ORIGINAL ARTICLE

Development of a risk prediction model for incident hypertension in a working-age Japanese male population

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The aim of this study was to develop a risk prediction model for incident hypertension in a Japanese male population. Study participants included 15 025 nonhypertensive Japanese male workers (mean age, 38.8 ± 8.9 years) who underwent an annual medical checkup at a company. The participants were followed-up for a median of 4.0 years to determine new-onset hypertension, defined as a systolic blood pressure (BP) ≥ 140 mm Hg, a diastolic BP ≥ 90 mm Hg, or the initiation of antihypertensive medication. Participants were divided into the following two cohorts for subsequent analyses: the derivation cohort ($n = 12\,020$, 80% of the study population) and the validation cohort ($n = 3005$, the remaining 20% of the study population). In the derivation cohort, a multivariate Cox proportional hazards model demonstrated that age, body mass index, systolic and diastolic BP, current smoking status, excessive alcohol intake and parental history of hypertension were independent predictors of incident hypertension. Using these variables, a risk prediction model was constructed to estimate the 4-year risk of incident hypertension. In the validation cohort, the risk prediction model demonstrated high discrimination ability and acceptable calibration, with a C-statistic of 0.861 (95% confidence interval 0.844, 0.877) and a modified Hosmer–Lemeshow χ^2 statistic of 15.2 ($P = 0.085$). A risk score sheet was constructed to enable the simple calculation of the approximate 4-year probability of incident hypertension. In conclusion, a practical risk prediction model for incident hypertension was successfully developed in a working-age Japanese male population. *Hypertension Research* (2015) 38, 419–425; doi:10.1038/hr.2014.159; published online 13 November 2014

Keywords: blood pressure; preventive medicine; risk prediction model; working-age Japanese male population

INTRODUCTION

Hypertension is a primary risk factor for cardiovascular disease, stroke and kidney disease.^{1,2} In Japan, hypertension is a nationwide epidemic, with more than 40 million Japanese estimated to have the condition.³ Prevention of hypertension in normotensive individuals, as well as medical treatment in patients with hypertension, is therefore a major public health concern in Japan. Accumulating evidence indicates that certain lifestyle modifications decrease blood pressure (BP) and reduce the risk of incident hypertension.^{4–9} Based on the evidence, guidelines for the management of hypertension^{10–12} explicitly indicate the need for lifestyle modifications to prevent or delay the onset of hypertension. In this regard, a simple and practical tool for estimating the risk of hypertension would assist healthcare providers in identifying individuals at high risk for incident hypertension and in guiding them as they modify their lifestyles.

Several risk prediction models for incident hypertension have been recently developed in Western,^{13–17} Middle Eastern¹⁸ and Asian^{19,20}

countries. Most of these models^{13,14,16–20} consist of simple clinical parameters and self-reported data, including information regarding lifestyle factors. The simplicity and user-friendliness of these models allow for their easy application in daily clinical practice as tools designed to prevent hypertension. However, to the best of our knowledge, prediction models for the risk of incident hypertension that specifically target the Japanese population have not yet been developed.

To fill this research gap, we aimed to develop a simple and practical risk prediction model for incident hypertension in working-age Japanese men.

METHODS

Study population

This study was conducted at an electrical equipment manufacturing company in Japan. Under the Industrial Safety and Health Law of Japan, all employers are required to conduct medical checkups of all employees at least once a year

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to ensure their health. We analyzed a personal information-free database of medical checkups at the company. A total of 20 909 workers underwent an annual medical checkup in 2008 (baseline examination). Among them, female subjects were excluded because they represented a markedly smaller proportion of the sample ($n=3024$) compared with the male subjects ($n=17\,885$). Among the male subjects, those with hypertension ($n=2043$) and those with a history of cardiovascular disease ($n=109$) or malignancy ($n=113$) were excluded. Subjects who did not provide the full amount of information needed for the present analysis ($n=460$) were also excluded. Additionally, 135 subjects who underwent baseline examinations (2008) but did not undergo any follow-up medical checkups (between 2009 and 2012) were excluded because of the lack of follow-up data. As a result, the present analysis included 15 025 subjects (age range, 19–63 years). This study was approved by the Ethics Committee of Nippon Medical School (Tokyo, Japan) and was conducted in accordance with the principles of the Declaration of Helsinki.

