

# Risk estimates of cardiovascular diseases in a Sri Lankan community

U K Ranawaka<sup>1</sup>, C N Wijekoon<sup>1</sup>, A Pathmeswaran<sup>1</sup>, A Kasturiratne<sup>1</sup>, D Gunasekera<sup>1</sup>, S Chackrewarthy<sup>1</sup>, N Kato<sup>2</sup>, A R Wickramasinghe<sup>1</sup>

(Index words: epidemiology, cardiovascular diseases, risk estimates, risk prediction tools)

## Abstract

**Objectives** Quantifying the risk of cardiovascular disease (CVD) in a community is important in planning preventive strategies, but such data are limited from developing countries, especially South Asia. We aimed to estimate the risks of coronary heart disease (CHD), total CVD, and CVD mortality in a Sri Lankan community.

**Methods** A community survey was conducted in an urban health administrative area among individuals aged 35-64 years, selected by stratified random sampling. Their 10-year CHD, total CVD, and CVD mortality risks were estimated using three risk prediction tools: National Cholesterol Education Program - Adult Treatment Panel III (NCEP-ATP III), Systematic Coronary Risk Evaluation (SCORE), and World Health Organisation/ International Society of Hypertension (WHO/ISH) charts.

**Results** Among study participants (n=2985), 54.5% were females, and mean age (SD) was 52.4 (7.8) years. According to NCEP-ATP III ('hard' CHD risk), WHO/ISH (total CVD risk), and SCORE (CVD mortality risk) criteria, 25.4% (95% CI 23.6-27.2), 8.2% (95% CI 7.3-9.2), and 11.8 (95% CI 10.5-13.1) respectively were classified as at 'high risk'. The proportion of high risk participants increased with age. 'High risk' was commoner among males (30.3% vs 20.6%,  $p<0.001$ ) according to NCEP-ATP III criteria, but among females (9.7% vs. 6.7%,  $p<0.001$ ) according to WHO/ISH criteria. No significant gender difference was noted in SCORE risk categories.

**Conclusions** A large proportion of individuals in this community are at risk of developing cardiovascular diseases, especially in older age groups. Risk estimates varied with the different prediction tools, and were comparatively higher with NCEP-ATP III charts.

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<sup>1</sup>Faculty of Medicine, University of Kelaniya, Ragama, Sri Lanka and <sup>2</sup>International Medical Centre of Japan, Shinjuku-ku, Tokyo, Japan.

Correspondence: UKR, e-mail: <[udayaran@yahoo.com](mailto:udayaran@yahoo.com)>. Received 22 September and revised version accepted 13 December 2015.

## Introduction

Cardiovascular diseases (CVD) is the leading cause of mortality in the world [1,2]. The broad disease category CVD comprises atherosclerosis related coronary heart disease (CHD), stroke and peripheral vascular disease. Almost 80% of deaths and disease burden due to CVD is seen in developing countries [2]. CVD prevalence and mortality rates are expected to double from 1990 to 2020, and over 80% of this increase is estimated to be in developing countries [3]. The burden of CVD is especially high in South Asia, where the prevalence and incidence of CVD, mortality due to CVD, and the prevalence of risk factors of CVD are higher than in many other regions [4,5]. This increase is seen not only among those resident in South Asia, but also in migrant South Asian communities in Western countries [6,7]. Sri Lanka is a South Asian developing country in epidemiological transition. The community prevalence of CHD in Sri Lanka is estimated to be 9.3%, and prevalence of stroke in the Colombo district is 1.04% [8, 9]. CHD and stroke together account for 23% of hospital deaths in Sri Lanka [10].

Estimating the CVD risk in a community is important in planning preventive and treatment strategies [1,11]. Several risk prediction tools are available to estimate CHD and CVD risks in different populations [1, 11]. They use several variables to calculate an individual's absolute 10-year risk of CHD and CVD. This calculated absolute risk is considered a better estimate of an individual's total CVD risk than the sum of several risk factors, and is more useful in decision making regarding therapeutic interventions [1,11-13]. Thus several international and country-specific guidelines make recommendations on CVD prevention strategies based on individual's CVD risk calculations using risk prediction tools. [13-23]. The risk prediction tools to calculate the absolute CVD risk have been developed, and used, mainly in the developed world [13, 24-31]. Quantifying the cardiovascular risk in developing



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countries needs to be based on them, until population-specific risk prediction tools derived from prospective cohort studies from these communities are developed. The World Health Organisation with the International Society of Hypertension has developed WHO/ISH cardiovascular risk prediction charts for use in different epidemiological sub-regions in the world, which partly addresses this need [11].

