Heliyon 9 (2023) e20396

Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

Agreement between ten-years cardiovascular disease risk assessment tools: An application to Iranian population in Shahedieh Cohort Study

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ARTICLE INFO

Keywords:
Cardiovascular diseases
Framingham risk scores
WHO/ISH risk chart
Cardiovascular risk
Risk assessment

ABSTRACT

Background and aim: Cardiovascular risk-prediction models are efficient primary prevention tools to detect high-risk individuals. The study aims to use three tools to estimate the 10-year risk of developing cardiovascular disease (CVD) and investigate their agreement in an Iranian adult population.
Methods: The current cross-sectional study was carried out on 8569 adults between 35 and 70 who participated in the first phase of the Shahedieh cohort study in Yazd, Iran, and were free of CVDs (cardiac ischemia or myocardial infarction or stroke). World Health Organization/International Society of Hypertension (WHO/ISH) chart, Laboratory-Based (LB) and Non-Laboratory-Based (NLB) Framingham Risk Score (FRS) were used to predict the 10-year risk of developing CVD. The agreement across tools was determined by Kappa.
Results: WHO/ISH chart indicated the highest prevalence of low CVD risk for males (96.10%) and females (96.50%), while NLB Framingham had the highest prevalence of high CVD risk for males (19.40%) and females (5.30%). In total, there was substantial agreement between both FRS models (Kappa = o.70), while there was a slight agreement between WHO/ISH and both FRS tools. For under 60 years males and females, substantial agreements were observed between FRS methods (kappa = 0.73 and kappa = 0.68). For males and females over 60 years, this agreement was moderate and substantial, respectively (kappa = 0.54 and kappa = 0.64). WHO/ISH and LB Framingham model had substantial agreement for over 60 years females (kappa = 0.61).
Conclusions: Framingham models classified more participants in the high-risk category than WHO/ISH. Due to the lethality of CVDs, categorizing individuals based on FRS can ensure that most of the real high-risk people are detected. Remarkable agreement between FRS methods in all sex-age groups suggested using the NLB Framingham model as a primary screening tool, especially in a shortage of resources condition.

1. Introduction

Cardiovascular disease (CVD) is known as the most important non-communicable diseases globally [1]. Commonly, CVD refer to a group of diseases including stroke, heart failure, hypertension, rheumatic heart disease, peripheral arterial disease, and several other

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https://doi.org/10.1016/j.heliyon.2023.e20396
Received 17 May 2023; Received in revised form 20 September 2023; Accepted 21 September 2023
Available online 22 September 2023

vascular, and cardiac problems [2]. Despite the global advances in the availability of efficient preventive strategies, CVD remain the main cause of the high mortality rate and a major contributor to disability [1,3]. Between 1990 and 2019, the prevalence of CVD increased from 257 million to 550 million cases with an upward trend in associated deaths, disability-adjusted life years (DALYs), and years of life lost (YLL) [1,4]. The discrepancies in CVD prevalence across countries are due to a variety of factors, including genetic predisposition, dietary habits, and social interactions [5]. Although the incidence of CVD has significantly decreased in industrialized countries over the past 20 years, it has increased in developing nations including the Eastern Mediterranean region [4]. In Iran, CVD has been identified as the first leading cause of mortality as well as in Eastern Mediterranean countries [6]. In the Iranian population, 27.2% of YLL and 46% of all deaths are related to CVD due to adopting an unhealthy lifestyle (inactivity, smoking, obesity, poor diet, etc.) [4]. To lessen the incidence of CVD and their associated burden, the most cost-efficient and beneficial strategy is to regularly identify people who are more likely to develop CVD sequels in the future [7].

