

Supplementary Table 1 Formulae of serum biomarkers for liver fibrosis assessment ⁽¹⁾

NIT	Formula
FIB-4	$\text{age (yr)} \times \text{AST [U/L]} / (\text{platelets [10}^9\text{/L]} \times (\text{ALT [U/L]})^{1/2})$
Fibrotest® (Biopredictive, Paris, France)	patented formula combining α -2-macroglobulin, γ GT, apolipoprotein A1, haptoglobin, total bilirubin, age and gender
Forns Index	$7.811 - 3.131 \times \ln(\text{platelet count}) + 0.781 \times \ln(\text{GGT}) + 3.467 \times \ln(\text{age}) - 0.014 \times (\text{cholesterol})$
AST to Platelet Ratio (APRI)	$\text{AST (/ULN)} / \text{platelet (10}^9\text{/L)} \times 100$
FibroSpectII® (Prometheus Laboratory Inc, San Diego, USA)	patented formula combining α -2-macroglobulin, hyaluronate and TIMP-1
MP3	$0.5903 \times \log(\text{PIIINP [ng/ml]}) - 0.1749 \times \log(\text{MMP-1 [ng/ml]})$
Enhanced Liver Fibrosis score® (ELF) (Siemens Healthcare, Erlangen, Germany)	patented formula combining age, hyaluronate, MMP-3 and TIMP-1
Fibrosis Probability Index (FPI)	$10.929 + (1.827 \times \text{Ln[AST]}) + (0.081 \times \text{age}) + (0.768 \times \text{past alcohol use}) + (0.385 \times \text{HOMA-IR}) - (0.447 \times \text{cholesterol})$
Hepascore® (PathWest, University of Western Australia, Australia)	patented formula combining bilirubin, γ GT, hyaluronate, α -2-macroglobulin, age and gender
Fibrometer® (Echosens, Paris, France)	patented formula combining platelet count, prothrombin index, AST, α -2-macroglobulin, hyaluronate, urea and age
Lok index	$-5.56 - 0.0089 \times \text{platelet (10}^3\text{/mm}^3) + 1.26 \times \text{AST/ALT ratio} = 5.27 \times \text{INR}$
Goteborg University Cirrhosis Index (GUCI)	$\text{AST} \times \text{prothrombin} - \text{INR} \times 100 / \text{platelet}$
Virahep-C model	$-5.17 + 0.20 \times \text{race} + 0.07 \times \text{age (yr)} + 1.19 \ln(\text{AST [IU/L]}) - 1.76 \ln(\text{platelet count [10}^3\text{/ml]}) + 1.38 \ln(\text{alkaline phos- phatase [IU/L]})$
Fibroindex	$1.738 - 0.064 \times (\text{platelets [10}^4\text{/mm}^3) + 0.005 \times (\text{AST [IU/L]}) + 0.463 \times (\text{gamma globulin [g/dl]})$
HALT-C model	$-3.66 - 0.00995 \times \text{platelets (10}^3\text{/ml)} + 0.008 \times \text{serum TIMP-1} + 1.42 \times$

log(hyaluronate)

Supplementary Table 2 Details of the search strategy and search terms

MEDLINE	((aspartate aminotransferase-to-platelet ratio index) OR (aspartate aminotransferase/platelet count ratio index) OR (AST-to-platelet ratio index) OR (AST/PLT ratio index) OR APRI OR (FIB 4) OR (Fibrosis 4) OR Fibrotest Or Fibrosure OR (Forns index) OR FibrospectII OR (Fibrospect II) OR MP3 OR (Enhanced liver fibrosis score) OR ELF OR (Fibrosis probability index) OR FPI OR Hepascore OR Fibrometer OR (Lok index) OR (Göteborg university cirrhosis index) OR GUCI OR ((Viralhep C) AND model) OR (Fibroindex) OR ((HALT C) AND model) OR (Liver stiffness) OR elastography OR "Fibroscan" OR (acoustic radiation force impulse imaging) OR ARFI OR pSWE OR (point shear wave elastography) OR (2D AND SWE) OR (2D shear wave elastography) OR MRE OR (magnetic resonance elastography)) AND (outcome* OR prognosis OR predict* OR cirrhosis OR decompensat* OR cancer OR hepatocellular carcinoma OR HCC OR death OR mortality OR transplant) AND (chronic hepatitis C OR chronic viral hepatitis OR HCV)
EMBASE	("aspartate aminotransferase to platelet ratio index" OR "aspartate aminotransferase-to-platelet ratio index" OR "AST to platelet ratio index" OR "AST-to-platelet ratio index" OR "AST/PLT ratio index" OR "APRI" OR "FIB 4" OR "FIB-4" OR "Fibrosis 4" OR "Fibrosis-4" OR "Fibrotest" OR "Fibrosure" OR "Forns index" OR "FibrospectII" OR "Fibrospect II" OR "MP3" OR "Enhanced liver fibrosis score" OR "ELF" OR ("Fibrosis" AND "probability" AND "index") OR "FPI" OR "Hepascore" OR "Fibrometer" OR "Lok index" OR "Göteborg university cirrhosis index" OR "GUCI" OR "Viralhep C model" OR "Viralhep-C model" OR "Fibroindex" OR "HALT C model" OR "HALT-C model" OR "PGA" OR "Bonacini" OR "Pohl" OR (Liver stiffness) OR elastography OR "Fibroscan" OR "acoustic radiation force impulse imaging" OR ARFI OR pSWE OR "point shear wave elastography" OR "2D SWE" OR "2D-SWE" OR "2D shear wave elastography" OR "2D-shear wave elastography" OR MRE OR "magnetic resonance elastography") AND (outcome* OR prognosis OR predict* OR cirrhosis OR decompensat* OR cancer OR hepatocellular carcinoma OR HCC OR death OR mortality OR transplant) AND (chronic hepatitis C OR chronic viral hepatitis OR HCV)

