

ORIGINAL RESEARCH

# Clinical Risk Score for the Prediction of Incident Atrial Fibrillation: Derivation in 7 220 654 Taiwan Patients With 438 930 Incident Atrial Fibrillations During a 16-Year Follow-Up

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**BACKGROUND:** Although several risk schemes have been proposed to predict new-onset atrial fibrillation (AF), clinical prediction models specific for Asian patients were limited. In the present study, we aimed to develop a clinical risk score (Taiwan AF score) for AF prediction using the whole Taiwan population database with a long-term follow-up.

**METHODS AND RESULTS:** Among 7 220 654 individuals aged  $\geq 40$  years without a past history of cardiac arrhythmia identified from the Taiwan Health Insurance Research Database, 438 930 incident AFs occurred after a 16-year follow-up. Clinical risk factors of AF were identified using Cox regression analysis and then combined into a clinical risk score (Taiwan AF score). The Taiwan AF score included age, male sex, and important comorbidities (hypertension, heart failure, coronary artery disease, end-stage renal disease, and alcoholism) and ranged from  $-2$  to 15. The area under the receiver operating characteristic curve of the Taiwan AF scores in the predictions of AF are 0.857 for the 1-year follow-up, 0.825 for the 5-year follow-up, 0.797 for the 10-year follow-up, and 0.756 for the 16-year follow-up. The annual risks of incident AF were 0.21%/year, 1.31%/year, and 3.37%/year for the low-risk (score  $-2$  to 3), intermediate-risk (score 4 to 9), and high-risk (score  $\geq 10$ ) groups, respectively. Compared with low-risk patients, the hazard ratios of incident AF were 5.78 (95% CI, 3.76–7.75) for the intermediate-risk group and 8.94 (95% CI, 6.47–10.80) for the high-risk group.

**CONCLUSIONS:** We developed a clinical AF prediction model, the Taiwan AF score, among a large-scale Asian cohort. The new score could help physicians to identify Asian patients at high risk of AF in whom more aggressive and frequent detections and screenings may be considered.

**Key Words:** atrial fibrillation ■ incidence ■ Taiwan AF score

See Editorial by El Moheb and Refaat

**A**trial fibrillation (AF) is the most common sustained cardiac arrhythmia that is associated with increased risk of mortality, heart failure, ischemic stroke, and dementia.<sup>1</sup> The prevalence of AF is expected to rise substantially during the next few decades because of the aging population, improved

public awareness, and better diagnostic tools.<sup>2,3</sup> Although the incidence and prevalence of AF are generally lower for Asian patients compared with White patients,<sup>4</sup> the prevalence rates of AF in Asian countries will continuously increase in parallel to that of Western countries. For example, from year 2020 to 2050, the

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## CLINICAL PERSPECTIVE

### What Is New?

- The Taiwan atrial fibrillation score was derived from 7 220 654 patients with 438 930 incident atrial fibrillation events and included age, male sex, and important comorbidities (hypertension, heart failure, coronary artery disease, end-stage renal disease, and alcoholism) and ranged from -2 to 15.

### What Are the Clinical Implications?

- The annual risks of incident atrial fibrillation were 0.21%/year, 1.31%/year, and 3.37%/year for the low-risk (score -2 to 3), intermediate-risk (score 4-9), and high-risk (score ≥10) groups, respectively.
- The new score could help physicians to identify Asian patients at high risk of atrial fibrillation in whom more aggressive and frequent detections and screenings may be considered.

## Nonstandard Abbreviations and Acronyms

<b>ARIC</b>	Atherosclerosis Risk in Communities Study
<b>CHARGE-AF</b>	Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation
<b>FHS</b>	Framingham Heart Study
<b>NHIRD</b>	National Health Insurance Research Database

prevalence rates of AF are projected to increase from 1.51% to 4.0% in Taiwan and from 2.1% to 5.4% in South Korea.<sup>1,5</sup> Therefore, the overall burden of patients with AF will largely grow in Asian regions, and how to identify patients at risk of AF is important.

Several risk schemes have been proposed to predict new-onset AF, including the FHS (Framingham Heart Study) score,<sup>6</sup> the ARIC (Atherosclerosis Risk in Communities Study) score,<sup>7</sup> and the CHARGE-AF (Cohorts for Heart and Aging Research in Genomic Epidemiology–Atrial Fibrillation) score.<sup>8</sup> However, these scoring schemes were derived in White populations and may not be fully applied to Asian patients. Although the C2HEST score has been proposed to predict incident AF for Asian patients, there were only 921 incident AF events among 471 446 Chinese patients after a mean follow-up of 4.1 years.<sup>9</sup> The incidence of AF was around 0.5/1000 person-years in the study from which the

C2HEST score was developed and is lower than that reported from Taiwan (1.51/1000 person-years) and South Korea (1.77/1000 person-years).<sup>1,5</sup> This previous study may be limited by selected population from certain hospitals of 1 single China province.<sup>9</sup> In the present study, we aimed to develop a clinical risk score (Taiwan AF score) for AF prediction using the whole Taiwan population database with long-term follow-up.

## METHODS

### Database

The authors declare that all supporting data are available within the article and its online supplementary files. This study used data from the National Health Insurance Research Database (NHIRD) provided by Health and Welfare Data Science Center, Ministry of Health and Welfare, Taiwan. The National Health Insurance system is a mandatory universal health insurance program that was launched on March 1, 1995, and that offers comprehensive medical care coverage to all Taiwanese residents. NHIRD consists of detailed healthcare data from >23 million enrollees, representing >99% of Taiwan's population, from January 1, 1996, to December 31, 2016. In this cohort data set, the patients' original identification numbers have been encrypted to protect their privacy, but the encrypting procedure was consistent so that a linkage of the claims belonging to the same patient was feasible within the National Health Insurance database and can be followed continuously. The descriptions about Taiwan NHIRD have been reported in our previous studies.<sup>1,10,11</sup>

### Study Population

From January 1, 2000, to December 31, 2000, a total of 7 220 654 patients aged ≥40 years without a past history of cardiac arrhythmias were identified from the NHIRD. Information about important comorbid conditions of each individual was retrieved from the NHIRD based on the *International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)* codes (Table S1). The diagnostic accuracies of important comorbidities in NHIRD, such as hypertension, diabetes mellitus, heart failure, myocardial infarction, hyperlipidemia, and chronic obstructive pulmonary disease, have been validated previously.<sup>12,13</sup> AF was diagnosed using the *ICD-9-CM* code (427.31) registered by the physicians responsible for the care of patients. The diagnostic accuracy of AF based on the *ICD-9-CM* code in the Taiwan NHIRD has been validated previously.<sup>14</sup>

