**Supplementary Material**

# Comparison of models to predict incident chronic liver disease: a systematic review and external validation in Chinese adults

**BMC Medicine**

Xue Cong, BM[1], Shuyao Song, BM[1], Yingtao Li, MS[1], Kaiyang Song, BA[2], Cameron MacLeod, BA[2], Yujie Cheng, BM[1], Jun Lv, PhD[1,3,4], Canqing Yu, PhD[1,3,4], Dianjianyi Sun, PhD[1,3,4], Pei Pei, MSc[1,3], Ling Yang, PhD[5,6], Yiping Chen, DPhil[5,6], Iona Millwood, DPhil[5,6], Shukuan Wu, BS[7], Xiaoming Yang, PhD[5], Rebecca Stevens, MSc[5], Junshi Chen, MD[8], Zhengming Chen, DPhil[5], Liming Li, MD[1,3,4], Christiana Kartsonaki, DPhil[5,6*]#, Yuanjie Pang, DPhil[1,4*]# on behalf of the China Kadoorie Biobank Collaborative Group**

*Corresponding author (yuanjie.p@gmail.com, christiana.kartsonaki@dph.ox.ac.uk)

#Equal contributors

**The members of steering committee and collaborative group are listed in Supplementary material.

1. Department of Epidemiology & Biostatistics, School of Public Health, Peking University, Beijing 100191, China
2. Medical Sciences Division, University of Oxford, Oxford OX3 9DU, United Kingdom
3. Peking University Center for Public Health and Epidemic Preparedness & Response, Beijing 100191, China
4. Key Laboratory of Epidemiology of Major Diseases (Peking University), Ministry of Education
5. Clinical Trial Service Unit & Epidemiological Studies Unit (CTSU), Nuffield Department of Population Health, University of Oxford
6. Medical Research Council Population Health Research Unit at the University of Oxford, Oxford OX3 7LF, United Kingdom
7. Meilan Center for Disease Control and Prevention, Haikou 570100, China
8. China National Center for Food Safety Risk Assessment, Beijing 100022, China

**Address for correspondence:**

Dr. Yuanjie Pang
Department of Epidemiology & Biostatistics
School of Public Health
Peking University
38 Xueyuan Road
Beijing, 100191, China
Tel: 86-010-82801528
Fax: 86-010-82801530
yuanjie.p@gmail.com

Dr. Christiana Kartsonaki
Nuffield Department of Population Health
University of Oxford
Old Road Campus
Oxford, OX3 7LF, UK
Tel: 86-010-82801528
Fax: 86-010-82801530
christiana.kartsonaki@dph.ox.ac.uk

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## Members of the China Kadoorie Biobank collaborative group

**International Steering Committee:** Junshi Chen, Zhengming Chen (PI), Robert Clarke, Rory Collins, Yu Guo, Liming Li (PI), Jun Lv, Richard Peto, Robin Walters. **International Co-ordinating Centre, Oxford:** Daniel Avery, Derrick Bennett, Ruth Boxall, Sue Burgess, Ka Hung Chan, Yumei Chang, Yiping Chen, Zhengming Chen, Johnathan Clarke, Robert Clarke, Huaidong Du, Ahmed Edris Mohamed, Zammy Fairhurst-Hunter, Hannah Fry, Simon Gilbert, Alex Hacker, Mike Hill, Michael Holmes, Pek Kei Im, Andri Iona, Maria Kakkoura, Christiana Kartsonaki, Rene Kerosi, Kuang Lin, Mohsen Mazidi, Iona Millwood, Sam Morris, Qunhua Nie, Alfred Pozarickij, Paul Ryder, Saredo Said, Sam Sansome, Dan Schmidt, Paul Sherliker, Rajani Sohoni, Becky Stevens, Iain Turnbull, Robin Walters, Lin Wang, Neil Wright, Ling Yang, Xiaoming Yang, Pang Yao.

**National Co-ordinating Centre, Beijing:** Yu Guo, Xiao Han, Can Hou, Jun Lv, Pei Pei, Chao Liu, Canqing Yu, Qingmei Xia. **10 Regional Co-ordinating Centres: Qingdao CDC:** Zengchang Pang, Ruqin Gao, Shanpeng Li, Haiping Duan, Shaojie Wang, Yongmei Liu, Ranran Du, Yajing Zang, Liang Cheng, Xiaocao Tian, Hua Zhang, Yaoming Zhai, Feng Ning, Xiaohui Sun, Feifei Li. **Licang CDC:** Silu Lv, Junzheng Wang, Wei Hou. **Heilongjiang Provincial CDC:** Wei Sun, Shichun Yan, Xiaoming Cui. **Nangang CDC:** Chi Wang, Zhenyuan Wu,Yanjie Li, Quan Kang. **Hainan Provincial CDC:** Huiming Luo, Tingting Ou. **Meilan CDC:** Xiangyang Zheng, Zhendong Guo, Shukuan Wu, Yilei Li, Huimei Li. **Jiangsu Provincial CDC:** Ming Wu, Yonglin Zhou, Jinyi Zhou, Ran Tao, Jie Yang, Jian Su. **Suzhou CDC:** Fang Liu, Jun Zhang, Yihe Hu, Yan Lu, Liangcai Ma, Aiyu Tang, Shuo Zhang, Jianrong Jin, Jingchao Liu. **Guangxi Provincial CDC:** Mei Lin, Zhenzhen Lu. **Liuzhou CDC:** Lifang Zhou, Changping Xie, Jian Lan, Tingping Zhu, Yun Liu, Liuping Wei, Liyuan Zhou, Ningyu Chen, Yulu Qin, Sisi Wang. **Sichuan Provincial CDC:** Xianping Wu, Ningmei Zhang, Xiaofang Chen, Xiaoyu Chang. **Pengzhou CDC:** Mingqiang Yuan, Xia Wu, Xiaofang Chen, Wei Jiang, Jiaqiu Liu, Qiang Sun. **Gansu Provincial CDC:** Faqing Chen, Xiaolan Ren, Caixia Dong. **Maiji CDC:** Hui Zhang, Enke Mao, Xiaoping Wang, Tao Wang, Xi zhang. **Henan Provincial CDC:** Kai Kang, Shixian Feng, Huizi Tian, Lei Fan. **Huixian CDC:** XiaoLin Li, Huarong Sun, Pan He, Xukui Zhang. **Zhejiang Provincial CDC:** Min Yu, Ruying Hu, Hao Wang. **Tongxiang CDC**: Xiaoyi Zhang, Yuan Cao, Kaixu Xie, Lingli Chen, Dun Shen. **Hunan Provincial CDC:** Xiaojun Li, Donghui Jin, Li Yin, Huilin Liu, Zhongxi Fu. **Liuyang CDC:** Xin Xu, Hao Zhang, Jianwei Chen, Yuan Peng, Libo Zhang, Chan Qu.

## Method S1 Search strategy

| No. | Entry terms |
|---|---|
| **Pubmed** | |
| 1 | "hepatocellular carcinoma"[Title/Abstract] OR "liver cancer"[Title/Abstract] OR "cirrhosis"[Title/Abstract] OR "chronic liver disease*"[Title/Abstract] OR "severe liver disease*"[Title/Abstract] (n=220,289) |
| 2 | "risk assessment"[MeSH Terms] OR "risk prediction"[Title/Abstract] OR "risk score"[Title/Abstract] OR "risk calculation"[Title/Abstract] OR "prediction model"[Title/Abstract] OR "predict index"[Title/Abstract] OR "decision rule"[Title/Abstract] OR "discrimination"[Title/Abstract] OR "roc curve"[Title/Abstract] OR "calibration"[Title/Abstract] OR "AUC"[Title/Abstract] OR "area under the curve"[Title/Abstract] OR "scoring system"[Title/Abstract] OR "outcome prediction"[Title/Abstract] OR "risk classification"[Title/Abstract] OR "forecasting"[Title/Abstract] OR "forecast"[Title/Abstract] OR "decision tree"[Title/Abstract] OR "predictive score"[Title/Abstract] OR "validat*"[Title/Abstract] (n=1,355,701) |
| 3 | 1 AND 2 Filters: Humans (n=13,548) |
| 4 | ("prospective study"[Title/Abstract] OR "retrospective study"[Title/Abstract] OR "cohort study"[Title/Abstract] OR "case control study"[Title/Abstract] OR "prospective"[Title/Abstract] OR "retrospective"[Title/Abstract] OR "cohort"[Title/Abstract] OR "case control"[Title/Abstract] OR "case cohort"[Title/Abstract]) AND (humans [Filter]) Filters: Humans (n=1,570,078) |
| 5 | ("review"[Title] OR "letter"[Publication Type] OR "interview"[Publication Type] OR "comment"[Publication Type] OR "news"[Publication Type] OR "guideline"[Publication Type] OR "editorial"[Publication Type] OR "Bibliography"[Publication Type]) (n=2,995,276) |
| 6 | 3 AND 4 NOT 5 (n=4,021) |
| 7 | 3 Filters: meta-analysis Filters: systematic review (n=429) |
| 8 | 6 OR 7 (n=4,379) |
| **Embase** | |
| 1 | hepatocellular carcinoma.ab. or hepatocellular carcinoma.ti. or liver cancer.ab. or liver cancer.ti. or cirrhosis.ab. or cirrhosis.ti. or chronic liver disease*.ab. or chronic liver disease*.ti. or severe liver disease*.ab. or severe liver disease*.ti. (n=313,023) |
| 2 | exp risk assessment/ (n=690,077) |
| 3 | risk prediction.ab. or risk prediction.ti. or risk score.ab. or risk score.ti. or risk calculation.ab. or risk calculation.ti. or prediction model.ab. or prediction model.ti. or predict index.ab. or predict index.ti. or decision rule.ab. or decision rule.ti. or discrimination.ab. or discrimination.ti. or roc curve.ab. or roc curve.ti. or calibration.ab. or calibration.ti. or AUC.ab. or AUC.ti. or area under the curve.ab. or area under the curve.ti. or scoring system.ab. or scoring system.ti. or outcome prediction.ab. or outcome prediction.ti. or risk classification.ab. or risk classification.ti. or forecasting.ab. or forecasting.ti. or forecast.ab. or forecast.ti. or decision tree.ab. or decision tree.ti. or predictive score.ab. or predictive score.ti. or |

| | |
|---|---|
| | validat*.ab. or validat*.ti. (n=1,502,514) |
| 4 | 2 or 3 (n=2,121,759) |
| 5 | 1 and 4 (n=31,685) |
| 6 | limit 5 to human (n=29,515) |
| 7 | prospective study.ab. or prospective study.ti. or retrospective study.ab. or retrospective study.ti. or cohort study.ab. or cohort study.ti. or case control study.ab. or case control study.ti. or prospective.ab. or prospective.ti. or retrospective.ab. or retrospective.ti. or cohort.ab. or cohort.ti. or case control.ab. or case control.ti. or case cohort.ab. or case cohort.ti. (n=2,953,555) |
| 8 | limit 7 to human (n=2,768,117) |
| 9 | review.ti. or letter.pt. or interview.pt. or comment.pt. or news.pt. or guideline.pt. or editorial.pt. or Bibliography.pt. (n=2,689,154) |
| 10 | 6 and 8 (n=10,777) |
| 11 | 10 not 9 (n=10,579) |
| 12 | limit 6 to meta analysis (n=652) |
| 13 | limit 6 to "systematic review" (n=808) |
| 14 | 12 or 13 (n=1,001) |
| 15 | 11 or 14 (n=11,427) |

**Method S2 China Kadoorie Biobank (CKB) information**

The external validation population was derived from the China Kadoorie Biobank (CKB), a large prospective Chinese population-based cohort study. The CKB study conducted the baseline survey from June 2004 to July 2008 in five urban and five rural areas of China, recruiting 512,891 adults aged 30 to 79 years[1]. The survey included questionnaire assessments, physical measurements, and collection of blood samples. The questionnaire included sociodemographic characteristics, lifestyle factors, personal and family medical history, and current medication use, etc. Physical measurements included height, weight, hip and waist circumference, blood pressure, and heart rate, etc. See the table below for predictors detail. All survey staff underwent standardized training and implemented computerized data management throughout the project to ensure consistency in survey protocols across regions.

