ORIGINAL RESEARCH

# Predicting Short-Term Risk of Cardiovascular Events in the Elderly Population: A Retrospective Study in Shanghai, China

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**Introduction:** Cardiovascular diseases (CVD) represents a leading cause of morbidity and mortality worldwide, including China. Accurate prediction of CVD risk and implementation of preventive measures are critical. This study aimed to develop a short-term risk prediction model for CVD events among individuals aged  $\geq$ 60 years in Shanghai, China.

**Methods:** Stratified random sampling recruited elderly individuals. Retrospective data (2016–2022) were analyzed using Lasso-Cox regression, followed by a multivariable Cox regression model. The risk scoring was visualized through a nomogram, and the model performance was assessed using calibration plots and receiver operating characteristic curves.

**Results:** A total of 9,636 individuals aged  $\geq$ 60 years were included. The Lasso-Cox regression analysis showed male gender (HR=1.482), older age (HR=1.035), higher body mass index (HR=1.015), lower high-density lipoprotein cholesterol (HR=0.992), higher systolic blood pressure (HR=1.009), lower diastolic blood pressure (HR=0.982), higher fasting plasma glucose (HR=1.068), hypertension (HR=1.904), diabetes (HR=1.128), and lipid-lowering medication (HR=1.384) were related to higher CVD risk. The C-index in the training and validation data was 0.642 and 0.623, respectively. Calibration plots indicated good agreement between predicted and actual probabilities.

**Conclusion:** This short-term predictive model for CVD events among the elderly population exhibits good accuracy but moderate discriminative ability. More studies are warranted to investigate predictors (gender, high-density lipoprotein cholesterol, systolic blood pressure, diastolic blood pressure, hypertension, and lipid-lowering medication) of CVD incidence for the development of preventive measures.

Keywords: cardiovascular disease, elderly population, predictive model, short-term risk, Lasso-Cox regression, China

#### Introduction

Cardiovascular diseases (CVD) represent the most common cause of mortality and disability in adults worldwide.<sup>1</sup> It has been reported that over 17.9 million individuals develop CVD each year, accounting for approximately 32% of annual global mortality rate.<sup>2</sup> Aging is a significant and inevitable factor that can influence cardiovascular health,<sup>3</sup> and the rapid aging of the global population increases the prevalence and burden of CVD. Statistics from the Global Burden of Disease have shown that the proportion of CVD-related deaths in Chinese individuals aged 60–89 years increases from 75.0% to 80.5% between 1990 and 2019.<sup>4</sup> Although aging is inevitable, substantial evidence indicates that the control of some

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factors related to CVD events can prevent or delay the onset and progression of CVD.<sup>5,6</sup> Kannel et al reported that the identification of CVD related risk factors and administration of interventions in this group lead to a higher economic cost than in the middle-aged individuals.<sup>7</sup>

The occurrence and progression of CVD result from the combined effects of various risk factors, including age, gender, hypertension, dyslipidemia, and smoking.<sup>8–11</sup> Damen et al proposed that multivariable risk assessment models could aid general practitioners in understanding the impact of these factors on disease development, thereby facilitating early detection, prevention, and treatment of CVD.<sup>12</sup> However, major prediction models are mostly designed for long-term risk prediction among the Western populations, such as the Framingham Risk Score (FRS), Pooled Cohort Equations (PCE), and Systematic Coronary Risk Evaluation-Older Persons (SCORE-OP). Studies have shown that these models tend to significantly overestimate CVD risk and perform poorly in Asian populations, highlighting the need for appropriate modifications.<sup>13,14</sup> Additionally, these models have primarily been developed and applied to populations aged 35–64 years, with relatively fewer older adults. This discrepancy often leads to poorer predictive accuracy in the elderly population, frequently resulting in overestimation of CVD risk.<sup>15,16</sup> In addition, reverse epidemiology has even been observed, wherein factors such as body mass index (BMI), serum cholesterol, and blood pressure have inverse correlations with the risk of death among the elderly.<sup>17</sup>