There is a paucity of data on cardiovascular risk estimates in developing countries, especially South Asia, even with the existing risk prediction tools [11, 32-34]. The aim of this study was to estimate the risk of developing CHD or CVD, and death due to CVD in an urban Sri Lankan community using three different risk prediction tools.

## Methods

This study is a part of a community survey on non-communicable diseases [Ragama Health Study (RHS)] conducted in 2007. The survey methodology has been described previously [35]. The RHS is a collaborative effort between the Faculty of Medicine, University of Kelaniya and the International Medical Centre of Japan (IMCJ), Tokyo, Japan. Approval was obtained from Ethics Review Committees of both institutions.

### Setting and participants

This was a survey among adults aged 35-64 years in the Ragama Medical Officer of Health (MOH) area [area - 25 km<sup>2</sup>, 21 Grama Niladhari (GN) divisions, 15137 housing units, population at the time of study - 75,591]. The householders list of each GN division was used as the sampling frame, and the study population was stratified into three age groups: 35-44, 45-54 and 55-64 years. A random sample of 200 adults was obtained from each GN division, in a ratio of 1:2:2 in the age groups of 35-44, 45-54 and 55-64 years respectively. Random numbers were generated by the statistical programme PEPI [36]. Households of selected participants were visited, and invited to take part in the study.

### Measurements

A special screening clinic was set up at the Faculty of Medicine, University of Kelaniya where participants were evaluated after obtaining informed written consent. Demographic, anthropometric and clinical data were recorded by trained investigators. Blood pressure was measured in the seated position using an Omron 705CP automated blood pressure monitor. The mean value of two readings taken five minutes apart was used for analysis. Plasma glucose was measured according to the hexokinase method, total cholesterol by the method described by Stadtman, and LDL-C by the homogenous assay method using ALDL-Flex reagent cartridges (Dimension Clinical Chemistry System, Dade Behring, USA) [37]. A special follow-up clinic conducted by

consultant physicians was commenced at the Faculty of Medicine to provide treatment and follow-up care to those found to have abnormal findings.

### Estimating the risk of CHD and CVD

The 10-year absolute risk of each participating individual was calculated, and assigned to a risk category according to the NCEP-ATP III [13], WHO/ISH [11] and SCORE [25] risk prediction tools. The NCEP-ATP III algorithm estimates the 10-year risk of 'hard' CHD events (myocardial infarction or CHD death), and classifies individuals into three risk categories; low risk (10-year risk of less than 10%), medium risk (10-20%), or high risk (more than 20%) [13]. Persons with diabetes or previous CVD were assigned to the high risk category irrespective of the calculated risk score. The WHO/ISH risk prediction charts estimate the total risk of fatal and non-fatal CVD events [11]. They classify individuals into 5 risk categories, to facilitate high risk categorisation and intervention at different levels of risk, depending on the availability of resources. We classified all those with a risk  $\geq 20\%$  as the high risk category to enable comparison with the NCEP-ATP III categories. Persons with previous CVD were assigned to the high risk category irrespective of the calculated risk score. The WHO/ISH charts are region-specific, and we used the charts applicable to Sri Lanka (South-East Asia Region B). The SCORE algorithm estimates total CVD mortality, and classifies individuals into categories of low risk (10-year risk of less than 5%) and high risk (5% or more) [25]. When using the SCORE algorithm, it is recommended that those with previous CVD are assigned to the high risk category irrespective of the calculated risk score, and the 10-year risk for those with diabetes is obtained by multiplying the calculated risk score by two in diabetic men and by four in diabetic women [25]. We made these adjustments when calculating the risk scores.

