STATISTICAL ANALYSES TO VALIDATE THE WHO/ISH RISK PREDICTION CHARTS FOR SRI LANKA

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Degree of Master of Science in Business Statistics

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Abstract

The WHO/ISH (WHO/ International Society of Hypertension) risk prediction charts have been used widely by South East Asian Countries. The WHO/ISH risk prediction charts provide approximate estimates of cardiovascular risk in people who do not have established coronary heart disease, stroke or other atherosclerotic diseases. Based on the 10-year risk of fatal or non-fatal major cardiovascular events according to age, gender, smoking status, systolic blood pressure, presence or absence of diabetes and total serum cholesterol level. However, it has not been validated for the Sri Lankan population. Thus this study was initiated to validate the above mentioned WHO/ISH risk prediction chart for cardiovascular diseases using the database maintained at the Faculty of Medicine, University of Kelaniya for 10 years (2007 - 2017). The major risk factors for cardiovascular diseases are age, gender, higher blood sugar level and higher systolic blood pressure when considered individual effect on cardiovascular(CV) diseases from each risk factor. In both risk prediction methods (risk prediction with serum cholesterol readings and without serum cholesterol readings), the majority of the population had a <10% risk of a fatal or non-fatal cardiovascular event. Risk of cardiovascular diseases in the same population increased with age. Males had a significantly higher cardiovascular risk than females. The risk classification using total serum cholesterol was a better prediction chart than the one without it.

Keywords: WHO/ISH, cardiovascular disease, risk prediction charts, Sri Lanka, South East Asia Region.

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List of Abbreviations

ATP – Adult Treatment Panel

BMI – Body Mass Index

CABG – Coronary Artery Bypass Graft

CHD – Congenital Heart Disease

CV – Cardiovascular

CVD – Cardiovascular Disease

GN – Grama Niladhari

IMCJ – International Medical Centre of Japan

ISH –International Society of Hypertension

MI – Myocardial Infarction

MOH – Medical Officer of Health

NCD – Non-Communicable Disease

NCEP – National Cholesterol Education Program

OR – Odds Ratio

PCI – Percutaneous Coronary Intervention

PROCAM - Prospective Cardiovascular Munster

RHS – Ragama Health Study

SBP – Systolic Blood Pressure

SCORE - Systematic COronary Risk Evaluation

SEAR B – South East Asia Region B

WHO – World Health Organization

CHAPTER 1

INTRODUCTION

1.1 Background of Cardiovascular Disease (CVD)

Non communicable diseases are the leading cause of mortality according to the hospital admissions in Sri Lanka (Annual Health Bulletin, 2016). Ischemic heart disease is reported to be the leading cause of death and has risen by 14.3% in the span of 10 years from 2007-2017 (Healthcare Access and Quality in Sri Lanka, 2019). Globally the majority of cardiovascular disease (CVD) deaths take place in low and middle income countries as the tide has turned for a healthier lifestyle among the more developed nations. The burden of NCDs is increasing. The proportion of burden from NCD in middle-income countries has already exceeded 70% (Mathers and Loncar, 2005). According to WHO's latest statistics, 17.9 million people die each year from CVDs, an estimated 31% of all deaths worldwide. A major reason for the increasing risk of cardiovascular diseases is lifestyle changes (Ghorpade, *et al*., 2015).

Prevention of CVDs requires timely identification of effective dietary and lifestyle modification and/or drug interventions. The WHO/ISH risk prediction charts provide approximate risk estimates of CVD risk in people who do not have established coronary heart disease, stroke or other atherosclerotic diseases. The chart is used to calculate the 10-year risk of fatal or non-fatal major cardiovascular events based on age, gender, smoking status, presence or absence of diabetes and total cholesterol level (Ghorpade, *et al*., 2015). These data are easily accessible to both physicians as well as health care workers in the community or primary care setting.

Understanding the risks to physical health is the basic key to preventing disease and injuries. Sometimes many risk factors are involved for a particular disease or injury. To identify the risk factors, multiple interventions are available. Most risk factors are associated with one or more diseases and targeting those factors can reduce multiple causes of diseases. For example, reducing smoking will result in fewer deaths and

less disease from lung cancer, heart disease, stroke, chronic respiratory disease and other conditions.

To prevent disease, it is necessary to identify and deal with their causes. Currently, in many countries with low and middle income, the main focus of health care for NCD's is hospital centered acute care (Global status report on noncommunicable diseases, 2010). It is a very expensive approach that will not contribute to a significant reduction of the NCD. It also denies people the health benefits of taking care of their conditions at an early stage. To ensure early detection and timely treatment, NCDs need to be integrated into primary health care.

1.2 Estimation of Risk

Risk estimates identify people with a high risk of potential CVD events early who will be able to change their lifestyle or behavior, take appropriate medications to reduce the risk and be helpful to motivate patients to change risky lifestyles. The identified high risk groups can be targeted for preventive measures directing the limited health care resources to achieve the highest impact in preventing CVD in resource poor settings. The decline in CVD risk has been attributed to changes made to modifiable risk factors as opposed to treatment of disease (Otgontuya *et al*., 2013), hence the importance of identifying the groups that will benefit most from preventive measures. In the past few decades due to urbanization, increased life expectancy and harmful lifestyles (Ghorpade *et. al*, 2015), NCDs and CVDs have become a major cause of morbidity, early death and overburdening of the public health infrastructure (Ghorpade *et a*l, 2015). Based on the report of the WHO, the middle eastern countries are expected to have the highest incidence of diabetes (Sarrafzadegan *et al*, 2017). Nearly 58% of CVD deaths occur in those aged less than 60 years in low and middle income countries (Otgontuya *et al.*, 2013).

A reduction of CVD morbidity and premature mortality has been occurred through a combination of three factors such as population-level risk factor, Individual-based primary prevention targeted at high risk groups to prevent the onset of CVD through risk factor reduction and also secondary prevention and treatment to prevent disease

progression in people with established CVD. Evidence from high-income countries shows that a comprehensive focus on prevention and improved treatment following CVD events has led to dramatic declines in mortality rates (Global status report on noncommunicable diseases, 2010). However, survival rates in low and middle income countries remain very low.

1.3 Present Procedure of Identification of CVDs

There are different concerns when following or developing a risk prediction model for clinical assessment of a patient to determine treatment methods. First of all, the risk score should be applicable to the local patient setting in the country. The suitability of any risk prediction model is determined by the underlying incidence of disease and prevalence of its risk factors. Secondly, can the risk prediction model be fully assessed for its clinical utility to predict risk accurately in the local patient setting? Reports proved that some developing countries often lack the information on CVD events that are required for the full adjustments of CV risk prediction models (Selvarajah *et al.*, 2014).

In the view of multiple factors in the causation of CVDs, it will not be fair to use a single risk factor for predicting CV risk. The best approach will be to use a particular risk chart with considers a maximum number of all possible determinants (Ghorpade *et al.*, 2015). CV risk prediction models are important in the prevention and management of cardiovascular disease. The contribution of each risk factor can be ascertained for different regions.

1.4 CVD Risk Prediction Charts by WHO/IHS

The risk prediction charts introduced by WHO and the International Society of Hypertension (ISH) indicate 10-year risk of a fatal or nonfatal major cardiovascular events such as myocardial infarction or stroke, based on age group, gender, blood pressure level, status of smoking status, total blood cholesterol and status of diabetes (presence or absence). According to WHO these charts are applicable for 14 WHO epidemiological sub-regions such as African Region (AFR D, AFR E), American

Region (AMR A, AMR B, AMR D), Eastern Mediterranean Region (EMR B, EMR D), European Region (EUR A, EUR B, EUR C), South East Asian Region (SEAR B, SEAR D), and Western Pacific Region (WPR A, WPR B).

Two sets of charts developed by WHO to estimate the risk factors. Each set consists 14 charts for each region. One set can be used in settings where blood cholesterol can be measured. The other set is for settings in which blood cholesterol cannot be measured. The charts cannot be used in countries that are not belong to specific WHO epidemiological sub-region. The charts provide approximate estimates of CVD risk in people who are not suffered from coronary heart disease, stroke or other atherosclerotic disease. The charts are useful as risk estimation tools to help identify those at high cardiovascular risk, and to motivate patients, particularly to change behavior and, when appropriate, to take antihypertensive, lipid-lowering drugs and aspirin. Risk scores vary widely in terms of study characteristics, predictors and CVD outcomes investigated (Otgontuya *et al.*, 2013). The risk scores developed for high income countries may not be suitable for low resource settings.

In addition to the individual benefits, risk estimates allow for monitoring of CVD risk in a population and documentation of the trend which is useful for policy making in the health sector. Risk estimation models are used in clinical practice to identify and treat high-risk populations as well as to communicate risk effectively.

The benefit of using WHO/ISH regional risk prediction charts for the Sri Lankan population is that the risk charts have been developed based on population data in the relevant regions. Hence, the WHO charts are likely to provide better estimates as compared to the estimates generated using models that have been developed for Caucasian populations such as the Framingham risk scores.

1.5 Present Situation on WHO/ISH

The Ragama Health Study (RHS) was part of a large community based investigation on non-communicable diseases and it was a collaborative study between the International Medical Centre of Japan (JMCJ) and the Faculty of Medicine, University of Kelaniya, Sri Lanka. The RHS is a large community based cohort

study which was started in 2007 comprising 2986 adults aged 35 to 64 years in the Ragama Medical Officer of Health area (Fig. 1.1).

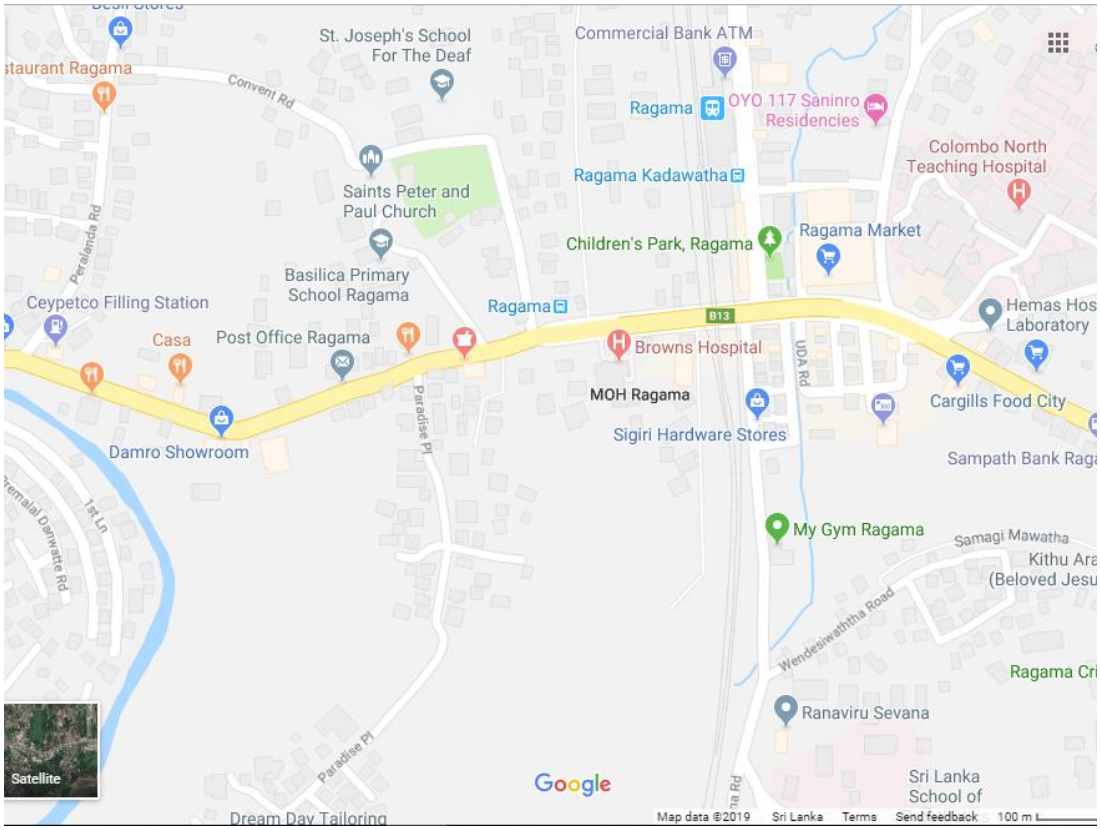

Figure1.1: Ragama Medical Officer of Health (MOH) area

Source: www.googlemaps.com

Sample was collected using stratified sampling using the house-holders list of each GN division. A random sample was obtained from each stratum. All selected individuals identified for selection were visited at their homes and invited to participate in the study (Dassanayake *et al.*, 2009); the procedures and benefits were explained to potential participants prior to obtaining informed written consent. All consenting adults were requested to participate in the interview, ultra-sonographic examination of the liver, anthropometric measurements and collection of blood samples (Dassanayake *et al.*, 2009). All subjects were requested to present to the clinic at the Faculty of Medicine after a 12 hour fasting with any available health records and the filled questionnaire (Appendix 1) which was given at the home visit.

Information on socio demographic variables, lifestyle habits with identification of alcohol consumption above the safe limit were obtained from the participants. For this study, 10-year information on 2517 participants was analyzed. There were 73 cardiovascular deaths during this period in this population.

1.6 Research Problem

The assessment of cardiovascular risk has been a key element in efforts to define risk factors for CVD, to identify novel markers of risk for CVD, to identify and assess potential targets of therapy, and to enhance the cost-effective implementation of therapies for both primary and secondary prevention of CVD (Cardiovascular Risk Prediction). Risk estimates can theoretically be used to raise population awareness of diseases (such as CVD) that cause a significant morbidity and mortality burden, to communicate knowledge about that risk to individuals and subgroups, and to motivate adherence to recommended lifestyle changes or therapies (Cardiovascular Risk Prediction). Cardiovascular risk assessment is a fundamental component of prevention of CVD. However, commonly used prediction models have not been validated within the specific regions.

As explained in Section 1.5, at baseline, the cohort comprised 2986 participants within the Ragama MOH area in 2007. In 2017, 2724 participants were contacted and among them only 2517 were 40 years and above in 2007. All of them were selected for the study as risk prediction charts are available only for persons aged 40 years and above.

1.7 Objective of the Study

On view of the above explanation, the objective of this study is, to carry out statistical analyses to test the accuracy of the WHO/ISH risk prediction chart for CVD for Sri Lanka using secondary data collected by Faculty of Medicine, Ragama

1.8 Outline of Dissertation

The dissertation comprises five chapters. Chapter 1 comprises the introduction, the justification for the study and the objectives of the study. Chapter 2 has the literature

review where both national and international studies related to the topic carried out previously were reviewed. Chapter 3 comprises the methodology used and a description of the data that was used for risk prediction. The Chapter 4 gives the statistical analyses to find the most affected risk categories on CVD in Sri Lanka based on WHO/ISH criteria. The Chapter 5 gives the validation result of WHO/ISH charts using Sri Lankan data. Conclusions and recommendation are given in Chapter 6.

CHAPTER 2

LITERATURE REVIEW

2.1 Status of NCD and CVD: Global Overview

Validation of a cardiovascular risk prediction model in a given population has been highlighted as being important before adoption to clinical practice (Lloyd-Jones *et al.*, 2010). All the risk prediction models may not be suited for a given population and some models might be better suited but WHO/ISH was a poor sensitivity in the Malaysian population where the high risk individuals were under-identified (Selvarajah *et al.*, 2014). This is detrimental to a developing nation as it would mean there is a higher chance of cardiovascular morbidity resulting in higher cost for the individual and the health care system even though the cost for screening has been incurred. In the above study FRS and Systematic Coronary Risk Evaluation were identified as better tools. They showed similar trends in prediction and had good discrimination for cardiovascular mortality (Selvarajah *et al.*, 2014).

It has been reported that CVD events such as myocardial infarction and stroke are rarely caused by a single potential risk factor but by the combined effect of several risk factors (Ghorpade *et al.*, 2015). Studies have highlighted the need raise awareness of cardiovascular risk. Heart diseases are increasing due to industrialization, globalization, urbanization and economic transition (Madhu *et al.*, 2016).