## Predictors of AF and the Development of Scoring Scheme

To develop the risk prediction model, general principles from the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis statement were followed.<sup>15</sup> Cox proportional hazards modeling tested each variable on the time to event of the occurrence of AF during the 16-year follow-up. An initial saturated Cox proportional hazards model was developed that forced all candidate variables into the model. An  $\alpha$  level of 0.1 from the saturated model was used as a threshold to enter a variable predictor into a backward elimination model.  $\beta$  coefficients are presented for the final Cox regression model, with significant associations reported as hazard ratios (HRs) with 95% CIs. The score weights of each significant predictors of incident AF in the multivariable Cox regression model were derived from their  $\beta$  coefficients using the methods described by Sullivan et al.<sup>16</sup> Thereafter, the score weight for each predictor variable was rounded to its closest integer to develop the score point and the scoring scheme. After the development of the risk prediction scheme, the Taiwan AF score, we reported the incidence of AF (%/year) after 1-year, 3-year, 5-year, 7-year, 10-year, 12-year, and 16-year follow-ups for

each score. Patients were classified into 3 different risk categories (low-risk, intermediate-risk, and high-risk groups) based on the tertile values of the Taiwan AF score of patients who developed AF after the 16-year follow-up.

## Statistical Analysis

Data are presented as the mean $\pm$ SD or median value (interquartile range) for continuous variables and proportions for categorical variables. The differences between median values were assessed using the Wilcoxon rank-sum test. The differences between nominal variables were compared by chi-square test. The incidence of AF was calculated from dividing the number of events by person-time at risk. The cumulative incidence curves of AF for different scoring strata were plotted via the Kaplan-Meier method, with statistical significance examined by the log-rank test. The diagnostic accuracy of the Taiwan AF score in the prediction of incident AF was assessed by calculating the C statistic based on the receiver operating characteristic curve. A bootstrap method of validation using 1000 replications was applied to the final scoring scheme. The area under the receiver operating characteristic curve (AUROC) of the Taiwan AF score was compared with other reported clinical schemes, including the CHADS<sub>2</sub>,<sup>17,18</sup> CHA<sub>2</sub>DS<sub>2</sub>-VASc,<sup>18</sup> and

**Table 1. Baseline Characteristics of Patients**

Variables	All Patients, n=7 220 654	Patients With AF, n=438 930	Patients Without AF, n=6 781 724	P Value
Age, y	53 (46–65)	68 (58–75)	52 (45–64)	<0.001
Male sex	3 494 582 (48.4)	233 562 (53.2)	3 261 020 (48.1)	<0.001
Hypertension	1 154 853 (16.0)	150 927 (34.4)	1 003 926 (14.8)	<0.001
Diabetes mellitus	522 767 (7.2)	50 023 (11.4)	472 744 (7.0)	<0.001
Heart failure	117 232 (1.6)	29 811 (6.8)	87 421 (1.3)	<0.001
Prior stroke	196 291 (2.7)	25 692 (5.9)	170 599 (2.5)	<0.001
Coronary artery diseases	423 288 (5.9)	72 083 (16.4)	351 205 (5.2)	<0.001
Without prior MI	391 906 (5.4)	66 536 (15.2)	325 370 (4.8)	<0.001
With prior MI	31 382 (0.4)	5547 (1.3)	25 835 (0.4)	<0.001
Peripheral vascular diseases	24 820 (0.3)	2993 (0.7)	21 827 (0.3)	<0.001
COPD	343 894 (4.8)	45 725 (10.4)	298 169 (4.4)	<0.001
Autoimmune diseases	71 341 (1.0)	6336 (1.4)	65 005 (1.0)	<0.001
Liver cirrhosis	52 234 (0.7)	3127 (0.7)	49 107 (0.7)	0.376
Cancer	165 367 (2.3)	11 786 (2.7)	153 581 (2.3)	<0.001
Hyperthyroidism	14 811 (0.2)	1218 (0.3)	13 593 (0.2)	<0.001
CKD	142 545 (2.0)	15 596 (3.6)	126 949 (1.9)	<0.001
Without ESRD	100 487 (1.4)	11 362 (2.6)	89 125 (1.3)	<0.001
With ESRD	42 058 (0.6)	4234 (1.0)	37 824 (0.6)	<0.001
Gout	246 587 (3.4)	27 634 (6.3)	218 953 (3.2)	<0.001
Alcoholism	34 583 (0.5)	2101 (0.5)	32 482 (0.5)	0.978

Data are provided as median (interquartile range) or number (percentage). AF indicates atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; and MI, myocardial infarction.

C2HEST scores,<sup>9</sup> using the DeLong test. The calibration, a measure of the goodness of model fit, was assessed by comparing the observed and predicted numbers of AF events in deciles of predicted risk as calculated by the Grønnesby-Borgan chi-square statistic.<sup>19</sup> The statistical significances were set at  $P < 0.05$ , and all statistical analyses were carried out by SPSS 17.0 (SPSS Inc.).

The present study was approved by the institutional review board at Taipei Veterans General Hospital, Taipei, Taiwan. Informed consent was waived because of the use of anonymous data.

## RESULTS

The median age of study population was 53 years, and 48.4% of them were men (Table 1). During a 16-year follow-up, 438 930 patients experienced incident AF with an incidence of 0.42 per 100 person-years. The baseline clinical characteristics of patients with or without incident AF are shown in Table 1. Generally, patients who experienced AF were older and had more comorbidities.

**Table 2. Predictors of Incident AF**

Variables	$\beta$ Coefficient	Multivariate Cox Regression Analysis	
		HR (95% CI)	P Value
Age, per y	0.077	1.080 (1.079–1.080)	<0.001
Male sex	0.232	1.261 (1.253–1.268)	<0.001
Hypertension	0.343	1.408 (1.398–1.419)	<0.001
Diabetes mellitus	0.082	1.086 (1.075–1.096)	<0.001
Heart failure	0.894	2.444 (2.413–2.475)	<0.001
Prior stroke	0.127	1.136 (1.121–1.151)	<0.001
Coronary artery disease			
Without MI	0.377	1.457 (1.444–1.471)	<0.001
With MI	0.435	1.545 (1.504–1.588)	<0.001
Peripheral vascular diseases	−0.038	0.963 (0.928–0.999)	0.042
COPD	0.151	1.163 (1.151–1.175)	<0.001
Autoimmune diseases	0.071	1.074 (1.047–1.101)	<0.001
Liver cirrhosis	0.139	1.149 (1.108–1.191)	<0.001
Hyperthyroidism	0.143	1.153 (1.090–1.216)	<0.001
CKD			
Without ESRD	0.104	1.109 (1.080–1.139)	<0.001
With ESRD	0.375	1.454 (1.419–1.490)	<0.001
Gout	0.146	1.158 (1.143–1.172)	<0.001
Alcoholism	0.338	1.402 (1.342–1.464)	<0.001

AF indicates atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; HR, hazard ratio; and MI, myocardial infarction.

