

Estimation of 10-Year Risk of Fatal and Nonfatal Ischemic Cardiovascular Diseases in Chinese Adults

Yangfeng Wu, MD, PhD; Xiaoqing Liu, MD; Xian Li, MD; Ying Li, MD; Liancheng Zhao, MD; Zuo Chen, MD; Yihe Li, MD; Xuxu Rao, MD; Beifan Zhou, MD; Robert Detrano, MD, PhD; Kiang Liu, PhD; for the USA-PRC Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology Research Group and the China Multicenter Collaborative Study of Cardiovascular Epidemiology (China MUCA) Research Group

Background—Stroke is much more prevalent than coronary heart disease in China; thus, any risk prediction model only for coronary heart disease may not be appropriate in application. Our objective is to develop a cardiovascular risk prediction model appropriate for the Chinese population.

Methods and Results—Cox proportional hazards regression was used to develop sex-specific optimal 10-year risk prediction models for ischemic cardiovascular disease (ICVD; including ischemic stroke and coronary events) from 17 years of follow-up data from the USA-PRC Collaborative Study of Cardiovascular Epidemiology cohort, in which 9903 participants were followed up every 2 years until 2000, and 371 ICVD events (266 strokes and 105 coronary heart disease events) occurred. The models showed ICVD was positively related to age, systolic blood pressure, serum total cholesterol, body mass index, current smoking status, and diabetes mellitus in both men and women. When the models were applied to the 17 329 participants in the China Multicenter Collaborative Study of Cardiovascular Epidemiology cohort, the areas under the receiver operating characteristic curve were 0.796 ± 0.036 for men and 0.791 ± 0.036 for women. The simplified point score model resulted in similar c statistics. Comparison of the observed with the estimated incidence of ICVD at different risk levels showed satisfactory precision. Meanwhile, application of recalibrated Framingham models significantly overestimated the coronary heart disease risk in both men (by $\approx 97\%$) and women (by $\approx 228\%$).

Conclusions—The Cox regression prediction models and simplified point score model have satisfying predictive capability for estimating the 10-year integrated cardiovascular risk in Chinese, in whom stroke is the predominant cardiovascular disease. (*Circulation*. 2006;114:2217-2225.)

Key Words: cardiovascular diseases ■ population ■ coronary disease ■ risk factors ■ stroke

The Framingham Heart Study and studies done in Europe have resulted in the development of several models and tools for predicting the risk of coronary heart disease (CHD) that serve well in developed countries.¹⁻⁶ Liu et al⁷ found that original Framingham functions overestimated the CHD risk in the Chinese population. Although recalibration of the Framingham functions improved the estimation and may be useful for some Chinese populations, this has not been confirmed in other studies. Furthermore, because risk factor patterns and the profile of cardiovascular disease^{8,9} are different in China, and because stroke is much more prevalent than CHD in China,¹⁰ more appropriate prediction models and tools that could estimate the total cardiovascular risk (both CHD and stroke) are needed for practical prevention. In the present report, we describe the derivation and validation of such a model.

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Methods

We used data from the USA–People’s Republic of China (PRC) Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology (the USA-PRC Study) cohort, as a derivation cohort, to generate the prediction models, and we used the independent China Multicenter Collaborative Study of Cardiovascular Epidemiology (MUCA) Cohort II as the validation cohort to test whether the derived models are applicable to recent Chinese populations and generalizable to other Chinese populations.

Derivation Cohort

The study protocols and the data collection forms in the USA-PRC Study for both baseline survey and follow-ups were developed by

Received November 19, 2004; de novo received February 19, 2006; revision received September 13, 2006; accepted September 15, 2006.

From the Cardiovascular Institute and Fuwai Hospital (Y.W., X. Li, Ying Li, L.Z., Z.C., B.Z.), Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China; Guangdong Provincial Cardiovascular Institute (X. Liu, Yihe Li, X.R.), Guangzhou, China; University of California (R.D.), Irvine; and Northwestern University School of Medicine (K.L.), Chicago, Ill. Dr Wu is currently at the Peking University School of Public Health, Beijing, China.

Correspondence to Dr Yangfeng Wu, MD, PhD, Professor and Chief, Department of Epidemiology, Cardiovascular Institute and Fu Wai Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100037, China. E-mail yangfengwu@263.net

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Circulation is available at <http://www.circulationaha.org>