Supplementary Table 3 Characteristics of the cohort studies included in the systematic review and meta-analysis

Supplementary Table 3A Characteristics of the cohort studies included in the meta-analysis

Study	Country	Enrolment year.	Follow-up	Number of patients	Age	Coinfection N (%)	Baseline fibrosis	HCV therapy N (%)	SVR N (%)	NIT*	Outcome N (%)	
Chun, 2020 ^[49]	Korea	2003-2016	median 49.0 months (IQR 21.9–84.9)	669	mean 59.6±11.6	0 (0)	FIB-4 2.3 ± 2.8 Cirrhosis 112 (16.7)	DAA 669 (100)	669 (100)	FIB-4 (post-Rx)	HCC 19 (2.84)	
Ogasawara, 2019 ^[38]	Japan	2011-2016	median 3.3 years (range 0.5–7.1)	398	median 70 (range 25–88)	0 (0)	LSM 8.6 kPa (range 2.4–49.6) FIB-4 3.00 (range 0.63–19.15)	DAA 398 (100)	398 (100)	FIB-4, TE (pre& post-Rx)	HCC 19 (4.77)	
Pons, 2019 ^[14]	Spain	2015-2016	median 2.9 years (range 0.3–3.8)	572	mean 63.7±11.1	0 (0)	LSM 20.2 kPa (SD 10.4) APRI 2.6 (SD 2.4) FIB-4 5.6 (SD 4.4)	DAA 572 (100)	572 (100)	TE (post-Rx)	HCC 25 (4.37)	
Ogasawara, 2019 ^[47]	Japan	1992-2014	median 8.9 years (range 1.0–26.7)	457	median 60 (range 36–78)	N/A	FIB-4 pretx: median 4.29 (range 3.25–27.3) FIB-4 24EOT median 2.69 (range 0.62–16.2)	IFN 457 (100)	457 (100)	FIB-4 (post-Rx)	OM 36 (7.8)	
Ioannou, 2019 ^[13]	United States	2000-2015	mean 5.4 years	Cirrhosis, IFN-treated [†]			DAA 29033 (60), IFN 19102 (40)	Cirrhosis 2251 (100)		48135 (100)	FIB-4 (pre-Rx)	HCC 1509 (3.13)
				2251	mean 56.9±6.2	HBV 49(2.2)/HIV 39 (1.7)						
				Cirrhosis, DAA-treated [*]								
				7533	mean 61.9±5.3	HBV 131(1.7)/ HIV 251 (3.3)						
				No cirrhosis, IFN-treated [†]								
16851	mean 53.1±7.0	HBV 172 (1.0)/ HIV 345 (2.0)	Cirrhosis 0 (0)									
No cirrhosis, DAA-treated [‡]												

Study	Country	Enrolment year.	Follow-up	Number of patients	Age	Coinfection N (%)	Baseline fibrosis	HCV therapy N (%)	SVR N (%)	NIT*	Outcome N (%)
				21500	mean 60.8±6.8	HBV 238 (1.1) / HIV 1063 (4.9)	Cirrhosis 0 (0)				
Na, 2019 ^[33]	Korea	2004-2014	mean 89.2 months (range 18–168)	no HCC				IFN 295 (100)	295 (100)	APRI, FIB-4 (pre & post-Rx)	HCC 12 (4.07)
				283	median 55 (20-80)	0 (0)	APRI median 0.94 (range 0.17–6.13) FIB-4 median 2.38 (range 0.46–17.83)				
				Developed HCC							
				12	median 63.5 (48-70)	0 (0)	APRI median 2.56 (range 1.08–4.62) FIB-4 median 5.80 (range 2.93–12.55)				
Tamaki, 2019 ^[30]	Japan	2015-2017	mean 26.4 months (range > 1 year, SD 7.9)	346	mean 68.2 ± 10	0 (0)	LSM 3.92 ± 1.9 kPa FIB-4 3.19 ± 2.1 F0-1/2/3/4 = 75/47/48/21	DAA 346 (100)	346 (100)	FIB-4, MRE (post-Rx)	HCC 24 (6.94)
Rinaldi, 2019 ^[15]	Italy	2015-2017	at least 1 year	258	median 68 years (61–74)	0 (0)	LSM median 25.5 kPa [18–35.6] Cirrhosis 258 (100)	DAA 258 (100)	N/A	TE (pre-Rx)	HCC 35 (13.6)
Hansen, 2019 ^[20]	Denmark	2007-2014	median 48.2 months (IQR 23.6–67.3)	591	46.1 (IQR 38.2–53.8)	0 (0)	LSM 6.8 kPa (IQR 5.3–11.6)	N/A	70 (11.8)	TE	OM 68 (11.5), LRM 27 (4.57), HD 30 (5.3)
Chen, 2019 ^[45]	China	2005-2016	median 4.8 years (IQR 3.3-7.6)	691	35 (31-40)	HBV 0 (0)/ HIV 691 (100)	FIB-4 1.78 (IQR, 1.19-3.00)	DAA 691 (100)	N/A	FIB-4	OM 131 (19.0)
Shili-Masmoudi, 2019 ^[28]	France	2005-2015	median 4.9 years (IQR 3.2–6.1)	1,062	45.7 (42.4–49.1)	HBV 22 (2.2)/ HIV 654 (61.6)	LSM 21.7% >12.5 kPa	unspecified 727 (68.5)	189 (26)	TE	OM 76 (7.16), LRM 26 (34.2)
Sou, 2019 ^[41]	China	2006-2013	at least 1 year	1884	mean 66.7±8.5	0 (0)	APRI 2.94±5.77 FIB-4 10.73±16.55 Cirrhosis 105 (5.57)	IFN 1884 (100)	1351 (71.6)	APRI, FIB-4 (pre & post-Rx)	HCC 122 (6.48)
Nakagomi, 2019 ^[34]	Japan	2004-2005	6.6 years (range >0.5)	1146	63.9 (IQR 55.1–70.9)	HBV 0 (0)/ HIV N/A	LSM median 7.9 kPa (IQR 5.4–14.3) kPa	DAA/IFN 461 (40.2)	229 (20.0)	TE	HCC 190 (16.6)

