Comparative performance of 14 HCC prediction models in CHB: a dynamic validation at serial on-treatment timepoints

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Supplementary appendix to the manuscript

Contents of supplementary appendix

Appendix 1

Overview of predictor variables, scores and/or formulas in 14 identified eligible HCC risk prediction models

Table S1-1. REACH-B model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	0.78798	2
Age	Per 1 year	0.09859	
	30-34		0
	35-39		1
	40-44		2
	45-49		3
	50-54		4
	55-60		5
	60-65		6
ALT(U/L)	<15	0	0
	15-44	0.38823	1
	≥45	0.96311	2
HBeAg	Negative	0	0
	Positive	0.81308	2
HBVDNA	<300(undetectable)	0	0
(copies/ml)	300-9999	0.11648	0
	10000-99999	1.31467	3
	100000-999999	2.27028	5
	$\geq 10^6$	2.09258	4

Average of LP = 6.12796; 3-year baseline disease free probability=0.99853; 5-year baseline disease free probability=0.9965.

Table S1-2. mREACH-B model

Predictors	Category	mREACH-BI score	mREACH-BII score
Sex	Female	0	0
	Male	2	2
Age	Per 5 years		
	30-34	0	0
	35-39	1	1
	40-44	2	2
	45-49	3	3
	50-54	4	4
	55-60	5	5
	60-65	6	6
ALT(U/L)	<15	0	0
	15-44	1	1
	≥45	2	2
HBeAg	Negative	0	0
	Positive	2	2
LSM(Kpa)	<8	0	0
	8-13kpa	1	2
	>13	2	4

Table S1-3. GAG-HCC model

Predictors	Category	Score
Sex	Female	0
	Male	14
Age	Per 1 year	Age
HBVDNA(Copies/ml in log)	Per 1 log	3*log
Cirrhosis	Presence	33
	Absence	0

Formula:

GAG-HCC score=14*sex(male=1, female=0)+age(in years)+3*HBVDNA levels(Copies/ml in log) +33*cirrhosis(presence=1, absence=0).

Table S1-4. CU-HCC model

Predictors	Category	Score
Age	>50	3
	≤50	0
ALB(g/L)	≤35	20
	>35	0
Tbil(μmol/l)	>18	1.5
	≤18	0
Cirrhosis	Yes	15
	No	0
HBVDNA(Log Copies/ml)	≤4	0
	4-6log	1
	>6	4

Table S1-5. LSM-HCC model

Predictors	Category	Score
Age	>50	10
	≤50	0
ALB(g/L)	≤35	1
	>35	0
LSM(Kpa)	≤8	0
	8.1-12.0	8
	>12	14
HBVDNA(IU/ml)	≤200000	0
	>200000	5

Table S1-6A. PAGE-B model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	1.4901	6
Age	Per 1 year	0.0527	
	16-29		0
	30-39		2
	40-49		4
	50-59		6
	60-69		8
	≥70		10
PLT	≥200	0	0
	100-199	1.5744	6
	<100	2.3258	9

5-year disease free probability=0.974.

Table S1-6B. PAGE-B risk score table

Score	5 years risk (%)
0	0.09
2	0.15
4	0.25
6	0.43
8	0.73
9	0.94
10	1.23
12	2.07
13	2.68
14	3.48
15	4.5
16	5.82
17	7.5
18	9.64
19	12.37
20	15.79
21	20.04
22	25.25
23	31.53
25	47.36

Table S1-7A. mPAGE-B model

Predictors	Category	Score
Sex	Female	0
	Male	2
Age	<30	0
	30-39	3
	40-49	5
	50-59	7
	60-69	9
	≥70	11
PLT	≥250	0
	200-250	2
	150-200	3
	100-150	4
	<100	5
ALB(g/dl)	≥4	0
	3.5-4	1
	3-3.5	2
	<3	3

Table S1-7B. mPAGE-B model risk score table

Score	3 years risk (%)	5 years risk (%)	Score	3 years risk (%)	5 years risk (%)
0	0.14	0.23	11	7.76	12.8
1	0.2	0.33	12	11.06	18.01
2	0.29	0.48	13	15.62	25.01
3	0.41	0.7	14	21.83	34.12
4	0.6	1.01	15	30.03	45.39
5	0.87	1.46	16	40.41	58.4
6	1.25	2.12	17	52.78	71.96
7	1.81	3.05	18	66.31	84.17
8	2.62	4.4	19	79.34	93.09
9	3.77	6.31	20	89.84	97.92
10	5.42	9.01	21	96.37	99.64

Table S1-8. NGM1-HCC model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	0.97709	2
Age	Per 1 year	0.50446	
	30-34		0
	35-39		1
	40-44		2
	45-49		3
	50-54		4
	55-59		5
	60-65		6
Family history of HCC	No	0	0
	Yes	0.94774	2
Alcohol intake	No	0	0
	Yes	0.7183	1
ALT(U/L)	<15	0	0
	15-44	0.74291	1
	≥45	1.38998	3
HBeAg	negative	0	0
	positive	1.69241	3

5-year disease free probability=0.99482; 10-year disease free probability=0.98572.

Table S1-9. NGM2-HCC model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	0.90474	2
Age	Per 1 year	0.50839	
	30-34		0
	35-39		1
	40-44		2
	45-49		3
	50-54		4
	55-59		5
	60-65		6
Family history of HCC	No	0	0
	Yes	0.94955	2
Alcohol intake	No	0	0
	Yes	0.77901	2
ALT(U/L)	<15	0	0
	15-44	0.53547	1
	≥45	0.93095	2
HBeAg/HBVDNA(copies/ml)	negative/<300	0	0
	negative/300-9999	0.44098	1
	negative/10000-99999	1.71424	3
	negative/100000-999999	2.18915	4
	negative/$\geq 10^6$	2.65376	5
	positive	3.1201	6

5-year disease free probability=0.9964; 10-year disease free probability= 0.98984.

Table S1-10A. CAMD model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	0.58779	2
Age(years)	<40	0	0
	40-49	1.50408	5
	50-59	2.19722	8
	≥60	2.76632	10
DM	No	0	0
	Yes	0.26236	1
Cirrhosis	No cirrhosis	0	0
	Cirrhosis with age<40y	2.93386	10
	Cirrhosis with age≥40y	1.52606	6

Table S1-10B. CAMD model risk score table

Score	3 years risk (%)
1	0.181
2	0.236
3	0.307
4	0.399
5	0.52
6	0.676
7	0.88
8	1.145
9	1.49
10	1.939
11	2.523
12	3.284
13	4.273
14	5.561
15	7.237
16	9.417
17	12.255
18	15.948
19	20.753

Table S1-11. RWS-HCC model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	1.80566	2
Age(years)	≤55	0	0
	>55	1.02747	1
Cirrhosis	No	0	0
	Yes	2.46606	2.5
AFP(μg/L)	<4.1	0	0
	4.1-20	1.86455	2
	>20	2.67387	2.5

Table S1-12A. AASL-HCC model

Predictors	Category	Score
Sex	Female	0
	Male	3
Age(years)	<30	0
	30-39	2
	40-49	4
	50-59	6
	60-69	8
	≥70	10
Cirrhosis	No	0
	Yes	11
ALB(mg/dl)	≥3.5	0
	2.8-3.4	3
	<2.8	5

Table S1-12B. AASL-HCC model risk score table

Score	5 years risk (%)	Score	5 years risk (%)
0	0.39	15	4.9
1	0.47	16	5.78
2	0.55	17	6.81
3	0.66	18	8.02
4	0.78	19	9.43
5	0.92	20	11.07
6	1.09	21	12.97
7	1.29	22	15.18
8	1.52	23	17.72
9	1.8	24	20.63
10	2.13	25	23.95
11	2.52	26	27.7
12	2.98	27	31.9
13	3.52	28	36.57
14	4.15	29	41.68

Table S1-13A. REAL-B model

Predictors	Category	Coefficient	Score
Sex	Female	0	0
	Male	0.48	1
Age	Per 10 years	0.51	
	18-29		0
	30-39		1
	40-49		2
	50-59		3
	60-69		4
	70-79		5
	≥80		6
Alcohol use	no	0	0
	yes	0.39	1
Cirrhosis	no	0	0
	yes	1.13	2
DM	No	0	0
	Yes	0.52	1
Baseline PLT<150	No	0	0
	Yes	0.35	1
Baseline AFP≥10	No	0	0
	Yes	0.48	1

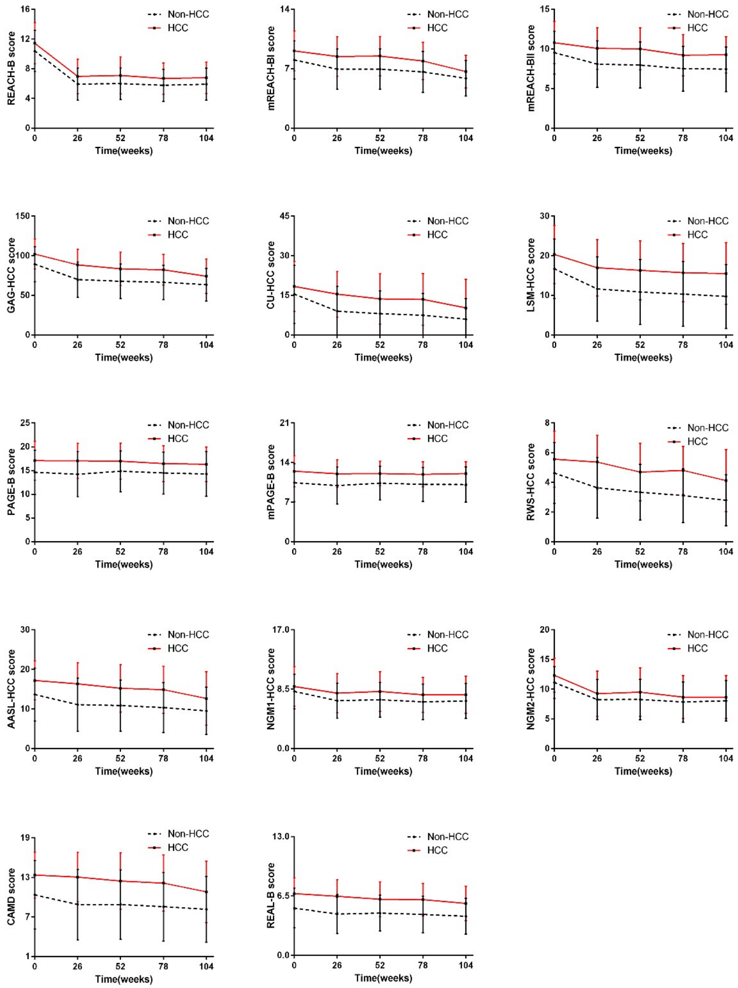
Table S1-13B. REAL-B model risk score table

Score	3 years risk (%)	5 years risk (%)
0	0.14	0.3
1	0.23	0.5
2	0.38	0.83
3	0.63	1.38
4	1.05	2.29
5	1.75	3.8
6	2.91	6.26
7	4.81	10.24
8	7.89	16.5
9	12.83	26
10	20.49	39.51
11	31.8	56.8
12	47.22	75.37
13	65.6	90.37

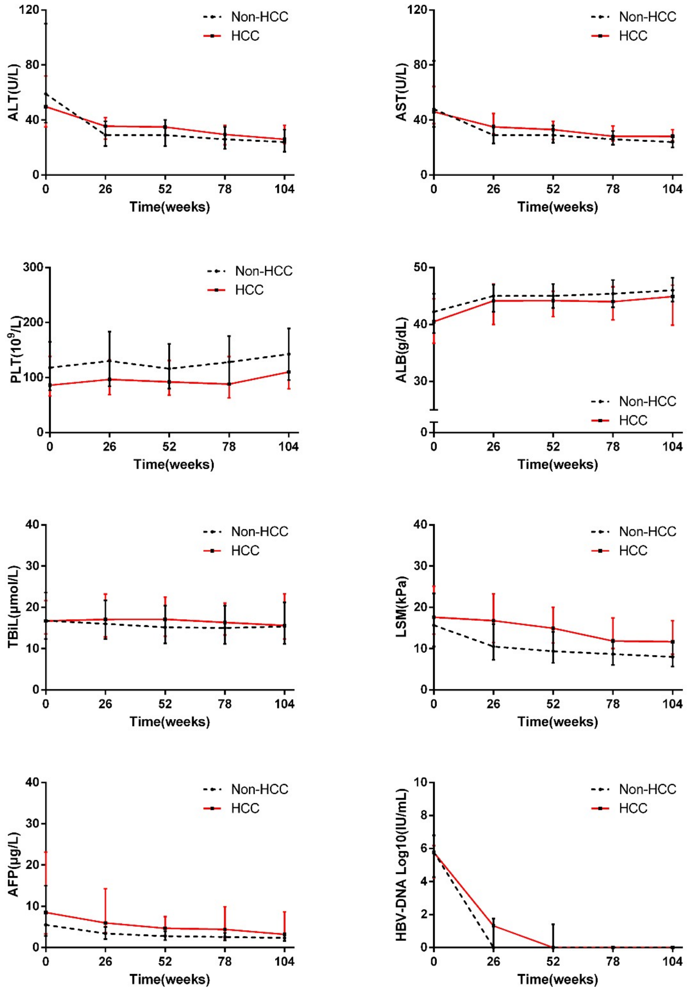
Appendix 2

On-treatment changes of 14 HCC risk prediction model scores and key predictors during 104 weeks

A.

