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General Cardiology

Validation of the Framingham General Cardiovascular Risk Score and Pooled Cohort Equations in a Community-Based Population: A Prospective Cohort Study Analysis 2006-2017

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Background: The 10-year atherosclerotic cardiovascular disease (ASCVD) risk — as assessed using the Framingham general cardiovascular risk score (FRS-CVD) or pooled cohort equations (PCE) — is commonly used in Western cohorts for the primary prevention of cardiovascular disease (CVD). However, the FRS-CVD and PCE have not been validated in Taiwanese cohorts.

Objectives: We aimed to validate the FRS-CVD and PCE for assessing the 10-year ASCVD risk using a Taiwanese community-based population.

Methods: We extracted patient data from the Landseed Integrated Outreaching Neighborhood Screening registry, a community-based prospective cohort study established in 2006. Cardiovascular events from 2006 to 2017 were determined from electronic medical records. The discriminative power and calibration of the FRS-CVD and PCE were evaluated.

Results: Overall, 5,139 subjects were analyzed; the 10-year follow-up rate was 99.6%. The mean age at baseline was 52.8 ± 13.1 years, and 44.6% of the subjects were male. In total, 430 of 4,631 (9.3%) and 227 of 4,022 (5.6%) of the FRS-CVD- and PCE-like cohorts, respectively, had ASCVD events. The calibration χ^2 of the FRS-CVD was 7.0267 ($p = 0.6343$) in males and 7.8845 ($p = 0.5458$) in females; the χ^2 of PCE was 13.007 ($p = 0.1623$) in males and 38.785 ($p < 0.001$) in females. The area under the receiver operating characteristic curve (AUROC) of the FRS-CVD was 0.76 (0.72-0.79) in males and 0.71 (0.67-0.74) in females; the AUROC of PCE was 0.68 (0.62-0.73) in males and 0.61 (0.56-0.67) in females.

Conclusions: Except for PCE in females, the FRS-CVD and PCE provided good calibration and modest discrimination in statin-naïve Taiwanese individuals without prior CVD.

Key Words: Atherosclerotic cardiovascular disease • Framingham general cardiovascular risk score • Pooled cohort equations • Primary prevention • Prospective cohort • Validation

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INTRODUCTION

Despite the progress in effective treatments, cardiovascular disease (CVD) remains the leading cause of death in Taiwan.[1] Atherosclerotic cardiovascular disease (ASCVD) encompasses coronary heart disease (CHD), cerebrovascular disease, and peripheral artery disease (PAD) due to the formation of atheroma in vascular beds. Heart failure (HF), the final common stage of ASCVD, is

Abbreviations

ACC	American College of Cardiology
AHA	American Heart Association
ASCVD	Atherosclerotic cardiovascular disease
AUROC	Area under the receiver operating characteristic curve
CHD	Coronary heart disease
CI	Confidence interval
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
EMR	Electronic medical records
FRS	Framingham risk score
FRS-CVD	Framingham general cardiovascular risk score
HDL-C	High-density lipoprotein cholesterol
HF	Heart failure
ICD	International Classification of Diseases
LDL-C	Low-density lipoprotein cholesterol
LIONS	Landseed Integrated Outreaching Neighborhood Screening
MI	Myocardial infarction
PAD	Peripheral artery disease
PCE	Pooled cohort equations
SBP	Systolic blood pressure

associated with high morbidity and mortality.[2] ASCVD and HF share common risk factors, including hypertension, dyslipidemia, diabetes, obesity, smoking, and an unhealthy lifestyle. Thus, modifying these risk factors is crucial for both primary and secondary prevention of ASCVD.[1-3]

Several risk prediction models have been developed to assess an individual's risk of ASCVD. The Framingham risk score (FRS) is the most well-known tool, and it has been widely used to predict the risk of CHD in middle-aged patients since 1998.[4] The Framingham Heart Study established the Framingham general cardiovascular risk score (FRS-CVD) to evaluate the risk of developing all types of CVD in 2008.[5] In addition, the 2013 and 2019 American College of Cardiology (ACC) and American Heart Association (AHA) guidelines for primary prevention released pooled cohort equations (PCE) to guide blood pressure and lipid treatments.[6,7] However, all of these tools were derived from studies of Western cohorts, and validation of these risk models in Asian populations has revealed inconsistencies with the original cohorts.[8-16] The lack of local epidemiologic surveys led to changes in the Taiwanese guidelines for dyslipidemia and hypertension published in 2022, which recommend the number of ASCVD risk factors that should be evaluated when making treatment decisions, rather than the 10-year ASCVD risk calculation.[17,18]