Study	Country	Enrolment year.	Follow-up	Number of patients	Age	Coinfection N (%)	Baseline fibrosis	HCV therapy N (%)	SVR N (%)	NIT*	Outcome N (%)
Watanabe, 2019 ^[44]	Japan	2014-2017	median 539 days	1174	66 (23–88)	N/A	N/A	DAA 1174 (100)	1174 (100)	APRI, FIB-4 (pre & post-Rx)	HCC 33 (2.81)
Hamada, 2018 ^[29]	Japan	2008-2016	26 months (5–109)	196	62 (29–89)	0 (0)	LSM 8.3 kPa (3.4–36.2) (kPa)	DAA 107 (55), IFN 89 (45)	197 (100)	FIB-4, SWE (post-Rx)	HCC 8 (4.1)
Thandassery, 2017 ^[43]	Qatar	2002-2014	median 6580.5 patient-years	1605	41.9 ± 9.7	0 (0)	F0/1/2/3/4 = 31/527/633/305/106 (1.9/32.9/39.5/19/6.6)	IFN 1605 (100)	1089 (67.8)	APRI, FIB-4 (pre-Rx)	HCC 11 (0.7), HD 52 (3.2), LRE 60 (3.8)
Cepeda, 2017 ^[25]	United States	2006-2014	median 5.9 years (IQR 4.3–6.5)	964	49 (IQR, 44–53 years)	HBV N/A/ HIV 337 (35.0)	LSM <8 kPa = 604 (62.7), 8–12.3 kPa = 218 (22.6), >12.3 kPa = 142 (14.7), FIB-4 <1.45 = 415 (47.7), 1.45–3.25 = 371 (42.6), >3.25 = 85 (9.8) F0-1/2-3/4 = 604 (62.7)/218 (22.6)/142 (14.7)	unspecified <5%	N/A	TE	OM 155 (16.1)
Sato, 2016 ^[40]	Japan	2004-2014	2.9 years (range 0.5–9.6)	355	median 2.9 years (range 0.5–9.6)	0 (0)	APRI median 0.61 (range 0.14–8.93) FIB-4 median 1.91 (range 0.31–16.22)	IFN 355 (100)	355 (100)	APRI, FIB-4 (pre-Rx)	HCC 12 (3.38)
Akuta, 2016 ^[39]	Japan	2008-2015	1.1 years (range 0.1–7.8)	958	median 64 (range 20–88)	0 (0)	FIB-4 median 2.7 (range 0.4–19.2)	IFN 304 (32) DAA 654 (68)	958 (100)	FIB-4 (pre-Rx)	HCC 14 (1.46)
Ng, 2016 ^[36]	China	2005-2011	4.38 years (range 1.13–9.27)	105	mean 58.3±10.4	HBV 10 (9.5)/ HIV 0 (0)	APRI 2.4±1.6	IFN 105 (100)	57 (54.3)	APRI (post-Rx)	HCC 15 (14.3)
Lee, 2016 ^[31]	Korea	1998-2010	median 5.1 years (range 0.1–14.3)	598	52 years (range 18–75)	HBV 0(0)/ HIV N/A	Cirrhosis = 34(5.69)	IFN 598 (100)	598 (100)	APRI (pre&post-Rx)	HCC 8 (1.34)
Tada, 2016 ^[48]	Japan	1994-2014	N/A (range > 3 years)	1723	median (IQR) 64.0 (57.0–69.0)	HBV 0(0)/ HIV N/A	FIB-4 median (IQR) 2.7 (1.7–11.5)	0 (0)	N/A	FIB-4 (pre-Rx)	LRM 225 (13.06), OM 465 (26.99)