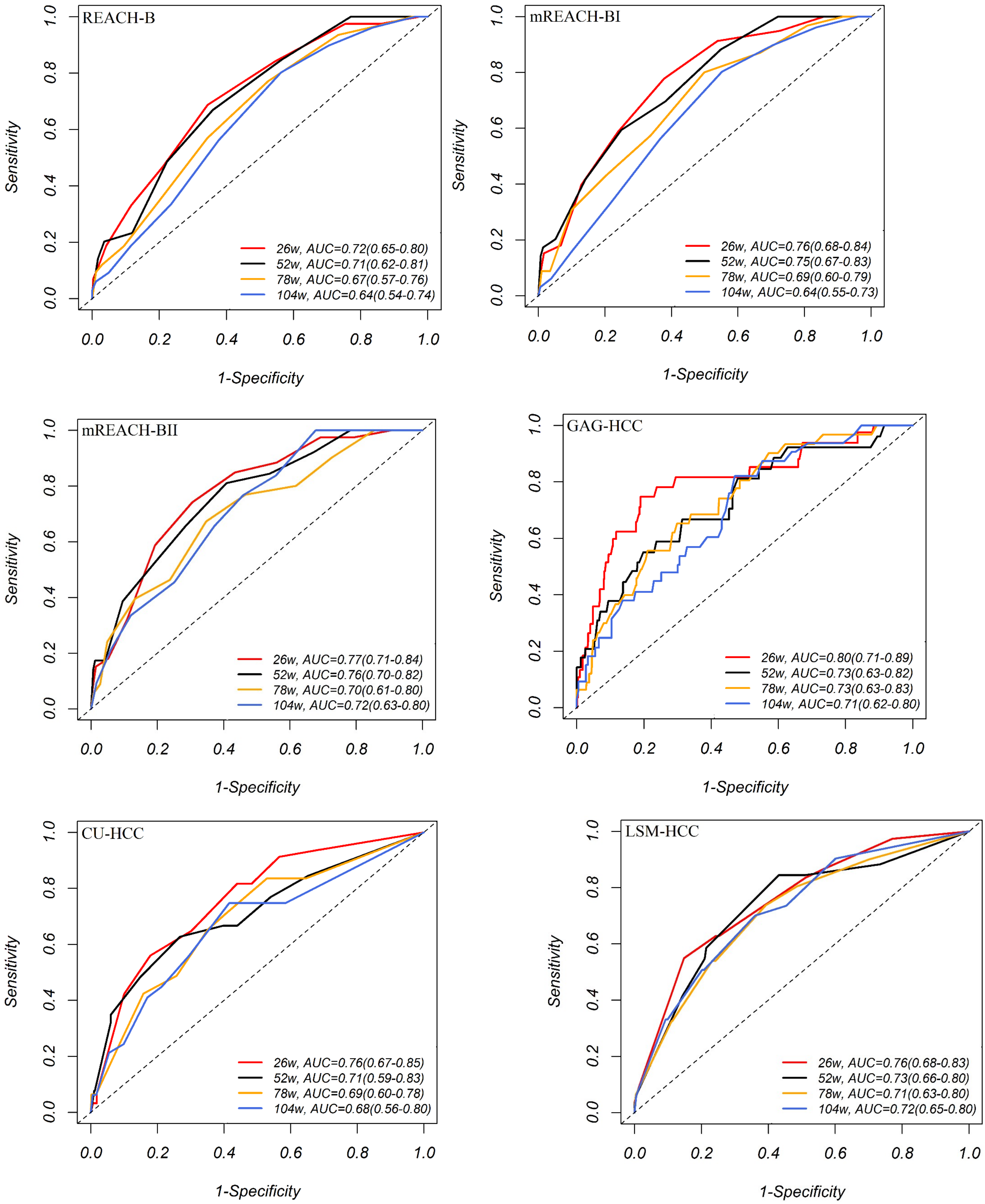

Non-HCC
HCC
REACH-B score
mREACH-BI score
mREACH-BII score
GAG-HCC score
CU-HCC score
LSM-HCC score
PAGE-B score
mPAGE-B score
RWS-HCC score
AASL-HCC score
NGM1-HCC score
NGM2-HCC score
CAMD score
REAL-B score
Time(weeks)

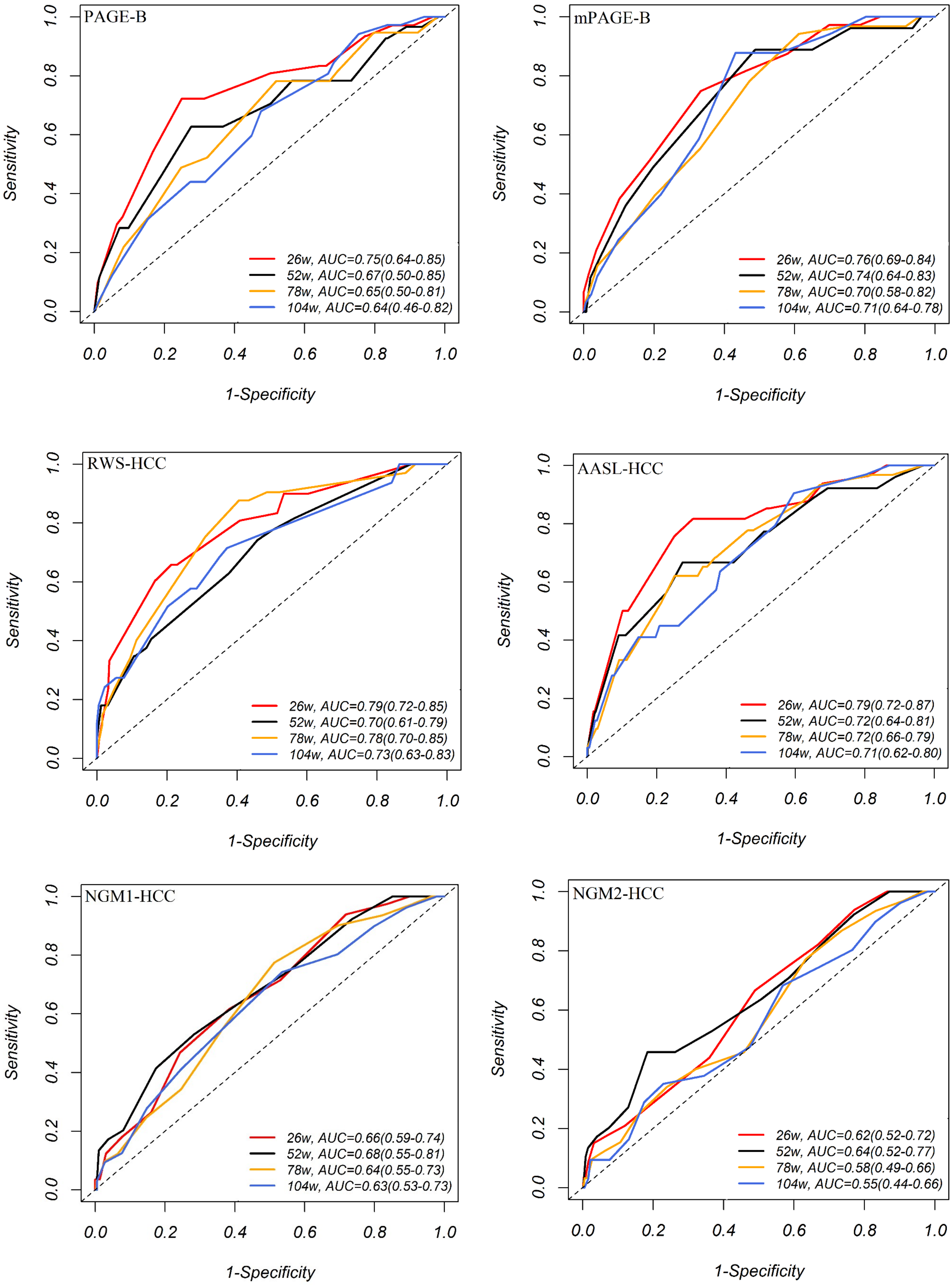
B.

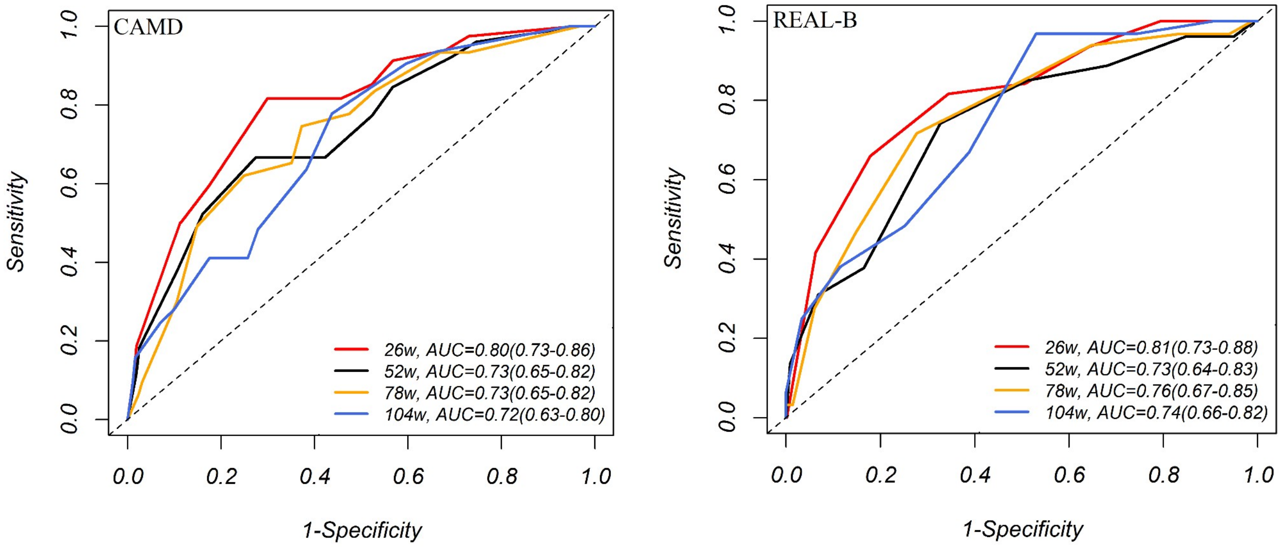

Non-HCC
HCC
ALT(U/L)
AST(U/L)
PLT(10^9/L)
ALB(g/dL)
TBIL(μmol/L)
LSM(kPa)
AFP(μg/L)
HBV-DNA Log10(IU/mL)
Time(weeks)

Appendix 3

3-year ROC curve of 14 HCC risk prediction models in BFH cohort using on-treatment values at different time-points

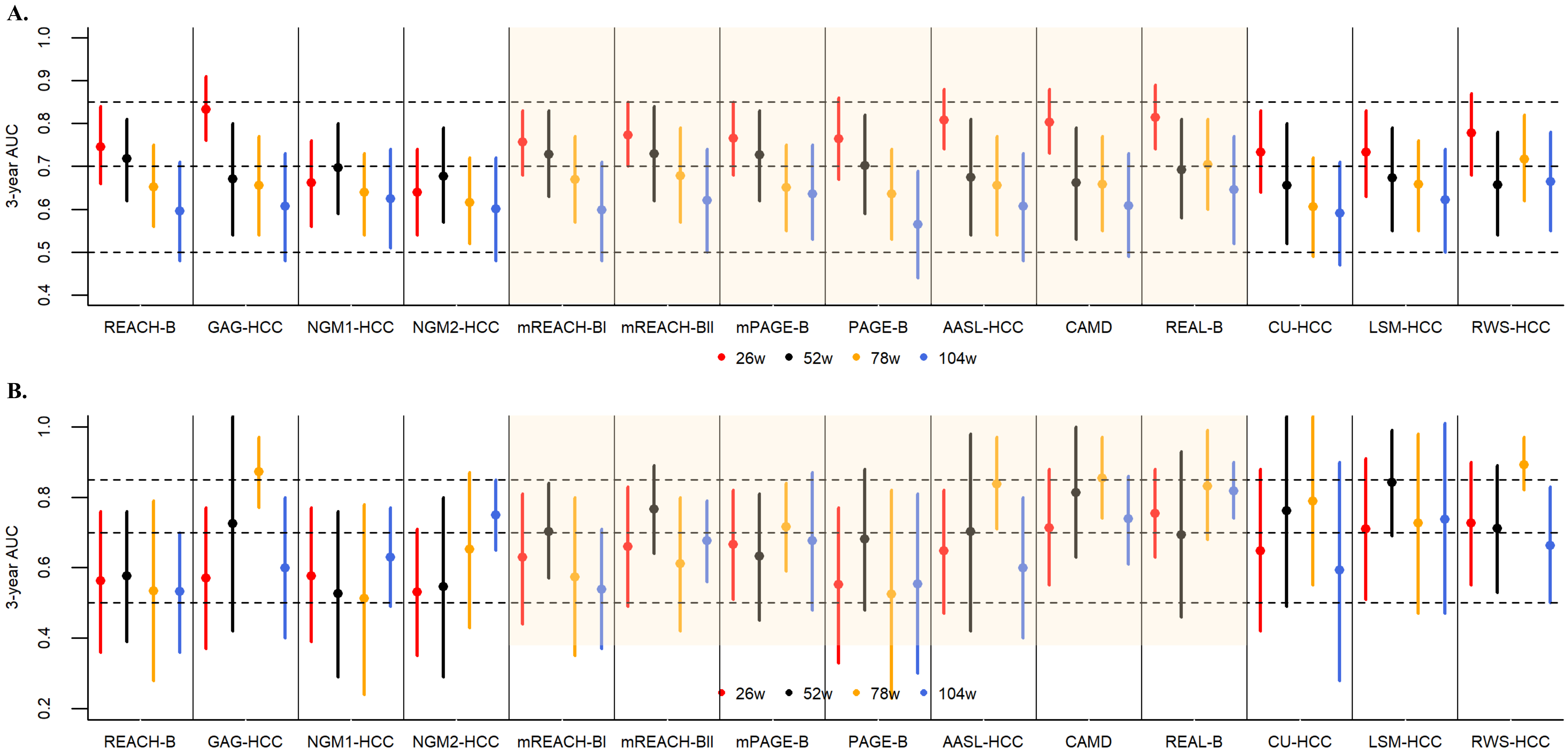

REACH-B
Sensitivity
1-Specificity
26w, AUC=0.72(0.65-0.80)
52w, AUC=0.71(0.62-0.81)
78w, AUC=0.67(0.57-0.76)
104w, AUC=0.64(0.54-0.74)
mREACH-BI
Sensitivity
1-Specificity
26w, AUC=0.76(0.68-0.84)
52w, AUC=0.75(0.67-0.83)
78w, AUC=0.69(0.60-0.79)
104w, AUC=0.64(0.55-0.73)
mREACH-BII
Sensitivity
1-Specificity
26w, AUC=0.77(0.71-0.84)
52w, AUC=0.76(0.70-0.82)
78w, AUC=0.70(0.61-0.80)
104w, AUC=0.72(0.63-0.80)
GAG-HCC
Sensitivity
1-Specificity
26w, AUC=0.80(0.71-0.89)
52w, AUC=0.73(0.63-0.82)
78w, AUC=0.73(0.63-0.83)
104w, AUC=0.71(0.62-0.80)
CU-HCC
Sensitivity
1-Specificity
26w, AUC=0.76(0.67-0.85)
52w, AUC=0.71(0.59-0.83)
78w, AUC=0.69(0.60-0.78)
104w, AUC=0.68(0.56-0.80)
LSM-HCC
Sensitivity
1-Specificity
26w, AUC=0.76(0.68-0.83)
52w, AUC=0.73(0.66-0.80)
78w, AUC=0.71(0.63-0.80)
104w, AUC=0.72(0.65-0.80)


