



The predictive accuracy of coronary heart disease risk prediction models in rural Northwestern China

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ABSTRACT

Cardiovascular risk models developed may have limitations when applied to rural Chinese. This study validated and compared the Framingham Risk Score (FRS) and Prediction for Atherosclerotic Cardiovascular Disease Risk in China (PAR) models in predicting 10-year risk of coronary heart disease (CHD) in a rural cohort in Ningxia, China from 2008 to 2019. The FRS and PAR models were validated by estimating predicted events, C index, calibration χ^2 and plots. 1381 adults without CHD at baseline were followed up for 9.75 years on average. 168 CHD cases were observed. The FRS and PAR underestimated CHD events by 22 % and 46 % for the total population, while overestimated for males by 152 % and 78 %, respectively. The C index was slightly higher for PAR than FRS. Both models showed weak calibration with chi-square values above 20 ($p < 0.001$). Bland-Altman plots indicated FRS predicted higher CHD risk than PAR, lacking consistency. Overall, FRS and PAR demonstrated limited performance in predicting 10-year CHD risk in this rural population. PAR had slightly better discrimination than FRS, but require further improvement in calibration and individual risk estimation to suit the rural population in Northwest China.

1. Background

Coronary heart disease (CHD) remains a significant global health issue and is the leading cause of mortality (Zaidi and Brueckner, 2017). Therefore, effective tools for assessing CHD are vital for early screening and primary prevention (Abd El-Wahab, 2021). Several cardiovascular disease risk assessment models are available worldwide, the classical Framingham Risk Score (FRS) established by the Framingham Heart Study (Mahmood et al., 2014), Systematic Coronary Risk Evaluation (SCORE), Pooled Cohort Equations (PCE), and the World Health Organization/International Society of Hypertension (WHO/ISH) risk prediction charts (Hense et al., 2008), etc. However, existing research suggests that the WHO/ISH model performs poorly in terms of cardiovascular risk stratification in Asian populations (Selvarajah et al., 2014). while the PCE equations provide poor accuracy in Hong Kong Chinese

(Lee et al., 2015). Although both the Framingham and SCORE models can stratify risk for Asian men and women, the FRS is more accurate in stratifying risk for women than the SCORE model (Tzoulaki, 2009). These models are based on data from Caucasians and Blacks in Europe and the United States. Because the nature or distribution of cardiac risk variables may be different in the Chinese population, these models may over or under predict CHD events in Chinese patients. Additionally, rural Chinese populations have a unique lifestyle compared to Europeans in terms of diet, physical activity, work, and rest (Colpani et al., 2018; Lv et al., 2017). Despite the use of risk assessment models in clinical practice to identify high-risk individuals, these models still have a long way to go in the Chinese population (Zhang et al., 2020).

The Framingham Risk Score is a crucial classical tool for predicting CHD events. However, its direct application in China may lead to an overestimation or underestimation of risk (Jiang et al., 2020; Sun et al.,

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2017). Fortunately, the Prediction for Atherosclerotic Cardiovascular Disease Risk in China (PAR), a new risk predictive model for Atherosclerotic Cardiovascular Disease (ASCVD) in China, was introduced in 2016 (Yang et al., 2016). In addition to the six major risk factors considered in existing risk projections, including age, treated and untreated systolic blood pressure, current smoking status, diabetes status, total cholesterol, and high-density lipoprotein cholesterol levels, PAR also includes other factors that explain Chinese characteristics, such as urbanization (urban or rural) and residence (north/south), family history of cardiovascular and cerebrovascular illnesses, and waist circumference (which offers better predictive power than BMI) (Zhang et al., 2020). Therefore, PAR equations may be superior to the FRS assessment tool in identifying ASCVD risk among Chinese adults (Li et al., 2019).

The objective of this study was to validate and compare the predictive abilities of the PAR Equations and FRS in estimating 10-year CHD risk using an external population cohort. The goal was to identify an accurate, convenient, and efficient tool for predicting CHD risk among rural Chinese populations and to establish a scientific basis for primary and secondary prevention (Bansilal et al., 2015).

2. Methods

2.1. Study population

This study is a retrospective, population-based cohort investigation. The baseline survey design was previously published (Zhao et al., 2020). In brief, from 2008 to 2012, a cross-sectional study was carried out in Qingtongxia county and Pingluo county of Ningxia, China. Two towns were randomly selected, and from those towns, two villages were randomly chosen, yielding a total of four administrative villages as research units. Stratified cluster sampling was used to recruit 2,209 subjects between the ages of 25 and 74 years from each county. Each participant completed a questionnaire survey, underwent a physical examination, and had their blood biochemistry levels measured. Those who were older than 75 years or younger than 30 years (43 subjects) and those who had CHD at baseline (93 subjects) were excluded from the study. All participants provided written informed consent. The study met institutional guidelines for the protection of human subjects safety and privacy and was approved by Ningxia Medical University Ethics Committee (Ethics ID 2018-012, 2020-689).

2.2. Baseline assessment

Trained investigators administered standardized questionnaires to collect information from participants on their age, gender, residence, smoking status, alcohol intake, physical activity, antihypertensive medicine usage, and history or family history of CHD in a face-to-face setting during the baseline assessment. Physical examinations were also conducted, which included taking blood pressure at sitting by an electronic sphygmomanometer (Omron-HEM 7301-IT, China) and taking blood pressure in the right arm three times for average analysis. In addition, a portable ruler was used to measure waist and hip circumference, while a weight scale (Omron, China) was used to measure height and weight. Before measuring body composition, individuals were instructed to remove their shoes and socks, wear light clothing, and remove any rings or other jewelry. Furthermore, blood samples were collected from participants after a minimum of 10 h of fasting and avoiding alcohol. Fasting plasma glucose (FPG), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) were measured using the enzymatic assay (CHOD-PAP, Roche diagnosis) (Zhao et al., 2020, 2014).

