Predicting the 10-Year Risks of Atherosclerotic Cardiovascular Disease in Chinese Population

The China-PAR Project (Prediction for ASCVD Risk in China)

Editorial, see p 1441

BACKGROUND: The accurate assessment of individual risk can be of great value to guiding and facilitating the prevention of atherosclerotic cardiovascular disease (ASCVD). However, prediction models in common use were formulated primarily in white populations. The China-PAR project (Prediction for ASCVD Risk in China) is aimed at developing and validating 10-year risk prediction equations for ASCVD from 4 contemporary Chinese cohorts.

METHODS: Two prospective studies followed up together with a unified protocol were used as the derivation cohort to develop 10-year ASCVD risk equations in 21 320 Chinese participants. The external validation was evaluated in 2 independent Chinese cohorts with 14 123 and 70 838 participants. Furthermore, model performance was compared with the Pooled Cohort Equations reported in the American College of Cardiology/American Heart Association guideline.

RESULTS: Over 12 years of follow-up in the derivation cohort with 21 320 Chinese participants, 1048 subjects developed a first ASCVD event. Sex-specific equations had C statistics of 0.794 (95% confidence interval, 0.775–0.814) for men and 0.811 (95% confidence interval, 0.787–0.835) for women. The predicted rates were similar to the observed rates, as indicated by a calibration χ^2 of 13.1 for men (P=0.16) and 12.8 for women (P=0.17). Good internal and external validations of our equations were achieved in subsequent analyses. Compared with the Chinese equations, the Pooled Cohort Equations had lower C statistics and much higher calibration χ^2 values in men.

CONCLUSIONS: Our project developed effective tools with good performance for 10-year ASCVD risk prediction among a Chinese population that will help to improve the primary prevention and management of cardiovascular disease.

Xueli Yang, PhD*
Jianxin Li, MD*
Dongsheng Hu, PhD
Jichun Chen, MD
Ying Li, MD
Jianfeng Huang, MD
Xiaoqing Liu, MD
Fangchao Liu, PhD
Jie Cao, MD
Chong Shen, PhD
Ling Yu, MD
Fanghong Lu, MD
Xianping Wu, MD
Liancheng Zhao, MD
Xigui Wu, MD
Dongfeng Gu, MD, PhD

*Drs Yang and Li contributed equally to this work.

Correspondence to: Dongfeng Gu, MD, PhD, Department of Epidemiology, Fuwai Hospital, State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, 167 Beilishi Rd, Beijing 100037, China. E-mail gudf@yahoo.com

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Clinical Perspective

What Is New?

- The China-PAR project (Prediction for ASCVD Risk in China) is the first study to develop and validate 10-year risk prediction equations for atherosclerotic cardiovascular disease (ASCVD) using data from 4 contemporary Chinese cohorts.
- The sex-specific equations had excellent performance of ASCVD risk prediction with good internal consistency and external validation; our findings also indicated that the Pooled Cohort Equations derived from Western populations were not appropriate for the Chinese population.

What Are the Clinical Implications?

- Risk assessment is a fundamental component of prevention of ASCVD.
- More aggressive risk factor modification should be required among individuals with a predicted high risk.
- The sex-specific China-PAR equations provide a valuable tool for identifying high-risk individuals and matching the intensity of preventive interventions to an individual's absolute risk of ASCVD development.
- The risk prediction equations will help clinicians guide preventive approaches, individualized counseling, and treatment decisions for ASCVD by more accurate estimation of 10-year risk of ASCVD.

Cardiovascular disease (CVD) is the leading cause of death and disease burden in China and worldwide.[1–3] In 2013, the number of CVD deaths reached 3.72 million in China.[2] During the past decades, stroke and ischemic heart disease have become the top 2 causes for years of life lost.[4] The total cost for hospitalization of acute myocardial infarction (MI) and stroke in China was 70.5 billion RMB (approximately US $10.7 billion) in 2013.[5]

The Framingham Heart Study identified several risk factors and developed the first coronary heart disease (CHD) risk equations in 1976.[6] Since then, several tools for CVD risk evaluation have been published and have guided public health and clinical practice in different populations. Well-known examples are the Framingham general CVD equations in the United States,[7] the Systematic Coronary Risk Evaluation model in Europe,[8] the QRISK in the United Kingdom,[9] and the most recent Pooled Cohort Equations (PCEs) for atherosclerotic CVD (ASCVD) reported in the American College of Cardiology/American Heart Association guideline.[10] However, these equations were all derived from Western samples, which limited their applicability to other populations.[10,11] Although equations have been developed by Barzi et al[12] for Asian populations, they only estimated 8-year CVD risk without information on diabetes mellitus and high-density lipoprotein cholesterol (HDL-C).

Rapidly increasing per-capita income, an aging population, westernization of lifestyle, and longer life spans led to dramatic changes in the CVD risk factors pattern in China during the past decade.[13] The disease burdens of CHD and stroke also increased and contributed to the major challenge of primary care in China.[4] Although Chinese risk prediction tools for CHD and ischemic CVD were developed 10 years ago and were based on Framingham equations,[14,15] data based on a large sample size of Chinese adults were limited for risk prediction models that focused on all ASCVD, defined as nonfatal acute MI or CHD death or fatal or nonfatal stroke. Therefore, we conducted the China-PAR project (Prediction for ASCVD Risk in China) to develop and validate the Chinese ASCVD risk equations in multiple contemporary Chinese cohorts with a total of 106 281 participants.

METHODS

Derivation Cohort

The China-PAR project used InterASIA (International Collaborative Study of Cardiovascular Disease in Asia) and China MUCA (1998) (China Multi-Center Collaborative Study of Cardiovascular Epidemiology) to develop the Chinese ASCVD risk equations as the derivation cohort. InterASIA, which was established from 2000 to 2001, selected a nationally representative sample 35 to 74 years of age in China using a 4-stage stratified sampling method. The sampling process was stratified by geographic region (northern/southern China, divided by the Yangtzi River) and urbanization (urban/rural); detailed information has been published elsewhere.[16] The China MUCA (1998) was established in 1998 with cluster random sampling. Fifteen clusters were selected that also were based on geographic region and urbanization, with ≈500 men and 500 women 35 to 59 years of age in each cluster.[17]

Among the 27 020 participants from these 2 studies, 24 334 (90.1%) completed the follow-up survey with an average follow-up duration of 12.3 years. After the exclusion of 418 participants with MI or stroke, 1094 participants with poor-quality measurements for blood specimens at baseline, and 1502 participants who were followed up only until 2008 and did not participate in the second follow-up survey from 2012 to 2015, we included 21 320 participants to derive the China-PAR equations (Figure I in the online-only Data Supplement).

Baseline examination was conducted by trained research staff under stringent quality control in both studies. Demographics, lifestyle information, and medical history were collected with standardized questionnaires. Current cigarette smoking was self-reported by participants. Family history of ASCVD was defined as at least a parent or a sibling with MI or stroke. Body weight and height were measured with the subject wearing light indoor clothes without shoes, and body mass index was calculated as kilograms per meters squared. Waist circumference (WC) was measured at 1 cm above the navel at minimal respiration. Three blood pressure (BP) measurements were taken after a 5-minute rest in subjects while seated. The mean of the 3 BPs was used in the analysis. In addition, blood samples were drawn from participants after fasting for at least 10 hours to measure serum glucose and lipids levels. Diabetes

mellitus was defined as having a fasting glucose ≥126 mg/dL or self-reported current treatment with antidiabetes medication (insulin or oral hypoglycemic agents).

The first follow-up survey for both InterASIA and the China MUCA (1998) was conducted during 2007 to 2008, and the second was conducted during 2012 to 2015. Study participants or their proxies were identified and interviewed to obtain disease status and vital information. Hospital records or death certificates were also collected. A study-wide end-point assessment committee at Fuwai Hospital in Beijing adjudicated the final end-point events by reviewing all incidence and death records. Two committee members independently verified the events, and discrepancies were resolved by discussion involving additional committee members.

ASCVD was defined as nonfatal acute MI or CHD death or fatal or nonfatal stroke. Acute MI was identified as a change in biochemical markers of myocardial necrosis accompanied by ischemic symptoms, pathological Q waves, ST-segment elevation or depression, or coronary intervention.[18] CHD death included all fatal events resulting from MI or other coronary deaths. Stroke included clinical signs and symptoms of subarachnoid or intracerebral hemorrhage or cerebral infarction, which were rapidly developing signs of focal (or global) disturbances in cerebral function lasting >24 hours without an apparent nonvascular cause.

Validation Cohort

Participants from China MUCA (1992–1994) and CIMIC (Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study) were used as validation cohorts to evaluate the performance of the equations. The China MUCA (1992–1994), established from 1992 to 1994, selected participants 35 to 59 years of age from 14 clusters in China.[19] A total of 14 392 participants in 9 of the 14 clusters were invited to participate in the subsequent follow-up survey. The cohort was followed up every 2 years from 1996 to 2004, and then a recent follow-up survey was conducted from 2012 to 2015. Methods for baseline and follow-up survey were the same as for China MUCA (1998). A total of 14 125 participants (98.1%) completed the follow-up survey until 2015. The average follow-up duration was 17.1 years. Data from 14 123 participants without MI or stroke at baseline were used for external validation (Figure I in the online-only Data Supplement).

The CIMIC was a large, community-based cohort that was established from 2007 to 2008. The study selected 4 survey sites from 3 provinces (Shandong, Henan, and Jiangsu) with different economic development levels in China. Two communities in rural areas were selected from each survey site. Approximately 10 000 participants were selected randomly in each community. In total, 86 428 participants ≥16 years of age completed the baseline study and were invited to participate in the follow-up survey from 2012 to 2015. The methods for the baseline and follow-up surveys were the same as for InterASIA. In total, 80 929 participants (93.6%) were followed up successfully, with an average follow-up duration of 5.9 years. Data from a 70 838 participants 35 to 74 years of age who were free of MI and stroke at baseline were used for external validation (Figure I in the online-only Data Supplement).

These preceding studies were all approved by the Institutional Review Board at Fuwai Hospital in Beijing. Written informed consent was obtained from each participant before data collection.

Statistical Analysis

Sex-specific means or corresponding percentages of baseline variables were calculated. Person-years of follow-up for each study participant were calculated as the difference between the date of the baseline examination and the date of occurrence of ASCVD, the date of death, or the last follow-up interview, whichever occurred first.