## Predictors of Incident AF and the Calculation Rules of the Taiwan AF Score

The significant clinical predictors of incident AF from the stepwise backward selection Cox regression model are shown in Table 2. The integer risk score, herein called the Taiwan AF score, which ranged from −2 to 15, was developed, and the calculation rules are shown in Table 3. An age group between 50 and 54 years was chosen as the reference group because the median age of the study population was 53 years. Figure 1 shows the distributions of Taiwan AF score of the study population.

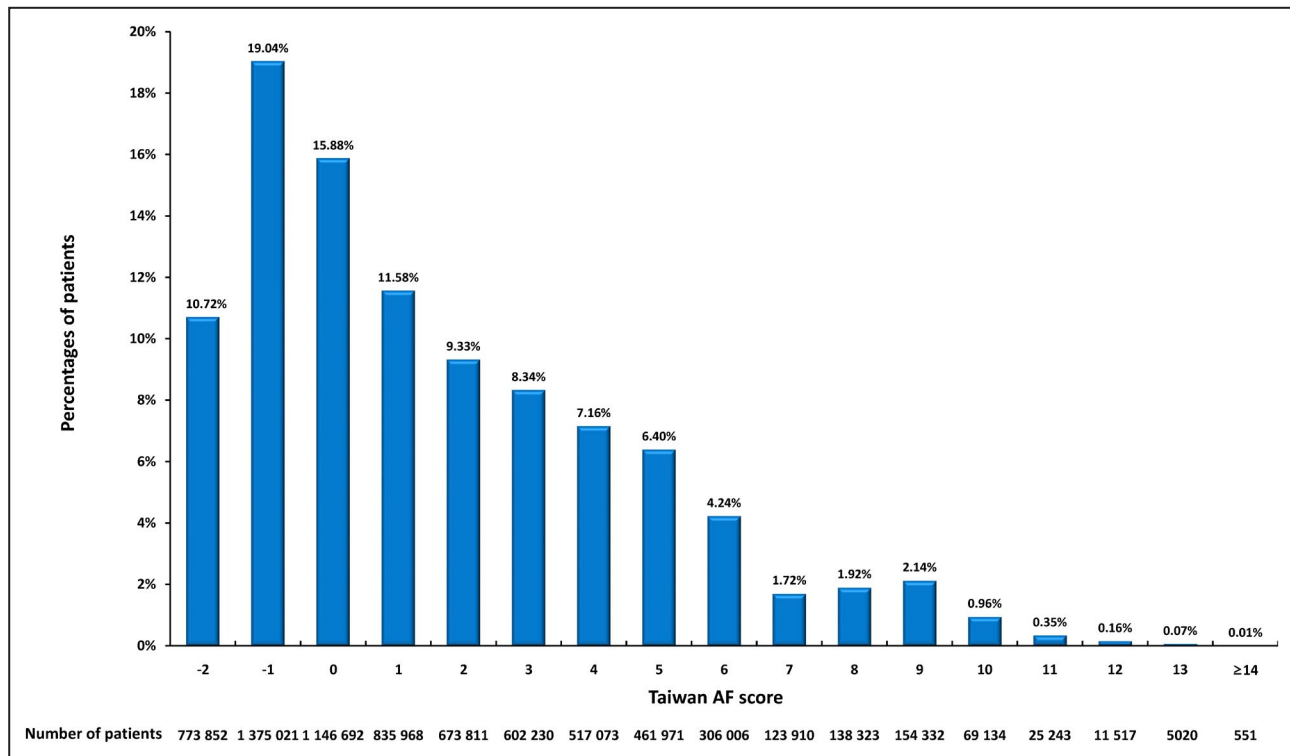
## Risk of Incident AF Stratified by Taiwan AF Score

The incidences of AF (%/year) of different Taiwan AF scores with different follow-up durations are shown in Table 4. After a 16-year follow-up, the risk of incident AF increased from 0.05%/year for patients with a score of −2 to 6.95%/year for those having a score  $\geq 14$ . Patients were classified as low risk for score −2 to 3, intermediate risk for score 4 to 9, and high risk for score  $\geq 10$ . The annual risks of AF of different scores and different risk categories based on the data of 16-year follow-up are shown in Figure 2. The annual risks of incident AF were 0.21%/year, 1.31%/year, and 3.37%/year for the low-risk, intermediate-risk, and high-risk groups, respectively. The cumulative incidence curves of incident AF of the low-risk, intermediate-risk, and high-risk groups are shown in Figure 3. The 2-year risks of AF were 0.08%, 2.03%, and 7.82% for the low-risk, intermediate-risk,

**Table 3. Calculations of Taiwan AF Score**

Variables	Score
Age, y	
40–44	−2
45–49	−1
50–54	0
55–59	1
60–64	2
65–69	3
70–74	4
75–79	5
>80	8
Male sex	1
Hypertension	1
Heart failure	2
Coronary artery disease	1
ESRD	1
Alcoholism	1
Total score	−2 to 15

AF indicates atrial fibrillation; and ESRD, end-stage renal disease.



**Figure 1.** The distributions of Taiwan AF score of the study population.

Taiwan AF score ranged from  $-2$  to  $15$  with a median value of  $1$  (interquartile range,  $-1$  to  $5$ ). AF indicates atrial fibrillation.

and high-risk groups, respectively. The 4-year risks of AF were  $0.31\%$ ,  $4.12\%$ , and  $13.58\%$  for the low-risk, intermediate-risk, and high-risk groups, respectively. The 10-year risks of AF were  $1.26\%$ ,  $11.13\%$ , and  $27.87\%$  for the low-risk, intermediate-risk, and high-risk groups, respectively. Compared with low-risk patients, the HRs of incident AF were  $5.78$  (95% CI,  $3.76$ – $7.75$ ) for the intermediate-risk group and  $8.94$  (95% CI,  $6.47$ – $10.80$ ) for the high-risk group.

