

Comparative performance of risk prediction models for hepatitis B-related hepatocellular carcinoma in the United States

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Table S1. Summary of Hepatitis B virus-Hepatocellular Carcinoma prediction models

Risk score	Race	Number	Cirrhosis (%)	Prior treatment	Medication	Risk parameter	Risk score cut-off
REACH-B Yang 2011	Asian (Taiwan)	3,584	0%	All naïve	Not on Tx	Age Male ALT HBeAg HBV DNA	Low risk: <10 Intermediate risk: 10-12 High risk: >12
PAGE-B Papatheodoridis 2016	Caucasian	1,350	20%	33%	ETV/TDF	Age Male Platelet	Low risk: <10 Intermediate risk: 10-17 High risk: >17
mPAGE-B Kim 2018	Asian (Korea)	2,001	19.1%	39.5%	ETV or TDF	Age Male Platelet Albumin	Low risk: ≤ 8 Intermediate risk: 9-12 High risk: ≥ 13:
CU-HCC	Asian (China)	1,005	38.1%	NA	Only 15.1% were on Tx	Age Albumin Bilirubin HBV DNA Cirrhosis	Low risk: <5 Intermediate risk: 5-19 High risk: ≥ 19
HCC-RESCUE Sohn 2017	Asian (Korea)	990	39%	All naïve	ETV	Age Male Cirrhosis	Low risk: ≤ 64 Intermediate risk: 65-84 High risk: ≥ 85
CAMD Hsu 2019	Asian (Taiwan)	23,851	26.4%	NA	ETV or TDF	Age Male Diabetes cirrhosis	Low risk: <8 Intermediate risk: 8-13 High risk: >13
APA-B Chen	Asian (Taiwan)	883	35.9%	All naïve	ETV	Age Platelet	Low risk: ≤ 5 Intermediate risk: 6-9

2017						(12 months after ETV) AFP (12 months after ETV)	High risk: ≥ 10
REAL-B Yang 2019	Asian- Pacific	8,048	20.2%	20%	Any anti-viral	Age Male Alcohol use Cirrhosis Diabetes Platelet AFP	Low risk: <4 Intermediate risk: 4-7 High risk: 8-13
AASL-HCC Yu 2019	Asian (Korea)	1,242	39.3%	All naïve	ETV or TDF	Age Male Albumin Cirrhosis	Low risk: ≤ 5 Intermediate risk: 6-19 High risk: ≥ 20
RWS-HCC Poh 2016	Asian (Singapore)	538	14.9%	NA	Any anti-viral	Age Male Cirrhosis AFP	Low risk: <4.5 High risk: ≥ 4.5
Abbreviation: ETV: Entecavir, TDF: Tenofovir disoproxil, AFP: alpha-fetoprotein							

Table S2. ICD codes for key variables.

Variable	ICD9	ICD10
Hepatocellular carcinoma	155.0	C22.0
Cirrhosis	456.1, 456.21, 456.0, 571.2, 571.5, 571.6, 789.5, 789.60, 789.59, 567.23, 572.2, 572.5, 573.5	E83.110, G93.40, I85.00, I86.40, I85.10, I85.01, I86.41, I85.11, K65.2, K70.30, K70.31, K70.11, K71.91, K71.51, K71.7, K72.11, K74.60, K74.69, K74.3, K74.4, K74.5, K76.7, K76.81, R18.8
Alcohol abuse	291.0, 291.1, 291.2, 291.3, 291.4, 291.5, 291.8X, 291.9, 303.00, 303.01, 303.02, 303.03, 303.90, 303.91, 303.92, 303.93, 305.0X, 357.5, 425.5, 535.3, 571.X, 790.3, V11.3	F10.10, F10.11, F10.120, F10.121, F10.129, F10.14, F10.150, F10.151, F10.159, F10.18X, F10.19, F10.20, F10.21, F10.220, F10.221, F10.229, F10.230, F10.231, F10.232, F10.239, F10.24, F10.250, F10.251, F10.259, F10.26, F10.27, F10.280, F10.281, F10.282, F10.288, F10.29, F10.920, F10.921, F10.929, F10.94, F10.950, F10.951, F10.959, F10.96, F10.97, F10.980, F10.981, F10.982, F10.988, F10.99, G62.1, I42.6, K29.20, K29.21, K70.0, K70.10, K70.11, K70.2, K70.30, K70.31, K70.40, K70.9

Table S3. Discrimination and calibration of ten HBV-HCC models for prediction of HCC risk using imputed dataset

	Total Number	Number of HCC in 3 years	Number of HCC in 5 years	AUC		Hosmer-Lemeshow χ^2	
				3 year (95% CI)	5 year (95% CI)	3 year (p-value)	5 year (p-value)
REACH-B	3101	53	83	0.57 (0.49, 0.65)	0.58 (0.51, 0.64)	8.02 (0.33)	10.35 (0.17)
PAGE-B	3101	53	83	0.73 (0.67, 0.79)	0.73 (0.67, 0.79)	5.25 (0.51)	5.01 (0.54)
mPAGE-B	3101	53	83	0.74 (0.68, 0.80)	0.74 (0.68, 0.80)	12.68 (0.12)	11.65 (0.17)
CU-HCC	3101	53	83	0.80 (0.76, 0.84)	0.80 (0.78, 0.82)	13.29 (0.07)	20.19 (<0.01)
HCC-RESCUE	3101	53	83	0.79 (0.69, 0.89)	0.77 (0.67, 0.87)	7.54 (0.48)	11.19 (0.19)
CAMD	3101	53	83	0.79 (0.73, 0.85)	0.77 (0.73, 0.81)	4.74 (0.69)	3.79 (0.80)
APA-B*	3101	53	83	0.86 (0.76, 0.96)	0.84 (0.80, 0.88)	9.09 (0.11)	12.31 (0.03)
REAL-B*	3101	53	83	0.83 (0.77, 0.89)	0.81 (0.77, 0.85)	2.20 (0.90)	9.60 (0.14)
AASL-HCC	3101	53	83	0.86 (0.82, 0.90)	0.86 (0.84, 0.88)	13.63 (0.09)	29.61 (<0.01)
RWS-HCC*	3101	53	83	0.91 (0.87, 0.95)	0.89 (0.87, 0.91)	6.76 (0.34)	12.25 (0.06)

REACH-B= Risk estimation for hepatocellular carcinoma in chronic hepatitis B; mPAGE-B= modified PAGE-B; CU-HCC=Chinese University HCC; HCC-RESCUE=HCC-Risk Estimating Score in CHB patients Under Entecavir; CAMD= cirrhosis, age, male sex, and diabetes mellitus; APA-B=age, platelet, AFP; REAL-B= Real-World Effectiveness From the Asia Pacific Rim Liver Consortium for HBV Risk Score; AASL-HCC= age, albumin, sex, liver cirrhosis-HCC; RWS-HCC= Real-world risk score for hepatocellular carcinoma
*: highlights the models incorporating AFP variable