2.3. Follow-up and events definition

Of the initial 2,209 participants, 1,655 subjects underwent

comprehensive follow-up between 2019 and 2020, with an average follow-up duration of 9.75 years, ranging from 7.33 years to 12.17 years. Among them, 124 individuals were lost to follow-up due to relocation, and 430 had missing data for blood pressure, lipid profiles, and waist circumference. There were 138 deaths from non-cardiac causes. In addition, 38 deaths from cardiac causes were included in the outcome events. And the tracking of death events was conducted through the local Center for Disease Control and Prevention's (CDC) monitoring system (including routine monitoring such as health records and cause-of-death surveillance, as well as targeted monitoring through village doctors). Among the survivors, 133 subjects were diagnosed with CHD. In the end, we conducted the analysis on a sample size of 1,381 individuals (as shown in Fig. 1).

The follow-up survey used the same questionnaire as the baseline survey, with body measurements taken using an InBody370 device from Seoul, Korea. CHD was defined as myocardial ischemia and hypoxia (angina) or myocardial necrosis caused by organic coronary artery (atherosclerosis or dynamic vasospasm) stenosis or obstruction (myocardial infarction) (ICD-10 code 120–125) based on self-reported verified by medical records (confirmed by secondary and above hospitals). Current smoking or non-smoking was defined as smoking one or more cigarettes per day, while alcohol intake for six months or more was defined as drinking at least once a week for six months or more. Hypertension was defined as systolic blood pressure higher than 140 mmHg, diastolic blood pressure higher than 90 mmHg, or the use of antihypertensive medication. Diabetes was defined as fasting blood glucose higher than 7.0 mmol/L or current self-reported use of insulin or oral hypoglycemic medicine (Zhao et al., 2014).

2.4. Predictive risk models

The FRS model includes seven risk factors such as age, gender, systolic blood pressure, TC, HDL-C, smoking status, and diabetes status. The 10-year risk score for the start of cardiovascular disease was calculated, and the results were grouped into low, medium, and high risk categories. However, the PAR Equations model includes eleven risk factors, which incorporates additional factors such as current residence, geographic area, waist circumference, blood pressure level, presence or absence of antihypertensive medicine, smoking and drinking habits, and family history of CHD. The PAR Equations model also provides 10-year risk stratification categories. Unlike the FRS, the PAR Equations take into account the Chinese geographical factors, making it more suitable for Chinese populations. In this cohort, we used both models to calculate scores for 10-year CHD risk prediction and compared their accuracy in predicting CHD.

2.5. Statistical analysis

The baseline characteristics of subjects were summarized as Mean (SD) for continuous variables and percentages for categorical categories. To account for potential bias due to loss of follow-up, the Kaplan-Meier method was used to adjust the observed number of events during follow-up. (D'Arrigo et al., 2021). This approach adjusted for the effect of censoring data on the number of incidents. The number of expected incidents after ten years was estimated using an exact formula derived from FRS and PAR, respectively. All risk scores were expressed as the median (Inter-Quartile Range, IQR).

After that, we evaluated the calibration for both the FRS and the PAR. This refers to the consistency of observed and expected risk. The discrimination, which refers to how well the model distinguishes between different risk levels, means that a model with superior discriminating ability will provide higher predicted probabilities (Alba et al., 2017; D'Agostino and Nam, 2003; Y et al., 2020, p. 202). These are used to demonstrate the effectiveness of risk prediction models. The area under the Receiver Operating Characteristic (ROC) curve was used for discriminating (Hanley and McNeil, 1982) using the R package

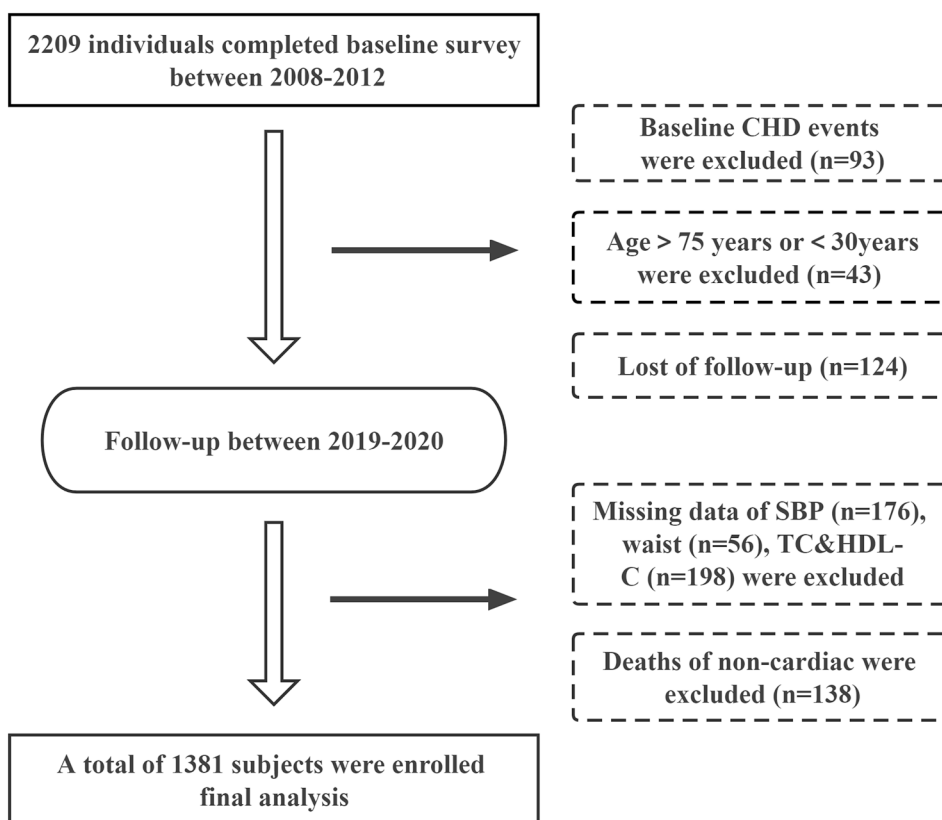


Fig. 1. Flowchart of the inclusion criteria used to choose study participants, RNC, 2008–2020. CHD, coronary heart disease; RNC, Rural Northwest China.