Measurements of variables

All subjects underwent anthropometrical evaluations, including body mass index, calculated as weight in kilograms divided by the square of height in meters. Obesity was defined as a body mass index $\geq 25.0\text{ kg m}^{-2}$.

Right brachial BP was measured by well-trained staff members while the subject was seated, following at least 5 min of rest, using a mercury sphygmomanometer with a cuff selected in accordance with the right-arm circumference. BP was measured twice, with a 1-min interval between measurements for recording the first and fifth Korotkoff sounds to determine systolic BP (SBP) and diastolic BP (DBP), respectively. The recording that provided the lower BP category was used for analysis. The BP category was defined as optimal (SBP < 120 mm Hg and DBP < 80 mm Hg), normal (SBP 120–129 mm Hg or DBP 80–84 mm Hg) and high-normal (SBP 130–139 mm Hg or DBP 85–89 mm Hg) according to the guidelines for the management of hypertension in Japan and in Europe.^{11,12} If both recordings fell within the same BP category, the recording that yielded the lower SBP was used. Hypertension was defined as a SBP ≥ 140 mm Hg, a DBP ≥ 90 mm Hg, or the current use of antihypertensive medication.

Blood samples were obtained from the antecubital vein following ≥ 8 h of fasting. Standard enzymatic methods were used to measure serum total cholesterol, triglycerides and plasma glucose levels. Serum high-density lipoprotein cholesterol levels were measured using the direct method. Low-density lipoprotein cholesterol was calculated using Friedewald's formula²¹ in subjects with triglyceride levels < 400 mg dl⁻¹. Hemoglobin A1c levels were measured using the latex coagulating method. Hemoglobin A1c levels were recorded in the form used by the Japan Diabetic Society and were converted to National Glycohemoglobin Standardization Program values in accordance with the following equation:²² hemoglobin A1c (National Glycohemoglobin Standardization Program) (%) = $1.02 \times \text{hemoglobin A1c (Japan Diabetic Society) (%)}$ + 0.25. Dyslipidemia was defined as a low-density lipoprotein cholesterol level ≥ 140 mg dl⁻¹, a triglyceride level ≥ 150 mg dl⁻¹, a high-density lipoprotein cholesterol level < 40 mg dl⁻¹ or the current use of antidiabetic medication. Diabetes was defined as a fasting plasma glucose level ≥ 126 mg dl⁻¹, a hemoglobin A1c level $\geq 6.5\%$ or the current use of glucose-lowering medication.

A self-reported questionnaire was administered to collect data regarding subjects' parental history of hypertension and lifestyle factors, including smoking status, exercise habits and alcohol intake. Smoking status was categorized as either current smoking or nonsmoking. Current smoking was defined as cigarette consumption on a regular basis (at least once daily) at the time of the examination. Regular exercise was defined as the performance of continuous exercise at an intensity sufficient to break a sweat for at least 30 min ≥ 2 days per week for at least 1 year. Excessive alcohol intake was defined as alcohol intake of ≥ 6 days per week.

Follow-up examinations

The outcome of this study was the incidence of hypertension. BP and antihypertensive medication use were followed-up for a median of 4.0 years (range, 0.3–4.7 years) via annual medical checkup data. The follow-up was censored when a subject was lost to follow-up or the 4-year follow-up (until

2012) period was completed. During a total follow-up period of 56 124 person-years, 1633 subjects developed hypertension; 12 623 were censored because of the completion of the 4-year follow-up period and the remaining 769 underwent an additional follow-up visit but were censored before completion of the 4-year follow-up period.