The following variables were assessed in risk estimation: sex, age, systolic blood pressure, smoking status, total cholesterol, HDL-cholesterol, diabetes and previous CVD. NCEP-ATP III risk estimation uses sex, age, systolic blood pressure, smoking status, total cholesterol and HDL cholesterol levels. WHO/ISH risk estimation charts use sex, age, systolic blood pressure, smoking status, total cholesterol level and presence of diabetes. SCORE risk estimation charts use sex, age, systolic blood pressure, smoking status and total cholesterol level. Fasting venous plasma glucose of  $\geq 7$  mmol/l or being on treatment for diabetes mellitus was considered as 'presence of diabetes mellitus'. A history of myocardial infarction, unstable angina, angina, stroke, transient ischaemic attack or treatment for CVD was considered as 'previous CVD'. Self-reported medical history supplemented by medical records such as diagnosis cards and clinic record books were utilised to document presence of and treatment for CHD (stable angina, unstable angina, myocardial infarction) and

ischaemic stroke/ transient ischaemic attacks. Those who have smoked within a period of one year were identified as smokers.

### Statistical analysis

Data were entered in a database using Epi Info 2000 (Centres for Disease Control and Prevention, Atlanta, GA) and logical and range checks were done. Statistical analysis was done using STATA version 8 (StataCorp, College Station, Texas 77845, USA). Continuous data were summarised using means and standard deviations as well as grouped frequency distributions. Categorical data were summarised as percentages. The overall prevalence of risk categories were calculated after standardising for age and sex. The statistical significance of the association between background variables and risk stratification was assessed using the Chi square test. A  $p$  value of  $<0.05$  was considered as significant.

### Results

Out of 3012 participants (response rate of 72%) data of 27 participants were incomplete and were excluded. A total of 2985 participants were evaluated for assessment of cardiovascular risk. The distribution of main clinical and biochemical features of the study population is shown in Table 1. The mean values (SD) for the variables studied were as follows; age - 52.4 (7.8) years, systolic blood pressure - 130.8 (29.8) mmHg, total cholesterol - 5.53 (1.98) mmol/l, HDL-cholesterol - 1.3 (0.24) mmol/l and fasting plasma glucose - 6.39 (3.9) mmol/l.

According to the NCEP-ATP III ('hard' CHD risk), WHO/ISH (total CVD risk), and SCORE (CVD mortality risk) criteria, 25.4%, 8.2%, and 11.8% respectively were classified as 'high risk' (Tables 2 and 3). Males were more likely to be categorised as 'high risk' based on NCEP-ATP III criteria (male - 30.3%, female - 20.6%,  $p<0.001$ ), while females were more likely to be classified as high risk on the WHO/ISH criteria (male - 6.7%, female- 9.7%,  $p<0.001$ ). There was no significant sex difference in 'high risk' categorisation according to SCORE risk estimates (male- 12.6%, female- 10.9%,  $p=0.211$ ) (Table 2). Risk increased with age in all prediction equations. According to NCEP-ATP III criteria, the percentages of 'high risk' participants in the age groups 35-44, 45-54 and 55-64 were 14.3%, 28.4% and 43.5% respectively ( $p<0.001$ ). According to WHO/ISH criteria, 1.9%, 9.2% and 19.8% were in the 'high risk' category in the 35-44, 45-54 and 55-64 age groups ( $p<0.001$ ), respectively. 'High risk' percentages for these age groups according to SCORE criteria were 6.9%, 13.5% and 18.8% respectively ( $p<0.001$ ) (Table 3).

### Discussion

Estimating the total cardiovascular risk in a community is important in developing targeted therapeutic and preventive strategies [7,11]. Ideally such strategies

should be based on population-specific risk prediction tools, as the validity of the tools vary from one population to another [1]. At present, there are no population-specific tools for Sri Lanka, as in many other developing countries. This is the first report from Sri Lanka to describe the cardiovascular risk in a community using different risk prediction tools. We found that one-fourth in this urban community was at high risk of developing a hard CHD event, and one-tenth was at risk of dying from CVD.