(timeROC) (Heagerty et al., 2000). It is widely believed that 0.7 or higher is better (Uno et al., 2011, p. 20). The Pearson Chi-square test statistic is used to calculate the calibration statistic (Hosmer and Lemeshow 1980). The χ^2 value of greater than 20 and the p value less than 0.05 indicate that the calibration effect is weak (Nattino et al., 2017). We also used calibration plots to show the projected ability of these models by decile of predicted risk. Participants were classified into three categories based on the cut-off points in the Chinese guidelines: <5.0 %, 5.0 %-9.9 %, and \geq 10.0 %.

We used decision curve analysis (DCA) to evaluate the net benefit of the FRS and PAR in predicting 10-year ASCVD risk to compare their clinical utility (Vickers and Elkin, 2006). Finally, we computed the ratio of expected occurrences to observed events among study participants based on the 10-year risk prediction. A ratio of 1.0 shows ideal calibration, with equal anticipated and observed rates, while a ratio less than 1.0 indicates an underestimation, and a ratio greater than 1.0 indicates an overestimation (Cook and Ridker, 2016). The statistical analyses were conducted using R software version 4.1.0 (<https://www.r-project.org>).

3. Results

3.1. Baseline characteristics

Our study included 1381 participants (570 men and 811 women) who met the inclusion and exclusion criteria. Table 1 presents the baseline characteristics of the 1,381 study participants. The mean age was 49.0 (SD = 9.8) years, with 58.7 % being female. The prevalence of current smoking and drinking was 17.3 % and 9.3 %, respectively. The mean waist circumference was 79.7–82.5 cm. Average total cholesterol was 4.0 (SD = 0.8) mmol/L and HDL-C was 1.3 (SD = 0.3) mmol/L. The mean SBP was 125.2 (SD = 19.0) mmHg and 8.0 % reported taking antihypertensive medication. The prevalence of diabetes and family

Table 1

Baseline characteristics stratified by sex of cohort participants, RNC, 2008–2012 (N = 1381).

Characteristics	No. (%) of participants Overall (n = 1381)	Men (n = 570)	Women (n = 811)
Age, yrs., Mean (SD)	49.0 ± 9.8	50.6 ± 10.0	47.9 ± 9.6
Smoking, n (%)			
Nonsmoker	1109 (80.3)	306 (53.7)	803 (99.0)
Smoker	239 (17.3)	231 (40.5)	8 (1.0)
Former smoker	33 (2.4)	33 (5.8)	0
Current drinker, n (%)			
Nondrinker	1226 (9.3)	426 (74.7)	800 (98.6)
Drinker	128 (9.3)	118 (20.76)	10 (1.2)
Former drinker	26 (1.9)	25 (4.4)	1 (0.1)
Waist circumference, cm, Mean (SD)	80.8 ± 9.1	82.5 ± 9.0	79.7 ± 9.0
Body mass index, Mean (SD)	23.5 ± 3.2	23.3 ± 3.0	23.7 ± 3.3
Lipid measurements, mmol/L, Mean (SD)			
Total cholesterol	4.0 ± 0.8	3.9 ± 0.8	4.0 ± 0.8
HDL cholesterol	1.3 ± 0.3	1.3 ± 0.3	1.4 ± 0.3
LDL cholesterol	2.0 ± 0.7	2.0 ± 0.6	2.0 ± 0.7
Diabetes mellitus, n (%)	26 (1.9)	9 (1.6)	17 (2.1)
SBP, mmHg, Mean (SD)	125.2 ± 19.0	125.1 ± 17.8	125.3 ± 19.9
DBP, mmHg, Mean (SD)	79.5 ± 11.3	80.1 ± 11.1	79.2 ± 11.4
Antihypertensive	110 (8.0)	49 (8.6)	61 (7.5)
Family history of CVD, n (%)	22 (1.6)	7 (1.2)	15 (1.8)
Ten-year CHD risk %, median(P ₂₅ -P ₇₅)			
Framingham Risk Score	4.0 (2.0–8.0)	7.0 (4.0–10.0)	3.0 (1.0–5.0)
China- PAR Equation	2.4 (0.9–5.5)	4.3 (1.9–8.33)	1.6 (0.7–3.5)

RNC, Rural Northwest China; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; CHD, coronary heart disease.

history of CVD was 1.9 % and 1.6 %, respectively.

3.2. Risk score

Among the 1381 participants, a total of 168 CHD events were identified, with 69 occurring in men and 99 in women. The median (IQR) 10-year predicted risk estimated by the FRS and PAR was 4.0 (2.0–8.0) and 2.4 (0.9–5.5), respectively. The FRS risk scores were higher than the PAR scores, and males had higher scores than females in both models. [Supplementary Fig. S1](#) compares the FRS and PAR for predicting the 10-year risk of CHD. The risk of CHD was concentrated in the 5 % to 10 % range for men and less than 5 % for women. The risk of CHD in the PAR model was significantly lower than in the FRS model.

3.3. Discrimination and calibration

[Table 2](#) displays the observed CHD event rates (adjusted using the Kaplan-Meier method) of 102.2 for men, while the predicted rates for FRS and PAR were 79.9 and 55.4, respectively. The expected-observed ratio (EOR) for males was 2.52 for FRS and 1.78 for PAR, whereas for females, it was 0.96 for FRS and 0.65 for PAR. This indicates that both models overestimated the risk for men but underestimated the risk for women. The PAR demonstrated good discrimination, as evidenced by the ROC Curve, with an overall C-index of 0.72 (greater than 0.7 for both men and women) compared to FRS of 0.64, as shown in [Supplementary Fig. S2](#). However, their calibration χ^2 values were greater than 20, indicating weak calibration ability, as shown in [Table 2](#).