PAGE-B
26w, AUC=0.75(0.64-0.85)
52w, AUC=0.67(0.50-0.85)
78w, AUC=0.65(0.50-0.81)
104w, AUC=0.64(0.46-0.82)
mPAGE-B
26w, AUC=0.76(0.69-0.84)
52w, AUC=0.74(0.64-0.83)
78w, AUC=0.70(0.58-0.82)
104w, AUC=0.71(0.64-0.78)
RWS-HCC
26w, AUC=0.79(0.72-0.85)
52w, AUC=0.70(0.61-0.79)
78w, AUC=0.78(0.70-0.85)
104w, AUC=0.73(0.63-0.83)
AASL-HCC
26w, AUC=0.79(0.72-0.87)
52w, AUC=0.72(0.64-0.81)
78w, AUC=0.72(0.66-0.79)
104w, AUC=0.71(0.62-0.80)
NGM1-HCC
26w, AUC=0.66(0.59-0.74)
52w, AUC=0.68(0.55-0.81)
78w, AUC=0.64(0.55-0.73)
104w, AUC=0.63(0.53-0.73)
NGM2-HCC
26w, AUC=0.62(0.52-0.72)
52w, AUC=0.64(0.52-0.77)
78w, AUC=0.58(0.49-0.66)
104w, AUC=0.55(0.44-0.66)
Sensitivity
1-Specificity
0.0
0.2
0.4
0.6
0.8
1.0

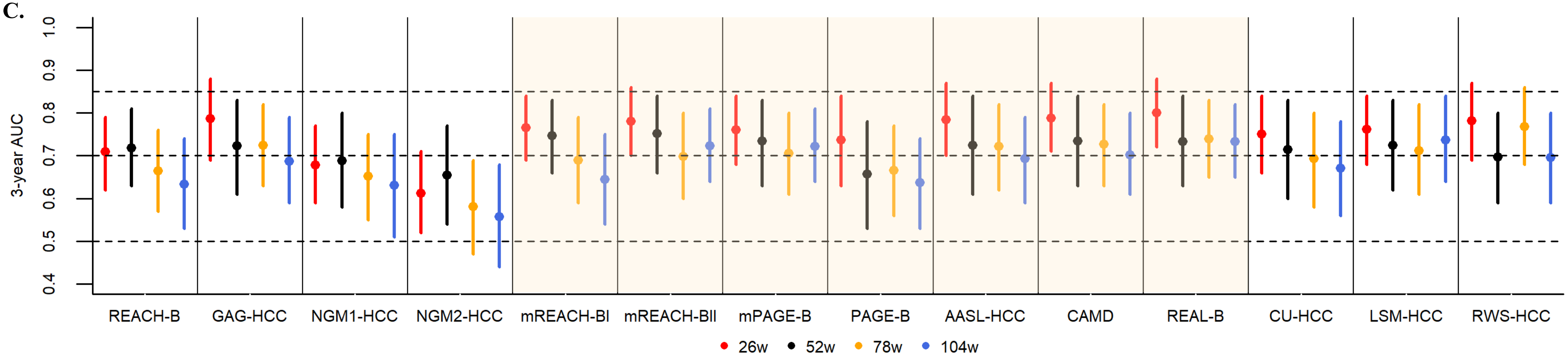

CAMD
Sensitivity
1-Specificity
0.0
0.2
0.4
0.6
0.8
1.0
26w, AUC=0.80(0.73-0.86)
52w, AUC=0.73(0.65-0.82)
78w, AUC=0.73(0.65-0.82)
104w, AUC=0.72(0.63-0.80)
REAL-B
26w, AUC=0.81(0.73-0.88)
52w, AUC=0.73(0.64-0.83)
78w, AUC=0.76(0.67-0.85)
104w, AUC=0.74(0.66-0.82)

Appendix 4

3-year ROC curve of 14 HCC risk prediction models in BFH cohort using on-treatment values at different time-points in patients with cirrhosis, non-cirrhosis or non-diabetes


A.
B.
3-year AUC
REACH-B
GAG-HCC
NGM1-HCC
NGM2-HCC
mREACH-BI
mREACH-BII
mPAGE-B
PAGE-B
AASL-HCC
CAMD
REAL-B
CU-HCC
LSM-HCC
RWS-HCC
26w
52w
78w
104w

C.



A. In patients with cirrhosis; B. In patients with non-cirrhosis; C. In patients with non-diabetes.

Table S4-1. 3-year ROC curve of 14 HCC risk prediction models using on-treatment values at different time-points in patients with cirrhosis, non-cirrhosis or non-diabetes

Model	3-year AUCs (95%CI)			
	Week 26	Week 52	Week 78	Week 104
In patients with cirrhosis				
REACH-B	0.75 (0.66, 0.84)	0.72 (0.62, 0.81)	0.65 (0.56, 0.75)	0.60 (0.48, 0.71)
GAG-HCC	0.83 (0.76, 0.91)	0.67 (0.54, 0.80)	0.66 (0.54, 0.77)	0.61 (0.48, 0.73)
NGM1-HCC	0.66 (0.56, 0.76)	0.70 (0.59, 0.80)	0.64 (0.54, 0.73)	0.62 (0.51, 0.74)
NGM2-HCC	0.64 (0.54, 0.74)	0.68 (0.57, 0.79)	0.62 (0.52, 0.72)	0.60 (0.48, 0.72)
mREACH-BI	0.76 (0.68, 0.83)	0.73 (0.63, 0.83)	0.67 (0.57, 0.77)	0.60 (0.48, 0.71)
mREACH-BII	0.77 (0.70, 0.85)	0.73 (0.62, 0.84)	0.68(0.57, 0.79)	0.62 (0.50, 0.74)
mPAGE-B	0.77 (0.68, 0.85)	0.73 (0.62, 0.83)	0.65 (0.55, 0.75)	0.64 (0.53, 0.75)
PAGE-B	0.76 (0.67, 0.86)	0.70 (0.59, 0.82)	0.64 (0.53, 0.74)	0.56 (0.44, 0.69)
AASL-HCC	0.81 (0.74, 0.88)	0.67 (0.54, 0.81)	0.66 (0.54, 0.77)	0.61 (0.48, 0.73)
CAMD	0.80 (0.73, 0.88)	0.66 (0.53, 0.79)	0.66 (0.55, 0.77)	0.61 (0.49, 0.73)
REAL-B	0.81 (0.74, 0.89)	0.69 (0.58, 0.81)	0.70 (0.60, 0.81)	0.65 (0.52, 0.77)
CU-HCC	0.73 (0.64, 0.83)	0.66 (0.52, 0.80)	0.61 (0.49, 0.72)	0.59 (0.47, 0.71)
LSM-HCC	0.73 (0.63, 0.83)	0.67 (0.55, 0.79)	0.66 (0.55, 0.76)	0.62 (0.50, 0.74)
RWS-HCC	0.78 (0.68, 0.87)	0.66 (0.54, 0.78)	0.72 (0.62, 0.82)	0.66 (0.55, 0.78)
In patients with non-cirrhosis				
REACH-B	0.56 (0.36, 0.76)	0.58 (0.39, 0.76)	0.53 (0.28, 0.79)	0.53 (0.36, 0.70)
GAG-HCC	0.57 (0.37, 0.77)	0.73 (0.42, 1.03)	0.87 (0.77, 0.97)	0.60 (0.40, 0.80)
NGM1-HCC	0.58 (0.39, 0.77)	0.53 (0.29, 0.76)	0.51 (0.24, 0.78)	0.63 (0.49, 0.77)
NGM2-HCC	0.53 (0.35, 0.71)	0.55 (0.29, 0.80)	0.65 (0.43, 0.87)	0.75 (0.65, 0.85)
mREACH-BI	0.63 (0.44, 0.81)	0.70 (0.57, 0.84)	0.57 (0.35, 0.80)	0.54 (0.37, 0.71)
mREACH-BII	0.66 (0.49, 0.83)	0.77 (0.64, 0.89)	0.61 (0.42, 0.80)	0.68 (0.56, 0.79)
mPAGE-B	0.67 (0.51, 0.82)	0.63 (0.45, 0.81)	0.72 (0.59, 0.84)	0.68 (0.48, 0.87)
PAGE-B	0.55 (0.33, 0.77)	0.68 (0.48, 0.88)	0.53 (0.23, 0.82)	0.55 (0.30, 0.81)
AASL-HCC	0.65 (0.47, 0.82)	0.70 (0.42, 0.98)	0.84 (0.71, 0.97)	0.60 (0.40, 0.80)
CAMD	0.71 (0.55, 0.88)	0.81 (0.63, 1.00)	0.85 (0.74, 0.97)	0.74 (0.61, 0.86)
REAL-B	0.75 (0.63, 0.88)	0.69 (0.46, 0.93)	0.83 (0.68, 0.99)	0.82 (0.74, 0.90)
CU-HCC	0.65 (0.42, 0.88)	0.76 (0.49, 1.00)	0.79 (0.55, 1.00)	0.59 (0.28, 0.90)
LSM-HCC	0.71 (0.51, 0.91)	0.84 (0.69, 0.99)	0.73 (0.47, 0.98)	0.74 (0.47, 1.00)
RWS-HCC	0.73 (0.55, 0.90)	0.71 (0.53, 0.89)	0.89 (0.82, 0.97)	0.66 (0.50, 0.83)
In patients with non-diabetes				
REACH-B	0.71 (0.62, 0.79)	0.72 (0.63, 0.81)	0.66 (0.57, 0.76)	0.63 (0.53, 0.74)
GAG-HCC	0.79 (0.69, 0.88)	0.72 (0.61, 0.83)	0.72 (0.63, 0.82)	0.69 (0.59, 0.79)
NGM1-HCC	0.68 (0.59, 0.77)	0.69 (0.58, 0.80)	0.65 (0.55, 0.75)	0.63 (0.51, 0.75)
NGM2-HCC	0.61 (0.52, 0.71)	0.65 (0.54, 0.77)	0.58 (0.47, 0.69)	0.56 (0.44, 0.68)
mREACH-BI	0.76 (0.69, 0.84)	0.75 (0.66, 0.83)	0.69(0.59, 0.79)	0.64 (0.54,0.75)
mREACH-BII	0.78 (0.70, 0.86)	0.75 (0.66, 0.84)	0.70 (0.60, 0.80)	0.72 (0.64, 0.81)
mPAGE-B	0.76 (0.68, 0.84)	0.73 (0.63, 0.83)	0.71 (0.61, 0.80)	0.72 (0.64, 0.81)
PAGE-B	0.74 (0.63, 0.84)	0.66 (0.53, 0.78)	0.67 (0.56, 0.77)	0.64 (0.53, 0.74)

AASL-HCC	0.78 (0.70, 0.87)	0.72 (0.61, 0.84)	0.72 (0.62, 0.82)	0.69 (0.59, 0.79)
CAMD	0.79 (0.71, 0.87)	0.73 (0.63, 0.84)	0.73 (0.63, 0.82)	0.70 (0.61, 0.80)
REAL-B	0.80 (0.72, 0.88)	0.73 (0.63, 0.84)	0.74 (0.65, 0.83)	0.73 (0.65, 0.82)
CU-HCC	0.75 (0.66, 0.84)	0.71 (0.60, 0.83)	0.69 (0.58, 0.80)	0.67 (0.56, 0.78)
LSM-HCC	0.76 (0.68, 0.84)	0.72 (0.62, 0.83)	0.71 (0.61, 0.82)	0.74 (0.64, 0.84)
RWS-HCC	0.78 (0.69, 0.87)	0.70 (0.59, 0.80)	0.77 (0.68, 0.86)	0.70 (0.59, 0.80)

Appendix 5

Head-to-head comparison of 14 HCC risk prediction models' discrimination in BFH cohort using on-treatment values at different time-points

Table S5-1. Head-to-head comparison of HCC risk model's discrimination in BFH cohort using on-treatment values at week 26 (N=937)

