Comparison of Cardiovascular Risk Estimation Tools in Thai Hospital Employees

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Abstract

OBJECTIVES: To compare cardiovascular disease (CVD) risks estimated by various estimators, we collected and analyzed the annual health checkup data of non-physician hospital employees (NPHEs) in 5 private hospitals in Thailand in 2018.

MATERIALS AND METHODS: This cross-sectional study employed five commonly used CVD risk calculators Thai Cardiovascular (CV) Risk score, modified Coronary Risk Chart (mCRC), Systematic Coronary Risk Evaluation (SCORE) chart, World Health Organization-Southeast Asian Region B (WHO SEAR B) risk prediction chart, and atherosclerotic cardiovascular disease (ASCVD) risk estimator plus) to compare risk levels estimated by each method. Statistical analysis was conducted using R code and STATA.

RESULTS: Among 7,286 eligible NPHEs invited to join, 3,687 consented to join. A total of 2,907 subjects were included in this study after excluding those with inadequate data and those with existing CVD. The majority (84.7%) of subjects were female and 75.3% of subjects were in the 30-59 years' age group. More than half (64.6%) had normal Body Mass Index (BMI). A small proportion had pre-existing hypertension (16.4%), diabetes mellitus (7.9%) and very few reported smoking behavior (5.1%) while a quarter (24.2%) reported regular alcohol use and 60.6% reported sedentary life. Pairwise comparison of future 10-year CVD risks between Thai CV Risk Score and (i) mCRC, (ii) European SCORE, (iii) WHO SEAR B risk chart and, (iv) ASCVD Risk Estimator Plus showed significant agreement of 94.15%, 98.25%, 97.80%, and 98.83% respectively, all with $p < 0.001$. Comparing results of Thai CV Risk Score when lipid profiles was used and not used also revealed high agreement (88.72%), $p < 0.001$. Subgroup comparison among those with moderate to high risks, agreement between Thai CV Risk Score with m-CRC, European SCORE, WHO SEAR-B and ASCVD Risk Estimator Plus dropped dramatically to 47.1%, 78.6%, 20.0%, and 41.7% respectively.

CONCLUSION: This study shows significant agreement between the Thai CV Risk Score with lipid profiles and mCRC, European SCORE Chart, WHO SEAR B, ASCVD Risk Estimator Plus and Thai CV Risk Score without lipid profiles. The Thai CV Risk Score could numerically detect more persons with moderate or high cardiovascular risk than other risk calculators. Clinical recommendation for those with moderate or even low risk should be made carefully, taking into account that the patient might actually be at a higher risk level.

Keywords: cardiovascular disease, risk calculator

Cardiovascular Diseases (CVD) have been the leading causes of morbidity and mortality worldwide for decades. Although there has been substantial development in CVD diagnosis and management in recent years, CVD remains the leading cause of morbidity and mortality worldwide. Approximately, half of the global burden of CVD is located in Asia.[1] In Thailand, the increasing prevalence of standard cardiovascular risk factors such as high blood pressure (BP), overweight, obesity, and diabetes mellitus has a massive impact on the prevalence and mortality from CVD in recent years.[2,3] Early management of cardiovascular risk factors which encompasses clinical evaluation, diagnostic testing and both pharmacological and behavioral treatments are still the cornerstones of primary CVD prevention.

For designing an optimal plan for risk factor management, the estimation of future cardiovascular risk is a very essential requirement. To facilitate this estimation and to encourage the physician's decision about preventive intervention, most national and international guidelines recommend using a CVD risk calculator to support the treatment decision.[4,5] Most of these risk calculators are available as electronic tools that mathematically combine multiple individual risk factors to predict an individual's probability of having an atherosclerotic cardiovascular event over the future of 5-10 years.