A CVD risk prediction model tailored to the elderly population may aid to accurately identify high-risk groups, helping to prevent risk overestimation and overtreatment. This also allows for precise, personalized interventions based on risk stratification, thereby reducing the burden of CVD. Nonetheless, available studies fail to comprehensively explain the influence of lifestyle and clinical factors on the cardiovascular risk in Asian older adults. This study aimed to establish a CVD risk prediction model for Chinese individuals aged  $\geq 60$  years to evaluate their risk of cardiovascular events in the near future. We speculate that the prediction model can be used for the risk recognition and to develop strategies for the prevention of CVD in the old population in developing countries or regions.

#### **Methods**

#### Study Design and Samples

This was a retrospective study, and a stratified random sampling approach was used for participant selection. Initially, 16 administrative districts in Shanghai were grouped into urban and rural ones according to their geographical locations. By using a random number table, two districts were randomly selected from each group, and the four community health service centers were then selected because the health information systems have been well established and the quality of data on medical examinations of the elderly is high. These centers were strategically located on streets (towns) reflecting the city's diverse living conditions, industrial and economic statuses, which ensures accurate and reliable data collection. Then, individuals aged  $\geq 60$  years were selected from each community in the training set.

In our analysis, the eligibility criteria at baseline were as follows: the individual had health examination records between January 1, 2016, and December 31, 2017; the individual was  $\geq 60$  years at the time of enrollment; the individual was free from various CVD according to their records of health information. Exclusions were as follows: the individual had a history of CVD events prior to enrollment; the individual had missing data exceeding 15%. In addition, regression imputation was employed for independent variables with missing data  $\leq 15\%$ , which is considered the most appropriate approach for handling missing data in Asian cardiovascular research.<sup>18</sup>

To minimize data bias, we also selected elderly individuals from the China Patient-Centered Evaluative Assessment of Cardiac Events Million Persons Project<sup>19</sup> as the validation set.

#### Data Collection

#### **Potential Risk Factors**

In this study, 15 potential risk factors associated with CVD were selected based on clinical significance, support from relevant studies, ease of collection from information management system of community health service, and high probability of occurrence. These factors included age, gender, smoking status (World Health Organization criterion: individuals who have smoked continuously or cumulatively for six months or more), systolic blood pressure (SBP), diastolic blood pressure

(DBP), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), total cholesterol (Total-C), fasting plasma glucose (FPG), BMI, hypertension (average SBP  $\geq$ 140 mmHg and/or DBP  $\geq$ 90 mmHg, history of hypertension, or taking antihypertensive medication), diabetes (fasting plasma glucose level  $\geq$ 7.0 mmol/L, history of diabetes, or taking antidiabetic medication), hypertension medication, diabetic medication, and lipid-lowering medication. All the data were collected from the health examination database, community resident health records, and mortality database between 2016 and 2022, with databases matched using each participant's identification number and name. The informed consent was obtained from all participants, and the local institutional board approved this study.

#### Follow Up and Outcome Events

All participants underwent continuous monitoring for CVD events and mortality for an average of 3.11±0.33 years. The definition of CVD in this study encompassed myocardial infarction and cerebrovascular events (such as ischemic stroke and hemorrhagic stroke). Data regarding participants' medical examinations, medical history, and mortality records were collected from above information management system of selected community health service. Suspected CVD events were evaluated by two experienced general practitioners who had received standardized training. In instances where participants experienced two or more CVD events during the follow-up period, only the initial event was considered as the endpoint for statistical analysis.

