The prevalence of undiagnosed cognitive impairment and prevalence of undiagnosed depressive mood in over 60's with type 2 diabetes in a Thai community: a cross-sectional study

Supaporn Trongsakul

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Faculty of Medicine and Health Sciences

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Abstract

Type 2 diabetes is a lifelong disease and a major health problem in Thai older people. Declining cognitive function and depressive mood can potentially present a barrier to self-care management. To date, there is no primary research data of cognitive impairment related to diabetes in Thailand, particularly in primary care settings which are the first important place for health care service in Thai community. This study contributes to the estimated prevalence of undiagnosed cognitive impairment and undiagnosed depressive mood in Thai older people with type 2 diabetes. In order to promote an early detection of cognitive impairment, a Thai version of Mini-Cog, a brief cognitive screening test for using in primary care settings was developed.

A cross-sectional study design was conducted in a group of older diabetic patients aged 60 and over in the primary care settings of San-sai district, Chiang Mai, Thailand. Overall 556 participants were recruited and the following screening tests were applied on them: Mini-Cog Thai version, Mini-Mental State Examination (MMSE) Thai 2002, and the depressive mood screening test of Thai Geriatric Depression Scale (TGDS).

The study shows the prevalence of Thai older people with type 2 diabetes who were probably undiagnosed with cognitive impairment to be 65.4% (95% CI 59.7%, 70.7%) for Mini-Cog, and 12.4% (95% CI 9.0%, 16.7%) for MMSE Thai 2002. The prevalence of people who were probably undiagnosed with depressive mood by TGDS is shown to be 19.4% (95% CI 15.2%, 24.4%). Logistic regression has been used to identify the associated characteristics of cognitive impairment and the associated characteristics of depressive mood. Using Mini-Cog, age, education, BMI and HDL were found to have effects on cognitive impairment. While using MMSE Thai 2002, only the effect of age and education were associated with cognitive impairment. The associated factor with depressive mood was retinopathy.

The differences of prevalence rate and associated characteristics between the two cognitive screening tests are probably due to the different foci on cognitive domain tests. Mini-Cog may be more sensitive in detecting an earlier stage of cognitive impairment better than MMSE Thai 2002. Mini-Cog Thai version shows a good inter-rater reliability ($K=0.8$, $p<0.001$, 95% CI 0.54, 1.06).

This study encourages health care providers' awareness of cognitive decline and depressive mood that may affect self-care diabetes. Mini-Cog Thai version might be used as a brief cognitive screening tool in primary care settings.

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Abbreviations and acronyms

AD	Alzheimer's disease
ADA	American Diabetes Association
Aβ	Amyloid beta
BMI	Body mass index
CDT	Cock Drawing Test
CERAD	Consortium to Establish a Registry for Alzheimer's disease
CI	Confidence Interval
CIB	Clock in a box
DALYs	Disability Adjusted Life Years
est.	establish
FBS	Fast Blood Sugar
HbA1c	Haemoglobin A1c
HDL	High density lipoprotein
IQCODE	Informant Questionnaire for Cognitive Decline in the Elderly
K	Kappa statistics
LDL	Low density lipoprotein
MCI	Mild Cognitive Impairment
MMSE	Mini-Mental State Examination Thai 2002
RA	Research Assistant
r	Parson's correlation coefficient
r_s	Spearman's correlation coefficient
SD	Standard deviation
SPSS	Statistical package for social science
sqrt	Square Root
TGDS	Thai Geriatric Depression Scale
TMSE	Thai Mental State Examination
UN	United Nations
VaD	Vascular dementia
WHO	World Health Organization

Chapter 1

Introduction

This thesis presents a prevalence study of undiagnosed cognitive impairment and undiagnosed depressive mood through associated factors in Thai older people with type 2 diabetes in one community. The study will achieve its goals using Mini-Cog and Mini-Mental State Examination (MMSE) Thai 2002, screening tools of cognitive impairment and Thai Geriatric Depression Scale (TGDS), a screening tool of depressive mood. In order to promote an early detection of cognitive impairment in the primary care setting in Thailand, this study also develops a Thai version of Mini-Cog, a short cognitive screening test specific to use in primary care centres. This test is studied along with MMSE Thai 2002, a Thai standard cognitive screening test. The information and results from this study will support appropriate self-care diabetes program and promote awareness of an early detection of cognitive impairment and/or depressive mood in older people with diabetes in primary care.

This chapter discusses the study background, the potential importance of this study and the linkage between type 2 diabetes and cognitive impairment and depressive mood. This study was conducted in Thailand, therefore the overview information of health care system and older people population are provided as well. Finally, a description of the structure of the thesis is outlined.

1.1 Background and significance of this study

Diabetes Mellitus is a disorder in which the body does not produce or utilize insulin, a hormone used in the metabolism of sugars, starches and other foods, properly. Absence or impairment of insulin functioning in the body results in high levels of glucose in the blood and urine (hyperglycaemia) (Clark 2004).There are two common forms of diabetes: type 1 diabetes or previously known as insulin dependent diabetes mellitus (IDDM), and type 2 diabetes or previously known as non-insulin dependent diabetes mellitus (NIDDM). Around 90% of people with

diabetes around the world are type 2 and about 10% have type 1 diabetes (World Health Organisation 2011).

Type 2 diabetes in adult is a global health issue. It has been estimated that the number of people with diabetes worldwide was 285 million in 2010 and will increase to 439 million in 2030 (Shaw et al. 2010). More than 80% of people with diabetes live in low and middle-income countries (World Health Organization 2011). Each year more than 3.96 million people worldwide die from diabetes and its complications (Egede and Ellis 2010). Diabetes care is important in lowering blood sugar level and maintaining a good metabolic control in order to help prevent complication of diabetes. However, less than 15 % of adults with type 2 diabetes met this goal in 2007 (Nam et al. 2011). For successful diabetes self-management, individuals must commit to lifelong daily self-care tasks such as adhering to diet, exercise, and medication regimens and checking blood glucose. The coordination of these tasks often requires complex cognitive functioning (Okura et al. 2009).

The prevalence of type 2 diabetes increases with age (Sicree et al. 2009). Research has linked the disease to cognitive impairment in the older people (Yeung et al. 2009, Ganzer and Crogan 2010). Recent evidence from epidemiological studies suggests that type 2 diabetes is a risk factor for cognitive impairment and dementia, both the vascular dementia (VaD) and Alzheimer's disease (AD), the two most common forms of dementia (Allen et al. 2004, Biessels et al. 2006, Luchsinger et al. 2007, Sastre and Evans 2008). Older individuals (aged 60-80) with type 2 diabetes are associated with approximately 1.5 fold risk of cognitive impairment compared to the control group (Cukierman et al. 2005). Given the potential for cognitive problems to interfere with the attempts to diabetes self-care management and following a physician's recommendation, cognitive decline among older people with diabetes could lead to further decline in health (Sinclair et al. 2000).

Another problem which may relate to cognitive impairment and affect self care diabetes is depressive mood. Depression is a common co-morbidity of type 2 diabetes (Lustman and Clausea 2005, Katon et al. 2010). People with diabetes are

likely to suffer twice as often from depression as those without diabetes. Depressive symptoms may hinder diabetic patients' ability to adhere to diet, physical activity and oral medication (Ciechanowski et al. 2000, Park et al. 2004, Wang et al. 2008). Moreover, depression by itself is the most common of the reversible causes of cognitive impairment or pseudo-dementia, particularly in memory part (Zrebiec 2006).

Although the association between cognitive impairment and type 2 diabetes is now well established in many countries (Bruce et al. 2001, Bruce et al. 2003, Munshi et al. 2006, Rajakumaraswamy et al. 2008, Alencar et al. 2010) to date, there is no investigation of the relationship between diabetes and cognitive impairment and depressive mood in Thailand, particularly in a primary care setting. A primary care centre in Thai community (rural areas or sub-district level) is the first place of heath care service that provides primary health care, prevention and promotion (Prakongsai et al. 2009). Type 2 diabetes is one of the main chronic diseases which causes a health problem in Thai older people (Assantachai and Maranetra 2005) and the numbers of older people people are expected to increase over the next few decades due to the growing of ageing population (Bureau of Health Policy 2007). This study intends to quantify and raise awareness of undiagnosed cognitive impairment and undiagnosed depressive mood in older people with type 2 diabetes. Early detection and establishing an association between type 2 diabetes and cognitive impairment as well as an association between type 2 diabetes and depressive mood could therefore be of great importance to provide optimal diabetic care and good quality life to Thai older people with type 2 diabetes in this community.

1.2 Definition of cognitive impairment and mild cognitive impairment

Cognitive impairment is a defining feature of dementia. Dementia is characterized by the development of multiple cognitive deficits that include memory impairment and at least one of the following cognitive disturbances: Aphasia (any impairment of the ability to use and/or understand words), Apraxia (difficulty in performing a learned movement or coordinated motor activity), Agnosia (loss of ability to recognize objects, people, sounds, shapes, or smells) or a disturbance in executive

functioning such as abstract thinking, judgement and problem solving accompanied by functional impairment (inability to perform independently in activities of daily living) (American Psychiatric Association 2000).
Mild cognitive impairment (MCI) is cognitive impairment in the presence of memory complaints which can detect memory impairment on neuropsychological tests but no impairment of daily life activities (Petersen 2004).

1.3 Type 2 diabetes, cognitive impairment and depressive mood: a potential linkage

There are many pathophysiological mechanisms through which diabetes may affect the underlying pathologies associated with cognitive impairment (Llorente and Malphurs 2007). In addition, depressive mood may be linked to diabetes and subsequent cognitive impairment. Both Alzheimer's disease (AD) and vascular dementia (VaD) are common types of cognitive impairment which can be found in these mechanisms as well as ageing itself (Biessels 2006). It is increasingly recognised that the brains of people with dementia, particularly in the very old, are likely to show a mixture of pathologies, particularly AD type and vascular changes (Neuropathology group 2001).

1.3.1 Type 2 diabetes and cognitive impairment

There are four main possible mechanisms which link type 2 diabetes and cognitive impairment. First, diabetes is a known risk factor for cerebrovascular diseases such as hypertension and dyslipdaemia (Halperin et al. 2006). Thus, it is expected that type 2 diabetes can cause the vascular form of cognitive impairment (Llorente and Malphurs 2007). Second, chronic hyperglycaemia in type 2 diabetes might lead to abnormalities in cerebral capillaries, such as basement membrane thickening. These microvascular changes might also lead to chronic and insidious ischemia of brain (Gispen and Biessels 2000). Third, the malfunction and damage of brain function due the alterations in insulin and glucose level either in hyperglycaemia (abnormally high level of sugar in blood) or hypoglycaemia (abnormally low level of sugar in blood). Hyperglycaemia affects the deposition of amyloid beta (Aβ), which is a protein fragment snipped from an amyloid precursor protein (APP). In a healthy brain, these protein fragments are broken down and eliminated. In

Alzheimer's disease, the fragments accumulate to form hard, insoluble plaques which contribute to the degradation of the nerve cells in the brain and the subsequent symptoms of Alzheimer's disease (AD) (Ritchie and Lovestone 2002). Hypoglycaemia can cause the damage of cortical area, particularly in the frontal lobe and hippocampus. However, due to the uncontrolled blood sugar, type 2 diabetic patients are more likely to have hyperglycaemia (World Health Organisation 2011). Fourth, ageing itself is associated with changes in insulin and its receptor in the brain and these changes might be even more pronounced in patients with AD (Craft and Watson, 2004).

1.3.2 Type 2 diabetes and depressive mood

There are two main possible mechanisms to explain the relationship between depressive mood and diabetes. First, depressive symptoms are associated with biochemical changes and related to the activation of the hypothalamic-pitutary-adrenal axia (HPA), which is a major part of the neuroendocrine system that controls reactions to stress and regulates many body processes, including digestion, the immune system, mood, emotions, energy storage and expenditure. Thus, this system is an important factor in disrupting overall metabolic control (Arvanitakis et al. 2004, Beeri et al. 2005). Second, the presence of depressive mood or symptoms may adversely affect life activities such as lack of exercise and poor diet that increase the risk of diabetes (Black et al. 2003, Saydah et al. 2003).

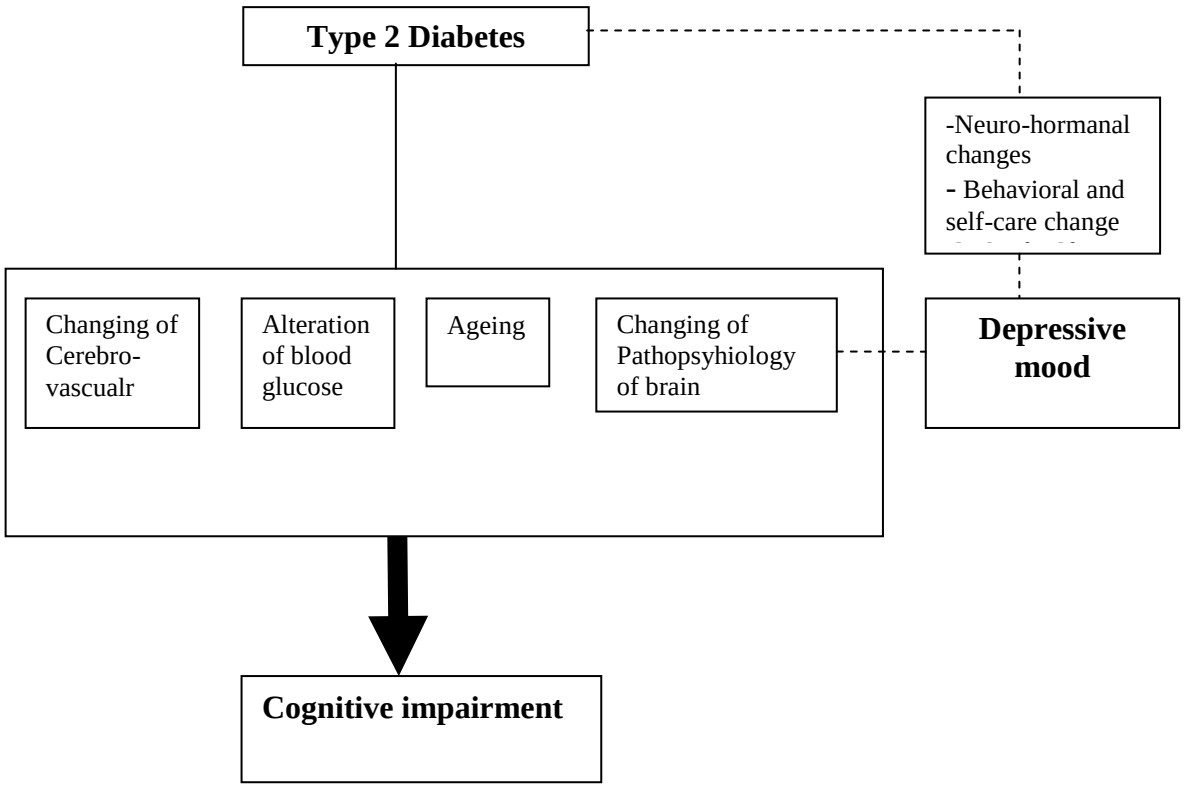
1.3.3 Depressive mood and cognitive impairment

Depressive mood affects the HPA disturbances and causes prolonged hypercortisolemia. As a result, it may promote hippocampal atrophy and functional decline. This also affects impairment in the memory functions of the brain served by the hippocampus (Campbell and Macqueen 2004).

In summary, the pathophysiological mechanisms suggest how diabetes-related factors can affect cognitive impairment through the brain. Vascular disease and alterations in glucose and amyloid metabolism seem to be important factors. In addition, the neuro-hormonal changes (activation of HPA) induced by depressive mood symptoms can lead to insulin resistance and develop type 2 diabetes.

Behavioural factors with depressive symptoms (lack of exercise and poor diet) also increase the risk of type 2 diabetes. The mechanisms linking depressive mood and type 2 diabetes may cause memory impairment.

Figure 1.1: Proposed scheme, association of type 2 diabetes with cognitive impairment and depressive mood through changes in pathophysiology



1.4 Cognitive function and depressive mood: Impact for diabetes self-care

Cognitive impairment and depression have important consequences for diabetic patients and diabetes self-care management (Bayer et al. 1994). They are crucial components in the individual needs to control an appropriate blood glucose level (an optimal goal for diabetes care) by maximizing adherence to diet, exercise, and dosing schedules of the medicine (Biessels et al. 2008). It is important to recognize these two co-morbidities and great insight is needed in how cognitive impairment and depressive mood influence the diabetes care and quality of life in the diabetic patients (Katon et al. 2010)

Although diabetes is considered to be a risk factor for cognitive impairment (Munshi et al. 2006, Allen et al. 2004, Gregg et al. 2000), the cognitive function of patients with type 2 diabetes is not usually evaluated in routine clinical care. Cognitive impairment might be another factor associated with poor diabetes control and also bad adherence of patients to educational approaches, such as diet orientations (Alencar et al. 2010).

1.5 The importance of the early detection of cognitive impairment and depressive mood

Although diabetes is considered to be a risk factor for cognitive impairment (Munshi et al. 2006, Allen et al. 2004, Gregg et al. 2000), the cognitive function of patients with type 2 diabetes is not usually evaluated in routine clinical care. Cognitive impairment might be another factor associated with poor diabetes control and poor adherence of patients to educational approaches, such as diet orientations (Alencar et al. 2010). In addition, type 2 diabetes relies heavily on the principles of self-management. This is in essence a series of complex behaviour required for lifestyle and behavioural changes as well as adherence to medical interventions. Successful disease management is dependent on the patient's ability to execute these interventions and maintain lifelong adherence to diabetes care (Llorente and Malphurs 2007).

Moreover, depression by itself is a reversible cognitive impairment, particularly in memory part (Dolan et al. 1992, Zrebiec 2006, Saez-Fonseca et al. 2007).

Depressive symptoms are also common in diabetic patients and may hinder their ability to adhere to diet, physical activity and oral hypoglycaemic agents (Ciechanowski et al. 2000, Park et al. 2004, Wang et al. 2008) and therefore cause poor glucose control as a result of reduced capacity to manage a self-care regimen (Goldney et al. 2004). Hence, early detection and management of cognitive impairment and depressive mood may become an important aspect of diabetes care.

1.6 An overview of Thailand

1.6.1 Thailand Profile

Thailand is situated in the southeast of continental Asia, and is part of the Indochina Peninsula (see map below, Figure 1.2), with an area of 514,000 kilometres^{2}is the world's 49thlargest country. Following Indonesia and Myanmar (otherwise known as Burma), it is the third largest country among the Southeast Asian nations. Thailand is a tropical country and is divided into 4 geographical regions: the central region (including the capital city of Bangkok), the North (including the country's second city Chiang Mai), the North-East (including Udon-Thani province) and the southern regions (Knodel and Choyavan 2008). Total population is around 66 million (2011 est.). The official national language, spoken and written by almost 100 percent of population, is Thai. More than half of the population (66%) lives in rural area. Life expectancy in 2011 was 71 years for males and 76 for females, with an average of 74 years (United Nation 2011).

Since 1961, the base of the Thai economy has rapidly changed from agriculture to service and manufacturing. The Gross Domestic Product (GDP) per capita was US $4,043 in 2009, representing Thailand as a middle income country (world rank 114/226). GDP-composition by sector is 11% in agricultural sector, 40% in industry and 49% in service (Sakunphanit and Suwanrada, 2011). The majority (80%) of people have health care insurance provided by the government (National Statistical Office of Thailand 2011).

Figure 1.2 Map of Thailand (Source: Sakunphanit, 2006)

1.6.2 Overview of health care structure in Thailand

Health care system in Thailand is an entrepreneurial health system with public and private providers. Public health facilities were rapidly expanded nationwide since 1961 when Thailand launched the first five-year National Economic and Social Development Plans (1961-1966). Private hospitals also play a role in health service. However, they are mostly in Bangkok, a capital city and urban areas. In the public sector, the largest agency is the Ministry of Public health (MOPH) with two-third of all hospitals and beds across the country. The other public health services are medical school hospitals under the Ministry of University, general hospitals under other ministries (such as Ministry of Interior, Ministry of Defence) (Sukunphanit 2006).

In 2004, 68.6% percent of hospital and 65.4% of beds belonged to the MOPH. The health care services in Thailand are divided in the following levels: general hospital (120-150 beds) or regional hospitals (501-1,000 beds) and few special centres/hospitals in provincial level, community hospitals (10-120 beds) in district level and primary care or health centre in sub-district level. The health care

structure under MOPH can be explained briefly as in Table1.1. It shows the relationship between administrative level, population size, level of care and providers. Currently, MOPH owns 891 hospitals which cover more than 90% of districts and 9,762 primary cares, which cover every sub-district or community in rural area (Wibulpolprasert 2004).

Table 1.1: Levels of health care system in Thailand: administrative level, population size, level of care and provider in Thailand

Administrative level	**Population**	**Level of care**	**Health care providers**
Province	300,000-1,000,000	Secondary care: General hospital	Specialists
District	20,000-100,000	Primary and secondary care: Community hospital	General practice, family practice
Sub-district	*2,000-5,000*	*Primary care: Primary care centre*	*Nurse/technical nurse/health worker*

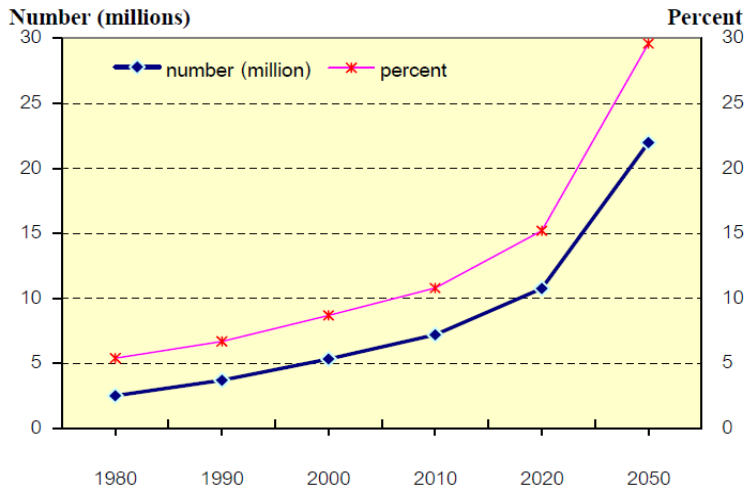
The importance of primary care system in Thailand

The primary care system is the first point of contact for people to access and utilize health service in Thailand. It is an important mechanism for enabling people to access quality health care service on a continuous basis. The primary care system is seen as a key mechanism and strategy to achieve health equity and progress on health system reform, and has received support from the World Health Organisation for over 30 years, since 1978. Evidence from international and Thai literature indicate that the primary care system plays an important role in improving equity in health and equitable to public health care service (Prakongsai et al. 2009).

1.6.3 Overview of Thai ageing population

Thailand has entered into the period of "the ageing society" since 2005, and the number of older people in Thailand is expected to rise significantly over the next 25 years (Ministry of Public Health and Ministry of Social Development and Human Security 2007). Population ageing is defined as the increasing proportion of older persons (60 years and above) in the total population (United Nations Population Fund Thailand 2006). The proportion of the population in their elderly years (60+) is anticipated to increase from 8.7 percent in 2000 to 10.8 percent in the year 2010, 15.2 percent in the year 2020, and 30 percent in the year 2050. The number of older persons will continue to rise, from approximately 5.3 million at present to 7.2 million in 2010 and will reach 11 million by 2020 (See Figure 1.3). The percent increase of the old-olds is greater than that of the overall aged population. Among older males and females, 71% and 48% have finished grade 4 (4 years in school) (Sakunphanit 2006). A majority (70 %) of Thai older persons live in rural areas and about 30 percent in municipal or urban areas. 93% of the older people live in the same households with many family members (The National Commission on the Elderly 2009). Among all persons aged 60 and above, especially in rural area, the most common source of income (80%) comes from their children (Ministry of Public Health of Ministry of Social Development and Human security 2007).

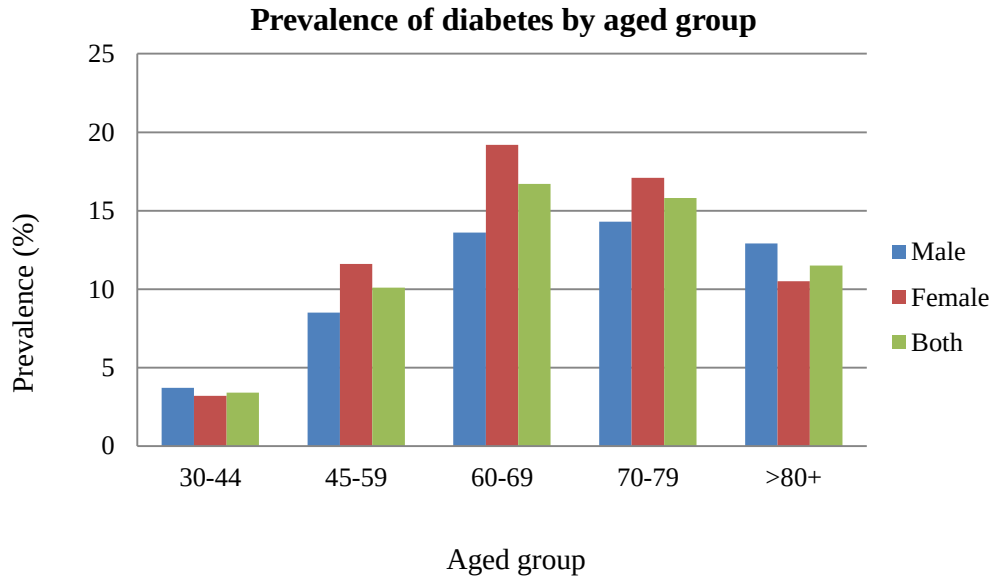
Figure 1.3: Total number and percent of the older population in Thailand, 1980-2050



1.7 The burden and gap problem of diabetes care in Thailand

Diabetes Mellitus is one of the important public health concerns of Thailand in recent years (Rawdaree et al. 2006, Nitiyanant et al. 2007). Recent economic change, reflected by rapid industrialization, urbanization and increased wealth at both national and household levels contribute to change of lifestyles, in particular high fat food diet and less physically active patterns. These factors have led to an increasing proportion of the Thai population living with diabetes from 2.3% in 1991 to 4.6% in 1997 and 6.9% in 2008-2009 (Akeplakorn et al. 2010, Chatterjee et al. 2011). In 2009, the National Health Examination Survey (NHES) IV reported the prevalence rate in female was higher than male. Overall in both genders, a highest prevalence rate (16.7%) was found in diabetic adults aged group 60-69 while the other adult aged groups were 3.4% (30-44), 10.1% (45-59), 15.8% (70-79) and 11.5% (80+) (see Figure 1.4) (Akeplakorn et al. 2011). Diabetes alone is responsible for 3.3 and 8.3% of total deaths in Thai men and women, respectively (Porapakkham et al. 2010). In addition, a high prevalence rate (6.7%) of diabetes in Thailand makes it among the top ten in Asia (Chan et al. 2009). While measuring the health status of Thai people using Disability Adjusted Life Years (DALYs) as an indicator, it was found that diabetes ranked eighth and third for males and females respectively in 2004. Moreover, the hospitalisation rate for diabetes in Thailand has increased and shown a rising trend. For example, the hospitalisation rate for diabetes has nearly doubled over 3 years from 380.7 (x 100, 000 population) in 2003 to 586.8 (x 100,000 population) in 2006 (Ministry of Public Health Thailand 2009).

Figure 1.4: Age-specific prevalence of diabetes in Thai adults



Source: NHES IV report 2009 (Akeplakorn et al. 2011)

People with diabetes are prone to consequences in both short-term and long-term complications (Chatterjeeet al. 2011). The chronic nature of diabetes and its devastating complications make it a very costly disease. A study based on four government hospitals in Thailand found that for outpatients, annual direct medical expenditure was more than five times higher for diabetic patients as compared to non-diabetics. For inpatients, the expenditure was more than two times higher in 2002 and 2003 (Pongcharoensuk et al. 2006). Chatterjee (2011) revealed that the cost average of illness per diabetic patient was US$ 881.50 which was about 21% of per capita GDP in Thailand. This study noted that the cost of informal care (care from family/friends) contributed 28% of the total cost of diabetes. Therefore, diabetes not only affected the individual but also the family members and friends. This study also found associations of diabetes cost with age and complications. Similarly, Chaikledkaew (2008) investigated factors associated with healthcare expenditures and hospitalisations in patients with diabetes in four public hospitals in Thailand. They showed that age, male gender, type of payment, health care

utilization (hospitalisation or outpatient visit), co-morbidities (hypertension, hyperlipidaemia) and complications (neuropathy, nephropathy, retinopathy) were associated with health expenditures. Both studies suggested that much of this cost associated with the disease is preventable through improved diabetes care, prevention initiatives to reduce the prevalence of diabetes and its co-morbidities (Chaikledkaew et al. 2008, Chatterjee et al. 2011).

Glycaemic control is fundamental to the management of diabetes (Llorente and Malphurs 2007). One measure of glycaemic control is glycated haemoglobin (HbA1c). The HbA1c is the most accepted indicator and accurately reflect longer-term glycaemic control (Saudek et al. 2006, Yavari 2011). The HbA1 is the compound in red blood cells that transports oxygen, and the most common form of haemoglobin is called haemoglobin A. Glucose binds to haemoglobin A, forming glycated haemoglobin (HbA1c), which is elevated when plasma glucose levels are high. American Diabetes Association (ADA) guidelines indicate that normal HbA1c is less than 6.0% (42 mmol/mol), while an HbA1c value greater than 7.0% (53 mmol/mol) represents poor glycaemic control (American Diabetes Association 2009). The decomposition of glycated haemoglobin is slow and the build up of glycated haemoglobin lasts between 1 and 4 months. HbA1c reflects mean glucose levels over the past 2 weeks to 3 months (Ross and Gadsby 2004). For diabetic patients, the goal of diabetic care and treatment is to achieve an HbA1c less than 7% (53 mmol/mol) in order to prevent the morbidity and mortality of diabetic complications (American Diabetes Association 2009). Nevertheless, a cross-sectional study survey of primary care settings in all regions of Thailand, Nitayanat (2007) revealed that the outcome of glycemic control was higher than the standard criteria. The mean $\pm$ SD of HbA1c was 8.6 $\pm$ 1.9 % (70.5 $\pm$ 2.3 mmol/mol). Furthermore, reports from health status surveys reveal that 60% of Thai people with diabetes are unable to maintain appropriate glycaemic control (Koshakri et al. 2009).

Barriers of glycaemic control in Thai literature included difficulty in making daily food choices, preparing food, and lack of knowledge (Wattana et al. 2007). The literature points out that proper diabetes health education programs for improving knowledge, diabetic control, and preventing complications for type 2 diabetic

patients are still needed. As mentioned earlier, diabetes self-management activities require complex cognitive functioning (Okura et al. 2009), however, no study was found to investigate the effects of cognitive function on glycemic control and diabetes self-care. Cognitive impairment might be another gap or factor associated with poor diabetes control and adherence of patients to educational approaches, such as diet orientations (Alencar et al. 2010). Therefore, early clinical recognition of cognitive impairment and its progression to dementia will bridge another gap toward effective self-care management in type 2 diabetic patients (Galluzzi et al. 2010).

In order to address these issues effectively, the present study will investigate the problem of cognitive impairment and depressive mood in Thai older people with type 2 diabetes at the primary care setting in a community which is required to provide baseline information for health care professionals (Ooi et al. 2011). In addition, understanding the epidemiology of cognitive impairment and dementia in Thai older people is crucial for planning public health strategies and rational allocation of resources to provide the optimal diabetic care and approach to Thai older people with type 2 diabetes. An early detection of cognitive decline may also afford individuals the opportunity to modify lifestyle and improve diabetes self-care management for a good quality of life.

It should be noted that, the incidence of type 2 diabetes increases with age, and 90% of diabetes is type 2. Thus, this thesis focuses only on the evidences relating type 2 diabetes to cognitive impairment and will not cover the cognitive complications of type 1 diabetes.

1.8 Structure of the thesis

This thesis is divided into 10 chapters. In order to understand the background of the research, this chapter (Chapter 1) provided an overview of Thailand profile and its older people population.

Chapter 2 will provide a review of the existing research related to the prevalence of cognitive impairment and the prevalence of depressive mood in type 2 diabetes.

The purpose of this chapter is to review the trend of prevalence rate, study setting and screening tools used in the previous studies. In addition, this information will provide an overview of factors related to the study of cognitive impairment in type 2 diabetes.

Chapter 3 will discuss and critique the existing cognitive screening tools commonly used in Thailand. The aim of this chapter is to provide a choice of the tests in this study.

Chapter 4 will focus on the development of the Thai version of Mini-Cog, a brief cognitive screening test specific to use in primary care setting. This chapter will present the validated processes to translate original version of the Mini-Cog from English to Thai.

Chapter 5 will present the study protocol including the research questions, aims, and objectives of this study. Procedures for recruitment, data collection and analysis will be outlined.

Chapter 6 is the pilot study. This chapter aims to investigate the feasibility of applying the study protocol as well as the Mini-Cog Thai version to collect the data in the main study. This study will present the inter-rater reliability and concurrent validity of the Mini-Cog. Lessons learned and a summary of changes for the methodology (Chapter 7) will be summarised.

Chapter 7 is methodology. This chapter will begin with a discussion of changes summarised from the lesson learned in the pilot study (Chapter 6). Then the second part will present an overall description of the methodology.

Chapter 8 will illustrate a summary of findings in this study. This chapter has two parts. In order to show the reliability of data collection in this study, the first part will provide the results of the inter-rater reliability between the researcher and research assistant in all screening tools. The second part is a summary of participant characteristics and results from the screening tools. This will be presented according to the research objectives.

Chapter 9 will critique and discuss the findings in relation to the existing literature and possible limitations. The outcomes of the study will be discussed and summarised.

Chapter 10 will provide an overall conclusion. Strengths and limitations of this study will be outlined. Implications for clinical and health care professions including recommendations for future research will be described.

1.9 Summary

Type 2 diabetes poses a major public health problem in Thailand and worldwide. The prevalence of type 2 diabetes in Thailand is about 7% and the highest prevalence (16.7%) is in the population aged 60 years and over. Diabetes alone is responsible for 3.3 and 8.3% of total deaths in Thai men and women. Keeping a good self-care management is an important factor in taking care of diabetes, a lifelong disease. Lifelong daily self-care activities include adhering to diet, exercise, and medication regimens including checking blood glucose. The coordination of these activities requires a complex cognitive functioning. Because of the prevalence of diabetes and cognitive impairment increase with age, screening cognition to identify early sign of cognitive impairment as well as screening depressive mood to detect a reversible cognitive impairment in older diabetic patients would benefit an optimal diabetes care and planning.

Chapter 2

Literature review

Evidence shows that cognitive impairment and depressive mood can be found in older people with type 2 diabetes (see Chapter 1). This chapter conducts a systematic search and synthesises of the published literature of the prevalence of cognitive impairment and the prevalence of depressive mood in the older people with type 2 diabetes. In addition, factors related to the cognitive impairment in the older people with type 2 diabetes will be presented.

This chapter consists of the following two parts. The first part focuses on the published studies that assess the prevalence of cognitive impairment and depressive mood in the older people with type 2 diabetes. The second part is an overview of factors related to the study of cognitive impairment in type 2 diabetes.

