Predictive Value for the Chinese Population of the Framingham CHD Risk Assessment Tool Compared With the Chinese Multi-provincial Cohort Study

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THE FRAMINGHAM HEART STUDY has contributed to the identification of risk factors for coronary heart disease (CHD) and has developed multivariable functions to predict absolute CHD risk. Risk reduction programs now focus on absolute risk of disease rather than on modification of individual risk factors. The Framingham prediction algorithms have been widely adopted to assess absolute risk and guide the intensity of risk factor interventions. However, since more than 99% of Framingham participants are of European descent, the Framingham functions cannot be generalized to other populations without evaluation of their appropriateness. Directly applying Framingham functions in some populations overestimates CHD risk. Recalibrating Framingham functions can substantially improve predictive ability and, thus, can be a useful approach to generalizing the Framingham model to other populations. This approach has been evaluated in co-

Context The Framingham Heart Study helped to establish tools to assess coronary heart disease (CHD) risk, but the homogeneous nature of the Framingham population prevents simple extrapolation to other populations. Recalibration of Framingham functions could permit various regions of the world to adapt Framingham tools to local populations.

Objective To evaluate the performance of the Framingham CHD risk functions, directly and after recalibration, in a large Chinese population, compared with the performance of the functions derived from the Chinese Multi-provincial Cohort Study (CMCS).

Design, Setting, and Participants The CMCS cohort included 30,121 Chinese adults aged 35 to 64 years at baseline. Participants were recruited from 11 provinces and were followed up for new CHD events from 1992 to 2002. Participants in the Framingham Heart Study were 5,251 white US residents of Framingham, Mass, who were 30 to 74 years old at baseline in 1971 to 1974 and followed up for 12 years.

Main Outcome Measures “Hard” CHD (coronary death and myocardial infarction) was used as the end point in comparisons of risk factors (age, blood pressure, smoking, diabetes, total cholesterol, and high-density lipoprotein cholesterol [HDL-C]) as evaluated by the CMCS functions, original Framingham functions, and recalibrated Framingham functions.

Results The CMCS cohort had 191 hard CHD events and 625 total deaths vs 273 CHD events and 293 deaths, respectively, for Framingham. For most risk factor categories, the relative risks for CHD were similar for Chinese and Framingham participants, with a few exceptions (ie, age, total cholesterol of 200-239 mg/dL [5.18-6.19 mmol/L], and HDL-C less than 35 mg/dL [0.91 mmol/L] in men; smoking in women). The discrimination using the Framingham functions in the CMCS cohort was similar to the CMCS functions: the area under the receiver operating characteristic curve was 0.705 for men and 0.742 for women using the Framingham functions vs 0.736 for men and 0.759 for women using the CMCS functions. However, the original Framingham functions systematically overestimated the absolute CHD risk in the CMCS cohort. For example, in the 10th risk decile in men, the predicted rate of CHD death was 20% vs an actual rate of 3%. Recalibration of the Framingham functions using the mean values of risk factors and mean CHD incidence rates of the CMCS cohort substantially improved the performance of the Framingham functions in the CMCS cohort.

Conclusions The original Framingham functions overestimated the risk of CHD for CMCS participants. Recalibration of the Framingham functions improved the estimates and demonstrated that the Framingham model is useful in the Chinese population. For regions that have no established cohort, recalibration using CHD rates and risk factors may be an effective method to develop CHD risk prediction algorithms suited for local practice.

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Methods
Participants
The CMCS Cohort. The CMCS was approved by the Beijing Institute of Heart, Lung and Blood Vessel Diseases for the entire duration and was conducted with informed consent from all participants. A total of 30,121 Chinese participants aged 35 to 64 years were included in the CMCS cohort, of whom 27,003 were recruited from 16 centers in 11 provinces of China in 1992 and 1993. Additionally, 3,118 participants from Beijing were added to the cohort in 1996 and 1999. A multistage sampling method was used. First, the centers were selected nonrandomly; the major requirements were having taken part in the Sino-MONICA Project and being able to conduct the study. Twelve centers (80.3% of participants) were in urban areas and 4 centers were in rural areas. Next, a stratified random sampling for each sex and 10-year age group was performed in each center for the baseline survey. The overall participation rate was 82%. The proportions of workers, peasants, and intellectuals were 34%, 13%, and 44%, respectively. Others were housewives and salesmen, etc.

