Development of a Risk Equation for the Incidence of Coronary Artery Disease and Ischemic Stroke for Middle-Aged Japanese
– Japan Public Health Center-Based Prospective Study –

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Background: Global risk assessment for the prevention of atherosclerotic cardiovascular diseases helps guide the intensity of behavioral and pharmacological interventions.

Methods and Results: The Japan Public Health Center-based prospective (JPHC) Study Cohort II (age range: 40–69 years at baseline in 1993–1994, n=15,672) was used to derive the risk equations for coronary artery disease (CAD) and ischemic stroke incidence via hazard regression. The model discrimination was evaluated by the area under the receiver-operating curve (AUC), and model goodness-of-fit by the Grønnesby-Borgan chi-squared statistic. During a mean of 16.4 years of follow up, 192 incident CAD cases and 552 ischemic stroke cases occurred. Variables selected for the CAD equation were age, sex, current smoking, systolic blood pressure, antihypertensive medication use, diabetes, and high-density lipoprotein cholesterol (HDLC) and non-HDLC. The same variables, except non-HDLC, were selected for the ischemic stroke equation. The equations discriminated incidence reasonably well (AUC: 0.81 for CAD, 0.78 for ischemic stroke). The AUC of the equation applied externally to Cohort I (n=11,598) was also good: 0.77 and 0.76 for CAD and ischemic stroke, respectively. Risk calculator application and color charts to visualize estimated risk according to the combinations of risk factors were prepared.

Conclusions: Risk equations were developed to estimate the 10-year probability of CAD and ischemic stroke in Japanese people, using variables that are routinely obtained. (Circ J 2016; 80: 1386–1395)

Key Words: Cholesterol; Coronary artery disease; Japan; Prediction; Risk factors

It is widely agreed that the intensity of lifestyle and pharmacological interventions for the prevention of cardiovascular disease (CVD) should be determined based on a patient’s estimated absolute risk of the disease.1 Although the American College of Cardiology and the American Heart Association (ACC/AHA) recently published a risk prediction model for atherosclerotic cardiovascular disease (ASCVD), consisting of coronary artery disease (CAD) and ischemic stroke,2 it cannot directly be applied to ethnicities other than non-Hispanic whites and African Americans in the US, as the ACC/AHA equation reportedly overestimates the risk in the other ethnic groups.

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In addition to differences in the incidence rates of CVD, the case mix of CVD differs by populations. Namely, in the US, the incidence rate of CAD is higher than that of ischemic...
stroke and ischemic stroke consists mostly of non-lacunar atherosclerotic stroke, which has similar risk factors to CAD. In contrast, in Japan, the incidence rate of CAD is much lower than that of ischemic stroke. Lacunar stroke accounts for a larger proportion of ischemic strokes in Japan compared to that in Western countries, and its risk factors vary somewhat from those for non-lacunar atherosclerotic stroke. This pattern of CVD case mix has also been observed in East Asian populations.

Considering this case mix of CVD in Japan, and that any risk equation would be applied to aid clinical decision-making involving statin use, developing a risk equation in Japan was considered most relevant for CAD. Therefore, we developed risk equations for CAD and for ischemic stroke separately in the Japanese population.

Although there have been a few CAD risk equations developed in Japan, they used either CAD mortality as the outcome, a meta-analysis of pre-existing cohorts, or participants residing in only one city. Furthermore, no previous study included antihypertensive medication use (Table S1). The Japan Public Health Center-based prospective (JPHC) Study is a cohort study of a Japanese representative population sample with standardized assessment of exposures and outcomes. The aim of the present study was to develop equations to estimate 10-year risk of CAD and ischemic stroke incidence in the JPHC Study.