2.1 Review studies of the prevalence of cognitive impairment and depressive mood

Prevalence refers to the proportion of a defined population at risk that has a defined health problem at a particular point in time (point prevalence) or during a period of time (period prevalence).Valid information of this basic epidemiological parameter is necessary to monitor trends of the disease burden and to highlight valuable information for preventing the problem and planning effective public health program (Webb and Bain 2011). In addition, prevalence study is an essential consideration to understand the current knowledge regarding cognitive impairment specific to type 2 diabetes that could lead to further primary research.

Therefore, the primary aims of this section are to synthesise and quantify the prevalence of cognitive impairment and depressive mood in published literature, including risk factors associated with type 2 diabetes in old adults.

2.1.1 Method

An electronic search was conducted using the following bibliographic databases: MEDLINE, AMED, CINAHL, EMBASE, PsycInfo and Cochrane library. These databases cover all the publications in medical and healthcare electronic resources. Each medical and healthcare database was separately searched from January 1985 to June 2012 for English articles. The year 1985 was chosen as the earliest year that the literature addressed across-sectional study examining the association between type 2 diabetes and cognitive impairment in the Cochrane review (Mattlar et al. 1985, Evans and Sastre 2009). All databases were searched continuously during the period of this research.

Search terms:

- type 2 near diab* or DM, type II near diab* or DM, type 2 diabet*, NIDDM, Non- Insulin Dependent Diabetes Mellitus, Diabetes Mellitus
- cognit*, dement*, alzheimer*, cognitive impair* , cognitive dysfunct*
- depres* , mood, low mood
- preval*, prevalence
- elderl*, older, age*

Both free text and the related thesaurus Medical Subject Heading (MeSH) terms were used for each search.

Inclusion criteria

- Primary studies reporting the frequency of (prevalence or incidence), or predictors for related cognitive impairment or dementia or depression in old adults with type 2 diabetes.
- Written and published in English.
- Focus on the measurement of the frequency of cognitive impairment or depressive mood in single point of time in order to see trend of burden disease

Exclusion criteria

- Qualitative research, single case studies and secondary research

2.1.2 Results

A total of 689 citations were retrieved from all database including duplicates. The search papers were narrowed and selected by title. Of the 689 citations, 457 were excluded due to the title and duplicates. Of 232 abstracts that addressed type 2 diabetes were read, and those that were relevant to inclusion criteria were identified and reviewed for the full-text.

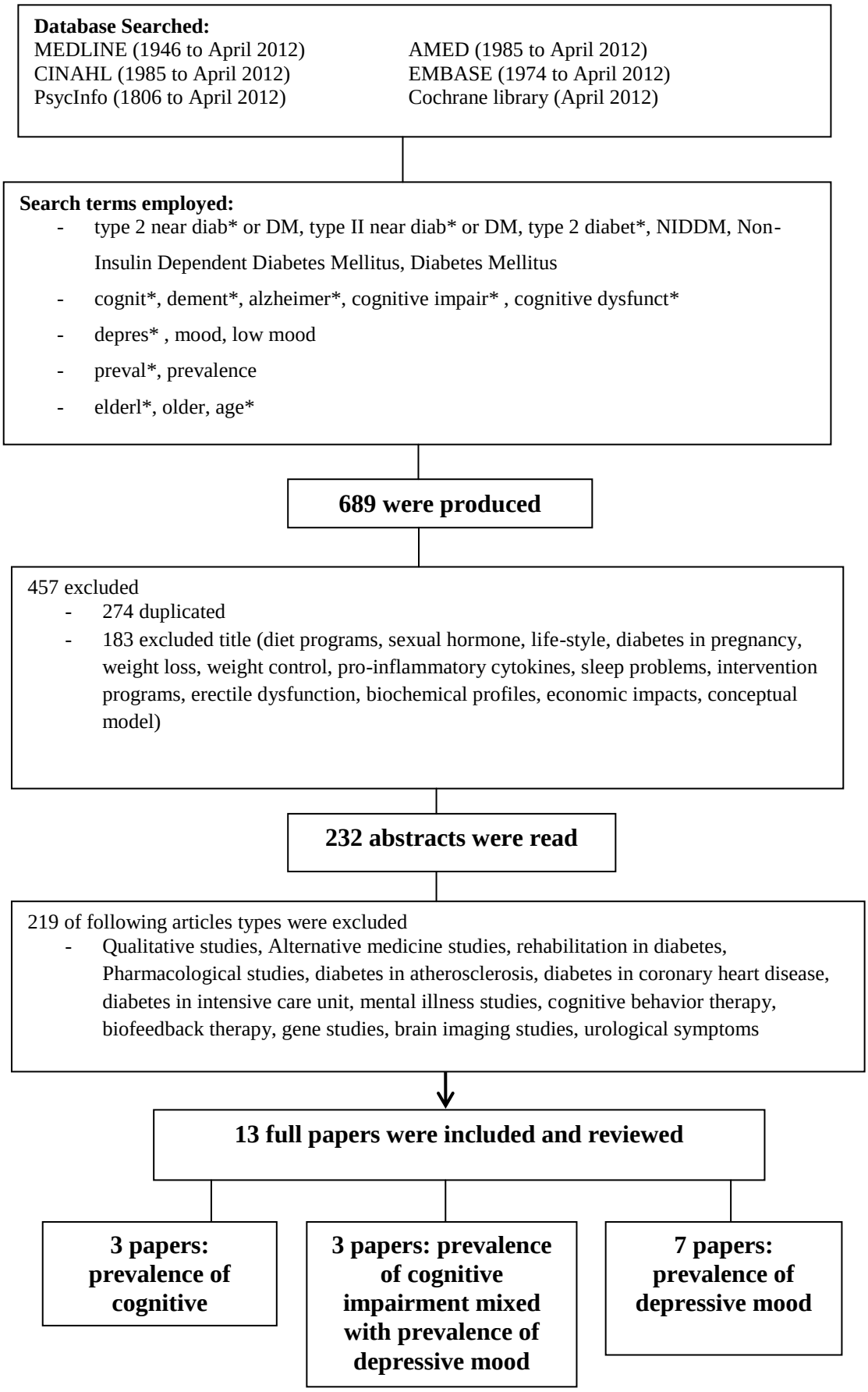
The search yielded that13 relevant studies met the criteria. The papers were read using Coughlan et al.'s (2007) guide to critique quantitative research. Prevalence studies were evaluated using a standardize checklist (Boyle, 1998). The papers were categorized into two categories related to cognitive impairment and depressive mood in type 2 diabetes as follows:

A) Prevalence of related cognitive impairment: 6 studies

B) Prevalence of depressive mood: 10 studies (3 papers overlapped with prevalence of cognitive impairment studies)

The search results are summarised in Figure 2.1

Figure 2.1: Results of Search Strategy



A) Prevalence studies related to cognitive impairment

Six studies estimated the prevalence of cognitive impairment in subjects with type 2 diabetes in old age. Two studies were designed to examine both cognitive impairment and depressive mood (Bruce et al. 2003, Munshi et al. 2006). One study focused on mild cognitive impairment and depressive mood (Thaneerat et al. 2009). Three published studies were conducted in hospital setting. The details in each study are described as the following:

In Australia, the prevalence of probable dementia was studied in a Fremantle Diabetes Study (FDS), a community-based study of diabetes care project in 2001 and 2003 (Bruce et al. 2001, Bruce et al. 2003). The study was conducted twice by the same researchers. The study in 2001 showed the prevalence rate at 11.3% of probable dementia with the limitation on small sample size (60). This study was conducted again in 2003 with a larger number of participants. In this study, 223 (42%) participants from a total number of 529 eligible surviving participants aged 70 were screened for cognitive impairment. MMSE and IQCODE were used to screen cognitive impairment. Participants who had MMSE score less than 24 and IQCODE score more than 3.61 (combining the results) were defined as probable dementia cases. The prevalence of probable dementia was found 15.3%.

Another study is related to Munshi et al. (2006) in the United States. They studied the association between cognitive dysfunction and glycaemic control with other barriers in 60 older adults with diabetes. The study took place at tertiary care specialty setting in the United States. Participants were recruited using convenience sampling. The Mini Mental State Examination (MMSE), Clock Drawing Test (CDT) and Clock-In-a-Box (CIB) were used as cognitive screening tools. This study pointed out two main weaknesses for MMSE: 1) low specificity (specificity = 64%, sensitivity = 96%) and 2) limitation of an executive function test. These weaknesses have an impact on the ability to detect the subtle changes in cognition and the early stage of cognitive impairment or mild cognitive impairment (MCI). Therefore, this study used CDT and CIB designed specifically to assess memory and executive function components in cognition, along with MMSE. The cut-off score for MMSE was less than 24/30 and the cut-off scores for

the CDT and CBT were 13/20 and 6/8, respectively. Of all the participants who were screened and were positive to cognitive impairment, 12% were diagnosed by MMSE, 38% by CDT and 35% by CIB. Munshi et al. (2006) stated that CDT and CIB were superior in identifying the patients with subtle changes in cognition and their vulnerability to cognitive dysfunction. They also suggested that cognitive impairment was one of the unrecognized barriers in diabetes control. However, due to the convenience sampling, the sample was unlikely to be representative of the population being studied because there was a high rate of Caucasian (82%) as compared to African American (13%) and Hispanics (5%). Another major limitation of this study was the small sample size.

In Thailand, Thaneerat et al. (2009) estimated the prevalence of depression with mild cognitive impairment (MCI) in 250 Thai older people with type 2 diabetes in a university hospital setting. Participants were recruited using systematic random sampling method and the patients with cognitive impairment who had been screened by Thai Mental Screening Test (TMSE) were excluded. This study used the Montreal Cognitive Assessment (MoCA) test to detect MCI. Overall, the number of people who had MCI was 77.6 % (194/250). This study was limited by the fact that the original version (English version) of the cognitive screening test was applied to non-English speaking population regardless of the report of reliability and validity of the test.

In Sri Lanka, Rajakumaraswamy et al. (2008) studied the frequency of cognitive function and dementia among Sri Lankan older people with type 2 diabetes in a diabetic clinic. The participants were recruited by random sampling of 204 participants from a specialist diabetic clinic database. MMSE was used as a cognitive screening test and a score of less than 25 was defined as cognitive impairment. Then the participants who had cognitive impairment (MMSE score less than 25) were screened further with the Cambridge Cognitive Assessment (CAMCOG) to detect dementia. The cut-off score of less than 80 was diagnosed with dementia. Psychiatric disorders were excluded in all these participants by a psychiatric blind to cognitive assessment scores. In total, the prevalence of cognitive dysfunction and dementia were 32.8 % (67/204) and 10.3 %, (21/204), respectively.

Alencar et al. (2010) conducted a study to find the prevalence of possible dementia in Brazilians with type 2 diabetes in a hospital setting in Brazil. The validated MMSE in the Brazilian version was used to detect possible dementia. The following criteria were set: cut-off score of MMSE of less than 26 (<26) for the participants who had more than 8 years in school and a cut-off score of less than 18 (<18) for those who had 1-8 years in school. Of the 346 participants who were screened by MMMSE, 12.1% (42/346) were classified as possible dementia cases. The limitation of this study is related to the representativeness of the population; that is illiterate participants were excluded from the study.

The 6 above-mentioned studies show the range of the prevalence of cognitive impairment in old adults 11.3% to 77.6%. It should be noted that the study of Thaneerat et al. (2009) focused on the prevalence rate of mild cognitive impairment (MCI) instead of cognitive impairment. Therefore, it could be possible that the estimated rate of MCI shows the distinctly high rate of (77.6%) compared to the other studies (i.e. Bruce et al. 2002, Bruce et al. 2003, Munshi et al. 2006, Rajakumaraswamy et al. 2008, Alencar et al. 2010). Overall, MMSE was the most common cognitive screening tool used in the prevalence study. Five of the six studies used MMSE as a screening tool for cognitive impairment. Although MMSE was used as a worldwide cognitive screening test, other short cognitive screening tools were used along with MMSE. There are two main reasons for applying the other cognitive screening tests along with MMSE. First, MMSE is not sensitive in early detection of dementia (Allen et al. 2004, Munshi et al. 2006). Second, MMSE is affected by age and education (Bruce et al. 2001, Bruce et al. 2003).

In summary, the prevalence rate of cognitive impairment in the literatures depends on the following factors:

1) The range of age groups

   For example, there was a variety of age range in each study, from the mean age of 59 to 79). None of the studies reported 95% CI with prevalence rate (Figure 2.1)
2) The difference of cognitive screening tools

3) The variety of cut-off scores in the same cognitive screening tool

For example, the cut-off score of MMSE, particularly, in the non-English versions varied. The study in Brazil used the cut-off score with the level of education (Alencar et al. 2010), while the study in Sri-Lanka used one cut-off score for all the levels of education (Rajakumaraswamy et al. 2008) (Figure 2.2). More importantly, the study in Thailand (Thaneerat et al. 2009) had a major limitation on the report of validated study of cognitive screening when applied to another culture and language.

Figure 2.2: Mean age in each prevalence study

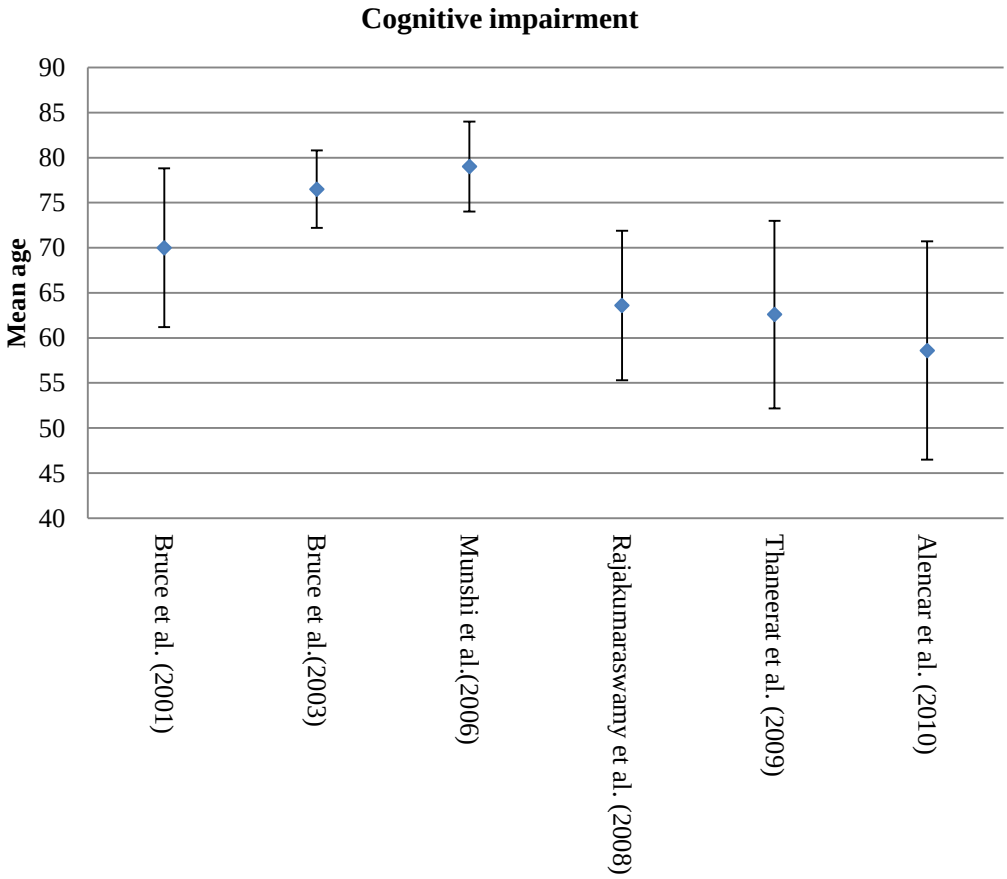


Figure 2.3: Prevalence rate and screening tools with cut-off scores

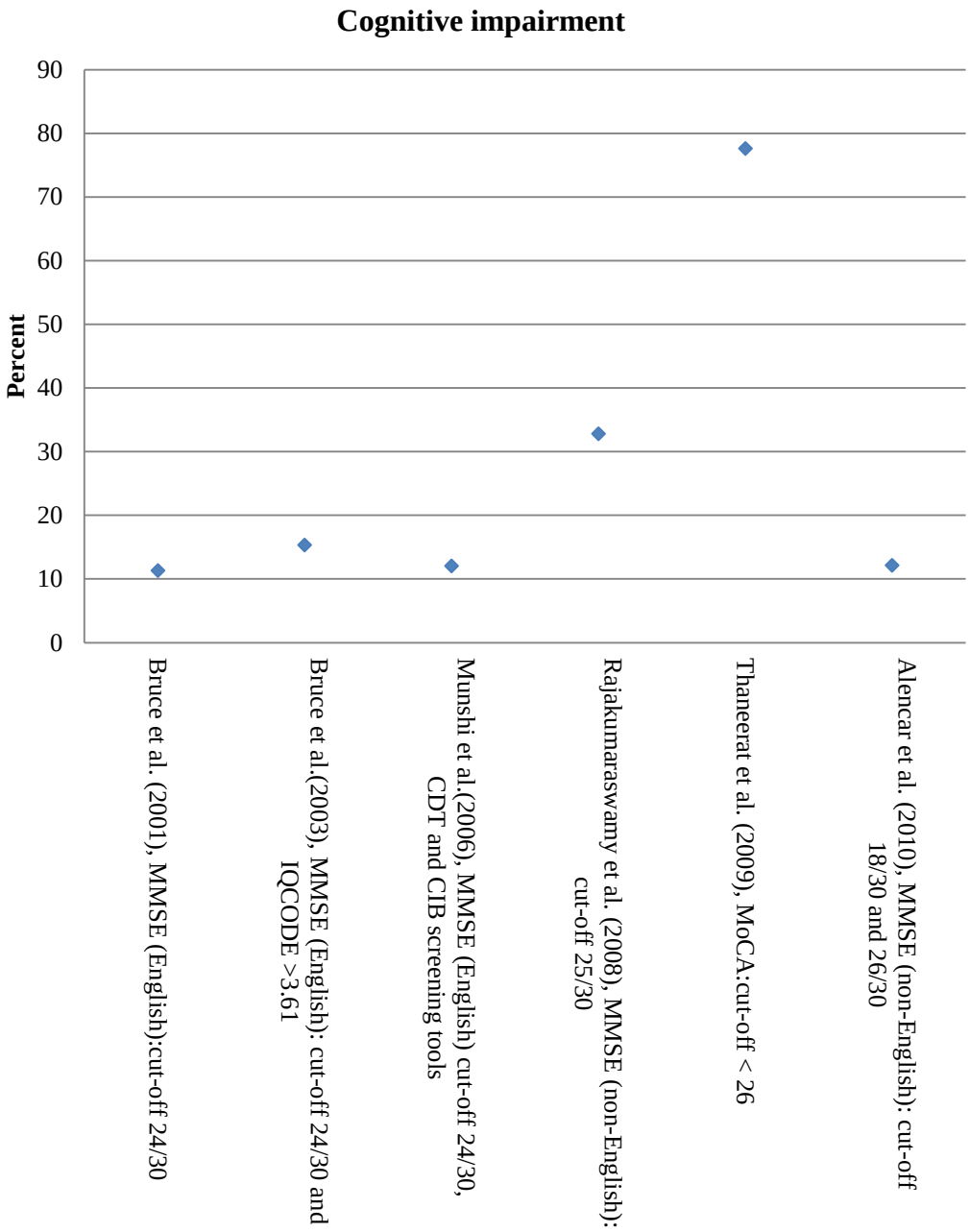


Table 2.1: Summary of the studies on the prevalence of related cognitive impairment in type 2 diabetes

Study and setting	Sample size	Probability sampling	Mean age / Age range	Prevalence (95% CI)	Measures	Comments
Bruce et al. (2001), Fremantle Diabetes Study (FDS), community- based study, Australia	63	no	70±8.8	11.3% of probable dementia	MMSE screening test: cut-off < 24/30 AND IQCODE screening test: cut-off > 3.61 defined as probable dementia	-No report of Confidence Interval (CI) with the prevalence -Exclude 10 cases when probable dementia was due to language barrier - IQCODE uncompleted due to the lack of suitable informant - Convenience sampling
Bruce et al. (2003), Fremantle Diabetes Study (FDS), community- based study, Australia	223	no	76.5±4.3	15.3% of probable dementia	MMSE screening test: cut-off < 24/30 AND IQCODE screening test: cut-off > 3.61 defined as probable dementia	-No report of Confidence Interval (CI) with the prevalence - Sensitivity = 93% and specificity = 85% for combining results of the two screening tests - Convenience sampling

Table 2.1: Summary of the studies on the prevalence of related cognitive impairment in type 2 diabetes (continued)

Study and setting	Sample size	Probability sampling	Mean Age /Age range	Prevalence (95% CI)	Measures	Comments
Munshi et al. (2006), Tertiary care specialty clinic, the United State	60	no	79±5.0	12% of cognitive impairment by MMSE 35% of cognitive impairment by CIB 38% of cognitive impairment by CDT	MMSE screening test: cut-off < 24 CIB (clock-in- a box):cut-off <6 (6/8) CDT: cut-off <13 (13/20)	-Small sample size -Convenience sampling - No report of CI
Rajakumaraswa-my et al. (2008), Specialist diabetic clinic, Sri Lanka	204	yes	63.6±8.3	32.8 % of cognitive impairment (MMSE) 10.3% of dementia (Neuropsychological tests)	two-phase design: 1. MMSE screening test (cut-off < 25) 2.Neuropsychological test for the diagnosis of dementia	-No report of Confidence Interval (CI) with the prevalence - No report of education level of subject when used MMSE in non-English group - The paper is in research letter format, the information of the study is restricted

Table 2.1: Summary of the studies on the prevalence of related cognitive impairment in type 2 diabetes (continued)

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Thaneerat et al. (2009), diabetic outpatient clinic, hospital-based study, Thailand	250	yes	62.58±10.41	77.6 % of mild cognitive impairment (MCI)	MoCA test (cut-off < 26)	-No report of Confidence Interval (CI) with the prevalence - No information of data collection method, i.e. no. of interviewer and process - No report of reliability and validity of the validated test
Alencar et al., (2010), Diabetic outpatient clinic, hospital-based study, Brazil	346	unknown	58.6± 12.1	12.1%	MMSE screening test with two-level cut-off score 1. cut-off < 26 for subjects with years of study more than 8 years 2.cut-off < 18 for subjects with years of study between 1 and 8 years	- No report of CI - No information of data collection method i.e. no. of interviewer and process - Exclude the illiterate participants

B) Prevalence studies of depressive mood in type 2 diabetes

Eleven papers were included in the review (Table 2.2). Five studies were conducted in a hospital-based setting and six studies were carried out in a community-based setting. The prevalence rate of depressive mood in the cross-sectional studies varies from 13.17 % to 33.4 %. The estimation of depression rate varied probably due to the difference of sample size, age range and depressive mood screening test in each study.

Three of these studies show that females are more likely to have depressive mood than males (Bruce et al. 2003, Pibernik-Okanovic et al. 2004, Sotiropoulous et al. 2008). Among these three studies, depressive mood is found to be related to gender in different subjects. For example, Bruce et al. (2003) found that females not only had depression, but also were more distressed than males. Pibernik-Okanovic et al. (2004) revealed that apart from gender (female), there were some psychological problems that could predict depression, such as unsatisfaction with social support or the existence of psychological problems in the past. In addition, the study from Sotiropoulous et al. (2008) found that depressive symptoms in women with diabetes were correlated with HbA1c and duration of diabetes, whereas there was no correlation between depressive symptoms and other testing variables in men.
Medical variables such as cholesterol, triglyceride and high-density lipoprotein (HDL) were found to have a relationship with depressive moods (Gary et al. 2000, Tsai et al. 2008). Other factors such as age (Bruce et al. 2003) and insulin injection as diabetes treatment (Tsai et al. 2008) were also correlated with depressive symptoms. Overall, some limitations were found in these studies that can be summarised as follows:

1) Missing 95% confidence interval (CI)

   Apart from Zahid et al.'s (2007) study, most of the previous studies do not report the 95% CI with the prevalence rate. Due to the varied sample size in prevalence studies, 95% CI is used to describe the results of the prevalence ratein which the actual estimation value is likely to fall. Thus, the report of 95% CI is crucial and represents the precision of an estimate (du Prel et al. 2004).

2) Drawback of self-report questionnaire

Recall bias and missing information are the drawbacks of self-report questionnaire screening tests. Screening test by self-report has limitation on recall bias. This can be found in the studies of Bruce et al. (2003) and Thaneerat et al. (2009). The possibility of a high number of missing information in the large sample study can be found in Net et al. (2012).

3) Uncertain cultural validity of the questionnaire test

Two studies used depressive mood-screening test in its English version regardless of the validated study (Zahid et al. 2017, Thaneerat et al. 2009). They reported the reliability and validity of the test in a non-English speaking population. Lack of precise translation of the research instruments may affect the generalisation of the results from the culture of origin. Likewise, the applicability of instruments from the original to the target version in different cultures and languages may be adversely affected if translation procedures are not validated (Su and Parham 2002). In addition, beyond the validated translation, the reliability and validity study of the instruments are important to ensure that the results of measurement are reliable in the target population (Kestenbaum 2009).

4) Generalisation of findings

There is a limitation in applying the results to the local populations in two of the above-mentioned studies. In the study of Nef et al. (2012) 97% of the sample was in one ethnic population, and the study of Gray et al. (2000) focused only on a group of African-Americans.

5) Study setting

The range of prevalence rate in a hospital setting is wider than the prevalence rate in a community setting (14-33% vs. 14-26%). Compared with the community setting, the prevalence studies in the hospital setting tend to focus on the association between other clinical variables such as glycaemic control (HbA1c) or cholesterol level and depressive mood, rather than the psychological problems.

Table 2.2: Summary of the studies on the prevalence of depressive mood in type 2 diabetes

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Gary et al. (2000), Primary care Unit, the US.	186	Random sample	59±9 (35-75)	30%	Center for Epidemiological Studies Depression Scale (CES-D) Cut-off score ≥ 22 Structure interview	1.No report of Confidence Interval (CI) with the prevalence 2. Depression correlated with higher serum of cholesterol and triglyceride ($p<0.05$) and higher serum of HDL ($p=0.047$). 3. The study may not represent other diabetic populations since it focused only on a group of African-Americans.

Table 2.2: Summary of the studies on the prevalence of depressive mood in type 2 diabetes (continued)

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Pibernik-Okanovic et al. (2001), Hospital-based study, Croatia	384	Random sample	57±7.8	22% (depressive mood by CES-D screening) 33% (clinical depression)	two-phase 1.Screen depression: Center for Epidemiological Studies Depression Scale (CES-D) Cut-off score ≥ 16 2. Structure clinical interview for DSM-IV Axis I Disorder (SCID) to identify clinical depression	1.No report of Confidence Interval (CI) with the prevalence 2. This study focused on psychological problems rather than disease -related variables. 3. Gender, experienced social support, and variables indicating emotional well-being (limitations due to emotional health, mental health and psychological wellbeing) were shown to be independent predictors of depression (standardized B coefficients were 1,78; 2,18; -0.08; -0,10 and -0,47, respectively).

Table 2.2: Summary of the studies on the prevalence of depressive mood in type 2 diabetes (continued)

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Bruce (2003), Fremantle Diabetes Study (FDS), community- based study, Australia	223	No	76.5 ±4.3	14.2%	Even Briefer Assessment Scale for depression (EBAS-DEP) Cut-off score of 4 or more out of 8 (contains sensitivity and specificity more than 80%)for clinically significant depression in community) Self-report	1. No report of Confidence Interval (CI) with the prevalence 2. Convenience sampling 3. Depression was not associated with age (Spearman's rho = 0.05, p=0.43). 4. Women were significantly more likely to have depression than men (43.5% vs. 27%, p =0.011and worry (54.6 vs. 39.6%, p=0.026).
Munshi (2006). Tertiary care specialty clinic, USA.	60	No	79 ± 5	33%	Short (15-item) Geriatric Depression Scale (GDS) Cut-off score ≥ 5 Interview	1. No report of Confidence Interval (CI) with the prevalence 2. Small sample size 3. Convenience sampling

Table 2.2: Summary of the studies on the prevalence of depressive mood in type 2 diabetes (continued)

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Zahid et al. (2007), rural community, Pakistan	1290	Cluster sampling 44 village	44	14.7% (6.6%-22.8%)	Montgomery-Asberg Depression Rating Scale (MADRS) Cut-off score ≥ 13	1.Direct translation of the original English version of MADRS to Urdu for interview 2. No report of reliability or validity of the Urdu version 3.No report of the validated study of Urdu version
Sotiropoulos et al. (2008), Hospital based study, Greek	320	Unknown	35-70	33.4 %	21-item Beck Depression Inventory (BDI) modified for diabetic patients Cut-off score ≥ 19	1.No report of Confidence Interval (CI) with the prevalence 2. Women were significantly more likely to have depression than men (48.4% vs. 12.7%, $p < 0.001$). 3. In women, depressive symptoms were correlated with HbA1c (p=04) and diabetes duration (p=0.004). 4.No correlation between depressive symptoms and testing variables in men

Table 2.2: Summary of the studies on the prevalence of depressive mood in type 2 diabetes (continued)

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Tsai et al. (2008) Hospital-based study, Taiwan, China	167	Unknown	60.2+11.0	13.17%	Beck Depression Inventory II (BDI-2) in Chinese version Cut-off score BDI ≥ 17 Self-report and interview for illiterate participants	1.No report of Confidence Interval (CI) with the prevalence 2.Excluding known cases of depression 3. Depression is correlated with insulin injection and total cholesterol level compared to non-depressed patients
Shehatah et al. (2009), Primary care setting, Saudi Arabia	458	Unknown	65+8.9	17.5%	Beck Depression Inventory II (BDI-2) but Cut-off score BDI ≥ 14 Self-report	1.No report of Confidence Interval (CI) with the prevalence 2. State language version was not used in BDI-2

Table 2.2: Summary of the studies on the prevalence of depressive mood in type 2 diabetes (continued)

Study and setting	**Sample size**	**Probability sampling**	**Mean Age /Age range**	**Prevalence (95% CI)**	**Measures**	**Comments**
Thaneerat et al. (2009), diabetic outpatient clinic, hospital-based study, Thailand	250	yes	62.5±10.4	28%	Thai-Hospital Anxiety Depression Scale (Thai-HADS) cut-off score ≥ 8 Self-report	-No report of Confidence Interval (CI) with the prevalence
Nef et al. (2012), Primary care, Netherland	2,460	Follow up	67±11	26%	Edinburgh Depression Scale Cut-off score ≥ 12 Self-report	1.No report of Confidence Interval (CI) with the prevalence 2. Strength: a large sample of primary care patients with type 2 diabetes 3. Weakness:27% missing data in demographic, clinical and psychological data 4. Not representing other diabetic populations since 97% of the cases were white in the study

2.2 Contribution of other factors on cognitive impairment in type 2 diabetes

Normally, type 2 diabetes does not exist in isolation. Other important factors that can affect cognition could take place in older diabetic patients leading to cognitive impairment (Asimakopoulou and Hampson 2002). Some factors that are likely to confound in the study of diabetes-related cognitive impairment are briefly discussed below.

Age

Cognitive impairment is often seen with the increasing age (Biessels et al. 2006). However, age does not seem to affect all the areas of cognition in elders in the same way (Asimakopoulou and Hampson, 2002). Ryan and Geckle (2000) state that older people with type 2 diabetes are more likely to be prone to diabetes-associated memory and learning difficulties than impairment in other areas of cognition. Ageing is also associated with changes in the brain. This change can be clearly seen in patients with Alzheimer's disease (AD) which show a decrease of glucose utilisation and deficient energy metabolism occur in the early of disease. This suggests for a role impaired insulin signaling pathogenesis of AD (Steen et al. 2005). Thus, the insulin receptor impaired in the brain due to ageing is also one of the causes of cognitive impairment.

Duration of diabetes

Longer duration of diabetes is associated with increased cognitive impairment (Cosway et al. 2001). In particular, longer duration of poor glycaemic control may lead to permanent cognitive impairment (Awad et al. 2004). Duration of diabetes may cause the development of vascular disease when combined with high blood glucose in body (Grodstein et al. 2001).

Obesity

Obesity or high BMI is associated with worse cognition (Berg et al. 2009), particularly in the cognitive flexibility and memory. BMI was included as a covariate in blood pressure and blood cholesterol level in Gustafson et al.'s (2003) study. There are many possibilities that BMI may link to cognitive decline in type

2 diabetes. A high BMI may lead to high blood pressure, and thus increase the risk of dementia (Zhang and Reisin, 2000). High blood cholesterol may also cause vascular risk factor and play a role in the etiology of AD (Skoog et al. 1996).

Diabetic complications

A diabetes complication in microvascular lead to renal failure, foot ulcer and vision loss (Nathan 1993). There is growing evidence that diabetes is associated with an increased risk of cognitive decline, physical disability and other conditions associated with geriatric syndrome (Strachan et al. 2003). These complications have an impact on the quality of life, loss of independence and may be of greater direct concern in older people with diabetes (Gregg et al. 2003). Diabetic complications may lead to chronic hyperglycaemia or long-term blood glucose and may also influence cerebral blood flow and neurotransmitter function, or nutrient to the brain (Strachan et al. 1997).

Diabetic treatment

Lack of diabetic pharmacological treatment seems to be associated with a worse performance of cognitive function in the older people with type 2 diabetes (Grostein et al. 2001). The study of Grodstein et al. (2001) suggest that women who receive treatment (oral medication) perform better on the cognitive measures than the diabetic women who are reported to receive no medication. Diabetes medications can help control type 2 diabetes by increasing insulin sensitivity and decreasing glucose output. Consistent use of diabetes medications also helps to control blood glucose level and keep oxygen and nutrient reach brain cells (Cukierman-Yaffe et al. 2009).

Advanced glycation end products (AGEs)

Advanced glycation end products (AGEs) are a heterogeneous group of modified proteins, lipids, and nucleic acids implicated in the aging process and diabetes (Rambhade et al. 2011).The modifications of proteins or lipids are the result of a chain of chemical reactions which follow an initial glycation reaction. Initial glycation involves covalent reactions between free amino groups of amino acids, such as lysine, arginine, and sugars (e.g. glucose, fructose and ribose), to create the

Schiff base and then Amadori products, of which the best known are fructosamine (FAM) and glycated haemoglobin (HbA1c) (Marchetti 2009).

A high level of blood glucose (hyperglycaemia) is known to enhance the forming of early FAM and HbA1c, intermediate and advanced glycation products. These glycation products are a primary factor that initiates and promotes diabetic complications (Hanssen 1997). FAM fraction reacts much more quickly than the HbA1c to a change in glucose situation and reflects a quality of diabetes control over the short period of 2-3 weeks, while the degree of glycation of haemoglobin provides information about the glucose level over the last 6-8 weeks (Gugliucci 2000, Kostolanska et al. 2009).