Cardiovascular risk assessment plays an important role in establishing convenient public health policies. It is an acceptable way to focus on preventive interventions for patients without symptoms the risk of developing cardiovascular disease. The risk functions that are obtained in cohort studies and randomized trials constitute the foundation of the risk prediction functions. These functions are simplified as charts, tables, computer programs, and web-based tools and are suitable for primary care [8]. Various tools have been designed to assess the CVD risk and Framingham Risk Score (FRS) and World Health Organization/International Society of Hypertension (WHO/ISH) risk charts are among the most commonly used and reliable models [9]. The FRS is a complex mathematical equation, which was developed by D'Agostino et al., in 2008, that calculates risk by applying either a laboratory-based (LB) or a non-laboratory-based (NLB) algorithm. To make Framingham's models more applicable in primary healthcare centers, the formula for calculation of the risk has been streamlined to a system that is based on points [7]. Studies conducted in Asian developing countries such as India and Malaysia showed that the FRS was more suitable than other models for predicting CVD risk [10,11]. WHO/ISH risk prediction charts, which are available for the WHO (World Health Organization) epidemiological sub-regions around the world, constitute a set of color-coded charts suggested based on the guidelines of the WHO for CVD prevention [12]. WHO has designed risk prediction charts for countries with limited resources that do not have a national cohort study to estimate the CVD risk [13].

Currently, there is no valid tool for estimating the CVD risk in Iran. Therefore, firstly, we determined the 10-year CVD risk level for each person in an Iranian population through WHO/ISH risk charts, LB and NLB Framingham models, which are among the most common and validated screening tools. Then, we examined the agreement between these methods in this population.

2. Methods

2.1. Study design and population

This was a cross-sectional study that was conducted on the data collected in the enrollment phase of the Shahedieh cohort study. This follow-up study was started in 2014 and is a part of the PERSIAN (Prospective Epidemiological Research Studies in Iran) multicenter cohort study. More details about the protocol of the PERSIAN cohort study are accessible elsewhere [14]. Shahedieh is conducted on 10,000 Iranian population adults, between 35 and 70 years old, who were residing in three towns of Yazd province (Shahedieh, Zarch, and Ashkezar). Demographic characteristics, lipid profiles, blood pressure, history of chronic diseases and medication usage, personal habits, and anthropometric indices of individuals were measured through questionnaires, clinical examinations, and blood test. Self-reported CVD were also defined as a history of ischemic heart diseases (heart failure, angina), Myocardial infarction (MI), and stroke.

The Ethics Committee of Shahid Sadoughi University of Medical Sciences approved the ethical considerations involved in this study (IR.SSU.SPH.REC.1400.088). The Shahedieh cohort study was carried out following the principles outlined in the Declaration of Helsinki, and either the participants or representatives of those who were illiterate provided informed consent.

2.2. Sample size and participants

At first, all the 35–70 years old adults from these regions were extended an invitation to take part in this study. The criteria for inclusion in this study were being of Iranian race and residing in three cities of Yazd province (Shahedieh, Zarch, and Ashkezar) for a minimum of 9 months of the year. Those with physical or psychological disabilities who could not finish the enrollment process were eliminated [15]. Considering the purpose of the study, of the 10,000 individuals who participated in the Shahedieh study, 590 with incomplete information, and 841 with CVD history (ischemic heart diseases or ischemic heart diseases or ischemic heart diseases) were excluded. Of 841 people with CVD, 546 (64.92%) had ischemic heart diseases, 14 (1.67%) had myocardial infarction, 63 (7.49%) had stroke, and 218 (25.92%) had at least two of the complications.

2.3. Tools to estimate cardiovascular risk

The FRS is a guideline to evaluate the 10-year CVD risk for individuals between 30 and 75 years with the initial goal of prevention. In this study, LB and NLB Framingham models were used to assess the 10-year CVD risk. Sex (male/female), age, total cholesterol (TC) and high-density lipoprotein (HDL) (in mg/dL), systolic blood pressure (SBP) (in mmHg), and status of its related treatment, diabetes (yes/no), and current smoking status (yes/no) were used to calculate FRS for the LB model. For the NLB model, this tool combines data on sex (male/female), age, SBP (in mmHg) and treatment status, diabetes (yes/no), current smoking status (yes/no), and BMI (kg/m^2) [7,9]. According to both FRS methods, individuals are categorized into three levels: Those with a risk score under 10% were considered as low-risk category, individuals with a risk score between 10% and 20% were considered as moderate risk category, and those with a risk score more than 20% were in the high-risk category. The third tool which was also utilized to estimate the risk of developing CVD (fatal or non-fatal) for the next ten years in the current study was the risk charts of WHO/ISH validated for Eastern Mediterranean Regional-B group countries (EMRE). To assess WHO/ISH risk, data on sex (male/female), age, SBP (in mmHg), TC (in mmol/l), current smoking status (yes/no), and diabetes status (yes/no) were required. The risk categories to predict CVD over 10-years, as determined by WHO/ISH, are as follows: low-risk (risk score <10%), moderate-risk (risk score between 10% and 19%), relatively high-risk (risk score between 20% and 29%), high-risk (risk score between 30% and 39%), and very high-risk (risk score ≥40%) [9]. To have similar categories in all methods, we defined the high-risk category by combining relatively high-risk to very high-risk groups in the WHO/ISH method.