The most frequent cause of death is NCDs in many countries. The four main types of non-communicable diseases are cardiovascular diseases (heart attacks and stroke), cancer, chronic respiratory diseases (such as chronic obstructed pulmonary disease and asthma) and diabetes.

In South Asia, the mortality rate due to CVD is very high (Ranawaka *et al.*, 2016). CVDs include: coronary heart disease, cerebrovascular disease, peripheral arterial disease, congenital heart disease, deep vein thrombosis and pulmonary embolism (Alwan *et al.*, 2011).

In 2015, 17 million of premature deaths reported due to NCDs (under the age of 70), 82% were in low- and middle-income countries, and 37% were caused by CVDs. In 2016, 17.9 million people died from CVD, it indicates 31% of all global deaths. Of these deaths, 85% were due to heart attack and stroke (Cardiovascular diseases (CVDs), 2018).

In 2015, 19.9 million CVD deaths occurred (one-third of all global deaths), and 423 million people had prevalent CVD (approximately 1 in 17 of the global population) (Cardiovascular diseases (CVDs), 2018).

2.2 NCD and CVD Status in South East Asian Region

The four main NCDs are the leading causes of illness and death worldwide including the SEAR. NCDs are increasing and constitute a serious concern, accounting for 52% of deaths and 38% of the disease burden in the SEAR. 3.6 million (45%) out of 7.9 million total NCD deaths in the region are due to CVDs (Cardiovascular diseases (CVDs), 2018). With ageing of the population and increasing exposure to risk factors for non-communicable diseases, the numbers are projected to increase to 4·2 million deaths in 2030 (Projections of mortality and burden of disease, 2004-2030, 2018). When adjusted for age, the proportions of deaths due to chronic NCDs in the South East Asian population aged 15years and older was greatest in countries with the highest gross national incomes such as Singapore, Brunei, and Malaysia. However, the age-adjusted death rates per 100 000 population were highest in low-income countries such as Myanmar, Cambodia, Laos, and Vietnam (Dans *et al.*, 2011).

Furthermore, about 30% of all deaths from NCDs occurred in people aged 15–59 years. These deaths represent premature and preventable mortality in a highly productive age group in South East Asia. In this age group, chronic NCDs accounted for 51% of deaths in ten countries (Dans *et al.*, 2011).Although CVDs are the main cause of death in most countries, types of CVDs vary between countries (Cardiovascular diseases (CVDs), 2018).

2.3 NCD Status in Sri Lanka

Like many countries in the WHO SEAR, Sri Lanka is witnessing a shift in the disease burden from communicable diseases to NCDs. In Sri Lanka, 103,500 people die each year due to NCDs, which accounts for 75% of all deaths in the country. The NCD epidemic poses a serious economic issue, as a significant proportion of the annual health budget is spent on NCD treatment. NCD prevention and control measures are a key priority.

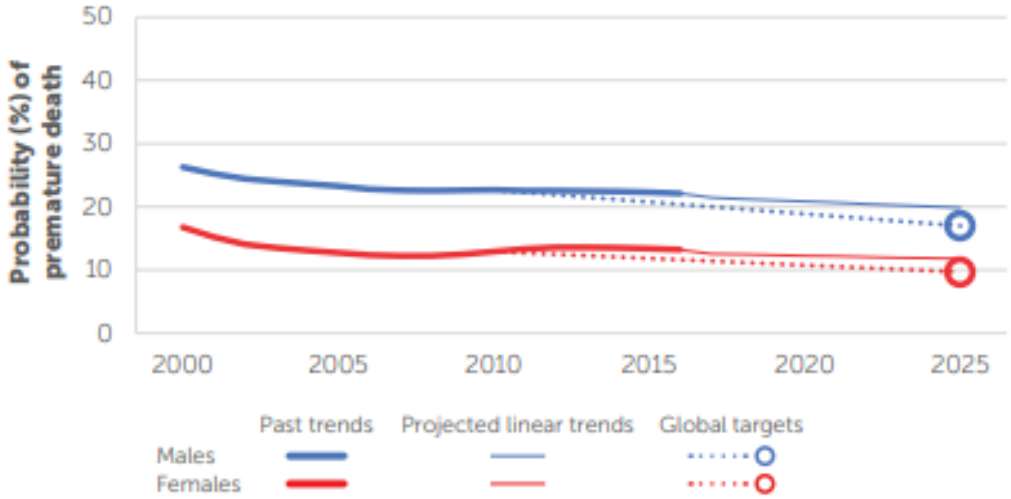

Figure 2.1: Risk of Premature Deaths due to NCDs in Sri Lanka

Source: Sri Lanka NCD profile 2016 (WHO)

Percentage of premature deaths due to NCDs in Sri Lanka were decreasing in 2000 to 2015. As shown in the figure 2.1, premature deaths among males were higher than females in the past trends and as future predicted trends, predicted death rate among males are higher. As predicted linear trends of NCD deaths among males and females, premature death percentage becoming lower compared to 2000 (Figure 2.1).

Table 2. 1: Proportional all-cause mortality in Sri Lanka

Cause of death	Percentage
Cardiovascular diseases	34%
Cancers	14%
Chronic respiratory disease	8%
Diabetes	9%
Other NCDs	18%
Communicable, maternal, perinatal and nutritional conditions	8%
Injuries	9%

Source: NCD statistics in Sri Lanka 2016 (WHO)

As the results of table 2.1, NCDs are reported 83% of all deaths. 34% of deaths were reported due to CVDs in Sri Lanka and it was the higher percentage among all deaths. Percentages of deaths were 14%, 8%, 9% and 18% due to cancers, chronic respiratory diseases, diabetes and other NCDs respectively (Table 2.1).

As mortalities due to NCDs are higher than the other deaths, it can be recommended to use preventive methods to assess or prevent the NCDs. WHO/ISH risk prediction charts have developed for assess the cardiovascular risk among individuals based on six risk factors. Use of the risk prediction charts can be useful to assess the cardiovascular risk.

2.4 Risk Prediction Charts

A number of risk prediction charts have been developed around the world for assessing the CVD risk prediction and prevention. A major limitation of the FRS was the small number of persons with diabetics in the cohort especially as diabetes is major risk factor of CVD. The Systematic Coronary Risk Evaluation (SCORE) is widely used in European countries. It also lacks risk prediction power of diabetes because of the unavailability of data (Sarrafzadegan *et al.*, 2017).

The assessment of risk has been a key element in efforts to define risk factors for CVDs, to identify novel markers of risk for CVD. In clinical practice, risk prediction algorithms have been used most directly to identify individuals at high risk of developing CVD in the short term to select those individuals for more intensive preventive interventions.

A Framingham score is a gender specific algorithm and it shows the risk of having heart disease over the next 10 years. The score is calculated based on risk factors identified in a large, long-term study which began in 1948 (Framingham heart study). To develop FRS, data was obtained from the Framingham heart study.

The European SCORE algorithm and the PROCAM have also been published (Shah *et al.*, 2018). The SCORE algorithm, derived from European data, has both region-specific and country-specific versions; however, this risk score system predicts only fatal cardiovascular events. PROCAM incorporates a larger number of covariates, which may limit clinical utility.

The SEAR B chart is recommended for Indonesia, Sri Lanka and Thailand. There are some limitations in the charts. Due to the insufficiency of data, charts have been compiled not for individual countries but for 14 WHO epidemiological sub-regions. It is likely that results will be most applicable to the largest country within the region. The accuracy and predictive value of the current risk prediction charts need to be improved as more epidemiological data becomes available from individual countries (WHO/ISH Cardiovascular Risk Prediction Charts, 2016).

2.5 Summary of Chapter 2

The WHO risk score charts have been developed using a modelling approach. The risks of non-fatal and fatal myocardial infarction and non-fatal and fatal stroke were modeled and combined to predict the individual risk of coronary heart disease and cerebrovascular disease. In brief, a set of individual level CVD risk factor profiles (age, sex, systolic blood pressure, total cholesterol, and the presence or absence of type -2 diabetes) were generated using information on the population distribution of

these risk factors from the WHO Comparative Risk Assessment study. The risk factor profiles were then combined with information on the relative risk of each risk factor, along with the population-level estimate of absolute risk.

They are useful as tools to help identify those at high cardiovascular risk, and to motivate patients, particularly to change behavior and, when appropriate, to take antihypertensive, lipid-lowering drugs and aspirin. However, it has not been tested to Sri Lankan environment.

CHAPTER 3

MATERIALS AND METHODS

The secondary data used for this study were collected from the database of RHS in 2007 at Faculty of Medicine, University of Kelaniya. Therefore the details given below were based on study undertaken by RHS.

3.1 Methodology

The RHS is a large community-based cohort study which was started in 2007 comprising 2986 adults aged 35 to 64 years. The RHS is a collaborative study between the International Medical Centre of Japan (IMCJ) and the Faculty of Medicine, University of Kelaniya. Ethical approval for the study was obtained from the Ethical Review Committees of the Faculty of Medicine, University of Kelaniya and the IMCJ.

3.2 Study Setting

This study was conducted in Ragama Medical Officer of Health (MOH) area (approximately 25km^2) situated 18 km north of the capital city, Colombo. The MOH area had a population of 75,591 persons resident in 15,137 housing units in 21 GN divisions which are the smallest administrative unit in the country (Dassanayake *et al.*, 2009).

3.3 Selection of Sample

The electoral lists maintained by Grama Niladharis in the Ragama MOH area were used as the sampling frame to invite persons into the study cohort (Ranawaka *et al.*, 2016). All persons 35-64 years were entered into a computer database, and then random samples were taken. All persons who agreed to participate signed the informed written consent form.

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, 55-64 years respectively. Thus, a sample of

40 individuals from the 35-44-year age group and 80 each of the 45-54 and 55-64-year age groups from each GN division were selected.

3.4 Follow Up of Cohort

At baseline in 2007, the study population was screened which included history taking and physical examination, recording clinical parameters and anthropometric measurements, and conducting biochemical assays. Age of the participant at recruitment was cross checked with their National Identity Cards which gives the date of birth based on what is given in the birth certificate of the individual. Smoking status was taken as what was given in the history.

The mean systolic and diastolic blood pressure readings of 3 measurements five minutes apart after rest were used. Weight and height of participants were measured as per WHO guidelines; weight and height were used to calculate BMI. Diabetes status was ascertained either by the patient giving a past medical history of diabetes confirmed with evidence such as blood testing, medical records and on current oral hypoglycemic agents, or a Fasting Plasma Glucose >126 mg/dL were considered as diabetics. A lipid profile assay was also done. All biochemical assays were done at certified laboratory of a leading private hospital in Colombo.

The same population was re-evaluated and screened in 2010 and 2014 (n=2148); the screening included a physical examination, and recording of clinical, anthropometric and biochemical findings. In these screenings, information was also obtained on cardiovascular events since the last screening which were also included in the analysis. In 2017, a survey was done among this population to record cardiovascular events that have taken place since the recruitment of participants in 2007.

In 2017, all residences of participants were traced based on the address given at the time of recruitment. Information on cardiovascular events were obtained from the participant or a family member if the participant was not able to communicate or if the participant had died. While collecting data, all attempts were made to obtain evidence of the event by confirming with information provided in diagnosis cards and death certificates. If the family of the participant was not resident in the given

address, attempts were made to contact them through telephone if a telephone number was available. If telephone contact was also not possible, then the neighboring houses were visited and information, if any, of the family was obtained and attempts were made to contact the recruited participant.

The cardiovascular (CV) events of interest were myocardial infarction, stroke, Coronary Artery Bypass Graft surgery or percutaneous coronary intervention. In the case of deaths, information on all deaths including the causes of deaths which were verified by cross checking with death certificates. For purposes of this analysis, only deaths due to cardiovascular events and non-fatal cardiovascular events were considered in the prediction models.

3.5 Risk Classification of Participants

The WHO/ISH Risk prediction charts gives the 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus. For this analysis the recommended chart for Sri Lanka - SEAR B was used. Participants were classified based on findings at recruitment.

3.5.1 Risk levels based on WHO/ISH risk prediction charts

The colour of the cell indicates the 10-year risk of combined myocardial infarction and stroke risk (fatal and non-fatal) as shown below.

Green	<10%	Low risk
Yellow	10% to <20%	Intermediate risk
Orange	20% to <30%	Moderate risk
Red	30% to <40%	High risk
Deep Red	≥ 40%	Very high risk

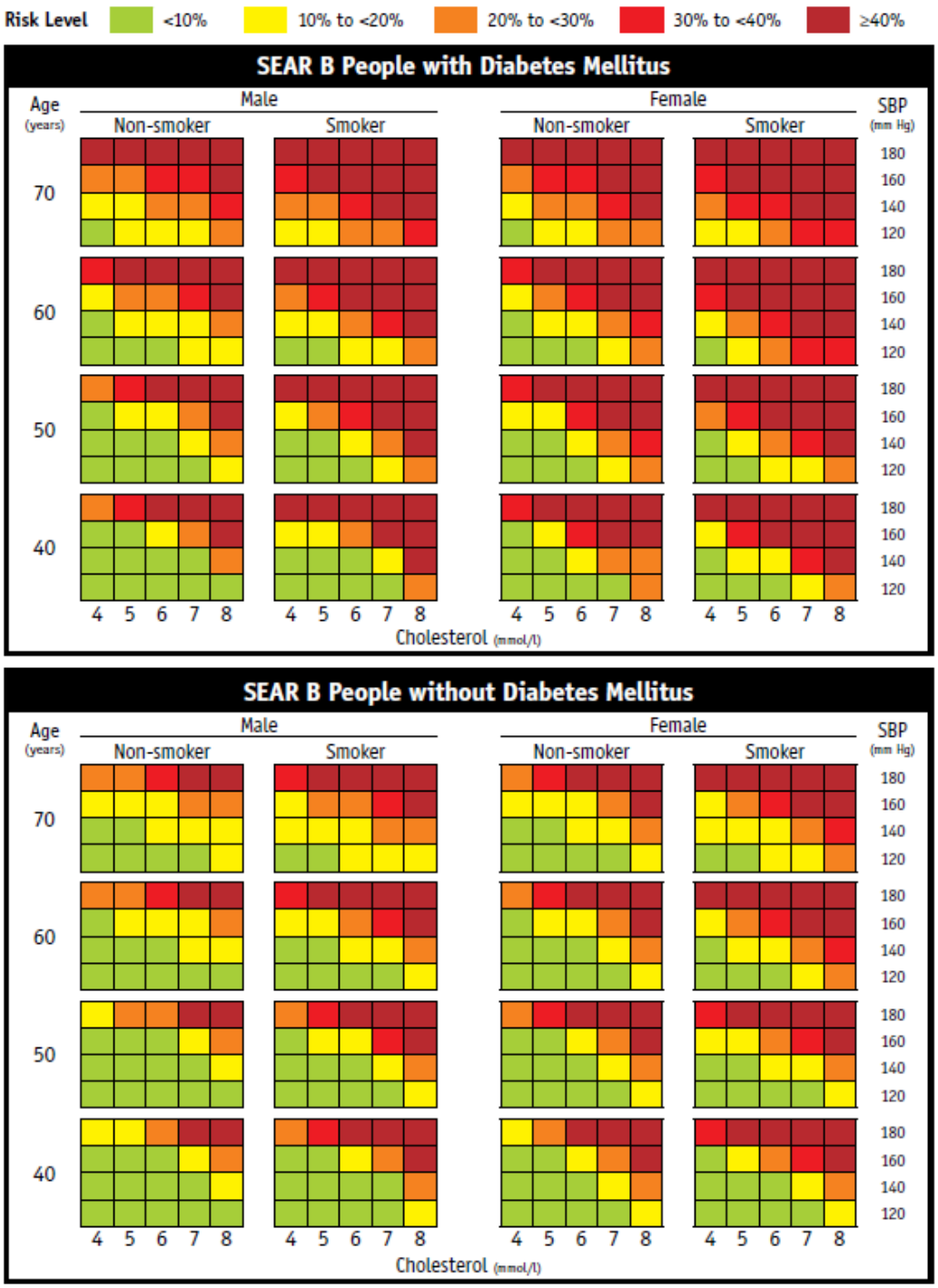

Figure 3. 1: WHO/ISH risk prediction chart for South East Asia Region B. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, total blood cholesterol, smoking status and presence or absence of diabetes mellitus