Statistical analysis

All statistical tests were performed using SPSS Statistics software, version 22 (IBM Japan, Tokyo, Japan) and R software, version 3.0.2. (R Foundation for Statistical Computing, Vienna, Austria, <http://cran.r-project.org/>). All continuous variables were expressed as the mean $\pm$ s.d., with the exception of one variable (triglyceride level) with a skewed distribution, which was expressed as a median (interquartile range). Categorical variables were expressed as numbers (percentage of the total). To test the internal validity of the risk prediction model, the subjects were randomly divided into the following two cohorts: the derivation cohort, which included 80% of the sample ($n=12\,020$), and the validation cohort, which included the remaining 20% ($n=3005$). The baseline characteristics of the two groups were compared using the unpaired *t*-test or the χ^2 -test, as appropriate. In the derivation cohort, the multivariate Cox proportional hazards model was used with forward selection procedure to determine significant predictors of incident hypertension. In this model, age, body mass index, SBP and DBP, dyslipidemia, diabetes, excessive alcohol intake, exercise status, smoking status and parental history of hypertension were used as explanatory variables. The following interaction terms were tested in the additional Cox model: SBP by age, DBP by age, parental history of hypertension by age or body mass index, smoking status by body mass index and excess alcohol intake by body mass index. Based on these results, the following general equation was used to calculate the risk of incident hypertension within the next 4 years:

$$\text{Probability} = 1 - S_0(t)^{\exp(\sum_{i=1}^p \beta_i X_i - \sum_{i=1}^p \beta_i \bar{X}_i)} \quad (1)$$

where $S_0(t)$ is the baseline survival function, assuming that all covariates are represented by average values for the study population, at follow-up time t (here $t=4$ years); β_i is the estimated regression coefficient; X_i is the value of the i th risk factor (if continuous); $\bar{X}_i$ is the corresponding mean; and p denotes the number of risk factors.

Using the validation cohort, the C-statistic of the resulting model was determined to estimate its discrimination ability, based on the method reported by Uno *et al.*²³ This method estimates the C-statistic of the model in predicting subject-level survival over a particular interval, independent of study-specific censoring distribution. A modified Hosmer–Lemeshow χ^2 statistic with 9 *df* was also applied to evaluate its calibration.²⁴ This equation uses the Kaplan–Meier estimator to determine the observed numbers of events in each decile of risk, which is based on the predicted probability of the Cox proportional hazards model. The C-statistics of the two groups were compared using the method reported by Uno *et al.*²³ A risk score sheet was constructed based on the method reported by Sullivan *et al.*²⁵ for facile calculation of the 4-year risk of incident hypertension. In the risk score sheet, continuous variables were divided into categories to facilitate risk estimation, with age divided into 4-year groups, with the exception of the group ≥ 59 years; SBP and DBP were divided into 5-mm Hg categories, with the exception of the ≤ 109 mm Hg and ≤ 64 mm Hg categories; and body mass index was divided into categories of ≤ 20.9 , 21.0–22.9, 23.0–24.9, 25.0–26.9, 27.0–29.9 and $\geq 30.0\text{ kg m}^{-2}$ in accordance with a report that demonstrated a relationship between body mass index and mortality risk in a pooled analysis of large-scale Japanese cohort studies.²⁶ All statistical tests were two-sided, and $P < 0.05$ was considered significant.

RESULTS

Baseline characteristics of the study participants are presented in Table 1. Overall, the mean age was 38.8 years. A significant difference in the prevalence of current smokers was noted between the derivation and validation cohorts.

In the derivation cohort, all variables used in the study were significant predictors of incident hypertension in the univariate Cox

Table 1 Baseline characteristics of the study population

Variable	Overall (n = 15 025)	Derivation cohort (n = 12 020)	Validation cohort (n = 3005)	P value
Age, years	38.8±8.9	38.9±8.9	38.7±9.0	0.32
Body mass index, kg m ⁻²	22.75±2.91	22.76±2.90	22.72±2.94	0.52
Obesity, n (%)	2847 (18.9)	2303 (19.2)	544 (18.1)	0.19
Systolic BP, mm Hg	115.5±11.3	115.6±11.3	115.3±11.3	0.31
Diastolic BP, mm Hg	70.1±9.1	70.1±9.1	69.9±9.1	0.27
Total cholesterol, mg dl ⁻¹	196.5±33.4	196.6±33.4	195.9±33.7	0.27
High-density lipoprotein cholesterol, mg dl ⁻¹	60.6±14.1	60.6±14.0	60.9±14.1	0.32
Low-density lipoprotein cholesterol ^a , mg dl ⁻¹	115.3±29.8	115.5±29.8	114.5±29.9	0.12
Triglycerides ^b , mg dl ⁻¹	84 (58, 124)	84 (60, 124)	84 (59, 125)	0.7
Dyslipidemia, n (%)	4864 (32.4)	3912 (32.5)	952 (31.7)	0.37
Medication for dyslipidemia, n (%)	346 (2.3)	276 (2.3)	70 (2.3)	0.91
Fasting plasma glucose, mg dl ⁻¹	90.1±11.6	90.2±11.8	89.9±10.6	0.33
Hemoglobin A1c, %	5.30±0.47	5.30±0.48	5.30±0.45	0.49
Impaired fasting glucose/diabetes, n (%)	493 (3.3)	398 (3.3)	95 (3.2)	0.68
Diabetes, n (%)	265 (1.8)	209 (1.7)	56 (1.9)	0.64
Medication for diabetes, n (%)	93 (0.6)	78 (0.6)	15 (0.5)	0.35
Current smoking status, n (%)	4592 (30.6)	3726 (31.0)	866 (28.8)	0.02
Regular exercise, n (%)	3516 (23.4)	2796 (23.3)	720 (24.0)	0.42
Excessive alcohol intake, n (%)	2453 (16.3)	1972 (16.4)	481 (16.0)	0.6
Parental history of hypertension, n (%)	3243 (21.6)	2560 (21.3)	683 (22.7)	0.088