DOI: 10.1161/CIRCULATIONAHA.105.607499

scientists from the 2 countries. The details of the baseline survey and follow-up methods were explained in prior publications.^{11,12} Briefly, the study included 11 336 men and women, aged 35 to 59 years, randomly selected in clusters (villages, residential households, or working organizations) from 4 approximately equally sized sub-samples, an urban and a rural district in Beijing and an urban and a rural district in Guangzhou. After a pilot study was completed that involved 6000 local residents, the formal baseline survey was performed on half of the cohort in September and October of 1983 and 1984. We chose this particular season to enhance participation: The farmers are not busy, and it is practical for participants to remove their clothes for anthropometric measurements in the temperate weather. All baseline survey interviewers received centralized training and passed a qualification test. The first follow-up for CHD and stroke events was done 4 years later in 1987 and 1988. After that, the cohort was followed up every 2 years until December 31, 2000. The follow-up data for CHD and stroke events were first collected by health workers in the villages or working places using a standardized form. Suspected events were further investigated with a doctor's revisit to the patient or family, or the hospital if applicable, to collect clinical data needed for diagnosis (including symptoms, personal history, ECGs, enzyme tests, or autopsy findings) and to complete the clinical records form. Seventy percent (74% in urban and 65% in rural districts) of nonfatal acute myocardial infarction diagnoses included cardiac enzyme tests, and 100% of the cases were hospitalized. For ischemic stroke, 90% (88% for urban and 92% for rural areas) were hospitalized. Final events were determined, without reference to the baseline risk factors, by an adjudication committee of 7 members from the Cardiovascular Institute and Fuwai Hospital in Beijing and the Guangdong Cardiovascular Institute in Guangzhou. Subjects were excluded for the following indications: prevalent disease at the baseline survey (8 myocardial infarction patients and 74 stroke patients); no baseline blood draw (1252 patients); and lost to any follow-up visit (99 patients). In this report, we used data from the remaining 9903 eligible participants. The years of follow-up were defined as the time from the baseline examination date to the date of disease onset for those who had had CHD or ischemic stroke (n=360), to the date of last follow-up for those who were lost to follow-up (n=494), and to the date (December 31, 2000) of the final follow-up survey for the remaining participants. The average length of follow-up was 15.1 years. At the baseline visit, all participants were provided with a description of the study and gave informed consent. Participants also gave informed consent at each follow-up visit.

Risk Factor Measurement

In the USA-PRC Study, the variables surveyed included demographic, medical, behavioral, and familial cardiovascular risk factors.¹¹ Briefly, these risk factors were measured as follows. Weight and height were measured with participants wearing light indoor clothing and no shoes; 3 consecutive blood pressure readings were taken on the right arm with a mercury sphygmomanometer, and the means were used for analysis; and a 12-hour fasting blood sample was collected and the blood lipids were measured with the standardized protocol of the National Heart, Lung, and Blood Institutes and the Centers for Disease Control and Prevention in the United States. Specifically, we used a high-performance enzymic reagent (Boehringer-Mannheim Diagnostics, Indianapolis, Ind) calibrated with precise standards on the Abbott Laboratories (Abbott Park, Ill) ABA 200 bichromatic analyzer to measure total cholesterol. The 12-hour fasting glucose was measured by an enzymatic method (SmithKline Instruments, Inc, Sunnyvale, Calif). Current smoking was defined as having smoked at least 1 cigarette per day for at least the past 1 year.

Events Criteria

The diagnostic criteria for events were those of the WHO-MONICA study (World Health Organization-MONItoring trends and determinants in Cardiovascular disease project).^{13,14} Briefly, the events reported as coronary events included (1) definite acute myocardial infarction, (2) possible acute myocardial infarction and coronary death, and (3) ischemic cardiac arrest with successful resuscitation

not fulfilling criteria for definite or possible myocardial infarction. We did not include silent myocardial infarction. Ischemic stroke was defined as brain infarction due to occlusion of precerebral arteries (*International Classification of Diseases*, 9th Revision, code 433) or embolic brain infarction (*International Classification of Diseases*, 9th Revision, code 434). It included patients who had clinical signs and symptoms suggestive of cerebral ischemic necrosis. It did not include transient cerebral ischemia or stroke events in cases of blood disease (eg, leukemia or polycythemia vera), brain tumor (or brain metastases), or trauma. In the present study, 81% of ischemic stroke patients underwent brain computed tomographic scanning. Ischemic cardiovascular disease (ICVD) events were defined as CHD events and ischemic stroke.

Identifying the Prediction Model Outcomes

In China, the incidence of CHD is approximately one fifth to one third that of stroke,⁸ and about two thirds of strokes are ischemic.¹⁵ It is therefore more appropriate to measure and use the integrated risk of ICVD¹⁶ rather than that of CHD alone from a prevention point of view. Thus, we used ICVD events as the dependent variable of the predictive model. If an individual had >1 event, the first event was used.

Fitting of the Optimal Prediction Model

Because of the large difference in ICVD incidence between the sexes, and because the reasons for this are not yet fully understood, separate models were developed and tested for men and women. The major risk factors included age, systolic blood pressure, body mass index [weight (kg)/height (m)²], total serum cholesterol, diabetes mellitus, and current smoking status. These factors were selected not on the basis of the best-fitted model for empirical data but rather on the basis of known and well-established risk factors for ICVD in China and the rest of the world.¹⁷⁻¹⁹ Distinct from models developed at Framingham and in Europe,^{4,6} high-density lipoprotein (HDL) cholesterol or the total cholesterol/HDL cholesterol ratio and low-density lipoprotein cholesterol were not included in our models, but body mass index was included. HDL cholesterol is not a routinely tested item in most local health services in China, and measurement error is expected to be large in many laboratories. Because low-density lipoprotein cholesterol is usually calculated in part based on HDL cholesterol, it will suffer from the same limitations. We defined diabetes as either a history of treatment or a fasting serum glucose level ≥ 126 mg/dL (7.0 mmol/L).²⁰ Because we found that systolic blood pressure is a more powerful predictor of events than diastolic blood pressure or the combination of systolic blood pressure and diastolic blood pressure, we included only systolic blood pressure in the model.