Models compared	3-year AUROC		
(model 1 VS model 2)	**Estimated difference (95%CI)**	**P value**	**Adjusted P value**
REACH-B VS mREACH-BI	-0.033(-0.079, 0.012)	0.155	0.339
REACH-B VS mREACH-BII	-0.048(-0.108, 0.011)	0.113	0.310
REACH-B VS GAG-HCC	-0.075(-0.146, -0.003)	0.041	0.168
REACH-B VS CU-HCC	-0.033(-0.117, 0.052)	0.447	0.636
REACH-B VS LSM-HCC	-0.032(-0.107, 0.043)	0.401	0.608
REACH-B VS PAGE-B	-0.022(-0.113, 0.068)	0.630	0.781
REACH-B VS mPAGE-B	-0.039(-0.112, 0.034)	0.297	0.491
REACH-B VS RWS-HCC	-0.062(-0.156, 0.033)	0.202	0.391
REACH-B VS AASL-HCC	-0.068(-0.141, 0.004)	0.065	0.236
REACH-B VS NGM1-HCC	0.062(-0.022, 0.146)	0.150	0.339
REACH-B VS NGM2-HCC	0.107(0.019, 0.195)	0.017	0.097
REACH-B VS CAMD	-0.073(-0.145, -0.002)	0.043	0.172
REACH-B VS REAL-B	-0.081(-0.162, 0.000)	0.051	0.192
mREACH-BI VS mREACH-BII	-0.015(-0.041, 0.010)	0.240	0.420
mREACH-BI VS GAG-HCC	-0.042(-0.108, 0.025)	0.220	0.397
mREACH-BI VS CU-HCC	0.000(-0.069, 0.070)	0.991	0.991
mREACH-BI VS LSM-HCC	0.001(-0.047, 0.049)	0.964	0.986
mREACH-BI VS PAGE-B	0.011(-0.070, 0.092)	0.794	0.881
mREACH-BI VS mPAGE-B	-0.006(-0.067, 0.055)	0.855	0.894
mREACH-BI VS RWS-HCC	-0.028(-0.116, 0.059)	0.526	0.712
mREACH-BI VS AASL-HCC	-0.035(-0.100, 0.030)	0.285	0.489
mREACH-BI VS NGM1-HCC	0.095(0.015, 0.174)	0.019	0.097
mREACH-BI VS NGM2-HCC	**0.140(0.055, 0.225)**	**0.001**	**0.017**
mREACH-BI VS CAMD	-0.040(-0.100, 0.019)	0.185	0.374
mREACH-BI VS REAL-B	-0.048(-0.125, 0.029)	0.223	0.397
mREACH-BII VS GAG-HCC	-0.026(-0.093, 0.041)	0.444	0.636
mREACH-BII VS CU-HCC	0.016(-0.049, 0.081)	0.635	0.781
mREACH-BII VS LSM-HCC	0.016(-0.024, 0.056)	0.421	0.629
mREACH-BII VS PAGE-B	0.026(-0.051, 0.103)	0.505	0.696
mREACH-BII VS mPAGE-B	0.010(-0.047, 0.067)	0.739	0.877
mREACH-BII VS RWS-HCC	-0.013(-0.095, 0.069)	0.754	0.877
mREACH-BII VS AASL-HCC	-0.020(-0.084, 0.045)	0.545	0.719
mREACH-BII VS NGM1-HCC	0.110(0.018, 0.202)	0.019	0.097
mREACH-BII VS NGM2-HCC	**0.155(0.066, 0.245)**	**0.001**	**0.012**
mREACH-BII VS CAMD	-0.025(-0.083, 0.033)	0.400	0.608
mREACH-BII VS REAL-B	-0.032(-0.106, 0.041)	0.386	0.606
GAG-HCC VS CU-HCC	0.042(-0.014, 0.098)	0.140	0.339

GAG-HCC VS LSM-HCC	0.043(-0.024, 0.109)	0.208	0.393
GAG-HCC VS PAGE-B	0.052(-0.005, 0.110)	0.074	0.250
GAG-HCC VS mPAGE-B	0.036(-0.01, 0.081)	0.123	0.329
GAG-HCC VS RWS-HCC	0.013(-0.039, 0.065)	0.624	0.781
GAG-HCC VS AASL-HCC	0.006(-0.017, 0.030)	0.605	0.776
GAG-HCC VS NGM1-HCC	0.136(0.038, 0.235)	0.007	0.057
GAG-HCC VS NGM2-HCC	**0.182(0.088, 0.275)**	**<0.001**	**0.004**
GAG-HCC VS CAMD	0.001(-0.031, 0.034)	0.942	0.974
GAG-HCC VS REAL-B	-0.006(-0.046, 0.034)	0.759	0.877
CU-HCC VS LSM-HCC	0.001(-0.064, 0.065)	0.983	0.991
CU-HCC VS PAGE-B	0.010(-0.074, 0.095)	0.809	0.883
CU-HCC VS mPAGE-B	-0.006(-0.064, 0.052)	0.836	0.892
CU-HCC VS RWS-HCC	-0.029(-0.102, 0.044)	0.439	0.636
CU-HCC VS AASL-HCC	-0.036(-0.085, 0.013)	0.153	0.339
CU-HCC VS NGM1-HCC	0.094(-0.012, 0.200)	0.081	0.256
CU-HCC VS NGM2-HCC	0.140(0.033, 0.247)	0.011	0.069
CU-HCC VS CAMD	-0.041(-0.099, 0.017)	0.168	0.355
CU-HCC VS REAL-B	-0.048(-0.107, 0.010)	0.106	0.301
LSM-HCC VS PAGE-B	0.010(-0.072, 0.091)	0.815	0.883
LSM-HCC VS mPAGE-B	-0.007(-0.074, 0.060)	0.843	0.892
LSM-HCC VS RWS-HCC	-0.030(-0.115, 0.056)	0.497	0.695
LSM-HCC VS AASL-HCC	-0.036(-0.104, 0.031)	0.290	0.489
LSM-HCC VS NGM1-HCC	0.094(-0.012, 0.199)	0.082	0.256
LSM-HCC VS NGM2-HCC	**0.139(0.046, 0.232)**	**0.004**	**0.036**
LSM-HCC VS CAMD	-0.041(-0.099, 0.016)	0.156	0.339
LSM-HCC VS REAL-B	-0.049(-0.123, 0.025)	0.197	0.390
PAGE-B VS mPAGE-B	-0.017(-0.078, 0.045)	0.597	0.776
PAGE-B VS RWS-HCC	-0.039(-0.096, 0.017)	0.174	0.360
PAGE-B VS AASL-HCC	-0.046(-0.106, 0.014)	0.132	0.339
PAGE-B VS NGM1-HCC	0.084(-0.032, 0.200)	0.154	0.339
PAGE-B VS NGM2-HCC	0.129(0.023, 0.236)	0.017	0.097
PAGE-B VS CAMD	-0.051(-0.109, 0.007)	0.084	0.256
PAGE-B VS REAL-B	-0.059(-0.123, 0.005)	0.072	0.250
mPAGE-B VS RWS-HCC	-0.023(-0.073, 0.027)	0.373	0.596
mPAGE-B VS AASL-HCC	-0.03(-0.069, 0.009)	0.137	0.339
mPAGE-B VS NGM1-HCC	0.101(0.006, 0.195)	0.037	0.168
mPAGE-B VS NGM2-HCC	**0.146(0.051, 0.240)**	**0.003**	**0.029**
mPAGE-B VS CAMD	-0.035(-0.076, 0.007)	0.101	0.297
mPAGE-B VS REAL-B	-0.042(-0.08, -0.005)	0.028	0.136
RWS-HCC VS AASL-HCC	-0.007(-0.055, 0.042)	0.782	0.881
RWS-HCC VS NGM1-HCC	0.123(0.006, 0.241)	0.039	0.168
RWS-HCC VS NGM2-HCC	**0.169(0.066, 0.272)**	**0.001**	**0.017**

RWS-HCC VS CAMD	-0.012(-0.073, 0.049)	0.705	0.856
RWS-HCC VS REAL-B	-0.019(-0.058, 0.019)	0.325	0.528
AASL-HCC VS NGM1-HCC	0.130(0.034, 0.226)	0.008	0.059
AASL-HCC VS NGM2-HCC	**0.175(0.083, 0.267)**	**<0.001**	**0.004**
AASL-HCC VS CAMD	-0.005(-0.041, 0.031)	0.788	0.881
AASL-HCC VS REAL-B	-0.013(-0.052, 0.027)	0.532	0.712
NGM1-HCC VS NGM2-HCC	0.045(-0.026, 0.117)	0.214	0.397
NMG1-HCC VS CAMD	**-0.135(-0.229, -0.041)**	**0.005**	**0.044**
NMG1-HCC VS REAL-B	-0.143(-0.249, -0.036)	0.009	0.061
NMG2-HCC VS CAMD	**-0.180(-0.269, -0.092)**	**<0.001**	**0.004**
NMG2-HCC VS REAL-B	**-0.188(-0.287, -0.089)**	**<0.001**	**0.004**
CAMD VS REAL-B	-0.008(-0.056, 0.041)	0.761	0.877

Note: AUROC: area under the ROC curve. Multiple tests were adjusted according to Benjamini and Hochberg method, one of the FDR (false discovery rate) methods. All bold model comparisons were statistically significant even after FDR adjusting, since all adjusted P values of bold model comparisons were less than 0.05.

Table S5-2. Head-to-head comparison of HCC risk model's discrimination in BFH cohort using on-treatment values at week 52 (N=899)

Models compared (model 1 VS model 2)	3-year AUROC Estimated difference (95%CI)	P value	Adjusted P value
REACH-B VS mREACH-BI	-0.035(-0.082, 0.011)	0.138	0.908
REACH-B VS mREACH-BII	-0.046(-0.112, 0.021)	0.177	0.908
REACH-B VS GAG-HCC	-0.011(-0.088, 0.065)	0.771	0.922
REACH-B VS CU-HCC	0.006(-0.113, 0.124)	0.926	0.983
REACH-B VS LSM-HCC	-0.019(-0.116, 0.078)	0.698	0.908
REACH-B VS PAGE-B	0.041(-0.187, 0.269)	0.726	0.912
REACH-B VS mPAGE-B	-0.022(-0.102, 0.058)	0.589	0.908
REACH-B VS RWS-HCC	0.013(-0.058, 0.083)	0.722	0.912
REACH-B VS AASL-HCC	-0.009(-0.092, 0.074)	0.834	0.937
REACH-B VS NGM1-HCC	0.037(-0.018, 0.091)	0.189	0.908
REACH-B VS NGM2-HCC	0.071(-0.035, 0.177)	0.188	0.908
REACH-B VS CAMD	-0.02(-0.113, 0.073)	0.671	0.908
REACH-B VS REAL-B	-0.019(-0.104, 0.065)	0.657	0.908
mREACH-BI VS mREACH-BII	-0.011(-0.036, 0.015)	0.412	0.908
mREACH-BI VS GAG-HCC	0.024(-0.026, 0.074)	0.351	0.908
mREACH-BI VS CU-HCC	0.041(-0.054, 0.136)	0.397	0.908
mREACH-BI VS LSM-HCC	0.016(-0.049, 0.081)	0.625	0.908
mREACH-BI VS PAGE-B	0.076(-0.152, 0.304)	0.514	0.908
mREACH-BI VS mPAGE-B	0.013(-0.048, 0.074)	0.672	0.908
mREACH-BI VS RWS-HCC	0.048(-0.004, 0.100)	0.071	0.908
mREACH-BI VS AASL-HCC	0.026(-0.033, 0.086)	0.382	0.908
mREACH-BI VS NGM1-HCC	0.072(-0.002, 0.146)	0.058	0.908
mREACH-BI VS NGM2-HCC	0.106(0.004, 0.209)	0.042	0.908
mREACH-BI VS CAMD	0.015(-0.050, 0.080)	0.650	0.908
mREACH-BI VS REAL-B	0.016(-0.040, 0.072)	0.571	0.908
mREACH-BII VS GAG-HCC	0.034(-0.017, 0.086)	0.193	0.908
mREACH-BII VS CU-HCC	0.051(-0.036, 0.139)	0.248	0.908
mREACH-BII VS LSM-HCC	0.027(-0.027, 0.080)	0.326	0.908
mREACH-BII VS PAGE-B	0.087(-0.140, 0.313)	0.455	0.908
mREACH-BII VS mPAGE-B	0.024(-0.038, 0.085)	0.450	0.908
mREACH-BII VS RWS-HCC	0.059(0.005, 0.113)	0.034	0.908
mREACH-BII VS AASL-HCC	0.037(-0.022, 0.095)	0.216	0.908
mREACH-BII VS NGM1-HCC	0.082(-0.008, 0.172)	0.073	0.908
mREACH-BII VS NGM2-HCC	0.117(0.006, 0.227)	0.038	0.908
mREACH-BII VS CAMD	0.026(-0.037, 0.088)	0.421	0.908
mREACH-BII VS REAL-B	0.027(-0.024, 0.078)	0.304	0.908
GAG-HCC VS CU-HCC	0.017(-0.062, 0.096)	0.672	0.908

GAG-HCC VS LSM-HCC	-0.008(-0.069, 0.053)	0.804	0.922
GAG-HCC VS PAGE-B	0.052(-0.184, 0.289)	0.666	0.908
GAG-HCC VS mPAGE-B	-0.011(-0.075, 0.054)	0.745	0.912
GAG-HCC VS RWS-HCC	0.024(-0.047, 0.096)	0.507	0.908
GAG-HCC VS AASL-HCC	0.003(-0.034, 0.039)	0.892	0.983
GAG-HCC VS NGM1-HCC	0.048(-0.056, 0.152)	0.365	0.908
GAG-HCC VS NGM2-HCC	0.082(-0.037, 0.201)	0.175	0.908
GAG-HCC VS CAMD	-0.009(-0.047, 0.029)	0.650	0.908
GAG-HCC VS REAL-B	-0.008(-0.053, 0.038)	0.738	0.912
CU-HCC VS LSM-HCC	-0.025(-0.105, 0.056)	0.546	0.908
CU-HCC VS PAGE-B	0.035(-0.219, 0.289)	0.786	0.922
CU-HCC VS mPAGE-B	-0.028(-0.132, 0.077)	0.604	0.908
CU-HCC VS RWS-HCC	0.007(-0.104, 0.119)	0.899	0.983
CU-HCC VS AASL-HCC	-0.015(-0.078, 0.049)	0.652	0.908
CU-HCC VS NGM1-HCC	0.031(-0.110, 0.171)	0.666	0.908
CU-HCC VS NGM2-HCC	0.065(-0.091, 0.221)	0.413	0.908
CU-HCC VS CAMD	-0.026(-0.091, 0.039)	0.436	0.908
CU-HCC VS REAL-B	-0.025(-0.113, 0.064)	0.583	0.908
LSM-HCC VS PAGE-B	0.06(-0.164, 0.284)	0.601	0.908
LSM-HCC VS mPAGE-B	-0.003(-0.087, 0.081)	0.944	0.983
LSM-HCC VS RWS-HCC	0.032(-0.054, 0.118)	0.466	0.908
LSM-HCC VS AASL-HCC	0.01(-0.053, 0.073)	0.751	0.912
LSM-HCC VS NGM1-HCC	0.056(-0.066, 0.177)	0.369	0.908
LSM-HCC VS NGM2-HCC	0.09(-0.046, 0.226)	0.195	0.908
LSM-HCC VS CAMD	-0.001(-0.058, 0.056)	0.970	0.983
LSM-HCC VS REAL-B	0.000(-0.066, 0.066)	0.998	0.998
PAGE-B VS mPAGE-B	-0.063(-0.301, 0.175)	0.605	0.908
PAGE-B VS RWS-HCC	-0.028(-0.257, 0.201)	0.811	0.922
PAGE-B VS AASL-HCC	-0.050(-0.294, 0.195)	0.691	0.908
PAGE-B VS NGM1-HCC	-0.004(-0.236, 0.228)	0.972	0.983
PAGE-B VS NGM2-HCC	0.030(-0.212, 0.272)	0.807	0.922
PAGE-B VS CAMD	-0.061(-0.299, 0.177)	0.616	0.908
PAGE-B VS REAL-B	-0.060(-0.300, 0.18)	0.624	0.908
mPAGE-B VS RWS-HCC	0.035(-0.037, 0.107)	0.344	0.908
mPAGE-B VS AASL-HCC	0.013(-0.053, 0.080)	0.697	0.908
mPAGE-B VS NGM1-HCC	0.059(-0.039, 0.156)	0.237	0.908
mPAGE-B VS NGM2-HCC	0.093(-0.022, 0.208)	0.113	0.908
mPAGE-B VS CAMD	0.002(-0.074, 0.078)	0.961	0.983
mPAGE-B VS REAL-B	0.003(-0.048, 0.054)	0.908	0.983
RWS-HCC VS AASL-HCC	-0.022(-0.101, 0.057)	0.590	0.908
RWS-HCC VS NGM1-HCC	0.024(-0.059, 0.107)	0.576	0.908
RWS-HCC VS NGM2-HCC	0.058(-0.051, 0.167)	0.296	0.908