Thus, we conducted the present study to (i) determine the 10-year incidence of ASCVD and its components, and (ii) validate the discriminative ability and calibration scores of the FRS-CVD and PCE to predict the risk of ASCVD using a large, prospective, community-based cohort in northern Taiwan.

METHODS

Study cohort

The Landseed Integrated Outreaching Neighborhood Screening (LIONS) community-based cohort study was established by Landseed International Hospital in Taiwan in 2006 to prospectively investigate chronic diseases and relevant risk factors. The design and implementation of the LIONS study have been previously described in depth.[19] Participants older than 30 were randomly selected using a probability-proportional-to-size sampling method from registered households in the Pingzhen district of Taoyuan City, Taiwan. The main ethnic groups in this cohort were Hakka, Minnan, and Chinese mainlander. The participants underwent on-site health screening examinations for four types of cancer and other common diseases (e.g., type 2 diabetes mellitus, hypertension, cancer, hyperlipidemia, osteoporosis, gout) as well as a face-to-face interview. A questionnaire survey was completed and blood samples were collected at enrollment and annual follow-up visits. The definitions of hypertension and diabetes were blood pressure > 140/90 mmHg or participants taking anti-hypertensive agents at baseline, and fasting glucose > 126 mg/dL or the use of hypoglycemic agents at baseline, respectively. The lipid profile of each participant was collected at baseline for analysis.

Study population

In this study, we included participants aged 30-74 and 40-79 years for analysis using the FRS-CVD and PCE, respectively. Individuals with previous CVD, those who had taken statins, and those with a serum low-density lipoprotein cholesterol (LDL-C) level > 190 mg/dL at baseline were excluded. According to the 2019 ACC/AHA guidelines for the primary prevention of CVD, patients

with an LDL-C level > 190 mg/dL are at high risk, and statin therapy is recommended.[6] In the current study, we aimed to validate the FRS-CVD and PCE in low- to intermediate-risk populations. The study started in 2006, and all participants were followed up for at least 10 years or censored by cardiovascular events. Individuals who missed a follow-up appointment were excluded from the study. We obtained ethical approval from the Institutional Review Board of Landseed International Hospital (LSHIRB 18-038-B1).

Study endpoint

The study endpoint was defined as the first diagnosis of CVD in an inpatient or at least two outpatient electronic medical records (EMR) of Landseed International Hospital during follow-up. Incident cardiovascular events were categorized based on the International Classification of Diseases Ninth (ICD-9) and Tenth Revision (ICD-10). The ICD codes used for analysis of CVD were: myocardial infarction (MI) ICD-9 410-411 and ICD-10 I20-24; stroke ICD-9 430-438 and ICD-10 G45-46, I60-63, I67, I69; HF ICD-9 402, 425, 428-429 and ICD-10 I11, I13, I42, I50, J81; PAD ICD-9 440, 441, 443-444, 447 and ICD-10 I70, I73-74, I76. Total CVD, the predicted outcome of the FRS-CVD, was defined as any fatal or nonfatal MI, stroke, angina, PAD, or HF events. Hard ASCVD, the predicted outcome of the PCE, was defined as any fatal or nonfatal MI or stroke event. We defined prior CVD as any history of MI, stroke, HF, or PAD.

Statistical analysis

Data were analyzed using SPSS version 25.0.0.2 (SPSS, Inc., Chicago, IL, USA) and R version 3.4.2 (R Foundation for Statistical Computing, Vienna, Austria). Non-normally distributed data (as determined using the Kolmogorov-Smirnov test) were natural-logarithmically transformed to obtain near normality before analysis. Values are reported as mean ± standard deviation or median with interquartile range, as appropriate.