Application of the Models to the Validation Cohort

The China MUCA study cohort II was established in 1993 to 1994 and is the validation sample used in the present report. It was considered appropriate because it was established more recently than the USA-PRC Study cohort and consisted of a large sample of 17 329 study subjects from 11 populations in China during a follow-up period of 11 years, and the sampling and survey methods, age at enrollment, and follow-up protocol were identical. We applied both the corrected and uncorrected prediction models to the China MUCA study cohort II and then assessed discrimination using receiver operating characteristic curve analysis, and accuracy was tested by comparing the predicted ICVD incidence with the observed person-year ICVD incidence.

Simplified Point-Score Risk Estimation

On the basis of the optimal models, we translated both discrete and continuous risk factor variables into categorized variables. Then, a simplified prediction model was fitted with the categorized variables. We set up a scoring system that assigned risk scores to different levels of the different risk factors, with reference to the corresponding regression coefficients (Figure 1). To translate the regression

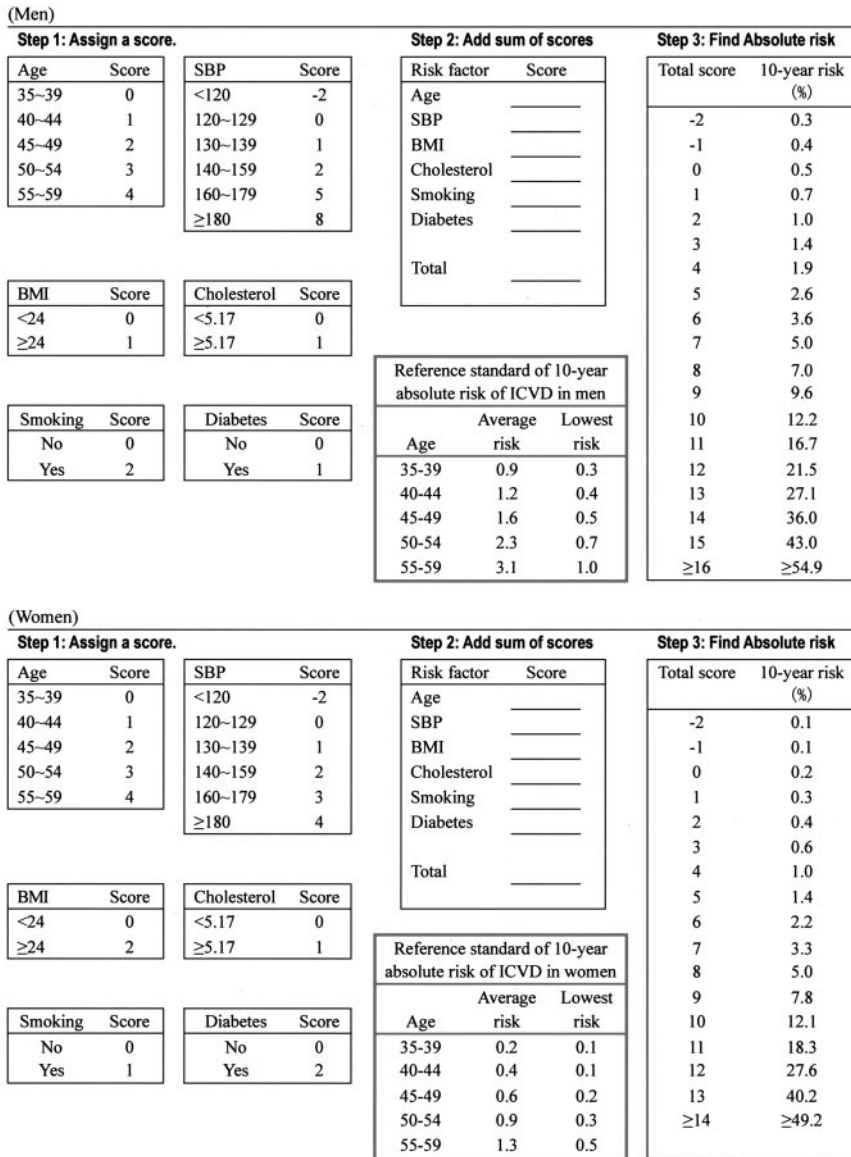


Figure 1. Simplified evaluation sheet for estimating 10-year risk of ICVD incidence for men and women. SBP indicates systolic blood pressure; BMI, body mass index.

coefficients into scores, we used the quantity of risk from every age increase of 5 years as 1 standard unit of risk and gave it an incremental score of 1. The mean 10-year risk of all possible combinations of risk factors for a specific total score was computed to obtain 10-year risk values (Figure 1).

Statistical Analysis

Statistical Model

We used the Cox proportional hazards model to fit the risk factors to the observed events²¹ after testing for the assumption of proportionality, with use of the SAS statistical package (SAS Institute, Inc, Cary, NC). To compare the coefficients of each major risk factor between the models for CHD and that for ischemic stroke, we used polytomous logistic regression to reproduce regression coefficients and then tested them with the z test.