RWS-HCC VS CAMD	-0.033(-0.120, 0.054)	0.457	0.908
RWS-HCC VS REAL-B	-0.032(-0.100, 0.036)	0.357	0.908
AASL-HCC VS NGM1-HCC	0.045(-0.061, 0.152)	0.403	0.908
AASL-HCC VS NGM2-HCC	0.080(-0.046, 0.205)	0.212	0.908
AASL-HCC VS CAMD	-0.011(-0.045, 0.022)	0.511	0.908
AASL-HCC VS REAL-B	-0.010(-0.060, 0.040)	0.689	0.908
NGM1-HCC VS NGM2-HCC	0.034(-0.043, 0.112)	0.381	0.908
NMG1-HCC VS CAMD	-0.057(-0.173, 0.060)	0.341	0.908
NMG1-HCC VS REAL-B	-0.056(-0.159, 0.048)	0.292	0.908
NMG2-HCC VS CAMD	-0.091(-0.223, 0.041)	0.176	0.908
NMG2-HCC VS REAL-B	-0.090(-0.209, 0.029)	0.137	0.908
CAMD VS REAL-B	0.001(-0.054, 0.057)	0.972	0.983

Note: AUROC: area under the ROC curve. Multiple tests were adjusted according to Benjamini and Hochberg method, one of the FDR(false discovery rate) methods. After FDR adjusting, all results were non-significant at 0.05 level.

Table S5-3. Head-to-head comparison of HCC risk model's discrimination in BFH validation cohort using on-treatment values at week 78 (N=844)

Models compared (model 1 VS model 2)	3-year AUROC Estimated difference (95%CI)	P value	Adjusted P value
REACH-B VS mREACH-BI	-0.027(-0.088, 0.035)	0.395	0.678
REACH-B VS mREACH-BII	-0.038(-0.107, 0.030)	0.274	0.608
REACH-B VS GAG-HCC	-0.065(-0.176, 0.046)	0.249	0.584
REACH-B VS CU-HCC	-0.024(-0.136, 0.088)	0.672	0.805
REACH-B VS LSM-HCC	-0.049(-0.143, 0.045)	0.311	0.630
REACH-B VS PAGE-B	0.011(-0.159, 0.181)	0.900	0.921
REACH-B VS mPAGE-B	-0.033(-0.139, 0.072)	0.535	0.736
REACH-B VS RWS-HCC	-0.113(-0.232, 0.006)	0.063	0.408
REACH-B VS AASL-HCC	-0.059(-0.184, 0.066)	0.357	0.634
REACH-B VS NGM1-HCC	0.022(-0.043, 0.087)	0.508	0.736
REACH-B VS NGM2-HCC	0.089(-0.033, 0.212)	0.152	0.543
REACH-B VS CAMD	-0.068(-0.182, 0.047)	0.245	0.584
REACH-B VS REAL-B	-0.097(-0.211, 0.017)	0.096	0.470
mREACH-BI VS mREACH-BII	-0.012(-0.050, 0.027)	0.555	0.736
mREACH-BI VS GAG-HCC	-0.038(-0.139, 0.062)	0.454	0.713
mREACH-BI VS CU-HCC	0.003(-0.103, 0.108)	0.961	0.961
mREACH-BI VS LSM-HCC	-0.022(-0.100, 0.056)	0.582	0.741
mREACH-BI VS PAGE-B	0.038(-0.112, 0.187)	0.621	0.774
mREACH-BI VS mPAGE-B	-0.007(-0.102, 0.089)	0.892	0.921
mREACH-BI VS RWS-HCC	-0.086(-0.188, 0.016)	0.098	0.470
mREACH-BI VS AASL-HCC	-0.032(-0.147, 0.083)	0.586	0.741
mREACH-BI VS NGM1-HCC	0.049(-0.025, 0.122)	0.193	0.577
mREACH-BI VS NGM2-HCC	0.116(0.008, 0.224)	0.035	0.286
mREACH-BI VS CAMD	-0.041(-0.145, 0.063)	0.436	0.696
mREACH-BI VS REAL-B	-0.070(-0.174, 0.033)	0.183	0.574
mREACH-BII VS GAG-HCC	-0.027(-0.120, 0.066)	0.573	0.741
mREACH-BII VS CU-HCC	0.014(-0.084, 0.112)	0.778	0.852
mREACH-BII VS LSM-HCC	-0.010(-0.080, 0.059)	0.768	0.852
mREACH-BII VS PAGE-B	0.049(-0.098, 0.196)	0.512	0.736
mREACH-BII VS mPAGE-B	0.005(-0.084, 0.094)	0.914	0.924
mREACH-BII VS RWS-HCC	-0.075(-0.168, 0.019)	0.117	0.531
mREACH-BII VS AASL-HCC	-0.021(-0.126, 0.085)	0.703	0.809
mREACH-BII VS NGM1-HCC	0.060(-0.024, 0.144)	0.161	0.543
mREACH-BII VS NGM2-HCC	0.128(0.012, 0.243)	0.030	0.286
mREACH-BII VS CAMD	-0.030(-0.123, 0.063)	0.531	0.736
mREACH-BII VS REAL-B	-0.059(-0.152, 0.035)	0.219	0.584
GAG-HCC VS CU-HCC	0.041(-0.042, 0.124)	0.334	0.634
GAG-HCC VS LSM-HCC	0.016(-0.073, 0.105)	0.718	0.817

GAG-HCC VS PAGE-B	0.076(-0.067, 0.219)	0.297	0.629
GAG-HCC VS mPAGE-B	0.032(-0.043, 0.107)	0.408	0.679
GAG-HCC VS RWS-HCC	-0.048(-0.128, 0.032)	0.241	0.584
GAG-HCC VS AASL-HCC	0.006(-0.032, 0.045)	0.747	0.839
GAG-HCC VS NGM1-HCC	0.087(-0.038, 0.212)	0.173	0.562
GAG-HCC VS NGM2-HCC	0.154(0.022, 0.287)	0.022	0.286
GAG-HCC VS CAMD	-0.003(-0.048, 0.043)	0.901	0.921
GAG-HCC VS REAL-B	-0.032(-0.100, 0.036)	0.355	0.634
CU-HCC VS LSM-HCC	-0.025(-0.104, 0.055)	0.546	0.736
CU-HCC VS PAGE-B	0.035(-0.135, 0.205)	0.687	0.809
CU-HCC VS mPAGE-B	-0.009(-0.098, 0.080)	0.839	0.905
CU-HCC VS RWS-HCC	-0.089(-0.162, -0.016)	0.017	0.286
CU-HCC VS AASL-HCC	-0.035(-0.131, 0.061)	0.480	0.730
CU-HCC VS NGM1-HCC	0.046(-0.087, 0.179)	0.499	0.736
CU-HCC VS NGM2-HCC	0.114(-0.036, 0.263)	0.136	0.543
CU-HCC VS CAMD	-0.044(-0.125, 0.038)	0.292	0.629
CU-HCC VS REAL-B	-0.073(-0.143, -0.002)	0.044	0.306
LSM-HCC VS PAGE-B	0.060(-0.084, 0.203)	0.418	0.679
LSM-HCC VS mPAGE-B	0.015(-0.051, 0.081)	0.650	0.788
LSM-HCC VS RWS-HCC	-0.064(-0.146, 0.018)	0.126	0.543
LSM-HCC VS AASL-HCC	-0.010(-0.112, 0.092)	0.845	0.905
LSM-HCC VS NGM1-HCC	0.071(-0.039, 0.180)	0.206	0.584
LSM-HCC VS NGM2-HCC	0.138(0.011, 0.265)	0.033	0.286
LSM-HCC VS CAMD	-0.019(-0.101, 0.062)	0.642	0.788
LSM-HCC VS REAL-B	-0.048(-0.131, 0.034)	0.250	0.584
PAGE-B VS mPAGE-B	-0.044(-0.167, 0.079)	0.482	0.730
PAGE-B VS RWS-HCC	-0.124(-0.265, 0.018)	0.087	0.468
PAGE-B VS AASL-HCC	-0.07(-0.217, 0.078)	0.354	0.634
PAGE-B VS NGM1-HCC	0.011(-0.154, 0.176)	0.896	0.921
PAGE-B VS NGM2-HCC	0.079(-0.088, 0.245)	0.355	0.634
PAGE-B VS CAMD	-0.079(-0.22, 0.062)	0.272	0.608
PAGE-B VS REAL-B	-0.108(-0.255, 0.039)	0.151	0.543
mPAGE-B VS RWS-HCC	-0.079(-0.154, -0.005)	0.036	0.286
mPAGE-B VS AASL-HCC	-0.025(-0.110, 0.060)	0.558	0.736
mPAGE-B VS NGM1-HCC	0.055(-0.064, 0.174)	0.362	0.634
mPAGE-B VS NGM2-HCC	0.123(-0.009, 0.254)	0.067	0.408
mPAGE-B VS CAMD	-0.035(-0.107, 0.038)	0.351	0.634
mPAGE-B VS REAL-B	-0.064(-0.124, -0.004)	0.038	0.286
RWS-HCC VS AASL-HCC	0.054(-0.028, 0.136)	0.196	0.577
RWS-HCC VS NGM1-HCC	0.135(0.011, 0.258)	0.033	0.286
RWS-HCC VS NGM2-HCC	0.202(0.069, 0.335)	0.003	0.267
RWS-HCC VS CAMD	0.045(-0.028, 0.118)	0.230	0.584

RWS-HCC VS REAL-B	0.016(-0.032, 0.064)	0.517	0.736
AASL-HCC VS NGM1-HCC	0.081(-0.055, 0.216)	0.244	0.584
AASL-HCC VS NGM2-HCC	0.148(0.017, 0.280)	0.027	0.286
AASL-HCC VS CAMD	-0.009(-0.055, 0.037)	0.695	0.809
AASL-HCC VS REAL-B	-0.038(-0.112, 0.036)	0.310	0.630
NGM1-HCC VS NGM2-HCC	0.068(-0.023, 0.158)	0.144	0.543
NMG1-HCC VS CAMD	-0.090(-0.215, 0.035)	0.159	0.543
NMG1-HCC VS REAL-B	-0.119(-0.249, 0.011)	0.073	0.417
NMG2-HCC VS CAMD	-0.157(-0.283, -0.032)	0.014	0.286
NMG2-HCC VS REAL-B	-0.186(-0.327, -0.045)	0.010	0.286
CAMD VS REAL-B	-0.029(-0.098, 0.040)	0.413	0.679

Note: AUROC: area under the ROC curve. Multiple tests were adjusted according to Benjamini and Hochberg method, one of the FDR(false discovery rate) methods. After FDR adjusting, all results were non-significant at 0.05 level.

Table S5-4. Head-to-head comparison of HCC risk model's discrimination in BFH validation cohort using on-treatment values at week 104 (N=751)

Models compared (model 1 VS model 2)	3-year AUROC Estimated difference (95%CI)	P value	Adjusted P value
REACH-B VS mREACH-BI	-0.005(-0.118, 0.108)	0.931	0.962
REACH-B VS mREACH-BII	-0.105(-0.186, -0.024)	0.011	0.235
REACH-B VS GAG-HCC	-0.117(-0.244, 0.011)	0.074	0.260
REACH-B VS CU-HCC	-0.088(-0.244, 0.069)	0.272	0.585
REACH-B VS LSM-HCC	-0.132(-0.252, -0.013)	0.030	0.235
REACH-B VS PAGE-B	-0.049(-0.220, 0.122)	0.574	0.790
REACH-B VS mPAGE-B	-0.118(-0.234, -0.002)	0.047	0.243
REACH-B VS RWS-HCC	-0.137(-0.291, 0.018)	0.083	0.260
REACH-B VS AASL-HCC	-0.117(-0.252, 0.019)	0.091	0.276
REACH-B VS NGM1-HCC	0.014(-0.100, 0.128)	0.811	0.878
REACH-B VS NGM2-HCC	0.079(-0.130, 0.288)	0.461	0.717
REACH-B VS CAMD	-0.124(-0.261, 0.014)	0.077	0.260
REACH-B VS REAL-B	-0.148(-0.261, -0.034)	0.011	0.235
mREACH-BI VS mREACH-BII	-0.100(-0.213, 0.013)	0.082	0.260
mREACH-BI VS GAG-HCC	-0.112(-0.244, 0.021)	0.098	0.287
mREACH-BI VS CU-HCC	-0.083(-0.258, 0.093)	0.358	0.651
mREACH-BI VS LSM-HCC	-0.127(-0.270, 0.015)	0.080	0.260
mREACH-BI VS PAGE-B	-0.044(-0.172, 0.084)	0.501	0.758
mREACH-BI VS mPAGE-B	-0.113(-0.226, 0.000)	0.051	0.243
mREACH-BI VS RWS-HCC	-0.132(-0.276, 0.012)	0.073	0.260
mREACH-BI VS AASL-HCC	-0.112(-0.259, 0.036)	0.139	0.373
mREACH-BI VS NGM1-HCC	0.019(-0.037, 0.075)	0.509	0.758
mREACH-BI VS NGM2-HCC	0.084(-0.045, 0.213)	0.204	0.511
mREACH-BI VS CAMD	-0.119(-0.251, 0.014)	0.081	0.260
mREACH-BI VS REAL-B	-0.143(-0.278, -0.007)	0.039	0.243
mREACH-BII VS GAG-HCC	-0.012(-0.090, 0.066)	0.769	0.871
mREACH-BII VS CU-HCC	0.017(-0.107, 0.142)	0.785	0.871
mREACH-BII VS LSM-HCC	-0.027(-0.101, 0.046)	0.463	0.717
mREACH-BII VS PAGE-B	0.056(-0.090, 0.201)	0.451	0.717
mREACH-BII VS mPAGE-B	-0.013(-0.094, 0.069)	0.758	0.871
mREACH-BII VS RWS-HCC	-0.032(-0.143, 0.079)	0.575	0.790
mREACH-BII VS AASL-HCC	-0.012(-0.103, 0.080)	0.804	0.878
mREACH-BII VS NGM1-HCC	0.119(0.012, 0.226)	0.029	0.235
mREACH-BII VS NGM2-HCC	0.184(-0.010, 0.377)	0.063	0.260
mREACH-BII VS CAMD	-0.019(-0.111, 0.074)	0.693	0.864
mREACH-BII VS REAL-B	-0.043(-0.117, 0.032)	0.260	0.585
GAG-HCC VS CU-HCC	0.029(-0.062, 0.120)	0.532	0.769