In this study, participant SBP was measured in a seated posture, following at least a 10-min break. Measuring blood pressure was repeated two times from both the right and left arms using a mercury sphygmomanometer. The mean of the second right and left arms blood pressure measurements was considered as the final blood pressure. Diabetes and hypertension status was determined based on the medical background of the disease and were self-reported. The status of cigarette smoking was also determined by self-report so that, individuals who claimed that they smoked regularly or occasionally were considered as current smokers. TC and HDL were tested in the laboratory. To calculate BMI, weight was measured by a trained researcher while the person wearing light clothes and without shoes using a digital scale (SECA, model 755, Germany). A tape measure which was attached to the wall without any bumps was used to measure the height of the subjects with a precision of 0.5 cm [14].

2.4. Statistical analysis

The frequency and percentage were reported to describe categorical variables and the mean and standard deviation were calculated for continuous variables. Using an independent sample T-test and Chi-Square test, the mean and frequency distribution of the CVD risk factors were compared among males and females through version 24 of SPSS. We calculated the ten-year risk of CVD using the points-based risk-scoring system of LB and NLB models [16]. The Ten-year WHO–EMR CVD risk level of the samples was also estimated using the whoishRisk package in version April 1, 1717 of RStudio [17].

The percentage of agreement between the two tools is obtained by dividing the frequency of people who were categorized in the same risk levels with both methods by the total number of people. This ratio is reported in terms of percentage. We also used Fleiss' kappa to study the agreement between three methods and weighted kappa statistics to determine the pairwise agreement. Based on Kappa statistic, the level of agreement is classified as follows: slight agreement (0–0.20); fair agreement (0.21–0.40); moderate agreement (0.41–0.60); substantial agreement (0.61–0.80); and almost perfect agreement (0.81–1.00) [18]. In all tests, a p-value less than 0.05 was deemed to be statistically significant.

3. Results

3.1. Descriptive statistics of risk factors

Of the total number of subjects (n = 8569), 4245 (49.50%) were male. The participants' mean (SD) age was 47.67 (9.28) years. According to the study results, there was a significant age mean difference between males and females ($P < 0.001$). The mean (SD) of TC, HDL-C, and SBP were 190.12 (41.01), 52.97 (12.24), and 109.68 (16.61), respectively. The mean (SD) of TC and HDL-C were higher in females while SBP was higher in males ($p < 0.001$). The prevalence of hypertension and diabetes was 17.60% and 15.80%. 79.40% of individuals used antihypertensive drugs. Furthermore, 1207 of the participants were current smokers. Of 4245 males 28.20% and of 4324 females 0.3% were current smokers. The mean (SD) of BMI was 28.41 (6.60) which was significantly higher in females ($p < 0.001$) (Table 1).

3.2. Prevalence of 10-year risk of developing CVD using the LB Framingham, NLB Framingham and WHO/ISH tools

Fig. 1 demonstrates the frequency distribution of the risk levels by each tool in total and by sex. It was observed that the WHO/ISH chart had the lowest proportion of high CVD risk level in total (0.90%) and for males (0.80%) and females (1.00%), while NLB

Table 1
Summary Statistics for components of Risk tools.