Based on the data presented in [Fig. 2](#), the observed incidence of 10-year CHD events was consistently higher than predicted for both FRS and PAR, regardless of the risk category. However, the predicted event rate for PAR was closer to the observed rate than for FRS in the high-risk category (>10 %). The calibration plot of deciles indicated a significant difference between FRS and PAR ($p < 0.05$), and both models underestimated event rates across all categories. Furthermore, both models deviated from the 45° calibration line, and the deviation was greater for higher predicted risk levels, particularly among women, as shown in [Fig. 3](#). The Bland-Altman plot revealed that the CHD risk predicted by FRS was higher than PAR, and the funnel-shaped chart demonstrated that the difference was more significant at higher CHD risk levels. These findings suggest that while PAR may have better discrimination, both models demonstrate poor calibration and consistently overestimate the risk of CHD.

3.4. Decision curve analysis (DCA)

As shown in [Fig. 4](#), we used DCA to compare the clinical usefulness of the two risk models in predicting 10-year ASCVD risks. For CHD risk thresholds ranging from approximately 0.1 to 0.2 in men, the net benefits of both FRS and PAR were similar. At a threshold of 10 %, the net benefits of both FRS and PAR were 0.045 and 0.022 higher, respectively, than the values obtained by assuming a positive result for all individuals.

Similarly, for women, the net benefits of FRS and PAR were 0.046 and 0.047, respectively. For risk thresholds ranging from approximately 0.1 to 0.4, the net benefits of FRS were slightly greater than those of PAR.

4. Discussion

Accurately assessing and calibrating cardiovascular risk is essential for the prevention and management of CHD, especially in rural populations ([Lloyd-Jones et al., 2019](#)). In this prospective rural cohort study with 9.75 years of follow-up, we found that the FRS and PAR models had limited performance in predicting 10-year CHD risk. Although the PAR model showed better discrimination, both models underestimated the risk in women and overestimated risk in men. The calibration was unsatisfactory for both models. The clinical utility appeared limited based on decision curve analysis. Our findings indicate that directly applying the existing FRS or PAR model to predict CHD risk in the rural Chinese population may have limitations. Further efforts to improve individual risk assessment tailored to this population are needed.

Numerous risk assessment tools have been developed to evaluate the risk of CHD, but many of them are derived from Western populations and may not apply to the Chinese population ([Sun et al., 2017](#)). More than ten years ago, Liu and Yang developed risk prediction models for coronary heart disease and ischemic heart disease in China based on the Framingham model. However, significant changes have occurred in cardiovascular risk factors in China due to changes in per capita income, an aging population, the westernization of lifestyles, and extended life expectancy ([Ahn et al., n.d.](#); [Janssen et al., 2009](#)). It remains unclear whether the FRS is still effective in predicting 10-year CHD events in China. Rodondi reported that the FRS underestimated the risk of CHD in both black and white older people ([Rodondi et al., 2012](#)). While other researchers believed that the FRS is a direct and feasible method that can be used as a clinical tool to predict coronary heart disease ([Sayin et al., 2014](#)).

In our study, the FRS demonstrated limited discrimination for predicting CHD risk with C-statistics of 0.65 and 0.67 for men and women, respectively. Although models specifically developed for the Chinese population like the PAR have been validated ([Yang et al., 2016](#)), their applicability in rural populations requires further evaluation ([Jiang et al., 2020](#)). The PAR incorporates a rural variable and has shown good discrimination in some Chinese cohorts, albeit with overestimation in women ([Tang et al., 2019](#)). The PAR takes into account the rural factor in the model, which may be more accurate for Chinese rural individuals. Tang ([Tang et al., 2019](#)) reported that the PAR performed well in predicting 5-year ASCVD disease in the Fangshan cohort, accurately predicting risk in men but overestimating risk in women (C-statistic 0.685 for men; 0.711 for women). However, our findings indicate that directly applying the PAR to rural populations may have limitations. Developing and validating optimized CHD risk assessment tools tailored for the rural Chinese population should be a focus of future research.

Cardiovascular risk is influenced by a complex interplay of genetic, biochemical, sociocultural and lifestyle factors ([Lv et al., 2017](#); [Sadeghi](#)

Table 2

External validation of CHD risk prediction equations between China-PAR and FRS among cohort participants, RNC, 2008–2012.

Variable	Overall		Men		Women	
	FRS	China-PAR	FRS	China-PAR	FRS	China-PAR
Actual events ^α , n	168	168	69	69	99	99
Kaplan-Meier-adjusted events (rate) ^β , n (%)	102.2 (7.4)	102.2 (7.4)	45.6 (8.0)	45.6 (8.0)	57.6 (7.1)	57.6 (7.1)
Predicted events, n	79.9	55.4	114.9	81.0	55.3	37.4
Expected-observed ratio	0.78	0.54	2.52	1.78	0.96	0.65
C statistic, %	64.02	72.45	65.45	74.78	67.33	74.5
95 % CI, %	56.80–71.24	66.25–78.65	55.50–75.41	64.77–84.78	58.72–75.94	67.91–81.09
Calibration χ^2	170.06	486.75	26.73	83.41	175.27	479.94
p value	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

RNC, Rural Northwest China; CI, confidence interval; CHD, coronary heart disease; α , the actual number of CHD events through follow-up; β , the observed number of CHD events (rate) after Kaplan-Meier adjustment through follow-up; FRS, Framingham Risk Score; China-PAR, China-PAR risk equation.