### Discrimination and Calibration of the Taiwan AF Score in the Prediction of AF

The AUROCs of the Taiwan AF score in the prediction of incident AF after different follow-up durations are shown in Table 5. The AUROCs of the Taiwan AF scores are  $0.857$  (95% CI,  $0.855$ – $0.860$ ) for the 1-year follow-up,  $0.825$  (95% CI,  $0.824$ – $0.826$ ) for the 5-year follow-up,  $0.797$  (95% CI,  $0.796$ – $0.798$ ) for the 10-year follow-up, and  $0.756$  (95% CI,  $0.755$ – $0.757$ ) for the 16-year follow-up, which were all higher than that of other scoring schemes (all DeLong  $P$  values  $<0.001$ ; Table S2). Receiver operating characteristic curves of the Taiwan AF score in the prediction of incident AF are shown in Figure S1. The model was validated internally by bootstrap with AUROCs of  $0.862$  (95% CI,  $0.860$ – $0.863$ ) for the 1-year follow-up,  $0.833$  (95% CI,  $0.831$ – $0.835$ ) for the 3-year follow-up,  $0.830$  (95% CI,

$0.827$ – $0.832$ ) for the 5-year follow-up,  $0.815$  (95% CI,  $0.814$ – $0.816$ ) for the 7-year follow-up,  $0.795$  (95% CI,  $0.793$ – $0.797$ ) for the 10-year follow-up, and  $0.755$  (95% CI,  $0.753$ – $0.757$ ) for the 16-year follow-up (Table 5). The AUROCs of the Taiwan AF score in the prediction of incident AF stratified by sex and age are shown in Table S3 and Table S4, respectively.

The predicted numbers of AF events in the 16-year risk deciles were similar to the observed events (Grønnesby-Borgan chi-square= $9.54$ ;  $P=0.388$ ). Figure S2 depicts the observed and expected risks of AF by decile of predicted risk, and the calibration was adequate (Grønnesby-Borgan chi-square= $13.8$ ;  $P=0.129$ ).

## DISCUSSION

In this nationwide cohort study, we identified clinical risk factors for new-onset AF among  $7\ 220\ 654$  patients with  $438\ 930$  incident AF after a 16-year follow-up, and the Taiwan AF score was derived accordingly. To the best of our knowledge, it was the largest study aiming to develop a clinical risk scheme for the predictions of incident AF, especially for Asian patients.

### Scoring Schemes for the Prediction of AF for Non-Asian Patients

Several prediction schemes for AF has been proposed for non-Asian patients, such as the FHS, ARIC,

**Table 4. Incidence of AF Stratified by Taiwan AF Score After Different Follow-Up Durations**

Follow-Up, y	Annual Risk (%/y) of AF Stratified by Taiwan AF Score																
	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	≥14
1	0.02	0.03	0.05	0.09	0.15	0.23	0.38	0.61	1.04	2.18	1.83	1.65	2.68	5.10	9.80	11.67	11.10
3	0.02	0.04	0.06	0.12	0.19	0.31	0.50	0.78	1.19	2.03	2.07	2.06	2.85	4.54	8.01	8.89	9.24
5	0.02	0.04	0.07	0.13	0.21	0.34	0.54	0.83	1.22	1.98	2.07	2.10	2.81	4.26	7.17	7.88	8.04
7	0.03	0.05	0.08	0.15	0.24	0.38	0.59	0.89	1.29	1.96	2.11	2.15	2.79	4.10	6.72	7.38	7.71
10	0.03	0.06	0.10	0.17	0.28	0.44	0.66	0.98	1.36	1.98	2.18	2.20	2.79	3.94	6.38	6.90	7.48
12	0.04	0.06	0.11	0.19	0.31	0.48	0.72	1.04	1.42	2.01	2.21	2.24	2.79	3.88	6.21	6.72	7.36
16	0.05	0.09	0.15	0.25	0.40	0.59	0.86	1.19	1.54	2.08	2.26	2.27	2.77	3.78	6.02	6.46	6.95

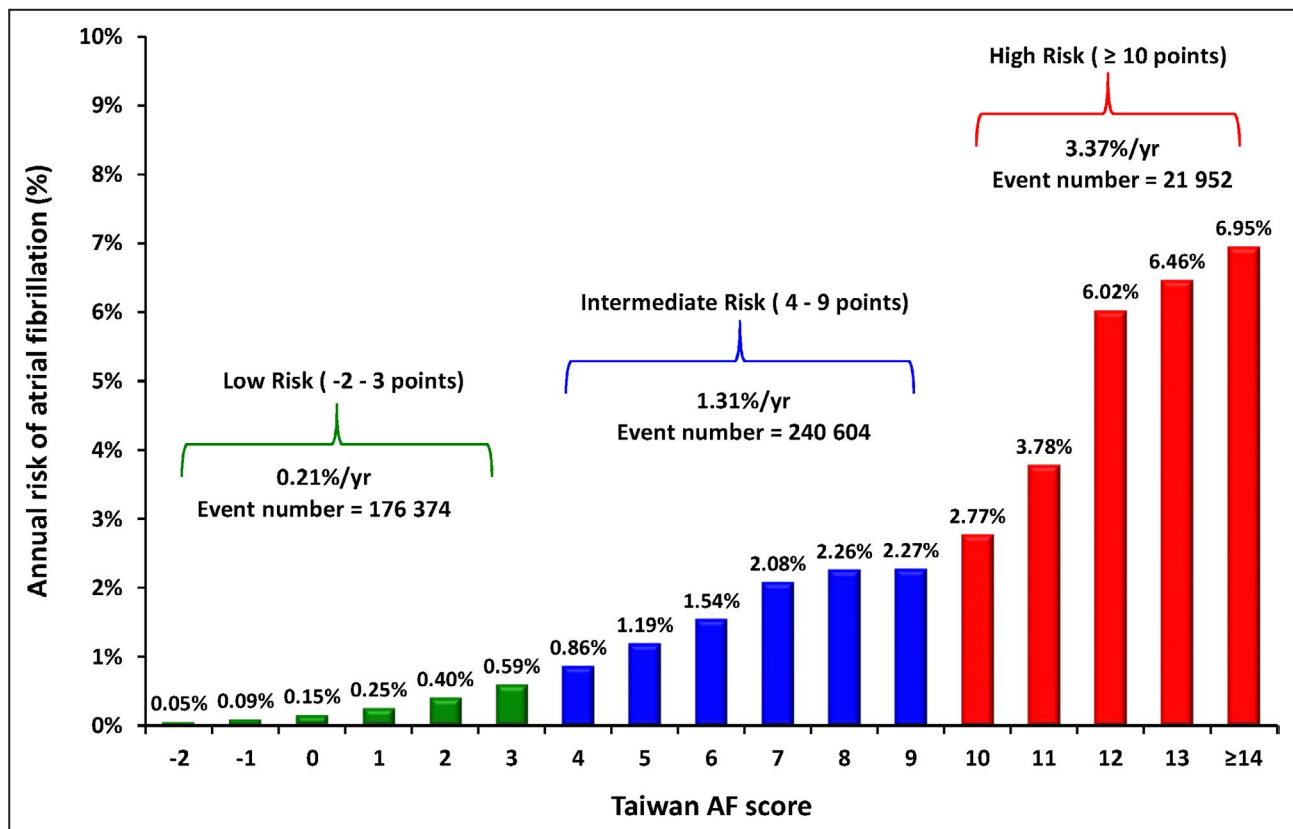
AF indicates atrial fibrillation.