There are many CVD risk assessment tools or calculators available, with at least 110 different risk-scoring methods for the general population and at least 45 calculators for diabetic patients.[6,7] The CVD risk calculator that is recommended in all Thai Practice Guidelines, is the Thai CV Risk Score. This risk score was derived from the longitudinal study of Electric Generating Authority of Thailand (EGAT) employees,[8] and is supposed to be the most reliable CVD risk calculator for Thai population. However, there are other well-accepted risk estimation systems that are also being used by many Thai physicians and healthcare workers such as the mCRC, European SCORE low risk chart, WHO SEAR B risk prediction chart, and ASCVD risk estimator plus. Many of these CVD risk calculators are being recommended in international guidelines which are well accepted by Thai practitioners, so they are still being widely used in CVD risk estimation in the Thai population.

There was a study in the Thai population showing that the risk score developed from Thai EGAT cohort had greater sensitivity and specificity than the Framingham CVD Score in predicting cardiovascular events.[9] However, there never was any study to compare the performances of these commonly used risk calculators with Thai CV Risk Score in the Thai population without clinical CVD.

As a result, we conducted this study to compare CVD risks estimated by various estimators. Results could be applied for clinical practices towards better risk classification of CVD patients.

Materials and Methods

This study was a cross-sectional study aiming to use information from annual health examination for employees of 5 private hospitals in Thailand in the year 2018. All hospitals are medium-sized private hospitals in the Bangkok Dusit Medical Services (BDMS) hospital network. All those NPHEs with a planned annual health examination with access to a pre-examination questionnaire survey and having made the decision to give informed consent to join the study via access to each hospital website took part. Only data from participants who had given written informed consent was used for this analysis. The study was approved by the BDMS Institutional Review Board (Project ID BMC-IRB 2018-02-03), and was conducted in accordance with the declaration of Helsinki and its amendments.

Participants

Participants were non-physician hospital employees from Bangkok Hospital Headquarters (BHQ), Bangkok Hospital Pattaya, Phayathai 2 Hospital, Bangkok Hospital Phuket and Bangkok Hospital Chiang Mai. The annual health examination in each hospital was performed between April to December 2018. All employees were informed about the study before their health examination and were freely allowed to decide whether to join the study. Employees with pre-existing clinical CVD cardiovascular disease were given the health examination but were excluded from the study analysis. In 2018, 7,286 NPHEs, were registered for an annual health examination. Among these, 3,687 NPHEs voluntarily consented to join the study. A total of 780 NPHEs who gave informed consent were excluded from the analysis because of inadequate data to calculate CVD risk (663 subjects), insufficient data on other aspects (105 subjects) and/or they had been diagnosed as CVD before entering the project (12 subjects). As a result, data from 2,907 subjects were included in the analysis of this study, as showed in Figure 1.
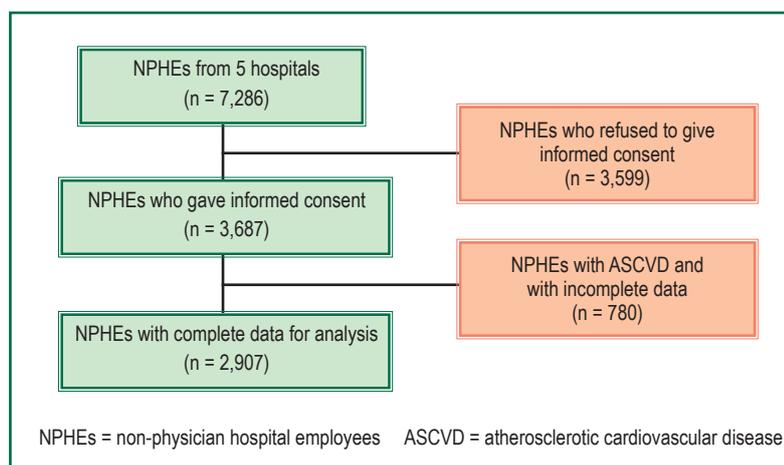

Figure 1: The study flow chart

Data collection

The health examination program consisted of history taking, complete behavior questionnaires, physical examination by physicians, chest x-ray and laboratory tests. Electrocardiograms were performed only for employees who were >35 years old. The health examination protocol was the same for every employee regardless of their allowance and status of the informed consent. The physicians, nurses and investigators were blind about the consent status of any employee.