In the CKB validation population, the following individuals were included:

1. General population: The total number of participants was 512,726. Individuals with baseline diagnoses of hepatitis or cirrhosis (n=6,193), cancer (n=2,578), or positive HBsAg results (n=27,285) at the baseline were excluded. The total study cohort included 478,930 individuals. For prediction models incorporating blood-based biomarkers, the sub-population analysis included 15,945 participants with GGT data, and 17,227 participants with ALT and AST data, applying the same exclusion criteria.
2. **HBV Infected individuals:** The total number of participants with positive HBsAg test was 15,552. Individuals with baseline diagnoses of hepatitis or cirrhosis (n=1,748) and cancer (n=98) at baseline were excluded, leaving 13,723 participants for the analysis. For prediction models involving blood-based biomarkers, the sub-population analysis included 394 participants with GGT and ALT data, applying the same exclusion criteria.

3. **Diabetes patient:** The total number of participants with diabetes was 30,301. Exclusion criteria for diabetes patients encompassed baseline diagnoses of hepatitis or cirrhosis (n=398), cancer (n=294), or positive HBsAg results (n=1,190) at the study baseline. The total number of diabetes patients included in the study was 28,540 individuals. In prediction models utilizing blood-based biomarkers, the sub-population analysis incorporated 1,540 participants with ALT biochemistry data and 1,348 participants with GGT biochemistry data, adhering to the established exclusion criteria.

The vital status of each participant was determined periodically through the China CDC's Disease Surveillance Points (DSP) system and the national health insurance system, supplemented by regular checks against local residential and health insurance records, and by annual active confirmation through street committees or village administrators. In addition, information about the occurrence of major diseases and any episodes of hospitalization was collected through linkages, using each participant's unique national identification number, with disease registries and national health insurance claims databases, which have almost universal coverage in the study areas. All events were coded using the International Classification of Diseases, 10th revision (ICD-10), by trained staff who were blinded to baseline information and reviewed centrally for consistency[2]. The ICD-10 of chronic liver disease (CLD) events in CKB is reported in **Method S4**. The present study included incident liver disease from enrollment until December 31, 2018, by which time a total of 56,552 (11.03%) participants had died and 4,028 (0.78%) were lost to follow-up.

**Method S3 The measurement and definition of CKB predictor variables**

| Predictor | Measurements | Units and definitions |
|---|---|---|
| Sex | Questionnaire | Female/male |
| Age | Questionnaire | Unit: year |
| Body mass index (BMI) | Formula: BMI=weight(kg)/height(m)$^2$. Instrument: height (self-made instrument), weight (TANITATBF-300GS body composition analyzer); accuracy: one decimal place. | Unit: kg/m$^2$ |
| Waist circumference (WC) | Measurement position: midpoint level of the line between the anterior superior iliac crest and the 12th costal edge; tool: plastic soft tape; precision: one after the decimal point; measurement time: at the end of normal expiration. | Unit: cm |
| Waist-to-hip ratio | Measurement position: maximum extension of hip; tool: soft tape; accuracy: one decimal place. | Unit: cm |
| Systolic Blood Pressure (SBP) | Instrument: UA-799 digital sphygmomanometer. Measurement time: sit for 5 min, repeat twice, and take the average value. If the difference is >10 mmHg, take the third measurement and average over the last two measurements. | Unit: mmHg |
| Diastolic blood pressure (DBP) | Same SBP | Unit: mmHg |
| Self-reported history of cirrhosis/chronic hepatitis | Questionnaire<br>Question: Have you been diagnosed with cirrhosis/chronic hepatitis by a doctor in a township/district hospital? | (Yes/no) |

| Predictor | Measurements | Units and definitions |
|---|---|---|
| Self-reported history of diabetes | Questionnaire<br>Question: Have you been diagnosed with diabetes by a doctor in a township/district hospital? | (Yes/no) |
| Newly detected diabetes during field investigation | Measurement tool: SureStep Plus System (LifeScan); Sample: Venous blood specimen. The object answered "yes" in question 1 was repeated if random blood glucose was 7.8-11.0 mmol/L. | Question 1 answered "no", the newly detected diabetes at site investigation was defined as follows: (1) random glucose value 7.0 mmol/L with fasting time 8 h; or (2) random glucose value 11.1 mmol/L with fasting time < 8 h; or (3) repeated random glucose measurement 7.0 mmol/L on the next day. |
| Triglyceride (TG) | Measurement of TG Beckman Chemistry Information Sheets: BLOSR6x118.04 2015-04. Beckman reagent (REF OSR6*118), analytical wavelength of primary 660 nm, secondary 800 nm, sample size of 1.6 μL, reagent volume(R1) 66 μL dilution of 57 μL, reagent volume(R2) 17 μL, dilution of 10 c. | Unit: Millimoles/Little |
| Total cholesterol (TC) | Reference for TC Beckman Coulter Cholesterol Chemistry Information Sheets: BLOSR6X16.07 2015-05. Beckman reagent (REF OSR6116), analyzed at primary 540 nm, secondary 600 nm, sample size of 1.6 μL, reagent volume(R1) of 24 μL, at 96 μL dilution. | Unit: Millimoles/Little |
| Smoking status | Questionnaire<br>(1) Current frequency of smoking:<br>Question 2 of l: How much time do you smoke once now? (A=non-smoking; B=occasional; C=most days; D=daily)<br>(2) Frequency of past smoking:<br>Question l 6: In the past, have you ever had the habit of smoking every day? (A=never; B=occasionally; C=most days; D=daily)<br>(3) Daily smoking volume | The current daily smoker was defined as: Question 2=D (Yes/No)<br>Quitters were defined as: Question 2=A and Question 6=B+C+D (Yes/No)<br>Daily smoking:<br>Tobacco content conversion: cigarette contains 1 gram of tobacco/cigarette, cigar contains 2 grams of tobacco/cigarette, grams of pipe/hookah, hand cigarette/dry tobacco are converted by the reported value. |
| Frequency of physical exercise | Questionnaire<br>Question 9: In the past year, how often do you usually take a | Metabolic equivalent (MET) for different types of physical activity was taken from the 2011 Physical Activity Outline. |

| Predictor | Measurements | Units and definitions |
|---|---|---|
| | physical exercise in your spare time? (A=never or almost absent; B=1-3 times/month; C=1-2 times/week; D=3-5 times/week; E=exercise every day or almost every day) | Unit: MET-hour/day |

**Method S4 ICD-10 of CLD events in CKB**

| ICD-10 | Diagnosis | No. cases |
|---|---|---|
| **HCC** | | |
| C22.0 | Liver cell carcinoma | 354 |
| C22.9 | Malignant neoplasm of liver and intrahepatic bile ducts, unspecified | 2,916 |
| **Total** | | 3,017 |
| **CLD** | | |
| K70 | alcoholic liver disease, ALD | 329 |
| K72.0 | Acute liver failure | 35 |
| K72.1 | Chronic liver failure | 12 |
| K72.9 | Liver failure unspecified | 251 |
| K74 | fibrosis and cirrhosis of liver | 2,708 |
| K76.7 | Hepatorenal syndrome | 31 |
| I85.0 | Esophageal varices with bleeding | 103 |
| I85.9 | Esophageal varices without bleeding | 45 |
| C22 | Liver cancer | 3,268 |
| **Total** | | 5,565 |

## Method S5 Predictors and equations for included models

**Predictors and equations for included models**

**HCC**

**1. HLI**

(1) Predictors: BMI, lifetime alcohol consumption, diet score, physical activity, smoking, hepatitis infection, diabetes

Predictor definition:

a. BMI (continuous, kg/m²), average lifetime alcohol intake (continuous, grams per day).
b. Diet score (The diet score combined six dietary items including cereal fiber, red and processed meats, ratio of polyunsaturated to saturated fatty acids, margarine (used as a surrogate marker for trans-fat from industrial sources), glycemic load, and fruits and vegetables. continuous).
c. Physical activity (continuous metabolic equivalents of task in metabolic equivalent hours per week).
d. Smoking (never, former smokers quit >10 y, former smokers quit c10 y, current smokers ≤15 cigarettes/d, current smokers >15 cigarettes/d).
e. Hepatitis infection (yes/no), and self-reported diabetes at baseline (yes/no). These are the components of an HLI used in EPIC, modified to include hepatitis and diabetes status.
f. Average lifetime alcohol intake was used instead of alcohol intake at recruitment to address potential bias related to reverse causality.

(2) Equation:

| Modified HLI variable | Scoring details |
|---|---|
| **BMI (kg/m$^2$)** | |
| 5th quintile (c30) | 0 |
| 4th quintile (26-29.9) | 1 |
| 3rd quintile (24-25.9) | 2 |
| 2nd quintile (22-23.9) | 3 |
| 1st quintile (<22) | 4 |
| **Lifetime alcohol consumption(g/day)** | |
| m: >30; w: >20 | 0 |
| m: 15-30; w: 10-20 | 1 |
| m: 5-15; w: 5-10 | 2 |
| 0.1-5 | 3 |
| Never | 4 |
| **Diet score** | |
| 1st quintile (6-21) | 0 |
| 2nd quintile (22-25) | 1 |
| 3rd quintile (26-28) | 2 |
| 4th quintile (29-33) | 3 |
| 5th quintile (34-46) | 4 |
| **Physical activity (METs-hour/week)** | |
| 1st quintile (<45) | 0 |
| 2nd quintile (46-69) | 1 |
| 3rd quintile (70-96) | 2 |
| 4th quintile (97-133) | 3 |
| 5th quintile (>=134) | 4 |
| **Smoking** | |
| Current smokers, >15 cigarettes/day | 0 |
| Current smokers, <=15 cigarettes/day | 1 |
| Former smokers, quit <=10 years | 2 |
| Former smokers, quit >10 years | 3 |
| Never | 4 |
| **Hepatitis Infection** | |
| Yes | 0 |
| No | 4 |
| **Diabetes at baseline** | |

| | |
|---|---|
| Yes | 0 |
| No | 4 |

(4) Equation in CKB:

```
3.9369385+0.081874441*bmi_q
-0.19685988*pa_q
-0.097734815*fruit
-0.22615716*cig_category
-0.047279255*alcohol_cat
-0.55157654*hepatitis
-0.16193887*diabetes
```

**2.1 Wen 1-2012**

(1) Predictors: sex, age, smoking, drinking, physical activity, diabetes

Predictor definition:

a. Smoking was classified by the number of pack-years (i.e. daily cigarette quantity*duration in years) among every smoker.

b. Alcohol consumption was classified into "regular drinkers" (those who consumed ≥2 drinks/day on ≥3 days/week) and "occasional drinkers" (those who consumed <2 drinks/day on <3 days/week).

c. Physical activity: regarding volume of leisure time physical activity (LTPA) (i.e. the product of intensity measured as metabolic equivalent tasks [MET]*duration of exercise in hours), the MET-hour per week of each individual was classified as: inactive (<3.75 MET-hour), low-active (3.75-7.49 MET-hour), and active (≥7.5 MET-hour; this group met the current LTPA recommendation)

(2) Equation:

| **Wen 1-2012 variable** | **Scoring details** |
|---|---|
| **Sex** | |
| Female | 0 |
| Male | 2 |
| **Age**, **year** | |
| 20-39 | 0 |
| 40-59 | 2 |
| ≥60 | 6 |
| **Smoking, pack-years** | |
| 0 | 0 |
| 1-9.9 | 1 |
| ≥10 | 1 |
| **Drinking** | |
| None or occasional | 0 |
| Regular | 1 |
| **Physical Activity, MET-hour** | |
| <3.75 | 0 |
| 3.75-7.49 | -1 |
| ≥7.5 | -1 |
| Diabetes | |
| No | 0 |
| Yes | 2 |

(3) Equation in CKB:

```
-1.0610638+0.24293881*data$age_category
+0.31523732*data$sex
+0.096166441*data$alc_category
+0.17316124*data$act_category
+0.47848429*data$diabetes
+0.37469387*data$cig_category
```

**2.2 Wen 2-2012**

(1) Predictors: sex, age, AST, ALT

(2) Equation:

| **Wen 2-2012 variable** | **Scoring details** |
|---|---|
| **Sex** | |
| Female | 0 |

| | |
|---|---|
| Male | 2 |
| **Age, year** | |
| 20-39 | 0 |
| 40-59 | 2 |
| ≥60 | 6 |
| **AST, IU/L** | |
| <25 | 0 |
| 25-39 | 5 |
| 40-59 | 9 |
| ≥60 | 13 |
| **ALT, IU/L** | |
| <25 | 0 |
| ≥25 | 2 |