We used Cox models of the FRS-CVD[5] and PCE[7] (for non-Hispanic white individuals) to calculate the 10-year risks of CVD and ASCVD, respectively, for Taiwanese subjects. We analyzed observed cardiovascular events using sex-specific Kaplan-Meier curves. The subjects were grouped into deciles of predicted CVD or ASCVD risk within 10 years of follow-up. The predictive accuracy of the FRS-CVD and PCE were evaluated using calibration, which was defined as the similarity between the observed events and predicted 10-year incident risk of CVD or ASCVD. We performed calibration by plotting the predicted 10-year risks against the observed incident CVD or ASCVD events and calculating the calibration chi-square statistic (χ^2); a p-value > 0.05 was considered to indicate good calibration. In addition, we assessed the discriminative ability of each cardiovascular risk model by measuring the area under the receiver operating characteristic curve (AUROC) using the predicted CVD or ASCVD risks estimated by each prediction model.

RESULTS

A total of 6,219 participants were eligible for the original LIONS cohort in 2006. On enrollment, we excluded 388 participants who had prior CVD, 483 who had taken statins, and 190 with serum LDL-C levels > 190 mg/dL. We also excluded 19 participants at follow-up because of missing data; therefore, 5,139 participants (10-year follow-up rate of 99.6%) were eligible for this analysis (Figure 1). In total, 4,631 participants aged 30-74 years were selected for FRS-CVD analysis, and 4,022 participants aged 40-79 years were chosen for PCE analysis. The median follow-up periods in the FRS-CVD and

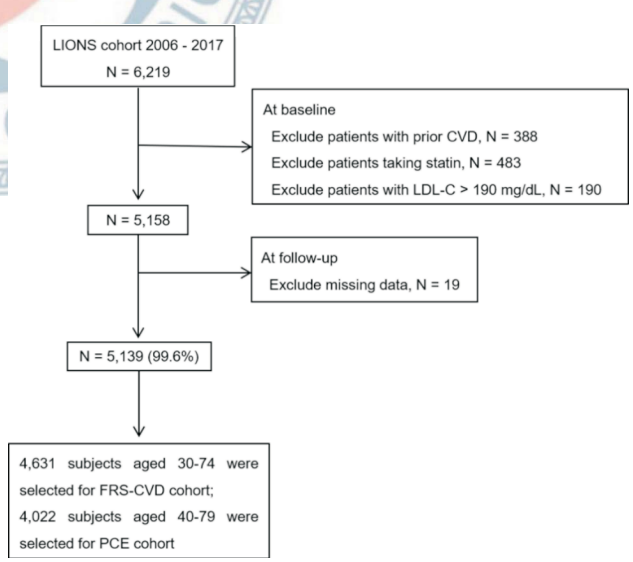


Figure 1. *Study design. CVD, cardiovascular disease; FRS-CVD, Framingham general cardiovascular risk score; LDL-C, low-density lipoprotein cholesterol; LIONS, Landseed Integrated Outreaching Neighborhood Screening; PCE, pooled cohort equations.*

PCE cohorts were 10.8 (interquartile range 9.6-11.6) and 11.0 (interquartile range 9.7-11.6) years, respectively. Table 1 summarizes the baseline characteristics of the study cohort in 2006. The mean age of the entire cohort was 52.8 ± 13.1 years, and 44.3% were male. One-third of the study participants had hypertension (mean blood pressure 124.8 ± 20.0 over 75.5 ± 12.2 mmHg), 8.3% had diabetes mellitus, and the mean serum total cholesterol and triglyceride levels were 198.0 ± 33.2 and 126.5 ± 133.5 mg/dL, respectively. Compared to the participants without incident cardiovascular events, those who had incident cardiovascular events were older, more likely to be male, had higher incidence rates of hypertension and diabetes mellitus, higher body mass index, systolic blood pressure (SBP), diastolic blood pressure (DBP) and serum fasting glucose, and lower serum high-density lipoprotein cholesterol at baseline.

