-1, hyaluronic acid)† Lok Index APRI Cirrhosis Discriminant Score	Unclear	513	Fibrosis (Ishak score ≥ 3): 93% Cirrhosis (Ishak 5 or 6): 38% (study excluded patients with Ishak 0 or 1) Biopsy quality: Mean 1.84 cm	Age: 49 years Female: 29% Genotype 1: Not reported All had Ishak 3 fibrosis within the last year
Fontanges, 2008 (101) France	Fibrotest	Prospective	96	Fibrosis (METAVIR F2-F4): 29% Cirrhosis (METAVIR F4): 6.2% Biopsy quality: Mean 22.5 mm and 19 portal tracts; 85% >15 mm	Age: 48 years Female: 36% Genotype 1: 83% 4.2% HIV and 1.0% HBV
Forns, 2002 (30) Spain	Forns Index (age, GGT, cholesterol, platelet count)†	Unclear	351 (index development sample) 125 (validation sample)	Fibrosis (Scheuer F2-F4): 24% (development sample) vs. 26% (validation sample) Cirrhosis (Scheuer F4): 6.0% vs. 3.2% Biopsy quality: All ≥ 6 portal tracts	Development vs. validation samples Age: 39 vs. 38 years Female: 36% vs. 36% Genotype 1: 86% vs. 84% All had elevated ALT
Fouad, 2012 (102) Egypt	Age-platelet Index AST/ALT ratio APRI Goteborg University Cirrhosis Index Pohl Index	Unclear	154	Cirrhosis (METAVIR F4): 19% Biopsy quality: Not reported	Age: 39 years Female: 32% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Friedrich- Rust, 2010 (103) Germany	Simplified ELF index Fibrotest	Retrospective	36	Fibrosis (METAVIR F2-F4): 66% Cirrhosis (METAVIR F4): 15% Biopsy quality: All >10 mm and >=6 portal tracts; mean 22 mm, median 20 mm	Age: 50 years Female: 57% Genotype 1: Not reported
Gabrielli, 1997 (104) Italy	Laminin P1 PIIIP	Unclear	99	Fibrosis (Scheuer F2-F4): Not reported Cirrhosis (Scheuer F4): 16% Biopsy quality: ≥5 portal tracts and ≥5 terminal hepatic veins	Age: 50 years Female: 36% Genotype 1: Not reported
Gara, 2013 (105) USA	APRI	Prospective	120	Fibrosis (Ishak ≥3): 29% Cirrhosis (Ishak 5 or 6): 13% Biopsy quality: Mean 13.4 mm and 13 portal tracts	Age: 42 years Female: 36% Genotype 1: Not reported
Giannini, 2006 (108) Italy and USA	AST/ALT ratio Platelet count	Retrospective	409	Fibrosis (Ishak ≥3 in Italian sample, METAVIR F2-F4 in US sample): 43% Biopsy quality: Not reported	Age: 47 (Italy) and 43 (USA) years Female: 27% and 36% Genotype 1: Not reported
Giannini, 2003a (106) Italy	AST/ALT ratio Platelet count AST/ALT ratio and platelet count (Pohl Index variant)†	Retrospective	252	Fibrosis (Scheuer F2-F4 or clinical signs of portal hypertension): 55% Cirrhosis (Scheuer F4 or clinical signs of portal hypertension): 36% Biopsy quality: Not reported	Age: 48 years Female: 26% Genotype 1: 57%

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Giannini, 2003b (107)	Italy	AST/ALT ratio APRI	Retrospective	239	Fibrosis (criteria not reported): 54% Cirrhosis (criteria not reported): 27% Biopsy quality: Not reported	Age: 47 years Female: 28% Genotype 1: Not reported
Gomes da Silva, 2008 (109)	Brazil	APRI	Retrospective	50	Fibrosis (METAVIR F2-F4): 56% Cirrhosis (METAVIR F4): 26% Biopsy quality: Not reported	Age: 50 years Female: 32% Genotype 1: 54%
Gordon, 2005 (110)	Australia	Cirrhosis Discriminant Score Hyaluronic acid	Unclear	104	Cirrhosis (METAVIR F4): 22% Biopsy quality: Mean 15 mm	Age: 39 years Female: 33% Genotype 1: 42% All had elevated ALT
Grigorescu, 2007 (111)	Romania	Fibrotest alpha-2 macroglobulin Haptoglobin Apolipoprotein-A1 Total bilirubin GGT	Retrospective	116	Fibrosis (METAVIR F2-F4): 63% Biopsy quality: Not reported	Age: 47 years Female: 63% Genotype 1: Not reported
Guechot, 2012 (115)	France	ELF	Retrospective	512	Fibrosis (METAVIR F2-F4): 48% Cirrhosis (METAVIR F4): 15% Biopsy quality: Mean 25 mm, >25 mm in 49%	Age: Median 50 years Female: 40% Genotype 1: Not reported
Guechot, 2010 (114)	France	Hepascore (with automated hyaluronic acid assay)	Prospective	512	Fibrosis (METAVIR F2-F4): 48% Cirrhosis (METVIR F4): 15% Biopsy quality: Mean 25 mm, >25 mm in 49%	Age: Median 50 years Female: 40% Genotype 1: Not reported

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Guechot, 1996 (113)	France	PIIIP Hyaluronic acid	Unclear	326	Severe fibrosis (Knodell F3-F4): 34% Cirrhosis (Knodell F4): 16% Biopsy quality: Not reported	Age: 44 years Female: 45% Genotype 1: Not reported All elevated ALT
Guechot, 1994 (112)	France	PIIIP Hyaluronic acid	Unclear	58	Fibrosis (Knodell F1-3): 76% Cirrhosis (Knodell F3): 17% Biopsy quality: Not reported	Age: Mean not reported (range 25-68 years) Female: 29% Genotype 1: Not reported
Guzelbulut, 2011 (116)	Turkey	APRI FIB-4 Forns' Index	Retrospective	150	Fibrosis (METAVIR F2-F4): 55% Cirrhosis (METAVIR F4): 34% Biopsy quality: Not reported	Age: 52 years Female: 48% Genotype 1: Not reported
Halfon, 2007a (119)	France	Fibrotest APRI Fibrometer Hepascore	Retrospective	356	Fibrosis (METAVIR F2-F4): 41% Cirrhosis (METAVIR F4): 4% Biopsy quality: All >15 mm	Age: 45 years Female: 47% Genotype 1: Not reported
Halfon, 2007b (120)	France	APRI FibroIndex Fibrotest Forns' Index	Prospective	125	Fibrosis (METAVIR F2-F4): 63% Biopsy quality: Not reported	Age: 47 years Female: 32% Genotype 1: Not reported
Halfon, 2006 (118)	France	Fibrotest	Prospective	504	Fibrosis (METAVIR F2-F4): 46% Cirrhosis (METAVIR F4): 5.8% Biopsy quality: Median 15 mm and 9 portal tracts; 55% ≥15 mm and ≥5 portal tracts	Age: 45 years Female: 46% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Halfon, 2005 (117) France	Hyaluronic acid	Prospective	151 (sample 1) 254 (sample 2)	Fibrosis (METAVIR F2-F4): 48% (sample 1) vs. 46% (sample 2) Cirrhosis (METAVIR F4): 7% vs. 5% Biopsy quality: All \geq 25 mm	Sample 1 vs. sample 2 Age: 51 vs. 47 years Female: 54% vs. 52% Genotype 1: Not reported
Hsieh, 2012 (121) Taiwan	Age-platelet Index AST/ALT ratio APRI Cirrhosis Discriminant Score FIB-4 FibroQ Lok Index Pohl Index	Retrospective	250	Fibrosis (METAVIR F2-F4): 83% (no patient with F0 fibrosis) Cirrhosis (METAVIR F4): 5.5%	Age: 54 years Female: 43% Genotype 1: Not reported
Hsieh, 2009 (22) Taiwan	FibroQ (age, AST, PT, platelets, ALT)† AAR APRI	Retrospective	113‡	Fibrosis (METAVIR F2-F4): 83% Cirrhosis (METAVIR F4): 4.3% Biopsy quality: Not reported	Age: 53 years Female: 35% Genotype 1: Not reported All treatment-naïve
Iacobellis, 2005a (122) Italy	Platelet count	Retrospective	1143	Fibrosis (Scheuer F2-F4): 57% Cirrhosis (Scheuer F4): 7.2% Biopsy quality: All \geq 5 portal tracts	Age: 53 years Female: 43% Genotype 1: Not reported All elevated aminotransferases