Correction for Change in Risk Factors

Since this research began, the prevalence and level of the major risk factors of ICVD have increased greatly in China.²² Some of the ICVD events observed might be due to risk factor increases since baseline. Thus, our model would overestimate the “true” risk of ICVD. To correct for this, we assumed that the true risk of ICVD during the follow-up is the direct function of the average level of risk

factors during the same period. Because we have risk factor data for the same cohort collected in 1993/1994, at about the middle of the follow-up period, we used those data as estimated average risk factor levels during the follow-up to correct the model for risk factor changes. The correction factors, the ratio of the risk factor levels in 1993/1994 to baseline levels, were 1.036 for systolic blood pressure, 1.045 for body mass index, 1.041 for total cholesterol, and 1.090 for glucose in men, and 1.041, 1.053, 1.051, and 1.076, respectively, for those values in women. We corrected the regression coefficients by dividing by these factors.

Area Under the Receiver Operating Characteristic Curve

To quantify the ability of the prediction models to discriminate events from nonevents, we calculated the area under the receiver operating characteristic curve (AUC) based on the application of the corrected Cox proportional hazards model and the simplified model to the validation cohort²³ using the trapezoid rule, as described by Hanley and McNeil.²⁴ We compared the AUCs using the method of Nam.²⁵

Applicability to an Independent Cohort

Applicability was evaluated by comparing the mean probability estimates in each decile of probability in the validation cohort with the observed disease incidence with the Hosmer-Lemeshow test.

Comparison With Recalibrated Framingham Model

We applied the recalibrated Framingham function for Chinese⁷ to the present validation cohort to compute the mean 10-year risk of CHD events and compared that with the observed 10-year incidence of CHD events and the estimated and observed 10-year risk of ICVD in the validation cohort. In the recalibrated Framingham functions, the regression coefficients were taken from the original Framingham Cox model,²⁶ but mean values from the Chinese Multi-Province Collaborative Study were used for risk factors and mean incidence rates.⁷ The CHD event end points used in the recalibrated Framingham functions were the same as those used in the present study, ie, they included acute myocardial infarction, sudden death, and other coronary deaths according to the criteria of the WHO-MONICA project.

The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Derivation Cohort Baseline Characteristics and Follow-Up Events

Table 1 describes the baseline characteristics of the USA-PRC cohort. The cohort had a typical distribution of education and occupation for the early 1980s in urban and rural areas in China. There were 371 ICVD events (360 cases), which included 105 CHD events (66 for men and 39 for women) and 266 ischemic strokes (158 for men and 108 for women).

Cox Proportional Hazards Results

The coefficients for predicting CHD events, ischemic stroke, and ICVD for each risk factor variable are listed in Table 2. Comparison of the coefficients between the CHD and ischemic stroke models showed that (1) the directionality of the relationship for all listed risk factors was similar (ie, they all were positively related to risk of CHD events and ischemic stroke); and (2) the magnitude of the relations for each of the risk factors was similar, with the exception of systolic blood pressure for women. The model for ICVD confirmed the directionality of relations and showed coefficients that were statistically significant for all risk factors except diabetes mellitus in men (Table 2).

Simplified Prediction Models and Tools

Table 3 contains the coefficients of the corrected simplified model, and Figure 1 displays the resulting clinical scoring system. Figure 1 also gives the average risk and lowest risk for different age/gender groups, to help doctors understand how their patient's risk level compares with average- and low-risk patients of the same age and gender. A computerized program that allows for Chinese individual 10-year risk evaluation of ICVD can be found at <http://www.healthyheart-china.com> under "Risk Assessment."

Comparison With Recalibrated Framingham Model

Figure 2 clearly shows that (1) the incidence of ICVD was much higher than that of CHD in Chinese; (2) the recalibrated Framingham model significantly overestimated the risk of CHD in both men (by $\approx 97\%$) and women (by $\approx 228\%$) and underestimated risk of ICVD in both men and women; and (3) the corrected ICVD model fit the observed ICVD incidence very well and better than the uncorrected model.

TABLE 1. Baseline Characteristics of Study Participants in the USA-PRC Cohort

	Men	Women	Total
Baseline characteristics			
No. of participants	4890	5013	9903
Age, y	46 \pm 6	45 \pm 6	46 \pm 6
Area, n			
Urban	2947	2545	5492
Rural	1943	2468	4411
Education, n (%)			
Illiterate	401 (8)	1795 (36)	2196 (22)
Primary school	2122 (44)	1825 (36)	3947 (40)
Secondary school	1428 (29)	862 (17)	2290 (23)
High school	753 (15)	436 (9)	1189 (12)
College and above	181 (4)	95 (2)	276 (3)
Occupation, n (%)			
Manual worker	2781 (57)	1993 (40)	4774 (48)
Farmer	1707 (35)	2039 (40)	3746 (38)
Office worker	375 (8)	202 (4)	577 (6)
Housewife	0 (0)	699 (14)	699 (7)
Other	27 (1)	79 (2)	106 (1)
Systolic blood pressure, mm Hg	120 \pm 18	119 \pm 20	119 \pm 19
Diastolic blood pressure, mm Hg	78 \pm 12	75 \pm 11	77 \pm 11
Serum total cholesterol, mmol/L	4.6 \pm 1.0	4.6 \pm 1.0	4.6 \pm 1.0
Serum glucose, mmol/L	4.5 \pm 1.0	4.6 \pm 1.2	4.5 \pm 1.1
Body mass index, kg/m ²	22 \pm 3	22 \pm 4	22 \pm 3
Smoking status, n (%)			
Current smoker	3591 (73)	866 (17)	4457 (45)
Ex-smoker	245 (5)	119 (2)	364 (4)
Never-smoker	1054 (22)	4028 (81)	5082 (51)
Hypertension, n (%)	990 (20)	813 (16)	1803 (18)
Hypercholesterolemia, n (%)	1127 (23)	1218 (24)	2345 (24)
Diabetes mellitus, n (%)	89 (2)	110 (2)	199 (2)
Overweight/obesity, n (%)	1153 (24)	1422 (28)	2575 (26)
Antihypertensive medication use in 2 weeks, n (%)	212 (5)	162 (4)	374 (4)
Follow-up data in 15 years, n (%)			
CHD events	66 (1)	39 (1)	105 (1)
Ischemic strokes	158 (3)	108 (2)	266 (3)
ICVD	219 (4)	141 (3)	360 (4)
Lost to follow-up	218 (4)	276 (5)	494 (5)