After 10 years of follow-up, 545 (11%) participants had had an incident cardiovascular event, of whom 0 and 98 had started to use statin and antihypertensive therapies before the event, respectively. In the group used to evaluate the FRS-CVD, 430 of 4,631 participants (9.1/1000 person-years) were censored for the primary outcome. In the group used to assess PCE, 227 of 4,022 participants (5.5/1000 person-years) were censored for the primary outcome (Table 2). As expected, males had a higher incidence of cardiovascular events than females in both study groups (9.7 vs. 8.7 per 1000 person-years in the FRS-CVD group; 7.0 vs. 4.4 per 1000 person-years in the PCE group). Interestingly, stroke and HF accounted for the majority of cardiovascular events in the FRS-CVD group, compared to stroke in the PCE group (Table 3). In the FRS-CVD group, females tended to have a higher incidence of heart failure than males (118 of 2,747 vs. 65 of 1,884; Table 3).

The observed and predicted event rates based on both the FRS-CVD and PCE for the decile groups are compared in Figure 2. Table 4 presents the discriminative power and calibration scores of each cardiovascular risk prediction model. The AUROC values of the FRS-CVD were 0.76 (0.72-0.79) and 0.71 (0.67-0.74) for males and females, compared to 0.68 (0.62-0.73) and 0.61 (0.56-0.67) for PCE, respectively. The calibration scores were optimal for both models, with the exception of PCE for females. The calibration χ^2 scores of the FRS-CVD were 7.0267 for males (p = 0.6343) and 7.8845 for females (p

Table 1. Clinical characteristics of the study population at baseline

Clinical characteristics	Original cohort				FRS-CVD cohort				PCE cohort			
	Total (N = 5,139)	With CV events (N = 545)	Without CV events (N = 4,594)	p value	Total (N = 4,631)	With CV events (N = 430)	Without CV events (N = 4,201)	p value	Total (N = 4,022)	With CV events (N = 227)	Without CV events (N = 3,795)	p value
Age (years)	52.8 ± 13.1	61.1 ± 13.1	51.8 ± 12.7	< 0.001	50.0 ± 10.1	56.2 ± 10.0	49.3 ± 9.9	< 0.001	54.8 ± 9.8	59.4 ± 11.1	54.6 ± 9.6	< 0.001
Male sex (%)	2,293 (44.6)	268 (49.2)	2,025 (44.1)	0.024	1,884 (40.7)	187 (43.5)	1,697 (40.4)	0.214	1,712 (42.6)	122 (53.7)	1,590 (41.9)	< 0.001
Body mass index (kg/m^2)	24.3 ± 3.6	25.2 ± 3.8	24.2 ± 3.5	< 0.001	24.3 ± 3.6	25.2 ± 3.9	24.2 ± 3.6	< 0.001	24.5 ± 3.5	24.6 ± 3.5	24.5 ± 3.5	0.561
Fasting glucose (mg/dL)	91.5 ± 26.1	96.0 ± 30.4	91.0 ± 25.5	< 0.001	90.9 ± 25.5	95.0 ± 30.9	90.5 ± 24.8	0.004	92.8 ± 27.4	98.3 ± 37.6	92.5 ± 26.6	0.023
Total cholesterol (mg/dL)	198.0 ± 33.2	196.8 ± 32.9	198.0 ± 33.2	0.373	198.8 ± 33.2	198.5 ± 32.7	198.8 ± 33.2	0.816	200.4 ± 32.9	195.3 ± 33.0	200.7 ± 32.9	0.016
HDL-C (mg/dL)	59.7 ± 15.4	57.8 ± 15.5	59.9 ± 15.4	0.002	60.0 ± 15.4	58.1 ± 15.1	60.2 ± 15.4	0.007	59.8 ± 15.5	57.3 ± 15.1	60.0 ± 15.5	0.010
LDL-C (mg/dL)	120.2 ± 29.0	120.2 ± 28.2	120.2 ± 29.1	0.953	120.6 ± 29.1	121.3 ± 28.7	120.5 ± 29.2	0.616	122.4 ± 28.7	119.3 ± 27.7	122.6 ± 28.8	0.099
Triglycerides (mg/dL)	126.5 ± 133.5	129.8 ± 108.0	126.1 ± 136.3	0.542	127.7 ± 138.3	134.1 ± 117.7	127.0 ± 140.3	0.317	127.3 ± 118.5	130.8 ± 93.7	127.1 ± 119.8	0.655
SBP (mmHg)	124.8 ± 20.0	134.5 ± 21.6	123.6 ± 19.5	< 0.001	123.2 ± 19.20	131.7 ± 21.4	122.3 ± 18.7	< 0.001	126.0 ± 19.9	132.9 ± 22.2	125.6 ± 19.7	< 0.001
DBP (mmHg)	75.5 ± 12.2	78.9 ± 14.1	75.1 ± 11.9	< 0.001	75.7 ± 12.1	79.9 ± 13.7	75.3 ± 11.9	< 0.001	76.3 ± 12.3	79.6 ± 14.1	76.1 ± 12.2	< 0.001
Current smoker (%)	915 (17.8)	97 (17.8)	818 (17.8)	0.993	829 (17.9)	83 (19.3)	746 (17.8)	0.429	670 (16.7)	46 (20.3)	624 (16.4)	0.134
Diabetes mellitus (%)	428 (8.3)	103 (18.9)	325 (7.1)	< 0.001	338 (7.3)	73 (17.0)	265 (6.3)	< 0.001	362 (9.0)	42 (18.5)	320 (8.4)	< 0.001
Hypertension (%)	1,615 (31.4)	240 (44.0)	1,375 (29.9)	< 0.001	1,362 (29.4)	175 (40.7)	1,187 (28.3)	< 0.001	1,281 (31.8)	96 (42.3)	1,185 (31.2)	0.001