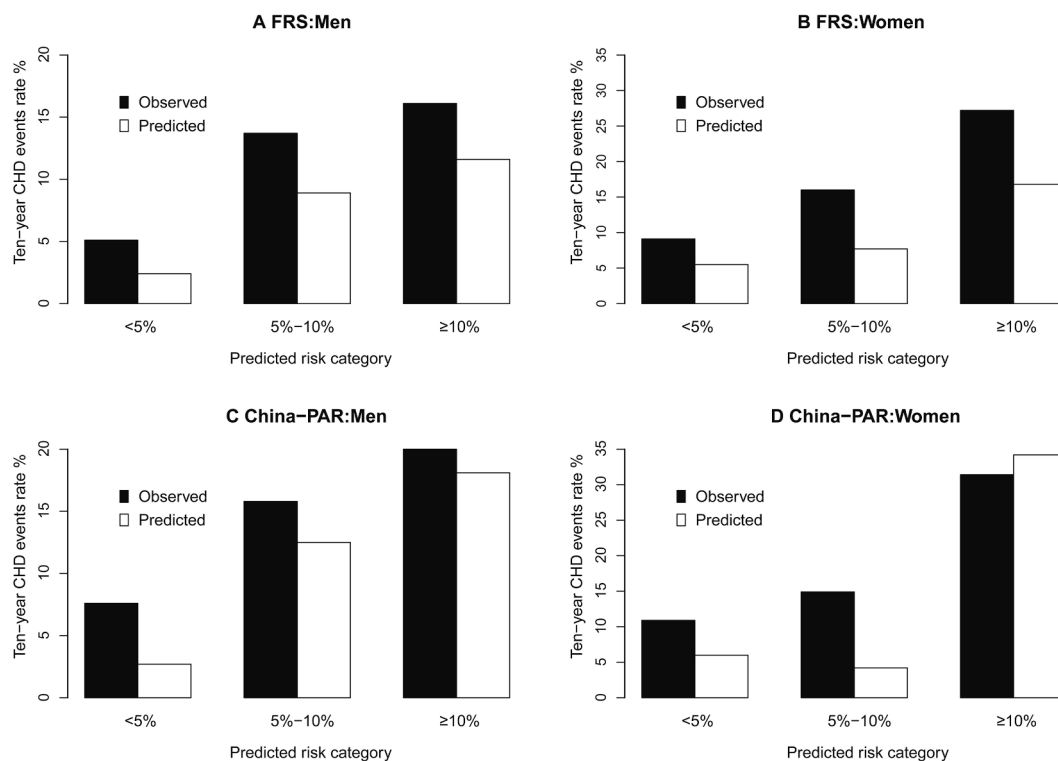


Fig. 2. Observed and Predicted Ten-year CHD events rates among participants in each risk category, RNC, 2008–2012. FRS, Framingham Risk Score; China-PAR, China-PAR risk equation; RNC, Rural Northwest China.

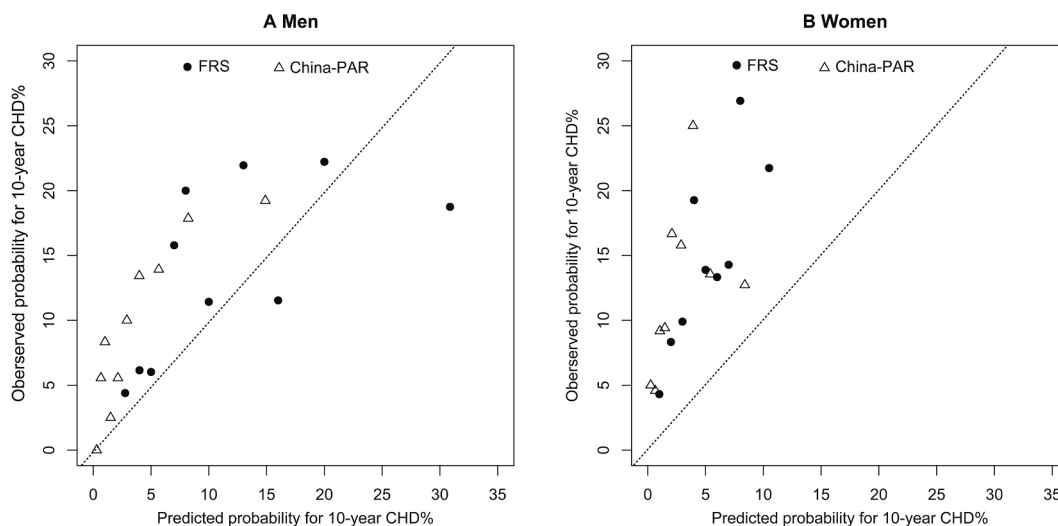


Fig. 3. Calibration plots for the external validation of ten-year CHD risk prediction among participants using the China-PAR and FRS, RNC, 2008–2012. FRS, Framingham Risk Score; China-PAR, China-PAR risk equation; RNC, Rural Northwest China.

et al., 2020). Our rural cohort has distinct characteristics including dietary habits, physical activity patterns and religious beliefs compared to the populations in which the FRS and PAR models were developed (Wang et al., 2015; Yi et al., 2010). However, current risk assessment tools are based on traditional risk factors and may not fully account for these unique factors. Additionally, external validation may lead to differences in accuracy between the original cohort and the validation population due to changes in population structure. The unique lifestyle behaviors and sociocultural characteristics of this cohort, including dietary patterns, physical activity levels, and spiritual beliefs, may not be fully captured by the variables included in the existing risk models. This could contribute to the underestimation of CHD risk.

Traditional risk factors such as gender, age and lifestyle behaviors are important predictors of CHD risk (Khamis et al., 2016; Nichols et al., 2013). In this study, the proportion of females was higher than males, and males had a higher average age than females, potentially leading to underestimation of risk. Moreover, the low smoking and drinking rates in the rural population may also lead to an underestimation of risk, especially among females. This reflects the unique characteristics of our rural cohort. As reflected in many Chinese references, the smoking and drinking rates among women in rural areas of northwest China are very low. Moreover, the women in this study are relatively older, these groups themselves have relatively low smoking and alcohol consumption rates. Therefore, the low prevalence of smoking and drinking