Ten-year ASCVD risk was defined as the risk of developing the first ASCVD event over a 10-year period among a population without ASCVD at baseline. The ASCVD risk prediction equations were developed from sex-specific Cox proportional hazards models. All continuous covariates in the models were natural log–transformed to improve the discrimination and calibration of the prediction models and to minimize the influence of extreme observations. The major risk factors were retained in our models directly, including age, treated or untreated systolic BP (SBP), total cholesterol, HDL-C, current smoking (yes/no), and diabetes mellitus (yes/no). In addition, we evaluated whether the model would be improved by the inclusion of additional variables, including body mass index, WC, geographic region (northern/southern China), urbanization (urban/rural), and family history of ASCVD (yes/no). The final models should include variables with a relative integrated discrimination improvement (IDI) index of ≥6%.[10] Interactions with age were also considered for each risk factor. The final models should include any interaction terms with value of $P<0.01$ or $P=0.01$ to 0.05 and the continuous net reclassification improvement for nonevents ≥15% or statistically significant IDI.[20,21] Model fit was evaluated by discrimination C statistics and calibration χ^2 using the modified Nam-D'Agostino test.[22–24]

Internal consistency of the discrimination and calibration performance measures was evaluated by a 10×10 cross-validation technique.[25] Means and percentiles of the discrimination C statistic, calibration χ^2, and calibration slope in internal validation were calculated and compared with those in the models for the whole population.

We evaluated the performance of the equations in predicting 10-year ASCVD events in the China MUCA (1992–1994) and 5-year ASCVD events in the CIMIC. For the CIMIC, the equations were adjusted for the reduced follow-up time by calculating 5-year baseline survival rate using methods developed by D'Agostino et al.[26] All other parameters were the same as the 10-year prediction equations. We assessed the equations by using predicted number of events, discrimination C statistic, and calibration χ^2 in validation cohorts. We also illustrated the prediction ability of the equations by using calibration charts. Participants in the validation cohorts were divided into 4 categories based on predicted ASCVD risk (<5%, 5%–7.4%, 7.5%–9.9%, and ≥10%), which were clinically meaningful cut points. Kaplan-Meier analysis was used to obtain the observed ASCVD event rate,[23] which was then compared with the predicted event rate in each category in calibration charts. The results were also shown in calibration plots comparing the predicted probabilities with the observed probabilities according to the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis statement.[27]

The PCEs released in the American College of Cardiology/American Heart Association guideline were evaluated in the derivation cohort and 2 validation cohorts. We calculated the predicted number of events, discrimination C statistic, and calibration χ^2 to assess the PCEs and made comparisons with those estimates from our equations. We also drew calibration charts in deciles of predicted risk to illustrate the difference of prediction between the PCEs and our equations.

All analyses were conducted with the SAS statistical package (version 9.2; SAS Institute, Inc., Cary, NC).

RESULTS

The baseline characteristics and ASCVD event rates of the derivation cohort are presented in Table 1. Men were slightly older and had a larger WC, higher SBP and diastolic BP, and lower total cholesterol and HDL-C levels than women. Men were more likely to be current smokers and less likely to have had antihypertensive treatment within the previous 2 weeks. During an average follow-up of 12.3 years, 1048 incident ASCVD events (645 in men and 403 in women) were identified, with a higher ASCVD event rate in men than in women after Kaplan-Meier adjustment.

Table 1. Baseline Characteristics and ASCVD Event Rates of the Derivation Cohort, by Sex

	Men (n=10 334)	Women (n=10 986)
Age, mean (SD), y	48.8 (9.4)	48.4 (9.2)
Northern China, n (%)	5286 (51.2)	5538 (50.4)
Urban, n (%)	4324 (41.8)	4582 (41.7)
Current smoker, n (%)	6269 (60.7)	489 (4.5)
Waist circumference, mean (SD), cm	80.1 (10.0)	76.5 (9.7)
SBP, mean (SD), mm Hg	124.8 (19.0)	122.5 (20.6)
DBP, mean (SD), mm Hg	80.1 (11.6)	76.9 (11.0)
Antihypertensive treatment within 2 wk, n (%)	595 (5.8)	808 (7.4)
Total cholesterol, mean (SD), mg/dL	186.6 (37.6)	188.2 (38.3)
HDL-C, mean (SD), mg/dL	50.4 (13.9)	53.4 (12.8)
Diabetes mellitus, n (%)	513 (5.1)	544 (5.1)
Family history of ASCVD, n (%)	1385 (13.4)	1424 (13.0)
Incident ASCVD events, n (%)	645 (6.2)	403 (3.7)
Incidence of ASCVD, n/100 000 person-y	514.2	293.4
10-y Kaplan-Meier ASCVD rate, %	4.6	2.7

ASCVD indicates atherosclerotic cardiovascular disease; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; and SBP, systolic blood pressure.

To convert total cholesterol and HDL-C to mmol/L, multiply by 0.0259.

Sex-specific equations were developed from the derivation cohort for assessing 10-year ASCVD risk among a Chinese population. Besides the major risk factors (age, treated or untreated SBP, total cholesterol, HDL-C, current smoking, and diabetes mellitus), 4 additional variables—WC, geographic region, urbanization, and family history of ASCVD (relative IDI=6.9%, 65.4%, 26.1%, and 24.3%, respectively)—were added to the equation for men, and 2 additional variables—WC and geographic region (relative IDI=9.6% and 21.3%, respectively)—were added to the equation for women. Available interaction terms of age with risk factors (treated or untreated SBP, current smoking, and family history of ASCVD) were also added to the equations as covariates. The parameters for the equations are shown in Table I in the online-only Data Supplement with the specification in Table II in the online-only Data Supplement. For example, the 10-year ASCVD risk was estimated for an individual 60 years of age with untreated SBP of 130 mm Hg, total cholesterol of 210 mg/dL, HDL-C of 55 mg/dL, and WC of 80 cm; who did not smoke; who had diabetes mellitus; who lived in an urban area of northern China; and who did not have a family history of ASCVD. According to the equations, the predicted 10-year ASCVD risk was 11.0% for men and 10.1% for women. Given the levels of risk factors that remained, the sex-specific predicted risk of ASCVD increased with aging, which ranged from 2.2% to 19.6% in men and from 2.4% to 17.1% in women (Table 2).

Our equations had good discrimination and calibration for ASCVD in both sexes. Women had a numerically higher C statistic than men (0.811 versus 0.794), although the difference is not significant. Calibration χ^2 values were 13.1 for men and 12.8 for women, which indicated excellent goodness of fit for our equations. Internal validation demonstrated that the means of discrimination C statistic, calibration χ^2, and calibration slope were similar to those from the models for the whole population, which indicated good internal consistency for our equations (Table 3).

Table 2. Age- and Sex-Specific 10-Year ASCVD Risk Predicted by a Specific Example*

	10-y ASCVD Risk, %	
Age, y	Men	Women
40	2.2	2.4
50	5.4	5.4
60	11.0	10.1
70	19.6	17.1

ASCVD indicates atherosclerotic cardiovascular disease; HDL-C, high-density lipoprotein cholesterol; and SBP, systolic blood pressure.

*Example: Individuals with untreated SBP of 130 mm Hg, total cholesterol 210 of mg/dL, HDL-C of 55 mg/dL, waist circumference of 80 cm; nonsmoking; with diabetes mellitus; living in an urban area of northern China; and without a family history of ASCVD.

Table 3. Internal Validation of 10-Year ASCVD Risk Prediction Equations Using 10×10 Cross-Validation Technique

	Original	Mean	SD	P5	Median	P95
Men						
n	10 334	1033.4	0.5	1033	1033	1034
C statistic	0.794	0.790	0.030	0.739	0.788	0.848
Calibration χ^2	13.1	8.4	5.7	2.5	6.8	18.5
Calibration slope*	1.000	0.976	0.144	0.755	0.962	1.220
Women						
n	10 986	1098.6	0.5	1098	1099	1099
C statistic	0.811	0.807	0.035	0.745	0.806	0.865
Calibration χ^2	12.8	7.2	6.4	1.5	5.6	15.3
Calibration slope*	1.000	0.977	0.137	0.773	0.963	1.185

ASCVD indicates atherosclerotic cardiovascular disease; P5, fifth percentile; and P95, 95th percentile.
*Calibration slope: β coefficient from the Cox proportional hazards model with the linear predictor used as the sole independent variable.

External validation was conducted to evaluate 10-year ASCVD risk prediction in China MUCA (1992–1994) and 5-year ASCVD risk prediction in CIMIC. The baseline characteristics and ASCVD event rates of the 2 validation cohorts are shown in Tables III and IV in the online-only Data Supplement. As shown in Table 4, compared with the Kaplan-Meier–adjusted events, a slight overprediction of ASCVD events was found in the 2 external validation cohorts. All C statistics in the validation were similar to those from the derivation cohort. Calibration χ^2 values in China MUCA (1992–1994) were 31.7 and 28.2 for men and women, respectively. Both calibration charts across 4 specific predicted risk categories (Figure 1A) and calibration plots (Figure 2A and 2B) indicated that no substantial differences existed between the observed rate and the predicted rate in China MUCA (1992–1994). Although the calibration χ^2 for the CIMIC cohort was much higher than 20 (χ^2=81.3 for men and χ^2=123.5 for women) in an extremely large sample size with a total of 70 838 subjects, the calibration charts and plots illustrated good agreement between the observations and the predictions (Figures 1B, 2C, and 2D).

Compared with our equations, the PCEs had lower C statistics and much higher calibration χ^2 values for men and women across most of the cohorts, whereas calibrations in the PCEs for women seemed better as the PCEs were applied to China MUCA (1992–1994) (Table 4). Generally speaking, our China-PAR equations were powerful in discrimination and had a better model fit than the PCEs. Furthermore, the PCEs for white Americans overestimated risk for Chinese men and underestimated risk for Chinese women. For example, in our China MUCA (1992–1994) validation cohort, the observed ASCVD events within the 10-year period in men were 218.7 adjusted by the Kaplan-Meier method. Our China-PAR equations overpredicted events by only 17% with estimated events of 255.9, but the PCEs for white Americans overpredicted by 54% with 336.9 estimated events in men. In addition, we found that the PCEs for blacks overestimated risk for both Chinese men and women (Table 4 and Figures II–IV in the online-only Data Supplement).

Recalibration analysis of PCEs was conducted in the current derivation cohort. In the recalibrated PCE functions, the coefficients were taken from the PCEs, but mean values from the Chinese derivation cohort were used for the risk factors and mean incidence rates. Recalibration did not affect the discriminatory ability according to the C statistic. In addition, the recalibration of PCEs overestimated ASCVD events much more and had higher calibration χ^2 than the current Chinese equations, as shown in Table V in the online-only Data Supplement, which suggested that the recalibrated prediction equations did not improve the calibration substantially.

DISCUSSION

The China-PAR project developed and validated the first equations for 10-year ASCVD risk prediction in a Chinese population from 4 large, contemporary, population-based Chinese cohorts. The sex-specific China-PAR equations had excellent performance of ASCVD risk prediction with good internal consistency and external validation. Our results also demonstrated that the PCEs in the American College of Cardiology/American Heart Association guideline were not appropriate for the Chinese population.

