


# BMJ Open Nomogram to predict risk of incident chronic kidney disease in high-risk population of cardiovascular disease in China: community-based cohort study

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## ABSTRACT

**Aims** To develop a nomogram for incident chronic kidney disease (CKD) risk evaluation among community residents with high cardiovascular disease (CVD) risk.

**Methods** In this retrospective cohort study, 5730 non-CKD residents with high CVD risk participating the National Basic Public Health Service between January 2015 and December 2020 in Guangzhou were included. Endpoint was incident CKD defined as an estimated glomerular filtration rate (eGFR) less than 60 mL/min/1.73 m<sup>2</sup> during the follow-up period. The entire cohorts were randomly (2:1) assigned to a development cohort and a validation cohort. Predictors of incident CKD were selected by multivariable Cox regression and stepwise approach. A nomogram based on these predictors was developed and evaluated with concordance index (C-index) and area under curve (AUC).

**Results** During the median follow-up period of 4.22 years, the incidence of CKD was 19.09% (n=1094) in the entire cohort, 19.03% (727 patients) in the development cohort and 19.21% (367 patients) in the validation cohort. Age, body mass index, eGFR 60–89 mL/min/1.73 m<sup>2</sup>, diabetes and hypertension were selected as predictors. The nomogram demonstrated a good discriminative power with C-index of 0.778 and 0.785 in the development and validation cohort. The 3-year, 4-year and 5-year AUCs were 0.817, 0.814 and 0.834 in the development cohort, and 0.830, 0.847 and 0.839 in the validation cohort.

**Conclusion** Our nomogram based on five readily available predictors is a reliable tool to identify high-CVD risk patients at risk of incident CKD. This prediction model may help improving the healthcare strategies in primary care.

## INTRODUCTION

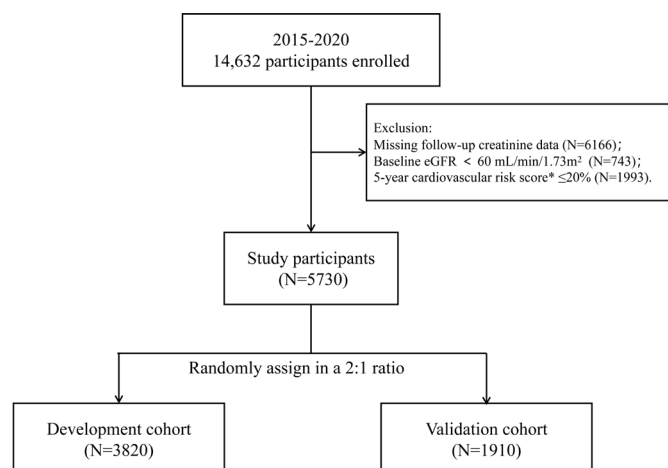
Chronic kidney disease (CKD) is a global burden with more than 5 million people die of it annually by 2040.<sup>1</sup> Generally, CKD is particularly challenging to tackle because it is often asymptomatic.<sup>2</sup> As such, CKD is often diagnosed late, and the global burden of CKD continues to be underappreciated.<sup>3</sup> In addition, like as hypertension and diabetes, CKD is an independent risk factor for

## Strengths and limitations of this study

- This study developed a simple nomogram for the prediction of 3-year, 4-year or 5-year risk of incident chronic kidney disease (CKD) in a cohort of primary health annual examination of high cardiovascular disease risk population.
- The nomogram with good discriminative power enables us to identify patients at high risk of CKD readily.
- The risk stratification of CKD based on nomogram had a good distinguish power.
- This study was based on data from a single centre.
- External validation is needed before clinical expansion.

cardiovascular disease (CVD) and all-cause mortality.<sup>4</sup> The ability to identify the individuals at risk of incident CKD may decrease the incidence of CVD. On the other hand, high CVD risk populations are often need to take medicines for multiple comorbidities, such as blood pressure (BP) lowering drugs, antidiabetic drugs or antithrombotic agents, these drugs may increase the burden on the kidney. Therefore, for these persons, early identify the high-risk CKD individuals is of great significance to guide prevention and treatment.

Risk predict tool to identify the individuals at high risk of incident CKD may help improving primary care for CKD.<sup>5–8</sup> However, the primary healthcare system is often faced challenges include insufficient medical staff, inadequate government funding and high intensity work.<sup>9</sup> Besides of improving the chronic disease management methods,<sup>10</sup> using the conventional data in the medical system to build a CKD risk prediction model is operable, convenient and acceptable. And then, through healthy education, dietary



**Figure 1** Flow chart of study design and participants. \*Cardiovascular risk assessment methods according to Thomas a Gaziano *et al.* eGFR, estimated glomerular filtration rate.

modification,<sup>11 12</sup> individualised medication<sup>13</sup> and a comprehensive approach to prevent CKD,<sup>7</sup> which may reduce the risk of cardiovascular events in high-risk population of CVD. In this study, data from a south Chinese high CVD risk population were used to develop and evaluate risk prediction nomogram for CKD.