(3) Equation in CKB:

```
-1.2420188+0.15651695*dat$age_category
+0.3586473*dat$sex
-0.076442133*dat$ALT_category
+0.12480102*dat$AST_category
```

**2.3 Wen 3-2012**

(1) Predictors: sex, age, smoking, drinking, physical activity, diabetes, AST, ALT

(2) Equation:

| Wen 3-2012 variable | Scoring details |
|---|---|
| **Sex** | |
| Female | 0 |
| Male | 1 |
| **Age, year** | |
| 20-39 | 0 |
| 40-59 | 2 |
| ≥60 | 6 |
| **Smoking, pack-years** | |
| 0 | 0 |
| 1-9.9 | 1 |
| ≥10 | 1 |
| **Drinking** | |
| None or occasional | 0 |
| Regular | 1 |
| **Physical Activity, MET-hour** | |
| <3.75 | 0 |
| 3.75-7.49 | 0 |
| ≥7.5 | -1 |
| **Diabetes** | |
| No | 0 |
| Yes | 1 |
| **AST, IU/L** | |
| <25 | 0 |
| 25-39 | 4 |
| 40-59 | 9 |
| ≥60 | 12 |
| **ALT, IU/L** | |
| <25 | 0 |

| | |
|---|---|
| ≥25 | 1 |

(3) Equation in CKB:

```
-1.2300978+0.15784406*dat$age_category
+0.61661131*dat$sex
-0.21056898*dat$ALT_category
+0.14130867*dat$AST_category
+0.11230019*dat$alc_category
+0.089372728*dat$act_category
+0.024911687*dat$diabetes
+0.071970998*dat$cig_category
```

**3. DM-HCC**

(1) Predictors: age, GGT, TG

(2) Equation:

| DM-HCC variable | Scoring details |
|---|---|
| Age, years | |
| >65 | 11 |
| ≤65 | 0 |
| GGT (IU/L) | |
| >80 | 16 |
| 41-80 | 8 |
| ≤40 | 0 |
| TG (mg/dL) | |
| <150 | 6 |
| ≥150 | 0 |

(3) Equation in CKB:

```
-0.50559487+0.071973603*dat$age_category
+0.10426216*dat$GGT_category
+0.038324225*dat$TG_category
```

**4. Li-2018**

(1) Predictors: age, gender, smoking habit, SGPT, variation of HbA1c, comorbidity, antidiabetes medications, antihyperlipidemia medication, THR

Predictor definition:

a. SGPT: serum ALT
b. HbA1c: RPG
c. Medication: as a user of specific medication when his/her number of prescription days for each specific drug was greater than 3 months. The anti diabetes medications of individual patients were further classified into 4 categories: no medication, oral anti diabetes drugs, insulin monotherapy, and insulin plus oral anti diabetes drugs.
d. Antihyperlipidemia medications considered were statins and fibrates.
e. THR: total/high-density lipoprotein (HDL) cholesterol ratio

(2) Equation:

```
Age (-2 to 8)
+Gender (0 if female, 2 if male)
+Smoking habit (0 if no smoking, 2 if smoking)
+SGPT (u/l) (0 if 6-45, 6 if <6 or >45)
+Variation of HbA1c (%) (0 if <8.5, 0 if 8.5-17.5, 1 if >17.5)
+Comorbidity (9 if Liver cirrhosis, 4 if Hepatitis B, 3 if Hepatitis C)
+Antidiabetes medications (0 if no medication, 0 if oral only, 2 if insulin, 3 if insulin+oral agent)
+Antihyperlipidemia medication:
-No medication:
-THR: male <5; female <4.5: Score 0
-THR: male 5-9.4; female 4.5-7: Score-1
-THR: male ≥9.5; female ≥7: Score 2
-Yes medication:
-THR: male <5; female <4.5: Score-2
-THR: male 5-9.4; female 4.5-7: Score-4
-THR: male ≥9.5; female ≥7: Score-3
```

(3) Equation in CKB:

```
-2.0077928+1.6373314*(dat$age_category=="-1")
```

-0.084629372*(dat$age_category=="0")
+1.5179949*(dat$age_category=="1")
+1.355421*(dat$age_category=="2")
+1.378663*(dat$age_category=="3")
+1.3509516*(dat$age_category=="4")
+1.7908917*(dat$age_category=="5")
+2.0393897*(dat$age_category=="6")
+2.2834965*(dat$age_category=="7")
-2.4928856*(dat$age_category=="8")
+0.37026501*dat$sex
-0.009137821*dat$smoke_category
+0.2810228*dat$SGPT_category+
0.76331689*dat$HbA1c_category
+0.39906606*dat$comorbidity_category
-2.095294*dat$antidiabetes_category
-0.064815973*dat$THR_category

**5. Sinn-2020**

(1) Predictors: age, gender, body mass index, smoking, diabetes,total cholesterol, ALT
Predictor definition:

a. BMI was classified according to Asian-specific criteria (underweight, BMI of <18.5 kg/$m^2$; normal weight, BMI of 18.5 to 22.9 kg/$m^2$; overweight, BMI of 23 to 24.9 kg/ $m^2$; and obese, BMI ≥25 kg/$m^2$).
b. Pre-hypertension was defined as a systolic blood pressure 130-<140 mmHg or a diastolic blood pressure 85-<90 mmHg at the baseline screening.
c. Hypertension was defined as the presence of at least one I10-I13 or I15 code during the year preceding the screening, or a systolic blood pressure 140 mmHg or a diastolic blood pressure 90 mmHg at the baseline screening.
d. Pre-diabetes was defined as a fasting glucose level of 100-<126 mg/dL at the baseline screening. Diabetes was defined as the presence of at least one E11-E14 code or a fasting glucose level of 126 mg/dL at the baseline screening.
e. Dyslipidaemia was defined as the presence of an E78 code or a total cholesterol level of >240 mg/dL at the baseline screening.
f. ALT level was classified into three groups: low (<30 U/L for males and <20 U/L for females), mildly elevated (30-89 U/L for males and 20-59 U/L for females) and elevated (90 U/L for males and 60 U/L for females)
g. Current alcohol consumption was categorized into none or modest (<30 g/day in men and <20 g/day in women).

(2) Equation:

| DM-HCC variable | Scoring details |
|---|---|
| **Age** | |
| <50 | 0 |
| 50-59 | 3 |
| 60-69 | 6 |
| ≥70 | 7 |
| **Sex** | |
| Female | 0 |
| Male | 2 |
| **Smoking** | |
| Never | 0 |
| Past | 0 |
| Current | 1 |
| **Diabetes** | |
| No diabetes | 0 |
| Pre-diabetes | 0 |
| Diabetes | 1 |
| **Total cholesterol(mg/dL)** | |
| <200 | 2 |
| ≥200 | 0 |
| **Alanine aminotransferasea** | |
| Low | 0 |

| | |
|---|---|
| Mildly elevated | 2 |
| Elevated | 6 |

(3) Equation in CKB:
-1.0888972+0.15591552*age_category
+0.44051948*sex
-0.042037495*current_smoking
-0.053377929*Diabetes
+0.159525*ALT_category
+1.3294444*Total_cholesterol

**6. Cao-2021**

(1) Predictor: age, sex, liver diseases in mother, BMI, alcohol consumption, psychological trauma
Predictor definition:
a. Liver diseases in mothers: including liver cancer, chronic hepatitis B, and other liver disease.

(2) Equation:
F(t)=1-S(t)exp(f,M);
f,M=0.058×(age in years)
+0.879 × (Female=0, Male=1)
+0.608 × (liver diseases in mother: Yes=1, No=0)
+0.380 × (BMI<25=1, BMI ≥25=0)
+0.753 × (alcohol consumption ≥550 g/week ethanol: Yes=1, No=0)
+0.480 × (psychological trauma: Yes=1, No=0)-4.010.

**CLD**

**1.1 CLivD score(nonlab)**

(1) Predictors: age, WHR, alcohol use (spline variable), GGT, diabetes, smoking status, sex*GGT, sex*smoking status

(2) Equation:
```
data$modellab <-(-6.7922721+0.044744302*data$AGE
+0.32961593*(data$WHR*10)+0.19860813*data$ALCOHOL
-0.0082096868*pmax(data$ALCOHOL-0.1,0)^3
+0.010575035*pmax(data$ALCOHOL-1,0)^3
-0.002004756*pmax(data$ALCOHOL-3,0)^3
-0.00033998925*pmax(data$ALCOHOL-9,0)^3
-2.0602882e-05*pmax(data$ALCOHOL-
33,0)^3+0.011813962*data$GGT+0.18721469*(data$SEX=="2")
+0.55249734*(data$DIABETES=="1")
+0.74679941*(data$SMOKING=="1")
+0.0054325769*data$GGT*(data$SEX=="2")
-0.64903176*(data$SEX=="2")*(data$SMOKING=="1"))
```

(3) Equation in CKB:
```
-1.7996042-0.13849959*data$alcohol_week
+0.0081373039*pmax(data$alcohol_week-1,0)^3
-0.016951927*pmax(data$alcohol_week-3,0)^3
+0.0090844935*pmax(data$alcohol_week-5,0)^3
-0.00025840613*pmax(data$alcohol_week-9,0)^3
-1.1464752e-05*pmax(data$alcohol_week-33,0)^3
+0.050087058*data$age
+0.45957616*data$whr
+0.42501114*data$diabetes
-0.27723986*data$smoking
-0.52580546*data$sex
+0.017439031*data$smoking*data$sex
```

**1.2 CLivD score(lab)**

(1) Predictors: age, WHR, alcohol use (spline variable), diabetes, smoking status, sex*smoking status

(2) Equation:
```
data$modelnonlab <-(-8.0940103+0.044177151*data$AGE+0.48927753*(data$WHR*10)
+0.19222894*data$ALCOHOL-0.00015029544*pmax(data$ALCOHOL-0.1,0)^3-
0.0021265611*pmax(data$ALCOHOL-1,0)^3+0.0029832769*pmax(data$ALCOHOL-3,0)^3-
0.00068765143*pmax(data$ALCOHOL-9,0)^3-1.8769011e-05*pmax(data$ALCOHOL-
33,0)^3+0.69669285*(data$DIABETES=="1")
```

+0.75968055*(data$SMOKING=="1")
+0.63248362*(data$SEX=="2")-0.59146649*(data$SMOKING=="1")*(data$SEX=="2"))

(3) Equation in CKB:
-1.0759261-0.04427105*data$alcohol_week
+4.3147139e-05*pmax(data$alcohol_week-0.1,0)^3
-9.0209853e-05*pmax(data$alcohol_week-15,0)^3
+5.0565399e-05*pmax(data$alcohol_week-30,0)^3
-3.502685e-06*pmax(data$alcohol_week-48,0)^3
+0.044255473*data$age
-1.1958386*data$whr
+0.01055964*data$ggt
-0.49321834*data$sex
+0.030192835*data$diabetes
+0.099859348*data$smoking
+0.0041691027*data$ggt*data$sex
-0.077726792*data$sex*data$smoking

**2. BARD**

(1) Predictors: BMI, AST, ALT, T2DM

(2) Equation:
(1 if BMI >28 kg/m²)
+(2 if AST/ALT ratio >0.8)
+(1 if T2DM)

(3) Equation in CKB:
-0.66609144-0.1319787*data$bmi_c
+0.33679484*data$diabetes_c
+0.34728017*data$ast_c

**3. dAAR**

(1) Predictors: age, ALT, AST

(2) Equation:
dataset$riskscore1<-10.129915+0.039811813*dataset$AGE
+0.25387407*dataset$ALT
-0.0023607234*pmax(dataset$ALT-11,0)^3
+0.0079492072*pmax(dataset$ALT-17,0)^3
-0.0076811579*pmax(dataset$ALT-22,0)^3
+0.0021985068*pmax(dataset$ALT-30,0)^3
-0.00010583268*pmax(dataset$ALT-58,0)^3
+3.5333535*dataset$astalt
-7.3473709*pmax(dataset$astalt-0.63,0)^3
+32.911587*pmax(dataset$astalt-0.92,0)^3
-44.937707*pmax(dataset$astalt-1.14,0)^3
+21.786619*pmax(dataset$astalt-1.41,0)^3
-2.4131284*pmax(dataset$astalt-2.13,0)^3