Prevalent cases (504 persons with clinical history of myocardial infarction or angina pectoris) were excluded from the baseline examination. A face-to-face follow-up interview to ascertain new CHD events was carried out at the end of each year for these 27,003 participants from 1992 to 1995, and the follow-up rate was 94%. From 1996 onward, 6 centers ceased follow-up because of completion of that national research project. The remaining 16,552 participants in 10 centers of the 1992-1993 cohort and the 3,118 participants of the 1996-1999 cohort were continuously followed up until the end of 2002, and the follow-up rate was 86% (65.3% of the total cohort).

“Hard” CHD events, comprising acute myocardial infarction, sudden death, and other coronary deaths, were recorded. The events were diagnosed based on symptoms, developments in electrocardiograms over time (using Minnesota codes for up to 4 records), serum enzymes, and autopsy findings according to the criteria of the World Health Organization (WHO) MONICA project. The diagnosis was made in 2 steps. First, when a new case was found during follow-up, trained physicians in the provincial collaborating unit were sent to visit the patient (or the relatives in fatal cases), review the hospital records, and complete a standard event form. Second, the form was sent to the collaborating center at the Beijing Institute of Heart, Lung and Blood Vessel Diseases and reviewed by a group of investigators. To ensure diagnostic validity, training was provided before the study started,case-based tests were given every 2 years, and about 20% of cases were verified by investigators from the collaborating center in Beijing.

The Framingham Cohort. All Framingham Heart Study participants provided written informed consent for the study using forms approved by the Boston University School of Medicine. This informed consent has been in effect throughout the duration of the study, beginning in 1948. As reported previously, Framingham Heart Study participants were 5,251 white US residents of Framingham, Mass, aged 30 to 74 years in 1971 to 1974 when they attended either the 11th examination of the original Framingham cohort (2152 participants) or the initial examination of the Framingham Offspring Study (3099 participants). Similar research protocols were used in these 2 studies, and CHD patients identified at baseline were excluded. Twelve-year follow-up was carried out for incidence of hard CHD events, which included CHD death and myocardial infarction.

Risk Factor Measurement
In the CMCS study, the baseline survey was conducted according to the WHO-MONICA protocol for risk factor surveys. The “smoking” variable comprised current smokers. Blood pressure (BP) was measured in the right arm with a regular mercury sphygmomanometer. Diastolic BP was defined as the beginning of Korotkoff phase 5. Two consecutive BP measurements were performed and the mean value of the 2 readings was used. Fasting glucose and total cholesterol (TC) levels were determined by the enzymatic method, and high-density lipoprotein cholesterol (HDL-C) was measured by the phosphotungstic acid/MgCl2 precipitation method. The methods used in the Framingham Heart Study have been described elsewhere.

Statistical Analysis
This analysis focused on 6 major risk factors: age, BP, smoking, diabetes, TC, and HDL-C. The predictive ability of the Framingham functions was assessed in 2 ways. First, the discriminatory power of the 6 risk factors in predicting CHD end points was assessed. Second, the calibration of the functions in predicting degree of risk was assessed. To ensure comparability with the established Framingham models, the stratification of BP, diabetes, TC, and HDL-C in the CMCS model was defined according to the criteria used in the Framingham model. Specifically, hypertension was categorized according to the Fifth Joint National Com-
Diabetes was defined according to 1985 WHO criteria. In the CMCS, diabetes was diagnosed if the fasting blood glucose level was at least 140 mg/dL (7.8 mmol/L) at the baseline examination or by a previous clinical diagnosis. In 44% of cases, diabetes diagnosis was based on fasting glucose level, 42% on clinical history, and 14% on both criteria. In the Framingham Heart Study, diabetes was defined as receiving hypoglycemic treatment (49% of diabetes patients), casual blood glucose level of at least 150 mg/dL (8.3 mmol/L) in the original cohort (24% of diabetes patients), or fasting blood glucose level of at least 140 mg/dL (7.8 mmol/L) at the initial examination of the Framingham Offspring Study participants (27% of diabetes patients). The cut points for TC and HDL-C were based on the National Cholesterol Education Program Adult Treatment Panel II (ATP-II), but we used more categories to test the association between extremely low or high levels of serum cholesterol and CHD in different populations. Specifically, TC of less than 200 mg/dL (5.18 mmol/L) in ATP-II was further classified into less than 160 and 160 to 199 mg/dL, and TC of at least 240 mg/dL (6.22 mmol/L) was further classified into 240 to 279 mg/dL and at least 280 mg/dL; HDL-C of at least 35 mg/dL (0.91 mmol/L) was further classified into 35 to 44, 45 to 49, 50 to 59, and at least 60 mg/dL.