## Statistical Analysis

#### Descriptive Statistical Analysis

Descriptive statistics were computed for all variables, with continuous variables presented as mean (standard deviation), and categorical variables as frequencies and percentages. Comparisons were done using two-sample *t*-test or Chi-square test. In addition, the balance in variable distribution between training and validation datasets was examined using the standard mean difference (SMD). A SMD below 0.1 indicated a balanced and comparable distribution of variables between two datasets.<sup>20</sup>

#### Cox Regression Analysis

Univariate Cox regression analyses were performed to identify the hazard ratio (HR), 95% confidence interval (CI), and P-value of candidate factors associated with CVD event. Lasso (least absolute shrinkage and selector operator) regression, incorporating variable selection and regularization, effectively addresses overfitting concerns and enhances the predictive accuracy and interpretability of statistical models.<sup>21–23</sup> Lasso-Cox regression integrating the Cox regression model with the lasso penalty was utilized to select candidate factors and construct the risk predictive model for CVD events in the training set. Subsequently, multivariate Cox regression was applied to assess the impact of selected variables on CVD event occurrence, and the results were visualized using a nomogram score.

#### Model Performance Evaluation

The discrimination ability of the prediction model was assessed and compared using Harrell's concordance index (C-index), Akaike information criterion (AIC) and Bayesian information criterion (BIC). A C-index below 0.5 indicates no predictive capability, a C-index of 0.6–0.75 suggests that the model can distinguish between CVD and non-CVD cases, and a C-index closer to 1 indicates superior discrimination.<sup>24</sup> Receiver operating characteristic (ROC) analysis was employed to assess the performance of this model in both training and validation datasets. Calibration curves were generated, with a well-calibrated model demonstrating predictions closely aligned with the 45-degree line on the plot.

All statistical analyses were conducted using R software, and two-sided P-value < 0.05 was considered statistically significant.

# Results

## Characteristics of Individuals

Table 1 presents the baseline characteristics of individuals in this study. A total of 9,636 participants without a history of CVD were included in the training and validation datasets.

Characteristics	Training data				Validation data				SMD
	Overall (n-9636)	Male (n=3988)	Female (n=5648)	P value	Overall (n-9636)	Male (n=3837)	Female (n=5799)	P value	
Age, mean (SD), y	68.58 (3.29)	68.77 (3.18)	68.45 (3.36)	<0.001	68.59 (3.41)	68.80 (3.37)	68.45 (3.43)	<0.001	0.001
BMI, mean (SD), kg/m²	24.70 (3.33)	24.73 (3.15)	24.69 (3.46)	0.625	24.74 (3.09)	24.93 (2.86)	24.62 (3.23)	<0.001	0.014
Smoking, n (%)	1217 (12.63)	1197 (30.02)	20 (0.35)	<0.001	1125 (11.67)	1110 (28.9)	15 (0.30)	<0.001	0.029
Total-C, mean (SD), mg/dL	192.36 (39.34)	180.32 (36.39)	200.78 (39.12)	<0.001	177.99 (44.27)	162.28 (40.63)	188.39 (43.51)	<0.001	0.343
HDL-C, mean (SD), mg/dL	62.40 (20.18)	59.17 (19.98)	64.67 (20.02)	<0.001	54.12 (15.68)	49.74 (14.91)	57.02 (15.51)	<0.001	0.458
LDL-C, mean (SD), mg/dL	115.47 (34.98)	109.39 (33.25)	119.62 (35.52)	<0.001	96.43 (36.02)	87.77 (32.77)	101.94 (36.90)	<0.001	0.536
SBP, mean (SD), mmHg	135.99 (17.36)	136.07 (17.16)	135.94 (17.50)	0.714	145.14 (15.95)	143.85 (15.79)	145.99 (16.00)	<0.001	0.548
DBP, mean (SD), mmHg	78.52 (9.17)	79.17 (9.14)	78.05 (9.16)	<0.001	80.86 (9.42)	82.35 (9.43)	79.87 (9.29)	<0.001	0.252
FPG, mean (SD), mmHg	5.67 (1.38)	5.73 (1.45)	5.62 (1.33)	<0.001	6.61 (1.81)	6.68 (1.85)	6.57 (1.78)	0.003	0.588
Hypertension, n (%)	7100 (73.68)	2933 (73.55)	4167 (73.78)	0.798	7061 (73.3)	2867 (74.7)	4194 (72.3)	0.009	0.009
Hypertension medication, n (%)	5861 (60.82)	2376 (59.58)	3485 (61.70)	0.035	6807 (70.6)	2772 (72.2)	4035 (69.6)	0.005	0.208
Diabetes, n (%)	2328 (24.16)	961 (24.10)	1367 (24.20)	0.576	1966 (20.4)	818 (21.3)	1148 (19.8)	0.070	0.09
Diabetic medication, n (%)	1804 (18.72)	721 (18.08)	1083 (19.17)	0.905	5385 (55.88)	2128 (55.5)	3257 (56.2)	0.483	0.789
Lipid-lowering medication, n (%)	2840 (29.47)	1004 (25.18)	1836 (32.51)	<0.001	5476 (56.83)	2186 (57.0)	3290 (56.8)	0.832	0.519