(3) Equation in CKB:
-10.334179-0.12283087*data$ALT
+0.0004243091*pmax(data$ALT-0.1,0)^3
-0.0012106484*pmax(data$ALT-11,0)^3
+0.00090314578*pmax(data$ALT-17,0)^3
-0.00031645783*pmax(data$ALT-22,0)^3
+0.00023916006*pmax(data$ALT-30,0)^3
-3.9508734e-05*pmax(data$ALT-58,0)^3
+10.649273*data$astalt
-4.8201285*pmax(data$astalt-0.1,0)^3
+7.4526922*pmax(data$astalt-0.63,0)^3
+10.855356*pmax(data$astalt-0.92,0)^3
-21.971644*pmax(data$astalt-1.14,0)^3
+10.031624*pmax(data$astalt-1.41,0)^3
-1.5478998*pmax(data$astalt-2.13,0)^3
+0.03380337*data$AGE

**4. CAP-B**

(1) Predictors: age, sex, income, chronic hepatitis C, diabetes mellitus, statin exposure, antiplatelet exposure, smoking, ALT, GGT

Predictor definition:

a. Income: medical aid <25%, low income=25-50%, intermediate=50-75%
b. Disease history: chronic hepatitis C; diabetes mellitus
c. Defined statin exposure as having filled at least 2 prescriptions within a six-month period,
d. Aspirin exposure as a prescription for at least once within 2 years prior to the index date
e. Smoking: smoking was based on the current status (i.e. yes or no) by patient health questionnaires
f. GGT*alcohol consumption:
g. Drinking: alcohol drinking was based on the current status (i.e. yes or no) by patient health questionnaires
h. Normal GGT: 3-50 U/L

(2) Equation:

0.677*(male)
+0.085*(age)
+0.310*(medical aid/<25%)
+0.249*(low income)
+0.146*(intermediate income)
+0.066*(chronic hepatitis C)
+0.406*(diabetes mellitus)
-0.426*(statin exposure)
+0.025*(antiplatelet exposure)
+0.230*(smoking)+0.539*(ALT >35)
+0.079*(normal GGT and drinking or abnormal GGT and & nondrinking)
+0.532*(abnormal GGT and drinking)+0.426
$P(t)=1-S0(t)\exp(\text{risk score}-0.43)$

## Table S1 Bias assessment

| No | Study | ROB | | | | Applicability | | | Overall | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Participants | Predictors | Outcome | Analysis | Participants | Predictors | Outcome | ROB | Applicability |
| 1 | Fredrik Åberg (2022) | Low | Low | Low | Low | Low | Low | Low | Low | Low |
| 2 | Vincent Wai-Sun Won (2010) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 3 | Hwai-I Yan (2010) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 4 | Man-Fung Yuen (2009) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 5 | Hwai-I Yang (2011) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 6 | Masayuki Kurosaki (2012) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 7 | Takehiro Michikawa (2012) | Low | Low | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 8 | Chi-Pang Wen (2012) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 9 | Juan Carlos Gavilán (2013) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 10 | Mei-Hsuan Lee (2013) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 11 | Yu-Ju Lin (2013) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 12 | Mei-Hsuan Lee (2014) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 13 | Talita Duarte-Salles (2016) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 14 | Beomseok Suh (2015) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 15 | Chunsun Fan (2019) | Low | Unclear | Unclear | High | Low | Low | Low | High | Low |
| 16 | Won Keun Si (2016) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 17 | Adeel A. Butt (2017) | Low | Unclear | High | Unclear | Low | Low | Low | High | Low |
| 18 | Wei-Yi Kao (2017) | Low | Unclear | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 19 | M. A. Konerman (2017) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 20 | Yeon Seok Seo (2017) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 21 | Hwai-I Yang (2016) | Low | Low | Low | Low | Low | Low | Low | Low | Low |
| 22 | Tsai-Chung Li (2018) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 23 | Lilian Yan Liang (2021) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 24 | Dong Hyun Sinn (2020) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 25 | Dong Hyun Sinn (2019) | Low | Low | High | High | Low | Low | Low | High | Low |
| 26 | Fredrik Åberg (2021) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 27 | Yuting Wang (2021) | Low | Low | Unclear | High | Low | Low | Low | High | Low |
| 28 | Mathias Daheim (2016) | Unclear | Unclear | Unclear | High | Low | Low | Low | High | Low |

| No | Study | ROB | | | | Applicability | | | Overall | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Participants | Predictors | Outcome | Analysis | Participants | Predictors | Outcome | ROB | Applicability |
| 29 | Ae Jeong Jo (2022) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 30 | Hannes Hagström (2019) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 31 | Dong Hyun Sinn (2016) | High | Unclear | Low | High | Low | Low | Low | High | Low |
| 32 | Chansik An (2021) | Low | Low | Low | Low | Low | Low | Low | Low | Low |
| 33 | Chengxiao Yu (2021) | Low | Low | Low | High | Low | Low | Low | High | Low |
| 34 | Thanachote Kamalapirat (2021) | Low | Unclear | Unclear | High | Low | Low | Low | High | Low |
| 35 | Alessandra Porto de Macedo Costa (2022) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 36 | Nada Assi (2018) | Low | Low | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 37 | Tai-Chung Tseng (2017) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 38 | Philip J. Johnson (2022) | Low | Unclear | Low | Low | Low | Low | Low | Low | Low |
| 39 | Do Young Kim (2013) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 40 | Monica A. Konerman (2019) | Low | Unclear | High | High | Low | Low | Low | High | Low |
| 41 | An K. Le (2021) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 42 | Maomao Cao (2021) | Low | Low | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 43 | Hannes Hagström (2019) | Low | Low | Unclear | High | Low | Low | Low | High | Low |
| 44 | Jae Seung Lee (2021) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 45 | Thierry Poynard (2019) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 46 | Jonathan Thomas (2022) | Low | Low | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 47 | Grace Lai-Hung Wong (2014) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 48 | Thierry Poynard (2021) | Low | Unclear | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 49 | Hsiao-Hsien Rau (2016) | Low | Low | Low | Unclear | Low | Low | Low | Unclear | Low |
| 50 | Seung Hwan Shin (2015) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 51 | Namyoung Paik (2018) | Low | Unclear | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 52 | Kyu Sik Jung (2015) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 53 | Mi Young Jeon (2018) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 54 | Mahmoud Abu-Amara (2016) | Low | Unclear | Unclear | Unclear | Low | Low | Low | Unclear | Low |
| 55 | W. P. Brouwer (2017) | Low | Unclear | Low | Unclear | Low | Low | Low | Unclear | Low |
| 56 | Zhongxian Poh (2016) | Low | Unclear | Low | High | Low | Low | Low | High | Low |
| 57 | Namkyu Kang (2021) | Low | Low | Low | High | Low | Low | Low | High | Low |

## Table S2 Predictors of prediction models for general population

| Model | Demographic | | Lifestyle | | | | | | | Blood-based biomarkers | | | | | | | | | | | | | | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Alcohol | BMI | Diet | PA | Smoking | WHR | Diabetes | AFP | ALB | ALP | ALT | AST | BIL | GGT | Glu | HBsAg | HBeAg | HBV DNA | TC | TG | PLT | |
| AGED | √ | √ | | | | | | | | | | | √ | | | | | | √ | √ | | | | |
| An-2021 | √ | √ | | √ | | | | | √ | | | | √ | | | √ | | | √ | √ | √ | | | income etc.‡ |
| CKB-PLR | √ | √ | √ | √ | | √ | √ | | √ | | | | | | | | √ | | | | | | | Family history of cancer etc.§ |
| CLivD (lab) | √ | √ | √ | | | | √ | √ | √ | | | | | | | √ | | | | | | | | |
| CLivD (non-lab) | √ | √ | √ | | | | √ | √ | √ | | | | | | | | | | | | | | | |
| dAAR | √ | | | | | | | | | | | | √ | √ | | | | | | | | | | |
| Duarte-Salles 1-2016 | | | | | | | | | | √ | | | | | | | | | | | | | | OPN |
| Duarte-Salles 2-2016 | | | | | | | | | | √ | | √ | | √ | | √ | | | | | | | | OPN |
| Duarte-Salles 3-2016 | | | | | | | | | | | | √ | | √ | | √ | | | | | | | | |
| Duarte-Salles 4-2016 | | | | | | | | | | | | √ | | √ | | √ | | | | | | | | OPN |
| Elaborate Base Model | √ | √ | √ | √ | √ | √ | | | √ | | | | | | | | | | | | | | | height, general health status |
| HLI | | | √ | √ | √ | √ | √ | | √ | | | | | | | | | | | | | | | hepatitis |
| LCR1 | √ | √ | | | | | | | | | | | | | | √ | | | | | | | | APOA1, Hp, A2M |
| LCR2 | √ | √ | | | | | | | | √ | | | | | | √ | | | | | | | | APOA1, Hp, A2M |
| LFS | | | | | | | | | | | √ | √ | √ | √ | √ | √ | | | | | | | | |
| LFS+lifestyle signature | | | √ | √ | √ | √ | √ | | √ | | | | | | | | | | | | | | | hepatitis |
| LFS+metabolic signature | | | | | | | | | | | | | | | | | √ | | | | | | | Metabolic signature¶ |
| Metabolic signature | | | | | | | | | | | √ | √ | √ | √ | √ | √ | √ | | | | | | | Metabolic signature¶ |
| Michikawa | √ | √ | √ | √ | | | | | √ | | | | | | | | | √ | | | | | | coffee consumption, Anti-HCV Ab |
| Parsimonious Base Model | √ | √ | √ | √ | √ | √ | | | √ | | | | | | | | | | | | | | | general health status |
| Sinn-020 | √ | √ | | | | | √ | | √ | | | | √ | | | | | | | | √ | | | |
| Sung(established)-2012 | | | | | | | | √ | | | | | √ | | | | √ | | | | | √ | √ | |
| Sung(new)-2012 | | | | | | | | √ | | | | | √ | | | | √ | | | | | √ | √ | |
| Wen 1-2012 | √ | √ | √ | | | √ | √ | | √ | | | | | | | | | | | | | | | |
| Wen 1'-2012 | √ | √ | √ | | | √ | √ | | √ | | | | | | | | | | | | | | | |
| Wen 2-2012 | √ | √ | | | | | | | | | | | √ | √ | | | | | | | | | | |

| Model | Demographic | | Lifestyle | | | | | | | Blood-based biomarkers | | | | | | | | | | | | | | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Alcohol | BMI | Diet | PA | Smoking | WHR | Diabetes | AFP | ALB | ALP | ALT | AST | BIL | GGT | Glu | HBsAg | HBeAg | HBV DNA | TC | TG | PLT | |
| Wen 2'-2012 | √ | √ | | | | | | | | | | | √ | √ | | | | | | | | | | |
| Wen 3-2012 | √ | √ | √ | | | √ | √ | | √ | | | | √ | √ | | | | | | | | | | |
| Wen 3'-2012 | √ | √ | √ | | | √ | √ | | √ | | | | √ | √ | | | | | | | | | | |
| Wen 4-2012 | √ | √ | √ | | | √ | √ | | √ | √ | | | √ | √ | | | | √ | | | | | | |
| Wen 4'-2012 | √ | √ | √ | | | √ | √ | | √ | √ | | | √ | √ | | | | √ | | | | | | |
| Wen 5'-2012 | √ | √ | √ | | | √ | √ | | √ | √ | | | √ | √ | | | | √ | | | | | | Anti-HCV Ab |

‡: Income, family history of chronic liver disease, disease history (chronic liver disease, chronic hepatitis virus infection, HIV infection, dyslipidemia, or schizophrenic/delusional disorders or mental disorders due to psychoactive substance use)
§: Family history of cancer, residential area, education, disease history (cancer, gallstone or gallbladder disease), cirrhosis
¶: Glutamic acid, Hexoses, SMC16:1, SM(OH)C14:1, SM(OH)C22:2, LysoPC aC28:1, PC aeC30:2
A2M: alpha2‐macroglobulin; AAR: aspartate-to-alanine aminotransferase ratio; AFP: alpha-fetoprotein; ALB: Albumin; ALP: alkaline phosphatase; ALT: alanine transaminase; Anti-HCV Ab: Anti-Hepatitis C Virus Antibody; APOA1: apolipoprotein A1; AST: aspartate transaminase; BIL:Bilirubin; GGT: gamma-glutamyl transferase; Glu: Glutamic acid; HBeAg: Hepatitis B e Antigen; HBsAg: Hepatitis B Surface Antigen; Hp: haptoglobin; PA: physical activity; PLT: Platelet count; TC: total cholesterol; TG concentration: triglyceride concentration; WC: waist circumference; WHR: waist-to-hip rate

