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Assessing the impact of reducing risk factors for cardio-vascular disease in Thailand

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Abstract

Cardiovascular disease (CVD) is a global health problem and there has been an epidemiological transition of CVD from high income countries to low-middle income countries. In the case of Thailand, the prevalence of heart disease and stroke is increasing. In order to reduce the risk of CVD, the Ministry of Public Health in Thailand has implemented a number of primary CVD prevention strategies within the last decade. These strategies are being specifically implemented to address the future potential economic burden of increasing CVD. However, the economic impact of reducing multiple risk factors, at a population level in Thailand, in terms of health care costs is unclear. In order to plan for investment in public health interventions within finite resources, it is imperative that decision makers have sufficient information to identify the target populations and risk reduction strategies, and to assess the impact of these strategies on the population.

This study aims to estimate the future prevalence of CVD in Thailand over the next 5 – 10 years and the potential economic and health benefits of strategies to reduce the population risk factors during this period.

The mathematic CVD cost-offset model has been developed in this study in 7 stages. 1) Descriptive analysis of the CVD risk profile data from the 4th National Health Examination Survey (NHESIV) 2008-2009 data set in order to explore the association of CVD risk factors in Thailand. 2) Calculate the probability of future CVD event which applies the CVD risk prediction equation. 3) Estimate of the number of future CVD events. 4) Validation of the estimated number of annual CVD event with the actual CVD hospitalisation event in Thailand. 5) Calculate the cost of hospital admission due to CVD from the Universal Coverage Health Care Scheme (UC) data in 2009. 6) Estimate the burden of CVD in terms of the DALYs. 7) Estimate the impact of reducing

CVD risk factors in different scenarios. The study outcomes being the number of hospitalisation cost savings, number of premature death savings, DALY savings and health care cost savings. The outcomes will also account for the uncertainty analysis.

As indicated above, no studies currently exist that focus specifically on the mathematic model for estimating the future situation of CVD in Thailand. Therefore, this study represents an original contribution to that knowledge. The findings of this study will contribute to health policy by providing specific new knowledge and information regarding Thai CVD risk factors and the impact of the risk reduction which will assist health policy makers in the planning and future investment in prevention programs for CVD in Thailand. Moreover, it is expected that the finding from this research will establish a CVD prediction model for Thailand, and one which may be applicable and compatible to the Asia and Pacific regions.

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Terms and Definitions

1. Cardiovascular diseases (CVD)

The World Health Organization (WHO) defined CVD as a group of disorders of the heart and blood vessels which include coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism. Coronary heart disease (CHD) is the disease of the blood vessels that supplyblood to the heart muscle. Cerebrovascular disease or stroke is the disease of blood vessels supplying blood to the brain. Peripheral arterial disease is disease of blood vessels supplying blood to the arms and legs. Rheumatic heart disease is caused by streptococcus bacterial infection which results in damage of the heart muscle and heart valves from the rheumatic fever. Congenital heart disease is the malformation of the heart structure which exists at birth. (World Health Organization, Regional Office for Euroupe 2011)

2. Coronary heart disease (CHD)

CHD is a condition where there is thickening of the coronary artery wall (Lindsay and Gaw 2004). It is also known as atherosclerosis, ischemic heart disease (IHD) or coronary artery disease (CAD) (World Health Organization 2004b). Atherosclerosis is the restriction of the blood supply to the heart due to either a blood clot or blockage in the circulation system (Healey 2012). The progression of CHD which often presents in clinical practice include, angina, acute coronary syndromes (ACS), myocardial infarction, ischemic cardiomyopathy, chronic heart failure and sudden cardiac death. Patients with CHD conditions may get the initial symptom of having chest pains which may be stable or unstable angina pectoris. Then, it is likely to develop to the next state, which is called acute coronary syndrome (ACS) (Luepker et al.

2003) . ACS covers unstable angina and myocardial infarction. The symptoms are prolonged ischemic chest pains which are not relieved by rest. Myocardial infarction (commonly known as a heart attack), occurs when there is a blood flow reduction, which may lead to chronic conditions such as intracoronary thrombosis, platelet aggregation and heart attack (Thygesen et al. 2012).

3. Cerebrovascular disease or Stroke

Stroke or cerebrovascular disease is a condition that occurs when there is an interruption of blood supply to the brain which may result in neurological symptoms (Sacco et al. 2013). There are two major types of stroke which are ischemic or haemorrhagic stroke. The former occurs when there is inadequate blood supply to some part of the brain caused by an obstruction in a blood vessel to the brain, thrombosis or embolism (American stroke association 2013b). The latter occurs as a spontaneous haemorrhage into the brain which is associated with hypertension (American stroke association 2013a). Both types can lead to an acute loss of brain function and disability.

IHD and Stroke are a major concern to health policy makers in Thailand. Therefore within this thesis, the definition of CVD refers specifically to IHD and Stroke and includes all fatal and non-fatal events. It does not include dysfunction of the vascular system caused by infection or disorder of the heart at birth (such as the congestive heart failure or rheumatic heart disease.

4. Disability Adjusted Life Years (DALYs)

The sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability. One DALY refers to the one year loss of healthy life. The sum of DALYs across the population can measure the gap between the current

situation of the health status and the ideal health status in terms of the lives with free of diseases and disability (World Health Organization 2011b).

5. The years of life lost (YLL)

The years of life lost (YLL) defined as potential years of life lost due to premature deaths. It takes into account the age weight which means giving the greater weight to deaths at a younger age and the lower weight to deaths at the older age (World Health Organization 2011b).

6. The years lost due to disability (YLD)

The years lost due to disability (YLD) defined as the number of the years of living with disability which can be calculated by multiplying the number of incident cases, duration of diseases and a disability weight according to the severity of the diseases. The disability weight is scale from 0 refers to the perfect health and 1 refers to dead.

7. Age and gender

There were gender and age differences in the risk of CVD, which have to be considered in the analysis. According to the ATPIII guideline, (Expert Panel on Detection, Evaluation,and Treatment of High Blood Cholesterol in Adults 2001), it was suggested that the risk to CVD was increasing with an advancing of age. Younger adults were less likely to be susceptible to CVD, whereas older adults were more prone to having a higher risk of suffering from CVD. In addition, middle age men, (35-65 years), had a higher risk of CHD than in women of the same age group. Women in the middle age groups who had high risk factors, may experience a delay in the occurrence of CHD by approximately 10-15 years, compared to men. In this analysis, age was categorised

into 7 age groups, according to the application of the Framingham 10-years CVD risk calculation, which are 15-24, 25-34, 35-44, 45-54, 55-64, 65-74 and ≥75 years.

8. Regular smoking

The definition of smoking behaviour in this study referred to people who smoked all kinds of tobacco products which were cigarettes, hand-rolled cigarettes, pipes, cigars and non-smoked tobacco. Regular smokers were classed as people who were current smokers during the past 12 months of the NHESIV survey period and smoked every day.

9. Body mass index (BMI)

Body mass index (BMI) is the measurement of human body shape, based on weight and height. The calculation of BMI is defined as body weight (kg) divided by the square of height (m) in metric measurements. The classification of BMI levels of the Asian population is different from American and European countries. According to the world health organization's guideline in 2004 (World Health Organization 2004a) , at BMI level ≥ 23 kg/m^2 is regarded as overweight and BMI level ≥ 25 kg/m^2 is regarded as obese, in the Thai population. The BMI was categorised by the WHO definition, BMI <18.5 kg/m^2 is regarded as underweight, 18.5-<25 kg/m^2 is normal, 25-<30 kg/m^2 is overweight and ≥30 kg/m^2 is obese.

10. Lipid profiles

Participants aged 15 years and over of the 4th National Health Examination Survey (NHESIV) 2009, Thailand were asked to undertake a fasting blood test. The lipid profiles were examined for total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglyceride (TG). Dyslipidemia was identified by using the international standard cutoff points from the Third Report of the Expert Panel on

Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III, ATPIII) (Expert Panel on Detection, Evaluation,and Treatment of High Blood Cholesterol in Adults 2001). The high total cholesterol referred to people who had a total cholesterol level ≥ 200 mg/dL. The high triglyceride level referred to people who had a serum triglyceride level ≥ 150 mg/dL. The low HDL-C was classified by using the cut-point at <40mg/dL for men and <50mg/dL for women.

11. Hypertension

Hypertension was defined according to the 7th JNC guideline for high blood pressure (Chobanian et al. 2003). The definition of high blood pressure in NHESIV referred to people who currently had systolic blood pressure ≥140 mmHg or had diastolic blood pressure ≥ 90 mmHg or on medication or received treatment for high blood pressure, during the past 12 months of the NHESIV survey period.

12. Diabetes mellitus

Diabetes mellitus is defined as people who had fasting plasma glucose ≥ 126 mg/dL or those who had been told, after being diagnosed by medical doctors or health personnel, that they had DM or those who were on medication and treatment for DM during the past 2 weeks of the NHESIV survey period.

List of Abbreviations

CVD	Cardiovascular disease
CHD	Coronary Heart Disease
IHD	Ischemic heart disease
CAD	Coronary Artery Disease
ACS	Acute coronary syndrome
MI	Myocardial infarction
TIA	Transcient Ischaemic Attack
DALYs	Disability Adjusted Life Years
YLL	Year of life lost
YLD	Year of living with disability
BMI	Body Mass Index
TC	Total cholesterol
TG	Triglyceride
HDL-C	High density lipoprotein cholesterol
LDL-C	Low density lipoprotein cholesterol
SBP	Systolic Blood Pressure
NHESIV	the 4th National health examination survey
NHESO	National health examination survey office
NHSO	National health security office
HISRO	Health Insurance System Research Office
JNC-V	Fifth Joint National Committee on Hypertension
NCEP ATPII	National Cholesterol Education Program, Adult treatment Panel II

APCS	Asia Pacific Cohort Study
UCS	Universal Coverage Health Care Scheme
SSS	Social Security Health Care Scheme
CSS	Civil Servant Health Care Scheme
ICD-10^{th}	International Classification of Diseases and related health problem 10^{th} revision
WHR	Waist to hip ratio
NHMRC	The National Health and Medical Research Council

Chapter 1 : Introduction

This introductory chapter outlines the background and rationale of the study; points out the research questions, aims and objectives and the original contribution of this work; describes the terms and definitions which are used in this thesis and provides an overview of the structure of the thesis.

1.1 Origins of the study/setting the scene

Cardiovascular diseases (CVD) are viewed as a global health problem. In 2008, the World Health Organization (WHO) estimated that there were 17.3 million deaths from CVD worldwide, which were primarily attributed to CHD and strokes.
This equates to approximately 30% of all global deaths. It was also estimated that the number of CVD deaths will reach 23.3 million by 2030 (World Health Organization September,2011). It was also reported that there has been an epidemiological transition of CVD from the high income countries to low and middle income countries, where 80% of CVD were taking place (World Health Organization 2011a). Although, over the past decade, the CVD mortality rate has declined in high income countries such as the United States of America, United Kingdom and some European countries, (i.e. Sweden and Switzerland), the CVD mortality rate in northern Asia or Eurasia countries, central Asia and Africa countries such as the Russian Federation, Ukraine and Sudan have incrementally increased year on year (Levi et al. 2002, Murray and Lopez 1997, Yach et al. 2004, Ueshima et al. 2008). It is noted that the CVD mortality rate is lower in south-east Asian countries such as Thailand, Malaysia and Singapore, (Mirzaei et al. 2009).

Although the mortality rate of CVD in Thailand is lower when compared to other countries in Northern Asia and Central Asia, CVD has become the leading cause of premature death and disability in Thailand. In 2009, strokes became the leading cause

of mortality accounting for 10.4% of all deaths in men and 14.4% of all deaths in women. Ischemic heart disease (IHD) ranked third and contributed to 7.7% of all deaths in men and 8.9% of all deaths in women (International Health Policy Program 2012). CHD and strokes are now in the top 5 causes of death in both men and women in Thailand (International Health Policy Program 2012). In 2010, the Global Burden of Diseases study estimated that CVD accounts for 27% of the total deaths in Thailand (Institute for Health Metrics and Evaluation 2013). The mortality rate of CVD and diabetes together are 343 (per 100,000) in males and 280 (per 100,000) in females, (World Health Organization 2011c). The trend of IHD mortality shows a continuous increase from 1998 to 2003. The trend of stroke mortality also increased rapidly from 1998 to 2004 but declined after 2004 due to improvements in health technology and accessibility to health care services (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2010) In terms of the morbidity, the prevalence of IHD and strokes have steadily increased year on year. (Health Information System Development Office 2011)

The increased prevalence of CVD in Thailand may be due to the effect of growth in economic development over the past decade. Thailand is also currently in transition from being primarily an agricultural based culture to one of industrialisation and urbanization. The increase of CVD in Thailand has been explained in terms of changing life styles and diet, with people doing less physical activities, having a high salty, fatty food, less fruit and vegetable consumption, increased alcohol consumption, cigarette smoking and an increasing ageing population (Aekplakorn, et al. 2010).
People are also more likely to experience stress than in the past (National Statistical Office 2011), and have shifted from a healthy diet to a high-fat and low-fibre diet (Satheannoppakoa et al. 2010). As a consequence this may result in a higher body mass index, hypercholesterolemia and subsequently result in an increased risk of CVD in the

population. The results from the National Health Examination Survey (NHES) in Thailand also show that the trend of obesity in Thai adults aged 18 to 59 year old has significantly increased in both men and women from 1997 to 2004 (Aekplakorn, et al. 2010). The prevalence of hypertension was relatively stable at 21% between 2004 to 2009 due to the rising of awareness of the pharmaceutical treatments and controls for managing blood pressure. Among individuals with high blood pressure there was also an increase in obesity between 2004 and 2009 (39.1% to 47.5% in men and 53.6% to 62.9% in women) (Aekplakorn, et al. 2010). The prevalence of hypercholesterolemia has increased from 11.3% to 15.5% and the prevalence of regular smoking has increased from 20.6% to 25.3% (Chooprapawan 1996, Porapakkham and Punyaratanapundhu 2006, Aekplakorn, et al. 2010). However, the overall trend of people smoking was continuously in decline over the past decade (World Health Organization, Regional Office for South East Asia 2009, World Health Organization 2009).

A possible explanation for the increasing prevalence of IHD and strokes, but declining mortality may be due to improvements in health care services, pharmaceutical and medical technology. As a result, patients who have CVD conditions may live longer, reducing their mortality rate, whilst increasing overall morbidity. The consequence of this being that this group of patients will arguably require more health care services and rehabilitation. Moreover, new cases of CVD patients are occurring every year, which will increase the economic burden within Thailand (International Health Policy Program 2012). Additionally, it also increases the economic burden of health care costs and the loss of productivity. An update of the burden of disease and injury studied in Thailand during 2009 reported that IHD and strokes were in the top rank causes of Disability Adjusted Life Years (DALYs) lost. DALY is the summation of years of potential life lost due to premature mortality and the years of productive life lost due to

disability. One DALY refers to one year loss of healthy life (Murray and Acharya 1997). The number of DALYs lost due to strokes was 368,701 DALYs in men (6.4% of DALYs overall) and 349,859 DALYs (8.0% of DALYs) overall in women. The number of DALYs lost due to IHD was 249,610 DALYs in men (4.3% of DALYs overall) and 177,894 DALYs (4.0% of DALYs overall) in women (International Health Policy Program 2012).

The combination of the multiple risk factors to CVD is increasing. The results from the national health examination survey 2008-2009 reported that 18.8% of the Thai population (aged 15 and over) have at least 2 CVD risk factors, and 21.1% have the metabolic syndrome (Aekplakorn et al. 2011). Most modifiable risk factors such as blood pressure, body mass index, blood cholesterol and cigarette smoking can be avoided and controlled, which will ultimately reduce the risk to the individual of getting CVD.

The linkages between the multiple risk factors of CVD have been identified. For example, reducing body weight reduces blood pressure (Mulrow et al. 2008) and lowering blood sugar level is likely to reduce the level of cholesterol (Welsh et al. 2010). Therefore, arguably each primary intervention has the potential to reduce the combination of CVD risk factors. Changing modifiable risk factors is more likely lead to change risk factor profiles among the Thai population (Sritara et al. 2003). It would be reflected the probability of absolute risk of CVD of the individual and decrease the burden of CVD in the future. Modifiable risk factors have been used in CVD risk assessment equations as the predictors for calculating the probability of getting CVD. The risk functions and risk scores such as the Framingham's equation, QRISK2 and SCORE, have been recommended as guidelines for the individual risk assessment, to identify the high-risk groups in the populations and provide suitable interventions for

the target population (National Vascular Disease Prevention Alliance 2009, National Institute for Health and Clinical Excellence 2008).

To reduce the risk of CVD, the Ministry of Public Health in Thailand has implemented a number of primary CVD prevention strategies within the last decade (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2010). These strategies include: the comprehensive tobacco programs, smoking regulation, dietary programs to reduce obesity, and early diagnosis of hypertension, diabetes and hypercholesterolemia. These strategies are being specifically implemented to address the future potential economic burden of increasing CVD. However, the economic impact of reducing multiple risk factors, at a population level in Thailand, in terms of health care costs is unclear (Teerawattananon, Russell and Mugford 2007).

In order to plan for investment in public health interventions within finite resources, it is imperative that decision makers have sufficient information to identify the target populations and risk reduction strategies, and to assess the impact of these strategies on the population. As a result of the above, the following factors need to be considered. Whether a primary intervention should be implemented to reduce the burden of CVD? What is the future trend of the CVD prevalence and burden in Thailand? What are the savings from the impacts on the number of hospitalisations, from CVD? How much benefit is gained from saving DALYs in the population? And, How much health care cost savings can be achieved as a direct result of the risk reduction strategies?

1.2 Rationale of the Study

There were a number of reasons for undertaking this study. Firstly, as indicated above, CVD is significant health problem in Thailand. There continues to be a year on

year increase in the prevalence of CVD, an increased number of hospitalisations, an increase in the number of patients who are living with disability and an increase in the associated long term health care. The impact of this is an increase in the government health care burden and spending. The Thai government spent approximately $36.5 million on inpatient health care in 2007 with 21% of this budget being spent on non-communicable diseases and injury and 10% on CVD (Garg and Evans 2011). Additionally, the loss due to premature death and disabilities have a direct impact on the individual's finances, productivity- and wellbeing.

Secondly, there are a limited number of studies that focus specifically on estimating the future prevalence of CVD in the population and the impact of reducing the CVD risk factors in Thailand. Previous studies have been conducted in several countries using the health economic modelling technique to estimate the prevalence of CVD, for example, the CHD policy model in the US-population and China (Weinstein et al. 1987), the CVD policy model in Australia (Mui 1999), the POHEM model in Canada (Statistic Canada 2010) and the IMPACT model in England (Unal, Critchley and Capewell 2005). However, to the best of my knowledge, there are no studies that have specifically focused on the development of the mathematic model for estimating the future situation of CVD in Thailand. Furthermore, few studies have been conducted in Thailand that have explored the impact of prevention interventions in this specific population. For example, the cost-effectiveness analysis of the pharmaceutical interventions to prevent an occurrence of CVD (Khonputsa et al. 2012) or the randomisation control trial for reducing the salt intake, (Aung et al. 2012) are examples of the studies on the impact and effectiveness of CVD interventions. Although it is well known that reducing CVD risk factors can prevent an occurrence of CVD in each individual, little is known regarding the impact in terms of the health care costs and DALYs avoidable at a population level in Thailand.

1.3 Research Questions

The research sets out to address the following questions:

- How will the prevalence of CVD develop in Thailand over the next 5 -10 years if the health system continues as it is?
- How much could the cost of hospital admissions and the number of DALYs from CVD be reduced, if the major multiple population risk factors, such as hypertension, obesity, diabetes, hypercholesterolemia and regular smoking were reduced through investment in public health initiatives?

1.3.1 Aims and Objectives

This study aims to estimate the future prevalence of CVD in Thailand over the next 5 – 10 years and the potential economic and health benefits of strategies to reduce the population risk factors during this period.

1.3.2 Research Objectives

1) To obtain a mathematical model that can be applied for estimating the future prevalence of CVD in Thailand if the health system remains as it is.
2) To estimate the potential reduction in the cost of hospital admissions and the number of hospital admission avoided, if the population level risk factors such as body mass index, smoking, hypertension and high cholesterol levels can be reduced or contained.
3) To estimate the potential DALYs from CVD which could be avoided if the population level risk factors such as body mass index, smoking, hypertension and high cholesterol levels can be reduced or contained.

1.4 Original contribution

As previously highlighted, no studies currently exist that focus specifically on the development of a mathematic model for estimating the future situation of CVD in Thailand. Therefore, this study represents an original contribution to that knowledge. This study will develop a decision model for predicting the impact of risk reduction strategies for CVD in the Thai population. This will be developed by applying the appropriate risk assessment equations which are specifically focused on the Thai population and will enhance the capability of the model to estimate the impact of the risk reduction strategies, not only for the health care costs but also the burden of diseases in terms of DALYs. The findings of this study will contribute to health policy by providing specific new knowledge and information regarding Thai CVD risk factors and the impact of the risk reduction which will assist health policy makers in the planning and future investment in prevention programs for CVD in Thailand. Moreover, it is expected that the finding from this research will establish a CVD prediction model for Thailand, and one which may be applicable and compatible to the Asia and Pacific regions.

1.5 The structure of the thesis

This thesis comprises 8 chapters:

Chapter 1: The introduction provides the background information and context of CVD in Thailand and the rationale for the research study. The research questions and research objectives are outlined in the structure of the thesis.

Chapter 2: The literature review provides a critical review of the literature used to derive the evidence for developing a CVD mathematic model. The literature review included 1) The natural history of CVD and epidemiology, 2) The risk assessment

equation for CVD, 3) The health economic modelling for CVD, 4) The Disability Adjuted Life Years and 5) The public health risk reduction strategies for CVD.

Chapter 3: Method; this chapter will describe the detailed design and methodology for the study. This will include stages of developing of the mathematic model. It will outline the study population, data requirement and data sources, data analysis, outcomes of interests in each stages. The data collection process, data management procedure and the ethical considerations will be described in this chapter.

The results will be presented from chapter 4 to chapter 7.

Chapter 4: Risk factors for CVD in Thailand. This chapter will outline and describe the results from the descriptive analysis of the 4th Thailand National Health Examination Survey (NHESIV) 2009 dataset, which has been used as the baseline data to simulate the model. All coronary risk factors which were included in the CVD model will be analysed for the distribution and the association with CHD and strokes.

Chapter 5: Application of CVD risk assessment equations to the Thai population. This chapter will present the results of the 8 to 10 years CVD probability when applied to the 3 difference equations such as the APCS equation, the Framingham-Asia equation and the original-Framingham equation. Then, the estimated number of CVD events and the validation of the CVD modelling will also be presented.

Chapter 6: Cost of hospitalisation for CVD patients in Thailand. This chapter will present the 10-years estimated outcomes of the cost of hospitalization in terms of both direct health care costs and indirect costs and the long term care or rehabilitation for the CVD patients.

Chapter 7: Impact of reducing risk factors for CVD in Thailand. This chapter will demonstrate the finding from the CVD modelling by comparing the "target risk

reduction scenario" against "without risk reduction scenario". The estimation of the disability adjusted life year (DALY) and the estimated burden of CVD in Thailand over a 8 year period will be presented. The expected outcomes will be presented in terms of the number of hospitalisation cost savings, number of hospital admission avoided, DALY savings and health care cost savings.

Chapter 8: Conclusion and Recommendations. This chapter discusses the finding arising from the study and examines the comparison to previous studies. The results will be discussed by using the conceptual link of the theoretical contribution to the published literature and knowledge to the area. It will also provide the methodological critique, the strength and limitation of the CVD model and the potential impact of this study on policy and practice. This chapter will also summarise the research and provide recommendations for further research and provide recommendations for public health policy and practice in Thailand.

Chapter 2 : Literature Review

2.1 Introduction

This chapter presents the literature review which is explored in five sections to achieve the research aims and objectives and address the research questions. The first section is the natural history of CVD and epidemiology. This section provides an overview of CVD, the global burden of diseases and trend of the mortality and morbidity of CVD in Thailand and compares this to the global epidemiological trend. The second section is the risk assessment equations for CVD. This provides a review of the CVD risk prediction equations and algorithms. Those CVD risk calculations have been derived from a number of cohort studies such as the Framingham's equation, QRISK, Asia pacific collaboration cohort studies etc. The third section reviews the health economic evaluation techniques and the health economic decision modelling. The most common three types of modelling techniques which have been used in the health economic studies, the decision tree model, Markov's model and the discrete event simulation model (DES), as well as the other types of model will also be discussed. Specifically, this section will explore the benefits and limitations of each model, as well as reviewing the previous studies of the CVD modelling in the health economic aspects. The fourth section provides a theoretical review of the concept of the summary measurement of population health and DALYs, which are the indicators that are used to present the burden of diseases. The final section presents the review of the public health risk reduction strategies for CVD and the target risk reduction strategies, which focus on the primary prevention interventions for the general population in Thailand. The literature search strategies are provided in the appendix A.

2.2 Natural history of CVD and Epidemiology

2.2.1 Natural history of CVD

This section reviews the natural history of CVD, the definition and the progression of disease. The World Health Organisation (WHO) defined CVD as a group of disorders of the heart and blood vessels, which include CHD, strokes, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis and pulmonary embolism (World Health Organization, Regional Office for Euroupe 2011). This review focuses on the natural history and the progression CHD and strokes, which are the major causes of death and disability among the Thai population. In general, most people have no sign or symptoms of CVD until they have a heart attack or stroke. Heart attacks or strokes occur in people who have an underlying condition affecting the blood vessels such as a blockage on the inner wall of a blood vessel, which blocks the flow of blood to the heart or brain. However, strokes can be caused by blood clots or rupturing of blood vessels in the brain.

2.2.1.1 Coronary heart disease (CHD)

Coronary heart disease (CHD) is a condition where there is thickening of the coronary artery wall (Lindsay and Gaw 2004). It is also known as atherosclerosis, ischemic heart disease (IHD) or coronary artery disease (CAD) (World Health Organization 2004b). Atherosclerosis is the restriction of the blood supply to the heart due to either a blood clot or blockage in the circulation system (Healey 2012). The progression of CHD which often presents in clinical practice include, angina, acute coronary syndromes (ACS), myocardial infarction, ischemic cardiomyopathy, chronic heart failure and sudden cardiac death. Patients with CHD conditions may get the initial symptom of having chest pains which may be stable or unstable angina pectoris. Then, it is likely to develop to the next state, which is called acute coronary syndrome (ACS)

(Luepker et al. 2003) . ACS covers unstable angina and myocardial infarction. The symptoms are prolonged ischemic chest pains which are not relieved by rest. Myocardial infarction (commonly known as a heart attack), occurs when there is a blood flow reduction, which may lead to chronic conditions such as intracoronary thrombosis, platelet aggregation and heart attack (Thygesen et al. 2012). The initial common symptoms of a myocardial infarction are central chest pains or the feeling of discomfort in the chest, arms, left shoulder, elbows, jaw or back. The person having a heart attack may experience difficulty in breathing, nausea or vomiting. This may then result in heart failure or sudden death. Individuals who get CHD conditions can move from one event to another event because there are different endpoints for the CHD developing process. It is important to consider that these events are interrelated to each other (Lindsay and Gaw 2004)

2.2.1.2 Stroke

Stroke or cerebrovascular disease is a condition that occurs when there is an interruption of blood supply to the brain which may result in neurological symptoms (Sacco et al. 2013). There are two major types of stroke which are ischemic or haemorrhagic stroke. The former occurs when there is inadequate blood supply to some part of the brain caused by an obstruction in a blood vessel to the brain, thrombosis or embolism (American stroke association 2013b). The latter occurs as a spontaneous haemorrhage into the brain which is associated with hypertension (American stroke association 2013a). Both types can lead to an acute loss of brain function and disability. The signs and symptoms of a stroke are weakness of the face muscles, arms and/or legs on either side of the body (World Health Organization 2004b). Depending on the region within the brain that the stroke occurs, the person with may have difficulties such as limitations in movement, loss of speech, loss of sensation and visual field defect (Sacco et al. 2013) .The symptoms may last for more than 24 hours or lead to death. However,

if the duration of the symptoms last for less than 24 hours, it is often referred to as a Transient Ischemic Attack (TIA) (Lindsay and Gaw 2004, Sorensen and Ay 2011) .

2.2.2 The global epidemiology and burden of CVD

This section provides a background and overview of the epidemiology and the global burden of CVD. The aims of the review are to address the global CVD epidemic and to address the specific CVD epidemic in Thailand. The review covers the incidence, prevalence, mortality, morbidity, trends and current situation, and the burden of CVD and disabilities globally and compares this to the situation of CVD in Thailand.

CVD is the leading cause of mortality around the world. WHO estimated that approximately 23.6 million people will die from heart diseases and strokes by 2030 (World Health Organization September, 2011). There was an epidemiological transition from the developed countries to the developing countries. According to the global age standardized mortality rate from CVD in 2004, the mortality rate increased in the low and middle-income countries, which are higher than in the high-income countries. It is estimated that the morbidity will increase in the Eastern Mediterranean region and mortality will rise in the South-East Asia region (Yach et al. 2004, Lopez et al. 2006, Gaziano et al. 2010).

The trend of CVD mortality has been different across geographical continents and ethnicity (Yusuf et al. 2001a). For example, CVD was considered as leading cause of death in USA over 50 years ago(Roger et al. 2012). However, the trend of CHD mortality in USA has continuously declined since this period, with a slower rate than from 1970 -1990. The stroke mortality has been decreasing slightly since 1990. The CHD mortality was respectively high in the black, non-Hispanic white and Hispanic population while the stroke mortality was high in black, non-Hispanic white and Asian race.

The trend of CVD mortality in the European countries has varied across regions (Levi et al. 2002). Western Europe had a similar trend of CHD mortality as in the USA with a rapid increase during 1965-1975 but then with a dramatic decline after 1975. The stroke mortality has also declined by more than 55% in both men and women during 1965-1975. In Eastern Europe such as Poland and the Czech Republic, both CHD and stroke mortality increased up to the early 1990s and then declined over a few years. Conversely, the mortality of CHD and CVD in the Russian republic has reached the highest rate worldwide (Levi et al. 2002). Stroke was a predominant cause of mortality over CHD in Asian countries. The trend of stroke mortality in Japan, South Korea and China was similar to that in the western countries (Ueshima et al. 2008).

CVD epidemiological patterns vary across geographical regions and continents (World Health Organization 2011a). Mirzaei (2009) examined CHD mortality data from 1950 to 2000 and reported trends of CHD mortality that were found to be different across continents, with three natural history patterns of CHD being suggested (Mirzaei et al. 2009). Firstly, the classic epidemic pattern which showed the rise and fall of CHD mortality. This pattern was found in many high income or developed countries such as Canada, United Stated, Australia, United Kingdom and the Scandinavian countries. A similar pattern was also found in many countries which have a lower case mortality rate such as western European countries, some South American countries such as Argentina, Brazil, Chile and some Asia countries such as Singapore, Japan and Hong Kong. Secondly, the rising pattern or the beginning of the CHD epidemic, which has been found in some countries in Central Asia such as the Russian Republic, Ukraine, Belarus, and Uzbekistan and some Asian countries such as urban China and Sri Lanka as well as Mexico in Central America. Thirdly, the "Flat" pattern or stable epidemic, which has been found in South Korea, rural China, Peru and Thailand.

The trend of stroke mortality of the population between the ages of 35 to 74 years was analysed in 48 countries worldwide, from 1950 to 2005 (Mirzaei et al. 2012). The highest mortality rates of stroke were in Japan, the Russian Republic and Bulgaria. On the other hand, the lowest mortality rates of stroke were in Canada and Australia. The mortality patterns for stroke were reported in "decline only", "rise and fall", "rise only" and "flat". The countries with the decline pattern in stroke mortality trends were the USA, Canada, the UK, Sweden, Denmark, Finland, Italy, Australia, and in Hong Kong. The rise and fall pattern was found in Japan, Portugal and in Eastern Europe. The rising pattern in the 20th century was in Kyrgyzstan, Kazakhstan and Armenia. The flat patterns were in Mexico, Cuba, El Salvador, Egypt, Kuwait, Peru and Thailand. The epidemiological characteristic of the stroke incidence and case fatality has also been reviewed and the pooled data analysed in 56 population-based studies from 1970 to 2008 (Feigin et al. 2009). This study reported that over four decades, the stroke incidence decreased by 42% in high-income countries, whereas, there was over a 100% increase in low to middle income countries. During 2000-2008, the stroke incidence rate continuously increased in the low to middle income countries. This was significant, as it was the first time that incidence of stroke, in low to middle income countries, had become as high as those in the high-income countries (Feigin et al. 2009).

Considering the epidemiological pattern above, most developing countries (such as in Africa, urban India, Latin America and some Asian countries) are in a stage of double burden, which includes both infectious disease and a chronic disease burden. Whilst on the other hand, many developed countries (such as in Western Europe, North America, Australia and New Zealand) are shifting to the next stage, which is the prevention and treatment for the CHDs and strokes, which is advancing the pharmaceutical and medical technology as well as enhancing the primary prevention programs. People in low and middle income countries are more exposed to CVD risk

factors but less likely to have access to adequate health care services than those who live in the high income countries. As a result, the death rates from CVD in these developed countries are decreasing and the life expectancy in the population is increasing, whilst in the developing countries both death rates and prevalence of CVD are increasing and the average life expectancy is also increasing but is still lower than that of developed countries (Yusuf et al. 2001a).

2.2.3 Epidemiology and burden of CVD in Thailand

Thailand is situated in the South East Asia region and has five geographical regions; north, central, north-east, south and Bangkok. The population in Thailand is approximately 63.9 million of which 23.1 million live in urban areas (inside municipalities), and 40.8 million live in rural areas (outside municipalities). The life expectancy at birth is 71 years in men and 77 years in women. However, when estimating healthy adjusted life years (HALE) or the years of living without any health problems or disability, the healthy life expectancy in Thailand was 65 years in men and 71 years in women (International Health Policy Program 2012).

The non-communicable diseases (NCDs) such as CVD, cancer, chronic respiratory disease and diabetes are a major concern in Thailand (Kaufman et al. 2011). In 2005, stroke was the number one cause of death accounting for 9.4% of all deaths in the male population and 11.3% of all deaths in the female population. CHD was the fourth most common cause of death in the male population (6.1%) and the third most common cause of death in the female population (7.5%) (Porapakkham 2009).

Recently, the burden of disease and injury in Thailand in 2009, (International Health Policy Program 2009), reported that the number of DALYs was calculated by combining the years of life lost due to premature death and the years of living with a disability. The number of DALYs lost due to stroke was 368,701 DALYs in men (6.4%

of DALYs overall) and 349,859 DALYs (8.0% of DALYs) overall in women. The number of DALYs lost due to IHD was 249,610 DALYs in men (4.3% of DALYs overall) and 177,894 DALYs (4.0% of DALYs overall) in women (International Health Policy Program 2012). shows the top 10 rankings of the number of DALYs lost in Thailand in 2009.

Table 2.1 The Ranking of the DALYs in Thailand 2009 by gender (International Health Policy Program 2012)

Rank	Male			Female		
	Diseases	**DALYs (x 1000)**	**%**	**Diseases**	**DALYs (x 1000)**	**%**
1	Alcohol addict	506	8.7	Diabetes mellitus	380	8.6
2	Road traffic injury	501	8.6	Stroke	350	8.0
3	Stroke	369	6.4	Depression	236	5.4
4	HIV/AIDS	282	4.9	Ischemic heart disease (IHD)	178	4.0
5	Liver Cancer	262	4.5	HIV/AIDS	160	3.6
6	Ischemic heart disease (IHD)	250	4.3	Cataract	154	3.5
7	Diabetes mellitus	218	3.8	Osteoarthritis	138	3.1
8	Chronic obstruction pulmonary disease (COPD)	206	3.5	Road traffic injury	129	2.9
9	Cirrhosis	176	3.0	Anaemia	117	2.7
10	Lung cancer	133	2.3	Liver cancer	114	2.6

Although CVD mortality trends in Thailand have had a slower decrease from 63.3 (per 100,000) in 2004 to 56.0 (per 100,000) in 2008, the inpatients hospitalization rate of CVD has steadily tripled from 614.3 (per 100,000) in 1999 to 1927.0

(per 100,000) in 2008 (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2010).

In terms of CVD trends, the mortality rate increased during 1998-2008. Geographical regional differences were also identified within Thailand, with Bangkok having the highest mortality rate from ischemic heart disease (IHD) and stroke. The current trend for IHD shows an increase in mortality from 1998, reaching an accelerated peak in 2003 and showing a continuing but slower increase up to 2008. (Figure **2.1**)

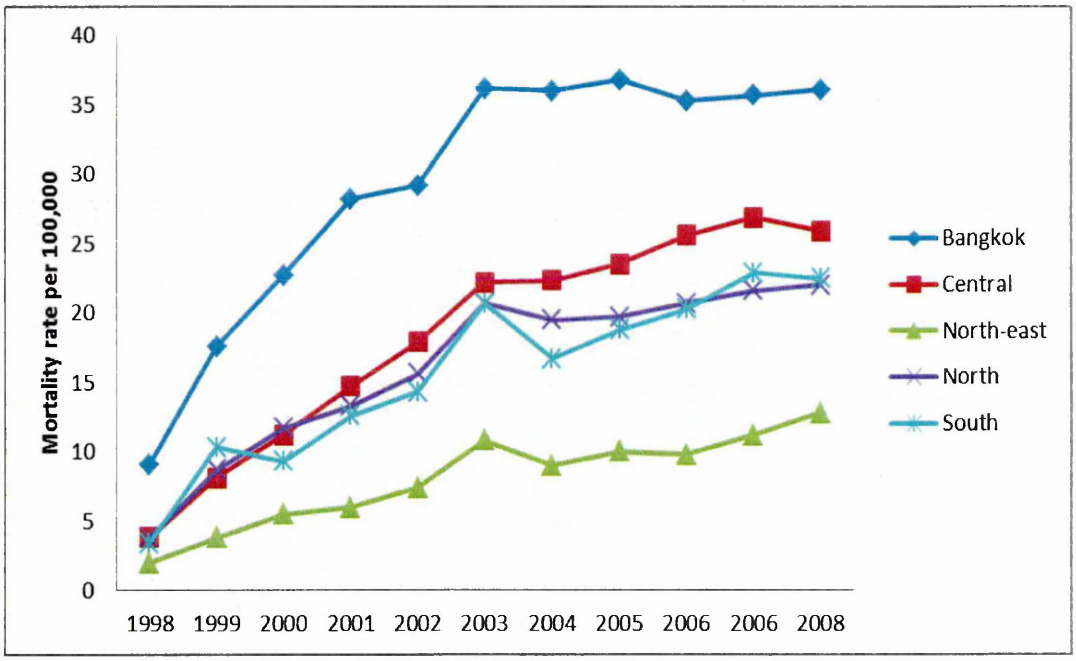


Figure 2.1 Mortality rate (per 100,000 populations) from ischemic heart disease by geographical regions in Thailand 1998-2008 (Health Information System Development Office 2011).

In addition, the trend of the mortality rate from stroke is different from the IHD mortality (Bureau of Non-Communicable Disease, Department of Disease Control,Ministry of Public health 2010). There was a dramatically increase in the stroke death rate from 1998 to 2004. Then, it rapidly decreased from 2004 to 2006. After 2006,

the stroke mortality has remained constant but is still at a higher level than in the past decade. The highest mortality rate was found in Bangkok when compared to other regions and the lowest death rate was found in north eastern Thailand. (Figure **2.2**)

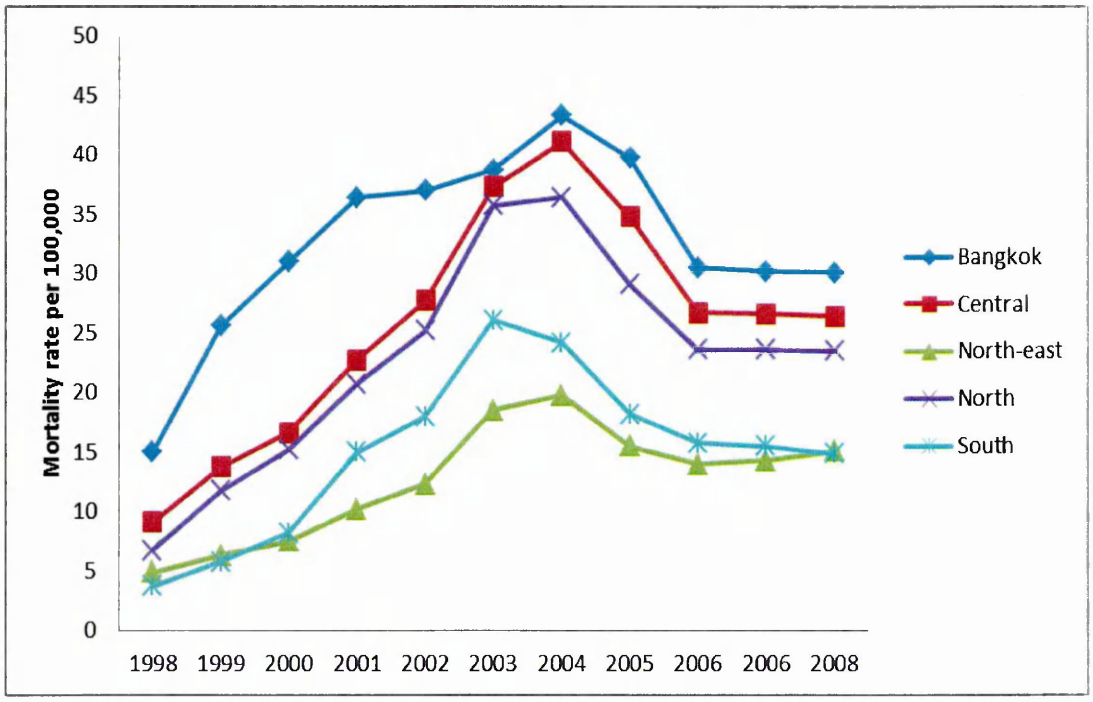


Figure 2.2 Mortality rate, (per 100,000 population) from stroke by region in Thailand 1998 – 2008, (Health Information System Development Office 2011).

The Thailand National Health Security Office (2010) recently reported that the hospital admission rate from CVD has dramatically increased. The rates of hospital admissions from IHD and stroke have increased three fold since 1992 (National Health Security office 2010). An increased number of patients to hospital has also resulted in an increase in the demand for treatment and medication in hospitals and an increase in the number of the patients receiving heart surgery through the Universal Coverage Scheme, which is a free national health care insurance scheme, from 21,162 (4.8%) in 2004 to 32,233 (5.99%) in 2009. Figure **2.3** demonstrates the rate of hospital admissions from stroke and IHD.

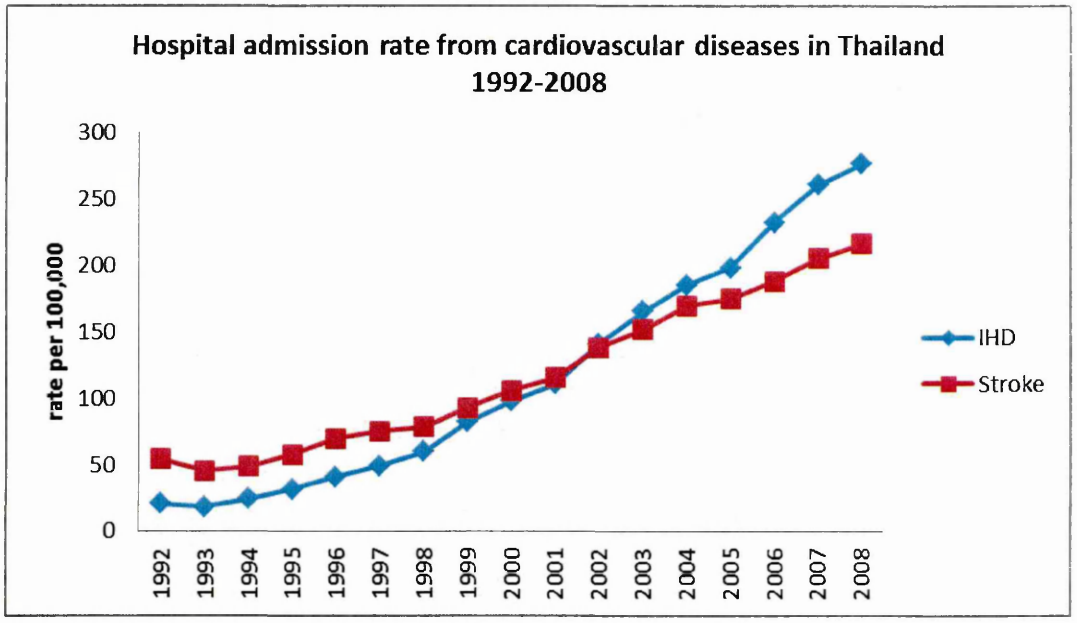


Figure 2.3 Inpatient admission rates from CVD in Thailand 1992-2008 (Bureau of Non-Communicable Disease,Department of Disease Control, Ministry of Public health 2010)

In terms of the incidence of CVD in Thailand, the chronic diseases surveillance system has been established since 2003 by the Bureau of Non-Communicable Disease (Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health 2012). This surveillance system was set up mainly for the public health care providers, such as the central hospitals, general hospitals and community hospitals, to report new cases from the non-communicable diseases (such as diabetes mellitus, hypertension, ischemic heart disease, stroke and chronic obstruction pulmonary disease), through the Ministry of Public Health. The incidence of IHD and stroke were recently reported in 2010. The incidence rate of hypertension was 566.17 per 100,000 population (360,658 cases), IHD was 59.93 per 100,000 population (38,176 cases) and stroke was 50.56 per 100,000 population (32,210 cases). The trends of the incidence rate of IHD and stroke from 2006 to 2010 showed that there was an increase in the incidence of cases during 2006 to 2009 but it slightly decreased in 2010. However, the prevalence of IHD and

stroke overall was continuously increasing (Bureau of Epidemiology, Department of Disease Control, Ministry of Public Health 2012).

2.2.4 The modifiable risk factor for CVD

Over the last decade, there has been an increase in mortality and morbidity globally which is related to the traditional risk factors. These risk factors are relating to globalisation, industrialisation and ageing populations (Yusuf et al. 2001b). Aside from the genetic factors such as age and gender, the modifiable risk factors have been confirmed. Common potential risk factors were hypercholesterolemia, hypertension, cigarette smoking, which can be long term predictors for CVD regardless of ethnicity or gender.

The following studies have confirmed the association between those multiple risk factors and CVD. The INTERHEART study was a case-controlled study of acute myocardial infarction in 52 countries across the world. This study found nine modifiable risk factors as being significantly associated with MI in both men and women (Yusuf et al. 2004). Risk factors identified included smoking, hypertension, diabetes, obesity, blood lipids, exercise, alcohol consumption, fruit and vegetable consumption and psychosocial factors (Yusuf et al. 2004).

More recently, a meta-analysis of 18 cohorts of the black and white population in the USA to identify the lifetime risk of CVD was undertaken (Berry et al. 2012). The cohorts were measured for the CVD risk factors every ten years at the ages of 45, 55, 65 and 75 years. The participants were stratified by blood pressure, cholesterol level, smoking status and diabetes status. The life time risk to CVD was calculated in terms of free from CVD conditions, fatal and non-fatal CVD. The finding from this study emphasized that the traditional risk factors continued to have the most influential effect on the lifetime risk of CVD. For example, participants aged 55 years with a low CVD

risk profile (total cholesterol <180mg/dL, blood pressure below 120/80 mmHg, non-smokers and non-diabetes) have a relatively lower risk of death from CVD than participants who had two or more major CVD risk factors. Overall, the mortality from CVD in the low risk groups was 4.7% in men and 6.4% in women, while the mortality from CVD in participants with more than two risk factors was 29.6 % of men and 20.5% of women. A low risk group also had approximately 10 times lower lifetime risks of death from CHD, MI or stroke. These findings were also consistent when comparing different ethnicity cohorts.