Table I Baseline Characteristics of Individuals in the Training and Validation Datasets

Abbreviations: SD, Standard Deviation; SMD, Standard mean difference.

In the training dataset, there were 3,988 males (41.39%) and 5,648 females (58.61%), and the mean age was 68.58  $\pm$ 3.29 years. Over the 3-year observation period, 263 participants experienced CVD events, resulting in an incidence rate of 2.73%. In the validation dataset, the mean age was 68.59 $\pm$ 3.41 years, and there were 3,837 males (39.82%). In the 3-year follow up period, the new-onset CVD was noted in 382 participants (3.96%).

### Selection of Predictors and Construction of Nomogram Model

In the training data, male gender, advanced age, elevated SBP and FPG, and low high-density lipoprotein cholesterol, hypertension, diabetes, and use of hypertension medication, diabetic medication, and lipid-lowering medication were correlated with higher risk of CVD. Lasso-Cox regression analysis revealed that the contribution coefficients of five variables were compressed to zero (Figure 1). Based on the above analysis, the multivariable Cox regression model further showed that male gender (HR=1.482, 95% CI:1.157–1.189, P = 0.002), age (HR=1.035, 95% CI: 0.997–1.074, P = 0.073), BMI (HR=1.015, 95% CI: 0.977–1.053, P = 0.449), HDL-C (HR=0.992, 95% CI:0.986–0.999, P = 0.016), SBP (HR=1.009, 95% CI:1.001–1.017, P = 0.033), DBP (HR:0.982, 95% CI=0.967–0.998, P = 0.023), FPG (HR =1.068, 95% CI:0.985–1.158, P = 0.109), hypertension (HR=1.904, 95% CI:1.32–2.746, P < 0.001), diabetes (HR=1.128, 95% CI: 0.846–1.503, P = 0.411), and lipid-lowering medication (HR=1.384, 95% CI: 1.076–1.78, P = 0.011) were significantly associated with the risk of CVD (Table 2).

A nomogram was then constructed to predict the 3-year risk of CVD events in the elderly adults, utilizing predictors selected through Lasso-Cox regression. As shown in Figure 2, each variable corresponded to the point scale at the top. By summing the scores of each variable, the total points were calculated. At the bottom of the nomogram, the total points were used to project a vertical line indicating the risk of CVD at 3 years.

## Model Performance for Derivation and Validation Data

The model had a C-index of 0.642, along with AIC = 4735.565 and BIC = 4771.211. The C-index of the validation data was 0.623, along with AIC = 5841.179 and BIC = 5878.893 (Figure 3A and B). In addition, the model calibration of the predicted and actual values associated with elderly individuals being CVD-free at 3 years was relatively good in both training and validation datasets (Figure 4A and B).

