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The Framingham Risk Score,Acc/Aha Pooled Cohort Equations And Who/Ish Cardiovascular Risk Prediction Models In The Estimation Of 10-Year Risk Of Cardiovascular Diseases –Review

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ABSTRACT
Cardiovascular diseases are a group of disorders of the heart andthe major blood vessels.It is always a major concern since they are the leading cause of morbidity and mortality worldwide.A risk factor can be defined as a characteristic that is associated with an increased or decreased likelihood of subsequent development of CVD.The knowledge regarding these risk factors helps topredict the risk of CVD in asymptomatic patients within a specified period using the risk scoring methods and also have a significant role in the prevention and management of cardiovascular diseases.This theoretically allows the targeting of health service resources to those most likely to benefit from preventive treatment and to avoid the cost, of unnecessary treatment and possible adverse effects in those at low risk.

KEYWORDS
Cardiovascular disease,Risk factor, Risk prediction models,Primary prevention,Framingham risk score,ACC/AHA Pooled cohort equations,WHO/ISH risk prediction chart.

AIM: To reviewthree different cardiovascular prediction models which are used in the estimation of 10-year risk of cardiovascular diseases.

I. INTRODUCTION

Cardiovascular diseases are the major cause of premature death in the developed world.According to WHO, an estimated 17.9 million people died from CVDs every year and contributes to 32% of global deaths. There are manywell-established, modifiable CVD risk factors which include elevated blood pressure,diabetes,hypercholesterolemia, obesity, lack of physical activity, inappropriate diet, excessive alcohol intake and smoking. Understanding these CVD risk factors makes prevention possible which led to the development of multivariable risk prediction models.They utilize data of multiple risk factors and make decisions regarding primary preventive strategy and clinic practice to identify and treat high-risk populations.Different guidelines recommend different risk scores to assess the 10-year cardiovascular risk and their management depending on the risk scores.

1.1) CARDIOVASCULAR DISEASES AND RELATED RISK FACTORS

Cardiovascular disease refers to a group of disorders,including diseases of the cardiac muscle and the vascular system supplying the brain,heartand other vital organs.CVD encompasses many clinical conditions, but all of them are caused by the common underlying pathophysiology of accelerated atherosclerosis.Among these, the leading cause of mortality and disability worldwide is the ischaemic heart disease and stroke which accountsfor 12.9milliondeathsworldwide in2013,orone inevery four of thetotals and also contribute to the escalating costs of health care according to the Global Burden of Disease study.

The incidence of cardiovascular disease in healthy and asymptomatic people is largely explained by several modifiable risk factors, which include smoking, abnormal lipid levels, hypertension, diabetes mellitus,an unhealthy diet with the low consumption of fruits and vegetables, excessive alcohol intake, abdominal obesity, psychosocial stress, and lack of regular physical activity. These nine modifiable risk factors account for more than 90% of the risk of future CVD events and contribute to the development of ischaemic heart disease and stroke worldwide.The benefit of these modifiable risk factorsis that they can be reduced or controlled with altered behaviour.Therefore, the primary targets of interventions to reduce the burden of Cardiovascular disease events would be throughthe prevention, treatment, and control of these risk

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factors before the manifestation of clinical symptoms.

1.2)CARDIOVASCULAR RISK PREDICTION MODELS

Cardiovascular disease is the leading cause of death worldwide and a major concern over public health. Therefore, its risk assessment is very important to many existing treatment guidelines.To calculate the absolute risk a riskassessment tool that evaluatesrelevant non-modifiable and modifiable risk factors is required and should be validated. Absolute risk is obtained bythe synergistic effect of all the cardiovascular risk factorspresent.The cardiovascular risk prediction tools estimate the probability of having a cardiovascular event based upon levels or presence of these known risk factorswithin a defined time frame, usually 10 years. Risk estimates are also being used to predict the magnitude of future cardiovascular disease mortality and morbidity at the population level and in specific subgroups to inform policymakers and health authorities about these risks. Additionally, risk prediction enables individuals to change their lifestyle, behaviour and to adhere to medications such as lipid-lowering drugs as a preventive measureand helps in the early identification of high-risk individuals for targeted intervention.

1.2.1)FRAMINGHAM RISK SCORE

The Framingham Risk Score is the first risk prediction scorethat was developed based on data obtained from the Framingham Heart Study andpredicts the fatal and non-fatal coronary heart disease events. Lately, the Framingham general CVD risk profile for primary care was developed in 2008, and this included cerebrovascular events,peripheral artery disease and heart failure as disease outcomes for assessing the 10-year cardiovascular disease risk.

Due to the increasing death rates for CVD since the beginning of the century which became an epidemic in the United States. In 1948, the Framingham Heart Study was initiatedunder the direction of the National Heart Institute (now known as the National Heart, Lung, and Blood Institute or NHLBI) as a project in health research to explore more about the general causes of heart disease and stroke which was little known.