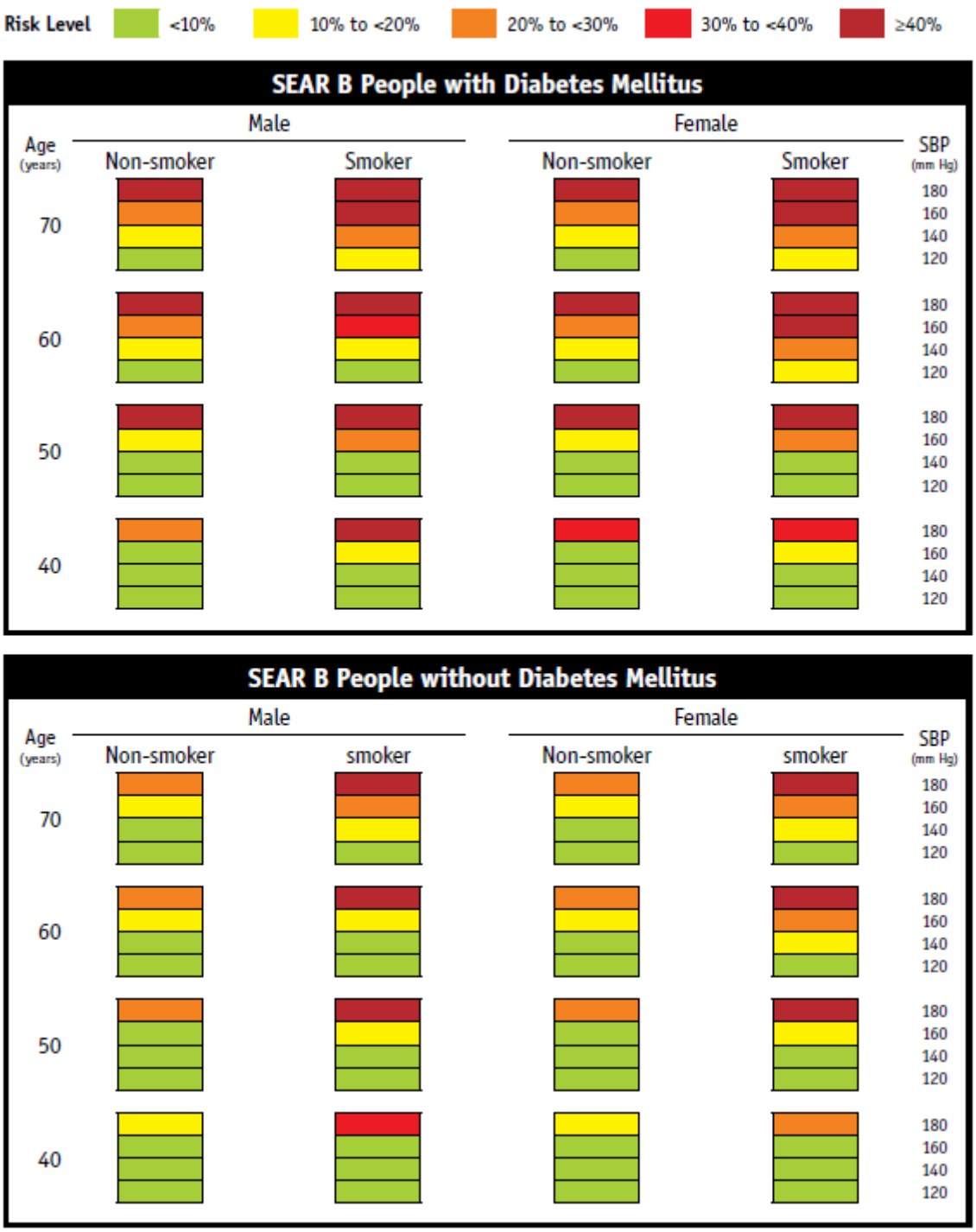

Figure 3. 2: WHO/ISH risk prediction chart for South East Asia Region B. 10-year risk of a fatal or non-fatal cardiovascular event by gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus (Without serum cholesterol readings)

The charts (figure 3.1, figure 3.2) indicate 10 year risk of fatal or non-fatal major cardiovascular event according to age, sex, blood pressure, smoking status, total blood cholesterol and presence or absence of diabetes mellitus for SEAR B where figure 3.1 with serum cholesterol measurements and figure 3.2 is without serum cholesterol measurements.

There are two sets of charts. One set (figure 3.1) can be used in settings where blood cholesterol can be measured. The other set (figure 3.2) is for settings in which blood cholesterol cannot be measured.

3.5.2 Assess the cardiovascular risk by using WHO/ISH risk prediction charts

When assess the cardiovascular risk of an individual by using WHO/ISH risk prediction charts, need to consider the following order.

First select the appropriate chart according to the region.
If blood cholesterol cannot be measured due to lack of resources, use the chart that do not have total cholesterol readings.
Before applying the chart to assess the 10-year cardiovascular risk of an individual, consider about the following information

- Presence or absence of diabetes
- Gender
- Smoker or non-smoker
- Age
- Systolic blood pressure
- Total blood cholesterol level

Once the above information is available, proceed to estimate the 10-years cardiovascular risk as follows;

First, select the appropriate chart depending on the presence or absence of diabetes, then, select male or female tables from the chart. After selecting the gender, select the smoking status. Next, select age group box (if age is 50-59 years select 50, if 60-69 years select 60 etc) (WHO/ISH Cardiovascular Risk Prediction Charts, 2016).

3.5.3 Important points to be considered when assess the risk

CVD risk may be higher than indicated by the charts in the presence of the following:

- Already on antihypertensive therapy.
- Premature menopause.
- Obesity (including central obesity).
- Sedentary lifestyle.
- Family history of premature coronary heart disease (CHD) or stroke.
- Raised triglyceride level (>2.0 mmol/L or 180mg/dL).
- Low HDL (High Density Lipoprotein) cholesterol level (<1 mmol/L or 40 mg/dL in males, <1.3mmol/L or 50 mg/dL in females).
- Raised pulse rate.
- Socioeconomic deprivation.

(WHO/ISH Cardiovascular Risk Prediction Charts, 2016)

3.6 Some Useful Definitions Used

Participants were followed up in 2017 after the data collection at the baseline in 2007. In 2017, focused on data regarding cardiovascular deaths and experienced cardiovascular events of the participants. If the participant experienced (with evidence) any one of the listed events during the follow up period: Myocardial Infarction (MI), Stroke, Coronary Artery Bypass Graft (CABG) surgery, Percutaneous Coronary Intervention (PCI) or if the participant died during the follow up period due to any of the following causes: myocardial infarction or stroke were considered for the analysis.

3.7 Statistical Analysis

IBM SPSS statistics, version 22.0 was used for statistical analysis. Independent sample t-test, Chi-square test and binary logistic regression were used to analyze the data. $P<0.05$ considered as significant.

3.8 Comparison of Two Means

In order to compare two population means, independent sample t-test was used under the following hypotheses:

H_0: There is no mean difference between two samples ($\mu_1 = \mu_2$)

H_1: There is a mean difference between two samples ($\mu_1 \neq \mu_2$)

The following test statistic was used.

Test statistic, $t_{(n1+n2-2)} = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\frac{s_1^2}{n_1} + \frac{s_2^2}{n_2}}}$ and under Ho, t~t (n_1+n_2-2)

$\bar{X}_1, \bar{X}_2$– Sample means

s_1,s_2 – Sample standard deviations

n_1, n_2 – Sample sizes

3.9 Analysis of 2-way Frequency Tables

In typical two factors (A & B) having 2 levels can be illustrated as shown below (table 3.1).

Table 3.1: Two-way Frequency Table

A	B		Total
	B_1	B_2	
A_1	f_{11}	f_{12}	$f_{1.}$
A_2	f_{21}	f_{22}	$f_{2.}$
Total	$f_{.1}$	$f_{.2}$	f..

Let $\{f_{ij}\}$ = Observed frequency of the row category = i and column category = j

Hypotheses:

H_0: Factor A is independent of factor B or there is no significant association between the two factors A and B.

H_1: There is a significant association between the two variables.

The Pearson's Chi-Square test statistics used to test the above hypothesis are based on 2-way frequency table.

Pearson's Chi-Square Test (exact) = $\chi_c^2 = \sum_{i,j=1}^{k} \frac{(O-E)^2}{E}$

Each statistic is distributed X^2 (r-1) (c-1) where, r – Number of rows and c – Number of columns.

3.10 Odds ratio

An OR is a statistical measure to test the association between an exposure and an outcome. The odds that an outcome will occur given a particular exposure compared to the odds of the outcome occurring in the absence of that exposure represented by OR.

The OR is commonly used in clinical research and decision-making. Because as an effect-size statistic, OR is useful and it gives clear and direct information to clinicians about which treatment approach has the best odds of benefiting the patient.

Table 3.2: Calculation of the odds ratio

Exposure status	Event occurred		Total
	Case (With disease)	Control (Without disease)	
Exposed	a	b	a+b
Not exposed	c	d	c+d
Total	a+c	b+d	a+b+c+d

Odds of an event = $\frac{p\,(event\ occurs)}{p\,(event\ does\ not\ occure)} = \frac{P}{1-P}$

Odds ratio (OR) between case and control = $\frac{Odds\ of\ a\ case}{Odds\ of\ a\ control}$

$$= \frac{\frac{p1}{(1-p1)}}{\frac{p2}{(1-p2)}}$$

From table 3.2,

Odds of that a case was exposed = $\frac{a}{c}$

Odds of that a control was exposed $= \frac{b}{d}$

Odds Ratio or relative odds $= \frac{a * d}{b * c}$

OR = 1 Exposure does not affect odds of outcome

OR > 1 Exposure associated with higher odds of outcome

OR < 1 Exposure associated with lower odds of outcome

3.11 Binary Logistic Regression Analysis

Logistic regression is the appropriate regression analysis to conduct when the dependent variable is dichotomous (binary). Like all regression analyses, the logistic regression is a predictive analysis. Logistic regression is used to describe data and to explain the relationship between one dependent binary variable and one or more nominal, ordinal interval or ratio-level independent variables. The goal of logistic regression is to correctly predict the category of outcome for individual cases using the most parsimonious model. To accomplish this goal, a model is created that includes all predictor variables that are useful in predicting the response variable.

Logistic regression is useful for situations in which we want to predict the presence or absence of an outcome based on a set of predictor variables. It is similar to a linear regression model but is suited to models where the dependent variable is dichotomous. Logistic regression coefficients can be used to estimate odds ratios for each of the independent variables in the model.

Hypothesis:

Ho: $\beta_1 = \beta_2 = \beta_3 \ldots\ldots \beta_k = 0$ vs

H_1: $\beta_1 \neq \beta_2 \neq \beta_3 \ldots\ldots \beta_k \neq 0$

3.11.1 Binary logistic regression major assumptions

The dependent variable should be dichotomous in nature (e.g., presence vs absent)

There should be no outliers in the data, which can be assessed by converting the continuous predictors to standardized scores.

There should be no high correlations (multicollinearity) among the predictors. This can be assessed by a correlation matrix among the predictors.

At the center of the logistic regression analysis is the task estimating the log odds of an event. Mathematically, logistic regression estimates a multiple linear regression function defines as:

$$\text{Log}\left(\frac{p_i}{1-p_i}\right) = \beta_0 + \beta_1 x_{1i} + + \beta_2 x_{2i} + \ldots\ldots\ldots\ldots + \beta_k x_{ki}$$

For i= 1,2,…..n

The relationship between log of odds and the independent variables are linear.

The model can alternatively be expressed in the form of,

$$p_i = \frac{\exp(\beta 0 + \beta 1 x 1 i + + \beta 2 x 2 i + \ldots\ldots\ldots\ldots + \beta k x k i)}{1 + \exp(\beta 0 + \beta 1 x 1 i + + \beta 2 x 2 i + \ldots\ldots\ldots\ldots + \beta k x k i)}$$

Where i= 1,2,…..n

The relationship between log of odds and the independent variables are non-linear.

Overfitting: when selecting the model for the logistic regression analysis, another important consideration is the model fit. Adding independent variables to a logistic regression model will always increase the amount of variance explained in the log odds (R2). However, adding more and more variables to the model can result in overfitting. (Sperandei, 2014)

3.11.2 Odd Ratios in logistic regression

The odds are simply the ratios of the proportions for the two possible outcomes of the binary logistic regression. If p is the proportion for the one outcome of an event then (1-p) is the proportion for the second outcome and the odds of an event is defined as,

$$Odds = \frac{p}{1-p}$$

The log transformation of p is also called as the logit of p or logit (p) and thus it is defined as,

$$Logit\ (p) = Log\left(\frac{p}{1-p}\right)$$

3.11.3 Variable selection methods in binary logistic model

Method of selection allows to specify how independent variables are entered into the analysis. Using different methods, we can construct a variety of regression models from the same set of variables.

Variable selection methods of binary logistic model are, enter, forward selection (Likelihood Ratio), forward selection (Wald), backward elimination (Wald), backward elimination (Likelihood Ratio).

3.11.4 Model selection procedure

Forward selection method (conditional) is used to select the most suitable model. This method starts with the null model (simplest model only with the intercept). Then the most significant variable (main effect) is added to the model. The variable with the lowest p value (at a given significant level) is considered to choose the most significant variable. In this way by adding one variable at a time to the each new model, the finalized model is defined when there is no further improvement. Similarly, higher order interactions are added thereafter.

Hypothesis:

H_0: The model fits data Vs H_1: The model does not fit data

3.11.5 Cox & Snell R2 and Nagelkerke R2

Both Cox & Snell R square and Nagelkerke R Square indicates percentage of variance of dependent variable explained by the model. Though it is similar to R^2 in regression those two statistics are not so powerful. Those values are sometimes referred to as pseudo R^2 values.

3.11.6 Deviance Test

Each of the two competing models, the null model and the alternative model is separately fitted to the data and the log-likelihood statistic shown below is computed at each step. The test statistic is often denoted by *D-Deviance* is twice as the difference in these log-likelihoods.

$$D = -2\log\left(\frac{likelihood\ for\ null\ model}{likelihood\ for\ alternative\ model}\right) = 2\log(L)$$

Under H_0: $D \sim X^2_1$

H_0: Model is adequately fits vs

H_1: Model is not significant

D statistic is the difference of log likelihood between two models.

3.11.7 Hosmer and Lemeshow Test

The Hosmer–Lemeshow test is a statistical test for goodness of fit for logistic regression models. It is used frequently in risk prediction models. The test assesses whether or not the observed event rates match expected event rates in subgroups of the model population.

The test statistic H is given by,

$$\mathrm{H} = \sum_{g=1}^{n} \frac{(O_g - E_g)^2}{N_g p_g (1-p_g)}$$

O_g – Number of observed cases in g^{th} group

E_g – Number of expected cases g^{th} group under the fitted model

g – Number of groups

Hypotheses:

H_0: Model is significant vs

H_1: Model is not significant

Under H_0, the test statistic is asymptotically follows Chi-square g-2 df (*Hosmer-Lemeshow Test: Definition*)

3.12 Ethical Considerations

This study was approved by the Ethics Review Committee of the Faculty of Medicine, University of Kelaniya.

CHAPTER 4

IDENTIFICATION OF RISK CATEGORIES ON CVDs IN SRI LANKA BASED ON WHO/ISH CRITERIA

This Chapter investigates the influence of each risk category on CV events separately to find the most influential variables on CV risk in Sri Lanka by performing tests for association and logistic regression.

4.1 Profile of Participants

At baseline, in 2007 study population was 2986 and participants of 35-64 years of age were enrolled to the RHS study. To validate the WHO/ISH risk prediction charts, values of six variables in 2007 are considered from the RHS database such as sex, age, fasting blood sugar level, serum cholesterol level, systolic blood pressure and smoking status. Variables are selected for the analysis based on the criteria of WHO/ISH risk prediction charts.

The baseline characteristics of selected variables are shown in table 4.1. Descriptive results are presented for the age, serum cholesterol level, fasting plasma glucose and systolic blood pressure variables in Table 4.1. The total population during 2007 was 2986 consists of 1349 (45.2%) male, 1737 (54.8%) females and 415 (13.9%) identified as smokers.