**Methods**

**Study Cohort**

The JPHC study cohorts were established in 1990 (Cohort I) and 1993–1994 (Cohort II) in 11 public health-center areas throughout Japan, initially enrolling 140,420 individuals. The study population was defined as participants with Japanese nationality from the 9 public health-center areas where data on CVD incidence were available, and who were aged 40–59 years (in Cohort I, n=54,376) or 40–69 years (in Cohort II, n=61,984). In the present study, we used Cohort I as a validation cohort because of the narrower age range at baseline (Figure 1). External validation methods are described in the Supplementary material. Regarding Cohort II, we excluded those with missing information on their lifestyle (smoking, alcohol drinking and physical activity; n=11,185) or missing biochemical data that was required for use in the analysis (n=34,489). From the remaining 16,310 participants, those with a self-reported history of CVD (myocardial infarction or stroke) or cancer (n=638) were excluded, leaving 15,672 (men: n=5,315, women: n=10,357) for the analysis. The study protocol, including the informed consent procedure of the JPHC study, was approved by the Human Ethics Review Committees of the National Cancer Center, Osaka University, and Fujita Health University (Issues related to human research ethics are described in the Supplementary material).
Follow up
The subjects were followed up from the date of the baseline survey through 2010. Residence and survival were ascertained annually using residential registries maintained by each municipality. In Japan, residency and death registration are required by law, and these registries are believed to be complete. Of the non-deceased participants (n=12,615), 731 (5.8%) moved out of the study area, but only 11 (less than 0.1% of 15,672) had unknown vital status (loss to follow up). Information on the cause of death was obtained through the death certificate provided by the Ministry of Health, Labor, and Welfare after the Ministry of Internal Affairs and Communications granted permission.

Definition of CAD and Ischemic Stroke
Ascertainment methods of CAD and ischemic stroke are described in the Supplementary material. CAD consisted of myocardial infarction or sudden cardiac death. Myocardial infarction was confirmed in the medical records according to the criteria of the Monitoring Trends and Determinants of Cardiovascular Disease (MONICA) project, which requires typical chest pain and evidence of infarction from the electrocardiogram and/or cardiac enzymes. For cases with typical prolonged chest pain (>20 min) but not confirmed by electrocardiograms or cardiac enzymes (1.1% of all myocardial infarctions), a possible myocardial infarction diagnosis was made and these were included as myocardial infarction cases. Sudden cardiac death was defined as a death of presumed cardiac origin that occurred within 1 h of the onset of symptoms. Strokes were confirmed according to National Survey of Stroke criteria, which require a constellation of neurological deficits of sudden or rapid onset lasting at least 24 h or until death. Ischemic stroke consisted of thrombotic or embolic stroke, and a definite diagnosis was established based on the examination of computed tomography scans, magnetic resonance images, or autopsy. For analysis, only first-ever CAD and ischemic stroke events during follow up were included; recurrent events were excluded.

Baseline Measurements
A self-administered questionnaire was used to assess smoking and drinking habits, and physical activity. Smoking status was categorized to current, past, and never, but dichotomized (current, non-smoker [reference]) in the final model because the past smoking category was not statistically significant. Pack-years were defined as the number of cigarettes per day divided by 20 multiplied by the number of years with the habit for both current and past smokers. The amount of alcohol consumption was estimated using responses to the questions on frequency, usual daily amount, and type of alcoholic beverages. It was grouped as 0–149 [reference], 150–299, 300–g/week; 150g/week ethanol is approximately equivalent to 1 bottle of beer or 1 serving of sake (Japanese wine) per day. Sport activity was assessed as the frequency (almost never, 1–3 days per month, 1–2 days per week, 3–4 days per week, and almost daily) of participation in non-occupational physical activity. Frequency of sports activity was categorized into 3 groups (almost none, 1–3 days per month, 1–2 days per week or more [reference]).