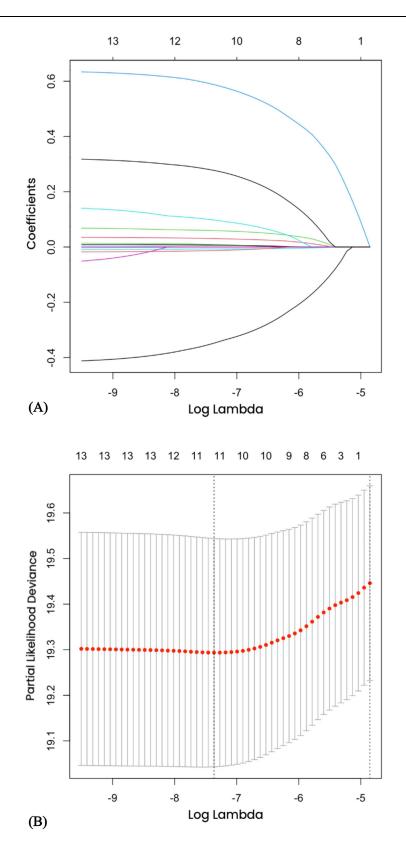


Figure 1 Screening of variables based on Lasso-Cox regression. (A) Variation characteristics of coefficient of variables; (B) Selection process of optimum value of parameter  $\lambda$  in the Lasso-Cox regression.

Predictors	Univariable C Regression		Lasso-Cox Regression	Multivariable Cox Regression		
	HR (95% CI)	Р	Lambda. min =0.00092	HR (95% CI)	Р	
Gender						
Female	Ref	Ref	0	Ref	Ref	
Male	1.505 (1.181–1.918)	<0.001	-0.32320	1.482 (1.157–1.189)	0.002	
Age	1.051 (1.013–1090)	0.008	0.02855	1.035 (0.997–1.074)	0.073	
BMI	1.034 (0.998–1.072)	0.063	0.00650	1.015 (0.977-1.053)	0.449	
Smoking						
No	Ref	Ref	0	—	—	
Yes	1.256 (0.897–1.759)	0.185	0	—	—	
Total-C	0.999 (0.995-1.002)	0.351	0	—	—	
HDL-C	0.990 (0.984–0.996)	0.002	-0.00667	0.992 (0.986-0.999)	0.016	
LDL-C	0.999 (0.983-1.010)	0.728	0	—	—	
SBP	1.009 (1.002–1.016)	0.009	0.00576	1.009 (1.001–1.017)	0.033	
DBP	0.996 (0.983-1.010)	0.590	-0.01037	0.982 (0.967,0.998)	0.023	
FPG	1.113 (1.034–1.197)	0.004	0.05637	1.068 (0.985–1.158)	0.109	
Hypertension						
No	Ref	Ref	0.56323	Ref	Ref	
Yes	2.251 (1.583-3.200)	<0.001		1.904 (1.32–2.746)	<0.001	
Hypertension medication						
No	Ref	Ref	0	—	_	
Yes	1.638 (1.251–2.144)	<0.001		—	_	
Diabetes						
No	Ref	Ref	0.08625	Ref	Ref	
Yes	1.420 (1.092–1.846)	0.009		1.128 (0.846–1.503)	0.411	
Diabetic medication						
No	Ref	Ref	0	—	—	
Yes	1.352 (1.024–1.785)	0.033		—	—	
Lipid-lowering medication						
No	Ref	Ref	0.25607	Ref	Ref	
Yes	1.425 (1.112–1.826)	0.005		1.384 (1.076–1.78)	0.011	

**Table 2** Extraction of Potential Predictors in the Training Dataset by Univariable and Multivariate Cox and LASSO-Cox Regression Analyses

Notes: "—" indicates that the variable was not selected in the final model. Abbreviations: HR, hazard ratio; Cl, confidence interval.

# Discussions

As the aging population grows, the burden of CVD is increasing, highlighting the need for effective preventive measures tailored to this group. Additionally, due to limited life expectancy and varying willingness to undergo interventions among the elderly, models that can be used to predict the short-term risk of CVD are of great significance. In this study, Lasso-Cox regression was employed to a 3-year CVD risk prediction model for community-dwelling adults aged  $\geq 60$  in Shanghai. The final model, visualized via a nomogram, integrates multiple factors to estimate individual risk, enhancing clinical decision-making. The final CVD risk prediction model included 10 variables: gender, age, BMI, HDL-C, SBP, DBP, FPG, hypertension, diabetes, and lipid-lowering medication. Similar to previous findings, factors such as gender,<sup>25–27</sup> age,<sup>26–28</sup> BMI,<sup>28</sup> SBP,<sup>28–30</sup> DBP,<sup>31</sup> HDL-C<sup>28–30</sup> and diabetes<sup>28–30</sup> were identified as predictors in the risk assessment model of CVD events.