## Table S3 Predictors of prediction models for HBV infected individuals

| Model | Demographic | | Lifestyle | | | Personal and family history | | | Blood-based biomarkers | | | | | | | | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Alcohol | BMI | Smoking | Diabetes | Cirrhosis | Family history | AFP | ALB | ALT | AST | GGT | HBeAg | HBV DNA | PLT | |
| Cao-2021 | √ | √ | √ | √ | | | | √‡ | | | | | | | | | Psychological trauma |
| CAP-B Score | √ | √ | √ | | √ | √ | | | | | √ | | √ | | | | income, CHC, statin exposure, anitplatelet exposure |
| D²AS | √ | √ | | | | | | | | | √ | | | √ | √ | | |
| GAG-HCC | √ | √ | | | | | √ | | | | | | | | √ | | core promoter mutations |
| GAG-HCC (non-core promoter mutations) | √ | √ | | | | | √ | | | | | | | | √ | | |
| Le-2021 | √ | √ | | | | √ | | | | | √ | √ | | √ | | | antiviral treatment |
| Lee-2013 | √ | √ | | | | | | √ | | | √ | | | √ | √ | | |
| Liang score | √ | √ | | | | | | | | | | | | | √ | | FIB-4 |
| Lin-Model I | √ | √ | | | | | | | | √ | √ | | | √ | √ | | |
| Lin-Model II | √ | √ | | | | | | | √ | | √ | √ | √ | | | | alpha-1 globulin |
| Lin-Model III | √ | √ | | | | | | | √ | √ | √ | √ | √ | | √ | | alpha-1 globulin |
| LSM-HCC | √ | | | | | | | | | √ | | | | | √ | | Liver stiffness |
| LSPS | | | | | | | | | | | | | | | | √ | Liver stiffness, spleen diameter |
| MALE-ABCD | √ | | | | | | | | √ | | | | √ | | | | |
| Methylation Profile | | | | | | | | | | | | | | | | | three methylated sites§ |
| Model 1-regression model | √ | √ | √ | | | | | √ | | | √ | | | √ | | | |
| Model 2-regression model | √ | √ | √ | | | | | √ | | | √ | | | √ | √ | | |
| Model 3-regression model | √ | √ | √ | | | | | √ | | | √ | | | √ | √ | | HBV genotype |
| NGM1-HCC | √ | √ | √ | | | | | √ | | | √ | | | √ | | | |
| NGM2-HCC | √ | √ | √ | | | | | √ | | | √ | | | √ | √ | | |
| NGM3-HCC | √ | √ | √ | | | | | √ | | | √ | | | √ | √ | | HBV genotype |
| REACH-B | √ | √ | | | | | | | | | √ | | | √ | √ | | |
| REACH-B IIa | √ | √ | | | | | | | | | √ | | | √ | √ | | |
| REACH-B IIb | √ | √ | | | | | | | | | √ | | | √ | | | |
| RWS-HCC | √ | √ | | | | | √ | | √ | | | | | | | | |
| Sinn-2019 | √ | √ | | | | | √ | | | | √ | | | √ | | √ | |
| Transient elastography-based risk estimation | √ | √ | | | | | | | | | | | | | √ | | liver stiffness |

| Model | Demographic | | Lifestyle | | | Personal and family history | | | Blood-based biomarkers | | | | | | | | Others |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | Alcohol | BMI | Smoking | Diabetes | Cirrhosis | Family history | AFP | ALB | ALT | AST | GGT | HBeAg | HBV DNA | PLT | |
| Won-2010 | √ | | | | | | √ | | | √ | | | | | √ | | |

‡: Liver diseases in mothers
§: cg00300879, cg06872964, and cg07080864
AFP: α-Fetoprotein; ALB: Albumin; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; CHC: chronic Hepatitis C; GGT: Gamma-Glutamyl Transferase; PLT: Platelet

## Table S4 Predictors of prediction models for other populations

| Model | Demographic | | Lifestyle | | Personal and family history | | | | Blood-based biomarkers | | | | | | | | other |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Age | Sex | BMI | Smoking | Diabetes | Cirrhosis | Hepatitis | Fatty liver | ALB | ALT | AST | AFP | BR | GGT | HBsAg | PLT | |
| ANN-model 1 | √ | √ | | | | √ | √ | √ | | | | | | | | | alcoholic cirrhosis etc.‡ |
| ANN-model 2 | √ | √ | | | | √ | √ | √ | | | | | | | | | alcoholic cirrhosis etc.§ |
| ANN-model 3 | √ | √ | | | | √ | √ | √ | | | | | | | | | nonalcoholic cirrhosis etc.¶ |
| CNN | | | | | | | | | | | | | | | | | |
| CRS | | | | | | | | | | | | | | | | | seven SNPs |
| CS boosting model | | | | | | | | | | | | | | | | | |
| DM-HCC | √ | | | | | | | | | | | | | √ | | | TG |
| GRU | | | | | | | | | | | | | | | | | |
| Li-2018 | √ | √ | | √ | | √ | √ | | | √ | | | | | | | Hba1C, antidiabetes medication, antihyperlipidemia medication and THR |
| HCC-4 Risk Score | √ | | | | | | | | | | | √ | | | | √ | gammaglobulin |
| HCC-RS | √ | √ | | | √ | | | | √ | √ | √ | | √ | | | √ | Cardiovascular disease etc.• |
| Liver Volume Index | | | | | | | | | | | | | | √ | | | Volume Index |
| longitudinal boosting model | | | | | | | | | | | | | | | | | |
| longitudinal Cox model | | | | | | | | | | | | | | | | | |
| LR-model 1 | √ | √ | | | | √ | √ | √ | | | | | | | | | alcoholic cirrhosis etc.‡ |
| LR-model 2 | √ | √ | | | | √ | √ | √ | | | | | | | | | alcoholic cirrhosis etc.§ |
| LR-model 3 | √ | √ | | | | √ | √ | √ | | | | | | | | | nonalcoholic cirrhosis etc.¶ |
| LS-Based Model 1 | √ | | | | | | | | | | √ | | | | | √ | Liver Stiffness |
| LS-Based Model 2 | √ | | | | | | | | | | √ | | | | | √ | Liver Stiffness |
| LS-Based Model 3 | √ | | | | | | | | | | √ | | | | | √ | Liver Stiffness |
| LSTM | | | | | | | | | | | | | | | | | |
| Kurosaki-2012 | √ | | | | | | | | √ | | | | | | | √ | |
| Lee-2014 | √ | | | | | √ | | | | √ | √ | | | | | | HCV RNA and HCV Genotype |

‡: alcoholic cirrhosis, nonalcoholic cirrhosis, alcoholic hepatitis, viral hepatitis, other types of chronic hepatitis, alcoholic fatty liver disease, other types of fatty liver disease and hyperlipidemia
§: alcoholic cirrhosis, alcoholic hepatitis, alcoholic fatty liver disease
¶: nonalcoholic cirrhosis, viral hepatitis, other types of chronic hepatitis, other types of fatty liver disease, and hyperlipidemia

•: Cardiovascular disease, Colorectal cancer, Lung cancers, Urinary/renal malignancies, Cervical cancer, Breast cancer, Lymphoma, Chronic kidney disease, Osteopenia, Osteoporosis, Hypertension, Anticoagulants, ACEI/ARB, Antiplatelet agents, Beta blockers, Histamine-2 receptor antagonist, Insulin, Immunosuppressant, Sulphonylurea, Thiazides, Other lipid-lowering agents, Other oral hypoglycaemic agents, Proton pump inhibitor, Potassium sparing diuretics, Statins, Loop diuretics, Metformin, NSAID
AFP: α-Fetoprotein; ALB: Albumin; ALT: Alanine Aminotransferase; AST: Aspartate Aminotransferase; BR: Bilirubin; GGT: Gamma-Glutamyl Transferase; HBsAg: Hepatitis B surface antigen; HbA1c: Hemoglobin A1c; PLT: Platelet; TG: Triglycerides

**Table S5 Sensitivity analysis for PLC and HCC**

| Model | Population | Time horizon (years) | PLC (C22) | | HCC (C22.0+C22.9) | | HCC (C22.0) | |
|---|---|---|---|---|---|---|---|---|
| | | | Events/total | C-index | Events/total | C-index | Events/total | C-index |
| HLI | General | 10 | 1,888/478,930 | 0.65 (0.64-0.67) | 1,709/478,930 | 0.68 (0.67-0.70) | 163/478,930 | 0.68 (0.63-0.73) |
| Wen 1-2012 | General | 5 | 875/478,930 | 0.72 (0.71-0.74) | 793/478,930 | 0.72 (0.70-0.74) | 71/478,930 | 0.76 (0.71-0.81) |
| Wen 1-2012 | General | 10 | 1,888/478,930 | 0.72 (0.70-0.73) | 1,709/478,930 | 0.72 (0.70-0.73) | 163/478,930 | 0.76 (0.72-0.80) |
| DM-HCC (all) | General | 5 | 30/15,818 | 0.69 (0.60-0.79) | 26/15,818 | 0.68 (0.57-0.79) | 3/15,818 | 0.71 (0.60-0.82) |
| Li-2018 (all) | General | 3 | 17/17,227 | 0.80 (0.70-0.90) | 12/17,227 | 0.83 (0.75-0.92) | 1/17,227 | 0.98 (0.98-0.98) |
| Li-2018 (all) | General | 5 | 32/17,227 | 0.75 (0.66-0.83) | 28/17,227 | 0.76 (0.68-0.84) | 3/17,227 | 0.92 (0.85-0.99) |
| Li-2018 (all) | General | 10 | 80/17,227 | 0.74 (0.68-0.79) | 72/17,227 | 0.74 (0.68-0.80) | 8/17,227 | 0.91 (0.84-0.98) |
| Sinn-2020 | General | 5 | 32/17,227 | 0.69 (0.60-0.77) | 28/17,227 | 0.70 (0.61-0.78) | 3/17,227 | 0.90 (0.81-0.99) |
| Sinn-2020 | General | 10 | 80/17,227 | 0.67 (0.61-0.73) | 72/17,227 | 0.66 (0.60-0.72) | 8/17,227 | 0.86 (0.77-0.95) |
| Wen 2-2012 | General | 5 | 32/17,227 | 0.68 (0.59-0.77) | 28/17,227 | 0.70 (0.62-0.79) | 3/17,227 | 0.82 (0.67-0.97) |
| Wen 2-2012 | General | 10 | 80/17,227 | 0.67 (0.61-0.73) | 72/17,227 | 0.67 (0.61-0.74) | 8/17,227 | 0.81 (0.66-0.96) |
| Wen 3-2012 | General | 5 | 32/17,227 | 0.69 (0.60-0.78) | 28/17,227 | 0.71 (0.62-0.80) | 3/17,227 | 0.98 (0.95-0.99) |
| Wen 3-2012 | General | 10 | 80/17,227 | 0.68 (0.62-0.73) | 72/17,227 | 0.68 (0.61-0.74) | 8/17,227 | 0.85 (0.69-0.99) |

## Table S6 CLD risk model for 5-year HCC discrimination in the published literature and CKB

| Model | Population | Time horizon | Development cohort | | | Published external validation cohort | | CKB | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Area | Events/total | C-index (95% CI) | Events/total | C-index (95% CI) | Events/total | C-index (95% CI) |
| **HCC** | | | | | | | | | |
| DM-HCC (all) | General | 5 | EAS | - | - | - | - | 26/15,818 | 0.68 (0.57-0.79) |
| Li-2018 (all) | General | 3 | EAS | - | - | - | - | 12/17,227 | 0.83 (0.75-0.92) |
| Li-2018 (all) | General | 5 | EAS | - | - | - | - | 28/17,227 | 0.76 (0.68-0.84) |
| Sinn-2020 | General | 5 | EAS | - | - | - | - | 28/17,227 | 0.70 (0.61-0.78) |
| Wen 1-2012 | General | 5 | EAS | - | - | - | - | 793/478,930 | 0.72 (0.70-0.74) |
| Wen 2-2012 | General | 5 | EAS | - | - | - | - | 28/17,227 | 0.70 (0.62-0.79) |
| Wen 3-2012 | General | 5 | EAS | - | - | - | - | 28/17,227 | 0.71 (0.62-0.80) |
| Cao-2021 | HBV infected | 3 | EAS | 203/110,536 | 0.73 (0.64-0.82) | - | - | 141/13,723 | 0.75 (0.72-0.79) |
| Cao-2021 | HBV infected | 5 | EAS | - | - | - | - | 250/13,723 | 0.74 (0.71-0.78) |
| DM-HCC | T2D | 5 | EAS | 36/2,364 | 0.86 (0.85-0.88) | - | - | 2/1,348 | 0.75 (0.44-0.99) |
| Li-2018 | T2D | 5 | EAS | 493/21,149 | 0.80 (0.77-0.83) | - | - | 2/1,490 | 0.99 (0.99-0.99) |