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Iacobellis, 2005b (123) Italy	AST/ALT ratio Platelet count Globulin/albumin ratio Combinations of the above APRI Forns' Index	Retrospective	1252	Fibrosis (Scheuer F3 or F4): 19% Cirrhosis (Scheuer F4): 6.2% Biopsy quality: All ≥ 5 portal tracts	Age: 54 years Female: 43% Genotype 1: Not reported All elevated aminotransferases
Ichino, 2010 (124) Japan	APRI Forns' Index FiboIndex	Unclear	165	Fibrosis (METAVIR F2-F4): 60% Cirrhosis (METAVIR F4): 15% Biopsy quality: Not reported	Age: 53 years Female: 46% Genotype 1: Not reported
Imbert- Bismut, 2001 (29) Thabut, 2003 (200) France	Fibrotest (original 6- marker version) [†] APRI	Prospective	205 (index development sample) 134 (validation sample)	Fibrosis (METAVIR F2-F4): 38% (development sample) vs. 45% (validation sample) Cirrhosis (METAVIR F4): 10% vs. 16% Biopsy quality: All ≥ 10 mm	Development vs. validation sample Age: 47 vs. 48 years Female: 47% vs. 34% Genotype 1: Not reported
Imperiale, 2000 (125) USA	AST/ALT ratio	Retrospective	177	Fibrosis: Not reported Cirrhosis (Hytiroglou 4): 23% Biopsy quality: Not reported	Age: 42 years Female: 37% Genotype 1: Not reported
Islam, 2005 (32) Sweden	Normalized AST Platelet count APRI Goteborg University Cirrhosis Index (GUCI) (AST, INR, platelet count) [†]	Retrospective	179	Fibrosis (Ishak ≥ 3): 41% Cirrhosis (Ishak 5 or 6): 11% Biopsy quality: ≥ 10 mm and ≥ 4 portal tracts	Age: 44 years Female: 44% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Jeffers, 2007 (126) USA	FIBROSpect II	Prospective	145 (7 with HBV infection)	Fibrosis (Batts-Ludwig F2-F4): 84% Biopsy quality: All >5 portal tracts	Age: 52 years Female: 44% Genotype 1: Not reported
Kalantari, 2011 (127) Iran	Hepascore	Unclear	80	Fibrosis (METAVIR F2-F4): 54% Cirrhosis (METAVIR F4): 20% Biopsy quality: All ≥10 mm	Age: 35 years Female: 15% Genotype 1: 100%
Kaul, 2002 (128) USA	4-item predictive model (sex, AST, platelet count, spider nevi)†	Retrospective	264 (index development sample) 102 (validation sample)	Fibrosis (Scheuer F2-F4): Not reported Cirrhosis (Scheuer F4): 33% (development sample) vs. 16% (validation sample) Biopsy quality: Not reported	Development vs. validation samples Age: 45 vs. not reported Female: 39% vs. not reported Genotype 1: Not reported All in derivation sample had elevated AST or ALT
Khairy, 2012 (129) Egypt	FIB-4 4-item index (age, AST, platelet count, alpha- fetoprotein)†	Retrospective	4289	Fibrosis (METAVIR F2-F4): 42% Biopsy quality: ≥15 mm and ≥4 portal tracts	Age: 41 years Female: 19% Genotype 1: Not reported
Khan, 2008 (130) Pakistan	APRI	Unclear	120	Fibrosis (METAVIR F2-F4): 54% Cirrhosis (METAVIR F4): 8% Biopsy quality: Not reported	Age: 37 years Female: 30% Genotype 1: Not reported
Khokhar, 2003 (131) Pakistan	Pohl Index	Retrospective	266	Fibrosis (METAVIR F2-F4): 80% Cirrhosis (METAVIR F4): 56% Biopsy quality: Not reported	Age: 45 years Female: 44% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Koda, 2007 (19) Japan	Fibro Index (platelet count, AST, GGT)† Forns Index APRI	Unclear	240 (index development sample) 162 (validation sample)	Fibrosis (METAVIR F2-F3): 51% (development sample) vs. 50% (validation sample) (excluding F4) Cirrhosis (F4): Excluded from primary analyses; 26% in secondary analysis of validation sample Biopsy quality: Mean 18 mm, all ≥10 mm	Age: 54 years Female: 40% Genotype 1: Not reported No alcohol >10 g/day
Lackner, 2005 (132) and Lackner, 2006 (197) Austria	AST/ALT ratio Cirrhosis Discriminant Score Age-platelet Index Pohl Index APRI Platelet count Lok Index	Unclear	194	Fibrosis (Ishak score ≥3): 50% Cirrhosis (Ishak score 5 or 6): 16% Biopsy quality: All ≥6 portal tracts	Age: 48 years Female: 43% Genotype 1: 84%
Leroy, 2008 (133) France	FibroMeter Fibrotest Hepascore APRI	Retrospective	825	Fibrosis (METAVIR F2-F4): 48% Cirrhosis (METAVIR F4): 11% Biopsy quality: 55% >20 mm; 84% >15 mm	Age: 44 years Female: 40% Genotype 1: Not reported
Leroy, 2007 (134) France	MP3 FibroMeter Fibrotest Hepascore Forns Index APRI	Unclear	180	Fibrosis (METAVIR F2-F4): 51% Cirrhosis (METAVIR F4): 14% Biopsy quality: Median 23 mm and median 17 portal tracts; 89% >15 mm and 45% >25 mm	Age: 44 years Female: 38% Genotype 1: 61%
				Not reported	

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Leroy, 2004 (37) France	Hyaluronic acid PIIIP MP3 score (MMP-1 and PIIIP)†	Unclear	188	Fibrosis (METAVIR F2-F4): 45% Cirrhosis (METAVIR F4): 7.4% Biopsy quality: Not reported	Age: 43 years Female: 36% Genotype 1: 51%
Liu, 2006 (135) Taiwan	APRI Age-platelet index AST/ALT ratio	Unclear	79	Fibrosis (METAVIR F2-F4): 27% Cirrhosis (METAVIR F4): 0% Biopsy quality: Mean 19 mm length and 1.4 mm diameter	Age: 43 years Female: 65% Genotype 1: 61% All had normal ALT
Lo Iacono, 1998 (136) Italy	Soluble ICAM-1 Soluble VCAM-1 PIIIP	Unclear	52	Fibrosis (Scheuer F2-F4): Not reported Cirrhosis (Scheuer F4): 21% Biopsy quality: Not reported	Age: 41 years Female: 37% Genotype 1: 73%
Loaeza-del- Castillo, 2008 (137) Mexico	APRI	Retrospective	164	Fibrosis (METAVIR F2-F4): 51% Severe fibrosis (METAVIR F3- F4): 41% Cirrhosis (METAVIR F4): 10% Biopsy quality: Not reported	Age: 49 years Female: 64% Genotype 1: 73%
Lok, 2005 (36) USA	Lok Index (platelet count, AST/ALT ratio, and INR)†	Prospective	783 (index development sample) 358 (internal validation sample) 265 (external validation sample)	Development vs. internal validation vs. external validation samples Fibrosis (Ishak score ≥ 3): 100% vs. 100% vs. 48% Cirrhosis (Ishak score 5 or 6): 39% vs. 34% vs. 15% Biopsy quality: 65% ≥ 1.5 cm, 14% >2.5 cm	Development vs. internal validation vs. external validation samples Age: 50 vs. 50 vs. 47 years Female: 28% vs. 27% vs. 36% Genotype 1: 90% vs. 87% vs. 74% All Ishak ≥ 3