A large multinational cohort study (WHO-MONICA project) (Evans et al. 2001, Kuulasmaa et al. 2000), found that over a ten year period (1980 - 1990) the coronary event rate had declined by 17% largely due to changes in risk factors (i.e. decreased blood pressure and serum cholesterols and increased BMI). Overall, trends of smoking rates decreased in males but increased in women. The trend of systolic blood pressure declined in both genders. There was a slight decrease in the trend of serum cholesterol levels, which had a significant effect on the risk of CVD. Conversely, BMI had increased in both genders. However, the change in the trends of CHD was partly associated with the change in the classical risk factors. This might be explained due to the time lag, the complexities in the relation between the changes in risk factors and event rates and the heterogeneity across populations (Kuulasmaa et al. 2000). In addition, there were strong negative correlations between regular smoking and high cholesterol in males and strong negative relation in regular smoking and high blood pressure.

In terms of the association between mortality and the risk factors, high blood pressure has the largest correlation of the risk factors with all the mortality measures, except for stroke mortality in males. High cholesterol has a strong negative association

with the stroke mortality in females (The World Health Organisation MONICA project 1994). A small change in the overall risk scores was found. There was a heterogeneity in stoke events across the populations. The changing of systolic blood pressure associated with stroke events only occurred in women. However, the combination risk factors score found a small association with the change in stroke events (Tolonen et al. 2002).

The trend of CVD risk factors such as total cholesterol, BMI, SBP has also changed globally. The worldwide trend of total cholesterol has changed less than 0.1 mmol/L per decade in both genders (Farzadfar, et al. 2011). There has been a decrease in the mean of total cholesterol (mmol/L) in high-income regions such as Australasia, North America and Western Europe. However, the mean total cholesterol has slightly increased 0.08-0.09 mmol/L per decade in East and South-East Asia and Pacific (Farzadfar, et al. 2011). Trends of Body Mass Index (BMI) have also increased globally 0.4-0.5 kg/m^2 per decade from 1980 to 2008. The highest mean BMI was in some Oceania countries (Nauru and Cook Islands), reaching 33.9 kg/m^2 in men and 35.0 kg/m^2 in women. The mean BMI has also increased in sub-Saharan Africa, and East, South and Southeast Asian countries (Finucane et al. 2011).

The age-standardized mean systolic blood pressure (SBP) has decreased by 0.8 mm Hg per decade in men and 1.0 mm Hg per decade in women. The trends of SBP have increased in both genders in Oceania, East Africa, South and Southeast Asia. However, in developed countries such as Australasia, North America and Western Europe, there has been a decrease (Danaei, et al. 2011).

2.2.5 CVD risk factors in Thailand

The increase of CVD in Thailand has been explained in terms of changing life styles and diet, with people doing less physical activities, having a high salty, fatty food, less fruit and vegetable consumption, increased alcohol consumption, cigarette smoking and an increasing ageing population (Aekplakorn, et al. 2010). The estimation from a population projection study (UNFPA Thailand October,2006) reported that the proportion of elderly people (defined as people who age 60 years and over) in the population will increase to nearly 30% of the total population by 2050 and therefore it will increase the target population of CVD in the future.

The National Health Examination Survey (NHES) in Thailand 1992 to 2004 has also demonstrated an increase in CVD risk factors and an increase in the prevalence of hypertension from 5.4% to 22.0%, hypercholesterolemia 11.3% to 15.5%, diabetes 2.3% to 6.6% and regular smoking 20.6% to 25.3% respectively (Chooprapawan 1996, Aekplakorn, et al. 2010). A survey from the National Statistical Office (National Statistical Office 2008, World Health Organization, Regional Office for South East Asia 2009) has identified the continuous decreasing trend of cigarette smoking during the past 16 years due to the smoking ban policy. Recently, the global tobacco adults survey (GATS) (World Health Organization, Regional Office for South East Asia 2009) in Thailand 2008 revealed that 15% of the overall Thai population has smoked manufactured cigarettes (29.6% men and 1.6% women), with more young adults engaging in smoking practices. Recently, the result from the 4th National Health Examination Survey (NHESIV) (Aekplakorn, et al. 2010) found that 27.2% of the Thai population had at least 2 CVD risk factors, which increased in women from 21.3% in 2004 to 25.2% in 2009, but remained the same 29.0% in men. Trends of obesity in the Thai population aged between 18– 59 increased from 1997 to 2004, with a significant increase in women. Perhaps, with the changing in life style, women are less likely to do

exercise and have increasingly unhealthy diets. Men residing in urban areas were more likely to become obese, whereas women residing in rural areas were less likely to have class II obesity than women residing in urban areas. In addition, men with a high educational level were more likely to be clinically obese. There was a converse relationship in women, where lower educational levels displayed a likelihood of becoming obese (Aekplakorn et al. 2007).

The cardiovascular risk factors also varied across administrative areas and regions. The International Collaborative Study of CVD in Asia (Inter-ASIA Collaborative Group 2003) was a complex cross-sectional study, which was conducted to estimate the CVD risk factors in the adult population in Thailand during the year 2000. The mean level of CVD risk factors was analysed and the sampling weight was applied to estimate the Thai population. It was found that the CVD risk factors in Thailand were high. When comparing the CVD risk factors in urban and rural area, smoking was higher in rural areas than other CVD risk factors. The mean level of blood pressure, total cholesterol, BMI, fasting plasma glucose and diabetes in urban areas were higher than in rural areas. However, the prevalence of high risk factor levels was in rural areas. The results from the Inter-ASIA study in 2000 suggested that the highest mortality rate of CVD was in Bangkok and the Central region. This might be the effect of the variation of CVD risk factors and health behaviour across five regions in Thailand. When comparing the risk factors across regions, it was found that Bangkok and the Central region had a higher prevalence of hypertension, high BMI, abdominal obesity, high LDL-c and diabetes mellitus, than the other regions. The highest prevalence of smoking and high triglyceride was in North Eastern region (Chongsuvivatwong et al. 2010). The association between the adiposity and serum glucose level was investigated in the Inter-ASIA study, in Thai adults who were aged 35 years and over. The adiposity was measured by using the waist circumference and the

distribution of fat was measured by using the waist to hip ratio (WHR). An increase in the plasma glucose was a linear association with the increasing of body weight, BMI, waist circumference and WHR. The waist circumference and WHR showed more relationship with plasma glucose and diabetes status, than body weight or BMI. This finding suggested that measuring the abdominal obesity may be more suitable for the Asia population, than BMI (Stolk et al. 2005).

In terms of the association of the risk factors, to date, only one CVD cohort study has been undertaken in Thailand (Sritara et al. 2003). This study followed up 3,499 adults aged 35- 54 years, who worked at the Electricity Generation Authority in Thailand (EGAT) from 1985 to 1997. There were 46 deaths from CVD during the 12 year follow-up period. This was significantly related to age, systolic and diastolic blood pressure, smoking status, diabetes, male gender and total cholesterol. The association between CVD mortality and serum lipid profile was explored after 17 years of follow-up. There was a significant association between HDL-C and CVD in this cohort (Sritara et al. 2008). Arguably the EGAT employees were not representative of the Thai population, i.e. most were middle-class, living in urban areas, well educated, and with only 23% of the participants being female. Another study in this cohort (Khonputsa et al. 2010) reported that an increase of 1 mmol/l in total cholesterol was associated with a fivefold increase in ischemic heart disease risk in adults aged 30-44 years but no significant association with stroke. The increase of 10 mmHg of blood pressure was associated with increasing the risk of ischemic heart disease and stroke, which the relative risk (RR) 1.31 and 1.46 respectively in this cohort.

2.2.6 Summary

In summary, when comparing the overall trend of CVD in Thailand with the global trend, although it appears that Thailand is considered as being low-risk in terms of CVD with the flat trend of prevalence compared to other high-income countries such as UK and USA the trend of CVD morbidity is rising continuously while the mortality rate is also steadily increasing. Overall the global trend of CVD risk factors are increasing in terms of body mass index, serum cholesterol and blood pressure is declining. Trends for cigarette smoking vary by country and gender. Comparing this with Thailand, there is an increase within the population in obesity, hypertension and hypercholesterolemia whilst the trend of cigarette smoking is in decline. However, the prevalence of CVD is increasing overall as a result from the changes in the modifiable risk factors.

2.3 The risk assessment equations for CVD

In the past decade, CVD risk assessment equations have been developed as a tool to estimate the risk of individuals developing CVD conditions, such as MI, CHD and stroke. The risk assessment tools assist in identifying the target population and target intervention, which is necessary for the policy implementation for planning the primary prevention program. Many cardiovascular risk assessments are derived from cohort studies, which follow up people who are initially free from CVD for a long period of time, until they experience the cardiovascular conditions. Most prediction equations are derived from statistical regression models, such as the Cox proportional hazard model, Weibull model and the multiple logistic regressions. Then, the prediction algorithm examines the effectiveness in terms of calibration and discrimination in identifying potential casualties. The calibration of models refers to the accuracy of the algorithm when comparing the number of the observed instances of CVD, to the

expected (Cui 2009). Discrimination refers to the capability of the algorithm to identify the target population who will contract a disease or who will be free from disease.

The advantage of using the risk assessment equation was the combination of the CVD risk factors. The set of factors that relate to CVD was included in the algorithm, which provides a better prediction than only considering a single risk factor. The concept of CVD risk prediction has been used in the clinical setting to calculate the absolute risk of the individual and raise the awareness of the 'high risk' group, to control or reduce the risk of CVD. The most classical risk prediction equation was derived from the Framingham heart study (Framingham Heart Study 2011), which has been used widely around the world and is recommended to be used as the standard risk assessment for the CVD in many countries, such as United States, Australia and New Zealand (Eichler et al. 2007). For example, the ACCF/AHA guidelines for the assessment of cardiovascular risk in the United States, recommended the use of Framingham's equation or another similar type of multivariate risk score, based on the classical CVD risk factors, for assessing the risk of CVD in all asymptomatic adults (Writing Committee members 2010). The National Health and Medical Research Council (NHMRC), in Australia, reviewed the guidelines for the assessment of absolute CVD risk, which mainly uses the risk calculation from the Framingham study, to identify the level of CVD risk to low, moderate or high risk groups (National Vascular Disease Prevention Alliance 2009). The CVD risk assessment equations and risk score has been developed in many studies in order to estimate the total CVD risk in the asymptomatic people. Those equations were derived from the follow-up studies in the different setting.

The modified Framingham equation (Anderson et al. 1991), has also been recommended to be incorporated as the risk assessment for primary prevention, by the

National Institute for Health and Clinical Excellence (NICE) in the UK. The recommendation has been changed to select the risk assessment algorithm most suitable to the population in 2010 (National Institute for Health and Clinical Excellence 2011). However, the Framingham's equation has been deemed suitable for populations who have the same baseline characteristics. Many cohort studies in other countries have been conducted in order to derive their own risk prediction equations and calibration, which are suitable to their populations, to be incorporated with the Framingham algorithm.

The purpose of this review is to explore the mathematical risk assessment methods, which have been used to estimate the CVD prevalence or incidence among populations and to establish the most appropriate CVD prediction equation suitable for use with the Thai population.

2.3.1 The Framingham's equation

The Framingham Heart Study (Framingham Heart Study 2011), undertaken in Framingham, Massachusetts, USA, is the first known cohort study to be undertaken that focuses on CVD and identifies the risk factors. Over 60 years, there have been 5 cohorts enrolled in this study. The original cohort included 2/3 of the adult population in Massachusetts (5,209 participants aged 30 - 62 years). The second generation cohort was the offspring cohort, consisting of the 5,124 offspring and spouses of the original cohort who were aged <10 - 70 years. The third generation cohort were recruited by enrolling participants who had a least one parent in the offspring cohorts and aimed to explore the genetics and clinical association of the cohort. The 103 new offspring spouses cohort were enrolled in 2005 and the Omni cohort which recruited 506 residents in 1994 with varied nationality, such as African-American, Hispanic, Asian, Indian, Pacific Islander and Native American origins. The Framingham's heart study

identified the modified risk factors which contributed to developing CVD, such as smoking, cholesterol level, triglyceride, high density lipoprotein (HDL), blood pressure, body mass index (BMI), diabetes, age and gender. The Framingham study derived several versions of prediction equations and risk scores to predict the cardiovascular event among the population. The following CVD risk scores and risk equations had been developed in this study.

The parametric model was developed in 1990 from 5,573 participants aged between 30- 74 years, from the Framingham original cohort and the Framingham offspring. The equation developed had been calculated using the baseline risk factors such as age, gender, systolic and diastolic blood pressure, cigarette smoking, diabetes and ECG-LVH level. There are 6 major outcomes of interest. These include CHD, myocardial infarction, death from CHD, stroke, CVD (including all cardiovascular events, CHF and PVD), and death from CVD. The strength of the parametric statistical equation is in its ability to calculate the probability of each outcome at a particular point of time until cardiovascular events occur (Anderson et al. 1991).

In 1998, Wilson et.al (1998) derived the risk prediction score from the original and the offspring Framingham study, aged 30 -74 years old, with a 12 year follow up period by using the Cox proportional hazard model. This study derived the multivariate CHD risk score, which included blood pressure, total cholesterol, LDL cholesterol, HDL cholesterol and gender. The β coefficients of each risk factor from the model were used to calculate the risk of developing fatal and non-fatal CHD and MI and coronary insufficiency. It was suggested that the risk score for CHD, using the risk factor categories, generalize in middle-aged white population samples or individuals, with the same characteristic (Wilson et al. 1998).

In the following year, a shorter time risk score for CHD was developed, to estimate risk over 1-4 years. The gender-specific risk equations were derived. The probability for initial and subsequent CHD could be calculated in the point estimation for 2-year risk to CHD or directly compute the risk at any time between 0 and 4 years by the Weibull accelerated failure regression model. The risk predictors in this equation were age, systolic blood pressure, cigarette smoking status, fasting lipid level, diabetes mellitus and the use of antihypertensive medication. Additionally, it also included the menopause status in the women's risk function (D'Agostino et al. 2000).

The risk prediction equations for the recurring CHD had been derived in another study, using the Weibull accelerated failure regression model. This study recruited 10,156 participants who were free from CVD and 1,176 participants who had experience of CHD or ischemic stroke. The recurring CHD events referred to subsequent CHD including mostly hospitalized events, consisting of myocardial infarction, coronary insufficiency, angina pectoris, and sudden and non-sudden coronary death, during a 4 year-period. The significant predictors for recurring CHD were age, lipid profiles (total cholesterol and HDL-c), and diabetes status (D'Agostino et al. 2000). The Weibull model was more feasible than the Cox proportional hazard model because it can calculate the risk at any period of time.

The estimated 10-year risk score for the Hard CHD had been derived in 2001, which was published in the third report of the national cholesterol education program (NCEP) expert panel. The Hard CHD referred to MI or coronary death. The risk score was presented by gender-specifically for men and women which included age, total cholesterol, smoking status, systolic blood pressure and treatment for hypertension (Expert Panel on Detection, Evaluation,and Treatment of High Blood Cholesterol in Adults 2001).

The general 10-year risk algorithms for the first ever CVD event were developed in 2007 by using the Cox proportional hazards model. This study recruited 8,491 participants from the original cohort and offspring cohort, who were free from CVD and had been followed up for 12 years (D'Agostino et al. 2008). The CVD events in this study referred to CHD, stroke, peripheral artery disease, or heart failure. Two versions of the risk algorithms had been derived, based on the traditional risk factors and the simpler version based on non-laboratory risk predictor, which can be used in the primary prevention care (Expert Panel on Detection, Evaluation,and Treatment of High Blood Cholesterol in Adults 2001).

A recent Framingham equation was derived in 2008 for estimating a 30-year risk of CVD. It was a longer-term risk equation than the previous version of Framingham's. The offspring cohort aged 20 to 59 years and free from CVD and cancer were being used as baseline study population. The modified Cox model was performed and adjusted for the competing risk of non-cardiovascular death, to derive the 30-year risk of the Hard CVD events. The Hard CVD events referred to coronary death, MI and stroke. The risk predictors in this equation were male gender, systolic blood pressure, antihypertensive treatment, total and high-density lipoprotein cholesterol, smoking and diabetes mellitus. However, the BMI was a weakly significant association; therefore, it was not including in the equation. The advantage of this equation was in predicting the long-term risk of CVD because the shorter period of the follow-up study may have missed cases, which might occur in the longer time periods. Additionally, the treatment effects might influence the short-term prediction equation. However, the limitation of this equation was pointed out. For example, the generalizability to other ethnic groups was limited because the base population comprised only of an all-white cohort, and the novel biomarkers risk factors were not included in the equation (Pencina et al. 2009). This 30-year risk prediction algorithm has been validated and compared to the earlier

version of Framingham algorithm (Anderson et al. 1991), in the Australian population in 2009. The results suggested that the older Framingham equations overestimated the CVD risks in the low risk group and under estimated the CVD risks in the high risk groups. It is essential to undertake a review of the calibration and validation parameters when applying the equation to specific populations (Zomer et al. 2011).

In terms of stroke, the risk predication algorithm had been developed in 1991, within the Framingham's cohort using the Cox proportional hazards regression model. Participants aged between 55-84 years were recruited onto this study. The 10-year risk score of the first ever stroke has been derived. The risk predictors were age, systolic blood pressure, the use of antihypertensive therapy, diabetes mellitus, cigarette smoking, prior instances of CVD, atrial fibrillation and left ventricular hypertrophy by electrocardiogram (D'Agostino et al. 1994). The stroke risk function had been developed further in 1994 by using the Cox proportional hazards regression model in participants within the same age groups and having the same risk predictors. However it was adjusted for the use of antihypertensive medication and systolic blood pressure. It provided a new predictor variable to be included into the risk function. The risk score derived provided a more accurate result allowing for a better understanding in controlling the systolic blood pressure impact (below 110 or greater than 200 mmHg) (D'Agostino et al. 1994).

Another version of the risk function for stroke had been developed for individuals who had ever experienced atrial fibrillation but never had stroke or TIA and were not on Warfarin medication. The Cox proportional hazard model derived two versions of the risk calculation, which were the 5 years-risk of stroke and the 5 years-risk of the combination of stroke or death. The risk predictors were age, female gender, systolic blood pressure, prior stroke or TIA, and diabetes status. Although, this risk

score was suitable for patients with atrial fibrillation, it may underestimate the stroke risk for the individual with left ventricular systolic dysfunction. The clinical diagnosis from echocardiograms was not included in this risk function, due to the limitation of using echocardiograms in the period prior to this study (Wang, Massaro and Levy 2003).

Several systematic reviews have been undertaken to verify the validity and accuracy of the Framingham's equation (Brindle et al. 2006, Eichler et al. 2007). The reviews tend to demonstrate similar comparable results. Brindle et al (2006) studied the accuracy and impact of the Framingham risk score for assessing the primary prevention of CVD. This study included 2 systematic reviews. First, a review of the external validity of the Framingham, Anderson and Wilson's equation, to observe the ratio predictions in the different cohort studies, for the 10 years risk prediction. Second, the review of the effectiveness of the CVD risk score in a randomised control trial by health care professionals. The former results suggested that there were heterogeneity considerations across the population.

The Framingham equation underestimated the risk of CVD 0.43 (95%CI, 0.27-0.67) in the high-risk population, for example: patients with diabetes and patients with a family history of CVD. Conversely, it over predicted the risk of CVD 2.87 (95%CI, 1.91-4.31) in the lower-risk population. The latter review found only 4 randomized control trials which investigated the risk score of CVD. It was concluded that there was no strong evidence for the performance of risk assessment in improving health outcomes, and there was insufficient information to conclude accurately the effectiveness of the risk assessment in clinical practice (Brindle et al. 2006). Beswick (2006) suggested that the risk scoring was variably accurate when transferred to a different ethnicity and social context. However, the recalibration method was required specifically to relate to the population (Beswick and Brindle 2006). Eichler Klans, et.al

(2007) conducted a systematic review of the Framingham score in 25 cohort studies in US and Non-US population. The review concluded that the Framingham score performed well in terms of predicting for a first coronary event, and was well calibrated for use in the US, Australia and New Zealand. However, it overestimated the cardiovascular risk in European cohorts (Eichler et al. 2007). Table 2.2 shows the summary of the Framingham's risk algorithms.

Table 2.2 Summary of the Framingham's risk algorithms for CVD

Authors, year of publication	Target population	Follow-up period	Model	Predictors	Outcome prediction
Anderson et al. 1991	Individual aged 30 to 74 years, free of CVD at base line	12 years	parametric statistical model (Weibull model)	Age, Gender, Systolic and Diastolic blood pressure, Smoking status, Diabetes status and ECG-LVH level	- Myocardial infarction (MI, including silent and un-recognised MI) -Death from CHD (sudden or non-sudden) -CHD (MI, CHD death angina pectoris and coronary insufficiency) -Stroke (stroke and TIA) -CVD (include all CVD events) -Death from CVD
Wilson et al. (1998)	Individual aged 30 to 74 years old and without overt CHD at baseline	12 years	Cox proportional hazard model	Age, Diabetes status, Smoking status, JNC-V blood pressure categories, NCEP Total cholesterol categories, LDL cholesterol categories	10- years risk of CHD

Authors, year of publication	Target population	Follow-up period	Model	Predictors	Outcome prediction
Pencina MJ, D'Agostino RB, et.al (2009)	Individual aged 20 to 59 years, free of CVD and cancer at baseline	35 years	Cox regression model	Gender, Age, Systolic Blood Pressure (SBP), Use of antihypertensive treatment, Smoking status, Diabetes status, Total cholesterol , HDL cholesterol ,BMI replacing lipids in a simpler model	30- year risk to "Hard" CVD (coronary death, myocardial infarction, stroke), "general" CVD (coronary death, myocardial infarction, coronary insufficiency, angina, ischemic stroke, haemorrhagic stroke, transient ischemic attack, peripheral artery disease, heart failure)
D'Agostino (2000)	Individual aged 35-74 years, free from of all CVD (CHD, stroke, transient ischemic attack, congestive heart failure and intermittent claudication)	4 years	Weibull accelerated failure regression model	Age, Systolic blood pressure (SBP),smoking status, Fasting lipid level (totals and HDL Cholesterol), Physician diagnosis of diabetes at the current or a previous examination, Use of antihypertensive medication	2-year risk of first ever CHD

Authors, year of publication	Target population	Follow-up period	Model	Predictors	Outcome prediction
D'Agostino et.al 2008	Individual aged 30-74 years, free from CVD at baseline	12 years	Cox proportional hazard model	Age, Diabetes status, smoking status, Treated and untreated Systolic Blood Pressure, Total cholesterol, HDL cholesterol, BMI replacing lipids in a simpler model	10-year CVD risk CHD, cerebrovascular disease, peripheral arterial disease and hearth failure)
Expert Panel on Detection, Evaluation, and Treatment of high blood cholesterol in adults, adult treatment panel III (2001)	Individual aged 20-79 years, free from CHD, intermittent claudication and diabetes	12 years	Cox proportional hazard model	Age, Total cholesterol, HDL, SBP ,Treatment for hypertension and Smoking status	Hard coronary heart disease (HCHD) (myocardial infarction or coronary death)
D'Agostino et.al (2000)	Individuals who had at least one CHD event or ischemic stroke before examination and survived the acute stage of that event.	4 years	Weibull accelerate failure regression model	Age, Systolic blood pressure (SBP), Cigarette smoking status , Fasting lipid level (total and HDL cholesterol), Physician diagnosis of diabetes at the current or a previous examination	2 year risk prediction of recurrence CHD

Authors, year of publication	Target population	Follow-up period	Model	Predictors	Outcome prediction
Wolf PA et.al (1991)	Individuals aged 55 to 84 years, free of stroke	10 years	Cox proportional hazard model	Age, systolic blood pressure, the use of antihypertensive medication, diabetes mellitus, cigarette smoking, Prior CVD, atrial fibrillation and left ventricular hypertrophy by electrocardiogram	10-year risk of first stroke
D'Agostino,R.B. et.al (1994)	Individuals aged 55 to 84 years, free of stroke at baseline	10 years	Cox proportional hazard model	Age, Systolic blood pressure, Diabetes mellitus, Cigarette smoking, Prior CVD, Atrial fibrillation, Left ventricular hypertrophy, Use of hypertensive medication (adjusted for the level of systolic blood pressure)	10-year risk of first stroke
Wang TJ , et.al (2003)	Individuals aged 54-94 years who had a new onset of atrial fibrillation, had an occurrence of new-onset Atrial Fibrillation (AF) without rheumatic mitral stenosis	10 years	Cox proportional hazard model	Age, Gender, Systolic blood pressure, Prior stroke or ischemic attack, Diabetes status	5-years risk for stroke alone 5-year risk for stroke or death

2.3.2 The Asia Pacific Cohort Studies (APCS) Collaboration

The Asia Pacific Cohort Studies (APCS) Collaboration is the largest cohort collaborative project in Asia, which includes over 650,00 participants, in 44 setting within China, Hong Kong, Taiwan, Japan, South Korea, Singapore, Thailand and Australia (Asia Pacific Cohort Studies Collaboration 2007). The APCS developed a CVD risk equation which was adjusted and reestimated with the Framingham's equations for the Asia population, with a limitation of risk factors data (only age, systolic blood pressure, total cholesterol and smoking status). This equation was derived from 172,077 Asia cohorts, 25,682 Chinese cohorts and 6,053 Framingham cohorts, during the 8 years of the follow-up period. The outcomes for this equation were any CVD event, such as cardiovascular death, non-fatal MI or non-fatal cerebrovascular event. This study derived both the Asia cohort cardiovascular risk prediction equation and the Framingham cohort equations for men and women. This prediction equation has been used to calculate the future cardiovascular events in the Thai cohort study data. When comparing the Asia cohort equation to the Framingham equation, it was found that the recalibrated Framingham equation overestimated the risk of CVD. Although the Asia cohort equations have used fewer parameters to estimate the risk of CVD, the Asia cohorts risk prediction equation is likely to provide the most reliable prediction tool for Asian populations. When compared to the recalibrated Framingham's equation, it was explained that there were broadly similar associations of most risk factors and systolic blood pressure showed the strongest association to cerebrovascular disease in the Asia cohort, than Framingham cohort. Another explanation was related to the CVD and background risk factors that were similar across APCS cohorts. The missing variables of the recalibrated Framingham equation might not effect to the overall risk prediction.

2.3.3 CVD risk assessment in Thailand

There have been few prospective cohort studies undertaken in Thailand. The only longitudinal study for CVD was established to explore the association of the modifiable risk factors. The setting was the Electricity Generating Authority of Thailand (EGAT) study, Bangkok, Thailand. This study was set up by a group of cardiologists from the Faculty of Medicine, Ramathibodi Hospital, Mahidol University. The EGAT study followed-up the 3,499 participants who were aged 35-54 years, since 1985 (EGAT1) and continuously recruited an additional cohort later in 1998 (EGAT2) and 2009 (EGAT3) (Vathesatogkit et al. 2012). The RAMA-EGAT heart score was developed by using the Cox-proportional hazard model. There were 3 versions of the RAMA-EGAT heart score which were: a risk score for use in the clinical assessment; a risk score for the general population with included the serum lipid variable and a simplified version of the risk score without any requirement of the laboratory variables. The outcome prediction was the 10-year risk for Coronary Artery Disease (CAD). The traditional risk factors included in the RAMA-EGAT score were, age, gender, serum total cholesterol, cigarette smoking status, diabetes mellitus, hypertension and waist circumference. This risk score was validated by comparing the actual number of observed clinical diagnosis by medical doctors and the estimated number from the RAMA-EGAT heart score and Framingham risk score. The finding showed the precision of the RAMA-EGAT risk score compared to the Framingham risk score. Overall, the Framingham risk score was 243.14% overestimated. The clinical diagnosis by medical doctors was overestimated by 21.44% and the RAMA-EGAT risk score for the general population was over predicted by 55.86%. There were some limitations of using this risk score. The participants in the EGAT cohort were mainly men, only 22% of participants were women (Yamwong 2005).

There were some limitations of the RAMA-EGAT heart score. Firstly, the risk score for use in the clinical assessment was developed based only on male data. However, a risk score for use in the general population was derived based on both men and women. It included gender as one of the prediction parameters of the risk score. Secondly, the RAMA-EGAT score was derived using middle-class participants who lived in urban areas. It was necessary to understand this constraint when applying the equation across different regions and socio-economic statuses. The finding suggested applying this risk score with the other Thai dataset to evaluate the performance of this risk score. However, the RAMA-EGAT score is the only available risk score based on the Thai population.

The validation of this risk score was evaluated in several studies in Thailand. The RAMA-EGAT score was applied to the 1,224 patients with moderate to high risk of CAD in Thailand. The risk score was evaluated against the CT angiography coronary for diagnosing the coronary stenosis. It was found that the RAMA-EGAT heart score was a good predictor for the CVD event, with a significant correlation between the clinical diagnosis and the estimation from the risk score (Pattanapichakul et al. 2007). The RAMA-EGAT risk score was also evaluated using the case-control study of the ACS patients at Siriraj hospital, Thailand. The case group was comprised 163 patients with CHD and a control group of 314 patients without CHD. The 3 versions of RAMA-EGAT score were applied to estimate the risk to ACS. It was found that the risk RAMA-EGAT for the general population, with serum lipid variables, was more accurate that the version than that developed for use in clinical practice and the risk score for general population without the lipid profile. The positive predictive value in the general population version was 82% in males and 93% in females. This finding suggested that the RAMA-EGAT score was an accurate predictor for screening for the risk of ACS in the Thai population. Another study was evaluated in the HIV

Netherlands, Australia, Thailand Collaboration (HIV-NAT) cohort study. This study followed 785 HIV-infected participants from 1996 to 2009. The Framingham's equation, RAMA-EGAT and Data Collection on Adverse Effects of Anti-HIV Drugs (D:A:D) risk equations were applied to this cohort. The D:A:D risk equation was derived from the HIV-infected in 20 countries across Europe and Australia. All three equations were used to estimate the 10-year risk of CHD. The comparison results showed a similar agreement between RAMA-EGAT equation and D:A:D risk equations. This study indicated the suitability of using the RAMA-EGAT or D:A:D equation in this cohort, rather than using the Framingham equation (Edwards-Jackson et al. 2011).

In terms of the recalibrated Framingham equation in Thailand, Khonputsa et.al (2011) has derived the recalibrated version of the Framingham equation which was applicable for the Thai population. The two equations were developed to project the risk, separately, for ischemic heart disease (IHD) and stroke within a specific time period for both men and women. The Weibull accelerator model had been used to derive the equations in the Framingham's original and offspring cohorts and provided the constants and regression coefficient, for each risk factor (Khonputsa, et al. 2011). The risk predictors in this equation were age, systolic blood pressure, total cholesterol, diabetes mellitus and cigarette smoking status. The equations were derived by incorporating those constants and risk factors separately by gender. The equations were then applied and compared to the average 10 year CVD observed risk ratio and the estimated ten-years risk calculated from the Framingham equation. This equation was applied to the 3rd National Health Examination Survey Dataset (2004), in participants who were aged 30 years and over, to calculate the individual probability of getting IHD or Stroke. It was found that the recalibrated Framingham equations decreased the CVD risk predicted by 10% in Thai women and by 97% in Thai men. The performance of this equation was tested by comparison with the Framingham's APCS equations. Both

recalibrated Framingham equations and the APCS equation were applied to the EGAT cohort study data set and projected the CVD risk over 8 years, in Thai men aged 30 years and over. The equations showed a similar estimation of the 8 years CVD risk. This study suggested using the recalibrated Framingham equation rather than using the APCSC equations, because it was more feasible when estimating the risks separately for IHD and stroke (Khonputsa, et al. 2011). However, there were some limitations in the recalibrated Framingham equation because the equation was recalibrated with the cumulative risks and CVD incidence. The incidence of non-fatal IHD or stroke was estimated by using the national hospitalization database in 2004. The proportion of first-ever IHD or Stroke came from a study in UK (Rothwell et al. 2005) and applied to the dataset by age and gender. There was an absent of up to date information on the proportion of the first ever IHD and stroke specifically for Asia.

2.3.4 The other global CVD risk equations

2.3.4.1 The QRISK equation

The QRISK algorithm was the first and largest algorithm to have been developed to predict the CVD events in the United Kingdom. The QRESERCH database has been used as a prospective open cohort study. The participants, aged 35 to 74 years were divided into two groups. These included 1.28 million participants, for derivation cohort, from 318 UK general practices and 0.61 million participants for the validation cohort, from 160 UK general practices. The outcomes that are of interest being CVD, including myocardial infarction, CHD, stroke and TIA or death from CVD, occurring within a 27 month period (Jan 1995 to April 2007). The risk factors included in the analysis were, age, gender, cigarette smoking status, systolic blood pressure, and ratio of total serum cholesterol (TC) to high density lipoprotein (HDL), left ventricular hypertrophy, family history of CVD, Townsend deprivation score and current

prescription of at least one anti-hypertensive drug. The Cox proportional hazards model was performed to estimate the coefficients of the association between risk factors and CVD in both males and females. The QRISK algorithm was performed and validated with the Framingham's equation and the ASSIGN equation, for the population in UK. It was found that the QRISK equation was extremely accurate in predicting CVD in the UK population (over-predicted CVD by 0.4%), whereas the Framingham's equation was over-predicted by 35% and the ASSIGN by 36% (Hippisley-Cox et al. 2007). The QRISK algorithm has been validated in The Health Improvement Network (THIN) cohort database (Hippisley-Cox et al. 2008). It also showed that the QRISK algorithm was more suitable to the UK population than the Framingham's algorithm, which over-estimated the risk by 23%.

In 2008, the QRISK2 algorithm was developed and validated, to estimate the risk of CVD in England and Wales across different ethnic groups. The 10 years follow-up opened cohort from the QRESEARCH database has been used to derive the QRISK2 equation, which included 2.3 million people and included the white population, south Asian, black African, black Caribbean, Chinese, other Asian and other ethnic groups. The outcomes were a prediction of CVD (CHDs, stroke and TIA).The risk factors which were incorporated in the risk algorithm were, self-assigned ethnicity, age, gender, cigarette smoking status, systolic blood pressure, ratio of total serum cholesterol / high density lipoprotein cholesterol, body mass index, family history of CHDs, Townsend deprivation score, treated hypertension, rheumatoid arthritis, chronic renal disease, type 2 diabetes and atrial fibrillation. The differences between the QRISK1 and QRISK2 algorithms were that the QRISK2 included more risk factor parameters, such as ethnicity, deprivation and clinical conditions. When comparing the QRISK2 to the modified Framingham equation, it was found that the QRISK2 was better at classifying the higher risk groups of cardiovascular events, than the modified Framingham's

equation, which was recommended by NICE (Hippisley-Cox et al. 2008). The QRISK2 has been evaluated in a 10 year prediction performance, in an independent UK cohort study. Comparing the QRISK1 to the QRISK1 and the Framingham's equation, QRISK2 demonstrated more accuracy in identifying the high risk CVD groups. However, the limitation of QRISK2 was the incompleteness of data for the total serum cholesterol and high density lipoprotein in the study population, which might introduce a bias in the analysis (Collins and Altman 2010).

The QRISK life time CVD risk function was developed further to estimate the lifetime risk of developing CVD which included stroke, TIA, angina or heart attack. The common risk factors with QRISK2 were included in this risk function, such as cigarette smoking status, ethnicity group, systolic blood pressure, ratio of total cholesterol and HDL-C, BMI, family history of CVD, Townsend deprivation score, treated hypertension, rheumatoid arthritis, chronic renal disease, diabetes mellitus and atrial fibrillation. There was some difference between QRISK2 and QRISK lifetime. The QRISK life time took into account the age and the risk of dying from the other causes. The smoking variable was classified to 5 categories according to the level of smoking habit; non-smoker, ex-smoker, light smoker (<10 a day), moderate smoker (10-19/day) and heavy smoker (≥20/day). The advantage of QRISK life time was the capacity of the risk identification in the younger population, which was difficult to identify in the 10-year risk function (Hippisley-Cox et al. 2010).

Dent (2010) reviewed the prediction equations for CHD which are: the Framingham's equation, SCORE, QRISK, PROCAM and ASSIGN. The review compared the strengths and limitations across the different algorithms. It was suggested that the recent development of the QRISK equation might be appropriate for the UK population, as the QRISK2 has good calibration predicting, when compare to the

observed number of the cardiovascular events. In addition, the model also comprises ethnicity and socio-economic deprivation, which has not been included in the Framingham's equation (Dent 2010).

2.3.4.2 The ASSIGN CVD risk score

The Scottish Heart Health Extended cohort (SHHEC) (Woodward, Brindle and Tunstall-Pedoe 2007) derived the ASSIGN score for predicting the risk of developing CVD. The cohorts were randomly selected from the Scottish MONICA project and the Scottish Heart Health study. A total of 13,297 participants aged between 30 to 74 years old were recruited to this study. The risk factors used including in the ASSIGN score were, age, gender, Scottish index of Multiple Deprivation, family history, cigarette smokers, the number of cigarettes smoked per day, systolic blood pressure, total cholesterol and HDL cholesterol. The main differences between the ASSIGN score and the Framingham equation are the addition of the social deprivation data, family history, and the quantity of cigarettes smoked. The outcomes of interest were death from the cardiovascular cause or discharging for CHD, cerebrovascular disease or for coronary artery intervention. The Cox proportional hazard model has been used to derive the ASSIGN risk score and then compare the number of observed and expected events to the Framingham's equation. The ASSIGN score showed a similar estimation to the Framingham equation (Woodward, Brindle and Tunstall-Pedoe 2007). However, it found that the ASSIGN score and the Framingham score were likely to overestimate the risk of CVD. When the ASSIGN score was validated to the Framingham equation with the THIN database, it was found that both algorithms overestimated the risk, especially in the higher risk population. The ASSIGN over predicted by 20%, whereas the Framingham equation over predicted by 16% (De la Iglesia et al. 2010).

2.3.4.3 The UKPDS risk engine

Because people with Type II diabetes have a significantly higher risk of developing CHD than the general population and there was no specific equation for predicting the risk in Type II diabetes patients, the UK Prospective Diabetes Study (UKPDS) (Stevens et al. 2001) derived the UKPDS risk engine to estimate the probability of getting CHD in Type II diabetes patients. Age, gender, ethnicity, cigarette smoking status, HbA1c, body mass index, systolic blood pressure, total cholesterol and duration of diagnosis to diabetes has been used in a parametric model. This risk engine was applicable for health care planning especially for diabetes patients.

2.3.4.4 The SCORE project

The SCORE project was a collaborative cohort study between 12 countries in Europe, (Finland, Russia, Norway, UK (England), Scotland, Denmark, Sweden, Belgium, Germany, Italy, France and Spain). The outcome of interest was the 10-year risk of death from CVD. This project focused on the mortality event as an outcome, because of the inconsistency of the end-point definition for morbidity in the other risk assessments. It also aimed to develop the comparable risk score for national level across Europe. The SCORE project derived the risk chart for identifying the high risk and low risk groups for the CVD according to age, gender, total cholesterol level, systolic blood pressure and cigarette smoking status. The risk score has been tested for the sensitivity and specificity under the ROC curve, which showed the area range from 0.71 to 0.84. However, the SCORE equation was limited to the principal risk factors and there are some associated risk factors which were not incorporated in the project, such as triglyceride, family history and the impaired glucose level (Conroy et al. 2003). The fourth joint task force of the European Society of Cardiology and other societies on CVD prevention in clinical practice, suggested using SCORE as the standard risk assessment for the population in Europe (Graham et al. 2007).

2.3.4.5 The FINRISK function

The FINRISK function was developed for estimating the risk of coronary events and stroke for the population in Finland. The risk function was derived from the FINRISK CVD factors survey dataset, which was conducted in 1982, 1987 and 1992 in the population aged between 30-64 years. The logistic regression was used to derive the risk functions after 10-year of follow-up periods. The prediction outcomes were coronary risk, stroke risk, and all CVD risk. The risk factors incorporated in the FINRISK function were age, gender, smoking status, serum cholesterol, systolic blood pressure, HDL-c, diabetes mellitus and the family history of infarction or stroke (Vartiainen et al. 2007).

2.3.4.6 ASCORE

A recent CVD risk score had been developed from the randomized clinical trial Anglo Scandinavian Cardiac Outcome Trial BPLA (ASCOT-BPLA). The ASCORE risk score was derived especially for the hypertensive patient. The study population was 15,995 the hypertensive patients who were initially free from CVD and never received any CVD preventive intervention. The Cox proportional hazard model derived the 5 year-risk function included age, gender, smoking, diabetes, blood pressure treatment history, systolic blood pressure, total cholesterol, HDL-C, fasting plasma glucose and creatinine. The ASCORE projected a 5-year risk of the first CVD event which was CVD death, myocardial infarction or stroke. The ASCORE performed a better prediction than the Framingham risk score which may overestimate the CVD risk in the hypertensive patients (Prieto-Merino et al. 2013).

2.3.4.7 PROCAM risk score

Prospective Cardiovascular Münster (PROCAM) study derived the PROCAM risk score for projecting the 10-year risk to the acute coronary event. This study was the

prospective cohort study which followed 5,389 men who aged 35-65 years in Germany. The Cox-proportional hazard model was used to produce the risk function. The risk predictors were age, LDL-c, smoking, HDL-c, systolic blood pressure, family history of premature MI, diabetes and triglyceride. However, this version of risk score was suitable to use in men, middle age, white population (Assmann, Cullen and Schulte 2002). The PROCAM study was developed further risk function to project the risk of MI and stroke based on the data from 18,460 men and 8,515 women in the north-west, Germany. The risk score for MI was derived by using the Weibull model. The risk predictors for MI were LDL-c, HDL-c, systolic blood pressure, smoking status, triglyceride and diabetes mellitus. The risk score for stroke was derive from the Cox proportional hazard model which included age, gender, diabetes status, smoking status and systolic blood pressure as the risk predictors (Assmann, et al. 2007).

2.3.4.8 The INTERHEART modifiable risk score (IHMR)

A new risk score for acute MI was developed from the INTERHEART study. This study was a large standardized case-control study in 52 countries which included 19,470 participants in the analysis. The risk score was developed by using the multiple logistic regressions model. The risk predictors were, Apo lipoprotein, smoking, second-hand smoke exposure, hypertension and diabetes. The strength of this risk score was more generalizable than the other risk scores, because the IHMR risk score was derived from data across the different ethnicities and global geographic regions. The case-control procedure allowed the recruitment of a larger number of participants than the prospective cohort study. However, it was argued that the case-control study, was not the ideal risk score for predicting the future instances of MI, because the case-control study did not allow to calculate the incidence or the absolute risk of disease, as risk functions that derived from the prospective study (McGorrian et al. 2011).

2.3.5 The CVD risk assessment in Asia

Several studies have applied the global CVD risk assessment algorithm to the Asia population. The Framingham risk score, JBS2 and QRISK2 have all been applied to calculate the 10-years risk of CVD, in the south Asian samples (Gujarati Indian origin), in the UK. It was found that all the three risk scores presented the moderate risk in agreement but QRISK2 estimated the proportion of participants who had 10-year risk >20% higher than the Framingham risk score (Rao et al. 2012). The Newcastle heart project also explored the CVD-risk engines by comparing Framingham risk score (1991), FINRISK and SCORE in the south Asian population (Bangladeshi, Pakistani and Indian). Those risk scores had calculated the risk of CVD mortality. The Framingham risk score and FINRISK showed similar results, while the SCORE presented lower 10-year risk estimations. The performance of SCORE was difference than the others, because it did not included HDL and diabetes as part of the predictors (Bhopal et al. 2005). The Singapore cardiovascular cohort study compared the predictability of the Framingham risk score, with the metabolic syndrome for estimating CVD mortality. By comparing the area under the ROC curve, the Framingham risk scores (Wilson et al. 1998) performed better in predicting CVD mortality than the metabolic syndrome, in healthy Chinese, Malays and Asian Indians (Lee et al. 2008).

2.3.5.1 The Chinese Multi-provincial Cohort Study (CMCS)

The Chinese Multi-provincial cohort study (CMCS) was a longitudinal study in 11 provinces in China (Liu, Hong and D'Agostino 2004). This study followed 30,121 participants aged between 35 to 64 years, from 1992 to 2002. This study derived the 10-year risk prediction equation for the 'Hard CHD', which referred to acute MI, sudden death or other coronary death. This study derived 2 versions of the CHD risk functions which were, the CMCS risk functions and the recalibrated Framingham's

equation for the population in China. The Cox-proportional hazard model had been used to derive the risk functions. It was found that the CMCS risk factor categories associated with the Hard CHD were similar to the Framingham risk function. Those risk factors were, age, smoking status, diabetes status, blood pressure, total cholesterol and HDL-C. When comparing the predictive capacity of the original Framingham equation with the CMCS equation, the original Framingham equation overestimated the absolute CHD risk. However, the recalibrated Framingham version, which was taken into account for the mean value of the risk factors and mean CHD incidence rate, enhanced the performance of the equation (Liu, Hong and D'Agostino 2004). Another risk algorithm for the population in China was derived from the USA-PRC, (USA –People's Republic of China) Collaborative Study of Cardiovascular Epidemiology cohort, that followed up 9,903 participants in China for 17 years and followed-up the participants every 2 years. The 10-year risk equation estimated the Ischemic Cardiovascular Disease (ICVD) such as ischemic stroke and coronary event. The simply 10 year risk score for ICVD had been derived. The Cox proportional hazard model showed statistically relationship of age, systolic blood pressure, total cholesterol, BMI, smoking status and diabetes mellitus. This risk algorithm was applied to the CMCS data set and compared with the recalibrated Framingham equations. The ICVD equation performed well in terms of the discrimination power, which considered the area under ROC was approximately 0.79 in both men and women. It also showed accuracy and precision when compared to the number of observed and estimated of CVD. Although, the recalibrated Framingham's equation showed the better prediction in the previous study, it demonstrated an overestimate in both Chinese men and women in this study. This result was controversial with Lui et.al (2004) arguing that the recalibrated Framingham risk function may not be applicable for the Chinese population because it projected the

CHD alone. The CVD risk function should include both stroke and CHD together, because stroke was a predominant cause of death in China (Wu et al. 2006).

2.3.5.2 The JMS Cohort Study

The JMS cohort study was a community-based longitudinal study in 12 rural districts in Japan, which followed 12,276 participants aged 19-93 years. The 10-year risk score for stroke was derived by using the Cox proportional hazards model. The prediction outcomes were 10-year risk score for all stroke risk, cerebral haemorrhage and cerebral infarction. The risk factors associated in the risk function were gender, age, smoking status, diabetes mellitus and systolic blood pressure. Those risk factors were common between cerebral haemorrhage and cerebral infarction. Although the JMS risk score was suitable for the Japanese population, the setting of this cohort was in the rural districts. Therefore, it should be used with caution when applying this risk score to populations in urban areas (Ishikawa et al. 2009).

2.3.5.3 WHO/ISH Risk prediction charts

In 2007 WHO provided the CVD risk prediction chart for 14 WHO epidemiological sub-regions (World Health Organization 2007), which included Africa, the Americas, Eastern Mediterranean, Europe, South East Asia and Western Pacific regions. The charts are used to estimate the 10-years risk of fatal or non-fatal, major CVD events such as MI or stroke for men and women who are aged 40 years and above. The risk charts are specifically used for each sub-region. Age, gender, systolic blood pressure, total cholesterol and cigarette smoking are used to estimate the individual risk of getting CVD in the next 10-years. However, there were 2 sets of the risk charts for use, one where the blood cholesterol measure data is available and the other set for when this data is unavailable. However, the risk equations were not published. Otgontuya et.al (2013) applied the WHO/ISH risk charts (World Health Organization

2007) to a cross-sectional survey conducted in Cambodia, Malaysia and Mongolia during 2005 to 2010 and estimated the prevalence of CVD over 10-years period (Otgontuya et al. 2013). It was found that using this risk assessment may underestimate the prevalence of CVD in people who are in the high risk group. Additionally, it also underestimated the treatment need in the high risk group, because it did not take into account the treatment effect in such instances as drug treatment for hypercholesterolemia and hypertension.