## Table S7 CLD risk model for 5-year CLD discrimination in the published literature and CKB

| Model | Population | Time horizon | Development cohort | | | Published external validation cohort | | CKB | |
|---|---|---|---|---|---|---|---|---|---|
| | | | Area | Events/total | C-index (95% CI) | Events/total | C-index (95% CI) | Events/total | C-index (95% CI) |
| **CLD** | | | | | | | | | |
| BARD | General | 5 | EUR | - | - | 232/75,303 | 0.57 (0.52-0.63) | 74/17,227 | 0.55 (0.51-0.59) |
| dAAR | General | 5 | EUR | 89/18,067 | 0.80 (0.74-0.85) | 343/126,941 | 0.74 (0.71-0.77) | 74/17,227 | 0.74 (0.68-0.81) |
| CAP-B | HBV infected | 3 | EAS | 5,781/401,745 | 0.78 (0.78-0.78) | - | - | 8/394 | 0.91 (0.83-0.98) |
| CAP-B | HBV infected | 5 | EAS | 10,278/401,745 | 0.78 (0.78-0.78) | - | - | 11/394 | 0.81 (0.67-0.94) |

**Table S8 CLD diseases and causes in high income countries and China in 2019**

| Diseases and causes | High income countries | | China | |
|---|---|---|---|---|
| | Number | Percent | Number | Percent |
| **Liver cancer (total)** | 261,313 | - | 290,373 | - |
| alcohol use | 62,969 | 24% | 25,488 | 9% |
| hepatitis B | 52,212 | 20% | 193,969 | 67% |
| hepatitis C | 118,240 | 45% | 41,078 | 14% |
| NASH | 15,984 | 6% | 12,831 | 4% |
| other causes | 11,908 | 5% | 17,007 | 6% |
| **Cirrhosis and other chronic liver diseases (total)** | 161,286,494 | - | 427,983,626 | - |
| alcohol use | 3,421,267 | 2% | 2,417,135 | 1% |
| hepatitis B | 11,557,512 | 7% | 111,315,938 | 26% |
| hepatitis C | 10,550,277 | 7% | 19,023,979 | 4% |
| NAFLD | 134,191,713 | 83% | 293,409,373 | 69% |
| other causes | 1,565,725 | 1% | 1,817,200 | 0% |

**Table S9 Risk factors for CLD in CKB and Western populations**

| Risk factors | CKB liver cancer | CKB cirrhosis | CUP liver cancer |
|---|---|---|---|
| Alcohol per 10 g/day | 1.11 (1.07-1.14)[3] | 1.18 (1.14-1.22)[4] | 1.04 (1.02-1.06) |
| BMI per 5 kg/m$^2$ | 1.05 (0.94-1.15)[5] | - | 1.30 (1.16-1.46) |
| Diabetes | 1.49 (1.30-1.70)[6] | 1.81 (1.57-2.09) | - |
| Physical activity | 0.81 (0.71-0.93) | 0.76 (0.66-0.88) | 0.54 (0.23-1.29) |
| Smoking | 1.29 (1.16-1.42)[7] | 1.08 (0.95-1.23) | - |

## Table S10 Summary of Liver Cancer Screening Strategies

| | EASL[8] | AASLD[9] | China screening strategy[10] |
|---|---|---|---|
| **Population** | 1. Cirrhotic patients, Child-Pugh stage A and B<br>2. Cirrhotic patients, Child-Pugh stage C awaiting liver transplantation<br>3. Non-cirrhotic HBV patients at intermediate or high risk of HCC[a] (according to PAGE-B[b] classes for Caucasian subjects, respectively 10-17 and ≥18 score points)<br>4. Non-cirrhotic F3 patients, regardless of aetiology may be considered for surveillance based on an individual risk assessment | 1. Child-Pugh A-B cirrhosis, any etiology<br>-Hepatitis B<br>-Hepatitis C (viremic or post-SVR)<br>-Alcohol associated cirrhosis<br>-Nonalcoholic steatohepatitis<br>-Other etiologies<br>2. Child-Pugh C cirrhosis, transplant candidate<br>3. Non-cirrhotic chronic hepatitis B<br>-Man from endemic country[c] age >40 years<br>-Woman from endemic country[c] age >50 years<br>-Person from Africa at earlier age[d]<br>-Family history of HCC<br>-PAGE-B score ≥10 | Males aged 45-74 and females aged 50-74 who meet at least one of the following criteria:<br>1. Positive Hepatitis B surface antigen (HBsAg)<br>2. History of HCV infection<br>3. History of liver cirrhosis<br>4. A first-degree/second-degree relative with a history of liver cancer |
| **Method** | Abdominal ultrasound | Ultrasound and AFP | Serum alpha-fetoprotein (AFP) test and abdominal ultrasound |
| **Frequency** | Every six months | Every six months | |

a Patients at low HCC risk left untreated for HBV and without regular six months surveillance must be reassessed at least yearly to verify progression of HCC risk.
b PAGE-B (Platelet, Age, Gender, hepatitis B) score is based on decade of age(16-29=0, 30-39=2, 40-49=4, 50-59=6, 60-69=8, ≥70=10), gender(M=6, F=0) and platelet count (≥200,000/ll=0, 100,000-199,999/ll=1, <100,000/ll=2): a total sum of ≤9 is considered at low risk of HCC(almost 0% HCC at five years) a score of 10-17 at intermediate risk(3% incidence HCC at five years) and ≥18 is at high risk(17% HCC at five years).
c Endemic country as defined by AASLD hepatitis B virus guidance.
d Surveillance can be initiated as early as third decade of life given median age 46 years at HCC diagnosis.
e Other risk calculators can be considered, although PAGE-B has been validated in Western populations on antiviral therapy.
EASL: European Association for the Study of the Liver; AASLD: American Association for the Study of Liver Diseases

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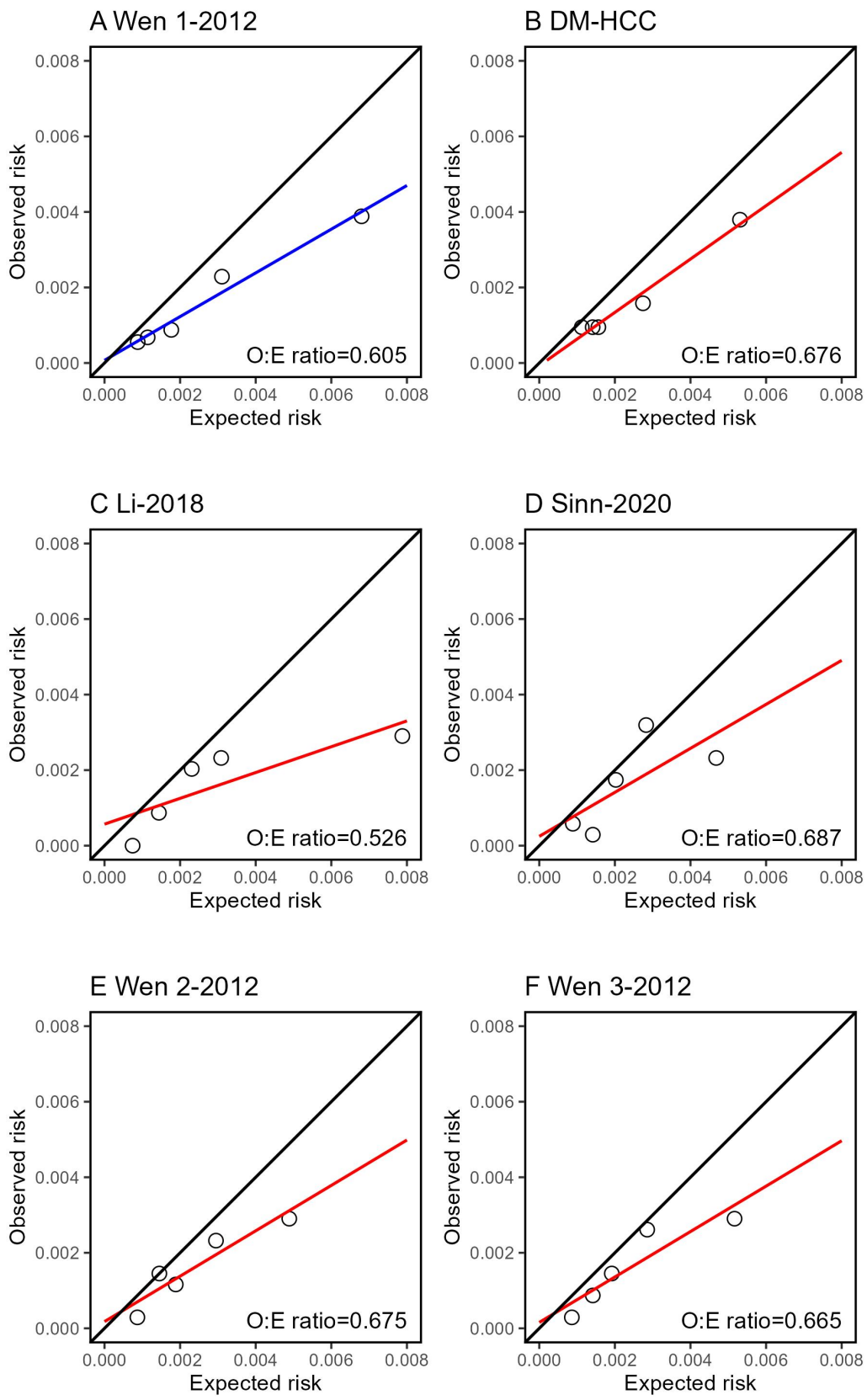
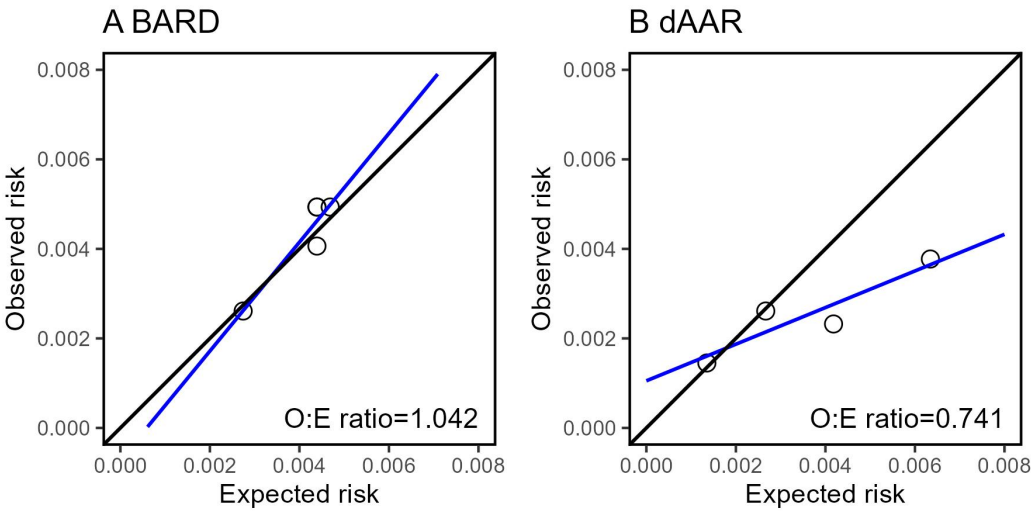
**Fig. S1 Calibration plots of 5-year HCC risk prediction models in the CKB**