Table 4. 1: Basic Statistics of the Initial Profile of Participants at baseline in 2007

Variable	Mean ±SE	95% CI
Mean age (±SE)	52.43±0.14	52.14 – 52.72
Mean serum cholesterol (±SE)	212.03±0.77	210.57 – 213.71
Mean plasma glucose (±SE)	118.08±0.81	117.21 – 119.44
Mean systolic blood pressure (±SE)	135.19±0.40	134.39 – 136.05

It is clear that female participation is higher than males. Irrespective of the gender the mean age (±SE) of the participants is 52.43±0.14. Mean serum cholesterol (±SE),

Mean plasma glucose (±SE), Mean systolic blood pressure (±SE) values are 212.03±0.77, 118.08±0.81, 135.19±0.40 respectively. In 2007, 415 participants (13.9%) were identified as smokers.

4.2 Distribution of Participants of Follow up Cohort in 2017

The initial 2986 (in 2007) had been monitored aged 35 – 64. During the follow up study from 2007 to 2017, only 2517 were left aged above 40 at the end of 2017 (Fig. 4.1). During 10 years, 238 persons were lost due to change their residencies (Fig. 4.1).

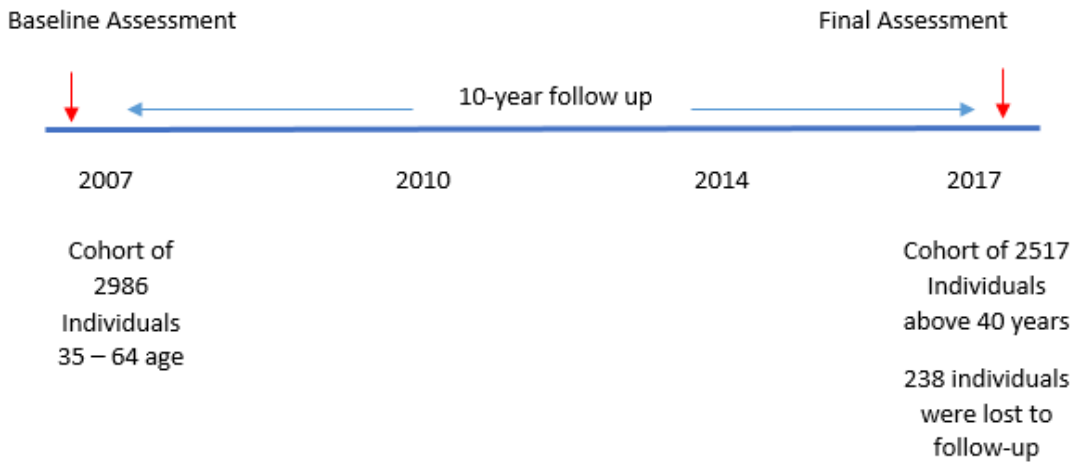

Figure 4. 1: Follow up of the cohort from 2007 to 2017

4.3 Cardiovascular events among participants during the follow up

The details of cardiovascular events and deaths during 10-years were collected from 2517 participants. Of them 168 (6.1%) was total deaths due to all-causes. Among total deaths, 73 (43.5%) were due cardiovascular events. The balance, 95 (56.5%) were due other causes (Fig. 4.2).

Furthermore, among the 215 cardiovascular events reported during the 10- year period, 73 were fatal and 142 were non-fatal CV events (Fig. 4.2). Among 142 non-fatal events, 98, 27, 10 and 7 were due to MI, Stroke, CABG and PCI respectively (Figure 4.2).

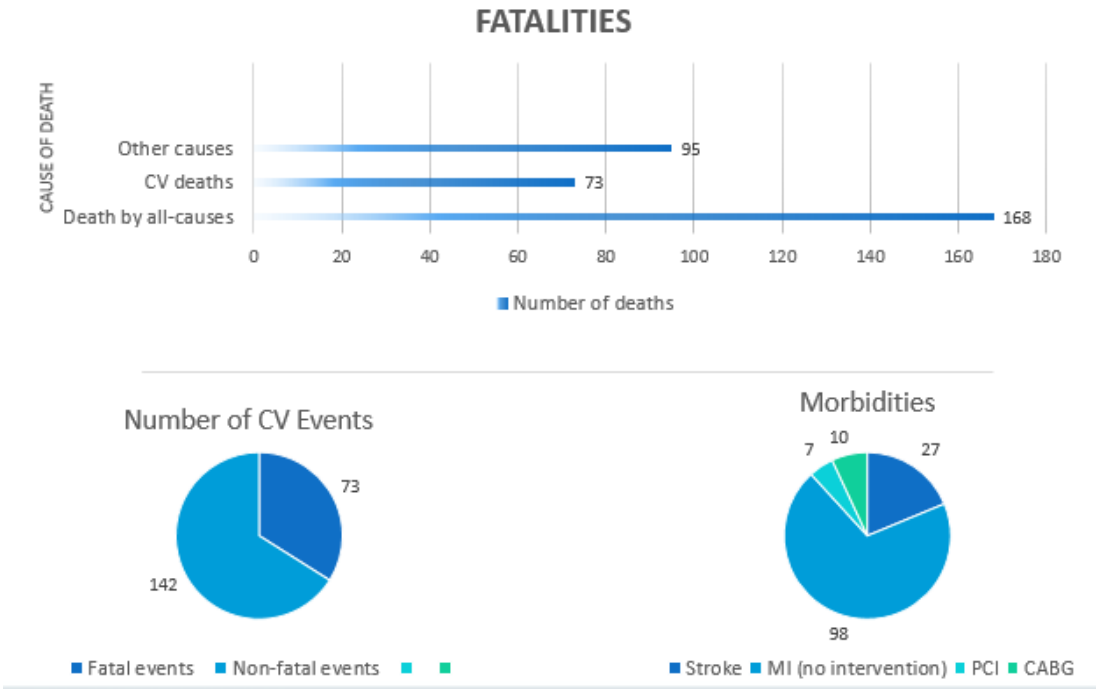

Figure 4. 2: Cardiovascular events among individuals from 2007 to 2017

4.4 Distribution of Participants Based on WHO/ISH criteria

According to the WHO/ISH risk prediction charts, there were cutoff values for the selected six variables. Those details are given in Table 4.2.

- Participants aged ≥ 40 years at the baseline (in 2007) were considered for the analysis according to the chart.
- Participants with a fasting plasma glucose level of >126 mg/dL, were considered as diabetic patients.
- Serum cholesterol level divided into five groups such as: <4 mmol/L, 4-4.9 mmol/L, 5-5.9 mmol/L, 6-6.9 mmol/L, 7-7.9mmol/L and > 8mmol.

- Systolic blood pressure level of the participants divided into four groups. Four groups are <140mmHg, 140-159.9mmHg, 160-179.9mmHg and >10mmHg.

Table 4. 2: List of variables used for the analysis based on the WHO/ISH risk prediction charts

Variables		Code
Gender	Male	1
	Female	2
Smoking status	Yes	1
	No	0
Fasting plasma glucose level	<126 mg/dL	0
	≥126 mg/dL	1
Age	40-49.9	1
	50-59.9	2
	>60	3
Serum cholesterol level	<4 mmol/L	1
	5-5.59 mmol/L	2
	6-6.69 mmol/L	3
	7-7.9 mmol	4
	>8 mmol/L	5
Systolic blood pressure	<140 mmHg	1
	140-159.9 mmHg	2
	160-179.9 mmHg	3
	>180 mmHg	4

4.5 Distribution of the Observed Statistics by Gender

According to the WHO/ISH risk prediction charts, risk can be predicted only for the persons who are aged ≥ 40 years. There were 2517 participants of aged above 40 years. Summary results are shown in Table 4.3.

Table 4. 3: Distribution of Each Variables within Categories by Gender

Parameter	Male [n (%)]	Female [n (%)]	Total [n (%)]
Age			
40-49.9	341(30.1%)	422(30.5%)	763(30.3%)
50-59.9	518(45.8%)	645(46.6%)	1163(46.2%)
>60	273(24.1%)	318(23.0%)	591(23.5%)
Total	1132(100.0%)	1385(100.0%)	2517(100.0%)
Diabetes (mg/dL)			
≥126	457 (40.4%)	552 (39.9%)	1009 (40.1%)
<126	675 (59.6%)	833 (60.1%)	1508 (59.9%)
Total	1132 (100.0%)	1385 (100.0%)	2517(100.0%)
Smoking	395 (34.9%)	0 (0.0)	395 (15.7%)
SBP (mm Hg)			
<140	732 (64.7%)	817 (59.0%)	1549 (61.5%)
140-159.9	263 (23.2%)	362 (26.1%)	625 (24.8%)
160-179.9	90 (8.0%)	133 (9.6%)	223 (8.9%)
>180	47 (4.2%)	73 (5.3%)	120 (4.8%)
Total	1132 (100.0%)	1385 (100.0%)	2517(100.0%)
Cholesterol (mmol/L)			
<4	463 (40.9%)	393 (28.4%)	856 (34.0%)
5-5.9	399 (35.2%)	497 (35.9%)	896 (35.6%)
6-6.9	198 (17.5%)	335 (24.2%)	533 (21.2%)
7-7.9	67 (5.9%)	123 (9.1%)	190 (7.7%)
>8	5 (0.4%)	37 (2.7%)	42 (1.7%)
Total	1132 (100.0%)	1385 (100.0%)	2517 (100.0%)

Results in Table 4.3 indicate that the percentage distribution among categories of age groups are almost the same between males and females. Between three age groups, highest percentage of participants are in 50-59.9 age group. Participation of >60 age group is 50% less compared to middle age group (40-49.9). 40.1% of the study

population was classified as diabetics with the percentages in both genders being almost the same at baseline.

There were no smokers among females. Almost 40 percent of study participants had a systolic blood pressure of 140 mmHg or above at baseline. Hypercholesterolemia of more than 4 mmol/L was present at baseline among 59.1% of the population (Table 4.3)

Almost 40 percent of study participants had a systolic blood pressure of 140 mmHg or above at baseline. Hypercholesterolemia of more than 4 mmol/L was present at baseline among 59.1% of the population (Table 4.3)

4.6 Distribution of cardiovascular (CV) risk factors of the participants aged > 40 from RHS database from 2007 to 2017

Table 4. 4: Distribution of Cardiovascular (CV) events collected at RHS study in 2017 (Sri Lankan population)

Cardiovascular events	Male	Female	Percentage from total population (%)
Fatal events	46(1.83%)	27(1.07%)	73(2.90%)
Non-fatal events			
Stroke	15(0.59%)	12(0.48%)	27(1.07%)
MI	55(2.19%)	43(1.70%)	98(3.89%)
PCI	6(0.24%)	1(0.04%)	7(0.28%)
CABG	8(0.32%)	2(0.07%)	10(0.39%)
Total CV events	130(5.16%)	85(3.37%)	215(8.53%)

All percentages in the parenthesis were from total population (n=2517). 6.67% deaths occurred during the follow up period from 2007 to 2017; 2.9% deaths were reported to be due to CVD. There were 98 Myocardial infarctions (3.89%) and 27 strokes (1.07%) reported among the study population during the follow up period.

PCI and CABG were done on 7 (0.28 %) and 10 (0.39%) persons, respectively (Table 4.4).

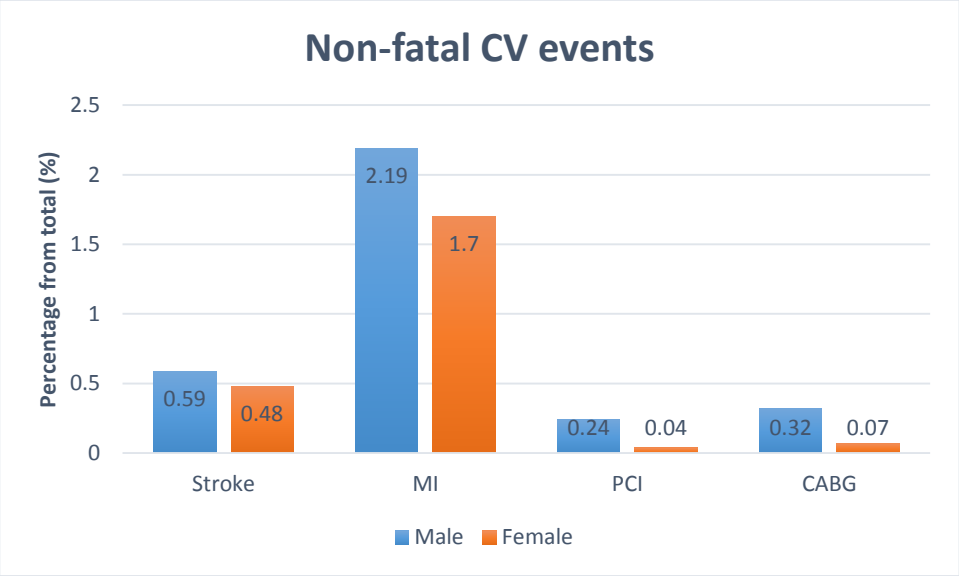

Figure 4. 3: Distribution of non-fatal CV events

According to figure 4.3, males reported higher percentage of all CV events. Higher percentage of MIs (Heart attack) reported among both males and females compared to other three events. PCI tests are the lowest among all events. Based on the above results, it can be seen that the males had higher CV risk than females (Figure 4.3).

The characteristics of six variables among two groups, persons who had a CV event and persons who had not from 2007 to 2017 are shown in table 4.4. Six variables are sex, age, serum cholesterol level, systolic blood pressure, fasting blood sugar level and smoking status. Descriptive statistics and frequencies are presented based on the baseline values (Table 4.5).

4.7 Distribution of Cardiovascular Events

Table 4. 5: Profile of participants at baseline

Variable	CV events during follow up (n=215)	No CV events during follow up (n=2302)	Total followed up (n=2517)
Male [n, (%)]	130 (11.5%)	1002 (43.5%)	1132 (45.0%)
Female [n,%]	85 (6.1%)	1300 (56.5%)	1385 (55.0%)
Mean age (±SE)	56.62 ±0.38	53.39 ±0.14	53.67 ±0.13
Mean serum total cholesterol (±SE) (mmol/L)	210.22±3.15	212.88± 0.87	212.65 ±0.84
Mean Fasting Plasma Glucose (±SE) (mg/dL)	132.79 ±3.79	117.55±0.88	118.86 ±0.87
Mean systolic blood pressure (±SE) (mmHg)	146.03±1.78	135.34±0.45	136.25 (0.44)
Smoking status [n (%)]	44 (11.1%)	351 (15.2%)	395 (15.7%)

[1]Total followed up in 2017 group includes the sum of (i) risk group (215) and (ii) non-risk group/control group (2302)

Among persons who had a fatal or non-fatal cardiovascular event during the 10 years, 11.5% of males and 6.1% of females experienced at least one CV event from 2007 to 2017. A larger proportion of males had experienced CV events as compared to other group. Although total followed up percentage of females (56.5%) are higher than males (43.5%), higher percentage of cardiovascular events reported among males. Mean age (±SE) of persons with at least one CV event is 56.62±0.38.

Persons who experienced cardiovascular events were older than that of other group and the corresponding mean ages are 56.6 years and 53.4 years. The mean serum

cholesterol in CV group (210.22 mmol/L ±3.15) is not significantly different that from none CV group.

The mean fasting plasma glucose in CV group (132.79) is significantly higher than the mean fasting plasma glucose level in none CV group (115.95mg/dL). Results in Table 4.5 indicate that mean systolic blood pressure in CV group is also significantly higher than that of none CV group.

Persons who experienced fatal or non-fatal CV events were older, had a higher mean Fasting Blood Sugar level, had a higher systolic blood pressure and were smokers at baseline as compared to the non-risk group and total followed up groups (Table 4.5).

4.8 Comparison of risk factors with CV events among participants from 2007 to 2017

The WHO/ISH risk classification charts indicate the cardiovascular risk of the individuals aged ≥40 years. Based on the chart, the impact of those risk factors were age, sex, fasting plasma glucose level, serum cholesterol level, systolic blood pressure and smoking status of each individual. In the below analysis, associations with CV events were calculated in each risk factor and the odds ratios were computed.