The aim of the Framingham heart study then was to identify the common factors or characteristics that are associated with an increased or decreased likelihood of subsequent development of CVD over a long period in a large group of participants who were free from symptoms of previous cardiovascular disease.In 1948, the first FHS cohort which included 5,209 men and women between the ages of 30 and 62 was enrolled from Framinghama town in Massachusetts, USA.Since 1948, detailed medical history, physical examination and laboratory tests were done for the subjects every two yearsand in 1971, the Study enrolled a second generation called the Offspring Cohort comprising 5,124 of the original participants' adult children and their spouses – to participate in similar examinations.Thenin April 2002, by the enrollment of the third generation of participants, the grandchildren of the Original Cohort the study entered into a new phase.

The Framingham heart studyevaluates the relationship betweencardiovascular risk factors and CVD, in particular Coronary heart disease. The Framingham risk score incorporated the effects of age, sex, systolic blood pressure, total cholesterol, high-density lipoprotein (HDL) cholesterol, smoking status, antihypertensive treatment status, and diabetes mellitus to estimate a 10-year risk of coronary heart disease.

The strength of the FHS is that it was a prospective study conducted at a single centreusing a similar protocol throughout the study during the period 1971-1986, an era when most of the patients were not on any medication. It led to the estimation of risk in subjects who were not on any medications.The limitations of the FHS score include the small number of participants, the predominance of a white population in the USA, the exclusion of family history of CHD and body mass index,the overestimation (or underestimation) of risk in populations other than the US population, and predicts only CHD.Later the current version of the Framingham Risk Score was published in 2008 with modified outcomes.

1.2.2) WHO/ISH

WHO/ISH Risk scores are developed by the World Health Organization and the International Society of Hypertension to estimate the 10-year risk of a cardiovascular event for persons aged 30-79 years. They are mainly used in countries with limited resources to derive a population-specific tool,especially in low-income and middle-income countries.In contrast to other risk prediction tools, Risk WHO havecorresponding risk charts for 14 sub regions of the world,including the South-East Asian region D chart is available.There are three sub regions

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among all European countries based on their mortality.

These charts indicate a 10-year risk of a fatal or non-fatal major cardiovascular event (Coronary heart disease,Myocardial Infarction,Stroke or any other Atherosclerotic disease) based on their age,sex,blood pressure,smoking status,total blood cholesterol levels and presence or absence of DM.For every sub region,simplified risk charts without variable total cholesterollevels as well as gender-specific risk charts using conventional prognostic risk factors and variable DM are presented.These risk charts are based on the guidelines published by WHO in 2007 for reducing disability and premature deaths from CVD. They were updated in 2019 taking relevant information from the 2007 guidelines and presented for 21 global regions to maximize between region-variability and minimize heterogeneity in mortality.They are categorized into laboratory-based and non-laboratory based charts.The former one included all risk factors including history of DM and total cholesterol whereas for the latter one diabetes Mellitus and total cholesterol were not necessary but included body mass index (BMI).Thiswas done bygenerating a dataset for each region based on the prevalence of risk factors in that area, their relative risk and the corresponding population-level estimate of absolute risks for CV events. Also, other statistical methods including the mean and standard deviation of risk factor levels which is measured as a part of the collaborative risk assessment study are determined.

The risk charts are having 5 categories of risk ; <10%,10-19.9%,20-29.9%,30-39.9%,>40%.A risk of >\= 30% is defined as a high cardiovascular risk.The Risk WHO is extremely helpful to mankind because they figure out people with high cardiovascular risk and motivate them to change their lifestyles and whenever needed to start taking antihypertensive,lipid-lowering agents and aspirin to prevent further complications. These are particularly useful to areas in the developing world that have limitedmedical facilities and financial capacity for obtaining biochemical measurements.

Themajor drawback of Risk WHO is they underestimate CV risk in Indian patients.Moreover, the non-laboratory based algorithm doesn't estimate extra CVD risk associated with DM and thereby underestimate CVD risk in individuals with diabetes Mellitus.Also,the WHO/ISH prediction model wasbased on hypothetical cohorts and not on actual cohorts. Other drawbacks of this model wereits methodology.Only a limited description of the methodology has been provided.In addition to that,the Risk WHO prediction model provides only approximate ranges for 10-year risk estimates.They donot provide regression equations to estimate absolute risk for individuals.So these methods need further investigation to determine accuracy and validity.

ACC/AHA POOLED COHORT EQUATIONS

The ACA/AHA pooled cohort equations have been developed in 2013 as sex- and race-specific tools by the American College of Cardiology and the American Heart Association which collaborated their guidelines with the national heart,lung and blood institute (NHLBI) for the management of cardiovascular diseases in the adult population. In 2008, the NHLBI provided systematic evidence on each topic by expert panels and developed critical questions. The report from the institute of medicine on the guidelines has been made in 2011 and thereby the joint guidelines have been released in 2013.