Hypertension was defined as systolic blood pressure ≥ 140 mm Hg and/or diastolic blood pressure ≥ 90 mm Hg and/or medication use in last 2 weeks. Hypercholesterolemia was defined as serum total cholesterol ≥ 5.17 mmol/L. The definitions of overweight/obesity and diabetes mellitus are given in the text.

Percentages for follow-up data are cumulative percentages during the 15 years of follow-up.

Discrimination

Figure 3 depicts receiver operating characteristic curves for men and women that show good, almost identical discrimination for the optimal model (for men, AUC=0.796, 95% CI=0.762 to 0.829; for women, AUC=0.791, 95% CI=0.755 to 0.828), the simplified model (for men,

TABLE 2. Coefficients (β) and P Values in Optimal Models for CHD Events, Ischemic Stroke, and ICVD, by Gender

Variable	CHD Model		Ischemic Stroke Model		Two-Model Comparison, P	ICVD Model	
	β	P	β	P		β	P
Men							
Age, 5 y	0.3267	0.0039	0.3314	<0.0001	0.90	0.3277	<0.0001
SBP, 20 mm Hg	0.5084	<0.0001	0.7102	<0.0001	0.17	0.6711	<0.0001
Total cholesterol, 1 mmol/L	0.1261	0.2661	0.1577	0.0262	0.76	0.1367	0.0260
BMI, 3 kg/m ²	0.0770	0.5033	0.1584	0.0291	0.62	0.1360	0.0287
Current smoker, yes/no	0.4675	0.1344	0.7630	0.0005	0.47	0.6894	0.0002
Diabetes, yes/no	0.4113	0.4318	0.0766	0.8351	0.81	0.1195	0.7030
Women							
Age, 5 y	0.6342	0.0002	0.3964	<0.0001	0.19	0.4641	<0.0001
SBP, 20 mm Hg	0.3993	0.0013	0.6825	<0.0001	0.04	0.6090	<0.0001
Total cholesterol, 1 mmol/L	0.2769	0.0375	0.1128	0.1810	0.34	0.1479	0.0423
BMI, 3 kg/m ²	0.3481	0.0020	0.0954	0.1731	0.07	0.1593	0.0087
Current smoker, yes/no	1.2023	0.0002	0.2819	0.2093	0.06	0.4457	0.0182
Diabetes, yes/no	1.0960	0.0145	1.0596	0.0003	0.85	0.9946	0.0001

SBP indicates systolic blood pressure; BMI, body mass index.

AUC=0.792, 95% CI=0.758 to 0.825; for women, AUC=0.783, 95% CI=0.746 to 0.821), and the score system (for men, AUC=0.791, 95% CI=0.757 to 0.825; for women, AUC=0.779, 95% CI=0.741 to 0.817) in the validation cohort, after correction of a long-term shift in the levels of risk factors.

Test of Generalizability in the Validation Cohort

In the 11-year follow up of the MUCA II cohort, there were 347 ICVD events (206 for men and 141 for women); 83 CHD events (56 for men and 27 for women), and 268 ischemic strokes (154 for men and 114 for women). The observed incidence of ICVD in the derivation cohort was not signifi-

TABLE 3. β -Coefficients and Hazard Ratios of the Multivariable Simplified Cox Proportional Hazard Model for 10-Year Risk of ICVD