The investigators transferred all health examination results from the hospital database to the study database. Each participant was assigned with a subject identification number to prevent exposure of their identity to investigators. The study flow chart is shown in Figure 1.

CVD risk assessment tools

We compared only CVD risk calculators that are commonly used among Thai physicians, i.e. Thai CV Risk score, mCRC, European SCORE chart, WHO SEAR B risk prediction chart, and ASCVD risk estimator plus.[10-12]

The European SCORE chart used in this study was the one designed for lower risk European countries (2016 age-adjusted CVD mortality rate < 150/100,000). This lower risk SCORE chart was selected because the CVD mortality rate in Thailand in 2016-2017 was also less than 150/100,000 and most Thai physicians use lower risk SCORE chart for risk estimation. The ASCVD Risk Estimator Plus in this study was that for non-white and non-African American race category.

The mCRC was firstly recommended in the 1994 European recommendations on coronary prevention.[13] The simplified method of deriving an approximate 10-year coronary heart disease (CHD) risk, based on a risk function derived from the Framingham study[14] was presented in the form of a Coronary Risk Chart. The Coronary Risk Chart originally was separated between the general and diabetic population. It was later modified by using impaired fasting glucose (>100 mg/dl) as an equivalent risk to DM and was used not only for prediction of CHD but also for stroke and mortality.[15,16]

For Thai CV Risk Score, the cardiovascular risk estimation can be performed both with and without the result of blood test for lipid profiles [total cholesterol, high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C)]. In this study we used the Thai CV Risk Score with blood test result for comparison with other risk calculators. We also used the data from this cohort to compare the performance of the Thai CV Risk score with and without blood test result.

The results of CVD risk estimation by each risk estimation tools were classified in 3 categories of low, moderate and high risk but only 2 categories which are 1) low and, 2) moderate or high risk categories were used in the correlation analysis. All risk calculators were developed to assist clinicians in risk estimation among population without clinical ASCVD and were aimed at primary CVD prevention. By classification of risk estimation results into only 2 categories, we assessed the performance of calculators in their ability to separate individuals with low future cardiovascular risk from those with moderate or high risk. For persons with low future risk, the general advice on lifestyle modification would be sufficient while pharmacological treatment or closer follow up can be essential for the population with moderate or high risk. In clinical practice, clinicians can identify individuals with high or very high CVD risk from their pre-existing clinical conditions or diagnosis such as long-standing diabetes, chronic kidney disease or the clinical history or presentation of ASCVD.

The threshold to define moderate or high risk category in each risk estimation tool is different. Thai CV Risk Score allows ≥ 10% of 10-year CVD risk as the definition of at least moderate risk as do the mCRC and WHO SEAR B. The ASCVD risk estimator plus uses ≥ 7.5% ASCVD risk as the diagnostic threshold for at least intermediate ASCVD risk. The European SCORE chart allows ≥ 1% for 10-year risk of fatal CVD to categorize moderate-to-high risk. To convert the risk of fatal CVD to risk of total (fatal + non-fatal) CVD, the SCORE users have to multiply the calculated risk by 3 in men and by 4 in women.

Statistical analysis

All statistical analysis was performed using R codes. Categorical data (e.g. gender, BMI category, BP status, and DM status) were presented as frequency and percentages while continuous data (e.g. age, bodyweight) were presented as mean and standard deviation.

CVD risk estimation among each risk estimator tools were classified in 3 categories as low, moderate and high risk and were presented both in numbers and percentages. The concordance correlation was used to estimate the level of agreement between the Thai CV Risk Score and other risk estimators with Cohen's kappa analysis presenting as a percentage of agreement, with $p < 0.05$ considered as statistically significant. For practical reasons as mentioned earlier we used only low and moderate or high risk categories for agreement analysis. The moderate or high risk group included all participants with higher than low risk in this category.