It has long been recognized that increased HbA1c (a precursor of AGEs) levels are associated with a higher incidence of vascular complications in diabetic patients (Marchetti 2009). Hence, hyperglycaemia or increased HA1c (a precursor of AGEs) will induce the formation of AGEs, which acts as an important pathophysiological mechanism in the development of diabetic complications through binding and interaction with their receptors (RAGE). RAGE is expressed in many tissues such as heart, lung, skeletal muscle, and vessel wall (Huijberts et al. 2008). The binding and interaction could then lead to an oxidative stress and activation of inflammatory pathways causing proatherosclerotic changes and inducing vessel damage (Leslie and Cohen 2009)

More importantly, hyperglycaemia (increased HbA1c) could cause cognitive impairment by several mechanisms. Acute changes in blood glucose are known to alter regional cerebral blood flow and could also cause osmotic changes in cerebral neurons. These same mechanisms may be operative in the brain and induce the changes in cognitive function that have been detected in diabetic patients (Vijayakumar et al. 2012). Moreover, AGEs are protein modifications that contribute to the formation of the histopathological and biochemical hallmarks of Alzheimer's disease (AD), i.e. amyloid plaques, neurofibrillary tangles and activated microglia in a brain (Stitt 2001).

AGEs may involve cognitive decline in type 2 diabetic patients from the glycation processes through hyperglycaemia or an increased HbA1c (precursor of AGEs). Therefore, reduction of blood glucose levels in diabetes, as documented by decreased HbA1c, remains the most appropriate way to reduce vascular complications in diabetic patients (Marchetti 2009).

Glycaemic control

Glycaemic control is associated with cognitive function in type 2 diabetes. In particular, chronic glucose level appears to be associated with cognitive impairment in type 2 diabetes (Cukierman-Yaffe et al. 2009, Grober et al. 2011, Mahakaeo et al. 2011). The level of glycaemic control (HbA1c) shows the association between the two cognitive domains (memory and executive function). HbA1c is defined in the two levels of controlled (HbA1c $\leq$ 7 or 53 mmol/mol) and inadequately controlled (HbA1c > 7 or 53 mmol/mol) (American Diabetes Association 2009, Grober et al. 2011). Memory impairment and executive dysfunction are associated with inadequately controlled diabetes in old adults with type 2 diabetes (Grober et al. 2011). Uncontrolled glycaemia can lead to hyperglycaemia and cause slowly progressive pathogenesis of brain abnormalities that may eventually induce Alzheimer's disease (AD) (See Chapter 1, Section 1.2.1). Therefore, chronic hyperglycaemia could be one of the determinants of cognitive changes in people with diabetes (Stewart and Liolitsa 1999).

Cardiovascular problems

Type 2 diabetes is a risk factor for vascular diseases such as hypertension. An interaction between type 2 diabetes and hypertension on cognitive performance is associated with a greater risk of poor performance on a test of memory and attention (Gregg et al. 2000). Hypertension may cause changes in vessel walls leading to ischemia or hypoxia of the brain, all of which are related to the development of AD pathology (Beeri et al. 2009).

Inflammation

Inflammation may also contribute to cognitive impairment associated with type 2 diabetes. There is a link between inflammation and diabetes. For example,

hyperglycaemia is associated with an increase in proinflammatory cytokines and other peripheral markers of inflammation (Stentz et al. 2004). Inflammation is also associated with an impaired glucose regulation and predicts the development of diabetes (Barzilay et al. 2001). A high level of the inflammatory marker of C-reactive protein (CRP) and interleukin-6 (IL-6) is not only associated with an increased risk of developing type 2 diabetes (Pradhan et al. 2007) but also accelerated cognitive decline in healthy older adults (Engelhart et al. 2004) and in older adults with metabolic syndrome (Yaffe et al. 2004). Moreover, decreasing brain levels of proinflammatory cytokines can reverse memory deficits (Balschun et al. 2004, Gemma et al. 2005)

Depression

Depression may also contribute to cognitive impairment in older people with type 2 diabetes because it is independently associated with poor cognitive function (Solanki 2009). A successful treatment of depression is associated with improvements in glycaemic control by increasing adherence with treatment (Anderson et al. 2001). Depression may also be associated with hippocampal atrophy caused by elevated glucocorticiod secretions, resulting in memory impairment and dementia in later life (Awad et al. 2004). Depression might also play an important role in the maintenance of optimal glycaemic control in supporting the treatment adherence.

2.3 Summary

Although the findings of the previous studies on prevalence can be used to guide this study, they are limited in terms of the differences in screening tools, method of administering and sample. There is no consensus on the measurement of cognitive impairment and depressive mood in type 2 diabetes. The differences in study tools depend on the purpose of the study and the group of subjects. This review provided the range of prevalence rate of cognitive impairment and depressive mood in the published papers in many regions.

The factors related to cognitive impairment in type 2 diabetes suggest that there are many factors related to cognitive impairment. Thus, in general, the study of cognitive impairment in type 2 diabetes contains a variety of factors (Asimakopoulou and Hampson 2002). It seems that none of these studies have been specially developed to address the cognitive process in older patients with type 2 diabetes.

In Thailand, there seems to be only one study on mild cognitive impairment and depressive mood in hospital setting. However, this study focuses on depression more than cognitive function. Moreover, although the study was conducted in a hospital setting in the capital city where patients tend to be highly motivated, educated and have excellent support system, there were still a certain number of the older people with diabetes who were undiagnosed with depression and mild cognitive impairment. These unrecognized conditions might affect the ability to perform self-management in diabetes patients in the long-term care. In order to perceive diabetes knowledge to perform in a long-term care, cognition of diabetic patients is crucial and needed to process diabetic self-care management.

Bearing in mind that uncontrolled diabetes is frequently found in community level and rural areas (Nitayanat, et al. 2007), no study on cognitive impairment and depressive mood in the older people with type 2 diabetes in community setting has been conducted. Considering that undiagnosed dementia is high in primary care settings in Thailand (Jitapunkul et al. 2009), there is a significant gap that requires further study in the prevalence rate to estimate the magnitude of these conditions in Thai older people in community level.

In order to support routine cognitive screening and promote the detection of cognitive impairment in primary care setting, the screening test should be efficient, specific and practical to be used in primary care settings. The significance of the study and screening test could help primary care staff to be aware of the early signs of cognitive impairment in the older people with type 2 diabetes and provide an appropriate care program. In the next chapter, an overview of cognitive screening tests in Thailand including the choice and rationale for the screening tests used in this study will be presented.

Chapter 3

Cognitive screening tests in Thailand and choice of the screening tests

In Chapter 2, a review of the previous prevalence studies and factor-related cognitive impairment and depressive mood was provided. To achieve the prevalence rate in this study, a review of the cognitive and depressive mood screening tests that used in Thailand are needed in order to select the screening tools or instruments in the current study. This chapter provides this information in two parts. The first part presents an overview of the commonly used cognitive screening tests in Thailand. The second part provides the rationale for the selection of cognitive and depressive mood screening tests in this study.

3.1 Cognitive screening tests in Thailand

In order to find the cognitive and depressive mood screening tests used in Thai older people either in clinical practice or literature, a manual search was conducted to locate Thai journals or literatures in the following databases: Journal of the Medical Association of Thailand, Siriraj Medical Journal, Thai Library Integrated System database and Mental Health Project database, the Ministry of Public Health, Thailand. It should be noted that this search was gathered before June 2009, prior to the development of this research protocol.

Five cognitive screening tests were found which were commonly used in Thai older people. A summary of the details including the advantages and disadvantages of all the tests are presented in Table 3.1.

3.1.1 Mini Mental State Examination (MMSE) Thai 2002

Mini Mental State Examination (MMSE) Thai 2002 is a current clinical mainstay cognitive screening instrument in Thailand (Prasat Neurological Institute 2008) (see Appendix D2). It has been used to detect cognitive impairment to follow the course of an illness and to monitor response to treatment (Ageingthai 2008). The MMSE Thai 2002 is translated from the original English version of MMSE

(Folstein et al. 1975). This is an 11 item test with a total score of 0 (severe impairment) to 30 (no impairment). These 11 items are grouped into seven categories: orientation to time, orientation to place, registration of three words, attention and calculation, recall of three words, language and visual construction. It has been assessed in four regions of Thailand and includes specific questions related to attention, orientation, memory, calculation, and language.

Since MMSE is created in a developed country, where education level is high with a standard cut-off score of MMSE (English version) 24, a score of 23 or below is at risk of cognitive impairment. The standard cut-off score may therefore produce false-positive results when used in developing countries, where the rate of low-educated population is high (Salmon and Lange 2001). In order to minimize the problem of score results when using MMSE in developing countries, it was suggested to adjust the cut-off score according to education levels in developing countries (Liu et al. 1994, Caldas et al. 2011). Thus, the MMSE Thai 2002was assessed in four regions of Thailand in order to find the suitable cut-off scores for Thai people. It includes specific questions related to attention, orientation, memory, calculation and language. The results show an appropriate measure's scoring for Thai older people based on 30 total scores as the following: a cut-off score of 14 is used for an uneducated person (illiteracy) (sensitivity = 0.35, specificity = 0.81), a cut-off score of 17 is used for those who attended primary school (sensitivity = 0.57, specificity = 0.94) and a cut-off score of 22 for those who attended secondary school or higher education (sensitivity = 0.92, specificity = 0.93) (Ageingthai 2008). The limitation of MMSE Thai 2002 is its low sensitivity in the group with a low level of education (Wongchaisuwan et al. 2005).

MMSE is the most commonly used cognitive screening test but it is not sensitive to detect the early sign of cognitive impairment or mild cognitive impairment (MCI) (Nasreddine et al. 2005, Nazem et al. 2009, Aggarwal and Kean 2010). In addition, MMSE does not have any tasks to assess executive functions like tests of the capacity to abstract. These intellectual abilities have been found to be altered in the early stage of Alzheimer's disease (Munshi et al. 2006, Hatfield et al. 2009).

Although several studies including the study in Thailand found the limitation of MMSE in the very old and those with limited education (Lorentz et al. 2002, Shulman and Feinstein 2003, Nys et al. 2005, Wongchaisuwan et al. 2005), it is most often used as a known reference standard against which other cognitive screening tests are compared (Clark et al. 1999, Cullen et al. 2007). Moreover, MMSE is a tool for cognitive screening used worldwide for global evaluation and has the major advantage of being very widely understood (Simard 1998).

3.1.2 Thai Mental Sate Examination (TMSE)

Thai Mental Sate Examination (TMSE) (Thai Train the Brain Forum committee 1993) was modified from MMSE as the standard mental status examination for Thai subjects. TMSE contains the six items of orientation (6 scores), registration (3 scores), attention (5 scores), calculation (3 scores), language (10 scores) and recall words (3 scores). The test was applied to 180 normal Thai older people, aged 60-70 throughout the country. The measure's scoring is based on 30 total scores. The mean total score of TMSE is 27.38 $\pm$ Standard deviation (SD) 2.02 and a cut-off score less than 23 is used for a cognitive impairment. The estimated time for applying the test is approximately 10 minutes. Although, the content validity is the strength of this test, the study of reliability or diagnosis of the test (sensitivity and specificity) could not be found in the literature search. Thus, the absence of diagnostic test information is the major weakness of the test. In addition, this test is limited to use only in the literate group.

3.1.3 Chula-test

Chula-test was modified from TMSE (Jitapunkul 1996). It contains 13 items that cover the areas of cognition, memory, orientation, perception, abstract thinking, judgment attention, language, and recall part. The test was applied to 212 older people in an older people home care in the capital city of Thailand. The total summation of scores was 19. The test score less than 15 (cut-off scores) indicated cognitive impairment with high sensitivity (74%) and specificity (86%). The estimated time for applying the test has not been reported. The limitation of the test is that this study was applied to the older people living in a care home. This cannot be a representative of general Thai older population. In addition, the test was

developed from TMSE which did not show basic evidences of psychometric property such as reliability and validity of the tool.

3.1.4 Clock drawing test-Chula (CDT-Chula)

CDT-Chula (Jitapunkul 2000) is a modified version of Clock drawing test (CDT) developed by Goodglass and Kaplan (1982). CDT is used to measure the executive function of the brain (Woodford 2007). A testee is asked to draw a clock on a preprinted 12-centimeter circle showing the time of 11.10. CDT-Chula uses the same assessment method as the original version except the scoring method. The CDT-Chula is scored using Chula Clock-drawing Scoring System (CCSS) developed and validated in 669 Thai older people in one community at the capital city. The CCSS is a quantitative systematic scoring system. It considers 5 domains consisting of number of digits, errors in number in the worst quadrant, spatial arrangement and number sequencing, hand and placement of hands (Kanchnatawan et al. 2006). The cut-off score is 7 (less than 7 means abnormal) and has the sensitivity and specificity of 88% and 74%, respectively. The estimated time for applying the test has not been reported. Although the test contains a good sensitivity and specificity, the limitation is that the testee must be illiterate. In addition, in order to score CDT test correctly, training is needed because there are 15 scoring criteria to score the drawing of CDT.

3.1.5 Informant Questionnaire for Cognitive Decline in the Elderly (IQCODE) Thai version

IQCODE Thai version (Sukhontha et al. 2006) is developed and modified from the original English version of the IQCODE by Jorm et al. (1989). The IQCODE assesses cognitive decline over time, based on ratings of everyday cognitive abilities. Informants are asked about the subject's change in capabilities in relation to performance 10 years ago, rating the changes on a 5-point scale (1 = much better, 3 = little change, 5 = much worse). The original 26-item version of IQCODE was translated into Thai and certified by a professional translator. In addition, six more items were added to the modified IQCODE in the Thai version; three of these items assessed cognitive functions, and three of them assessed daily life activities. The test was studied in 200 pairs of older people subjects and their

informants who visited a Geriatric Clinic in Bangkok, the capital city. The optimal cut-off score on the modified IQCODE Thai version was 3.42, with 90% sensitivity and 95% specificity. However, the estimated time for applying the test has not been reported. Although this test has a higher sensitivity and specificity, it needs an informant or proximal who can provide reliable information and should have known the older people for at least 10 years in order to report changes of the older people over the last 10 years (Jorm et al. 1989).

Table 3.1 Summary of the cognitive screening tools used in Thailand with some advantages and disadvantages

Screening test	Description	Estimated time to complete the test	Advantage	Disadvantage
MMSE Thai 2002 (Agingthai 2008)	11-item test with a total score of 0 (severe impairment) to 30 (no impairment).	10-20 minutes	Main instrument for test cognitive screening in Thailand and worldwide Cut-off score is adjusted and suitable for Thai population sensitivity and specificity compared to diagnosis by a health professional	-Influenced by education, and age (Wongchaisuwan et al.2005) -Low sensitivity in low education levels -Lack of sensitivity to the early sign of cognitive impairment or mild cognitive impairment (MCI)
TMSE (Thai Train the Brain Forum committee 1993)	6-item test with a total score of 0-30	10-minutes	Content validity by Thai experts	-No information of psychometric property -Testee must be literate

Table 3.1 Summary of cognitive screening tools used in Thailand with some advantages and disadvantages (continued)

Screening test	Description	Estimated time to complete the test	Advantage	Disadvantage
Chula test (Jitapunkul 1996)	13- items test with a total 19 scores	No report	sensitivity and specificity compared to diagnosis by a health professional	-The study was conducted in a specific group of Thai older people in a care home -Developed from TGDS which does not provide an evidence of psychometric property
CDT - Chula test (Jitapunkul 2000)	draw a clock on preprinted 12 centimeters circle showing time of 11.10	No report	sensitivity and specificity compared to diagnosis by a health professional	-Needs training for interpretation and scoring of clock drawing
IQCODE Thai version (Sukhontha et al. 2006)	Asking information about the subject's change in capabilities in relation to performance 10 years ago	No report	sensitivity and specificity compared to diagnosis by a health professional	-Needs an informant who has known the tester very well for at least 10 years -The relationship between the informant and testee may affect the score results

3.2 Limitations of using existing screening tools in primary care settings

A number of conclusions can be drawn with regard to the existing measures used for cognitive screening in Thailand. The obstacles and the practical time of using cognitive screening tests in primary care setting were mentioned in Section 3.1.The following limitations of the existing cognitive screening tests are mainly based on the feasibility and validation of using the tests in primary care settings, the study area in this research.

Based on the review of cognitive screening commonly used in Thailand, the screening tests can be divided in two types: the test is given to the patient (MMSE Thai 2002, TMSE, Chula test and CDT Chula test) or the test is given to the informant or carer who can provide reliable information about the patient (IQCODE). The MMSE Thai 2002 is the main clinical screening test that has been use in hospital (Ageingthai 2008). Since the test remains the most familiar and widely used cognitive screening test worldwide, it is also used as the reference standard with other cognitive tests for research purposes (Silpakit et al. 2007).

The main limitation of the MMSE Thai 2002 is the impracticality of its administration time in Thai primary care setting, low sensitivity of the test in low education level and lack of sensitivity to detect early sign of cognitive impairment. Nevertheless, the MMSE Thai 2002 is still a main clinical screening test that is used in Thai hospitals (Ageingthai 2008). TMSE is the most restricted test to be used in primary care settings not only because of the length of administration time but also because of lacking the validation study of the test. The length of time to administer the Chula-test, CDT-Chula test and IQCODE in Thai population is not clear. These three tests have varied limitations and biases to be used in primary care settings. The Chula-test may be susceptible to the older people in home care. The CDT-Chula is complicated on the scoring of the clock drawing test and training is needed before using it. The IQCODE is impractical for routine use at primary care settings because the test results depend on the informant who knows the subject very well and because not all older patients access informants.

It is clear from the review that none of the screening tests were considered to be used in the current study due to the major limitation of administration time as a routine screening test in Thai primary care settings. Therefore, the current study aims to find and use a cognitive screening test which is specific to and validated in primary care settings in order to overcome the limitations of the existing screening tests.

3.3 Choice of screening tests in the current study

3.3.1 Cognitive screening tests

3.3.1.1 Cognitive screening tests which specific for primary care setting

There have recently been few tests that are recommended to be used in primary care settings. Based on a systematic review of short cognitive screening for primary care setting, the following three tests are the most valid and best suited in primary care applications (Woodford and George 2007): the General Practitioner Assessment of Cognition (GPCOG) (Brodaty et al. 2002), the Memory Impairment Screen (MIS) (Buschke et al. 1999) and the Mini-Cog (Borson et al. 2000). In addition, another survey study of cognitive screening used in primary care setting show that these three tests are recommended for clinical practice by the general practitioner (GP) in primary care settings (Milne et al. 2008). The Mini-Cog, MIS, and GPCOG are identified as relevant to primary care setting and are recommended for use due to the brevity and validity of the tests (Ismail et al. 2010)

GPCOG has been designed for primary care settings with a six-item patients test and a six-item informant interview. The length of time to use the test is approximately 4.5 minutes with the sensitivity of 85% and specificity of 86%. Although GPCOG is suitable to use in primary care settings, this test needs informants which may not be practical in the routine use.

MIS is a test of memorisation task that requires the testee to read and remember items in response to its category i.e. city, animal, musical instrument and vegetable. The sensitivity and specificity are 80 and 96 %, respectively. The length of time to complete the test is around 4 minutes. This test is limited to literate subjects. Therefore, it may not be practical to use in Thai rural area.

Mini-Cog consists of a simple memory test (3-item recall) and an executive function test (clock drawing test-CDT) (see appendix D1). The test has a sensitivity of 99% and a specificity of 96%. The length of time to administer the test is approximately 2-4 minutes with a simple scoring system of CDT. The concordance for rating the test result between the expert and naïve is high at 96% (Scanlan and Borson 2001).

Based on the information of the three cognitive screening tests validated in primary care settings, GPCOG contains a good psychometric property. But this test needs informants and this may not be practical in routine use. MIS is limited to literate subjects, since it requires reading ability. Compared to the other two tests, Mini-Cog is less affected by education and is directly tested on the patients. Considering the length of time to administer, Mini-Cog is suitable to apply in Thai primary care settings compared to GPCOG and MIS. Since the duration of time to visit primary care settings in Thailand varies between 3 to 5 minutes, Mini-Cog, which can be used in approximately 2-4 minutes is appropriate. The overall information of the three tests shows that Mini-Cog has a balance between minimum administration time and maximum performance which makes it the most suitable tool to apply in primary care settings. Thus, Mini-Cog is selected as a cognitive screening test in the current study.

3.3.1.2 Mini-Cog

Mini-Cog (Borson et al. 2000) was originally developed in an ethnolinguistically diverse American sample, to screen dementia in primary care settings. It is composed of a memory test (recall of 3 unrelated words) and a very simple free-hand version of the clock drawing test (CDT) included as a distractor for the memory task. Mini-Cog can be administered in an average of 3.2 minutes and contains a high sensitivity (99%) and specificity (96%) in a community sample of 249 ethnolinguistically diverse older people, one-half of whom had dementia and one-half of whom were cognitively intact (Borson et al. 2000). In a community-based study with a low level of educated participants and non-English speaking groups it has proved to be superior to MMSE in identifying dementia. Mini-Cog's

sensitivity of 76% and specificity of 89% contrasts MMSE's sensitivity of 79% and specificity of 88% (Borson et al. 2003).

Unlike MMSE, Mini-Cog is not affected by education and language (Borson et al. 2000). Moreover, in a multiethnic sample, Mini-Cog detects most of the subjects with a mild cognitive impairment as well as subjects with a moderate and severe cognitive impairment, many of whom were not recognized by their physicians (Borson et al. 2006).

Mini-Cog is new and has not been validated in Thai population. In order to propose Mini-Cog as a new cognitive screening tool, the test should be compared with a known reference standard on the same population, such as MMSE, the most clinical cognitive screening test in Thailand (Deeks 2001, Lorentz 2002).

3.3.2 Depressive mood screening test

Thai Geriatric Screening Test (TGDS) is the only test that has been validated among Thai older people (Laing et al. 2009). The original version of GDS is a validated mood assessment tool for use among older people with dementia (O'Riordan et al. 1990).This test is also one of the most widely used measures of depression in older people (Nouwen and Oyebode 2009). Therefore, TGDS is selected and used as the screening test for depression in the current study.

Thai Geriatric Screening Test (TGDS)

Thai Geriatric Screening Test (TGDS) is developed from Geriatric Depression Scale (GDS) by Yesavage et al. (1983). TGDS was studied for validity and reliability by Train the Brain Forum Thailand (1994). The objective for the study was to develop a clinical standard questionnaire for screening depression among Thai older people throughout the country. It has been tested for reliability (internal consistency) in 275 Thai older people, 154 females and 121 males, aged between 60-70 years old in all the regions of the country. The results show that the average time to complete the questionnaire is 10.09 minutes. The reliability of internal consistency with the high Cronbach's α coefficients degree is 0.93.This means that each item in this questionnaire measures the same characteristic. The questionnaire

contains 30 questions with a “yes/no” answer format. The optimal cut-off score of TGDS yields at 0-12 for normal, 13-18 for mild depression, 19-24 for moderate depression and 25-30 for severe depression. TGDS questionnaire has recently been used for both research and clinical assessment of geriatric depression in Thailand (Ageingthai 2008).

3.4 Summary

A routine cognitive screening in primary care is useful in many ways. It can help the health care staff to be aware of cognitive decline in older diabetic patients. This may affect their quality of care, decrease the burden of health cost and support the health care strategies for diabetic patients and their families. In order to support a routine cognitive screening and promote the detection of cognitive impairment in primary care settings, a screening test which is superior because of its brevity, effectiveness and simplicity will be used and studied in a primary care setting.

A typical visit to Thai primary care is short, about 3-5 minutes, because primary care is the first contact of medical service and consultant for a large number of people in the rural and semi-rural areas with no appointment (Lotrakul and Saipanish 2006). Due to limitation in time, a cognitive screening test such as Mini-Cog that can be administered in 5 minutes or less seems the most suitable and useable in primary care settings (Borson et al. 2003, Moorhouse 2009).

As mentioned earlier in chapter 1, it is important that patients who undergo a cognitive screening test should then undergo a mood screening test such as GDS (Sinclair 2011). Cognitive impairment and depression may share similar symptomologies, such as memory loss (Sinclair 2011). Although the time to screen cognitive function by Mini-Cog is suitable for a typical visit in primary care (5 minutes), it is suggested that when combining the cognitive and depressive mood screening tests, the time allowed for the visit is longer than 5 minutes. If a significant depressive mood is detected, the patient will be offered and received further appropriate treatment (Sinclair and Aimakopoulou 2009).

Overall the three choices of selected screening tools in the current study are

1) Mini-Cog for the cognitive screening test
2) MMSE Thai 2002 for the cognitive screening test and used as a standard test in Thailand to compare and study validation with Mini-Cog
3) TGDS for depressive mood screening test

The original version of Mini-Cog is in English and it has never been used in the Thai population. In order to ensure the validity of the use of Mini-Cog in Thai culture, it is necessary to develop its Thai version. The reliability and validity of the test should also be studied in the target population before proceeding to data collection. All these processes of developing Mini-Cog in its Thai version will be presented in the following chapter.

Chapter 4

Development of Mini-Cog Thai Version

As mentioned in Chapter 3, Mini-Cog will be used for data collection in Thai older people. However, the original version of Mini-Cog is in English, and it is necessary to translate it from English into Thai before its administration in this study. Therefore, this chapter presents the development of the Thai version of Mini-Cog, describes the background and composition of Mini-Cog including the processes of developing the Thai version Mini-Cog.

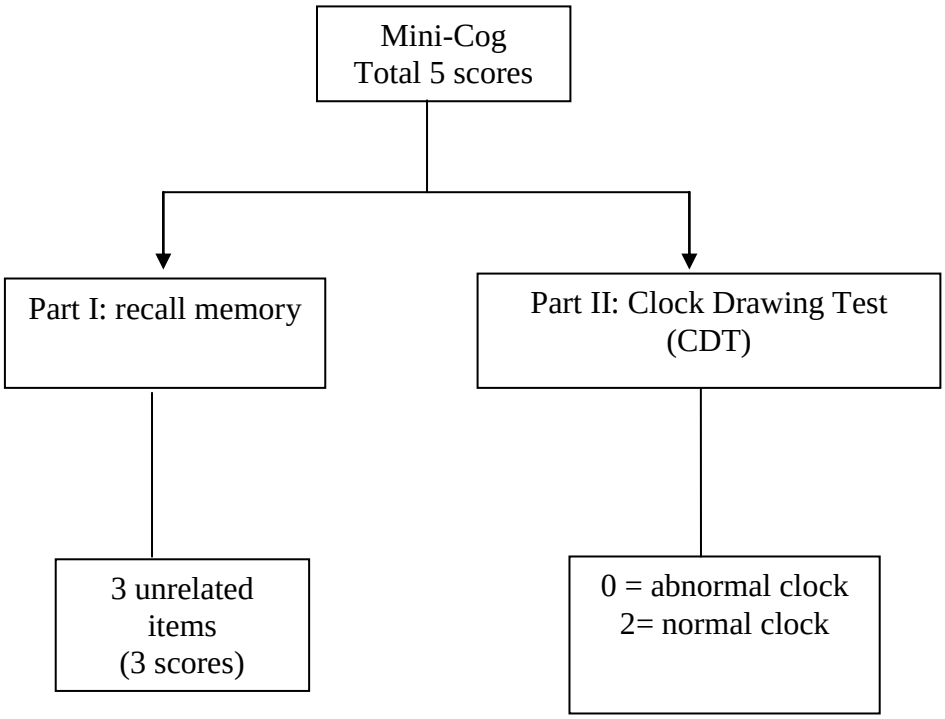
4.1 Background and development of Mini-Cog

Mini-Cog was originally developed from a very simple free-hand version of clock drawing test (CDT) (Borson et al. 1999). The free hand version of CDT is uncomplicated to score and requires little language interpretation in a community sample of multi-ethnic and multilingual older adults. The overall sensitivity is adequately at 79% but it still lacks a test of new learning, which is a critical point for the diagnosis of dementia. In order to enhance the psychometric properties in including a test of new learning into this cognitive screening test, Borson et al. (2000) added a simple 3-item memory test based on the Cognitive Abilities Screening Instrument (CASI) (Teng et al. 1994) to the clock drawing test and created a composite screening instrument named Mini-Cog. CASI is a screening test designed for cross-cultural application. The 3-item memory test of CASI is simple to adapt for a variety of language groups (Teng et al. 1994).

The original scoring of the CDT in Mini-Cog was based on the Consortium to Establish a Registry for Alzheimer's disease (CERAD). The CERAD is standardised, reliable and valid instruments for the evaluation and diagnosis of patients with Alzheimer's disease (AD). They are used by all Alzheimer Disease Centres established by the National Institute on Aging (NIA) in the United States (Fillenbaum et al. 2008). The CDT scoring of CERAD generates four possible scores based on an overall mark of the clock (0 = normal, 1 = mild, 2 = moderate and 3 = severe impairment). In order to minimise the complexity of CDT that can

be scored without reference to the complex system of rules, Borson et al. (2000) finally reduced the scoring of the CDT into the binary scores of 0 and 2(0 = abnormal or incorrectly clock, 2 = normal or correctly clock) (see Figure 4.1).

Figure 4.1: Composition of Mini-Cog test



Mini-Cog has been studied in a population-based sample of ethnically and linguistically diverse older adults (Borson et al. 2006, Borson et al. 2000). It takes 3-5 minutes to administer and performs as well as or better than the Mini-Mental State Examination (MMSE) for screening cognitive impairment and dementia. Borson et al. (2006) show the overall accuracy of cognitive impairment detection at 83% for Mini-Cog and 81% for MMSE. Mini-Cog is superior in recognizing patients with Alzheimer-type dementias (P = 0.05) and is not influenced by language and education (interclass correlation = 0.97, sensitivity = 0.99, specificity = 0.93) (Borson et al. 2003, Borson et al. 2000). In addition, Scanlan and Borson (2001) show the results of the high level of concordance (98 %) between expert and naive rater for scoring Mini-Cog.

4.2 Development of the Thai version of Mini-Cog

There were 3 phases for the development and validation of the Thai version of Mini-Cog in:

Phase 1: Permission for copyright
Phase 2: Selection of an expert panel
Phase 3: Translation processes

Phase 1: Copyright permission

Mini-Cog was created by Dr. Soo Borson (Borson et al. 2000) and the publisher's permission was necessary before beginning the translation. Therefore, the researcher requested Dr. Borson for copyright explaining the purposes of the translation. In the original version of Mini-Cog, the 3-item recall words are apple, table and penny. These words are not familiar in the Thai culture. Thus, following a discussion with Dr. Borson, the researcher was granted the copyright for the translation using a new set of the 3-item words consisting of house, cat and green. The selected 3-item recall words are based on the simplicity of the words and that they can be recognised by Thai older people and culture (see the attached permission email and copyright of Mini-Cog Thai version in Appendix A3).

Phase 2: Selecting the expert panel in the research team for translation

The expert panel in the research team for translation is required to assists in determining whether the translation of the questionnaire test is well constructed and suitable for testing. According to McGartland Rubio et al. (2003), a range of two to twenty experts is suggested to establish the number of the expert panel in research team for translation. This depends on the desired level of expertise and knowledge diversity. In addition, the panel of experts should be comprised of content and lay experts. The content experts are professionals who have work experience relevant to the measure and the lay experts are people who can address issues on language and understanding (McGartland Rubio et al. 2003).

In this study, the expert panel in research team for translation consisted of Dr. Nahathai Wongpakaran, a physician in geriatric psychology and expert on psychogeriatric screening tests. She acted as the content expert. The lay expert was the researcher, an academic staff in Thai university.

Phase 3: Translation of Mini-Cog

When an instrument is used in a different language, across-cultural translation process is needed to reduce the risk of introducing bias into a subsequent study (Gjersing et al. 2010). An individual clinician may make a mistake when translating verbally, which could lead to inconsistency and misunderstanding when administering the test. This may in turn make an analysis of results more difficult (Bradley 1994).

Beaton et al. (2002) suggested that if the instruments are to be used across cultures, not only should they be translated well linguistically, but the content validity of the instrument should also be contained at the same level across different cultures. Thus the aims for the translation of Mini-Cog into Thai are as follows:

- To achieve the conceptual equivalence of Mini-Cog Thai version to Mini-Cog English version
- To ensure equivalence of meaning
- To prevent the participants of being misled and to ensure the instruction of the test is correct

Although there is agreement that it is not suitable to simply translate and use an instrument in another linguistic and cultural context, there is no universal standard guideline on how to translate an instrument for use in another cultural setting (Gjersing et al. 2010). Maneesriwongul and Dixon (2004) recommend applying multiple techniques into the translation processes.

In the current study, the guidelines for cross-cultural translation of medical health research (Beaton et al. 2000) and diabetic psychology (Bradley et al. 1994) were primarily applied. These suggest that there are four steps for the development and validation of the cross-cultural instrument. They are as the following:

Step 1: Forward translation

Forward translation is the first stage in the instrument adaptation. It is recommended that at least two forward translations be made of the instrument from the original language to the target language (Beaton et al. 2000). In this way, obscure wording in the original version or difference in the translation will be noticed. In order to choose the suitable wording in translation, however, fluency in language alone is not a sufficient qualification for the translation. The translator needs to understand the purpose of the instrument and the basic aim of designing the instrument (Bradley et al. 1994).

In this study, both translators (1 and 2) speak Thai fluently (target language) and English (original language). Both translators have doctoral degrees from Australia and the United States and have experience in neuro-cognitive screening questionnaire design and development. Therefore, they are familiar with the terminology covered by the screening test. Both translators produced an initial forward translation of Mini-Cog independently. They were instructed to aim for conceptual rather than literal translation, and to keep the language easy to understand for the individuals without the knowledge of technical terminology (see Appendix B1).

Step 2: Synthesis of the translation

In this step, the results of the translation from the two translators were compared by the expert panel. They looked for discrepancies of meaning in the translations. If any discrepancies were found, both the translators would discuss them and come to an agreement (Bradley et al. 1994). Consensus of translation is important rather than one person's opinion to resolve the issue. This process is called the synthesis process (Beaton et al. 2000) (see Appendix B2).

Step 3: Back translation

Back-translation is important and is needed to identify any discrepancies between the meaning of the translation and the original version (Bradley et al. 1999). In the process of backward translation, a target language version is translated back into the source language version, and then the two language translations are compared

in order to verify the translation of the test (Maneeseriwongul and Dixon 2004). The two back-translators should preferably be without the knowledge in the area covering the instrument. The main reasons are to avoid information bias and to bring out unexpected meaning in the translated questionnaire (Beaton et al. 2000).

In this study the Thai version of Mini-Cog was back-translated blindly into an English version by two back-translators in order to verify the translation of Mini-Cog. Two different translators (3 and 4) were invited for back translation. The back-translators were bilingual and bicultural. They spoke Thai and English fluently (both were half Thai-British who had grown up in Thailand and graduated from a university in the UK). The back translators did not have a background in medicine or the area that covers cognitive screening test. They were blinded to the original version of Mini-Cog and translated the approved Thai Mini-Cog into English. No discrepancies of meaning between the two back-translators were found (see Appendix B3).

Stage 4: Equivalence testing

The back translation of the original and the back-translated version need to be examined and compared by an original developer who will examine the differences found in back-translation. Basically, the measuring of equivalence in the instrument translation is mostly evaluated in two types: semantic and content equivalence (Willgerodt et al. 2005). Semantic equivalence is used to ensure that the contents of the translation in the two versions keep the same meaning (Maneesriwongul & Dixon 2004), while content equivalence is used to ensure that the contents in the two versions have a consistent cultural relevance.

The results of back-translation in this study indicate that there was no difference in the meaning of the words or concepts between the two English versions of Mini-Cog test (original and back-translated version).

4.3 Summary

Mini-Cog will be used as the cognitive screening tool in this study. Since there was no formal translation of Mini-Cog available for use with Thai population, the Thai version of Mini-Cog was developed by the researcher who aimed to screen cognitive function of Thai older people with type 2 diabetes at the primary care setting.