## METHODS

### Participants

A retrospective cohort study was conducted among participants of National Basic Public Health Service Project of China in Guangzhou, Guangdong between January 2015 and December 2020. To participate in this national project, one must be elderly adults (aged  $\geq 65$  years) or aged  $\geq 35$  years complicating diabetes or hypertension. For this current analysis, we included patients with 5-year cardiovascular risk score  $>20\%$  according to the assessment methods build by Gaziano *et al.*<sup>14</sup> Patients from the national project would be excluded from the current study if they met the following exclusion criteria: (1) pre-existing CKD and (2) missing follow-up creatinine data. All eligible participants were followed up every 1 year after enrolment until December 2020. All included participants were randomly assigned to a development cohort and a validation cohort in a 2:1 ratio (figure 1). The development cohort was used to establish the prediction model, and the validation cohort was used for validation of the nomogram.

### Definitions

CKD was defined as estimated glomerular filtration rate (eGFR)  $<60$  mL/min/ $1.73$  m<sup>2</sup>.<sup>15</sup> The Modification of Diet in Renal Disease equation was used to calculate eGFR.<sup>16</sup> Serum creatinine was measured by enzymatic method. Diabetes mellitus (DM) was defined as random blood glucose level  $\geq 11.1$  mmol/L or fasting plasma glucose level  $\geq 7.0$  mmol/L or haemoglobin A1c  $\geq 6.5\%$ . The BP

measurements were taken using Omron upper arm electronic sphygmomanometer after 5 min rest. Hypertension was defined as systolic BP (SBP)  $\geq 140$  mm Hg, diastolic BP  $\geq 90$  mm Hg and/or use of antihypertensive medications. Body mass index (BMI) was defined as weight in kilograms divided by the square of height in metres. Smoking was classified as ever smoking vs never smoking. Exercise was divided into five categories according the frequency: never, once a week, few times a week and daily.

### Endpoint

The endpoint of this study was incident CKD, defined as incident eGFR  $<60$  mL/min/ $1.73$  m<sup>2</sup> during follow-up period. And participants without CKD events during the whole follow-up period were defined as CKD-free. All eligible participants were followed up every 1 year after enrolment until December 2020.

### Patient and public involvement

The study was an retrospective cohort study. Demographic characteristics, history, physical examination, laboratory test results, examination results, medication history, life style were obtained from the regional chronic disease management platform of Zengcheng District of Guangzhou for all included patients. And we thanks all participants for their valuable contribution.

### Sample size calculation and statistical analysis

#### Determination of minimum sample size

Use pmsampsize package of R<sup>17 18</sup> to calculate the minimum sample size required for developing a multi-variable prediction model with a survival outcome using five candidate predictors. We know an existing prediction model-Chien equation in the same field has an area under the curve (AUC) value of 0.765,<sup>19</sup> so we selected the related predicted value of R<sup>2</sup>D from table 1 in the work of Jinks *et al.*<sup>20</sup> according to this AUC. The mean follow-up of the entire cohort was 3.51 years, and overall event rate was 0.1909. We select a timepoint of interest for prediction using the newly developed model of 5 years. Therefore, the events per candidate predictor parameter was 12.2. In the development cohort, the minimum sample size required 640 participants. And because of the proportion of development cohort and validation group is 2:1, so the validation cohort need at least 320 participants.

### Statistical analysis

Continuous variables were compared with an unpaired, two-tailed t-test and are expressed as the mean $\pm$ SD or were compared through the Wilcoxon rank-sum test and are expressed as the median  $\pm$ IQR. Categorical variables were compared using the  $\chi^2$  test or Fisher's exact test and are expressed as percentages. And Restricted cubic spline was used to do nonlinear correlation analysis for the risk of CKD over the range of continuous variables.