Sex-specific Cox proportional hazards models were derived after testing for the assumptions underlying its use. For each risk factor, the regression coefficients for the CMCS and Framingham cohorts were compared using a 2-tailed $z$ statistic, where $z = (b_{F} - b_{C}) / SE$. The SE is the standard error of the difference in coefficients, and $SE = (SE[F]^{2} + SE[C]^{2})^{0.5}$. The $b_{F}$ and $b_{C}$ are the beta coefficients of the CMCS model and the Framingham model, respectively. The $SE[F]$ and $SE[C]$ are the standard errors of $b_{F}$ and $b_{C}$, respectively. Because the relative risk (RR) of a risk factor is the exponential function of its regression coefficient $\exp(\theta)$, the $z$ statistic was used to test the difference in RR between the 2 cohorts. To put a heavier test on the functions, $P < .10$ was defined as significant.

The absolute 10-year risk of hard CHD was predicted with a Cox regression model developed by Framingham investigators, where

$$P = 1 - S(t)^{exp(\theta)}$$

and

$$f(x,M) = \beta_1(x_1 - M_1) + \ldots + \beta_p(x_p - M_p).$$

Here, $\beta_1, \ldots \beta_p$ are the regression coefficients, $x_1 \ldots x_p$ represent an individual’s risk factors, $M_1 \ldots M_p$ are the mean values of the risk factors in the cohort, and $S(t)$ is the survival rate at the mean values of the risk factors at time $t$ ($t = 10$ years). Discrimination and calibration were used to evaluate the predictive capabilities. The discriminatory power of a model was assessed by the area under the receiver operating characteristic curve (AUROC) or $c$ statistic. A test developed by Nam was used to compare the AUROCs of 2 models. The second approach was calibration, which measured how closely the predicted risk fit the actual risk. The CMCS participants were divided into deciles of 10-year CHD risk predicted by the CMCS functions, the original Framingham functions, and the recalibrated Framingham functions. The predicted and actual risk in each decile were compared, and the difference was assessed by the Hosmer-Lemeshow $\chi^2$ test. Values exceeding 20 indicate significant lack of calibration ($P < .01$). SAS software, version 6.12 (SAS Institute Inc), was used for all statistical analyses.

### RESULTS

#### CHD Rates and Baseline Risk Factors

A total of 191 CHD events and 625 total deaths occurred during follow-up in the CMCS cohort. In the Framingham cohort, 273 hard CHD events and 293 total deaths occurred. The 10-year CHD event rates were 1.5% for men and 0.6% for women in the CMCS, without adjusting for age. The corresponding crude incidence rates in Framingham men and women were 8.0% and 2.8%, respectively. Numbers of participants, person-years of follow-up, and CHD events are shown in Table 1 and Table 2.

Tables 1 and 2 also display the risk factor levels at the baseline examination of the 2 cohorts, unadjusted for age. In comparison with the Framingham cohort, the smoking rate was higher in Chinese men but lower in Chinese women, the prevalence of hypercholesterolemia and hypertension was lower in both sexes, and the prevalence of reduced HDL-C was lower in Chinese men. Similar prevalence rates for diabetes in men and women and for low HDL-C in women were observed in the Chinese and US samples.

#### $\beta$ Coefficients and RRs

The $\beta$ coefficients and RRs for major CHD risk factors were obtained from Cox regression models for the 2 cohorts (Table 3). Major risk factors showed a similar relation to CHD in both cohorts, except that smoking was inversely related to CHD risk in Chinese women. This unexpected trend may be attributable to the low smoking rate among CMCS women, with small numbers leading to unstable estimates. The coefficient for age squared was significant in Framingham women, but this was not found in Framingham men or CMCS participants. For most risk factor categories, the magnitude of the RRs did not differ significantly. The few exceptions that nearly reached statistical significance were that among CMCS men, age was associated with a higher RR ($P = .06$) and TC of 200 to 239 mg/dL and HDL-C of less than 35 mg/dL were associated with lower RRs ($P = .07$ for both); among CMCS women, smoking was associated with a lower RR ($P = .07$). The effects of BP on CHD risk were similar in both studies.