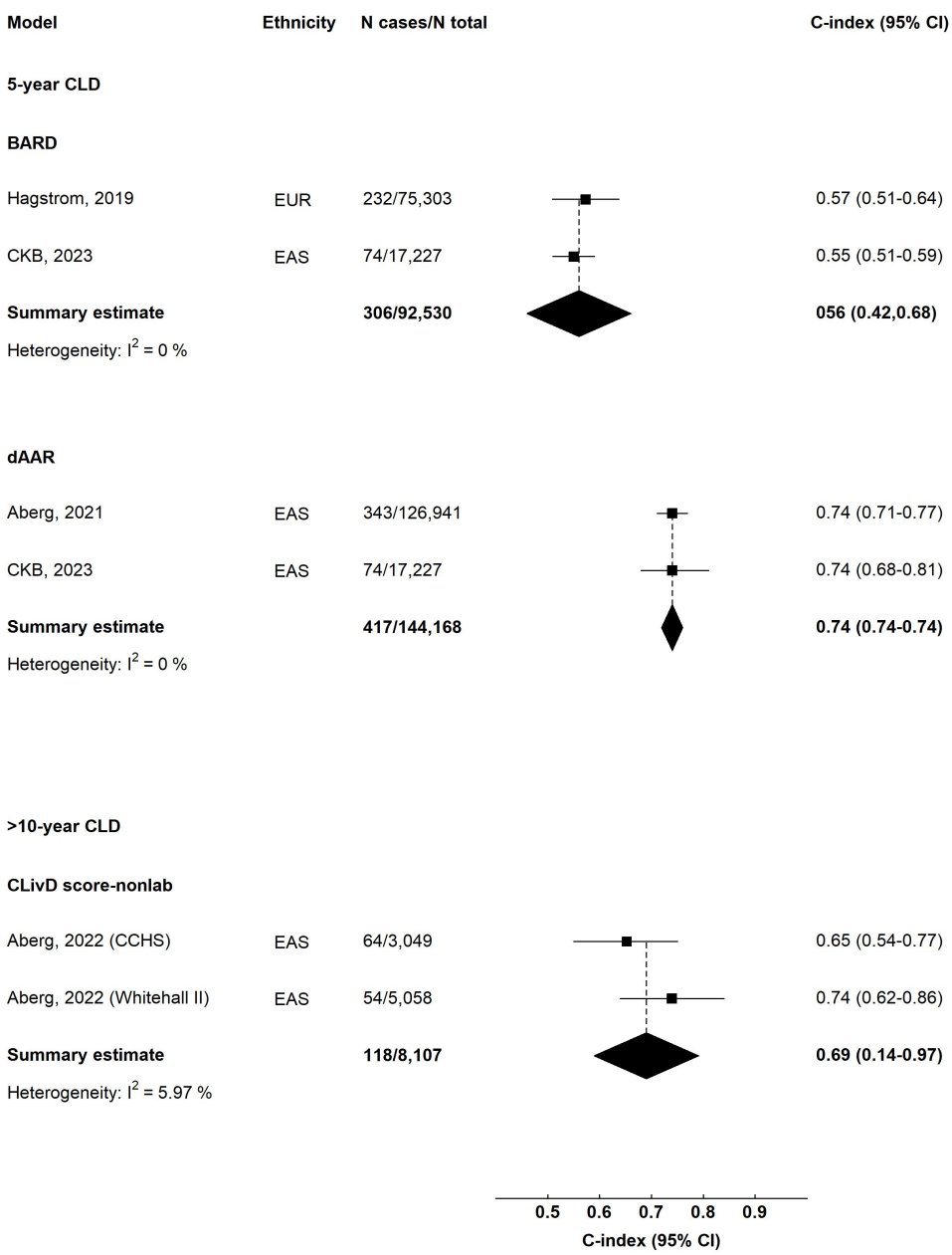



Blue color represents models with non-lab predictors, while red color indicates models that include lab predictors.

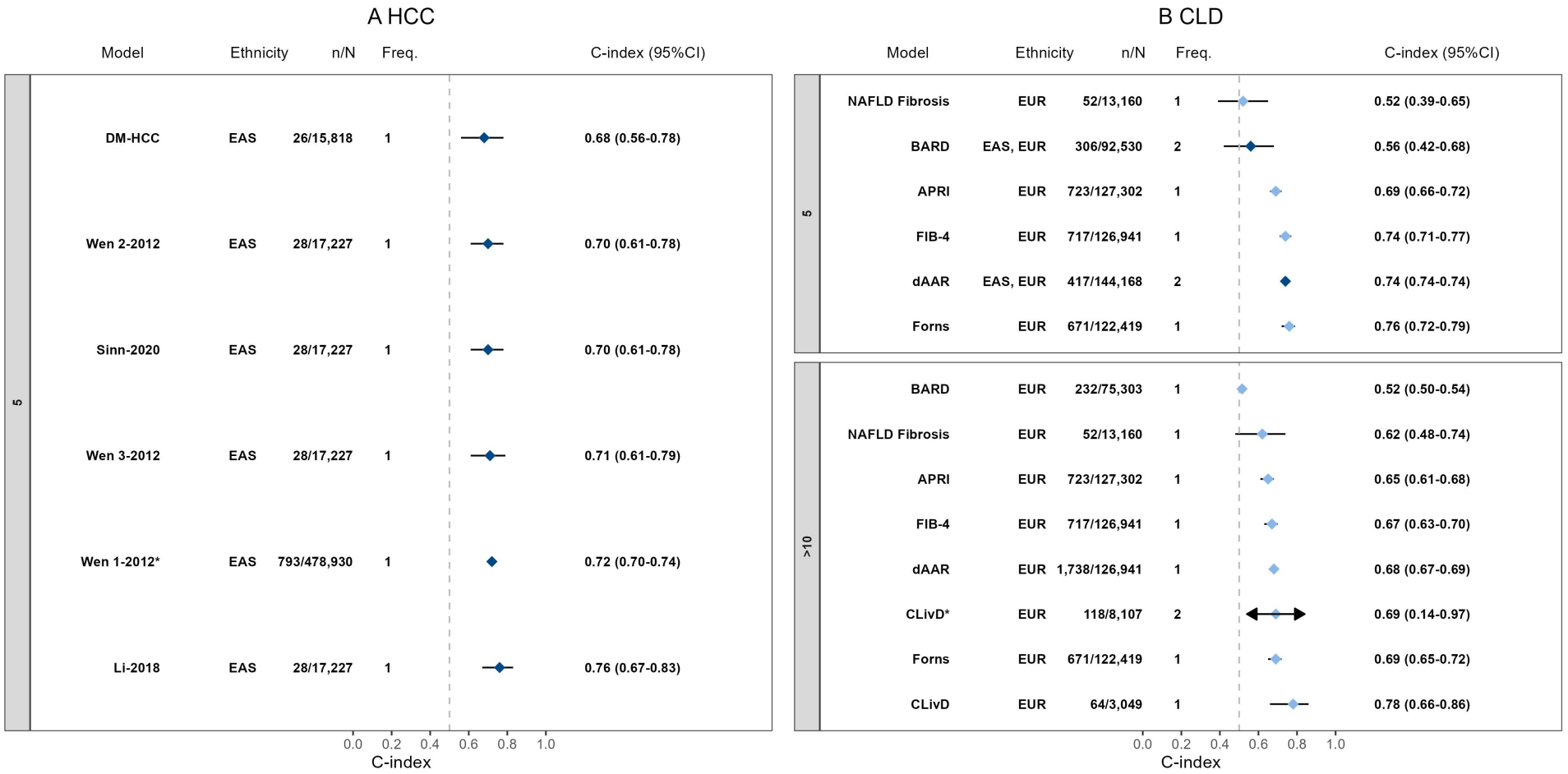
**Fig. S2 Calibration plots of 5-year CLD risk prediction models in the CKB**