and CHARGE-AF scores, with the AUROCs around 0.77 to 0.78.<sup>6-8</sup> The AF prediction score derived from the FHS (4764 participants with 457 incident AF), including age, body mass index, systolic blood pressure, hypertension medications, PR interval, age when cardiac murmur developed, and age of heart failure, had an AUROC of 0.78.<sup>6</sup> The additional incorporation of echocardiographic measurements into the FHS scheme only slightly improved the C statistic from 0.78 to 0.79 without the improvement in risk reclassification ( $P=0.18$ ).<sup>6</sup> The CHARGE-AF scheme was developed using individual-level data from 3 large cohorts in the United States (ARIC study, the Cardiovascular Health Study, and the FHS), including 18 556 men and women (19% Black participants, 81% White participants) with 1186 incident AF cases in the derivation cohorts and 585 in the validation cohorts.<sup>8</sup> The variables included in the CHARGE-AF model were age, race, height, weight, systolic and diastolic blood pressure, current smoking, use of antihypertensive medication, diabetes mellitus, and history of myocardial infarction and heart failure, which result in an AUROC around 0.765, and the addition of variables from the ECG did not improve the overall model discrimination.<sup>8</sup> The findings from the FHS and CHARGE-AF scores may suggest that a scoring scheme based on clinical factors without detailed information from the ECG and echocardiogram may be good enough for the prediction of incident AF in the clinical setting of daily practice.

Interestingly, the AUROC of the FHS score in the prediction of incident AF was only around 0.65 for Black patients in the ARIC cohort, which seems to be lower than that in the FHS cohort (AUROC=0.78).<sup>7</sup> It is reasonable that the FHS score performs better in the original cohort from which the scoring scheme was derived. Another possibility is that a scoring scheme for the prediction of incident AF developed for White patients may not be applied well to other races. Therefore, these preexisting scoring models may not predict incident AF for Asian patients as well as they did for non-Asian patients.

### Taiwan AF Score and the Prediction of Incident AF

In the present study, we developed an AF prediction scheme (Taiwan AF score) for Asian patients using a Taiwan nationwide database with 7 220 654 patients and 438 930 incident AF events. The AUROCs of the Taiwan AF scores are 0.857 for the 1-year follow-up, 0.825 for the 5-year follow-up, 0.797 for the 10-year follow-up, and 0.756 for the 16-year follow-up, which were higher than that of other scoring schemes, including the CHADS<sub>2</sub>, CHA<sub>2</sub>DS<sub>2</sub>-VASc, and C2HEST scores. The Taiwan AF scheme included age, sex,



**Figure 2.** The annual risks of AF of different Taiwan AF scores and different risk categories based on the data of a 16-year follow-up.

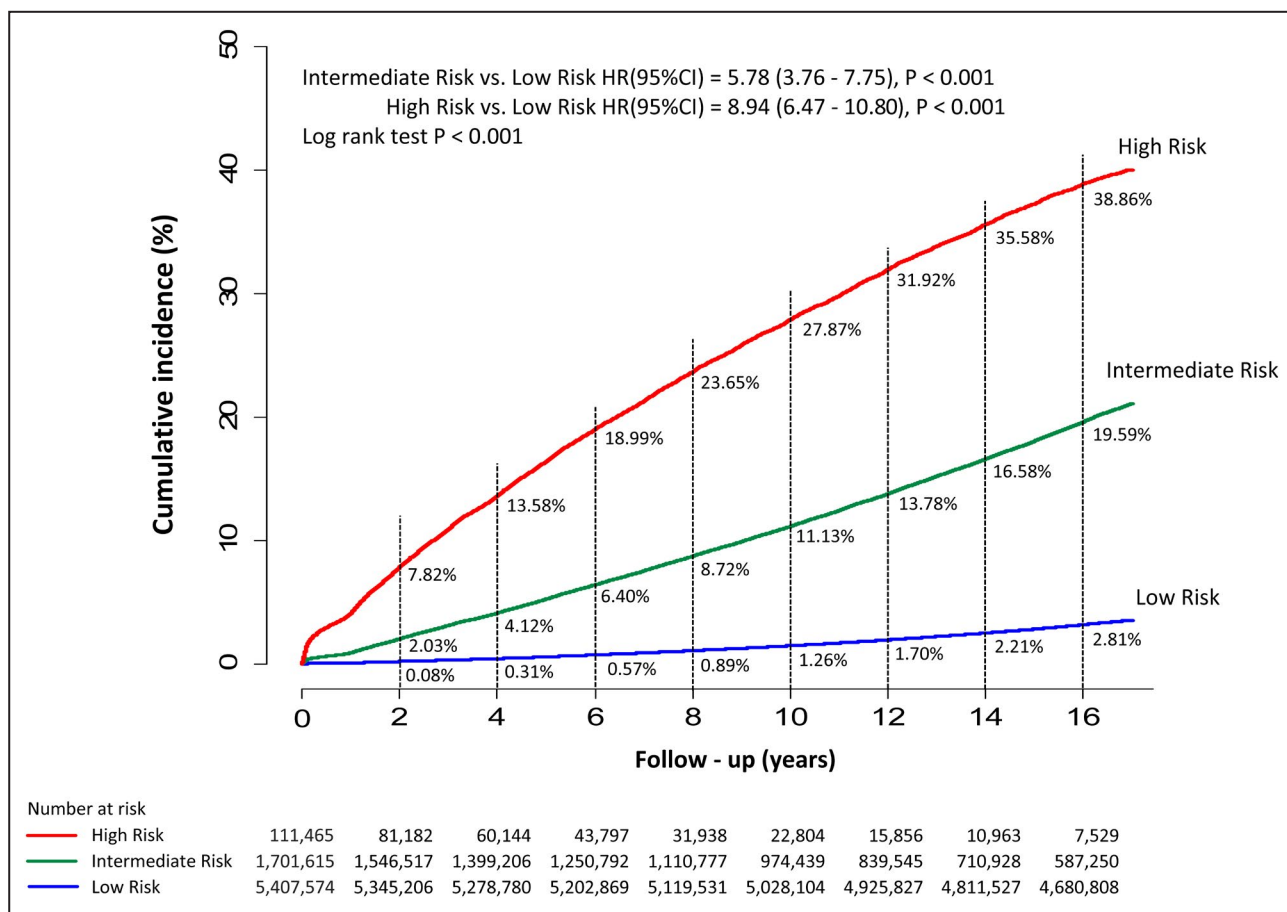
After a 16-year follow-up, the risk of incident AF increased from 0.05%/year for patients with a score of  $-2$  to 6.95%/year for those having scores  $\geq 14$ . Patients were classified as low risk for scores  $-2$  to 3, intermediate risk for scores 4 to 9, and high risk for scores  $\geq 10$ . The annual risks of incident AF were 0.21%/year, 1.31%/year, and 3.37%/year for the low-risk, intermediate-risk, and high-risk groups, respectively. AF indicates atrial fibrillation.