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Lu, 2006 (138)	Taiwan	Platelet count	Retrospective	244	Cirrhosis (Knodell F4): Proportion not reported	Age: Not reported Female: Not reported Genotype 1: Not reported
Luo, 2002 (31)	Taiwan	AST/ALT ratio Globulin/albumin ratio Platelet count AST/ALT ratio + globulin/albumin ratio AST/ALT ratio + platelet count Globulin/albumin ratio + platelet count	Unclear	103	Fibrosis (Scheuer F2-F4): 48% Cirrhosis (Scheuer F4): 21% Biopsy quality: All >5 portal tracts	Age: 52 years Female: 31% Genotype 1: Not reported All elevated ALT
Martinez, 2011 (139)	Spain	Forns Index APRI Simplified ELF index (PIIP, Hyaluronic acid and TIMP-1, without age)† FIB-4	Unclear	340	Fibrosis (METAVIR F2-F4): 67% Cirrhosis (METAVIR F4): 36% Biopsy quality: Mean 15 mm, 72% >15 mm	Age: 48 years Female: 36% Genotype 1: 74%
McHutchison, 2000 (140)	USA	Hyaluronic acid	Prospective	486	Fibrosis (Knodell 1-3): 76% Cirrhosis (Knodell 3): 17% Biopsy quality: ≥1 cm and at least 3 portal tracts	Age: Median 41 years Female: 27% Genotype 1: not reported
Metwally, 2007 (141)	USA	3-item predictive index (platelet count, AST, albumin)†	Prospective	137	Severe fibrosis (METAVIR F3- F4): 23% Cirrhosis (METAVIR F4): Not reported Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Morali, 2007 (142) Israel	Fibrotest	Unclear	81	Fibrosis (METAVIR F2-F4): Unclear Biopsy quality: Not reported	Age: 40 years Female: 51% Genotype 1: Not reported
Morra, 2007 (143) France	Eight peak proteomic index Fibrotest	Retrospective	191	Fibrosis (METAVIR F2-F4): 54% Cirrhosis (METAVIR F4): 14% Biopsy quality: All ≥ 10 mm and >5 portal tracts; mean 19 mm and 24% ≥ 25 mm	Age: 48 years Female: 36% Genotype 1: 53%
Mossong, 2011 (144) Luxembourg	Fibrotest Forns' Index 3-item predictive index (AST, alpha- macroglobulin, GGT)	Retrospective	186	Fibrosis (METAVIR F2-F4): 76% Cirrhosis (METAVIR F4): 5.4% Biopsy quality: Not reported	Age: 39 years Female: 36% Genotype 1: 60%
Murawaki, 2001a (146) Japan	Type-IV collagen Platelet count	Unclear	165	Fibrosis (Desmet F2-F3): 47% Cirrhosis (Desmet F4): 0% (excluded) Biopsy quality: Not reported	Age: 53 years Female: 33% Genotype 1: Not reported All had elevated ALT
Murawaki, 2001b (145) Japan	7S fragment of type IV collagen (PIVNP) PIIIIP Hyaluronic acid MMP-2 TIMP-1 ALT	Unclear	169	Fibrosis (Desmet F2-F3): 48% Cirrhosis (Desmet F4): 0% (excluded) Biopsy quality: Not reported	Age: 53 years Female: 34% Genotype 1: Not reported All had elevated ALT
Myers, 2003 (147) France	Fibrotest 7-item index (Fibrotest items plus PT and platelet count)	Unclear	323	Fibrosis (METAVIR F2-F4): 41% Cirrhosis (METAVIR F4): 13% Biopsy quality: All ≥ 10 mm	Age: 47 years Female: 42% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Myers, 2002 (148) France	Fibrotest Historical index (age at infection and biopsy, sex, and alcohol consumption)†	Unclear	211	Fibrosis (METAVIR F2-F4): 40% Cirrhosis (METAVIR F4): 9% Biopsy quality: All ≥10 mm	Age: Median 42 years Female: 44% Genotype 1: Not reported
Obrador, 2006 (39) Spain	Sabadell NIHCED (non- invasive hepatitis C related cirrhosis early detection) index (age ≥60 years, platelet count ≤100, AST/ALT index ≥1, PT ≥1.1, right hepatic lobe atrophy, splenomegaly, caudate lobe hypertrophy)†	Unclear	170 (index development sample) 162 (validation sample)	Fibrosis: Not reported Cirrhosis (Knodell F4): 28% (development sample) and 12% (validation sample) Biopsy quality: Mean 11.6 mm, 12.2 portal tracts	Development vs. validation samples Mean age: 52 vs. 45 years Female: 44% vs. 44% Genotype 1: Not reported All elevated liver enzymes
Ohta, 2006 (24) Japan	Fibrosis Index (albumin, platelet count)†	Retrospective	368 (index development sample) 249 (validation sample)	Fibrosis (Desmet F2-F4): 50% (development sample) and 63% (validation sample) Cirrhosis (Desmet F4): 8.4% and 9.6% Biopsy quality: Not reported	Reported for development sample only Mean age: 44 years Female: 39% Genotype 1: Not reported All elevated liver enzymes
Omran, 2011 (18) Egypt	Fibro-□ (alpha-fetoprotein, AST, ALT, platelet count)†	Unclear	199 (index development sample) 135 (validation sample)	Fibrosis (METAVIR F2-F4): 32% (development sample) and 42% (validation sample) Cirrhosis (METAVIR F4): 7.5% and not reported Biopsy quality: All ≥15 mm and/or >5 portal tracts	Development vs. validation samples Mean age: 44 years vs. not reported Female: 30% vs. 33% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Paggi, 2008 (149) Italy	APRI	Unclear	430	Fibrosis (METAVIR F2-F4): 70% Cirrhosis (METAVIR F4): 37% Biopsy quality: Median 4.1 cm	Age: Median 43 years Female: 45% Genotype 1 or 4: 55% All elevated liver enzymes
Parise, 2006 (150) Brazil	Hyaluronic acid APRI GGT AST/ALT ratio	Prospective	206	Fibrosis (Batts-Ludwig F2-F4): 42% Cirrhosis (Batts- Ludwig F4): 21% Biopsy quality: Not reported	Age: 47 years Female: 44% Genotype 1: 61%
Park, 2011a (152) Korea	APRI Multibiomarker score (alpha-2 macroglobulin, hyaluronic acid)†	Prospective	91	Fibrosis (METAVIR F2-F4): 67% Cirrhosis (METAVIR F4): 7.7% Biopsy quality: Not reported	Age: 50 years Female: 42% Genotype 1: 47%
Park, 2011b (153) Korea	Age-platelet Index APRI	Prospective	40	Fibrosis (METAVIR F2-F3): 42% Cirrhosis (METAVIR F4): 0% Biopsy quality: All >=15 mm and >=6 portal tracts	Age: 45 years Female: 60% Genotype 1: 45% All treatment-naïve Excluded for alcohol >20 g/day All with normal ALT
Park, 2000 and 2005 (151, 201) Australia	AST/ALT ratio	Retrospective	153	Fibrosis: Not reported Cirrhosis (Scheuer F4): 20% Biopsy quality: Not reported	Age: 47 years Female: 36% Genotype 1: Not reported
Parkes, 2011 (154) UK	Simplified Enhanced Liver Fibrosis index (ELF) (TIMP-1, hyaluronic acid, PIIIP)†	Prospective	347	Fibrosis (METAVIR F2-F4 or Ishak ≥3): 51% Cirrhosis (F4 or Ishak 5-6): 14% Biopsy quality: Not reported	Age: Median 42 to 45 years (3 cohorts) Female: Not reported Genotype 1: Not reported