Study	Country	Enrolment year.	Follow-up	Number of patients	Age	Coinfection N (%)	Baseline fibrosis	HCV therapy N (%)	SVR N (%)	NIT*	Outcome N (%)
Macías, 2015 ^[21]	Spain	1990-2013	median 3 years (IQR 1.9-4.3)	1046	median (IQR) 43 (40-47)	HBV 19(1.8)/ HIV 1046(100)	LSM median (IQR) 7.9 kPa (5.8-13.1)	unspecified 305 (29)	0 (0)	TE	HD 53 (5.1), OM 69 (6.6)
Narita, 2014 ^[35]	Japan	2007-2011	median 722 days (range 189-1378)	151	median 62 (range 22-82)	HBV 0(0)/ HIV N/A	LSM median 8.8 kPa (range 2.8-45.7) F0-2/3-4 = 115/36	IFN 151 (100)	83 (55)	TE (pre-Rx)	HCC 9 (6)
Nojiri, 2014 ^[37]	Japan	2008-2009	median 3.1 years	142	mean 66.1±12.4	0 (0)	N/A	IFN 39 (27.5)	27 (19.0)	APRI, FIB-4, Forns index	HCC 21
Tamaki, 2014 ^[42]	Japan	1991-2010	Paired biopsy group			0(0)	FIB-4 3.15 F0/1/2/3/4 = 405 (38.72)/ 326 (31.17)/ 229 (21.89)/ 35 (3.44)	IFN 1046 (100)	0 (0)	FIB-4 (pre & post-Rx)	HCC 119 (11.38)
			mean 6.4 years	171	56.1±8.5						
			Validation group								
			mean 5.9 years	875	58.0±10.3						
Bambha, 2012 ^[16]	United States	1994-1995, 2001-2002	median 6.6 years (IQR 3.2-9.8)	450	median (IQR) 43 (40-47)	HBV 9 (2)/ HIV 450 (100)	N/A	unspecified 17 (1.8)	N/A	APRI, FIB-4	OM 191 (42.44)
Masuzaki, 2009 ^[32]	Japan	2004-2005	3.0 years (2,627 person-years)	984	mean 62.2±11.3	HBV 0(0)/ HIV N/A	LSM 11.9±9.7 kPa Cirrhosis 196(22.6)	IFN 173 (20.0)	83 (9.6)	TE	HCC 77 (9.8)
Yu, 2006 ^[11]	China	1992-2002	No treatment			0 (0)	Cirrhosis 68(12.1)	0 (0)	N/A	APRI (post-Rx)	HCC 41, OM 15
			5.15 years (SD 4.21)	562	mean 43.6±14.0						
			IFN-treated								
			4.75 years (SD 2.43)	776	mean 46.8±11.5	0 (0)	Cirrhosis 127(16.4)	IFN 776 (100)	483 (62.2)		

N/A not available

*NITs are not classified as either pre-treatment or post-treatment if the study did not specify when the NIT measurement was done with regards to the initiation of HCV therapy

APRI: aspartate aminotransferase to platelet ratio index; DAA: direct-acting antiviral; FIB-4: fibrosis-4 index; HCC: hepatocellular carcinoma; HD: hepatic decompensation; IFN: interferon-based regimen; LRM: liver-related death; LSM: liver stiffness measurement; LRE: liver-related event; NIT: non-invasive test; OM: overall mortality; pre-Rx: pre-treatment; post-Rx: post-treatment; pre&post-Rx: document both pre-treatment and post-treatment.

Supplementary Table 3B Characteristics of the cohort studies included only in the systematic review

Study	Country	Enrolment year.	Follow-up	Number of patients	Age	Coinfection N (%)	Baseline fibrosis	HCV therapy N (%)	SVR N (%)	NIT*	Outcome N (%)
Peleg, 2019 ^[23]	Israel	2015-2018	mean 24.2 months (95%CI 4-39)	Liver steatosis				DAA 515 (100)	515 (100)	TE (post-Rx)	HCC 27 (5.24), OM 27(5.24), HCC or OM 44(8.54), HD 24(4.66)
				211	mean 57.26 (55.84-58.83)	0 (0)	LSM 13.88 kPa (8.56-15.11) APRI 1.72 (1.36-2.08) FIB-4 3.69 (3.07-4.30) Cirrhosis 23.30 (49)				
				No liver steatosis							
				304	mean 54.07 (52.42-55.52)	0 (0)	LSM 12.93 kPa (7.88-13.97) APRI 1.31 (1.10-1.52) FIB-4 2.92 (2.56-3.29) Cirrhosis 17.80 (54)				
Chalouni, 2019 ^[18]	France	N/A	median 4.2 years (IQR 2.0–5.8)	998	median 46.8 years (IQR 43.3–50.7)	HBV N/A/ HIV 998 (100)	LSM median 6.9 kPa (IQR 5.5–11.1) APRI median 0.6 (IQR 0.4–1.4) FIB-4 median 1.6 (IQR 1.1–2.5)	unspecified 283 (28.4)	N/A	APRI, FIB-4, TE	LRE 39 (3.91)
Munteanu, 2018 ^[22]	France	1997-2012	median 6.0 years (range 0.1- 19.3)	3449	48.0 (IQR 41.0-57.5)	HBV 0 (0)/ HIV 454 (14.8)	F0/1/2/3/4 = 1143 (33.1)/682 (19.8)/349 (10.1)/516 (15.0)/759 (22.0)	N/A	457 (13.3)	Fibrotest	OM 449 (13), LRM 226 (6.6)
Bloom, 2018 ^[17]	Australia	2014-2016	median 15.2 months (IQR 9.6–21.8)	780	43 (IQR 36 – 50)	HBV 15 (1.9)/ HIV N/A	LSM median 6.9 kPa (IQR 5.3–10.4) (kPa)	unspecified 421 (54.0)	N/A	TE	LRE (HCC included) 12 (1.54)
Gomez-Moreno, 2017 ^[19]	Spain	2008-2014	median 5.1 years (IQR 2.9–6.9)	343	49.7 (43.5–57.9)	0 (0)	LSM 6.8 kPa (5.3–10.2) (kPa) F0-1/2/3/4 = 187 (54.5)/58 (16.9)/38 (11.1)/60 (17.5)	IFN 215 (62.7)	71 (21.1)	TE	HCC 6 (1.7), HD 10 (2.9), LRM 6 (1.7)
Merchante, 2017 ^[26]	Spain	2006-2009	median 49 months (IQR 25–68)	446	49 (IQR, 46–53 years)	HBV 9 (2)/ HIV 446 (100)	LSM 22 kPa (17–35), <21 kPa = 197 (44), 21 – 39.9 kPa = 166 (37), >40 kPa = 83 (19)	unspecified 104 (23)	67 (38%)	TE	HD 15 (3.36)