To build the prediction model, the entire cohort were randomly assigned to a development cohort and a validation cohort in a 2:1 ratio. The development cohort was used to establish the prediction model, and the validation

**Table 1** Baseline characteristics of participants with and without follow-up chronic kidney disease (CKD) in the development cohort

	Missing data (%)	No CKD (n=3093)	CKD (n=727)	P value
Age (years)	0 (0.00)	68.18±6.26	70.71±7.07	<0.001
Female, n (%)	0 (0.00)	1646 (53.2)	430 (59.1)	0.004
Weight (kg)	3 (0.08)	60.46±10.37	61.00±10.24	0.204
BMI (kg/m <sup>2</sup> )	3 (0.08)	24.58±3.59	25.16±3.54	<0.001
Waist (cm)	0 (0.00)	85.55±9.27	87.07±9.07	<0.001
SBP (mm Hg)	4 (0.10)	149.67±19.35	152.60±20.92	<0.001
DBP (mm Hg)	4 (0.10)	82.94±11.12	82.52±11.67	0.366
Diabetes mellitus, n (%)	123 (3.22)	730 (24.5)	218 (30.2)	0.002
Hypertension, n (%)	0 (0.00)	2454 (79.3)	634 (87.2)	<0.001
Ever smoking, n (%)	0 (0.00)	756 (24.4)	135 (18.6)	0.001
Ever drinking, n (%)	0 (0.00)	493 (15.9)	88 (12.1)	0.011
Exercise	3 (0.08)			<0.001
Never, n (%)		1374 (44.5)	373 (51.3)	
Once a week, n (%)		460 (14.9)	117 (16.1)	
Few times a week, n (%)		148 (4.8)	44 (6.1)	
Daily, n (%)		1108 (35.9)	193 (26.5)	
<b>Laboratory examination</b>				
RCC (×10 <sup>12</sup> /L)	61 (1.60)	4.69 (4.38, 5.07)	4.59 (4.30, 4.97)	<0.001
Haemoglobin (g/L)	40 (1.05)	138.00 (129.00, 147.00)	136.00 (128.00, 146.00)	0.006
WCC (×10 <sup>9</sup> /L)	16 (0.42)	6.60 (5.66, 7.75)	6.90 (5.92, 8.10)	<0.001
PLT (×10 <sup>9</sup> /L)	87 (2.28)	212.00 (178.00, 253.00)	208.00 (175.00, 248.00)	0.025
ALT (U/L)	8 (0.21)	22.20 (17.30, 30.20)	23.10 (17.30, 32.10)	0.067
Fasting glucose (mmol/L)	2 (0.05)	4.94 (4.43, 5.70)	4.97 (4.46, 5.78)	0.306
Cholesterol (mmol/L)	2 (0.05)	5.37 (4.62, 6.17)	5.31 (4.65, 6.06)	0.423
Triglyceride (mmol/L)	4 (0.10)	1.42 (0.99, 2.10)	1.62 (1.08, 2.30)	<0.001
Uric acid (umol/L)	860 (22.51)	365.90 (302.65, 436.25)	407.90 (332.10, 477.40)	<0.001
BUN (mmol/L)	18 (0.47)	5.22 (4.50, 6.19)	5.80 (5.00, 6.60)	<0.001
Scr (umol/L)	0 (0.00)	64.10 (54.20, 76.34)	76.21 (64.80, 89.80)	<0.001
eGFR (mL/min/1.73 m <sup>2</sup> )	0 (0.00)	96.66 (83.79, 113.43)	75.94 (68.04, 89.35)	<0.001
eGFR 60–89 (mL/min/1.73 m <sup>2</sup> )	0 (0.00)	1143 (37.0)	550 (75.7)	<0.001
<b>Medications</b>				
Antihypertension drugs	0 (0.00)			0.136
Yes, n (%)		700 (22.6)	184 (25.3)	
No, n (%)		2393 (77.4)	543 (74.7)	
<b>Classifications</b>				
ACEI/ARB, n (%)		239 (8.2)	59 (8.7)	0.679
CCB, n (%)		303 (10.3)	81 (12.0)	0.237
β-blocker, n (%)		87 (3.0)	24 (3.6)	0.504
Diuretics, n (%)		21 (0.7)	5 (0.7)	1
Other antihypertension drugs, n (%)		203 (6.6)	56 (7.7)	0.309
Antidiabetic drugs	0 (0.00)			0.190
Yes, n (%)		245 (7.9)	69 (9.5)	
No, n (%)		2848 (92.1)	658 (90.5)	

ACEI, ACE inhibitor; ALT, alanine aminotransferase; ARB, angiotensin II receptor blockers; BMI, body mass index; BUN, blood urea nitrogen; CCB, calcium channel blocker; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; PLT, platelet; RCC, red cell count; SBP, systolic blood pressure; Scr, serum creatinine; WCC, white cell count.