Table 2.3 presents the comparison of the CVD risk equations. The strengths and limitations in each equation are presented as follow;

Table 2.3 Comparison of the risk equations

Risk functions	**Target populations**	**Outcome prediction**	**Strengths**	**Limitations**
Framingham	US, white population	10 years risk to CVD, maximum projection is a 30 years CVD risk	1)Well-known equations 2)Feasible to calculate the risk of the different CVD outcomes 3)Recommended as the standard guideline	1) Not generalizable with other ethnicities 2) Needs a calibration when applying to specific populations.
QRISK2	UK population and across different ethnic groups	10 years risk to CVD (CHD, stroke and transient ischaemic attack)	New and up to date risk score with the accurate validation among UK population and some other ethnicities	The equations were not revealing in the research article. However, the risk calculation engine was available online.
QRISK lifetime	UK population and across different ethnic groups	Life time risk of CVD	First ever risk assessment equation that is capable to calculate the life	The same limitation as QRISK2

Risk functions	Target populations	Outcome prediction	Strengths	Limitations
			time risk	
ASSIGN	Scottish population	10 years CVD risk	Specific risk score for Scottish population and included the social deprivation variables	Over predict in the high risk population
UKPDS risk engine	UK diabetics patients	Risk to CHD	Risk engine specific for diabetic patients	Population specific
SCORE	European population	10 year risk of death from CVD	Use as the standard risk assessment for the European population	Predict only the death from CVD
FINRISK	Finland population	10 year risk of all CVD, CHD and stroke	Accurate among the population in Finland	Risk function derived from the cross-sectional data
ASCORE	Scandinavian cohort	5 year risk of CVD	Valid for the Scandinavian population	Population specific
PROCAM	German population	10 year risk of acute coronary events	Valid for the German population	Population specific
INTERHEART	International based on 52 countries worldwide	Risk for acute stroke	New risk score for predicting stroke in the international level	Based on the case-control studies
Chinese multi provincial cohort study (CMCS)	Chinese population	10 year risk of the Hard CVD	Valid for Chinese population	Population specific
JMS cohort study	Japanese population	10 year risk for stoke	Valid for Japanese population	Population specific
APCS cohort study	Asia population	8 year risk of CVD	Generalizable for the Asia population	Capable to project the risk only for CVD overall

Risk functions	Target populations	Outcome prediction	Strengths	Limitations
WHO/ISH risk prediction charts	14 WHO epidemiological sub-regions	10 year risk of fatal or non-fatal, major CVD events	The risk chart has been specifically used for each sub-region.	The equations were not published.
RAMA-EGAT risk score	Thailand population	10 year risk of CVD	First ever CVD risk specific for Thai population	1)RAMA-EGAT Published the risk score but not published the equation 2)RAMA-EGAT mostly base on Thai men, middle age and living in Urban area

2.3.6 Summary

This section presented the concept of the classical prediction model for CVD, which mostly use the risk equations or the risk score that have been derived from regression models such as the multiple logistic regressions, Cox proportional hazard model and Weibull model. Those risk functions were used widely to assess the risk of getting CVD events, such as total CVD, CHD or stroke, in both fatal and non-fatal events. The risk function was used as a standard guideline for assessing the risk of the individual in many countries and also assessing the risk to identify the high risk population for prevention and control. However, there were some limitations when applying the risk equation to a diverse population. The Framingham's equations overestimate the risk of CVD in the low risks population and under estimates in the high risk populations for several reasons. First, the Framingham equation was derived during

the high prevalence and high risk factors level in the US middle-aged white population, while some risk factors in other countries tend to decrease, for example with the decline of cigarette smoking. Secondly, the improvement of CVD treatment and medication has reduced the incidence and mortality of CVD in the population. Thirdly, the Framingham's equation has not included some associated risk factors, such as the socio-economic deprivation and ethnicity.

Although the prediction equation is not capable of calculating the exact number of future CVD events, it is an effective tool for assessing the risk of developing CVD in the future. Those equations had been used in routine CVD risk assessment, which was more accurate than the assessment by using only a single risk factor. This thesis will use the equation from the calibrated Framingham version for the Thai population and the APCSC cohort study as it represents CVD in the Asia/Pacific region and has been applied in the Thai population. Additinally, these equations was available in the publication and the list of independent risk factors in the equations are applicable to apply in the Thai data. The selection criteria of the CVD risk equation has explained in chapter 3. However, as discussed, the APCSC equation uses fewer parameters than the Framingham equation and it is possible to overestimate the CVD event. Therefore, it will be necessary to adjust with the Framingham algorithm.

2.4 Health economic modelling for CVD

This section reviews the application of the health decision modelling techniques related to the CVD, which have been conducted in many studies. The various types of model which have been applied to estimate the Future CVD events are, decision tree model, Markov model, Discrete event simulation or micro-simulation, cell-based simulation and system dynamic simulation. The impact of the primary prevention of the CVD risk has been estimated in terms of mortality saving, morbidity saving, life year

saving and economic saving. This review presents the up to date literature of CVD decision modelling, which has been used for the health economic evaluation and policy implication.

Modelling for economic evaluation has been used widely in public health in many countries and is increasingly used in the UK (Brennan, Chick and Davies 2006, Barton, Bryan and Robinson 2004). The increase in the variation of health care interventions and new technologies such as pharmaceuticals, surgery, diagnostic tests and primary prevention interventions, leads to increased consideration for the policy planner, to manage and allocate budgets and resources which are limited in availability. Drummond et.al (2005) defines economic evaluation as "the comparative analysis of the alternative courses of action in terms of their cost and consequence" (Drummond, et al. 2005). The decision analytic model was developed by performing the mathematical algorithm, to capture the relationship between the series of consequences and the evaluation of the alternative options. The consequences address the probability or a chance of getting to events and it can calculate the cost and outcome of each consequence. For example, Mar et.al (2008) developed the Markov model for calculating the stroke prevalence and economic impact of thrombolytic treatment (Mar, Sainz-Ezkerra and Miranda-Serrano 2008). The expected cost and expected outcome can be estimated by the decision model; however the variability and uncertainty should be taken into account (Briggs, Sculpher and Buxton 1994). The decision modelling, such as the cost-effectiveness modelling, provides the information for a decision maker to prioritise and select the most suitable interventions for a health problem (Briggs, Claxton and Sculpher 2006). In addition, it is able to estimate costs, effectiveness or benefits and evaluate treatment decisions.

The following section provides an overview of the decision modelling techniques which have been used in health economic evaluations. The aim of the review is to address which type of economic decision model will be most appropriate to use within the study. The review focuses on the decision trees model, the Markov Model, the discrete event simulation model and the other types of health economic modelling, which are most often used for the health economic evaluation (Briggs, Claxton and Sculpher 2006). The review includes the theoretical concepts of modelling, the comparison of strengths and limitations of the model, and the previous studies of health economic modelling which relate to the estimation of the future burden of CVD and the primary prevention intervention.

2.4.1 The Decision tree model (DTM)

The decision tree model is the most commonly used model for economic evaluation (Briggs, Claxton and Sculpher 2006). The model illustrates the health situation as a tree like diagram. The expected costs and outcomes are calculated by summation of the pathway weight by the probability of each pathway.

Whitfield et al (2006) developed the cost offset model which was a spreadsheet based decision tree model. The model applied the Framingham algorithm and the UKPDS risk engine, to estimate the economic impact of CVD risk reduction strategies. The findings found that a 2-4% risk reduction in CVD would save the cost, in acute admission rates, of about £5.4 million over 5 years and prevent approximately 4,000 people from having cardiovascular events from a population base of 185,000 (Whitfield et al. 2006).

Liew et.al (2006) demonstrated the health effect from the hypothetical intervention of primary prevention strategies for CVD by conducting a decision-analysis tree and underpinning life-course analysis and Markov processes. Uncertainty

and sensitivity analyses were undertaken by Monte Carlo simulation (Liew et al. 2006). This study showed the strength of the models in terms of its generic nature and is applicable to any population which has data available. The model included both CHD and Stroke which have shared risk factors and treatment. The model was also shown to be capable of simulating temporary factors, such as lag-time and discontinued therapy, and allowed for uncertainty analysis.

The decision tree model draws the explicit picture of the relationship and the progression of each pathway. However, the limitation of the decision tree model is that it does not take into account the outcome over time. (Drummond, et al. 2005, Briggs, Claxton and Sculpher 2006).

2.4.2 Markov Model

The Markov Model is more complex than the decision tree model. It is commonly used in decision analysis when the progression of diseases and risk are dynamic, when time is involved and with possible recurrence of events occurring over time. The Markov model moves forward by using the transition probability of the beginning stage to the next stage. The Markov chain model is used widely for health economic evaluations (Briggs, Claxton and Sculpher 2006).

The CHD policy model (Weinstein et al. 1987) was a Markov state transitional model, which was originally developed for projecting the CHD event in the US population. The CHD policy model consisted of three sub-models: the demographic epidemiologic sub-model, the bridge sub-model and the disease history sub-model. The demographic-epidemiologic sub-model simulated the distribution of risk factors and the incidence of CHD in a general population. The bridge sub-model simulated the events in the first CHD patients. The disease history sub-model simulated the event for people who previously got CHD. The model was built up based on the number of the US

population in 1980 and estimated the risk by using the data from the national health and nutrition examination survey (NHANSII). The Framingham's equation was applied to calculate the probability of getting CHD event in the population. The outcomes of the projection were the number and rate of fatal and non-fatal CHD, number of people who survived until age 85 years old with and without CHD; number of CHD events including cardiac arrest, MI, angina pectoris and the cost of intervention including both therapeutic intervention and prevention intervention up to 30 years period. However, the CHD policy model assumed that the CVD risk factors would remain stable, even as the time changed (Weinstein et al. 1987). This model also estimated the impact of coronary risk factors reduction and the change in CHD events among the US population between 1980 and 1990. It was found that the decline of CHD prevalence was substantially related to the risk reduction interventions, such as changing life styles and habits, which resulted in life saving and health care cost saving of approximately $5400 per year of life save (Goldman et al. 2001).

The CHD policy model (Moran et al. 2008) was applied to project the change of the Future CHD in China and the impact due to the change of demographics. The CHD policy model, which was calibrated for China, was applied to estimate the future prevalence of CHD. The CHD event, CHD mortality and DALY were calculated. The results from the model showed a continuously increase of CHD events in the Chinese population during 2010 to 2029, because of the growing age of the population (Moran et al. 2008). This result was confirmed by the further development of the CHD policy model. The model simulated the CHD event at a national scale, which projected the CHD event in China's population aged 35-84 years (Moran et al. 2010). This has allowed the projection of trends for stroke and CHD from 2010 to 2030. The finding reported a 23% increase in a cardiovascular event during a 20 year period. It

demonstrated that although the level of risk factors remains, CVD will possibly increase with the effects of an ageing population and a continuous population growth.

The Rotterdam ischemic heart disease and stroke computer simulation (RISC) model was developed by using the Monte Carlo Markov model in the Netherlands (Kempen et al. 2012). This model aimed to estimate the effect of the modifying risk factors on the burden of CVD, as well as performing the internal validation with the Rotterdam 5-years of follow-up study. The model simulated the 13-years risk of getting CHD, stroke, CVD death and non-CVD death, in the Rotterdam cohort. The Monte Carlo Markov model was performed with six states: 1) the CVD death state; 2) non-CVD death state; 3) CHD state; 4) Stroke state; 5) CHD and stroke state; and 6) the well state (alive without any CVD conditions). The probability of changing the health state was calculated from the Cox-proportional hazard model. It was found that the risk of CVD event was increase from year 5 to year 12. In terms of the validation, the model performed well when comparing the number of observed and expected occurrences within 5-10 years period.

The Markov's model for projecting the burden of stroke was conducted in South Korea (Kang et al. 2011). The Markov state transitional included the post primary stroke event, alive post stroke and dead. The model simulated the life time stroke by using the transitional probability, based on the epidemiological study in South Korea and the literature review. The life time cost of stroke was calculated and included both the health care aspect and economic aspect, such as the cost of treatment and cost of the loss of productivity. It was estimated that people who start getting stroke at age 45 years have the year of life lost from stroke was 15.5 years for men and 17.62 years for women. The life time cost for stroke also depended on the age of onset, which means that the

younger the age of getting the first stroke, the more life time costs to pay (Kang et al. 2011).

The evaluation of the effectiveness of the primary prevention and the risk reduction strategies to reduce the CVD events was studied in some previous studies using the Markov's state transitional model. Pletcher et.al (2009) estimated the impact of the primary prevention strategies on lowering cholesterol level, to the reduction of CHD risk. The CHD policy model was applied to the US population aged 35 – 85 years. The input parameters were the risk factors from the National Health Survey during 1999 to 2004, vital statistics, cost of treatment for statin and other publish data. The Framingham risk function was used to calculate the probability of getting CHD. The model projected the number of CHD events between 2010 to 2014 and the impact of lowering serum cholesterol based on the public health impact of adult treatment panel III (ATPIII) guideline. The ATPIII guideline recommended treatment for the serum cholesterol lowering based on the cholesterol level and the calculation of the individual CHD risk. It was found that lowering the cholesterol level, according to the ATPIII guideline, with statin would prevent 20,000 events of MI and 10,000 CHD deaths per year and the incremental cost effectiveness of statin contributed to $42,000 per quality adjusted life year (QALY).

Martin et.al (2004) developed the Markov's model for projecting the 20 year survival from CVD in the UK cohort aged 35 to 65 years. The Whickham cohort was used as the baseline data. The transitional probability was derived from the Framingham's equation. The model evaluated the accuracy with the number of observed events in this cohort. The impact of changing the coronary risk factors, such as cigarette smoking, has been evaluated. It was found that the model's performance closely estimated the actual survival events. The elimination of CVD risk factors would

gain an increased life expectancy of 4 years for all 35 year old men and 1.8 years for all 35 year old women. It was concluded that the model performed an accurate prediction in the CVD free people, who had systolic blood pressure below 180mmHg and underestimated for people who had systolic blood pressure over 180 mmHg (Martin, Vanderpump and French 2004). Mistry et.al (2012) investigated the cost-effectiveness of the primary prevention intervention for CVD by using the Markov's modelling approach in the EUROACTION study across 6 countries in Europe. The purpose of modelling was to compare the cost-effectiveness of the CVD primary prevention intervention, to the usual care, after implementing the intervention for 1 year in the high risk group. The intervention group received the lifestyle changing intervention and management for controlling blood pressure and lipids. At an individual level, Markov's model was used to simulate the CVD events over an 11 years period, in both the intervention group and the usual care group. The transitional probability came from the published literature, expert opinion and the Framingham equation. The incremental cost per QALY gain was calculated, to compare the cost-effectiveness of the intervention group against the usual care group. It was found that changing the lifestyle intervention was more costly and more effective over the usual care approach (Mistry et al. 2012).

Another study in Sweden also estimated the effects of a primary prevention program, to reduce the CHD in the elderly population, using Markov's model (Lindgren et al. 2003). The primary intervention focused on the dietary program, exercise and combining both dietary and exercise. The Markov's model was developed with the CHD states, such as without CHD, first year of MI, second year of CHD events, the following year of disease and death. The Framingham equation was used to calculate the risk of CHD. The model predicted the effect of the primary intervention and presented the cost-effectiveness of the intervention, life year gain and the cost per life year gain. It was found that the most cost-effective intervention was a dietary program

which contributed to save 0.0228 life years compare to no intervention (Lindgren et al. 2003).

Cobiac et.al (2012) identified the most cost-effectiveness intervention for primary prevention in Australia by developing a discrete time Markov model. The model projected the ischemic heart disease and stroke event over the life time, in the general population aged 35 to 84 years, and estimated the impact of the mix-primary prevention programs such as lifestyle change, pharmaceutical intervention and the population wide primary prevention intervention. There were four health states in the Markov model, which were: fatal or non-fatal IHD, and fatal or no-fatal stroke. The cost-effectiveness analysis was presented in both cost per QALY and cost per DALY. The finding from this study suggested that the most cost-effective invention was the limitation of salt in the manufactured food product, which would produce more impact than the pharmaceutical intervention. However, changing the lifestyle intervention and exercise did not produce a strong impact in this study (Cobiac et al. 2012).

The Markov model is more flexible than the decision tree model but the restriction of the Markov model is the assumption that the model has no memory for the previous states. For example, once patients move to the next state, the model has no memory of which state they came from and will treat all patient as homogenous. Therefore, it might be difficult to model more complex prognoses using the Markov model (Drummond, et al. 2005, Briggs, Claxton and Sculpher 2006).

2.4.3 Discrete event simulation (DES)

The discrete event simulation is sometimes referred to as micro-simulation or individual sampling models. It performs the advance simulation at the patient-level by tracking the individual's progression to each stage, instead of using aggregated data. The discrete event simulation allows simulating the events of an individual, when the

state can occur more than once. The model is transited by the probability of the individual. The variation of time of the individual throughout the process is included in the analysis, which allows more complexity and flexibility such as the time. It is suitable for modelling complicated disease conditions or specific health problems (Briggs, Claxton and Sculpher 2006).

The CVD policy model was the microsimulation model in Australia. This model projects the incidence of CHD and hospitalization (Mui 1999). The model found a decline of 13% and 24% in the incidence of CHD in the male and female population respectively. However, the model projected an increase in the number of hospitalisations by 40%, this largely being due to the increasing aging population. This study suggested that the micro-simulation model is advantageous for projecting and planning in the future health problem, however, the availability of data required is a concern. Battes et.al (2013) discussed the benefits of the microsimulation technique over the classical regression model and Markov's model. The microsimulation was more feasible in calculating the lifetime risk and incorporated the change of some risk factors over time, such as patient age. It allowed estimating the multiple outcomes of the individual patients with the time dependent or the repeated outcomes which might occur in the patients. These were the strengths of microsimulation when compared to the regression analysis, which just calculates single events over a certain period of time and Markov's model which has no memory of the previous health state (Battes et al. 2013).

The PREVENT model(Gunning-Schepers 1989) was a microsimulation model which was originally developed for predicting the effects of changes in risk factor prevalence and the health effects in the population levels in the Netherlands. The results from the PREVENT model provided suggestions to use in policy making to

help determine the target population and compare scenarios with and without intervention, on the change of the future prevalence of events (Gunning-Schepers 1989). The PREVENT model showed a reasonable estimation when testing the model validity against other models. The model was applied to predict the mortality of IHD in the Danish population, with the effect of reducing the CVD risk factors, such as hypertension, hypercholesterolemia, cigarette smoking and physical activity (Bronnum-Hansen and Juel 2000). The PREVENT model took into account the change of risk factors over time. The input parameters in the model were the population size during 1993 from Statistics Denmark, the cause-specific mortality rate for the year of the model start, the all causes mortality and the relative risk of each individual risk factors. The risk factors data came from the various sources such as: the prevalence of hypertension and hypercholesterolemia from part of the MONICA study, the prevalence of smoking from the nationwide survey, and the physical activity data from the Danish Health and Morbidity Survey. All those risk parameters came from the same period of the year onset in the model. It was showed that the most effective intervention on the reduction of IHD mortality was the reduction of smoking. The IHD would be reduced by one-third within 10 years from reduction of the prevalence of smoking, to be 10% lower for men and 15% lower for women. The other risk reduction interventions which affected the IHD mortality, was the reduction of the prevalence of hypercholesterolemia by 25%, and undertaking gentle exercise of at least 4 hours a week, would reduce death from IHD by 3-6%, at ages below 65 years (Bronnum-Hansen 2002).

The Canadian's Population Health Model (POHEM) (Will et al. 2001) was a dynamic microsimulation model which was developed by Statistic Canada. The model was designed based on the interaction between the set of risk factors and specific chronic diseases. The individual-level data on health care cost, the health-related quality of life and the Health Utility Index Mark 3 (HUI3) were included in the analysis.

The POHEM model is currently developing a sub-model for specific chronic diseases. The common risk factors such as smoking, BMI, total cholesterol and blood pressure were incorporated into the model. There are four disease specific sub-models which are: a heart diseases model, a diabetes model, an osteoarthritis model and a cancer model. The dynamic model was allowed to simulate the continuous-time, the population age change, the co-morbidities, the change in risk factors and the progression of disease. It provided a lifetime projection for a large population representative for Canada (Statistic Canada 2010, Will et al. 2001).

Babad et al. (2002) described the development of a new CHD Policy Model which uses the discrete event simulation technique. This study was a collaborative project between the Department of Health at the London School of Hygiene and Tropical Medicine (LSH andTM) and the University of Southampton and the University of Birmingham (Babad et al. 2002). The model was purposed to estimate the impact of the primary prevention strategies to prevent CHD for the UK population. A discrete event simulation model was created to simulate the CHD events of the individual, with their CHD risk profile. The CHD events were simulated for each individual by sampling from the probability distribution. It allowed the change in risk factors, disease status and event rates by taking into account new distribution parameters and the sample of discrete event time. A number of data were required to conduct this model. The health survey for England (HSE) was used as the baseline data for the population characteristic and coronary risk factors. The Framingham study was used to derive the time-to-disease-event distribution and provided information on the natural history of CHD, with the capability to distinguish between the CHD states, to stable or unstable angina, MI or Stroke. The Framingham equation was considered for use for the risk calculation. The British Regional Heart Study (BRHS) was used to calibrate the results with the Framingham study. The model contained the modifiable risk factors such as age, gender,

systolic blood pressure, total cholesterol and smoking. The outcome events were: stable or unstable angina, MI (heart attack), sudden cardiac death, stroke death, other CVD death, cancer death, and death from the other causes. The effect of primary prevention programs were evaluated in the model, such as the reduction in blood pressure, cholesterol and smoking. The treatment parameters were determined to further analyse such changes as the uptake rate, compliance rate and the effectiveness. The model was running the PASCAL simulation, which was known as POST (Patient Oriented Simulation Techniques). The data from the health survey for England was manipulated to generate a population size factor in the database. The model will run for the life-time of each individual. This model was under the development process. However, there was no published literature to date about the results from the model.

The World Health Organization (WHO) and the Organization Economic Co-operation and Development (ODEC), developed the chronic disease prevention model named the CDP model (Sassi 2010). The CDP model is a dynamic micro-simulation model, which is capable of estimating the impact of health investment on the intervention to prevent chronic diseases. The web of causation was used to link the causal relationship between the modifiable risk factors and the occurrence of chronic diseases. The CDP model individually estimated the health outcome by age, gender and socio-economic status. The strength of the CDP model was that it is unique from the other exiting models. The simulation was designed for the dynamic risk factors and the environmental factors, with the continuously interaction and capability to simulate the complexity of the reality. It was the first and only model too date, which simulates the health behaviour and obesity to chronic diseases, with the pooled data analysis from individuals across 30 countries (Sassi 2010). Cecchini et.al (2010) used the CDP model to investigate the health effect due to the unhealthy behaviour such as unhealthy diet, physical inactivity and obesity, in 6 low-middle income countries: Brazil, China, India,

Mexico, Russia, and South Africa. It was found that increasing the price of the unhealthy diet and reducing the price of a healthy diet, had the largest effect on the heath gain from chronic diseases in the short term. The intervention that targeted on child obesity, such as the restriction of food advertising, was more effective than the school-based intervention (Cecchini et al. 2010).

The discrete event simulation has some limitation with regard to data availability and the computational burden. The model requires individual data, such as patient characteristics, remission and recurrent experience, type of intervention undertaken and the time the individual remained in each stage. The model provides a precise evaluation when all data are available. The computational burden is discussed in terms of the complexity of the model, which requires time for development, especially in a large cohort data set. Furthermore, there is difficulty when performing, in terms of the uncertainty of the expected cost and outcome, because the sensitivity analysis has to run all uncertainties of every parameter in the model. It also requires specialist software and hardware to perform the analysis (Briggs, Claxton and Sculpher 2006).

2.4.4 The other types of CVD modelling

Other types of CVD modelling include the mathematic model which have been developed for specific purposes of different studies.

The IMPACT model was developed to estimate the CHD death in England and Wales between1981-2000 (Unal, Critchley and Capewell 2005). This IMPACT model was a cell-based mortality model, which was developed in a Microsoft Excel spreadsheet. The detail of the IMPACT model was described elsewhere in an online website (www.healthimpact.org.uk). The IMPACT model was validated to estimate the change in CHD mortality in several countries such as UK, USA and China (Critchley et al. 2004, Unal, Critchley and Capewell 2004, Ford et al. 2007). The IMPACT model

was used to investigate whether the primary prevention in a healthy population, was more effective than the secondary prevention, (Unal, Critchley and Capewell 2005). This model estimated the numbers of CHD patients, treatment, trends of CVD risk factors and mortality saving, due to the reduction of specific risk factor changes in a healthy population and in patients with CHD. The model used a 35.5 million population base, aged between 25 to 84 years. The estimation of change in risk factors and mortality in the general population, was calculated from the regression equation from the systematic review of the MONICA study. The impacts of risk factors change involved smoking, total cholesterol and blood pressure. Patients in this model were divided into group categories which were: an acute MI, survival of MI, revascularization patients, patients with unstable angina, chronic angina and chronic heart failure. Statin and other treatment interventions were taken into account as the impact of secondary prevention in patients. This study estimated that reduction in primary prevention had a fourfold impact on the larger reduction in the mortality of CHD, when compared to the secondary intervention. The decline of 35% in smoking effected the reduction of around 29,715 deaths in the UK population. The fall of serum total cholesterol of 4.2% contributed to 5,770 fewer deaths. Blood pressure reduction by 7% resulted in saving approximately 5,870 deaths. Overall the reduction in those three major risk factors resulted in 81% fewer deaths in a health population and 19% fewer deaths in CHD patients.

2.4.5 Selection of the appropriate modeling approach

Selection of the appropriate modeling approach is a crucial step for the model developer to construct an effective model which can identify the whole picture of health problems according to the objectives and the characteristic of the data. Several studies have been reviewed in order to select the most appropriate health economics modeling for this study.

Karnon and Brown (1998) showed the difference approach of the decision tree, Markov model and the discrete event simulation model by demonstrating the breast cancer scenario and comparing the strengths and limitations of each method. These authors suggested that the decision tree was suitable to model an event and intervention in a short-time period. The Markov chain models are suggested as being most appropriate when events occur over a long period. The discrete event simulation was modeled by shifting the probability of the individual in each stage which showed more flexibility than the decision trees and Markov model. If using adequate and reliable data, it can provide confidential information. However, it requires time and specialist software to conduct the model (Karnon and Brown 1998). Karnon (2003) also compared the Markov model to the discrete event simulation by demonstrating the calculation of the cost-effectiveness in the alternative adjuvant therapies for breast cancer. Even though the discrete event simulation was more flexible and more complex than the Markov model, both models showed similar results. Therefore, the discrete event simulation is appropriate to use when the available data points out specific characteristic. This is due to the time and resources required to build up the complex model while the simpler analytic modeling can answer the same questions (Karnon 2003).

Barton (2004) suggested the model selecting approach which is illustrated in the diagram below (Figure **2.4**). When selecting the type of model, it need to consider the potential interaction between the individual, the level of modeling need (cohort or individual), path way structure and the number of the extensive stages. For example, if the health problem address the interaction between the individuals or having a complex number of stages the discrete event simulation is more appropriate to use than the decision tree or Markov model (Barton, Bryan & Robinson 2004). Brennan (2006) described the model structural and the selection criteria which is classified by a taxonomy of the models. The taxonomy classified the economic evaluation model by

the modeling level (cohort or individual), the interaction allowance and time consideration. Brennan provided the checklist for selecting the model which emphasized the need to consider the timing for cost and health outcome, whether or not heterogeneity population, the population size, the interaction between individual and the need of the sensitivity analysis (Brennan, Chick & Davies 2006).

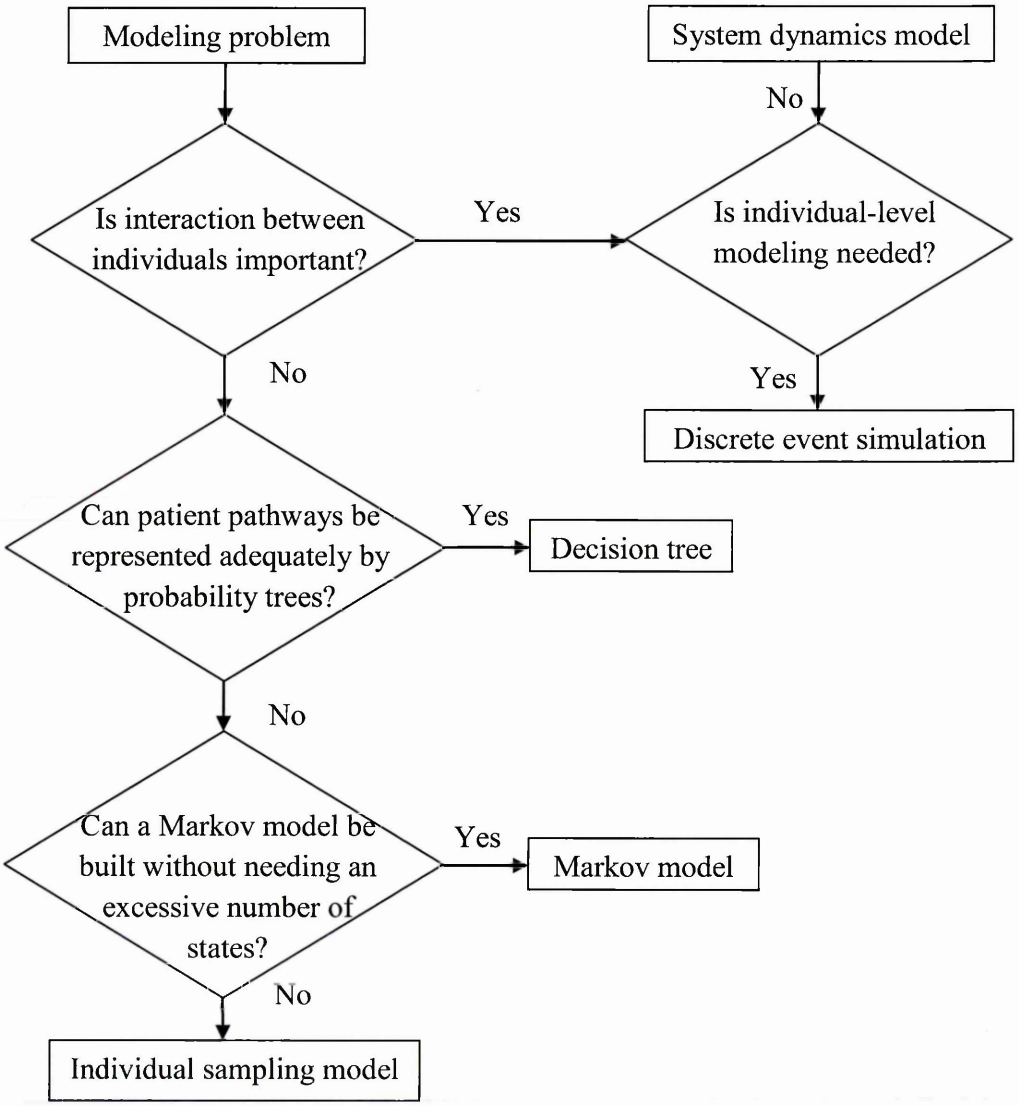


Figure 2.4 Diagram for selecting an appropriate model (Barton, Bryan and Robinson 2004)

Table 2.4 Comparison of the health economic decision modelling techniques

Content	Decision Tree	Markov Model	Discrete-event simulation	Other types of modelling
Key Methodology	To determine the optimal strategies when it has decision alternative under conditions of uncertainty	To model the health state and the effect of intervention over the state transition by time of an evaluation into cycles.	To simulate the patient-level for the specific events experienced for each individual. It usually uses Monte-Carlo simulation method.	To estimate the future health problems and the impact of the interventions
Use for	1)Any decision process which can be classified into the tree-like structure 2)Event occur over a short time period	1)The progression of disease 2) The ongoing risk which occur more than once. (recurrent event) 3) The progression through the different state	1) Modelling the specific events which are experienced by the individual. 2) Event oriented based on each individuals. 3) Simulate the time to event	1) Estimating the future events and the impact of the intervention. 2)Specific purposed of study or specific population
Structure	Tree-like structure	Cycle of the transition state depend on the disease	Pathways are tracked independently by the individual data over time	Various
Move state by	Probability	Probability of transition (assume that it is constant over time)	Transition probabilities vary by time of the individual in each state.	Various
Timing	Untimed	Timed	Discrete or continuous timed	Untimed
Interaction	No	No	Allowed	No
Benefit	1) Capable to project the outcomes and evaluate the optimal alternative. 2)Develop the clinical	1) Possible to model the repeated set of the outcome over time. 2) Allow to model for long time	1)Allow more complexity of the model 2) Incorporate each individual history and the interaction between the	1)Capable to project the health outcome events. 2) Reflect a large population

Content	Decision Tree	Markov Model	Discrete-event simulation	Other types of modelling
	guideline 3)Clearly and exactly for explaining and criticizing 4) Capable to measure the variability of the number of individual in each state. 5)Reflecting to a large population assumption	period.	individual which is suitable for modelling the infectious diseases. 3) More Flexible and confidential.	assumption 3)Capable to design for the specific population 4) Capable to apply when the data is limited.
Limitation	1) not able to calculate the recurrent of diseases and looping 2)suitable only for a short period of time	1) When moving to the next state, the model will not memorize the previous state. It focuses only on the current cycle. 2) Has a fixed length of the operation cycle.	1)Require specific software to construct 2) Cannot perform without the adequate data. 3) Require the specialist analysis, control and validation, or else it will be lead to the miss-interpretation. 4) Demand for time to develop model 5) Concern for the over complexity.	1) The model is static and not taking into account the time or the change over time. 2) May not capture all complexity of the event as in the reality

2.4.6 Summary

In summary, this section reviewed the principal concepts of decision modelling techniques, which are widely used in health economic evaluation in many countries (Brennan, Chick and Davies 2006, Barton, Bryan and Robinson 2004). Table 2.4 Comparison of the health economic decision modelling techniques provides a summary of each type of model in terms of the key methodology, advantages, timing, interaction,

benefits and limitations. Overall, the decision tree and Markov model use the aggregated data while the discrete simulation uses the individual level data.

According to Barton (2004) and Brennen (2006) criteria for selecting modeling approch, this study will focus on modeling data at population level with no interaction between the individual and the population aggregated data of risk factors. So, the discrete event simulation are not considered in this study. Hence, during the period of study, there are lack of the information on the CVD probability, particularly in Thailand such as the transitional probability of the disease progression, the probability of the severity of disease, the remission rate, the recurrence rate and information related to the time to event of CVD patients. This is why we can not consider the Markov model or the Simulation model for the analysis. In this end, this study will develop a CVD model for Thailand, which adapted the concept of the cost offset model. The model was mainly to focus to incorporate the risk assessment algorithm to estimate the number of CVD events (such as a number of hospital admission and death from CVD) over 5 to 10 years period if population level risk factors such as smoking, systolic blood pressure and cholesterol level can be reduced or contain.

2.5 Disability Adjusted Life Years (DALYs)

2.5.1 The concept of summary measures of population health

Health indicators are used for comparing the health status between populations or between times, studying on the inequality of the health status, such as the difference between gender and the socioeconomic status, measuring the size of the health problems, prioritizing the health problems, planning for the health investment and assessing the health outcome (Global Forum for Health Research et al. 2006). In the past, single health indicators such as the mortality rate or morbidity rate were widely used to reflect the health problems in the population, by measuring the mortality event or the mortality event and disability (Murray, Salomon and Mathers 2000). However, using the single health indicator captures the health situation in only one dimension. The summary measures of population health are the composite health indicators, which are combined of both fatal and non-fatal health outcomes, to measure the health status in the population. They are divided into two concepts: the health expectancies and the health gaps (Robine, Romieu and Cambois 1999), which are explained below;

1) The health expectancy is the years of living with full health or the healthy life year span, which is adjusted for the year of living with disability or year of living with illness. It demonstrates the quality of life and is mostly used in cost-effectiveness analysis. Some indicators are adjusted for the disability free or healthy life year such as the Disability Free Life Expectancy (DFLE), Disability Adjusted Life Expectancy (DALE) or Health Adjusted Life Expectancy (HALE).

2) The health gaps present the difference between the ideal health status and the actual health status. It calculates the gap between the years of premature death, illness or disability and the year of living with full health. For example, the DALYs are the

indicator that measures the health gaps between the year of life lost and the year of living with disability.

2.5.2 Disability adjusted life years (DALYs)

DALYs are one type of the health indicator to measure the overall health status in the population, which combines mortality, morbidity and disability and use it as one indicator to compare with the different health problems. This indicator had been developed by researchers at Harvard University, World Bank and the World Health Organization (WHO) in 1993 (Lopez, et al. 2006) . It was widely used in prioritizing health problems, planning for health investment and assessing the health outcome. To calculate DALYs, it requires various data sources, such as the number of death by ages and gender, size of the population, the epidemiological data, such as the prevalence rate, incidence rate, remission rate, case-fatality rates or the relative risks, duration of diseases and the age at onset of the diseases (Murray 1994, Devleesschauwer et al. 2014, Rushby and Hanson 2001).

The DALY calculation formulas are as follows:

$$DALY = YLL + YLD \quad (2.1)$$

$$YLL = N \times L \quad (2.2)$$

Where, N is the number of deaths, L is the age-specific life expectancy

$$YLD = I \times DW \times L \quad (2.3)$$

Where, I is number of new cases or the incident case in the period of time, DW is the disability weight and L is the duration of illness

2.5.3 Years of Life Lost (YLL)

The Years of Life Lost (YLL) is one of the components of DALYs. It measures the number of years of the life that are lost from premature death and compares thi to an average life expectancy of the individual in each age group, based on the underlying assumption that the life years lost are different in each age groups. The life table is used to calculate YLL and the unit of measurement is life years (Mathers et al. 2005). There are four methods that are used to calculate YLL, based on the different patterns of death and the type of life tables (Murray 1994) which are: 1) Potential Years of Life Lost (PYLL), 2) Period Expected Year of Life Lost (PEYLL), 3) Cohort Expected Year of Life Lost (CEYLL) and 4) Standard Expected Year of Life Lost (SEYLL). Each method is described below.

1) Potential Years of Life Lost (PYLL) is the measurement of the years of life lost due to the premature death prior to the referenced age. The number of life years are compared with the life years lost at the specific age, e.g., PYLL(70) refers to year of life lost compared to the death at age 70. The data from the death registration system and the case fatality data from the Ministry of Public Health are used in the calculation. The benefit of using PYLL is it presents the loss from premature death and has the capability to be compared across the different populations. However, the limitation of PYLL is that people who die at ages beyond the reference age are not included in the calculation and there are no standards for determining the reference age. PYLL is calculated by using the formula below.

$$PYLL = \sum_{x=0}^{L} d_x(L-x) \tag{2.4}$$

Where, L is the highest age which expects everybody will dead , d_x is the number of deaths in each age group and x is the Age at death.

2) Period Expected Year of Life Lost (PEYLL) is the number of years of life lost from premature death which is calculated by using the period life table. The data sources that are used in this method are: the number of deaths by age and gender from the death registration system, case fatality data and the national life table. The benefit of using PEYLL is that it uses the period life table, which can be used to calculate the life years lost in a specific age group.

$$PYLL = \sum_{x=0}^{L} d_x e_x \tag{2.5}$$

Where, e_x is the expected age of living in each age group, d_x is the number of deaths in each age group and L is the highest expected age of death.

3) Cohort Expected Year of Life Lost (CEYLL) is the number of life years lost from premature death which is calculated by using the cohort life table in each generation. The data from death registration, number of case fatalities by age group and the cohort life table are used in the calculation. CEYLL is well suited to present the life years lost in the cohort but it cannot be used to compare over long periods of time because the cohort life table changes. It is a generation and country specific formula. In the case of Thailand, there are no cohort life tables available to perform this calculation.

$$CEYLL = \sum_{x=0}^{L} d_x e_x^c \tag{2.6}$$

Where, e_x^c is the age interval of living in each age group from the cohort life table, d_x is the number of deaths in each age group and L is the highest age of death.

4) Standard Expected Year of Life Lost (SEYLL) is the number of life years lost due to premature death which use the standard life table (West level 26) in the calculation. Using the standard life table in calculating SEYLL allows the comparison of the number of life years lost across countries and over time. However, SEYLL is not suitable for some countries which have high life expectancy, such as Japan, Sweden, Australia and Switzerland, because their populations live longer than the highest age in the standard life table. The data required to calculate SEYLL are from the death registration, case fatality data and the standard life table (West level 26). The burden of diseases and injury, (BOD) studied in Thailand also used the SEYLL to calculate the number of years of life lost because of the availability of mortality data and using the standard life table (West level 26) for the life expectancy by age and gender.

$$SEYLL = \sum_{x=0}^{L} d_x e_x^s \tag{2.7}$$

Where, e_x^s is the expected age of living in each age group from the standard life table, d_x is the number of deaths in each age group and L is the highest age of death.

2.5.4 Years of life lost due to disability (YLD)

YLD is one of the components of DALYs. It presents the number of years of life lost during the disability from health problems. It requires data from the disability incidence, the disability duration and the age onset of the disability. The disability weights are used in the calculation according to the level of severity of disease (Vos et al. 2013).

$$\text{YLD} = \text{I} \times \text{DW} \times \text{L} \tag{2.8}$$

Where, I is the number of new cases or the incident case in the period of time, DW is the disability weight and L is the duration of illness.

2.5.5 Disability Weights (DW)

The disability weights are the valuations of the health status and the severity of disease, based on the social perspective of the health problems or disability compare to the ideal health status. The maximum value of disability weights is 1 which refers to death and the minimum is 0, equivalent to the perfect health. The disability weight is used to calculate the years lost due to disability, (YLD), by multiplying it with the number of cases and duration of illness. In this study the disability weights of the cardiovascular and circulatory disease from the global burden of disease study in 2010 are used (Murray et al. 2012a).

2.5.6 Discounting

Discounting is the method used for adjusting the future value to the present value. The present value means the value of cost, utility and benefit at the present time, which is adjusted for the changing of value in the future. When implementing the interventions in the health care system, discounting is involved in both the monetary benefit and the health benefit. In terms of the monetary benefit, the discounting will be taken into account with the opportunity cost and the time preference. For example, if one deposits a £1000 in the bank for 1 year, it will earn interest at a value of £2.50 per year. However, if one spends a £1000 on investment, there may be more benefit than saving the money in the bank. The time preference referred to the uncertainty of the value and the declining of marginal utility. This assumed that the present value is more valuable than the value of money in future. If personal income is increasing in the future, the value of £1 in the present will be more than £1 in the future. In terms of the health benefits, there is the uncertainly of the health problems in each individual age group and the opportunity to die from the disease. The discounting will determine the value of death in different age groups; therefore the value of years of death in younger people is

different from an older age group. WHO and the World Bank Health Sectors use the discounting rate at 3% to transfer the value of a year in the future to the current year. For example, when using 3% of the discount rate, it means 1 healthy year in the next 10 years is less than 24% of the current year. Therefore, if there is a gain of 1 healthy year in the next 10 years, it will equal to 0.76 of the current year.

Discounting formulas

1) Present value

$$Cost_{PV} = \frac{Cost}{(1+r)^t} \tag{2.9}$$

Where, $Cost_{PV}$ is the present value of cost, $Cost$ is the future number of money that must be discount, r is the discounting rate, t and the number of time (in year) where the discount rate has been applied (r and t have to be in the same range of time)

2) Discounting continuous streams of life

2.1) Discrete formula

$$n_{PV} = (1+r)^{0.5} \times \frac{1}{r} \times \left[1 - \left[\frac{1}{1+r}\right]^n\right] \tag{2.10}$$

2.2) Continuous formula

$$n_{PV} = \frac{1}{r} - \left[\frac{1}{r} \times e^{-r \times n}\right] \tag{2.11}$$

Where, n_{PV} is the present value of the number of years, n is the number of years that must be discount, r is the discounting rate , 0.5 is the weighting value and e is the exponential function.

2.5.7 Age weighting

The age weighting is used to value the year of life according to the age preferences. If there are 2 patients who are aged 20 years old and 3 years old are admitted to the emergency unit at the same time, most people may decide to save the life of 20 years old patient because of the external factors, such as the family relationship, family bonding and social prospective. The age weighting will focus only on the age difference and will not consider the external factors. However, there are some arguments for using the age weighting to value the life of people. In terms of the human capital approach, it is assumed that the value of years of life is difference between different ages. Labour age gains more productivity than children and the elderly. They have the potential to produce more than they consume and can support the other age groups. Therefore, saving the life of a labour age person will gain more benefit than saving the life of a child. On the other hand, when considering the life lost approach, most people will choose to save the life of younger age groups over older age groups, because more life years can be saved in children than in the elderly. In addition, rather than considering the benefit in a static time, it should take into account the future benefit. When the government implements the intervention for children, such as health care or education, they will gain more benefit in the future and increase the future productivity. In terms of the cost-of-illness approach, it will focus only the differential of age groups but does not include any other factors. Children and elderly are both considered as the dependency age groups, which require the support of the labour force age group. The mathematical formulation of differential age weights is shown below.

$$Age\ weight = Cxe^{-\beta x} \quad (2.12)$$

Where, β is the relative age weight function, which determines the important value of each age groups. C is the adjustment constant, WHO using c= 0.1658 in the global burden of disease study.

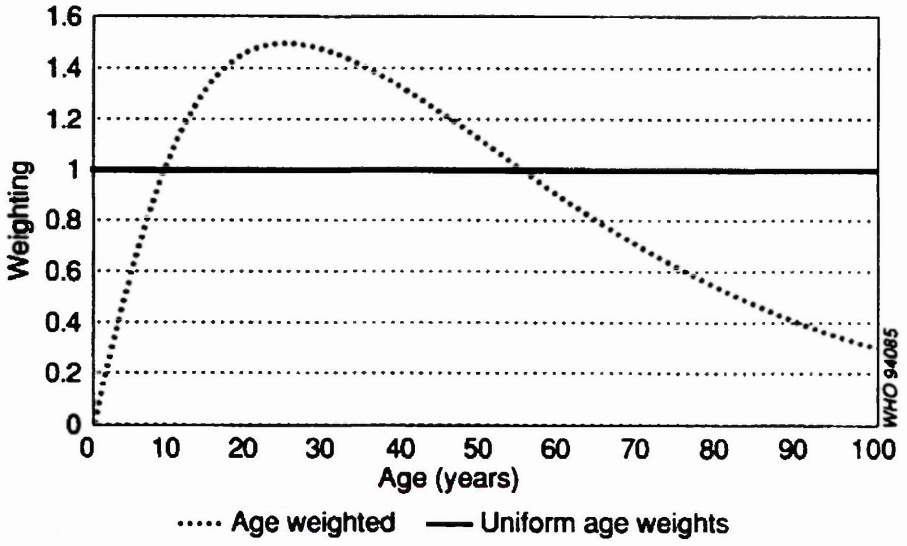


Figure 2.5 The age weight functions (β)

Source: (Murray 1994)

2.5.8 Summary

DALYs are the combination of the measurement which can present the health status of the population in both morbidity and mortality. It is capable of comparing the health status in different populations and over different periods of time. In addition, DALYs presents the burden of disease for the non-fatal health outcomes. It can be used in prioritizing health problems for the health policy because it presents the health problem in the same unit of measurement. These are the benefit of DALYs over the other single health indicators, such as the mortality rate, incidence or prevalence rate.

For example, when using the only the mortality rate, prioritising the health problem in Thailand in 2000, the top 5 health problems were cancer, road traffic injury, CHD, hypertension and stroke. On the other hand, when using DALYs to prioritise the health problems in the same years, the top 5 health problems were AIDS, road traffic injury, CVD, cancer and suicide. Furthermore, it also widely used in the cost-effectiveness analysis of health intervention. However, there are some limitations of using DALYs. First, it needs various data sources to calculate the DALYs. Furthermore, there are some arguments in the method of calculation, such as using the disability weight from the expert opinions, using age weight, which values the year of life in younger people more than the older people. Moreover, the definition of the cause of death and disability uses a single cause, so it may not cover the complication of diseases and the multiple causes of death and disability.

2.6 The public health risk reduction strategies for CVD

This section reviews the public health risk reduction strategies to reduce the prevalence of CVD in the population. The reviews focus on both global target risk reduction goals and the national goals specifically for Thailand.