Pérez-Latorre, 2016 ^[24]	Spain	2006-2014	median 5.8 years (IQR 3.4–7.1)	957	44 (41–48)	HBV N/A/ 957 (100)	LSM 8 kPa (6–12) Cirrhosis by TE = 24.6%	N/A	0 (00)	TE	LRE 90 (9.40), OM 73 (7.62)
Study	Country	Enrolment year.	Follow-up	Number of patients	Age	Coinfection N (%)	Baseline fibrosis	HCV therapy N (%)	SVR N (%)	NIT*	Outcome N (%)
Lee, 2016 ^[46]	Korea	2005-2014	median 43.0 months (range 6-120 months)	190	mean 54.1±11.4	0 (0)	LSM 7.1±5.4 kPa Cirrhosis 85(44.7)	IFN 190 (100)	190 (100)	TE (post-Rx)	LRE 10 (5.3) (8 HCC, 1HD, 1LRM)
Berenguer, 2015 ^[12]	Spain	2000-2008	median 62 months (IQR 42.5-80.3)	903	median (IQR) 40 (37-43)	HBV 34(3.8)/ HIV 903(100)	F0/1/2/3/4 = 71 (7.9)/242 (26.8)/236 (26.1)/236 (26.1)/118 (13.1)	IFN 903 (100)	328 (36.32)	FIB-4 (pre-Rx)	LRE (HD or HCC) 71 (7.86), OM 46 (5.09)
Nunes, 2010 ^[27]	United States	N/A	5.15 years (SD 2.87)	303	44	HBV 5 (1.65)/ HIV 207 (68.3)	APRI HIV + median 0.69, HIV – median 0.63 FIB-4 HIV + median 1.75, HIV – median 1.39	N/A	N/A	APRI, FIB-4	LRM 33 (10.9)

N/A not available

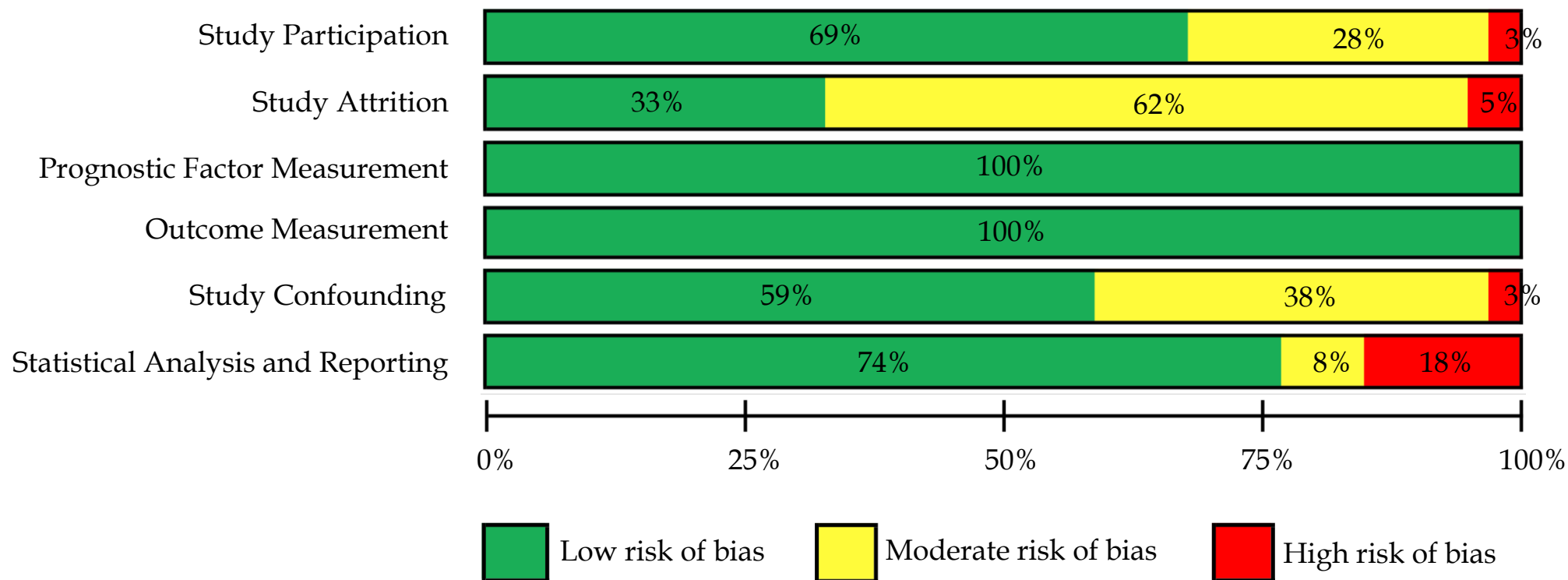
*NITs are not classified as either pre-treatment or post-treatment if the study did not specify when the NIT measurement was done with regards to the initiation of HCV therapy