Accurate translation is a first requirement in the process of transferring a test from the original (English) version to target (Thai) version (Beaton et al. 2000). An individual's direct translation of the test without any reference to the formal version can affect validity and reliability of results (Bradley 1994). In order to ensure a conceptually equivalent version, this study showed the translation methodology used for transferring Mini-Cog from English to Thai version. This chapter also revealed the success of the translated Mini-Cog that ensured consistency and quality in the content or face validity between the original and target versions of the screening test. Content or face validity refers to the subject matter based on the judgements of experts concerned with whether the test measures the content are accurately (Crookes and Davies 2004).

The translation does not guarantee the good quality of instruments, such as inter-rater reliability in different cultures (Kimberlin and Winterstein 2008). Inter-rater reliability (also called inter-observer agreement) refers to the equivalence of ratings obtained with an instrument when used by different observers. If a measurement process involves ratings by observers, a reliable measurement will require consistency between different raters (Crookes and Davies 2004).

Mini-Cog is new and has not been validated in Thai population. Thus, in order to propose Mini-Cog as a new cognitive screening tool in Thailand, Mini-Cog is needed to establish the concurrent validity by comparing its performance with a known reference standard, such as MMSE Thai 2002, on the same population (Lorentz 2002). The concurrent validity means measuring the relationship between the new and the existing standard test (Sim and Wright 2000). Therefore, following the translation, the inter-rater reliability and concurrent validity of the translated

Mini-Cog Thai was measured. This will be addressed in Chapter 6 (the pilot study).

In the next chapter, the research protocol of the current study will be presented in order to reveal the research aims and objectives including the overall steps of the study.

Chapter 5

Study protocol

This chapter provides information regarding the study protocol which is common to both the pilot study (Chapter 6) and the main study (Chapter 7). The chapter starts with the research questions and objectives of this study. It then provides the details regarding the research design, criteria of the participants, plan and processes of data collection in the fieldwork including the ethical issues and considerations.

5.1 Research questions

As stated in Section 1.1 (Chapter 1), to the best of the researcher's knowledge, there is no investigating study to date of Thai older people with type 2 diabetes related to cognitive impairment and depressive mood in community or rural areas. The present study addresses this issue. The two main questions of the study are:

1. What is the prevalence rate of cognitive impairment in rural Thai older people with type 2 diabetes who have never received a formal diagnosis of cognitive impairment in the primary care setting?
2. What is the prevalence rate of depressive mood in rural Thai older people with type 2 diabetes who have never received a formal diagnosis of depressive mood in the primary care setting?

To investigate this main question in detail, there are four secondary questions as the following:

i) What are the predictors of rural Thai older people with type 2 diabetes who have cognitive impairment?
ii) What are the predictors of rural Thai older people with type 2 diabetes who have depressive mood?
iii) What is the relationship between cognitive impairment and depressive mood?

iv) What is the relationship between cognitive impairment and glycaemic level, and what is the relationship between depressive mood and glycaemic level?
v) Are there any differences between good (HbA1c ≤ 7 % or ≤ 53 mmol/mol) and poor (HbA1c > 7% or > 53 momol/mol) glycaemic control groups in the cognitive screening tests and depressive mood-screening test?

5.2 Research objectives

In order to find out an accurate answer for the research questions, in this study the following specific objectives are set to achieve:

- Ascertaining the prevalence of undiagnosed cognitive impairment in Thai older people (aged 60+ years) with type 2 diabetes
- Ascertaining the prevalence of undiagnosed cognitive impairment and undiagnosed depressive mood in Thai older people (aged 60+ years) with type 2 diabetes
- Investigating the characteristics of rural Thai older people with type 2 diabetes who have and have not experienced cognitive impairment
- Investigating the characteristics of rural Thai older people with type 2 diabetes who have and have not experienced depressive mood
- Examining the association between cognitive impairment and depressive mood in rural Thai older people with type 2 diabetes
- Identifying the association between the level of cognitive impairment or depressive mood with the degree of glycaemic control (HbA1c)
- Comparing the results of cognitive and depressive mood screening tests between the good (HbA1c ≤ 7 % or ≤ 53 mmol/mol) and poor (HbA1c > 7% or > 53 momol/mol) glycaemic control groups

5.3 Research design

An observational study using cross-sectional research design is applied in this study. In order to achieve the aims of the study, the logic of cross sectional study is suitable for this research for a number of reasons. First, it is the best method of determining the prevalence of disease or any other health-related event in a defined population at a point in time (Mann 2003). In other words, the current disease status is examined in relation to the current exposure level. All participants are contacted at a point in time and relevant information is obtained from them (Mann 2003). Second, the basis of this information is classified as having or not having the outcome of interest (e.g. cognitive impairment or depressive mood). Last, a cross-sectional study is carried out to investigate the associations between potential risk factors (e.g. clinical variable of diabetes) and the outcome of interest (e.g. cognitive impairment and depressive mood) (Levin 2006).

The advantage of a cross-sectional study is an ability to study a large number of subjects at a relatively small cost and time when compared with other methods such as a longitudinal study (Mann 2003). More importantly, the data from the cross-sectional study provides a good picture of health care needs of target population. A prevalence study is a valuable method of obtaining information on the pattern of morbidity of a population and to assist health care staff to plan and establish health priorities. The data can generate hypotheses for other related studies in the same population or area (Levin 2006). A disadvantage of this type of study is that it does not provide a cause and effect study (Mann 2003). This issue does not affect the research area of this study which examines association at one point in time or a short period of time.

To conclude, using a cross-sectional study to execute the research objectives is considered to be sufficient to discover the precise answer to the research questions in this study.

5.4 Sample size

In order to ensure that the proposed number of participants to be recruited into this study is appropriated to answer the research objectives, an appropriate sample size calculation is selected and applied.

There are two main approaches to sample size calculation. One is based on the concept of power of a study, that is, the ability to detect a statistically significant change if the true magnitude of the effect is anticipated. This approach focuses on the significant test that will be performed at the end of the study or intervention. The second approach focuses on the precision of the estimate, that is, the level of sampling error regarded as acceptable (Dos Santos Silva 1999). The 95% Confidence Interval (CI) provides an indication of how precise the sample estimate is in relation to the true population value (Shakespeare et al. 2001). Thus, this approach focuses on the width of confidence interval that will be obtained when the results of the study are analysed.

In this study, the primary research objective focuses on the detection and estimation of the prevalence rate (percent) in the true population rather than statistically significant change of intervention. The sample size calculation is therefore based on the precision of 95% Confidence Interval (CI) if true prevalence is required.

Formula for 95% Confidence Interval (CI) for prevalence is calculated by

$p \pm z_{(\alpha/2)}\text{sqrt}\ (pq)/n$ (Daniel, et al 1999)

where

p = prevalence in sample

α = probability of type I error, = 0.05 (2-sided)

$z_{(\alpha/2)}$ = z-score (the z-score for 95% CI is the value of z such that 0.025 is in each tail of the distribution (Peacock and Peacock 2011)

n = sample size

q = 1-p

In order to estimate pwith 95% CI of size d (width of the interval)

d (size of the width of the interval) is $z_{\alpha/2}$ sqrt (pq)/n

Hence, given a required size is needed to solve the equation for n

$d = z_{(\alpha/2)}$ sqrt (pq)/n

This given

$d^2 = (z_{(\alpha/2)})^2$ x pq/n

$n = (z_{(\alpha/2)})^2$ x pq $/d^2$

d = size of width of the interval in this study estimated from $d = z_{(\alpha/2)}$ sqrt (pq)/n (in this formula, n = total number of older people with type 2 diabetes with HbA1c test = 283. As mentioned earlier in Chapter 1, HbA1c test in the most widely accepted measure of overall, long term blood glucose control in diabetes (Llorente and Malphurs 2007,Saudek et al. 2006). It reflects a beneficial effect on the immediate clinical consequence of diabetes (hyperglycaemic), which may affect the study outcome measures (either in cognitive function or mood) (Alencar et al. 2010). In addition, based on Chapter 2, this study intends to 1) assess the generalisability of association between HbA1c test and the outcome measures and 2) estimate the effect of poor glycaemic control (indicated by the presence of HbA1c result) on the outcome measures. Thus, HbA1c is important to select as an appropriated primary endpoint to support a claim based on glycaemic control.
Therefore, $d = (1.96)^2$ 0.5 x (1-0.5) / 283, thus total width= 0.12 (12%) and the margin of error $\pm$ 6% (0.06).

Since there are no previous studies on the rate of cognitive impairment in Thai older people with type 2 diabetes, this study uses the proportion at 50% (use 0.5 in the formula), which is the most conservative estimate in the maximum value of error in order to yield the maximum sample size (Daniel et al 1999, Peacock and Peacock 2011).

Sample size in this study $n = (1.96)^2\ 0.5 \times (1-0.5) / (0.06)^2$

$n = 267$

In the current study, the calculation of sample size equals 267, the required number of participants in this study.

5.5 Research setting and target population

This study is carried out in primary care settings. It was mentioned in Chapter 1 that Thai primary care settings are health care centres at the sub-district level (rural areas). The primary care provides frontier, ongoing, comprehensive, and co-ordinate care (Ministry of Public Health 2009). Primary prevention including health promotion and specific protection from disease are the key activities of Thai primary care settings. Since type 2 diabetes prevalence increases with age, the numbers of older persons with diabetes are expected to grow as the older population increases in number (Cukierman et al. 2005, Aekplakorn et al. 2007). In this study, the older people with type 2 diabetes in all the primary care settings of San-sai district are found to be a good representative of patient population because San-sai district is located in the northern part of Thailand which has the highest old population (12.6%). It should further be mentioned that primary care centres are important public healthcare services in Thai community (National Statistical Office Thailand 2007). As stated in Chapter 1, Section 1.6.2, the health care system in Thailand consists of public and private providers. Private clinics and polyclinics are wide spread only in the capital city and urban areas. Due to the financial problems and poverty in Thailand, it is difficult to encourage private health facilities to provide services in rural area (Sukunphanit 2006). Therefore, it is uncommon for people in the rural areas to use private clinic.

Public health facilities were rapidly expanded nationwide since 2001 when Thailand launched the Universal Healthcare Coverage Scheme (Prakongsai et al. 2009). This scheme is provided mainly by the public sector-in primary health care centres and district hospitals geographically accessible to the rural poor (Sukunphanit 2006). Ministry of Public health (MOPH) is the largest agency with

two-third of all hospitals and beds across the country. The other public health services are medical school hospitals under the Ministry of University, general hospitals under other ministries (such as Ministry of Interior, Ministry of Defence) (Sukunphanit 2006). MOPH owns 891 hospitals that cover more than 90% of the districts, and 9,762 primary care centres that cover every sub-district or community in rural area (Wibulpolprasert 2004).

According to the Ministry of Public Health (MOPH), 98% of all the primary care centres are registered with Universal Healthcare Coverage Scheme (Prakongsai et al. 2009). Distribution of health care infrastructure nationwide is a necessity for the universal coverage of health (Prakongsai et al. 2009). All primary care centres under the scheme of Universal Healthcare Coverage must have the same infrastructure, premises and equipments. As the primary care centres in San-sai district are under MOPH, they are similar to the other ones in Thailand. In addition, chronic diseases (e.g. diabetes, hypertension and heart disease) are a major problem of non-communicable diseases (NCD) in ageing population at primary care centres in Thailand (National Statistical Office of Thailand 2011). Moreover, a higher prevalence rate (16.7%) of diabetic adults from the national health survey was found in the aged group of 60-69 (Akeplakorn et al. 2011) comprising to 64% of the population visiting the diabetic clinic in San-sai district.

In addition, diabetic clinics have been set in all primary care settings at San-sai district, thus, it is possible to identify and recruit diabetic patients in the community or rural areas. In addition, more than half (67%) of the diabetic patients in the primary care centres of San-sai district are unable to maintain appropriate glycaemic control, defined as FBS >140 mg/dl or mmol/l or 7.8 mmol/l (San-sai district health office 2009). The increasing number of diabetic cases and the persistent ineffective management of patients with diabetes present a serious challenge in identifying cognitive impairment or depressive mood in older people aged 60 and over with type 2 diabetes in San-sai district.

5.6 The criteria of the participants

In order to provide clear and manageable limits to the information that would be gathered and synthesized as evidence, certain parameters are set to refine the criteria of the participants in this study. These parameters, called inclusion and exclusion criteria, are then used to select the studies that best provide the information needed to answer the research questions (Boyle 1998). The inclusion criteria enlist characteristics of potential participants who accurately represent a target population in the study. The exclusion criteria are the characteristics of participants that may confound the results of the study (Lunsford and Lunsfords 1995).

5.6.1 Inclusion criteria

In this study, participants are included if they meet the following main criteria for eligibility.

- Thai people aged over 60 years with type 2 diabetes who have had at least one year of diagnosis.
    - A one-year time period following the diagnosis is selected in order to know the HbA1c result of the participants. Because of the limitation of resources, primary care settings in San-sai district perform physical examination and laboratory tests including HbA1c test once a year

- Thai people aged over 60 years with type 2 diabetes who have had all types of diabetic treatment (e.g diet control alone, medication or insulin injection or combined diabetic treatments) were included in this study.
    - This criterion is preserved for generalisability of the diabetic patients in the study.

- The result of HbA1c test must have not been obtained more than one year prior to the date of recruitment.
    - In order to see the valid findings of an association between glycaemic control (HbA1c result) and cognitive function /

depressive mood, the result of HbA1c test must be updated within a year of recruitment and the screening tests applied. According to the recommendation of Diabetes UK, a one-year period of HbA1c is appropriate. Doctors should check the long-term diabetes control of diabetic patients by HBA1c test (Diabetes United Kingdom (UK) 2011).

- The participants must be competent Thai speakers.
    - In order to complete the screening tools, the participants must communicate and understand the instructions provided by the researcher.

5.6.2 Exclusion criteria

Participants are excluded if they have the following criteria.

- Thai people aged over 60 years with type 2 diabetes who have been previously diagnosed with any stage of dementia or Alzheimer's disease (AD) either before or after diabetes diagnosis because this group of people are classified as known cases of cognitive impairment and dementia.

- Participants with a formal diagnosis of depressive disorder, schizophrenia or epilepsy in any stages. Schizophrenia and epilepsy are chronic disorders that are characterized by abnormalities in thinking, emotions and behaviour. Since the screening tools for cognitive impairment have not been validated in this group, they have been excluded in the study.

- Those who are receiving medical treatment with psychoactive drugs (anti-cholinergics, anti-convulsants, anti-parkinsonians or anti-psychotics), complicated hypertension and renal failure were excluded due to the effect of these medications on the cognitive function. The effect of these medications can be described as follows:
    - Anti-cholinergic agents have been causally linked to the development of memory impairment in healthy subjects. Memory impairment may be associated with basal forebraincholinergic

pathways. Moreover, acetylcholine is also involved with attention and other aspects of cognitive functioning (Rumman et al. 1995)

- All anticonvulsants may cause drug-induced delirium or dementia, even at therapeutic drug levels. These effects appear to be dose related. Furthermore, uncontrolled seizures can affect cognition (Flaherty 1998). Anti-depressants have side effects to central nervous system such as delirium, disorientation. Short-term memory dysfunction can be found in persons on anti-depressant drugs (Oxman 1996).
- Anti-parkinsonism such as Levodopa is one of the anti-parkinsonism drugs associated with changes in cognitive function and mental status (Cummings 1991).
- Anti-psychotics such as thioridazine and chlorpromazine may partly cause cognitive decline and delirium in patients who are on anti-psychotics drugs (Moore and O'Keeffe 1999).
- A cerebrovascular disease such as stroke or complicated hypertensions, and renal failure is the most common cause of cognitive impairment and dementia. Severe hypertension may cause damage to the brain i.e. a stroke, which is an accumulation of lacunar infarcts, ischemic white matter disease and cerebral hypoperfusion that are the most common causes of cognitive impairment/dementia. Severe damage to the kidneys leading to renal failure is also a cause of cognitive impairment (Llorente and Malphurs 2007).

- Participants who have communication difficulty such as hearing loss
  - The participants must have a good hearing in order to participate in the cognitive tests to recall words told only once by the researcher.

5.7 Study instruments and outcome measure

In order to investigate cognitive impairment and depressive mood in the target population, the screening tests of cognitive impairment and depressive mood are selected and used as study instruments in this study. As mentioned earlier in Chapter 3, the overview and rationale for selecting the cognitive and depressive mood screening tests are appropriated to use in this study. Following are the three selected study instruments:

5.7.1 Cognitive screening tests

- Mini-Cog

  Mini-Cog was developed as a very brief screening tool for primary care settings (Borson et al. 2000, Borson et al. 2006). It is a simple tool to screen cognition and has been validated in a population-based sample of ethnically and linguistically diverse older adults. It consists of two orally presented tasks (a three-item word recall) combined with an executive clock drawing task (CDT). It takes 3 minutes to administer the test. Mini-Cog scores, therefore, range from 0 (worst) to 5 (best) (Borson et al. 2006). A cut-off of 2 out of 5 provides the optimal combination of sensitivity (99%) and specificity (96%) for detecting cognitive impairment (Borson et al. 2000, Borson et al. 2003, Borson et al. 2005, Scanlan and Borson 2001). (see Chapter 3 for more details and Chapter 4 for translated version of Mini-Cog from English to Thai).

- Mini Mental State Examination (MMSE) Thai 2002

  The Mini Mental State Examination (MMSE) Thai 2002 (Boonkerd et al. 2003) is translated from its original version in English (Folstein et al. 1975). MMSE remains the most commonly used screening instrument as a global cognitive test (Nazem et al. 2009) and is used as a current clinical mainstay cognitive screening instrument in Thailand. The MMSE Thai 2002 is scored in terms of the number of correctly completed items; lower scores indicate poorer performance and greater cognitive impairment. The total score ranges from 0 to 30 (perfect performance), a cut-off score of 14

is used for uneducated participants (illiteracy), a cut-off score of 17 is used for those who completed primary school, and a cut-off score of 22 for those who completed secondary school (Ageingthai 2008). (see Chapter 3 for details).

5.7.2 Depression screening test

- Thai Geriatric Screening Test (TGDS)

  Thai Geriatric Screening Test (TGDS) is used as a depressive mood screening test in this study. It is developed from the Geriatric Depression Scale (GDS) by (Yesavage et al. 1983). The TGDS questionnaire contains 30 questions with a "yes/no" answer format. The optimal cut-off score of TGDS yields 0-12 for normal, 13-18 for mild depression, 19-24 for moderate depression and 25-30 for severe depression (Ageingthai 2008). In the available literature, TGDS is the only test that has been studied for validity and reliability specific to the Thai older population (Ageingthai 2008, Liang et al. 2009). (see refer to Chapter 3 for more details).

5.8 Study plans and processes

5.8.1 Pilot study

- A pilot study is undertaken in order to test the translated Mini-Cog Thai version and the study protocol including data collection and processes in preparation for the main study. The pilot study provides tentative information regarding the impact of the instruments and feasibility study.

5.8.2 Main study

- The information from the pilot study is considered to make changes in the research protocol. The main study is carried out in 15 primary care settings in San-sai district, Chiang Mai, Thailand.

5.9 Data collection

There are three steps for the data collection as follows;

Step 1: Demographic data interview

Interview is used to collect the demographic data (Appendix E1). It comprises of basic demographic data including age, education, and years in school, marital status, living arrangement (alone or with family), income and type of health cost support. Information is collected directly from the participant to ensure the accuracy of the data. This information is used to study the characteristics of participant with the outcome of interests (cognitive impairment and depressive mood).

Step 2: Application of the screening tests

The second stage is applying the screening tests. This stage takes around 25 minutes. The screening tests are applied in the following order:

1. Mini-Cog (5 minutes)
2. MMSE Thai 2002 (10 minutes)
3. TGDS (10 minutes)

Mini-Cog is applied first not only because it is the priority test in this study but the short duration of the test is also perceived as less stressful to the patient compared to MMSE test which is a longer test with a series of questions for concentration and attention (Doerflinger 2007). TGDS is the last test to administer because of its simple yes/no format which can easily be used and understood by older people who have short attention spans or feel easily fatigued which may happen after testing the cognitive screening tests (Holroyd and Clayton 2000).

Step 3: Recording medical information

After the researcher administers the screening tests, the recording medical data of each participant is recorded on a separate sheet by viewing the medical history profile.

5.10 Statistic analysis

The data analysis is performed using the Statistical Package for Social Sciences (SPSS) program for Windows version 16. The statistical analysis consists of descriptive and inferential statistics.

Descriptive statistics

Percentage, mean and standard deviation are used to explain the characteristics of the participants, and provide initial views of the data prior to applying inferential statistics.

Interferential statistics

The prevalence rates of cognitive impairment and depressive mood are estimated by calculating the percentage of individuals at the cut-off point score and 95% confidence intervals is constructed.

A logistic regression analysis is conducted on the binary outcome data through which the relationship between cognitive impairment and independent potential risk factors is examined. A similar analysis is undertaken for depression.

To study the correlation between Min-Cog and MMSE Thai 2002 tests and TGDS test, Pearson's correlation is used for parametric data and Spearman's correlation is used for nonparametric data. In order to compare the score result of cognitive impairment and depressive mood in the levels of glycaemic control (HbA1c), statistics comparing the two groups is used.

5.11 Ethical approval

Ethical approval is obtained separately for the pilot and the main study (Appendix A1 and A2, respectively). The research proposal and related documents in the pilot and main studies are submitted initially to the Faculty of Health Research Ethics Committee, University of East Anglia (UEA), the United Kingdom (UK). When approved, the research proposals are submitted further for ethical approval to the

Ethical Review Committee for research in Human Subjects, Department of Medical Service of Public Health, Ministry of Public Health, Thailand.

5.12 Ethical considerations

Eligible patients are invited to participate on a voluntary basis. They are invited to provide written informed consents and are informed of their right to withdraw from the study at any time without any negative effect or prejudice to their regular or further service at the primary care centre.

Confidentiality and anonymity are assured through the following procedures:

- None of the patients' personal data is reported in any study report.
- All personal details and completed questionnaires are stored in a locked cupboard in each primary care setting (this has already been negotiated with each of the primary care settings to which only the researcher has access or password protected on the researcher's computer.
- If an emerging health problem is identified for any patient during the study by the researcher, the researcher would, with the consent of the patient, notify a clinical member of staff within the primary care setting to enable appropriate care to be provided. If necessary, any interview is terminated, and/or the patient's participation in the trial is ended.

5.13 Summary

The study plan and protocol is provided in order to present the research questions and objectives. The details of the research design, instruments and criteria of the participants will be presented in Chapters 6 and 7 (pilot and main studies). A pilot study is conducted to test the Mini-Cog Thai version and to establish the feasibility of the study protocol for the main study. The lesson learned and the information achieved from the pilot study will be used to adjust into the methodology in the

main study. The information and details of the pilot study will be presented in the next chapter.

Chapter 6

Pilot study

This chapter provides details of and information about the pilot study in the current research. First, a definition and the objectives of the pilot study are provided. Next, the procedures and outcomes of the pilot study are discussed. Finally, a summary of the pilot study and its application are included; and the lesson learned from the pilot study in adjusting the methodology in the main study is presented.

6.1 What is a pilot study?

The pilot, or feasibility study, is a small version of the study designed, as well as the specific pre-testing of a particular research instrument (Thabane 2010). The advantage of conducting a pilot study is that it might reveal whether the proposed methods or instruments are inappropriate or too complicated in the main study. Pilot study provides vital information to improve the quality and efficiency of the main research protocol (Teijlingen and Vanora 2001). Therefore, the pilot study is set in order to test the logic of the study and gather the appropriate research procedure and method to prevent the potential pitfall in the main study.

6.2 Objectives of the pilot study

This pilot study has two objectives:

1. As mentioned in Section 6.1, the pilot study tests the study protocol and its feasibility in applying it in the main study.
2. It was mentioned in Chapter 4 that Mini-Cog has never been used in Thailand. In order to propose Mini-Cog as a new cognitive screening tool, it is necessary to establish the good quality of the test already in use in Thai population. Therefore, the second objective of the pilot study is measuring the inter-rater reliability and the concurrent validity of Mini-Cog. The inter-rater reliability (also called inter-observer agreement) refers to the equivalence of ratings obtained from an instrument used by different observers. If a measurement process involves ratings by different

observers, a reliable measurement will require consistency between the raters (Crookes and Davies 2004). The purpose of the inter-rater reliability of Mini-Cog is supporting the practical, effective and uncomplicated method for the scoring system in the clock drawing part (CDT) of Mini-Cog. In addition, in order to see the performance of the new test with a known reference standard on the same population (Lorentz 2002), the concurrent validity is used to measure the relationship between Mini-Cog, a new test in Thailand and MMSE Thai 2002, the existing standard test (Sim and Wright 2000).

6.3 Setting and population

As stated earlier in the study protocol (Chapter 5), this study was conducted in Chiang Mai because it has the highest older population in Thailand (12.6%) (National Statistical Office Thailand 2007). The primary care centre is an important public health care service in community or rural areas (Ministry of Public Health 2009). The pilot study was conducted in one primary care centre (Nong-han) in San-sai district, the study area for the current study in Chiang Mai, Thailand. The potential participants who visited the diabetic clinic in April 2010 on a regular basis at Nong-han primary care were invited to participate in the pilot study.

6.4 Sample size

It was suggested that in general a minimum number of 30 participants or greater is appropriate to estimate a parameter for the pilot study and that it has adequate power to detect any trends in the study (Lancaster 2004, Thabane et al. 2010). In this study thirty-two (32) participants took part in the pilot study based on the availability of the potential participants visiting Nong-han primary care during the study.

6.5 Procedure

In order to access the participants, two weeks before the beginning of the pilot data collection in Nong-han primary care, the researcher contacted and informed the nurse in the diabetes clinic at Nong-han primary care centre about the purpose, processes and inclusion/exclusion criteria for the potential participants in the pilot study. It should be mentioned that this primary care centre had already agreed to be a part of this study.

The potential participants visited the primary care centre on the date. After they received the routine diabetes care, the nurse identified the older patients with type 2 diabetes and asked whether they were interested to participate in the study. If they were interested, the researcher contacted them individually, explained the study and gave them the "information sheet" (Appendix C) containing the purpose of the research. All the interested potential participants were given time (at least 24 hours) to decide whether they wanted to participate in the study. Those individuals who agreed to join the study had an opportunity to ask any questions. They were assured that they could refuse to participate in the research without giving reasons at any time if they disagreed or were unsatisfied during the process with no effect on their medical care. If the participants decided to take part in the study, they had to sign a consent form (Appendix C) in writing or by thumb print (if they were illiterate) to show their willingness to participate. After receiving the informed consent, the participants were interviewed and asked to complete all the questionnaires by the researcher within the primary care centre.

6.6 Measure outcomes

6.6.1 Inter-rater reliability of Mini-Cog

The inter-rater reliability is a method of measuring reliability of the test to determine the extent to which two or more raters obtain the same result when using the same instrument to measure a concept (Porta 2008). Kappa statistics measures the degree of non-random agreement between two raters of the same categorical

variables the equivalence and consistency of ratings obtained with an instrument between different raters (Crookes and Davies 2004).

In this study, the reliability of CDT scoring was assessed by comparing the scores given by the researcher and an expert on 32 participants. The score results (normal and abnormal) of CDT between the researcher and the expert were blinded to each other. The rationale for studying the inter-rater reliability only in the CDT part of the study is the following. First, the recall memory part of Mini-Cog is a short-term memory test of unrelated 3 objects. The raters would score exactly the same if the participants answered the recall word correctly, unlike the CDT part where the scoring criteria are applied, the score of CDT may be biased depending on the judgement of raters. Second, the previous study of inter-rater reliability of Mini-Cog focused only on the CDT part. Thus this study can be compared with the previous study. To compare the inter-rater reliability of Mini-Cog in Thai with the previous study, the inter-rater reliability was focused in the part of CDT scoring.

6.6.2 Concurrent validity

The concurrent validity is meant to measure the relationship between the new test and the existing standard test. In order to validate a new measure, the results of the measure are compared to the results of the standard obtained at approximately the same point in time (Sim and Wright 2000). This approach is useful in situations when a new or untested tool is potentially more efficient, easier to administer and more practical than another more established tool and is being proposed as an alternative instrument (Porta 2008). In order to see whether Mini-Cog can used as an alternative tool of cognitive screening test in Thai primary care settings, the concurrent validity was conducted by measuring the correlation between the score results of Mini-Cog and MMSE Thai 2002.

6.7 Data analysis

The data were entered and the analyses were performed using SPSS Software Package version 16.

- Kappa (K) statistic (Fleiss et al. 2003) was applied to measure the inter-rater reliability between the researcher and the expert on the scores of CDT.

- Pearson Product-Moment Correlation Coefficients (Pearson's r) (Cohen and Cohen 1983) was applied to examine the concurrent validity or correlation between the score results of Mini-Cog and MMSE Thai 2002.

- Descriptive statistics, including percentages, mean, median and standard deviation were used to summarise the data collected from the sample (demographic and clinical characteristic of the participants).

6.8 Ethical approval

The research protocol and related documents were submitted to the Faculty of Health Research Ethics Committee, University of East Anglia, the United Kingdom. After the ethical approval was obtained from the UEA in November 2009 (Appendix A1), the research protocol was then submitted again to the Ethical Review Committee for research in Human Subjects, Department of Medical Service of Public Health, Ministry of Public Health, Thailand. The ethical approval of the pilot study was obtained from Thailand in April 2010 (Appendix A2).

6.9 Ethical considerations

Eligible participants were invited to participate on a voluntary basis. They were invited to provide written informed consents or thumb print and were informed of their right to withdraw from the study at any time without any negative effect or prejudice to their regular or further service at the primary care setting.

Confidentiality and anonymity were assured. None of the participants' personal data was reported in any study report. All questionnaire tests were stored safety in a locked cupboard or password protected in the researcher's computer file. All information obtained from the participants was coded and kept in the researcher's locked files in the post-graduate research room during and after the study. Only the researcher holds the key to the code.

In case of emerging any health problem on the part of any participant, the researcher would immediately cease the interview or study, and refer the participant to the nurse in the diabetic clinic or a health professional who can offer support in the primary care setting.

6. 10 Results

Inter-rater reliability of CDT scoring in Mini-Cog

Both the raters' scores for each participant in CDT scoring are presented in Table 6.1 The inter–rater reliability of CDT scoring *r* in the Mini-Cog classified as 'normal CDT' and 'abnormal CDT' are presented in Table 6.2. Rater 1 and 2 both agreed on the 'normal CDT of 25% and the 'abnormal CDT' of 65.6%. In9.4% of the cases rater 2 disagreed with rater 1 on 'normal CDT'. In total, the agreement on normal and abnormal CDT from both raters is 90.6 %. The Kappa statistics for the inter-rater reliability of CDT scoring shows a good agreement (K = 0.8, p <0.001, 95% CI= 0.54, 1.00). The levels of agreement by Kappa (K) value are suggested by Altman (1991) and can be interpreted as follows:

Value of K	Strength of agreement
< 0	less than chance agreement
<0.20	Poor
0.21-0.40	Fair
0.41-0.60	Moderate
0.61-0.80	Good
0.81-1.00	Very good

Table 6.1: Raw data scores of CDT in Mini-Cog Thai version from the researcher and expert, a pilot study in a sample of 32 older people with type 2 diabetes in Nong-han primary care centre, San-sai district.

	Mini-Cog score	
Participant	Researcher	Expert
1	2	2
2	0	0
3	2	2
4	0	0
5	0	0
6	2	2
7	2	2
8	2	2
9	0	0
10	0	0
11	2	2
12	0	0
13	2	2
14	0	0
15	0	0
16	0	0
17	0	0
18	0	0
19	2	2
20	0	0
21	2	2
22	0	0
23	2	0
24	0	0
25	0	0
26	0	0
27	0	0
28	2	0
29	0	0
30	0	0
31	2	0
32	0	0

Table 6.2: 32 participants are scored by the researcher and expert for Mini-Cog. 0 (zero) denotes the participants with incorrectly drawn clock, 2 (two) denotes the participants are classified with correctly drawn clock

		Expert N (%)		Total N (%)
		0	2	
Researcher N (%)	0	21(65.6%)	0(0%)	21(65.6%)
	2	3(9.4%)	8(25%)	11(34.4%)
Total		24(75%)	8(25%)	32(100%)

Concurrent validity of Mini-Coq

Table 6.3: Pearson correlation coefficients between the scores of Mini-Cog Thai version and MMSE Thai 2002

	MMSE Thai 2002		
	Pearson's r (*r*)	P	95% Confidence Interval (CI)
Mini-cog	0.47	0.007	0.37-0.55

In order to see the concurrent validity between Mini-Cog and MMSE Thai 2002, Pearson correlation was analysed. The scores of Mini-Cog showed a significantly positive and moderate correlation with Pearson correlation (*r*) of 0.47, 95% CI 0.37, 0.55 (p = 0.007) with the scores of MMSE Thai 2002 (Table 6.3). Pearson correlation (*r*) ranges from -1 to 1, including 0. Each level of measurement has an appropriate test of association. Values closer to +1 indicate a positive relationship while values closer to -0.1 indicate a negative relationship (Pallant 2009). Values closer to 0 represent the absence of relationship between the two tests. Below is the interpretation of Pearson correlation (*r*) (Cohen and Cohen 1983).

Correlation coefficient (*r*)	Interpretation
0.10-0.29	small correlation
0.30-0.49	moderate correlation
0.50-1.00	strong correlation

Characteristics of the participants

Of the 32 participants, 75% were female with the mean age of 70 ± 6 years old. Half of the participants (50%) were married, 44% were widowed and 6% were single. More than half of the participants (81%) finished primary school and had a duration of 4 years in schools. Most of the participants (97%) lived with family and 31% lived with their children.

The mean BMI (24.63±4.1 kg/m^2) was in the normal range for international classification of BMI (19-25 kg/m^2). The mean cholesterol (206±48 mg/dl or 11.4 mmol/l) was higher than the normal level guideline (200 mg/dl or 11.1 mmol/l) but triglyceride (137±64 mg/dl or 7.6 mmol/l) was in the normal range of the guideline (< 150 mg/dl or 8.3 mmol/l) (Diabetes Association of Thailand 2009). The average duration of time for having diabetes in the participant was 4 years. As for the treatment of diabetes, 50% of the participants were on oral medication, 47% on diet control and 3% took insulin injection. Demographic and clinical characteristics of the participants are summarised in Table 6.4.