Characteristics	Total (n = 8569)	Male (n = 4245)	Female (n = 4324)	P
Age, mean (SD), year	47.67 (9.28)	48.18 (9.39)	47.16 (9.15)	P < 0.001
TC, mean (SD), mg/dL	190.12 (41.01)	187.92 (40.27)	192.29 (41.61)	P < 0.001
HDL-C, mean (SD), mg/dL	52.97 (12.24)	48.97 (10.71)	56.90 (12.39)	P < 0.001
SBP, mean (SD), mm Hg	109.68 (16.61)	111.91 (15.99)	107.50 (16.92)	P < 0.001
Hypertension, n (%)	1509 (17.60%)	559 (13.20%)	950 (22.00%)	P < 0.001
BP treatment, n (%)	1198 (79.40%)	431 (77.10%)	767 (80.70%)	0.09
Diabetes, n (%)	1351 (15.80%)	563 (13.30%)	788 (18.20%)	P < 0.001
Smoking, n (%)	1207 (14.10%)	1196 (28.20%)	11 (0.30%)	–
BMI (kg/m^2)	28.41 (6.60)	27.21 (7.69)	29.59 (5.05)	P < 0.001

Framingham had the highest prevalence in high-level of CVD risk in overall (12.30%) and for males (19.40%) and females (5.30%).

3.3. Agreement between LB Framingham, NLB Framingham, and WHO/ISH tools

In total, there was a fair agreement between the three methods (Fleiss' kappa = 0.29). It can be seen that there was slight agreement to fair agreement between methods in terms of rating participants as having low (kappa = 0.37), intermediate (kappa = 0.15), and high (kappa = 0.36) CVD risk.

To assess the pairwise risk agreement, weighted kappa was also calculated. Kappa statistic indicated that both FRS models had substantial agreement (Kappa = o.70) while slight agreement was observed between the risk score of the WHO/ISH and LB Framingham model (Kappa = 0.20) and the risk score of WHO/ISH and NLB Framingham model (Kappa = 0.12). The pairwise agreement was also investigated by age and sex.

For less than 60 years males, 77% agreement was observed between Framingham models (kappa = 0.73). According to the NLB model, 403 people were identified as high-risk individuals, and 2290 people were categorized in the low-risk level, while in the LB model, 205 people were detected as high-risk, and 2838 individuals were classified in the low-risk level, therefore, it is observed that NLB model placed more individuals in the high-risk category and fewer people in the low-risk group than LB model, which led to a slight disagreement between two models. It was observed that NLB model tended to indicate a higher risk, 761 (20%) males were in higher risk categories while only 31 (0.85%) males were classified in the lower risk levels compared to the LB model. For males under 60, no agreement was observed between risk score of the WHO/ISH and LB Framingham model (kappa = 0.05) and NLB Framingham model (kappa = 0.03). The considerable observed percent of agreement between WHO/ISH and LB (78%) and NLB (63%) Framingham model was due to categorizing a large number of individuals in the low-risk level according to both WHO/ISH and LB Framingham model (n = 2838) and WHO/ISH and NLB Framingham model (n = 2290). Comparing WHO/ISH and LB Framingham model, the low-risk group had a higher number of participants (3617 vs. 2838) and high-risk group had fewer participants (9 vs. 205) in WHO/ISH chart than in the LB Framingham model. The LB model classified 593 (16.31%) subjects in the higher-risk groups and only 2 (0.05%) in the lower-risk levels. A similar result was obtained by comparing the WHO/ISH chart and NLB model. The proportion of samples in the low-risk group is higher in WHO/ISH (99.50%) than in NLB model (62.99%). There were 949 (26.10%) males in the higher-risk groups but no participants in the lower-risk groups in the NLB model.

For males over 60 years old, the agreement between the NLB and the LB FRS categories was 59% (kappa = 0.54). The NLB model tended to classify more males in the high-risk group (419 vs. 276). The frequency of the low-risk level of this model is 0. Among 610 males over 60 years, 240 (39.34%) were in higher risk levels, and 4 (0.65%) were in lower risk groups in the NLB model compared to the LB model. For males more than 60 years old, there was no agreement between the WHO/ISH and NLB Framingham model (agreement = 5%, kappa = 0.07) and slight agreement between the WHO/ISH model and LB Framingham model (agreement = 23%, kappa = 0.20). More samples are placed in the low-risk category (462 vs. 97, 462 vs. 0) and fewer samples in the high-risk group (32 vs. 276, 32 vs. 419) using the WHO/ISH chart than LB and NLB Framingham models, respectively. Furthermore, there were 327 (53.60%) and 299 (49.01%) males in the lower risk groups but no males in the higher risk groups based on WHO/ISH chart than LB and NLB Framingham models, respectively (Table 2).