Abbreviation: BP, blood pressure.

^aCalculated using the Friedewald's formula in 14 884 subjects with a triglycerides level < 400 mg dl⁻¹.^bMedian (Interquartile range).**Table 2** Regression coefficients and HR for incident hypertension

Variable	Univariate model				Age-adjusted model				Multivariate model ^a			
	β	s.e.	HR	95% CI	β	s.e.	HR	95% CI	β	s.e.	HR	95% CI
Age (per 1-year increase)	0.074	0.003	1.08	1.07, 1.08	—				0.040	0.004	1.04	1.03, 1.05
Body mass index (per 1.0 kg m ⁻² increase)	0.174	0.007	1.19	1.17, 1.21	0.166	0.008	1.18	1.16, 2.00	0.071	0.009	1.07	1.06, 1.09
Systolic BP (per 1 mm Hg increase)	0.113	0.003	1.12	1.11, 1.13	0.107	0.003	1.11	1.11, 1.12	0.061	0.004	1.06	1.05, 1.07
Diastolic BP (per 1 mm Hg increase)	0.164	0.004	1.18	1.17, 1.19	0.154	0.004	1.17	1.16, 1.18	0.096	0.005	1.10	1.09, 1.11
Current smoking status (yes/no = 1/0)	0.295	0.057	1.34	1.20, 1.50	0.246	0.057	1.28	1.14, 1.43	0.242	0.058	1.27	1.14, 1.43
Excessive alcohol intake (yes/no = 1/0)	0.661	0.063	1.94	1.71, 2.19	0.323	0.064	1.38	1.22, 1.57	0.202	0.065	1.22	1.08, 1.39
Parental history of hypertension (yes/no = 1/0)	0.602	0.060	1.83	1.63, 2.05	0.477	0.060	1.61	1.43, 1.81	0.282	0.060	1.33	1.18, 1.49
Regular exercise (yes/no = 1/0)	-0.190	0.069	0.83	0.72, 0.95	-0.250	0.069	0.78	0.68, 0.89	Not selected			
Dyslipidemia (yes/no = 1/0)	0.795	0.056	2.21	1.99, 2.47	0.531	0.057	1.70	1.52, 1.90	Not selected			
Diabetes (yes/no = 1/0)	0.963	0.143	2.62	1.98, 3.47	0.351	0.145	1.42	1.07, 1.89	Not selected			

Abbreviations: β, regression coefficient; BP, blood pressure; CI, confidence interval; HR, hazard ratio; s.e., standard error.

^aForward selection procedure.

proportional hazard model (Table 2). In the age-adjusted Cox model, all variables (except for age) remained significant predictors. The multivariate Cox model indicated that age, body mass index, SBP and DBP, current smoking status, excessive alcohol intake and

parental history of hypertension were independent predictors of incident hypertension. The 4-year baseline survival function ($S_0(4)$) was 0.963. When the interaction terms were included in the model in the manner described in the previous section, DBP by age, in addition

to age, body mass index, SBP and DBP, current smoking status, excessive alcohol intake and parental history of hypertension, was identified as a significant predictor of incident hypertension (Supplementary Table 1).