Estimation of absolute risk of CVD commonly relies on prediction models derived from prospective cohort studies. Liu et al[14] formulated prediction models for CHD in a Chinese cohort from 1992 to 2002 that were based on

Table 4. External Validation of ASCVD Risk Prediction Equations as Applied to the Validation Cohorts and Comparison With the PCEs

	Men			Women		
		Validation Cohort			Validation Cohort	
	Derivation Cohort*	China MUCA (1992–1994)*	CIMIC†	Derivation Cohort*	China MUCA (1992–1994)*	CIMIC†
Total, n	10334	6565	26872	10986	7558	43966
Actual events, n‡	451	216	755	285	168	738
Kaplan-Meier–adjusted events, n§	472.7	218.7	746.7	296.3	166.4	716.0
Chinese equations						
Predicted events¶	509.3	255.9	836.0	326.9	182.0	912.6
C statistic	0.794	0.809	0.793	0.811	0.829	0.805
95% CI	0.775–0.814	0.778–0.839	0.778–0.808	0.787–0.835	0.801–0.856	0.791–0.819
Calibration χ^2	13.1	31.7	81.3	12.8	28.2	123.5
P value	0.16	<0.001	<0.001	0.17	<0.001	<0.001
PCEs for white Americans						
Predicted events¶	719.2	336.9	1249.3	268.8	121.6	646.3
C statistic	0.762	0.768	0.761	0.783	0.786	0.785
95% CI	0.740–0.783	0.733–0.803	0.744–0.778	0.755–0.810	0.752–0.820	0.771–0.800
Calibration χ^2	131.9	118.8	359.7	19.4	18.7	65.9
P value	<0.001	<0.001	<0.001	0.02	0.03	<0.001
PCEs for blacks						
Predicted events¶	840.7	453.4	1322.6	414.4	209.6	1087.7
C statistic	0.769	0.790	0.750	0.796	0.807	0.792
95% CI	0.748–0.790	0.758–0.823	0.733–0.766	0.771–0.822	0.775–0.839	0.777–0.806
Calibration χ^2	456.7	538.8	506.7	77.4	19.8	174.8
P value	<0.001	<0.001	<0.001	<0.001	0.02	<0.001

ASCVD indicates atherosclerotic cardiovascular disease; China MUCA (1992–1994), China Multi-Center Collaborative Study of Cardiovascular Epidemiology (1992–1994); CI, confidence interval; CIMIC, Community Intervention of Metabolic Syndrome in China and Chinese Family Health Study; and PCE, pooled cohort equation.

*Based on 10-year risk prediction.

†Based on 5-year risk prediction.

‡Actual number of events through follow-up.

§Observed number of events after Kaplan-Meier adjustment through follow-up.

¶Predicted number of events based on the ASCVD equation through follow-up.

the Framingham CHD Risk Assessment Tool. Wu et al[15] developed 10-year risk prediction models for ischemic CVD, including ischemic stroke and coronary events, using derivation and validation cohorts with 9903 and 17329 subjects, respectively. However, both of these prediction models were derived at least 10 years ago. The epidemics of CVD and risk factors have changed during the past decade. The risk prediction equations developed from recent data will generalize better to contemporary populations and identify high-risk individuals with appropriately predicted risk probability. Furthermore, the previous Chinese equations as mentioned above could not evaluate ASCVD outcome. The current China-PAR equations are focused on risk prediction of ASCVD events, were developed from the most recent cohorts with a high follow-up rate of 90.1% among 21320 Chinese participants, and were validated by 2 independent cohorts with 14123 and 70838 participants. In addition, the adjudication for outcomes with a standardized review process using the same diagnosis criteria across cohorts further strengthened the present investigation.

Several key risk factors have been established to account for ASCVD risk and were conjointly used to devise multivariable risk prediction tools previously.[10,14,15,28] Thus, our equations directly included age, SBP, total cholesterol, HDL-C, current smoking, and diabetes mel-

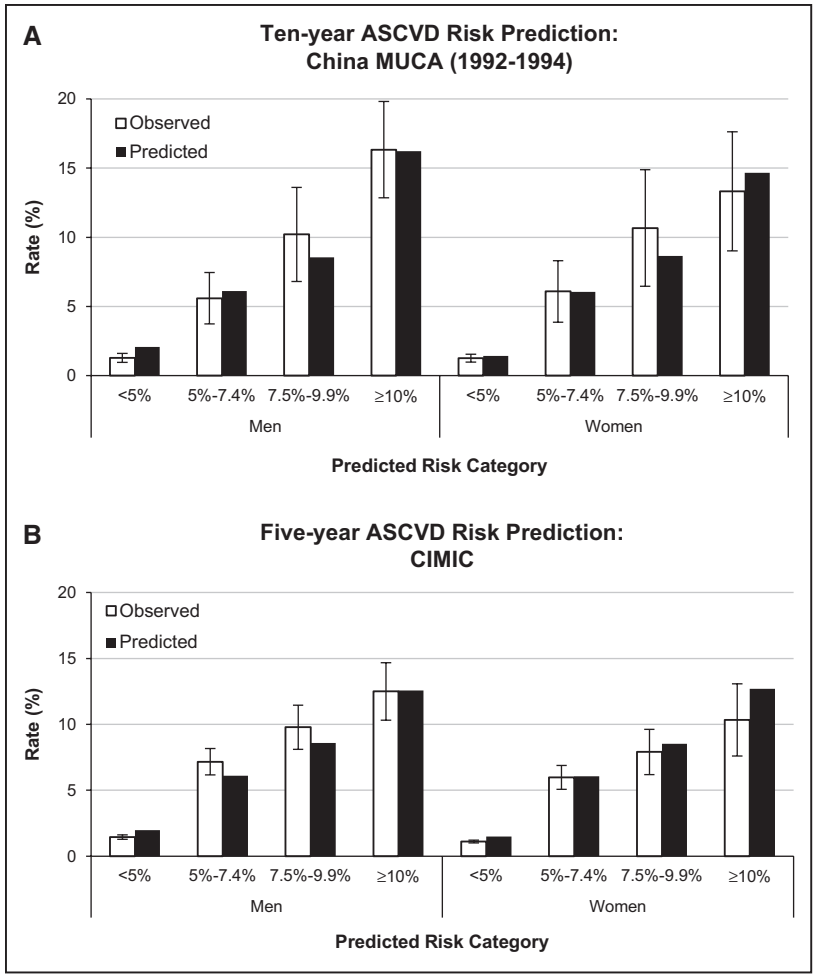

Figure 1. Ten-year (A) and 5-year (B) Kaplan-Meier observed and predicted atherosclerotic cardiovascular disease (ASCVD) event rates in the external validation cohorts using the China-PAR (Prediction for ASCVD Risk in China) equations.
China MUCA (1992–1994) indicates the China Multi-Center Collaborative Study of Cardiovascular Epidemiology (1992–1994); and CIMIC, the Community Intervention of Metabolic Syndrome in China and Chinese Family Health Study.

litus. Four additional covariates (WC, geographic region, urbanization, and family history of ASCVD) met the predefined inclusion criteria based on relative IDI (≥6%), whereas they were not included in Chinese prediction models previously.[14,15] These 4 factors were incorporated to improve the discrimination ability of our equations. Some studies supported WC as a better predictor for CVD than body mass index,[29,30] and in our equations, WC had a higher relative IDI than body mass index in both men (6.9% versus 3.2%) and women (9.6% versus 9.2%). Although risk of obesity appeared to be mediated via total cholesterol, HDL-C, hypertension, and diabetes mellitus, the association of WC with ASCVD risk was still significant after controlling for these other factors in our populations. This suggested that central obesity deserves more attention in the primary prevention of ASCVD among Chinese adults. In addition, considering residential differences in profiles of CVD burden and risk factors,[3,31] the variables of geographic region and urbanization further improved the prediction capability and the generalizability of our equations. Furthermore, ASCVD events yielded familial aggregation possibly as a result of genetic determinants of risk factors or shared environmental factors.[32] Both the QRISK and ASSIGN (Assessing Cardiovascular Risk Using SIGN Guidelines to Assign Preventive Treatment) scores incorporated the variable of family history to predict CVD events in Europeans because of better calibrations.[9,33] Likewise, family history was ascertained in our cohorts, and adding the information enhanced the prediction usefulness of our equations for Chinese.

Compared with established risk prediction tools such as the Framingham general CVD equations,[7] the PCEs reported in the 2013 American College of Cardiology/American Heart Association guideline obtained good discrimination and calibration with internal validation by 10×10 cross-validation and external validation among Americans.[10,34] However, it did not work well when applied to East Asian populations.[28,35] Similar results were found in our analysis. For example, compared with the PCEs for white Americans, the China-PAR equations had a lower calibration χ^2 in men (31.7 versus 118.8) when applied to our external validation cohort, China MUCA (1992–1994) (Table 4). Our equations predicted an ASCVD risk of 11.0% for a man and 10.1% for a woman with the baseline characteristics shown in Table I in the online-only Data Supplement, whereas the corresponding 10-year risk would increase to 16.0% for the man

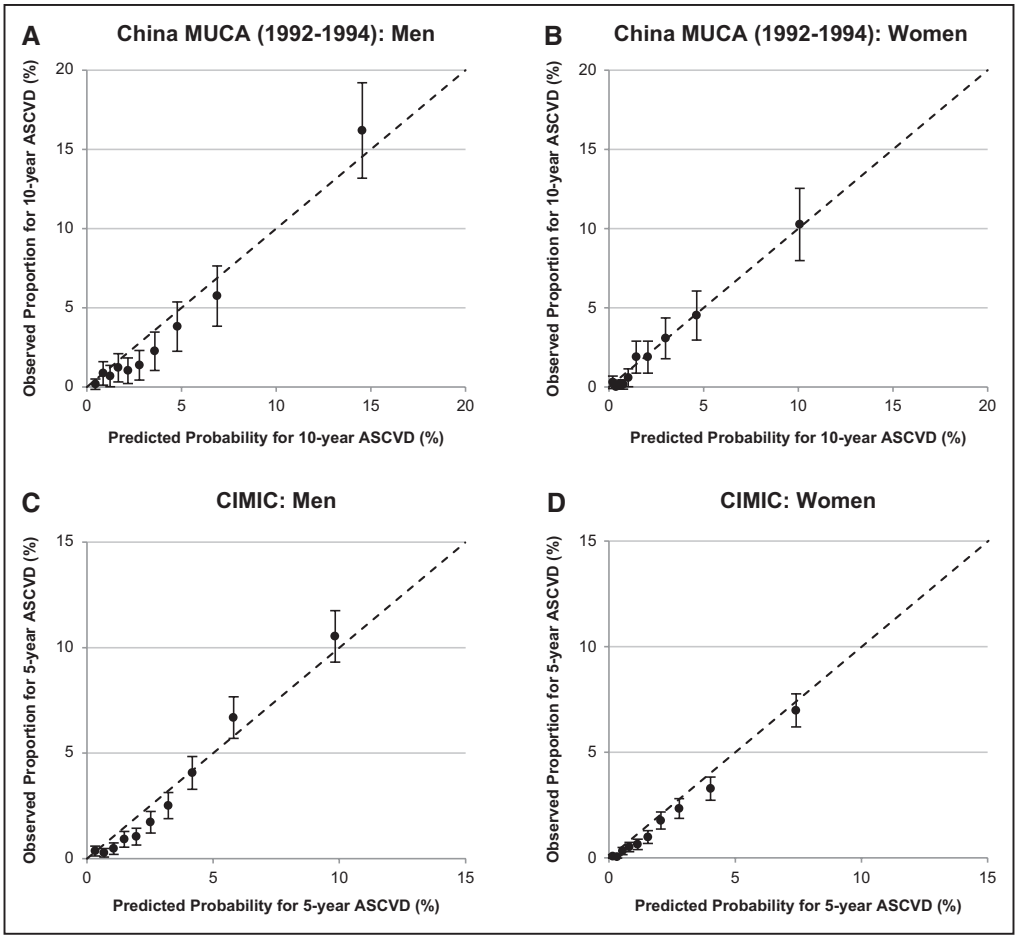

Figure 2. Calibration plots for the China MUCA (1992–1994) (China Multi-Center Collaborative Study of Cardiovascular Epidemiology, 1992–1994; A and B) and the CIMIC (Community Intervention of Metabolic Syndrome in China and Chinese Family Health Study; C and D) using the China-PAR (Prediction for ASCVD Risk in China) equations.