For females under 60 years, 92% agreement was observed between two Framingham models (kappa = 0.68). More participants were in the low-risk category (3593 vs. 3406) and fewer people were in the high-risk level (26 vs. 89), according to the LB model. It is worth mentioning that this model categorized 10 (0.26%) females in higher groups and 256 (6.76%) females in lower risk levels. Although the percent of agreement between WHO and LB (95%) and NLB (90%) Framingham model tended to be 100% due to observing a large number of participants in the low-risk level, there was no agreement between WHO/ISH chart and Framingham models based on the kappa statistic. Comparing LB and NLB models to WHO/ISH, fewer participants were in lower risk group in the LB

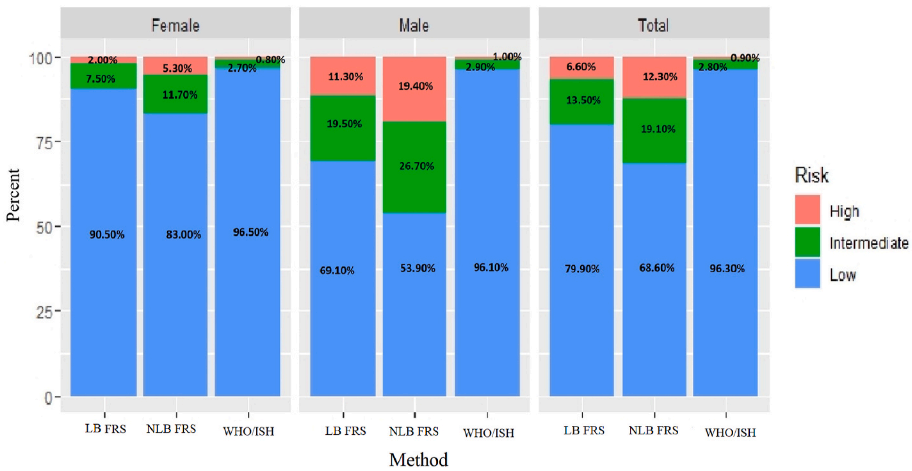

Fig. 1. Percentages of 10-year CVD risk levels applying the LB Framingham, NLB Framingham, and WHO/ISH tools.

Table 2
The agreement between LB Framingham model, NLB Framingham model, and WHO/ISH chart 10-year CVD risk categories in males.

Age	method		NLB Framingham model				WHO/ISH			
		Risk level	**Low**	**Intermediate**	**High**	**Total**	**Low**	**Intermediate**	**High**	**Total**
		Low	2273	557	8	2838	2838	0	0	2838
		Intermediate	17	371	204	592	587	3	2	592
	LB Framingham model	**High**	0	14	191	205	192	6	7	205
		Total	2290	942	403	3635	3617	9	9	3635
		Kappa (95% CI[a])	0.73 (0.71, 0.74)				0.05 (0.02, 0.08)			
<60 years (n = 3635)		**Agreement (%)**	77%				78%			
		Low	2290	941	386	3617	–	–	–	–
		Intermediate	0	1	8	9	–	–	–	–
	WHO/ISH	**High**	0	0	9	9	–	–	–	–
		Total	2290	942	403	3635	–	–	–	–
		Kappa (95% CI[a])	0.03 (0.01, 0.04)				–			
		Agreement (%)	63%				–			
		Low	0	95	2	97	97	0	0	97
		Intermediate	0	92	145	237	224	13	0	237
	LB Framingham model	**High**	0	4	272	276	141	103	32	276
		Total	0	191	419	610	462	116	32	610
>60 years (n = 610)		**Kappa (95% CI[a])**	0.54 (0.50, 0.57)				0.20 (0.17, 0.23)			
		Agreement (%)	59%					23%		
		Low	0	187	275	462	–	–	–	–
		Intermediate	0	4	112	116	–	–	–	–
	WHO/ISH	**High**	0	0	32	32	–	–	–	–
		Total	0	191	419	610	–	–	–	–
		Kappa (95% CI[a])	0.07 (0.05, 0.08)				–			
		Agreement (%)	5%				–			

[a] CI: Confidence Interval.

model (3593 vs. 3769) and the NLB model (3406 vs. 3769) but more people were in the high-risk group in the LB model (26 vs. 6) and the NLB model (89 vs. 6). Also, both LB and NLB models tended to classify 161 (4.25%) and 291 (7.69%) participants in higher risk groups and 5 (0.13%) and 1 (0.02%) in lower risk levels, respectively.