Figure 1 Modified Hosmer–Lemeshow goodness-of-fit analysis of the risk prediction model for incident hypertension in the validation cohort.

The models with and without interaction terms were virtually identical with regard to their C-statistics (0.861, 95% confidence interval 0.844, 0.877 and 0.861, 95% confidence interval 0.844, 0.877, respectively) in the validation cohort. Therefore, the interaction-term-excluded model was used in subsequent analyses to enable construction of a simpler and more user-friendly risk calculation equation and risk score sheet.

The results of the modified Hosmer–Lemeshow χ^2 statistic using the validation cohort indicated an acceptable calibration of the risk prediction model, yielding a value of 15.2 ($P=0.085$, Figure 1).

A simple and practical risk score sheet was finally developed to calculate the 4-year risk of incident hypertension (Figure 2). In this score sheet, 1-point was set as the risk associated with a 4-year increase in age. For scoring of continuous values, the range of possible values was divided into anywhere from 6–11 categories to enable the awarding of points depending on the category selected. For the scoring of binary questions, 1 or 2 points were assigned if the subject answered affirmatively, and 0 points were assigned if the subject answered negatively. Although each point was originally computed as a decimal value, it was then rounded to the nearest integer for facile calculation. The approximate 4-year risk of incident hypertension was then estimated via summation of the points awarded to each of the items.

The total score obtained from the risk score sheet demonstrated good discrimination ability for incident hypertension in the validation cohort, as its C-statistic was 0.858 (95% confidence interval 0.840, 0.876). The total score also indicated good calibration in the validation cohort, as its χ^2 statistic was 9.30 ($P=0.41$, Figure 3a). A comparison

Risk factor	Categories	Point	Risk factor	Categories	Point
Age, years	19 ~ 22	-5	Body mass index, kg/m ²	~ 20.9	-1
	23 ~ 26	-4		21.0 ~ 22.9	0
	27 ~ 30	-3		23.0 ~ 24.9	1
	31 ~ 34	-2		25.0 ~ 26.9	2
	35 ~ 38	-1		27.0 ~ 29.9	3
	39 ~ 42	0		30.0 ~	4
	43 ~ 46	1	Current smoking	No	0
	47 ~ 50	2		Yes	2
	51 ~ 54	3	Excessive alcohol intake	No	0
	55 ~ 58	4		Yes	1
Systolic BP, mmHg	59 ~ 63	5	Parental history of hypertension	No	0
	~ 109	-4		Yes	2
	110 ~ 114	0	Total score		
	115 ~ 119	2	Total score	4-year estimated risk (%)	
	120 ~ 124	4	~ -5	< 1	
	125 ~ 129	6	-4 ~ 6	1 ~ < 5	
Diastolic BP, mmHg	130 ~ 134	8	7 ~ 10	5 ~ < 10	
	135 ~ 139	10	11 ~ 15	10 ~ < 20	
	~ 64	-6	16 ~ 18	20 ~ < 30	
	65 ~ 69	0	19 ~ 20	30 ~ < 40	
	70 ~ 74	3	21 ~ 22	40 ~ < 50	
	75 ~ 79	6	23 ~ 24	50 ~ < 60	
	80 ~ 84	9	25 ~	60 ~	
	85 ~ 89	12			

Figure 2 Risk score sheet for predicting the approximate 4-year risk of incident hypertension.

Figure 3 (a) Modified Hosmer–Lemeshow goodness-of-fit analysis of the total score obtained from the risk score sheet for incident hypertension in the validation cohort. (b) Comparison between the estimated risk categories obtained from the risk score sheet and the observed incident rate of hypertension.

between the estimated risk categories obtained from the risk score sheet and the observed incident rate of hypertension is presented in Figure 3b, which indicates that the range of estimated risk is consistent with the observed incident rate in each risk category.

The steps followed in using the risk calculation equation and risk score sheet are described in the Appendix.

We attempted to construct a risk prediction model for incident hypertension in female subjects who fulfilled the inclusion criteria of this study ($n=2711$); their baseline characteristics are presented in Supplementary Table 2. The multivariate Cox proportional hazards model indicated that age, SBP and DBP and body mass index were independent predictors of incident hypertension (Supplementary Table 3). By contrast, neither excessive alcohol intake nor current smoking status was a predictor, although they were completely modifiable lifestyle factors. Therefore, we concluded that a risk prediction model constructed without these variables would have low utility, and a risk prediction model was not constructed for female subjects.