#### Predictive Capacities

CMCS Functions. In the CMCS functions, the $\beta$ coefficients in the CMCS Cox model, mean values of the risk factors, and mean incidence rates in the CMCS cohort were used. In the discriminatory analysis, the AUROCs for men and women were 0.736 (95%
### Table 1. Baseline Risk Factors, Person-Years of Follow-up, and CHD Events in Men in the CMCS and Framingham Cohorts

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>CMCS Men</th>
<th>Framingham Men*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants With Risk Factor, %</td>
<td>No. of Participants</td>
</tr>
<tr>
<td>Total‡</td>
<td>16,056</td>
<td>94,655</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimal</td>
<td>36</td>
<td>5783</td>
</tr>
<tr>
<td>Normal</td>
<td>22</td>
<td>3534</td>
</tr>
<tr>
<td>High normal</td>
<td>13</td>
<td>2089</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>19</td>
<td>9052</td>
</tr>
<tr>
<td>Stage 2-4 hypertension</td>
<td>10</td>
<td>1607</td>
</tr>
<tr>
<td>TC, mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;160</td>
<td></td>
<td></td>
</tr>
<tr>
<td>160-199</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200-239</td>
<td>22</td>
<td>3534</td>
</tr>
<tr>
<td>≥280</td>
<td>3</td>
<td>482</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>22</td>
<td>3534</td>
</tr>
<tr>
<td>45-49</td>
<td>14</td>
<td>2249</td>
</tr>
<tr>
<td>50-59</td>
<td>25</td>
<td>4016</td>
</tr>
<tr>
<td>≥60</td>
<td>33</td>
<td>5302</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>6</td>
<td>964</td>
</tr>
</tbody>
</table>

Abbreviations: CMCS, Chinese Multi-provincial Cohort Study; CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol.  
SI conversions: To convert HDL-C and TC to mmol/L, multiply by 0.0259.  
*Data for the Framingham risk factors are from D’Agostino et al.  
†Hard CHD events were for 10 years of follow-up.  
‡Mean ages of CMCS and Framingham men were 47.4 years and 48.3 years, respectively.

### Table 2. Baseline Risk Factors, Person-Years of Follow-up, and CHD Events in Women in the CMCS and Framingham Cohorts

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>CMCS Women</th>
<th>Framingham Women*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Participants With Risk Factor, %</td>
<td>No. of Participants</td>
</tr>
<tr>
<td>Total‡</td>
<td>14,056</td>
<td>85,127</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optimal</td>
<td>36</td>
<td>5783</td>
</tr>
<tr>
<td>Normal</td>
<td>22</td>
<td>3534</td>
</tr>
<tr>
<td>High normal</td>
<td>13</td>
<td>2089</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>19</td>
<td>9052</td>
</tr>
<tr>
<td>Stage 2-4 hypertension</td>
<td>10</td>
<td>1607</td>
</tr>
<tr>
<td>TC, mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;160</td>
<td></td>
<td></td>
</tr>
<tr>
<td>160-199</td>
<td></td>
<td></td>
</tr>
<tr>
<td>200-239</td>
<td>22</td>
<td>3534</td>
</tr>
<tr>
<td>≥280</td>
<td>3</td>
<td>482</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-44</td>
<td>22</td>
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<td>45-49</td>
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<td>2249</td>
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<tr>
<td>50-59</td>
<td>25</td>
<td>4016</td>
</tr>
<tr>
<td>≥60</td>
<td>33</td>
<td>5302</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>6</td>
<td>964</td>
</tr>
</tbody>
</table>

Abbreviations: CMCS, Chinese Multi-provincial Cohort Study; CHD, coronary heart disease; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol.  
SI conversions: To convert HDL-C and TC to mmol/L, multiply by 0.0259.  
*Data for the Framingham risk factors are from D’Agostino et al.  
†Hard CHD events were for 10 years of follow-up.  
‡Mean ages of CMCS and Framingham women were 46.3 years and 49.6 years, respectively.
**CHD RISK ASSESSMENT IN A CHINESE POPULATION**

Women had a mean age of 75.3 years (range: 23-100 years) and 14.2 years (range: 23-100 years), respectively, showing good ability to distinguish cases from noncases. In the calibration, the Hosmer-Lemeshow \( \chi^2 \) was 12.6 for men \( (P = .13) \) and 14.2 for women \( (P = .08) \), showing that the actual CHD rates in the CMCS cohort were similar to the event rates predicted by CMCS functions (FIGURE 1).