For females over 60 years old, 59% agreement was observed between both Framingham models (kappa = 0.64). Compared to the LB model, the frequency of the high-risk group was higher (141 vs. 60) and the frequency of the low-risk group was lower (184 vs. 320) in the NLB model. 209 (38.63%) participants were in higher risk groups and 4 (0.73%) in the lower risk levels according to the NLB model. Furthermore, 72% agreement was between WHO/ISH and LB model (kappa = 0.61). The slight disagreement between these

Table 3
The agreement between LB Framingham model, NLB Framingham model and WHO/ISH chart 10-year CVD risk categories in females.

Age	method		NLB Framingham model				WHO/ISH			
		Risk level	**Low**	**Intermediate**	**High**	**Total**	**Low**	**Intermediate**	**High**	**Total**
		Low	3397	194	2	3593	3590	2	1	3593
		Intermediate	9	93	62	164	158	3	3	164
	LB Framingham model	**High**	0	1	25	26	21	3	2	26
		Total	3406	288	89	3783	3769	8	6	3783
		Kappa (95% CI[a])	0.68 (0.64, 0.72)				0.14 (0.06, 0.23)			
<60 years (n = 3783)		**Agreement (%)**	92%				95%			
		Low	3404	286	79	3769	–	–	–	–
		Intermediate	1	2	5	8	–	–	–	–
	WHO/ISH	**High**	1	0	5	6	–	–	–	–
		Total	3406	288	89	3783	–	–	–	–
		Kappa (95% CI[a])	0.08 (0.03, 0.13)				–			
		Agreement (%)	90%				–			
		Low	182	132	6	320	303	17	0	320
		Intermediate	2	82	77	161	92	65	4	161
	LB Framingham model	**High**	0	2	58	60	9	27	24	60
		Total	184	216	141	541	404	109	28	541
>60 years (n = 541)		**Kappa (95% CI[a])**	0.64 (0.60, 0.69)				0.61 (0.54, 0.68)			
		Agreement (%)	59%					72%		
		Low	179	174	51	404	–	–	–	–
		Intermediate	5	40	64	109	–	–	–	–
	WHO/ISH	**High**	0	2	26	28	–	–	–	–
		Total	184	216	141	541	–	–	–	–
		Kappa (95% CI[a])	0.36 (0.30, 0.41)				–			
		Agreement (%)	45%				–			

[a] CI: Confidence Interval.

models was in both directions, so that, more individuals were in the low-risk level (404 vs. 320) and fewer in the high-risk group (28 vs.60) based on the WHO/ISH model. In this model, 21 (3.88%) females were in the higher-risk groups and 119 (21.99%) females were in the lower-risk groups. The agreement between WHO/ISH and NLB model was 45% (kappa = 0.36). Based on the WHO/ISH chart, a larger number of females were in the low-risk level (404 vs. 184) and a smaller number of females were in a high-risk group (28 vs. 141). This model categorized 7 (1.29%) in the higher-risk groups and 238 (43.99%) in the lower-risk groups (Table 3).

4. Discussion

This study aimed to predict CVD using LB and NLB Framingham model and WHO/ISH chart among 35-70 year-old adults in Shahdieh cohort study since there isn't a particular tool to calculate the risk of CVD in Iran. The agreement between the categorization of 10-year predicted CVD risk presented by the studied methods was also investigated. The findings indicated that the agreement between LB and NLB Framingham models was substantial. The comparison of Kappa agreement coefficients obtained by gender and age groups showed that the highest agreement between the models was related to LB and NLB Framingham models. Findings showed that the highest kappa coefficient was related to men under 60 years old (kappa = 0.73), and the lowest coefficient was for men over 60 years old (kappa = 0.54). In the study of Rezaei et al. the lowest coefficient of agreement between the two Framingham models was related to men over 60 years of age [7].