CV, cardiovascular; DBP, diastolic blood pressure; FRS-CVD, Framingham general cardiovascular risk score; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PCE, pooled cohort equations; SBP, systolic blood pressure.

Table 2. Observed incidence of cardiovascular events in the study groups

	Total	Males	Females
Framingham general cardiovascular risk score	4,631	1,884	2,747
Total number of person-years	47,015	19,073	27,942
Number of incident cases of CVD	430	187	243
Cumulative CVD incidence (per 1000 person-years)	9.1	9.7	8.7
Pooled cohort equations	4,022	1,712	2,310
Total number of person-years	41,270	17,476	23,794
Number of incident cases of CVD	227	122	105
Cumulative CVD incidence (per 1000 person-years)	5.5	7.0	4.4

Abbreviation as Figure 1.

Table 3. Distribution of observed cardiovascular events in the study groups

Endpoints	FRS-CVD (30-74 years) (N = 4,631)		PCE (40-79 years) (N = 4,022)	
	Males (n = 1,884)	Females (n = 2,747)	Males (n = 1,712)	Females (n = 2,310)
Myocardial infarction	29 (1.5%)	18 (0.7%)	27 (1.6%)	18 (0.8%)
Stroke	74 (3.9%)	85 (3.1%)	95 (5.5%)	87 (3.8%)
Heart failure	65 (3.5%)	118 (4.3%)	N/A	N/A
Peripheral artery disease	19 (1.0%)	22 (0.8%)	N/A	N/A

N/A, not available; the others as Figure 1.