Results

A total of 2,907 subjects were female (2,463 (84.7%)). Mean age of the whole group was 36.9 ± 8.5 years with 75.3% aged between 30-59 years, (Figure 2). Mean body weight was 59.6 ± 12.1 kilograms (kg), most of them (64.6%) had BMI between 18.5-24.9 kg/m², while 28.3% had BMI ≥ 25 kg/m³. About one-third (31.8%) of subjects had waist circumferences greater than normal limit for Asian population. A total of 16.4% of subjects had pre-existing HT and 7.9% had pre-existing diabetes mellitus. A few (5.1%) reported smoking behavior, a quarter (24.2%) reported regular alcohol use and 60.6% had sedentary life, (Table 1).
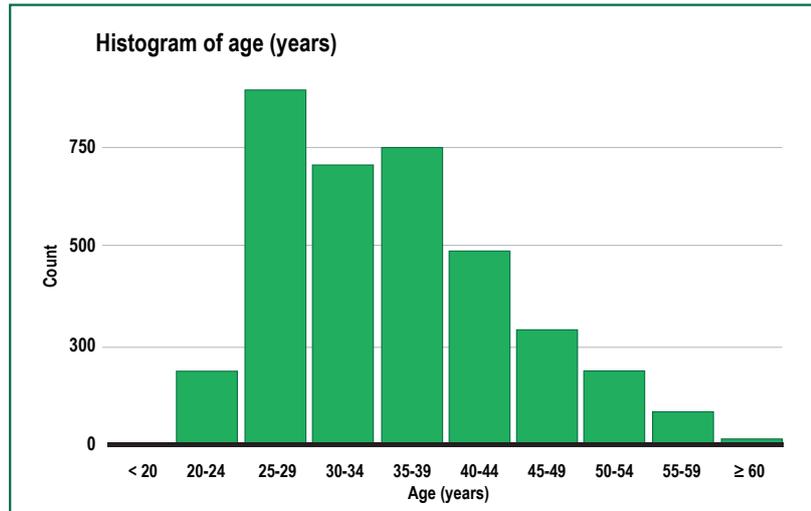
Figure 2: Age distribution of subjects

Table 1: Subjects' characteristics (n = 2,907)

Characteristics	n (%)
n	2,907 (100.0)
Mean age	36.9 ± 8.5
Female	2,463 (84.7)
Mean Body weight	59.6 ± 12.1
High Body Mass Index (BMI) (≥ 25 kg/m²)	823 (28.3)
High Waist Circumference (> 80 cm for female, > 90 cm for male)	925 (31.8)
Underlying diseases	n = 599 (20.6)
Hypertension (HT)	98 (16.4)
Diabetic Mellitus (DM)	47 (7.9)
Behavioral risk	2,907 (100.0)
Currently Smoking	148 (5.1)
Regular alcohol use	705 (24.2)
Sedentary	1,762 (60.6)

By using the Thai CV Risk Score, 2,858 (98.3%) NPHEs were classified as low risk and 49 (1.7%) were classified as moderate or high risk. Other risk calculators revealed little difference, i.e. those who were classified as low risk by mCRC were 2,714 (93.3%), European SCORE, 2,837 (97.6%) WHO SEAR B 2,904 (99.8%) and ASCVD Risk Estimator Plus 2,836 (97.5%). The numbers of NPHEs who were classified as moderate or high risk by mCRC, European SCORE, WHO SEAR B and ASCVD Risk Estimator Plus were 193 (6.7%), 70 (2.4%), 3 (0.2%) and 71 (2.5%) respectively. The pairwise comparison of future 10-year cardiovascular risk between the Thai CV Risk Score and mCRC, European SCORE, WHO SEAR B risk chart and ASCVD Risk Estimator Plus showed significant agreement of 94.15%, 98.25% 97.80% and 98.83% all with $p < 0.001$ (Table 2).