ASCVD indicates atherosclerotic cardiovascular disease.

but decrease to 6.7% for the woman using the PCEs for white Americans (data not shown). The substantial differences in prediction capability between the PCEs and the China-PAR equations might be explained by ethnic heterogeneities, distinct risk profiles of CVD burden, and different treatment and control rates for risk factors (eg, hypertension, hyperlipidemia, and diabetes mellitus).[36–41]

Our project provided sex-specific equations for 10-year ASCVD risk estimation in China, and prediction of ASCVD risk made it easy to match the probability of ASCVD reducing with the intensity of risk factor lowering. In addition, multivariable risk assessment took seriously high-risk ASCVD candidates with clustering of multiple marginal risk factors and avoided unnecessary warnings to individuals a sole isolated risk factor. However, it should be highlighted that risk score per se cannot be converted into better outcomes for patients or declines in ASCVD unless it can be used appropriately by physicians and understood by high-risk individuals. In the future, training among physicians is required to communicate predicted 10-year risk of ASCVD to patients appropriately when the equations are applied in prevention practice.

Several limitations in our modeling should be addressed. First, the outcome events in the present research encompass only hard end points of ASCVD, whereas some atherosclerosis-related events such as angina pectoris and intermittent claudication were not included. The predicted absolute risks of these events could not be evaluated by the present equations. Thus, caution should be used when the equations are applied in practice. Second, information about lipid-lowering treatment was not collected in the China MUCA (1998), and it was not considered in our equations. However, the lipid-lowering treatment rate in China was only 3.4% in 2000 and 5.1% in 2008.[40,42] Thus, overlooking lipid-lowering treatment in the algorithm should have no substantial impact on our equations. Third, although the China-PAR equations were well validated in China MUCA (1992–1994), our equations overestimated ASCVD events with

high calibration χ^2 in the CIMIC cohort that had a large sample size of 70838 participants with 5.9 years of follow-up. However, the statistical test for calibration χ^2 was sensitive to sample size,[24] and testing should be accompanied by assessment of calibration plots, which showed good agreement in the CIMIC cohort (Figure 2C and 2D). The findings were tolerable for the external validation. Further investigation is warranted to examine whether the 10-year risk prediction equations could have good performance in other large-scale cohorts with short durations of follow-up. The China-PAR equations focused on estimating risk of ASCVD developed within a 10-year period. Lifetime risk evaluation should otherwise be considered when individuals are classified as having a low absolute 10-year risk.

CONCLUSIONS

The China-PAR project developed equations with good ability to predict 10-year ASCVD risk among Chinese population. Applying this tool will help to identify high-risk individuals and match the intensity of preventive interventions to an individual's absolute risk of ASCVD development. It will be important in the practice of ASCVD management in China. The risk prediction equations provide a valuable tool to quantify risk and to guide individualized primary care among Chinese populations. More aggressive risk factor modification should be required among individuals with a predicted high risk. In addition, serial ASCVD risk assessments will be beneficial to monitor the improvement in control of risk factors at individual level. Further studies are warranted to link the ASCVD risk prediction to goals of therapy for risk factors in future guidelines for ASCVD prevention and management in China.

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DISCLOSURES

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AFFILIATIONS

From Department of Epidemiology, Fuwai Hospital, State Key Laboratory of Cardiovascular Disease, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China (X.Y., J.L., J.C., Y.L., J.H., F. Liu, J.C., L.Z., X.W., D.G.); Department of Prevention Medicine, Shenzhen University School of Medicine, Shenzhen, China (D.H.); Division of Epidemiology, Guangdong Provincial People's Hospital and Cardiovascular Institute, Guangzhou, China (X.L.); Department of Epidemiology and Biostatistics, School of Public Health, Nanjing Medical University, Nanjing, China (C.S.); Department of Cardiology, Fujian Provincial People's Hospital, Fuzhou, China (L.Y.); Cardio-Cerebrovascular Control and Research Center, Institute of Basic Medicine, Shandong Academy of Medical Sciences, Jinan, China (F. Lu); and Sichuan Center for Disease Control and Prevention, Chengdu, China.

FOOTNOTES

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Predicting the 10-Year Risks of Atherosclerotic Cardiovascular Disease in Chinese Population: The China-PAR Project (Prediction for ASCVD Risk in China)

Xueli Yang, Jianxin Li, Dongsheng Hu, Jichun Chen, Ying Li, Jianfeng Huang, Xiaoqing Liu, Fangchao Liu, Jie Cao, Chong Shen, Ling Yu, Fanghong Lu, Xianping Wu, Liancheng Zhao, Xigui Wu and Dongfeng Gu

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SUPPLEMENTAL MATERIAL

Supplemental Table 1. Gender-specific Parameters of Equations for Predicting 10-year ASCVD Risk with Specific Example

	Men			Women		
	Coefficient	Individual Example Value*	Coefficient ×Value†	Coefficient	Individual Example Value*	Coefficient ×Value†
Example: 60 years of age with untreated SBP 130 mm Hg, total cholesterol 210 mg/dL, HDL-C 55 mg/dL, waist circumference 80 cm, nonsmoking, diabetes, living in urban area of northern China, and without family history of ASCVD						
Ln(age), y	31.97	4.09	130.88	24.87	4.09	101.84
Ln(treated SBP), mmHg	27.39	-	-	20.71	-	-
Ln(untreated SBP), mmHg	26.15	4.87	127.28	19.98	4.87	97.26
Ln(total cholesterol), mg/dL	0.62	5.35	3.32	0.06	5.35	0.31
Ln(HDL-C), mg/dL	-0.69	4.01	-2.78	-0.22	4.01	-0.87
Ln(waist circumference), cm	-0.71	4.38	-3.12	1.48	4.38	6.46
Current smoker(1=Yes, 0=No)	3.96	0	0.00	0.49	0	0.00
Diabetes (1=Yes, 0=No)	0.36	1	0.36	0.57	0	0.00
Geographic region(1=Northern China, 0=Southern China)	0.48	1	0.48	0.54	1	0.54
Urbanization (1=Urban, 0=Rural)	-0.16	1	-0.16	N/A	N/A	N/A
Family history of ASCVD(1=Yes, 0=No)	6.22	0	0.00	N/A	N/A	N/A
Ln(age)*Ln(treated SBP)	-6.02	-	-	-4.53	-	-
Ln(age)*Ln(untreated SBP)	-5.73	19.93	-114.21	-4.36	19.93	-86.90
Ln(age)*Current smoker	-0.94	0	0.00	N/A	N/A	N/A
Ln(age)*Family history of ASCVD	-1.53	0	0.00	N/A	N/A	N/A
Individual sum	N/A	N/A	142.04	N/A	N/A	119.22
Mean (coefficient × value)	N/A	N/A	140.68	N/A	N/A	117.26
Baseline survival	N/A	N/A	0.97	N/A	N/A	0.99
Estimated 10-year risk (%)	N/A	N/A	11.0	N/A	N/A	10.1

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; SBP, systolic blood pressure; HDL-C, high-density lipoprotein cholesterol; Ln, natural logarithm; N/A, covariate was not included in the equation; –, this value was not included in the example.
SI conversion factors: To convert total cholesterol and HDL-C to mmol/L, multiply by 0.0259.
[*]Individual Example Value: The natural log of continuous covariates, and 0 or 1 for category covariate, interaction terms are the products of the natural log of age multiplied by the natural log of other continuous covariates, or by the value of category covariates.
[†]Coefficient × Value: The product of the coefficient multiplied by the individual example value.

Supplemental Table 2. Predicting an Individual's 10-year Risk for a First ASCVD Event

We assume an individual aged 60 years with untreated SBP 130 mm Hg, total cholesterol 210 mg/dL, HDL-C 55 mg/dL, waist circumference 80 cm, nonsmoking, diabetes, living in urban area of northern China, and without family history of ASCVD. For the equations, the values for age, SBP, total cholesterol, HDL-C, and waist circumference are log transformed. Current smoker, diabetes, and family history of ASCVD are dichotomous variables with 1 for "Yes" and 0 for "No". Geographic region is dichotomous variable with 1 for "Northern China" and 0 for "Southern China". Urbanization is also dichotomous variable with 1 for "Urban" and 0 for "Rural". Interaction terms are the products of the natural log of age and the natural log of other continuous variables, or the value of categorical variables. See the "Individual Example Value" column in Supplemental Table 1.

These values above are multiplied by the coefficients from the gender-specific equations ("Coefficient" column in Supplemental Table 1), and the results are in the "Coefficient × Value" column in Supplemental Table 1. The sum of the "Coefficient × Value" column is then calculated for the individual in each gender group, and shown as "Individual sum".

The estimated 10-year risk of the first ASCVD event is formally calculated as formula below:

$$1 - S_{10}^{e^{(IndX'B - MeanX'B)}}$$

S_{10} is the survival rate for ASCVD at 10 years ("Baseline survival" in Supplemental Table 1), IndX'B is gender-specific "Individual sum" in Supplemental Table 1, MeanX'B is gender-specific overall mean "Coefficient × Value" sum, which is shown as "Mean (coefficient × value)" in Supplemental Table 1.

Below is the equation using men as an example to estimate the 10-year ASCVD risk:

$$1 - 0.9707^{e^{(142.04 - 140.68)}}$$

which equals to a 11.0% probability of the first ASCVD event occurring within 10 years.

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; SBP, systolic blood pressure; HDL-C, high-density lipoprotein cholesterol.