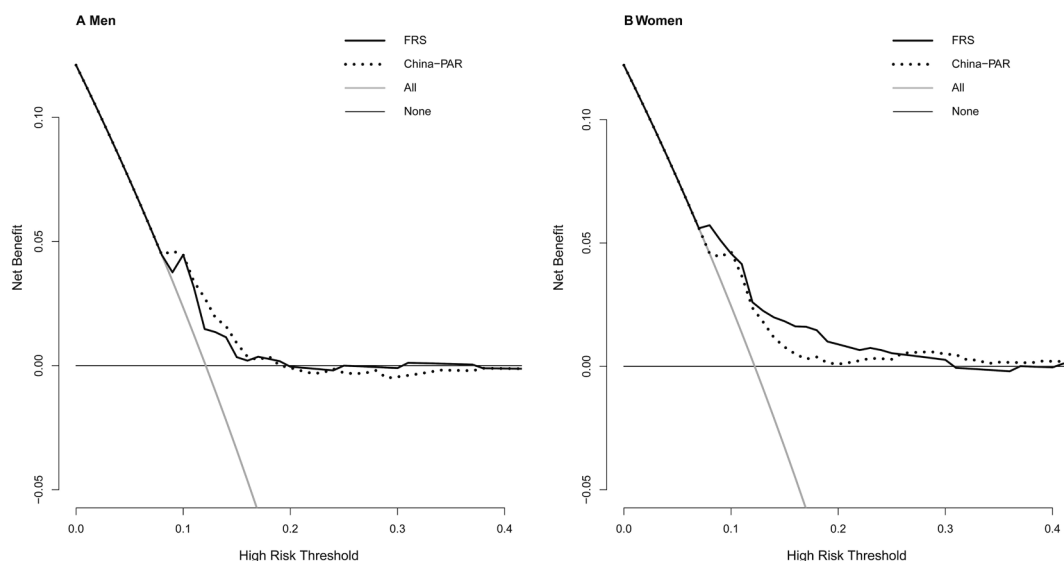


Fig. 4. Decision curves among participants for the FRS and China-PAR, RNC, 2008–2012. FRS, Framingham Risk Score; China-PAR, China-PAR risk equation; RNC, Rural Northwest China.

represents the distinctive lifestyle pattern in this population, which is markedly different from other regions. Additionally, as Ningxia is located in the “stroke belt” and has a high prevalence of metabolic syndrome among rural adults (Xu et al., 2013; Yi et al., 2010), the risk of CHD in rural populations may be higher than in urban populations. Therefore, it is crucial to account for these unique factors when assessing CHD risk in the rural population.

There are several limitations that need to be addressed. First, the outcome event of this study was CHD, but there are other atherosclerosis-related events that could also be associated with the risk models. Second, while the diagnosis of coronary heart disease was based on oral reports, we used medical documents from patients to ensure accurate diagnosis and avoid underestimation of risk. Nonetheless, the lack of clear diagnosis documents based on the hospital information system is still a limitation of our study. Third, the single follow-up design at 10 years is a limitation. Additional follow-up assessments could have allowed evaluation of the changes in predictive abilities and calibration of the models over longer periods. Finally, the loss to follow-up was 25.1% in our study. Although we used statistical approaches such as the Kaplan-Meier method to minimize the potential influence of missing data.

Our study validated the Framingham Risk Score and PAR model for predicting 10-year CHD risk in a prospective rural Chinese cohort. Although the PAR model showed better discrimination, both models demonstrated limitations in risk estimation and calibration. The findings indicate that directly applying existing tools to the rural population may have reduced accuracy due to unaccounted sociocultural and lifestyle factors. Developing and validating risk assessment models tailored for the rural Chinese population through incorporating additional biomarkers and lifestyle variables is warranted. Our study provides valuable insights into the predictive performance of current cardiovascular risk models in the understudied rural population. Future research should focus on optimizing CHD risk assessment strategies suitable for diverse Chinese subgroups.

5. Conclusion

Our study suggests that the performance of the PAR Equations and Framingham Risk Score in predicting 10-year CHD risk is limited for the rural Northwest population cohort. Overall, both models underestimated risk in females but slightly over-predicted risk in males. While PAR showed better discrimination, its calibration was similar to FRS and

unsatisfactory. In addition, the DCA curve indicated controversial clinical utility of these models. Although the Risk Score was developed to estimate the risk of CHD occurrence within a 10-year time-frame rather than providing a specific risk estimate at 10 years, our findings indicate that directly applying existing risk assessment tools to this population may have certain limitations. Further research could benefit from increased follow-up times to obtain more informative data. However, the present study confirms that developing risk assessment tailored to Chinese rural populations is necessary for more precise individual risk estimation and primary prevention in the future.

6. Ethics approval

This study was approved by the Ningxia Medical University Ethics Committee (Ethics ID 2018-012, 2020-689). All of the participants provided their written informed consent before the start of the study.

Authors contributions

All authors contributed to the study conception and design. Conceptualization and resources were provided by [Yuhong Zhang] and [Yi Zhao]. Material preparation, data collection and analysis were performed by [Kai Wang], [Kexin Chen], [Jiaying Zhang], [Juan Li] and [Chan Yang]. Visualization was performed by [Qingan Wang]. The first draft of the manuscript was written by [Jiangwei Qiu] and [Zhenqi Chang], and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.pmedr.2023.102503>.