To perform bivariate analysis and to find odds ratio, each variable divided into two groups. For age, serum cholesterol level, SBP and FBS level, lower value considered as reference group. For gender, reference group is female and for smoking status, reference group is non-smokers (Table 4.6).

Table 4. 6: Cutoff values of the variables for bivariate analysis

Variables	Value	Code
Gender	Male	1
	Female	2
Age	<50	0
	≥50	1
Serum Cholesterol Level	<4 mmol/L	0
	≥4 mmol/L	1
Fasting Blood Sugar Level	<126 mg/dL	0
	≥ 126 mg/dL	1
Systolic Blood Pressure	<140 mmHg	0
	≥140 mmHg	1
Smoking Status	Yes	1
	No	0

4.8.1 Impact of Gender

Table 4. 7: Influence of Sex on CV events

			CV events		
			No	Yes	Total
Sex	Female	Unt	1300	85	1385
		% within sex	93.9%	6.1%	100.0%
	Male	Count	1002	130	1132
		% within sex	88.5%	11.5%	100.0%
Total		Count	2302	215	2517
		% within sex	91.5%	8.5%	100.0%

Chi-square test statistic (χ^2_1) = 22.80 (p = 0.000 < 0.001), Odds ratio = 1.984

The Chi square test statistic (22.8, p<0.001) confirms that there is a significant association between the gender and CV events among participants aged ≥40. The

percentage of males who had a CV event was (11.5%). It is significantly higher than that of females (6.1%).

The odd ratio is significant. It can be claimed that the odds of risk of males are 1.984 times more likely to have a CV event than females (95% CI, 1.491 – 2.640). Thus it can be concluded that gender is significantly influenced on having a CV event irrespective of other risk factors (Table 4.7).

4.8.2 Impact of Age on having a CV events

Table 4. 8: Association between age and CV events

			CV events		
			No	Yes	Total
Age (in yrs)	<50	Count	737	26	763
		% within Age	96.6%	3.4%	100.0%
	≥50	Count	1565	189	1754
		% within Age	89.2%	10.8%	100.0%
Total		Count	2302	215	2517
		% within Age	91.5%	8.5%	100.0%

Chi-square test statistic (χ^2_1) = 14.973 (p = 0.000 < 0.001), Odds ratio = 3.423

Results in Table 4.8 indicate that there is a significant association between age category and having CV events among participants during follow up. The percentage of participants who aged ≥ 50 had a significantly higher CV events (10.8%). The odd ratio is also significant as the 95% CI is [2.25, 5.21]. Thus it can be concluded that the odds of risk of having a CV event among persons of aged ≥50 years are 3.423 times higher compared to the lower age group (age<50) (Table 4.8).

According to table 4.9, mean age and standard error of persons who had a CV event during the follow up were 56.62 and 0.38 and mean age of individuals who did not experienced a CV event during follow up was 53.39. Test results of the independent sample t-test statistics (-7.893, p<0.001) confirmed that the mean age of participants who had a CV event was significantly higher irrespective gender and other factors (Table 4.9).

Table 4. 9: Comparison of age with CV events

CV events	N	Mean age	Std. Error Mean
No	2302	53.39	.141
Yes	215	56.62	.384

T-test statistic = - (7.893), p=0.000< 0.001

4.8.3 Impact of fasting blood sugar level and CV events of participants

Table 4. 10: Influence of FBS level on CV events

			CV events		
			No	Yes	Total
FBS level (mg/dL)	<126	Count	1417	91	1508
		% within FBS level	94.0%	6.0%	100.0%
	≥126	Count	885	124	1009
		% within FBS level	87.7%	12.3%	100.0%
Total		Count	2302	215	2517
		% within FBS level	91.5%	8.5%	100.0%

Chi-square test statistic (χ^2_1) = 30.274 (p = 0.000 < 0.001), Odds ratio = 2.182

Based on the results of table 4.10 concluded, persons who had a higher FBS level (≥126mg/dL), had a higher risk of having a CV event (12.3%) than persons who had lower FBS level (<126 mg/dL). Thus it can be concluded that the FBS level and the CV events are significantly associated (Chi-square test statistic = 30.274 (p = 0.000 < 0.001). The odds of risk of having a CV event of persons who had FBS level ≥ 126mg/dL are 2.182 (95% CI, 1.644 – 2.896) times higher compared to the other group (Table 4.10).

4.8.4 Impact of serum cholesterol level and CV events of participants

Table 4. 11: Influence of serum cholesterol level on CV events

			CV events		
			No	Yes	Total
Serum cholesterol level (mmol/L)	<4	Count	170	23	193
		% within chol. Level	88.1%	11.9%	100.0%
	≥4	Count	2132	192	2324
		% within chol. Level	91.7%	8.3%	100.0%
Total		Count	2302	215	2517
		% within chol. Level	91.5%	8.5%	100.0%

Chi-square test statistic (χ^2_1) = 3.048 (p = 0.081 > 0.05), Odds ratio = 0.666

Serum cholesterol level of the participants is not significantly associated with the CV events as Chi-square test statistic = 3.048 (p = 0.081 > 0.05). As odds ratio is 0.666 it indicates, odds of risk of having a CV event of individuals who had ≥4 mmol/L cholesterol level are 0.666 times less. Serum cholesterol level is not significantly influenced on CV events irrespective of other risk factors such gender, SBP level, FBS level, age and smoking status (Table 4.11).

4.8.5 Impact of systolic blood pressure level and CV events of participants

Table 4. 12: Influence of SBP level on CV events

			CV events		
			No	Yes	Total
SBP level (mm Hg)	<140	Count	1445	104	1549
		% within SBP level	93.3%	6.7%	100.0%
	≥140	Count	857	111	968
		% within SBP level	88.5%	11.5%	100.0%
Total		Count	2302	215	2517
		% within SBP level	91.5%	8.5%	100.0%

Chi-square test statistic (χ^2_1) = 17.226 (p = 0.000 < 0.001), Odds ratio = 1.800

Results of table 4.12 shows, persons who had high SBP level (≥140 mmHg), had a higher percentage of CV events (11.5%) than persons who had lower SBP level (<140 mmHg). Thus, it can be concluded that the SBP level and the CV events are significantly associated (Chi-square test statistic = 17.226 (p = 0.000 < 0.001)). The odds of risk of having a CV event of persons who had SBP level ≥ 140mmHg are 1.800 (95% CI, 1.359 – 2.382) times higher (Table 4.12).

4.8.6 Impact of Smoking Status on CV events

Table 4. 13: Influence of Smoking Status on CV events

			CV events		
			No	Yes	Total
Smoking status	No	Count	1951	171	2122
		% within smokers	91.9%	8.1%	100.0%
	Yes	Count	351	44	395
		% within smokers	88.9%	11.1%	100.0%
Total		Count	2302	215	2517
		% within smokers	91.5%	8.5%	100.0%

Chi-square test statistic (χ^2_1) = 4.046 (p = 0.044 < 0.05), Odds ratio = 1.430

Chi-square test statistics (4.046, p<0.05) confirms that there is a significant association between smoking and having CV events. 11.1% CV events were recorded during the follow up among participants who were identified as smokers. Thus it can be concluded that smoking status is significantly influenced on CV events. Based on the results, the odds of risk of having a CV event of smokers are 1.430 (95% CI, 1.008 – 2.030) times higher than non-smokers (Table 4.13)

4.9 Logistic Regression Approach

The Chi-square analysis confirmed that out of all the selected variables namely, age, gender, smoking status, SBP level, and FBS level have significant impact while serum cholesterol level is not significantly impact on CV events of the individuals in Sri Lankan population. In this section, the effects of each of the significant variables

from bivariate analysis have been analyzed simultaneously by using binary logistic regression method.

The dependent variable for the logistic regression analysis is, CV events during the follow up (had a CV event = 1, not had a CV event = 0). The reference groups that used for the logistic regression are indicated in table 4.14.

Table 4. 14: Categorical variables coding in logistic regression

Variable	Value	Code as SPSS	Parameter coding			
			(1)	(2)	(3)	(4)
Sex	Male	1	1			
	Female	2	0			
Smoking status	Yes	1	1			
	No	0	0			
Fasting plasma glucose level	<126 mg/dL	0	0			
	≥126 mg/dL	1	1			
Age	40-49.9	1	0			
	50-59.9	2	1			
	>60	3		1		
Serum cholesterol level	<4 mmol/L	1	0			
	5-5.59 mmol/L	2	1			
	6-6.69 mmol/L	3		1		
	7-7.9 mmol	4			1	
	>8 mmol/L	5				1
Systolic blood pressure	<140 mmHg	1	0			
	140-159.9 mmHg	2	1			
	160-179.9 mmHg	3		1		
	>180 mmHg	4			1	

Reference categories for sex, smoking status, fasting plasma glucose, age, serum cholesterol level and systolic blood pressure are female, non-smokers, FBS level < 126 mg/dL, (40 – 49.9) , <4mmol/L and < 140 mmHg respectively (Table 4.14).

Forward conditional method was applied to the cohort to analyze the main effects and obtained results are as follows.

4.9.1 Goodness of Fit of the Fitted Model (Main effects)

Table 4. 15: Classification table of the model

Observed			Predicted		
			CV events		Percentage Correct
			.00	1.00	
Step 0	CV events	.00	2302	0	100.0
		1.00	215	0	.0
	Overall Percentage				91.5

As 91.5% of people were correctly classified. The addition of explanatory variables should increase the percentage of correct classification significantly if the model is good (Table 4.15).

Table 4. 16: Model summary for the main effects

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	1421.243[a]	.019	.042
2	1398.670[a]	.028	.062
3	1373.257[a]	.037	.084
4	1356.095[a]	.044	.099

Model Summary table gives the values for two pseudo R^2 values. From the table above, it can be concluded that between 4.4% and 9.9% of the variation in CV events can be explained by the model. However, it should be pointed out these statistics are not similar to R^2 in linear regression analysis, these are named as pseudo R^2 for logistic regression (Table 4.16).

Table 4. 17: Hosmer and Lemeshow test statistics

Step	Chi-square	df	Sig.
1	.000	1	1.000
2	.994	4	.911
3	5.405	6	.493
4	7.158	8	.520

The Hosmer & Lemeshow test of the goodness of fit suggests the model is a good fit to the data as p = 0.520 (>0.05) at the 4th step. In this case, the model is statistically significant (Table 4.17).

Table 4. 18: Final results of the Logistic Regression model (Forward LR Method)

Explanatory Variable	B	S.E.	Wald	Df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Sex(1)	.747	.150	24.939	1	.000	2.111	1.574	2.829
FBS(1)	.616	.150	16.969	1	.000	1.852	1.381	2.482
Age			24.401	2	.000			
Age(1)	.955	.227	17.686	1	.000	2.599	1.665	4.057
Age(2)	1.182	.242	23.844	1	.000	3.261	2.029	5.240
SBP			25.195	3	.000			
SBP(1)	.050	.181	.076	1	.783	1.051	.737	1.500
SBP(2)	.607	.225	7.280	1	.007	1.835	1.181	2.851
SBP(3)	1.137	.254	20.013	1	.000	3.116	1.894	5.128
Constant	-4.046	.235	295.766	1	.000	.017		

In the logistic regression output in table 4.18, four steps has improved from the beginning. At the last step, there is a fitted model with four significant variables

($p<0.05$ and exp (β) > 1) such as sex, FBS level, age and SBP as the result of the logistic regression with main effects. Individuals aged above 50 and had a SBP level above 180mmHg and males had a higher risk of having a CV event as exp (β) > 2 and regression coefficients (0.747, 0.955, 1.182 and 1.137 respectively) are higher compared to other variables.

On average, holding all other risk factors constant, individuals age >60 had 118.2% of higher chance of having a CV event than individuals aged<50. As in SBP, those who had SBP level >180mmHg had a 113.7% of higher chance of having a CV event than those who had a SBP <140mmHg.

Results confirm that all four factors are significantly influenced on CV events and also it can be concluded that impact is also significantly different between levels with factors.

The fitted model can be written as:

$Log\ (\frac{P}{1-P})$ = - 4.046 + 0.747 * Sex $_{(Male)}$ + 0.616 * FBS $_{(\geq 126)}$ + 0.955 * Age $_{(50\text{-}59.9)}$ + 1.182 * Age $_{(>60)}$ + 0.607 * SBP $_{(160\text{-}179.9)}$ + 1.137 * SBP $_{(>180)}$

Thus p = Probability of cardiovascular event present can by written as,

$p = \frac{e^k}{(1-e^k)}$ Where k = - 4.046 + 0.747 * Sex $_{(Male)}$ + 0.616 * FBS $_{(\geq 126)}$ + 0.955 * Age $_{(50\text{-}59.9)}$ + 1.182 * Age $_{(>60)}$ + 0.607 * SBP $_{(160\text{-}179.9)}$ + 1.137 * SBP $_{(>180)}$

Thus it can be concluded that those four risk factors have a combined effect on CV events. Results in table 4.17, logistic regression results concluded, the most affected risk categories for having a CV event from the selected variables according to the WHO/ISH criteria are male gender, increased FBS level (>126mg/dL), higher age (age >50) and increased SBP (>160 mmHg) level as odds ratio (exp β >1) and p value are significant in above variables. According to the variables selected based on the WHO/ISH criteria, sex, age, systolic blood pressure and fasting blood sugar level can be considered as most affected risk factors on CVDs in Sri Lanka (Table 4.18).

4.9.2 Logistic Model with 2-way interactions

As it is difficult to interpret higher order interaction in logistic regression with categorical variables as explanatory variables, a best fitted model was tried with 2-way interaction only using the same criteria as above in logistic regression. Variables used for the two-way interaction model are as follows.

Individual variables are age, gender, SBP, FBS level and smoking status. Interaction terms are serum cholesterol level*age, serum cholesterol level*gender, serum cholesterol level*SBP, serum cholesterol level*FBS and serum cholesterol level*smoking status.

Table 4.19: Final results with two way interaction terms (Forward LR method)

Explanatory Variable	B	S.E.	Wald	df	Sig.	Exp(B)	95% C.I.for EXP(B)	
							Lower	Upper
Sex(1)	.717	.159	20.387	1	.000	2.047	1.500	2.794
FBS(1)	.643	.151	18.189	1	.000	1.902	1.415	2.556
Age			24.446	2	.000			
Age(1)	.941	.228	17.059	1	.000	2.564	1.640	4.007
Age(2)	1.193	.243	24.077	1	.000	3.296	2.047	5.307
SBP			26.101	3	.000			
SBP(1)	.047	.183	.066	1	.797	1.048	.733	1.499
SBP(2)	.620	.225	7.554	1	.006	1.858	1.195	2.890
SBP(3)	1.158	.255	20.663	1	.000	3.183	1.932	5.245
Chol.*Smoking(1)			10.893	4	.028			
Chol.(1)* Smoking (1)	-.055	.299	.034	1	.854	.946	.526	1.701
Chol.(2)* Smoking (1)	-.067	.380	.031	1	.860	.935	.444	1.971
Chol.(3)* Smoking (1)	1.566	.482	10.554	1	.001	4.790	1.862	12.324
Chol.(4)* Smoking (1)	-18.772	22630.95	.000	1	.999	.000	.000	.
Constant	-4.062	.237	294.813	1	.000	.017		

The fitted model with two way interactions can be written as,

$$\text{Log}\left(\frac{P}{1-P}\right) = -4.062 + 0.717 * \text{Sex}_{(\text{Male})} + 0.643 * \text{FBS}_{(\geq 126)} + 0.941 * \text{Age}_{(50\text{-}59.9)} + 1.193 * \text{Age}_{(>60)} + 0.047 * \text{SBP}_{(140\text{-}159.9)} + 0.620 * \text{SBP}_{(160\text{-}179.9)} + 1.158 * \text{SBP}_{(>180)} - 0.055 * \text{Cholesterol}_{(4\text{-}4.9)} * \text{Smoking}_{(\text{Yes})} - 0.067 * \text{Cholesterol}_{(5\text{-}5.9)} * \text{Smoking}_{(\text{Yes})} + 1.566 * \text{Cholesterol}_{(7\text{-}7.9)} * \text{Smoking}_{(\text{Yes})}$$

Results in Table 4.18 indicate that two-way interaction (smoking*cholesterol) and four main risk factors are (gender, age, Fasting plasma glucose level, & serum cholesterol level) significant ($p < 0.05$). It should be pointed out in this case, cholesterol level was not forcefully included according to the principals of hierarchical modelling. It was not identified as a significant main factor.