Table 2: Concordance (percent agreement) in pairwise comparison of 10-year cardiovascular disease risk calculators across 2 risk categories in 2,907 NPHEs

		n	Thai CV risk score		Agreement (%)	p
			Low Risk <10% (n = 2,858) n (%)	Moderate or High Risk ≥ 10% (n = 49) n (%)		
A. Comparing risk estimation by Thai CV Risk Score and mCRC						
mCRC	Low < 10%	2,714	2,701 (94.5)	13 (26.5)	94.15	< 0.001
	Moderate or High ≥10%	193	157 (5.5)	36 (73.5)		
B. Comparing risk estimation by Thai CV Risk Score and European SCORE Chart						
SCORE	Low < 1%	2,837	2,822 (98.7)	15 (30.6)	98.25	< 0.001
	Moderate or High ≥1%	70	36 (1.3)	34 (69.4)		
C. Comparing risk estimation by Thai CV Risk Score and WHO SEAR B risk prediction chart						
WHO SEAR B	Low < 10%	2,882	2,838 (99.3)	44 (88.8)	97.80	< 0.001
	Moderate or High ≥10%	25	20 (0.7)	5 (10.2)		
D. Comparing risk estimation by Thai CV Risk Score and ASCVD Risk Estimator Plus						
ASCVD Risk Estimator Plus	Low < 7.5%	1,868	2,846 (99.6)	22 (44.9)	98.83	< 0.001
	Moderate or High ≥7.5%	39	12 (0.4)	27 (55.1)		

Thai CV Risk Score without lipid profiles result could be applied in 2,820 NPHEs and 2,457 (87.1%) and 363 (12.9%) NPHEs were categorized as low risk and moderate or high risk respectively. When the Thai CV Risk Score with lipid profiles was applied to these 2,820 NPHEs, 2,775 (98.4%) were categorized as low risk and 45 (1.6%) were categorized as moderate or high risk. There was a significant agreement of 88.72% between these two sub-types of Thai CV Risk Score with $p < 0.001$. (Table 3)

Including all subjects, comparison between the Thai CV Risk Score with the remaining four estimators resulted in high agreement, i.e. with European SCORE (98.7%), WHO SEAR-B (98.0%) and ASCVD (97.5%), and mCRC (83.0%). However, when only non-low risk subjects were included, the agreements dropped dramatically, with the lowest of 20.0% with WHO SEAR-B, Table 4.

Table 3: Risk estimation by Thai CV Risk Score with and without lipid profile (n = 2,820)

Without Lipid profile	n	Thai CV risk score		Agreement (%)	p
		Low Risk <10% (n = 2,775) n (%)	Moderate or High Risk ≥10% (n = 45) n (%)		
Low < 10%	2,457	2,457 (100.0)	0	88.72	< 0.001
Moderate or High ≥10%	363	318 (87.6)	45 (12.4)		

Table 4: Agreement between the Thai CV Risk Score and the other four estimators when all subjects were included and when only non-low risk subjects were included.

	Thai CV Under estimation, n(%)	Matched Estimation, n(%)	Thai CV Over estimation, n(%)	Agreement (All subjects)	Agreement** (excluded low and low risk)
mCRC	405 (16.9)	1,993 (83.0)	4 (0.2)	83.0%*	47.1%
European SCORE	20 (0.8)	2,619 (98.7)	15 (0.6)	98.7%*	78.6%
WHO/ISH (SEAR-B)	19 (0.7)	2,601 (98.0)	34 (1.3)	98.0%*	20.0%
ASCVD (American)	39 (1.9)	2,023 (97.5)	13 (0.6)	97.5%*	41.7%

** low and low risks indicate low risk classified by both Thai CV and another estimator
* $p < 0.01$

The Thai CV Risk Score is more sensitive in detection of NPHEs with moderate or high CV Risk than WHO SEAR B and ASCVD Risk Estimator Plus. The number of individuals screened to have moderate or high CV Risk using Thai CV Risk Score was 49 from the 2,907 NPHEs screened while the number of individuals with moderate or high CV risk detected by WHO SEAR B and ASCVD Risk Estimator Plus were 3/2,907 and 71/2,907 respectively. On the contrary, the European SCORE Chart and mCRC were numerically more sensitive than the Thai CV Risk Score because they could detect more NPHEs with moderate or high CV risk (70/2,907 and 193/2,907 respectively).