Table 6.4 Demographic and clinical characteristics of the participants

Demographic variables	N (%)
Gender	
- male	25% (8)
- female	75% (24)
Age (years)	70±6
Education	
- never attended school	6% (2)
- primary school (4 yr in school,)	81% (26)
- secondary school (7-9 yr. in school)	10% (3)
- high school (10-12 yr. in school)	3% (1)

Demographic variables	N (%)
Marital status	
- single	6% (2)
- married	50% (16)
-widowed	44% (14)
Living status	
- alone	6% (2)
- not alone (multiple answers)	94% (30)
- with spouse 13% (4)	
- with son/daughter 31 % (10)	
- with grandchild 6% (2)	
- with spouse+son/daughter 16%(5)	
- with spouse+grandchild 3 %(1)	
- with spouse+son/daughter+grandchild 19%(6)	
- with son/daughter+grandchild 6% (2)	
Income support (multiple answers)	
-from government (500 baht or 10 pounds/month)	100% (32)
-from bank saving	16% (5)
-from son/daughter	22% (7)
Clinical variables	
Body Mass Index(kg/m^2)	24.63±4.1
Blood pressure (mm Hg)	
-systolic	130 (100-150)
-diastolic	73 (60-90)
Fasting Blood Sugar (mg/dl or mmol/l)	109 mg/dl (91-190) 6 mmol/l (5-10.5)
Haemoglobin A1c (% or mmol/mol)	7.58% (5.8% -12.5% 59.34 mmol/mol (40-113)
Duration of HaemoglobinA1c result (months)	10 (9-11)
Total Cholesterol (mg/dl or mmol/l)	206±48 mg/dl 11.4±3 mmol/l
Low density lipoprotein (mg/dl or mmol/l)	118 ± 42 mg/dl 6.5±2 mmol/l
High density lipoprotein (mg/dl or mmol/l)	44 (24-89) mg/dl 2.4 (1.3-4.9) mmol/mol
Triglyceride (mg/dl or mmol/l)	137±64 mg/dl 7.6±3.5

Clinical variables	N (%)
Diabetes treatment	
-diet control	47% (15)
-oral medication	50% 16)
-insulin injection	3% (1)
Duration of HbA1c test (months)	10 (9-11)
Diabetes complication	
- retinopathy	6% (2)
History of chronic disease	
- Hypertension	72% (23)
- Chronic obstructive pulmonary disease (COPD)	6% (2)
- dyslipidemia	9% (3)
- Osteoarthitis (OA)	3% (1)
- Osteoarthitis (OA)+dyslipidemia	3% (1)
Health behaviour (present)	
Drinking	
Yes	16% (5)
Smoking	
Yes	10% (3)

Data are given as % (N), Mean± SD and median (range).

6.11 Discussion

There is a good level of agreement (inter-rater reliability) of CDT scoring in the Mini-Cog Thai version with a Kappa (K) value of 0.8 ($p<0.001$, 95% CI 0.54,1.06). According to Altman (1991) and Fleiss et al. (2003), the value of K = 0.61-0.80 shows a good strength of agreement. The inter-rater reliability in this study is in line with the Mini-Cog in Italian version, which shows the inter-rater reliability (intraclass correlation coefficient) of $r_i = 0.89$ (Scanlan et al. 2007). Both Kappa value and the intraclass correlation coefficient measure inter-rater reliability (Fleiss 2003). The results of inter-rater reliability in both Thai and Italian studies show a good inter-rater reliability for clinical measurement (Altman 1991, Portney and Watkins 2000). Kappa requires that the two raters should use the same rating categories, while the intraclass correlation coefficient is used when the raters are

preferably more than two (Howell 2006). In this study, there were two raters for the CDT scoring, whereas in the study of Scanlan et al. (2007), there were 40 raters due to the large area of study setting (11 regions of Italy).Concurrent validity was established by comparing the performance of Mini-Cog against MMSE Thai 2002, an independent standard clinical cognitive screening test in Thailand, in respect of the same entity at the same time (Sim and Wright 2000, Polit et al. 2006). Pearson's correlation (r = 0.467, 95% CI 0.37, 0.55, p = 0.007) between Mini-Cog and MMSE indicated a positive correlation between Mini-Cog and MMSE Thai 2002 scores. This information shows an acceptable validity of Mini-Cog with MMSE Thai 2002. This implies that Mini-Cog Thai version is a relatively new instrument producing data that agrees with the existing measure use in Thailand.

The results of the pilot study gave an overview of characteristic data in the target population. In particular, the result shows that most of the participants (81%) finished primary school. This makes Mini-Cog suitable for applying within this group because it is designed for low educated people, people with language barrier or the two combined (Borson 1999). It was found that the proportion of females was three times more than males, which might be due to the higher number of females in Thai community (Jitapunkul and Bunnag 1999). In addition, 97% of the participants do not live alone and 31% live with their children. This demonstrates the Asian culture where the primary responsibility for the older people has traditionally been with the family (Knodel et al. 1999).

The pilot study carried out in this research demonstrates the feasibility of conducting data collection in the main study. It suggests that the research design is appropriate to conduct data collection. In other words, Mini-Cog Thai version is practical to administer and acceptable in Thai language and culture. The participants demonstrate that they can clearly understand the wordings and instructions of the test and there is no need for revision. The time of interview and administration of the test (5 minutes) are acceptable to the participants, as well.

Recruitment of the potential participants was practical in the study area. The participants were willing to participate. However, due to the limitation of public transport and the travelling cost of Thai older people in rural areas, the potential

participants who decided to take part in the study provided informed consents on the date of receiving “information sheet” rather than taking time (at least 24 hours) to consider their participation. It is to be noted that sending “information sheet” by post would not suit Thai rural older people who have limited abilities in reading and understanding information. In particular, a formal letter from the primary care centre would make them worried about the details of the letters and cause increased anxiety. A Verbal explanation of “the information sheet” is much more suitable for Thai rural older population.

Three lessons are learned from the pilot study. They are summarised below.

1. Although the identification and recruitment of Thai older people with type 2 diabetes in San-sai district were feasible through the existing research protocol, it became apparent that the limitation of HbA1c measurement in the research area might result in a biased sample. Because of the limited resources and budget of primary care settings in San-sai district, only the patients who have a good ability to control their FBS (<140 mg/dl or 7.8 mmol/l) in two of the last three visits to the primary care centre receive HbA1c measurement. Uncontrolled and unstable FBS (>140 mg/dl or >7.8 mmol/l) in the three last visits imply that the patient has poor control of blood sugar and would be prone to have the HbA1c more than target control (>7% or >53 mmol/mol). Due to the limitation of the resources in primary care centres, this group of patients are not selected to receive HbA1c measurement from the health care staff. Another reason for selecting only the group of stable FBS for HA1c test is to follow one of the recommendations for HbA1c measurement in American Diabetes Association (ADA) diabetes care, which suggests that the HbA1c test should be performed at least twice a year, particularly in the patients meeting treatment goals (who have stable glycaemic control) (American Diabetes Association 2012).

2. Therefore, in this study, the participants who receive HbA1c measurement tend to have a better control of FBS than the participants who do not receive it.

The research question in this study aims to find out the prevalence of cognitive impairment and depressive mood in Thai older people with type 2 diabetes in the community. Prevalence data shows the actual number of the outcome measures in the target population; however, if the data is influenced by differences in some variables in the population, it then may have an impact on the validity of the prevalence study (Dolin et al, 1999).

It is necessary, therefore, to prevent the selection bias of the participants from the study area and to ensure that the difference in criterion for receiving HbA1c measurement may not influence the outcome measures (cognitive impairment and depressive mood). This study needs to assess the outcome measures in the participants who do not receive HbA1c measurement and then to compare it with the participants who receive HbA1c measurement. The comparison of the prevalence between the two groups is likely to measure whether there is a problem of selection bias between the groups with and without HbA1c in the study.

3. The information from the pilot study reveals that diabetic clinics in all primary care settings in San-sai district are open two days a week, and that some of these primary care settings run diabetic clinic on the same day and time. Due to the constraints of time for data collection including the need to collect the data of the participants with and without HbA1c, this study required a research assistant (RA) to help with the main data collection.

4. With regard to RA in the main data collection and in order to assure the reliable administration of all the instruments used by the researcher and the RA, the study of inter-rater reliability of all the instruments used in the main study must be tested.

6.12 Summary

The findings of the pilot study show that the inter-rater reliability of CDT is in good agreement (K=0.8) between the researcher and the expert. Although Mini-Cog Thai version is relatively new in Thailand, the findings reveal a positive correlation, concurrent validity or the same direction of the screening results with MMSE Thai 2002. Thus, Mini- Cog can perform with MMSE Thai 2002, which is a standard test of cognitive screening in Thailand.

In conclusion, the identification and recruitment of the older people with type 2 diabetes in primary care centres in San-sai district were feasible through the research protocol. However, drawing on the results of the pilot study, the methodology for the main study should be adjusted to the following three issues

a) The number of the older people with type 2 diabetes who do not receive HbA1c measurement should be added to the main study
b) A research assistant should help with data collection in the main study
c) The inter-rater reliability of all the instruments used by the researcher and the research assistant should be tested in the main study.

All the details of these adjustments will be explained and summarised in the following chapter.

Chapter 7

Methodology

The pilot study in the previous chapter demonstrated the feasibility of the study protocol to be carried out in the main study. This chapter presents the methods and procedures used to collect data for the main study. Firstly, a summary of the lessons learned in the pilot study about the necessary changes in the methodology is outlined. This is followed by a rationale and discussion of the changes. Secondly, an overall description of the methodology for the main study is provided.

7.1 Summary of the necessary changes for the study protocol

Changing the number of the sample size

As mentioned in Chapter 5 (Study Protocol), only the potential participants who have a HbA1c test will be included in the current study. However, due to the limited resources of primary care settings, not every diabetic patient receives a HbA1c test. The selection of diabetic patients who receive HbA1c measurement is based on their ability to control FBS (< 140 mg/dl or 7.8 mmol/l) in two of the last three visits to the primary care centre. Hence, the patients who receive HbA1c measurement tend to have a better control of blood sugar than the participants who do not. As a result, the inclusion criteria for this study, that intends to focus on the potential participants with HbA1c results, seems to have a selection bias of the sample in the study area.

In order to test for selection bias of the participants in the study area it is important to ensure that the criterion difference in the group who receives HbA1c measurement will not influence the outcome measures (cognitive impairment and depressive mood). This study, therefore, needs to assess prevalence of cognitive impairment and prevalence of depressive mood in the participants who do not receive HbA1c measurement and then compare the prevalence with the participants who receive HbA1c measurement. This comparison of the prevalence

between the two groups is likely to measure whether there is a problem of selection bias between the groups with and without HbA1c. If the results show that there is no difference of the outcome measures between the group with HbA1c and the group without HbA1c, only the group with HbA1c will be used in data analysis in order to 1) assess the generalisability of association between HbA1c test and the outcome measures and 2) estimate the effect of poor glycaemic control (indicated by the presence of HbA1c result) on the outcome measures. In summary, the sample size in the research protocol will be doubled to include the participants without HbA1c test. In total, the minimum sample size of five hundred and thirty-four (534) older people with type 2 diabetes (two hundred and sixty-seven (267) with HbA1c test plus two hundred and sixty-seven (267) without HbA1c test) will be used in the main study.

The importance of HbA1c result

As mentioned in Chapters 1 and 2 , glycaemic control (HbA1c) appears to play a role and may be related to cognitive impairment and depressive mood in the older people with type 2 diabetes (please see Chapter 2). For example, three studies have demonstrated an inverse relationship between HbAlc and working memory, executive functioning, learning and complex psychomotor performance (Reaven et al. 1990, Munshi et al. 2006, Ryan et al. 2006) in patients with type 2 diabetes. These findings support the hypothesis that worsening glycaemic control leads to worsening cognitive function. Moreover, HbA1c is a precursor of AGEs, which may involve cognitive decline in type 2 diabetic patients from the glycation processes through hyperglycaemia. Therefore, document blood glucose levels by HbA1c are important to see the possibility of vascular complications, which may affect to cognitive impairment in diabetic patients (Marchetti 2009).

Glycaemic control (HbA1c) is a vital goal for diabetes treatment and may be related to the outcome measures. In addition to the knowledge of the researcher through the literature search, no study in Thailand has investigated the association between glycaemic control (HbA1c) and cognitive impairment in the older people with type 2 diabetes. It would therefore be of interest to see whether glycaemic control (HbA1c) is related to cognitive impairment and depressive mood. The

findings will be compared with the previous studies from other countries in order to find out the different or similar trends of glycaemic control (HbA1c) towards cognitive impairment.

The need for a Research Assistant (RA)

During the pilot study, the researcher found that each primary care setting in the study area provide services in its diabetic clinics two days a week. Some primary care settings run diabetic clinics on the same date and time. Considering the time constraints for data collection (4 months) and sample size, a research assistant is required for the main study. The recruitment and training of RA will therefore be added to the research protocol in the main study. The details of this process will be presented later in this chapter.

Inter-rater reliability of all the study instruments

Prior to data collection in the main study, all the instruments (Mini-Cog, MMSE Thai 2002 and TGDS) will be tested between the researcher and the RA in order to assure the reliable administration of the tests. The details and processes will be presented later in Section 7.6.

To summarise, the following three strategies are added to the methodology in the main study in order to meet the already mentioned issues

a) The number of older people with type 2 diabetes who do not receive HbA1c measurement will be added to the main study
b) A Research Assistant (RA) will help collect the data in the main study
c) The inter-rater reliability between the researcher and the research assistant will be studied

Table 7.1: Summary of the differences between the pilot and the main study

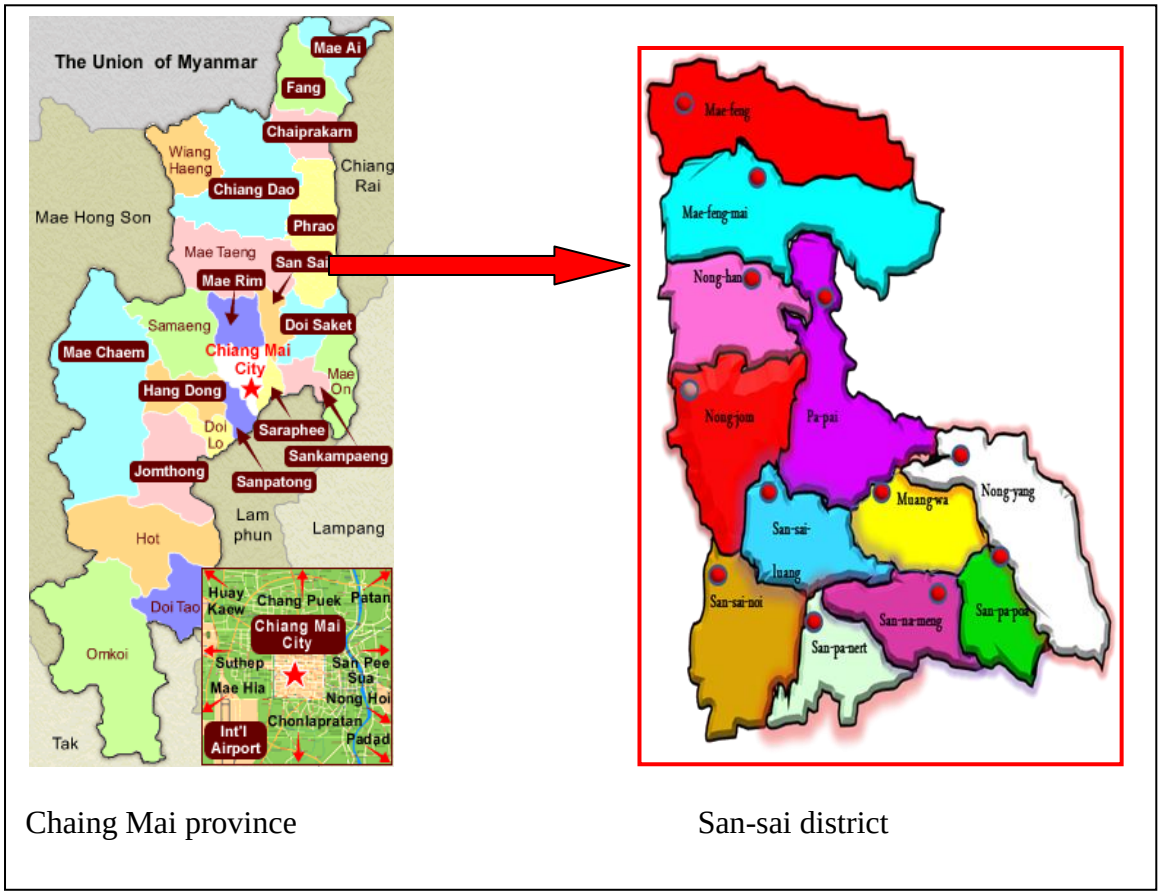
Consideration issues in the pilot study	Old protocol	Changes in the main study	Rationale
Sample size	Sample with HbA1c test	Adding the number of participants in the sample without HbA1c test	Testing the selection bias in the study sample
Research Assistant (RA)	No RA	Adding RA	Time restriction in data collection because diabetic clinics are run on the same day and time
Inter-rater reliability study of the application of all instruments	No study of inter-rater reliability in the application of the study instruments	Adding the study of inter-rater reliability	To ensure the reliable administration of the tests and achieving valid results

After discussing the changes concerning the information in the research protocol, the methodology for the main study is presented below.

7.2 Area of the study

This study was conducted in San-sai district which is one of the districts in Chiang Mai, Thailand. Chiang Mai is located in north of Thailand. It is approximately 700 kilometres from Bangkok, the capital of Thailand. The province consists of 24 districts, 204 sub-districts, 1,999 villages and 262 primary care settings. With a population of 1.6 million, Chiang Mai is one of the largest provinces in the northern part of Thailand with the highest older people population (12.6%) (National Statistical Office, Thailand 2007). For more details, please refer to Chapter 5 (The Study Protocol).

Figure 7.1 Map of Chiang Mai provinces and sub-districts community within San-sai district, Thailand



Chaing Mai province San-sai district

Sources: http://chaingmai.sawasdee.com and courtesy map from San-sai district health office

7.3 Study population and sampling procedures

Population

The target population will include all the patients aged 60 and over, who reside and are registered with the primary care settings in San-sai district.

Sample size and sampling

As mentioned earlier, in order to test the selection bias of HbA1c results in the participants and to ensure that the target population (group with HbA1c) is representative of the actual population (the entire older people with type 2 diabetes), the sample size of the methodology is amended by adding an equal number of participants without HbA1c results. The comparison between the prevalence of the outcome between the groups with and without HbA1c is analysed to see whether this study assesses the actual population value.

The total minimum number of the participants in this study is planned to be 534 (267 with HbA1c result and 267 without HbA1c result). All the eligible older people with type 2 diabetes from 15 PCUs in San-sai district have the same probability of being included in the sample.

A list of the target population (participants with HbA1c results) will be provided by the gatekeeper, a diabetes nurse of San-sai hospital where HbA1c is measured. It should be mentioned that the target population is dispersed within 13 of the 15 primary care settings. Random sampling will be applied in this study so that an eligible target population of 267 patients with HbA1c measure and 267 patients without HbA1c measure are included in the study

7.4 Ethical issues and considerations

The ethical approval for the main study will be sought first from the Faculty of Health Research Ethics Committee, University of East Anglia, the United Kingdom; and then from the Ethical Review Committee for research in Human Subjects, Department of Medical Service of Public Health, Ministry of Public

Health , Thailand (see Appendices A1 and A2). Ethical considerations are given in relation to the following:

- After giving the participant an information sheet in Thai, the researcher asks them if they feel comfortable to receive the information in written form or they want it explained verbally. If the participant is illiterate, the researcher will read the form out. The patients are assured that their participation or non-participation will not have any impact on their routine health care service. If the potential participants agree to take part, they will be invited to give their consent either in writing or by thumb-print (in case they are illiterate). As with all other documents, the consent form will be read to the illiterate participants who have 'signed' using their thumb print in the presence of two health care staff as witnesses. The researcher will also sign the consent form to indicate that the she has explained the purpose of the study to the participants. Participants will have an opportunity to ask any questions, and may refuse to participate without giving reasons at any time if they disagree or are unsatisfied during the process. Many Thai older people in the study area have only a primary school level of education and require extra help. The researcher will therefore explains verbally all the information on the information sheet.

- The researcher will be alert for any emerging health problems that may arise during the study in the participants. If any problem arises, the researcher will, with the consent of the patient, notify a clinical member of staff within the primary care setting to provide appropriate care for the patient. If necessary, any interview will be terminated, and the participation in the study will be ended.

- All the data produced in this study is anonymous and is kept strictly confidential. Each study participant is given a code number for identification purposes. The researcher is the only person to know the identity of the participants. All the data is kept in a secure storage on a UEA computer and is protected by the researcher's personal identification number. It can only be accessed by the researcher during the lifetime of the

study. Once the Doctorate Thesis and any publications arising from the work have been completed, all recordings will be confidentially erased and all transcripts will be stored in electronic form for 5 years.

7.5 Identification and recruitment of the participants

There are two steps for the identification and recruitment of the participants as follows:

1) Prior to data collection, the researcher will formally contact the nurse who works in the diabetic clinic of each primary care centre and will explain the aims and objectives including the inclusion and exclusion criteria in this study.

2) A list of the potential participants who have a routine visit date at the diabetic clinic during the researcher's visit for data collection will be provided by the nurse at each primary care centre. On the date that the potential participants visit the primary care centre and after receiving the routine diabetes care, the nurse will assist the researcher by identifying the older people with type 2 diabetes and enquires if they are interested in to take part in the study. If the potential participant is willing to take part, the researcher will explain the project and give them the "information sheet" (Appendix C). Those that agree to join the study will be invited to sign a consent form (Appendix C) to show their willingness to participate. After obtaining informed consent, the participants will be interviewed and asked to complete all the questionnaires by the researcher within the primary care centre. It should be noted that due to the context of the study area in a Thai older people population, it is not possible to hand out "the information sheet" to the potential participants and allow them time for consideration (see Chapter 6 Section 6.11).

7.6 Recruitment and training of the research assistant

A research assistant is recruited at the psychogeratric department, Faculty of Medicine, Chiang Mai University. The assistant is qualified as a registered nurse and works as a research assistant on psychogeriatric research with Dr.Nahathai Wongpakaran, a specialist psychogeriatric physician and the fieldwork mentor for

this study. A one-day training is provided to the qualified research assistant by the researcher. The purpose of the training is to ensure that the research assistant fully understands the research objectives, and that the questionnaire tests are consistently conducted under the research protocol.

Inter-rater reliability study of the instruments

After establishing the training, an inter-rater reliability of all the instruments (Mini-Cog, MMSE Thai 2002 and TGDS) between the researcher and the research assistant is assessed in the first twenty-one (21) participants of the main study.

The instruments (Mini-Cog, MMSE Thai 2002 and TGDS) used for data collection are investigated to establish the reliability and accuracy of the administration process between the researcher and the RA. The researcher and RA perform the test independently from the individual participants in an alternating fashion and are blinded to each other's results. The researcher and RA's results obtained from each instrument are then analysed for inter-rater reliability. This discussion will be presented in Chapter 8.

7.7 Data collection for the main study

The data collection of the main study was conducted January-April 2011. The researcher and RA collected the data from the individual participants separately as the following:

Procedure for applying the instruments

- Demographic data interview

  The interview of demographic data is the first stage of applying the instrument. It comprises of basic demographic data including age, education, and years in school, marital status, living arrangement (alone or with family), income and type of health cost support. The information is collected directly from the participants to ensure its accuracy. It is then used to study the characteristics of the participants. (see Appendix E1).

- Application of the screening tests

The second stage is applying the screening tests. The screening tests are applied in the following order: first Mini-Cog (5 minutes), then MMSE Thai 2002 (10 minutes) and last the TGDS (10 minutes). This whole stage will take 25 minutes. Mini-Cog is applied first because it is the primary test in this study, and the short duration of the test is perceived as less stressful to the patient compared to MMSE, which is longer with a series of questions for concentration and attention span (Doerflinger 2007). TGDS is the last test to administer because of its simple yes/no format. It can easily be understood by older people who have short attention spans or may feel easily fatigued after testing the cognitive screening tests (Holroyd and Clayton 2000).

- Recording data

The details of data record are divided into three parts. The first part is the demographic data that provides the characteristics and personal information of the participants through the interview and patients' profile record. The second part is the medical information obtained by viewing the medical annual report profile recorded 5-9 months prior to the recruitment. Only FBS is recorded on the day of recruitment. The last part is the results of cognitive screening and depressive mood screening tests. The details of all the data records are in Appendix E1.

7.8 Data analysis and statistical procedures

The researcher used the Statistical Package for Social Sciences (SPSS) program for Windows version 16 for data management including data entry, checking and analysing.

7.8.1 Preparing the data for analysis

This step include scoring the data by assigning numeric values to each response, cleaning data entry errors from the database, recording items on instruments with

inverted scores or computing new variables that comprise multiple items from scales.

- Data coding: the variables of the study are divided into numeric and string. The data from the outcome measure of the screening tests are categorized as numeric, and some demographic data are categorised as string. Although categorical variables are entered into the statistical package for social science (SPSS) as labels, it is easier to code the labels and to facilitate statistical analysis, it is recommended to enter the codes as numeric data (Creswell and Plano Clark 2011).Therefore, males are coded as 0 and females are coded as 1. For the dichotomous variables such as the results of the screening tests, 0 and 1 are used as codes to show the patients' normal and impaired conditions, respectively (Appendix E2).

- The major descriptive statistics such as minimum and maximum values, means and standard deviations are calculated by SPSS in order to check briefly the range and distribution of the variables.

- To ensure the accuracy of the data file, 10% of the computerised data file is randomly selected to proofread against the original file (Tabachnick and Fidell 2007). The errors in the database are found to be acceptable at 0.1 %. The six errors of data are found in the following variables: height, Low Density Lipoprotein (LDL), duration time of HbA1c before recruitment, DM duration (groups), DM treatment and co-morbid diseases.

7.8.2 Analysing the data by using inferential statistics

Before using inferential statistics, several assumptions such as normal distribution, multicollinearity and outlier are required to ensure the validity and reliability statistical calculation as follows:

- *Assumption of normality*

Checking the normality of variables is one of the important assumptions of using statistical test. A Kolmogorov-Smirnov testis used to assess the normality of the distribution of variables. In statistics, a non-significant result (p value more than 0.05) indicates normality (Pallant 2009). In this study, the Kolmogorov-Smirnov test shows the significant p value (less than 0.05) of the data set suggesting the non-normality of the data (Pallant 2009) (see Appendix F1).

- *Assumption of multicollinearity*

In order to analyse the reliable data of logistic regression, it is important to check the multicollinearity, which can pose a threat to the validity of correlation and a logistic regression analysis (Field 2009). Mutlicollinearity exists when there is a strong correlation between two or more predictors in correlation and logistic regression. The variance inflation factor (VIF) indicates whether a predictor has a strong linear relationship with other predictors. If the value of VIF is more than 10, it indicates problem with multicollinearity, which may be biasing the correlation and logistic regression analysis. Tolerance, which is VIF's reciprocal (1/VIF), is another statistics to check the multicollinearity. Values of tolerance are very low (below0.1) indicating that the variable has high correlations with other variables in the model (Pallant 2009). In this study, the VIF and tolerance value were checked and multi-collinearity was not found in the data set (Appendix F2).

Demographic data

Descriptive statistics, including percentages, mean, and standard deviation are used to examine the demographic data and study the variables of the participants with and without HbA1c

Comparison of the demographic and clinical data between the groups with and without HbA1c group

A Mann-Whitney U test is used to compare the difference in the demographic and clinical data in two categorical variables, while the Kruskal-Wallis test is used to compare the difference in three or more sets of categorical variables between the groups with and without HbA1c.

Prevalence study

Crude prevalence rate (percentage number) with the 95% confidence interval (CI) of screening positive for cognitive impairment by Mini-Cog test and MMSE Thai 2002 and the crude prevalence rate with the 95% confidence interval (CI) of depressive mood screening by TGDS are calculated in the groups with and without HbA1c test result.

Comparison of prevalence study

The chi-square test ($\chi 2$) is calculated to compare the prevalence of cognitive impairment and depressive mood between the groups with and without HbA1c test. To ensure the results of the p-value from Chi-square test, the difference of proportion in 95% confidence interval (CI) is analysed to see whether or not there is a difference on the study outcomes.

Relationship between cognitive impairment and depressive mood

Partial correlation analysis involves studying the linear relationship between two dependent variables after excluding the effect of one or more independent variables (Choudhury 2010). In order to get a correct picture of the relationship between two variables, the influence of confounding variables should be removed. As in simple correlation, the strength of the linear relationship between two variables is measured without taking into consideration the fact that both these variables may be influenced by a third variable or confounding variable (Pallant 2009).

Based on the discussion in chapters 2 and 3, age and years in school are the confounding variables of performance scores on cognitive and depressive mood

screening tests. In order to obtain an accurate picture of the relationship between the cognitive function and depressive mood, partial correlation analysis is applied in this study to analyse the relationship between cognitive impairment and depressive mood by excluding the effect of age and years in school.

Predictors of cognitive impairment and depressive mood in Thai older people with type 2 diabetes

In order to investigate the independent predictor or individual characteristics associated with cognitive impairment and depressive mood, logistic regression is used in the data analysis. The logistic regression is used to explore which characteristics are associated with cognitive impairment and depressive mood by univariate logistic regression. Based on the results of univariate logistic regression, the variables that were significant at $p = 0.10$ level are applied in multivariate logistic regression with Backward Elimination Likelihood Ratio or Backward LR method. The results of this step will create a prognostic model, which might be individual predictors associated with the cognitive impairment and individual predictors associated with depressive mood.

Backward LR is important in the process to distinguish between relevant and less relevant predictors, meaning that the final model can be developed with as few predictors as possible, but would still lead to reliable predictions. Subsequently the variables with the highest p-values are manually removed. Then the model is re-run. This step is repeated until there are no variables left with a p-value smaller than 0.10.A p-value of 0.10 or 0.20 is commonly used in prognostic models, as variables that are less strongly associated with the outcome may still make a relevant contribution to the prediction. Final pruning of the model in this study is carried out with backward LR at $p < 0.05$ (Bursac 2008).

Differences of test score between the good glycaemic control (HbA1c ≤ 7% or 53 mmol/mol) and poor glycaemic control (HbA1c > 7% or or 53 mmol/mol) groups

In order to investigate and compare whether there is a difference between the cut-off score in the cognitive screening tests and depressive mood test, and between the level of good glycaemic control (HbA1c ≤7% or 53 mmol/mol) and poor glycaemic control (HbA1c > 7% or 53 mmol/mol) groups, A Mann-Whitney U test) is used. It is meant to compare the difference in the score results of the screening tests between the participants with good and poor glycaemic control (Field 2009).

7.9 Summary

In order to achieve the research aims and objectives for the current study, this chapter provided the methodology, which is adapted and based on the practical information from the pilot study. The results of data collection from the main study are analysed and presented in the next chapter.

Chapter 8

Results

In the previous chapter the methodology employed within this study was presented and discussed. In this chapter the results from the data analysis of the main study will be presented. The results are organised into eight parts. The first part includes the results of the inter-rater reliability between the researcher and the RA of all the instruments initially conducted during the data collection. The second through the six parts of this chapter outline the findings of the data analysis.

8.1 Inter-rater reliability of Mini-Cog, MMSE Thai 2002 and the TGDS

The raw scores of 21 participants in all the instruments (Mini-Cog, MMSE Thai 2002 and TGDS), used in this study between the researcher and the RA are presented in Table 8.1. The results of inter-rater reliability of Mini-Cog , MMSE Thai 2002 and TGDS are presented in Tables 8.2 ,8.3 and 8.4 respectively.

Table 8.1: Raw data scores of Mini-Cog Thai version, MMSE Thai 2002 and TGDS between the researcher and the RA in a sample of 21 older people with type 2 diabetes in the main study

Participants	Mini-Cog		MMSE Thai 2002		TGDS	
	Researcher	RA	Researcher	RA	Researcher	RA
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	1	1	0	0	0	0
4	0	0	0	0	1	1
5	0	0	0	0	0	0
6	0	0	0	0	1	1
7	0	0	0	0	0	0
8	0	0	0	1	1	1
9	1	1	0	0	0	1
10	0	0	0	0	1	1
11	0	0	0	0	0	0
12	0	0	0	0	0	0
13	1	1	0	0	0	0
14	0	0	0	0	0	0
15	0	0	0	0	0	0
16	1	1	1	1	1	1
17	0	1	0	0	0	0
18	0	0	0	0	0	0
19	0	0	0	0	0	0
20	1	1	1	1	0	0
21	0	0	0	0	0	0

Inter-rater reliability of Mini-Cog

The researcher and RA both agreed in Mini-Cog on the 'normal cognition' (57.1%) and the 'cognitive impairment' (33.3%). In 9.5% of the cases RA and the researcher disagreed on the 'normal cognition'. In total, the agreement on 'normal cognition' and 'cognitive impairment' between the researcher and RA was 90.4% (Table 8.2).

Table 8.2: 21 participants are scored by the researcher and RA for Mini-Cog. 0 (zero) denotes the participants with normal cognition. 1 (one) denotes the participants with cognitive impairment.

		RA N (%)		Total N (%)
		0	1	
Researcher N (%)	0	12(57.1%)	2 (9.5%)	14 (66.7%)
	1	0 (0%)	7 (33.3%)	7 (33.3 %)
Total		12 (57.1%)	9 (42.9%)	21 (100%)

Inter-rater reliability of MMSE Thai 2002

In MMSE Thai 2002, the researcher and RA both agreed on ‘normal cognition’ (85.7%) and ‘cognitive impairment’ (9.5%). In 4.8% of the cases the RA disagreed with the researcher on ‘normal cognition’. In total, the agreement on the ‘normal cognition’ and ‘cognitive impairment’ between the researcher and RA was 95.2% (see Table 8.3).

Table 8.3: 21 participants are scored by the researcher and RA for MMSE Thai 2002. 0 (zero) denotes the participants with normal cognition, 1 (one) denotes the participants with cognitive impairment.

		RA N (%) 0	1	Total N (%)
Researcher N (%)	0	18 (85.7%)	1(4.8%)	19 (90.5%)
	1	0 (0%)	2 (9.5%)	2 (9.5%)
Total		18 (85.7%)	3(14.3%)	21 (100%)

Inter-rater reliability of the TGDS

In the TGDS, the researcher and RA both agreed on ‘normal mood (76.2%) and ‘depressive mood’ (19.0%). In 5.9% of the cases the RA disagreed with the researcher on ‘normal mood’. In total, the agreement on ‘normal mood’ and ‘depressive mood’ between the researcher and RA was 95.2 % (see Table 8.4).

Table 8.4: 21 participants are scored by the researcher and RA for the TGDS. 0 (zero) denotes the participants with normal mood, 1 (one) denotes the participants with depressive mood

		RA N (%) 0	1	Total N (%)
Researcher N (%)	0	16 (76.2%)	1(5.9%)	17 (81%)
	1	0 (0%)	4 (19%)	4 (19%)
Total		16 (76.2%)	5 (23.8%)	21 (100%)

The Kappa (K) statistics for the inter-rater reliability between the researcher and RA showed a good agreement for all the instruments used in this study. The results are as the following (see Table 8.5); K = 0.8, p = 0.000, 95% CI 0.54, 1.06 for Mini-Cog, K = 0.77, p = 0.001, 95% CI 0.51, 0.90 for MMSE Thai 2002 and K = 0.86, p = 0.000, 95% CI 0.68, 0.94).

Table 8.5: Agreement between the researcher and RA on the instruments (Mini-Cog, MMSE Thai 2002 and the TGDS) used in the study.