APRI: aspartate aminotransferase to platelet ratio index; DAA: direct-acting antiviral; FIB-4: fibrosis-4 index; HCC: hepatocellular carcinoma; HD: hepatic decompensation; IFN: interferon-based regimen; LRM: liver-related death; LSM: liver stiffness measurement; LRE: liver-related event; NIT: non-invasive test; OM: overall mortality; pre-Rx: pre-treatment; post-Rx: post-treatment; pre&post-Rx: document both pre-treatment and post-treatment.

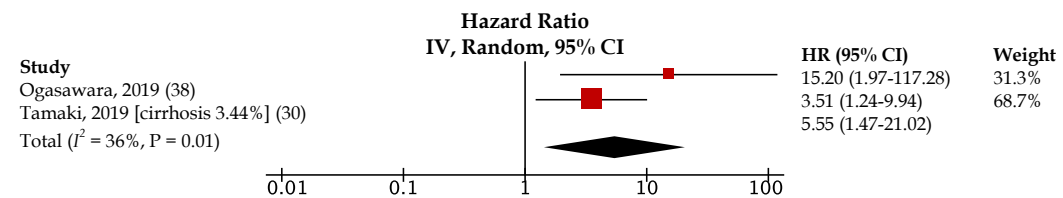
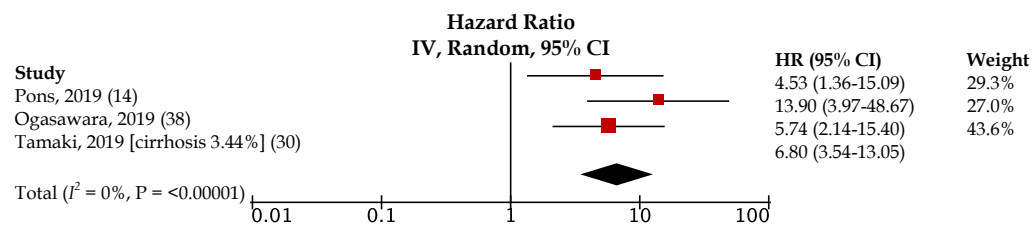
Supplementary Table 4 Quality assessment of the included studies using the Quality In Prognosis Studies tool ^[10]

Study	Participation	Attrition	Prognostic factor measurement	Outcome measurement	Confounding	Analysis and reporting	Overall
Chun, 2020 ^[49]	low	moderate	low	low	moderate	high	high
Ogasawara, 2019 ^[38]	low	moderate	low	low	moderate	low	low
Pons, 2019 ^[14]	low	low	low	low	moderate	low	low
Ogasawara, 2019 ^[47]	moderate	high	low	low	moderate	low	moderate
Ioannou, 2019 ^[13]	low	low	low	low	low	low	low
Peleg, 2019 ^[23]	low	moderate	low	low	moderate	low	low
Na, 2019 ^[33]	low	moderate	low	low	low	low	low
Chalouni, 2019 ^[18]	moderate	moderate	low	low	low	moderate	moderate
Tamaki, 2019 ^[30]	low	moderate	low	low	low	low	low
Rinaldi, 2019 ^[15]	low	moderate	low	low	moderate	high	high
Hansen, 2019 ^[20]	low	low	low	low	low	low	low
Chen, 2019 ^[45]	moderate	low	low	low	high	high	high
Shili-Masmoudi, 2019 ^[28]	moderate	low	low	low	low	low	low
Sou, 2019 ^[41]	low	moderate	low	low	moderate	high	high
Nakagomi, 2019 ^[34]	moderate	moderate	low	low	low	high	high
Watanabe, 2019 ^[44]	high	low	low	low	moderate	low	low
Munteanu, 2018 ^[22]	low	low	low	low	moderate	low	low
Bloom, 2018 ^[17]	moderate	low	low	low	moderate	moderate	moderate
Hamada, 2018 ^[29]	low	moderate	low	low	low	low	low
Gomez-Moreno, 2017 ^[19]	low	moderate	low	low	low	low	low
Thandassery, 2017 ^[43]	low	moderate	low	low	low	low	low
Cepeda, 2017 ^[25]	moderate	moderate	low	low	low	low	low
Sato, 2016 ^[40]	low	moderate	low	low	low	high	high
Merchante, 2017 ^[26]	low	moderate	low	low	low	low	low
Pérez-Latorre, 2016 ^[24]	low	low	low	low	moderate	moderate	moderate
Akuta, 2016 ^[39]	low	moderate	low	low	low	low	low
Ng, 2016 ^[36]	low	low	low	low	low	low	low
Lee, 2016 ^[31]	moderate	moderate	low	low	moderate	low	moderate
Lee, 2016 ^[46]	low	moderate	low	low	low	low	low
Tada, 2016 ^[48]	low	moderate	low	low	low	low	low