	Men				Women			
	n	β	HR	95% CI	n	β	HR	95% CI
Age, y	4890	0.0656	1.07‡	1.04–1.10	5013	0.0851	1.09‡	1.05–1.13
SBP, mm Hg								
<120	2777	-0.5488	0.58*	0.36–0.92	3104	-0.8267	0.44†	0.24–0.82
120–129	954	Referent	1.00	...	842	Referent	1.00	...
130–139	526	0.4011	1.49	0.93–2.41	428	0.2294	1.26	0.68–2.32
140–159	452	0.8073	2.24‡	1.43–3.51	399	0.7970	2.22†	1.28–3.84
160–179	140	1.7041	5.50‡	3.43–8.80	174	1.3674	3.93‡	2.23–6.91
≥180	41	2.5327	12.59‡	7.45–21.28	66	1.8483	6.35‡	3.42–11.80
BMI, kg/m ²								
<24	3737	Referent	1.00	...	3591	Referent	1.00	...
≥24	1153	0.2864	1.33	1.00–1.78	1422	0.6762	1.97‡	1.34–2.88
Total cholesterol, mmol/L								
<3.62	681	Referent	1.00	...	819	Referent	1.00	...
3.62–5.16	3082	-0.0070	0.99	0.59–1.69	2976	-0.0866	0.92	0.44–1.93
≥5.17	1127	0.3040	1.36	0.79–2.34	1218	0.2654	1.30	0.62–2.73
Current smoker, yes/no	3591	0.7082	2.03‡	1.42–2.90	866	0.4699	1.60*	1.11–2.32
Diabetes, yes/no	89	0.0651	1.07	0.58–1.98	110	0.9599	2.61‡	1.57–4.33
Baseline survival function at 10 years, S(10)	...	0.9835	0.9948

SBP indicates systolic blood pressure; BMI, body mass index.

*0.01 < P < 0.05; †0.001 < P < 0.01; ‡P < 0.001.

Coefficients and baseline survival functions listed at the bottom of the table are used to compute an exponential model based on the variables listed in the table in a method exactly analogous to that used in the Framingham model in the United States.⁴

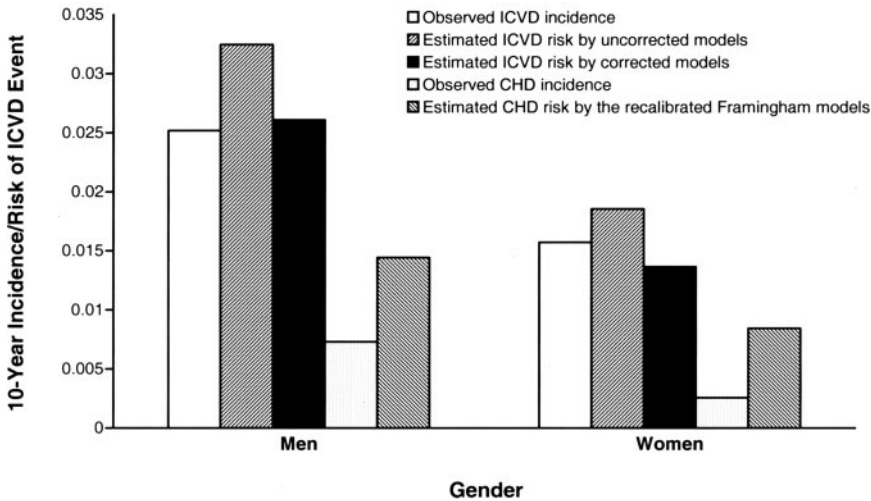


Figure 2. Comparison of applicability of different models. Compared with the observed 10-year incidence of ICVD, the uncorrected models overestimated the risk significantly in men ($P=0.010$) but not in women ($P=0.167$). The corrected models predicted risk very well in both men ($P=0.733$) and women ($P=0.274$). Compared with the observed 10-year incidence of CHD events, the calibrated Framingham models overestimated the risk significantly in men ($P<0.0001$) and in women ($P<0.0001$).

cantly different from the estimated ICVD risk by uncorrected models. There was, however, a significant difference between the observed ICVD incidence in the validation cohort and the estimates from the uncorrected model. The corrected models improved the accuracy in the validation cohort (Figure 4.)

Comparison between participants included and excluded in the derivation cohort showed that excluded participants were 3.3 years older, had body mass indices that were 0.6 kg/m² lower, and had systolic blood pressures that were 2 mm Hg higher and diastolic blood pressures that were 1.3 mm Hg lower. However, age- and sex-specific means did not differ significantly. Although heart attack and stroke incidence or mortality were slightly higher in the included group, the difference was not statistically significant.

Discussion

Cardiovascular disease risk is a result of the integration of multiple risk factors. The concept of “integrated risk” evaluation is well recognized. The current clinical guidelines^{27–30} all adapted the strategy of applying interventions according to the magnitude of integrated risk. The Framingham Heart Study began its exploration in 1967¹ of prediction models to estimate the global risk of CHD for individuals. After many years of study,^{2–4} its evaluation models and tools were

produced and have been widely used in the United States and other countries.

Although a study by Liu et al⁷ suggested a recalibrated Framingham model can be applied to Chinese populations to estimate 10-year risk of CHD events, findings in the present study do not support this. Furthermore, we consider it inappropriate to estimate the total cardiovascular risk on the basis of the risk of CHD alone without considering stroke in a population in which the predominant type of cardiovascular disease is stroke. We use the term “integrated risk” to address not only the integrated risk from the combination of multiple risk factors (eg, blood pressure, hypercholesterolemia, and diabetes mellitus) but also the combined risk of multiple atherosclerotic diseases (eg, CHD and ischemic stroke). Although CHD and stroke have some differences in origin, atherosclerosis is the common pathophysiological basis for both. Hypertension, hyperlipidemia, smoking, diabetes mellitus, obesity, age, and sex are widely accepted as major risk factors for atherosclerosis, CHD, and ischemic stroke. These factors, together with our own findings, support the use of ICVD as the outcome for prediction of the global risk of ischemic vascular diseases. The concept of integrating the risk of CHD and ischemic stroke into a single model and then using the resulting model in clinical practice is particularly