The current study demonstrated that the agreement of two Framingham models among women in both age groups was substantial. In the study of Boateng et al. the agreement between the two Framingham models was substantial (kappa = 0.63) [19]. Jones et al. reported that the agreement between BMI-based and Cholesterol-based Framingham models was moderate in all groups except for men over 60 years who had fair agreements [20]. A study conducted on the South Asian population showed that each LB model had a good agreement with its NLB model. In this study the agreement of the LB and NLB version of WHO/ISH chart (kappa = 0.804) and the agreement of the LB and NLB Framingham model (Kappa = 0.736) were substantial. In another study, a high agreement was observed between two Framingham models. They stated that the NLB Framingham model can be a good substitute for the LB Framingham if a country's resources are limited [21]. However Rezaei et al. reported that the NLB Framingham model cannot be a suitable substitute for the LB Framingham because it may overestimate the risk of CVDs [7]. A study that compared 6 models for predicting the risk of CVD indicated that the Framingham model had a better performance in predicting the people at risk than WHO/ISH. The author also noted that the Framingham model estimates more consequences of CVD, while other models, like WHO/ISH, estimate only myocardial infarction (fatal and non-fatal) and stroke [10]. Therefore, direct comparison of the Framingham model with other models doesn't seem correct and may lead to overestimating the CVD risk [22,23]. A study that investigated the performance of the Framingham method to predict the risk of CVD showed that the Framingham model performed relatively well in distinguishing between risk categories, but may overestimate the CVD risk for high-risk populations [24]. Mettanada et al. believed that the Framingham model could not perform well in the Asian population because it was designed based on the American data in a period when CVD had a high prevalence in America and low prevalence in Asia. Also, some factors like lack of exercise, abdominal obesity, and family history are not considered for Asian populations in the Framingham model [25].

The findings indicated that the agreement of the two Framingham models with the WHO/ISH chart was slight. The results also showed that the highest agreement of the WHO/ISH method with the two Framingham models was related to LB Framingham in women over 60 years old (kappa = 0.61) and NLB Framingham in women over 60 years old (kappa = 0.36). Comparison of other Kappa coefficients by age-gender groups indicated fair agreement between WHO/ISH method and the two Framingham models. Samaniyan et al. also showed that the lowest agreement between the models was related to the WHO/ISH and the Framingham model [9]. In Mirzaei et al.'s study, the agreement between risk classification in the Framingham and WHO/ISH method was slight. The authors believed that WHO/ISH charts cannot be used for risk assessment in developing countries [26]. Samaniyan et al. stated that because the WHO/ISH methods are not obtained from a future cohort study, they are not compatible with the Framingham method and have low sensitivity. Also, the authors believed that heterogeneity in different populations is the reason for underestimating the risk of CVDs in WHO/ISH [9].

The evidence from this study suggested that NLB Framingham model was remarkably different from the other methods in terms of risk classification. In the current study, 12.3% were in the high-risk level based on the NLB Framingham model. Meanwhile, LB Framingham model placed 6.6% of people and WHO/ISH chart placed less than 1% in the high-risk level. This finding shows the high tendency of NLB Framingham method to place more people in the high-risk level compared to the other two methods while WHO/ISH model tended to place more people in the low-risk level. This difference in the classification of people has been reported in other studies, which is consistent with our findings [11,27–29]. Selvarajah et al. evaluated the performance of CVD risk prediction models including FRS, SCORE (Systematic Coronary Risk Evaluation)-high and -low models, and WHO/ISH chart in a Malaysian population. In their study, the WHO/ISH chart grouped 89% of individuals in the low cardiovascular risk level in total. Furthermore, all models showed similar trends in categorizing women but the WHO/ISH chart had the highest category of low-risk populations in men [11]. 10-year predicted CVD risk was assessed in Carmarthenshire, south Wales by various models including NLB Framingham model. The results showed that more males were categorized at high-risk level in FRS [28]. Bansal et al. also examined the difference between the predicted risk of CVD by FRS and WHO/ISH chart. The results of this study also indicated that WHO/ISH significantly underestimated CVD risk than FRS [29]. Consistent with the present study, WHO/ISH chart tended to place people in the low-risk level in the Shahrekord cohort study. Based on the LB Framingham model, 9.8% of the people were in the high-risk level but, based on WHO/ISH chart, 1.8% were in the high-risk level [9]. Considering that the frequency of factors such as smoking and senility in the Shahrekord cohort study was higher compared to the present study, it was expected that a higher percentage of the Shahrekord cohort study population was categorized in the high-risk group [9]. Rezaei et al. also stated that the NLB Framingham model tended to show a higher risk than the LB Framingham, and men and women who were placed in the high-risk group in the NLB Framingham model were slightly more than twice as the LB model [7]. In our study, the percentage of men and women who were detected as high-risk individuals by the NLB Framingham model is less than twice compared to the LB Framingham model.