Study	Participation	Attrition	Prognostic factor measurement	Outcome measurement	Confounding	Analysis and reporting	Overall
Macías, 2015 ^[21]	low	low	low	low	low	low	low
Nojiri, 2014 ^[37]	moderate	low	low	low	moderate	low	low
Berenguer, 2015 ^[12]	low	moderate	low	low	low	low	low
Tamaki, 2014 ^[42]	low	moderate	low	low	low	low	low
Narita, 2014 ^[35]	low	moderate	low	low	low	low	low
Bambha, 2012 ^[16]	moderate	moderate	low	low	moderate	low	low
Nunes, 2010 ^[27]	moderate	high	low	low	moderate	low	moderate
Masuzaki, 2009 ^[32]	low	low	low	low	low	low	low
Yu, 2006 ^[11]	low	moderate	low	low	low	low	low

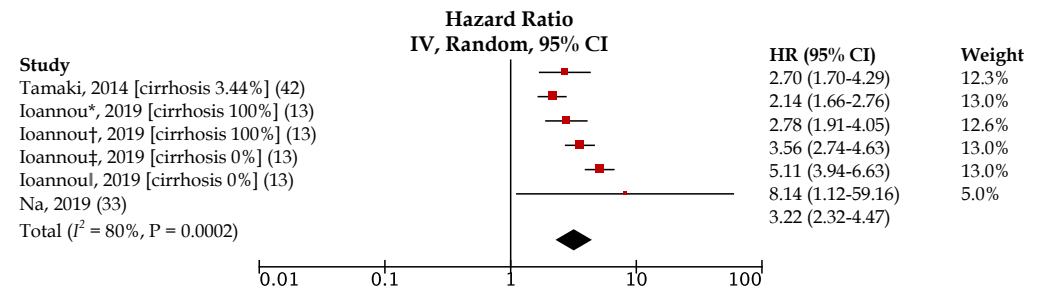
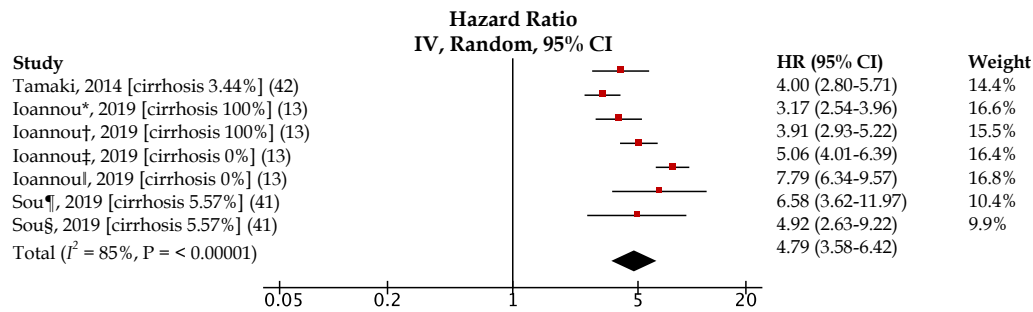


Supplementary figure 1 Quality assessment of the included studies using the Quality In Prognosis Studies tool ^[10]



Supplementary figure 2 Unadjusted and adjusted hazard ratios of LSM and HCC risk in patients achieving SVR after DAA, respectively

DAA: direct-acting antiviral; HCC: hepatocellular carcinoma; LSM: liver stiffness measurement; pegIFN/RBV: pegylated interferon and ribavirin; SVR: sustained virologic response.

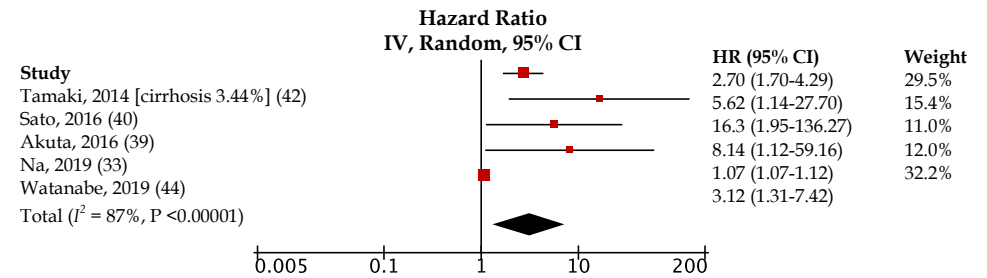
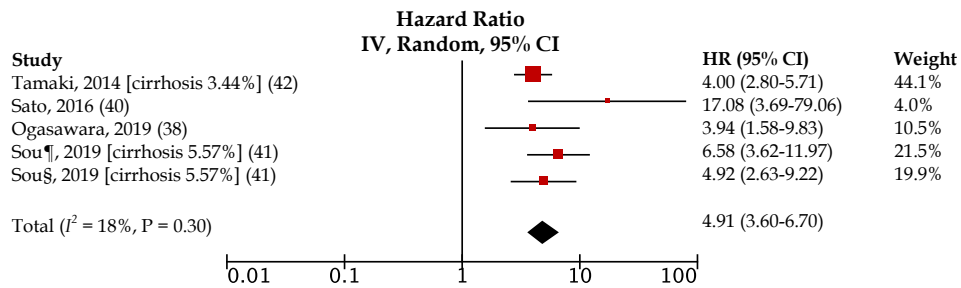