The following items were obtained at the baseline health check up: height and weight were measured, and body mass index (BMI) was calculated as weight (kg) divided by the square of the height in meters (m²). Blood pressure (BP) was measured using a standard mercury sphygmomanometer applied to the right arm of the seated participant after a 5-min rest. Either fasting (61% of total samples) or non-fasting (casual, 39%) blood samples were collected. Serum total and high-density lipoprotein cholesterol (TC and HDL-C) and glucose were measured in 23 laboratories. The non-HDL-C level was obtained by subtracting HDL-C from TC. The precision and accuracy of lipid measurement in all laboratories were satisfactory, according to the Osaka Medical Center for Health Science and Promotion, a member of the cholesterol Reference Method Laboratory Network. Diabetes was defined as a glucose level of 7.0 (fasting) or 11.1 or higher (non-fasting) mmol/L and/or self-reported use of glucose-lowering medications. Antihypertensive medication use was also self-reported. The validity of questionnaire items has been reported.

Statistical Analysis
All analyses were conducted using SAS for Windows, version 9.4 (SAS/STAT 13.1) (SAS Institute, Cary, North Carolina, USA). Sex, logarithmically transformed values of age, systolic blood pressure (SBP), HDL-C, and non-HDL-C, and the aforementioned lifestyle and medical history variables were considered for the prediction model. Logarithmic transformation of continuous variables was performed to improve discrimination and calibration of the models and to minimize the influence of extreme observations. Significant (P<0.10) risk factors from the univariate models were then pooled into a single multivariate model, and a backward selection procedure was used to determine the final model, while retaining significant (P<0.10) predictors. All possible interactions of risk factors with sex as well as with age were tested, and significant interaction (P<0.10) of sex with age was observed, and the term was retained in the CAD model. Also, the interaction term between BP and antihypertensive medication was significant in both CAD and ischemic stroke models (P<0.10).

The equation to estimate the 10-year probability of developing CAD and ischemic stroke was derived from all the significant predictors by the method used by the Framingham Study. We have used all of the observed person-time to derive coefficients in the present analysis. Fine and Gray’s sub-distribution hazard model was used under the assumption that death is a competing risk. The statistical procedure dealing with competing risk is described in the Supplementary material.

The discrimination of the equation was estimated using the area under the receiver operating characteristics (ROC) curve (AUC) based on a method to estimate time-dependent AUC for long-term risk prediction. The degree of calibration, a measure of the model’s goodness of fit, was assessed by comparing the observed and predicted number of events in deciles of predicted risk, as calculated by the Gronnesby-Borgan (GB) chi-squared statistic. Methods for the internal and external validations are provided in the Supplementary material.

Subsequently, we created risk charts to visualize the estimated risk of each endpoint for categories defined by the combination of predictors in the equation. We initially developed 1 chart based on our single risk equation including sex and diabetes as covariates, but because the chart became so big, we split it into 2 parts for presentation by stratifying on sex. We also created risk calculators for both endpoints (images are provided in the Supplementary material), which will eventually be posted as a web application.

Meanwhile, Cohort II subjects used to develop the equation were older, less likely to be men and current smokers, and the age- and sex-adjusted incidence rates of CAD and ischemic...
stroke were still lower compared to those of the subjects excluded due to missing data (Table S2). Therefore, instead of restricting these indicators to the analyzed subjects, we used incidence rates of the entire Cohort II who did not have a CVD history (n=854, crude incidence rate: 0.75 per 1,000 person-years) when estimating absolute risks.

**Results**

The mean age of the subjects was 57.4 years and 33.9% were men. The prevalence of diabetes mellitus was 4.6% at baseline. The average SBP, HDLC, and non-HDLC were 132.3 mmHg, 56.8 mg/dl and 146.2 mg/dl, respectively (Table S3).