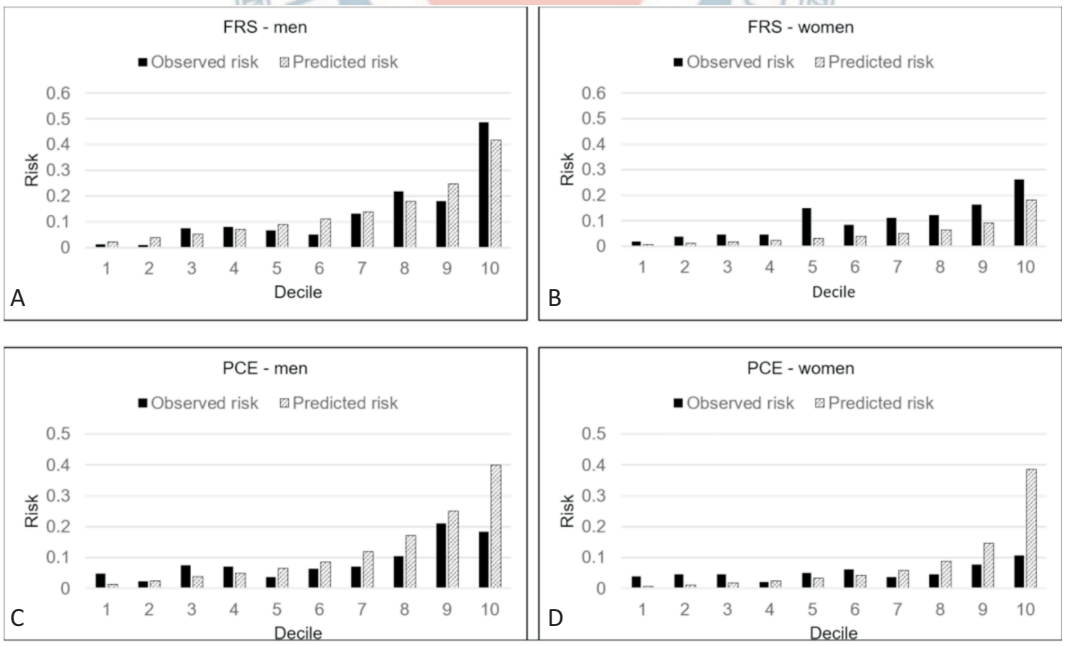


Figure 2. *Comparison of the observed vs. predicted cardiovascular risks for the cohort stratified by sex and prediction model. (A) men, FRS model; (B) women, FRS model; (C) men, PCE model; and (D) women, PCE model. FRS, Framingham risk score; PCE, pooled cohort equations.*

= 0.5458). The calibration χ^2 scores of PCE were 13.007 for males (p = 0.1623) and 38.785 for females (p < 0.001), respectively. A significant degree of miscalibration was observed for females in the PCE group.

The FRS-CVD model exhibited different predictive power in males and females. The average predicted risk and average observed risk were comparable for males (13.61 vs. 13.13%); however, the FRS-CVD model underestimated the risk of CVD for females (5.19 vs. 10.43%). In contrast, the PCE model overestimated the risk of

hard CVD in both males and females, with average predicted risks of 12.18% [95% confidence interval (CI) 11.61-12.75] for males and 8.19% (95% CI 7.70-8.68) for females, compared to average observed risks of 8.91% (95% CI 8.79-9.03) and 5.35% (95% CI 5.30-5.40), respectively (Table 4). A subgroup analysis by age (< 60 vs. ≥ 60 years) showed that the PCE model also overestimated the risk in the elderly (Supplementary Table 1).

DISCUSSION

Numerous risk prediction models have been proposed with the aim of stratifying patients into different CVD risk groups. The FRS is commonly used to predict the risk of CHD, and D'Agostino et al. expanded the algorithm to calculate the 10-year general CVD risk.[5] The ACC/AHA guidelines for the assessment of cardiovascular risk introduced race- and sex-specific PCE as the default ASCVD risk prediction calculator for adults aged 40 to 75 years.[6,7] However, both models were derived from Western cohorts and have not been validated in a Taiwanese population. This is the first community-based prospective cohort study to externally validate the FRS-CVD and PCE based on discriminative ability and calibration analyses in Taiwanese adults. We demonstrated that both the FRS-CVD and PCE had good calibration scores, except for PCE in females (Central Illustration). The FRS-CVD underestimated the risk of CVD in females, and PCE overestimated the risk of ASCVD in males and females. Both risk models had modest discriminative ability in our cohort.

In this community-based cohort, the data were collected from 2006 and the participants mainly lived in Taoyuan. Some selection bias may have resulted from the exclusion of participants who had taken statins, however they were probably not a high-risk population by definition. We believe it was subtle because that the distribution of our cohort was similar to previous population surveys.[20,21] The prevalence of diabetes mellitus in our study was 8.3%, compared to 7.45% reported in patients aged 20-79 years in Taiwan in 2006 in the previous study.[20] The difference may be due to undiagnosed diabetes in the general population. On the other hand, 45% of this cohort were male. In 2006, population statistics from the Taiwan government showed that males accounted for 49.87% of people aged 30-79 years living in Taoyuan County.[21]