Study, Year	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Patel, 2009 (155) France, Germany, Canada	Fibrotest FIBROSpect II APRI Forns Index FIB-4	Unclear	95	Fibrosis (METAVIR F2-F4): 95% Cirrhosis: Not reported Biopsy quality: Mean 18 mm	Age: 46 years Female: 40% Genotype 1: Not reported
Patel, 2004 (28) USA and France	FIBROSpect II (TIMP-1, alpha-2-macroglobulin, Hyaluronic acid)†	Retrospective	294 (index development sample) 402 (validation sample)	Fibrosis (METAVIR F2-F4): 0.52 (both samples) Cirrhosis (METAVIR F4): 18% (development sample) and 16% (validation sample) Biopsy quality: All ≥10 mm and at least 5 portal tracts	Development vs. validation samples Age: 45 vs. 46 years Female: 31% vs. 35% Genotype 1: Not reported
Plevris, 2000 (156) UK	Hyaluronic acid	Prospective	69	Fibrosis: Not reported Cirrhosis (Knodell F4): 22% Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported
Pohl, 2001 (38) USA	AST/ALT ratio Pohl Index (AST/ALT ratio and platelet count)†	Retrospective	153	Fibrosis (METAVIR F2-F4): 35% Cirrhosis (METAVIR F4): 13% Biopsy quality: Not reported	Age: 46 years Female: 48% Genotype 1: 49%
Poynard, 2003 (158) Europe, Canada, Argentina, and USA	Fibrotest	Retrospective	352	Fibrosis (METAVIR F2-F4): 38% Cirrhosis (METAVIR F4): 8.5% Biopsy quality: Not reported	Age: 45 years Female: 36% Genotype 2 or 3: 27% All patients had elevated ALT

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Poynard, 2002 (157)	France	Fibrotest Hyaluronic acid	Retrospective	165	F3 fibrosis (Knodell F3): 33% Cirrhosis (Knodell F4): 0% Biopsy quality: Not reported	Age: 41 years Female: 40% Genotype 1: Not reported All patients had ALT >1.5 x upper limit of normal
Poynard, 1997 (12)	Europe	Age-platelet index†	Retrospective	500	Fibrosis (METAVIR F2-F4): 69% Biopsy quality: Not reported	Age: 59 years Female: 41% Genotype 1: Not reported All had elevated transaminases
Pradat, 2002 (159)	Europe	ALT	Unclear	864	Fibrosis (METAVIR F2-F4): 71% Cirrhosis (METAVIR F4): 7.5% Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported
Reedy, 1998 (160)	USA	AST/ALT ratio	Retrospective	71	Fibrosis: Not reported Cirrhosis (Knodell F4): 32% Biopsy quality: Not reported	Age: 44 years Female: 31% Genotype 1: Not reported
Renou, 2001 (161)	France	Platelet count	Unclear	104	Fibrosis (METAVIR F2-F4): 45% Cirrhosis (F4): 13% Biopsy quality: Not reported	Age: Not reported Female: Not reported Genotype 1: Not reported All had elevated ALT
Romagnuolo, 2001 (162)	Canada	Platelet count ALT Albumin Bilirubin	Prospective	54	Fibrosis (Hytiroglou F2-F4): 31% Cirrhosis (Hytiroglou F4): 7.4% Biopsy quality: All ≥6 portal tracts	Age: 40 years Female: 32% Genotype 1: Not reported All had elevated ALT

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Romera, 2006 (163)	Spain	Forns Index APRI Fibrosis Probability Index (Sud or Sydney Index)	Retrospective	131	Fibrosis (Scheuer F2-F4): 47% Cirrhosis (Scheuer F4): 17% Biopsy quality: Mean 10 portal tracts	Age: 40 years Female: 40% Genotype 1: 43% All treatment-naïve
Rosenberg, 2004 (16)	Europe	European Liver Fibrosis test (age, hyaluronic acid, amino-terminal propeptide of type III collagen, and TIMP-1)†	Prospective	521 in sample, number with HCV infection not reported	Proportion with fibrosis or cirrhosis: Not reported Biopsy quality: >12 mm and >5 portal tracts	Age: Not reported Female: Not reported Genotype 1: Not reported All abnormal liver function tests for >6 months
Rossi, 2003 (164)	Australia	Fibrotest □-2 macroglobulin Apolipoprotein A1 Bilirubin GGT Haptoglobin	Unclear	125	Fibrosis (METAVIR F2-F4): 38% Cirrhosis (METAVIR F4): 7.2% Biopsy quality: Not reported	Age: 40 years Female: 34% Genotype 1: Not reported
Saadeh, 2001 (165)	USA	Cirrhosis Discriminant Score	Retrospective	111	Fibrosis: Not reported Cirrhosis (Knodell F4): 31% Biopsy quality: Not reported	Age: 44 years Female: 25% Genotype 1: Not reported All had elevated ALT
Said, 2010 (166)	Tunisia	Fibrotest	Prospective	65	Fibrosis (METAVIR F2-F4): 71% Severe fibrosis: (METAVIR F3-F4): 39% Cirrhosis (METAVIR F4): 10% Biopsy quality: Mean 17.7 mm, 10.5 portal spaces; 88% >15 mm	Age: 50 years Female: 57% Genotype 1: 92%

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Saitou, 2005 (167)	Japan	Type IV collagen PIIIP Hyaluronic acid YKL-40	Unclear	109	Fibrosis (METAVIR F2-F4): 71% Cirrhosis (METAVIR F4): 28% Biopsy quality: Not reported	Age: 54 years Female: 43% Genotype 1: Not reported
Schneider, 2006 (168)	Germany	APRI	Prospective	83	Fibrosis (Ishak 3-6): 57% Cirrhosis (Ishak 5 or 6): 23% Biopsy quality: Not reported	Age: 48 years Female: 51% Genotype 1: 84%
Sebastiani, 2012 (173)	Europe	Fibrotest APRI Forns Index SAFE algorithm Fibropaca algorithm Leroy algorithm	Retrospective	1013	Fibrosis (METAVIR F2-F4): 54% Cirrhosis (METAVIR F4): 11% Biopsy quality: Mean 20 mm and 11 portal tracts, 45% >20 mm	Age: 48 years Female: 43% Genotype 1: 65%
Sebastiani, 2011 (172)	Europe	APRI Fibrotest FIB-4 AST/ALT ratio Forns Index Lok Index	Retrospective	1810	Fibrosis (METAVIR F2-F4): 45% Cirrhosis (METAVIR F4): 9.0% Biopsy quality: Mean 18 mm and 11 portal tracts, 43% >20 mm	Age: 47 years Female: 44% Genotype 1: Not reported
Sebastiani, 2009 (169)	Europe	APRI SAFE fibrosis algorithm SAFE cirrhosis algorithm	Retrospective	2035	Fibrosis (METAVIR F2-F4): 46% Cirrhosis (METAVIR F4): 9.4% Biopsy quality: Mean 18 mm and mean 10.6 portal tracts	Age: 47 years Female: 44% Genotype 1: 68%