	Kappa	P	95% CI	
			Upper	Lower
Mini-Cog	0.80	0.000	0.56	0.92
MMSE Thai 2002	0.77	0.000	0.51	0.90
TGDS	0.86	0.000	0.68	0.94

Summary of the inter-rater reliability between the researcher and RA

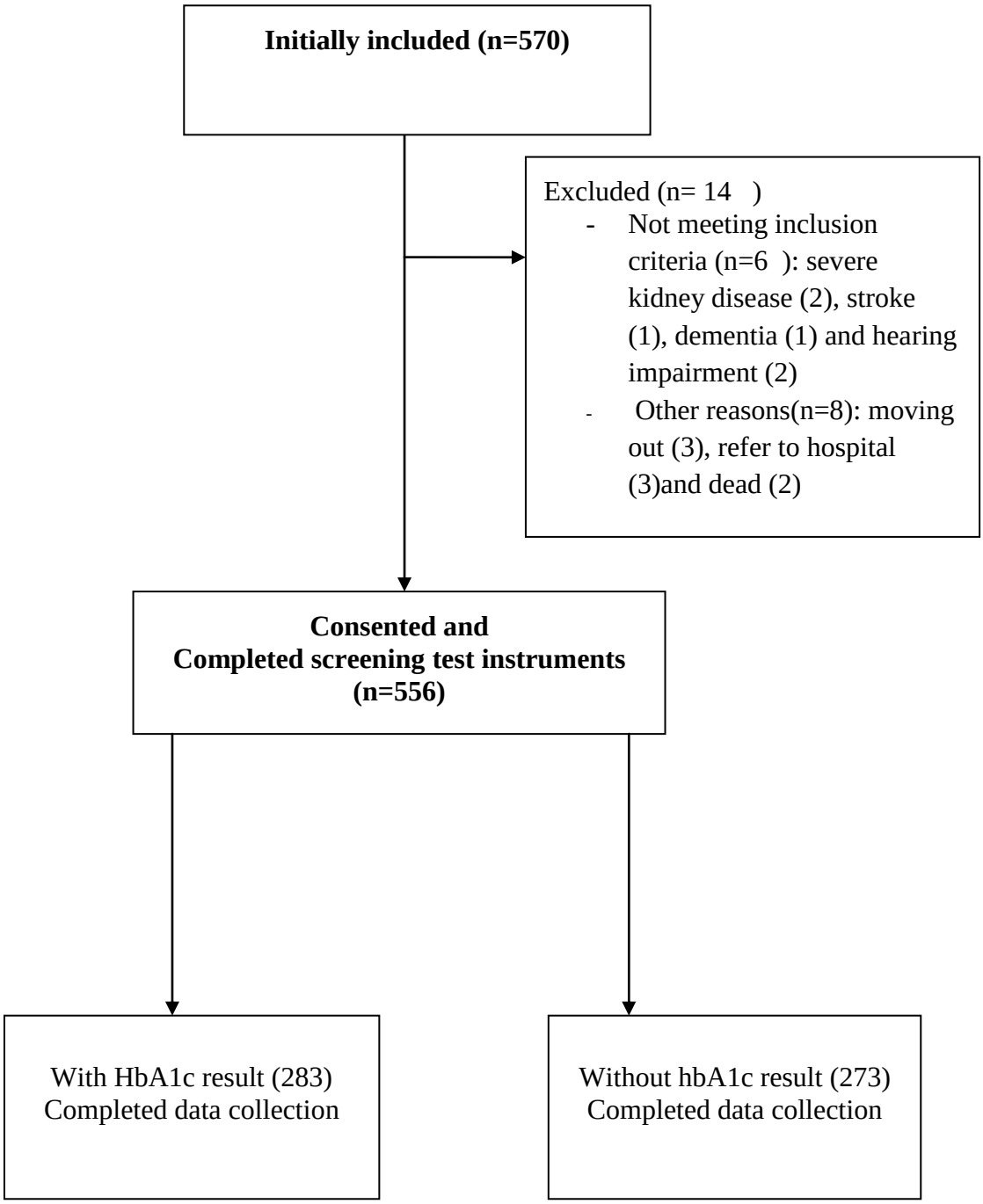
The findings of the inter-rater reliability of all the instruments used in this study were in the good level of agreement at K=0.8 for Mini-Cog, K= 0.77 for MMSE Thai 2002 and K=0.87 for the TGDS (Altman, 1991) (see section 6.10 for the levels of agreement). These findings showed the evidence of a good reliability between the researcher and the RA.

As mentioned earlier in Chapter 7, using the RA was needed in this study. Because of limitation of time with a double increased number of subjects, and some primary care settings ran diabetic clinics in the same date and time. This finding suggests that the researcher and RA could administer all the instruments with each other in a reliable manner for the data collection in the main study.

8.2 Participant recruitment

The initial recruitment of the sample for this study identified 570 Thai older people with type 2 diabetes who had routine visits at diabetic clinic from January to mid of May 2011 within 13 primary care centres at San-sai district. Potential participants were invited to take part in the study. Fourteen (14) potential participants were excluded due to: moving out (3), dying (2), not meeting inclusion criteria (6), and being referred to hospital (3). Five hundred and fifty six (556) Thai older people with type 2 diabetes who participated and completed data collection were subsequently divided into the group with HbA1c (283) and the group without HbA1c (273). All the participants gave informed consents and completed screening test instruments. A flow chart diagram (see Figure 8.1) shows the summary of the recruitment in this study.

Figure 8.1: Flow chart diagram of participant recruitment



8.3 Demographic characteristic data of the participants

The characteristics of 556 participants who participated in the study and completed the data collection and screening test instrument are outlined in Table 8.6. In this study 556 participants took part, 367 (66%) of which were females and 189 (34%) of which were males. A similar pattern of gender representation was found in both groups of with and without HbA1c test. There were 180 (63.6%) females in the group with HbA1c test and 187 (68.5%) females in the group without HbA1c test. Males represented 103 (36.4%) in the group with HbA1c test and 86 (31.5%) in the group without HbA1c test. There was no statistically significant difference in the mean age between the two groups (68±6 with HbA1c test vs. 68±7 without HbA1c test, p=0.709). Likewise, there was no statistically significant difference in the age group between the two groups. 93% of all the participants (with and without HbA1c test) had attended school. The percentage of the participants who attended school for less than 4 years was found to be the same between the groups with and without HbA1c test, with no statistically significant difference (89.4% and 89.7% in the group with HbA1c and without HbA1c respectively, p=0.894). Nevertheless, the data showed that the number of people who lived alone in the group without HbA1c test was higher than the group with HbA1c test (20 vs. 10) with a statistically significant difference (p=0.048). Health behaviours (current smoking, drinking and exercise) between the two groups were not statistically significant. Ninety percent (90%) of the participants in both groups received health cost support from the government.

Overall, it can be observed that living arrangement was the only one demographic characteristic data that was found to be statistically significant between the two groups. It is possible that the people who lived alone were less likely to have HbA1c test compared to people who live with family.

Table 8.6: Characteristics of participants

Characteristics	With HbA1c n=283	Without HbA1c n=273	Total N=556	P
Gender				
Male	103 (36.4%)	86 (31.5%)	189 (34%)	0.224
Female	180 (63.6%)	187(68.5%)	367 (66%)	
Age[a]	67.60±6.42	67.59+6.77	556 (100%)	0.709
Age (years)				
60-64	121 (42.8%)	124 (45.4%)	245(44.1%)	0.695
65-69	60 (21.2%)	53 (19.4%)	113(20.3%)	
70-74	52 (18.4%)	46 (16.8%)	98 (17.6%)	
75+	50 (17.7%)	50 (18.3%)	100 (18%)	
Education				
Never attended to school	19 (6.7%)	20 (7.3%)	39 (7%)	0.778
Attended to school	264 (93.3%)	253 (92.7%)	571 (93%)	
Year in school				
≤4	253 (89.4%)	245 (89.7%)	498(89.6%)	0.894
>4	30 (10.6%)	28 (10.3%)	58 (10.4%)	
Living arrangement				
Alone	10 (3.5%)	20 (7.3%)	30(5.4%)	0.048*
With family	273 (96.5%)	253 (92.7%)	526(94.6%)	
Working				
Yes	99 (35.0%)	108 (39.6%)	207(37.2%)	0.265
No	184 (65.0%)	165 (60.4%)	349(62.8%)	
Current smoking				
Yes	20 (7.1%)	25 (9.2%)	45 (8.1%)	0.367
No	263 (92.9%)	248 (90.8%)	511(91.9%)	
Current drinking				
Yes	23 (8.1%)	31 (11.4%)	54 (9.7%)	0.199
No	260 (91.9%)	242 (88.6%)	502(90.3%)	
Current exercise				
Yes	149 (52.7%)	160 (58.6%)	309(55.6%)	0.158
No	134 (47.3%)	113 (41.4%)	247(44.4%)	
Health cost support				
- national health care (30 baht scheme policy)	261 (92.2%)	247 (90.5%)	508(91.4%)	0.548
- Social/Welfare health care	6 (2.1%)	10 (3.7%)	16 (2.9%)	
- Self-funding/family support	16 (5.7%)	16 (5.9%)	32 (5.8%)	

*$p \leq 0.05$, [a] mean ± SD

Characteristics of the clinical data

The clinical characteristics data in Table 8.7 shows that the group without HbA1c test had a significantly higher number of people with a BMI range of 23-25 $kg/m^2$and > 25+ kg/m^2 than the group with HbA1c test (p = 0.043). As expected, the group without HbA1c had a poor control of FBS (> 140^+ mg/dl or >7.8 mmol/l) and a total cholesterol level of > 200^+ mg/dl or 11.1 mmol/l when compared to the group with HbA1c (with a statistical significance of p = 0.000 and p=0.017 respectively). Systolic and diastolic blood pressure, LDL, HDL, triglyceride, HbA1c, diabetes complications and co-morbidity diseases were not found to be statistically different between the two groups.

Diabetes treatment between the two groups was statistically significant (p = 0.006). The group with HbA1c test had a higher number (48) of people who were on diet alone (without medication) than the group without HbA1c test (25); while the group without HbA1c test had a higher number of participants who were on oral medication, insulin injection and combined treatment (oral medication plus insulin injection) than the participant with HbA1c test (234 vs. 225, 9 vs. 8 and 5 vs. 2, respectively). Duration range of diabetes (years) was also significantly different between the two groups (p = 0.01). The group without HbA1c test had a higher number of participants in the duration range of 1-4 years than the group with HbA1c (111 vs. 74); whereas the participants with HbA1c test had a higher number of participants in the duration range of 5-8 years and 8+ years than the group without HbA1c (105 vs. 78 and 104 vs. 84, respectively).

The criteria for selecting the diabetic patients who would have HbA1c test in the primary care based on a good ability to control FBS < 140 mg/dl or <7.8 mmol/l in two of the last three visits to the primary care. Therefore, it was not surprising to see that the group with HbA1c test was able to control blood sugar (FBS) and some metabolic variables such as BMI and cholesterol levels better than the group without HbA1c test. In addition, the data showed that the diabetes duration and treatment were significantly different between the two groups. It can be observed that the number of participants in the group without HbA1c who had a diabetes duration of 1-4 years, was higher than the number of participants in the group with

HbA1c. However, the number of participants in the group without HbA1c who were on diet alone (without medication) was lower than the group with HbA1C.

Table 8.7: Characteristics of the clinical data

Characteristics	With HbA1c n=283	Without HbA1c n=273	Total N=556	P
Body Mass Index(kg/m2)				
<23	119 (42.0%)	82 (30.0%)	201(36.2%)	0.043*
23-25	47 (16.6%)	68 (24.9%)	115(20.7%)	
>25+	117 (41.3%)	123 (45.1%)	240(43.2%)	
Blood Pressure (BP)				
Syatolic (mmHg)				
≤130 normal	112 (39.6%)	106 (38.8%)	218(39.2%)	0.857
>130	171(60.4%)	167 (61.2%)	338(60.8%)	
Diastolic (mmHg)				
≤80 normal	180 (63.6%)	187 (68.5%)	367(66.0%)	0.224
>80	103 (36.4%)	86 (31.5%)	189 (34.0%)	
Fasting Blood Glucose (mg/dl or mmol/l)				
≤140 (or ≤7.8) normal	184 (65%)	98 (35.9%)	282(50.7%)	0.000**
>140 (>7.8)	99 (35.0%)	175 (64.1%)	274(49.3%)	
Total Cholesterol (mg/dl or mmol/l)				
≤200 (or ≤11.1) normal	150 (53.0%)	117 (42.9%)	267 48.0%)	0.017*
>200 (>11.1)	133 (47.0%)	156 (57.1%)	289(52.0%)	
Low density lipoprotien (mg/dl or mmol/l)				
≤100 (or ≤5.5) normal	78 (27.6%)	66 (24.2%)	144(25.9%)	0.362
>100 (>5.5)	205 (72.4%)	207 (75.8%)	412 (74.1	
High density lipoprotien (mg/dl or mmol/l)				
> 41 (>2.2)normal	236 (83.4%)	234 (85.7%)	470(84.5%)	0.449
≤ 40 (or ≤2.2) abnormal	47 (16.6%)	39 (14.3%)	86 (15.5%)	

Characteristics	With HbA1c n=283	Without HbA1c n=273	Total N=556	P
Triglyceride (mg/dl or mmol/l)				
≤ 150 (or ≤8.3) normal	177 (62.5%)	161 (59.0%)	338(60.8%)	0.389
>150 (>8.3)	106 (37.5%)	112 (41.0%)	218(39.2%)	
Duration of diabetes (years)				
1-4	74 (26.1%)	111 (40.7%)	185(33.3%)	0.003**
5-8	105 (37.1%)	78 (28.6%)	183(32.9%)	
8+	104 (36.7%)	84 (30.8%)	188(33.8%)	
Diabetes treatment				
Diet alone	48 (17.0%)	25 (9.2%)	73 (13.1%)	0.006**
Oral medication+diet	225 (79.5%)	234 (89.7%)	459(82.6%)	
Insulin injection+diet	8 (2.8%)	9 (3.3.%)	17 (3.1%)	
Combined oral medication+ insulin injection+ diet	2 (0.7%)	5 (1.8%)	7 (1.3%)	
Diabetes complication				
Neuropathy	11 (3.9%)	9 (3.3 %)	20 (3.6%)	0.709
Retinopathy	46 (16.3%)	37 (13.6%)	83 (14.9%)	0.372
Nephropathy	39 (13.8%)	30 (11.0%)	69 (12.4%)	0.318
Co-morbid disease				
Heart disease	7 (2.5%)	12 (4.4%)	19 (3.4%)	0.213
Hypertension	209 (53.5%)	182 (66.7%)	391(70.3%)	0.064
Chronic obstructive pulmonary disease (COPD)	4 (1.4%)	5 (1.8%)	9 (1.6%)	0.696
Gout	6 (2.1%)	9 (3.3%)	15 (2.7%)	0.392
Arthritis	3 (1.1%)	1 (0.4%)	4 (0.7%)	0.334
Dyslipidemia	79 (27.9%)	72 (26.4%)	151(27.2%)	0.683
Asthma	4 (1.4%)	2 (0.7%)	6 (1.1%)	0.438
Others*	6 (2.1%)	5 (1.8%)	11 (3.9%)	0.317

*p ≤ 0.05 **p ≤ 0.01/*Thyroid/Anemia/Tuberculosis/Thalassemia/Osteoporosis

8.4 Prevalence study

This part shows the results of the data analysis on the prevalence study of cognitive impairment and the prevalence study of depressive mood in the groups with and without HbA1c. The data is presented by calculating the percentage, p-value and 95% confidence interval (CI) which indicates how precise the sample estimate is likely to be in relation to the true population value (Dos Santos Silva 1999)

As shown in Table 8.8, the prevalence of probable cognitive impairment by Mini-Cog was 65.4% in the group with HbA1c test and 64.4% in the group without HbA1c test. The prevalence of probable cognitive impairment by MMSE Thai 2002 in the group with HbA1c was 12.4% and in the group without HbA1c test was 12.1%. The prevalence of probable depressive mood was equally 19.4% in both groups.

Table 8.8: Estimation of the prevalence of probable cognitive impairment and depressive mood in the group with and without HbA1c

Screening tests	With HbA1c (N=283)	Without HbA1c (N=273)	P	95% CI of the difference
Mini-Cog				
-Probable cognitive impaired	65.4 % (185)	64.8% (177)	0.895	-0.073-0.085
MMSE Thai 2002				
- Probable cognitive impaired	12.4% (35)	12.1% (33)	0.920	-0.052-0.058
TGDS				
-Probable depressed	19.4% (55)	19.4% (53)	0.995	-0.066-0.066

8.5 Comparison of the prevalence of cognitive impairment and depressive mood between the groups with and without HbA1c test

In order to check the selection bias in HbA1c test, the comparison of the prevalence between the two groups is analysed to see whether having or not having HbA1c test in this population affects the outcome measures (cognitive impairment and depressive mood) in the current study.

As presented in table 8.8, there were no statistically significant differences in the prevalence of cognitive impairment by Mini-Cog (p =0.895, 95% CI 0.073, 0.085) and by MMSE Thai 2002 (p = 0.920, 95% CI -0.052, 0.058) between the two groups. Likewise, the difference of the prevalence of depressive mood by TGDS between the two groups was not found (p = 0.995, 95% CI -0.066, 0.066).

In a descriptive epidemiology, the p-values should generally not be reported alone because they are designed to help deciding whether a set of observation is compatible with some hypothesis, and they do not provide information on the difference of effect (Dos Santos Silva 1999). For example, small effects of no epidemiological relevance can become 'statistically significant' with a large sample size, whereas important effects may be 'statistically non-significant' because the size of the sample studied was too small. In contrast, the confident interval (CI) provides an idea of likely difference of effects, and their width (margin of error) indicates the degree of uncertainty in the estimate of effect (Shakespeare et al. 2001). If the 95% confidence interval for a difference does not include the null hypothesis value of zero, then P-value is lower than 0.05. Conversely, if this CI includes the value of zero, i.e. one limit in positive and the other is negative, then P-value is greater than 0.05 (Du Prel 2009).

Thus, in order to confirm the non-significant p-value of the differences in the three screening tests between the two groups, 95% CI for the difference between the two independent proportions (prevalence) was calculated. It can been observed in Table 8.10 that the 95% confidence interval for the difference between the two proportions of the three screening tests included zero. As mentioned above, this

means that the p value is greater than 0.05 confirming a non-significant difference (Du Prel 2009).

This result shows clearly that there is no statistically significant difference in the prevalence data between the groups with and without HbA1c. This means that neither the group with HbA1c test nor the group without HbA1c influenced the outcome measures (cognitive impairment and depressive mood).

This result reveals that neither the group with HbA1c test nor the group without HbA1c influenced the outcome measures (cognitive impairment and depressive mood). Thus, the selection bias of HbA1c test towards the outcome measures has not been found in this population. Regarding the importance of focusing on glycaemic control by HbA1c test in this study, which was mentioned earlier in Chapters 1 and 7, only the data in the group with HbA1c test was used to analyse and represent the results of the target population in this study. The results are presented in Sections 8.6 – 8.8.

8.6 Characteristics associated with cognitive impairment and depressive mood

All univariate analyses were performed in relation to Mini-Cog scores. These associations were further explored to identify the potential individual predictors of the characteristics associated with cognitive impairment by Mini-Cog (multivariate logistic regression). The results were also reported as odds ratio (OR) and respective 95% confidence interval (CI). Odds ratios are used to compare the relative odds of the occurrence of the outcome of interest (e.g. cognitive impairment or depressive mood), and given exposure to the variable of interest (e.g. demographic or clinical characteristics). The odds ratio can be used to determine whether a particular exposure is a risk factor for a particular outcome, and to compare the magnitude of various risk factors for that outcome (Szumilas 2010).

OR=1 Exposure does not affect odds of outcome

OR>1 Exposure associated with higher odds of outcome

OR<1 Exposure associated with lower odds of outcome

The 95% CI is often used as a proxy for presence of statistical significance if it does not overlap the null value (e.g. OR=1) (Du Prel 2009).

Univariate models describe the crude relationship between a variable (risk factor) and an outcome measure (cognitive impairment/ depressive mood). However, the crude relationship may not only reflect the effect of the viable, but may also reflect the effect of a confounder, which is associated with the risk factor (Heinze, 2009). A confounder defines as a variable that we may or may not has measured other than the risk factors in which we are interested that potentially affect the outcome measure (Field, 2009).

This implies that the crude measure of effect reflects a mixture of the effect of the exposure and the effect of confounding factors. When confounding exists, analytical methods must be used to separate the effect of the exposure from the effects of the confounding factor(s). Multivariable modelling is one way to control. Thus, it has been proposed to include important factors from univariate into multivariable modelling to reduce the variability of the outcome measure (Heinze, 2009).

For a logistic regression model with only one independent variable, the OR is considered ‘‘unadjusted’’ because there are no other variables whose influence must be adjusted for or subtracted out. In contrast, if the logistic regression model includes multiple independent variables, the ORs are now ‘‘adjusted’’ because they represent the unique contribution of the independent variable after adjusting for (or subtracting out) the effects of the other variables in the model (Stoltzfus, 2011).

The analysis with MMSE Thai 2002 scores and TGDS scores was carried out in the same manner in order to find the independent predictors on cognitive impairment by MME Thai 2002 and individual predictors associated with depressive mood (see Chapter 7 for more details).

8.6.1 Association between the predictors and cognitive impairment by Mini-Cog

The univariate and multivariate logistic regression revealed a number of associations (see Table 8.9). The characteristics of participants who were more likely to be reported as having cognitive impairment were as the following: they were 60-64 years old (OR = 3.84, 95% CI 1.92, 7.67), had attended school for more than 4 years (OR = 8.56, 95% CI 1.99, 36.75), and they were working (OR = 1.8, 95% CI 1.06, 3.09). The other clinical associations with cognitive impairment were BMI 23-25 kg/m^2 and more than 25 kg/m^2 (OR = 2.60, 95% CI 1.18, 5.70 and OR = 1.40, 95% CI 0.82, 2.38, respectively), FBS more than 140 mg/dl or 7.8 mmol/l (OR = 1.95, 95% CI 1.13, 3.34), total cholesterol less than 200 mg/dl or 11.1mmol/l and HDL less than 40 mg/dl or 2.2 mmol/l (OR = 2.20, 95% CI 1.04, 4.64 and OR=1.55, 95% CI 0.95, 2.53 respectively).

The important independent predictors of cognitive impairment by Mini-Cog in the prognostic model were as the following: being aged 60-64 (OR = 3.62, 95% CI 1.70, 7.71), being aged 65-69 (OR = 2.90, 95% CI 1.25, 6.72), being aged 70-74 (OR = 2.39, 95% CI 1.02, 5.57), having more than 4 years in school (OR= 9.31, 95% CI = 2.11, 41.05), with BMI 23-25 kg/m2 (OR = 2.78, 95% CI 1.21, 6.38), high BMI of more than 25 kg/m^2 (OR = 1.05, 95% CI 0.58,1.89), and poor HDL of less than 40 mg/dl or 2.2 mmol/l (OR = 2.43, 95% CI 1.10, 5.38).

As shown in Table 8.9, in the univariate analysis, having FBS of more than 140 mg/dl or 7.8 mmol/l by its own showed a statistically significant association with cognitive impairment by Mini-Cog with an unadjusted OR = 1.95, 95% CI 1.13, 3.34, P = 0.016). It showed that the participants who had an FBS of more than 140 mg/dl or 7.8 mmol/l were 1.95 times more likely to have cognitive impairment than those with an FBS of more than 140 mg/dl or 7.8 mmol/l. The P value of 0.016 was less than 0.05 indicating that the upper (3.34) and lower limits (1.13) of the 95% confidence interval excluded the null value. However, in the multivariable model logistic regression analysis, having an FBS of more than 140 mg/dl or 7.8 mmol/l was not a statistically significant and not important contribution to the model (adjusted OR = 1.66, 95% CI 0.93, 2.98, P = 0.088), controlling for all other factors in the model. This indicates that the participants having an FBS of more

than 140 mg/dl or 7.8 mmol/l were not strongly associated with cognitive impairment by Mini-Cog. The P value at 0.08 was more than 0.05. This indicates that the upper (2.98) and lower limits (0.93) of the 95% confidence interval were close to the null value. Thus, having FBS of more than 140 mg/dl or 7.8 mmol/l had a low risk of cognitive impairment and may be a potential confounding variable in this study. Nevertheless, the lower limit of 95% CI adjusted OR of having an FBS of more than 140 mg/dl or 7.8 mmol/l was at 0.93, which was close to 1. If the alpha level was set at 10% ($P<0.1$), this variable (having an FBS of more than 140 mg/dl or 7.8 mmol/l) might therefore be considered significant evidence and contributed to the model.

Table 8.9: Univariate and Multivariate logistic regression of Mini-Cog

Characteristics	Impair/Total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Gender					
-Male	72/103 (69.9%)	1.38(0.82-2.31)	0.23		
-Female	113/180 (62.8%)	1			
Age (years)					
60-64	89/121 (73.6%)	3.84 (1.92-7.67)		3.62 (1.70-7.71)	
65-69	42/60 (70%)	3.22 (1.47-7.08)		2.90 (1.25-6.72)	
70-74	33/52 (63.5%)	2.40 (1.08-5.32)		2.39 (1.02-5.57)	
75+	21/50 (42%)	1	0.002	-	0.009
Education					
-Never attended to school	10/19 (52.6%)	1			
-Attending the school	175/264 (66.3%)	1.77 (0.69-4.51)	0.232		
Year in school					
≤4	157/253 (62.1%)	1		1	
>4	28/30 (93.3%)	8.56 (1.99-36.75)	0.004	9.31 (2.11-41.05)	0.003
Living alone					
- No	180/273 (65.9%)	1.94 (0.55-6.86)	0.306		
-Yes	5/10 (50%)	1			
Working					
-No	112/184 (60.9%)	1			
-Yes	73/99 (73.7%)	1.8 (1.06-3.09)	0.031		
Smoking					
-No	170/263 (64.6%)	1			
-Yes	15/20 (75%)	1.64 (0.58-4.66)	0.352		
Drinking					
-No	168/260 (64.6%)	1			
-Yes	17/23 (73.9%)	1.55 (0.59-4.07)	0.372		
Exercise					
-No	93/134 (69.4%)	1.41 (0.86-2.30)	0.177		
-Yes	92/149 (61.7%)	1			
Body Mass Index(kg/m2)					
<23	70/119 (58.8%)	1	0.053	1	0.045
23-25	37/47 (78.7%)	2.60 (1.18-5.70)		2.78 (1.21-6.38)	
>25+	78/117 (66.7%)	1.40 (0.82-2.38)		1.05 (0.58-1.89)	
Blood Pressure (BP)					
Systolic (mmHg)					
≤130 normal	74/112(66.1%)	1.05(0.64-1.74)	0.841		
>130	111/171(65%)	1			
Diastolic (mmHg)					
≤80 normal	117/180 (65%)	1			
>80	68/103 (66%)	1.05 (0.63-1.74)	0.862		

Characteristics	Impair/Total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Fasting blood Sugar (mg/dl or mmol/l)					
≤140 (≤7.8) normal	111/184 (60.3%)	1		1	
>140 (>7.8)	74/99 (74.7%)	1.95 (1.13-3.34)	0.016	1.66 (0.93-2.98)	0.088
Total Cholesterol (mg/dl or mmol/l)					
≤200 (≤11.1) normal	105/150 (70%)	1.55 (0.95-2.53)	0.083		
>200 (>11.1)	80/133 (60.2%)	1			
Low density lipoprotein (LDL) (mg/dl or mmol/l)					
≤100 (≤5.6) normal	48/78 (61.5%)	1			
>100 (>5.6)	137/205 (66.8%)	1.26 (0.73-2.16)	0.404		
High density lipoprotein (HDL) (mg/dl or mmol/l)					
≤ 40 (≤2.2) abnormal	37/47 (78.7%)	2.20 (1.04-4.64)	0.038	2.43 (1.10-5.38)	0.028
> 40 (>2.2) normal	148/236 (62.7%)	1			
Triglyceride (mg/dl or mmol/l)					
≤ 150 (≤8.3) normal	116/177 (65.5%)	1.02 (0.62-1.69)	0.940		
>150 (>8.3)	69/106 (65.1%)	1			
HbA1c (% or mmol/mol)	24/40(60%)	1.31(0.66-2.60)	0.442		
≤ 7 (≤ 53)	161/243(66%)	1			
>7 (> 53)					
Duration of diabetes (years)					
1-4	50/74 (27%)	1.36 (0.73-2.54)	0.430		
5-8	72/105 (38.9%)	1.42 (0.80-2.51)			
8+	63/104 (34.1%)	1			
Diabetes treatment					
diet alone	26/48 (54.2%)	1.18 (0.70-20.01)	0.317		
oral medication+ diet	153/225 (68%)	2.13 (0.13-34.46)			
insulin injection+diet	5/8 (62.5%)	1.67 (0.07-37.73)			
Combined (oral medication+ insulin injection+diet	1/2 (50%)	1			
Diabetes complication					
Neuropathy					
-No	177/272 (65.1%)	1	0.603		
-Yes	8/11 (72.7%)	1.43 (0.37-5.52)			

Characteristics	Impair/Total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Retinopathy					
-No	160/237 (67.5%)	1.74 (0.92-3.31)	0.088		
-Yes	25/46 (54.3%)	1			
Nephropathy					
-No	159/244 (65.2%)	1			
-Yes	26/39 (66.7%)	1.07 (0.52-2.19)	0.855		
Co-morbid disease					
Heart disease					
-No	179/276 (64.9%)	1			
-Yes	6/7 (85.7%)	3.25 (0.39-27.40)	0.278		
Hypertension					
-No	47/74 (63.5%)	1			
-Yes	138/209 (66%)	1.12 (0.64-1.94)	0.696		
Chronic obstructive pulmonary disease (COPD)					
-No	182/279 (65.2%)	1			
-Yes	3/4 (75%)	1.60 (0.16-15.58)	0.686		
Gout					
-No	179/277 (64.6%)	1			
-Yes	6/6 (100%)	N/A	N/A		
Arthritis					
-No	183/280 (65.4%)	1			
-Yes	2/3 (66.7%)	1.06 (0.1-11.84)	0.962		
Dyslipidemia					
-No	131/204 (64.2%)	1			
-Yes	54/79 (68.4%)	1.2 (0.7-2.1)	0.512		
Asthma					
-No	182/279 (65.2%)	1			
-Yes	3/4 (75%)	1.6 (0.16-15.58)	0.686		
Others *					
-No	183/279 (65.6%)	1.91 (0.26-13.74)	0.522		
-Yes	2/4 (50%)	1			

*Thyroid/Anemia/Tuberculosis/Thalassemia/Osteoporosis

N/A: The predictor could not be applied to the analysis in the multivariate logistic regression because the analysis requires at least 10 positives and 10 negatives variables per predictor (Peacock and Kerry 2007).

8.6.2 Association between the predictors and cognitive impairment by MMSE Thai 2002

Table 8.10 shows that the participants aged 65-69, 70-74 and more than 74 are more likely to have cognitive impairment than the participants aged 60-64 (OR = 1.57, 95% CI 0.52, 4.75, OR = 1.84, 95% CI 0.61, 5.61 and OR = 6.10, 95% CI 2.37, 15.47). Participants who had a total cholesterol of more than 200 mg/dl or 11.1 mmol/l seemed to have more cognitive impairment than the participant who had total cholesterol of less than 200 mg/dl or 11.1 mmol/l (OR = 1.82, 95% CI 0.89, 3.75). Participants who never attended school were more probable to have cognitive impairment than the participants who attended school (OR = 8.24, 95% CI 3.01, 22.11).

The important characteristics which were independently associated with cognitive impairment by MMSE Thai 2002 were the aged group of more than 74 and never attending school (OR = 4.57, 95% CI 1.72,12.14 and OR = 6.19, 95% CI 2.12, 18.10 respectively) .

Table 8.10:Univariate and multivariate logistic regression of the MMSE Thai 2002

Characteristics	Impair/Total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Gender					
-Male	10/103 (9.7%)	1			
-Female	25/180 (13.9%)	1.5 (0.69-3.26)	0.306		
Age (years)					
60-64	8/121 (6.6%)	1	0.001	1	0.011
65-69	6/60 (10.6%)	1.57 (0.52-4.75)		1.50 (0.49-4.58)	
70-74	6/52 (11.5%)	1.84 (0.61-5.61)		1.30 (0.40-4.21)	
75+	15/50 (30.0%)	6.10 (2.37-15.47		4.57 (1.72-12.14)	
Education					
-Never attended school	9/19 (47.4%)	8.24 (3.01-22.11)	0.001	6.19 (2.12-18.10)	0.001
-Attending school	26/264 (9.8%)	1			
Year in school					
≤4	30/253 (11.9%)	1			
>4	5/30 (16.7%)	1.49 (0.53-4.178)	0.452		
Living alone					
- No	35/273 (12.8%)	N/A	N/A		
-Yes	0/10 (0%)	1			
Working					
-No	25/184(13.6%)	1.4 (0.64-3.05)	0.397		
-Yes	10/99 (10.1%)				
Smoking					
-No	32/263 (12.2%)	1			
-Yes	3/20 (15%)	1.27 (0.35-4.60)	0.711		
Drinking					
-No	34/260 (13.1%)	3.31 (0.43-25.36)	0.249		
-Yes	1/23 (4.3%)	1			
Exercise					
-No	20/134 (14.9%)	1.57 (0.77-3.20)	0.218		
-Yes	15/149 (10.1%)	1			
Body Mass Index(kg/m2)					
<23	18/119 (15.1%)	1.72 (0.77-3.82)	0.414		
23-25	6/47 (12.8%)	1.41 (0.50-4.10)			
>25+	11/106 (9.4%)	1			
Blood Pressure (BP)					
Systolic (mmHg)					
≤130 normal	14/112(12.5%)	1.02(0.50-2.10)	0.956		
>130	21/171(12.3%)	1			
Diastolic (mmHg)					
≤80 normal	24/180 (13.3%)	1.29 (0.60-2.75)	0.515		
>80	11/103 (10.7%)	1			

Characteristics	Impair/Total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Fasting Blood Sugar (mg/dl or mmol/l)					
≤140 (≤7.8) normal	19/184 (10.3%)	1			
>140 (>7.8)	16/99 (16.2%)	1.67 (0.82-3.42)	0.158		
Total Cholesterol (mg/dl or mmol/l)					
≤200 (≤11.1) normal	14/150 (9.3%)	1			
>200 (>11.1)	21/133 (15.8%)	1.82 (0.89-3.75)	0.103		
Low density lipoprotein (LDL) (mg/dl or mmol/l)					
≤100 (≤5.6) normal	7/78 (9%)	1			
>100 (>5.6)	28/205 (13.7%)	1.61 (0.67-3.84)	0.288		
High density lipoprotein (HDL) (mg/dl or mmol/l)					
≤ 40 (≤2.2) abnormal	4/47 (8.5%)	1	0.380		
> 40 (>2.2) normal	31/236 (13.1%)	1.63 (0.55-4.84)			
Triglyceride (mg/dl or mmol/l)					
≤ 150 (≤8.3) normal	23/177 (13%)	1.17 (0.56-2.46)	0.679		
>150 (>8.3)	12/106 (11.3%)	1			
HbA1c (% or mmol/mol)					
≤ 7 (≤ 53)	20/136(14.7%)	1.51 (0.74-3.10)	0.253		
>7 (> 53)	15/147(10.2%)	1			
Duration of diabetes (years)					
1-4	10/74 (28.6%)	1.00 (0.42-2.40)	0.760		
5-8	11/105 (31.4%)	0.75 (0.32-1.74)			
8+	14/104 (40.0%)	1			
Diabetes treatment					
diet alone	5/48 (10.4%)	N/A	0.737		
oral medication+ diet)	28/225 (12.4%)	N/A			
insulin injection+diet)	2/8 (25%)	N/A			
Combined (oral medication+ insulin injection+diet)	0/2 (0)%)	1			
Diabetes complication					

Characteristics	Impair/Total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Neuropathy					
-No	33/272 (12.1%)	1			
-Yes	2/11 (18.2%)	1.61 (0.33-7.78)	0.554		
Retinopathy					
-No	29/237 (12.2%)	1			
-Yes	6/46 (13%)	1.10 (0.42-2.76)	0.879		
Nephropathy					
-No	30/244 (12.3%)	1			
-Yes	5/39 (12.8%)	1.10 (0.38-2.90)	0.926		
Co-morbid disease					
Heart disease	33/276 (12%)	1			
-No	2/7 (28.6%)	2.95 (0.55-15.80)	0.207		
-Yes					
Hypertension	8/74 (10.8%)	1			
-No	27/209 (12.9%)	1.22 (0.53-2.83)	0.636		
-Yes					
Chronic obstructive pulmonary disease (COPD)	32/279 (11.5%)	1			
-No	32/279 (11.5%)	1			
-Yes	3/4 (75%)	23.16 (2.34-229.34)	0.007[a]		
Gout					
-No	33/277 (11.9%)	1			
-Yes	2/6 (33.3%)	3.70 (0.65-20.98)	0.140[a]		
Arthritis					
-No	33/280 (11.8%)	1			
-Yes	2/3 (66.7%)	15.0 (1.32-169.66)	0.029[a]		
Dyslipidemia					
-No	25/204 (12.3%)	1			
-Yes	10/79 (12.7%)	1.04 (0.47-2.27)	0.926		
Asthma					
-No	35/279 (12.5%)	N/A	N/A		
-Yes	0/4 (0%)	1			
Others *					
-No	34/279 (12.2%)	1			
-Yes	1/4 (25%)	2.40 (0.24-23.75)	0.454		

*Thyroid/Anemia/Tuberculosis/Thalassemia/Osteoporosis

[a] and N/A : The predictor could not be applied to the analysis in the multivariate logistic regression because the analysis requires at least 10 positives and 10 negatives variables per predictor (Peacock and Kerry 2007).