We identified 192 CAD cases (126 in men and 66 in women) during the 256,692 person-years of follow up and 552 ischemic stroke cases (299 men and 253 women) during the 254,765 person-years of follow up among the initially 40–69 year olds of Cohort II (crude incidence rate: 0.75 and 2.17 per 1,000 person-years, respectively). Univariate analyses of baseline variables identified 10 potential risk factors for CAD incidence and 9 potential risk factors for ischemic stroke (Table S4). Male sex, older age, current smoking, higher SBP, antihypertensive medication use, diabetes, lower HDLC, higher non-HDLC, 300 g or more alcohol drinking per week, and pack-years of smoking were significantly positively associated with the incidence of CAD. The same risk factors, except for higher non-HDLC, were also associated with ischemic stroke incidence. Alcohol intake and pack-years were eliminated from the final multivariable model for both endpoints by the backward variable selection procedure. The coefficients and standard errors of all the risk factors in the final models to predict 10-year incidence of CAD and ischemic stroke are shown in Table.

The AUCs of the final model (0.81 for CAD and 0.78 for ischemic stroke) indicated good discrimination. The numbers of predicted CAD and ischemic stroke events generally matched the numbers of observed CAD and ischemic stroke events in 10-year risk deciles (Figures 2A,B; GB P=0.74 and 0.51, respectively).

An equation for CAD that used TC instead of non-HDLC had nearly identical discrimination (AUC: 0.81, 95% confidence interval: 0.78–0.84) and calibration (GB P=0.74). Results for the internal and external validations are provided in the Supplementary material (Figure S1). The proportions of individuals who were classified as having intermediate (5.0–7.4%) or high (7.5%–) 10-year CAD risk were 2.9% and 2.2% in the non-HDLC model. These respective proportions were 1.4% and 0.8% in the TC model. The proportions of individuals who were classified as having intermediate (5.0–7.4%) or high (7.5%–) 10-year ischemic stroke risk were 9.1% and 6.2%, respectively.

Finally, we presented risk charts, which can be used to visualize predicted risk according to specific combinations of risk factors (Figures 3A,B for CAD, Figures S2A,B for ischemic stroke, and Figures S3A,B for CAD using TC for men and women, respectively). In creating charts and calculators, we used incidence rates of the entire Cohort II who did not have a CVD history (CAD: n=854, crude incidence rate 0.9/1,000 person-years, ischemic stroke: n=1,950, 2.1/1,000 person-years).

**Discussion**

We developed equations to predict 10-year risk of CAD as well as of ischemic stroke in Japanese men and women aged 40–69 years. The discrimination of the equation was reasonably good (AUC=0.81 for CAD and 0.78 for ischemic stroke) and comparable to those of the ACC/AHA ASCVD risk equation, which had AUCs ranging from 0.71 (African-American men) to 0.82 (African-American women). The discrimination of the model for CAD was also comparable to values reported by other Japanese studies, namely, the Japan Atherosclerosis Longitudinal Study (JALS): 0.83 for the model that used non-HDLC, and the Suita Study: 0.84 for the model that included chronic kidney disease. The discrimination of the ischemic stroke model was comparable to values reported in the Atherosclerosis Risk in Communities Study (0.75 for men and

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**Table. Multivariate Regression Coefficients (Standard Errors) of CAD and Ischemic Stroke Risk Prediction Model in the Derivation Cohort; JPHC Study Cohort II, 1994–2010**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Coefficient (SE)</th>
<th>p-value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.059261 (1.31786)</td>
<td>&lt;0.0001</td>
<td>0.059071 (0.46144)</td>
</tr>
<tr>
<td>Sex (men=1)</td>
<td>12.5268 (6.36665)</td>
<td>0.049</td>
<td>0.50464 (0.009945)</td>
</tr>
<tr>
<td>Current smoking (+=1)</td>
<td>0.69074 (0.16068)</td>
<td>&lt;0.0001</td>
<td>0.36247 (0.11190)</td>
</tr>
<tr>
<td>Antihypertensive medication (+=1)</td>
<td>10.28406 (5.67383)</td>
<td>0.07</td>
<td>12.06829 (6.36397)</td>
</tr>
<tr>
<td>Prevalent diabetes mellitus (+=1)</td>
<td>0.55877 (0.21938)</td>
<td>0.01</td>
<td>0.84434 (0.12785)</td>
</tr>
<tr>
<td>Log of SBP (mg/dl)</td>
<td>2.09871 (0.71122)</td>
<td>0.003</td>
<td>2.21016 (0.37810)</td>
</tr>
<tr>
<td>Log of HDL cholesterol (mg/dl)</td>
<td>−1.09968 (0.27743)</td>
<td>&lt;0.0001</td>
<td>−0.59896 (0.16076)</td>
</tr>
<tr>
<td>Log of non-HDL cholesterol (mg/dl)</td>
<td>1.46938 (0.30763)</td>
<td>&lt;0.0001</td>
<td>– –</td>
</tr>
<tr>
<td>Antihypertensive medication × log of SBP (mg/dl)</td>
<td>−1.95968 (1.14438)</td>
<td>0.09</td>
<td>−2.37428 (0.73207)</td>
</tr>
</tbody>
</table>