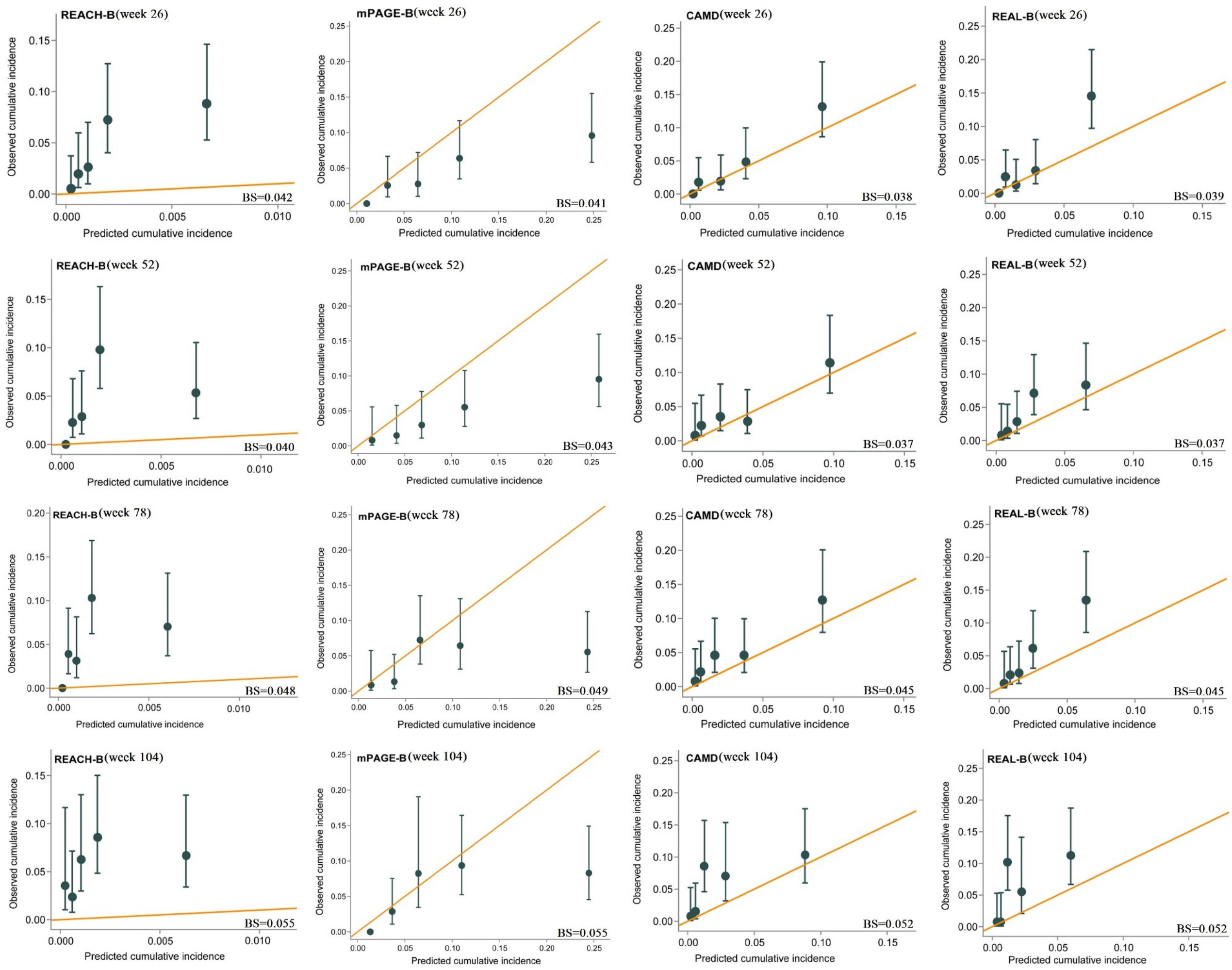
GAG-HCC VS LSM-HCC	-0.016(-0.097, 0.065)	0.704	0.866
GAG-HCC VS PAGE-B	0.068(-0.069, 0.204)	0.331	0.627
GAG-HCC VS mPAGE-B	-0.001(-0.068, 0.066)	0.974	0.986
GAG-HCC VS RWS-HCC	-0.020(-0.092, 0.051)	0.582	0.790
GAG-HCC VS AASL-HCC	0.000(-0.036, 0.036)	0.996	0.996
GAG-HCC VS NGM1-HCC	0.131(0.000, 0.261)	0.050	0.243
GAG-HCC VS NGM2-HCC	0.195(0.005, 0.385)	0.044	0.243
GAG-HCC VS CAMD	-0.007(-0.050, 0.036)	0.753	0.871
GAG-HCC VS REAL-B	-0.031(-0.101, 0.039)	0.382	0.656
CU-HCC VS LSM-HCC	-0.045(-0.131, 0.042)	0.311	0.615
CU-HCC VS PAGE-B	0.039(-0.150, 0.227)	0.690	0.864
CU-HCC VS mPAGE-B	-0.030(-0.128, 0.067)	0.543	0.772
CU-HCC VS RWS-HCC	-0.049(-0.146, 0.048)	0.320	0.620
CU-HCC VS AASL-HCC	-0.029(-0.107, 0.049)	0.465	0.717
CU-HCC VS NGM1-HCC	0.101(-0.066, 0.269)	0.235	0.547
CU-HCC VS NGM2-HCC	0.166(-0.051, 0.383)	0.133	0.368
CU-HCC VS CAMD	-0.036(-0.124, 0.052)	0.421	0.696
CU-HCC VS REAL-B	-0.060(-0.145, 0.025)	0.166	0.433
LSM-HCC VS PAGE-B	0.083(-0.069, 0.235)	0.283	0.585
LSM-HCC VS mPAGE-B	0.015(-0.055, 0.084)	0.681	0.864
LSM-HCC VS RWS-HCC	-0.004(-0.091, 0.083)	0.921	0.962
LSM-HCC VS AASL-HCC	0.016(-0.074, 0.106)	0.730	0.871
LSM-HCC VS NGM1-HCC	0.146(0.014, 0.279)	0.031	0.235
LSM-HCC VS NGM2-HCC	0.211(0.017, 0.405)	0.034	0.235
LSM-HCC VS CAMD	0.009(-0.075, 0.093)	0.837	0.897
LSM-HCC VS REAL-B	-0.015(-0.079, 0.049)	0.637	0.828
PAGE-B VS mPAGE-B	-0.069(-0.194, 0.056)	0.281	0.585
PAGE-B VS RWS-HCC	-0.088(-0.226, 0.050)	0.213	0.511
PAGE-B VS AASL-HCC	-0.067(-0.216, 0.081)	0.374	0.654
PAGE-B VS NGM1-HCC	0.063(-0.068, 0.194)	0.346	0.642
PAGE-B VS NGM2-HCC	0.128(-0.031, 0.286)	0.115	0.327
PAGE-B VS CAMD	-0.074(-0.205, 0.056)	0.265	0.585
PAGE-B VS REAL-B	-0.099(-0.253, 0.056)	0.210	0.511
mPAGE-B VS RWS-HCC	-0.019(-0.098, 0.06)	0.636	0.828
mPAGE-B VS AASL-HCC	0.001(-0.075, 0.077)	0.975	0.986
mPAGE-B VS NGM1-HCC	0.132(0.024, 0.240)	0.017	0.235
mPAGE-B VS NGM2-HCC	0.196(0.023, 0.370)	0.027	0.235
mPAGE-B VS CAMD	-0.006(-0.068, 0.056)	0.855	0.905
mPAGE-B VS REAL-B	-0.030(-0.096, 0.036)	0.373	0.654
RWS-HCC VS AASL-HCC	0.020(-0.060, 0.100)	0.620	0.828
RWS-HCC VS NGM1-HCC	0.151(0.012, 0.289)	0.033	0.235
RWS-HCC VS NGM2-HCC	0.215(0.038, 0.393)	0.018	0.235

RWS-HCC VS CAMD	0.013(-0.059, 0.086)	0.721	0.871
RWS-HCC VS REAL-B	-0.011(-0.088, 0.066)	0.778	0.871
AASL-HCC VS NGM1-HCC	0.130(-0.015, 0.276)	0.079	0.260
AASL-HCC VS NGM2-HCC	0.195(-0.009, 0.400)	0.061	0.260
AASL-HCC VS CAMD	-0.007(-0.056, 0.042)	0.779	0.871
AASL-HCC VS REAL-B	-0.031(-0.106, 0.043)	0.412	0.694
NGM1-HCC VS NGM2-HCC	0.065(-0.060, 0.190)	0.311	0.615
NMG1-HCC VS CAMD	-0.137(-0.27, -0.005)	0.041	0.243
NMG1-HCC VS REAL-B	-0.162(-0.289, -0.034)	0.013	0.235
NMG2-HCC VS CAMD	-0.202(-0.383, -0.022)	0.028	0.235
NMG2-HCC VS REAL-B	-0.226(-0.417, -0.036)	0.020	0.235
CAMD VS REAL-B	-0.024(-0.097, 0.049)	0.516	0.758

Note: AUROC: area under the ROC curve. Multiple tests were adjusted according to Benjaminiand Hochberg method, one of the FDR(false discovery rate) methods. After FDR adjusting, all results were non-significant at 0.05 level.

Appendix 6

3-year calibration of REACH-B, mPAGE-B, CAMD and REAL-B models using on-treatment values at different time-points



REACH-B(week 26)
BS=0.042
mPAGE-B(week 26)
BS=0.041
CAMD(week 26)
BS=0.038
REAL-B(week 26)
BS=0.039
REACH-B(week 52)
BS=0.040
mPAGE-B(week 52)
BS=0.043
CAMD(week 52)
BS=0.037
REAL-B(week 52)
BS=0.037
REACH-B(week 78)
BS=0.048
mPAGE-B(week 78)
BS=0.049
CAMD(week 78)
BS=0.045
REAL-B(week 78)
BS=0.045
REACH-B(week 104)
BS=0.055
mPAGE-B(week 104)
BS=0.055
CAMD(week 104)
BS=0.052
REAL-B(week 104)
BS=0.052
Observed cumulative incidence
Predicted cumulative incidence

Appendix 7

3-year calibration of REACH-B, mPAGE-B, CAMD and REAL-B models using on-treatment values at different time-points in patients with cirrhosis, non-cirrhosis or non-diabetes

Table S7-1. 3-year calibration of REACH-B, mPAGE-B, CAMD and REAL-B models using on-treatment values at different time-points in patients with cirrhosis, non-cirrhosis or non-diabetes.

Model	Brier score			
	Week 26	**Week 52**	**Week 78**	**Week 104**
In patients with cirrhosis				
REACH-B	0.054	0.054	0.065	0.081
mPAGE-B	0.052	0.055	0.065	0.079
CAMD	0.048	0.050	0.061	0.076
REAL-B	0.049	0.050	0.061	0.076
In patients with non-cirrhosis				
REACH-B	0.021	0.016	0.020	0.017
mPAGE-B	0.023	0.023	0.024	0.022
CAMD	0.020	0.015	0.019	0.017
REAL-B	0.020	0.015	0.019	0.016
In patients with non-diabetes				
REACH-B	0.039	0.037	0.042	0.051
mPAGE-B	0.039	0.040	0.044	0.051
CAMD	0.036	0.035	0.040	0.048
REAL-B	0.036	0.035	0.040	0.048

Note: For mREACH-BI, mREACH-BII, GAG-HCC, CU-HCC, LSM-HCC, PAGE-B, RWS-HCC, AASL-HCC, NGM1-HCC and NGM2-HCC models, no disease-free probability at specific time-point could be obtained for these models constructed with Cox regression.

Appendix 8

K-M cumulative incidence of HCC in low/intermediate/high risk groups according to each risk prediction model cut-off values in BFH cohort using on-treatment values at different time-points

Table S8-1. K-M cumulative incidence of HCC in low/intermediate/high risk groups according to each risk prediction model cut-off values using on-treatment values at week 26.