Supplemental Table 3. Baseline Characteristics and ASCVD Event Rates of the China MUCA (1992-1994) by Gender

	Men (n=6565)	Women (n=7558)	*P* Value[a]
Age, mean (SD), y	46.5 (7.4)	46.6 (7.4)	0.75
Northern China, No. (%)	2753 (41.9)	3423 (45.3)	<0.001
Urban, No. (%)	2266 (34.5)	2202 (29.1)	<0.001
Current smoker, No. (%)	4536 (70.1)	577 (7.6)	<0.001
Waist circumference, mean (SD), cm	77.4 (9.3)	75.2 (9.6)	<0.001
SBP, mean (SD), mm Hg	123.2 (18.0)	122.5 (20.2)	0.02
DBP, mean (SD), mm Hg	80.0 (11.7)	77.7 (11.4)	<0.001
Antihypertensive treatment within 2 weeks, No. (%)	217 (3.3)	275 (3.6)	0.28
Total cholesterol, mean (SD), mg/dL	176.7 (37.4)	177.0 (38.2)	0.67
HDL-C, mean (SD), mg/dL	50.0 (13.7)	52.1 (13.3)	<0.001
Diabetes, No. (%)	179 (2.9)	248 (3.5)	0.07
Family history of ASCVD, No. (%)	1198 (18.2)	1253 (16.6)	0.009
Incident ASCVD events, No. (%)	511 (7.8)	405 (5.4)	
Incidence of ASCVD (/100,000 person-year)	472.6	314.4	
10-year Kaplan-Meier ASCVD rate (%)	3.3	2.2	

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; China MUCA (1992-1994), the China Multi-center Collaborative Study of Cardiovascular Epidemiology (1992-1994).
SI conversion factors: To convert total cholesterol and HDL-C to mmol/L, multiply by 0.0259.
a Continuous variables were examined by t-test, and categorical variables were examined by χ^2 test.

Supplemental Table 4. Baseline Characteristics and ASCVD Event Rates of the CIMIC by Gender

	Men (n=26 872)	Women (n=43 966)	*P* Value[a]
Age, mean (SD), y	55.3 (10.2)	53.9 (10.2)	<0.001
Northern China, No. (%)	13 108 (48.8)	20 891 (47.5)	0.001
Urban, No. (%)	0 (0)	0 (0)	-
Current smoker, No. (%)	13 473 (50.2)	682 (1.6)	<0.001
Waist circumference, mean (SD), cm	82.9 (9.9)	81.3 (10.0)	<0.001
SBP, mean (SD), mm Hg	131.6 (20.5)	130.3 (22.4)	<0.001
DBP, mean (SD), mm Hg	80.6 (11.9)	78.9 (11.9)	<0.001
Antihypertensive treatment within 2 weeks, No. (%)	4443 (16.5)	7495 (17.0)	0.08
Total cholesterol, mean (SD), mg/dL	168.9 (31.8)	176.5 (34.0)	<0.001
HDL-C, mean (SD), mg/dL	50.2 (13.0)	51.7 (12.3)	<0.001
Diabetes, No. (%)	1585 (6.2)	2784 (6.7)	0.01
Family history of ASCVD, No. (%)	2612 (9.7)	4258 (9.7)	0.88
Incident ASCVD events, No. (%)	1204 (4.5)	1242 (2.8)	
Incidence of ASCVD (/100,000 person-year)	775.2	476.7	
5-year Kaplan-Meier ASCVD rate (%)	2.8	1.6	

Abbreviations: ASCVD, atherosclerotic cardiovascular disease; SD, standard deviation; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; CIMIC, the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study.

SI conversion factors: To convert total cholesterol and HDL-C to mmol/L, multiply by 0.0259.

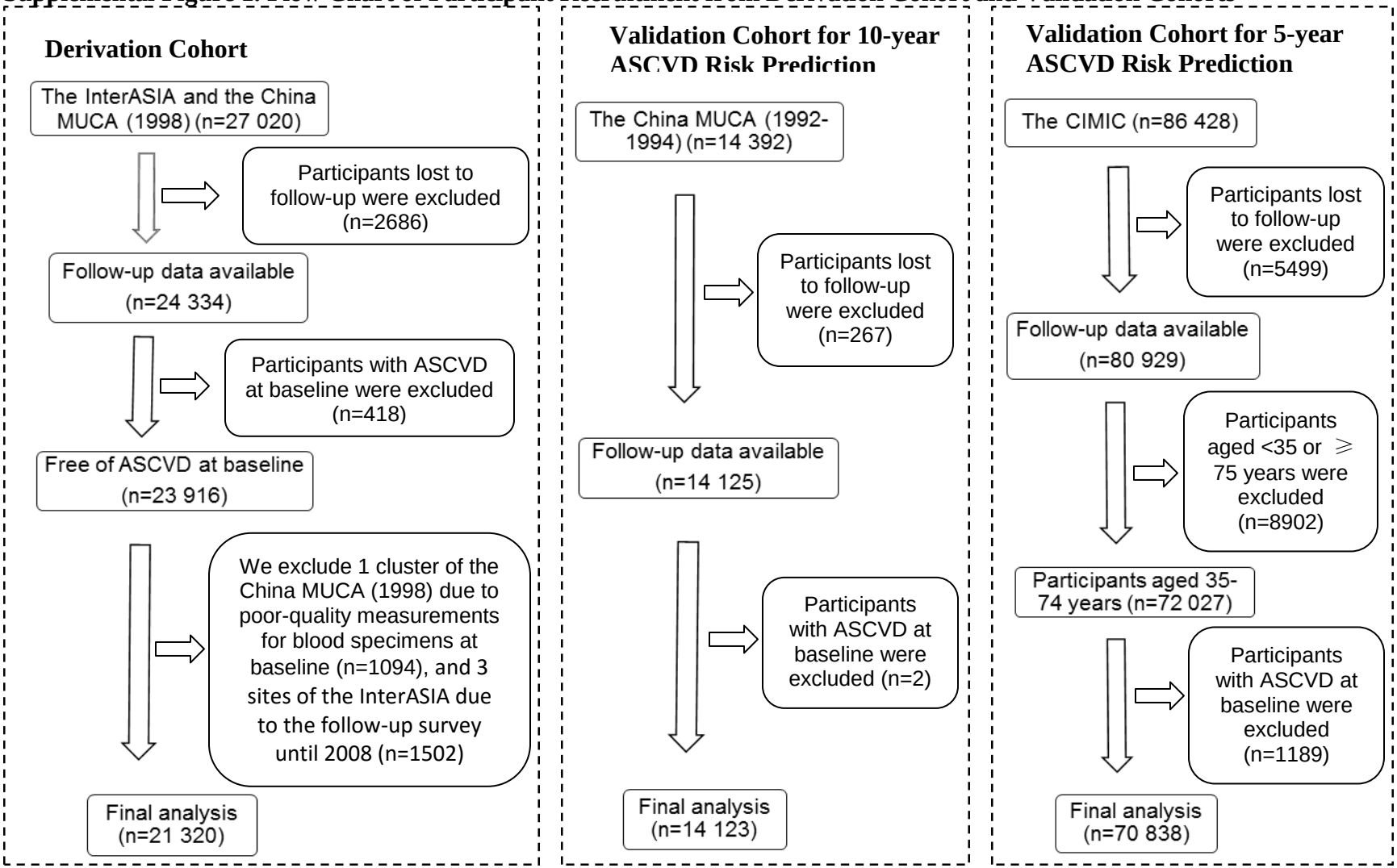
a Continuous variables were examined by t-test, and categorical variables were examined by χ^2 test.

Supplemental Table 5. Comparison the Current Chinese Equations with the Recalibrated PCE in the Derivation Cohort

	Algorithm Derivation Cohort	
	Men	Women
Total N	10 334	10 986
Actual events*	451	285
Kaplan-Meier adjusted events†	472.7	296.3
Chinese Equations		
Predicted events‡	509.3	326.9
C-statistic	0.794	0.811
95% CI	(0.775-0.814)	(0.787-0.835)
Calibration χ^2	13.1	12.8
P value	0.16	0.17
Recalibration PCE for White American		
Predicted events‡	769.4	631.6
C-statistic	0.762	0.783
(95% CI)	(0.740-0.783)	(0.755-0.810)
Calibration χ^2	187.3	402.1
P value	<0.001	<0.001
Recalibration PCE for African American		
Predicted events‡	600.0	852.6
C-statistic	0.769	0.796
(95% CI)	(0.748-0.790)	(0.771-0.822)
Calibration χ^2	123.8	1076.3
P value	<0.001	<0.001

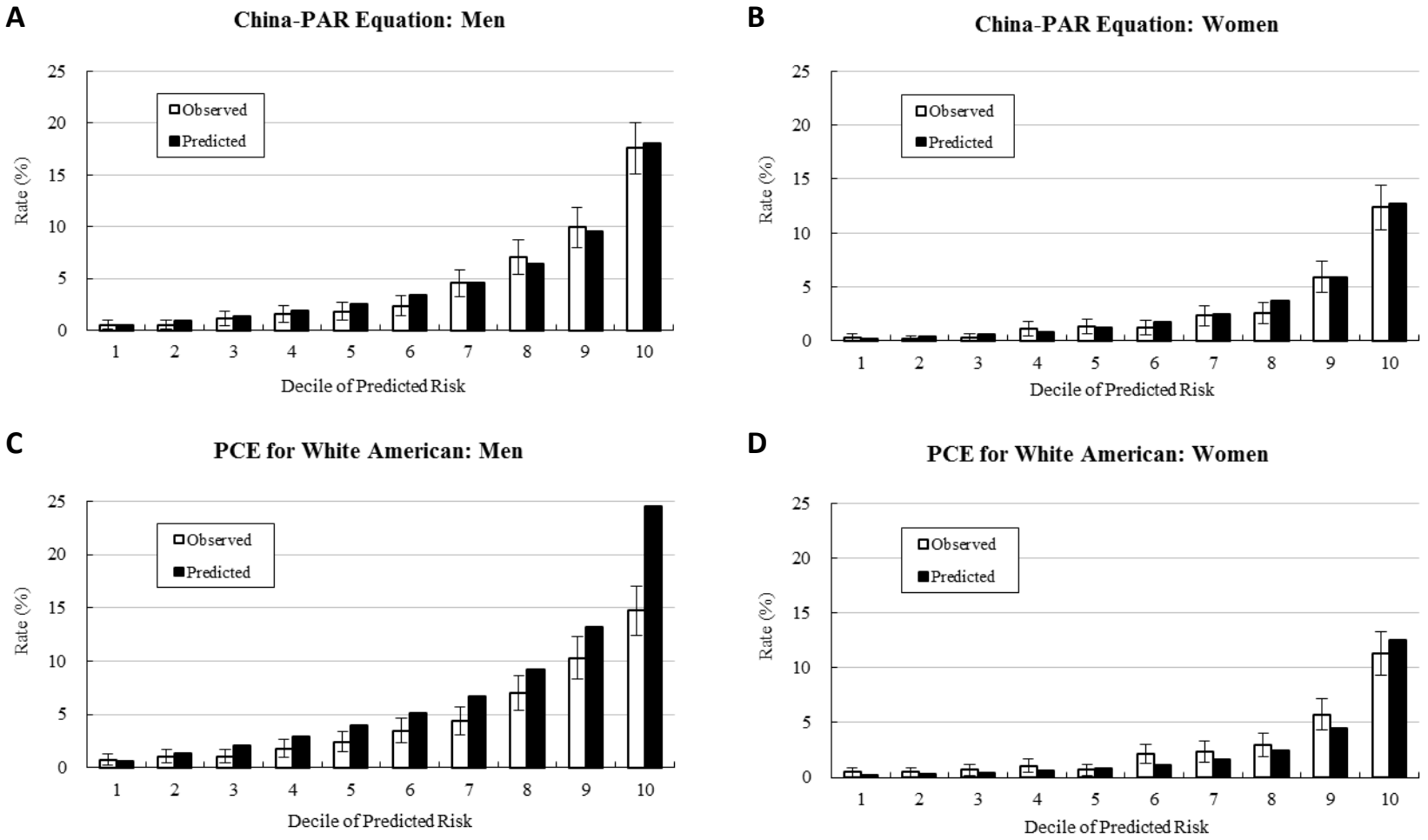
* Actual number of events through follow-up period;
† Observed number of events after Kaplan-Meier adjustment through follow-up period;
‡ Predicted number of events based on the ASCVD equation through follow-up period.