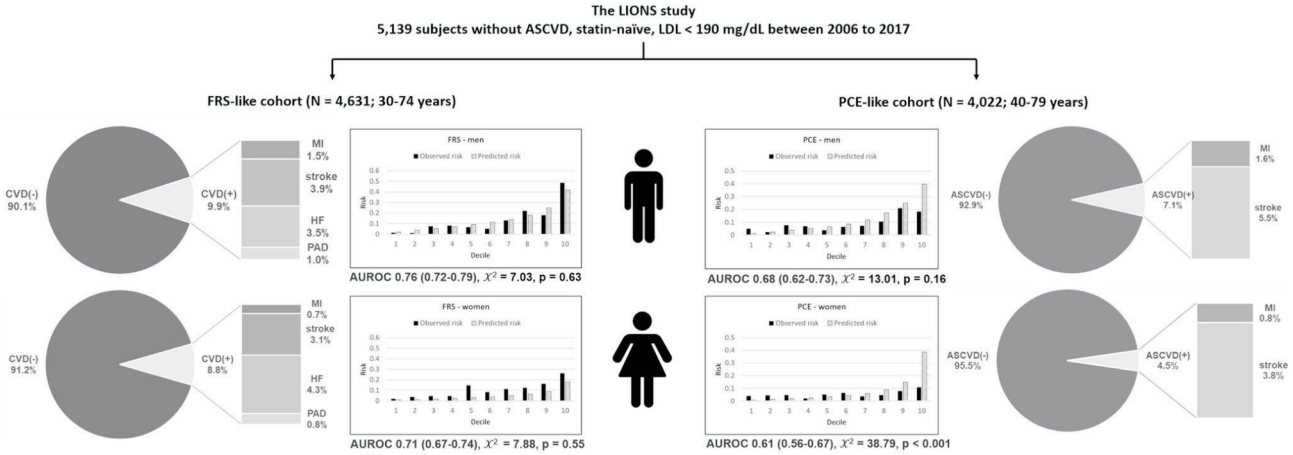
In terms of hard CVD events, the risk of CHD in our study was similar to prior studies in East Asia but lower than studies in South Asia.[10,16] Overall, both the PCE and FRS models overestimated the risk of CHD in East Asian populations.[8-16,22] Moreover, the discriminative power was modest (AUROC ranging from 0.705 to 0.809), and calibration scores were poor among these studies. Possible reasons for the overprediction could be different eligibility criteria and baseline characteristics, progress in treatment for primary prevention, ethnic heterogenicity, and under-ascertainment or misclassification of outcome events.[22]

When stroke was included into the risk prediction model, the risk of ASCVD was higher in our study than in a previous meta-analysis of Asian patients (7.0 vs. 3.45

Table 4. Discriminative power and calibration scores of the FRS-CVD and PCE

Outcome of interest	FRS-CVD	PCE
Age, years	30-74	40-79
Males, *n* (%)	187 (9.9)	122 (7.1)
AUROC (95% CI)	0.76 (0.72-0.79)	0.68 (0.62-0.73)
Calibration χ^2	7.0267 (p = 0.6343)	13.007 (p = 0.1623)
Average predicted risk (95% CI)	13.61 (13.07-14.15)	12.18 (11.61-12.75)
Average observed risk (95% CI)	13.13 (12.85-13.41)	8.91 (8.79-9.03)
Females, *n* (%)	243 (8.8)	105 (4.5)
AUROC (95% CI)	0.71 (0.67-0.74)	0.61 (0.56-0.67)
Calibration χ^2	7.8845 (p = 0.5458)	38.785 (p < 0.001)
Average predicted risk (95% CI)	5.19 (4.99-5.39)	8.19 (7.70-8.68)
Average observed risk (95% CI)	10.43 (10.28-10.57)	5.35 (5.30-5.40)

AUROC, area under the receiver operating characteristic curve; CI, confidence interval; FRS-CVD, Framingham general cardiovascular risk score; PCE, pooled cohort equations.



Central Illustration. *To validate the 10-year ASCVD risk using FRS and PCE in Taiwan. ASCVD, atherosclerotic cardiovascular disease; AUROC, area under the receiver operating characteristic curve; FRS, Framingham risk score; HF, heart failure; LDL, low-density lipoprotein; LIONS, Landseed Integrated Outreaching Neighborhood Screening; MI, myocardial infarction; PAD, peripheral artery disease; PCE, pooled cohort equations.*

per 1000 person-years in men, 4.4 vs. 1.95 per 1000 person-years in women);[10] this finding may be associated with the higher prevalence of hypertension in our cohort compared to the prior study.[23] This finding also suggests that stroke is more prevalent in Taiwan, and this observation merits more attention.