Baseline survival function at 10 years

<table>
<thead>
<tr>
<th>CAD</th>
<th>Ischemic Stroke</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.99248</td>
<td>0.98310</td>
</tr>
<tr>
<td>0.98430</td>
<td>– –</td>
</tr>
</tbody>
</table>
As expected, non-HDLC was found not to be a risk factor for ischemic stroke. However, it is beyond the scope of the current study to discuss whether statin therapy would still lower the risk of developing ischemic stroke or not in the studied population. This finding also indicates appropriateness of creating separate risk equations for CAD and ischemic stroke in Japan. BMI was not related to the risks of CAD and ischemic stroke in the same population, which makes the present study unique.

Furthermore, the variables selected for prediction of CAD in the present study were essentially the same as those in the ACC/AHA ASCVD equation and the JALS Study equation. However, we did not find that the non-HDLC model was superior to the TC model, as the JALS Study did. Nevertheless, we externally validated the equation, using Cohort I of the JPHC Study; validation was not done in the previous Japanese studies. We also contrasted risk models for CAD and ischemic stroke.

Figure 2. (A) Calibration of the prediction model for 10-year CAD incidence by decile of risk. Observed (blue bar) and expected (red bar) numbers of CAD events showed good agreement. The P-value from the Grønnesby-Borgan chi squared test was 0.74. (B) Calibration of the prediction model for 10-year ischemic stroke incidence by decile of risk. Observed (blue bar) and expected (red bar) numbers of ischemic stroke events showed good agreement. The P-value from the Grønnesby-Borgan chi squared test was 0.51. CAD, coronary artery disease.
<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Diabetes (No)</th>
<th>Diabetes (Yes)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Current Smoking (%)</td>
<td>Current Smoking (%)</td>
</tr>
<tr>
<td></td>
<td>Untreated SBP (mmHg)</td>
<td>Treated SBP (mmHg)</td>
</tr>
<tr>
<td>40-44</td>
<td>110</td>
<td>120</td>
</tr>
<tr>
<td>45-49</td>
<td>110</td>
<td>120</td>
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<td>50-54</td>
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<tr>
<td>65-69</td>
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<td>120</td>
</tr>
<tr>
<td>70-74</td>
<td>110</td>
<td>120</td>
</tr>
</tbody>
</table>