Points	0 10 20 30 40 50 60 70 80 90 10
Gender	Male Female
Age	60 64 68 72 76
BMI	10 20 30 40 45
HDL	160 140 120 100 80 60 40 20 0
SBP	90 110 130 150 170 190 200
DBP	130 120 110 100 90 80 70 60 50 40
FPG	3 4 5 6 7 8 9 11 13 14 Yes
Hypertension	Yes No <sub>Yes</sub>
Diabetes	
Lipid-lowering Medicine	No Yes No
Total Points	0 50 100 150 200 250 300 35
Linear Predictor	-2 -1.5 -1 -0.5 0 0.5 1 1.5 2
3-year risk of CVD	

Figure 2 Nomogram for predicting the 3-year risk of CVD in elder adults.

In this study, the results indicated that the use of lipid-lowering medication was associated with a higher risk of CVD. Lipid-lowering drugs primarily aim to reduce cholesterol and triglycerides. However, results on the predictive performance of cholesterol and triglycerides for CVD events are conflicting in available studies,<sup>32,33</sup> which might be ascribed to multiple factors such as cholesterol type, study outcomes, participant demographics, and comorbidities.<sup>34</sup> One possible explanation for our findings is that certain lipid-lowering medications (eg, statins and niacin) may affect glucose metabolism and insulin sensitivity, potentially increasing the risk of diabetes and, in turn, the risk of CVD events.<sup>35,36</sup> It is also possible that individuals prescribed lipid-lowering medications are already at elevated cardiovascular risk due to pre-existing hyperlipidemia, which may partially account for the observed association.

FPG, though rarely included in other models, emerged as an important predictor. Evidence from middle-aged and elderly populations in Japan has shown that elevated FPG levels are associated with a higher incidence of CVD.<sup>37</sup> Experimental studies have further revealed that high blood glucose level can influence several etiologies of CVD, such as atherosclerosis and oxidative stress.<sup>38–40</sup> The role of FPG, one of the factors in our risk assessment model, in the occurrence and development of CVD still needs to be further investigated.

Hypertension was also included as a predictor in our model, which is often not contained in the final model. In China, hypertension is the most critical risk factor for CVD events, with approximately 43% of CVD events attributable to hypertension.<sup>41</sup> Different racial and ethnic groups exhibit varying characteristics of hypertension,<sup>42</sup> which may affect its predictive performance in CVD, and further investigation is warranted in future studies. This also underscores the importance of monitoring and management of hypertension in the elderly population to prevent CVD events.

In our study, the C-index was 0.642 in the training set and 0.623 in the validation set, consistent with previous models for older adults, which typically show moderate discriminative performance.<sup>25</sup> Several factors may explain this limitation. First, existing predictors may not fully capture risk factors specific to the elderly.<sup>43,44</sup> Second, the elderly population often concomitantly experiences multiple chronic diseases, which requires further optimization of the prediction model algorithms. Third, exposure to multiple risk factors among the elderly results in a higher degree of overlap in risk factors between diseased and non-diseased individuals, leading to less variability in disease risk

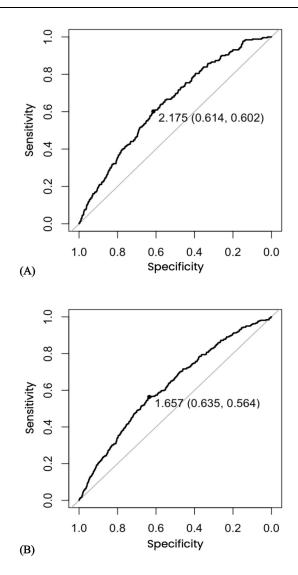


Figure 3 ROC curves of the model in the training and validation datasets. (A) ROC curve of the model in the training dataset. (B) ROC curve of the model in the validation dataset.