2.6.1 The global target risk reduction strategies for CVD

In 2011, The United Nations (UN) General Assembly declared the 25 × 25 millennium goal, to reduce the global mortality of four non-communicable diseases by 25% by 2025 (United Nations General Assembly 2011). Those four non-communicable diseases (NCD) are CVD, chronic respiratory diseases, cancer and diabetes. The six risk factors were targeted, which were: 1) reduction of 30% in prevalence of tobacco smoking, 2) reduction of 10% in alcohol consumption per person, 3) reduction of 30% of salt intake in average the population, 4) Stop the rising in the prevalence of obesity, 5) reduction of 25% of the prevalence of high blood pressure and 6) Stop the rising in

prevalence of diabetes (The NCDs alliances 2014). Furthermore, WHO also set the additional goals of treating the NCD patients which are providing 80% coverage of the NCD medicine and technologies and 50% coverage of the drug therapy and counselling (World Health Organization 2014). Kontis et.al (2014) estimated the impact of reducing risk factors, according to the UN 25 × 25 millennium goal by conducting the systematic analysis and meta-analyses (Kontis et al. 2014). It was found that if all six risk factors are reached in a population who are between 30 to 70 years old, the probability of dying from those 4 non-communicable diseases will decline by 22% in men and 19% in women, between 2010 and 2025. Additionally, it will also save a number of premature deaths by approximately 37 million worldwide.

Table 2.5 The UN millennium goal target risk reduction in the population

Risk factors	**Target risk reduction in the population** **(UN millennium goal by 2025)**
Smoking	Reduce 30% in prevalence of tobacco smoking
Alcohol use	Reduce 10% of alcohol use per person consumption
Salt intake	Reduce 30% in average population intake
Obesity	Stop rising in prevalence
Blood pressure	Reduce 25% of the prevalence of high blood pressure
Blood glucose and Diabetes	Stop rising in the prevalence of diabetes

2.6.2 The target risk reduction strategies for CVD in Thailand

The 11th National Health Development Plan in Thailand (2012-2016), states that:

"All Thai citizens are healthy and take part in creating a sufficient health system with equity, leading to social wellbeing" (Ministry of Public Health 2012).

The goals of the 11th National Health Development Plan are targets to reduce morbidity from preventable diseases and unhealthy lifestyles, improve the quality of the health care system and health care service providers, improve the disaster monitoring system and put in place an active health promotion and disease prevention plan. The 10 years targets of this plan are to increase the life expectancy at birth of Thai people to 80 years of age and state that the healthy life expectancy should be at least 72 years. For the target strategies related to CVD in Thailand, It was stated that within 3-5 years, the mortality rate for CVD (included both MI and stroke), should be less than 20 per 100,000 population and 90% of Thai people who are aged 15 years and over receive screening for diabetes and hypertension. Every single year, at least 50% of the diabetes patients who are identified are capable of controlling their blood sugar levels. At least 40% of newly identified hypertension patients could control their blood pressure and 100% of diabetes and hypertension patients, who have these disease complications, are treated and have access to the health care services, (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2013).

According to the Thailand healthy lifestyle strategic plan (2011-2020), the aims are to reduce the non-communicable diseases due to an unhealthy life style, namely: diabetes, hypertension, heart disease, cerebrovascular disease and cancers (Ministry of Public Health 2011). The risk reduction strategies are promoting the sufficiency life styles, which are having a balanced diet, undertaking adequate physical exercise and having suitable emotional management. This strategy is divided into three phases, short

term (1-3 years, 2011-2013), medium term (5 years, 2011-2015) and long term (10 years, 2011-2020). The main development goals of the short-term strategies are: emphasize the collaborative policies on the healthy diet, advocate physical activity and healthy environment for all target populations at central, regional and provincial level. Increase the satisfaction with the health policy in the target population and improve their health behaviours to prevent the occurrence of chronic disease due to lifestyle. Increase fruit and vegetable consumption and decrease the sweet, salty, fatty, chemically contaminated food intake and decrease alcohol consumption and tobacco smoking. The medium-term goals are targeting on the metabolic risk factors, which are decreasing obesity among children younger than 15 years old and obesity in adults who are aged 15 years and older, increasing an active physical lifestyle, decreasing blood cholesterol and the prevalence of metabolic syndrome among population age 15 years and older, increasing the skill of emotional management amongst the population age 15 years and older and reducing the proportion of the disease complication among the patients who have the chronic diseases. The ultimate long-term goals of this plan are increased disease-free, and disability free life expectancy of the Thai population, a decrease in the mortality rate of the lifestyle diseases, a decrease in the health care expenditure of treatment of the lifestyle diseases and no increase in the prevalence of the lifestyle diseases.

2.6.3 The target CVD risk reduction for the individual in Thailand

According to the national guideline for reducing CVD risk factors in the Thai population, there are three groups in the target population, diabetes mellitus patients, hypertension patients and the general population (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2013). The general population's level of risk of CVD is classified by the probability of 10-years risk to

CVD events of the individual, calculated by using the CVD risk assessment from WHO/ISH (Otgontuya et al. 2013). The low risk group of CVD refers to people who have 10-years risk lower than 10%, the medium risk group are 10% to <20%, the high risk group are 20% to <30% and the severe risk group are more than 30% of 10-years CVD risk. The multiple CVD risk factors are targeting on blood pressure, blood glucose, total cholesterol, LDL, HDL, Triglycerides, cigarette smoking, weight, waist circumference, physical activities and food consumption. For blood pressure control in diabetes patients, the target risk reduction strategy is using the suggestions from an evidence-based guideline report, from the panel members appointed to the 8th Joint National Committee, 2014 (JNC8) (James et al. 2014), for the management of high blood pressure in adults. The following table summarizes the target of reducing CVD risk factors for the individual in Thailand.

Table 2.6 The target CVD risk reduction for the individual who aged 40 years and over in Thailand

Target	DM patients	HT patients	General population (no DM and HT conditions)
Blood pressure (mmHg)	<140/90*	<140/90	<140/90 (age<60years) and <150/90 (age≥60 years)
Blood glucose			
FPG(mg/dL)	70-130		60-100
HbA1c(%)	6-7		
Lipid Profiles			
Total Cholesterol (TC)mg/dL	<280 (for medium risk group**) <200 (for high and severe risk group***)		
Low Density Lipoprotien (LDL) mg/dL	<160 (for medium risk group) <100 (for high risk group) <70 (for severe risk group)		
HDL (mg/dL)	>40 (men) >50 (women)		
Triglyceride	<150 (mg/dL)		
Cigaratte smoking	Smoking cessation		
BMI	18.5 – 24.9 kg/m^2		
Waist circumference	< hight/2 (cm)		
Physical activity	Moderate physical activity, at least 30 minutes/time and 5 times/week		
Food consumption	Reducing sweet, fatty and salty food consumption Increasing fruit and vegetable consumption		

Source: (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2012)

*The JNC 8th guideline (James et al. 2014)

**Medium risk group refer to 10-years risk probability of CVD events 10-<20%

***High risk group refer to 10-year risk probability of CVD events 20-<30% and Severe risk group refer to 10-year risk probability of CVD events ≥30%

2.6.4 Summary

The public health risk reduction strategies have been reviewed at both global and national level. The global level is the UN millenniums goal for reducing the mortality rate from NCDs, which targets six modifiable risk factors. For the national policy level in Thailand, there are two plans of health development stated by the Ministry of Public Health. The 11th health development plan and the Thailand healthy style strategies plans which are both aims to reduce the number of deaths from the lifestyle diseases in the general population and improve the health care coverage for people with the CVD complication. However, it was not stated clearly in the Thailand healthy life style strategies plan, by what percentage of reducing the risk factors among population it wanted to achieve. It stated only "increase", "decrease" or maintains the level of risk factors at the same state. For the individual risk reduction goal in Thailand, it has been focused on the population at the high risk age of 40 years old.

The study target risk reduction will be assessed according to the national guidelines. The UN mellenium development goal will also be used as the target risk reduction scenario in this study.

Chapter 3 : Method

3.1 Introduction

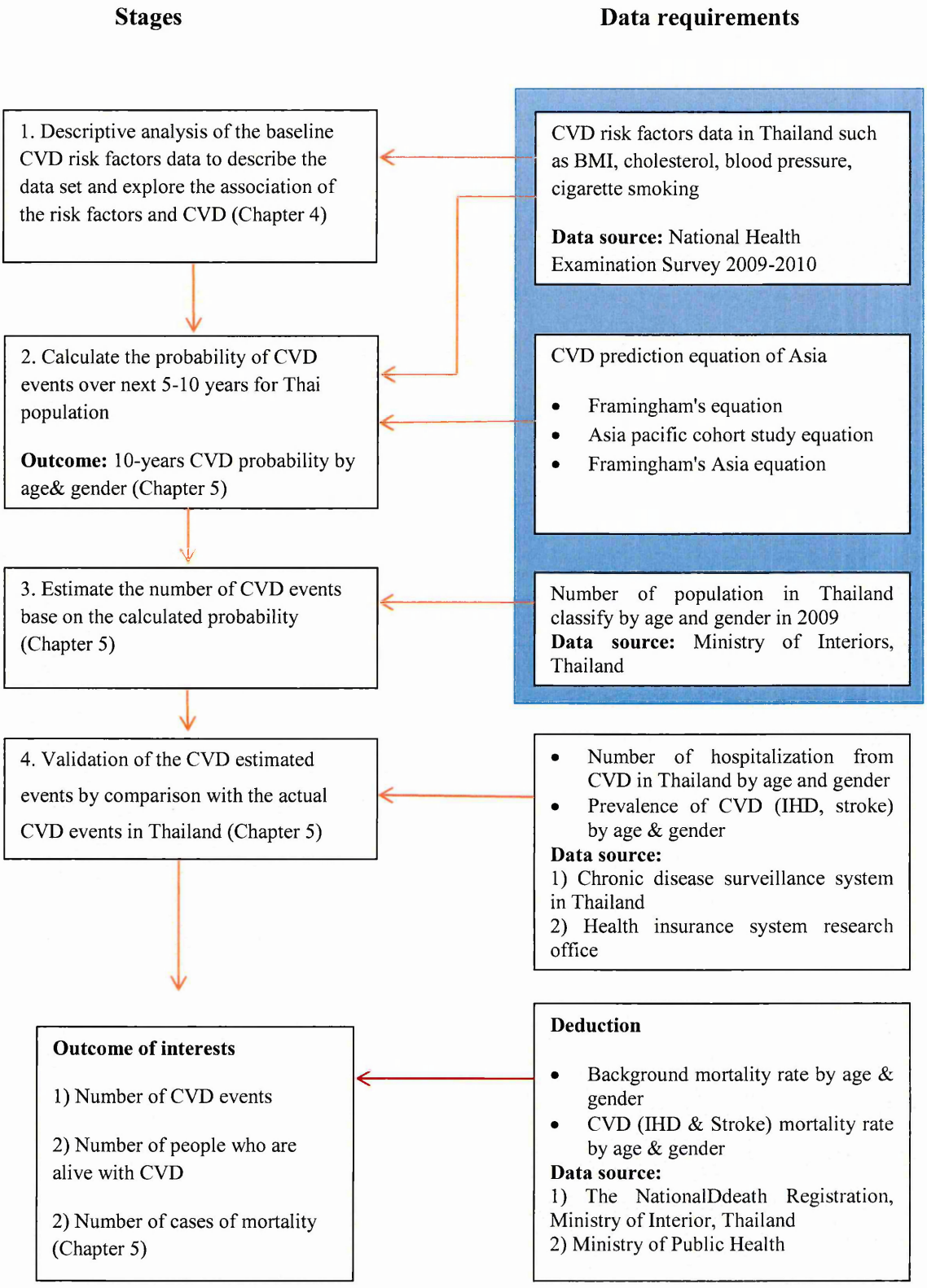
Obesity, hypertension, hypercholesterolemia and cigarette smoking are common risk factors for CVD. These classical risk factors, apart from smoking, have continuously increased in Thailand over a decade, which has led to an increase in the prevalence of CHD and stroke among the Thai population (Aekplakorn, et al. 2010). Although the Ministry of Public Health has implemented many primary prevention programs, the effects of reducing these multiple risk factors in the population, in terms of health benefit and health care cost savings, are still unclear, because the number of health economic and decision models in Thailand are limited. This study will obtain a mathematical model which can be used to estimate the future prevalence and the impacts of reducing risk factors through the public health strategies. The model will calculate the future possible events of CVD, such as MI, stroke and mortality, for people who have those multiple risk factor profiles. In addition, it will also estimate the expected cost for hospital admissions, the expected burden in terms of the DALYs, as well as simulating the potential impacts of the prevention interventions strategies, such as DALYs saving and hospitalisation cost saving. The purpose of this chapter is to address the aims, objectives and the two main key questions about this study. This research will focus on two main areas. First is the CVD modelling for Thailand, by applying mathematical models to estimate the 8 to 10 years prevalence and the DALYs of CVD. Secondly, an exploration of the cost of CVD hospital admissions in Thailand and to estimate the impact of reducing CVD risk factors in the population level on the health care cost and DALYs. This section will outline the research methodology to be adopted in this study.

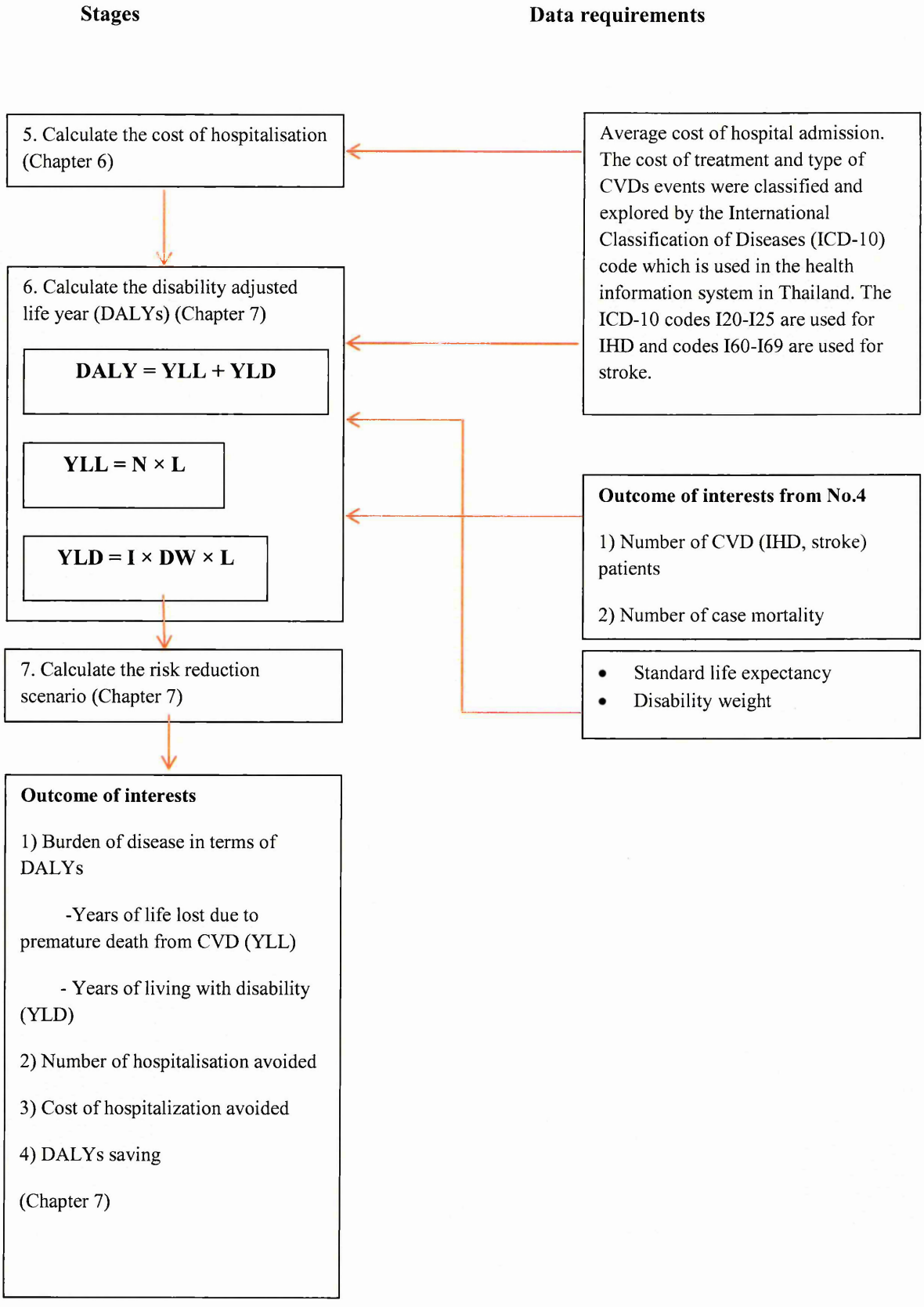
3.2 Research methods

This study has used the concept of the cost offset model approach, which previously developed for estimating the possible clinical and potential financial impact of the population-level health risk reduction program in the UK over a 5 year period (Whitfield et al. 2006). Whitfield's model estimated the impact of reducing population level CVD risk factors on the acute hospital admissions avoided, premature death avoided and potential revenue cost saving.

This study will develop the model further by not only estimated the impact in terms of the number of hospital admisssion and cost, but also estimated the future burden of CVD in term of DALYs. The model using individual risk data for estimating the probability of future CVD events, and then apply those probabilities to the data held on the Thai population in 2009. The model is used to estimate the number of hospital admissions and calculate the consequences of the risk reduction strategies, in terms of the burden of diseases (DALYs). A spreadsheet cost offset model has been developed, based on the risk factors data from the 4th National Health Examination Survey (2008-2009) (NHESIV) Thailand. The CVD risk profiles of the individuals included BMI, systolic blood pressure, total cholesterol and regular cigarette smoking. These risk factors data were entered into the spreadsheet to calculate the probability of all fatal and non-fatal CVD events, MI or stroke and the number of acute hospital admissions over 8 to 10 year period. The model will integrate the background knowledge of epidemiology and health economics. The model will also combine various data sources to address the study research questions, for example population level data, the demographic data, the epidemiology, risk factor level, health services and health care cost analysis. The methods, data set and data analysis are explained in the following stages diagram of developing CVD cost offset model.

Stages of developing CVD cost offset model




Stages
Data requirements
5. Calculate the cost of hospitalisation (Chapter 6)
Average cost of hospital admission. The cost of treatment and type of CVDs events were classified and explored by the International Classification of Diseases (ICD-10) code which is used in the health information system in Thailand. The ICD-10 codes I20-I25 are used for IHD and codes I60-I69 are used for stroke.
6. Calculate the disability adjusted life year (DALYs) (Chapter 7)
DALY = YLL + YLD
YLL = N × L
YLD = I × DW × L
Outcome of interests from No.4
1) Number of CVD (IHD, stroke) patients
2) Number of case mortality
7. Calculate the risk reduction scenario (Chapter 7)
Standard life expectancy
Disability weight
Outcome of interests
1) Burden of disease in terms of DALYs
-Years of life lost due to premature death from CVD (YLL)
- Years of living with disability (YLD)
2) Number of hospitalisation avoided
3) Cost of hospitalization avoided
4) DALYs saving
(Chapter 7)

3.2.1 Stage1. The descriptive analysis of the baseline CVD risk factors data to describe the data set and explore the association of the risk factors and CVD. (Chapter 4)

3.2.1.1 Study population

The 4th National Health Examination Survey (2008-2009) (NHESIV) dataset (Aekplakorn, et al. 2010), has been used as the baseline population and provided the risk factors profile of the Thai population. This survey is the most up to date and the largest national representative cross-sectional survey currently available in Thailand. This survey presents the health status, the prevalence of health problems and potential CVD risk factors among the Thai population. This survey sampled 20,450 individuals who were aged ≥ 15 years old in 2009, classified by age and gender in 5 geographical regions; northern, central, north eastern, southern and Bangkok. This data was input to the model as the base population. The sampling procedure of the NHESIV has been described elsewhere (Aekplakorn et al. 2011). The data collection included the health behaviour risk factors that were collected on the questionnaires by the interviewers and a blood sample was taken from each participant to examine for lipid profiles (total cholesterol, HDL, Triglyceride, LDL), fasting blood sugar, haemoglobin, haematocrit and red blood cell morphology. In addition the anthropometry (such as body weight, height, waist and hip circumference, arm span), and physical examination (such as blood pressure, near vision test, walk test and hand grip strength test), were performed in each individual participant. The following are inclusion and exclusion criteria for the data analysis.

1) Inclusion criteria

NHES participants who were aged 15 years and over and had completed the full data collection on the CVD risk factors, such as the lipid profiles, fasting blood sugar, BMI, blood pressure and cigarette smoking status. Of 20,450 participants who were aged 15 years and above, 19,342 participants have been included in the analysis.

2) Exclusion criteria

1,108 participants have been excluded in this analysis because there were some incomplete data of the CVD risk factors.

3.2.1.2 Data analysis

The descriptive analysis of the baseline data from NHESIV was performed to explore the distribution of CVD risk factors. Descriptive statistics are used to explore the characteristics of the study sample, such as mean, percentage and standard deviations. The bivariate and multiple logistic regressions have been performed to explore the association to the CHD and stroke by using the statistical software package, STATA version 12 (StataCorp LP 2011).

3.2.1.3 Outcome of interests

1) The mean level of CVD risk factors by age and gender.

2) The prevalence of CHD and stroke in the NHESIV data set.

3) The mean level of risk factors by CVD conditions (CHD or stroke).

4) The factors that are associated with CHD or stroke in the Thai population based on the national health examination survey data.

3.2.2 Stage 2. Calculate the probability of CVD events over next 5-10 years for the Thai population (Chapter 5)

3.2.2.1 Selecting CVD risk assessment equations for Thai population

CVD risk equations have been critically reviewed through the literature review. There are 5 criteria for selecting the CVD risk equations which are suitable for the Thai population.

1) Setting of studies: The CVD risk prediction equations were derived from the cohort studies which were set in the Asia Pacific regions or Thailand. CVD risk equations, where the population characteristics of the studies were closely matched to the Thai population, were selected. The other well-known equations from the Framingham cohort study, where the characteristics of the study population are different to Thai population, have been selected to compare the performance of the CVD risk equations.

2) Availability of the equations: The CVD risk assessment equations are available in the publications reviewed and clearly described how the equations have been derived and how to apply to the population.

3) Applicability of the equations: The independent variables in the risk assessment equations are applicable to the risk factors data that are available in Thailand.

4) Period of the risk estimations: The risk assessment equations are capable of estimating the CVD risk in the next 5 to 10 year period.

5) Outcome of the estimation: The outcomes are 5 to 10 years probability of getting fatal or non-fatal CVD, IHD, MI or stroke.

According to the selection criteria above, three equations have been selected in the model. First, the Asia-Pacific Collaborative Cohort Study equations (APCS equation), which uses the concept of the Cox's proportional hazard model, which had been derived from 177,077 participants of the cohort studies around Asia and 25,682 Chinese cohorts. The Electricity Generating Authority of Thailand (EGAT) cohort studies also included in this APCS (Asia Pacific Cohort Studies Collaboration et al. 2007). Second, the recalibrated Framingham's equation or the low information Framingham's equation (Framingham Asia), which has applied the Cox's proportional hazard model concept derived from 6,053 participants of the Framingham studies and adjusted for the Asian population, where some risk data is not available (Asia Pacific Cohort Studies Collaboration et al. 2007). Third, the Framingham's equation (Framingham original), using the concept of the Weibull accelerated failure-time models, which have been applied to the Thai population (Khonputsa, et al. 2011). Table 3.1 shows the summary of CVD risk assessment equations which has been selected to estimate the risk of CVD in 8 to 10 year period.

Table 3.1 The selected CVD risk assessment equations

Equations	APCS equation	Framingham Asia	Framingham original
Type of model	Cox's proportional hazard model	Cox's proportional hazard model	Weibull accelerated failure-time models
Follow-up years	8	8	10
Study populations	172,077 participants from the Asian cohorts; 25,682 participants from Chinese cohorts.	6,053 participants from the Framingham Study.	9,373 men and 11,198 women free of previous stroke were included in the risk prediction equation for first-ever stroke, and 8,754 men and 10,783 women free of previous IHD were included in the risk prediction equation for first-ever IHD
Independent factors	Age, gender, systolic blood pressure, total cholesterol, smoking	Age, gender, systolic blood pressure, total cholesterol, smoking	Age, gender, total cholesterol, systolic blood pressure, smoking, diabetes
Outcomes	Fatal and non-fatal CVD events	Fatal and non-fatal CVD events	IHD, Stroke and Overall CVD (IHDandStroke)

3.2.2.2 Data analysis

Calculation of the CVD probability

The NHESIV individual data and the individual risk factor variables were entered into a Microsoft Excel spreadsheet to use as the baseline population. The Framingham's equations (Konputsa et.al 2010), the APCSC equations and the Asia Framingham's equations (Asia Pacific Cohorts Studies Collaboration 2011), were applied to calculate the risk of the population who might be likely to contract CVD. The main outcome prediction is the of probabilities of CVD related events, such as stroke, heart attacks and heart failure. The details of the equations are described below.

1) The APCS equation. The Asia cohort CVD risk prediction equations (Asia Pacific Cohorts Studies Collaboration 2011)

The probability of getting a cardiovascular event within 8 years

For Asian men is:

$$p(8)_{men} = 1 - S(8)_{men} \exp\left\{\begin{matrix} 0.065(age_i - \overline{age}) + 0.027(SBP_i - \overline{SBP}) \\ + 0.095(TC_i - \overline{TC}) + 0.33(smoke_i - \overline{smoke}) \end{matrix}\right\} \quad (3.1)$$

For Asian women is:

$$p(8)_{women} = 1 - S(8)_{women} \exp\left\{\begin{matrix} 0.072(age_i - \overline{age}) + 0.023(SBP_i - \overline{SBP}) \\ + 0.027((TC_i - \overline{TC}) + 0.31(smoke_i - \overline{smoke}) \end{matrix}\right\} \quad (3.2)$$

2) The Framingham's Asia equation for estimating the probability of getting a cardiovascular event within 8 years

For men is:

$$p(8)_{men} = 1 - S(8)_{men} \exp\left\{\begin{matrix} 0.068(age_i - \overline{age}) + 0.012(SBP_i - \overline{SBP}) \\ + 0.015(TC_i - \overline{TC}) + 0.37(smoke_i - \overline{smoke}) \end{matrix}\right\} \quad (3.3)$$

For women is:

$$p(8)_{women} = 1 - S(8)_{women} \exp\left\{\begin{matrix} 0.078(age_i - \overline{age}) + 0.017(SBP_i - \overline{SBP}) \\ + 0.14(TC_i - \overline{TC}) + 0.55(smoke_i - \overline{smoke}) \end{matrix}\right\} \quad (3.4)$$

Where, $S(8)$ is the survival free from the cardiovascular event (in the 8 years average). $\overline{age}$ is the mean age of the NHESIV participants, age_i is the age of the individual, $\overline{SBP}$ is the mean systolic blood pressure of the NHESIV participants, SBP_i is the systolic blood pressure of the individual, $\overline{TC}$ is the mean of total cholesterol of the NHESIV participants, TC_i is the total cholesterol of the individual, $\overline{smoke}$ is the

prevalence of regular smoking of the NHESIV participants, $smoke_i$ is the smoking status of the individual (1=being a regular smoker, 0=not smoking).

3) The Framingham original equation for estimating 10 year probability of CVD event.

Using the Framingham's equation for Thai population from Weibull accelerated failure-time model regression coefficients (Khonputsa P, et.al 2011)

$$m = \text{Constant}1 + \sum_{i=1}^{i=n} \beta_i x_i \tag{3.5}$$

$$u = \frac{\log(t) - m}{\text{constant}2} \tag{3.6}$$

$$p = 1 - e^{-e^u} \tag{3.7}$$

$$\text{CVD risk} = 1 - (1 - P_{IHD})(1 - P_{stroke}) \tag{3.8}$$

Where, m is the interim variables, x_i are the risk factors, β are coefficients estimated from the Framingham study , u is the interim variables for calculating p, t is the time of follow-up in years, and p is the predicted probability of IHD/Stroke by time t. The further information about the constants and the β coefficients of the original Framingham equation shows in (appendix B).

3.2.2.3 Outcome of interests

8 to 10 years probability of getting CVD, IHD or Stroke of the individuals and the 8 to 10 years probability of getting CVD, IHD or Stroke events by age groups and gender.

3.2.3 Stage 3. Estimate the number of CVD event base on the calculated probability (Chapter 5)

Stage 3 estimates the number of CVD events at the national level according to the outcome from stage 2. The study population, data collection and data analysis at this stage are described below.

3.2.3.1 Study population

The Thai population who were aged 15 years and above in 2009.

Table 3.2 Number of the mid-year Thai population in 2009 by age groups and gender

Age groups	Men	Women
15-24	4,683,981	4,532,018
25-34	5,149,508	5,130,746
35-44	5,154,963	5,408,488
45-54	4,058,120	4,388,770
55-64	2,399,309	2,694,633
65-74	1,362,752	1,655,159
≥ 75	749,125	1,086,374
Total	23,557,758	24,896,188

3.2.3.2 Data requirement and data sources

1) The number of mid-year population in Thailand in 2009 has been collected from the Ministry of Interior.

2) The CVD mortality data, the number of CVD deaths by age groups and gender has been collected from the Thailand national health statistic report over the past 10 year period, to calculate an average 10-year probability of dying from CVD by

age groups and gender. The mortality data available to calculate the mortality rate by age groups and gender in Thailand are from 1996 to 2006.

3.2.3.3 Data analysis

The mean of a probability of getting CVD, IHD or Stroke which has been calculated in stage 2 were used at this stage. The underlying assumption at this stage was that the NHESIV data represents the health status of the Thai population during 2008-2009. Thus, the mean probability of getting any CVD event in the NHESIV sample can reflect the probability of getting CVD in the general population, by age groups and gender. The number of Thai population who are aged 15 years and over was used to estimate the number of future CVD events. When multiplying the number of Thai population, with the probability of getting CVD events by age groups and gender, the result was an estimate of the number of people who are likely to have CVD events over 8-10 year periods. The probability of CVD events will include both fatal and non-fatal occurrences. Therefore, the model deduced the number of people who are likely to die before admission to the hospital, which will estimate the number of CVD acute admission events over the next 10 years. Moreover, the model was also adjusted for the different proportion of the population structures between NHESIV and the general population, by age groups and gender.

3.2.3.4 Outcomes of interest

1) The estimated number of CVD patients in Thailand over the next 10 years.

2) The estimated number of the Case-fatality in Thailand over the next 10 years.

3.2.4 Stage 4. Validation of the CVD estimated events by comparison with the actual CVD events in Thailand (Chapter 5)

The estimated number of CVD events using the CVD risk assessment equations was validated for accuracy by comparison with the actual CVD events that occurred in Thailand.

3.2.4.1 Data requirement and data sources

1) The number of inpatient hospitalisation in Thailand

The number of inpatient hospital admissions due to CVD by age and gender during 2007 to 2011 from the national hospitalisation database of the Universal Health Care Coverage (UC) (Supachutikul 1996). The UC is the main health insurance system in Thailand, which covered 75% of the population, approximately 47 million people. This health care scheme is financed by tax revenue to UC cover in and out-patients, health care expenditure, denture, pharmaceuticals, medical equipment, food, hospital admission (common room) and maternal delivery of mainly public health care services (National Health Security office 2008). The number of inpatient admissions from CVD is collected from the National Health Security Office (NHSO). The inpatient cases are classified by ICD-10 which was I00-I99 referred to all CVD, I20-I25 referred to IHD and I60-I69 regard to stroke.

3.2.4.2 Data analysis

The model validation has been performed on the Microsoft Excel spreadsheets. The average of the estimated number of hospital admission per year has been compare with the actual number of hospital admission in 2009. The validation classified by the same age group and gender to make it comparable.

3.2.5 Stage 5. Calculate the cost of hospitalisation due to CVD (Chapter 6)

The average cost of hospital admission for CVD in Thailand were estimated and calculated by using the costing data from the National Health Security Office (NHSO). These analyses were limited to the health care service provider perspective and not include the patients and other indirect expenditure. The cost of treatment and type of CVD events were classified and explored by the International Classification of Diseases (ICD-10^{th}) code, which is used in the health information system in Thailand. The ICD-10^{th} codes I20-I25 are used for CHD and codes I60-I69 are used for stroke and I00 – I99 for all CVD events.

3.2.5.1 Data requirement and data sources

1) The national inpatient cost of hospitalisation data in 2009, Thailand, which included the universal coverage health care schemes from the National Health Security Office (NHSO), Thailand
2) The estimated number of CVD patients.

3.2.5.2 Data analysis

An average cost of hospitalisation and the standard deviations are calculated. The unit of hospitalisation cost were presented in Thai currency. The cost of hospital admission were calculated by multiplying the estimated number of CVD patients with an average cost of hospital admission.

3.2.5.3 Outcomes of interest

The estimated of cost of hospitalisation over an 8 to 10 year period.

3.2.6 Stage 6. Estimation of the burden of CVD (Chapter 7)

Once the model has estimated the CVD events, stage 5 will estimate the burden of CVD in terms of the DALYs.

3.2.6.1 Data requirement and data sources

1) Standard life table west level 26 (World Health Organization 2000) is used to calculate YLL
2) The estimated number of CVD events from stage 3
3) The estimated number of CVD mortality from stage 3
4) The disability weight of the Global Burden of Diseases (GBD) study (Murray et al. 2012a)
5) The number of mid-year population by age and gender in 2009

3.2.6.2 Data analysis

Calculate the disability adjusted life year (DALYs)

DALYs were calculated to estimate the burden of CVD in Thailand. DALYs are the summation of years of potential life lost (YLL) due to premature death and the years of productive life lost due to disability (YLD). The calculation formula for DALY is described below:

$$DALY = YLL + YLD \tag{3.9}$$

Where, YLL is the Year of Life Lost measure the lost years of life due to premature death, calculated by the number of deaths (N) multiplied by the standard life expectancy at of death occur in years (L).

$$YLL = N \times L \tag{3.10}$$

YLD is the Year of Life with Disability corresponds to the number of the lost years of living with disability. It is calculated by multiplying the number of incident cases in that period (I), the average duration of disease (L) and the disability weight (DW) which indicate the severity of the disease from perfect health = 0 to death = 1. The YLD is calculated by:

$$YLD = I \times DW \times L \tag{3.11}$$

To calculate the DALYs, the prevalence of CVD were estimated from the model by the number of hospital admissions. The mortality rate and remission rate will come from the literature reviews. Incident and average duration were derived from the Dismod Software (Barendregt et al. 2003). The disability weights were applied from the Global Burden of Diseases (GBD) study (Murray et al. 2012a).

3.2.6.3 Outcomes of interests

1) Burden of disease in terms of DALYs

2) Year of life lost due to premature death from CVD or IHD or Stroke (YLL)

3) Year of living with disability (YLD)

3.2.7 Stage 7. The risk reduction scenario (Chapter 7)

The targets of the CVD risk reduction were determined from the literature reviews of previous studies, regarding the level of reduction in the potential multiple risk factors such as hypertension, hypercholesterolemia and regular smoker. The model will compare the CVD in 4 different scenarios: the do nothing scenario, the optimistic scenario, achieve the UN millennium development goal scenario and the worst case scenario.

3.2.7.1 Data analysis

The scenario of the percentage of effective reduction were used to calculate the avoidable CVD admission rate, CVD deaths avoided, the average cost of hospital admission saved and DALYs saved. The risk reduction scenario were calculated on the Microsoft Excel spreadsheet.

3.2.7.2 Outcomes of interest

1) Number of hospitalisations avoided

2) The number of deaths avoided

3) Cost of hospitalisation avoided

4) DALYs saving

3.3 Data sources

This section summarises all data requirements and data sources that are used in this study.

3.3.1 List of all data requirements and data sources

The data requirements and data sources for populating the model are shown in.

Table 3.3 Data requirement and data sources

Data requirement	Data sources
1. Baseline population data sampling from the National Health Survey in Thailand in 2009	The National Health Examination Survey 2008-2009 from the National Health Examination Survey Office, Health System Research Institute, Thailand
2. Risk factor data 1) Baseline variables • Age • Gender • Geographical regions 2) Risk factor variables • Height (cm) • Body Mass Index (BMI) • Diabetes status (yes/no) • Fasting Blood Sugar (mg/dL) • Total Cholesterol (mmol/L) • HDL (mmol/L) • LDL (mmol/L) • Triglyceride (mmol/L) • Systolic blood pressure (mmHg) • Diastolic blood pressure (mmHg) • HypertensionStatus (yes/no) • Regular smoking status (yes/no)	The National Health Examination Survey 2008-2009 from the National Health Examination Survey Office, Health System Research Institute, Thailand
3. The admission rate and cost of hospital admissions	The National Health Security Office, Thailand.
4. The mortality rate by age and gender	The national death registration, Ministry of Interior, Thailand and the national health statistic, Ministry of Public Health
5. The mortality rate from CVD or MI or stroke	The national health statistic, Ministry of Public Health
6. Probability of CVD events	Calculated by using the risk assessment equations.

3.4 Data collection

3.4.1 Phase I: The national health examination survey data

The secondary anonymous population data have been collected for the analysis from the National Health Examination Survey Office (NHESO). A letter outlining the proposed research, showing the detailed research proposal and the analysis plan were submitted to the NHESO during January 2011, in order to seek access to use their data. The use of the secondary data is followed by the criteria of the data sharing policy from the Health System Research Institute (HSRI), Thailand. Permission to access and use the data was granted by the National Health Examination Survey Office Thailand (NHESO) in January 2011. (See Appendix C).

3.4.2 Phase II: the number of hospital admissions and the cost of hospitalisation due to CVD

The number of hospital admissions and the cost of hospitalisation has been collected from the National Health Security Office (NHSO). A letter outlining the study including the research protocols, dummy tables, plans for data analysis and the data requested form, was submitted to NHSO during September 2013. The data permission was approved and granted in May 2014. The use of the anonymous hospitalisation data is defined under the criteria of the data sharing policy from NHSO, Thailand (See Appendix C).

3.5 Overall of outcomes of interests

The CVD cost off-set model estimated the various outputs which are:

1) Number of hospitalisations for non-fatal CVD events;
2) Number of DALY lost due to CVD;

3) Cost of hospitalisation;

4) Number of hospitalisation savings due to the reduction of CVD risk factors;

5) Number of DALY savings due to the reduction of CVD risk factors;

6) Health care cost savings due to the reduction of CVD risk factors.

3.6 Other information

3.6.1 Data management procedures

The National Health Examination Survey Office Thailand (NHESO) has agreed to provide anonymous population data in the STATA file format (*. data). This data were kept confidentially on a researcher's computer which is kept secured and is password protected. Only the researcher and the lead supervisor will have access to the data. The data were initially analysed for the general characteristics and risk factor information categorized by age, gender and geographical region. The statistical analysis were performed by using the percentages, mean, standard deviation and 95% confidence interval. The initial results were presented in an aggregate of the population level before being entered into the modelling process.

3.6.2 Ethical considerations

The study does not include UK NHS participants or services, therefore ethics approval from the UK NHS is not required. However, ethical considerations were taken into account to ensure that the well-being of individuals is not compromised. The ethical issues considered are as described below:

1) Recruitment – The data collected is secondary anonymous population data from Thailand. Full permission to access this data has been granted by the National Health Examination Survey Office (NHESO), Thailand and the

National Health Security Office (NHSO), to use for the purposes of secondary data analysis (modelling).

2) Confidentiality – All records of the secondary data were kept confidential and it is strictly anonymous. The name and the identity of the individuals are not associated with the research finding in any way. The data were kept securely and only use by the researcher. The data usage is restricted to the data sharing policy of the Health System Research Institute, Thailand.
3) Consent – This project does not collect data from the individuals, so a consent form is not applicable.
4) Risks and benefits – There are no known risks, harmful and/or discomforts to the individuals associated with this project.

The study was submitted to the Sheffield Hallam University, Faculty of Health and Wellbeing Research Ethics Committee during April 2011 and subsequently received ethics approval during April 2011 (See approval letter Appendix C).

Chapter 4 : Risk factors associated with CVD in Thailand from the 4th National Health Examination Survey 2008-2009

Abstract

Coronary heart disease (CHD) and stroke are ranked in the top five causes of death, in both males and females, as well as a cause of premature death and disability in Thailand. The aim of this chapter is to describe the current situation of CVD and to explore the association of the modifiable risk factors with CHD and stroke in Thailand.

The 4th National Health Examination Survey (NHESIV) dataset has been used in this study. 19,342 participants aged ≥15 years who have completed the data gathering process on CVD risk factors, have been included in the analysis, which comprise 9,246 men and 10,096 women. The descriptive statistic, the bivariate analysis and the multiple logistic regression have been performed to describe and explore the association among CVD risk factors, CHD and stroke. The modifiable risk factors included in the analysis are age, BMI, total cholesterol, triglyceride, high density lipoprotein cholesterol (HDL-C), systolic blood pressure(SBP), diabetes and regular smoking.

The mean age of the participants is 52.7 years. The prevalence of CHD was 2.5% in men and 2.3% in women and the prevalence of stroke was 2.5% in men and 1.6% in women. The overall prevalence of diabetes was 10.1% and regular smoking was 17.9%. When exploring the association of the modifiable risk factors with CHD and stroke, using the bivariate and multivariate analysis, the results show that factors associated with both CHD and stroke are being aged 55 and over, high blood pressure and diabetes. Obesity, high triglyceride level and low HDL-C, only showed association with CHD but does not show any significant association to stroke. Having a high triglyceride level was related to stroke only in women but does not show any association in men. The factors that do not show significant association in both CHD and stroke are high total cholesterol and being a regular smoker.

Although the analysis of the cross-sectional data was not able to identify the cause and effect of the factors relating to CHD or stroke, it showed some association of these modifiable risk factors for CVD. The modifiable risk factors, such as high blood pressure, obesity and diabetes need to be of concern in considering the CVD prevention strategies in Thailand.

4.1 Introduction

CVD has become the leading causes of death and disability in Thailand (International Health Policy Program 2012). The number of patients who were admitted to hospital with CVD conditions has increased year on year (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2010). Over the past decade, the modifiable risk factors, such as obesity, dyslipidemia, systolic blood pressure, diabetes and regular smoking, have been proved to be associated with the cause of CVD in many studies(Hubert et al. 1983, Asia Pacific Cohort Studies Collaboration 2003, Ezzati et al. 2002, Huxley, Barzi and Woodward 2006, Lee et al. 2008, Anand et al. 2008). The increase of CVD patients in Thailand may be caused by changes in lifestyles, such as being less physically active and having an unhealthy diet, which leads to an increase in the level of metabolic risk factors of the individual (Aekplakorn, et al. 2010). The EGAT study, which was a CVD cohort study in Thailand, found that the trend of the mean level of CVD risk factors such as SBP, BMI, total cholesterol, HDL-C and the prevalence of diabetes, increased over a 12-year follow-up period (Sritara et al. 2003), whereas the prevalence of regular smoking declined (World Health Organization, Regional Office for South East Asia 2009). Although it is well known that these modifiable risk factors are related to CVD conditions, the metabolic risk factors may change over time.

This chapter presents the results from the descriptive analysis of the risk factors for CVD. This study aims to describe the current situation of CVD and explore the risk factors that are associated with the CVD conditions, such as CHD and stroke, especially in Thailand. The CVD conditions referred to in this chapter are CHD and stroke.

4.2 Dataset and method

4.2.1 Dataset

The 4th National Health Examination Survey (NHESIV) Thailand is a cross-sectional, population based survey which was conducted in 2008-2009. The main objective of this survey is to present the prevalence of chronic diseases and the potential health risk factors to the Thai population. This survey is a national representative of the Thai health status by age, gender, administrative area (urban/rural) and geographic regions. Stratified four stage random sampling has been applied to the sampling in the Thai population, at the age of 1 year and above, in 20 provinces and the Bangkok metropolitan area. The survey sampling was divided into 3 age groups, 1-14 years, 15-59 years old and 60 years old and above for both sexes. This survey recruited 20,450 adults who were aged 15-59 years and 60 years and above to represent the health status in both the labour force and the elderly. The sampling method has been described elsewhere (Aekplakorn, et al. 2010). The data has been collected by interview using a questionnaire, physical examination, blood examination and urine examination.

4.2.2 Method

The secondary anonymous dataset has been collected from the National Health Examination survey office, National Health System Research institute, Thailand. Full permission was granted including ethical approval to allow access to data to use in this study. Of 20,450 participants aged 15 years and above, 19,342 participants have been included in the analysis. 1,108 participants have been excluded from this analysis because the data was incomplete. The descriptive analysis has been performed on the 4 main classical risk factors for CVD, such as body mass index (BMI), lipid profiles (total cholesterol, triglyceride, HDL and LDL), systolic blood pressure and regular smoking.

It has been descriptively analysed for CVD related conditions that have been reported in participants in the survey, such as hypertension, diabetes mellitus, CHD and stroke. Multiple logistic regressions have been performed to explore the association between these risk factors and CVD conditions.

4.3 The outcome variables

The definition of the outcome variables use a similar definition as that of the National Health Examination Survey IV. The outcome variables are CHD and stroke. For the further information see (Terms and definitions page xiv) of the Thesis.

4.4 Results

Table 4.1 shows the general characteristic of the NHESIV participants aged ≥ 15 years. There were 9,246 men and 10,096 women included in the analysis. 20.8% of participants are at age 55 to 64 years. Although 60.4% of men and 50.6% of women had normal BMI levels (BMI 18.5 to <25 kg/m^2), 22.2% of men and 29.2% of women were overweight (BMI 25 to <30 kg/m^2). Additionally, 5.6% of men and 11.4% of women were obese (BMI ≥ 30 kg/m^2).

In terms of the lipid profile, 51.1% of men and 60.5% of women had high total cholesterol levels. 38.9% of men and 33.9% of women had high triglyceride level. Furthermore, 35 % of men and 57.7% of women had low levels of the HDL-C which is considered as a risk for CVD.

Moreover, 33.3% of men and 31.9% of women had high blood pressure. 9.3% of men and 10.9% of women had diabetes. 34.4% of men were current regular smokers, whereas, 2.7% of women were regular smokers.

Table 4.1 The general characteristic of the NHESIV participants aged ≥15 years classified by risk factors of CVD and gender

Risk factors	Men (n=9,246)	Women (n=10,096)	Total (n=19,342)
Age groups (years)			
15-24	9.9%(919)	8.3%(834)	9.1%(1,753)
25-34	9.6%(889)	9.5%(962)	9.6%(1,851)
35-44	13.9%(1,287)	15.7%(1,581)	14.8%(2,868)
45-54	13.6%(1,256)	15.9%(1,600)	14.8%(2,856)
55-64	20.8%(1,920)	20.8%(2,096)	20.8%(4,016)
65-74	21.4%(1,975)	19.5%(1,969)	20.4%(3,944)
≥75	10.8%(1,000)	10.44(1,054)	10.6%(2,054)
BMI categories (kg/m^2)			
<18.5	11.8%(1,090)	8.8%(885)	10.2%(1,975)
18.5 - <25	60.4%(5,584)	50.6%(5,106)	55.3%(10,690)
25 - <30	22.2%(2,054)	29.2%(2,952)	25.9%(5,006)
≥30	5.6%(518)	11.4%(1,153)	8.6%(1,671)
High total cholesterol (TC≥200mg/dL)			
No	48.9%(4,519)	39.5%(3,989)	44.0%(8,508)
Yes	51.1%(4,727)	60.5%(6,107)	56.0%(10,834)
High triglyceride (TG≥150mg/dL)			
No	61.2%(5,654)	66.1%(6,669)	63.7%(12,323)
Yes	38.9%(3,592)	33.9%(3,427)	36.3%(7,019)
Low HDL-C (<40mg/dL in male and <50 mg/dL in female)			
No	65.0%(6,014)	42.3%(4,273)	53.2%(10,287)
Yes	35.0%(3,232)	57.7%(5,823)	46.8%(9,055)
High blood pressure			
No	66.7%(6,168)	68.1%(6,873)	67.4%(13,041)
Yes	33.3%(3,078)	31.9%(3,223)	32.6%(6,301)
Diabetes mellitus			
No	90.7%(8,384)	89.1%(9,000)	89.9%(17,384)
Yes	9.3%(862)	10.9%(1,096)	10.1%(1,958)
Regular smoking			
No	65.6%(6,062)	97.3%(9,820)	82.1%(15,882)
Yes	34.4%(3,184)	2.7%(276)	17.9%(3,460)

Table 4.2 presents the prevalence of CHD and Stroke in the NHESIV for participants aged 15 years and over, classified by risk factors of CVD. The modified risk factors are the gender, age groups, BMI categories, high total cholesterol, high triglyceride, low HDL-C, high blood pressure, diabetes and regular smoking.