As all the predictor variables should be included into the hierarchical model, the final model selected by using enter method. The model can be written as,

$$\text{Log}\left(\frac{P}{1-P}\right) = -21.513 + 0.587 * \text{Sex}_{(\text{Male})} + 0.440 * \text{FBS}_{(\geq 126)} + 17.672 * \text{Age}_{(40\text{-}49.9)} 18.588 * \text{Age}_{(50\text{-}59.9)} + 19.299 * \text{Age}_{(>60)} - 0.121 * \text{Smoking}_{(\text{Yes})} + \text{Chole}_{(5\text{-}5.9)} + 17.161 * \text{Chole}_{(7\text{-}7.9)} + 0.176 * \text{SBP}_{(140\text{-}159.9)} - 0.013 * \text{SBP}_{(160\text{-}179.9)} + 1.038 * \text{SBP}_{(>180)} + 0.037 * \text{Chole}_{(5\text{-}5.9)} * \text{Sex}_{(\text{Male})} + 0.008 * \text{Chole}_{(6\text{-}6.9)} * \text{Sex}_{(\text{Male})} + 1.135 * \text{Chole}_{(7\text{-}7.9)} * \text{Sex}_{(\text{Male})} + 0.330 * \text{Chole}_{(5\text{-}5.9)} * \text{FBS}_{(\geq 126)} + 0.170 * \text{Chole}_{(6\text{-}6.9)} * \text{FBS}_{(\geq 126)} + 0.247 * \text{Chole}_{(7\text{-}7.9)} * \text{FBS}_{(\geq 126)} + 19.246 * \text{Chole}_{(>8)} * \text{FBS}_{(\geq 126} - 0.369 * \text{Chole}_{(5\text{-}5.9)} * \text{SBP}_{(140\text{-}159.9)} + 0.836 * \text{Chole}_{(5\text{-}5.9)} * \text{SBP}_{(160\text{-}179.9)} + 0.189 * \text{Chole}_{(5\text{-}5.9)} * \text{SBP}_{(>180)} + 0.271 * \text{Chole}_{(6\text{-}6.9)} * \text{SBP}_{(140\text{-}159.9)} + 0.914 * \text{Chole}_{(6\text{-}6.9)} * \text{SBP}_{(160\text{-}179.9)} + 0.358 * \text{Chole}_{(6\text{-}6.9)} * \text{SBP}_{(>180)} - 1.348 * \text{Chole}_{(7\text{-}7.9)} * \text{SBP}_{(140\text{-}159.9)} + 0.783 * \text{Chole}_{(7\text{-}7.9)} * \text{SBP}_{(160\text{-}179.9)} - 0.867 * \text{Chole}_{(7\text{-}7.9)} * \text{SBP}_{(>180)} + 0.276 * \text{Chole}_{(5\text{-}5.9)} * \text{Smoking}_{(\text{Yes})} + 0.249 * \text{Chole}_{(6\text{-}6.9)} * \text{Smoking}_{(\text{Yes})} + 1.133 * \text{Chole}_{(7\text{-}7.9)} * \text{Smoking}_{(\text{Yes})}$$

Based on the best fitted model, it can be concluded that, sex, higher FBS level, higher age, higher SBP level are the most affected risk factors on CV risk. In interaction terms with serum cholesterol level, smokers with higher cholesterol level

is significant ($p = 0.001$, $\exp \beta > 1$). The odd ratio for smoking*chol. Level (3) is very high (4.79) compared with odd ratios for other variables.

Most affected risk categories on CV risk are: SBP > 180mmHg ($p < 0.001$, odd ratio = 3.18), age 50-59.9 ($p < 0.001$, odd ratio = 2.564) age > 60 ($p < 0.001$, odd ratio = 3.296) and males ($p < 0.001$, odd ratio = 2.052). And regression coefficients of those variables are 1.158, 0.941, 1.193, and 0.717 respectively (Table 4.19).

4.10 Summary of Chapter 4

When considered individual effect from the risk factors on CV risk, most affected risk categories based on the WHO/ISH criteria are higher FBS level ($\geq$126 mg/dL), male gender, higher SBP level (>160mmHg) and higher age (age $\geq$ 50). When considered interactions of total cholesterol level with each individual risk factors, only smokers with higher serum cholesterol level (7-7.9) mmol/L is significant. No individual effect on CV risk from serum cholesterol level. When interaction presents, smokers who had higher serum cholesterol level had a higher CV risk.

CHAPTER 5

VALIDATION OF THE WHO/ISH RISK PREDICTION CHARTS

Based on the WHO/ISH risk prediction charts for SEAR B, the 10-year risk of a fatal or non-fatal cardiovascular events were derived for all persons aged 40 years and above based on the status of the predictor variables at baseline. Two risk estimates were calculated: (i) with gender, diabetes status, systolic blood pressure, age, smoking status and serum cholesterol level; and (ii) with gender, diabetes status, systolic blood pressure, age, and smoking status (Without serum cholesterol level). The results of the two methods are described separately.

5.1 Risk Prediction with Gender, Diabetes Status, Systolic Blood Pressure, Age, Smoking Status and Serum Cholesterol Level

Table 5. 1: Distribution of participants by risk and gender

10-year risk of a fatal or non-fatal cardiovascular event	Male	Female	Total
<10%	987(87.2%)	1045(75.5%)	2032(80.7%)
10-20%	73(6.4%)	177 (12.8%)	250 (9.9%)
20-30%	41 (3.6%)	55 (3.9%)	96 (3.8%)
30-40%	14 (1.2%)	48 (3.5%)	62 (2.5%)
>40%	17 (1.5%)	60 (4.3%)	77(3.1%)
Total	1132	1385	2517

Parenthesis indicated the column percentage with respect to column total

According to the WHO/ISH chart for SEARB, the 10-year predicted risk of CVD is shown in table 5.1 for the each gender. The majority (80.7%) of the study population had a low risk (<10%) of CVD. Intermediate/moderate risk (10% to <20%), high risk (20% to < 30%) and very high risk (>30%) were 9.9%, 3.8% and 5.6% respectively (Table 5.1).

5.2 Risk Prediction Chart with all Risk Factors

Of the 1132 males and 1385 females, CV events were found only in 130 males and 85 females. That is 8.5% of the total population.

The validation results varied between males and females. The observed CVD events among males were within the expected ranges of the prediction charts for risk groups <10% and >40%. In risk group 20%-30%, the observed number of CVD events was 14.6%; in risk group 30%-40%, the observed number of CVD events was 28.6%, it was closer to the lower limit of the interval. If the risk groups 10%-20% and 20%-30% are amalgamated, then the observed CVD events are 21.9% which will lie in the interval 10%-30%. Observed results validated the expected numbers. (Table 5.2)

Table 5. 2: Validation of Risk Prediction of Cardiovascular Events Using Diabetes Status, Systolic Blood Pressure, Age, Smoking Status and Serum Cholesterol Level Based on WHO/ISH Chart for SEAR B

Risk (%)	Male			Female			Total		
	N	CVD events	%	N	CVD events	%	N	CVD events	%
<10%	987	94	**9.5**	1045	48	**4.6**	2032	142	**7.0**
10-20%	73	19	26.0	177	12	6.8	250	31	**12.4**
20-30%	41	6	14.6	55	6	10.9	96	12	12.5
30-40%	14	4	**28.6**	48	8	16.7	62	12	19.4
>40%	17	7	**41.2**	60	11	18.3	77	18	23.4
Total	1132	130	11.5	1385	85	6.1	2517	215	8.5

Among females, the observed number of CVD events was less than the expected in all risk categories except in the category <10%, the observed percentage being 4.6%

However, there was an increasing trend in the observed number of events with increasing risk category unlike in the males (Table 5.2)..

5.3 Risk Prediction with Gender, Diabetes Status, Systolic Blood Pressure, age, and Smoking Status (Without Serum Cholesterol Level)

10-year risk of a fatal or non-fatal cardiovascular event using gender, age, systolic blood pressure, smoking status and presence or absence of diabetes mellitus (without total cholesterol) was obtained by applying the WHO/ISH risk prediction chart for SEAR B.

Table 5. 3: Distribution of participants by gender and risk[1]

10-year risk of a fatal or non-fatal cardiovascular event	Male	Female	Total
<10%	931 (82.2%)	1084 (78.3%)	2015 (80.1%)
10-20%	157 (13.9%)	239 (17.3%)	396 (15.7%)
20-30%	31 (2.7%)	62 (4.5%)	93 (3.7%)
30-40%	1 (0.1%)	0 (0.0%)	1 (0.0%)
>40%	12 (1.1%)	0 (0.0%)	12 (0.5%)
Total	1132	1385	2517

[1]Risk prediction using gender, diabetes status, systolic blood pressure, age and smoking status

The majority 80.1% (n=2015) of the study population had a low risk (<10%) of CVD. When risk calculated without serum cholesterol readings, there were no CVD events recorded among females in risk groups >30%.12(1.1%) CVD events were observed among males having a predicted risk of >40%. (Table 5.3)

Table 5. 4: Distribution of participants by gender and combined risk groups

			CV risk		
			<10%	≥10%	Total
Sex	F	Count	1084	301	1385
		% within sex	78.3%	21.7%	100.0%
	M	Count	931	201	1132
		% within sex	82.2%	17.8%	100.0%
		% of Total	80.1%	19.9%	100.0%

Chi-square test statistic (χ^2_1) = 6.169 (p = 0.013 < 0.05)

Due to lack of numbers for the risk prediction for higher risk groups in table 5.4, combined all higher risk groups together to compare with lower risk group (<10%). Chi-square test statistics confirms that there is a significant difference between males and females. Females had a significantly higher risk than males (χ^2= 6.17, p<0.05) when <10% category was considered as low risk and all the other risk categories combined (≥10%) considered as high risk (Table 5.4).

5.4 Risk Prediction without Serum Cholesterol Readings

Table 5.5: Validation of risk prediction with diabetes status, systolic blood pressure, age, smoking status with gender and cardiovascular events

Risk (%)	Male			Female			Total		
	N	CVD events	%	N	CVD events	%	N	CVD events	%
<10%	931	89	**9.6**	1084	49	**4.5**	2015	138	**6.8**
10-20%	157	28	**17.8**	239	26	**10.9**	396	54	**13.6**
20-30%	31	10	7.7	62	10	16.1	93	20	**21.5**
30-40%	1	0	0.0	0	0	0.0	1	0	0.0
>40%	12	3	2.3	0	0	0.0	12	3	25.0
Total	1132	130	11.5	1385	85	6.1	2517	215	8.5

Risk is correctly classified for the lower risk categories (<10% and 10-20%) for males, females and the total population. The trends of observed events using the risk classification without serum cholesterol is poor except in the categories <10% and 10%-20% in males, females and in the total population with the expected number of events being within the risk ranges. For the higher risk categories>30%, no recorded events for the risk prediction for females and only 3 events for males. Thus it can be concluded, risk prediction is poor for males, females and the total population when serum cholesterol level is not involved for the analysis (Table 5.5).

5.5 Comparison of two risk predictions

It is obvious that both prediction charts do not match perfectly. In order to compare both charts, the probabilities of correctly classifying into different categories in Chart II, given that it is in a category of Chart I were computed (Table 5.6). Similarly, the probabilities of correctly classifying into different categories in Chart I, given that it is in a category of Chart II were also computed (Table 5.7).

Table 5. 6: Frequencies and the corresponding raw percentage under each category

Risk classification (diabetes status, systolic blood pressure, age, smoking status, gender)- Chart I	Risk classification (diabetes status, systolic blood pressure, age, smoking status, gender and serum cholesterol) – Chart II					
	<10%	(10-20) %	(20-30) %	(30-40) %	>40 %	Total
(<10%)	**1866 (92.7)**	107 (5.3)	36 (1.8)	5 (0.2)	1 (0.0)	2015
(10-20%)	165 (41.7)	**140 (35.4)**	38 (9.6)	27 (6.7)	26 (6.6)	396
(20-30%)	1 (1.1)	3 (3.2)	**20 (21.5)**	26 (28.0)	43 (46.2)	93
(30-40%)	0 (0.0)	0 (0.0)	1 (100.0)	**0 (0.0)**	0 (0.0)	1
(>40%)	0 (0.0)	0 (0.0)	1 (8.3)	4 (33.3)	**7 (58.4)**	12
Total	2032	250	96	62	77	2517

Parenthesis indicates the row percentages.

Table 5. 7: Frequencies and the corresponding column percentage under each category

Risk classification (diabetes status, systolic blood pressure, age, smoking status, gender)- Chart I	Risk classification (diabetes status, systolic blood pressure, age, smoking status, gender and serum cholesterol) – Chart II					
	<10%	(10-20) %	(20-30) %	(30-40) %	>40 %	Total
(<10%)	**1866 (91.8)**	107 (42.8)	36 (37.5)	5 (8.1)	1 (1.3)	2015
(10-20%)	165 (8.1).	**140 (56.0)**	38 (39.6)	27 (43.5)	26 (33.8)	396
(20-30%)	1 (0.1)	3 (1.2)	**20 (20.9)**	26 (41.9)	43 (55.8)	93
(30-40%)	0 (0.0)	0 (0.0)	1 (1.0)	**0 (0.0)**	0 (0.0)	1
(>40%)	0 (0.0)	0 (0.0)	1 (1.0)	4 (6.5)	**7 (9.1)**	12
Total	2032	250	96	62	77	2517

Parenthesis indicates the column percentages.

Results in Table 5.6 indicates that the probability correctly classifying into <10% category in Chart II given that those subjects are in the same category in Chart I is 92.7%. Results in Table 5.7 indicate that the probability correctly classifying into <10% category in Chart II given that those subjects are in the same category in Chart I is 91.8%. Both probabilities are very high confirming that both charts give almost similar results for < 10% group. However, for other categories reasonable higher probabilities were not observed, Nevertheless the probability of overall correctly classification irrespective of the category is 80%.

That is, (1866+140+20+7)*100/2517.

CHAPTER 6

CONCLUSIONS AND RECOMENDATIONS

Asians, in particular Sri Lankans have a higher incidence of CVDs and have different risk factor profiles. However, there are no cardiovascular risk prediction models developed specifically for Sri Lankans or South Asians. This study validated the WHO/ISH risk prediction chart for South East Asia Region B by calculating the 10-year risk of a cardiovascular event of a population resident in the Ragama Medical Officer of Health area which was followed for 10 years. Risk predictions were made using age, sex, systolic blood pressure, presence of diabetes, smoking status and with and without total serum cholesterol level. This is the first study to validate WHO/ISH risk prediction charts in a South Asian / Sri Lankan population.

Conclusions and recommendation derived from the statistical inferences derived in this study are given below.

6.1 Conclusions

- Most affected risk factors on CVDs were age, gender, fasting plasma glucose level and systolic blood pressure. Among them, male gender, higher age (>50) and higher systolic blood pressure level (>160mmHg) can be considered as highly affected risk categories on CVD.
- Smokers who had higher serum cholesterol level at baseline, had a higher risk of having a CV event.
- Participants who experienced any CV event were older than the normal persons and males had higher CV risk than females
- When total serum cholesterol was used in risk prediction, the observed CVD events among males were within the expected ranges of the prediction charts only for risk groups <10% and >40%. In risk group 30-40%, predicted risk among males is 28.6% and in risk group 20%-30%, the observed number of CVD events was 14.6% both predictions are closed to the lower limit of the respective intervals.

- Even though serum cholesterol level is not associated with CV events, when we consider the collective risk for the risk prediction, the risk analysis were accurate with serum cholesterol values.
- Among females, the observed number of CVD events was less than the expected in all risk categories except in the category <10%. There was an increasing trend in the observed number of events with increasing risk category in females.
- When risk prediction was done without using total serum cholesterol, the observed number of CVD events were correctly predicted in the two lower risk categories (<10%, 10-20%) in males, females and total population.
- In both risk predictions methods, the majority of the population had a <10% risk of a fatal or non-fatal CVD event.
- Participants who had a CV event, had a significantly higher fasting blood sugar level and systolic blood pressure, and were a higher percentage of smokers at baseline.
- In both classifications used in this study, females had a significantly higher CVD risk than males with higher percentages being in the higher risk groups.
- Males were more likely to be categorized as 'high risk' based on NCEP-ATP III criteria while females were more likely to be classified as high risk on the WHO/ISH criteria.