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Sebastiani, 2008 (170)	Italy	Fibrotest AST/ALT ratio Forns Index Fibroindex APRI	Unclear	244	Fibrosis (METAVIR F2-F4): 60% Cirrhosis (METAVIR F4): 9.8% Biopsy quality: All ≥ 15 mm and ≥ 7 portal tracts	Age: 48 years Female: 45% Genotype 1: 57%
Sebastiani, 2006 (171)	Italy	Fibrotest APRI	Unclear	190	Fibrosis (METAVIR F2-F4): 59% Cirrhosis (F4): 15% Biopsy quality: All ≥ 1.5 cm and ≥ 7 portal tracts	Age: 49 Female: 44% Genotype 1: 63%
Sheth, 1998 (174)	USA	AST/ALT ratio	Retrospective	139	Fibrosis: Not reported Cirrhosis (Hytiroglou F4): 34% Biopsy quality: Not reported	Age: 44 years Female: 33% Genotype 1: Not reported All had elevated ALT
Shlomai, 2013 (175)	Israel	Serum bile acids Fibrotest Serum bile acid-based model (serum bile acids, age, BMI, AST, cholesterol, glucose) GGT	Unclear	135	Severe fibrosis (METAVIR F3-F4): 33% Biopsy quality: Not reported	Age: 47 years Female: 30% Genotype 1: 79%
Silva, 2004 (176)	Brazil	GGT	Retrospective	201	Severe fibrosis (Desmet 3 or 4): 28% Cirrhosis (Desmet 4): 16% Biopsy quality: Not reported	Age: 40 years Female: 29% Genotype 1: Not reported
Sirli, 2010 (177)	Romania	APRI Forns' Index Lok Index FIB-4 Platelet count	Retrospective	150	Fibrosis (METAVIR F2-F4): 89% Cirrhosis (METAVIR F4): 10% Biopsy quality: All ≥ 20 mm and ≥ 8 portal tracts	Age: 50 years Female: 68% Genotype 1: Not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Snyder, 2007 (178) USA	APRI FIBROSpect II APRI + FIBROSpect II	Prospective	93	Fibrosis (Batts-Ludwig F2-F4): 54% Cirrhosis (Batts-Ludwig F4): 20% Biopsy quality: Mean 25 mm	Age: 47 years Female: 30% Genotype 1: 69%
Snyder, 2006 (179) USA	APRI	Retrospective and prospective	339 (retrospective sample) 151 (prospective sample)	Fibrosis (Batts-Ludwig F2-F4): 49% (retrospective sample) and 52% (prospective sample) Cirrhosis (Batts-Ludwig F4): 1.8% and 17% Biopsy quality: Not reported	Retrospective vs. prospective samples Age: 44 vs. 48 years Female: 28% vs. 30% Genotype 1: 76% vs. 74%
Stibbe, 2011 (180) The Netherlands	Fibrotest FIB-4	Prospective	41	Fibrosis (METAVIR F2-F4): 54% Cirrhosis (METAVIR F4): 27% Biopsy quality: All ≥ 20 mm	Age: 47 years Female: 66% Genotype 1: Not reported
Sud, 2004 (25) Australia	Fibrosis probability index (age, AST, total cholesterol, insulin resistance, alcohol intake) [†]	Prospective	170 (index development sample) 126 (validation sample)	Fibrosis (Scheuer F2-F4): 49% (development sample) and 59% (validation sample) Cirrhosis (Scheuer F4): 6% and 13% Biopsy quality: Not reported	Reported for development sample only Age: 41 years Female: 35% Genotype 1: Not reported
Testa, 2006 (181) Italy	Body mass index Platelet-spleen diameter ratio APRI Fibrosis model 1 (BMI, APRI, PLT/SPD) [†]	Unclear	75	Fibrosis (Ishak ≥ 3): 49% Cirrhosis (Ishak 5 or 6): 12% Biopsy quality: All ≥ 15 mm; mean 24 mm	Age: 50 years Female: 32% Genotype 1b: 43% All elevated transaminases

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Trocme, 2006 (182)	France	PIIIP/MMP-1 index†	Retrospective	79	Fibrosis (METAVIR F2-F4): 66% Cirrhosis (METAVIR F4): 8.9% Biopsy quality: Not reported	Age: 46 years Female: 43% Genotype 1: 62% All elevated ALT
Usluer, 2012 (183)	Turkey	Age-platelet Index APRI FIB-4 Fibrotest	Prospective	77	Fibrosis (Ishak 3 or 4): 25% (no Ishak 5 or 6) Biopsy quality: All ≥20 mm	Age: 49 years Female: 57% Genotype 1: Not reported
Uyar, 2010 (184)	Turkey	Fibrotest	Unclear	25	Fibrosis (METAVIR F2-F4): 12% Biopsy quality: Mean 14 mm and 8.9 portal tracts	Age: Not reported Female: 56% Genotype 1: Not reported All treatment-naïve
Vallet-Pichard, 2007 (185)	France	FIB-4	Retrospective	847	Fibrosis (METAVIR F2-F4): 36% Cirrhosis (METAVIR F4): 7.2% Biopsy quality: Not reported	Age: 44 years Female: 46% Genotype 1: Not reported
Verbaan, 1997 (186)	Sweden	Procollagen III propeptide (PIIIP) Type-IV collagen	Retrospective	98	Fibrosis: Not reported Cirrhosis (Scheuer F4): 11% Biopsy quality: Not reported	Age: 46 years Female: 34% Genotype 1: Not reported
Viana, 2009 (187)	Brazil	APRI	Prospective	200 (sample 1) 200 (sample 2)	Fibrosis (METAVIR F2-F4): 60% (sample 1) vs. 63% (sample 2) Cirrhosis (METAVIR F4): 20% vs. not reported Biopsy quality: All >10 portal tracts	Sample 1 vs. sample 2 Age: 51 vs. 50 years Female: 46% vs. 61% Genotype 1b: 54% vs. not reported

Study, Year Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, <i>n</i> *	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Wai, 2003 (13) USA	Aspartate aminotransferase to platelet ratio index (APRI)†	Retrospective	270 (combined index development and validation sample)	Fibrosis (Ishak ≥ 3): 48% Cirrhosis (Ishak 5 or 6): 15% Biopsy quality: Not reported	Age: 48 years Female: 36% Genotype 1: 74%
Walsh, 2000 (189) UK	Type-IV collagen Serum laminin ALT	Unclear	37	Advanced liver disease (Ishak score ≥ 3 and HAI ≥ 6): Not reported Biopsy quality: Not reported	Age: Not reported Female: 32% Genotype 1: Not reported
Walsh, 1999a (188) UK	PIIIP ALT	Unclear	30	Advanced liver disease (Ishak score ≥ 3 and HAI ≥ 6): Biopsy quality: Not reported Biopsy quality: Not reported	Age: Not reported Female: 36% Genotype 1: Not reported
Walsh, 1999b (190) UK	TIMP-1 TIMP-2 MMP-2 ALT	Unclear	43 (TIMP-1 and ALT) 30 (TIMP-2 and MMP-2)	Advanced liver disease (Ishak score ≥ 3 and HAI ≥ 6): Not reported Biopsy quality: Not reported	Age: Not reported Female: 33% Genotype 1: Not reported
Westin, 2008 (191) Europe	GUCI	Prospective	231	Fibrosis (Ishak 3-6): 37% Cirrhosis (Ishak 5-6): 15% Biopsy quality: All ≥ 4 portal tracts and ≥ 15 mm	Age: Not reported Female: Not reported Genotype 1 or 4: 71%
Williams, 1988 (14) USA	AST/ALT ratio	Unclear	44	Fibrosis: Not reported Cirrhosis (Hoofnagle criteria): 25% Biopsy quality: Not reported	Age: 51 years Female: Not reported Genotype 1: Not reported All elevated aminotransferases