distribution.<sup>45</sup> Some investigators have proposed that model calibration may be more meaningful than discrimination for this demographic.<sup>29</sup>

Clinical practice guidelines recommend the use of risk assessment systems so that preventive measures can be tailored for high-risk individuals against CVD. Our study contributes to the existing evidence in this field. Specifically, the risk prediction model designed in our study addresses the issue of overestimation when using general population models to estimate risk for the elderly, thus reducing the risk of overtreatment in clinical practice. It is advisable for general practitioners to monitor the changes in blood pressure, cholesterol, and other indicators, particularly when drug therapy is associated with increased adverse reactions in the elderly. Under this condition, they should assess the risk and benefit, and adjust treatment plans accordingly. Additionally, our findings suggest that, for high-risk individuals, primary care physicians should design individualized interventions targeting key risk factors, such as weight reduction, improved exercise and dietary habits.

However, this study has several limitations. First, as a retrospective analysis based on community health center data, it may be subject to incomplete records and limited disease coverage. Second, confounding factors like mental health, psychology, family history, and lifestyle may also influence the results, but they were not adjusted in this study. Lastly,

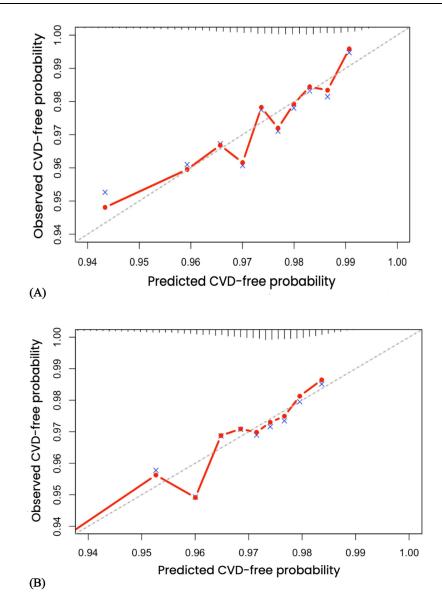


Figure 4 Calibration curves for the training and validation datasets. (A) Calibration curve of the model in the training dataset. (B) Calibration curve of the model in the validation dataset. The grey dotted line represents an ideal predictive model, and the red solid line shows the actual performance of the predictive model.

the validation set included high-risk elderly individuals with baseline differences from the training set, potentially affecting generalizability. Further prospective, multicenter studies with larger samples are warranted to refine the model.

## Conclusion

This study developed a 3-year cardiovascular disease risk prediction model for adults aged 60 years and older in Shanghai. The final model included 10 risk factors: gender, age, BMI, HDL-C, SBP, DBP, FPG, hypertension, diabetes, and use of lipid-lowering medication. The model showed moderate predictive performance and can help primary care providers identify high-risk individuals and take early preventive actions. It is simple to use and suitable for routine practice in community settings.

## Abbreviations

AIC, Akaike information criterion; BIC, Bayesian information criterion; BMI, Body mass index; CI, Confidence interval; CVD, Cardiovascular disease; DBP, Diastolic blood pressure; FPG, Fasting plasma glucose; FRS, Framingham risk

score; HDL-C, High-density lipoprotein cholesterol; HR, Hazard ratio; Lasso, Least absolute shrinkage and selection operator; LDL-CLow-density lipoprotein cholesterol; ROC, Receiver operating characteristic; SBP, Systolic blood pressure; SMD, Standard mean difference; Total-C, Total cholesterol.

## **Data Sharing Statement**

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

# **Ethics Approval and Consent to Participate**

The study complies with the Declaration of Helsinki, was approved by the Public Health and Nursing Research Ethics Committees, which is affiliated with the Shanghai Jiao Tong University School of Medicine (ref: SJUPN20211). The studies were conducted in accordance with the local legislation and institutional requirements. The participants provided their written informed consent to participate in this study.

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# Disclosure

The authors report no conflicts of interest in this work.

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