6.2 Recommendations

The WHO/ISH risk prediction charts provide a guide to assess CV risk among Sri Lankans and should be routinely used. WHO/ISH charts for SEAR B can also be used for CV risk prediction in Sri Lankan population.

The risk prediction was more accurate with serum cholesterol values based on the reported number of CVD events. Risk classification is significantly improved by including serum cholesterol. The risk classification using total serum cholesterol was a better prediction chart than the one without it.

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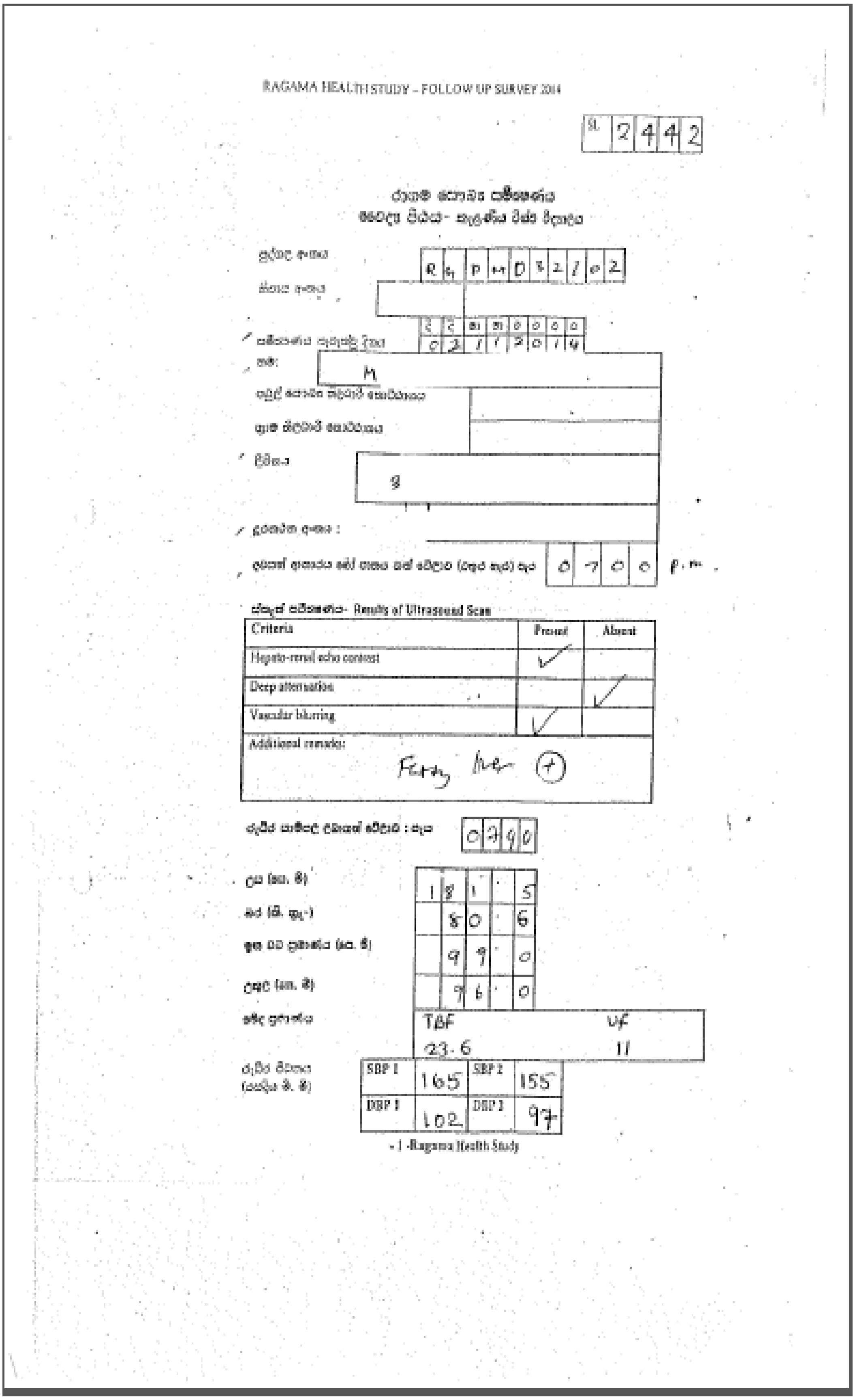
APPENDIX 1

Questionnaire



RAGAMA HEALTH STUDY – FOLLOW UP SURVEY 2014

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R G P M D 3 2 / 0 2

0 2 / 1 2 / 2 0 1 4

M

9

0 7 0 0 p.m.

Results of Ultrasound Scan

Criteria	Present	Absent
Hepato-renal echo contrast	✓	
Deep attenuation		✓
Vascular blurring	✓	
Additional remarks: Fatty liver (+)		

0 7 4 0

	1 8 1 . 5
	8 0 . 6
	9 9 . 0
	9 6 . 0
	TBF 23.6 VF 11

SBP 1	165	SBP 2	155
DBP 1	102	DBP 2	97

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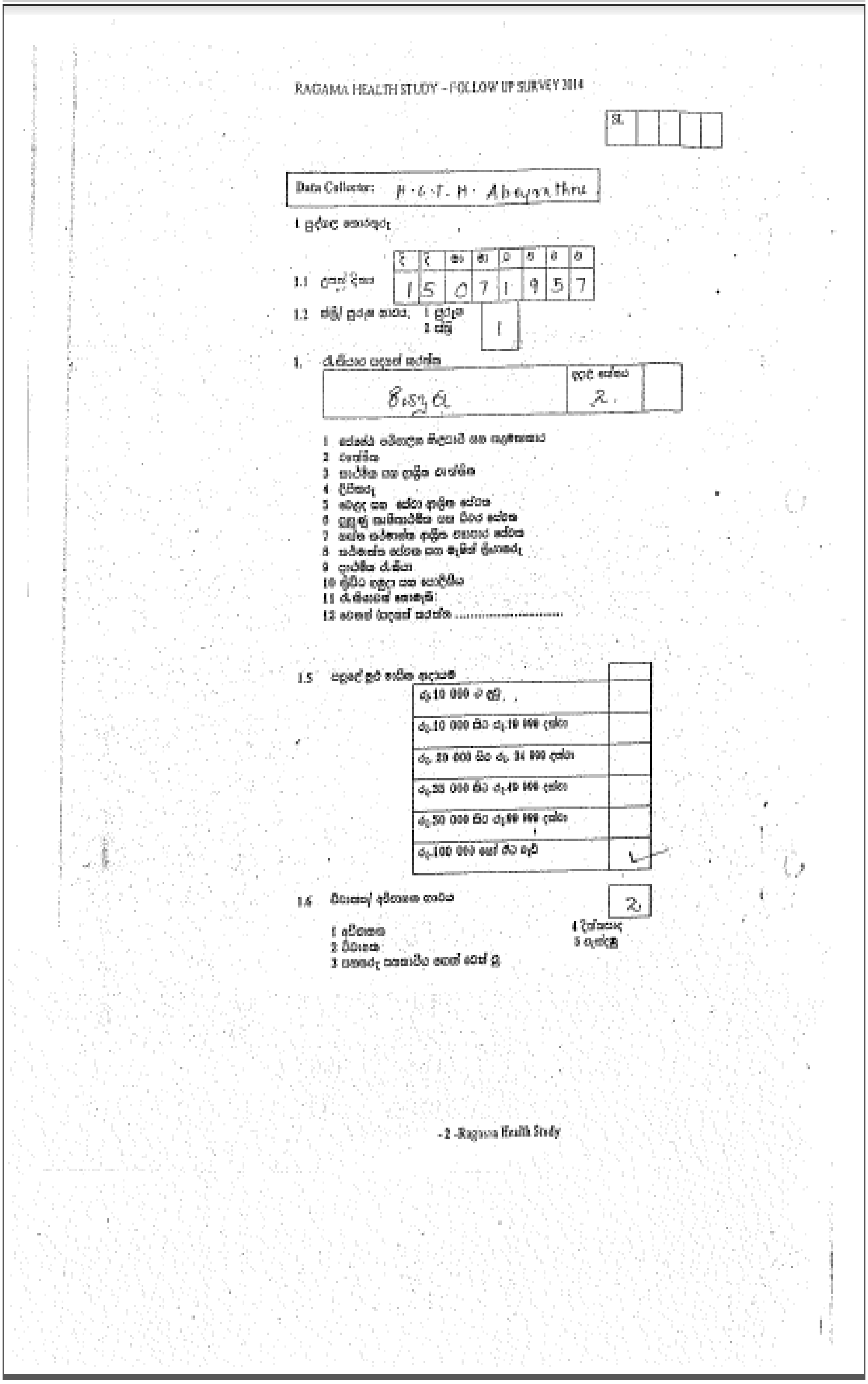

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SL | | | |

Data Collector: H. L. T. H. Abayrathne

1 [illegible]

1.1 [illegible]

[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
1	5	0	7	1	9	5	7

1.2 [illegible] 1 [illegible] 2 [illegible] — 1

1. [illegible]

[illegible]	[illegible] 2.	

1 [illegible]
2 [illegible]
3 [illegible]
4 [illegible]
5 [illegible]
6 [illegible]
7 [illegible]
8 [illegible]
9 [illegible]
10 [illegible]
11 [illegible]
12 [illegible] ....

1.5 [illegible]

[illegible] 10 000 [illegible]	
[illegible] 10 000 [illegible] 19 999 [illegible]	
[illegible] 20 000 [illegible] 34 999 [illegible]	
[illegible] 35 000 [illegible] 49 999 [illegible]	
[illegible] 50 000 [illegible] 99 999 [illegible]	
[illegible] 100 000 [illegible]	✓

1.6 [illegible] — 2

1 [illegible]
2 [illegible]
3 [illegible]
4 [illegible]
5 [illegible]

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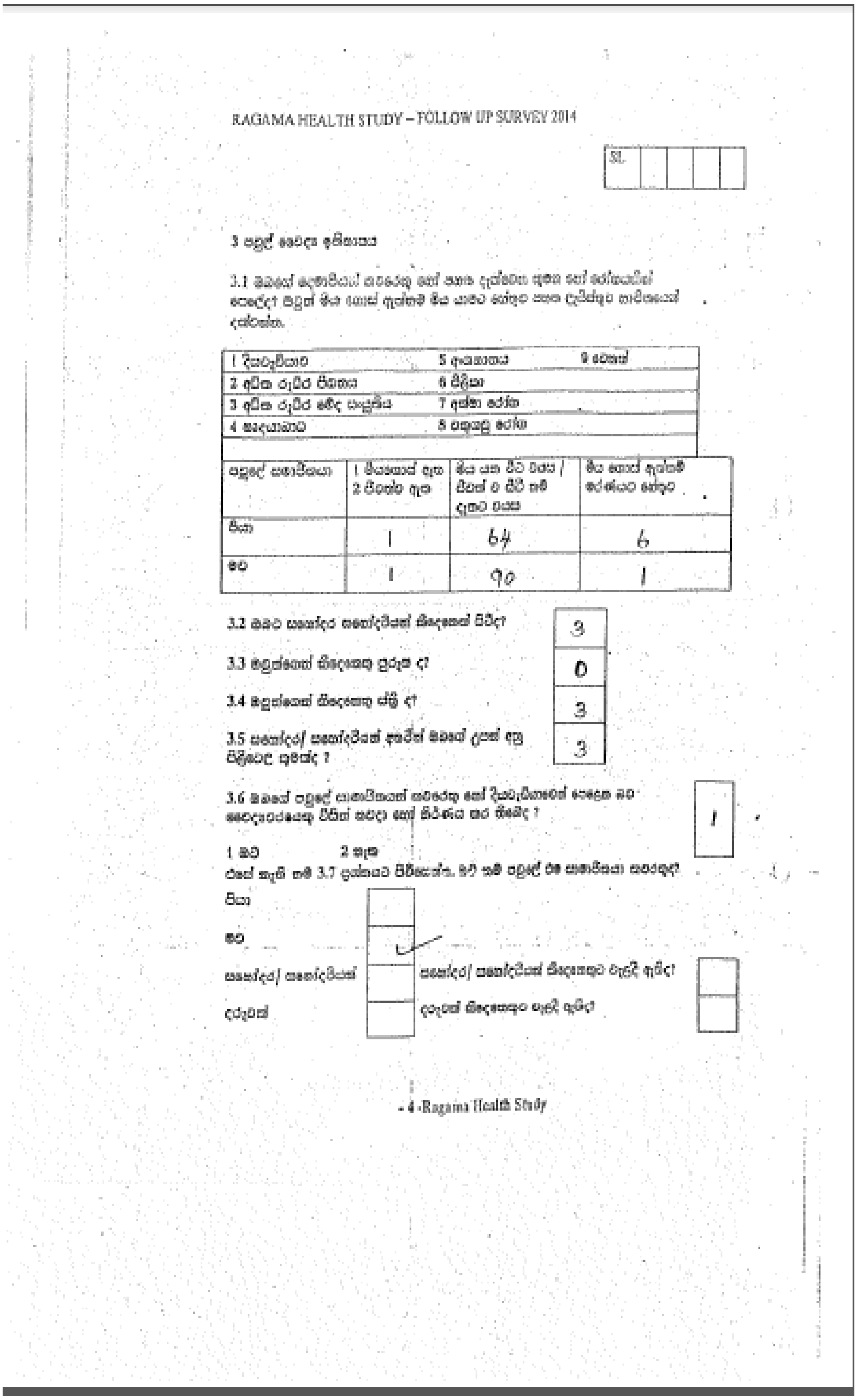
2 ඔබ පහත සඳහන් ඕනෑම හෝ රෝගයකින් පෙළෙන බව වෛද්‍යවරයෙකු විසින් කවදා හෝ තීරණය කර තිබේද?

1 ඇත
2 නැත

රෝග තත්වය		දැනට භාවිතා වන බෙහෙත් වර්ග		දිනකට භාවිතා වන වාර ගණන	හඳුනාගත් වර්ෂය	වෛද්‍ය වාර්තා මගින් තහවුරු විය
දියවැඩියාව	2	1 ඉන්සියුලින් විදීම 2 දියවැඩියා පාලන පෙති ගැනීම 3 අංක 1 සහ 2 4 ආහාර පාලනය පමණක් 5 වෙනත් 6 ප්‍රතිකාර නොගනී				
අධික රුධිර පීඩනය	2	1 අධික රුධිර පීඩන පාලන ඖෂධ ගැනීම 2 ලුණු අඩු කිරීම 3 අංක 1 සහ 2 4 වෙනත් 5 ප්‍රතිකාර නොගනී				
අධික රුධිර මේද සංයුතිය (අධික කොලෙස්ටරෝල් මට්ටම ඇතුළත්ව)	2	1 මේදය අඩු කරන ඖෂධ ගැනීම 2 ආහාර පාලනය 3 අංක 1 සහ 2 4 වෙනත් 5 ප්‍රතිකාර නොගනී				



RAGAMA HEALTH STUDY – FOLLOW UP SURVEY 2014

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3 පවුලේ වෛද්‍ය ඉතිහාසය

3.1 ඔබගේ දෙමාපියන් [illegible] දක්වන්න.