Several strengths in our study merit emphasis. Firstly, our sample size was large, and our findings are likely to be statistically robust, as evidenced by the narrow confidence intervals. Therefore, we believe these findings are representative of our population. Secondly, our results were based on primary data from a community survey,

**Table 1. Clinical and biochemical characteristics of the study population**

	Male n (%)	Female n (%)	Total n (%)
Age (years)			
35-39	104 (7.7)	127 (7.8)	231 (7.8)
40-44	138 (10.1)	146 (9.0)	284 (9.5)
45-49	236 (17.4)	317 (19.5)	553 (18.5)
50-54	269 (19.8)	318 (19.5)	587 (19.7)
55-59	307 (22.6)	368 (22.6)	675 (22.6)
60-64	304 (22.4)	351 (21.6)	655 (21.9)
Systolic blood pressure (mmHg)			
<120	358 (30.8)	403 (32.5)	761 (31.7)
120-129	259 (20.1)	294 (20.7)	553 (20.4)
130-139	280 (21.9)	310 (19.4)	590 (20.6)
140-149	196 (12.0)	219 (10.5)	415 (11.2)
150-159	109 (7.2)	190 (8.3)	299 (7.7)
160 or above	156 (8.0)	211 (8.8)	367 (8.4)
Total cholesterol (mmol/l)			
<4.2	172 (11.4)	119 (8.3)	291 (9.8)
4.2-5.2	456 (33.1)	461 (32.3)	917 (32.7)
5.3-6.2	464 (34.8)	584 (35.2)	1048 (35.0)
6.3-7.3	194 (14.8)	337 (17.9)	531 (16.3)
7.4 or above	72 (6.0)	126 (6.4)	198 (6.2)
HDL-cholesterol (mmol/l)			
1.6 or above	9 (0.8)	21 (1.3)	30 (1.1)
1.3-1.6	728 (53.9)	1038 (60.6)	1766 (57.3)
1.1-1.3	569 (41.1)	544 (37.0)	1113 (39.0)
<1.1	52 (4.2)	24 (1.2)	76 (2.6)
Diabetes	303 (19.4)	411 (19.4)	714 (19.4)
Smoking	476 (37.7)	10 (0.8)	486 (19.0)
Previous CVD	67 (3.3)	61 (2.2)	128 (2.7)
Total	1358 (45.5)	1627 (54.5)	2985 (100.0)

whereas several previous studies have used retrospective secondary data [27, 28]. Thirdly, we used three different risk equations. Most previous studies have used the Framingham equation, its derivative the NCEP-ATP III, or the SCORE equation. We used the WHO/ISH charts in addition to the NCEP-ATP III and the SCORE equations. The Framingham equations and the SCORE risk equations are among the most widely used, and are used in most clinical guidelines on CVD prevention. The WHO/ISH charts have been designed to be region-specific, taking into consideration the varying population mix and risk factor prevalence, based on available data [11]. Fourthly, evaluating the total CVD risk, and not only the CHD risk, is important in individual risk assessment [6, 11]. We studied the CHD risk (NCEP-ATP III), the total CVD risk (WHO/ISH), and the risk of CVD mortality (SCORE). Finally, some previous studies have been confined to those with selected risk factors [28, 29], whereas others had excluded participants with certain risk factors. We did not select participants according to the presence or absence of risk factors, and therefore our data may be more applicable to the community at large.

There are several limitations to our study. Firstly, the study population was drawn from an urban community, and these results are not generalisable to the entire country. The risks are likely to vary in different areas, especially in rural parts. However, the risk of CHD and CVD are likely to be highest in urban areas, and risk estimation and therapeutic intervention should start in these communities. Secondly, the risk of CHD and CVD in extreme age groups (< 35 years and > 64 years) is not captured in this study, as only those in the 35-64 year age range were included. However, assessment of risk outside

this age range was not possible, as the WHO/ISH and SCORE algorithms have been developed for use in this age group. Thirdly, the risk calculations were based on a single evaluation for the presence of risk factors, and this may not be an entirely accurate reflection of an individual's risk. This is a drawback that affects all community based risk estimation studies. Repeated measurements would improve the accuracy of data, but would be difficult in a large community survey. Fourthly, use of self-reported data as evidence for CVD and diabetes may lead to inaccuracies, and possible under- or overestimation of risk. This cannot be avoided as many patients with previously detected CVD and diabetes would already be on treatment, and may not have biochemical or other evidence of disease at time of assessment. Furthermore, the distribution of systolic blood pressure in our sample was skewed to the right, and 68% of the population had a systolic blood pressure over 120 mmHg. This may be due to overrepresentation of the higher age groups in the study sample. Finally, most of the risk algorithms have been developed based on data from Caucasian populations. The NCEP-ATP III charts are an adaptation of the original Framingham equations derived from an American population [38], and the SCORE charts are based on data derived from several European countries [25]. Their validity in South Asian countries has not been established in prospective cohort studies.