cohort was used for validation of the nomogram. Candidate variables that were imbalanced between groups in the development cohort or that are clinically important were included in the univariable Cox regression analysis. Variables with >10% missing values were not considered candidates. Significant variables from the univariable Cox regression analysis were then included in the multivariable Cox regression analysis. A backward stepwise approach was performed to screen the variables by successively removal of nonsignificant ( $p > 0.05$ ) covariates until all the remaining variables were statistically significant. Then, we manually investigated the contribution of the remaining variables to determine the final predictors according to previous reports and clinical meaning of these variables. A nomogram was then formulated based on the filtered variables and by using the rms package of R. To form the nomogram, each regression coefficient in the multivariable Cox regression was proportionally converted into a 0–100 point scale. The variable with the highest  $\beta$  coefficient (absolute value) was assigned 100 points. The points are added across each variable to calculate the total points, which are finally converted to predicted probabilities. And the individual point of each subject in the validation cohort was calculated by using the nomogram established by the development cohorts. Finally, the total point was used to predict and verify its CKD risk.

The nomogram was evaluated in both the development and validation cohorts. Discriminative ability was assessed using the concordance index (C-index) and the AUC time-dependent receiver operating characteristic curve. Calibration was assessed using a bootstrap approach with 1000 resamples to compare the predicted CKD-free with the CKD-free observed in the study. Missing data were not imputed. And multivariable Fine-Gray model was used to test the sensitivity of predictors included in the multivariable Cox regression model. In all analyses, a  $p < 0.05$  was considered statistically significant. All analyses were conducted with R software (V.4.0.3; R Foundation for Statistical Computing, Vienna, Austria) and SPSS (V.26.0).

## RESULTS

### Population characteristics

A total of 5730 high CVD risk populations were categorised into the development ( $n=3820$ ) and the validation cohort ( $n=1910$ ). The baseline characteristics of the entire cohort are listed in online supplemental table 1. In the entire cohort, the mean age was  $68.64 \pm 6.49$  years, and the median eGFR was  $92.95 \text{ mL/min/1.73 m}^2$ . No significant differences were identified between the development and validation cohorts.

Within the development cohort, participants who developed CKD tended to be older, BMI and waistline were more than those who are free of CKD. As for laboratory examinations, lower eGFR and blood platelet and higher uric acid and triglyceride were found among

those developing CKD. Patients developing CKD during the follow-up period were also more likely to have hypertension and diabetes, whereas they were less likely to be ever smokers or drinkers. And adjusted spline plots for the risk of CKD over the range of eGFR (online supplemental figure 1) shown that when eGFR lightly declined to  $60\text{--}89 \text{ mL/min/1.73 m}^2$ , the risk of incident CKD was significantly increased, and the non-linear value was 55.6 ( $p < 0.001$ ). Therefore, continuous variable eGFR was changed into binary categorisation variable (eGFR  $60\text{--}89 \text{ mL/min/1.73 m}^2$  vs eGFR  $\geq 90 \text{ mL/min/1.73 m}^2$ ).

During the median follow-up period of 4.22 years, the incidence of incident CKD was 19.09% ( $n=1094$ ) in the entire cohort, 19.03% ( $n=727$ ) in the development cohort and 19.21% ( $n=367$ ) in the validation cohort. In the entire cohort, 23 (0.4%) death occurred during the follow-up period, among which 7 patients died after developing CKD and 16 patients died without developing CKD. The main causes of death were stroke (26.09%), myocardial infarction (21.74%), cardiac death (except myocardial infarction) (13.04%), pulmonary death (13.04%), malignant tumour (8.70%), septic shock (4.35%) and unexplained death (13.04%). In order to avoid the competitive risk caused by death, we conducted the multivariable Fine-Gray test for the included predictors.

### Development of the incident CKD-predicting nomogram

The results of univariable COX regression analysis are detailed in table 2. Through multivariable COX regression analysis and a backward stepwise approach, age (HR: 1.07, 95% CI: 1.06 to 1.08), BMI (HR: 1.04, 95% CI: 1.02 to 1.06), eGFR  $60\text{--}89 \text{ mL/min/1.73 m}^2$  (HR: 5.59, 95% CI: 4.70 to 6.65), diabetes (HR: 1.63, 95% CI: 1.38 to 1.91) and hypertension (HR: 1.40, 95% CI: 1.13 to 1.75) were selected as predictors of incident CKD (table 2). In the Fine-Gray test, variables of the nomogram were also demonstrated to be the risk factors, The HRs of these predictors were 1.06, 1.03, 5.40, 1.48, 1.84, respectively (online supplemental table 3). The nomogram for predicting 3-year, 4-year and 5-year CKD risk was then built based on these five variables (figure 2).