For CHD, the prevalence of this in men is 2.5% and in women is 2.3%. The prevalence increases respectively with an increase of the age groups. The highest prevalence of CHD is 5.3% in participants who are aged over 75 years old. The lowest prevalence of CHD is 0.2% in ages 15-24 years and 25-34 years.

The prevalence of CHD also increases, according to an increase of the BMI categories, the highest prevalence of CHD occurs in 3.7% of participants who had an obesity condition (BMI $\geq$30 kg/m^2). The second highest prevalence of CHD is 3.2% of participants who had been classified as overweight (BMI between 25 and <30 kg/m^2). The prevalence of CHD is lower in BMI lower than 18.5 kg/m^2 (1.8%) and BMI between 18.5 and < 25 kg/m^2 (2.0%).

In terms of the lipid profile, the prevalence of CHD in participants with high total cholesterol ($\geq$200 mg/dL) is less than those who had normal levels of total cholesterol (2.2% vs. 2.7%). In addition, the prevalence of CHD in participants who had a high triglyceride level was higher than those who had a normal triglyceride level (2.8% vs. 2.2%). Furthermore, the prevalence of CHD in people in the population with low HDL-C was higher than in those who had high levels of HDL-C (2.7% vs. 2.1%).

Moreover, the prevalence of CHD in participants with diabetes mellitus are 5 times higher than those who did not have diabetes (6.5% vs. 1.9%). On the other hand, the prevalence of CHD in regular smokers was lower than in nonsmokers (1.3% vs. 2.6%).

In terms of stroke, the prevalence of stroke in men is 2.5% and 1.6% in women. The prevalence of stroke also arises with an increase in age groups. Therefore, the highest prevalence of stroke was in participants who were aged 75 years and over. The second high prevalence of stroke was in participants aged between 65 and 74 years old and the third highest prevalence in ages between 55 and 64 years old. The prevalence of stroke was less than 1% of participants who are aged lower than 45 years old.

When looking at the prevalence of stroke by BMI categories, it was found that the prevalence of stroke was higher in participants who have a BMI lower than 18.5 kg/m^2 and second highest in those who were overweight, (BMI between 25 and less than 30 kg/m^2). In the total cholesterol level, there was not difference in the prevalence of stroke. 2.1% of participants who had high total cholesterol had a stroke condition and 2.0% of those who had normal levels of total cholesterol had a stroke. In terms of the triglyceride level, the prevalence of stroke in participants who had a high triglyceride level were higher than those who had a normal triglyceride level (2.6% vs. 1.7%). Additionally, the prevalence of stroke in participants who had a low HDL-C level was higher than those who had the highest level of HDL-C (2.2% vs. 1.9%).

In terms of blood pressure, 3.6% of participants with high blood pressure had stroke conditions, whereas 1.3% of participants with normal blood pressure had strokes. The prevalence of stroke in participants with diabetes was higher than those who did not have diabetes (4.4% VS. 1.8%). Conversely, the prevalence of stroke in the regular smoking group was lower than in the non-smoking group (1.6% VS.2.1%).

Table 4.2 The prevalence of CHD and Stroke (%) classified by risk factors in the NHESIV participants aged ≥15 years

Risk factors	N (N=19,342)	CHD (n=466)	STROKE (n=395)
Gender			
Men	9,246	2.5% (233)	2.5% (234)
Women	10,096	2.3% (233)	1.6%(161)
Age groups (years)			
15-24	1,753	0.2%(4)	0.3%(6)
25-34	1,851	0.2%(4)	0.4%(8)
35-44	2,868	0.5%(13)	0.8%(24)
45-54	2,856	1.4%(39)	1.2%(33)
55-64	4,016	3.4%(136)	2.7%(110)
65-74	3,944	4.1%(161)	3.5%(139)
≥75	2,054	5.3%(109)	3.7%(75)
BMI categories (kg/m^2)			
<18.5	1,975	1.8%(36)	2.6%(51)
18.5 - <25	10,690	2%(209)	1.9%(199)
25 - <30	5,006	3.2%(160)	2.3%(115)
≥30	1,671	3.7%(61)	1.8% (30)
High total cholesterol (TC≥200mg/dL)			
No	8,508	2.7%(228)	2%(170)
Yes	10,834	2.2%(238)	2.1%(225)
High triglyceride (TG≥150mg/dL)			
No	12,323	2.2%(271)	1.7%(214)
Yes	7,019	2.8%(195)	2.6%(181)
Low HDL-C (<40mg/dL in men and <50 mg/dL in women)			
No	10,287	2.1%(215)	1.9%(198)
Yes	9,055	2.7%(251)	2.2%(197)
High blood pressure			
No	13,041	1.3%(170)	1.3%(169)
Yes	6,301	4.7%(296)	3.6%(226)
Diabetes mellitus			
No	17,384	1.9%(338)	1.8%(308)
Yes	1,958	6.5%(128)	4.4%(87)
Regular smoking			
No	15,882	2.6%(420)	2.1%(341)
Yes	3,460	1.3%(46)	1.6%(54)

Table 4.3 shows the unadjusted odds ratio and adjusted odds ratio of the association of the individual risk factors and CVD conditions. The bivariate analysis and multiple logistic regression has been performed in the NHESIV participants aged 15 years and over. The risk factors that had significant association with CHD are described as follows.

The middle and elderly age groups were associated with CHD and the advancing of age also increases the risk of getting CHD. When compared with the unadjusted odds ratio to the younger age group (15-24 years old), being in age group 55-64 years is 1.6 times increased risk of CHD (OR=1. 6. 95% CI 1.3-1.9), age group 65 – 74 years is 2.1 times increased risk of CHD (OR=2. 1. 95% CI 1.7-2.6) and age group 75 years and over is 2.7 times increased risk of CHD (OR=2. 7. 95% CI 2.1-3.3) than the younger age group. In terms of stroke, the risk factors that presented the most significant association with stroke were similar to the risk factors of CHD. People in the middle age group and the elderly were more likely to have stroke than people in younger age group. People at age 55-64 years were 1.48 times more likely to suffer a stroke than those who were aged 15-24 years (OR=1.48. 95% CI 1.18-1.85). The risk of stroke increased to 2.16 times at age 65-74 years (OR=2. 16.95% CI=1.75-2.66). At age 75 years and over, the risk of stroke were 2.09 times greater than people in the younger age group. When modified for the effects of the other variables, the adjusted odds ratio showed that the middle age groups of 45-54 years, 55-64 years and elderly age groups 65-74 years and 75 years and above had significant association with both CHD and stroke.

For the lipid profile, the bivariate analysis showed that participants who had high triglyceride level were 1.3 times more likely to have CHD than those who had a normal triglyceride level (OR=1.3, 95% CI 1.1-1.5). The low level of the good lipid

profile such as HDL-C was also associated with CHD. People who had low HDL-C were 1.3 times more likely to have CHD than those who had the high level of HDL-C (OR=1.3, 95% CI 1.1-1.6). For stroke, the high triglyceride level was associated with stroke. However, the high level of total cholesterol and low level of HDL-C showed no association with stroke. The un-adjusted odds ratio showed that people with high triglyceride level were 1.49 times more likely to suffer stroke than those who had a normal triglyceride level (OR=1. 49, 95% CI=1.22-1.82). However, the adjusted odds ratio of the lipid profiles, such as high total cholesterol, high triglyceride and low HDL-C, did not show association with both CHD and stroke, when controlling the effects of the other variables.

Obesity (BMI≥25 kg/m^2) showed significant association with CHD in both unadjusted and adjusted odds ratio. The bivariate analysis showed that people with the obesity condition (≥25 kg/m^2) were 1.7 times more likely to experience CHD than those who had BMI at the normal level (OR=1.7, 95% CI 1.4-2.1). In addition, the adjusted odds ratio of BMI showed that people who were obese were 1.6 times more likely to experience CHD than those who had a normal BMI level (OR=1. 6, 95% CI 1.31-1.96). On the other hand, there was no association between obesity and stroke.

High blood pressure was significantly associated with both CHD and stroke in both bivariate and multivariate analysis. The unadjusted odds ratio showed that people with high blood pressure had 3.7 times the risk of CHD, than those who had normal blood pressure (OR=3.7, 95% CI=3.1-4.5) and were 2.83 times more likely to suffer stroke (OR=2.83, 95% CI=2.31-3.46). Furthermore, the adjusted odds ratio showed that people who had high blood pressure were 1.81 times at greater risk of experiencing CHD (OR=1. 81, 95% CI 1.47-2.22) and 1.63 times more likely to suffer a stroke (OR=1. 63, 95% CI 1.31-2.03) than those who had normal blood pressure.

Additionally, diabetes also showed a significant association with both CHD and stroke. The unadjusted odds ratio showed that people who had diabetes were 3.5 times more likely to experience CHD than those who did not have diabetes (OR=3.5, 95% CI=2.9-4.3) and 2.57 times more likely to get stroke (OR=2.57, 95% CI = 2.02 – 3.28). Whenthe multivariated analysis was performed , people who had the diabetes condition were 1.85 times more likely to get CHD (OR=1.85, 95% CI 1.49-2.31) and 1.59 times more likely to get stroke (OR=1.59, 95% CI 1.23-2.05).

However, there were some risk factors which did not show any significant association of being a risk to CHD and stroke, such as being women, having high cholesterol and regular smoking.

Table 4.3 The unadjusted and adjusted odds ratio of the association between risk factors and CVD conditions (CHD and Stroke) in the NHEISV participants aged ≥ 15 years

Risk factors	CHD (n=466)				STROKE (n=395)			
	Unadjusted odds ratio	95%CI	Adjusted Odds ratio	95%CI	Unadjusted Odds Ratio	95%CI	Adjusted Odds ratio	95%CI
Gender								
Men	-ref		-ref		-ref		-ref	
Women	0.9	0.8 – 1.1	0.79	0.65-0.97	0.62	0.5-0.76	0.56	0.45-0.70
Age groups (years)								
15-24	-ref		-ref		-ref		-ref	
25-34	0.1	0.03-0.2	0.95	0.24-3.82	0.19	0.09-0.38	1.28	0.44-3.7
35-44	0.2	0.09 -0.3	1.79	0.58-5.51	0.36	0.24-0.55	2.31	0.94-5.69
45-54	0.5	0.4-0.7	4.9*	1.74-13.84	0.52	0.36-0.75	2.96*	1.23-7.15
55-64	1.6*	1.3-1.9	10.53*	3.85-28.8	1.48*	1.18-1.85	6.09*	2.64-14.06
65-74	2.1*	1.7-2.6	12.25*	4.48-33.46	2.16*	1.75-2.66	7.39*	3.21-17.01
≥75	2.7*	2.1-3.3	16.9*	6.14-46.5	2.09*	1.55-2.59	7.63*	3.26-17.85
High total cholesterol (TC≥200mg/dL)								
No*	-ref		-ref		-ref		-ref	
Yes	0.8	0.7-0.98	0.68	0.56-0.83	1.04	0.85-1.27	0.92	0.74-1.14

Risk factors	CHD (n=466)				STROKE (n=395)			
	Unadjusted odds ratio	95%CI	Adjusted Odds ratio	95%CI	Unadjusted Odds Ratio	95%CI	Adjusted Odds ratio	95%CI
High triglyceride (TG≥150mg/dL)								
No*	-ref		-ref		-ref		-ref	
Yes	1.3*	1.1 – 1.5	0.96	0.78-1.18	1.49*	1.22-1.82	1.21	0.97-1.51
Low HDL-C (<40mg/dL in men and <50 mg/dL in women)								
No*	-ref		-ref		-ref		-ref	
Yes	1.3*	1.1 – 1.6	1.03	0.84-1.27	1.13	0.92-1.38	1.01	0.81-1.26
Obesity (BMI≥25kg/m^2)								
No*	-ref		-ref		-ref		-ref	
Yes	1.7*	1.4-2.1	1.6*	1.31-1.96	1.1	0.89-1.35	1.01	0.81-1.25
High blood pressure								
No*	-ref		-ref		-ref		-ref	
Yes	3.7*	3.1-4.5	1.81*	1.47-2.22	2.83*	2.31-3.46	1.63*	1.31-2.03
Diabetes mellitus								
No*	-ref		-ref		-ref		-ref	
Yes	3.5*	2.9-4.3	1.85*	1.49-2.31	2.57*	2.02-3.28	1.59*	1.23-2.05
Regular smoking								
No*	-ref		-ref		-ref		-ref	
Yes	0.5	0.4-0.7	0.57	0.41-0.79	0.72	0.54-0.96	0.64	0.47-0.87

Table 4.4 presents the association between risk factors and CVD conditions in male participants aged 15 years and over, by using the multiple logistic regression. When controlling for the effects of the other variables, the factors associated with CHD in both men and women were being in the middle and elderly age groups (aged 55 and above), being obeses, having high blood pressure and diabetes.

The risk of getting CHD in men and women increased with an advance in age. Men aged 55-64 years had 8.49 times higher risk of CHD (OR=8.49, 95% CI 2.62-27.46) and men aged 65-74 years were 9.44 times more likely to have a risk of CHD, than those who were aged 15-24 years (OR=9.44, 95% CI 2.92-30.49). The risk of CHD was highest at age 75 years and above which was 13.67 times higher than those who were aged 15-24 years (OR=13. 67, 95% CI 4.19-44.61). In addition, women who were in the middle age and elderly age groups were more likely to get both CHD and stroke and the risk increased with an advance in age. Women aged 55-64 years had 16.8 times the risk (OR=16. 8, 95% CI 2.3-123.0), at age 65-74 years had 20.5 times the risk (OR=20. 5, 95%CI 2.81-149.43) and at age 75 years and over had 26.45 times the risk (OR=26. 45,95% CI 3.59-194.5) of getting CHD than women aged 15-24 years.

Furthermore, men who had an obesity condition (BMI$\geq$ 25 kg/m^2) were 1.74 times more likely to experience CHD than those who had a normal BMI (OR=1. 74, 95% CI 1.30-2.32). Women who were obese (BMI$\geq$25 kg/m^2) were 1.49 times more likely to experience CHD than those who had a normal BMI (OR=1. 49, 95% CI 1.12-1.97).

Men who had high blood pressure were 1.72 times more likely to experience CHD than those who had normal blood pressure (OR=1. 72, 95% CI 1.29 - 2.30). Women who had high blood pressure were 1.89 times more likely to experience CHD than those who had normal blood pressure (OR=1.89, 95% CI=1.42-2.54).

Additionally, men who had diabetes were 1.68 times more likely to get CHD than those who did not have diabetes. Women who had diabetes were 2.02 times more likely to experience CHD than those who did not have diabetes.

However, dyslipidemia and being regular smokers did not show any significant association with CHD in both men and women.

The factors associated with stroke in both men and women were being in the middle and elderly age groups, having high blood pressure and diabetes. The middle and elderly age groups showed significant association to stroke in men as well as CHD. Men aged 55-64 years had 4.78 times the risk of experiencing CHD (OR=4. 78, 95% CI 1.88-12.11) than men in the younger age group (15-24 years). The risk of stroke in men was highest at age 65-74 years, which is 6 times higher than the younger age group (OR=6. 00, 95% CI 2.38-15.12). For women, the age group that showed association with stroke were being aged 55-64 years, 65-74 years and 75 years and above. The adjusted odds ratio were presented as follow 55-64 years (OR=12. 22, 95% CI 1.65-90.22), 65-74 years (OR=13. 72, 95% CI 1.86-101.29) and 75 years and above (OR=15. 59, 95% CI 2.08-116.76).

In addition, men who had high blood pressure were 1.52 times more likely to experience a stroke than those who had normal blood pressure (OR=1.52, 95% CI 1.15-2.03). Women who had high blood pressure were 1.8 times more likely to experience a stroke than those who had normal blood pressure (OR=1.8, 95% CI 1.27-2.55).

Men who had a diabetic condition also had a 1.56 times greater risk of experiencing stroke than those who did not have diabetes (OR=1.56, 95% CI 1.11-2.21). Women with a diabetic condition were 1.59 times more likely to experience stroke than those who did not have diabetes (OR=1.59, 95% CI 1.09-2.32).

Furthermore, the factor that showed a significant association with stroke only in women was a high triglyceride level. Women who had a high triglyceride level were 1.51 times more likely to experience a stroke than those who had a normal triglyceride level (OR=1. 51, 95% CI 1.07-2.13).

On the other hand, dyslipidemia, obesity and regular smoker factors were not associated with stroke, when controlled against the effects of the other variables in men. Furthermore there were no associations found between high total cholesterol, low HDL-C, being obese, being a regular smoker and stroke in women.

Table 4.4 The multivariate analysis of the association between risk factors and CVD conditions (CHD and Stroke) in the NHESIV participants aged ≥15 years by gender

Risk factors	CHD (n=466)				Stroke (n=395)			
	Men (n=233)		Women (n=233)		Men (n=234)		Women (n=161)	
	Adjusted odds ratio	95%CI	Adjusted odds ratio	95%CI	Adjusted odds ratio	95%CI	Adjusted odds ratio	95%CI
Age groups (years)								
15-24	-Ref		-Ref		-Ref		-Ref	
25-34	0.38	0.04-3.64	2.44	0.25-23.49	0.42	0.81-2.19	4.98	0.59-41.5
35-44	1.67	0.43-6.51	2.62	0.31-21.85	2.3	0.84-6.32	3.23	0.39-26.4
45-54	4.43*	1.29-15.18	7.33	0.97-55.14	2.52	0.93-6.87	5.44	0.71-41.9
55-64	8.49*	2.62-27.46	16.84*	2.31-123.0	4.78	1.88-12.11	12.22*	1.65-90.22
65-74	9.44*	2.92-30.49	20.48*	2.81-149.43	6	2.38-15.12	13.72*	1.86-101.29
≥75	13.67*	4.19-44.61	26.45*	3.59-194.5	5.83	2.25-15.07	15.59*	2.08-116.76
High total cholesterol (TC≥200mg/dL)								
No	-Ref		-Ref		-Ref		-Ref	
Yes	0.6	0.45-0.80	0.77	0.58-1.02	1.03	0.78-1.37	0.77	0.55-1.08
High triglyceride (TG≥150mg/dL)								
No	-Ref		-Ref		-Ref		-Ref	

Risk factors	CHD (n=466)				Stroke (n=395)			
	Men (n=233)		Women (n=233)		Men (n=234)		Women (n=161)	
	Adjusted odds ratio	95%CI	Adjusted odds ratio	95%CI	Adjusted odds ratio	95%CI	Adjusted odds ratio	95%CI
Yes	0.89	0.66-1.21	1.01	0.75-1.34	1.02	0.76-1.36	1.51*	1.07-2.13
Low HDL-C (<50mg/dL in male and <40 mg/dL in femaie)								
No	-Ref		-Ref		-Ref		-Ref	
Yes	1.01	0.81-1.45	0.98	0.73-1.31	1.13	0.84-1.52	0.87	0.61-1.23
Obesity (BMI≥25kg/m^2)								
No	-Ref		-Ref		-Ref		-Ref	
Yes	1.74	1.30-2.32	1.49	1.12-1.97	0.91	0.67-1.24	1.15	0.83-1.59
High blood pressure								
No	-Ref		-Ref		-Ref		-Ref	
Yes	1.72	1.29-2.30	1.89	1.42-2.54	1.52	1.15-2.03	1.8	1.27-2.55
Diabetes mellitus								
No	-Ref		-Ref		-Ref		-Ref	
Yes	1.68	1.21-2.33	2.02	1.49-2.73	1.56	1.11-2.21	1.59	1.09-2.32
Regular smoking								
No	-Ref		-Ref		-Ref		-Ref	
Yes	0.52	0.36-0.75	0.97	0.47-2.09	0.59	0.43-0.82	0.97	0.39-2.41

4.5 Discussion

This chapter has showed the analyses of the national cross-sectional data which was collected during 2008-2009. The strength of the NHESIV is that it is the largest national representative cross-sectional survey, which can present the health status of the general Thai population during that period. However, there are some limitations. Although the bivariate analysis and multivariate analysis present the associations between the risk factors and the CVD conditions, it is not able to present the causal relationship between these risk factors and CVD. Therefore, the results do not show the cause and effect of risk factors to CVD.

The risk factors that show no association with CHD or stroke in both bivariate analysis and multivariate analysis are high total cholesterol and regular smoking (Table 4.3 and 4.4).This might be because people who already had CHD or stroke had received treatment to control their blood total cholesterol, such as receiving a cholesterol lowering drug. Additionally, once they had been diagnosed that they had CHD or stroke, they also changed their unhealthy lifestyle and stopped smoking.

When adjusted for an effect of the other variables in both men and women (Table 4.4), the risk factors that are associated with CHD, in both genders, are being in the middle and elderly age groups, having high triglyceride levels, having low HDL-C, being obese (BMI $\geq$ 25 kg/m^2), having high blood pressure and diabetes. The analysis did not show significant associations with higher total cholesterol and regular smoking and the result also showed no association in the bivariate analysis. However, when analysing the association with gender, all lipid profiles were not related to CHD. This might be due to the limited number of CHD cases, when performing the analysis by gender, which was not a large enough sample to show any significant association.

Furthermore, the factors associated with stroke were being in the middle age and elderly age groups, having high blood pressure and diabetes. There was no association between all lipid profiles, obesity and regular smoking, when performing the multivariate analysis in both genders. However, having high triglyceride level showed significant association with stroke but only in women.

Although the middle age and elderly age groups show a significant association with both CHD and stroke in women, the 95% confidence interval among women was very wide across the age groups factor (Table 4.4). This was because there are very few numbers of stroke cases in the reference age groups of 15-24 years and the number of stroke cases in women aged 55 years and over, was higher than in the other age groups. Another reason was the NHESIV randomly selected the sampling in the general population, there are few numbers of CHD and stroke cases found in the survey. If there were a larger number of cases, it may have showed a more precise association in 95% confidence interval.

Chapter 5 Application of CVD risk assessment equations to the Thai population

Abstract

The CVD risk assessment equations have been developed in many studies in order to estimate the risk of getting CVD in asymptomatic people. However, those CVD risk equations have been deemed suitable for the specific target population and there are a limited number of CVD risk equations in Thailand. The objectives of this chapter are 1) To calculate the probability of CVD events by applying 3 different equations, which are: the APCS equation, the Framingham-Asia equation and the original Framingham equation, to the individual risk factors data from the NHESIV, Thailand. 2) To estimate the number of 8-10 years CVD events. 3) To validate and identify the most suitable CVD risk equations for the Thai population.

The individual risk factors from the NHESIV dataset has been entered into a Microsoft excel spreadsheet as the baseline population. The APCS equation, the Framingham-Asia equation and the original Framingham equation, are applied to calculate the probability of 8 to 10 years CVD events by age groups and gender. The CVD events in this analysis refer to all fatal and non-fatal CVD events (ICD10, I00-I99), which include IHD (ICD10, I20-I25) and stroke (ICD10, I60-I69). The individual CVD probability from the NHESIV participants, will calculate the average probability of CVD by age groups and gender. Then, it will be applied to the national population to estimate the number of future CVD events in Thailand. The average CVD mortality rates over a 10-year period are used to calculate the 10-year probability of dying from CVD and estimate the number of CVD deaths. The number of CVD deaths has been deduced in the estimated CVD events, to estimate the number of people who are alive with CVD condition. The estimated number of CVD events has been validated against the actual events in Thailand. The national hospitalisation database has been used to validate the mathematical model.

The following results were recorded when the APCS, the Framingham-Asia and the original Framingham equations, were applied to the NHESIV dataset. The APCS equation calculated the average 8-years probability of getting CVD as 8.3% in men and 7.8% in women. The 8-year probability of CVD in the Framingham-Asia equation were 7.2% in men and 8.1% in women. The original Framingham equation showed the highest probability of 10-years CVD which were 18.8% in men and 11.1% in women.Over the next 8 years, the APCS equation estimated overall 5.0 million CVD cases and the Framingham-Asia estimated 4.8 million CVD cases. While, the original Framingham estimated 8.3 million CVD cases in the next 10 years. Through the validation, we found that all CVD equations overestimated the risk of CVD in the elderly age groups. The original Framingham equation overestimated the risk of CVD in the Thai population in all age groups.

The APCS and the Framingham-Asia equation both performed a better estimation than the original Framingham equation in both men and women.

5.1 Introduction

CVD risk prediction models have been developed in many studies, as a tool to predict the levels of CVD in the future. The most influential prediction models, using statistical multivariate analysis equations, were derived from the Framingham Study (Sritara et al. 2003, Wilson et al. 1998, Cui 2009, Wu et al. 2006). Many studies found that the Framingham's function was suitable for predicting future CVD in the middle aged, US white population and others with similar profiles of CVD risks (Diverse Populations Collaborative Group 2002, Liao et al. 1999). However, some studies showed an overestimated prediction for groups which have different risk profiles and ethnicity such as Asian and some EU populations (Liu, Hong and D'Agostino 2004, Thomsen et al. 2002, Haq et al. 1999, Brindle et al. 2003).

Nevertheless, the Framingham equation gives a generalized prediction, in terms of the biomarker risk factors, such as blood pressure and cholesterol level. Several studies have developed adjustments to the Framingham CVD risk prediction equation, to adapt it for use in specific populations. For example: the QRISK risk score in the United Kingdom and the Asia Pacific Cohort Studies Collaboration (APCSC) (Hippisley-Cox et al. 2007, Asia Pacific Cohort Studies Collaboration et al. 2007).

In Thailand, to date, there is only one CVD risk score, which has been derived from the EGAT cohort study (Vathesatogkit et al. 2012). This study has followed-up 3,499 participants aged 35 to 54 years since 1985. Several studies found that RAMA-EGAT risk score provided a better prediction of CVD than the Framingham equation (Pattanapichakul et al. 2007). Although the CVD risk score was derived specifically for the Thai population, this cohort study was well representative only for Thai middle-class men aged 35 years and over but it was not well representative in women (Sritara et al. 2003).

The objectives of this study are: 1) To calculate the probability of CVD events by applying the three difference equations, which are APCS equation, the Framingham-Asia equation and the original Framingham equation, to the individual risk factors data from the NHESIV, Thailand; 2) To estimate the number of 8-10 years CVD events; 3) To validate and identify the most suitable CVD risk equations for the Thai population.

This chapter presents the results of the application of the CVD risk assessment equations to the Thai populations. The details of the analysis and CVD risk assessment equations has been described in chapter 3, at stage 2 to stage 4. The outcome of interest in this chapter were the probability of CVD events using the three different equations, the estimated number of non-fatal CVD events in the Thai population and the validation of the mathematic model.

5.2 Methods

5.2.1 Selecting CVD risk assessment equations for Thai population

The available CVD risk equations have been critically reviewed through the literature. The APCS, Framingham- Asia and the original Framingham equations have been applied. For more information about the selection criteria of the CVD risk equations see (chapter 3, page 101). The APCS and the Framingham-Asia equations both have been applied to the Asia Pacific cohort study collaboration. The original Framingham equation has also been applied to the Thai population. The APCS and the Framingham-Asia equations both use the same independent factors such as age, gender, systolic blood pressure, total cholesterol and smoking status. The original Framingham equation also included the diabetes status as one of the independents factors. The outcome of the estimation are fatal and non-fatal CVD events. Hence, the original

Framingham equation is able to calculate the risk of getting IHD or stroke seperately. The period of CVD estimation are 8 to 10 years.

5.2.2 Calculation of the CVD probability

The NHESIV dataset has been used as the study population. The individual data and risk factors profile have been entered to an Excel spreadsheet. The APCS, Framingham-Asia and the original-Framingham equations have been applied to the data to calculate the probability of getting CVD in each individual. Then, the mean of 8-10 years probablity has been calculated by age groups and gender. The main outcomes are the probablity of IHD, stroke and all CVD events.

5.2.3 Estimated number of CVD events

The number of CVD events at the national level are estimated by multiplying the CVD probability to the number of the mid-year population in 2009, by age groups and gender, to obtain the number of all CVD events over the next 8 to 10 year period. The probablity of CVD events includes both fatal and non fatal CVD. The analysis excluded those who died based on the statistical information. The average 10-years probability of dying from CVD conditions has been calculated based on the Thailand Health Statistic Report during 1996 to 2006 (appendix H). The 10-years probability of dying from CVD has been multiplied with the population in 2009 (mid-year population) to get the number of people who are likely to die from CVD over the next 10 years . The number of people who are likely to die from CVD has been deducted from the estimated number of CVD events, in order to estimate the number of people who are alive with the CVD conditions over the next 10 years. The number of current CVD cases in 2009 has been statistically estimated from the NHESIV by age groups and gender. Then, the number of current CVD cases in 2009 has been added to the estimated number of people who are

alive with CVD over the next 10 years, to get the number of future prevalence cases of CVD.

5.2.4 Validation of the CVD estimated events

The estimated number of CVD events are validated with the actual number of CVD hospital admissions in Thailand in 2009. The number of CVD cases will be classified by the ICD-10 code in which I0-I99 refers to all CVD events, I20-I25 refers to IHD and I60-I69 refers to stroke. The actual number of CVD admissions come from the National health Security Office, Thailand (NHSO) which covers 75% of all hospital admissions in Thailand and includes the patients who were in the universal coverage health care scheme.

5.3 Results

5.3.1 The probability of CVD events

Table 5.1 shows the comparison of mean probability of CVD, which has been calculated by using the APCS equation, the Framingham-Asia equation and the original Framingham equation in the NHESIV dataset. The mean probability of CVD has been calculated by age groups and gender.

When applying the APCS equation, the overall mean of 8-year CVD probability are 8.3% in men and 7.8% in women. The trend of 8-year probability increased according to age groups in both men and women. The probability of CVD is lowest at age 15-24 years. The probability of CVD starts to increase from the 45-54 years age group The CVD probability in men is higher than in women from the ages 15 to 74 years. Whereas, women have CVD probability higher than men at age 75 years and over.

The mean 8-year probabilities of CVD when using the Framingham-Asia equation are 7.2% in men and 8.1% in women. The minimum CVD probability is at age 15-24 year. At age 45-54 years, the CVD probability in men is 3.2% and 2.6% in women. The CVD probability is equal to 6.7% in both men and women at age 55-64 years. The CVD probability increases with an increase of age groups. Although the trends of CVD probability of the Framingham-Asia equation are similar to the CVD probability that are calculated with APCS equation, the Framingham-Asia calculated the CVD probability in women as higher than in men from age 65 years and over. The 8-year probability of CVD is highest at age 75 years and over.

In terms of the 10-year original Framingham equation, the overall mean of 10-year CVD probability is 18.8% in men and 11.1% in women. The CVD probability in men is higher than in women in all age groups. The lowest CVD probabilities are 1.9% in men and 0.8% in women at age 15-24 years. The CVD probability continuously increases when age increases, in both men and women. The CVD probability is 2 times higher in men than in women at the age 35-44 and 45-54 years. In elderly age groups, the 10-year CVD probability is higher than in the younger age groups and the highest probability of CVD is at age 75 years and over, which are 47.6% in men and 30.8% in women.

Table 5.1 The mean probability of CVD events by age groups and gender amongs APCS equation, the Framingham-Asia equation and the Framingham original equation

Age (years)	8 years-probability of CVD (%)				10-year probability of CVD (%)	
	APCS		Framingham-Asia		Framingham original	
	Men	Women	Men	Women	Men	Women
15-24	0.3	0.2	0.3	0.2	1.9	0.8
25-34	0.8	0.5	0.8	0.4	4.1	1.6
35-44	1.7	1.1	1.6	1.0	6.8	2.8
45-54	3.6	2.7	3.2	2.6	11.5	5.8
55-64	7.8	6.6	6.7	6.7	19.5	11.8
65-74	14.4	13.9	12.1	14.4	30.5	19.6
≥75	26.0	29.5	22.4	30.9	47.6	30.8
Total	8.3	7.8	7.2	8.1	18.8	11.1

Table 5.2 shows the 10-year probabilities of CVD, which are calculated by the Framingham original equation in the NHESIV data set. This equation is capable of calculating three events, which are IHD, stroke, and all CVD events. Table 5.2 presents the mean 10-year probability, by CVD condition, age groups and gender.

The overall mean of 10-year IHD probability is 14.5% in men and 8.0% in women. The trend of IHD probability rises with an increase in age groups. Men have more probability of getting IHD than women in all age groups. The IHD probability is lowest at age 15-24, which are 1.9% in men and 0.7% in women. The probability of IHD at age 25-34 is 3.9% in men and 1.4% in women. The IHD probability in men continually increases in the middle age and elderly age groups. At age 35-44 years, the IHD probability in men is nearly triple that in women, which is 6.3% in men and 2.4% in women. The IHD probability is twice as high in men than in women at age 45-54 years, which is 10.2% in men and 4.8% in women. At age 55-64, the IHD probability in men is 15.9% and 9.1% in women. The IHD probability in elderly age groups, 65-74 years and 75 years and above is higher than the IHD probability in younger age groups.

At age 65-74 years, there are 22.8% of men and 14.0% of women who have a chance of getting IHD. The IHD probability reaches the highest at age 75 years and over, which is 32.4% in men and 20.15 in women.

The average 10-years probability of stroke is 6.2% in men and 3.8% in women. The graph shows that the stroke probability is below 1% from age 15 to 44 years in both men and women. At age 45 – 54 years, there is 1.5% probability in men and 1.2% of women who suffer a stroke. The trend of stroke probability increase from the age of 55 years and men are more likely to have a chance of suffering a stroke than women. The stroke probability is 4.5% in men and 3.1% in women at age 55-64 years. Then, the stroke probability increases in the elderly age groups, which is 10.6% in men and 6.8% in women at age 65-74 years. The stroke probability reaches 24.7% in men and 14.6% in women at age 75 years and above. Compared to figure 5.3, the mean of 10-year probability of stroke is lower than the probability of IHD, in both men and women in all age groups. The overall mean of stroke probability is twice as high than the mean of IHD probability. In men, the probability of IHD is 14.5% and stroke 6.2%. In women, the probability of IHD is 8.0%, while the probability of stroke is 3.8%.

Table 5.2 The mean probability of CVD events by age groups, gender and CVD conditions using the original Framingham equations

Age (years)	10-years probability (%)					
	IHD		Stroke		CVD	
	Men	Women	Men	Women	Men	Women
15-24	1.9	0.7	0.1	0.1	1.9	0.8
25-34	3.9	1.4	0.2	0.2	4.1	1.6
35-44	6.3	2.4	0.5	0.5	6.8	2.8
45-54	10.2	4.8	1.5	1.2	11.5	5.8
55-64	15.9	9.1	4.5	3.1	19.5	11.8
65-74	22.8	14.0	10.6	6.8	30.5	19.6
≥75	32.4	20.1	24.7	14.6	47.6	30.8
total	14.5	8.0	6.2	3.8	18.8	11.1

The graph that compare the probability of CVD when applying the the three differences equation shows in (appendix F).

5.3.2 The estimated number of CVD events in the Thai population over 8 to 10 year periods.

This section presents the estimated number of CVD events when multiplying the probability of CVD in an 8-year and 10-year period, to the number of the national mid-year populuation in Thailand in 2009. The number of CVD events, which have been calculated using three different equations, are the number of total CVD events which included both fatal and non-fatal events of IHD and stroke. Therefore, the number of estimated CVD events will deduct the number of people who are dead from CVD, to obtain the number of people who are alive with CVD. The number of deaths from CVD are estimated by appling the average of 10-year CVD mortality probability, which has been calculated from the national CVD mortality rate in Thailand over 10-year period (1996-2006).

Table 5.3 shows the estimated number of people who are alive with CVD in Thailand in the next 8 to 10 years. In men, the APCS equation estimated 2.5 million, the Framingham Asia equationestimated 2.2 million and the original Framingham equation estimated 5 million, of men who are alive with CVD. The table shows that the original Framingham equation estimated a higher number of CVD events than either the APCS or the Framingham-Asia equations in all age group. The number of estimated CVD patients increase according to age groups. The APCS equation estimated the number of CVD cases as nearly the same at ages 15 to 44 years. However, at age 45 year and above, the APCS equation estimated number of CVD cases higher than the Framingham-Asia equation. The lowest number of CVD cases are at at age 15 to 24

years. The number of CVD cases increases at age 45 years and above. The highest number of CVD cases are at ages 65 to 74.

The estimated number of CVD cases in women in Thailand in the next 8 to 10 years, when applying the 8-year and 10-year probability of CVD from the APCS equation, the Framingham-Asia equation and the original Framingham equation. The total number of estimated CVD cases in women are 3.3 million when applied the 10-year probability of CVD from the original Framingham equation, whilst, the Framingham-Asia equation estimated 2.6 million cases and the APCS equation estimated 2.5 million cases overall in an 8-year period. The table shows that the original Framingham equation estimated a higher number of CVD cases in women than either the APCS equation or the Framingham-Asia equation in most age groups, except at age 75 and over. The lowest number of estimated CVD cases are at age 15 to 74 years. The APCS equation estimates the number of CVD cases in women higher than the Framingham-Asia equation from age 15 to 54 years. On the other hand, the Framingham-Asia equation estimated the number of CVD cases higher than the APCS equation at age 55 years and above. The original Framingham equations estimated the highest number of CVD cases at age 65 to 74 years. However, at age 75 years and above the Framingham-Asia equation estimated the higher number of CVD cases than the original Framingham equation or the APCS equations.

Table 5.3 The estimated number of people who are alive with CVD in Thailand during the next 8-10 years by age groups and gender amongs APCS equation, the Framingham-Asia equation and the Framingham original equation

Men	Estimated number of people who are alive with CVD		
Age	APCS	Framingham Asia	Framingham original
	8-years	8-years	10-years
15-24	24,711	24,403	62,084
25-34	22,065	21,794	96,848
35-44	139,848	137,442	308,877
45-54	248,721	237,687	501,574
55-64	566,300	510,851	1,139,557
65-74	818,176	703,639	1,627,409
≥75	722,779	630,331	1,273,257
Total	2,542,599	2,266,147	5,009,607
Women	**Estimated number of people who are alive with CVD**		
Age	**APCS**	**Framingham Asia**	**Framingham original**
	8-years	**8-years**	**10-years**
15-24	12,512	11,869	25,354
25-34	53,255	52,135	79,660
35-44	93,754	90,281	160,900
45-54	253,433	250,647	377,651
55-64	536,927	544,755	807,650
65-74	761,026	782,969	1,034,955
≥75	827,332	862,479	860,526
Total	2,538,238	2,595,135	3,346,695

The graphs of the estimated number of people who are alive with CVD in Thailand during the next 8-10 years by gender shows in (appendix F).

5.3.3 The validation of the mathemetic model

This section presents the validation of the mathemetic model. The estimated number of people who are alive with CVD calculated from the APCS, the Framingham-Asia and the original Framingham equations have been validated against the actual number of CVD events in Thailand.

The national hospitalisation data in 2009 from NHSO, Thailand, have been used to validate the model which covers the in-patients hospital admissions for the whole country. The in-patients admissions from the Universal Coverage Health Care Scheme (UCS), which accounts for 75% coverage of the all hospitalisation data in Thailand. The average number of the estimated CVD patients per year, has been calculated to make it comparable with the 1-year hospital admissions in Thailand and is compared by age groups and gender. The CVD conditions have been indentified by using the ICD-10 code, which I00-I99 refers to all CVD, I20-I25 refers to IHD and I60-I69 refers to stroke.

Table 5.4 shows the validation of the estimated number of CVD patients which has been calculated from the APCS equation, Framinham-Asia equation and the original Framingham equation. The actual number of CVD patients who were admitted to hospitals in 2009 in has been used to validate the estimated number of CVD patients using each equation. In men, The APCS and the Framingham-Asia equations estimated the total number of patients closer to the actual number, than the original Framinham equation. The original Framingham equation overestimated the number of CVD patients by a factor of two.

When comparing across age groups in men, the APCS equation and the Framingham-Asia equation both slightly over-estimated the number of CVD patients at age 15 to 24 years but under-estimated the number of patients from age 25 to 34 years. Both APCS and the Framingham-Asia equations over-estimated the number of patients at age 55 years and over. The APCS equation and the Framingham-Asia equation performed a close estimation at age 35 to 44 years and 45 to 54 years. The original Framingham equation over-estimated the number of CVD patients in almost all age

groups, with estimates at double the actual number at age 25 to 54 years and triple the actual number at age 15 to 24 years and 55 years and over.

Overall, the three equations overestimated the number of CVD patients in women. When comparing across age groups, the APCS and the Framingham-Asia equations both under estimated the number of CVD patients at age 15 to 24 years, whereas, the original Framingham performed a close estimation in this age group. In addition, at age 35 to 44 years and 45 to 54 years the APCS equation and the Framingham-Asia equation both closely estimate the actual number of CVD patients. Whereas, the original Framingham equation overestimated the number of CVD events. In the elderly age groups, all three equations have overestimated the number of CVD patients. The validation graph is shown in (appendix F).

Table 5.4 Comparing the actual number of CVD hospital admissions with the estimated number of CVD patients per year in the three different equations amongst Thai men by age groups, in 2009

Men	Observed number of CVD patients in 2009 (only UC)	The average of estimated number of people who are alive with per year		
Age		APCS	Framingham Asia	Framingham original
15-24	2,479	3,089	3,050	6,208
25-34	4,661	2,758	2,724	9,685
35-44	13,135	17,481	17,180	30,888
45-54	27,217	31,090	29,711	50,157
55-64	37,721	70,788	63,856	113,956
65-74	40,861	102,272	87,955	162,741
≥75	32,122	90,347	78,791	127,326
Total	158,196	317,825	283,268	500,961
Women	**Observed number of CVD patients in 2009 (only UC)**	**The average of estimated number of people who are alive with CVD per year**		
Age		**APCS**	**Framingham Asia**	**Framingham original**
15-24	2,227	1,564	1,484	2,535
25-34	3,768	6,657	6,517	7,966
35-44	11,459	11,719	11,285	16,090
45-54	25,308	31,679	31,331	37,765
55-64	36,352	67,116	68,094	80,765
65-74	45,637	95,128	97,871	103,495
≥75	44,488	103,417	107,810	86,053
Total	169,239	317,280	324,392	334,670

5.4 Discussion

The probability of CVD events, which are calculated by the APCS equation, the Framingham-Asia equation, and the original Framingham equation, increases accordingly with an increase in the age groups, in both men and women (Table 5.1 and 5.2). However, the original Framingham equation projects a higher CVD probability than either the APCS equation or the Framingham-Asia equation, in both men and women at all age groups. This might be because the original Framingham equation was derived from the Framingham cohort, who have different characteristics of CVD risk factors and ethnicity, compare to the Asian population. Many studies have found that the Framingham's function was suitable for predicting future CVD in middle aged US white populations, and others with similar profiles of CVD risks (Liao et al. 1999, Diverse Populations Collaborative Group 2002). However, some studies showed an overestimated prediction for groups which have different risk profiles and ethnicity, such as Asian and some EU populations (Liu, Hong and D'Agostino 2004, Thomsen et al. 2002, Haq et al. 1999, Brindle et al. 2006). The APCS equation was derived from the pooled data of the cohort studies around Asia and included the EGAT cohort study in Thailand. Hence, the Framingham-Asia equation was also recalibrated with the APCS cohort. Therefore, the APCS equation and the Framingham-Asia equation are more suitable than the original Framingham equation, when applied to the Thai population.

When comparing genders, the original Framingham equation calculated the higher probability of CVD in men than in women. Conversely, the probability of CVD in women is higher than in men in the Framingham Asia equation (Table 5.1). This might because the Framingham Asia equation was reported to overestimated the risk of CVD by an average 4% in women and underestimate the CVD risk by an average 2% in

men, in the non-chinese cohorts (Asia Pacific Cohort Studies Collaboration et al. 2007). In addition the prevalence of regular smoking in women is lower than in men, which might have an impact and affect the calculations.There are some metabolic risk factors in women which are higher than men. For example, the mean of BMI in women is 24.36 kg/m^2 but in men is 23 kg/m^2. The mean of total cholesterol in women is 5.58 mmol but in men is 5.27 mmol. Hence, the prevalence of diabetes in women is 10.9% but in men is 9.3%.

In terms of the mathematical equations, there are some limitations of using the APCS equation, the Framingham-Asia equation and the original Framingham equation. Firstly, the setting of mathematical models are different. The APCS equation and the Framingham-Asia applied the Cox's model but the original Framingham equation was derived from the Weilbull's model.

Secondly, the input parameters of the risk factors in the APCS and the Framingham-Asia equations are limited because the APCS and the Framingham-Asia were trying to derive equations that can be used with the limited sources of information and also be applicable to many countries around Asia. Therefore, the APCS and the Framingham-Asia equation used BMI, age, gender, blood pressure and total cholesterol to project the CVD events. On the other hand, the original Framingham equation included all of those variables and diabetes status, which is another potential risk factor of CVD.

Thirdly, the time frame differences, the APCS and the Framingham Asia equations are both based on an 8-years cohort study, while the original Framingham equation is based on 10-years of follow-up period. Therefore, when conducting the validation of the mathematical models, the average number of CVD patients per year

has been used to compare the number of actual CVD hospital admissions in a single year.

In term of the outcome limitations, the APCS equation and the Framingham-Asia equation estimated only the number of all CVD events but cannot estimate the CVD conditions seperately. The original Framingham equation is more flexible in being able to calculate the CVD events sepreately for IHD or Stroke. However, all three equations calculate both fatal and non-fatal events together, which cannot identify the exact number of people who die from or are alive with CVD. Therefore, the CVD mortaliy probability is applied to the number of all CVD events, to get the number of people who are likely to die from CVD. Then, deduct this number from the number of all CVD events to obtain the number of people who are alive with a CVD condition (Table 5.3).

Additionally, this analysis assumed that all individual had no previous history of CVD because the APCS, Framingham-Asia and the orginal Framininghamequation were derived based on the general population. However, in reality, the general population may contain healthy or asymptomatic people and people who currently have CVD conditions. Ideally, the estimation should remove the people who currently have CVD, but according the descriptive analysis of the NHESIV, Thailand (Chapter 4), there were a small proportion of the population of people who have CHD or Stroke, which can effectively be ignored from the analysis.

When validating the equations against the actual number of the hospital admissions due to CVD in Thailand, the APCS equation and the Asia-Framingham equation both closely estimated the total number of CVD patients (Table 5.4). The original Framingham equation overestimated the total number of CVD patients in both men and women. The validation showed a close estimation at age 35 to 44 years and 45

to 54 years in both men and women when applying the APCS and the Framingham-Asia equations. However, all three equations overestimated the risk in the older population, because the CVD risk equations are derived from middle age groups populations. The APCS and the Framingham Asia equations are derived from cohorts age 30 to 75 years. The original Framingham equation was derived from cohorts aged 30 to 62 years. When applying the equations to the younger age groups (15 to 34 years), they did not estimate CVD events accurately. Additionally, the younger generation in Thailand may have a different lifestyle than the older generation, such as undertaking less physical acitivites and an unhealthy diet. Moreover, there are a limited number of studies that derieved CVD risk equations for a population aged under 30 years old.

In terms of the mortality data, the number of deaths from CVD may be underestimated, because the average 10-year CVD mortality probability has been calculated from the national CVD mortality rate in Thailand during 1996 to 2006, but the estimation is based on the year 2009. Hence, the death registry in Thailand might be under-reporting or miss classifying the causes of death in its data. Moreover, the CVD mortality rate in 2009 was presented as a total mortality rate, but not presented by age groups and gender. Therefore, the 10-years mortality during 1996 to 2006 was used instead because it was the best available data during the period of this study.

In conclusion, the APCS equation and the Asia Framingham equation performed the better estimation than the original Framingham equation for the Thai population. Although the Asia Framingham equation has perform the estimation nearly the same as the APCS equation, the Asia Framingham equation was derived from the Framingham cohort which has the different population characteristic with the Asia population. The APCS equation was derived from the Asia cohort studies which including the Thai EGAT cohort study. Additionally, the actual number of CVD event that use in the

validation covered 75% of the hospital admission data in Thailand which may underreport the number of CVD cases overall. Moreover, The APCS equation is applicable for the Asia population which will enhance the capability of the model to apply it in different setting. Therefore, this study will use the APCS equation as the risk engine in the next stages of modelling.