Study, Year	Country	Tests Evaluated	Retrospective or Prospective Data Collection	Sample Size, n*	Proportion with Fibrosis or Cirrhosis/ Biopsy Quality	Population Characteristics
Wilson, 2006 (192)	USA	Fibrotest APRI ALT AST	Prospective	119	Ishak 3-4 fibrosis: 9.2% Cirrhosis (Ishak 5-6): 0% (excluded) Biopsy quality: Not reported	Age: 42 years Female: 18% Genotype 1: 97%
Wong, 1998 (193)	UK	Hyaluronic acid ALT a-glutathione-S transferase (GST)	Unclear	130	Fibrosis (modified Ishak 3-5 {max 5}): 34% Cirrhosis (modified Ishak 5): 8.5% Biopsy quality: Not reported	Age: median 37 years Female: 28% Genotype 1: not reported
Yilmaz, 2011 (194)	Turkey	APRI	Unclear	108	Proportion with fibrosis or cirrhosis: Not reported Biopsy quality: Not reported	Age: 53 years Female: 75% Genotype 1: Not reported
Zaman, 2007 (195)	USA	FIBROspect II	Prospective	108	Fibrosis (METAVIR F2-F4): 36% Cirrhosis (METAVIR F4): 2% Biopsy quality: All >15 mm and >5 portal tracts	Age: 44 years Female: 35% Genotype 1: Not reported
Zarski, 2012 (196)	France	FibroTest FibroMeter Forns Index APRI MP3 ELF Hepascore FIB-4 Hyaluronic acid	Prospective	436	Fibrosis (METAVIR F2-F4): 46% Cirrhosis (METAVIR F4): 14% Biopsy quality: All >=20 mm or >=15 mm and >=11 portal tracts	Age: 51 years Female: 38% Genotype 1: Not reported

*Sample sizes restricted to patients with HCV infection.

† Index originally developed in this study.

‡ All patients evaluated in Hsieh et al 2009 were included in Hsieh et al 2012

Abbreviations: a2MG = Alpha-macroglobulin, AAR = Aspartate aminotransferase-alanine aminotransferase ratio, ALT = Alanine aminotransferase, APRI = Aspartate aminotransferase-Platelet Ratio Index, AST = Aspartate aminotransferase, DM = Diabetes mellitus, ELF = Enhanced Liver Fibrosis Index, GGT = Gamma-glutamyl transferase, GST a-glutathione-S transferase, GUCI=Goteborg University Cirrhosis Index, HA=Hyaluronic acid, HBV =Hepatitis B virus, HCV = Hepatitis C virus, HIV = Human immunodeficiency virus, ICAM-1 = Inter-cellular adhesion molecule 1, INR = International normalized ratio, METAVIR=Meta-analysis of histologic data in viral hepatitis, mm = Millimeter, MMP-1 = Matrix metalloproteinase-1, MMP – 2 = Matrix metalloproteinase-2, NIHCED = Non-Invasive Hepatitis C Related Cirrhosis Early Detection, PIIIP = Procollagen III propeptide, PLT/SPD = Platelet count/spleen diameter ratio, PT = Prothrombin time, SAFE = Sequential algorithm for fibrosis evaluation, TIMP = Tissue inhibitor of metalloproteinase, VCAM-1 = Vascular cell adhesion protein 1, YKL-40 = Human cartilage glycoprotein-39

Table 2 of the Supplement. Strength of Evidence Domains and Overall Ratings

Key Question	Number of Studies	Quality (Good, Fair, Poor)	Consistency (High, Moderate, Low)	Directness (Direct or indirect)	Precision (High, Moderate, Low)	Number of Subjects, <i>n</i> *	Strength of Evidence
Diagnostic accuracy (vs. liver biopsy)							
Platelet counts	18	Fair	Moderate	Direct	Low	8,267 (for fibrosis) and 5,733 (for cirrhosis)	Moderate
Hyaluronic acid	8	Fair	Moderate	Direct	Low	1,509 (for fibrosis) and 1,471 (for cirrhosis)	Moderate
Age-platelet index	11	Fair	High	Direct	Moderate	1,937 (for fibrosis) and 1,584 (for cirrhosis)	Moderate
AST-platelet ratio index	7	Fair	High	Direct	High	25,183 (for fibrosis) and 16,694 (for cirrhosis)	High
AST/ALT ratio	32	Fair	High	Direct	High	2,292 (for fibrosis) and 34,226 (for cirrhosis)	High
Cirrhosis Discriminant Score (also known as Bonacini Index)	12	Fair	High	Direct	Moderate	1,761 (for fibrosis) and 2,170 (for cirrhosis)	Moderate
Enhanced Liver Fibrosis or Simplified ELF Index	8	Fair	High	Direct	Moderate	1,471 (for fibrosis) and 1,247 (for cirrhosis)	Moderate

Key Question	Number of Studies	Quality (Good, Fair, Poor)	Consistency (High, Moderate, Low)	Directness (Direct or indirect)	Precision (High, Moderate, Low)	Number of Subjects, <i>n</i>*	Strength of Evidence
FIB-4	19	Fair	High (two studies)	Direct	Moderate	2,797 (for fibrosis) and 2,297 (for cirrhosis)	Moderate
FibroIndex	9	Fair	High	Direct	Low	6,512 (for fibrosis) and 5,837 (for cirrhosis)	Moderate
Fibrometer	8	Fair	High	Direct	Moderate	4,306 (for fibrosis) and 3,131 (for cirrhosis)	Moderate
FibroSpect II	7	Fair	High	Direct	Low	1,730 (for fibrosis)	Low
Fibrotest	32	Fair	High	Direct	High	9,549 (for fibrosis) and 6,893 (for cirrhosis)	High
Forns' Index	22	Fair	High	Direct	High	8,834 (for fibrosis) and 1,336 (for cirrhosis)	High
Goteborg University Cirrhosis Index	5	Fair	Moderate	Direct	Low	776 (for fibrosis) and 526 (for cirrhosis)	Low
Hepascore	12	Fair	High	Direct	High	4,669 (for fibrosis) and 3,953 (for cirrhosis)	High
Lok Index	10	Fair	High	Direct	Moderate	3,215 (for cirrhosis)	Moderate

Key Question	Number of Studies	Quality (Good, Fair, Poor)	Consistency (High, Moderate, Low)	Directness (Direct or indirect)	Precision (High, Moderate, Low)	Number of Subjects, <i>n</i>*	Strength of Evidence
Pohl Index	12	Fair	High (two studies)	Direct	Low	1600 for fibrosis) and 1368(for cirrhosis)	Low
APRI vs. Fibrotest	17	Fair	High	Direct	Moderate	8,734 (excluding overlapping populations)	Moderate
AST/ALT ratio vs. other indices	20 studies	Fair	High	Direct	Moderate	11,139	Moderate

*For studies of diagnostic accuracy, based on studies reporting the area under the receiver operating characteristic curve.