### Validation of the incident CKD-predicting nomogram

In both cohorts, the nomogram demonstrated a good discriminative power with C-index of 0.778 in the development cohort and 0.785 in the validation cohort. The 3-year, 4-year and 5-year AUCs in the development cohort were 0.817, 0.814 and 0.834, respectively. The 3-year, 4-year and 5-year AUCs were 0.830, 0.847 and 0.839 in the validation cohort (figure 3).

The calibration plots for the 3-year, 4-year and 5-year CKD indicated that there was good agreement between the actual observations and predictions made using the nomogram in both the development cohort and the validation cohort (figure 4).



**Table 2** Univariable and multivariable Cox regression analysis of predictors of chronic kidney disease

Variables	Univariable Cox analysis		Multivariable Cox analysis	
	HR (95% CI)	P value	HR (95% CI)	P value
Age (years)	1.07 (1.06 to 1.08)	<0.001	1.06 (1.05 to 1.07)	<0.001
BMI (kg/m <sup>2</sup> )	1.04 (1.02 to 1.06)	<0.001	1.02 (1.00 to 1.05)	0.02
Diabetes mellitus	1.27 (1.08 to 1.49)	<0.01	1.63 (1.38 to 1.91)	<0.001
Hypertension	1.99 (1.57 to 2.53)	<0.001	1.40 (1.13 to 1.75)	0.003
eGFR 60–89 mL/min/1.73 m <sup>2</sup>	5.95 (5.02 to 7.06)	<0.001	5.59 (4.70 to 6.65)	<0.001
Female, (%)	1.33 (1.14 to 1.54)	<0.001		
Waist (cm)	1.02 (1.01 to 1.03)	<0.001		
SBP (mm Hg)	1.01 (1.00 to 1.01)	<0.001		
Ever smoking	0.70 (0.58 to 0.85)	<0.001		
Ever drinking	0.83 (0.67 to 1.05)	0.127		
Exercise				
Never	Reference			
Once a week	0.97 (0.80 to 1.20)	0.81		
Few times a week	1.05 (0.76 to 1.46)	0.76		
Daily	1.17 (0.99 to 1.39)	0.069		
RCC (×10 <sup>12</sup> /L)	0.61 (0.53 to 0.71)	<0.001		
Haemoglobin (g/L)	0.99 (0.98 to 0.99)	<0.001		
WCC (×10 <sup>9</sup> /L)	1.05 (1.01 to 1.10)	0.014		
PLT (×10 <sup>9</sup> /L)	1.00 (1.00 to 1.00)	0.722		
ALT (U/L)	1.00 (0.99 to 1.00)	0.322		
BUN (mmol/L)	1.00 (1.00 to 1.01)	0.855		
Triglyceride (mmol/L)	1.12 (1.06 to 1.19)	<0.001		

ALT, alanine aminotransferase; BMI, body mass index; BUN, blood urea nitrogen; eGFR, estimated glomerular filtration rate; PLT, platelet; RCC, red cell count; SBP, systolic blood pressure; WCC, white cell count.

### Risk evaluation of incident CKD based on the nomogram scores

Based on the predicted 3-year, 4-year and 5-year incidence of CKD in relation to different total nomogram scores, we further divided the participants into two score categories based on the median value of total points calculated by the nomogram: low-risk group (scores < 106, 3-year risk = 3.14%, 4-year risk = 5.23%, 5-year risk = 9.51%), high-risk group (scores ≥ 106, 3-year risk = 18.49%, 4-year risk = 28.79%, 5-year risk = 45.84%). The predicted rates of CKD in the validation cohort were closed to those in the development cohort inside each of the three risk groups (figure 5). And Kaplan-Meier curves of incident CKD for patients in the low-risk and high-risk groups shown that this risk classification system had a good discriminative power, the incidence of CKD was significantly increased in the high-risk group (HR: 6.33,  $p < 0.001$ ) (online supplemental figure 2).