Chapter 6 : Health care costs of CVD in Thailand

Abstract

Cardiovascular disease (CVD) has become a leading cause of death and disability in Thailand because the life style of population has changes to the unhealthy life style which increase the level of CVD risk factors. The number of hospital admissions from CVD has continuously increased year by year, which increases health care expenditure for the health care service providers. This chapter undertakes to analyse the costs of hospitalisation for CVD inpatients in Thailand, 2009.

The costs of hospital admission have been analysed from the health service providers perspective. The direct medical costs and direct non-medical expenditure during hospital admission have been included in the analysis. The descriptive analysis has been performed, to present the overall health care costs of CVD, in mean and absolute total costs of hospital admissions, which will reflect the burden of health care expenditure at the national level.

The secondary anonymous inpatient data from the "Universal Coverage" (UC) health care scheme during 2009 has been obtained from the National Health Security Office (NHSO), Thailand. 327,435 CVD inpatients were classified according to ICD-10 code, of which I20-I25 referred to IHD, I60-I69 referred to stroke and I00-I99 referred to all CVD conditions.

Of the 327,435 CVD inpatients, 26.42% were aged 65 to 74 years old and 23% were aged 75 years old and over, 51.69% were women and 48.31% were men. The average health care cost for all CVD conditions (I00-I99) was ฿21,921per patient (£1 = ฿50*). The average health care cost for IHD patients was ฿32,884 per patient, while stroke patients had health care expenditure on average of ฿25,617. The average length of stay in hospital for stroke patients was higher than IHD patients and other CVD conditions. The average health care cost per day of IHD patients was higher than stroke patients. The absolute total cost increased as the age groups increased. Male patients had a higher cost of hospital admission than women. Overall in 2009, the health service providers spent ฿7,177 million on treatment of CVD. The total cost of IHD was ฿2,544 million and the total cost of stroke was ฿1,920 million.

CVD was a significant proportion of healthcare expenditure from a health care provider perspective.

*฿ is the symbol of Thai currency (Baht).

6.1 Introduction

Over the past decade, CVD have been one of the leading causes of premature death and disability and have become an increasing burden in Thailand (International Health Policy Program 2009). As a result of Thailand's urbanisation the peoples' lifestyles have changed, such as a decrease in the level of physical activities, changing their dietary patterns and habits which increase metabolic risk factors such as BMI, total cholesterol and blood pressure (Aekplakorn et al. 2012, Satheannoppakoa et al. 2010, Chongsuvivatwong et al. 2010, Stolk et al. 2005, Roth et al. 2011).

The National Health Security Office, Thailand reported that the number of hospital admissions which are caused by CVD conditions has continuously increased and has tripled since 1992 (National Health Security office 2010). This has not only resulted in the increase of the number of the hospital admissions but has also affected the loss of productivity due to absence from work, a decline in the quality of life and increased health care expenditure, of both health care services providers and the patients' families. In 2007, Thailand spent $36.5 million on inpatients medical care for non-communicable diseases, of which 10% of this expenditure was attributable to CVD (Garg and Evans 2011). There were several studies on the health care cost of CVD in Thailand. In 2007, the median cost of treatment for acute coronary syndrome (ACS) patients was ฿47,908 (£1 = ฿50). However, the cost of treatment varied depending on the diagnosis group, treatment procedures and complication of the diseases (Moleerergpoom et al. 2007). The annual hospital charges for treatment of multiple chronic conditions varied from ฿611 to ฿16,794, depending on the health status and severity of the disease in the patient (Thanapop, Pannarunothai and Chongsuvivatwong 2009). Some studies estimated the medical costs attributable to risk factors such as cigarette smoking and obesity. The average direct out-of-pocket cost of CHD which was

attributable to smoking was estimated at ฿33,716.40 per patient or ฿1,773.68 million in total (Leartsakulpanitch, Nganthavee and Salole 2007). The total economic cost attributable to obesity has been estimated at ฿2,168.4 million spending on IHD and ฿ 2,017.6 million spending on stroke, which includes health care costs, cost of premature death and the cost of productivity loss due to hospital-related absenteeism (Pitayatienanan et al. 2014).

In terms of the cost of the stroke rehabilitation, Archongka et.al (2008) found that stroke patients spent, on average ฿11,170.56 ± 5641.73 per patient at the medical rehabilitation (Archongka et al. 2008). Additionally, out of pocket expenses of stroke patients occurs when they need informal care, which is usually provided by their family, friends or neighbours.The cost of informal care for stroke patients has been estimated at ฿4,642.6 per month, based on 2006 prices. The average time spent on the domestic care of stroke patients was 94.6 hours, which implies that there is a loss of opportunity costs which are forgone because of unpaid work undertaken in caring for the patient (Riewpaiboon et al. 2009).

Although it is already known that CVD has become an economic burden in Thailand, the studies on the costs of hospital admissions is not up to date and is mostly limited to single health care units or single groups of patients. This chapter aims to calculate the national level of the total cost of CVD for Thailand during 2009.

6.2 Methods

This is a prevalence-based study of the health care expenditure of CVD in-patients in Thailand, 2009.

6.2.1 CVD

In this study, CVD is defined according to the international classification of diseases 10th version (ICD-10). The CVD conditions have been classified by the ICD-10th codes of which I20 to I25 refer to ischemic heart diseases, I60 to I69 refer to stroke and I00 to I99 refer to all CVD conditions. The list of ICD-10 codes is in appendix E.

6.2.2 Data sources

The health care costs of CVD have been analysed using data from the inpatients services in Thailand in 2009. The numbers and the costs of the anonymous inpatient data were obtained from the National Health Security Office (NHSO), Thailand. This data includes the inpatient hospital admissions in the Universal Coverage health care scheme (UC), which is the major health care insurance system in Thailand. Approximately 47.24 million of the population or 75.29% of the total population of 64 million are in the UC scheme. The health care services cover 11,460 health care units nationwide, which include public hospitals managed under the ministry of public health, other public hospitals, private hospitals and sub-district health promoting hospitals. The data collection process has been described in chapter 3.

6.2.3 Data cleaning and verification

The anonymous CVD inpatients data has been classified by the ICD-10 code. A descriptive analysis of all variables in the data set has been performed to look at data coding, frequency and the distribution of data. If the total cost, the length of stay and the

average cost per day is inconsistent, those records will be recorded as missing. The continuous variable has been checked for the outlier value. For example, the length of stay and the total cost of hospital admission. The length of stay has been examined for the outlier. The inpatients who were admitted into hospital for more than 365 days have been recoded to be missing. The outlier value of the total cost of hospitalisation data has been identified by calculating the cost of hospital admissions per day. The minimum cost of hospital admission was set at ฿500 per day (£10 per day) which was the minimum payment when patients were admitted to a public hospital. The maximum cost of hospital admission was up to ฿65,000 per day (£1300 per day), which was the possible maximum cost if the patients received a specialist medical procedure or were admitted to an intensive care unit (ICU).

6.2.4 Health care cost

This study has focused only on the health care service providers' perspective. The total cost of treatment and hospitalisation included both direct medical cost and direct non-medical cost such as; room rates and meals, the prosthesis / medical devices used in treatment, medication that was used in hospitals, the medical diagnosis and the clinical resources, therapeutic radiology, medical equipment, medical procedure fees, nursing services, physical and rehabilitation services in hospital and other specialist diagnostic methods and the other treatments from health professionals. However, this study has not focused on the patient's perspective. Therefore, the indirect costs, such as the cost of productivity loss due to absence from work and the patients and their family out of pocket expenses have not been included in this analysis.

6.2.5 Statistical Analysis

The descriptive analysis has produced the results in percent, mean and absolute total cost of hospitalisation. The unit of hospitalisation cost will be presented in Thai

currency (Baht, (£1 = ฿50)).The total cost of hospital admissions will be calculated by multiplying the number of CVD patients by an average cost of hospital admission per patient. The statistical analysis has been performed by STATA software version 12 (StataCorp LP 2011).

6.3 Results

Table 6.1 shows the number and percentage of the 327,435 patients who had a primary diagnosis with CVD conditions (ICD-10, I00-I99), classified by CVD condition, age group, gender, length of stay and the discharge status. Of the 327,345 patients, 23.6% had IHD, 22.9% had stroke and 53.5% had other CVD conditions. The number of CVD inpatients increased respectively by age groups but slightly decreased at age 75 years and over. The number of IHD and stroke patients was high in the middle and elderly age groups, with the number of patients increasing at age 45-54 years and reach the highest at age 65-74 years. Although the number of CVD inpatients in younger adults aged 15-24 years and 25-34 years was lower than in the older age groups, the proportion of patients who had other CVD conditions was higher than the older age groups. For examples, at age 15-24 years, of 4,706 patients, 3.1% had IHD, 12.8% had stroke and 84.2% had other CVD conditions. While at age 55-64 years, of 74,073 patients, half of them had IHD and stroke and half of them had the other CVD conditions.

When comparing between genders, the number of inpatients with IHD and stroke in men was higher than in women. Conversely, the number of patients with other CVD conditions was higher in women than in men. However, overall more women were admitted to hospital with CVD conditions than men.

When classifying patients by the length of stay, patients with CVD condition were mostly admitted to hospital for less than one month. 24% of patients in this group

were admitted with IHD, 22% admitted with stroke and 54% admitted with other CVD conditions. However, there were 4,438 inpatients who were admitted between 1 to 3 months, 52% of them admitted with stroke, 15% admitted with IHD and 34% admitted with other CVD conditions. Additionally, patients who were admitted to hospital for more than 3 months were mostly stroke patients.

For the discharge status, 273,787 patients had improved from their illness when discharged from the hospital. 23.7% of them improved from IHD, 20.1% improved from stroke and 56.2% improved from the other CVD conditions. 1,163 patients had complete recovery after being admitted to hospital of which 21.2% recovered from IHD, 13.2% of them recovered from stroke and 65.5% recovered from the other CVD conditions. However, there were 30,969 patients who did not improve from their illness and 21,399 patients were discharged because they died in hospital.

Table 6.1 Number and percentage of CVD patients classified by CVD conditions, Universal coverage health care scheme (UC), Thailand 2009

Categories	IHD	Stroke	Other CVD	All CVD
Age				
15-24	146(3.1%)	600(12.8%)	3,960(84.2%)	4,706(100%)
25-34	614(7.3%)	1,266(15%)	6,549(77.7%)	8,429(100%)
35-44	3,483(14.2%)	4,774(19.4%)	16,337(66.4%)	24,594(100%)
45-54	10,997(20.9%)	12,211(23.3%)	29,317(55.8%)	52,525(100%)
55-64	19,945(26.9%)	16,902(22.8%)	37,226(50.3%)	74,073(100%)
65-74	23,894(27.6%)	20,129(23.3%)	42,475(49.1%)	86,498(100%)
≥75	18,314(23.9%)	19,067(24.9%)	39,299(51.2%)	76,610(100%)
Gender				
Men	42,692(27%)	40,736(26%)	74,768(47%)	158,196(100%)
Women	34,701(21%)	32,213(20%)	100,325(59%)	169,239(100%)
Lengths of stay				
< 1month	76,720 (24%)	72,289(22%)	173,487(54%)	322,496(100%)
≥1-3 months	646(15%)	2,290(52%)	1,502(34%)	4,438(100%)
≥3-6 months	22(6%)	281(71%)	92(23%)	395(100%)
≥6-9 months	1(1.6%)	56(84.9%)	9(13.6%)	66(100%)
≥9-12months	2(15.4%)	9(69.2%)	2(15.4%)	13(100%)
Unspecified	2(7.4%)	24(88.9%)	1(3.7%)	27(100%)
Discharge Status				
Complete recovery	247(21.2%)	154(13.2%)	762(65.5%)	1,163(100%)
Improve	64,988(23.7%)	54,949(20.1%)	153,859(56.2%)	273,787(100%)
Not improve	7,162(23.1%)	10,492(33.9%)	13, 1315(42.9%)	30,969(100%)
Died	4,969(23.2%)	9,340(43.7%)	7,090(33.1%)	21,399(100%)
Unspecified	27(23.1%)	23(19.7%)	67(57.3%)	117(100%)
Total	77,393(23.6%)	74,949(22.9%)	175,093(53.5%)	327,435(100%)

Table 6.2 shows the absolute total cost of hospital admissions by categories and CVD conditions. Overall, CVD patients cost ฿7,199 million (£143million) of which IHD patients cost ฿2,531 million (£50million), stroke patients cost ฿1,907 million (£38 million) and the other CVD conditions cost ฿2,680 million (£53 million). The absolute total cost increased with each increasing along with age but slightly decreased at age 75 years and over. When compared between genders, male patients had an absolute total cost of hospital admission more than women, which was ฿3,888 million (£77million) in men and ฿3,231 million (£64 million) in women. The health care costs to treat men with IHD and stroke cost more than women. On the other hand, more was spent on women than men with other CVD conditions. The graph which compares the absolute total costs by age groups, gender and CVD conditions is presented in appendix G.

In terms of the length of stay, the absolute total health care cost was highest in patients who were admitted to the hospital for less than one month because the number of patients in this group was higher than the other groups. The total cost spent on patients who had IHD and were admitted to hospital for less than 1 month was ฿2,353 million (£47 million). Patients with stroke and admitted to hospital for less than 1 month cost ฿1,261 million (£25 million). Additionally, patients with other CVD conditions cost as much as IHD patients, which was ฿2,328 million (£46 million). Furthermore, patients who were admitted between 9 to 12 months had a higher absolute total cost than patients who were admitted between 1 and up to 9 months.

When classified by the discharge status, the highest absolute health care cost was in patients who improve from illness, which cost ฿5,710 million (£114 million) in total, of which ฿2,215 million (£44 million) was spent on IHD patients and ฿1,268 million (£25 million) spent on stroke patients and ฿2,227 million (£44 million) spent on

other CVD patients. However, the total cost of hospital admissions was higher in patients who died from CVD.

Table 6.2 The Absolute total cost of hospital admission by categories and CVD condition (THB (฿)*)

Categories	IHD	stroke	other CVD	All CVD
Age groups				
15-24	2,257,119	27,325,711	79,120,065	108,702,894
25-34	14,390,400	37,450,052	127,964,733	179,805,186
35-44	108,533,174	141,845,311	319,239,325	569,617,811
45-54	380,368,138	325,286,934	532,507,274	1,238,162,346
55-64	744,748,695	419,013,435	579,576,458	1,743,338,588
65-74	814,269,234	489,638,746	582,287,556	1,886,195,536
75+	466,645,916	466,828,809	460,208,145	1,393,682,870
Gender				
Men	1,532,931,439	1,038,994,870	1,316,312,781	3,888,239,089
Women	998,281,238	868,394,128	1,364,590,777	3,231,266,142
Length of stay				
< 1month	2,353,265,367	1,261,968,543	2,328,073,213	5,943,307,123
≥1-3 months	159,254,375	462,529,711	297,183,150	918,967,236
≥3-6 months	15,696,554	129,767,646	44,386,186	189,850,386
≥6-9 months	573,153	28,518,983	9,063,731	38,155,866
≥9-12months	1,883,622	6,503,539	1,716,157	10,103,318
Discharge Status				
Complete recovery	8,020,575	3,389,411	17,132,857	28,542,843
Improve	2,215,026,299	1,268,554,308	2,227,019,320	5,710,599,928
Not improve	77,724,478	164,419,209	134,613,690	376,757,378
Died	229,479,019	470,848,354	301,279,921	1,001,607,294
Total	2,531,212,676	1,907,388,998	2,680,903,557	7,119,505,231

*Note: (£1 = ฿50)

Table 6.3 shows the summary of total cost of hospitalisation by CVD conditions in 2009. There were 327,435 CVD patients admitted to hospital under the UC health care scheme. 77,393 patients were admitted for IHD, 74,949 patients were admitted for stroke and 175,093 patients were admitted for the other CVD conditions.

The average length of stay was highest in stroke patients which was 6.72 days, IHD patients stayed in hospital on average 4.12 days, while patients who had other CVD conditions stayed in hospital on average 3.99 days. The average cost per day was highest in IHD patients, which cost ฿10,681 per day and second highest in stroke patients which cost ฿4,067 per day, while the other CVD conditions cost ฿3,614 per day.

The average cost per patients was highest in IHD patients, stroke and other CVD respectively. IHD patients cost on average ฿32,884, stroke patients cost on average ฿25,617 and the other CVD patients cost on average ฿15,465 .

The total cost of IHD was ฿2,544 million and the total cost of stroke was ฿1,920 million. The total cost of the other CVD conditions was ฿2,707 million, which was higher than IHD and stroke.

Overall, the CVD patients admitted to hospital stayed on average 4.65 days, the average cost per day was ฿5,393 and the average cost per patients was ฿21,921. The health service providers spent in total ฿7,177 million on treatment of CVD.

Table 6.3 Summary of total cost of hospitalisation by CVD conditions in 2009

CVD Conditions	Total number of cases	Average length of stay (days)	Average cost per day (THB*)	Average cost per patient (THB*)	Total cost (THB*) =(number of cases* average cost per patients)
IHD (I20-I25)	77,393	4.12	10,681	32,884	2,544,991,412
Stroke (I60-I69)	74,949	6.72	4,067	25,617	1,920,018,748
other CVD	175,093	3.99	3,614	15,465	2,707,858,769
All CVD (I00-I99)	327,435	4.65	5,393	21,921	7,177,705,909

*Note: (£1 = ฿50).

6.4 Discussion

Although the analyses focused only on patients covered under the UC health care scheme, it covered the majority (75.29%) of the total population. The other health care schemes that were not included in the analysis were the Social Security health care scheme (SS), which covered 15.42% of population and the Civil Servant health care scheme (CS) which covers 8.2% of population. Another limitation is that data covers mainly public hospitals, and only 60 private hospitals. Therefore, the cost of hospital admission is not properly representative in This data. Additionally, this analyses focuses only on the total expenditure that occurred when patients were admitted to hospital. So, it was only from a health service provider perspective. There may have been hidden costs occurring when the patients were discharged from hospital. They may have needed long-term care and rehabilitation. Other cost related to patients as well as the productivity loss and absenteeism were not the focus of this study. Furthermore, there was a limitation of the dataset which did not provide the information on the type of

medical procedures that had been used for treatment, which may have an affect on the cost of hospitalisation when patients required specialist treatments.

Considering the health care costs by age groups (Table 6.2), the absolute total health care cost was higher in the middle to elderly age groups because the number of cases was higher than younger age groups. Although the younger age groups had lower numbers of hospital admissions which 1.44% of CVD inpatients were in age 15 to 24 years, when exploring the primary diagnosis of this age group, it was found that most patients at age 15 to 24 had been diagnosed with other CVD conditions such as arteritis hypotension, endocarditis etc.

When comparing the health care cost by discharge status (Table 6.2), it was found that patients who died from CVD had the highest expenditure compared to those who completely recovered and those who did not improve. This was because the patients who died were more likely to have stayed in hospital longer than patients in the other groups. When investigating the average length of stay by discharge status, it was found that patients who died from CVD had an average length of stay 7.23 days. While, patients who improved from CVD after admission to hospital stayed on average 4.6 days and patients who completely recovered from CVD stayed on average 4.05 days. On the other hand, patients who did not improve from CVD stayed on average 3 days.

Although the average cost per patients in the other CVD conditions is lower than IHD and stroke, the total cost of other CVD conditions was at the highest at ฿2,707 million, because the number of total cases in this group is higher than IHD and stroke. However, IHD and stroke have a higher cost per patient (Table 6.3).

In conclusion, this study found that CVD had a significant impact on the hospitalisation costs and economic burden on Thailand. In 2009, the health service providers spent ฿7,177 million on hospital admissions due to CVD conditions. The total

expenditure for IHD patients was ฿2,544 million and for stroke patients was ฿1,920 million.

Chapter 7 : : The impact of reducing risk factors for CVD in Thailand

Abstract

Cardiovascular disease (CVD) is considered as one of the main health problems in Thailand, which is not only increasing in the number of hospital admissions year by year, but is also having an effect of increasing the health care expenditure for the treatment and long-term care of CVD patients. The aim of this chapter is to carry out a CVD cost-offset model at population level to estimate the impact of risk reduction strategies on the number of CVD hospital admissions, Disability Adjusted Life Years (DALYs) and the costs of hospitalisation.

The CVD cost-offset model has been implemented on a Microsoft Excel spreadsheet. The number of the mid-year population, classified by age, gender and the CVD risk factors profile from the NHESIV in 2009 have been used as the baseline population data. The CVD risk factors profile included age, gender, systolic blood pressure, total cholesterol and cigarette smoking status. The APCS equation (Asia Pacific Cohort Studies Collaboration et al. 2007) has been applied to calculate the probability of getting CVD over the next eight year period. The model has provided an estimate number of CVD events, both fatal and non-fatal and by deducting the projected number of deaths from that total, will provide the number of patients who will live with CVD. The model also calculates the DALYs from the estimated number of fatal and non-fatal events. The cost of hospital admissions has been estimated by using the costs of hospitalisation from 2009. A 3 percent discounted rate has been applied in both the costs and DALYs, for adjusting the costs and benefits that occur in the different time periods. Four CVD risk scenarios have been investigated, these are:1) do nothing scenario; 2) optimistic scenario; 3) achieve the UN millennium development goal; and 4) worst case scenario.

The model has estimated the impact of reducing the risk factors among the population. If the level of risk factors remain the same as it was in 2009, (do nothing scenario), the number of CVD cases will reach 3,361,472 patients over the next eight years, which is estimated to be 5,620,626 DALYs and cost approximately ฿58,169 million for hospital admissions. However, if the health policy can reduce the levels of risk factors, as in the optimistic scenario or achieve the UN millennium development goal, there will be a significant reduction in the number of hospital admissions of 540,097 cases or 533,052 cases respectively. This will result in saving health care expenditure of approximately ฿9,000 million and 750,000 DALYs during the next eight years. On the other hand, if the trend of risk factors increases as predicted in the worst case scenario, there will be an increase of 442,963 CVD cases. This will increase the DALYs figure by 623,925 and increase the hospitalisation costs by approximately ฿7,000 million.

The findings of this study suggest that reducing the levels of CVD risk factors in the population will have a significant impact on reducing the number of CVD cases, saving DALYs and saving health care costs. The health policy should enhance the primary prevention programs which are targeted at reducing the CVD risk factors in the population.

7.1 Introduction

CVD is considered one of the main potential health problems in Thailand. The burden of disease and injury study in Thailand in 2009 estimated 1,146,064 DALYs lost from CVD, which includes both IHD and stroke (International Health Policy Program 2012). The DALYs lost from stroke was ranked as the third highest in men and the second highest in women. While, IHD was ranked as the sixth and fourth highest cause of death and disability in men and women respectively. Although the overall mortality rate in Thailand has decreased during the past decade due to the improvement in the health care services; the prevalence of CVD has continuously increased (Bureau of Non-Communicable Disease,Department of Disease Control,Ministry of Public health 2010). The increase in the prevalence of CVD has affected the increasing need for medical and long term care for CVD patients. As a consequence, CVD has become a burden for both patients and the health service providers in terms of health care expenditure.

The increase in the prevalence of CVD is related to socio-economic and lifestyle changes in the population in Thailand, which has increased the risk of CVD (Aekplakorn, et al. 2010). It has been proved that the classical CVD risk factors such as ageing, high blood pressure, high total cholesterol and cigarette smoking are related to instances of CVD (Yusuf et al. 1998, Lloyd-Jones et al. 1999, McGorrian et al. 2011, Yusuf et al. 2004). The Ministry of Public Health, Thailand has encouraged the reduction of these modifiable risk factors at the population level. Many public health interventions have been implemented, such as health education, advocating physical activity, promoting healthy diets and changing smoking regulations (Ministry of Public Health 2012). However, this raises the following questions: will the investment in public health programs reduce the further demand for health care in the population and,

if so, how much benefit will be gained from reducing the risk factors at population level? among population?

In terms of CVD modelling, several studies have projected the number of future CVD events and future health care expenditure for the country, based on the current information of the risk factors levels in the population (Mui 1999, Heidenreich et al. 2011, Kang et al. 2011). Some studies have found that reducing the levels of risk factors among the population will reduce the number of deaths and disability from CVD as well as saving costs on the number of hospital admissions (Grover et al. 1998, Capewell, Morrison and McMurray 1999, Goldman et al. 2001, Whitfield et al. 2006, Moran et al. 2010). Many studies in the health economic field have investigated the cost-effectiveness of secondary prevention programs and treatment strategies, such as comparing the multidrug regimen for prevention of CVD (Lim et al. 2007, Conly et al. 2011, Cobiac et al. 2012), coronary artery revascularization procedures (Mannan, Knuiman and Hobbs 2008), treatment of high blood pressure (Dodhia et al. 2012).

This study steps back from the secondary prevention strategies, but focuses on the primary prevention strategies which should be implemented in the general population, to prevent them from being admitted into hospital due to CVD. The aim of this chapter is to estimate the impact of public health risk reduction strategies on the potential benefits of investment. The mathematical model has been conducted, which integrated the modified risk equation from the Asia Pacific Cohort study collaboration. The eight year probability of CVD events has been calculated based on the population level risk factors information from 2009. The model has estimated the number of people who are likely to be admitted to the hospital with CVD conditions which include both IHD and stroke, as well as the burden of the disease in terms of DALYs. The outcomes

of interest in this chapter are represented by the impact in terms of the number of CVD hospital admissions avoided, DALYs saving and the health care financial savings.

7.2 Method

7.2.1 The CVD cost-offset model

A CVD cost-offset model has been carried out in order to: 1) estimate the number of CVD hospital admissions during the next eight year period; 2) estimate the burden of disease in terms of DALYs; and 3) estimate the cost of hospital admissions due to CVD conditions. The CVD cost-offset model has been used to assess the impact of risk reduction strategies on the number of hospital admissions, DALYs and direct health care costs. The impact of changing the risk factors at the population level has been investigated through 4 different scenarios. The analysis process has been described below.

The CVD cost-offset model has been conducted using a Microsoft Excel spreadsheet. The number of the mid-year population by age group and gender in 2009 has been used as the baseline population. The CVD risk factors such as age, systolic blood pressure, total cholesterol and regular smoking, from the 4th National Health Examination Survey (NHESIV) in 2009 (Aekplakorn, et al. 2010), have been used as the input parameters to represent the mean level of risk factors of the Thai population, by age group and gender. Table 7.1 shows the input data of the cost-offset model based on the number of mid-year population and the risk factors profile during 2009.

Table 7.1 The input data: number of mid-year population and the mean level of risk factors by age group and gender in 2009

Men	Mid-year population 2009	The mean level of risk factors at 2009			
		Age (years)	SBP (mmHg)	TC (mmol)	Smoking prevalence (%)
15-24	4,683,981	18.76	117.24	4.60	28.5%
25-34	5,149,508	29.92	120.80	5.27	42.3%
35-44	5,154,963	39.75	122.56	5.43	39.9%
45-54	4,058,120	49.33	126.44	5.46	42.6%
55-64	2,399,309	60.11	131.44	5.40	34.4%
65-74	1,362,752	69.17	134.60	5.31	30.5%
≥75	749,125	79.22	137.22	5.20	23.5%
Total	23,557,758	52.80	128.39	5.28	34.0%

Women	Mid-year population 2009	The mean level of risk factors at 2009			
		Age (years)	SBP (mmHg)	TC (mmol)	Smoking prevalence(%)
15-24	4,532,018	18.97	106.19	4.90	0.7%
25-34	5,130,746	29.87	110.19	5.21	1.4%
35-44	5,408,488	39.65	116.04	5.30	1.8%
45-54	4,388,770	49.10	123.92	5.70	2.6%
55-64	2,694,633	60.02	129.45	5.92	3.0%
65-74	1,655,159	69.24	134.53	5.80	3.5%
≥75	1,086,374	79.48	139.19	5.66	5.2%
Total	24,896,188	52.60	124.70	5.58	3.0%

The probability of experiencing CVD events within an eight year period has been calculated by using the APCS equations (Asia Pacific Cohort Studies Collaboration et al. 2007). The risk factors that are included in the equation are age, systolic blood pressure, total cholesterol and smoking.

The model has calculated the probability of CVD events within an eight year period by age group and gender. Then, the eight year probability of CVD events has been multiplied with the number of the mid-year population to get the estimated number of CVD events in the next eight years. However, the APCS equation calculated the probability of all CVD events, which included both fatal and non-fatal CVD events. The number of CVD events resulting in mortality has been estimated by using the average 10 year probability of dying from CVD in the general population during 1996 to 2006 by age and gender. The probability of dying from CVD is shown in Appendix F. The number of people who are likely to die from CVD has been estimated by multiplying the number of the population in 2009 with the probability of dying from CVD by age groups and gender. Then, the model has deducted the number of people who are likely to die from CVD to obtain the number of people who will be alive with CVD conditions. The outcomes of interest are the number of people with CVD who are alive and the number of deaths from CVD conditions over the eight year period.

7.2.2 Disability Adjusted Life Years (DALYs)

Once the model had estimated the number of CVD events over an eight year period, the total DALYs for each age group and gender was calculated as the summation of the years lost due to disability (YLD) and the years of life lost due to premature death (YLL). Therefore, DALYs will present the burden of CVD which includes both non-fatal burden and the burden of premature death. The calculation procedure follows the WHO national burden of disease studies (Mathers, et al. 2001).

$$DALY = YLD + YLL \quad (7.1)$$

Where, YLD is the number of years lost due to disability and YLL is the number of years of life lost due to premature death.

7.2.2.1 Discounting and age weighting

It is a standard practice for a health economic analysis to discount the future benefits (Drummond, et al. 2005). This study has applied a 3% discount rate to years of life lost in the future, to estimate the net present value of years of life lost and for adjusting both future costs and health outcomes. A 3% discount rate has been applied in this study because it has been used in the Global burden of Disease study project (GBD) (Murray and Lopez 1996) and the burden of disease study project in Thailand (Bundhamcharoen et al. 2011).

The standard age weight from the GBD Study has been applied in the analysis. The assumption of using the age weight was based on the social preference which value a year life in younger adult higher than a year lived by someone in the elderly age group because the younger adult are consider as in the labour force which have more economic productivity than the elderly age group. The GBD study performs an exponential function to express the age-weighting as follows:

$$\text{Age weight} = C \times e^{-\beta x} \quad (7.2)$$

Where, C is the age-weighting correction constant (GBD standard value 0.1658), β is determines the importance of age-weights (GBD standard value 0.04).

7.2.2.2 Calculating YLL

YLL is the number of years of life lost due to premature death which is calculated by multiplying the number of deaths with the standard life expectancies in each age-gender group.

$$YLL = N \times L \tag{7.3}$$

Where, N is the number of deaths and L is the standard life expectancy at age of death in years.

The estimated number of deaths in each age group has been entered to the spreadsheet to calculate YLL. The average age at death for each age group has been calculating by using the mid-point of age at death in each age interval.

Then, the standard life expectancies of these average age at death has been calculated by interpolation between the standard life expectancies at exact ages of death given from the West standard life tables(World Health Organization 2000). by single year of age

With 3% discounting and uniform age weights; YLL has been calculated with this formula:

$$YLL = \frac{N}{0.03}\left(1 - e^{-0.03L}\right) \tag{7.4}$$

Where, N is number of deaths and L is the Standard life expectancy at age of death in years.

When taking into account the 3% discount rate and age weight, YLL has been calculated with the full formula as follows:

$$YLL = NCe^{(ra)}/(\beta + r)^2\left[e^{-(\beta+r)(L+a)}\left[-(\beta + r)(L + a) - 1\right] - e^{-(\beta+r)a}\left[-(\beta + r)a - 1\right]\right] \tag{7.5}$$

Where,r is the discount rate (using GBD standard discount rate at 0.03 (3%)), C is the age-weighting correction constant (using GBD standard value 0.1658), β is the parameter form age weighting function (using GBD standard value 0.04), a is the age of

onset at death and L is the standard life expectancy at age of death in years which is the duration of time lost due to premature death (calculated from the standard life table).

7.2.2.3 Calculating YLD

YLD presents the years lost due to disability which is the one component of DALYs. The basic formula of YLD is:

$$YLD = I \times DW \times L \tag{7.6}$$

Where, I is the number of incidence cases in the reference period, DW is the disability weight and L is the average duration of disability in years.

In this analysis, the estimated number of people who are alive with CVD conditions by age and gender has been entered into the spreadsheet as the number of incidence cases occurring during the eight year period (I). The disability weight that has been used as the average disability weight at 0.18 for all CVD conditions is taken from the GBD study undertaken in 2010 because the model has limitations on calculating the probability of CVD events by the specific CVD condition and it did not taken into account the severity of disease. The disability weight by CVD conditions of the GBD study is shown in Appendix G. The average age onset of disability and the duration of disability have been calculated by using DISMOD II software.

DISMOD II software has been developed by Jan J Barendregt, department of Public health, Erasmus University, Netherlands (EpiGear International Pty Ltd 2010). This software has been used as an analytical tool in the GBD study for checking the consistency of various data and for estimating the incidence, prevalence, duration and case fatality, when the partial data was not available. DISMODII has been commonly used in YLD calculations for estimating the incidence and duration of the disease from the available information about the country. An underlying generic disease model

concept has been developed in DISMOD software to explore the causal relations and the disease process as shown in Figure 7.1.

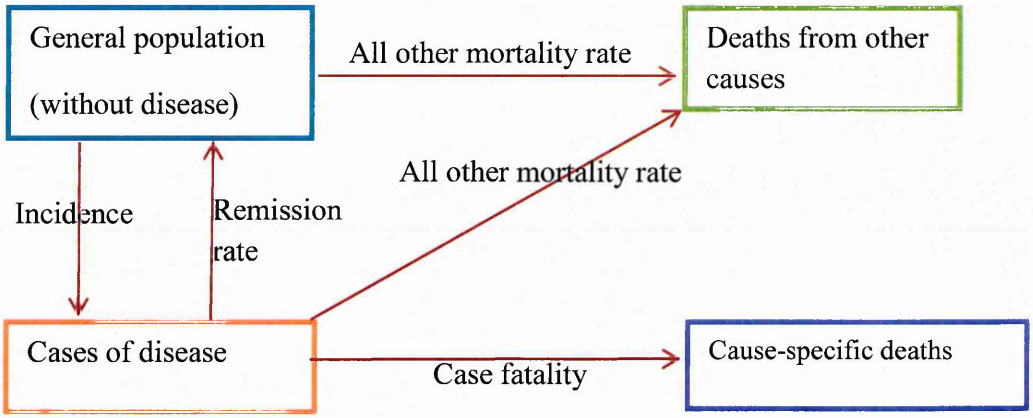


Figure 7.1 The conceptual generic disease model in DISMOD software (Barendregt et al. 2003)

The number of mid-year population, the background mortality, the prevalence of CVD and CVD mortality rate in the Thai population classified by age and gender in 2009have been entered as the input information in the DISMOD software. This analysis assumed the remission rate from CVD is equal to zero. The DISMOD software will estimate the age onset of getting CVD and the duration of disability from CVD by age and gender. Then, the YLD has been calculated by using the following formula:

With a 3% discount rate and uniform age weight, YLD has been calculated using the formula as follows:

$$YLD = \frac{I \times DW \times \left(1 - e^{-0.03L}\right)}{0.03} \qquad (7.7)$$

Where, I is the number of incidence cases in the reference period, DW is the disability weight and L is the average duration of disability in years.

When applying the discount rate and non-uniform age weight, the full formula of YLD is:

$$YLD = I \times DW \times Ce^{(ra)} /(\beta + r)^2 \left[e^{-(\beta+r)(L+a)}\left[-(\beta + r)(L + a) - 1\right] - e^{-(\beta+r)a}\left[-(\beta + r)a - 1\right]\right] \quad (7.8)$$

Where, DW is the disability weight, r is the discount rate (using GBD standard value 0.03), C is the age-weighting correction constant (using GBD standard value 0.1658), β is the parameter for standard age function (using GBD standard value 0.04), a is the age onset of disability (calculated from DISMODII software), and L is the duration of disability (calculated from DISMODII software).

Once the model has calculated the YLL and YLD, DALYs will be calculated by the summation of YLL and YLD together to obtain the number of total DALYs, which takes into account both death and disability to reflect the burden of CVD in Thailand.

7.2.3 Health Care Cost for CVD patients

The average total cost of hospital admissions from CVD has been calculated from the inpatient services in Thailand during 2009. The costing data obtained from the national health security office includes the universal coverage health care scheme. The results of the health care costs have been analysed and presented in Chapter 6. The health care service providers spent on IHD ฿32,884 (£657) per patient, on stroke ฿ 25,618 (£512) per patient and on all CVD conditions ฿21,921 (£438) per patient. Because of the limitations of the APCS equation, which estimates the total CVD event only, the average cost of all CVD conditions has been used to estimate the total health care costs for the next eight years. The estimated total health care cost has been calculated by multiplying the average cost per patient with the estimated number of CVD cases. However, this analysis is based on the price at 2009; the discount rate has

been applied to estimate the present value of the health care expenditure with the following formula:

$$P = \frac{F}{(1+r)^t} \tag{7.9}$$

Where, P is the present value, F is the payment that will be made t years in future, r is the discount rate (0.03), and t is time (years).

7.2.4 The impact of changing CVD risk factors

The model has taken into account the CVD risk reduction scenario analysis which targets the following three CVD risk factors; systolic blood pressure, total cholesterol and the prevalence of smoking at population level. The model estimates the impact of changes in only three CVD risk factors due to the input variables in the APCS equations. There are some underlying assumptions in the CVD cost offset analysis. The model assumes that the population structure and the health care system remains the same as they were in 2009. Therefore, there is no change in the number of the population by age group and gender over time and the mean age of each of the age group remain the same in the model.

The model has estimated the impact of changing the risk factors on the number of CVD patients, the number of DALYS and the cost of hospitalisation in four different scenarios. Table 7.2 shows the summary of the percentages of changing the risk factors in the scenario analysis for the CVD cost offset model which are described as follows:

Table 7.2 Summary of the risk reduction scenario analysis for the CVD cost offset model

Scenario	% Change of the risk factors level		
	Systolic blood pressure	**Total Cholesterol**	**Smoking**
1)Do nothing scenario	0%	0%	0%
2)The optimistic scenario	-5%	-5%	-5%
3)Reach the UN millennium development goal	-5%	0%	-30%
4) The worst case scenario	+3.35%	+11.7%	-30%

1) Do nothing scenario: this scenario assumes that there is no change in CVD risk factors over time. The level of CVD risk factors remain the same.

2) The optimistic scenario: this scenario assumes that all CVD risk factors have been reduced in the population through public health initiative strategies. The target risk factors have been reduced 5%.

3) Reach the UN millennium development goal: this scenario estimates what will happen if the risk reduction strategies in Thailand can achieve the UN millennium development goals. The target of this goal is to reduce 25% of the global premature mortality from non-communicable disease (NCDs) based on the 2010 levels and to achieve it by 2025. This is a goal referred to by some as the "25 x 25" target (Kontis et al. 2014). The target risk reductions are: a reduction of 30% in the prevalence of tobacco smoking; reducing alcohol consumption by 10%, reduction of 30% in the average salt intake of the population, stop the rising prevalence of obesity, reduce 25%

of the prevalence of high blood pressure and stop the rise in prevalence of diabetes. Based on the information available for the model, this scenario analyses the targets on reducing 30% of smoking and assumes that the level of systolic blood pressure has been reduced by 5% to achieve this goal and the other risk factors remain the same as in 2009.

4) The worst case scenario: This scenario assumes that the trend of risk factors in the population will be changed according to the information provided from the WHO global observatory, Thailand country profile data (WHO 2011). The trends of the risk factors of the Thai population who are aged 25 years and over have been presented in Appendix J. The percentage of change has been calculated by:

$$\%\text{Change} = \frac{\text{current value - starting value}}{\text{starting value}} \times 100 \qquad (7.10)$$

During 1980 to 2009, there was a +3.35% increase in the level of systolic blood pressure in the population and +11.7% increase in the total cholesterol level. However, the percentage of smoking in the population reduced by 30% because of the effectiveness of the smoking regulation policy in Thailand (Sangthong et al. 2011).

7.3 Results

7.3.1 The estimated number of CVD patients over an 8 year period

Table 7.3 shows the estimated number of CVD patients over the next eight years by age group, gender and the risk reduction scenarios. The model estimates the highest number of patients in the "worst case scenario", which is 3,804,435 patients and the second highest figure is in the "do nothing scenario" which is 3,361,472 patients. However, if the public health interventions can reduce the level of CVD risk factors, as in the "optimistic scenario", the estimated number of CVD patients will decline to

2,821,375 patients. Additionally, if the health policies achieve the UN millennium development goal, the number of total CVD patients will decrease to 2,828,420 patients.

When comparing the estimated number between men and women by age group and the risk reduction scenarios; overall, the model estimated the number of CVD patients was higher amongst women than men. However, the UN millennium goal scenario estimated the number of male CVD patients to be higher than the figures for women in most age group except at age 75 years and over. This might be because reducing cigarette smoking by 30% could have a higher impact on men as they have a higher prevalence of regular smoking than women (Appendix K).

When comparing the total estimated number of CVD patients by age group and the risk reduction scenarios, the estimated number of CVD patients increases respectively with the increasing of age group in both men and women. The worst case scenario estimated the highest number of CVD patients, following by the do nothing scenario. While, the optimistic scenario and the reaching UN millennium development goal estimated nearly the same number of patients (Appendix K).

Table 7.3 The estimated number of CVD patients over an eight year period in the different scenarios

Conditions	Age group	15-24	25-34	35-44	45-54	55-64	65-74	≥75	Total
Do nothing	**Men**	5,869	14,046	43,475	90,007	312,329	603,699	573,332	1,642,758
scenario	**Women**	3,355	9,481	37,588	91,175	299,959	595,675	681,480	1,718,714
	Total	9,224	23,527	81,064	181,181	612,289	1,199,375	1,254,812	3,361,472
Optimistic	**Men**	4,752	11,179	35,121	72,727	254,043	493,302	473,179	1,344,303
scenario	**Women**	2,912	8,198	32,487	78,165	256,877	510,297	588,136	1,477,072
	Total	7,665	19,377	67,608	150,892	510,920	1,003,599	1,061,315	2,821,375
Reaching UN	**Men**	4,743	11,048	34,850	72,024	253,355	493,311	475,480	1,344,812
millennium goal	**Women**	2,932	8,252	32,683	78,620	258,318	512,792	590,011	1,483,607
	Total	7,675	19,300	67,533	150,644	511,673	1,006,104	1,065,491	2,828,420
Worst case	**Men**	6,775	16,200	49,972	103,180	359,751	695,069	658,427	1,889,374
scenario	**Women**	3,726	10,557	41,858	102,064	335,929	665,861	755,066	1,915,061
	Total	10,501	26,757	91,830	205,244	695,680	1,360,930	1,413,492	3,804,435

7.3.2 The estimated DALYs over 8 year period

Table 7.4 shows the estimation of the absolute total DALYs and DALYs lost from CVD per 1,000 population over the next eight years by age group gender and the risk reduction scenarios. The total DALYs overall is highest in the worst case scenario, which has a total loss of 6,244,551 DALYs. The second high is in the do nothing scenario which has a total loss of 5,620,626 DALYs. In addition, when the model assumed that the CVD risk factors have been reduced, as in the optimistic scenario, the total DALYs lost will be reduced to 4,859,439 DALYs. Furthermore, if the model assumed that CVD risk factors can be reduced as in the UN millennium goal scenario, the total DALYs lost will be reduced to 4,868,151. Both the optimistic scenario and the UN millennium goal scenario estimated the DALYs as nearly the same.

When comparing DALYs across age group, it was found that the number of DALYs lost from CVD increase respectively with an increase in age group. The DALYs is higher in the older adults, (age 35 years and older) than in the younger adults (ages 15 to 34). The absolute total DALYs is highest at ages 65 to 74 years.

Table 7.4 The Estimated of the absolute total DALYs over an eight year period in different scenarios, Standard Life table, with age weight and mean disability weight

	Estimated the absolute total DALYs (years)											
	Do nothing scenario			Optimistic scenario			Reaching UN millennium goal			Worst case scenario		
Age group	Men	Women	Total	Men	Women	Total	Men	Women	Total	Men	Women	Total
15-24	34,080	17,215	51,295	33,008	16,467	49,475	33,000	16,500	49,500	34,949	17,842	52,791
25-34	92,784	47,585	140,369	88,752	44,614	133,366	88,568	44,738	133,306	95,813	50,078	145,891
35-44	181,361	139,217	320,578	165,457	125,778	291,235	164,941	126,294	291,235	193,729	150,466	344,195
45-54	314,503	296,525	611,028	277,500	264,105	541,604	275,995	265,238	541,233	342,712	323,661	666,373
55-64	714,223	704,801	1,419,024	602,320	614,633	1,216,953	600,999	617,650	1,218,648	805,267	780,082	1,585,349
65-74	922,451	962,034	1,884,485	769,512	835,095	1,604,607	769,525	838,805	1,608,330	1,049,030	1,066,385	2,115,414
≥75	534,697	659,150	1,193,847	447,067	575,131	1,022,197	449,080	576,819	1,025,898	609,151	725,385	1,334,536
Total	2,794,098	2,826,528	5,620,626	2,383,616	2,475,823	4,859,439	2,382,108	2,486,043	4,868,151	3,130,652	3,113,899	6,244,551

7.3.3 Estimate the impact of the risk reduction scenario

Table 7.5 presents the summary results of the CVD cost-offset model compared the four scenario analysis and the impact of changing CVD risk factors, on the number of CVD hospital admissions, total costs of hospitalisation and the DALYs. Do nothing scenario in the model has estimated that over the next eight year period there will be 3,361,472 CVD patients if the levels of risk factors remain the same as in 2009. However, if the levels of risk factors decline as in the optimistic scenario (all risk factors reduce by 5%), it will reduce the number of CVD hospital admissions by 540,097 people. Additionally, if the health interventions can achieve the UN millennium development goal, there will be a reduction in the number of CVD hospital admissions by 533,052 people. On the other hand, if the trends of risk factors increase amongst the population as in the worst case scenario, the number of CVD hospital admissions is estimated to be 3,804,435 which will be an increase of 442,963 CVD patients.

In terms of the total cost of hospitalisation, when applying the discount rate of 3%, it is estimated that the health service providers will spent ฿58.1 thousand million (£1,163 million) on medical expenditure for CVD patients over the next eight year period. However, if the health interventions can reduce the levels of risk factors as in the optimistic scenario, there will be ฿9,346 million (£186 million) saving on the hospitalisation costs. In addition, if the health policy can achieve the UN millennium development goal, it will save ฿9,224 million (£184 million) of the health care expenditure. Conversely, if the trend of CVD risk factors continuously increase as in the worst case scenario, the health care expenditure will increase by ฿7,665 million (£153 million) over the next 8 year period.

Furthermore, the model estimate 5,620,626 DALYs lost due to CVD in Thailand over the next eight years if the levels of risk factors remain the same as in 2009. However, the government would be able to save 761,187 DALYs if all levels of risk factors could be reduced as in the optimistic scenario. Moreover, if the health policy can reach the UN millennium development target, there will be 752,475 DALYs saving in the next eight years. Or, if the trend of CVD risk factors continuously increase as in the worst case scenario, the total DALYs will reach to 6,244,551 DALYs during the next eight year period, which is an increase of 623,925 DALYs overall in the Thai population.

Table 7.5 Summary of the CVD cost-offset model showing the four differences scenarios

Conditions	**Scenario**			
	1) Do nothing scenario	**2) Optimistic scenario**	**3) Achieve the UN millennium development goal**	**4) Worst case scenario**
Number of CVD patients	3,361,472	2,821,375	2,828,420	3,804,435
Number of CVD hospital admission saving, compare to "Do nothing scenario"	-ref	540,097 (saving)	533,052 (saving)	442,963(increasing)
Total cost (THB)	73,686,851,301	61,847,395,792	62,001,814,904	83,397,048,087
Total cost (THB) of hospitalisation with 3% Discount rate	58,169,080,864	48,822,905,356	48,944,805,230	65,834,399,874
Cost of hospitalisation saving (THB)	-ref	9,346,175,508 (saving)	9,224,275,634 (saving)	7,665,319,010 (increasing)
Total DALYs (years)	5,620,626	4,859,439	4,868,151	6,244,551
DALYs saving (years)	-ref	761,187 (saving)	752,475 (saving)	623,925 (increasing)

7.3.4 Sensitivity analysis

The sensitivity analysis has been performed in 4 different parameters.