Supplementary figure 3 Unadjusted and adjusted hazard ratios of pretreatment FIB-4 cutoff of 3.25 and HCC risk,

respectively

‡cirrhosis and interferon-treated cohort; *cirrhosis and DAA-treated cohort; †non-cirrhotic and interferon-treated cohort; ‡non-cirrhotic and DAA-treated cohort; §SVR cohort; ¶non-SVR cohort.

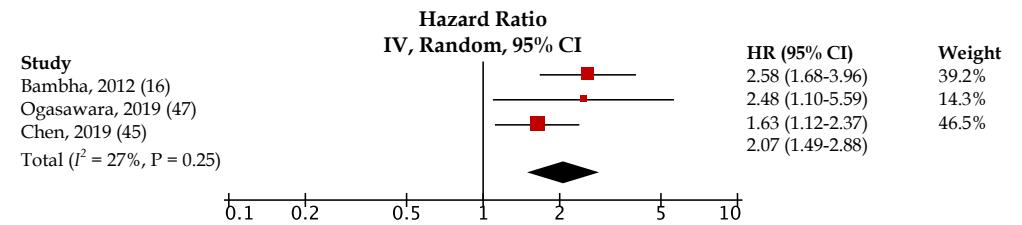
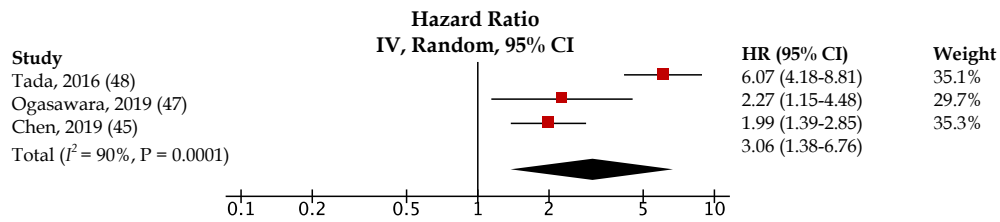
DAA: direct-acting antiviral; FIB-4: fibrosis-4 index; HCC: hepatocellular carcinoma; pegIFN/RBV: pegylated interferon and ribavirin; SVR: sustained virologic response.



Supplementary figure 4 Unadjusted and adjusted hazard ratios of pre-treatment FIB -4 and HCC risk of studies conducted in Eastern countries, respectively

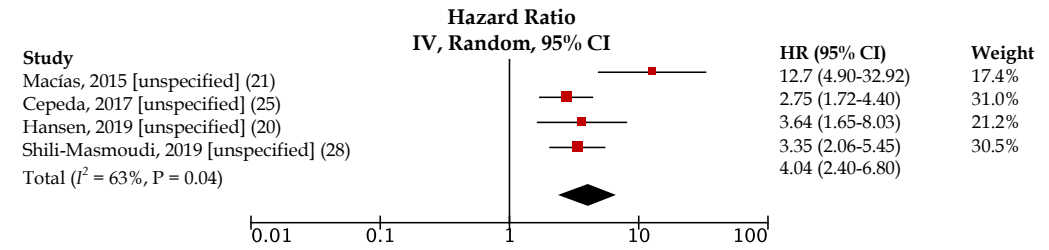
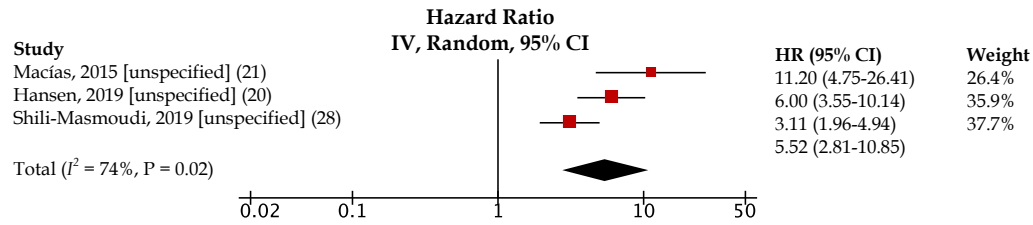
†cirrhosis and interferon-treated cohort; *cirrhosis and DAA-treated cohort; †non-cirrhosis and interferon-treated cohort; ‡non-cirrhosis and DAA-treated cohort; §SVR cohort; ¶non-SVR cohort.

DAA: direct-acting antiviral; FIB-4: fibrosis-4 index; HCC: hepatocellular carcinoma; pegIFN/RBV: pegylated interferon and ribavirin; SVR: sustained virologic response.



Supplementary figure 5 Pooled unadjusted and adjusted hazard ratios of FIB-4 and overall mortality risk, respectively

FIB-4: fibrosis-4 index.



Supplementary figure 6 Pooled unadjusted and adjusted hazard ratios of LSM and overall mortality risk, respectively

LSM: liver stiffness measurement.