### DISCUSSION

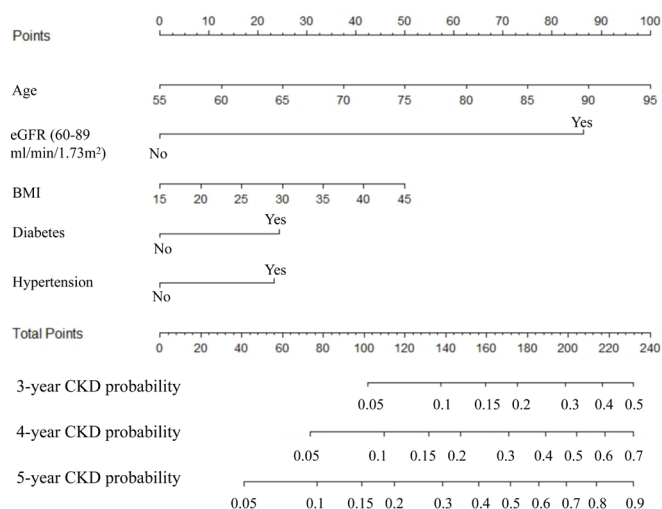
This study developed a simple nomogram for the prediction of 3-year, 4-year or 5-year risk of incident CKD in a cohort of high CVD risk population. Using the

demographic, clinical and laboratory variables from electronic health records, our visualised nomogram with only five variables (age, BMI, eGFR, diabetes and hypertension) demonstrated good discriminative power, which enables us to identify patients at high risk of incident CKD readily.

CKD has long been proven a strong cardiovascular risk factor.<sup>21</sup> Since Professor Bright established the concept of ‘renal origin of CVD’ which means renal disease is the primary disorder and cardiovascular changes are secondary.<sup>22</sup> Many studies have confirmed and extended this association.<sup>4 22 23</sup> Therefore, it is urgent to identify high CVD risk individuals who are at risk of developing CKD. Once identified individuals at risk of incident CKD, besides of conducting strategies to prevent diabetes, hypertension and obesity,<sup>7</sup> type and dose of potentially nephrotoxic medications (such as non-steroidal anti-inflammatory drugs) should be taken with care.<sup>24</sup>

Several risk prediction models for incident CKD have been developed in various population.<sup>19 24–37</sup> O’Seaghdha *et al* equation<sup>26</sup> made a risk score based on three models for CKD prediction among the general population, and the c-statistic is 0.786, 0.812 and 0.813, respectively.