*Figure 3 continued the next page.*
Figure 3. (A) Predicted probability of incident CAD within 10 years by specific combinations of non-HDLc, HDLc, SBP, current smoking and diabetes mellitus for Japanese men; JPHC Study, 1994–2010. JPHC Study, Japan Public Health Center-based Prospective Study; CAD, coronary artery disease; HDLc, high-density lipoprotein cholesterol; SBP, systolic blood pressure. To convert mg/dl to mmol/L, multiply the value by 0.02586. Non-HDLc is defined as TC minus HDLc. Colors in the charts indicate: (white) predicted 10-year probability of CAD <1%; (blue) predicted 10-year probability of CAD 1%–<5%; (green) predicted 10-year probability of CAD 5%–<7.5%; (yellow) predicted 10-year probability of CAD 7.5%–<10%; (orange) predicted 10-year probability of CAD 10%–<12.5%; (dark orange) predicted 10-year probability of CAD 12.5%–<15%; (red) predicted 10-year probability of CAD 15%–.
incidence in the present study independent of other risk factors (data not shown). Inclusion of BMI in the ischemic stroke prediction model did not improve discrimination (0.77 in the model with BMI vs. 0.78 without BMI) or calibration (GB chi-statistic P=0.68 in the model with BMI vs. 0.51 without BMI) although BMI would have remained in the final model. Although previous similar analyses indicated independent associations of BMI with CAD and total stroke, the effect of BMI would likely be mediated by the established risk factors in the present study, indicating importance of obesity prevention and control. Other measures of obesity were not reported to be superior to BMI at population level.

The proportion of subjects whose 10-year CAD risk was 5.0–7.4% or 7.5%+ in the present sample was small (5.1% in total), reflecting the low incidence rate of CAD in the cohort (crude rate: 0.91 per 1,000 person-years). The incidence rate was low partly because we included only hard CAD outcomes. Although we do not have data on how many more cases angina and coronary interventions might have added, a surveillance study in Japan indicated that 20–30% of softer CAD events might be added. The low rate of CAD in Japan may negate the value of assessing CAD risk from the beginning, as it would identify only a small fraction of individuals as being at high risk. However, the cut-off values for defining individuals with intermediate and high risk typically vary according to the population. For example, the sensitivity for identifying individuals who would develop CAD during the entire follow up by using a cut-off of 7.5% was only 15.6% (30/192), whereas it would increase to 66.1% (130/192) if a cut-off of 2.0% (approximately 80th percentile) was used in a non-HDLc model. Corresponding values using the TC model were 16.6% (32/192) and 45.3% (87/192), respectively. Furthermore, individual data meta-analysis of randomized trials has indicated that statins benefit even people at low CAD risk to lower CAD rates without increasing adverse outcomes.

In addition to conducting further studies that add coronary interventions to the outcome, the effectiveness and efficiency of CAD risk estimator-guided statin therapy with varying cut-off values for defining high-risk individuals, are warranted.

We found significant positive associations of antihypertensive medication use with CAD and ischemic stroke incidence independent of SBP in the present study. As there is massive evidence to support the benefits of antihypertensive medication use to lower CVD risk, users of antihypertensive medication in observational studies typically are participants with more severe hypertension and with greater subclinical atherosclerosis burden. In addition, the period during which antihypertensive medication was used, as well as the age at which the treatment was initiated, might have confounded the association. We did not consider medications for hyperlipidemia in the present study because the proportion of those taking these medicines was very small (1.9%) at baseline. Also, it was not related to CAD incidence when it was examined in the statistical model.

Strengths of the present study include its large sample size with long follow up that provided one of the largest number of CAD cases among Japanese studies, its standardized case ascertainment, and nearly complete follow up. We also used state-of-the-art methods to evaluate the performance of the prediction model, validated it in a second cohort, and the presented risk charts to aid risk communication.