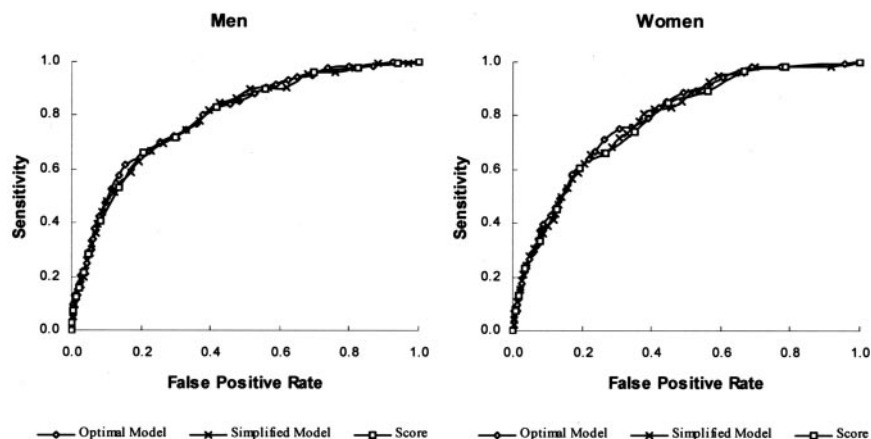


Figure 3. Receiver operating characteristic (ROC) curves for men and women showing almost identical discrimination for optimal model, simplified model, and score system in the validation cohort.

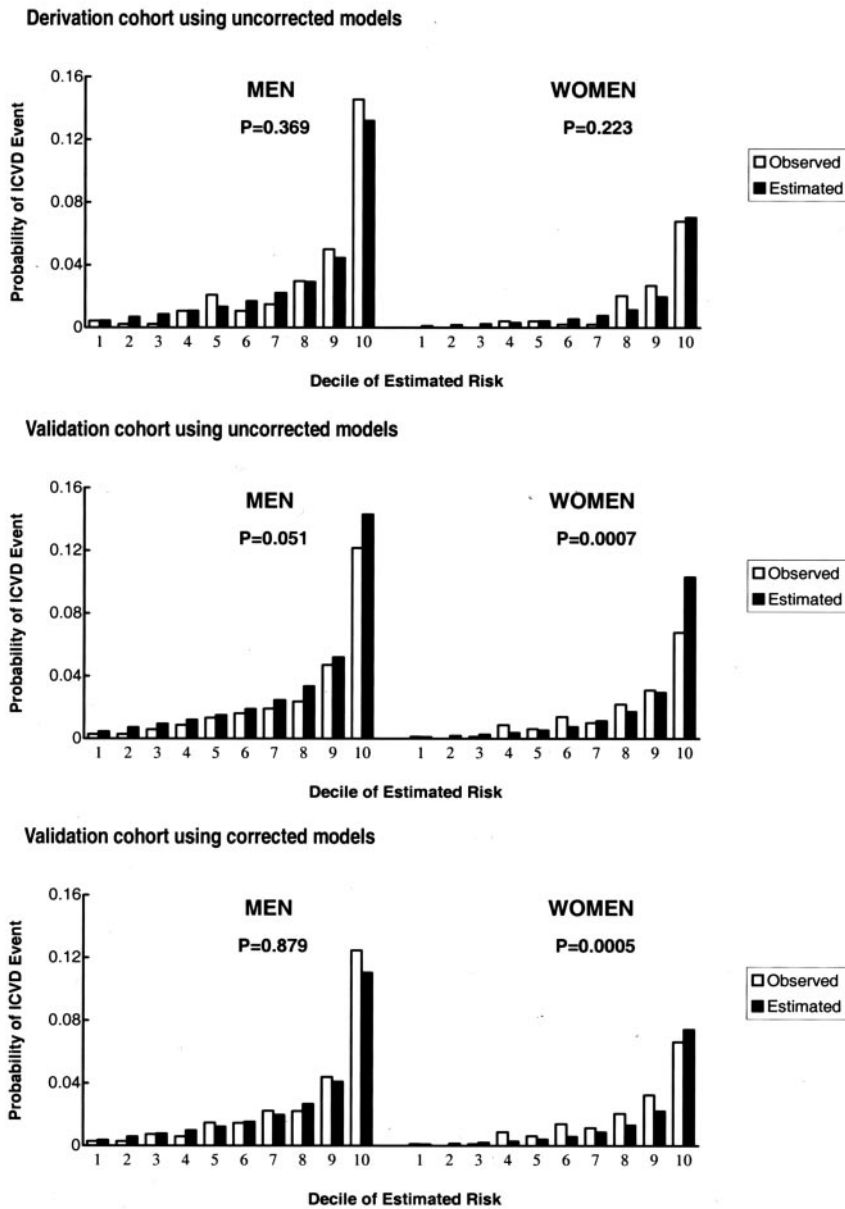


Figure 4. Comparison between observed and estimated 10-year incidence of ICVD for men and women in the derivation and validation cohorts with uncorrected and corrected models.

valuable in countries where stroke risk is high, as it is in China.