**Original Framingham Functions.** In the original Framingham functions, the \( \beta \) coefficients in the Framingham Cox model, mean values of the risk factors, and mean incidence rates in the Framingham cohort were used directly. In the discriminatory analysis, the original Framingham functions separated cases from noncases in the CMCS cohort nearly as well as the CMCS functions. The AUROCs were 0.705 (95% CI, 0.665-0.746) for men and 0.742 (95% CI, 0.686-0.798) for women. However, in calibration, the original Framingham functions statistically overestimated the event rates observed in the CMCS cohort. The Hosmer-Lemeshow \( \chi^2 \) was 645.9 for men \( (P < .001) \) and 147.6 for women \( (P < .001) \) (FIGURE 2). Larger differences were observed in higher deciles. For example, in the 10th decile in men, the predicted rate was 20% and the actual rate was only 3%.

**Recalibrated Framingham Functions.** In the recalibrated Framingham functions, the \( \beta \) coefficients were taken from the Framingham Cox model, but mean values from the CMCS cohort were used for the risk factors and the mean incidence rates. Recalibration did not affect the discriminatory ability but improved the calibration substantially, especially in women. The \( \chi^2 \) was 31.5 for men \( (P < .001) \) and 16.9 for women \( (P = .03) \) (FIGURE 3). The largest difference between the actual rate and the predicted rate after recalibration was 1.5% (in the 10th decile in men), compared with the difference of 17% for the original Framingham functions.

**Additional Analyses**

The prevalence of body mass index of at least 25 was 33.5% in men and 33.9% in women. When body mass index (calculated as weight in kilograms divided by the square of height in meters) was included in the CMCS model, the RR for body mass index of 25 or higher was 1.29 for men and 1.68 for women, both nonsignificant. Moreover, RRs for diabetes, TC, HDL-C, and BP were all reduced after including body mass index. The AUROC had a nonsignificant increase (from 0.736 to 0.739 in men and from 0.759 to 0.763 in women) and the calibration did not change significantly (data available from authors). Data on exercise were ob-

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**Table 3. Cox Regression Coefficients and RRs for CHD Risk Factors in Men and Women in the CMCS and Framingham Cohorts**

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>CMCS</th>
<th>Framingham*</th>
<th>CMCS</th>
<th>Framingham*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age squared</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>−0.001</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>−0.51</td>
<td>0.60 (0.34-1.05)</td>
<td>0.09</td>
<td>1.10 (0.67-1.82)</td>
</tr>
<tr>
<td>High normal</td>
<td>0.21</td>
<td>1.24 (0.69-2.20)</td>
<td>0.42</td>
<td>1.53 (0.98-2.36)</td>
</tr>
<tr>
<td>Stage 1 hypertension</td>
<td>0.33</td>
<td>1.39 (0.84-2.31)</td>
<td>0.66</td>
<td>1.93 (1.28-2.92)</td>
</tr>
<tr>
<td>Stage 2-4 hypertension</td>
<td>0.77</td>
<td>2.16 (1.27-3.68)</td>
<td>0.90</td>
<td>2.45 (1.59-3.79)</td>
</tr>
<tr>
<td>TC, mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;160-199</td>
<td>−0.51</td>
<td>0.60 (0.37-0.98)</td>
<td>−0.38</td>
<td>0.69 (0.31-1.52)</td>
</tr>
<tr>
<td>200-239</td>
<td>0.07</td>
<td>1.08 (0.71-1.63)</td>
<td>0.57</td>
<td>1.77 (1.25-2.50)</td>
</tr>
<tr>
<td>240-279</td>
<td>0.32</td>
<td>1.37 (0.74-2.55)</td>
<td>0.74</td>
<td>2.10 (1.43-3.10)</td>
</tr>
<tr>
<td>≥280</td>
<td>0.52</td>
<td>1.68 (0.67-4.20)</td>
<td>0.83</td>
<td>2.29 (1.39-3.76)</td>
</tr>
<tr>
<td>HDL-C, mg/dL</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;35</td>
<td>−0.25</td>
<td>0.78 (0.35-1.74)</td>
<td>0.61</td>
<td>1.84 (1.17-2.88)</td>
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<tr>
<td>35-44</td>
<td>0.01</td>
<td>1.01 (0.60-1.70)</td>
<td>0.37</td>
<td>1.45 (0.94-2.21)</td>
</tr>
<tr>
<td>45-49</td>
<td>0.08</td>
<td>1.09 (0.47-2.49)</td>
<td>0.60</td>
<td>1.82 (1.05-3.16)</td>
</tr>
<tr>
<td>≥50-59</td>
<td>−0.07</td>
<td>0.92 (0.56-1.55)</td>
<td>0.00</td>
<td>1.00 (0.62-1.60)</td>
</tr>
<tr>
<td>Diabetes</td>
<td>0.09</td>
<td>1.09 (0.57-2.08)</td>
<td>0.53</td>
<td>1.69 (1.11-2.57)</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.62</td>
<td>1.86 (1.31-2.64)</td>
<td>0.73</td>
<td>2.07 (1.60-2.68)</td>
</tr>
</tbody>
</table>