There are limitations to our study that warrant consideration. First, the number of CAD cases was low preventing us from performing analyses stratified on sex or diabetes. However, as sex did not interact with other risk factors, combining men and women was acceptable. Nevertheless, a pooled analysis of all Japanese and Asian cohorts would provide a more precise risk equation with stratification by sex. The number of CAD cases in Cohort I was also small. Although the analysis indicated good levels of discrimination and calibration for the external validation, the analysis might have been underpowered. So, applying the equation to other populations may require caution. Second, electrocardiographic findings were not available in this study. Because atrial fibrillation is a strong risk factor for ischemic stroke, especially for cerebral embolism, its inclusion may improve performance of the prediction model for ischemic stroke. However, because it is so strong a predictor, individuals with clinically evident atrial fibrillation would normally be under medical control; therefore, its inclusion in the prediction model may not be so clinically useful. Nevertheless, future studies with atrial fibrillation and other electrocardiographic information may be needed to clarify these issues. Third, many individuals were excluded due to missing information. There were differences between included subjects and the others (Table S2). To tackle this problem, we used incidence rates, and proportions and mean values of risk factors from the entire Cohort II, if available, when creating risk charts and risk calculators. This strategy is similar to recalibration methods used by others. This resulted in an upward shift of the risk distribution; for example, the percentages with intermediate or high absolute risk of CAD (5.0%+) increased from 2.9% to 5.1%. Consequently, the sensitivity of identifying CAD cases by absolute risk criterion of 5.0% increased from 22.3% to 30.2%. Fourth, the number of individuals undergoing cholesterol lowering therapy (statin) at baseline were small, and the association with CAD could not be fully evaluated. However, given the fact that the main application of the CAD risk model is to aid decision-making involving statin use, it may be unnecessary to incorporate statin use in the risk model. Fifth, duration of diabetes, which might contribute additionally to CAD and ischemic stroke risk was not considered in the present analysis. Sixth, change in the behaviors (smoking status) or drug treatment (initiation/termination) during follow up were not considered. CAD and ischemic stroke risks related to current smoking may be underestimated if current smokers at baseline quit smoking during follow up. Finally, the sample included only Japanese people aged 40–69 years. It would be ideal to include young individuals, because it would be reasonable to consider risk factor modification as early as possible, and some risk factors (smoking, high BP, high blood cholesterol) are already prevalent before middle age. For this aim, estimation of lifetime risk may be warranted, as younger individuals would have even lower CVD incidence rates than observed here. Of course, a population-wide approach to promote control of CVD risk factors should complement any assessment to identify high-risk individuals by the use of risk equations in Japan.

Conclusions

In conclusion, the present study developed, calibrated and validated equations to estimate 10-year CAD and ischemic stroke risks using a large population-based cohort of Japanese men and women. Whether the prediction equation would be helpful for risk stratification to guide clinical decision-making to prevent CAD and ischemic stroke would need to be tested in a future clinical trial. In addition, population-wide effort to control levels of each risk factor should complement an approach to identify high-risk individuals by the risk estimator.
in order to improve public health in Japan, because a majority of the population would have a low risk.

Acknowledgments

We thank the participants and staff of the JPHC Study for their important contributions. We are also grateful to Professor Aaron R. Folsom (University of Minnesota) for valuable comments and suggestions on this manuscript.

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Disclosures

None of the authors had a personal or financial conflict of interest.

References


Supplementary Files

Methods and Results

Appendix

Table S1. Comparison of risk models for CAD incidence in Japan

Table S2. Comparison of selected characteristics among the analyzed participants, excluding subjects that had missing lifestyle and biochemical information in cohort II, JPHC study, 1993–1994

Table S3. Mean (standard deviation) or percentage of baseline characteristic in the derivation and validation cohorts; JPHC study, 1993–1994

Table S4. Univariate HRs of CAD and ischemic stroke risk prediction model in the derivation cohort; JPHC study cohort II, 1994–2010

Figure S1. (A) Calibration of the prediction model for 10-year CAD incidence by decile of risk in the validation cohort.

Figure S2. (A, men) Predicted probability of incident ischemic stroke within 10 years by specific combinations of HDLC, SBP, current smoking and diabetes mellitus for Japanese men.

Figure S3. (A, men) Predicted probability of incident CAD within 10 years by specific combinations of TC, HDLC, SBP, current smoking and diabetes mellitus for Japanese men. JPHC study, 1994–2010.

Figure S4. Image of coronary artery disease (CAD) risk calculator.

Figure S5. Image of ischemic stroke risk calculator.

Please find supplementary file(s): http://dx.doi.org/10.1253/circj.CJ-16-0081