Comparison of our data with previous studies is difficult, as the risk factor profiles are likely to vary between populations, and different studies have used different risk equations and recruitment criteria, especially with regard to the age groups and the presence of risk factors. There are only a few studies using similar risk equations in Asian

**Table 2. Risk stratification by sex, according to NCEP-ATP III, WHO/ISH and SCORE criteria**

	<i>Low risk</i>		<i>Moderate risk</i>		<i>High risk</i>		<i>p value</i>
	<i>n</i>	<i>% (95% CI)</i>	<i>n</i>	<i>% (95% CI)</i>	<i>n</i>	<i>% (95% CI)</i>	
<b>NCEP-ATP III ('hard' CHD)</b>							
Male	406	46.1 (42.8-49.5)	430	23.6 (21.2-26.1)	522	30.3 (27.5-33.2)	<0.001
Female	1168	78.9 (76.7-81.0)	16	0.5 (0.3-0.8)	443	20.6 (18.5-22.8)	
All	1574	62.8 (60.7-64.8)	446	11.8 (10.7-13.2)	965	25.4 (23.6-27.2)	
<b>WHO/ISH (fatal or non-fatal CVD event)</b>							
Male	1142	89.9 (88.4-91.4)	75	3.4 (2.6-4.3)	141	6.7 (5.5-8.0)	<0.001
Female	1207	82.9 (80.9-84.6)	180	7.4 (6.3-8.7)	240	9.7 (8.4-11.2)	
All	2349	86.4 (85.1-87.5)	255	5.4 (4.7-6.2)	381	8.2 (7.3-9.2)	
<b>SCORE (CVD mortality)</b>							
Male	1157	87.4 (85.3-89.3)	-	-	201	12.6 (10.7-14.8)	0.211
Female	1388	89.1 (87.3-90.6)	-	-	239	10.9 (9.4-12.7)	
All	2545	88.2 (86.9-89.5)	-	-	440	11.8 (10.5-13.1)	

Percentages are adjusted for age; NCEP-ATP III, National Cholesterol Education Program-Adult Treatment Panel III; WHO/ISH, World Health Organization/International Society for Hypertension; SCORE, Systematic Coronary Risk Evaluation; CHD, Coronary Heart Disease; CVD, Cardiovascular Disease.

**Table 3. Risk stratification by age, according to NCEP-ATP III, WHO/ISH and SCORE criteria**

	<i>Low risk</i>		<i>Moderate risk</i>		<i>High risk</i>		<i>p value</i>
	<i>n</i>	<i>% (95% CI)</i>	<i>n</i>	<i>% (95% CI)</i>	<i>n</i>	<i>% (95% CI)</i>	
<b>NCEP-ATP III ('hard' CHD)</b>							
35-44 years	421	81.2 (77.6-84.4)	22	4.5 (3.0-6.8)	72	14.3 (11.5-17.6)	<0.001
45-54 years	659	55.9 (53.0-58.8)	161	15.7 (13.7-18.0)	320	28.4 (25.8-31.0)	
55-64 years	494	35.8 (33.3-38.4)	263	20.7 (18.6-23.0)	573	43.5 (40.8-46.2)	
All	1574	62.8 (60.7-64.8)	446	11.8 (10.7-13.2)	965	25.4 (23.6-27.2)	
<b>WHO/ISH (fatal or non-fatal CVD event)</b>							
35-44 years	500	97.2 (95.3-98.3)	5	0.9 (0.4-2.3)	10	1.9 (1.0-3.5)	<0.001
45-54 years	955	84.2 (81.9-86.2)	79	6.6 (5.4-8.2)	106	9.2 (7.6-10.9)	
55-64 years	894	67.5 (65.0-70.0)	171	12.7 (11.0-14.6)	265	19.8 (17.7-21.9)	
All	2349	86.4 (85.1-87.5)	255	5.4 (4.7-6.2)	381	8.2 (7.3-9.2)	
<b>SCORE (CVD mortality)</b>							
35-44 years	480	93.1 (90.5-95.0)	-	-	35	6.9 (5.0-9.5)	<0.001
45-54 years	986	86.5 (84.3-88.3)	-	-	154	13.5 (11.7-15.7)	
55-64 years	1079	81.2 (78.9-83.2)	-	-	251	18.8 (16.8-21.0)	
All	2545	88.2 (86.9-89.5)	-	-	440	11.8 (10.5-13.1)	