Abbreviations: CI, confidence interval; CMCS indicates Chinese Multi-provincial Cohort Study; HDL-C, high-density lipoprotein cholesterol; NA, not applicable; RR, relative risk; TC, total cholesterol.

SI conversions: To convert HDL-C and TC to mmol/L, multiply by 0.0259.

*Data for the Framingham cohort are from D’Agostino et al.†Relative risk in the CMCS cohort is significantly different from that in the Framingham cohort \( (P < .10) \).

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A total of 19.4% of men and 13.8% of women reported physical activity (defined as physical activity regularly during off hours at least once per week and lasting more than 20 minutes each time). Those who reported less exercise also tended to have higher BP, higher glucose levels, and lower HDL-C levels. After adjusting for these factors, the association of exercise with CHD was not significant (data available from authors). Performance of the functions were compared in urban vs rural residents. Performance of the CMCS and recalibrated Framingham functions for urban vs rural men and women were all very similar, with overlapping 95% CIs (data available from authors).

To assess the effect of the portion of the study population that had only 3 years of follow-up, a separate model was created after exclusion of the participants who dropped out. The RRs, 10-year CHD rates, and prediction capabilities did not differ from the current cohort. Nevertheless, the total person-years of follow-up and CHD events were reduced and the 95% CIs for some risk factor categories were wider after the exclusion (data available from authors).

**COMMENT**

In the present analysis, we tested the performance of the Framingham functions in a large Chinese population, both directly and after recalibration, and compared them with the usefulness of functions derived from the Chinese cohort itself to determine absolute risk of CHD. Estimation of absolute risk of CHD to treat and prevent CHD commonly relies on prediction models derived from the experience of prospective cohort studies. Although prediction algorithms developed by Framingham investigators have been widely adopted to formulate clinical guidelines in the United States and elsewhere, the Framingham functions have overestimated CHD risk in some populations, leading to concern that it is not appropriate to generalize the results to other populations. Framingham func-
tions have been recalibrated in some co-

munity of CHD, and exercise were not in-

cluded. Because the risk of obesity ap-

pears to be mediated through TC,

HDL-C, hypertension, and diabetes, the

ATP-III did not include it as a factor in-

fluencing treatment.14 Body mass in-

dex was not significant after control-

ling for these other factors, nor was exercise. Similar results were found in the Framingham study.5 Family his-


tory was ascertained in the CMCS and

in the original Framingham cohort but

was not included in the prediction model because its independent effect is difficult to quantify. Familial influence on risk status is often mediated through other major CHD risk factors, which run in families.

The RR indicates the importance of

a risk factor categories were not statistically

by others.31 The unex-

served for the relation of BP with CHD,

significant. Homogeneity was ob-

ferences between RRs in most of the risk

levels in the 2 cohorts differed, the dif-

ham baseline.

Although CHD rates and risk factor

levels in the 2 cohorts differed, the dif-

erences between RRs in most of the risk

factor categories were not statistically

significant. Homogeneity was ob-

served for the relation of BP with CHD,

as reported by others.24,25 To show the ac-

ual magnitudes in the 2 cohorts, the

rates and risk factor levels were not ad-

justed for age. The 10-year CHD rate

of the Framingham cohort was 5 times

higher than that for the CMCS cohort. The CMCS

can counterparts, and the prevalence

rates for diabetes in both sexes and low

HDL-C in women were similar in the

2 samples, but all other risk factor lev-

els at the CMCS baseline examination

were lower than those at the Framing-

ham baseline.