DISCUSSION

In this study of a working-age Japanese male population, predictors of incident hypertension included age, body mass index, SBP and DBP, current smoking status, excessive alcohol intake and parental history of hypertension. Using these predictors, a risk prediction equation for estimating the 4-year risk of incident hypertension was developed. Testing of the internal validity of the risk prediction equation in the validation cohort indicated that it has a high discrimination ability and acceptable calibration. A risk score sheet was developed for facile determination of the approximate risk of incident hypertension, a system with high discrimination ability and good calibration.

Age, SBP and DBP, body mass index, current smoking status and parental history of hypertension were predictors of incidental hypertension in this study, findings similar to those of previous studies that developed a hypertension risk prediction model.^{14,16–20} These findings are also consistent with the results of other epidemiologic studies.^{27–32} Additionally, excessive alcohol intake was a predictor of incident hypertension in this study, and the present model included this variable in its risk calculation. By contrast, previously reported risk prediction models did not include data regarding alcohol intake,

because in those studies, these data itself were lacking^{18,20} or alcohol intake was not a significant predictor of hypertension.^{14,16,17,19} However, excessive alcohol intake has been shown to be significantly associated with an increased risk of incident hypertension in several other studies.^{33–35} Therefore, our results regarding the relationship between excessive alcohol intake and the risk of hypertension are somewhat in line with those reported by previous studies.

Regular exercise was not associated with the risk of hypertension in the present study, although it has been reported to have protective effects against BP elevation and hypertension onset.^{7,36} One possible explanation for this conflicting finding is that body mass index and BP of subjects who engage in regular exercise were already low at baseline as a result of its favorable effects on BP control. In fact, both baseline body mass index and DBP were significantly lower in subjects engaging in regular exercise compared with those who did not engage in regular exercise (data not shown). Our hypothesis is supported by the results of the Cox analysis; regular exercise was a significant predictor of incident hypertension in both the univariate and age-adjusted models, but not in the multivariate model, which simultaneously included body mass index and BP as covariates. Therefore, it would be inappropriate to use this finding to conclude that engaging in regular exercise does not reduce the risk of incident hypertension.

Risk assessment tools are thought to be useful in motivating individuals at high risk for future health problems to modify their lifestyles in a manner that decreases their risks.³⁷ In this regard, a unique advantage of the risk prediction model developed in this study is its ability to provide information that shows individuals how lifestyle modifications may reduce their future risk. When considering Case 2, as described in the Appendix, a decrease in the frequency of alcohol intake to 3 days per week, as well as a 6 kg decrease in body weight and a decrease in SBP/DBP by 4/2 mm Hg following 1 year of lifestyle modification, will result in a decrease in his 4-year risk of hypertension from 64.2 to 38.6% (age, 50 years old; body mass index, 24.7 kg m⁻²; no excessive alcohol intake; and BP, 132/82 mm Hg). Application of the risk prediction model in this manner may be used to assist individuals in understanding the benefits of engaging in recommended lifestyle modifications and may increase the likelihood that they do so.

This study has several limitations. First, we did not construct a risk prediction model for female subjects. Second, study participants

included individuals employed by only a single company. Therefore, determining whether the risk prediction model may be applied to other populations, including the elderly, requires testing of the external validity of the model. Third, the BP values used in this study were not average values but the lower values between two measurements. This is not consistent with the guidelines for hypertension.^{10–12} However, the lower value of the two measurements was chosen before we obtained data from the existing database; therefore, we could not use average BP values in this study. Therefore, risk calculation based on the present risk model using the average BP values may reduce its reliability. Fourth, because of the difficulties in performing BP measurements over several days, as well as in performing ambulatory BP measurements in an occupational setting, BPs were measured on only 1 day, which may have resulted in less accurate BP values. Fifth, the frequency of alcohol intake was used to define excessive alcohol intake, whereas the amount of alcohol intake was not used due to lack of data. However, previous studies have demonstrated reductions in BP by decreasing the amount, rather than the frequency, of alcohol intake.⁸ Therefore, we should help individuals with excessive alcohol intake to decrease not only their frequency of alcohol intake but also their amount of alcohol intake, to reduce their risk of hypertension. Sixth, salt intake and vegetable intake are important dietary factors in the risk of incident hypertension; however, in this study, these data were not available. Seventh, although the risk prediction model demonstrated acceptable calibration ($P > 0.05$, Figure 1), the differences between the observed and predicted risks were somewhat greater in the seventh to ninth deciles than in the other deciles. Finally, although several potential confounders were examined in the multivariate analysis, other confounders that could not be tested due to lack of data, such as educational status and other socioeconomic factors,^{38,39} may have affected the results.