The Thai CV Risk Score without lipid profiles also appeared to be numerically more sensitive in detection of moderate or high CV risk individuals than the Thai CV Risk Score with lipid profiles. The number of NPHEs screened to have moderate or high CV risk without blood test was 363 out of 2,820 screened while the number detected by using the Thai CV Risk Score with blood test result was only 45 out of 2,820 screened.

Discussion

We used five CVD risk calculators to estimate future CVD risk among 2,907 NPHEs from five private hospitals in Thailand.

Comparing concordance in classification into two risk categories between Thai CV Risk Score (with blood test results) and mCRC, European SCORE Chart, WHO SEAR B and ASCVD Risk Estimator Plus showed the significant agreement of 94.15%, 98.25% 97.80% and 98.83% respectively, all with $p < 0.001$.

There was also significant agreement of 88.72% ($p < 0.001$) between the Thai CV Risk Score with and without lipid profiles. The Thai CV Risk Score with lipid profiles uses the following eight specific risk indicators to calculate ASCVD risk: age, sex, smoking status, systolic BP, DM, total cholesterol, HDL-C and, LDL-C. The other studied risk calculators use from five to nine specific standard risk indicators to estimate ASCVD risk. The mCRC uses triglyceride level instead of LDL-C level in their risk estimation and use family history of premature ASCVD and family history of high cholesterol in the calculator. The WHO SEAR B uses the same six risk indicators as the Thai CV Risk Score but does not use LDL-C and, HDL-C levels. For the European SCORE Chart, only five risk factors were included, and total cholesterol was the only laboratory result that was included. For people with DM type 2, the use of the European SCORE Chart is not usually indicated. The ASCVD Risk Estimators Plus uses the same specific risk indicators as the Thai CV Risk Score but includes diastolic BP in the calculation.

When the similar characteristics of the assessed risk calculators were considered, it was not surprising that their performances were all in agreement with Thai CV Risk Score. However, when considering the ability of each calculator to detect those healthy individuals with moderate or high future CVD risk the performance of mCRC and the European SCORE Chart seemed to be better than Thai CV Risk Score.

There are two risk calculators that allow risk estimation by using non-laboratory-based parameters. The first is Thai CV Risk Score which uses waist circumference and height in the risk estimation, the second is WHO SEAR B which uses BMI in the calculator. The WHO SEAR B risk estimator tested in this study was the one that uses cholesterol level for risk estimation.

If the purpose for population screening is to find the moderate or high CV risk individuals so that their future CVD risk can be modified, then the risk calculator which is most sensitive will be more useful than the rest. In this context of awareness creation and disease prevention, the mCRC might be the best CVD risk calculator for this purpose.

Surprisingly, the Thai CV Risk Score without laboratory test was numerically the most sensitive calculator in the detection of moderate or high risk NPHEs compared to the rest of calculators assessed in this study. The Thai CV Risk Score without laboratory test could detect 363 (12.9%) moderate or high risk individuals from 2,820 healthy NPHEs. While the data from 2,907 NPHEs in this study showed that mCRC, European SCORE Chart, Thai CV Risk Score with blood test, ASCVD Risk Estimator Plus and WHO SEAR B risk prediction chart could detect the moderate or high risk category in only 193(6.6%), 70(2.4%), 49(1.7%), 71(1.4%) and 3(0.9%) persons respectively.