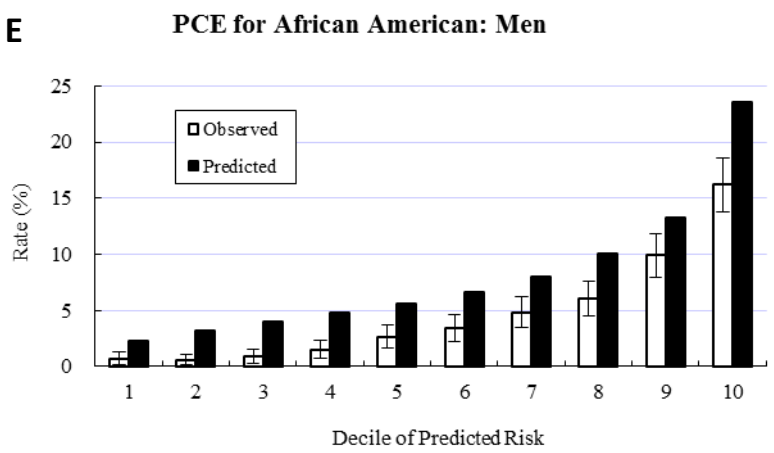
Supplemental Figure 1. Flow Chart of Participant Recruitment from Derivation Cohort and Validation Cohorts

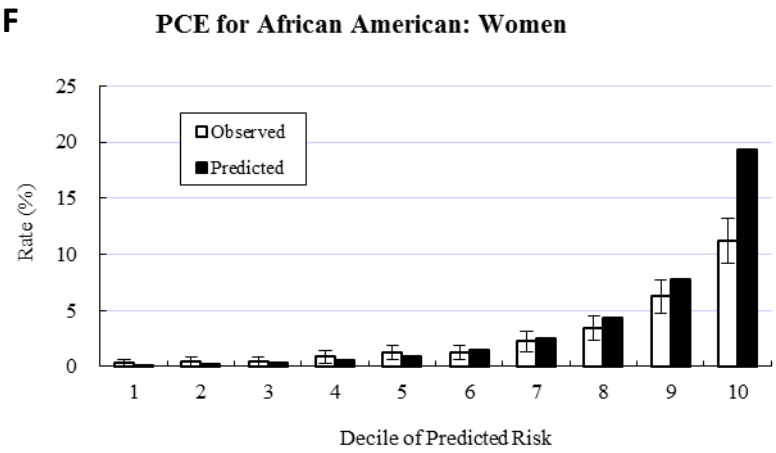


Abbreviations: ASCVD, atherosclerotic cardiovascular disease; InterASIA, the International Collaborative Study of Cardiovascular Disease in Asia; China MUCA (1998), the China Multi-center Collaborative Study of Cardiovascular Epidemiology (1998); China MUCA (1992-1994), the China Multi-center Collaborative Study of Cardiovascular Epidemiology (1992-1994) ; CIMIC, the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study.

Supplemental Figure 2. Kaplan-Meier Observed and Predicted 10-year ASCVD Event Rate in the Derivation Cohort Using the China-PAR Equations (A, B) and the PCE (C, D, E, F)

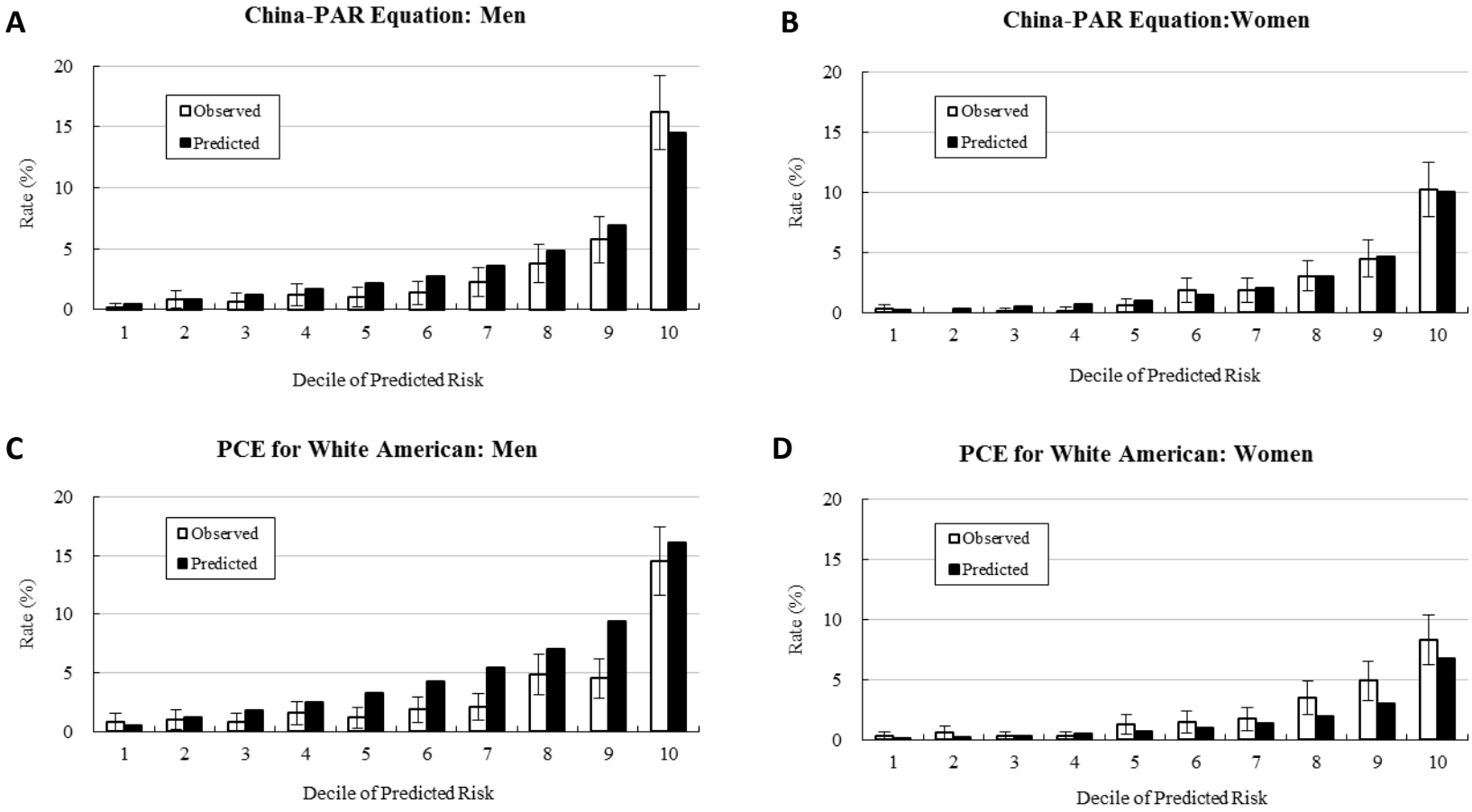


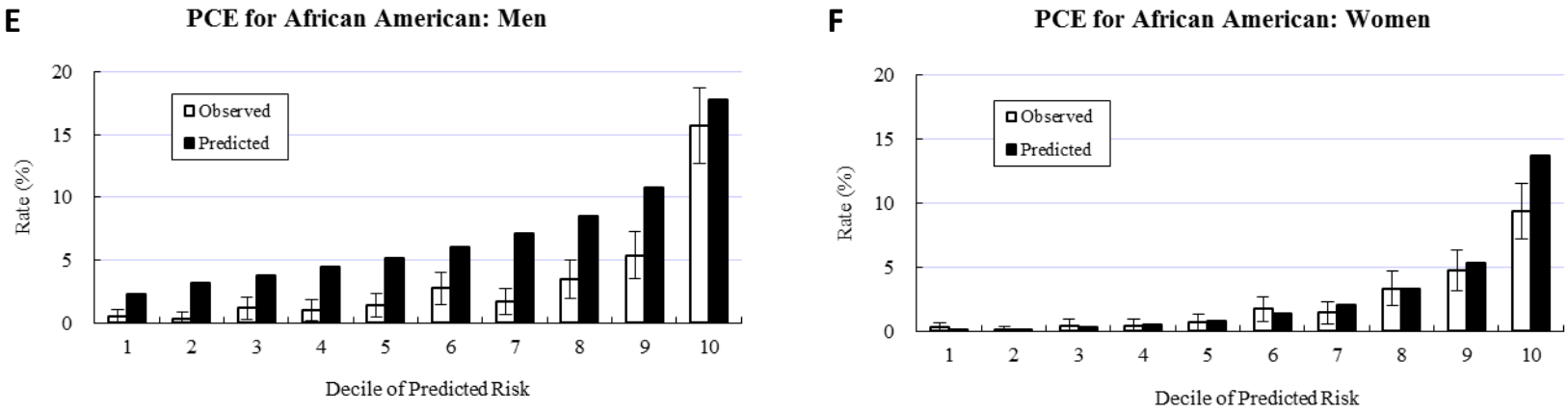




Abbreviations: ASCVD, atherosclerotic cardiovascular disease; China-PAR, Prediction for ASCVD Risk in China; PCE, Pooled Cohort Equations.