and important clinical comorbidities that were significantly associated with the occurrence of incident AF. Because the Taiwan AF score is based on clinical factors with no need for ECG, echocardiogram, and laboratory evaluations, it is easy to calculate and apply in the clinical practice and allows for good identification of patients at risk for incident AF. Compared with other previously published schemes developed among the selected cohorts,<sup>6-9</sup> the present study used a nationwide Taiwanese cohort that consists of detailed healthcare data of  $>99\%$  of Taiwan's population and therefore may be less likely to have significant selection bias. A high Taiwan AF score suggesting a higher risk of incident AF may justify more aggressive and frequent evaluations and detections of AF, especially for patients with symptoms or after an ischemic stroke.

### Study Limitations

There were several limitations of the present study. First, some personal information such as smoking habit, physical activity, and body mass index was not

available from this nationwide registry. However, the goal of the present study was to provide a straightforward clinical scheme to estimate the risk of incident AF. Second, we were not able to compare the predictive accuracies of the Taiwan AF score to the FHS, ARIC, and CHARGE-AF scores because some variables (eg, blood pressure and body mass index) were not recorded in our database. As we discussed in the Discussion section, scoring models derived from 1 race may not perform well among other races, and the goal of the present study was to develop a scoring scheme specific for Asian patients. However, further studies are necessary to compare the predictive accuracy of the Taiwan AF score to these published scoring schemes. Third, the diagnoses of comorbidities and alcoholism were made on the basis of *ICD-9-CM* codes registered by physicians responsible for the care of the patients without further confirmations. Although the diagnostic accuracies of important comorbidities in the Taiwan NHIRD have been validated previously,<sup>12,13</sup> the accuracy of "alcoholism" defined using *ICD-9-CM* codes may not be as accurate as that



**Figure 3. The cumulative incidence curves of incident AF of the low-risk, intermediate-risk, and high-risk groups.** The 2-year risks of AF were 0.08%, 2.03%, and 7.82% for the low-risk, intermediate-risk, and high-risk groups, respectively. The 4-year risks of AF were 0.31%, 4.12%, and 13.58% for the low-risk, intermediate-risk, and high-risk groups, respectively. The 10-year risks of AF were 1.26%, 11.13%, and 27.87% for the low-risk, intermediate-risk, and high-risk groups, respectively. Compared with low-risk patients, the HRs of incident AF were 5.78 (95% CI, 3.76–7.75) for the intermediate-risk group and 8.94 (95% CI, 6.47–10.80) for the high-risk group. AF indicates atrial fibrillation; and HR, hazard ratio.

of comorbidities in the registry-based data set, and further external validation studies using different types of databases are necessary. Lastly, the present study was performed among Chinese patients, and whether our findings could be generalized to other Asian races remains uncertain.

### CONCLUSIONS

We developed a clinical prediction model, the Taiwan AF score, among 7 220 654 patients with 438 930 incident AF to assess the individual risk for Asian patients. The new score could help physicians to identify

**Table 5. AUROCs of Taiwan AF Score in the Prediction of AF After Different Follow-Up Durations**

Follow-up Duration, y	Taiwan AF Score		Taiwan AF Score, Bootstrap	
	AUROC (95% CI)	P Value	AUROC (95% CI)	P Value
1	0.857 (0.855–0.860)	<0.001	0.862 (0.860–0.863)	<0.001
3	0.838 (0.837–0.840)	<0.001	0.833 (0.831–0.835)	<0.001
5	0.825 (0.824–0.826)	<0.001	0.830 (0.827–0.832)	<0.001
7	0.814 (0.813–0.815)	<0.001	0.815 (0.814–0.816)	<0.001
10	0.797 (0.796–0.798)	<0.001	0.795 (0.793–0.797)	<0.001
12	0.786 (0.785–0.787)	<0.001	0.786 (0.784–0.787)	<0.001
16	0.756 (0.755–0.757)	<0.001	0.755 (0.753–0.757)	<0.001

AF indicates atrial fibrillation; and AUROC, area under the receiver operating characteristic curve.



Asian patients at high risk of AF in whom more aggressive and frequent detections and screenings may be considered.

## ARTICLE INFORMATION

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### Disclosures

None.