The FRS has been validated in various Asian populations, primarily for predicting the risk of CHD but not the FRS-CVD model. In Asian cohorts, the FRS-CVD has been shown to overestimate the incident risk of CVD, but to have acceptable discriminative power and calibration.[13,16] As in our study, the FRS-CVD performed better than PCE in both sexes, which may be due to the higher incidence of CVD other than CHD. In terms of the composite cardiovascular outcomes in our cohort, females had a lower incidence of MI, stroke, and PAD but a higher incidence of HF than males. This finding is compatible with prior studies which reported that females tend to develop HF at an older age than males and have a higher risk of admission for HF, which has been attributed to higher co-morbidity rates.[24]

PCE have been reported to have varied predictive performance for the risk of ASCVD in Asian cohorts.[13,14,25] In a community-based cohort study conducted in northern California to validate PCE for disaggregated race/ethnic subgroups, PCE overestimated the risk of ASCVD for American Asians by a wide range.[25] Among all Asian subgroups, the extent of overestimation was greatest for Chinese participants (predicted/observed risk ratio of 1.9) and lowest for Vietnamese participants (predicted/observed risk ratio of 0.9). In our study, PCE overestimated the risk of ASCVD for Taiwanese males and females by 37% and 53%, respectively; much less than the overestimations for American Chinese individuals in the previous study.[25] These results imply that environmental factors may have an important influence on the performance of this risk prediction model, in addition to race and traditional atherosclerotic risk factors.

The 2019 ACC/AHA guidelines for the primary prevention of CVD endorse PCE as a class I recommendation for 10-year ASCVD risk prediction in patients with hyperlipidemia and hypertension.[6] Statin therapy is recommended for individuals at intermediate risk (7.5%) with risk enhancers. The initiation of pharmacological treatment is also recommended for adults with a 10-year ASCVD risk of > 10% and an average SBP > 130 or DBP > 80 mmHg. The Taiwan hypertension and lipid guidelines in 2022 used the number of risk factors rather than ASCVD risk calculation to guide primary care.[17,18] Our study showed that 1291 of 4,631 (28%) participants in the FRS-CVD group and 855 of 4,022 (21%) participants in the PCE group met the criteria of the ACC/AHA guidelines based on predicted risks of 10% or 7.5% or higher. HF and stroke were the main events observed in the present study, and prevention of these CVDs should not only focus on dyslipidemia, diabetes, and hypertension, but also on unhealthy diet, smoking, obesity, and the rapidly aging population. Thus, incorporating the FRS-CVD into Taiwan guidelines for the primary prevention to assess the 10-year general CVD risk is a reasonable alternative.

The strength of this study is the prospective cohort design with a high 10-year follow-up rate. Data on all risk factors for risk prediction were available, and cardiovascular outcomes were collected annually using a questionnaire. However, recall bias is still possible as the patients may not have accurately defined the cardiovascular events. We cross-checked the cohort using ICD codes in the EMR of the local hospital, however definite diagnoses may not be available for patients who sought medical aid directly from other medical centers. A limitation of this study is that only subjects with EMR-documented CVD were included for risk analysis, which may have caused underestimation. Finally, the risk prediction models for ASCVD-free, statin-naïve populations with LDL-C < 190 mg/dL may not be accurate for other individuals who do not meet these criteria.

CONCLUSIONS

The FRS-CVD and PCE models provided good calibration and had modest discriminative power in CVD-free, statin-naïve Taiwanese individuals with serum LDL-C < 190 md/dL, with the exception of PCE for females. Further investigations to improve model performance should focus on women.

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DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary Table 1. Predicted vs. observed rate of cardiovascular diseases by age subgroup

	N	Predicted CVD	Observed CVD	P/O ratio	p value*
FRS-CVD					
< 60 years	3,834	6%	8.9%	0.7	0.05144
≥ 60 years	797	19%	23%	0.8	0.3441
PCE					
< 60 years	2,960	5%	5.6%	0.9	0.1726
≥ 60 years	1,062	24%	10.5%	2.3	< 0.001

P/O ratio, predicted-to-observed ratio; the others as Figure 1.
* Differences between predicted and observed CVD risk based on chi-square test.