8.6.3 Association between the predictors and depression by TGDS

Table 8.11 shows that the female participants (OR = 1.68, 95% CI 0.88, 3.21), the participants aged 65-69, 70-74 and more than 74 (OR = 1.53, 95% CI 0.68, 3.45; OR = 2.72, 95% CI 1.25, 5.94 and OR = 1.53, 95% CI 0.65, 3.62 respectively), those who had less than 4 years in school (OR = 3.71, 95% CI 0.86, 16.07), those who did not work (OR = 2.21, 95% CI 1.11, 4.42), and did not exercise (OR = 1.89, 95% CI 1.04, 3.44) were also associated with depression.

Other clinical associations with depression were a high total cholesterol of more than 200 mg/dl or 11.1 mmol/l (OR = 1.60, 95% CI 0.88, 2.89), HDL of more than 40 mg/dl or 2.2 mmol/l (OR = 2.26, 95% CI 0.85, 6.01), LDL of less than 100 mg/dl or 5.6 mmol/l (OR = 1.23, 95% CI 0.17, 1.18) and having retinopathy as a diabetes complication (OR = 3.07, 95% CI 1.54, 6.13).

Overall, the major important predictor for depression in this study was having retinopathy as the diabetic complication (OR = 3.28, 95% CI 1.57, 6.90).

Table 8.11: Univariate and Multivariate logistic regression of the TGDS

Characteristics	Impair/total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Gender					
-Male	15/103 (14.6%)	1			
-Female	40/180 (22.2%)	1.68 (0.88-3.21)	0.120		
Age (years)					
60-64	17/121 (14%)	1	0.098		
65-69	12/60 (20%)	1.53 (0.68-3.45)			
70-74	16/52 (30.8%)	2.72 (1.25-5.94)			
75+	10/50 (20%)	1.53 (0.65-3.62)			
Education					
-Never attended to school	6/19 (31.6%)	2.03 (0.73-5.60)	0.173		
-Attending the school	49/264 (18.6%)	1			
Year in school					
≤4	53/253 (20.9%)	3.71 (0.86-16.07)	0.080		
>4	2/30 (6.7%)	1			
Living alone					
- No	53/273 (19.4%)	1			
-Yes	2/10 (20%)	1.04 (0.21-5.03)	0.963		
Working					
-No	43/184 (23.4%)	2.21 (1.11-4.42)	0.025		
-Yes	12/99 (12.1%)	1			
Smoking					
-No	52/263 (19.8%)	1.40 (0.39-4.95)	0.605		
-Yes	3/20 (15%)	1			
Drinking					
-No	52/260 (20%)	1.67 (0.48-5.82)	0.424		
-Yes	3/23 (13%)	1			
Exercise					
-No	33/134 (24.6%)	1.89 (1.04-3.44)	0.038		
-Yes	22/149 (14.8%)	1			
Body Mass Index(kg/m2)					
<23	26/93 (21.8%)	1.21 (0.64-2.28)	0.582		
23-25	7/40 (14.9%)	0.76 (0.30-1.91)			
>25+	22/117 (18.8%)	1			
Blood Pressure (BP)					
Systolic (mmHg)					
≤130 normal	22/112(19.6%)	1.02(0.56-1.87)	0.943		
>130	33/171(19.3%)	1			

Characteristics	Impair/total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Diastolic (mmHg)					
≤80 normal	37/180 (20.6%)	1.22 (0.66-2.28)	0.529		
>80	18/103 (17.5%)	1			
Fasting Blood Sugar(mg/dl or mmol/l)					
≤140 (≤7.8)	37/184 (20.1%)	1.13 (0.61-2.12)	0.696		
>140 (>7.8)	18/99 (18.2%)	1			
Total Cholesterol (mg/dl or mmol/l)					
≤200 (≤11.1)	24/150 (16%)	1			
>200 (>11.1)	31/133 (23.3%)	1.60 (0.88-2.89)	0.123		
Low density lipoprotein (LDL) (mg/dl or mmol/l)					
≤100 (≤5.6)	17/78 (21.8%)	1.23 (0.17-1.18)	0.103		
>100 (>5.6)	38/205 (18.5%)	1			
High density lipoprotein (HDL) (mg/dl or mmol/l)					
≤ 40 (≤2.2)	5/47 (10.6%)	1	0.103		
> 40 (>2.2)	50/236 (21.2%)	2.26 (0.85-6.01)			
Triglyceride (mg/dl or mmol/l)					
≤ 150 (≤8.3)	34/177 (19.2%)	1			
>150 (>8.3)	21/106 (19.8%)	1.04 (0.57-1.91)	0.901		
HbA1c (% or mmol/mol)					
≤7 (≤ 53)	28/136 (20.6%)	1.15(0.64-2.08)	0.637		
>7 (> 53)	27/147 (18.4%)	1			
Duration of diabetes (years)					
1-4	15/74 (27.3%)	1.07(0.51-2.26)	0.977		
5-8	20/105 (36.4%)	1.0 (0.50-1.97)			
8+	20/104 (36.4%)	1			
Diabetes treatment					
diet alone	15/48 (31.2%)	0.455 (0.027-7.766)	0.132		
oral medication+ diet	39/225 (17.3%)	0.210 (0.013-3.425)			

Characteristics	Impair/total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Insulin-injection+diet	0/8 (0%)	N/A			
Combined (oral medication+ insulin injection+diet)	1/2(50%)	1			
Diabetes complication					
Neuropathy					
-No	54/272 (19.9%)	2.48 (0.31-19.77)	0.392		
-Yes	1/11 (9.1%)	1			
Retinopathy					
-No	38/237 (16%)	1		1	
-Yes	17/46 (37%)	3.07 (1.54-6.13)	0.001	3.28 (1.57-6.36)	0.002
Nephropathy					
-No	50/244 (20.5%)	1.75 (0.65-4.71)	0.266		
-Yes	5/39 (12.8%)	1			
Co-morbid disease					
Heart disease	54/276 (19.6%)	1.46 (0.17-12.38)	0.729		
-No	1/7 (14.3%)				
-Yes					
Hypertension	13/74 (17.6%)	1			
-No	42/209 (20.1%)	1.18 (0.59-2.35)	0.637		
-Yes					
Chronic obstructive pulmonary disease (COPD)					
-No	54/279 (19.4%)	1			
-Yes	1/4 (25%)	1.39 (0.14-13.61)	0.778		
Gout					
-No	53/277 (19.1%)	1	0.395		
-Yes	2/6 (33.3%)	2.11 (0.38-11.84)	0.395		
Arthritis					
-No	54/280 (19.3%)	1			
-Yes	1/3 (33.3%)	2.09 (0.19-23.50)	0.550		
Dyslipidemia					
-No	38/204 (18.6%)	1			
-Yes	17/79 (21.5%)	1.20 (0.63-2.28)	0.582		
Asthma					
-No	55/279 (19.7%)	N/A	N/A		
-Yes	0/4 (0%)	1			

Characteristics	Impair/total (%)	Univariate logistic regression		Multivariate logistic regression	
		OR (95% CI)	P	OR (95% CI)	P
Others *					
-No	55/279 (19.7%)	N/A	N/A		
-Yes	0/4 (0%)	1			

*Thyroid/Anemia/Tuberculosis/Thalassemia/ Osteoporosis

N/A : The predictor could not be applied to the analysis in the multivariate logistic regression because the analysis requires at least 10 positives and 10 negatives variables per predictor (Peacock and Kerry 2007)

8.7 Relationship between cognitive impairment and depressive mood (controlling for potential confounders)

As documented in Chapter 2, the variables potentially confounding the cognitive screening test and depressive mood screening test in Thai population are age and years of education (Wongchaisuwan et al. 2005, Thaneerat et al. 2009). Thus, partial correlations were performed to examine the relationship between the cognition scores and depressive mood scores while adjusting for the effects of variables such as age and years of education.

Age and years of education are most likely to be positive confounders. The association between cognitive impairment and depressive mood is more extreme. On controlling, this would be expected to weaken the association (Pallant 2009) (see Tables 8.12 - 8.14).

Table 8.12: Correlation coefficients between cognitive function scores and TGDS scores (partial correlations controlling age)

Scores	Mini-Cog	MMSE Thai 2002
TGDS	-0.2*	-0.3**

* p<0.01 ** p<0.001

After controlling age, the depressive mood scores were significantly negative and correlated with cognitive scores by Mini-Cog (r_s = -0.2, p<0.01). Similarly, the depressive mood scores were significantly negative and correlated with cognitive scores by MMSE Thai 2002 (r_s = -0.3, p<0.001).

Table 8.13: Correlation coefficients between cognitive function scores and TGDS scores (partial correlations controlling years of education)

Scores	Mini-Cog	MMSE Thai 2002
TGDS	-0.1*	-0.2**

* $p<0.05$ ** $p<0.001$

After controlling for the years of education, the depressive mood scores were significantly negative and correlated with cognitive scores by Mini-Cog (r_s = -0.1, $p<0.05$). Similarly, the depressive mood scores were significantly negative and correlated with cognitive scores by MMSE Thai 2002 (r_s = -0.2, $p<0.001$).

Table 8.14: Correlation coefficients between cognitive function scores and TGDS scores (partial correlations controlling for age and years of education)

Scores	Mini-Cog	MMSE Thai 2002
TGDS	-0.1	-0.2*

* $p<0.01$

After controlling the age and years of education, the depressive mood scores were still significant and correlated with cognitive scores from MMSE Thai 2002 (r_s = -0.2, $p<0.01$) but there was no significant correlated between the depressive mood scores and cognitive scores from Mini-Cog (r_s = -0.1, p = 0.06).

Overall, the negative correlation coefficients in Tables 8.12-8.14 show that higher level of depression scores was associated with lower level of cognitive function. This implies that the participants who had high scores in depressive mood screening test (scores > 12 showing low mood) tended to have low level of cognitive function (scores ≤ 2 for Mini-Cog and scores ≤ 14 for MMSE Thai 2002 showing low cognitive function).

It can be seen from Tables 8.12 - 8.14 that the scores from Mini-Cog and MMSE Thai 2002 were modest negatively correlated with TGDS scores. It shows that the higher score (cognitive impairment) in Mini-Cog and MMSE Thai 2002 were associated with the lower score in TGDS (depressive mood). In other words, the participants who had cognitive impairment seemed to have depressive mood.

In order to see the correlation between Mini-Cog and MMSE Thai 2002, the Spearman correlation was analysed. As can be observed in Table 8.15, there was a significant positive correlation between the scores of Mini-Cog and MMSE Thai 2002 with Spearman's rank order correlation coefficient r_s = 0.44, P= 0.001. It is clear that the scores in Mini-Cog were moderate positively correlated with the scores in MMSE Thai 2002. The higher score in Mini-Cog were associated with the higher score in MMSE Thai-2002. Therefore, it was shown that Mini-Cog and MMSE Thai 2002 screening tests yielded the results in the same direction.

Table 8.15: Correlation coefficients between the scores of Mini-Cog Thai version and MMSE Thai 2002

	MMSE Thai 2002	
	Spearman rho(r_s)	p
Mini-cog	0.44	0.001

For the agreement between Mini-Cog and MMSE Thai 2002, the kappa agreement was analysed. As can be seen in Table 8.16, Mini-Cog and MMSE Thai 2002 agreed on the result of 'impaired' (4.9%) and 'not impaired' (27.2%). In 60.4% of the cases Mini-Cog disagreed with MMSE Thai 2002 on 'not impaired'. In total, the agreement on the 'impaired' and 'not impaired' between Mini-Cog and MMSE was 32.1%. The Kappa (K) statistics for the agreement between the Mini-Cog and MMSE Thai 2002 was less than chance agreement with K = -0.1, p= 0.001 , 95% CI -0.169, -0.031 (Altman, 1991) (see Section 6.10 for the levels of agreement).

These findings show that Mini-Cog and MMSE Thai 2002 were in potential disagreement between the results of cognitive impairment.

Table 8.16: 2x2 Table of the agreement between the Mini-Cog and MMSE Thai 2002

		MMSE Thai 2002		Total N (%)
		Impaired	Not impaired	
Mini-Cog	Impaired	14(4.9%)	171(60.4%)	185(65.4%)
	Not impaired	21(7.4%)	77(27.2%)	98 (34.6%)
Total N (%)		35(12.4%)	248(87.6%)	283 (100%)

8.8 Comparison of the results (by cut-off scores) of cognitive and depressive mood screening tests between good and poor glycaemic control (HbA1c) groups

In order to see that participants who had good glycaemic control (HbA1c ≤ 7% or 53 mmol/mol) and poor glycaemic control (HbA1c > 7% or 53 mmol/mol) show similar or different patterns of scores in cognitive screening tests and depressive mood screening tests, the Man-Whitney U was conducted for the analysis.

Table 8.17: Comparison of the score results based on the cut-off score between good and poor glycaemic control

	Good glycaemic control (Hba1c ≤7% 53 mmol/mol) (N=136)	Poor glycaemic control (HbA1c > 7% 53 mmol/mol) (N=147)	P	95% CI of difference
Mini-Cog	3 (0-5)	3 (0-5)	0.215	-0.49-0.49
MMSE Thai 2002	22 (12-22)	22(16-22)	0.362	-1.10-1.10
TGDS	6 (0-22)	(0-25)	0.921	-2.77-0.77

*Data is presented in median (range)

As can be observed in Table 8.16, the data shows that there were no differences in the result scores of Mini-Cog, MMSE Thai 2002 and TGDS between the good and poor glycaemic control groups. The above result shows that the levels of glycaemic control between the good (HbA1c ≤ 7% or 53 mmol/mol) and poor (HbA1c > 7% or 53 momol/mol) glycaemic control might not have an impact on the score results of cognitive screening tests and depressive mood screening test in the current study. Therefore, it is unlikely that the level of glycaemic control in this study affects the score results of screening tests.

8.9 Summary

This chapter showed the substantial level of agreement (K = 0.8, p< 0.000) between the researcher and the RA. This information provides the support for the researcher and the RA in performing all screening tools in the same manner with reliable results in the main study. This study found 65.4% and 12.4% prevalence of cognitive impairment and 19.4% of depressive mood in Thai older people with type 2 diabetes at the primary care settings. The potential characteristics of cognitive impairment by Mini-Cog test are young old age (age < 75 years), having

years in school more than 4 years, high BMI (> 25 kg/m^2, poor level of HDL (<40 mg/dl or 2.2 mmol/l), whereas the potential characteristics of cognitive impairment by MMSE Thai 2002 are old age (age 75+ years) and never attending school. Retinopathy was found to be a strong predictor for depressive mood in the current study. The results also showed that cognitive impairment was related to depressive mood. This means that the diabetic patients who had cognitive impairment seemed to have depressive mood and vice versa. However, the study did not find the differences of score results (by the cut-off point) in cognitive and depressive mood screening tests between the good and poor control of glycaemic control (HbA1c). This shows that either good or poor level of glycaemic control did not relate to the cognitive impairment and depressive mood in this study. In order to see whether the findings in the current study support or differ from the previous studies and the existing knowledge, the discussion of the findings including the difference of prevalence rate between Mini-Cog and MMSE Thai 2002 and implications of the prevalence study will be presented in the next chapter.

Chapter 9

Discussion

This is the first epidemiological cross-sectional study of the prevalence of undiagnosed cognitive impairment and the prevalence of undiagnosed depressive mood in Thai older people with type 2 diabetes in Thai primary care settings. The aims of the study areas are the following:

a) estimating the prevalence of cognitive impairment in rural Thai older people (aged 60+ years) with type 2 diabetes who have never received a diagnosis of cognitive impairment
b) estimating the prevalence of depressive mood in rural Thai older people (aged 60+ years) with type 2 diabetes who have never received a diagnosis of depressive mood
c) examining the association between cognitive function and depressive mood
d) examining the relationship between the cognitive function or depressive mood and glycaemic control

This chapter discusses the findings of the study in relation to the relevant literature and existing knowledge. The discussion is presented in accordance with the research findings.

9.1 The characteristics of the groups with and without HbA1c test

The data of demographic and clinical characteristics between the groups with and without HbA1c was different in the following variables (see Tables 8.6 and 8.7 in Chapter 8):

9.1.1 Living arrangement

The data in Table 8.6 shows that the group without HbA1c test tended to live alone compared to the group with HbA1c test ($p = 0.048$). The criteria of diabetic patients who received the HbA1c test in this study setting depended on the ability of having a good control of blood sugar by FBS. Thus, it is possible that living alone might have an impact on the ability to control blood sugar. Living alone

influences the ability to control blood glucose level in terms of diabetic self-care of the patients. Diabetes is a life-long disease that requires daily planning and decision-making (Thorne et al. 2003). In this long process, social support is crucial for diabetic patients in terms of sharing emotions and feelings or receiving help from family and friends in everyday life to achieve a good glycaemic control (Lo 1999, Toljamo and Hentinen 2001). In addition, it is possible that lack of social support may lead to less attention and adherence to self-care among patients with diabetes (Cameron 1996). As a result, this study supports the previous studies of Lo 1999, and Toljamo and Hentinen 2001 showing that living alone may have an impact on poor blood sugar control. Therefore, it is more likely for health care staff to be aware of poor control of blood sugar level in the older people who live alone.

9.1.2 Clinical characteristics

As expected, based on the selection criteria of HbA1c test in the setting, the group with HbA1c seemed to be healthier than the group without HbA1c test. Table 8.7 shows that the group with HbA1c test had a better control of BMI, FBS and total cholesterol than the group without HbA1c with statistically significant differences ($p=0.043$, $p=0.000$, $p=0.017$, respectively). The data also shows the significant difference in diabetes treatment and duration between the groups with and without HbA1c test ($p=0.006$, $p=0.003$, respectively). The difference of these characteristics is explained below.

The number of the participants in the group with HbA1c test who were on diet control (no medication) was higher than the group without HbA1c test. According to the clinical practice guideline of diabetes in Thailand (Diabetes Association of Thailand 2011), diabetic patients who have a blood sugar (FBS) between 126-200 mg/dl or 7-11.1 mmol/l do not receive medication and instead they receive self-care knowledge from the health staff in order to reduce their blood sugar level by exercising or increasing physical activity and having healthy nutrition (reduced food that contains high levels of sugar and fat). After 3 months of self-control regime, the health staff checks the blood sugar level (FBS) of the patients again to see whether the patients should receive anti-diabetic medicine. This information implies that the participants in this study who were on diet alone (without

medication) may have the range of blood glucose level that was in an early stage of diabetes. Thus, the possibility is that the progress and metabolic control were not complicated for the individuals care, and that the disease had a low impact on health conditions (Turner 2008). These could be the reasons why the group with HbA1c test containing a higher number of participants who were on diet alone (without medication) had a better control of blood glucose level (FBS) and some clinical variables (BMI and cholesterol) than the group without HbA1c.

In addition, Table 8.7 (Chapter 8) shows that there were a number of participants in the group without HbA1c who had a diabetes duration of 1-4 years more than the participants in the group with HbA1c. Snoek (2002) states that the diagnosis of diabetes may come as a shock, and can induce serious emotional distress in patients. Diabetic patients have an individual psychological adjustment varying from several months to one year after the diagnosis because they have to learn and integrate diabetes into their daily lives (Snoek 2002). For example, patients always have to think about what they can or cannot eat. This is found to be burdensome for the patients in an early state of the disease. Thus, stress and anxiety can seriously disrupt an ability to control blood glucose level (Engum 2007). It is possible that the psychological problems in the early stage of diabetes may have an impact on the self-control of blood sugar in this study. Therefore, compared to the group with HbA1c, the group without HbA1c seemed to have a poorer control of blood sugar.

Summary of the characteristics

Due to the lack of social support and help from family members, living alone was a demographic characteristic that might have an impact on the ability to control blood glucose in the older people. In addition, it was found that compared to the group without HbA1c test, the group with HbA1c test had a higher number of participants who were on diet alone (without medication). The treatment without medication may describe the early stage of diabetes with an uncomplicated metabolic control. Therefore the group with HbA1c test showed a better control of BMI, FBS and cholesterol compared to the group without HbA1c test. Moreover, the data indicates that the group without HbA1c test had a higher number of participants with a diabetes duration of 1-4 years than the group with HbA1c. It

could be possible that the psychological adjustment in the beginning period of diabetes may affect the ability to control the blood sugar level. Thus, the group without HbA1c had a poorer control of their blood sugar compared to the group with HbA1c.The information of the characteristic differences between the group with and without HbA1c may be useful for the health care staff to consider the potential factors that may affect the ability to control blood sugar level in this selected population.

As mentioned in chapter 1, glycaemic control is fundamental in the management of diabetes (Llorente and Malphurs 2007). Glycaemia control by HbA1c is the most accepted indicator. It accurately reflects a longer-term glycaemic control (Saudek et al. 2006). In addition, glycaemic control (HbA1c) appears to play a role and may relate to cognitive impairment and depressive mood in the older people with type 2 diabetes (see chapter 2). Therefore, it would be of interest to see whether glycaemic control (HbA1c) is related to cognitive impairment and depressive mood in this study.

Not all participants in this study received HbA1c measurement. The selection bias was checked by comparing the prevalence of the outcome measures (prevalence of cognitive impairment and depressive mood) between the groups with and without HbA1c. The results show that there is no difference between the two groups in terms of the outcome measures (Mini-Cog, $p = 0.895$, 95% CI 0.073, 0.085, MMSE Thai 2002, $p = 0.920$, 95% CI -0.052, 0.058 and TGDS, $p = 0.995$, 95% CI -0.066, 0.066 in Table 8.8). The importance of the use of HbA1c test in the study protocol and methodology was mentioned in Chapters 5 and 7. In brief, this study intends to 1) assess the generalisability of the association between HbA1c test and the prevalence of cognitive impairment / depressive mood, and 2) estimate the effect of poor glycaemic control (indicated by the presence of HbA1c result) on the prevalence of both cognitive impairment and depressive mood.

9.2 The prevalence of possible cognitive impairment and depressive mood

9.2.1 The prevalence rate of possible cognitive impairment by Mini-Cog and MMSE Thai 2002

It was discussed in Chapter 2 that the prevalence of cognitive impairment in the older people with type 2 diabetes in many regions including Thailand was found to be 11.3% - 77.6% (see Table 2.1). The prevalence rates in each study depend on the study purposes, study tools and cut-off scores. It should however be noted that Thaneerat et al.'s 2009 study in Thailand focused on the prevalence rate of mild cognitive impairment (MCI) instead of cognitive impairment. Thus, the MoCA test, a specific tool for screening MCI, was used to estimate the prevalence rate of mild cognitive impairment, while the other previous studies used MMSE as a screening tool for screening cognitive impairment. As a result, it could be possible that the estimated rate of cognitive impairment in the previous study in Thailand show the distinctly high rate of (77.6%) compared to the other previous studies (Bruce et al. 2002, Bruce et al. 2003, Munshi et al. 2006, Rajakumaraswamy et al. 2008, Alencar et al. 2010). Apart from MoCA test, by using MMSE as a screening tool the range of estimated rate from many regions was shown to be between 11.3-32.8% (see Chapter 2).

This study estimates the prevalence of cognitive impairment in Thai older people with type 2 diabetes by Mini-Cog and MMSE Thai 2002 to be 65.4% (95% CI 59.7%, 70.7%) and 12.4% (95% CI 9.0%, 16.7%), respectively (see Table 8.8). The prevalence rate by Mini-Cog agrees with the previous study in Thailand that reveals the prevalence rate of mild cognitive impairment (MCI) in the older people with type 2 diabetes to be 77.6% (Thaneerat et al. 2009). The previous study (Thaneerat et al. 2009) used MoCA as a screening tool and showed only the estimated rate of MCI rather than dementia. The MoCA is specifically used to screen the clinical state between normal cognitive ageing and mild state of cognitive impairment (Nasreddine et al. 2005, Smith et al. 2007). The current finding confirms Thaneerat et al.'s (2009) study in Thailand, and shows that the cognitive impairment among Thai older people with type 2 diabetes is found not only in the hospital setting but also in the primary care setting.

This study shows the estimated rate of cognitive impairment by MMSE Thai 2002 to be 12.4% (95% CI 9.0%, 16.7%). This result is similar to the ones in the literature (see Chapter 2, Table 2.1) indicating that in Brazil the estimate is 12.1% and in Australia the rate is 15.3% (Bruce at al. 2003, Alencar et al. 2010). The rate of cognitive impairment in Australia is 2.9% higher than the current study. This may probably be due to the differences in the cut-off scores of the study tools. As mentioned earlier in Chapter 3, Section 3.1.1, MMSE was developed in an English speaking country, where education level is high with a standard cut-off score of 24, that is, a score of 23 or below is considered to have cognitive impairment. However, when using MMSE in non-English speaking countries with a high rate of low-educated population (Salmon and Lange 2001), it is suggested to adjust the cut-off score according to education levels in those countries (Liu et al. 1994, Caldas et al. 2011). Therefore, the study in Australia used the higher cut-off scores of MMSE compared to MMSE Thai 2002. Whereas, the study in Brazil used MMSE with the cut-off score similar to MMSE Thai 2002, particularly in subjects with a low level of education. Thus, the rate of cognitive impairment in Brazil is very close to the current study with a small difference of 0.3%.

This study can be compared with the study in Sri Lanka (Rajakumaraswamy et al. 2008), in which the prevalence of cognitive impairment in the older people with type 2 diabetes by MMSE is 32.8 % (see Chapter 2, Table 2.1). It is possible that the estimated rate in this study is 20.4 % lower than the study in Sri Lanka due to the high cut-off score (less than 25) in Sri Lanka's study, yielding the high estimate rate of cognitive impairment. The study in Sri lanka did not report the education levels of subjects. As stated above, when MMSE is used in a non-English speaking group, the cut-off score should be adjusted according to the variety of education levels, particularly in developing countries (Salmon and Lange 2001). Thus, using one cut-off score for all education levels in Sri lanka's study may have caused the high prevalence rate of cognitive impairment. The finding in this study shows a similar prevalence rate when compared to the study of Munshi et al. (2006) in the United States. In addition, the difference of prevalence rate in cognitive impairment between the Mini-Cog and MMSE in this study reveals a similar pattern to that of Munshi et al.'s study. The present study shows the prevalence rate of Mini-Cog is higher than MMSE Thai 2002 (64.5% vs. 12.4%).

Similarly, Munshi's study reveals that the prevalence rate of cognitive impairment from clock-drawing test (CDT) (38%) and the prevalence rate of cognitive impairment from clock-in-a-box (CIB) (35%) are higher than the prevalence rate of cognitive impairment by MMSE (12.5%) (see Chapter 2, Table 2.1).

As mentioned earlier in Chapter 2, the prevalence rate of cognitive impairment in each study is affected by a variety of cut-off points of MMSE and sample size. The literature reveals the range of prevalence rate by MMSE to be between 11.3-32.8% (see Chapter 2, Section 2.1.3). This study supports the prevalence of cognitive impairment by MMSE in type 2 diabetes within the range of the previous rate and confirms the estimated rate of 12.4%.

There is a large difference of prevalence rate in cognitive impairment between Mini-Cog Thai version and MMSE Thai 2002 (64.5% vs. 12.4%). The difference between the two tests could be described as follows:

1. Since one third (10/30) of the total score in MMSE is orientation test, it is highly possible that the subjects who have good orientation but perform poorly in other cognitive domain tests would get the normal score range, particularly in the subjects who are illiterate or have low education level in which the low cut-off score would be used. For example, the orientation part contains 10 scores; hence, the subjects who are illiterate with good orientation but have poor function in other cognitive domains would easily get 10 scores from the total cut-off score of 14 if they pass one domain test. As a result, the participants who passed only one domain test (orientation test) of the total eleven tests could get a higher possibility of yielding the score result in normal range. In particular, when the lowest cut-off score is used in the group with illiterate or low education.

2. Short term memory and executive function (judgment, decision-making, planning), are found to have an impact on the early stage of cognitive impairment (Doerflinger 2007). The scores in these two parts are therefore important in the current study. With regard to the cognitive screening tests in this study focusing on different foci, Mini-Cog contains two tests of

short term memory and executive function, whereas MMSE includes a variety of 11 cognitive domain tests. The high score in some parts of MMSE may have a limitation in detecting cognitive impairment in early phases of dementia or mild cognitive impairment (MCI) (Blake et al. 2002, Bak et al. 2005, Woodford and George 2007). Thus, the subjects with good orientation may have poor short term memory loss, which is a significant initial sign of cognitive impairment and dementia (Ratchie and Lovestone 2002, Liorente and Malphurs 2007).

3. As stated earlier in Chapter 3, Section 3.1.1, MMSE is insensitive to the early stage of cognitive impairment or MCI (Nasreddine et al. 2005, Nazem et al. 2009, Aggarwal and Kean 2010). In addition, MMSE does not contain an executive function task which is the domain that found to be altered in the early stage of Alzheimer's disease (AD) (Munshi et al. 2006, Hatfield et al. 2009). In contrast, Mini-Cog consists of clock drawing test (CDT) which is an executive function test. Therefore, it is possible that the Mini-Cog is more likely to be sensitive than MMSE Thai 2002 in detecting people with an early stage of cognitive impairment or mild cognitive impairment. This explanation is supported by Munshi et al. (2006) stating that MMSE has a limitation on specificity (specificity = 64%, sensitivity = 96%) and executive function tests (see Chapter 2). Thus, in their study the clock drawing test (CDT) and clock in a box (CIB) which are specifically designed for executive function tests, detected a higher number of people with cognitive impairment compare to that of MMSE. As a result, the prevalence rate of cognitive impairment by CDT and CIB in Munshi et al.'s study was higher than the prevalence rate of cognitive impairment by MMSE (See Chapter 2, Sections 2.1.2 and section 9.2.1). Moreover, the prevalence rate of cognitive impairment in this study is confirmed with the previous study in Thailand (Thaneerat et al. 2009) which found that the prevalence rate of mild cognitive impairment (MCI) in Thai older people with type 2 diabetes (aged 60+) in hospital setting was 77.6% (see Section 9.2.1).

4. The difference of prevalence rate between the two cognitive screening tests may come from disease spectrum bias, which is the phenomenon of the sensitivity and/or specificity of a test varying with features and severity of disease (Sica 2006, Leeflang et al. 2009). In this study, MMSE Thai 2002 is highly specific but less sensitive in identifying cognitive impairment, particularly in illiterate subjects (sensitivity = 0.35, specificity = 0.81) and educated primary school subjects (sensitivity = 0.57, specificity = 0.94) (Ageingthai 2008). As a result, the screening test of MMSE Thai 2002 may be unable to detect the cognitive impairment in the group with low education which consisted of 89.6% of the total participants (Table 8.6). This information is supported by previous studies which have found that MMSE is insensitive in subjects with an early stage of cognitive impairment due to the low sensitivity of the test and being less concerned with the subtypes of dementia (Wind et al. 1997, Nasreddine et al. 2005, Heiss et al. 2006, Munshi et al. 2006, Hatfield et al. 2009). Alternatively, it could be possible that there were a higher number of participants in the early stage of cognitive impairment or mild cognitive impairment (MCI) in the current study.

In summary, the prevalence of cognitive impairment in the older people with type 2 diabetes supports and agrees with the previous studies either in Thailand or other countries. However, the difference of prevalence rate between Mini-Cog Thai version and MMSE Thai 2002 may result from the low sensitivity of MMSE Thai 2002 in detecting cognitive impairment in the low education group and at the early stage of cognitive impairment or mild cognitive impairment (MCI). It is possible that in the current study, Mini-Cog is more likely to be sensitive and identify a higher number of participants with an early stage of cognitive impairment than MMSE Thai 2002 due to a high number of participants with an early stage of cognitive impairment or MCI.

9.2.2 The prevalence of possible depressive mood by TGDS

The estimated rate of depression in this study was found to be 19.4% in the older people with type 2 diabetes (Table 8.8). This finding agrees with the previous studies that showed the prevalence of depression in diabetes between 13.2%-33.4% (see Chapter 2). However, compared with the previous study in Thailand, the figure rate in the current study is lower and this is probably due to the difference in study setting and screening tool. The previous study in Thailand was conducted in a hospital setting where the number of depressed patients may be higher than the primary care setting, particularly in an urban area (Akepakorn et al. 2007, Suttajit et al. 2010). Another explanation is that the previous study used the Hospital Anxiety Depression Scale (HAD) as the screening tool for depression. Therefore, it could be possible that the screening tool in the previous study detected not only depression but also anxiety in the patients with type 2 diabetes (Snaith 2003). It is difficult to compare the estimated rate in this study with those of other studies in literature because of the different assessments. Although one study from the United States (Munshi et al. 2006) used the same depressive mood-screening test, the depression rate could not be clearly compared due to the small sample size (60 subjects) of the previously mentioned study.

Similar to the prevalence of cognitive impairment in type 2 diabetes, the wide range of reported prevalence of depression in type 2 diabetes is not only from the assessments but also due to several factors such as the characteristics of the sample size, the age range of the sample, the clinical symptom of depressive disorders and the study setting. Overall, the finding demonstrates that the prevalence rate (19.4%) of depressive mood concurs with the previous studies and that depression appears to be a common co-morbid health problem in the primary care patients with type 2 diabetes. In the present study, 19.4% of the older patients with type 2 diabetes were undiagnosed of depressive mood in the primary care setting at San-sai district. In addition, the prevalence rate is concordant with the range of depressive mood at the primary care setting in the previous studies in which the rate showed between 14.2-33.0% (see Chapter 2).