In conclusion, we have developed a practical risk prediction model for estimating the probability of incident hypertension in working-age Japanese men. Following confirmation of its validity via external validation studies, we anticipate that this risk prediction model will be used in diverse healthcare environments to guide individuals attempting to modify their lifestyles and prevent or delay the onset of hypertension.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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Supplementary Information accompanies the paper on Hypertension Research website (<http://www.nature.com/hr>)

APPENDIX

Estimating the 4-year risk of incident hypertension via direct calculation and risk score sheet

Case 1

Consider a 36-year-old man with an SBP/DBP of 124/72 mm Hg and a body mass index of 24.5 kg m^{-2} who does not smoke or engage in excessive alcohol intake but has a parental history of hypertension. The regression coefficient (Table 2), 4-year baseline survival function ($S_0(4) = 0.963$), mean values of the relevant risk factors in the derivation cohort (Table 1) and personal risk factor information were entered in the general formula (1), as follows:

$$\begin{aligned} \sum_{i=1}^p \beta_i X_i &= (0.040 \times \text{age} + 0.071 \times \text{body mass index} \\ &\quad + 0.061 \times \text{SBP} + 0.096 \times \text{DBP} \\ &\quad + 0.242 \times \text{current smoking} \\ &\quad + 0.202 \times \text{excessive alcohol intake} \\ &\quad + 0.282 \times \text{parental history of hypertension}) \\ &= (0.040 \times 36 + 0.071 \times 24.5 + 0.061 \times 124 \\ &\quad + 0.096 \times 72 + 0.242 \times 0 + 0.202 \times 0 + 0.282 \times 1) \\ &= 17.938 \end{aligned}$$

$$\begin{aligned} \sum_{i=1}^p \beta_i \bar{X}_i &= (0.040 \times 38.87 + 0.071 \times 22.756 + 0.061 \times 115.55 \\ &\quad + 0.096 \times 70.12 + 0.242 \times 0.310 + 0.202 \times 0.164 \\ &\quad + 0.282 \times 0.213) \\ &= 17.119 \end{aligned}$$

∴ 4-year probability from the direct equation

$$= 1 - 0.963^{\exp(17.938 - 17.119)} = 0.082$$

In accordance with the risk score sheet, as shown in Figure 2, -1 points are assigned for age; 4 and 3, for SBP and DBP, respectively; 1, for body mass index; 0, for smoking status; 0, for excessive alcohol intake; and 2, for parental history of hypertension, yielding a total score of 9 points. Therefore, he has a 4-year risk of incident hypertension of 5 to <10%.

Case 2

Consider a 49-year-old man with an SBP/DBP of 136/84 mm Hg, a body mass index of 26.8 kg m^{-2} (height, 1.70 m and weight, 77.5 kg) and excessive alcohol intake but who does not smoke or have a parental history of hypertension.

$$\begin{aligned} \sum_{i=1}^p \beta_i X_i &= 0.040 \times 49 + 0.071 \times 26.8 + 0.061 \times 136 \\ &\quad + 0.096 \times 84 + 0.242 \times 0 + 0.202 \times 1 + 0.282 \times 0) \\ &= 20.425 \end{aligned}$$

∴ 4-year probability from the direct equation

$$= 1 - 0.963^{\exp(20.425 - 17.119)} = 0.642$$

Completion of the risk score sheet in the manner described for Case 1 would yield a total score of 24 points, indicating that his 4-year risk of incident hypertension is 50 to <60%.

When completing the risk score sheet, it is important to note that the continuous variables are categorized and that each point is rounded to the nearest integer. Therefore, the estimated risk according to the risk score sheet is not necessarily comparable to that determined by direct calculation.