Abbreviations: ALT = Alanine aminotransferase, APRI = Aspartate aminotransferase-platelet patio index, AST = Aspartate aminotransferase, AUROC = Area under the receiver operating characteristic curve, ELF = Enhanced Liver Fibrosis Index

Table 3 of the Supplement. Discrepancies

Author, Year	Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Attallah, 2013 (21)		Fibronectin \geq 0.35	Severe fibrosis: 36% (52/145)	0.60	0.58	31	39	21	54	0.59 vs. 0.44	0.44 vs. 0.72
Attallah, 2012 (27)		FiboIndex \geq 3.3	Cirrhosis: 10.5% (337/3212)	0.06	1.0	20	4	317	2660	0.70 vs. 0.83	0.90 vs. 0.89
Ben Jazia, 2009 (68)		APRI $>$ 0.72	Fibrosis: 77% (27/35)	0.93	0.58	25	3	2	5	0.87 vs. 0.83	0.60 vs. 0.71
Cheung, 2008 (26)		AAR \geq 1.0	Severe fibrosis: 45% (210/465)	0.19#	0.97#	40*	7*	170*	248*	0.42 vs. 0.85	0.63 vs. 0.59
Crisan, 2012 (90)		A: Forns Index $>$ 4.47 B: Hepascore $>$ 0.34	Fibrosis: 63% (283/446)	A: 0.80 B: 0.57	A: 0.49 B: 0.72	A: 226 B: 182	A: 82 B: 45	A: 57 B: 101	A: 81 B: 118	A: 0.41 vs. 0.73 B: 0.82 vs. 0.80	A: 0.61 vs. 0.69 B: 0.43 vs. 0.54

Author, Year Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Ehsan, 2008 (94)	A: APRI >5 B: Lok index >0.6 C: CDS >7 D: GUCI >1.5 E: APRI >1.5 F: Pohl Index positive G: AAR >1.5	Cirrhosis: 30% (35/116)	A: 0.72 B: 0.79 C: 0.48 D: 0.74 E: 0.66 F: 0.34 G: 0.44	A: 0.93 B: 0.88 C: 0.99 D: 0.89 E: 0.94 F: 0.99 G: 0.91	A: 25 B: 28 C: 17 D: 26 E: 23 F: 12 G: 15	A: 6 B: 10 C: 1 D: 9 E: 5 F: 1 G: 7	A: 10 B: 7 C: 18 D: 9 E: 12 F: 23 G: 20	A: 75 B: 71 C: 80 D: 72 E: 76 F: 80 G: 74	A: 0.91 vs. 0.81 B: 0.87 vs. 0.74 C: 0.98 vs. 0.94 D: 0.87 vs. 0.74 E: 0.92 vs. 0.82 F: 0.92 vs. 0.92 G: 0.83 vs. 0.68	A: 0.77 vs. 0.88 B: 0.80 vs. 0.91 C: 0.66 vs. 0.82 D: 0.77 vs. 0.89 E: 0.74 vs. 0.86 F: 0.60 vs. 0.78 G: 0.72 vs. 0.79
El- mezayen, 2012 (96)	Fibrosis Discriminant Score A: >0.55 B: >0.60	Fibrosis: 57% (120/210)	A: 1.0 B: 0.95	A: 0.73 B: 0.81	A: 120 B: 114	A: 24 B: 17	A: 0 B: 6	A: 66 B: 73	A: 0.91 vs. 0.83 B: 0.90 vs. 0.87	A: 0.97 vs. 0.66 B: 0.67 vs. 0.92
Guehot, 2012 (115)	ELF index >9.0 (fibrosis), >9.33 (severe fibrosis), or >9.35 (cirrhosis)	1: Fibrosis: 48% (247/512) 2: Severe fibrosis: 30% (155/512) 3: Cirrhosis: 15% (76/512)	1: 0.86 2: 0.90 3: 0.83	1: 0.62 2: 0.63 3: 0.75	1: 212 2: 140 3: 63	1: 101 2: 132 3: 109	1: 35 2: 15 3: 13	1: 164 2: 225 3: 327	1: 0.80 vs. 0.68 2: 0.73 vs. 0.51 3: 0.44 vs. 0.37	1: 0.70 vs. 0.82 2: 0.85 vs. 0.94 3: 0.95 vs. 0.96

Author, Year Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Iacobellis, 2005a (122)	Platelet count <140 x 10 ⁹ /L	Fibrosis: 57% (648/1143)	0.51	0.90	330	49	318	446	0.96 vs. 0.87	0.29 vs. 0.58
Iacobellis, 2005b (123)	A: AAR >=1 B: Platelet count <140 x 10 ⁹ /L C: Globulin/albumin ratio >1 D: B and C E: A and B F: A and C G: A, B, and C H: A and platelet count <150 x 10 ⁹ /L I: APRI >1.5 (fibrosis) or >2.0 (cirrhosis)	1: Fibrosis: 19% (243/1252) 2: Cirrhosis: 6.2% (78/1252)	B1: 0.71 C1: 0.31 D1: 0.29 E1: 0.19 F1: 0.11 G1: 0.09 H1: 0.20 B2: 0.86 C2: 0.38 F2: 0.20 G2: 0.17 H2: 0.03	B1: 0.86 C1: 0.85 D1: 0.84 E1: 0.84 F1: 0.82 G1: 0.82 H1: 0.84 B2: 0.87 C2: 0.96 F2: 0.95 G2: 0.95 H2: 0.96	B1: 172 C1: 74 D1: 70 E1: 47 F1: 27 G1: 22 H1: 48 B2: 67 C2: 30 F2: 15 G2: 13 H2: 2	B1: 136 C1: 151 D1: 159 E1: 164 F1: 180 G1: 182 H1: 164 B2: 156 C2: 49 F2: 60 G2: 61 H2: 45	B1: 71 C1: 169 D1: E1: 173 F1: 196 G1: H1: C2: B2: 11 C2: 48 F2: 63 G2: 65 H2: 76	B1: 873 C1: 858 D1: 850 E1: 845 F1: 829 G1: 827 H1: 845 B2: 1018 C2: 1125 F2: 1114 G2: 1113 H2: 1129	B1: 0.77 vs. 0.56 C1: 0.58 vs. 0.33 D1: 0.91 vs. 0.31 E1: 0.82 vs. 0.22 F1: 0.64 vs. 0.13 G1: 0.88 vs. 0.11 H1: 0.74 vs. 0.23 B2: 0.29 vs. 0.30 C2: 0.23 vs. 0.38 F2: 0.36 vs. 0.20 G2: 0.50 vs. 0.18 H2: 0.34 vs. 0.04	B1: 0.93 vs. 0.92 C1: 0.95 vs. 0.83 D1: 0.995 vs. 0.83 E1: 0.99 vs. 0.81 F1: 0.98 vs. 0.79 G1: 0.997 vs. 0.79 H1: 0.98 vs. 0.81 B2: 0.87 vs. 0.99 C2: 0.91 vs. 0.96 F2: 0.98 vs. 0.95 G2: 0.99 vs. 0.94 H2: 0.96 vs. 0.94

Author, Year Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Leroy, 2004 (37)	MP3 Score >0.50	Severe fibrosis: 19% (36/188)	0.26 [@]	0.97 [@]	9	5	27	147	0.77 vs. 0.64	0.85 vs. 0.85
Mossong, 2011 (144)	Forns' Index >4.2	Fibrosis: 44% (81/186)	0.58	0.77	47	24	34	81	0.50 vs. 0.66	0.77 vs. 0.70
Saitou, 2005 (167)	A: Type IV collagen >5.75 B: PIIP >0.835 C: Hyaluronic acid >75.7 D: YKL-40 >186.4 E: Type IV collagen >6.55 F: PIIP >0.995 G: Hyaluronic acid >183.5 YKL-40 >284.8	1: Fibrosis: 71% (77/109) 2: Cirrhosis: 28% (30/109)	A1: 0.65 B1: 0.78 C1: 0.75 D1: 0.78 A2: 0.60 B2: 0.77 C2: 0.80 D2: 0.80	A1: 0.69 B1: 0.75 C1: 0.81 D1: 0.81 A2: 0.61 B2: 0.66 C2: 0.80 D2: 0.71	A1: 50 B1: 60 C1: 58 D1: 60 A2: 18 B2: 23 C2: 24 D2: 24	A1: 10 B1: 8 C1: 6 D1: 6 A2: 31 B2: 27 C2: 16 D2: 23	A1: 27 B1: 17 C1: 19 D1: 17 A2: 12 B2: 7 C2: 6 D2: 6	A1: 22 B1: 24 C1: 26 D1: 26 A2: 48 B2: 52 C2: 63 D2: 56	A1: 0.67 vs. 0.83 B1: 0.76 vs. 0.88 C1: 0.79 vs. 0.91 D1: 0.80 vs. 0.91 A2: 0.61 vs. 0.37 B2: 0.69 vs. 0.46 C2: 0.80 vs. 0.60 D2: 0.73 vs. 0.51	A1: 0.66 vs. 0.45 B1: 0.77 vs. 0.59 C1: 0.76 vs. 0.58 D1: 0.79 vs. 0.60 A2: 0.60 vs. 0.80 B2: 0.67 vs. 0.88 C2: 0.80 vs. 0.91 D2: 0.78 vs. 0.90