1) Using the WHO Standard Life Table (the Standard Life Table west level 26) vs. Thailand Life Table.

2) The application of age weight vs. without age weight.

3) Using upper and lower 95% confidence limits of the disability weight (mean = 0.181, 95%CI (0.08-0.29))

4) Using upper and lower 95% confidence limits of the cost of hospital admission (mean=฿21,921, 95%CI(฿21,717-฿22,125).

The model has applied both WHO standard Life table vs. Thailand Life Table in the analysis. Each life table has re-estimated the DALYs when using age weight vs. no age weight. In each analysis of applying age weight vs. no age weight, it also used the upper vs. lower limit of the disability weight to get the range of estimated DALYs under the uncertainty of the different parameters. The 95% confidence limit of the cost of hospital admission was also applied in the model to estimate the possible range of the total expenditure that the health care providers have to pay for treatment of CVD patients.

Table 7.6 presents the estimation of the absolute total DALYs and the total cost of hospital admission when applying to the different parameters in the sensitivity analysis. In terms of DALYs estimation, when using the Standard Life Table vs. Thailand Life Table, there is no difference when the age weight has been applied in both life tables. However, the Thailand Life Table estimated DALYs slightly lower than the Standard Life Table when not using age weight. Comparing using age weight and no age weight in both life tables, the estimated DALYs using age weight is lower than no

age weight. The use of upper and lower 95% Confidence Limit of the disability weight shows the possible range of DALYs when the severity of disability was taken into account. The lower limit of disability weight refers to mild CVD condition and the upper limit of disability weight refers to severe CVD condition. For example, in the do nothing scenario, when using the standard life table and age weight, the model estimates total DALYs lost from CVD is 5,620,626 which the possible DALYs are ranged between 2,987,263 to 8,462,573. The DALYs estimated by age groups and gender shows in the appendix L and appendix M.

In terms of the sensitivity analysis of the cost of hospital admission, the model estimates the total cost when applying the upper and lower 95% confidence limit of cost to estimate the range of total cost with the 3% discount rate and compare between four scenarios as shown in Table 7.6.

Table 7.6 The sensitivity analysis of the absolute total DALYs and the cost of hospital admission by different parameters.

Conditions	Scenario				
	mean and 95% CI analysis	**1) Do nothing scenario**	**2) Optimistic scenario**	**3)Achieve the UN mellenium millennium development goal**	**4) Worst case scenario**
1) The WHO Standard Life Table* / with age weight (DALYS)	mean DW**	5,620,626	4,859,439	4,868,151	6,244,551
	lower limit	2,987,263	2,650,826	2,654,677	3,263,030
	upper limit	8,462,573	7,242,991	7,256,950	9,463,231
2) The WHO Standard Life Table /no age weight (DALYS)	mean DW	8,395,031	7,168,467	7,184,889	9,401,686
	lower limit	4,122,236	3,580,108	3,587,367	4,567,166
	upper limit	13,006,266	11,041,053	11,067,364	14,619,138
3) Thailand Life Table / with age weight (DALYS)	mean DW	5,623,737	4,862,549	4,871,262	6,247,661
	lower limit	2,990,373	2,653,936	2,657,787	3,266,141
	upper limit	8,465,684	7,246,101	7,260,061	9,465,341
4) Thailand Life Table / no age weight (DALYS)	mean DW	8,349,070	7,122,507	7,138,929	9,355,725
	lower limit	4,076,275	3,534,147	3,541,406	4,521,206
	Upper limit	12,960,305	10,995,092	11,021,404	14,573,178

Conditions		Scenario			
	mean and 95% CI analysis	**1) Do nothing scenario**	**2) Optimistic scenario**	**3)Achieve the UN mellenium millennium development goal**	**4) Worst case scenario**
5) Cost of hospital admission (THB) with 3% Discount rate	mean cost	58,169,080,864	48,822,905,356	48,944,805,230	65,834,399,874
	lower limit	57,628,175,795	48,368,908,892	48,489,675,238	65,222,216,217
	Upper limit	58,709,959,398	49,276,879,548	49,399,912,894	66,446,553,499

*The WHO standard life table = the standard life table west level 26

**DW = Disability Weight

7.4 Discussion

In 2009, there were 327,435 CVD patient admissions to hospitals which had a total health care expenditure of ฿7,177 million (£143 million) and the BOD Thailand study in 2009 estimated the total DALYs of IHD and Stroke together was 1,146,064 DALYs (International Health Policy Program 2012). If the levels of CVD risk factors remain the same as in 2009, the number of CVD patients will increase approximately 10 times and the total DALYs of CVD will increase to 5,620,626 DALYs over the next eight year period. However, if the trend of risk factors increase as in the worst case scenario, the number of CVD patients will increase to 3,804,435 and increase to 6,244,551 DALYs over the next eight year period. As a consequence the health care expenditure will increase as well as the DALYs also increasing (Table 7.3-7.5).

The CVD cost off-set model has estimated that there are potential benefits of reducing the CVD risk factors at the population level. The optimistic risk reduction scenario and reaching the UN millennium goal scenario are both estimated to have the potential benefit of reducing CVD risk factors on the number of CVD hospitalisations avoided, total cost of hospital admissions savings and the DALYs saving being nearly the same. Although in the UN millennium goal did not take into account the reduction of total cholesterol, there are still high impacts on reducing level of systolic blood pressure and reducing the prevalence of smoking.

In terms of the DALYs estimation (Table 7.4), the DALYs calculation incorporated the age weight which considers the value of the years of life lost at an elderly age as less than in younger adults. The use of age weighting is controversial because the societal perspective is concerned about the economic productivity, the value of the years of life are weighted different among age group but in the equality

perspective, the values the years of life are weighted equally for all age group. However, this model allows for the analysis to perform the estimation of DALYs with and without using an age weight. The DALYs calculation without the age weight has been presented in (Appendix L). When applying age weight in the analysis, it found that DALYs in the younger age group (15-34) has increased and DALYs in the older age group has decreased.

Additionally, this analysis has used the standard life table West Level 26 to calculate the life expectancy in the population because the GBD study and BOD study in Thailand had used the standard life table, instead of the country life table, for comparing the results with the other studies. However, the DALYs estimation which used the recent Thailand specific life table at 2012 has been analysed and presented in (Appendix M). When applying the country specific life table to calculate DALYs, it was found that the number of DALYs lost was not different with applied age weight but it has slightly dropped without applied age weight, compared to the standard life table, because the standard life table has a higher life expectancy at birth than Thailand life table (World Health Organization 2000). The life expectancy at birth in the standard life table is 80 years in men and 82.5 years in women. While, the life expectancy at birth in the Thailand life table in 2012 is 71 years in men and 79 years in women.

7.4.1 Limitation

There are some limitations of the CVD cost-offset model. Firstly, the model has been carried out under limited conditions and there are some underlying assumptions. The model is static and compares the estimation at two points of time from 2009 and over the next 8 year period, apart from 2009. The model assumed that the number of mid-year of population and the population structure by age group and gender remain the same as in 2009, but the reality is that people in the cohort of 2009 will gain more age.

Several studies have suggested that Thailand will become an ageing society by 2050 because of the falling fertility rate in the Thai population, (Knodel and Chayovan 2008, National Statistical Office 2007). It was estimated that in a few decades, Thailand will for the first time have a greater population aged 60 years and over, than the population aged less than 15 years old (Knodel and Chayovan 2008). Therefore, the population structure in the future may be different from now because there may be more people in the elderly age group.

Secondly, the CVD risk factors are modifiable. Some risk factors might vary with the age difference and can change over time. Younger adults and older adults experience different levels of risk factors. For example, older adults may experience high blood pressure more than younger adults. Some behavioural risk factors are dynamic which may change anytime based on individual behaviour, such as cigarette smoking. This model is not able to capture the dynamic changing of the CVD risk factors of the individual because the estimation is based on the mean level of the risk factors by each age group and gender.

Thirdly, the model uses the APCS equation to calculate the eight year probability of getting CVD. This equation has some limitations in terms of the number of independent variables, such as age, gender, systolic blood pressure, total cholesterol level and cigarettes smoking status. Some potential risk factors such as diabetic status and BMI level were not included in the equation which may have underestimated the risk of CVD in people who have a high BMI or diabetes. Furthermore, although the equation is able to calculate the overall probability of getting CVD, it is not able to calculate the probability of specific CVD conditions, such as stroke and IHD, separately. However, this equation is suitable for the Asian population. It has been validated in the performance of the equations in the Thai cohort (Asia Pacific Cohort Studies

Collaboration et al. 2007) and also in this study (Chapter 5). The model could perform a more precise estimation if the country-specific CVD risk assessment equation was available.

Chapter 8 : Conclusion and recommendation for future research

8.1 Conclusion

This study was carried out to estimate the future prevalence of CVD in Thailand and the potential economic and health benefits of strategies to reduce the population risk factors during an eight year period. The main empirical findings and discussions have been presented and summarized within the respective chapters: Chapter 4: risk factors associated with CVD in Thailand from the 4th National health examination survey 2008-2009, Chapter 5: application of CVD risk assessment equations to the Thai population, Chapter 6: health care cost of CVD in Thailand, and Chapter 7: the impact of reducing risk factors for CVD in Thailand. This section will synthesise the main empirical findings to answer the study's two research questions.

1) How will the prevalence of CVD develop in Thailand over the next 5-10 years if the health system remains as it is?

- This study estimated the number of CVD patients over an eight year period by undertaking the mathematical CVD cost-offset model. If the health system continues as it is and the CVD risk factor remain the same as it was in 2009; the number of CVD patients will increase from 327,435 patients in 2009 to 3,361,472 patients over the next 8 years.

2) How much could the cost of hospital admissions and the number of DALYs from CVD be reduced, if the major multiple population risk factors were reduced through investment in public health initiatives?

- Findings from this study suggested that reducing any combination of the CVD risk factors can reduce incidence of aquiring CVD in a healthy population, as well as saving the burden of disease in terms of DALYs and savings on health care expenditure.
- If the public health initiatives achieve the UN millennium development goal or achieve a reduction of 5% in the level of CVD risk factors such as systolic blood pressure, total cholesterol and prevalence of cigarette smoking in the population, the health service provider will save approximately ฿9,000 million and achieve savings of approximately 750,000 DALYs over the next eight years.
- On the other hand, if the trend of risk factors increases, there will be an increase in health care expenditure of ฿7,600 million and an increase of 623,925 DALYs during the eight year period.

The main findings of this study are consistent with other studies on CVD modelling that focus on primary prevention and which target a reduction in modifiable risk factors. Moran et al. (2010) projected the trend of CVD in China will increase during 2010 to 2030, which relates to the aging population, increases in blood pressure and diabetes levels but decreases in the trend of active smoking. Whitfield (2006) presented the benefits of investment in primary prevention, which could prevent the number of deaths and also reduce the number of hospital admissions as well as saving costs of acute hospital admissions from CVD in the UK. Kontis (2014) has estimated that there will be delay or reduction in the number of deaths worldwide from the chronic disease, including CVD, if the UN millennium development goal is achieved (Kontis et al. 2014). Some CVD policy model studies found the effectiveness of treatment intervention, such as using statins, aspirin and beta-blockers on the number of deaths prevented, years of life gained without CVD and hospital admissions avoidable was

significant (Grover et al. 1998, Capewell, Morrison and McMurray 1999, Babad et al. 2002). However, the effectiveness of treatment interventions is beyond the scope of this study.

8.2 Strengths and limitations of the research

8.2.1 Strengths

To the best of the author's knowledge, this is the first study that has developed a CVD policy model specifically for use in Thailand. The benefit of mathematic modelling is the capability to estimate the future occurance of CVD events based on the current available information and the scientific evidence, instead of following-up people over a long period of time. This study provides the information for the health policy developers to plan and invest in primary prevention programs for chronic diseases such as CVD, rather than waiting until the problems occur or the prevalence of CVD increases in the population.

In terms of the implications for policy and practice in Thailand, many primary prevention programs for CVD have been implemented. Some primary interventions have been successfully implemented, such as smoking regulation which has reduced the prevalence of smoking in the Thai population during the last decade (Sangthong et al. 2011). However, some primary prevention programs such as promoting a healthy diet and undertaking physical activity have not been evaluated regarding their impact on reducing the risk factors of CVD. This is because CVD is caused by a combination of risk factors and it is difficult to measure the impact on the health benefits during a short-term period. The CVD cost-offset model can be used as the financial tool for helping develop the health policy for long-term planning and targeting the investment in primary prevention programs for reducing the instances of CVD. The findings in this

study show that there will be huge benefits of reducing the CVD risk factors by preventing the number of hospitalisations, reducing the burden of disease (DALYs) and savings in the future health care expenditure.

Additionally, the CVD cost offset model that has been developed in this study usd the APCS equation as the risk engine to calculate the probability of instances of CVD events during the eight year period. The APCS equation is generalisable for applying to other Asian populations because it was derived from the pools of data from the cohort studies around Asia. Therefore, this model can be replicate to other settings in Asian countries, if the esssential information of the population data and the risk factors profiles are available.

Moreover, the estimated number of CVD patients has been validated with the actual number of CVD patients who admitted in the hospital in 2009 which shows an accurate estimation in the middle and elderly age groups.

8.2.2 Limitations

This study encounterd a number of limitations, which need to be considered.

8.2.2.1 Model limitation

In terms of the model's limitation, the CVD cost-offeset model is static, as it performs the estimation at two points in time between 2009 and the following eight years. The model did not taken into account the dynamic changing of the risk factors and changes in the population age structure over time. In addition, the risk engine that has been used in this study is the APCS equation. Although, this equation is suitable for Asian populations and has been validated with the actual CVD events in Thailand; the number of independent variables that have been applied in the equation are limited. The equation incorporated age, gender, systolic blood pressure, total cholesterol and the

prevalence of smoking, but some risk factors such as diabetic status and BMI were not included in the analysis. Additionally, the equation has been able to calculate the probability of all CVD events which included both fatal and non-fatal CVD events, but it cannot calculate the probability of stroke or IHD separately.

8.2.2.2 Data limitation

In terms of the limitation of data availability, various data sources are required to conduct the model. The model was developed based on the population information of demographic and risk factors data in 2009. Therefore, the essential information for that year was gathered to apply and validate the model, such as the number of hospital admissions classified by age group and gender and the number of people who died from CVD in 2009. However, some information from 2009 is missing because it is not accessible and available during the period of study, such as the number of CVD patients in private hospitals, the number of patients in the social security health care scheme and in the civil servant health care scheme, which accounts for approximately 25% of the population and is missing from the validation data. The same limitation was encountered with the CVD mortality data in Thailand. It was gathered by a review of the informationcontained in the health statistic report and the annual report from the ministry of Public Health. Most documents present the overall mortality data,but do not classify it by age group and gender, as is required by the model. Therefore, the 10-year trend of CVD mortality during 1996 to 2006 has been used instead of the CVD mortality in 2009 because of the limitation of data availability.

8.3 Challenges of this study

This study used a combination of the various evidence, background knowledgeand literature, such as the epidemiology, biostatistics, mathematics, demographics and health economics to construct the mathematic CVD cost offset

model. A number of challenges occured whilst undertaking the study on health economic modelling. Completing the study required both technical skills, such as the advanced use of Microsoft Excel spreadsheets, learning how to perform analysis on statistical packages and how to calculated DALYs, as well as integrating all of this background knowledge to carry out the development of the model.

Another challenge was aquiring the various data required in this study, such as the demographic data on the number of the population classified by age and gender, the background mortality rate, the probability of dying from CVD in the general population, the CVD risk factor profile from the health survey, the actual number of hospital admissions due to CVD classified by age and gender and the cost of hospitalisation. The model needed different data from different sources. Some data can be accessed and gathered through the literature review, such as the mortality data from the national health statistical report. However, some of data needed to be collected from organisations in Thailand such as the national health examination survey data, hospitalisation data and the health care cost of CVD. To aquire this data, authority was required and permission had to be sought and obtained in writing before access to the data was granted. Although these are the secondary data sources, the data collection process took time because of the need to contact many organisations and some data source owners did not allow access to their data, such as the hospitalisation data from the social security health insurance system and the civil servant health insurance system. However, this study used the best available data in Thailand, which could be accessed during the period of the study to carry out the model.

8.4 Recommendations for future research

This study contributes to the initial CVD cost-offset model for estimating the future burden of CVD events and the future potential benefits of reducing the risk

factors of CVD in the population level in Thailand. However, the future development of the model is required to fullfill the gap of this study. The areas for future research are suggested as follows:

- A more sophisticated and dynamic model can be developed by applying the Markov model or Discrete event simulation model, if the specific CVD risk equations and the data are available.
- Further study can focus more on the CVD risk factors in younger adults. During the period of this study, there was no CVD risk equation available that was suitable for the younger adult (aged under 30 years) Thai population. Although, several studies have derived the CVD risk equation for projecting the CVD risk in younger adults (Pencina et al. 2009, Expert Panel on Detection, Evaluation,and Treatment of High Blood Cholesterol in Adults 2001), it was derived using western countries data which is not suitable for use with the Thai population.
- The APCS equation can be jusified to the Thai setting. However, a country specific CVD risk equation should be applied to get the precise estimation. During the study period, Thailand had the RAMA-EGATs risk score but it was only suitable for middle aged men in urban areas (Supina et al. 2009) and the equation was not published. Once, a country-specific CVD risk equation is available, the model can be configured with the equation to calculate the risks of getting CVD specifically for the Thai population.
- A future study may develop the model which takes into account the complexity of the risk factors. For example, the people with the highest risk conditions related to CVD, such as having diabetes mellitus, having chronic kidney dieases and being obese, are more likely to have a higher probability than the general

population of getting CVD. The specific CVD risk equation for these groups may be applied in the model.

- The dynamics of the risk factors should be taken into account in a further study because in reality most CVD risk factors are modifiable and can change over time when people change their health behaviour. For example, cigaratte smoking behaviour is dynamic as people can start and stop smoking at anytime during their life.
- Thailand has been estimated to become a more aging population than the labour force population in the next few decades. This study has estimated a high probability of getting CVD in an aging population because they are in the high risk groups of CVD, which have higher levels of CVD risk factors, such as higher blood pressure and higher total cholesterol, compared to the younger population. A future study should take into account the changes in the population age structure, which will benefit in supporting the information on the health care financial costs and the burden of disease related to CVD for the health policy, to prepare for an aging society in the future.
- The cost-effectiveness study of the specific primary preventions programs in Thailand should be studied to provide information on which intervention is the best value for money for the health policy implementation and an evaluation study on the cost-effectiveness of the existing CVD prevention interventions will be useful for encouraging investment in the prevention programs.
- Future research should investigate health care expenditure from the patients perspective because CVD patients require long-time care.There are many hidden and out-of-pocket costs that occur with patients and their family but few studies have been undertaked in Thailand.

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Appendix A: The literature search strategies

The literature search strategies

The literature search strategies are followed as descript below;

Inclusion criteria

The literature review included primary studies and research which have been relevant to the research topic such as the cardiovascular disease study, mathematical risk CVD risk assessment equation and the health economic modelling. The review included research articles, journal articles, reports, books, websites and theses. The published literatures are reviewed in electronically searching on the online database or hand searching for the hard copies. The review is focus on both English and Thai languages which was published in 1990 onwards. However there might be some unpublished literature which have related to the topic will be selected such as; the ministry of public health policy documents, conference papers and reports.

Exclusion criteria

The literature review excluded primary studies or research which were not directly relevant to the research topic. The review excluded non-English or non-Thai languages and the pre 1990 studies. The literature search excluded congenital heart disease which is caused by the dysfunction of the heart at birth. Rheumatic heart disease which is caused by infection is also excluded from the literature search because it is beyond the scope of the study.

Limitation of the literature reviews

The cardiovascular diseases are focused on the cardiovascular related diseases such as coronary heart disease, heart failure, heart attack, ischemic heart disease, stroke and myocardial infarction. However, some type of cardiovascular diseases which related the infection or genetic disorder will not covered in the reviews such as Rheumatic heart disease, Congenital or birth heart defects and Arrhythmia.

List of electronic databases

- Cochrane Library
- Medline (EBSCO)
- Applied Social Sciences Index and Abstracts (ASSIA) database
- Scopus
- Web of Science
- Cumulative Index to Nursing and Allied Health Literature (CINAHL)
- Ethos, British library database

University databases

- Centre for Review and Dissemination (CRD) database, University of York
- SCHARR Library, University of Sheffield

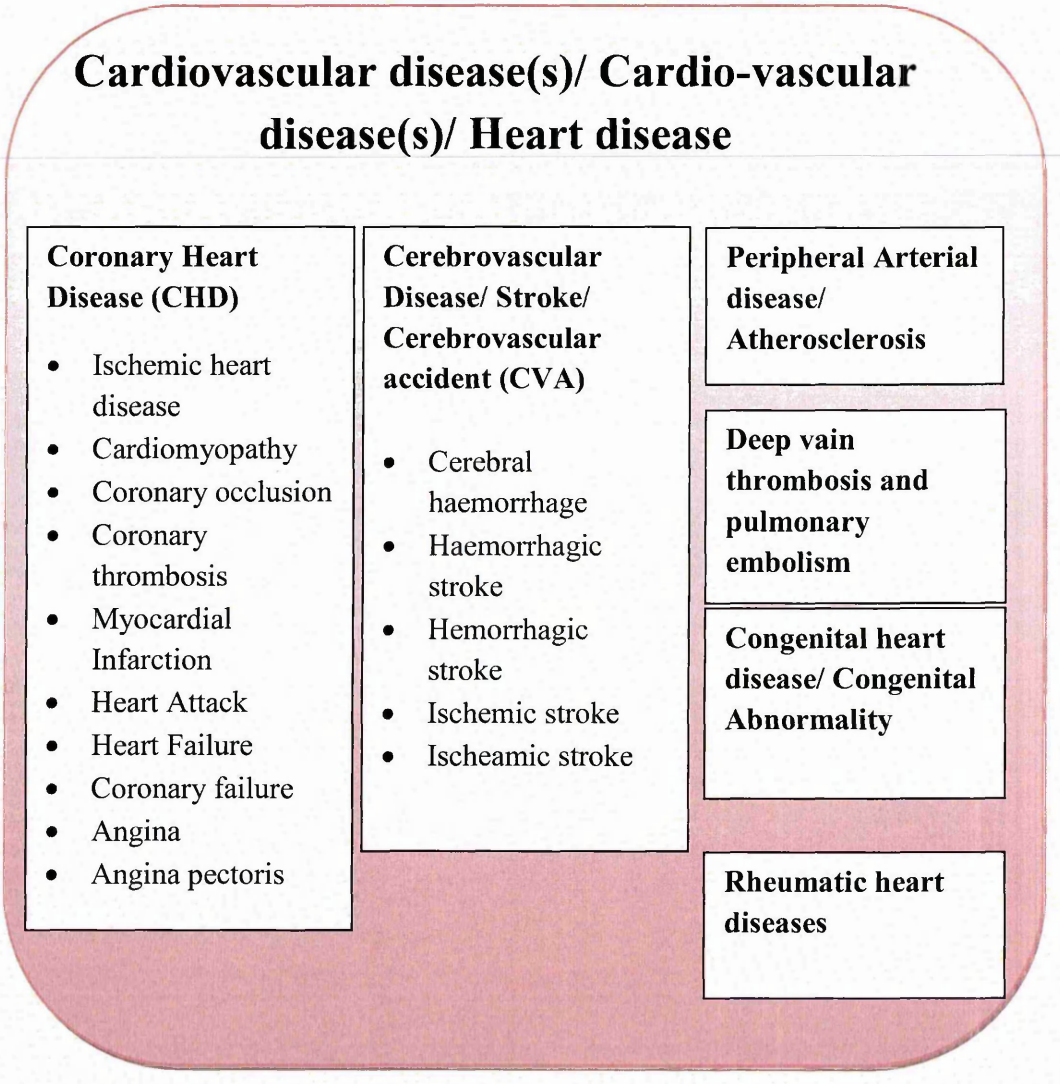
Other electronic sources

- Netting the evidence Google search engine
- Google scholar
- Organization websites
    - World health organization
    - National Institute for Health and Clinical Excellence (NICE)
    - Ministry of Public Health, Thailand
    - National Health Security Office, Thailand
    - Health System Research Institute, Thailand
    - International Health Policy Program, Thailand

Search Terms and Keywords

Cardiovascular diseases are a group of diseases. The main heading search terms used in Medical Subject Heading (MeSH) were "cardiovascular diseases", "cardio-vascular disease" , "heart disease", "coronary heart disease", "ishemic heart disease" "stroke", "cerebrovascular disease", "cerebrovascular accident".

Figure 1A: Overall terms of cardiovascular diseases



1. Prevalence and burden of cardiovascular diseases

Explanation of search terms used: / = MeSH Heading exp = exploded MeSH Heading; aterisk (*) denotes any character; ti = title word; ab = abstract word; pt = publication type; adj = adjacency; "" = phrase search; unless otherwise stated, terms searched all fields.

1. cardiovascular*:ti,ab.
2. cardiovascular disease*ti,ab.
3. cardiovascular diseses/
4. heart disese*ti,ab.
5. heart adj1 disease*ti,ab.
6. heart disease/
7. coronary heart disease*ti,ab.
8. coronary adj1 heart adj1 disease*.ti,ab.
9. coronary disease/
10. ischemic heart disease*ti,ab.
11. ischemic adj1 heart adj1 disease*.ti,ab.
12. myocardial ischemia/
13. myocardial infarc*ti,ab.
14. myocardial adj1 infarc*.ti,ab
15. myocardial infarction/
16. stroke*.ti,ab.
17. stroke/
18. cerebrovascular disease*.ti,ab.
19. cerebrovascular adj1 disease*.ti,ab.
20. cerebrovascular disease/

21. cerebrovascular accident*.ti,ab.

22. cerebrovascular adj1 accident*.ti,ab.

23. cerebrovascular accident/

24. cerebrovascular*.ti,ab.

25. heart attack*.ti,ab.

26. heart failure*.ti,ab.

27. heart failure/

28. or/1-27

29. epidemiology*,ti,ab.

30. burden*,ti ab.

31. burden adj1 disease*.ti,ab.

32. global* adj1 burden*.ti,ab.

33. disabilit* adj1 adjust* adj1 life adj1 year*

34. disabilit* adjust* life* year*

35. DALY*.ti,ab.

36. or/29-35

37. prevalence*.ti,ab.

38. incidence*.ti,ab.

39. mortalit*.ti,ab.

40. morbidit*.ti,ab.

41. trend*.ti,ab.

42. distribution*.ti,ab.

43. situation*.ti,ab.

44. pattern*.ti,ab.

45. or/37-44

46. 28 and 29

47. 28 and 36 and 45

48. 46 or 47

2. Mathematical risk assessment methods

Explanation of search terms used: / = MeSH Heading exp = exploded MeSH Heading; aterisk (*) denotes any character; ti = title word; ab = abstract word; pt = publication type; adj = adjacency; "" = phrase search; unless otherwise stated, terms searched all fields.

1. cardiovascular*:ti,ab.
2. cardiovascular disease*ti,ab.
3. cardiovascular diseses/
4. coronary heart disease*ti,ab.
5. coronary adj1 heart adj1 disease*.ti,ab.
6. coronary disease/
7. stroke*.ti,ab.
8. stroke/
9. cerebrovascular disease*.ti,ab.
10. cerebrovascular adj1 disease*.ti,ab.
11. cerebrovascular disease/
12. cerebrovascular accident*.ti,ab.
13. cerebrovascular adj1 accident*.ti,ab.
14. cerebrovascular accident/
15. cerebrovascular*.ti,ab.
16. or/ 1-15
17. Prediction model*.ti,ab.

18. Prediction*.ti,ab.

19. Estimation*.ti,ab.

20. Cohort study*.ti,ab.

21. Follow up study*.ti,ab.

22. Prediction equation*.ti,ab.

23. Risk score*.ti,ab.

24. logistic regression equation*.ti,ab.

25. Risk prediction equation*.ti,ab.

26. Multiple risks prediction*.ti,ab.

27. or/17-26

28. 16 and 27

3. Modelling technique

Explanation of search terms used: / = MeSH Heading exp = exploded MeSH Heading; aterisk (*) denotes any character; ti = title word; ab = abstract word; pt = publication type; adj = adjacency; "" = phrase search; unless otherwise stated, terms searched all fields.

1. cardiovascular*:ti,ab.
2. cardiovascular disease*ti,ab.
3. cardiovascular diseses/
4. coronary heart disease*ti,ab.
5. coronary adj1 heart adj1 disease*.ti,ab.
6. coronary disease/
7. stroke*.ti,ab.
8. stroke/

9. cerebrovascular disease*.ti,ab.

10. cerebrovascular adj1 disease*.ti,ab.

11. cerebrovascular disease/

12. cerebrovascular accident*.ti,ab.

13. cerebrovascular adj1 accident*.ti,ab.

14. cerebrovascular accident/

15. cerebrovascular*.ti,ab.

16. or/ 1-15

17. Mathematic* Model* *.ti,ab.

18. Decision* model* *.ti,ab.

19. Economic* model* *.ti,ab.

20. Decision tree model*.ti,ab.

21. Markov's Model* *.ti,ab.

22. Simulation* Model**.ti,ab.

23. Micro-simulation* model* *.ti,ab.

24. or/17-23

25. 16 and 24

Appendix B: The constants and β coefficient for the original Framinham equation.

Table 1B: Weibull accelerated failure-time model regression coefficients of risk factors and CVD in the Framingham heart study (Khonputsa, et al. 2011)

Risk factor	Men	Women
	Ischemic heart disease	
Age (years)	-0.037	-0.036
Total cholesterol (mg/dL)	-0.005	-0.006
Diabetes mellitus (yes=1, no=0)	-0.461	-0.695
Systolic blood pressure (mmHg)	-0.009	-0.01
Smoking (yes=1, no=0)	-0.384	-0.221
Constant1	8.39	9.32
Constant2	0.82	0.83
	Stroke	
Age (years)	-0.081	-0.06
Total cholesterol (mg/dL)	Non-significant	Non-significant
Diabetes mellitus (yes=1,no=0)	-0.391	-0.684

Appendix C: The letter of approval for data accessing

National Health Examination Survey Office (NHESO)
126 Fifth Floors, Boromarajonani College of Nursing Building,
Bamrasnaradura Infectious Disease Institute
Talad-Kwan, Muang District, Nonthaburi 11000, Thailand

January 24, 2011

Dear Dr. Malcolm David Whitfield,

The National Health Examination Survey Office (NHESO), Thailand agrees to support Miss Rungkarn Inthawong for her PhD research work at Sheffield Hallam University. The NHESO will support her research activities in accessing to the National Health Examination Survey IV, 2008-2009 (NHESIV) data of the requested variables, providing work facilities and assisting in contact with other organizations in Thailand.

Sincerely yours,

(Dr. Wichai Aekplakorn)
Principal Investigation of NHES IV
National Health Examination Survey Office
Email address: *rawap@mahidol.ac.th*

Other address:
Dr. Wichai Aekplakorn
Department of Community Medicine,
Faculty of Medicine, Ramathibodi Hospital, Mahidol University
Rama VI Rd. Rajdevi,
Bangkok 10400, Thailand
Tel: +662 2011518

สปสช.
สำนักงานหลักประกันสุขภาพแห่งชาติ

สำนักงานหลักประกันสุขภาพแห่งชาติ
๑๒๐ หมู่ ๓ ชั้น ๒-๔ อาคารรวมทางน้ำยงานราชการB สุมย์ราชการเฉลิมพระเกียรติ ๘๐ พรรษา ๕ ธันวาคม ๒๕๕๐
ถนนแจ้งวัฒนะ แขวงทุ่งสองห้อง เขตหลักสี่ กรุงเทพฯ๑๐๒๑๐ โทร.๐๒ ๑๔๓๙๐๐๐ โทรสาร ๐๒ ๑๔๓๙๓๑๐

ที่ สปสช. ๑.๕๔/ ๐๐๒๗๖

๘ กรกฎาคม ๒๕๕๘

เรื่อง อนุญาตให้ใช้ข้อมูลเพื่อนำไปประกอบเป็นหลักฐานอ้างอิงของข้อมูลแนบท้ายวิทยานิพนธ์

เรียน นางสาวรุ่งกานต์ อินทวงศ์

อ้างถึง หนังสือของ มหาวิทยาลัย Sheffield Hallam: ลงวันที่ ๓๐ มกราคม ๒๕๕๘

สิ่งที่ส่งมาด้วย (๑) เอกสารโครงการวิจัย จำนวน ๑ ชุด

ตาม หนังสือของนางสาวรุ่งกานต์ อินทวงศ์ นักเรียนทุนรัฐบาลกระทรวงวิทยาศาสตร์และเทคโนโลยี ซึ่งเป็นนักศึกษาปริญญาเอกสาขา PhD (health and wellbeing) จากมหาวิทยาลัย Sheffield Hallam ประเทศอังกฤษ ขอความกรุณาออกหนังสืออนุญาตให้ใช้ข้อมูลเพื่อนำไปประกอบเป็นหลักฐานอ้างอิงของข้อมูลแนบท้ายวิทยานิพนธ์ ในการทำวิจัยในหัวข้อ "Assessing the impact of reducing Risk factors for cardiovascular disease in Thailand" เพื่อพัฒนาแบบจำลองคณิตศาสตร์คาดประมาณสถานการณ์โรคหัวใจและหลอดเลือดในประเทศไทย รวมทั้งประเมินผลกระทบทางด้านค่าใช้จ่ายในการรักษาพยาบาล จำนวนผู้ป่วย จำนวนผู้เสียชีวิตจากโรคหัวใจและหลอดเลือด และจำนวนปีในการเสียสุขภาวะ หากมีการลดปัจจัยเสี่ยงต่อการเกิดโรคหัวใจและหลอดเลือดในระดับประชากร นั้น

ในการนี้ สำนักงานหลักประกันสุขภาพแห่งชาติ (สปสช.) อนุญาตให้นางสาวรุ่งกานต์ อินทวงศ์ ใช้ข้อมูลดังกล่าวได้ เพื่อนำไปประกอบเป็นหลักฐานอ้างอิงของข้อมูลแนบท้ายวิทยานิพนธ์ และเมื่อโครงการวิจัยเสร็จสิ้นแล้ว ทางสำนักงานหลักประกันสุขภาพแห่งชาติ ขอความร่วมมือท่านนำส่งรายงานการวิจัยฉบับสมบูรณ์มายังสำนักสารสนเทศเพื่อการบริหาร ทั้งนี้เพื่อใช้ประโยชน์ต่อไป

จึงเรียนมาเพื่อโปรดทราบ และดำเนินการต่อไป จะเป็นพระคุณ

ขอแสดงความนับถือ

(นายอภิจ ธรรมลัยชารี)
ประธานกรรมการ
ปฏิบัติงานแทน เลขาธิการสำนักงานหลักประกันสุขภาพแห่งชาติ

สำนักสารสนเทศเพื่อการบริหาร
โทรศัพท์ ๐๒ ๑๔๑ ๕๐๖๘
โทรสาร ๐๒ ๑๔๓ ๙๗๓๔
ผู้ประสานงาน : นายวันชัย มากเลาะเลย์
Email : wanchai.m@nhso.go.th

Appendix D: Letter of approval from Sheffield Hallam University,

Faculty of Health and Wellbeing Research Ethics Committee

Centre for
Health and Social Care
Research

Faculty of Health and Wellbeing Research Ethics Committee
Health & Social Care Research Ethics Review Group

Report Form

Title:	Assessing the impact of reducing risk factors for cardio-vascular disease in Thailand.
Principal Investigator:	Rungkarn Inthawong
Recommendation:	
Acceptable:	✓
Not acceptable, see comments:	
Acceptable, but see comments:	

Comments:

See attached feedback on review forms.

Signature : Peter Almk ..... Date: 19 April 11

Peter Almark,
Chair
HSC Research Ethics Review Group

Please remember that an up-to-date project file must be maintained for the duration of the project and afterwards. The project file might be inspected at any time.

Note: *Approval applies until the anticipated date of completion unless there are changes to the procedures, in which case another application should be made.*

Centre for Health and Socal Care Research
Faculty of Health and Wellbeing Sheffield Hallam University Montgomery House
32 Collegiate Crescent Collegiate Crescent Campus Sheffield S10 2BP UK
Telephone +44 (0)114 225 5854 Fax +44 (0)114 225 4377
E-mail chscr@shu.ac.uk www.shu.ac.uk/chscr

Sheffield Hallam University

Research proposal review form: Sept 2010

Faculty of Health and Wellbeing
Faculty Research Ethics Committee
Health and Social Care Division

Research Proposal Review Form

Review Summary

Name of researcher: Rungkarn Inthawong

Project title: Assessing the impact of reducing risk factors for cardio-vascular diseases in Thailand

Name of supervisor: Prof. Malcolm D. Whitfield
Dr. Karen Collins

Code for Decision: Satisfactory Review Achieved
Satisfactory Review with some advice
Unsatisfactory Review - needs amendments
[PLEASE SELECT ONE OF THESE THREE]

Signature of Reviewer: Peter Allmark

Date: 18/04/2011

Feedback : This proposal has already been approved in terms of the RF1 process. In terms of ethics it involves using anonymous data which the student has permission to access from its owner. It is a well-written protocol and I have no concerns about the ethics. I have decided that a single ethics review is sufficient in this case given that the proposal has been reviewed already for the RF1 and that it is very low risk.

Site/Project files
An up-to-date project or site file must be maintained for the duration of the project and afterwards. The file might be inspected at any time.

Mental Capacity
Special procedures now apply to any research that involves adults without mental capacity to consent to that research. This applies both to the NHS and to

Social Care Research. Please contact Peter Allmark to discuss if that applies to this study.

Checklist for Independent Scientific Review -
PA - This has already been done as part of the RF1 process

General	Yes	No	N/A
The aims of the project are clearly stated			
The project is original in concept with evidence to support the project's originality in the literature review			
The project is useful and relevant to clinical practice, policy making or workforce planning			
The project is feasible in the time available			
Service users have been involved in the development of the proposal where possible			
A completed project safety plan is included with the proposal			
A completed registration form is included			

Method / design / analysis	Yes	No	N/A
The design is appropriate for the identified aims			
A clear rationale for the use of systematic literature review is included			
The review procedure chosen is appropriate			
The sampling strategy chosen is appropriate for the identified aims.			
A power calculation has been undertaken if appropriate.			
Methods to be used to identify, approach and recruit participants have been included			
Trustworthiness and rigour of data collection are considered			
Measurement issues are addressed in relation to clinically appropriate measuring tools.			
The validity and reliability of the outcomes measures chosen have been considered (this included questionnaires to be used)			
An appropriate plan of analysis is included with reflection on the implications of the sample size.			
The project attempts to look at individual data as well as aggregated data			
There is a logical and feasible research time plan with clearly delineated milestones.			
Itemised costings are included			
Issues concerning racial and cultural diversity have been considered			
Participant information and consent forms have been included			

Have issues around controlling bias been considered			
Has a statistical opinion been included if appropriate			
Have indemnity issues been considered (FIN 12 included if appropriate.)			
Have funding arrangements been made clear (ENT 1 enclosed if appropriate)			
Have methods for the dissemination of results been considered.			
Have intellectual property arrangements been considered (if appropriate)			

Checklist for Ethical Approval

SAFETY ISSUES - Refer to the project safety plan as well as the protocol.	**Yes**	**No**
Is there is any potential for physical or psychological harm or distress to research participants?		x
If Yes: a) Are adequate mechanisms in place to minimise the risk and to tackle any harm or distress that occurs?		
b) Is the potential risk of harm balanced by potential benefit to participants?		
Is there is any potential for physical or psychological harm or distress to the researcher(s)?		x
If Yes: a) Are adequate mechanisms in place to minimise the risk and to tackle any harm or distress that occurs?		
Are any of the participants likely to belong to a so-called vulnerable group, for example, children, people with mental health problems or with learning disability, people in a dependent relationship to the researcher(s)?*		x
Is there a named Project Safety Supervisor?	x	

* See note on Mental Capacity on the front sheet.

RIGHTS ISSUES	**Yes**	**No**
Are issues of confidentiality, privacy and data protection adequately covered in relation to:	x	
a) The recruitment of participants?		
b) The protection of the privacy of participants?		
c) The protection and storage of confidential information generated by the study?		
Will informed consent be obtained from the participants?		x
Is there a satisfactory:		
a) Participant information sheet?		
b) Participant consent form? [Note: a consent form is not required for questionnaire studies.]		
Does the research involve the removal of any human tissue from participants? Human tissue is, in effect, any sample taken from the human body apart from nails and hair.		x
Does this proposal adequately address any issues of ethnic diversity or other diversity issues?	x	
Do you believe this proposal needs specialist ethics review?		x

4

Appendix E: The international statistical classicfication of diseases and related health problems 10th revision

Diseases of the circulatory system (I00-I99)

Code	Diseases
I00-I02	**Acute rheumatic fever**
I00	Rheumatic fever without mention of heart involvement
I01	Rheumatic fever with heart involvement
I02	Rheumatic chorea
I05-I09	**Chronic rheumatic heart diseases**
I05	Rheumatic mitral valve diseases
I06	Rheumatic aortic valve diseases
I07	Rheumatic tricuspid valve diseases
I08	Multiple valve diseases
I09	Other rheumatic heart diseases
I10-I15	**Hypertensive diseases**
I10	Essential (primary hypertension)
I11	Hypertensive heart disease
I12	Hypertensive renal disease
I13	Hypertensive heart and renal disease
I15	Secondary hypertension
I20-I25	Ischaemic heart diseases
I20	Angina pectoris
I21	Acute myocardial infarction
I22	Subsequent myocardial infarction
I23	Certain current complications following acute myocardial infarction
I24	Other acute ischaemic heart disease
I25	Chronic ischaemic heart disease
I26-I28	**Pulmonary heart disease and diseases of pulmonary circulation**

Code	Diseases
I26	Pulmonary embolism
I27	Other pulmonary heart diseases
I28	Other diseases of pulmonary vessels
I30-I52	**Other forms of heart disease**
I30	Acute pericarditis
I31	Other diseases of pericardium
I32	Pericarditis in diseases classified elsewhere
I33	Acute and subacute endocarditis
I34	Nonrheumatic mitral valve disorders
I35	Nonrheumatic aortic valve disorders
I36	Nonrheumatic tricuspid valve disorders
I37	Pulmonary valve disorders
I38	Endocarditis, valve unspecified
I39	Endocarditis and heart valve disorders in diseases classified elsewhere
I40	Acute myocarditis
I41	Myocarditis in disease classifield elsewhere
I42	Cardiomyopathy
I43	Cardiomyopathy in diseases classified elsewhere
I44	Atrioventricular and left bundle-branch block
I45	Other conduction disorders
I46	Cardiac arrest
I47	Paroxysmal tachycardia
I48	Atrial fibrillation and flutter
I49	Other cardiac arrhythmias
I50	Heart failure
I51	Complications and ill-defined descriptions of heart disease
I52	Other heart disorders in diseases classified elsewhere
I60-I69	**Cerebrovascular diseases**

Code	Diseases
I60	Subarachnoid haemorrhage
I61	Intracerebral haemorrhage
I62	Other nontraumatic intracranial haemorrhage
I63	Cerebral infarction
I64	Stroke, not specified as haemorrhage or infarction
I65	Occlusion and stenosis of precerebral arteries, not resulting in cerebral infarction
I66	Occlusion and stenosis of cerebral arteries, not resulting in cerebral infarction
I67	Other cerebrovascular diseases
I68	Cerebrovascular disorders in diseases classified elsewhere
I69	Sequelae of cerebrovascular disease
I70-I79	**Diseases of arteries, arterioles and capillaries**
I70	Atherosclerosis
I71	Aortic aneurysm and dissection
I72	Other aneurysm and dissection
I73	Other peripheral vascular diseases
I74	Arterial embolism and thrombosis
I77	Other disorders of arteries and arterioles
I78	Diseases of capillaries
I79	Disorders of arteries, arterioles and capillaries in diseases classified elsewhere
I80-I89	**Diseases of veins, lymphatic vessels and lymph nodes , not elsewhere classified**
I81	Portal vein thrombosis
I82	Other venous embolism and thrombosis
I83	Varicose veins of lower extremities
I84	Haemorrhoids
I85	Oesophageal varices
I86	Varicose veins of other sites

Code	Diseases
I87	Other disorders of veins
I88	Nonspecific lymphadenitis
I89	Other noninfective disorders of lymphatic vessels and lymph nodes
I95-I99	**Other and unspecified disorders of the circulatory system**
I95	Hypotension
I97	Postprocedural disorders of circulatory system, not elsewhere classified
I98	Other disorders of circulatory system in disease classified elsewhere
I99	Other and unspecified disorders of circulatory system

Appendix F: The mean of 8-10 years probability of CVD and the estimated number of 8-10 years CVD patients.

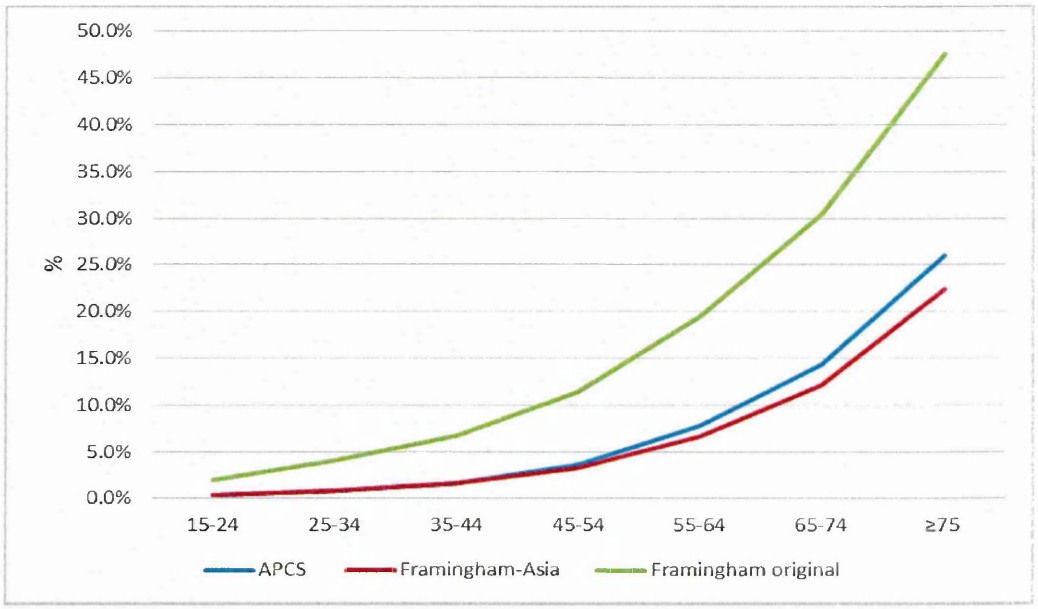


Figure 1F The mean of 8-10 years probability of CVD in men who aged ≥ 15 years, NHESIV

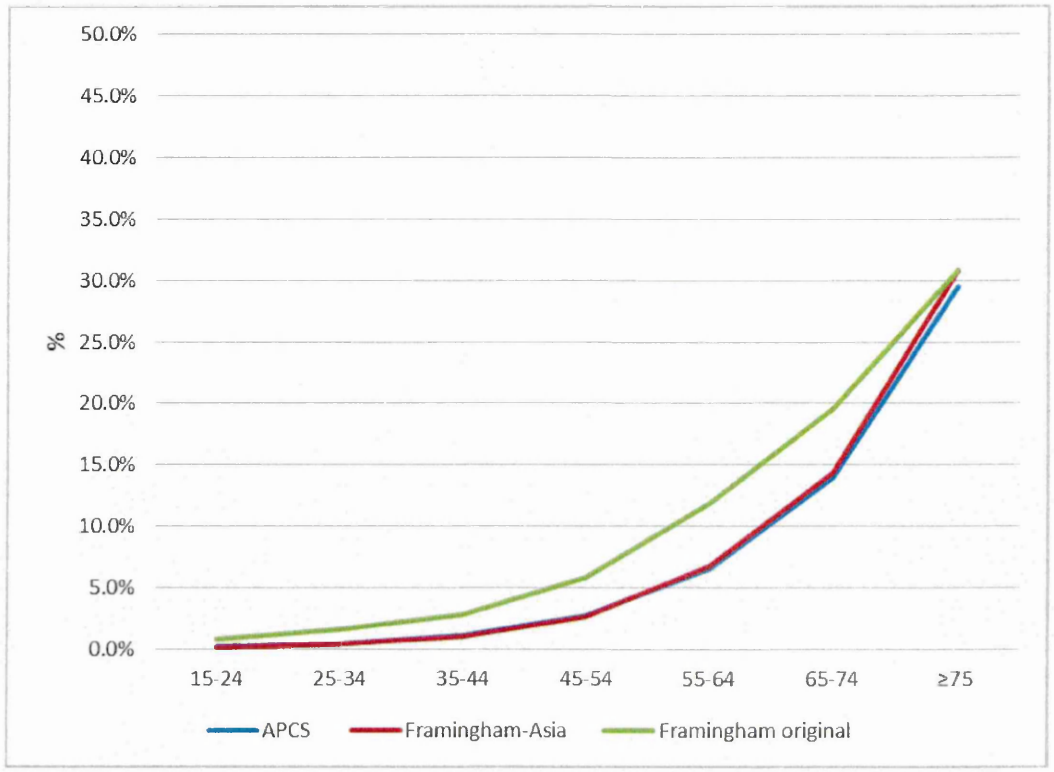


Figure 2F The mean of 8-10 years probability of CVD in women who are aged ≥ 15 years, NHESIV.