The aim of the ACA/AHA pooled cohort equations is to predict 10-year risk of hard atherosclerotic cardiovascular disease events in the population especially in African-American individuals of age 20- 59 years forprimary prevention. The endpoints such as fatal and non-fatal stroke, Diabetes mellitus and racehas been used as characteristics thathelp in better risk prediction in individuals. The equationshave been designed to predict ASCVD events such as nonfatal myocardial infarction, fatal coronary heart disease, nonfatal or fatal stroke etc.The variables included in the pooled cohort equations are age, sex, race (White, Black, or other), smoking status, systolic blood pressure, hypertension treatment status, diabetes status, and total and high-density lipoprotein (HDL) cholesterol levels in the specific individual. The risk factors such as chronic kidney disease and social deprivation have been omitted as measures from the risk prediction.

The FRS which was used earlier was not able to estimate the risk of stroke which led to the introduction of ACC/AHA pooled cohort risk equations.The ACC/AHAhadthe same parameters as that of Framingham risk score and in addition, it also addsendpoints such as fatal and nonfatal stroke, myocardial infarction etc.One of the main limitations of the ACC/AHA is that it resulted in the overestimation of ASCVD risk. Thereby it led to the prescription of statin therapy in many individuals with lower risk than the intended 7.5% 10-year ASCVD risk.In addition,ACC/AHApooled

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cohort equations excluded the family history of premature CVD and also led to an underestimation of risk in individuals with a strong family history of CVD events. The Other limitation of ACC/AHA pooled cohort equations is that it had Diabetes mellitus as one of the endpoints but it excluded the factors that affect diabetes such asduration whether it was type 1 or type 2 and other cardiovascular risk factors.One of the main advantages of the equations is that they have been subjected to rigorous validation when compared to Framingham CHD risk score and other European scores.

CHARACTERISTICS OF 3 COMMON CARDIOVASCULAR PREDICTION MODELS:

	FRS	WHO/ISH	FRS CVD	ACC/AHA
Data	Prospective study: Framingham Heart Study	Methods differ from other risk estimation functions—not based on prospective data	Prospective studies: Framingham Heart Study and Framingham Offspring Study	National Heart, Lung, and Blood Institute-sponsored cohort studies, such as the ARIC (Atherosclerosis Risk in Communities) study, the CHS (Cardiovascular Health Study), and the CARDIA (Coronary Artery Risk Development in Young Adults) study, Framingham Original and Offspring Studycohorts.
Population assessed	General population, Framingham, Mass, U.S. Volunteer	Not applicable	General population, Framingham, Mass, U.S. Volunteer	African American population
Year	1998	2003	2008	2013
Age range(years)	30-74	40-70	30-74	20-79
Variables	Age, gender, DM, SBP, smoking, TC or LDL-C, HDL-C	Sex, age, SBP, smoking status, diabetes,± total cholesterol; different charts available for worldwide region	CVD RF + treated BP	Age,gender,race,TC ,HDL-C,DBP,DM,smokin gtreatment of HTN
Outcomes	Fatal and non - fatalCHD events(including angina)	Fatal and nonfatal MI and Stroke	CHD (coronary death, angina, coronary insufficiency), cerebrovascular events (all strokes and TIA), PAD, HF	CHD death, non-fatal MI,fatal stroke,nonfatal stroke
Time prediction	10-year risk of CHD events	10-year risk of CVD events.	The 10-year risk of CVD events, Risk age.	10-year risk
Guidelines	NCEP guidelines	WHO guidelines on CVD prevention	NCEP guidelines	ACC/AHA

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Formats	Online calculator	Colour-coded charts	Online calculator	Online calculator

II. CONCLUSION

The review comprises the characteristics of three prominent cardiovascular risk prediction models which includes Framingham risk score, WHO/ISH risk score and ACC/AHA pooled cohort equations.The overall objective of these cardiovascular risk assessment strategies discussed above is predicting and reducing the risk of future CVD events in asymptomatic patients.The benefits of these risk scores concerning the individuals,societies and the complete health care system are it enables clinicians to identify and stratify individuals at risk for CVD and aids communication with them to helpunderstand the importance of lifestyle modification and drug therapy.Many validated cardiovascular prediction tools can be used but they differ in various ways like the methods by which they were derived, population assessed, variables included and defined outcomes.So it is important to use a model correctly for the global cardiovascular risk assessment without failureand in the right contextto not avoid the opportunity for intervention.

ABBREVIATIONS

CVD;Cardiovascular disease, FHS;Framingham heart study, FRS; Framingham Risk Score,ACC/AHA; American College of Cardiology/American Heart Association,WHO/ISH; World health organization/International Society of Hypertension, NHLBI; National Heart, Lung, and Blood Institute, NCEP; National Cholesterol Education Program ASCVD; Atherosclerotic cardiovascular disease, DM; Diabetes mellitus, HTN; Hypertension, CHD; Coronary heart disease, MI; Myocardial infarction, TIA; Transient ischemic attack, PAD; Peripheral artery disease, HF; Heart failure, HDL-C; High-density lipoprotein cholesterol, LDL-C; Low-density lipoprotein cholesterol, TC; Total cholesterol, DBP; Diastolic blood pressure,SBP; Systolic blood pressure.

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