### Risk prediction model for incident CKD

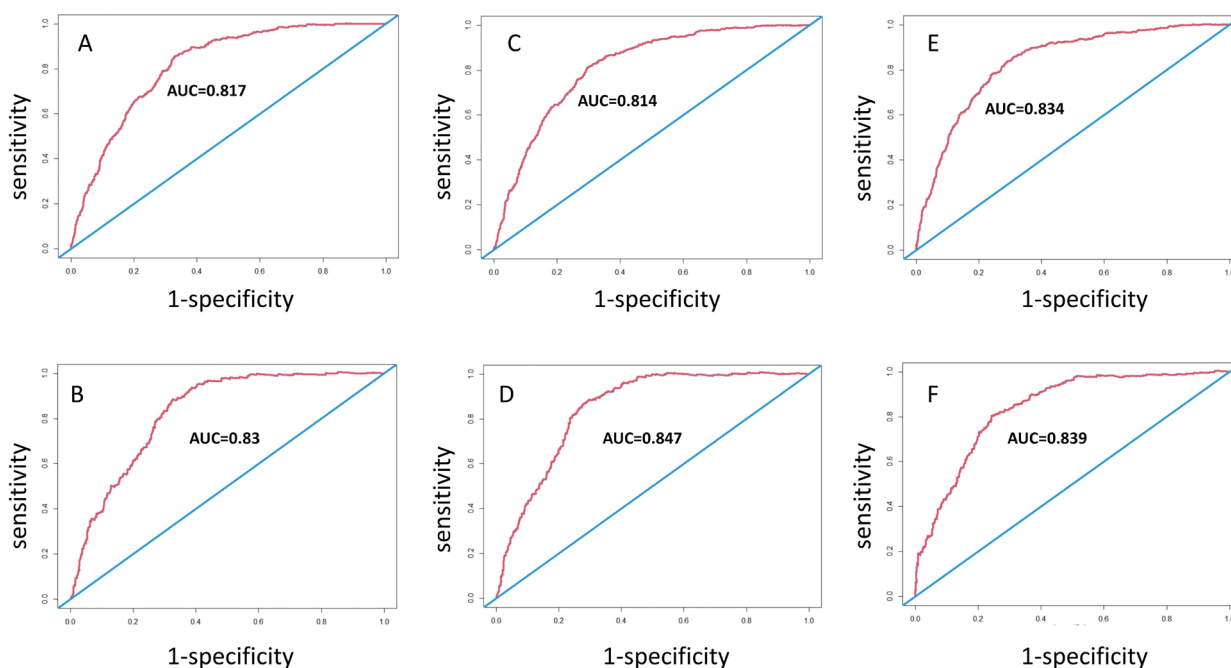


**Figure 2** Nomogram to predict the 3 years, 4 years and 5 years risk of chronic kidney disease (CKD). To use the nomogram, find the position of each variable on the relative axis, draw a line to the points axis for the number of points, add the points derived from all the variables together, and refer to the total points axis to determine the 3 years, 4 years or 5 years CKD probabilities. For example, one 75-year-old person with hypertension and diabetes, and his BMI and EGFR are 25 and 80 mL/min per 1.73 m<sup>2</sup>. The points of each item are 50, 22.5, 25, 15, 87.5, respectively. And the total points is 200, it is obtained by adding those points. BMI, body mass index; eGFR, estimated glomerular filtration rate.

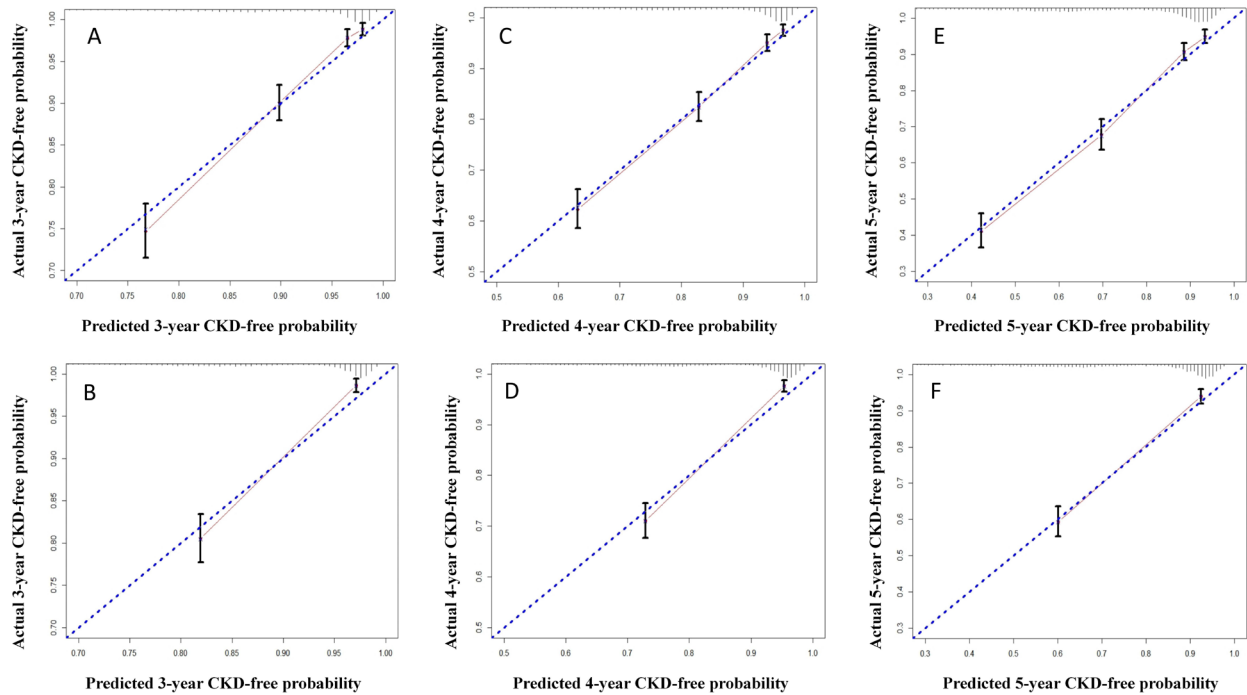
However, another study made an external validation of previous models<sup>19 24 26–30</sup> by using population-based electronic health records from Salford, UK.<sup>38</sup> The results showed that most of models were poorly calibrated, and

only the QKidney Scores performed well in their population. Considering the heterogeneity of the population, we developed a nomogram for Chinese high CVD risk population. And we divided the eGFR category according to the classification of eGFR by K/DOQI clinical practice guidelines.<sup>15</sup> By using multivariable Cox regression analysis, the HR of the stage of 60–89 mL/min/1.73 m<sup>2</sup> of eGFR is 5.59 (95% CI: 4.70 to 6.65). It seems that this stage of eGFR is the most important factor for incident CKD.