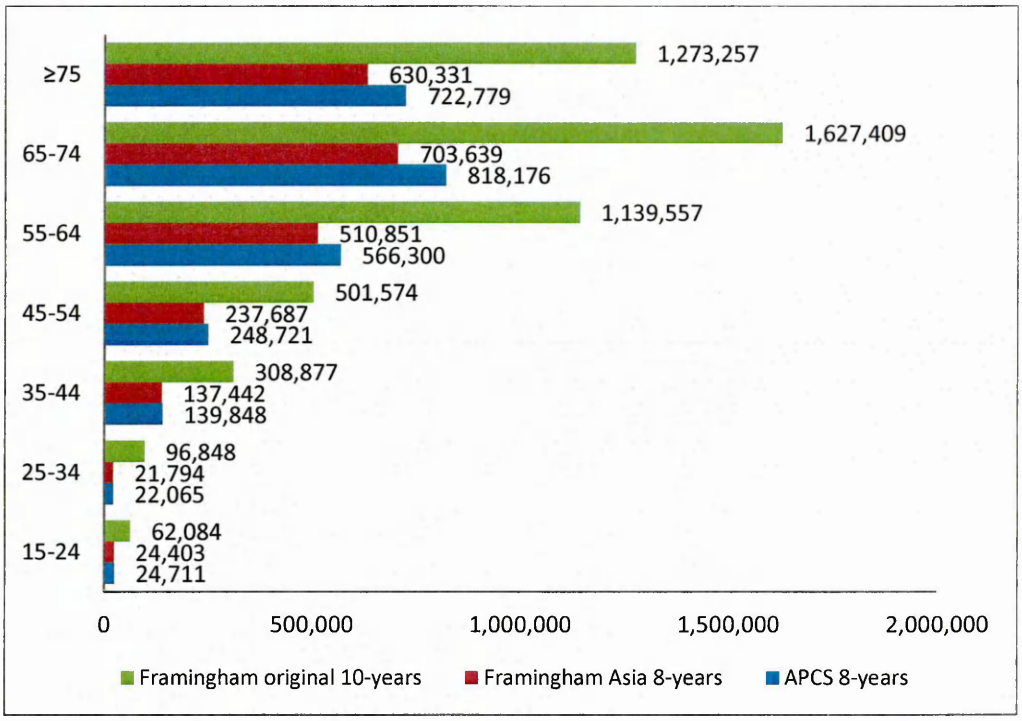


Figure 3F The estimated number of men who are alive with CVD in Thailand in 2017-2019

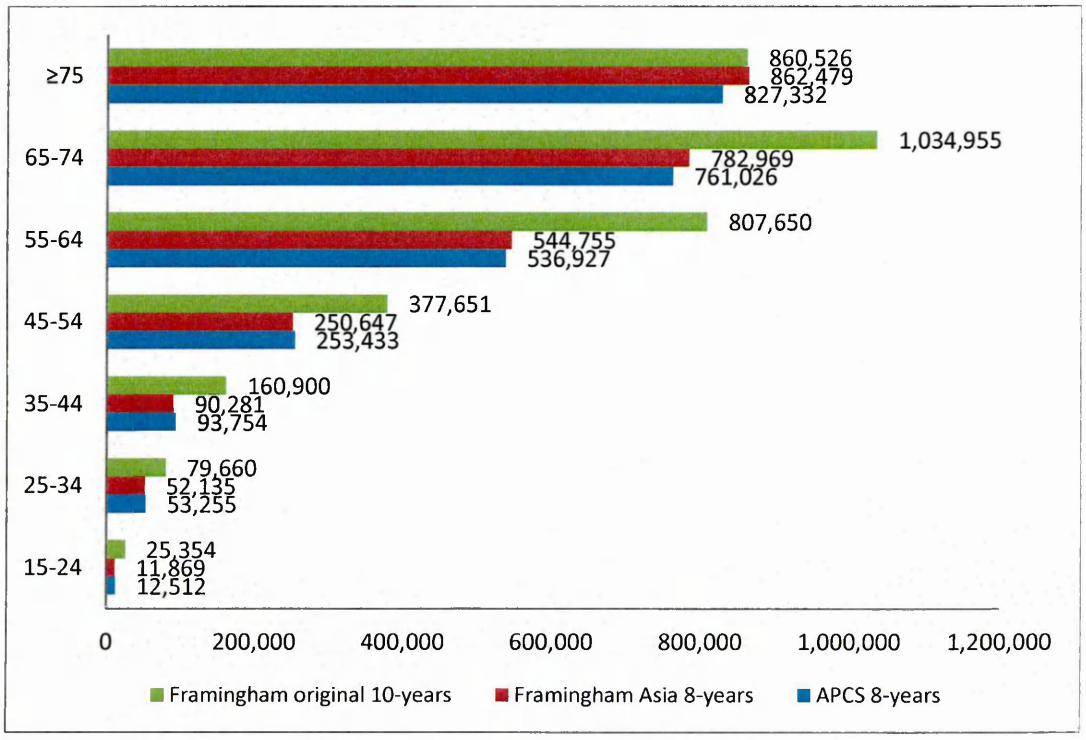


Figure 4F The estimated number of women who are alive with CVD in Thailand during the next 8-10 years

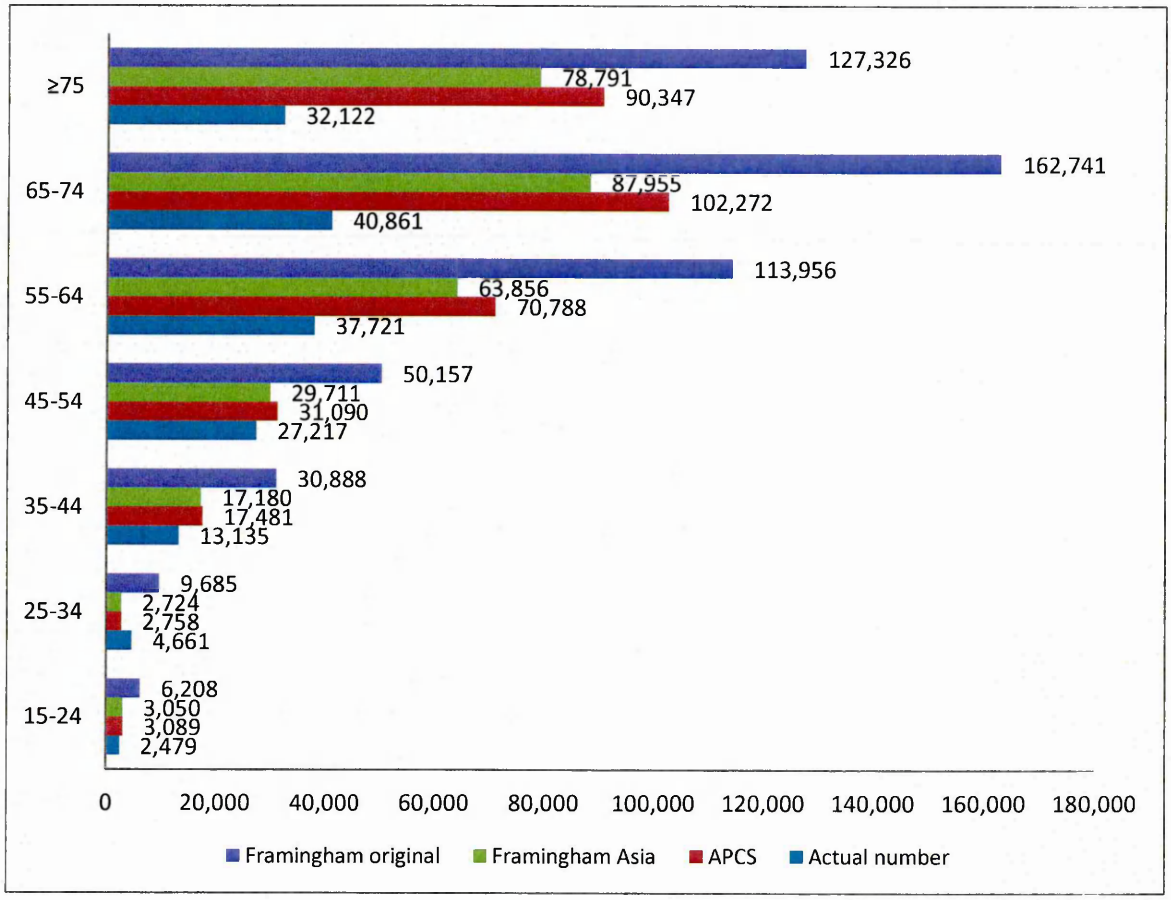


Figure 5F Comparing the actual number of CVD patients with the estimated number of CVD patients in the 3 different equations amongst Thai men by age groups, in 2009

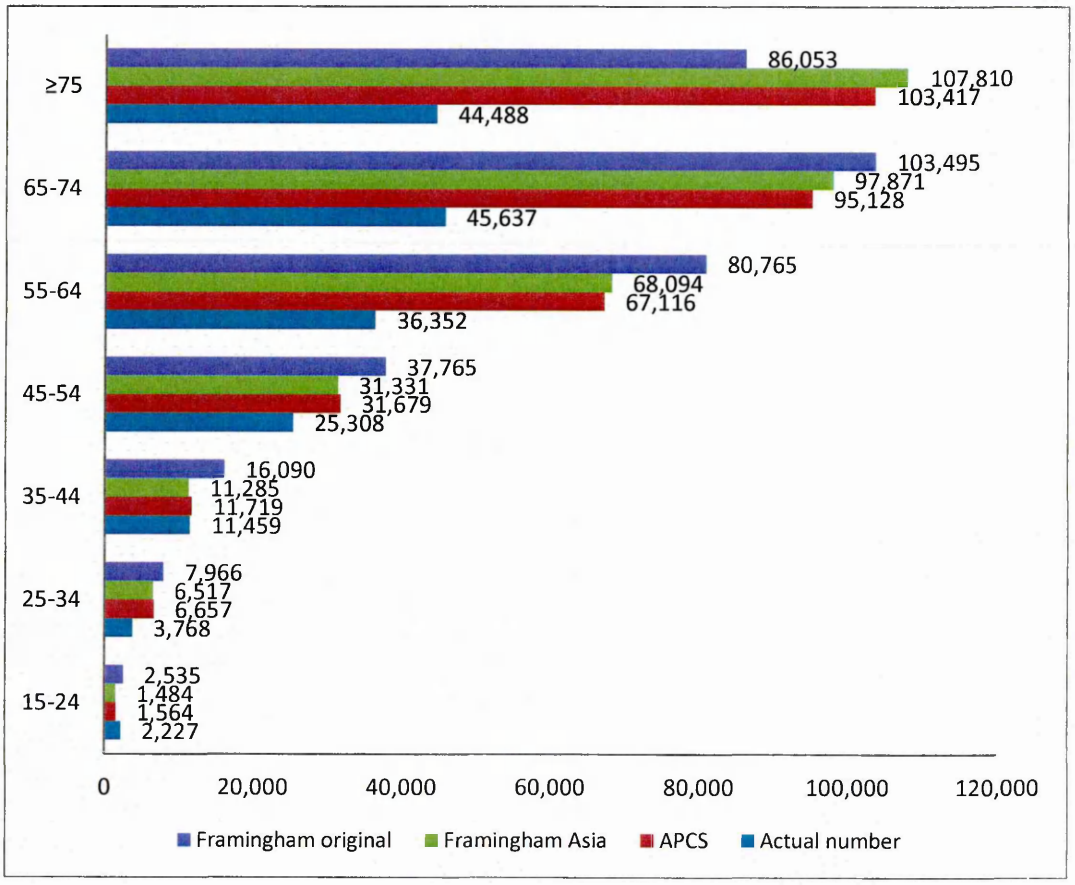


Figure 6F Comparing the actual number of CVD patients with the estimated number of CVD patients in 3 different equations among Thai women by age groups in 2009

Appendix G: The absolute total cost of hospital admission by age group gender and CVD condition

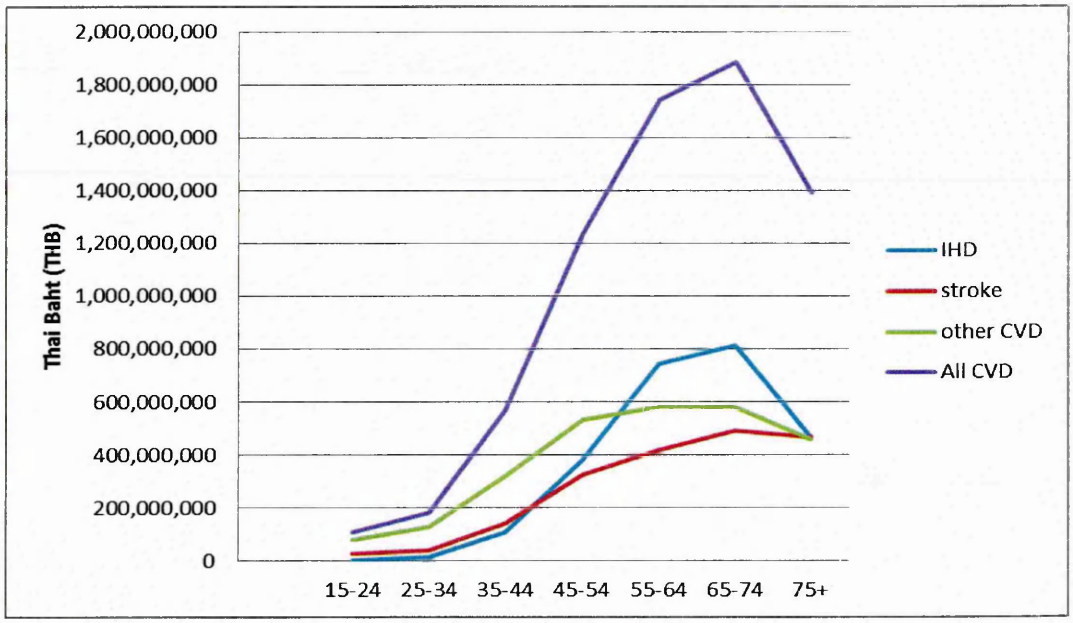


Figure 1E The absolute total cost of hospital admission by age group and CVD condition, Thailand 2009 (THB)

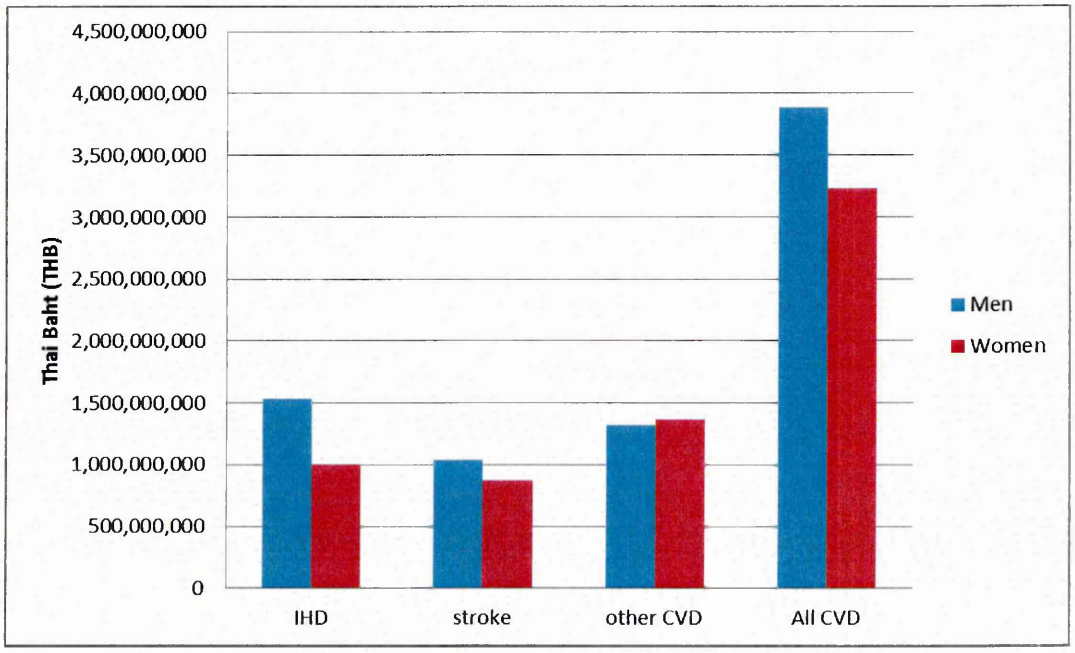


Figure 2E The absolute total cost of hospital admission by gender and CVD conditions, Thailand 2009 (THB)

Appendix H: Probability of dying from all CVD (1996-2006), Thailand

Table 1H presents the probability of dying in the Thai population during 1996 to 2006. The probability of dying from CVD has been calculated from the number of death from CVD divided by the number of mid-year population in each year and classified by age group and gender

Table 1H Probability of dying from all CVD (1996-2006) in Thai population

Age	1996			1997			1998		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
15-24	0.000398794	0.000145262	0.000274213	0.00036604	0.000146244	0.000257992	0.000230343	0.000126603	0.000179248
25-34	0.000952812	0.000281999	0.000621294	0.000980456	0.000315141	0.000651967	0.000901672	0.000302012	0.000605674
35-44	0.001253676	0.000474107	0.000862295	0.001215292	0.000431124	0.000821186	0.00108842	0.000411782	0.000747959
45-54	0.002050223	0.001055035	0.001541176	0.001852103	0.001019558	0.00142603	0.001697635	0.000906511	0.001292959
55-64	0.003771456	0.002187529	0.002943464	0.003329804	0.00209481	0.002683261	0.003036482	0.001847158	0.002413529
65-74	0.006341359	0.004154046	0.005176651	0.005541879	0.003706673	0.004559946	0.004817827	0.0034094	0.004061503
75+	0.011155654	0.008667278	0.009715244	0.009550196	0.007534551	0.00838527	0.008421561	0.006909529	0.007547073
total	0.001701233	0.00098959	0.001342764	0.001569198	0.000931843	0.001247898	0.00139975	0.000858852	0.001126749
Age	**1999**			**2000**			**2001**		
	Male	**Female**	**Total**	**Male**	**Female**	**Total**	**Male**	**Female**	**Total**
15-24	0.000150838	0.000080	0.000116	0.000089	0.000050	0.000070	0.000087	0.000040	0.000064
25-34	0.000538701	0.000203	0.000373	0.000285	0.000132	0.000210	0.000217	0.000104	0.000161
35-44	0.000761657	0.000323	0.000541	0.000505	0.000215	0.000359	0.000458	0.000217	0.000336
45-54	0.001253283	0.000725	0.000983	0.000987	0.000544	0.000761	0.000995	0.000577	0.000781
55-64	0.002425317	0.001486	0.001932	0.001882	0.001116	0.001480	0.001972	0.001176	0.001553
65-74	0.004232015	0.003004	0.003571	0.003468	0.002462	0.002926	0.003689	0.002654	0.003129
75+	0.007553248	0.006001	0.006660	0.006353	0.005300	0.005748	0.007603	0.006748	0.007110
total	0.001077724	0.000710	0.000892	0.000815	0.000562	0.000687	0.000842	0.000623	0.000731

Age	2002			2003			2004		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
15-24	0.000079	0.000033	0.000057	0.000115	0.000036	0.000076	0.000107	0.000034	0.000071
25-34	0.000159	0.000070	0.000114	0.000154	0.000060	0.000108	0.000183	0.000069	0.000126
35-44	0.000355	0.000163	0.000257	0.000372	0.000158	0.000264	0.000421	0.000178	0.000297
45-54	0.000886	0.000474	0.000674	0.000771	0.000432	0.000597	0.001046	0.000544	0.000786
55-64	0.001825	0.001173	0.001484	0.001650	0.000982	0.001304	0.002217	0.001309	0.001741
65-74	0.003489	0.002424	0.002908	0.003144	0.002413	0.002755	0.004192	0.002894	0.003483
75+	0.005880	0.005070	0.005406	0.004198	0.003873	0.004013	0.006670	0.005648	0.006071
total	0.000765	0.000569	0.000665	0.000833	0.000635	0.000733	0.000939	0.000669	0.000801

Age	2005			2006		
	Male	Female	Total	Male	Female	Total
15-24	0.000088	0.000030	0.000060	0.000064	0.000030	0.000047
25-34	0.000151	0.000065	0.000108	0.000128	0.000052	0.000090
35-44	0.000386	0.000149	0.000265	0.000327	0.000137	0.000230
45-54	0.000993	0.000458	0.000716	0.000854	0.000404	0.000620
55-64	0.002028	0.001128	0.001555	0.001815	0.001011	0.001392
65-74	0.003708	0.002650	0.003129	0.003411	0.002417	0.002867
75+	0.006318	0.005688	0.005948	0.006099	0.005147	0.005540
total	0.000870	0.000625	0.000745	0.000797	0.000576	0.000684

Table 2F Average 10-year probability of dying from CVD classified by age group and gender

Age	Average 10-years probabilities		
	Male	**Female**	**Total**
15-24	0.0001615	0.0000682	0.0001157
25-34	0.0004228	0.0001504	0.0002881
35-44	0.0006494	0.0002597	0.0004527
45-54	0.0012168	0.0006489	0.0009253
55-64	0.0023593	0.0014100	0.0018620
65-74	0.0041849	0.0029262	0.0035060
75+	0.0072546	0.0060533	0.0065584
total	0.0010553	0.0007045	0.0008777

Appendix I: The disability weight of the cardiovascular disease from GBD study 2010

Cardiovascular and circulatory disease	Estimate	95%CI
Acute myocardial infarction: days 1-2	0.422	0.284-0.566
Acute myocardial infarction: days 3-28	0.056	0.035-0.082
Angina pectoris: mild	0.037	0.022-0.058
Angina pectoris: moderate	0.066	0.043-0.095
Angina pectoris: severe	0.167	0.109-0.234
Cardiac conduction disorders and cardiac dysrhythmias	0.145	0.097-0.205
Claudication	0.016	0.008-0.028
Heart failure: mild	0.037	0.021-0.058
Heart failure: moderate	0.07	0.044-0.102
Heart failure: severe	0.186	0.128-0.261
Stroke: long-term consequences, mild	0.021	0.011-0.037
Stroke: long-term consequences, moderate	0.076	0.050-0.110
Stroke: long-term consequences, moderate plus cognition problems	0.312	0.211-0.433
Stroke: long-term consequences, severe	0.539	0.363-0.705
Stroke: long-term consequences, severe plus cognition problems	0.567	0.394-0.738

source: (Murray et al. 2012b)

Appendix J: The global health observatory data repository, non-communicable risk factors

Table 1J Mean (95% CI) of blood pressure trends (crude estimate) for population aged 25 years and over in Thailand (mmHg)

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989
Male	121.3 (112.3-130.3)	121.3 (113.1-129.2)	121.2 (113.8-128.2)	121 (114.4-127.4)	120.9 (114.9-126.7)	120.9 115.3-126.1)	120.8 (115.7-125.7)	120.8 (116.1-125.3)	120.9 (116.5-125.2)	121 (116.8-125.1
Female	116.6 (107.6-126.0)	116.7 (108.6-125.2)	116.8 (109.4-124.4)	116.9 (109.9-123.7)	117 (110.7-123.2)	117 (111.3-122.7)	117.1 (111.7-122.3)	117.2 (112.1-122.0)	117.3 (112.6-121.8)	117.4 (113.1-121.7
	1990	**1991**	**1992**	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Male	121.1 (117.1-125.2)	121.3 (117.4-125.2)	121.5 (117.7-125.3)	121.7 (118.0-125.4)	121.9 (118.3-125.6)	122.2 (118.6-125.8)	122.4 (118.9-126.1)	122.6 (119.1-126.4)	122.8 (119.2-126.4)	122.9 (119.4-126.5
Female	117.6 (113.5-121.6)	117.8 (113.8-121.7)	117.9 (114.2-121.7)	118.1 (114.5-121.8)	118.4 (114.8-121.9)	118.6 (115.1-122.1)	118.8 (115.4-122.2)	133.9 (125.9-141.7)	119.1 (115.8-122.5)	119.3 (116.0-122.7
	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**
Male	123.1 (119.7-126.6)	123.2 (119.9-126.7)	123.4 (120.2-126.8)	123.6 (120.5-126.9)	123.8 (120.7-127.1)	124.1 (120.9-127.3)	124.3 (121.1-127.6)	124.5 (121.1-128.0)	127.4 (121.0-128.5)	124.8 (120.6-129.1
Female	119.5 (116.2-122.8)	119.7 (116.5-122.8)	119.8 (116.7-123.0)	120 (116.8-123.2)	120.2 (117.1-123.5)	120.4 (117.2-123.8)	120.6 (117.2-124.1)	120.8 (117.1-124.5)	120.9 (116.9-124.9)	121 (116.6-125.4

Table 2J Mean (95%CI) of thetotal cholesterol trends (crude estimate) for population aged 25 years and over in Thailand (mmol/L)

	1980	1981	1982	1983	1984	1985	1986	1987	1988	1989
Male	4.7 (3.9-5.4)	4.7 (4.0-5.3)	4.7 (4.0-5.3)	4.7 (4.1-5.2)	4.7 (4.1-5.2)	4.7 (4.2-5.1)	4.7 (4.3-5.1)	4.7 (4.3-5.1)	4.7 (4.3-5.0)	4.7 (4.4-5.0)
Female	4.7 (3.8-5.6)	4.7 (3.9-5.5)	4.7 (3.9-5.4)	4.7 (4.0-5.3)	4.7 (4.1-5.3)	4.7 (4.2-5.2)	4.7 (4.2-5.2)	4.7 (4.3-5.1)	4.7 (4.3-5.1)	4.7 (4.4-5.1)
	1990	**1991**	**1992**	**1993**	**1994**	**1995**	**1996**	**1997**	**1998**	**1999**
Male	4.7 (4.4-5.0)	4.7 (4.5-5.0)	4.8 (4.5-5.0)	4.8 (4.5-5.0)	4.8 (4.5-5.1)	4.8 (4.6-5.1)	4.8 (4.6-5.1)	4.9 (4.6-5.1)	4.9 (4.6-5.1)	4.9 (4.6-5.1)
Female	4.8 (4.4-5.1)	4.8 (4.4-5.1)	4.8 (4.5-5.1)	4.8 (4.5-5.1)	4.8 (4.5-5.2)	4.9 (4.5-5.2)	4.9 (4.6-5.2)	4.9 (4.6-5.2)	4.9 (4.6-5.3)	4.9 (4.6-5.3)
	2000	**2001**	**2002**	**2003**	**2004**	**2005**	**2006**	**2007**	**2008**	**2009**
Male	4.4 (3.8-4.9)	4.3 (3.8-4.9)	5 (4.7-5.2)	5 (4.8-5.2)	5 (4.8-5.2)	5 (4.8-5.3)	5.1 (4.8-5.3)	5.1 (4.9-5.3)	5.1 (4.9-5.4)	5.2 (4.5-5.4)
Female	4.9 (4.7-5.2)	4.9 (4.7-5.2)	5 (4.7-5.3)	5.1 (4.8-5.3)	5.1 (4.8-5.4)	5.1 (4.9-5.4)	5.1 (4.9-5.4)	5.2 (4.9-5.5)	5.2 (4.9-5.5)	5.3 (4.9-5.6)

Table 3J The average change in the level of risk factors between 1980 to 2009 in Thai population who aged 25 years and over

Risk Factors	Average change per year		%Change between 1980 to 2009		
	Male	Female	Male	Female	Total
Blood pressure (mmHg)	6.1	4.3	2.9	3.8	3.35
Total cholesterol (mmol/L)	0.4	0.5	10.6	12.8	11.70

Appendix K: Estimated number of CVD patients over the next 8 years in Thailand

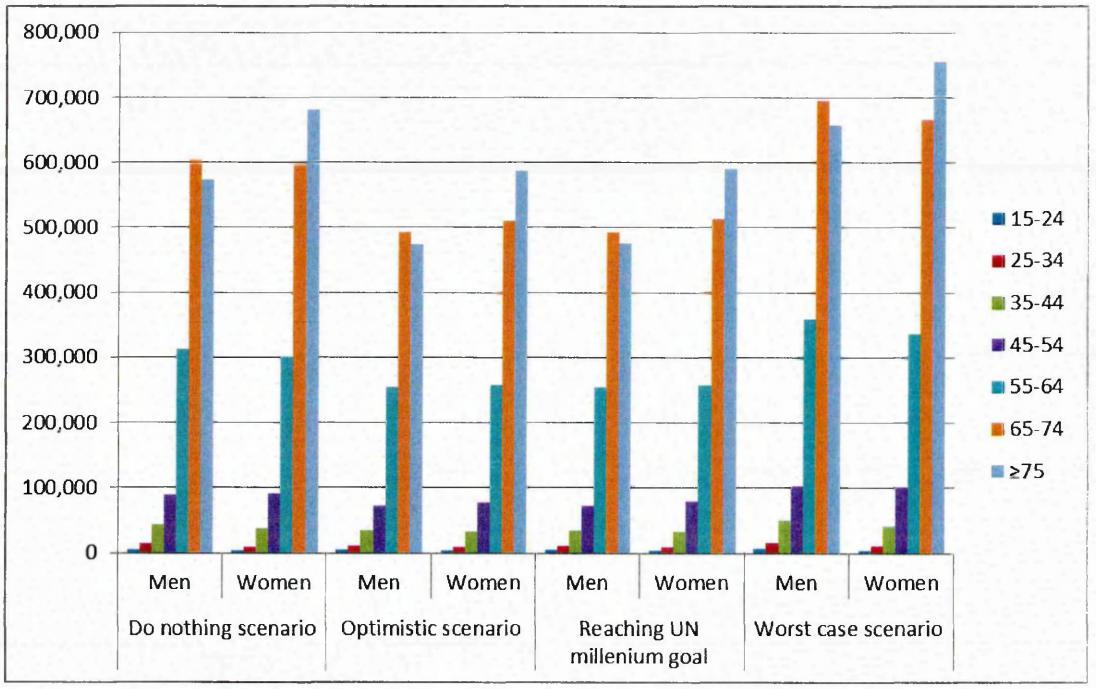


Figure 1K Estimated number of CVD patients over the next 8 years in Thailand by genders and risk reduction scenario

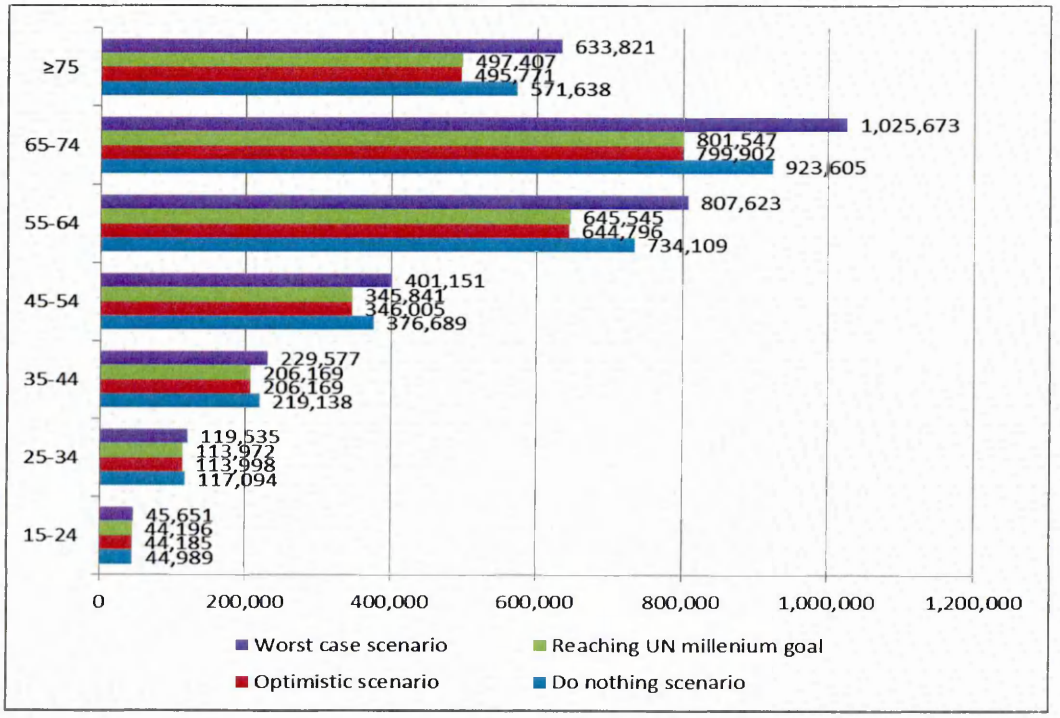


Figure 2K Estimated number of CVD patients over the next 8 years in Thailand by age groups and risk reduction scenarios

Appendix L: The total DALYs estimation from CVD over an eight year period using the Standard Life Table in different scenario

Table 1L: Estimate total DALYs: Standard Life Table, with age weight, Disability weight= 0.08 (lower limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	30,938	14,052	44,989	30,464	13,721	44,185	30,460	13,736	44,196	31,322	14,329	45,651
25-34	81,761	35,333	117,094	79,978	34,020	113,998	79,897	34,075	113,972	83,100	36,435	119,535
35-44	135,178	83,960	219,138	128,149	78,020	206,169	127,921	78,248	206,169	140,645	88,932	229,577
45-54	206,953	169,736	376,689	190,598	155,407	346,005	189,933	155,908	345,841	219,421	181,730	401,151
55-64	379,617	354,491	734,109	330,158	314,638	644,796	329,574	315,971	645,545	419,858	387,765	807,623
65-74	455,768	467,837	923,605	388,171	411,731	799,902	388,176	413,371	801,547	511,714	513,959	1,025,673
≥75	254,774	316,865	571,638	216,042	279,729	495,771	216,932	280,475	497,407	287,682	346,139	633,821
Total	1,544,988	1,442,274	2,987,263	1,363,560	1,287,266	2,650,826	1,362,893	1,291,784	2,654,677	1,693,741	1,569,289	3,263,030

Table 2L: Estimate total DALYs: Standard Life Table, with age weight, Disability weight= 0.29(upper limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	37,471	20,628	58,099	35,754	19,430	55,184	35,740	19,483	55,223	38,864	21,633	60,497
25-34	104,681	60,807	165,488	98,221	56,046	154,267	97,926	56,246	154,172	109,535	64,801	174,336
35-44	231,202	198,851	430,053	205,720	177,319	383,039	204,894	178,145	383,039	251,018	216,874	467,891
45-54	430,571	433,357	863,928	371,285	381,412	752,697	368,874	383,229	752,103	475,769	476,834	952,603
55-64	1,075,331	1,082,859	2,158,190	896,040	938,391	1,834,431	893,923	943,224	1,837,146	1,221,203	1,203,475	2,424,678
65-74	1,426,099	1,495,376	2,921,475	1,181,059	1,291,993	2,473,052	1,181,080	1,297,937	2,479,017	1,628,905	1,662,567	3,291,472
≥75	836,792	1,028,548	1,865,340	696,390	893,931	1,590,321	699,615	896,635	1,596,251	956,084	1,134,670	2,090,754
Total	4,142,147	4,320,426	8,462,573	3,484,468	3,758,522	7,242,991	3,482,053	3,774,898	7,256,950	4,681,377	4,780,854	9,462,231

Table 3L: Estimated total DALYS : Standard Life Table, no age weight, Disability weight = 0.18 (mean DW)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	24,880	12,511	37,392	24,172	12,019	36,191	24,167	12,040	36,207	25,455	12,925	38,379
25-34	70,402	36,057	106,459	67,640	33,966	101,605	67,514	34,053	101,567	72,477	37,812	110,289
35-44	147,463	119,080	266,543	134,511	107,577	242,088	134,091	108,018	242,109	157,535	128,708	286,243
45-54	307,671	317,452	625,124	267,927	280,891	548,818	266,311	282,170	548,481	337,971	348,054	686,025
55-64	894,799	933,377	1,828,176	745,018	809,005	1,554,023	743,249	813,165	1,556,415	1,016,661	1,037,215	2,053,876
65-74	1,474,645	1,588,366	3,063,012	1,217,038	1,369,852	2,586,890	1,217,060	1,376,239	2,593,299	1,687,853	1,767,995	3,455,848
≥75	1,093,820	1,374,506	2,468,326	907,362	1,191,490	2,098,852	911,646	1,195,166	2,106,812	1,252,244	1,518,782	2,771,026
Total	4,013,681	4,381,351	8,395,031	3,363,668	3,804,799	7,168,467	3,364,037	3,820,852	7,184,889	4,550,195	4,851,491	9,401,686

Table 4L: Estimate total DALYs: Standard Life Table, no age weight, Disability weight= 0.08 (lower limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	22,804	10,427	33,231	22,491	10,209	32,701	22,489	10,219	32,708	23,058	10,610	33,668
25-34	62,850	27,432	90,282	61,629	26,508	88,137	61,573	26,547	88,120	63,767	28,208	91,975
35-44	109,853	71,784	181,636	104,128	66,700	170,828	103,943	66,894	170,837	114,304	76,039	190,344
45-54	192,154	174,470	366,625	174,588	158,311	332,898	173,873	158,876	332,749	205,546	187,996	393,542
55-64	446,932	450,181	897,114	380,731	395,210	775,941	379,949	397,049	776,999	500,794	496,077	996,871
65-74	688,572	737,652	1,426,224	574,712	641,072	1,215,784	574,722	643,894	1,218,616	782,807	817,046	1,599,854
≥75	498,204	628,919	1,127,123	415,792	548,028	963,819	417,685	549,653	967,338	568,226	692,687	1,260,913
Total	2,021,369	2,100,866	4,122,236	1,734,071	1,846,037	3,580,108	1,734,234	1,853,132	3,587,367	2,258,503	2,308,663	4,567,166

Table 5L: Estimate total DALYs: Standard Life Table, no age weight, Disability weight= 0.29(upper limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	27,121	14,761	41,881	25,987	13,971	39,958	25,977	14,006	39,983	28,041	15,423	43,464
25-34	78,552	45,365	123,917	74,126	42,014	116,140	73,924	42,154	116,079	81,877	48,177	130,054
35-44	188,051	170,123	358,175	167,300	151,693	318,993	166,628	152,400	319,027	204,189	185,549	389,738
45-54	432,339	471,760	904,098	368,660	413,181	781,841	366,070	415,230	781,300	480,885	520,790	1,001,675
55-64	1,378,140	1,454,845	2,832,985	1,138,159	1,255,575	2,393,735	1,135,326	1,262,241	2,397,567	1,573,388	1,621,215	3,194,603
65-74	2,322,982	2,506,463	4,829,446	1,910,241	2,156,358	4,066,599	1,910,276	2,166,590	4,076,867	2,664,585	2,794,267	5,458,852
≥75	1,736,614	2,179,149	3,915,763	1,437,869	1,885,919	3,323,787	1,444,732	1,891,809	3,336,541	1,990,442	2,410,310	4,400,752
Total	6,163,799	6,842,467	13,006,266	5,122,342	5,918,711	11,041,053	5,122,934	5,944,431	11,067,364	7,023,407	7,595,731	14,619,138

Appendix M: The total DALYs estimation from CVD over an eight year period using the Thailand Life Table in different scenario

Table 1M: Estimated total DALYS : Thailand Life Table, with age weight, Disability weight = 0.181 (mean DW)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	34,721	17,311	52,033	33,650	16,564	50,213	33,641	16,597	50,238	35,591	17,939	53,529
25-34	94,727	47,894	142,621	90,694	44,923	135,618	90,511	45,048	135,558	97,756	50,387	148,143
35-44	183,772	139,800	323,572	167,868	126,361	294,229	167,353	126,876	294,229	196,140	151,049	347,188
45-54	315,765	297,321	613,086	278,763	264,900	543,662	277,258	266,034	543,292	343,975	324,457	668,432
55-64	711,963	704,835	1,416,798	600,060	614,667	1,214,727	598,739	617,683	1,216,422	803,007	780,116	1,583,123
65-74	918,143	961,067	1,879,210	765,205	834,127	1,599,332	765,218	837,837	1,603,055	1,044,722	1,065,417	2,110,139
≥75	534,667	661,750	1,196,417	447,037	577,730	1,024,767	449,050	579,418	1,028,468	609,122	727,984	1,337,106
Total	2,793,759	2,829,978	5,623,737	2,383,277	2,479,272	4,862,549	2,381,769	2,489,493	4,871,262	3,130,313	3,117,348	6,247,661

Table 2M: Estimate total DALYs: Thailand Life Table, with age weight, Disability weight= 0.08 (lower limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	31,579	14,149	45,728	31,105	13,818	44,923	31,101	13,833	44,934	31,963	14,426	46,389
25-34	83,703	35,643	119,346	81,921	34,329	116,250	81,839	34,384	116,224	85,042	36,745	121,786
35-44	137,589	84,543	222,132	130,560	78,603	209,163	130,332	78,831	209,163	143,056	89,515	232,570
45-54	208,216	170,532	378,747	191,861	156,202	348,063	191,196	156,703	347,899	220,684	182,526	403,210
55-64	377,358	354,525	731,883	327,898	314,672	642,570	327,314	316,005	643,319	417,598	387,798	805,397
65-74	451,460	466,869	918,330	383,863	410,763	794,627	383,869	412,403	796,272	507,407	512,991	1,020,398
≥75	254,744	319,464	574,208	216,013	282,328	498,341	216,903	283,074	499,976	287,653	348,738	636,391
Total	1,544,649	1,445,724	2,990,373	1,363,221	1,290,716	2,653,936	1,362,554	1,295,233	2,657,787	1,693,402	1,572,738	3,266,141

Table 3M: Estimate total DALYs: Thailand Life Table, with age weight, Disability weight= 0.29(upper limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	38,113	20,725	58,837	36,396	19,527	55,922	36,382	19,580	55,961	39,506	21,730	61,235
25-34	106,624	61,116	167,740	100,163	56,356	156,519	99,868	56,555	156,424	111,477	65,111	176,587
35-44	233,613	199,434	433,047	208,131	177,902	386,033	207,305	178,727	386,033	253,429	217,457	470,885
45-54	431,834	434,152	865,986	372,548	382,207	754,755	370,136	384,024	754,161	477,032	477,630	954,661
55-64	1,073,072	1,082,892	2,155,964	893,780	938,424	1,832,205	891,663	943,257	1,834,920	1,218,944	1,203,508	2,422,452
65-74	1,421,791	1,494,408	2,916,200	1,176,751	1,291,025	2,467,776	1,176,772	1,296,969	2,473,741	1,624,597	1,661,599	3,286,197
≥75	836,762	1,031,147	1,867,909	696,360	896,530	1,592,890	699,586	899,234	1,598,820	956,054	1,137,269	2,093,323
Total	4,141,808	4,323,875	8,465,684	3,484,129	3,761,971	7,246,101	3,481,714	3,778,347	7,260,061	4,681,038	4,784,303	9,465,341

Table 4M: Estimated total DALYS : Thailand Life Table, no age weight, Disability weight = 0.181 (mean DW)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	23,867	12,363	36,230	23,159	11,870	35,029	23,153	11,892	35,045	24,442	12,776	37,218
25-34	66,694	35,530	102,224	63,932	33,438	97,370	63,806	33,526	97,331	68,769	37,285	106,054
35-44	141,319	117,870	259,189	128,367	106,367	234,734	127,947	106,808	234,755	151,391	127,498	278,888
45-54	298,283	314,759	613,042	258,539	278,198	536,737	256,923	279,476	536,399	328,583	345,361	673,944
55-64	884,110	929,808	1,813,918	734,329	805,436	1,539,765	732,561	809,596	1,542,157	1,005,972	1,033,646	2,039,618
65-74	1,467,366	1,585,640	3,053,006	1,209,758	1,367,127	2,576,885	1,209,781	1,373,513	2,583,293	1,680,573	1,765,269	3,445,843
≥75	1,093,789	1,377,672	2,471,462	907,331	1,194,656	2,101,987	911,615	1,198,332	2,109,947	1,252,213	1,521,948	2,774,161
Total	3,975,429	4,373,642	8,349,070	3,325,416	3,797,091	7,122,507	3,325,786	3,813,143	7,138,929	4,511,943	4,843,782	9,355,725

Table 5M: Estimate total DALYs: Thailand Life Table, no age weight, Disability weight= 0.08 (lower limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	21,791	10,279	32,070	21,478	10,061	31,539	21,476	10,070	31,546	22,045	10,461	32,506
25-34	59,142	26,905	86,047	57,921	25,980	83,902	57,866	26,019	83,885	60,059	27,681	87,740
35-44	103,709	70,573	174,282	97,984	65,489	163,473	97,799	65,684	163,483	108,161	74,829	182,989
45-54	182,766	171,777	354,543	165,200	155,617	320,817	164,485	156,182	320,668	196,158	185,303	381,461
55-64	436,244	446,612	882,856	370,042	391,641	761,683	369,260	393,480	762,741	490,105	492,507	982,613
65-74	681,293	734,927	1,416,219	567,433	638,346	1,205,779	567,443	641,168	1,208,611	775,528	814,321	1,589,848
≥75	498,173	632,085	1,130,258	415,761	551,194	966,955	417,654	552,819	970,473	568,195	695,853	1,264,048
Total	1,983,118	2,093,158	4,076,275	1,695,819	1,838,328	3,534,147	1,695,983	1,845,423	3,541,406	2,220,251	2,300,954	4,521,206

Table 6M: Estimate total DALYs: Thailand Life Table, no age weight, Disability weight= 0.29(upper limit)

	Do nothing scenario			Optimistic scenario			Reaching UN millenium goal			Worst case scenario		
Age groups	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**	**Men**	**Women**	**Total**
15-24	26,108	14,612	40,720	24,973	13,823	38,796	24,964	13,858	38,822	27,028	15,275	42,302
25-34	74,845	44,838	119,682	70,419	41,486	111,905	70,217	41,627	111,843	78,169	47,650	125,819
35-44	181,908	168,913	350,820	161,156	150,483	311,639	160,484	151,189	311,673	198,045	184,339	382,384
45-54	422,951	469,066	892,017	359,272	410,487	769,759	356,682	412,536	769,219	471,497	518,097	989,593
55-64	1,367,451	1,451,276	2,818,727	1,127,471	1,252,006	2,379,477	1,124,637	1,258,672	2,383,309	1,562,699	1,617,646	3,180,345
65-74	2,315,703	2,503,738	4,819,440	1,902,961	2,153,632	4,056,594	1,902,997	2,163,864	4,066,861	2,657,306	2,791,541	5,448,847
≥75	1,736,583	2,182,316	3,918,899	1,437,838	1,889,085	3,326,923	1,444,701	1,894,976	3,339,677	1,990,411	2,413,476	4,403,887
Total	6,125,547	6,834,758	12,960,305	5,084,090	5,911,002	10,995,092	5,084,682	5,936,722	11,021,404	6,985,155	7,588,022	14,573,178