### Supplementary Material

Table S1–S4  
Figure S1–S2

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# **Supplemental Material**

**Table S1. ICD-9-CM codes used to define the comorbidities.**

Comorbidities	ICD-9-CM codes	Diagnostic criteria
Hypertension	401-405	Discharge or outpatient department $\geq 2$ times
Diabetes mellitus	250	Discharge or outpatient department $\geq 2$ times
Heart failure	428	Discharge diagnosis
Prior stroke	433, 434, 436	Discharge diagnosis
Coronary artery disease	411, 413, 414	Discharge or outpatient department $\geq 2$ times
Myocardial infarction	410, 412	Discharge diagnosis
Peripheral vascular diseases	443.8, 443.9	Discharge or outpatient department $\geq 2$ times
COPD	491, 492, 493.2, 496	Discharge or outpatient department $\geq 2$ times
Autoimmune diseases	279.4, 710, 714, 711.1, 711.2	Discharge or outpatient department $\geq 2$ times
Liver cirrhosis	571.2, 571.5	Discharge or outpatient department $\geq 2$ times
Hyperthyroidism	242	Discharge or outpatient department $\geq 2$ times
CKD	580-589	Discharge or outpatient department $\geq 2$ times
ESRD	585.6	Discharge or outpatient department $\geq 2$ times
Anemia	280-285	Discharge or outpatient department $\geq 2$ times
Alcoholism	305.00-305.03, 303.90-303.93	Discharge or outpatient department $\geq 2$ times

CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; ESRD = end-stage renal disease

**Table S2. AUCs of different scoring schemes in the prediction of AF after different follow-up durations.**

Follow up duration	C2HEST Score		CHA <sub>2</sub> DS <sub>2</sub> -VASc score		CHADS <sub>2</sub> score	
	AUC (95% CI)	P value	AUC (95% CI)	P value	AUC (95% CI)	P value
1 year	0.840 (0.837 – 0.843)	< 0.001	0.809 (0.806 – 0.812)	< 0.001	0.811 (0.808 – 0.814)	< 0.001
3 years	0.792 (0.790 – 0.794)	< 0.001	0.777 (0.775 – 0.779)	< 0.001	0.766 (0.764 – 0.767)	< 0.001
5 years	0.769 (0.767 – 0.770)	< 0.001	0.760 (0.758 – 0.761)	< 0.001	0.745 (0.743 – 0.746)	< 0.001
7 years	0.750 (0.748 – 0.751)	< 0.001	0.745 (0.743 – 0.746)	< 0.001	0.728 (0.726 – 0.729)	< 0.001
10 years	0.724 (0.723 – 0.725)	< 0.001	0.723 (0.722 – 0.724)	< 0.001	0.704 (0.703 – 0.705)	< 0.001
12 years	0.708 (0.706 – 0.709)	< 0.001	0.710 (0.709 – 0.711)	< 0.001	0.690 (0.689 – 0.691)	< 0.001
16 years	0.670 (0.669 – 0.671)	< 0.001	0.676 (0.675 – 0.677)	< 0.001	0.655 (0.654 – 0.656)	< 0.001

AF = atrial fibrillation; AUC = area under the receiver operating characteristic curve; CI = confidence interval

**Table S3. AUCs of Taiwan AF score in the prediction of AF after different follow-up durations for males and females.**

Follow up duration	Taiwan AF score			
	Males		Females	
	AUC (95%CI)	P value	AUC (95%CI)	P value
1 year	0.863 (0.861 - 0.864)	< 0.001	0.864 (0.862 - 0.867)	< 0.001
3 years	0.835 (0.833 - 0.837)	< 0.001	0.831 (0.829 - 0.833)	< 0.001
5 years	0.831 (0.829 - 0.833)	< 0.001	0.829 (0.827 - 0.831)	< 0.001
7 years	0.813 (0.812 - 0.814)	< 0.001	0.816 (0.813 - 0.818)	< 0.001
10 years	0.794 (0.792 - 0.796)	< 0.001	0.793 (0.792 - 0.795)	< 0.001
12 years	0.782 (0.78 - 0.785)	< 0.001	0.783 (0.781 - 0.786)	< 0.001
16 years	0.754 (0.752 - 0.757)	< 0.001	0.753 (0.751 - 0.755)	< 0.001

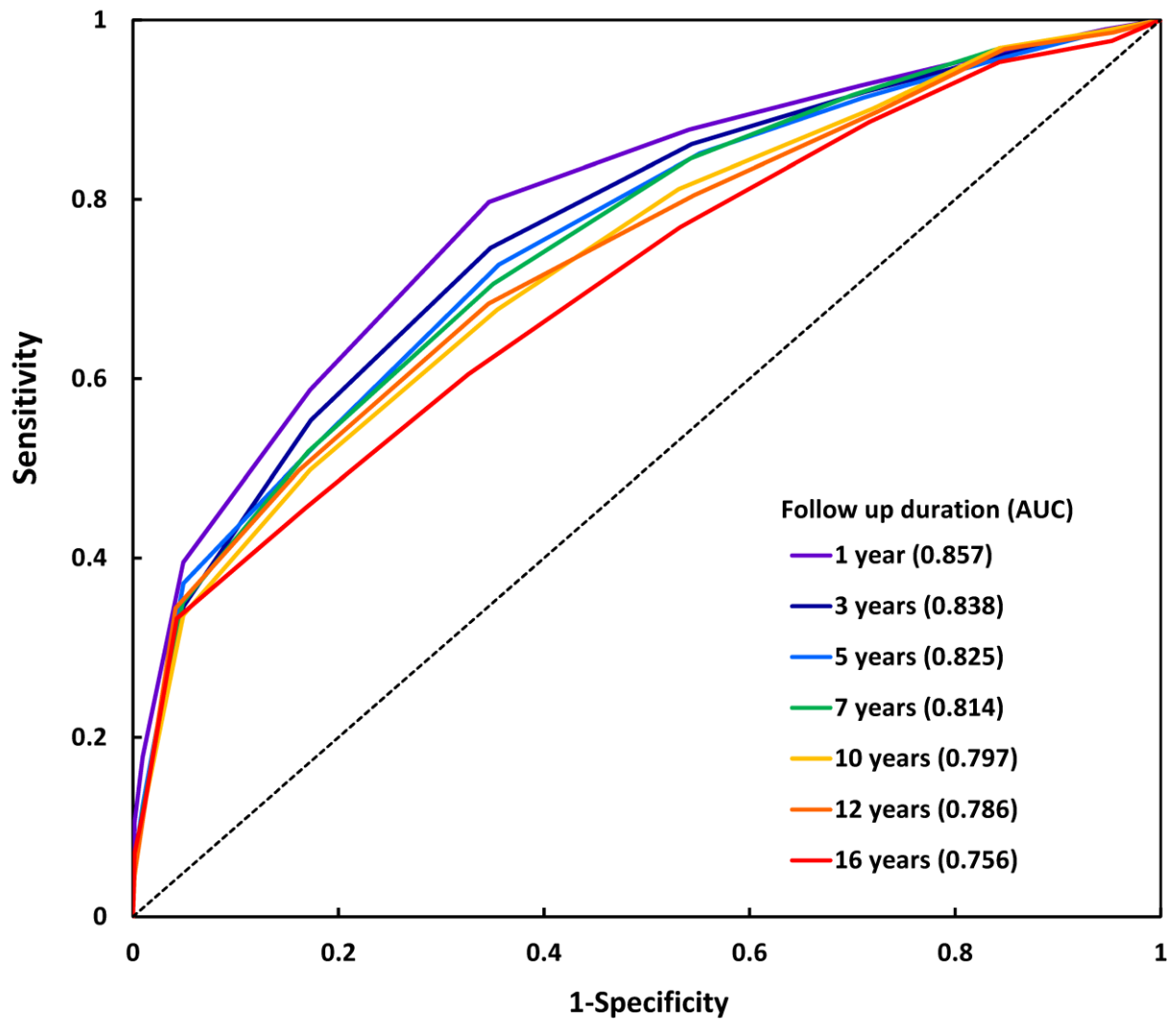
AF = atrial fibrillation; AUC = area under the receiver operating characteristic curve; CI = confidence interval