Model	Using on-treatment values at week 26			
	Risk category (N, %)	At 1 year (%)	At 2 years (%)	At 3 years (%)
GAG-HCC	Low risk (N=841, 89.7)	0.85(0.41, 1.78)	1.71(1.00, 2.94)	2.71(1.73, 4.24)
	high risk (N=96, 10.3)	7.47(3.63, 15.04)	10.05(5.34, 18.52)	18.37(11.13, 29.46)
CU-HCC	Low risk (N=488, 52.1)	0.41(0.10, 1.64)	0.89(0.33, 2.36)	1.44(0.65, 3.20)
	Intermediate risk (N=419, 44.7)	2.93(1.68, 5.11)	4.37(2.73, 6.96)	7.19(4.89, 10.52)
	high risk (N=30, 3.2)	0	6.67(0.97, 38.74)	13.85(3.64, 45.03)
LSM-HCC	Low risk (N=422, 45.0)	0.24(0.03, 1.68)	0.50(0.13, 2.00)	1.47(0.61, 3.52)
	high risk (N=515, 55.0)	2.59(1.51, 4.42)	4.27(2.78, 6.56)	6.57(4.56, 9.43)
PAGE-B	Low risk (N=194, 20.7)	0	0.59(0.08, 4.10)	1.29(0.32, 5.10)
	Intermediate risk (N=482, 51.4)	0.63(0.20, 1.93)	1.17(0.48, 2.81)	1.76(0.83, 3.68)
	high risk (N=261, 27.9)	4.33(2.42, 7.69)	6.57(4.07, 10.52)	11.04(7.49, 16.12)
mPAGE-B	Low risk (N=369, 39.4)	0.27(0.04, 1.91)	0.58(0.14, 2.29)	1.32(0.49, 3.50)
	Intermediate risk (N=365, 39.0)	1.40(0.59, 3.33)	2.76(1.44, 5.26)	3.92(2.23, 6.83)
	high risk (N=203, 21.6)	4.06(2.05, 7.96)	5.88(3.29, 10.39)	10.44(6.55, 16.43)
RWS-HCC	Low risk (N=522, 55.7)	0.19(0.03, 1.35)	0.89(0.33, 2.36)	1.41(0.63, 3.14)
	high risk (N=415, 41.3)	3.22(1.88, 5.49)	4.69(2.97, 7.36)	7.92(5.46, 11.41)
AASL-HCC	Low risk (N=283, 30.2)	0.35(0.05, 2.48)	0.35(0.05, 2.48)	0.85(0.21, 3.41)
	Intermediate risk (N=525, 56.0)	0.97(0.41, 2.32)	1.67(0.84, 3.33)	3.27(1.94, 5.48)
	high risk (N=129, 13.8)	6.43(3.26, 12.45)	11.34(6.71, 18.82)	16.52(10.46, 25.55)
CAMD	Low risk (N=382, 40.8)	0.53(0.13, 2.09)	0.53(0.13, 2.09)	0.89(0.28, 2.78)
	Intermediate risk (N=354, 37.8)	0.87(0.28, 2.68)	1.54(0.64, 3.68)	3.51(1.89, 6.46)
	high risk (N=201, 21.4)	4.60(2.42, 8.65)	8.45(5.15, 13.70)	12.40(8.10, 18.75)
REAL-B	Low risk (N=306, 32.7)	0	0.37(0.05, 2.57)	0.81(0.20, 3.23)
	Intermediate risk (N=548, 58.5)	1.30(0.62, 2.71)	2.45(1.39, 4.29)	3.76(2.34, 6.01)
	high risk (N=83, 8.8)	8.85(4.31, 17.69)	11.72(6.26, 21.37)	21.50(13.11, 34.09)

Table S8-2. K-M cumulative incidence of HCC in low/intermediate/high risk groups according to each risk prediction model cut-off values using on-treatment values at week 52.

Model	Using on-treatment values at week 52			
	Risk category (N, %)	**At 1 year (%)**	**At 2 years (%)**	**At 3 years (%)**
GAG-HCC	Low risk (N=830, 92.3)	0.52(0.20, 1.39)	1.46(0.78, 2.70)	3.28(2.15, 5.00)
	high risk (N=69, 7.7)	4.60(1.51, 13.61)	6.59(2.50, 16.76)	13.84(6.71, 27.36)
CU-HCC	Low risk (N=507, 56.4)	0.22(0.03, 1.54)	0.97(0.36, 2.57)	2.29(1.20, 4.37)
	Intermediate risk (N=377, 41.9)	1.70(0.77, 3.74)	3.11(1.68, 5.74)	5.84(3.65, 9.28)
	high risk (N=15, 1.7)	0	0	20.0(5.41, 59.13)
LSM-HCC	Low risk (N=471, 52.4)	0	0	1.14(0.43, 3.01)
	high risk (N=428, 47.6)	1.75(0.84, 3.64)	3.95(2.35, 6.62)	7.39(4.99, 10.87)
PAGE-B	Low risk (N=144, 16.0)	0	0.89(0.13, 6.17)	1.86(0.47, 7.22)
	Intermediate risk (N=494, 55.0)	0.22(0.03, 1.56)	0.76(0.24, 2.34)	2.19(1.10, 4.34)
	high risk (N=261, 29.0)	2.45(1.11, 5.37)	4.40(2.40, 8.13)	8.71(5.55, 13.52)
mPAGE-B	Low risk (N=301, 33.5)	0	0.41(0.06, 2.90)	1.34(0.43, 4.09)
	Intermediate risk (N=392, 43.6)	0.54(0.14, 2.14)	1.84(0.83, 4.08)	3.60(2.00, 6.42)
	high risk (N=206, 22.9)	2.62(1.10, 6.19)	3.95(1.89, 8.17)	8.97(5.38, 14.77)
RWS-HCC	Low risk (N=537, 59.7)	0.21(0.03, 1.45)	0.92(0.34, 2.43)	2.44(1.32, 4.49)
	high risk (N=362, 40.3)	1.78(0.80, 3.92)	3.26(1.76, 6.00)	6.48(4.11, 10.14)
AASL-HCC	Low risk (N=262, 29.1)	0	0	1.06(0.27, 4.16)
	Intermediate risk (N=528, 58.7)	0.61(0.20, 1.87)	1.59(0.76, 3.32)	3.42(2.03, 5.72)
	high risk (N=109, 12.1)	3.97(1.51, 10.25)	7.79(3.76, 15.78)	15.04(8.74, 25.21)
CAMD	Low risk (N=372, 41.4)	0	0.35(0.05, 2.47)	1.48(0.56, 3.89)
	Intermediate risk (N=342, 38.0)	0.62(0.16, 2.45)	1.36(0.51, 3.60)	3.33(1.74, 6.32)
	high risk (N=185, 20.6)	2.93(1.23, 6.90)	5.95(3.12, 11.20)	10.97(6.71, 17.66)
REAL-B	Low risk (N=271, 30.1)	0	0.46(0.06, 3.21)	1.48(0.48, 4.52)
	Intermediate risk (N=551, 61.3)	0.58(0.19, 1.80)	1.75(0.88, 3.49)	3.78(2.33, 6.12)
	high risk (N=77, 8.6)	5.47(2.09, 13.93)	7.32(3.08, 16.86)	14.97(7.99, 27.08)

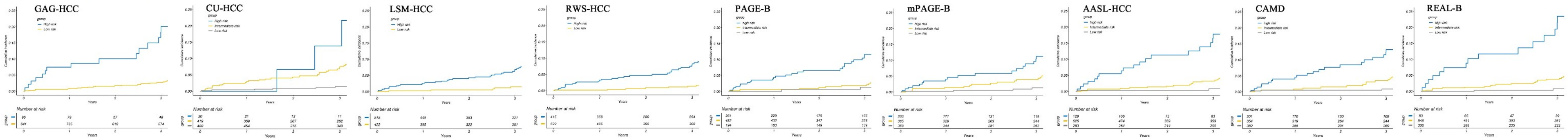
Table S8-3. K-M cumulative incidence of HCC in low/intermediate/high risk groups according to each risk prediction model cut-off values using on-treatment values at week 78.

Model	Using on-treatment values at week 78			
	Risk category (N, %)	**At 1 year (%)**	**At 2 years (%)**	**At 3 years (%)**
GAG-HCC	Low risk (N=783, 92.8)	0.70(0.29, 1.68)	1.85(1.05, 3.25)	3.95(2.66, 5.84)
	high risk (N=61, 7.2)	5.66(1.85, 16.65)	15.29(7.53, 29.68)	17.79(9.23, 32.69)
CU-HCC	Low risk (N=511, 60.6)	0.66(0.21, 2.04)	1.42(0.63, 3.10)	2.71(1.51, 4.85)
	Intermediate risk (N=319, 37.8)	1.72(0.72, 4.09)	4.71(2.69, 8.19)	7.94(5.12, 12.22)
	high risk (N=14, 1.6)	0	8.33(1.22, 46.10)	16.67(4.45, 51.83)
LSM-HCC	Low risk (N=479, 56.8)	0	0.79(0.26, 2.43)	2.18(1.10, 4.32)
	high risk (N=365, 43.2)	2.43(1.22, 4.81)	5.39(3.33, 8.68)	8.56(5.80, 12.55)
PAGE-B	Low risk (N=154, 18.3)	1.45(0.36, 5.69)	1.45(0.36, 5.69)	1.45(0.36, 5.69)
	Intermediate risk (N=463, 54.9)	0.26(0.04, 1.86)	1.39(0.58, 3.30)	4.09(2.44, 6.82)
	high risk (N=227, 26.9)	2.36(0.99, 5.59)	6.47(3.71, 11.16)	8.96(5.56, 14.27)
mPAGE-B	Low risk (N=310, 36.7)	0.34(0.05, 2.39)	0.34(0.05, 2.39)	0.76(0.19, 3.05)
	Intermediate risk (N=349, 41.4)	1.02(0.33, 3.13)	2.92(1.47, 5.76)	6.57(4.13, 10.38)
	high risk (N=185, 21.9)	2.27(0.86, 5.95)	6.49(3.53, 11.79)	8.70(5.12, 14.56)
RWS-HCC	Low risk (N=553, 65.5)	0.62(0.20, 1.91)	1.08(0.45, 2.58)	1.81(0.91, 3.59)
	high risk (N=291, 34.5)	1.85(0.77, 4.40)	5.99(3.58, 9.94)	10.88(7.41, 15.84)
AASL-HCC	Low risk (N=257, 30.5)	0	0	1.03(0.26, 4.05)
	Intermediate risk (N=492, 58.3)	0.90(0.34, 2.39)	2.76(1.53, 4.94)	5.03(2.23, 7.79)
	high risk (N=95, 11.2)	4.67(1.77, 12.03)	10.48(5.34, 19.99)	15.09(8.59, 25.77)
CAMD	Low risk (N=370, 43.8)	0	0.34(0.05, 2.40)	1.79(0.74, 4.24)
	Intermediate risk (N=320, 37.9)	1.05(0.34, 3.24)	3.07(1.54, 6.06)	4.37(2.44, 7.77)
	high risk (N=154, 18.3)	3.54(1.48, 8.34)	8.05(4.39, 14.54)	13.89(8.69, 21.81)
REAL-B	Low risk (N=269, 31.9)	0.43(0.06, 3.01)	0.43(0.06, 3.01)	0.91(0.23, 3.60)
	Intermediate risk (N=510, 60.4)	1.10(0.46, 2.63)	2.65(1.47, 4.75)	5.39(3.54, 8.17)
	high risk (N=65, 7.7)	3.13(0.79, 11.92)	13.62(6.68, 26.66)	18.26(9.85, 32.42)

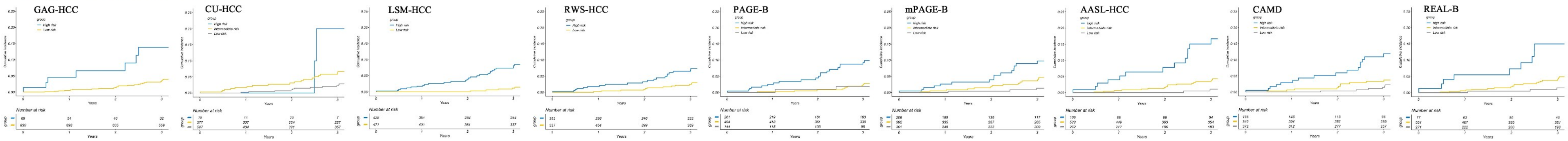
Table S8-4. K-M cumulative incidence of HCC in low/intermediate/high risk groups according to each risk prediction model cut-off values using on-treatment values at week 104.

Model	Using on-treatment values at week 104			
	Risk category (N, %)	**At 1 year (%)**	**At 2 years (%)**	**At 3 years (%)**
GAG-HCC	Low risk (N=706, 94.0)	0.93(0.42, 2.05)	2.58(1.59, 4.18)	5.01(3.37, 7.40)
	high risk (N=45, 6.0)	2.63(0.37, 17.25)	15.01(6.52, 32.47)	15.01(6.52, 32.47)
CU-HCC	Low risk (N=537, 71.5)	0.79(0.30, 2.10)	2.29(1.28, 4.11)	3.80(2.36, 6.08)
	Intermediate risk (N=203, 27.0)	1.71(0.55, 5.21)	4.75(2.40, 9.28)	9.89(5.39, 17.79)
	high risk (N=11, 1.5)	0	25.0(6.91, 68.52)	25.0(6.91, 68.52)
LSM-HCC	Low risk (N=447, 59.5)	0	1.05(0.39, 2.76)	2.47(1.29, 4.70)
	high risk (N=304, 40.5)	2.56(1.23, 5.31)	6.52(4.10, 10.29)	10.27(6.69, 15.60)
PAGE-B	Low risk (N=158, 21.0)	0.65(0.09, 4.49)	1.34(0.34, 5.24)	1.34(0.34, 5.24)
	Intermediate risk (N=384, 51.1)	0.89(0.29, 2.74)	2.77(1.45, 5.25)	6.04(3.55, 10.16)
	high risk (N=209, 27.8)	1.58(0.51, 4.82)	5.62(3.06, 10.20)	8.23(4.94, 13.40)
mPAGE-B	Low risk (N=285, 38.0)	0.36(0.05, 2.51)	1.15(0.37, 3.53)	1.56(0.59, 4.10)
	Intermediate risk (N=291, 38.8)	0.80(0.20, 3.16)	2.85(1.37, 5.88)	7.66(4.43, 13.06)
	high risk (N=175, 23.2)	2.57(0.97, 6.71)	7.61(4.28, 13.34)	9.20(5.43, 15.36)
RWS-HCC	Low risk (N=557, 74.2)	0.76(0.29, 2.02)	2.21(1.23, 3.95)	3.22(1.94, 5.32)
	high risk (N=194, 25.8)	1.82(0.59, 5.56)	6.42(3.50, 11.62)	12.96(7.88, 20.91)
AASL-HCC	Low risk (N=236, 31.4)	0	0.94(0.24, 3.72)	1.43(0.46, 4.37)
	Intermediate risk (N=436, 58.1)	1.26(0.53, 3.00)	2.90(1.62, 5.19)	6.40(4.00, 10.16)
	high risk (N=79, 10.5)	3.11(0.79, 11.91)	13.35(6.90, 24.97)	15.32(8.26, 27.46)
CAMD	Low risk (N=358, 47.7)	0	1.59(0.67, 3.79)	2.26(1.08, 4.68)
	Intermediate risk (N=281, 37.4)	1.95(0.82, 4.64)	3.22(1.62, 6.35)	8.11(4.80, 13.53)
	high risk (N=112, 14.9)	2.10(0.53, 8.17)	8.95(4.57, 17.12)	10.29(5.47, 18.89)
REAL-B	Low risk (N=285, 38.0)	0	0.40(0.06, 2.81)	0.40(0.06, 2.81)
	Intermediate risk (N=414, 55.1)	1.30(0.54, 3.11)	3.62(2.11, 6.15)	7.62(4.95, 11.64)
	high risk (N=52, 6.9)	5.07(1.29, 18.78)	18.42(9.22, 34.82)	21.55(11.37, 38.64)