## Fig. S3 Discrimination of CLD risk prediction models in the published literature and CKB

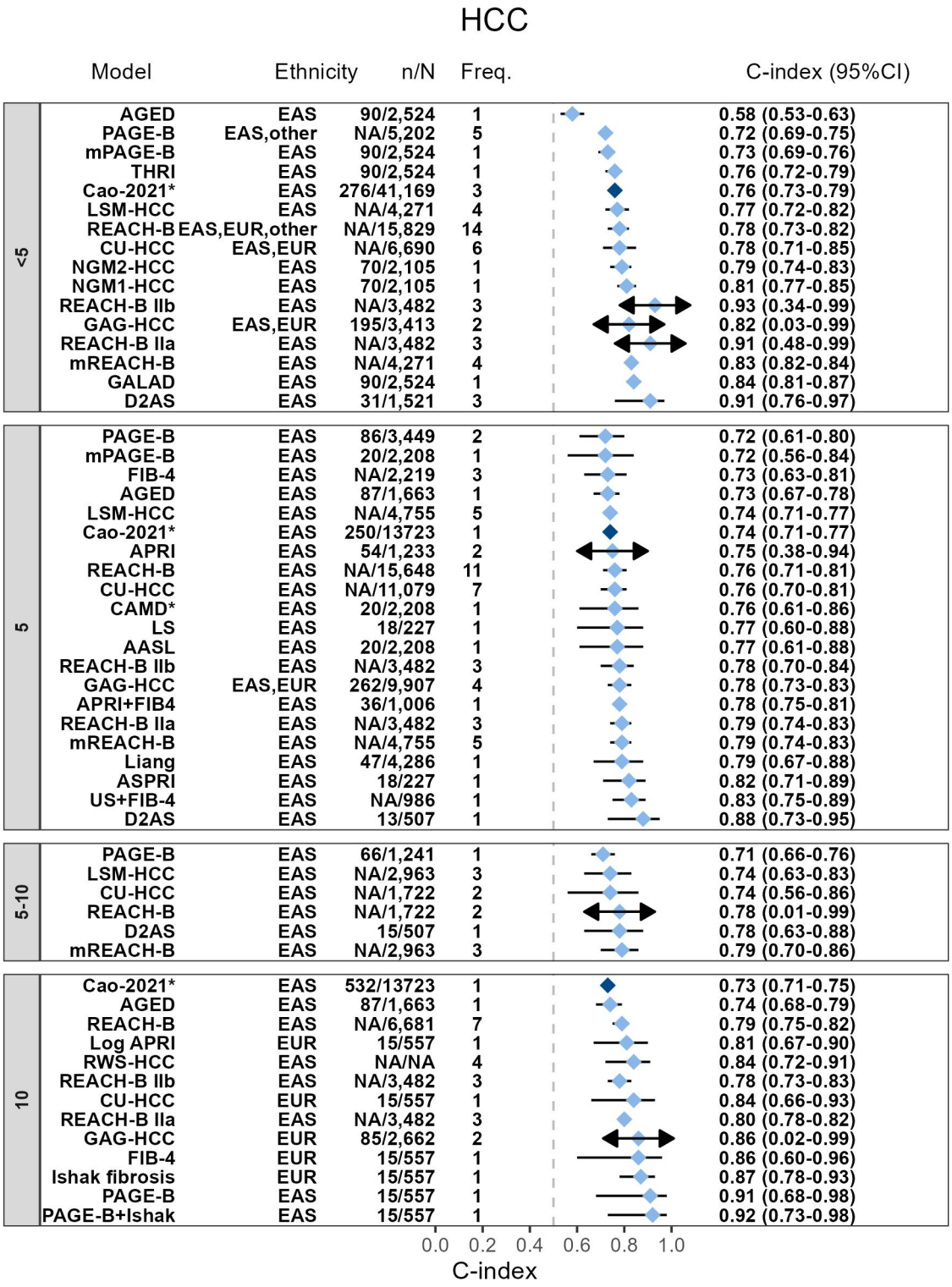


## Fig. S4 Discrimination of HCC risk prediction models in the general population



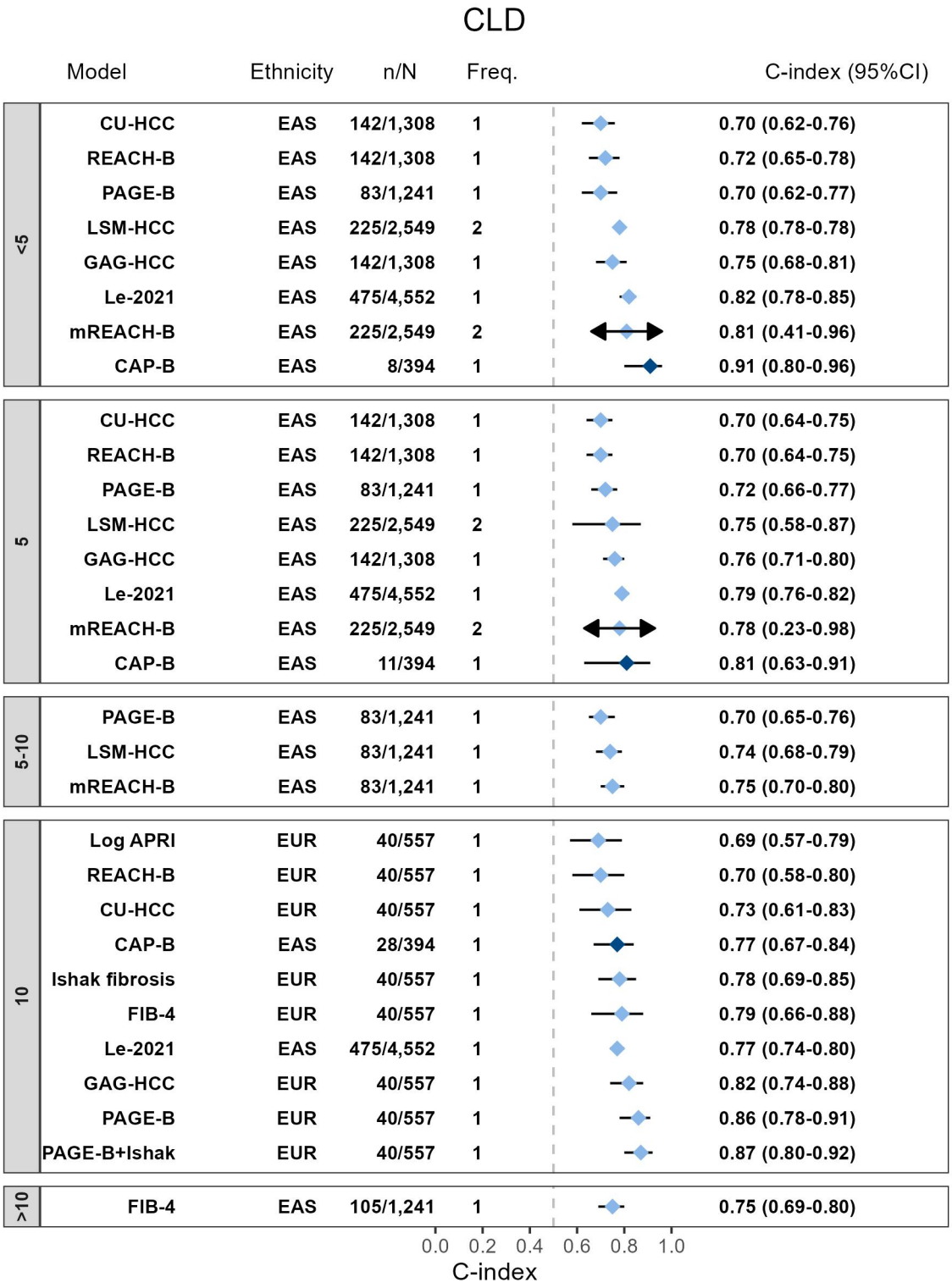

An asterisk (*) represents a predictive model comprising all non-lab predictors. Dark blue color denotes models externally validated in CKB, while light blue color represents models not externally validated in CKB. "Ethnicity" represents the development population, and "Freq." represents the model's external validation frequency. The REAL-B model was not included due to the population being post-treatment or intervention liver disease patients.

**Fig. S5 Discrimination of HCC risk prediction models in the HBV infected individuals**



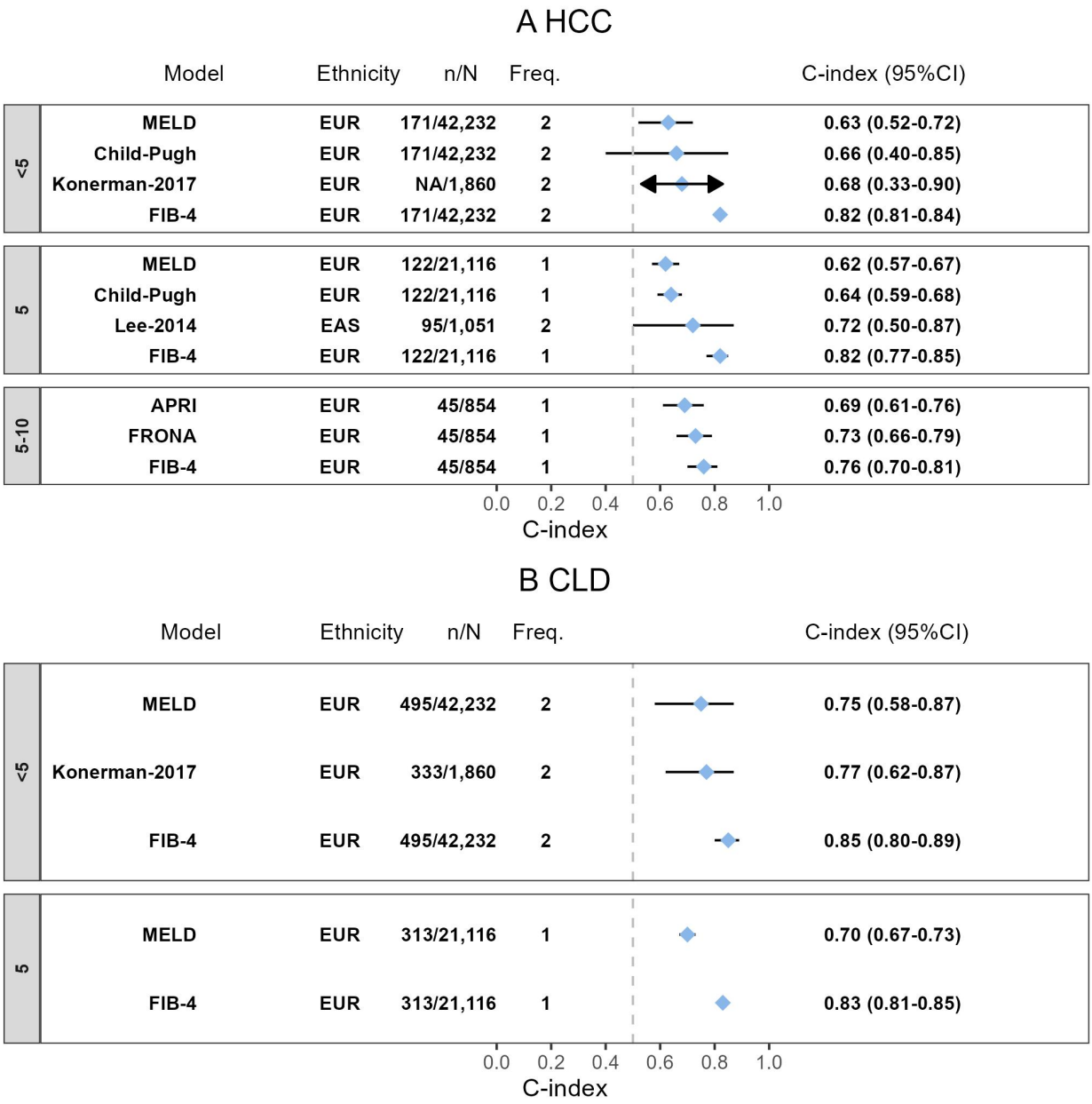

An asterisk (*) represents a predictive model comprising all non-lab predictors. Dark blue color denotes models externally validated in CKB, while light blue color represents models not externally validated in CKB. "Ethnicity" represents the development population, and "Freq." represents the model's external validation frequency. The REAL-B model was not included due to the population being post-treatment or intervention liver disease patients.

**Fig. S6 Discrimination of CLD risk prediction models in the HBV infected individuals**



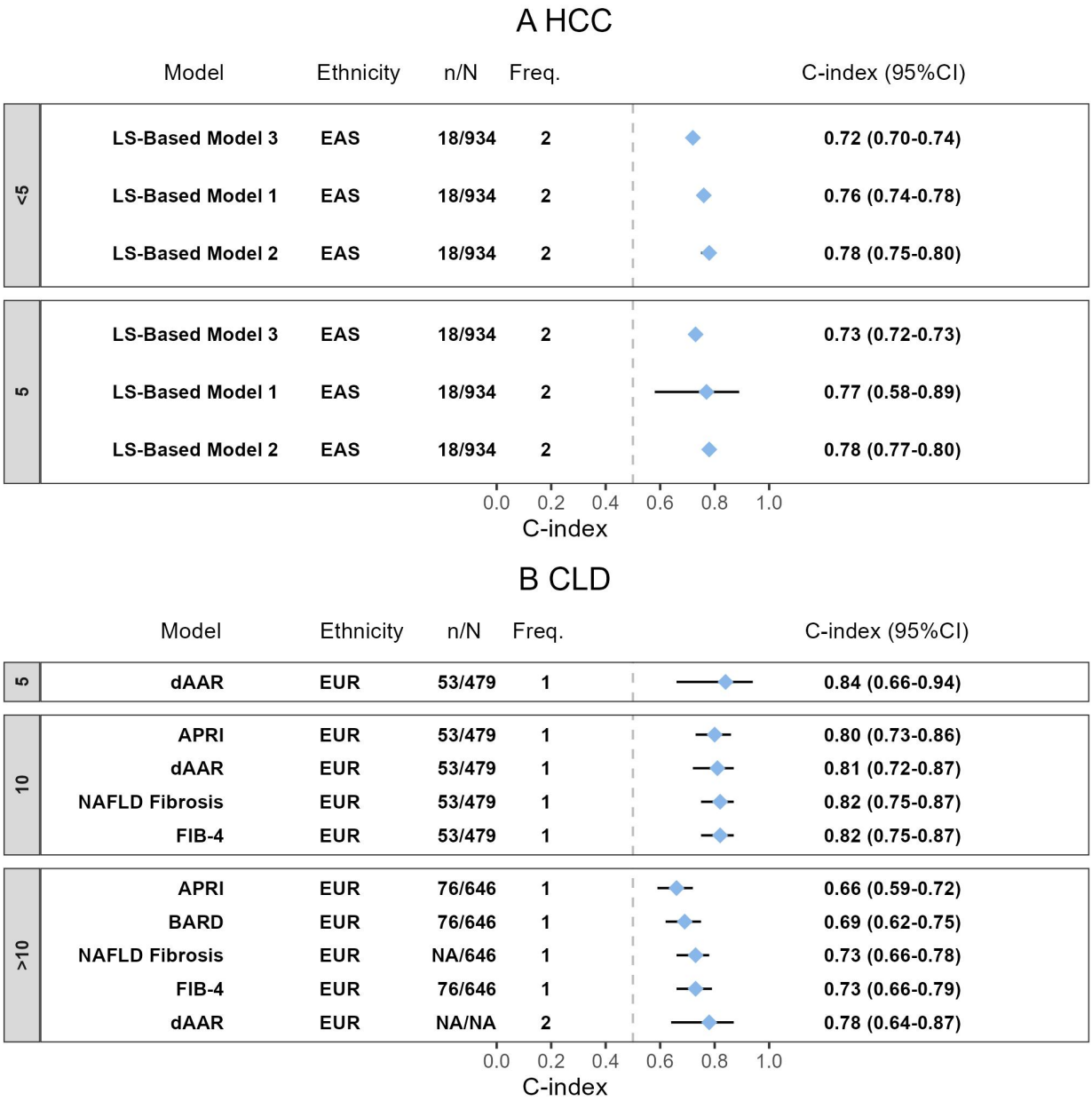

An asterisk (*) represents a predictive model comprising all non-lab predictors. Dark blue color denotes models externally validated in CKB, while light blue color represents models not externally validated in CKB. "Ethnicity" represents the development population, and "Freq." represents the model's external validation frequency. The REAL-B model was not included due to the population being post-treatment or intervention liver disease patients.

**Fig. S7 Discrimination of CLD risk prediction models in the HCV infected individuals**




An asterisk (*) represents a predictive model comprising all non-lab predictors. Dark blue color denotes models externally validated in CKB, while light blue color represents models not externally validated in CKB. "Ethnicity" represents the development population, and "Freq." represents the model's external validation frequency. The REAL-B model was not included due to the population being post-treatment or intervention liver disease patients.

## Fig. S8 Discrimination of CLD risk prediction models in the NAFLD patients




An asterisk (*) represents a predictive model comprising all non-lab predictors. Dark blue color denotes models externally validated in CKB, while light blue color represents models not externally validated in CKB. "Ethnicity" represents the development population, and "Freq." represents the model's external validation frequency. The REAL-B model was not included due to the population being post-treatment or intervention liver disease patients.