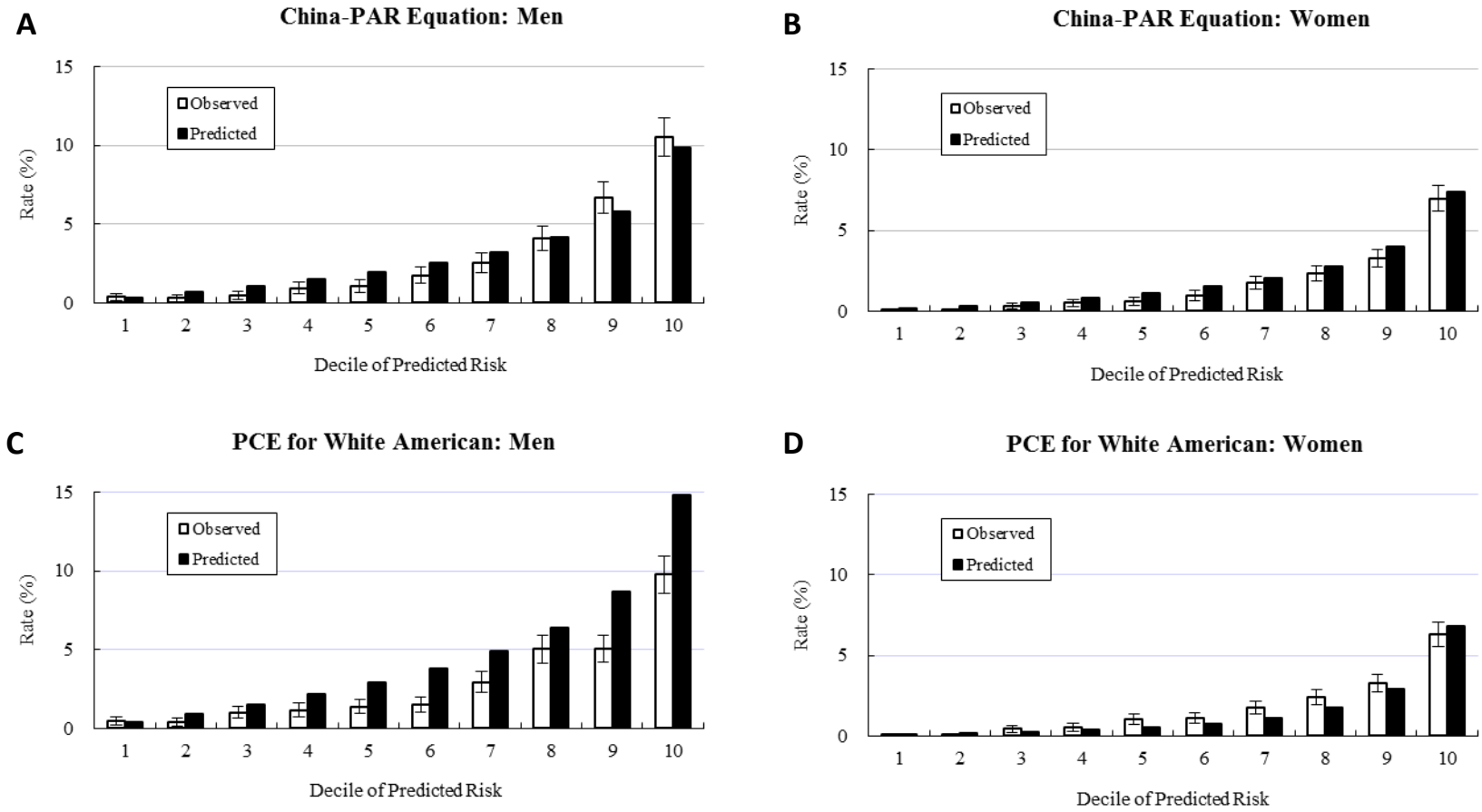
Supplemental Figure 3. Kaplan-Meier Observed and Predicted 10-year ASCVD Event Rate in the China MUCA (1992-1994) Using the China-PAR Equations (A, B) and the PCE (C, D, E, F)

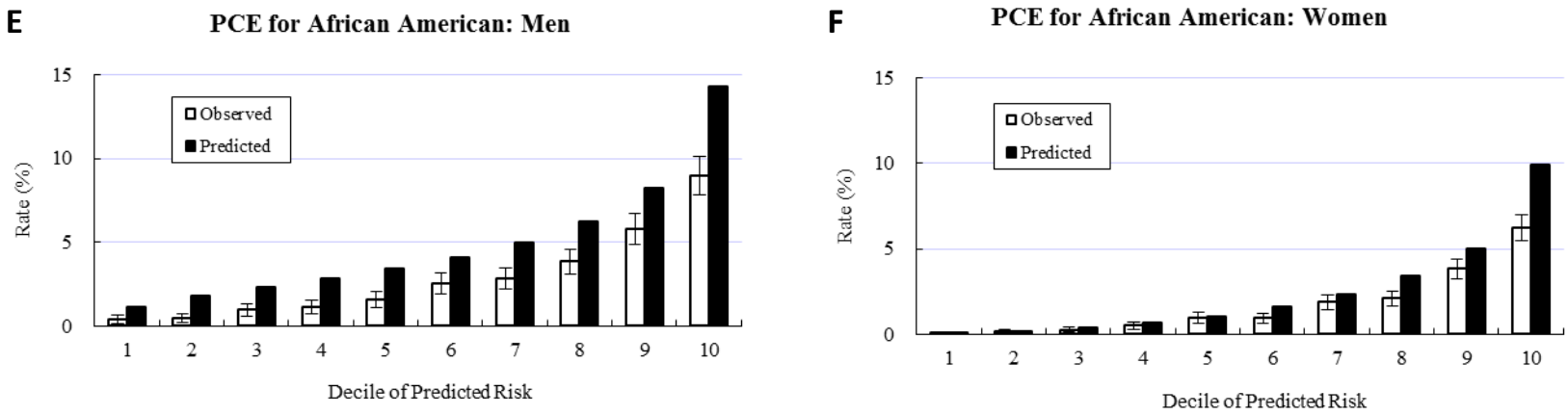




Abbreviations: ASCVD, atherosclerotic cardiovascular disease; China-PAR, Prediction for ASCVD Risk in China; PCE, Pooled Cohort Equations; China MUCA (1992-1994), the China Multi-center Collaborative Study of Cardiovascular Epidemiology (1992-1994).

Supplemental Figure 4. Kaplan-Meier Observed and Predicted 5-year ASCVD Event Rate in the CIMIC Using the China-PAR Equations (A, B) and the PCE (C, D, E, F)





Abbreviations: ASCVD, atherosclerotic cardiovascular disease; China-PAR, Prediction for ASCVD Risk in China; PCE, Pooled Cohort Equations; CIMIC, the Community Intervention of Metabolic Syndrome in China & Chinese Family Health Study.

Dr. Carolyn Lam: Welcome to circulation on the run. Your weekly podcast summary and backstage pass to the journal and its editors. I'm Dr. Carolyn Lam associate editor for the National heart center and Duke National University of Singapore. Our podcast is really going around the world, and today's feature interview comes to you live from China. Where we will be discussing the prediction of ten year risks of cardiovascular disease in the Chinese population. So now to all our Chinese colleagues out there: Chinese dialect

First here's your summary of this week's journal. The first study challenges the assumption that all patients with vascular disease are at high risk of recurrent vascular events. First author Dr. Kasenbrud corresponding author Dr. Viceren and colleagues form the University Medical center Utric in the Netherlands, provide new data on the estimation of ten year risk of recurrent vascular events and a secondary prevention population. In other words, in patients with established cardiovascular disease they applied the second manifestations of arterial disease or 'smart' score for the ten year risk prediction of myocardial infarction, stoke or vascular death in more than six thousand-nine hundred Dutch patients with vascular diseases ranging for coronary artery disease, cerebral-vascular disease, peripheral artery disease, abdominal aortic aneurysm and poly-vascular disease. Predictors included in the SMART risk score included age, sex, current smoking, diabetes, systolic blood pressure, total cholesterol, HGL cholesterol, presence of coronary artery disease, cerebral-vascular disease, peripheral artery disease, abdominal aortic aneurysm, estimated glomariaol fruition rate, high sensitivity CRP and years since the first manifestation of vascular disease. They further externally validated the risk score in more than eighteen thousand four hundred patients with various types of vascular disease fro the TNT ideals Sparkle and Capri trials.

The overall findings was that the external performance of the SMART risk score was reasonable apart from over-estimation of risk in patients which a ten year risk of more than forty percent. What was striking was the substantial variation in the estimated ten year risk. The median ten year risk of a reoccurring major vascular event was 17 percent but this varied for less than 10 percent in 18 percent to more than 30 percent in 22 percent of patients.

The authors further estimated residual risk at guideline recommend targets by applying the relative risk reductions form meta-analysis to estimated risks for targets for systolic pressure, LDL, smoking, physical activity and use of anti-thrombotic agents. They found that if all modifiable risk factors were at guideline recommend targets only half of the patients would have ten year risk of less than 10 percent. Even with optimal treatment many patients with vascular disease appear to remain at more than a 20 percent or even more than 30 percent of a ten year risk.

The take home message is that a single secondary prevention strategy for all patients with vascular disease may not be appropriate. Instead novel risk stratification approaches may be helpful to individualize secondary prevention by identifying high risk patient which may derive the greatest benefit from novel

interventions.

The next study provides experimental evidence that an indigenous-gastro transmitter hydrogen sulfide may potentially be a therapeutic target in diabetic patients with cardiovascular diseases. In this paper by first author Dr. Chen, corresponding author Dr.Kisher and Colleagues from the Louis Cat's school of medicine Temple University in Philadelphia. Authors aim to evaluate the role of hydrogen sulfide deficiency in diabetes induced bone marrow cell dysfunction and to examine the therapeutic effects of restoring hydrogen sulfide production in diabetic bone marrow cells on ischemic high limb injury in diabetic DBDB mice. They further specifically investigated the effects of hydrogen sulfide deficiency on the nitric oxide pathways under conditions of high glucose. They found that bone marrow cells for diabetic DBDB mice had decreased hydrogen sulfide production and lower levels cystathonine gamma lyaze which is the primary enzyme that produces hydrogen sulfide in the cardiovascular system. Administration of a stable hydrogen sulfide donor and over expression of cystathonine gamma lyaze in diabetic bone marrow cells restore their functional and restorative properties. Further more they demonstrated that the therapeutic actions of hydrogen sulfide were mediated by nitric oxide pathway involving endothelial nitric oxide synthase PT495.

In summary these results support the hypothesis that hydrogen sulfide deficiency plays critical role in diabetes induced bone marrow cell dysfunction and suggests that modulating hydrogen sulfide production in diabetic bone marrow cells may have transformational value in treating critical limbs ischemia.