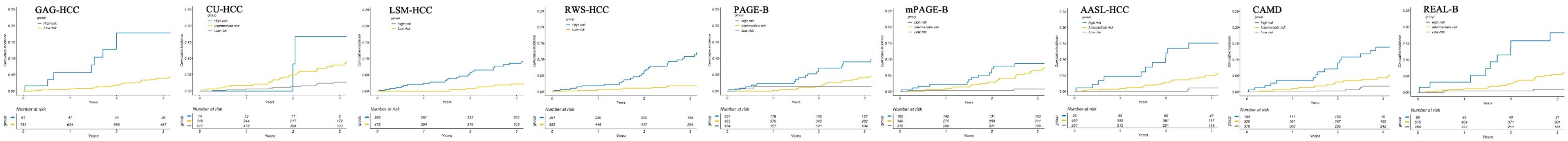
A. using on-treatment values at week 26



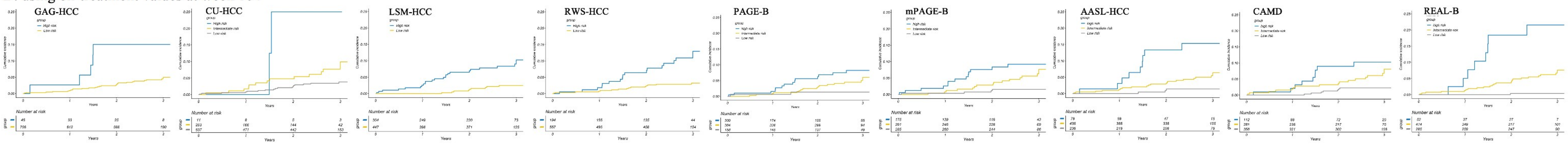
B. using on-treatment values at week 52



C. using on-treatment values at week 78



D. using on-treatment values at week 104



Appendix 9

Differences in failure rates between different HCC risk models in independent BFH cohort using on-treatment values at different time-points

Table S9-1. Differences in failure rates between different prediction models in BFH validation cohort using on-treatment values at week 26

Comparison (model 1 VS model 2)	Difference between failure rates (%, 95%CI)
GAG-HCC VS CU-HCC	**1.25(0.21,2.37)**
GAG-HCC VS LSM-HCC	1.23(-0.11,2.60)
GAG-HCC VS PAGE-B	1.47(-0.44,3.13)
GAG-HCC VS mPAGE-B	**1.36(0.18,2.74)**
GAG-HCC VS RWS-HCC	**1.27(0.32,2.39)**
GAG-HCC VS AASL-HCC	**1.90(0.42,3.32)**
GAG-HCC VS CAMD	**1.83(0.50,3.17)**
GAG-HCC VS REAL-B	**1.91(0.57,3.28)**
CU-HCC VS LSM-HCC	-0.03(-1.24,1.24)
CU-HCC VS PAGE-B	0.22(-1.30,1.59)
CU-HCC VS mPAGE-B	0.11(-0.54,0.93)
CU-HCC VS RWS-HCC	0.04(-0.67,0.67)
CU-HCC VS AASL-HCC	0.59(-0.43,1.80)
CU-HCC VS CAMD	0.53(-0.22,1.52)
CU-HCC VS REAL-B	0.64(-0.28,1.85)
LSM-HCC VS PAGE-B	0.20(-1.17,1.76)
LSM-HCC VS mPAGE-B	0.17(-1.22,1.56)
LSM-HCC VS RWS-HCC	0.09(-1.31,1.43)
LSM-HCC VS AASL-HCC	0.65(-0.76,2.09)
LSM-HCC VS CAMD	0.58(-0.48,1.78)
LSM-HCC VS REAL-B	0.64(-0.23,1.92)
PAGE-B VS mPAGE-B	-0.03(-1.31,1.22)
PAGE-B VS RWS-HCC	-0.21(-1.51,1.47)
PAGE-B VS AASL-HCC	0.38(-0.83,1.92)
PAGE-B VS CAMD	0.34(-1.01,2.04)
PAGE-B VS REAL-B	**0.44(0.00,1.25)**
mPAGE-B VS RWS-HCC	-0.11(-0.96,0.63)
mPAGE-B VS AASL-HCC	0.42(-0.37,1.57)
mPAGE-B VS CAMD	0.39(-0.53,1.49)
mPAGE-B VS REAL-B	0.48(-0.20,1.63)
RWS-HCC VS AASL-HCC	0.56(-0.52,1.70)
RWS-HCC VS CAMD	0.51(-0.50,1.64)
RWS-HCC VS REAL-B	0.59(-0.37,1.70)
AASL-HCC VS CAMD	-0.04(-0.73,0.46)
AASL-HCC VS REAL-B	0.03(-1.04,1.10)
CAMD VS REAL-B	0.11(-0.99,1.16)

Table S9-2. Differences in failure rates between different prediction models in BFH validation cohort using on-treatment values at week 52

Comparison (model 1 VS model 2)	Difference between failure rates (%, 95%CI)
GAG-HCC VS CU-HCC	0.99(-0.08,2.29)
GAG-HCC VS LSM-HCC	**2.12(0.86,3.48)**
GAG-HCC VS PAGE-B	1.56(-1.12,3.73)
GAG-HCC VS mPAGE-B	**1.95(0.45,3.64)**
GAG-HCC VS RWS-HCC	0.87(-0.22,1.99)
GAG-HCC VS AASL-HCC	**2.24(0.56,3.90)**
GAG-HCC VS CAMD	**1.78(0.33,3.48)**
GAG-HCC VS REAL-B	**1.83(0.23,3.59)**
CU-HCC VS LSM-HCC	**1.11(0.20,2.32)**
CU-HCC VS PAGE-B	0.51(-2.00,2.49)
CU-HCC VS mPAGE-B	0.93(-0.31,2.29)
CU-HCC VS RWS-HCC	-0.14(-0.97,0.70)
CU-HCC VS AASL-HCC	1.22(-0.18,2.83)
CU-HCC VS CAMD	0.75(-0.21,2.03)
CU-HCC VS REAL-B	0.79(-0.54,2.20)
LSM-HCC VS PAGE-B	-0.57(-3.32,1.35)
LSM-HCC VS mPAGE-B	-0.17(-1.50,0.99)
LSM-HCC VS RWS-HCC	**-1.24(-2.48, -0.24)**
LSM-HCC VS AASL-HCC	0.05(-0.88,1.15)
LSM-HCC VS CAMD	-0.31(-1.32,0.50)
LSM-HCC VS REAL-B	-0.30(-1.77,0.91)
PAGE-B VS mPAGE-B	0.48(-0.96,2.43)
PAGE-B VS RWS-HCC	-0.65(-2.75,1.84)
PAGE-B VS AASL-HCC	0.61(-1.10,3.24)
PAGE-B VS CAMD	0.22(-1.80,3.13)
PAGE-B VS REAL-B	0.37(-1.14,2.15)
mPAGE-B VS RWS-HCC	-1.05(-2.58,0.22)
mPAGE-B VS AASL-HCC	0.24(-0.31,1.35)
mPAGE-B VS CAMD	-0.16(-1.41,1.25)
mPAGE-B VS REAL-B	**-0.12(-0.41,0.00)**
RWS-HCC VS AASL-HCC	1.34(-0.03,2.97)
RWS-HCC VS CAMD	0.92(-0.42,2.44)
RWS-HCC VS REAL-B	0.91(-0.46,2.49)
AASL-HCC VS CAMD	-0.36(-1.63,0.47)
AASL-HCC VS REAL-B	-0.40(-1.57,0.11)
CAMD VS REAL-B	0.03(-1.50,1.35)

Table S9-3. Differences in failure rates between different prediction models in BFH validation cohort using on-treatment values at week 78

Comparison (model 1 VS model 2)	Difference between failure rates (%, 95%CI)
GAG-HCC VS CU-HCC	**1.23(0.03,2.49)**
GAG-HCC VS LSM-HCC	**1.72(0.51,3.12)**
GAG-HCC VS PAGE-B	**2.52(0.12,4.7)**
GAG-HCC VS mPAGE-B	**3.14(1.52,4.94)**
GAG-HCC VS RWS-HCC	**2.08(0.92,3.49)**
GAG-HCC VS AASL-HCC	**2.83(1.04,4.71)**
GAG-HCC VS CAMD	**2.12(0.60,3.74)**
GAG-HCC VS REAL-B	**2.98(1.3,4.83)**
CU-HCC VS LSM-HCC	0.52(-0.92,1.97)
CU-HCC VS PAGE-B	1.30(-1.35,3.39)
CU-HCC VS mPAGE-B	**1.91(0.29,3.62)**
CU-HCC VS RWS-HCC	**0.85(0.12,1.86)**
CU-HCC VS AASL-HCC	**1.64(0.05,3.43)**
CU-HCC VS CAMD	0.86(-0.23,2.18)
CU-HCC VS REAL-B	**1.73(0.27,3.49)**
LSM-HCC VS PAGE-B	0.83(-2.08,3.08)
LSM-HCC VS mPAGE-B	1.38(-0.07,2.99)
LSM-HCC VS RWS-HCC	0.34(-1.03,1.68)
LSM-HCC VS AASL-HCC	1.12(-0.59,2.96)
LSM-HCC VS CAMD	0.37(-0.92,1.78)
LSM-HCC VS REAL-B	1.24(-0.41,2.85)
PAGE-B VS mPAGE-B	0.59(-0.92,3.02)
PAGE-B VS RWS-HCC	-0.47(-2.23,2.00)
PAGE-B VS AASL-HCC	0.31(-2.04,3.25)
PAGE-B VS CAMD	-0.40(-2.76,2.49)
PAGE-B VS REAL-B	0.46(-1.13,2.69)
mPAGE-B VS RWS-HCC	-1.04(-2.41,0.27)
mPAGE-B VS AASL-HCC	-0.19(-1.65,0.88)
mPAGE-B VS CAMD	-0.99(-2.66,0.34)
mPAGE-B VS REAL-B	-0.10(-1.33,0.92)
RWS-HCC VS AASL-HCC	0.83(-0.90,2.36)
RWS-HCC VS CAMD	0.04(-1.26,1.22)
RWS-HCC VS REAL-B	0.89(-0.30,2.27)
AASL-HCC VS CAMD	-0.70(-2.10,0.32)
AASL-HCC VS REAL-B	0.07(-1.24,1.60)
CAMD VS REAL-B	0.84(-0.69,2.57)

Table S9-4. Differences in failure rates between different prediction models in BFH validation cohort using on-treatment values at week 104

Comparison (model 1 VS model 2)	Difference between failure rates (%, 95%CI)
GAG-HCC VS CU-HCC	1.15(-0.04,2.77)
GAG-HCC VS LSM-HCC	**2.57(0.94,4.40)**
GAG-HCC VS PAGE-B	**3.73(1.33,6.12)**
GAG-HCC VS mPAGE-B	**3.42(1.54,5.72)**
GAG-HCC VS RWS-HCC	**1.74(0.48,3.42)**
GAG-HCC VS AASL-HCC	**3.62(1.55,5.81)**
GAG-HCC VS CAMD	**2.76(0.89,4.74)**
GAG-HCC VS REAL-B	**4.57(2.90,6.73)**
CU-HCC VS LSM-HCC	1.30(-0.22,3.01)
CU-HCC VS PAGE-B	**2.51(0.29,4.75)**
CU-HCC VS mPAGE-B	**2.24(0.60,4.09)**
CU-HCC VS RWS-HCC	**0.55(0.07,1.32)**
CU-HCC VS AASL-HCC	**2.39(0.57,4.35)**
CU-HCC VS CAMD	**1.52(0.15,3.15)**
CU-HCC VS REAL-B	**3.39(1.75,5.33)**
LSM-HCC VS PAGE-B	1.11(-1.12,3.17)
LSM-HCC VS mPAGE-B	0.90(-0.57,2.51)
LSM-HCC VS RWS-HCC	-0.75(-2.52,0.92)
LSM-HCC VS AASL-HCC	1.05(-0.40,2.58)
LSM-HCC VS CAMD	0.21(-0.89,1.49)
LSM-HCC VS REAL-B	**2.07(0.75,3.72)**
PAGE-B VS mPAGE-B	-0.18(-1.68,1.10)
PAGE-B VS RWS-HCC	-1.90(-3.92,0.06)
PAGE-B VS AASL-HCC	-0.11(-1.92,1.90)
PAGE-B VS CAMD	-0.92(-2.89,1.14)
PAGE-B VS REAL-B	0.89(-0.80,3.16)
mPAGE-B VS RWS-HCC	-1.69(-3.42,0.04)
mPAGE-B VS AASL-HCC	0.09(-0.44,1.07)
mPAGE-B VS CAMD	-0.67(-2.19,0.68)
mPAGE-B VS REAL-B	**1.13(0.00,2.63)**
RWS-HCC VS AASL-HCC	1.80(-0.12,3.77)
RWS-HCC VS CAMD	0.97(-0.47,2.53)
RWS-HCC VS REAL-B	**2.82(1.35,4.52)**
AASL-HCC VS CAMD	-0.78(-2.29,0.36)
AASL-HCC VS REAL-B	**0.98(0.00,2.46)**
CAMD VS REAL-B	**1.80(0.56,3.58)**