The possible mechanism for better detection of CVD using the Thai CV Risk Score without blood test in this study was hard to explain. Nevertheless, we speculated that probably a number of factors could contribute to this phenomenon. First, the EGAT employees, which the Thai CV Risk Score was derived from, were largely middle-class, well educated, urban-dwelling individuals receiving an above-average level of income and were quite similar to the NPHEs in this study. Second, there was no significant relationship between total cholesterol and vascular death among 3,318 Thai individuals followed for an average of 12 years in the EGAT study.[8] The Thai CV Risk Score with lipid profile derived from the EGAT cohort were influenced by the fact that cholesterol levels might not be a strong predictor for future CVD in the Thai population. This could explain the agreement between Thai CV Risk Score with and without lipid results. Third, the Thai CV Risk Score without blood test uses waist circumference in the risk estimation instead of BMI because the EGAT Study did not show a significant relationship between BMI and vascular death in the Thai population.[8] In our study, the mean age of participants was 36.9 years which was younger than in the EGAT cohort (mean 49.5 years), so the cardiovascular risk

in our population was not influenced by age but could have very strong influence from larger waist circumference as in our study, there were 34.8% of NPHEs with waist circumference beyond the normal limits for Asians. Fourth, there was about 50% (3,599 persons) of NPHEs, who refused to give informed consent. This could lead to a bias in our study from the possibility that many NPHEs with known personal risk might refuse to participate in the trial, many of them might have higher standard risk factors than those included.

Our finding that agreement between the Thai CV Risk Score and the other estimators dropped dramatically when only non-low risk subjects were included in the analysis calls for special attention. A patient who is actually at "high" risk could be judged as "moderate" risk by an estimator being used by her or his preferred clinician. As a result, clinical recommendations should be made taking into account additional clinical, behavioral and life style data, with perhaps results of other risk estimators.

The strength of the present study was adequate sample size. The results showed not only the significant agreement between the Thai CV Risk Score and the other commonly used cardiovascular risk assessment tools, but also suggested the benefits of Thai CV Risk Score without blood test for the younger population. The agreement of Thai CV Risk Score without blood test with the Thai CV Risk Score with blood test suggested that the lipid profile assessment may not be routinely used for CV risk assessment in Thai healthy population, because it did not add any benefit in this large population. Limitations of the study were the large number of NPHEs who refused to give informed consent which could lead to a possible error in our conclusions and the high proportion of female participants which could limit the generalization of our results. The possibility that NPHEs who refused to give consent might have different levels of cardiovascular risk could not be ruled out. The other limitations were the nature of the cohort studied, a young, middle-class, well-educated Thai population with above average income, so the results of the study may not be generalizable to the rest of the Thai population as a whole.

Conclusion

This study shows significant agreement between Thai CV Risk Score with lipid profiles and mCRC, European SCORE Chart, WHO SEAR B, ASCVD Risk Estimator Plus and the Thai CV Risk Score without lipid profiles. The Thai CV Risk Score could numerically detect more persons with moderate or high cardiovascular risk than other risk calculators, thus it could be very practical in terms of rapid and cost-saving risk assessment for the Thai population. More study on concurrent application of various estimators among non-low risk patients is recommended. For the interim, clinical recommendation for those with moderate or even low risk should be made with caution taking into account that the patient might actually be at a higher risk level.

What is already known on this topic?

The Thai CV Risk Score is useful in cardiovascular risk estimation for a healthy Thai population without preexisting CVD and it can be used either with or without lipid profile. The other commonly used cardiovascular risk estimation tools share similar standard risk indicators as the Thai CV Risk Score with some minor deviations from each other. However, there may be a difference between level of risks and characteristics of cohorts used in the design and validation of each risk estimation tools.

What does this study add?

There was significant agreement among the Thai CV Risk Score with lipid profiles and the other commonly used risk calculators which are mCRC, European SCORE Chart, WHO SEAR B and ASCVD Risk Estimator Plus when applied to a group of middle-aged, middle-class, and a well-educated Thai population. The Thai CV Risk Score without lipid profiles also had significant agreement with the Thai CV Risk Score

with lipid profiles when applied to this same population. The Thai CV Risk Score may be more sensitive in detection of moderate or high risk individuals than the rest of risk calculators tested, especially in this population.

Conflicts of interest

All investigators declared no personal or professional conflicts of interest regarding any aspect of this study.

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