Author, Year Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Sebastiani, 2008 (170)	A: FibroIndex >1.25	Fibrosis: 40%	A: 0.41 B: 0.09	A: 0.77 B: 1.0	A: 13 B: 3	A: 11 B: 0	A: 19 B: 29	A: 37 B: 48	A: 0.75 vs. 0.54	A: 0.43 vs. 0.66
	B: Fibroindex >2.25	(32/80), subgroup	C: 0.36 D: 0.14	C: 0.91 D: 1.0	C: 12 D: 4	C: 4 D: 0	C: 20 D: 28	C: 44 D: 48	B: 1.0 vs. 1.0	B: 0.39 vs. 0.62
	C: APRI >0.5	with	E: 0.66	E: 0.85	E: 21	E: 7	E: 11	E: 41	C: 0.90 vs. 0.75	C: 0.42 vs. 0.69
	D: APRI >1.5	normal	F: 0.13	F: 0.88	F: 4	F: 6	F: 28	F: 42	D: 1.0 vs. 1.0	D: 0.57 vs. 0.63
	E: Fibrotest >0.49	ALT levels	G: 0.56 H: 0.06	G: 0.67 H: 1.0	G: 18 H: 2	G: 16 H: 0	G: 14 H: 30	G: 32 H: 48	E: 0.88 vs. 0.75	E: 0.61 vs. 0.79
	F: AAR >1								F: 0.70 vs. 0.40	F: 0.30 vs. 0.60
	G: Forns Index >4.2								G: 0.75 vs. 0.53	G: 0.47 vs. 0.70
	H: Forns Index >6.9								H: 1.0 vs. 1.0	H: 0.38 vs. 0.62

Author, Year Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Sebastiani, 2011(172)	A: APRI >1.0	1: Fibrosis:	D1: 0.56	D1: 0.79	D1: 461	D1: 209	D1:	D1: 781	D1: 0.84	D1: 0.68 vs.
	B: APRI >1.5	45%	E3: 0.54	E3: 0.90	E3: 88	E3: 163	359	E3:	vs. 0.69	0.69
	C: APRI >2.0	(820/1810)	B2: 0.27	B2: 0.89	B2: 48	B2: 47	E3: 75	1484	E3: 0.53 vs.	E3: 0.95 vs.
	D: Fibrotest >0.49	2: Fibrosis: 40%	A4: 0.33	A4: 0.87	A4: 6	A4: 75	B2: 128	B2: 372	0.35	0.95
	E: Fibrotest >0.75	(176/595)^	C4: 0.26	C4: 0.90	C4: 5	C4: 60	A4: 13	A4: 501	B2: 0.71 vs.	B2: 0.61 vs.
	F: FIB-4 >3.25	3:	E4: 0.33	E4: 0.94	E4: 6	E4: 35	C4: 14	C4: 516	0.51	0.74
	G: Forns' Index >4.2	Cirrhosis: 9.0%	F2: 0.53	F2: 0.59	F2: 93	F2: 173	E4: 13	E4: 541	A4: 0.26	A4: 0.94 vs.
	H: Forns' Index >6.9	(163/1810)	G2: 0.57	G2: 0.67	G2: 100	G2: 140	F2: 83	F2: 246	vs. 0.07	0.97
	I: Platelets <150 x 10 ⁹ /L	3:	H2: 0.18	H2: 0.89	H2: 31	H2: 46	G2: 76	G2: 279	C4: 0.40 vs.	C4: 0.96 vs.
	J: AAR >1	(19/595)^	I4: 0.44	I4: 0.90	I4: 8	I4: 57	H2:	H2: 373	0.08	0.97
	K: Lok Index >0.2		J4: 0.12	J4: 0.88	J4: 2	J4: 72	145	I4: 519	E4: 0.27 vs.	E4: 0.94 vs.
	L: Lok Index >0.5		K4: 0.67	K4: 0.35	K4: 13	K4: 374	I4: 11	J4: 504	0.15	0.98
			L4: 0.52	L4: 0.60	L4: 10	L4: 228	J4: 17	K4: 202	F2: 0.70 vs.	F 2: 0.41 vs.
							K4: 6	L4: 348	0.35	0.75
						L4: 9		G2: 0.75	G2: 0.47 vs.	
								vs. 0.42	0.79	
								H2: 0.90	H2: 0.34 vs.	
								vs. 0.40	0.72	
								I4: 0.34 vs.	I4: 0.94 vs.	
								0.12	0.98	
								J4: 0.70 vs.	J4: 0.30 vs.	
								0.03	0.97	
								K4: 0.40	K4: 0.84 vs.	
								vs. 0.03	0.97	
								L4: 0.65 vs.	L4: 0.45 vs.	
								0.04	0.97	

Author, Year Country	Test	Prevalence of Fibrosis	Sensitivity	Specificity	TP	FP	FN	TN	Reported vs. Calculated Positive Predictive Value	Reported vs. Calculated Negative Predictive Value
Sebastiani, 2012 (173)	A: APRI >1.0	1: Fibrosis:	A2: 0.75	A2: 0.79	A2: 84	A2: 185	A2: 29	A2: 715	A2: 0.68	A2: 0.96 vs.
	B: APRI >1.5	54 %	B1: 0.29	B1: 0.95	B1: 160	B1: 21	B1: 392	B1: 440	vs. 0.31	0.96
	C: Fibrotest >0.75	(552/1013) 2: Cirrhosis: 11% (111/1013)	C2: 0.30	C2: 0.89	C2: 34	C2: 100	C2: 79	C2: 800	B1: 0.90 vs. 0.88	B1: 0.39 vs. 0.53
Stibbe, 2011 (180)	A: Fibrotest >0.58	1: Severe fibrosis:	A1: 0.91	A1: 0.41	A1: 16	A1: 13	A1: 2	A1: 9	A1: 0.68	A1: 0.78 vs.
	B: Fibrotest >0.75	45% (1840) 2: Cirrhosis: 28% (11/40)	B2: 1.0	B2: 0.24	B2: 11	B2: 22	B2: 0	B2: 7	vs. 0.55	0.82
									B2: 0.64 vs. 0.33	B2: 1.0 vs. 1.0

*True positives, false positives, false negatives, and true negatives provided by study

#Based on 2 x 2 data (true positives, false positives, false negatives, and true negatives) provided by the study. Reported sensitivity of 0.21 and reported specificity of 0.82 inconsistent with reported 2 x 2 data

^Normal ALT subgroup

~Results for aspartate aminotransferase-to-platelet index not reported; reported data inconsistent with expected decrease in sensitivity and increase in specificity at progressively higher cutoffs

Abbreviations: AAR = Aspartate aminotransferase to alanine transaminase ratio, ALT= Alanine aminotransferase, APRI = Aspartate aminotransferase-to-platelet index, CDS = Cirrhosis discriminant score, GUCI= Goteborg, University Cirrhosis Index, FN = False negatives, FP = False positives, TN = True negatives, TP = True positives