References

- Abd El-Wahab, E.W., 2021. Predicting coronary heart disease using risk assessment charts and risk factor categories. *J. Public Health (Berl.)* 29, 1037–1045. <https://doi.org/10.1007/s10389-020-01224-z>.
- Ahn, K.A., Yun, J.E., Cho, E.R., Nam, C.M., Jang, Y., Jee, S.H., n.d. Framingham Equation Model Overestimates Risk of Ischemic Heart Disease in Korean Men and Women. *Epidemiol. Health* 28, 162–170.
- Alba, A.C., Agoritsas, T., Walsh, M., Hanna, S., Iorio, A., Devereaux, P.J., McGinn, T., Guyatt, G., 2017. Discrimination and Calibration of Clinical Prediction Models: Users' Guides to the Medical Literature. *J. Am. Med. Assoc.* 318, 1377–1384. <https://doi.org/10.1001/jama.2017.12126>.
- Bansilal, S., Castellano, J.M., Fuster, V., 2015. Global burden of CVD: focus on secondary prevention of cardiovascular disease. *Int. J. Cardiol.* 201 (Suppl 1), S1–S7. [https://doi.org/10.1016/S0166-5273\(15\)31026-3](https://doi.org/10.1016/S0166-5273(15)31026-3).
- Colpani, V., Baena, C.P., Jaspers, L., van Dijk, G.M., Farajzadegan, Z., Dhana, K., Tielmans, M.J., Voortman, T., Freak-Poli, R., Veloso, G.G.V., Chowdhury, R., Kavousi, M., Muka, T., Franco, O.H., 2018. Lifestyle factors, cardiovascular disease and all-cause mortality in middle-aged and elderly women: a systematic review and meta-analysis. *Eur. J. Epidemiol.* 33, 831–845. <https://doi.org/10.1007/s10654-018-0374-z>.
- Cook, N.R., Ridker, P.M., 2016. Calibration of the Pooled Cohort Equations for Atherosclerotic Cardiovascular Disease: An Update. *Ann. Intern. Med.* 165, 786–794. <https://doi.org/10.7326/M16-1739>.
- D'Agostino, R.B., Nam, B.-H., 2003. Evaluation of the Performance of Survival Analysis Models: Discrimination and Calibration Measures, in: *Handbook of Statistics, Advances in Survival Analysis*. Elsevier, pp. 1–25. doi: 10.1016/S0169-7161(03)23001-7.
- D'Arrigo, G., Leonardi, D., Abd ElHafeez, S., Fusaro, M., Tripepi, G., Roumeliotis, S., 2021. Methods to Analyse Time-to-Event Data: The Kaplan-Meier Survival Curve. *Oxid. Med. Cell. Longev.* 2021, 2290120. <https://doi.org/10.1155/2021/2290120>.
- Heagerty, P.J., Lumley, T., Pepe, M.S., 2000. Time-dependent ROC curves for censored survival data and a diagnostic marker. *Biometrics* 56, 337–344. <https://doi.org/10.1111/j.0006-341x.2000.00337.x>.
- Hense, H.-W., Koesters, E., Wellmann, J., Meisinger, C., Völzke, H., Keil, U., 2008. Evaluation of a recalibrated systematic coronary risk evaluation cardiovascular risk chart: results from systematic coronary risk evaluation Germany. *Eur. J. Prev. Cardiol.* 15, 409–415.
- Janssen, K.J.M., Vergouwe, Y., Kalkman, C.J., Grobbee, D.E., Moons, K.G.M., 2009. A simple method to adjust clinical prediction models to local circumstances. *Can. J. Anesth./J. Can. Anesth.* 56, 194. <https://doi.org/10.1007/s12630-009-9041-x>.
- Jiang, Y., Ma, R., Guo, H., Zhang, X., Wang, X., Wang, K., Hu, Y., Keerman, M., Yan, Y., Ma, J., Song, Y., Zhang, J., He, J., Guo, S., 2020. External validation of three atherosclerotic cardiovascular disease risk equations in rural areas of Xinjiang, China. *BMC Public Health* 20, 1471. <https://doi.org/10.1186/s12889-020-09579-4>.
- Khamis, R.Y., Ammari, T., Mikhail, G.W., 2016. Gender differences in coronary heart disease. *Heart* 102, 1142–1149. <https://doi.org/10.1136/heartjnl-2014-306463>.
- Lee, C.H., Woo, Y.C., Lam, J.K.Y., Fong, C.H.Y., Cheung, B.M.Y., Lam, K.S.L., Tan, K.C.B., 2015. Validation of the Pooled Cohort equations in a long-term cohort study of Hong Kong Chinese. *J. Clin. Lipidol.* 9, 640–646.e2. <https://doi.org/10.1016/j.jacl.2015.06.005>.
- Li, H.H., Huang, S., Liu, X.Z., Zou, D.J., 2019. Applying the China-PAR Risk Algorithm to Assess 10-year Atherosclerotic Cardiovascular Disease Risk in Populations Receiving Routine Physical Examinations in Eastern China. *Biomed. Environ. Sci.* 32, 87–95. <https://doi.org/10.3967/bes2019.014>.
- Lloyd-Jones, D.M., Braun, L.T., Ndumele, C.E., Smith Jr, S.C., Sperling, L.S., Virani, S.S., Blumenthal, R.S., 2019. Use of risk assessment tools to guide decision-making in the primary prevention of atherosclerotic cardiovascular disease: a special report from the American Heart Association and American College of Cardiology. *Circulation* 139, e1162–e1177. doi: 10.1161/cir.0000000000000638.
- Lv, J., Yu, C., Guo, Y., Bian, Z., Yang, L., Chen, Y., Tang, X., Zhang, W., Qian, Y., Huang, Y., Wang, X., Chen, J., Chen, Z., Qi, L., Li, L., China Kadoorie Biobank Collaborative Group, 2017. Adherence to Healthy Lifestyle and Cardiovascular Diseases in the Chinese Population. *J. Am. Coll. Cardiol.* 69, 1116–1125. doi: 10.1016/j.jacc.2016.11.076.
- Mahmood, S.S., Levy, D., Vasan, R.S., Wang, T.J., 2014. The Framingham Heart Study and the epidemiology of cardiovascular disease: a historical perspective. *Lancet* 383, 999–1008. [https://doi.org/10.1016/S0140-6736\(13\)61752-3](https://doi.org/10.1016/S0140-6736(13)61752-3).