1 දියවැඩියාව	5 අංශභාගය	9 වෙනත්
2 අධික රුධිර පීඩනය	6 පිළිකා	
3 අධික රුධිර මේද සංයුතිය	7 අක්මා රෝග	
4 හෘදයාබාධ	8 වකුගඩු රෝග	

පවුලේ සාමාජිකයා	1 මියගොස් ඇත 2 ජීවත්ව ඇත	මිය යන විට වයස / ජීවත් ව සිටී නම් දැනට වයස	මිය යාමට හේතුව
පියා	1	64	6
මව	1	90	1

3.2 ඔබට සහෝදර සහෝදරියන් කීදෙනෙක් සිටීද? 3

3.3 ඔවුන්ගෙන් කීදෙනෙකු පුරුෂ ද? 0

3.4 ඔවුන්ගෙන් කීදෙනෙකු ස්ත්‍රී ද? 3

3.5 සහෝදර/ සහෝදරියන් අතරින් ඔබගේ උපන් අනු පිළිවෙළ කුමක්ද ? 3

3.6 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකු හෝ දියවැඩියාවෙන් පෙළෙන බව වෛද්‍යවරයෙකු විසින් සොයා හෝ නිර්ණය කර තිබේද ? 1

1 ඔව් 2 නැත

එසේ නැති නම් 3.7 ප්‍රශ්නයට පිවිසෙන්න. ඔව් නම් පවුලේ එම සාමාජිකයා කවරෙක්ද?

පියා			
මව	✓		
සහෝදර/ සහෝදරියන්		සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළඳී ඇතිද?	
දරුවන්		දරුවන් කීදෙනෙකුට වැළඳී ඇතිද?	

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3.7 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකුට හෝ හෘදයාබාධයක් සැලුන බව වෛද්‍යවරයෙකු විසින් කවදා හෝ සිථිණය කර තිබේද ?

1 ඔව් 2 නැත 2

එසේ නැති නම් 3.8 ප්‍රශ්නයට පිවිසෙන්න ඔව් නම් පවුලේ එම සාමාජිකයා කවරතුද?

පියා

මව

සහෝදර/ සහෝදරියන් සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළදී ඇතිද?

දරුවන් දරුවන් කීදෙනෙකුට වැළදී ඇතිද?

3.8 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකුට හෝ අධි රුධිර පීඩනයෙන් පෙළෙන බව වෛද්‍යවරයෙකු විසින් කවදා හෝ සිථිණය කර තිබේද ?

1 ඔව් 2 නැත

1

එසේ නැති නම් 3.9 ප්‍රශ්නයට පිවිසෙන්න ඔව් නම් පවුලේ එම සාමාජිකයා කවරතුද?

පියා

මව

සහෝදර/ සහෝදරියන් ✓ සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළදී ඇතිද? 1

දරුවන් දරුවන් කීදෙනෙකුට වැළදී ඇතිද?

SL				

3.9 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකු හෝ අධික රුධිර මේද සංයුතියකින් පෙළෙන බව වෛද්‍යවරයෙකු විසින් කවදා හෝ නිර්ණය කර තිබේද ?

1 ඔව් 2 නැත [1]

එසේ නැති නම් 3.10 ප්‍රශ්නයට පිවිසෙන්න ඔව් නම් පවුලේ එම සාමාජිකයා කවරෙක්ද?

පියා			
මව			
සහෝදර/ සහෝදරියන්	✓	සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළදී ඇතිද?	1
දරුවන්		දරුවන් කීදෙනෙකුට වැළදී ඇතිද?	

3.10 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකුට හෝ ආඝාතය සැදුන බව වෛද්‍යවරයෙකු විසින් කවදා හෝ නිර්ණය කර තිබේද ?

1 ඔව් 2 නැත [2]

එසේ නැති නම් 3.11 ප්‍රශ්නයට පිවිසෙන්න ඔව් නම් පවුලේ එම සාමාජිකයා කවරෙක්ද?

පියා			
මව			
සහෝදර/ සහෝදරියන්		සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළදී ඇතිද?	
දරුවන්		දරුවන් කීදෙනෙකුට වැළදී ඇතිද?	

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3.11 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකු හෝ පිළිකා රෝගයෙන් පෙළෙන බව වෛද්‍යවරයෙකු විසින් සඳහා හෝ තීරණය කර තිබේද ? [1]

1 ඔව් 2 නැත

එසේ නැති නම් 3.12 ප්‍රශ්නයට පිවිසෙන්න ඔව් නම් පවුලේ එම සාමාජිකයා කවරෙකුද ?

පියා	✓	ඔව් නම් ප්‍රාථමික ස්ථාන	[illegible]
මව		ඔව් නම් ප්‍රාථමික ස්ථාන	
සහෝදර/ සහෝදරියන්		ඔව් නම් සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළදී ඇත්ද?	
දරුවන්		ඔව් නම් දරුවන් කීදෙනෙකුට වැළදී ඇත්ද?	

ඔබගේ සහෝදර/ සහෝදරියන්ගේ/ දරුවන්ගේ පිළිකාවේ ප්‍රාථමික ස්ථාන මොනවාද?

3.12 ඔබගේ පවුලේ සාමාජිකයන් කවරෙකු හෝ වකුගඩු රෝගයකින් පෙළෙන බව වෛද්‍යවරයෙකු විසින් සඳහා හෝ තීරණය කර තිබේද ? [2]

1 ඔව් 2 නැත

එසේ නැති නම් 3.13 ප්‍රශ්නයට පිවිසෙන්න ඔව් නම් පවුලේ එම සාමාජිකයා කවරෙකුද ?

පියා			
මව			
සහෝදර/ සහෝදරියන්		සහෝදර/ සහෝදරියන් කීදෙනෙකුට වැළදී ඇත්ද?	
දරුවන්		දරුවන් කීදෙනෙකුට වැළදී ඇත්ද?	

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3.13 ඔබගේ පවුලේ දෘෂ්ටිකයෙක් සහෝදර හෝ අක්කා රෝහමින් පෙළෙන බව පෙදෙසවරයෙකු විසින් හෙදියා හෝ තිරණය කර තිබේද ?

1 ඔව් 2 නැත

2

එසේ නැති නම් 4 ප්‍රශ්නයට පිවිසෙන්න මේ සඳහා පවුලේ එම දෘෂ්ටිකයා කවරකු ද ?

පියා			
මව			
සහෝදර/ සහෝදරියන්		සහෝදර/ සහෝදරියන් සිදෙනකුට වැඩි ඇතිද?	
දරුවන්		දරුවන් සිදෙනකුට වැඩි ඇතිද?	

SL

4. මධ්‍යසාර භාවිතය

4.1 ඔබ කවදා හෝ මධ්‍යසාර භාවිතා කර තිබේද?

නැත

මම කලින් භාවිතා කර නවතා ඇත

මම වර්තමානයේදීත් භාවිතා කරමි ✓

4.2 ඔව් නම් පසුගිය වසර සඳහා පිළිතුරු සපයන්න භාවිතා කරන මධ්‍යසාර වර්ගය/ ප්‍රමාණය හා භාවිතා කරන වාර ගණන පහත ඇති උපදෙස්වලට අනුව සඳහන් කරන්න

වර්ගය	.	වාර ගණන										ප්‍රමාණය		
		1	2	3	4	5	6	7	8	9	10	බෝතල්	ජෝගු	වීදුරු
බීර (මි.ලි 330 / ½ පයින්ට ඒකක 1)														
අරක්කු (මි.ලි 30 ඒකක 1)							✓					1/4		
වයින් (වීදුරු 1, ඒකක 1 මි.ලි 50 ඒකක 1)														
කසිප්පු														
වෙනත් විශේෂයන්........................														

1 දවසට දෙවතාවට වැඩියි නම් ඒ කී වතාවක්දැයි දක්වන්න..............

2 දවසට දෙවතාවක්

3 දිනපතා

4 සතියකට 5-6 අතරතුර දවසට වතාවක්

5 සතියකට 3–4 වතාවක්

6 සතියකට වතාවක් හෝ දෙවතාවක්

7 මසකට 2–3 වතාවක්

8 මසකට වතාවක්

9 වසරකට 6–11 වතාවක්

10 වසරකට 1–5 වතාවක්

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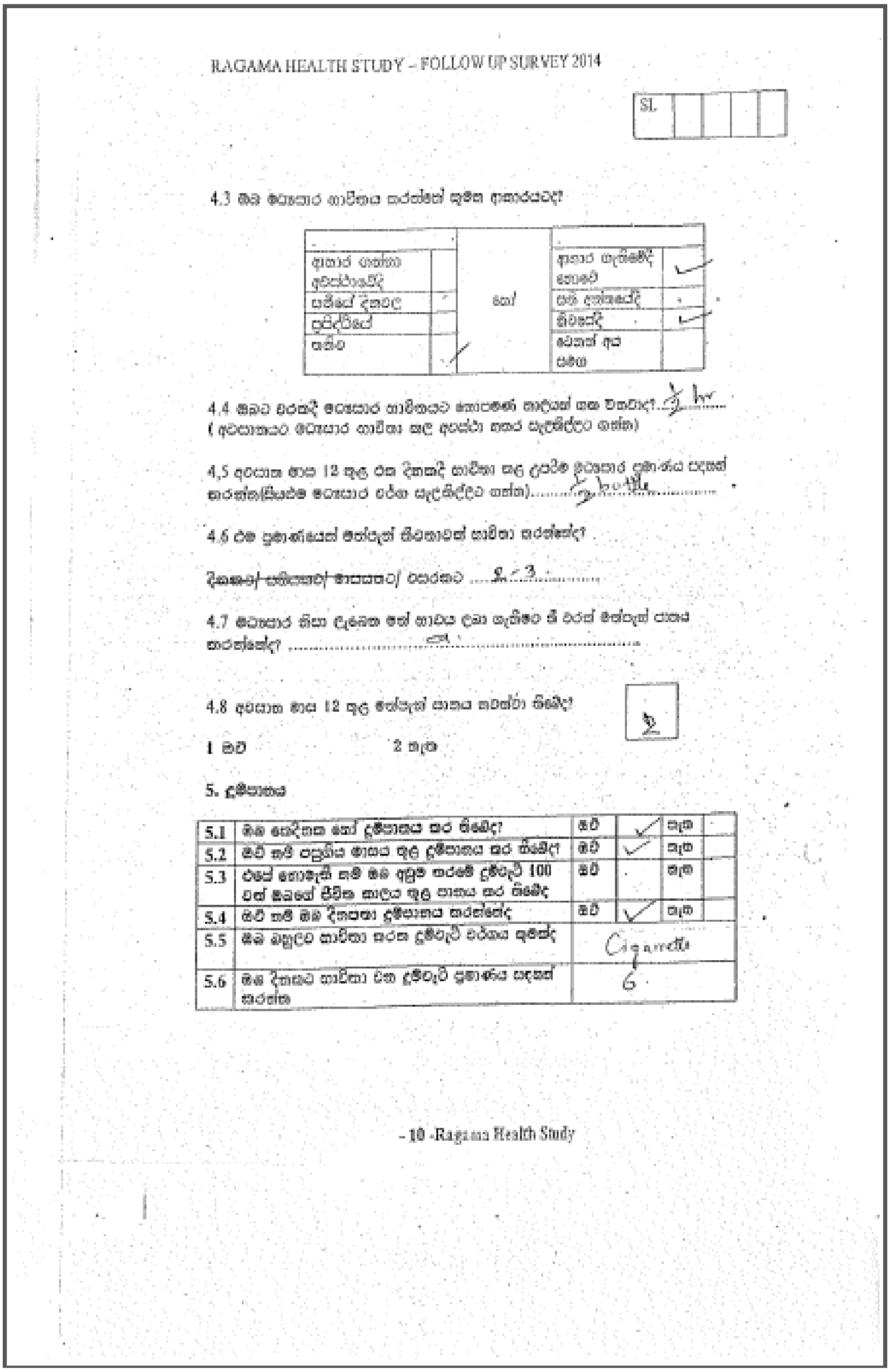

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4.3 ඔබ මධ්‍යසාර භාවිතය කරන්නේ කුමන ආකාරයටද?

ආහාර ගන්නා අවස්ථාවේදී		හෝ	ආහාර ගැනීමේදී නොවේ	✓
සතියේ දිනවල			සති අන්තයේදී	
[illegible]			නිවසේදී	✓
තනිව	✓		වෙනත් අය සමග	

4.4 ඔබට වරකදී මධ්‍යසාර භාවිතයට කොපමණ කාලයක් ගත වනවාද?...½ hr...
(අවසානයට මධ්‍යසාර භාවිතා කළ අවස්ථා තුන සැලකිල්ලට ගන්න)

4,5 අවසාන මාස 12 තුළ එක දිනකදී භාවිතා කළ උපරිම මධ්‍යසාර ප්‍රමාණය සඳහන් කරන්න(සියළුම මධ්‍යසාර වර්ග සැලකිල්ලට ගන්න)........½ bottle..........

4.6 එම ප්‍රමාණයෙන් මත්පැන් කීවතාවක් භාවිතා කරන්නේද?

~~දිනකට/ සතියකට/ මාසයකට/~~ වසරකට ....2-3..........

4.7 මධ්‍යසාර නිසා ඇතිවන මත් භාවය ලබා ගැනීමට කී වරක් මත්පැන් පානය කරන්නේද? ....

4.8 අවසාන මාස 12 තුළ මත්පැන් පානය නවත්වා තිබේද? [2]

1 ඔව් 2 නැත

5. දුම්පානය

5.1	ඔබ කෙදිනක හෝ දුම්පානය කර තිබේද?	ඔව්	✓	නැත	
5.2	ඔව් නම් පසුගිය මාසය තුළ දුම්පානය කර තිබේද?	ඔව්	✓	නැත	
5.3	එසේ නොමැති නම් ඔබ අවම තරමේ දුම්වැටි 100 වත් ඔබගේ ජීවිත කාලය තුළ පානය කර තිබේද	ඔව්		නැත	
5.4	ඔව් නම් ඔබ දිනපතා දුම්පානය කරන්නේද	ඔව්	✓	නැත	
5.5	ඔබ බහුලව භාවිතා කරන දුම්වැටි වර්ගය කුමක්ද	Cigarette			
5.6	ඔබ දිනකට භාවිතා වන දුම්වැටි ප්‍රමාණය සඳහන් කරන්න	6			

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SL 2442

රාගම [illegible] පර්යේෂණ සම්මුති පත්‍රය

සහභාගිවන්නන් විසින් මෙම පත්‍රය කියවා සම්පූර්ණ කළ යුතුය. මේ සඳහා පළමුව සහභාගිවන්නන් සඳහා වූ තොරතුරු පත්‍රිකාව කියවන්න.

(කියවීමට අපහසු අය සඳහා පර්යේෂණ නිලධාරියා විසින් මෙය කියවනු ඇත.)

කැමති ප්‍රතිචාරය වටුම් කරන්න.

1	ඔබ තොරතුරු පත්‍රිකාව කියවූවාද හෝ කිසිවෙකු විසින් කියවනු ලැබුවාද?	ඔව්/ නැත
2	මෙම පර්යේෂණය [illegible] පිළිබඳව [illegible] ඔබට [illegible]?	ඔව්/ නැත
3	මෙම පර්යේෂණය ගැන පර්යේෂණ නිලධාරියා සමඟ සාකච්ඡා කිරීමට හා ප්‍රශ්න ඇසීමට අවස්ථාව ලැබුණාද?	ඔව්/ නැත
4	ඔබගේ ප්‍රශ්න සඳහා සෑහීමකට පත්විය හැකි පිළිතුරු ලැබුණේද?	ඔව්/ නැත
5	මෙම පර්යේෂණයෙන් ඔබ [illegible] ඔබට [illegible] ඔබ වටහා ගත්තේද?	ඔව්/ නැත
6	කිසිම හේතුවක් [illegible] මෙම පර්යේෂණයෙන් ඉවත් වීමට [illegible] ඇති බව වටහා ගත්තේද?	ඔව්/ නැත
7	ඔබට මෙම තීරණය ගැනීම සඳහා ප්‍රමාණවත් කාලයක් ලැබුණේද?	ඔව්/ නැත
8	ඔබ මෙම පර්යේෂණයට සහභාගිවීමට එකඟද?	ඔව්/ නැත

ඉහත පර්යේෂණයට සහභාගිවීමට මම කැමැත්ත පළ කරමි.

සහභාගිවන්නාගේ අත්සන ....

සහභාගිවන්නාගේ නම M. P. S. Saparamadu.

දිනය 2014/11/02.

මා විසින් පර්යේෂණය ගැන සහභාගිවන්නාට පැහැදිලි කර දුන් අතර [illegible]

පර්යේෂණ නිලධාරියාගේ අත්සන ....

පර්යේෂණ නිලධාරියාගේ නම H. A. T. H. Abeyrathne.

දිනය 2014/11/02.