**Table S4. AUCs of Taiwan AF score in the prediction of AF after different follow-up durations in different age strata.**

Follow up duration	Taiwan AF score							
	<50 years		50-64 years		≥65 years		≥75 years	
	AUC (95%CI)	P value	AUC (95%CI)	P value	AUC (95%CI)	P value	AUC (95%CI)	P value
1 year	0.859 (0.858 - 0.861)	< 0.001	0.860 (0.858 - 0.862)	< 0.001	0.864 (0.862 - 0.867)	< 0.001	0.866 (0.864 - 0.869)	< 0.001
3 years	0.827 (0.825 - 0.829)	< 0.001	0.831 (0.829 - 0.833)	< 0.001	0.834 (0.832 - 0.836)	< 0.001	0.835 (0.833 - 0.837)	< 0.001
5 years	0.826 (0.824 - 0.828)	< 0.001	0.829 (0.827 - 0.831)	< 0.001	0.832 (0.83 - 0.835)	< 0.001	0.831 (0.829 - 0.834)	< 0.001
7 years	0.809 (0.806 - 0.811)	< 0.001	0.810 (0.808 - 0.812)	< 0.001	0.816 (0.813 - 0.818)	< 0.001	0.814 (0.811 - 0.817)	< 0.001
10 years	0.784 (0.782 - 0.786)	< 0.001	0.796 (0.794 - 0.799)	< 0.001	0.797 (0.795 - 0.799)	< 0.001	0.794 (0.792 - 0.796)	< 0.001
12 years	0.781 (0.779 - 0.783)	< 0.001	0.782 (0.779 - 0.786)	< 0.001	0.786 (0.783 - 0.789)	< 0.001	0.787 (0.784 - 0.790)	< 0.001
16 years	0.748 (0.746 - 0.749)	< 0.001	0.753 (0.751 - 0.756)	< 0.001	0.754 (0.752 - 0.756)	< 0.001	0.756 (0.754 - 0.757)	< 0.001

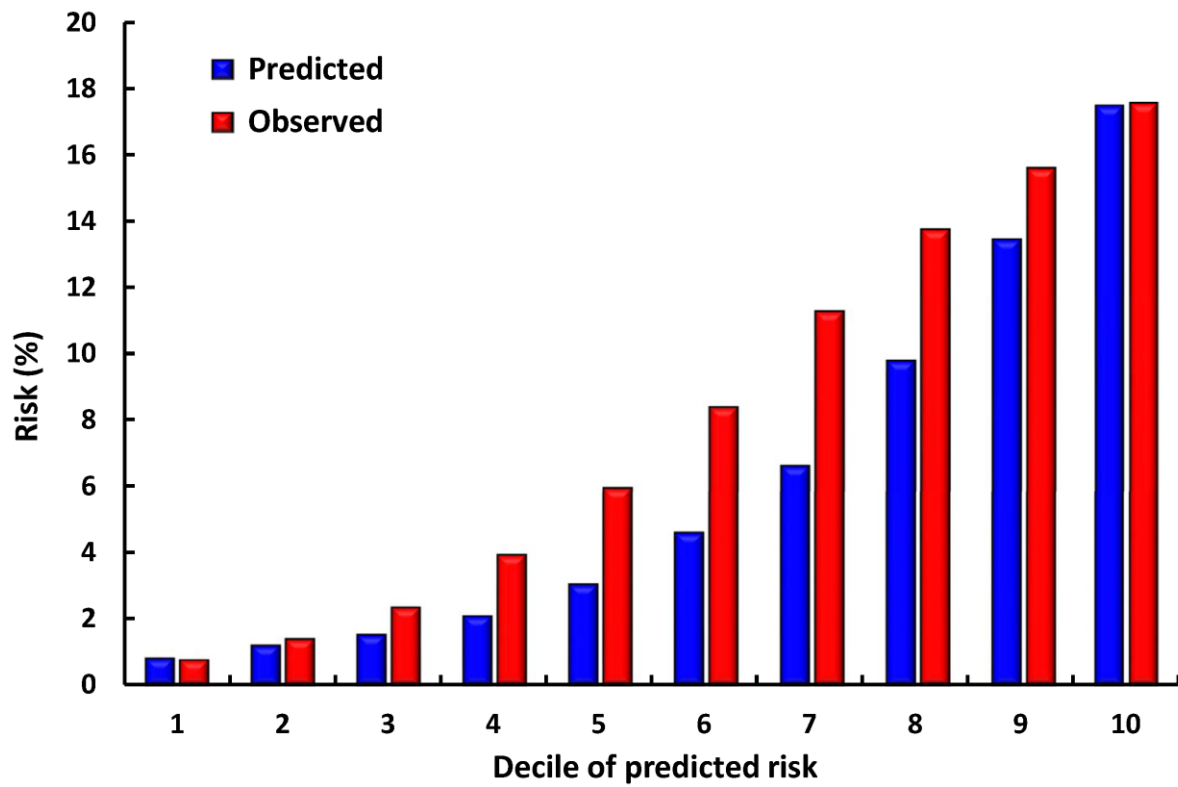
AF = atrial fibrillation; AUC = area under the receiver operating characteristic curve; CI = confidence interval

**Figure S1. ROC curves of Taiwan AF score in the prediction of incident AF.**



AF = atrial fibrillation; AUC = area under the receiver operating characteristic curve; ROC curve = receiver operating characteristic curve

**Figure S2. Observed and expected AF risks by decile of predicted risk.**



The predicted risk of AF in the 16-year risk deciles was similar to the observed risk and the calibration was adequate (Grønnesby-Borgan chi-square = 13.8,  $p = 0.129$ ).

AF = atrial fibrillation.