The USA-PRC study cohort study provides an optimal base for developing the prediction model for several reasons. Internationally standardized study methodology and quality control protocols were used both in the baseline risk factor survey and in the follow-up procedures. In particular, the laboratories used for lipid measurements participated in the US Centers for Disease Control and Prevention’s long-term quality control program. In addition, this population-based cohort had a large sample size of >10 000 and a follow-up period that averaged 15 years. Finally, collection of the follow-up data on ICVD outcomes was prospective and was done periodically (every 2 years).

Study Limitations

Despite the many strengths of the present study, there are some limitations that need to be addressed. First, those

individuals who were excluded due to missing values were 3.3 years older than included subjects; however, age- and sex-specific risk factor mean values were comparable between the 2 groups. Because the age distribution of the people included in the analyses covers the entire spectrum of the age distribution, it is unlikely that the exclusion of the people with missing values would cause a serious bias. We did not collect data on atrial fibrillation, left ventricular hypertrophy, or heart failure, and this limited our ability to refine the prediction models. We used presence or absence for current smoking status in the prediction model and did not consider the effect of quitting smoking, because the rate of quitting was only 3.7%. We repeated the analysis with hypertension therapy included and found that the coefficient was almost unaffected by inclusion of this variable in the model. Because the effect size was small, we did not include antihypertensive medication use in our risk model.

Because >80% of stroke diagnoses were confirmed by computed tomography, the misclassification of events between ischemic and hemorrhagic stroke would be small. In terms of multicollinearity and effect modification, we examined the correlation coefficients among risk factors. They ranged from 0.0022 to 0.3704, which demonstrates that there was not much effect from multicollinearity or effect modification.

There might be some incomplete case findings. This would attenuate the association between risk factors and ICVD and thus cause some underestimation of risk. However, because the number of noncases was very large compared with the number of misclassified cases, the potential bias should be very small and can be ignored.

Because of these and other considerations, caution should be used when the tools of the present study are applied. (1) The study was based on data from those without known cardiovascular disease, and the models should not be directly applied to those with known cardiovascular disease. (2) Because the outcome events in the present study did not encompass other ICVD events such as angina pectoris or claudication, the predicted absolute risk of ICVD events will be lower than actual risk when these other outcomes are included. When applied in clinical work, this should be taken into consideration. (3) The study population was aged 35 to 59 years; thus, application to persons older than 60 years should be used cautiously if at all. (4) This method only estimates the risk of developing ICVD within a 10-year time period. Caution should be used in applying these results to young persons. For these cases, we strongly recommend the use of the score sheet in Figure 1 and comparing the estimated risk with the average risk and low risk of the same age-sex group. (5) The findings from testing in an independent group showed the prediction model and score tool satisfied generalizability in Chinese individuals living in the mainland of China; however, we recommend caution in applying our model to other Chinese persons.

Acknowledgment

We deeply appreciate the participation of our colleagues and coworkers at the USA-PRC and MUCA participating centers and especially the contribution of the research participants in these studies.

Sources of Funding

This study was supported by the People's Republic of China Ministry of Science and Technology and the Ministry of Health through the 8th through 10th National Five-Year Plan projects (contracts 85-915-01-01, 96-906-02-01, and 2001BA703B01); the United States National Heart, Lung, and Blood Institute (contracts NO1HV12243 and NO1HV8112); Cardiovascular Institute and Fu Wai Hospital, Beijing, China; and Guangdong Provincial Cardiovascular Institute, Guangzhou, China. The authors are also grateful to Pfizer Pharmaceuticals Limited, China, for its generous support of the 10th National Five-Year project.

Disclosures

None.

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CLINICAL PERSPECTIVE

The present report displays clinically applicable risk prediction models. These models are based on up-to-date clinical data taken from 2 large and widely quoted studies: the USA–People's Republic of China (PRC) Collaborative Study of Cardiovascular Epidemiology and the China Multicenter Collaborative Study of Cardiovascular Epidemiology. These results have practical applicability, particularly among healthcare providers caring for Chinese patients. The models published in this report can be used to calculate risk of ischemic cardiovascular disease in individual patients in China, where stroke is much more common than coronary heart disease. Because such patients make up $\approx 20\%$ of such persons worldwide, these models can be of great clinical benefit for prevention and control of cardiovascular disease in the world. Furthermore, by more accurate estimation of the individual's total cardiovascular risk, more active interventions will be initiated among those high-risk individuals whose cardiovascular risk would have been underestimated previously only for coronary heart disease. Doctors can use the formally published results and the Web-published results to predict the joint risk of coronary heart disease and ischemic stroke in their patients on the basis of demographic and risk factor data.

Estimation of 10-Year Risk of Fatal and Nonfatal Ischemic Cardiovascular Diseases in Chinese Adults

Yangfeng Wu, Xiaoqing Liu, Xian Li, Ying Li, Liancheng Zhao, Zuo Chen, Yihe Li, Xuxu Rao, Beifan Zhou, Robert Detrano and Kiang Liu
for the USA-PRC Collaborative Study of Cardiovascular and Cardiopulmonary Epidemiology Research Group and the China Multicenter Collaborative Study of Cardiovascular Epidemiology (China MUCA) Research Group

Circulation. 2006;114:2217-2225; originally published online November 6, 2006;
doi: 10.1161/CIRCULATIONAHA.105.607499

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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