About the risk predictors of CKD, researchers of QKidney Scores model has sought the opinions of two senior nephrologists from the National Clinical Director for Kidney Services in England, and factors like age at study entry, BMI, SBP (mm Hg), smoking status, diabetes, treated hypertension and so on, should be thought of the potential risk predictors.<sup>24</sup> The QKidney Scores included comprehensive predictors, but it is difficult to conduct in majority medical system because of missing relevant data. The same problem exist in some other models included cardiovascular or cerebrovascular medical history as predictors. Considering the current medical situation in China, medical institutions have not yet achieved medical data sharing.<sup>9</sup> The CVD history of residents is often obtained from questionnaire, and memory bias could not be avoided. Therefore, although CVD history is a risk predictor for CKD, it is difficult for these models to be applied in regions or countries with difficulty in obtaining medical history data. Our nomogram just includes five predictors without CVD history and shows a good discriminative power with the 3-year, 4-year and 5-year AUCs all over 0.8 in the development cohort and validation cohort.



**Figure 3** Receiver operating characteristic curves for the risk prediction model applied to the study population. The 3-year AUCs in the development cohort (A) and in the validation cohort (B). The 4-year AUCs in the development cohort (C) and in the validation cohort (D). The 5-year AUCs in the development cohort (E) and in the validation cohort (F). AUC, area under the curve.



**Figure 4** Validity of the predictive value of the nomogram in estimating the risk of the 3 years, 4 years and 5 years of incident chronic kidney disease (CKD). Validity of the predictive value in the development cohort (A) and in the validation cohort (B) of the 3 years CKD probability. Validity of the predictive value in the development cohort (C) and in the validation cohort (D) of the 4 years CKD probability. Validity of the predictive value in the development cohort (E) and in the validation cohort (F) of the 5 years CKD probability.

### Strengths and limitations

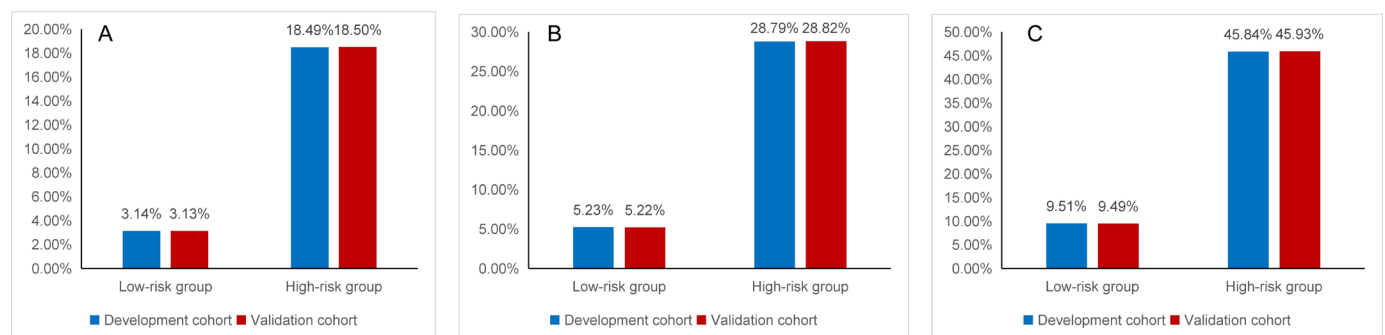
This study developed a nomogram for the prediction of 3-year, 4-year and 5-year risk of incident CKD in a high CVD risk population. Our nomogram with only five variables (age, BMI, eGFR, diabetes and hypertension) is clinically applicable and simple to use. And the nomogram with good discriminative power enables us to identify patients at high risk of CKD readily and take action in time.

This study has several limitations. First, majority of participants lack of albuminuria data at baseline. Considering there were about 1000–2000 participants have no albuminuria data every year, we developed a prediction model without albuminuria. Second, we defined the endpoint as incident  $eGFR < 60 \text{ mL/min/1.73 m}^2$ , and it could

include cases with a slight decrease of eGFR. Change the endpoint from an absolute value to a percentage maybe an alternative way<sup>39</sup> More studies focusing on the clinical meaning of different decline of eGFR are in need. Third, there was no external validation of our model, whereas it shows good C-index and AUCs in the internal validation cohort.

### CONCLUSIONS

The present nomogram with five predictors (age, BMI, eGFR, DM, hypertension) is a simple and reliable tool for CKD risk stratification among high CVD risk populations, which enables physicians to identify individuals at risk and implement precise prevention strategies in time.



**Figure 5** Risk stratification of 3 years, 4 years and 5 years incident chronic kidney disease (CKD) based on the nomogram scores (A, B, C). Low-risk group (scores  $< 106$ ), high-risk group (scores  $\geq 106$ ). The predicted rates of CKD in the validation cohort were closed to those in the development cohort inside each of the three risk groups.

However, further external validations are needed before clinical generalisation.

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