Percentages are adjusted for sex; NCEP-ATP III, National Cholesterol Education Program-Adult Treatment Panel III; WHO/ISH, World Health Organization/International Society for Hypertension; SCORE, Systematic Coronary Risk Evaluation; CHD, Coronary Heart Disease; CVD, Cardiovascular Disease.

populations [6, 32, 33, 39]. In these studies, the estimates of the CHD risk derived from the Framingham functions were comparatively higher. Similar findings have been reported by several authors when Framingham functions were used even in European populations [27, 30, 40].

In our study, risk estimates with the three equations were different, similar to the findings from previous studies using different risk algorithms [6, 27-29]. The high risk group was largest (25.4%) when risk estimation was done with NCEP-ATP III criteria, and smallest (8.2%) when the risk was estimated using WHO/ISH criteria. Different risk categorisation seen with different risk assessment tools may be due to several reasons. Firstly, the end-points assessed are different – 'hard' CHD events with NCEP-ATP III, total CVD events with WHO/ISH, and total CVD

mortality with SCORE. Secondly, the methods used in risk calculation are different. In the NCEP-ATP III algorithm, participants with diabetes or pre-existing CVD (considered CHD equivalents) are automatically assigned to the 'high risk' category. In the WHO/ISH risk assessment, separate charts are available for those with and without diabetes, but the presence of diabetes automatically does not equate with 'high risk'. Those with previous CVD are assigned to the high risk category. The SCORE algorithm does not consider the higher risk conferred by diabetes and previous CVD in the risk calculation, but it is recommended that the risk scores are adjusted to reflect this increased risk [25]. The prevalence of diabetes was high (19.4%) in our study population, and this may largely explain the disparity between the high risk rates seen with the NCEP-ATP III charts and other risk charts.

The proportion at high risk of death due to CVD would be expected to be much lower than the proportion at high risk of all CVD events. However, in our study, the proportion of the population at high risk of CVD mortality (by SCORE criteria) was actually higher than the proportion at high risk of fatal or non-fatal CVD events as estimated by WHO/ISH criteria. It raises the possibility that the WHO/ISH prediction charts may underestimate the population risk of CVD events. The SCORE charts were previously shown to underestimate the mortality risk in South Asians, and this may render this difference in risk estimates even more significant [6].

In our study, males predominated in the high risk category in the NCEP-ATP III estimates, whereas more females were at high risk with the WHO/ISH criteria. One possible explanation for this apparent disparity may be that males are at higher risk of hard CHD events (NCEP-ATP III), but females may be at higher risk of total CVD events.

In conclusion, we have estimated the risks of developing CHD and CVD events, and death due to CVD, in an urban Sri Lankan community. We believe our findings are useful in quantifying the disease burden, and would help in planning targeted preventive strategies. With the available data, we cannot make recommendations on the most suitable risk estimation tool for Sri Lankan patients. Using a tool like NCEP-ATP III (derived from Framingham functions) that categorises more individuals in to the high risk group will lead to selection of more people for treatment, but with the inherent cost implications and risk of adverse drug reactions. On the other hand, using a tool (such as the WHO/ISH) that categorises fewer individuals in to the high risk group may deprive eligible people of potentially life saving treatment. The differing risk estimates obtained with the different equations in this cross sectional study highlight the need for developing risk prediction tools based on nationally representative data of incident cardiovascular events in Sri Lanka.

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## Conflicts of interests

There are no conflicts of interest.

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