Similar to the present study, 6.8% of people were in the high-risk level based on the Framingham model in a study conducted on adults in Mashhad [30]. In Mirzaei et al.'s study, the Framingham model put 26.5% of the participants in the high-risk level, and WHO/ISH method put 4.2% in the high-risk group, which indicates the greater tendency of the WHO/ISH method to place people in the low-risk level [26]. The higher percentage of the high-risk level and the lower percentage of the low-risk level in the Mirzaei et al. study compared to this study may be due to the population under study [26]. Shahedieh cohort study was conducted in three small towns while Mirzaei et al. study, was done in an urban area. Rezaei et al. stated that the NLB Framingham model tended to state a higher risk than the LB Framingham, and men and women who were placed in the high-risk level in the NLB Framingham model were slightly more than twice as the LB model [7].

The findings of this study showed that in all three models, men were more at risk for CVD than women, which is consistent with similar studies [30]. Based on the LB Framingham method, 11.3% of men and 2% of women were at the high-risk level. Following the present study, 16.2% of men and 3.4% of women in the Shahrekord cohort study, and 8.8% of men and 2.1% of women in a study in northern Iran were at the high-risk level [9,31]. The Kappa coefficient in the current study showed that the agreement between models in women of all ages was better than in men except the agreement between the two Framingham models in individuals under 60 years, which was better in men than women. In the study of Rezaei et al. the two Framingham models were better for women of all age groups than men [7].

The comparison of Kappa coefficients to investigate the agreement of the two Framingham models indicated that the agreement was more in people under 60 years old than older people for both genders, which is aligned with the findings of Rezaei et al. [7]. Conversely, the agreement of the WHO/ISH with Framingham models indicated that the agreement was more in individuals more than 60 years than the younger people for both sexes. Rezaei et al. showed that the agreement of the two Framingham models in men under 60 years old (kappa = 0.71) was close to the present study. Also, the agreement of the two Framingham models in men over 60 years old was less than the younger people (Kappa = 0.44) [7].

This is the first study that assessed the agreement between the LB Framingham model, NLB Framingham model, and WHO/ISH chart. It was carried out with a relatively high sample which is considered as another strength. The results of this study were generated based on the data of the recruitment phase of the cohort study. We may be able to compare the prediction power of the tools and also determine the best scoring tool for 10-year predicted CVD risk in the next phases of the study.

This study had some limitations. As the Framingham model predicts a wider range of CVD than the WHO/ISH model, interpreting and comparing the results need discretion. Another limitation is that the population under study was from three small towns around Yazd city which were not industrialized. Therefore, extending the obtained results to the urban populations should be done with caution.

Based on the findings, it was observed that both Framingham models classified more individuals in the high-risk group compared to WHO/ISH. Due to the lethality of CVDs and the importance of their early detection, even if there are some false cases in the high-risk group based on Framingham models, we can ensure that most of the true high-risk people are detected. Since considerable agreements were observed between Framingham models in all sex-age categories, the NLB model may be preferred to the LB model as a primary screening tool, especially in a shortage of resources condition, where laboratory markers are not available or people cannot afford the laboratory test expenses. Furthermore, since FRS can be calculated through a points-based system, which does not need a computer or calculator, this tool is particularly useful where primary healthcare is delivered.

Author contribution statement

All authors listed have significantly contributed to the development and the writing of this article.

Data availability statement

The data that has been used is confidential.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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