The next study reinforces the importance of hypertension as a critical risk factor for inter-cerebral hemorrhage, and suggests that Blacks and Hispanics may be a particularly high risk. In this study by DR. Walsh and colleagues for the University of Cincinnati, authors conducted the largest case controlled study to date on treated and untreated hypertension as a risk factor for inter-cerebral hemorrhage. They also investigated whether there was variation by ethnicity. The ethnic racial variations of inter-cerebral hemorrhage or eriche study is a prospective multi-center case controlled study of inter-cerebral hemorrhage among Whites, Blacks and Hispanics. Cases were enrolled from 42 recruitment cites, controls were matched cases one to one by age, sex, ethnicity and metropolitan area. A total of 958 white, 880 black and 766 Hispanic cases of inter-cerebral hemorrhage were enrolled. Untreated hypertension was more highly prevalent in Blacks at almost 44 percent and Hispanics at almost 47 percent compared to whites at 33 percent. Treated hypertension was a significant independent risk factor and untreated hypertension was substantially greater risk factor for all three ethnic groups and across all locations. There was a striking interaction between ethnicity and risk of inter-cerebral hemorrhage, such that untreated hypertension conferred a greater risk of inter-cerebral hemorrhage in Blacks and Hispanics relative to Whites.

The nest study provides the first prospective multi-centered data on mortality and morbidity in rheumatic heart disease from low and middle income countries. First

author Dr. Zulky, corresponding author Dr. Mayoci and authors from Gertrude hospital and University of Cape Town in South Africa present the results of two year follow up of the global rheumatic heart disease registry or remedy study in 3343 children and adults with rheumatic heart disease from 14 low and middle income countries. They found that although patients were young with a median age of only 28 years the 2 year case fatality rate was high at almost 17 percent. The median age at death was 28.7 years. Mortality was higher in low income and low middle income regions compared to upper middle income countries. Independent predictors of death was severe valve disease, more advanced functional class, atrial fibrillation and older age. Where as post primary education and female sex were associated with a lower risk of death. The authors carefully noted that apart from age and gender the independent risk factors for mortality such as severity of valve disease heart failure, atrial fibrillation and low education were all modifiable and thus they called for programs focused on the early detection and treatment on clinical rheumatic heart disease.

Well that's it for the summaries, now lets go over to China

For our feature interview today we are going all the way to Beijing at the great Wall meeting where we will be meeting authors as well as editors. So here we have first and corresponding author Professor {Dong Fen Gu} and co-author Professor {Sherliang} both from {Fu Y} hospital Chinese academy of medical sciences in Beijing. Welcome

Dr.Gu: Welcome we are so delighted to be interviewed by you

Dr. Carolyn Lam: Thank you so much we are so excited to be talking about your paper predicting the ten year risks of cardiovascular disease in the Chinese population. And here we have as well editor in chief Dr. Joe Hill as well as Dr. Amid Kira digital strategies editor and associate editor. Gentlemen how is it in Beijing? And I hear that you have a Chinese greeting for everyone as well.

Joe Hill: {Ni how} and {nuchme and senchmen}

Amid Kira: I can't top that but I agree with what Joe said

Dr. Carolyn Lam: Dr. Gu, could you please tell us what is it that is so different about cardiovascular disease in China compared to what we heard about in the western world.

Dr.Gu: Okay cardiovascular disease is both leading cause of death in China and in United States as well in European countries. However the patterns for components of cardiovascular disease including coronary arteries and stroke are still quite different in the Chinese populations compared united states. For example there are coronary arteries mortality rate in the united states is along the 100 thousand per year and this is the first leading cause of death in the united states. And for stroke the annual mortality rate is along 36 per 100 thousand in the united states populations. However in china the stroke mortality rate among Chinese

populations is around the 160 per 100 thousand, so that almost 3.5 to 4 as high as in untied states. Obviously for our lifestyle in including battery behavior quite different you can easily identify one kind of difference in the united states and the Europe restaurants from Chinese restaurants and some western style restaurants you can figure it out.

And another example, smoking rate is major component for risk of cardiovascular disease it is very high in Chinese adult men. It over 50 percent right now but in the united states in the past 50 years it declined immensely. And around maybe less than around 20 percent and from the previous experiment from studies by Dr. Liu Chin from and my colleague Dr.WU they used the questions for predictions of coronary arteries compared to equations and also use the similar prediction model compares that its chemical cardiovascular disease from the united states population and the Chinese population. That to over estimation if we use the united states produced this kind of equation. So based on this kind of scenario we based on Chinese long term larger scales cohort to precede and study our own prediction model.

Dr. Carolyn Lam: Wow that is really fascinating Dr. Gu and I really could not agree with you more because I sort of trained in the united states for quite some time and then I moved back to Singapore and saw for myself in Asia the tremendously high rates of stroke. I was also very struck by the relative youth of the patients suffering cardiovascular disease and the differences in risk factors, the smoking but not just that, obesity is almost defined on a different scale in our relatively sized smaller Chinese population compared to that in the western. Congratulations to you and your team for a successful amazing effort. Could you or Dr. Yang now just let us know what are your main findings.

Dr. Yang: Well I think there are 2 major finding for our work. First we developed a new prediction risk model you know after analysis is for high risk score or equations released by AJ and ACC and is some other risk scores. We included 6 conditional risk factors in combination with our previous knowledge that included age, treated or untreated ISBP, total classical, HDLC current smoking and diabetes. So this traditional risk factors were set up as a base model and then we use the predefined statistical to include new additional variables they were Chinese special elements. Finally in our model there were rates as constraints and geographic region which means northern part versus the southern part in China and also organization is rural or urban area. And finally the forth one is family history as a CVD so this for additional variables in our model suggest that we maybe as a Chinese prediction and equations has something special. For example we feel more attention for central obesity in primary prevention in Chinese populations and also you know the norther part and the southern part there are large differences in the risk profiles. And so maybe according to our risk prediction model we pay more attentions for the residence living in northern part in China.

And then for the second points I think we found that PCE equation which shows for equations was not appropriate to predict ten year risk of in Chinese populations.

For example in our revelation cohort we found that our model just slightly over predicts severity risk by 17 percent in Chinese man but when we use the PCE models released form AHA the over-estimation come to 50 percent so maybe equations from western populations are not appropriate to Chinese populations.

Dr. Carolyn Lam: Thank you so much Dr. Yang I mean those are just such important findings applicable to a huge population in china, like you said. And just as important as the second point that the pooled equations derived from western populations may not be the most appropriate for certain other ethnic populations. I think that a very important message and that why we are so proud to be publishing this in Circulation. Could I ask then are you applying these new equations in your personal clinical practice?

Dr.Gu: Risk assessment is a fundamental components for prevention of ASSVD. In Chinese we question {turn the PA on} provide a valuable to identify high risk individuals in Chinese populations. And not with just complicated [inaudible 00:18:02] for further analysis. And propose three levels of groups of risk stratification could be identified by cut off 5 percent and 10 percent. So lower risk individuals with predicted activity risk of less than 5 percent should be offered lifestyle wise to maintain the lower risk status. While the moderate risk individual is predicted risk of 5 to 10 percentage for intensive therapeutic lifestyle change wit drug therapy if necessary. For the high individual risk high or large 10 percent teheraph of clinical aliment taken account for physicians recommendation should be required with therapy for the lifestyle modification. Then annually clinic up, including an echocardiographic information for carotid artery back and even for outer [inaudible 00:19:09] CT examinations for coronary artery are recommended. Also blood pressure, lipids, glucose measurement if necessary are suggest according to Chinese guideline. While cardiovascular disease prevention as well as for the epidemic of this kind a lines. For ACVD patients those are different kinds of risk assessment we could know whether their risk profile had been improved or be progressed so that appropriate clinical elements should be taken in clinical practice.

Dr. Carolyn Lam: Thank you very much Dr. Gu so that just show that these findings are immediately clinically applicable and I trust that means you're suing it in your clinics too, and once again were so happy to be publishing this in Circulation so in the rest of the time in going to now direct questions at Joe and Amid.

How's China been? How are your chopstick skills and any word on how Circulation is being received there?

Joe Hill: Well Carolyn its a delight to be here this is a bustling media that get better and better every year. In about 2 hours we have our first ever Circulation session, we brought several editors here to discuss the types of content that we are looking to publish, the type of work across prevention and population and electrophysiology of heart failure. This is an extraordinary media that is now internationally acclaimed and as we've heard here, the face of cardiovascular disease in Asia is changing. And as you pointed out 60percent of the human race lives in Asia and we want to do

everything we can to be here on the ground, in Asia trying to address this curve that is already present and is worsening by the day.

Dr. Carolyn Lam: Amid, you know you've seen the latest statistic on our podcasts and you highlighted that we have quite a number of listeners over there as well. Would you like to tell me how this is all blending it to the digital strategies and anything else you might want to highlight?

Amid Kira: Sure its been an incredible meeting and we get to meet great colleagues like our colleagues today on this podcast and learning so much from this meeting. Our podcast as you pointed out quite a sizable and growing cadre of people in Asia and Japan and China who are listening and we truly want to enhance that as Joe mentioned with the large splurge of cardiovascular disease and the great science that is going on here. Want to make sure that we are able to be apart of that conversation and interact with researcher and clinitions here. In addition to podcast, we are exploring some other options involving social media, specifically in China so stayed tuned in how those develop but we certainly appreciate the importance of being her and interacting where so much of cardiovascular disease and cardiovascular science is occurring.

Dr. Carolyn Lam: That's so great. Joe or Amid now there's a specific we would like to highlight to our listeners the doodle, either of you want to pick that up a bit about blipping the doodle?

Amid Kira: So there is as you know Circulation now has this doodle where we change it periodically and its sort of a fun themed thing. Right now I think it Halloween and we've had several other ones that people have designed to sort of keep thing fresh and light and interesting. There's a new app called blippar which you can download from iTunes or android stores and you can essentially scroll that over with your phone with the doodle and that will take you to new content either table of contents of videos, different kinds of content that it can navigate you to. So I hope people will not only enjoy the doodle kind of anticipate what's next in terms of seasons but will take the time t blip the doodle when they get a chance.

Dr. Carolyn Lam: That great and that blippar- B l I P P A R. You really c should check it out, anyone who is listening to this really check it out you'll be floored. Joe could I just turn the mic to you for any last words about the global outreach of Circulation, I mean its just so amazing that you're there in China

Joe Hill: Well heart disease Carolyn knows no boundaries nor does Circulation. There was a day when cardiovascular disease was largely an issue in the developed world that is long since gone and that's why the study that we are talking about today with these authors is so important because the face of cardiovascular disease is different than in the west, the ways in which it is evolving id different here than in the west and I like many others foresee an increase a significant increase in the types and prevalence of heart disease here in Asia. for all the reasons that we have been talking about, hypertension, obesity, type two diabetes, smoking the environment

all of these challenges I fear are going to lead to a substantial increase in the prevalence of heart disease in Asia and that why we're here on the ground with Circulation in Asia that's why we have one of our major leaders Chong Shong Ma who is here in Beijing. Circulation is in China everyday, it’s in Beijing everyday to try and address this problem.

Dr. Carolyn Lam: And you heard it from our editor and chief, so thank you everyone for listening to this episode of Circulation on run. Tune in next week.