- Nattino, G., Lemeshow, S., Phillips, G., Finazzi, S., Bertolini, G., 2017. Assessing the calibration of dichotomous outcome models with the calibration belt. *Stata J.* 17, 1003–1014.
- Nichols, M., Townsend, N., Scarborough, P., Rayner, M., 2013. Trends in age-specific coronary heart disease mortality in the European Union over three decades: 1980–2009. *Eur. Heart J.* 34, 3017–3027. <https://doi.org/10.1093/eurheartj/ehi159>.
- Rodondi, N., Locatelli, I., Aujesky, D., Butler, J., Vittinghoff, E., Simonsick, E., Satterfield, S., Newman, A.B., Wilson, P.W.F., Pletcher, M.J., Bauer, D.C., for the Health ABC Study, 2012. Framingham Risk Score and Alternatives for Prediction of Coronary Heart Disease in Older Adults. *PLoS ONE* 7, e34287. doi: 10.1371/journal.pone.0034287.
- Sadeghi, M., Daneshpour, M.S., Khodakaram, S., Momenan, A.A., Akbarzadeh, M., Soori, H., 2020. Impact of secondhand smoke exposure in former smokers on their subsequent risk of coronary heart disease: evidence from the population-based cohort of the Tehran Lipid and Glucose Study. *Epidemiol. Health* 42, e2020009.
- Sayin, M.R., Cetiner, M.A., Karabag, T., Akpınar, I., Sayin, E., Kurcer, M.A., Dogan, S.M., Aydin, M., 2014. Framingham risk score and severity of coronary artery disease. *Herz* 39, 638–643. <https://doi.org/10.1007/s00059-013-3881-4>.
- Selvarajah, S., Kaur, G., Haniff, J., Cheong, K.C., Hiong, T.G., van der Graaf, Y., Bots, M. L., 2014. Comparison of the Framingham Risk Score, SCORE and WHO/ISH cardiovascular risk prediction models in an Asian population. *Int. J. Cardiol.* 176, 211–218. <https://doi.org/10.1016/j.ijcard.2014.07.066>.
- Sun, C., Xu, F., Liu, X., Fang, M., Zhou, H., Lian, Y., Xie, C., Sun, N., Wang, C., 2017. Comparison of validation and application on various cardiovascular disease mortality risk prediction models in Chinese rural population. *Sci. Rep.* 7, 43227. <https://doi.org/10.1038/srep43227>.
- Tang, X., Zhang, D., He, L., Wu, N., Si, Y., Cao, Y., Huang, S., Li, N., Li, J., Dou, H., Gao, P., Hu, Y., 2019. Performance of atherosclerotic cardiovascular risk prediction models in a rural Northern: Results from the Fangshan Cohort Study. *Am. Heart J.* 211, 34–44. doi: 10/gmxbnk.
- Tzoulaki, I., 2009. Assessment of Claims of Improved Prediction Beyond the Framingham Risk Score. *J. Am. Med. Assoc.* 302, 2345. <https://doi.org/10.1001/jama.2009.1757>.
- Uno, H., Cai, T., Pencina, M.J., D'Agostino, R.B., Wei, L.J., 2011. On the C-statistics for evaluating overall adequacy of risk prediction procedures with censored survival data. *Statist. Med.* 30, 1105–1117. <https://doi.org/10.1002/sim.4154>.
- Vickers, A.J., Elkin, E.B., 2006. Decision curve analysis: a novel method for evaluating prediction models. *Med. Decis. Making* 26, 565–574. <https://doi.org/10.1177/0272989X06295361>.
- Wang, Z., Koenig, H.G., Al Shohaib, S., 2015. Religious involvement and tobacco use in mainland China: a preliminary study. *BMC Public Health* 15, 155. <https://doi.org/10.1186/s12889-015-1478-y>.
- Xu, G., Ma, M., Liu, X., Hankey, G.J., 2013. Is there a stroke belt in China and why? *Stroke* 44, 1775–1783. <https://doi.org/10.1161/STROKEAHA.113.001238>.
- Y, H., W, L., F, M., Ra, G., L, O.-M., 2020. A tutorial on calibration measurements and calibration models for clinical prediction models. *J. Am. Med. Inform. Assoc. JAMIA* 27, doi: 10.1093/jamia/ocz228.
- Yang, X., Li, J., Hu, D., Chen, J., Li, Y., Huang, J., Liu, X., Liu, F., Cao, J., Shen, C., Yu, L., Lu, F., Wu, X., Zhao, L., Wu, X., Gu, D., 2016. Predicting the 10-Year Risks of Atherosclerotic Cardiovascular Disease in Chinese Population: The China-PAR Project (Prediction for ASCVD Risk in China). *Circulation* 134, 1430–1440. <https://doi.org/10.1161/circulationaha.116.022367>.
- Yi, Z., Jing, J., Xiu-ying, L., Hongxia, X., Jianjun, Y., Yuhong, Z., 2010. Prevalence of the metabolic syndrome among rural original adults in Ningxia, China. *BMC Public Health* 10, 140. doi: 10/b9jz26.
- Zaidi, S., Brueckner, M., 2017. Genetics and Genomics of Congenital Heart Disease. *Circ. Res.* 120, 923–940. <https://doi.org/10.1161/CIRCRESAHA.116.309140>.
- Zhang, Y., Fang, X., Guan, S., Wu, X., Liu, H., Wang, C., Zhang, Z., Gu, X., Liu, C., Cheng, J., 2020. Validation of 10-Year Stroke Prediction Scores in a Community-Based Cohort of Chinese Older Adults. *Front. Neurol.* 11, 986. <https://doi.org/10.3389/fneur.2020.00986>.
- Zhao, Y., Liao, S., He, J., Jin, Y., Fu, H., Chen, X., Fan, X., Xu, H., Liu, X., Jin, J., Zhang, Y., 2014. Association of vitamin D receptor gene polymorphisms with metabolic syndrome: a case-control design of population-based cross-sectional study in North China. *Lipids Health Dis.* 13, 129. doi: 10/gpkzng.
- Zhao, Y., Wang, B., Wang, G., Huang, L., Yin, T., Li, X., Liu, X., Wang, Q., Jing, J., Yang, J., Zhang, Y., 2020. Functional interaction between plasma phospholipid fatty acids and insulin resistance in leucocyte telomere length maintenance. *Lipids Health Dis.* 19, 11. <https://doi.org/10.1186/s12944-020-1194-1>.