Although CHD rates and risk factor

levels in the 2 cohorts differed, the dif-

ferences between RRs in most of the risk

factor categories were not statistically

significant. Homogeneity was ob-

served for the relation of BP with CHD,

as reported by others.31 The unex-

spected association of smoking in CMCS

women may be attributable to the low

smoking rate and few CHD events, re-

sulting in unstable estimates of risk of

smoking. The effects of diabetes ap-

peared to be weaker in the CMCS, but the low prevalence rates led to wider 95% CIs and nonsignificant results.

In the present analysis, only 6 ma-

or risk factors were included in the risk prediction. Body mass index, family his-

ory of CHD, and exercise were not in-

cluded. Because the risk of obesity ap-

pears to be mediated through TC,

HDL-C, hypertension, and diabetes, the

ATP-III did not include it as a factor in-

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tory was ascertained in the CMCS and

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The functions derived from the CMCS were used to represent the “best” possible predictive value against which the performance of the Framingham functions could be tested. However, if the CMCS prediction functions are to be generalized across China, the functions should be further tested in another validation cohort. In the present analysis, only Framingham predictions were evaluated in this Chinese cohort. Both the original and the recalibrated Framingham functions discriminated between CHD cases and noncases in the CMCS cohort as well as did the CMCS functions. Nevertheless, the discriminatory ability could not evaluate the ability to estimate absolute risk of events. In the calibration analysis, a systematic overestimation was observed when the original Framingham functions were applied directly to the CMCS cohort, especially in the higher deciles.

Overestimation of CHD risk in Chinese persons could result in inappropriate treatment. The estimation of 10-year absolute CHD risk for a non-smoking man aged 57 years with TC of 222 mg/dL, HDL-C of 55 mg/dL, fasting blood glucose of 95 mg/dL, and stage 1 hypertension was 11.7% using the original Framingham functions. However, the estimation from the CMCS functions was only 2.9%. Thus, if the Framingham predictive tool was used, it would be necessary to consider drug therapy according to ATP-III, but it would not be necessary if the CMCS prediction was used.

From the public health perspective, the direct use of original Framingham functions in Chinese guidelines is inappropriate, as that would lead to overestimation of CHD risk and incorrect health resource allocation. For instance, by Framingham estimates, the proportion of Chinese people whose 10-year CHD risk exceeded 10% was 9.9%, but the CMCS functions estimated that only 0.3% experience that level of CHD risk. Thus, the burden of CHD in the Chinese population would be overestimated if the original Framingham prediction were applied directly.

This study has several limitations. Although the CMCS cohort was nearly 6 times larger than the Framingham cohort, it had fewer CHD cases than the Framingham Study because of lower CHD incidence. In addition, 34.7% of the study participants were followed up for only 3 years. However, exclusion of this group did not materially affect the results.

Our study oversampled individuals in urban areas compared with rural areas. However, results of the functions were very similar in the 2 groups.

Finally, levels of risk factors increased in China during the past decades. These changes appeared to have limited impact on the prediction capabilities. For example, the levels of most of these risk factors were higher in the 1996-1999 cohort than those in the 1992-1993 cohort. However, the predictive functions with and without the 1996-1999 data set were basically the same. Similarly, although population characteristics changed in the Framingham cohort, the present functions are still valid within US cohorts with more recent profiles of risk factors.

The success of the recalibrated Framingham functions in this Chinese cohort suggests that recalibration could be of great value for assessment of CHD risk in other countries. For populations for which CHD risk factor and event data are available, Framingham functions could also be recalibrated. For example, several European countries that participated in the WHO-MONICA project have data on risk factor levels and CHD incidence rates. A recent study recalibrated Framingham functions using cross-sectional data on risk factors and monitoring data on CHD rates in a Spanish population.

In conclusion, the original Framingham functions overestimates the risk of CHD for CMCS participants, and they should not be directly incorporated into estimates of CHD risk in China. Recalibration of the Framingham functions corrects the overestimation and, thus, can be a useful approach for the generalization of the Framingham model in other populations. For populations that have no established cohort, recalibration may be an effective method to develop a CHD risk prediction tool suited for local practice of CHD prevention.


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