9.3 Predictors associated with possible cognitive impairment and depressive mood

9.3.1 Major predictors associated with possible cognitive impairment

This section reveals the important characteristics associated with cognitive impairment by Mini-Cog Thai version and MMSE Thai 2002 (see Tables 8.9-8.11). Each characteristic will now be discussed in turn.

a) The aged group

One of the important factors for cognitive impairment by Mini-Cog is being aged less than 75.This study is in contrast with the study of Scanlan et al. (2007) which is the only study that used Mini-Cog in the older people with type 2 diabetes (16 % of the total subjects) and found that cognitive impairment increas with age. This contradiction is probably due to the difference in age group between this study and the previous studies. This study shows the mean age of 67 whereas the mean age in the previous study was 75. In addition, the highest proportion (40%) of the individual age group in the current study was the younger old aged (60-64 years old). It can be observed that this study had a sample with the mean age lower than the previous studies and also had a high proportion of sample in the younger old age; hence, the result in this study may rely on the younger old age (less than 75 years old). In addition, the Thai older people had the average life expectancy of 74 in both female and male, thus most of the older people subjects in this study were younger old age (less than 75 years old) (United Nations 2011). Compared to the previous study, it could be possible that the Thai older people had a life expectancy shorter than the previous study conducted in Italy (78 vs. 85 for females, 71 vs.79 for males) (United Nations 2011). Therefore the Italian older subjects in the previous study seem to be healthier and live longer than the older people subjects in Thailand.

Unlike the individual characteristics associated with cognitive impairment by Mini-Cog, old age (aged more than 74 years old) was found to be a strong predictor related to cognitive impairment by MMSE Thai 2002. This is probably because the older people (over 65 years of age) with the chronic diseases are

generally found to be impaired in learning and verbal memory as well as in psychomotor functioning (Asimakopoulou and Hampson 2002, Worrall et al. 1993). In addition, Ryan and Geckle (2000) proposed that learning and memory impairment in older adults with type 2 diabetes may be the result of "a synergistic interaction between diabetes-related metabolic derangements and the structural and functional changes occurring in the central nervous system that are part of the normal aging process" (p. 308). Thus, it could be possible that the diabetic subjects aged more than 74 in this study may fail in learning and memory parts of MMSE Thai 2002.

Although age group was found to be a strong predictor associated with cognitive impairment in both Mini-Cog and MMSE Thai 2002, the range of the age group was different. The younger old age (less than or equal 74 years) was an individual characteristic for Mini-Cog, while the old age (more than 74 years) was the strong predictor in MMSE Thai 2002. This difference is probably because MMSE Thai 2002 was unable to detect the early state of cognitive impairment (see Section 9.2.1). In addition, it could be possible that the participants in the younger old age group (less than 75 years) had a mild cognitive impairment, while the old age group (more than 75 years) had a moderate to severe cognitive impairment, which is the level MMSE could clearly detect better than the mild level of cognitive impairment.

b) Never attending school

Never attending school is a strong predictor for cognitive impairment by MMSE Thai 2002. This finding is in line with the study of Ishizaki et al. (1998) which investigated the cognitive impairment in a community based data and found that ageing and poor education are the risk factors for cognitive impairment by MMSE. They demonstrated that not only the education level not only influences the total score on MMSE but affects the clinical care of the participants. This might have an impact on health and cognitive function. This explanation agrees with the previous studies which support that participants with a low education have a reduced cognitive reserve and lead to an earlier manifestation of the distinctive signs and symptoms of dementia in the screening test (Scarmeas et al. 2006, Musicco et al. 2009). This information implies and supports the unclear MMSE result when used

in the low education group. Although this study used the cut-off score with the level of education in Thai subjects, low sensitivity of cut-off score in the illiterate group may provide ambiguous results. Thus, a further study using a neuropsychological test battery such as the Addenbrooke's Cognitive Examination-Revised (ACE-R), an extended version of MMSE which covers a wider range of cognitive domains (Hodges, 2007) may be needed to produce clearer results of MMSE in illiterates.

c) Years in school

More than 4 years of attending school is a potential predictor for cognitive impairment by Mini-Cog. Although the original version of Mini-Cog (English version) is not affected by education (Borson et al. 2000), this study finds out that the participants who attended school for more than 4 years showed an increased possibility of having cognitive impairment. 89% of the participants had less than 4 years of school and 11 % of the participants had more than 4 years of school (see Table 8.6). When compared to the study of Mini-Cog in the non-English version (Italian) which contains average years in school similar to this study (5 years), the study in Italy shows that 33% of the subjects have less than 4 years of school, 54% with 5-8 years in school and 13% with more than 9+ years in school (Scanlan et al. 2007). Thus, it can be seen that the data in the current study does not contain homogeneous distribution with regard to the level of education compared to the previous study in Italy. As a result, a huge difference in the proportion of years in school provides the wide range of confidence interval (CI) around the odd ratio (OR= 9.31, 95% CI= 2.11, 41.05). The data implies that this study still needs a larger sample to investigate the effect of education on the cognitive impairment as measured by Mini-Cog.

d) High BMI

This study reveals that a high range of BMI (BMI 23-25 kg/m^2 and more than 25 kg/m^2) is one of the predictors of cognitive impairment by Mini-Cog. This finding agrees with the review study of Berge et al. (2009) on the effect of obesity related to cognitive impairment. The review assesses six population-based study designs which used BMI cut-off 25 kg/m^2 and over as a measure of obesity and compared cognitive performance in the individual subjects. Overall, they found that the

association between obesity and cognition differ across the individual domains: cognitive flexibility was significantly affected in 67%, perception and construction was affected in 50%, memory 40%, and processing speed 33%. In addition, the study of Gustafson (2003) reveals an association between being overweight (BMI $\geq$ 25 kg/m^2) and the age of 70 increasing the risk of Alzheimer's disease (AD) in women. They show that after controlling a number of potential confounders, the relationship between BMI and AD still remained. Moreover, three previous studies have shown that midlife obesity measured by BMI was approximately two to five-fold and increased the risk of mild cognitive impairment (MCI) and dementia (Rosengren et al. 2005, Whitmer et al. 2005, Lu et al. 2012). This information shows that obesity or high BMI affects cognitive function and is related to cognitive impairment.

The link between obesity or high BMI and cognitive impairment could be explained with the following possibilities. First, people with high BMI may have a higher adipose tissue which underlines many of cardiovascular diseases such as hypertension, cardiovascular disease including diabetes. Thus, it is possible that the high BMI may lead to these conditions that could aggravate the process of dementia (Gustafson et al. 2003). Second, adipose tissue is an active endocrine organ that produces adipokines known to have both pro and anti-inflammatory properties including adiponectin, leptin, resistin, as well as pro-inflammatory cytokines such as interleukin-6 (IL-6) (Trujillo et al. 2005). A high level of IL-6 is associated with accelerated cognitive impairment in older adults with metabolic syndrome (Yaffe et al. 2004). In addition, two studies have shown that decreasing brain levels of proinflammatory cytokines can reverse memory deficits (Balschun et al. 2004, Gemma et al. 2005). Therefore, these mechanisms in body could affect the cognitive function in the brain.

It is possible that obesity or high BMI has an impact on Mini-Cog score through these mechanisms, particularly in the memory part. Therefore, the current study reinforces the role of obesity or high BMI associated with the risk of dementia.

It is important to mention that in this study BMI of 23 kg/m^2 and higher are moderate to high health risk. The cut-off BMI in this study is different from an

international classification of BMI, which defines the BMI of 23- 25 kg/m^2 as low to moderate health risk (World Health Organisation (WHO) 2000). The view of BMI cut-off at 23 kg/m^2 in this setting area is based on the recommendation from WHO expert consultation, which suggest that the percentage of body fat different BMIs varies within populations. They suggest that for many Asian populations trigger points for public health action are identified to be 23 kg/m^2 and higher (WHO expert consultant, 2004). Therefore, BMI of 23 kg/m^2 is set as the cut-off for moderate health risk in this setting area.

e) The level of HDL

Low level of HDL (less than 40 mg/dl or 2.2 mmol/l) is one of the clinical predictors of cognitive impairment by Mini-cog in this study. This result is in accordance with the study of Singh-Manoux et al. (2010) that found the low level of HDL (< 40 mg/dl or 2.2 mmol/l) is related to poor memory in middle-aged adults. They showed the association between low HDL and poor memory (OR = 1.73; 95% CI 1.20, 2.50) remained after the effect of education, occupation, prevalent disease, medication use and APOE4. A potent risk of Alzheimer's disease (AD) was adjusted. Total cholesterol and triglycerides levels did not show any association with memory decline in their study (P= 0.49 and P= 0.37, respectively). Considering that HDL plays a critical role in the maintenance of neuronal functions in the hippocampal neurons, there is a plausibility of a link between mild cognitive impairment (MCI) or AD and HDL (Michikawa 2003).

There are a number of possible mechanisms connecting the low level of HDL to memory. First, HDL is one of the important lipoproteins in the brain (Olesen and Dago 2000). It involves the regulation of Amyloid Beta (Aβ), protein metabolism and deposition in the brain (Reiss et al. 2004). Aβ has an essential role in the mechanisms of synaptic protein that underline learning and memory (Koudinov and Berezov 2004). The deposition of amyloid protein in the brain is the pathogenesis of AD. Second, a low level of HDL in the neurodegenerative process might involve its anti-inflammatory (Gauthier et al. 2006) or antioxidant properties (Singh-Manoux et al. 2008). Moreover, HDL can bind the excess Aβ and inhibit its oligomerisation (Olesen and Dago 2000), a step in the transformation of the monomeric nontoxic peptide to the aggregated neurotoxic form, which can account

for memory impairment (Lesne et al. 2006). Therefore, HDL may link to AD and poor memory through the variable biochemical mechanisms in the brain.

Overall, it could be summarised that the potential characteristics associated with cognitive impairment by Mini-Cog in this study are the younger old age group (equal or less than 74 years), attending school for more than 4 years, high BMI (more than 23 kg/m^2) and poor level of HDL (less than 40 mg/dl or 2.2 mmol/l). Meanwhile, the strong predictor associated with cognitive impairment by MMSE Thai 2002 includes those who never attended school and the old age group (more than 75 years). Since it is possible that Mini-Cog and MMSE Thai 2002 consist of different foci of the domain test including the limitation of MMSE Thai 2002 in the low education group (see section 9.2.1), it is not surprising to see the different results of the characteristics related to cognitive impairment between the two tests. More importantly, the current study shows that the potential clinical characteristics (BMI and HDL) of cognitive impairment by Mini-Cog are related to mild cognitive impairment (MCI). Therefore, this may confirm that Mini-Cog could detect the people with MCI. It also shows higher number of cognitive impairment than MMSE Thai 2002. However, the potential characteristic of years in school in Mini-Cog test needs a larger sample to confirm the results. The predictor of the characteristic of never attending school for MMSE Thai 2002 may also have limitations in the illiterate group. A further investigation using a diagnostic test would provide a clearer trend of the results.

9.3.2 The major predictor of depression

An important predictor of depression in the current study is retinopathy as a diabetes complication. This result agrees with a cohort study of depression and diabetic retinopathy in the United States which found that co-morbid depression has a significantly higher risk of developing diabetic retinopathy in 2,359 adults with type 2 diabetes (mean age 64) in the primary care settings. After five years of following up, their data showed that severity of depression was associated with the risk of retinopathy (OR = 1.026, 95% CI 1.002, 1.051). This information may imply that improving diabetic retinopathy treatment in the primary care could contribute to depressive mood prevention or vice versa. This finding is also

consistent with the study of Grot et al. (2001) which found that depression had a clinically significant association with retinopathy ($P < 0.00006$), nephropathy ($P < 0.0002$), neuropathy ($P < 0.0002$) and macro-vascular disease $P < 0.00001$) in a meta-analysis of 27 studies.

The results in this study are different from the previous study in Thailand which found that nephropathy is a strong predictor of depression in Thai older people with type 2 diabetes in the hospital setting (Thaneerat et al. 2009). The different result is probably due to the difference in the study settings. The current study was conducted in a primary care setting where medical resources and equipment were limited compared to the hospital setting. Thus, the suspected patient with diabetic nephropathy in the primary care will refer to the hospital care. Therefore, the number of diabetic retinopathy patients in primary care settings was higher than the number of diabetic retinopathy patients in the hospital settings (Nitiyanant 2007).

The link between diabetic retinopathy and depression may come from the malfunctioning of the hypothalamic-pituitary-adrenal axis, activation of the sympathetic nervous system and an increase in pro-inflammatory factors (Katon et al. 2005, Golden et al. 2007, Lustman et al. 2007). Depression, through the increase of cortisol (Miller et al. 2002, Katon et al. 2005) accompanied with inflammation may increase insulin resistance and glycaemic fluctuation which play roles in the progression of micro-vascular and macro-vascular complications in the patients with type 2 diabetes (Golden et al. 2007). Furthermore, it could be possible that in depressed patients, retinopathy could reflect the changing of cerebral micro-vascular associated with depression (Ding et al. 2010).

As mentioned in Chapter 1, depression and depressive symptoms might affect the neuroendocrine system and diabetes self-care behaviour. This could lead to an uncontrolled or increase in blood sugar level (hyperglycaemic) and glucose alteration in vascular system. Hence, type 2 diabetic patients are at risk of accelerated atherosclerosis and microvascular disease (Leiter 2005). Many clinical complications of diabetes are caused by small and large vessel pathology throughout the body. In addition, small vessels throughout the body are affected by

diabetes, including those in the brain, heart, and peripheral vascular system (Rambhade 2011). Normally, the vascular smooth muscle receives continuous regulatory nerve signals and a continual supply of vasodilating nitric oxide (NO) from blood vessels. These regulatory mechanisms adjust microvascular flow instantaneously to meet the metabolic needs of the tissue. A prolonged hyperglycaemia causes a thickening of capillary basement, which is found as a structural hallmark of diabetic microvascular disease. The thickening of the basement membrane impairs the amount and selectivity of transport of metabolic products and nutrients between the circulation and the tissue (Dokken 2008).

Overall, depression has an impact on diabetic retinopathy through biochemical processes leading to macro and micro-vascular lesions. This study therefore, reinforces the probability of diabetic retinopathy as a predictor of depressive mood in type 2 diabetes.

9.4 Correlation between cognitive impairment and depressive mood

The scores of both cognitive screening tests (Mini-Cog and MMSE Thai 2002) are negatively correlated with the score of depressive mood test (TGDS) in this study. This implies that the participants who had high scores in cognitive tests (showing possible cognitive impairment) seem to have low scores in depressive mood screening test (showing depressive mood). This study is consistent with the previous studies of Munshi et al. (2006), Zrebiec (2006), Katon (2010).

In addition, the association between the scores of cognitive screening tests and depressive mood screening test persisted after controlling age, years in school and potential confounding factors in cognitive and depressive mood screening test (Wongchaisuwan et al. 2005 Thaneerat et al. 2009). The correlation between cognitive impairment by Mini-Cog and depressive mood seem not to correlate after controlling age and years in school. As stated earlier in Section 9.2, this study has limitations in the heterogeneity of education in the population. The vast majority of the sample in this study (89%) had equal or less than 4 years in school. Therefore, the evidence is still ambiguous in the variable of years in school. However, the

result shows the trend of the correlation between cognitive impairment and depressive mood.

Depressive mood may relate to cognitive impairment in many possible ways. First, prolonged hypercortisolemia associated with depressive symptom may have negative impact on memory through hippocampal damage (O'Brien et al. 1996, Jacobson and Sapolsky 1991). Second, depressive symptoms are common in diabetic patients and may hinder their ability to adhere to diet, physical activity and medication and therefore cause poor glucose control (hyperglycaemia) which may also affect vascular and brain function (Ciechanowski et al. 2000, Park et al. 2004, Wang et al. 2008). Lastly, hyperglycaemia and hyperinsulinaemia can affect brain tissue and its metabolism by decreasing the neurotransmitter function, which induce organ damage (Kodl and Seaquist 2008).

The current finding indicates a poor score on cognitive tests in depressed individuals (poor score in depressive mood test). It is supported that depression is more common in people with type 2 diabetes and could be the reversible causes of memory impairment and people with diabetes (Lustman et al. 2002). Thus, it would be of interest to propose that when cognitive impairment is suspected, screening depression is recommended. As the literature in this area suggests, the prevalence of depression is found among people with type 2 diabetes. Moreover, depression could be the reversible cause of memory impairment and people with diabetes (Lustman et al. 2002). Treatment of depression may improve the cognitive function, which may also support self-care management and behaviour of the older people with type 2 diabetes (Rubin and Peyrot 2001).

9.5 Correlation between Mini-Cog and MMSE Thai 2002

As mentioned in Chapter 4, Mini-Cog is recently new and has not been validated in Thai population. Thus, in order to propose Mini-Cog as a new cognitive screening tool in Thailand, it is necessary to compare the results of Mini-Cog with MMSE Thai 2002, which is a known reference standard in Thailand (Lorentz 2002).

The data in this study shows that both Mini-Cog and MMSE Thai 2002 seem to detect the cognitive impairment in the same direction. The results clearly indicate that the scores in Mini-Cog are moderate positively correlated (r_s = 0.44, p = 0.001) with the result the scores of MMSE Thai 2002 (Table 8.15). This finding demonstrates significant correlations between Mini-Cog as a new test and MMSE Thai 2002 as a standard test in Thailand. This means that Mini-Cog seems to perform adequately with MMSE Thai 2002, a standard test, for screen cognitive impairment in this study. However, the disagreement between Mini-Cog and MMSE Thai 2002 (Table 8.16) could be explained in two possible ways. The first possibility is that MMSE Thai 2002 could not detect an early state of cognitive impairment or mild cognitive impairment (MCI) due to the lack of an executive function test. This explanation is supported by the study of Munshi et al. (2006) stating that MMSE has a limitation on specificity (specificity = 64%, sensitivity = 96%) and executive function tests (see Chapter 2). The second possibility is that kappa value can be strongly influenced by prevalence (the relative frequency of the condition of interest) (Fleiss 2003). It is possible that this study may have a high number of people with MCI or an early state of cognitive impairment, which MMSE is not sensitive to detect at this state (Allen et al. 2004, Munshi et al. 2006). In summary, an overall disagreement kappa value in the results of cognitive impairment between Mini-Cog and MMSE Thai 2002 might come from the differences of foci in cognitive domain tests and the prevalence of MCI.

With regard to the different foci on cognitive domain tests between Mini-Cog and MMSE Thai 2002 (Chapter 3 and Section 9.2.1), it is possible that the participants with the early stage of cognitive impairment or MCI can detected by Mini-Cog. Mini-Cog consists of short term memory and executive function tests (judgment, decision-making, planning), while MMSE Thai 2002 has seven category tests: orientation to time, orientation to place, registration of three words, attention and calculation , recall of three words, language and visual construction. Apart from short term memory, executive function is found to have an impact on the early stage of cognitive impairment (Doerflinger 2007). The major reason for MMSE's inability in detecting early phases of dementia or mild cognitive impairment (MCI) could be its limitation as an executive function test (Blake et al. 2002, Bak et al. 2005, Woodford and George 2007) .

9.6 Cognitive impairment and depressive mood with the degree of good and poor glycaemic control (HbA1c)

Previous studies have found that glycaemic control (HbA1c) is associated with cognitive function in type 2 diabetes (Cukierman-Yaffe et al. 2009, Grober et al. 2011, Makkakaeo et al. 2011) (see Chapter 2). In particular, uncontrolled glycaemic control can lead to hyperglycaemia which may cause slow and progressive functional and structural abnormalities in the brain affecting cognitive function (Biessels et al. 2006). Thus, the levels of glycaemic control (HbA1c) show the association with cognitive function. HbA1c divides the level into controlled (HbA1c ≤ 7 or 53 mmol/mol) and inadequately controlled (HbA1c > 7 or 53 mmol/mol) (American Diabetes Association, 2009, Grober et al. 2011).

This study investigated and compared whether there was a difference between the levels of good (control (HbA1c ≤ 7% or 53 mmol/mol) and poor (HbA1c > 7% or 53 mmol/mol) glycaemic control and the cut-off score in the all screening tools. The study showed that there was no difference in the scores of cognitive and depressive mood screening tests between the group with good (HbA1c ≤ 7% or 53 mmol/mol) and poor (HbA1c > 7% or 53 mmol/mol) control. The finding from this study either agrees or disagrees with the literatures. Following are the details.

The current finding is controversial with the literature which mostly showed that a better glycaemic control is associated with a less cognitive impairment in the older people with type 2 diabetes (Cukierman-Yaffe et al. 2009, Grober et al. 2011, Mahakaeo et al. 2011). However, the literature could not provide a clear answer that whether a better glycaemic control is related to a better cognitive functioning due to the limitations of each study. By contrast, this study shows the similar results and agrees with the three previous studies which found no association between glycaemic control measured by HbA1c and cognitive screening test (MMSE) in the evaluation period (Munshi et al. 2006, Bruce et al. 2008, Alencar et al. 2010). However, there is no study in the literature, to the best of the researcher's knowledge, on the association between the level of glycaemic control (HbA1c) and cognitive impairment measured by Mini-Cog.

According to the results of HbA1c test, it is important to mention that HbA1c test result in this study was recorded from medical profile and HbA1c was measured before the administration of the screening tests. Thus, the value of HbA1c on the day of administering the tests may have varied from the previously recorded test in the medical profile. Moreover, this study was limited to the information of the medicine used in individual treatments. It could be possible that some of the diabetic patients changed the anti-diabetic agent and some of them used other classes of medication such as anti-hypertensive medicine or alternative medicines after the HbA1c measurement. These conditions may have affected the cognitive function in older people with type 2 diabetes (Wu et al. 2003, Logroscino et al. 2004).

Regarding depression, this result is also in line with the study of Munshi et al. (2006) that observed no correlation between depression and depressive mood screening test (GDS). However, this finding contradicts with some studies in the literature that found HbA1 correlated with depressive symptoms (Sotiropoulos et al. 2008, Tsai et al. 2008, Thaneerat et al. 2009). As stated earlier, the results of depression studies have to be cautious due to the variety of depressive mood screening tests, the purpose of the study including the definition of depression in each study.

9.7 Summary

This prevalence study has documented the undiagnosed cognitive impairment and depressive mood in the older people with type 2 diabetes in the primary care setting. The prevalence of cognitive impairment by Mini-Cog and MMSE was found to be 65.4 % and 12.4 % respectively. With regard to the executive function test in Mini-Cog, it could be possible that Mini-Cog could detect the number of people with an early stage of cognitive impairment or mild cognitive impairment (MCI), whereas MMSE Thai 2002 has a limitation on executive test. Therefore, MMSE Thai 2002 may be not be able to detect the participants with the early stage of cognitive impairment or MCI. Hence, this may be a major reason for the difference of prevalence rate between the two tests. The prevalence of depressive mood was found to be 19.4%. The prevalence of cognitive impairment and

depressive mood amongst Thai older people was consistent with the previous studies in many regions of the world. This study further highlighted the possibility of early cognitive impairment in Thai older people, particularly the younger old age of less than 75. This study revealed the associated characteristics of the older people with type 2 diabetes that may result from cognitive impairment and depressive mood. Although age and education variables may need further study to confirm the results, other variables of clinical indicators such as BMI, HDL and diabetes retinopathy may contribute to the increased risk of cognitive impairment and depressive mood in Thai older people at the primary care setting. In addition, BMI and HDL are the clinical risk factors of MCI and Alzheimer's disease (AD) (Michikawa 2003, Whitmer et al. 2005). This study found that these two clinical factors were the potential clinical characteristics of cognitive impairment by Mini-Cog. Thus, this may be a supportive reason for the difference of prevalence rate between Mini-Cog and MMSE.

Although this study had a limitation in accessing the HbA1c test result at the same time and date of the assessment of the screening tests, it should be noted that a long term of poor glycaemic control (hyperglycaemia) may affect the macro and micro-vascular system in the brain and body and could indirectly influence cognitive impairment and depressive mood (Biessels et al. 2006).

The findings of this study are significant for Thai older people with type 2 diabetes in a community or rural areas. The information implies that inadequately recognised cognitive impairment and depressive mood in diabetic patients may lead to health problem and affect self-care diabetes management. It is important that health care staff at the primary care setting be aware of undiagnosed cognitive impairment and depressive mood in the older people with type 2 diabetes. An appropriate program for prevention and care with any signs of cognitive impairment or depressive mood is needed to provide either the diabetic patients or family members for the good quality of life.

In the next chapter the strengths and limitations of the study will be provided including recommendation for other implications and further research studies.

Chapter 10

Summary and Recommendations

This chapter is divided into four parts. The first part is an overall summary of the study. The second part presents the strengths and limitations of this study. The third part includes recommendations and implications for clinical or health care professionals. The last part provides some ideas for further research

10.1 Overall summary

The present study demonstrated the prevalence of Thai older people with type 2 diabetes who were undiagnosed with cognitive impairment (65.4% for Mini-Cog and 12.4% for MMSE Thai 2002) and undiagnosed with depressive mood (19.4%) in Thai rural areas. This study revealed that the individual potential characteristics related to predicting cognitive impairment by Mini-Cog are younger old age group (equal or less than 74 years), more than 4 years of attending school, a high level of BMI (more than 23 kg/m2) and a low level of HDL (less than 40 mg/dl or 2.2 mmol/l). The individual characteristics associated with cognitive impairment by MMSE Thai 2002 were old age (more than 75 years) and never attending school. An important predictor for depressive mood was retinopathy. This study found an association between cognitive impairment and depressive mood. The patient with cognitive impairment was likely to have depressive mood and vice versa. However, the levels of glycaemic control, which were divided into the good and poor levels, did not show the differences between the performance of cognitive and depressive mood tests.

This study entailed the development of a Thai version of Mini-Cog test, a brief cognitive screening test specifically used in primary care settings (Borson et al. 2000, Lorentz et al. 2002, Ismail et al. 2010). In addition, the Thai Mini-Cog test was developed to address the need for short cognitive screening test specifically used in primary care settings where time for health care services is limited (Borson et al. 2000, Wilber et al. 2005, Lotrakul et al. 2006, Brodaty et al. 2007). The validity and reliability studies demonstrated that Mini-Cog Thai version is reliable to screen cognitive impairment in the study subjects. The results of Mini-Cog

demonstrated significant correlation with MMSE Thai 2002, a standard Thai cognitive screening test. This information implies that Mini-Cog yield the result in the same direction with the standard test in Thailand. Thus, Mini-Cog seemed to perform acceptable to a Thai standard cognitive screening test. Short memory and executive function are cognitive domains that are found to changes in an early stage of cognitive impairment or mild cognitive impairment (MCI). As mentioned in Chapter 9, MMSE Thai 2002 has limitation on specificity and execution function test which may not detect the MCI. Mini-Cog, on the contrary, contains the executive function test. Therefore, it could be possible that Mini-Cog is more likely to detect MCI cases and, therefore, has a higher prevalence rate of cognitive impairment than MMSE Thai 2002.

10.2 Strengths and limitations of the study

10.2.1 Strengths of the study

There is one study conducted by Thaneerat (2009) which is carried out in a hospital setting in the urban area of Thailand and focuses on mild cognitive impairment (MCI). Apart from that, this is the first study to investigate the prevalence of cognitive impairment and depressive mood including the potential factors and the association between cognitive impairment and depressive mood among Thai older people with type 2 diabetes in primary care settings. It shows the number of older diabetic patients who have cognitive impairment and depressive mood in primary care settings in rural areas. The study of diabetic older people at primary care setting in rural areas is important because 70 % of Thai older people live in rural areas (The National Commission on the Elderly 2009) (Chapter 1, Section 1.6.3). Moreover, primary care setting is the first gateway to access health service and plays an important role in improving equity in health (Prakongsai et al. 2009) (Chapter 1 , Section 1.6.2).

This study initially developed a Thai version of Mini-Cog, a brief cognitive screening test originally based on its utility in primary care settings (Borson et al. 2000). This test is practical, convenient to administer and only requires a pen or a pencil and a piece of paper, no special equipment. The test takes 5 minutes to

implement and can be administered by health care staff with a minimal training and a simple scoring system. The use of cross-cultural translation ensures the equivalence of meaning and concept between Mini-Cog original (English) and its Thai version. The study of the inter-rater reliability of the Thai version of Mini-Cog contained a high agreement value (Kappa (K) = 0.8, $p < 0.001$, 95% CI 0.54, 1.06). It indicates a reliable test to use between the raters (Altman, 1991). Finally, the study of the concurrent validity of Mini-Cog test ($r = 0.47$, $p = 0.007$, 95% CI 0.37, 0.55) and MMSE Thai 2002 increases the likelihood of the test to be practically useful in Thailand.

10.2.2 Limitations of the study

This study shows the empirical prevalence of cognitive impairment and depressive mood in the older people with type 2 diabetes. However, considerations need to be given to the factors that may have influenced the results of this study.

- *Research design*

  The results in the current study are reported on the basis of the data from the cross-sectional study collected at a specific point of time. However, the conditions of cognitive impairment and depressive mood are likely to be changeable, which might cause patients' cognition and depressive mood to change over time (Gagliardi 2008). Therefore, the results of this research may not reflect the prevalence of cognitive impairment and depressive mood over a period of time.

  In addition, since the present study is a cross-sectional design in which participants are assessed at the same instant in time, it is implausible to interpret and discuss the findings in terms of cause and effect (Sutton 2002). The potential risk factor and outcome measures (cognitive impairment and depressive mood) are measured at the same time, and it is not usually possible to determine a temporal relationship between the two (Sutton 2002). In this study, the research design (cross-sectional study) could not inform the causation of cognitive impairment and depressive mood in the subjects; however the findings could show the potential

associations between the individual characteristics and cognitive impairment, and the potential associations between individual characteristics and depressive mood.

- *HbA1c test result*

  The results of the glycaemic control level by HbA1c were the limitation in this study. As mentioned earlier, HbA1c was not measured on the same date of the administration of the screening test. Therefore, we should be aware that the real levels of glycaemic control (HbA1c) results on the day of administering the tests might vary from the medical record. This is because the blood glucose level varies from day to day (American Diabetes Association 2009) in response to changes in diet and life style (Nitin 2010). Moreover, changing medication and treatment may affect HbA1c level in diabetic patients (Logroscino et al. 2004, Sherifali et al. 2010).

  Regarding the limitation of HA1c test in Thai primary care centres, postprandial blood glucose (PPG), a measure of oral glucose tolerance, can be used to diagnose diabetes and monitor diabetes management. Since postprandial hyperglycaemia develops early in type 2 diabetes that is often found before observing fasting hyperglycaemia (Sikaris 2009), PPG remains a more sensitive (and specific) marker of glucose intolerance. In addition, approximately 92% of all patients with type 2 diabetes are insulin resistant (Parkin and Brooks 2002).PPG depends altogether on insulin resistance, hepatic glucose output, and insulin secretory capacity of the pancreas in response to meals (Dinneen et al. 1992). Whereas, FBG concentrations are fairly stable in type 2 diabetic patients but can vary by about 15 percent from day to day (Ollerton et al. 1999). Thus, PPG rather than FBG would better reflect the overall pathophysiological process of the disease, i.e., insulin resistance, inadequately suppressed hepatic glucose output, and defective insulin response to meals (Avignon et al. 1997). Moreover, PPG is a marker of glycaemic burden and is as predictive of the risk for diabetic complications when compared with FPG(Avignon et al. 1997). Furthermore, PPG levels have been found to correlate with HbA1c better than fasting levels (Avignon et al. 1997, Rosediani et al. 2006).

Therefore, it is important to identify and utilize the PPG where possible in the primary care centres in order to monitor the glycaemic control level and risk of diabetic complications more accurately. Nevertheless, PPG is not recommended to be used in a standard practice of diabetes care in Thailand because clinical practice of diabetes care and treatment in Thailand is based on the American Diabetes Association (ADA) guidelines, which uses only HbA1c test as a monitor of diabetes management (Diabetes Association Thailand 2012).

- *The coexistence of depression*

  As stated in Chapter 1, depression is a reversible cognitive impairment (Zrebiec 2006). This study focused on the prevalence of cognitive impairment and depressive mood. Thus, depression was not definitely excluded. This means that the results of cognitive impairment could have been influenced by the presence of an underlying depressive condition and vice versa. However, this study intended to show the prevalence rate of undiagnosed depression in order to encourage an awareness of depression as a co-morbidity in diabetic older people for a further appropriate treatment.

- *Diagnostic test*

  This study did not use a complete battery of neurological instruments to establish a diagnosis of dementia or mild cognitive impairment in order to ensure the accuracy of screening tests. There is no report of an empirical data of the prevalence rate of cognitive impairment and depressive mood of the older people with type 2 diabetes in the community level. This study focused on the potential number of outcome measures in order to give an overview trend and blueprint of the existing problem of the health care in taking care of diabetic patients. The data of this study should be used as the primary data for future prospective studies.

- *Generalisation of findings*

  This study only examined a sample of Thai older people from one district in the north part of Thailand. The results were based on one community

(San-sai district) where most of the subjects were located in the rural areas with the limitation of HbA1c test. Therefore, the findings may not be generalisable to all the community dwellings of Thai older people, particularly the urban areas.

10.3 Clinical implication

10.3.1 Implication of Mini-Cog

Mini-Cog can be used when there is a suspicion of cognitive impairment or during a routine screening of an older adult (Borson et al. 2006, Brodaty et al. 2006). In particular the test consists of short memory and executive function tests which are found to decline in an early stage of cognitive impairment (Doerflinger 2007). The strength of this tool is its efficiency, brevity (3-5 minutes of administration) and cost-effectiveness in equipment (only a pen and a piece of paper needed). Another advantage is that the test is not complicated and requires minimal training before use (Scanlan and Borson 2001, Borson et al. 2003). Thus, Mini-Cog can be used as a screening tool to facilitate early identification of cognitive impairment (Borson et al. 2006, Borson et al. 2007) in primary care settings.

Three studies suggest that the use of a combination of a brief cognitive screening test with MMSE resulted in a higher sensitivity and greater accuracy in identifying a case that was achieved by MMSE alone (Flicker et al. 1997, Xu et al. 2002, Palmqvist et al. 2009). Thus, it could be possible to use Mini-Cog and MMSE Thai 2002 in combination in order to ensure the accuracy of the screening tests to each other.

The patients identified as positive in one or more screening tools should be aware of early cognitive impairment. In addition, this early detection would help the health care staff to make diagnostic and treatment decisions by further referring to qualified professionals (Boustani 2003). An early diagnosis provides patients and families with an appropriate care and sufficient time to prepare for future care while the patients still have the capacity to participate in the process (Leifer 2009).

To the researcher's knowledge, this is the first investigation of cognitive impairment in diabetic patients in Thai rural areas. Most of the diabetic patients in this study may have an early or mild symptom of cognitive impairment. The range of the findings represents a potential limitation for generalisability to more severely impaired subjects. Although, without additional neuropsychological testing, it is difficult to provide accurate results and further research will be needed to support this evidence. Nevertheless, the findings in this research support the previous study by Thaneerat et al. (2009) in Thailand, which reported a similar percentage of mild cognitive impairment of Thai older diabetic patients in hospital (77.6%). In addition, this study agrees with the finding of Munshi et al. (2006) suggesting that MMSE fails to sample the executive function test adequately, with a corresponding loss of sensitivity to an early state of cognitive impairment.

In primary care centres with a limited time and specialist availability, it is vital that cognitive impairment be screened reliably, using a tool that requires minimal or little training so that further service can be arranged in time. Even though MMSE Thai 2002 is considered to be the gold-standard for assessing cognitive impairment but this assessment is too time-consuming to be done routinely and requires trained assessors in primary care centres. Moreover, MMSE Thai 2002 misses the point of mild cognitive impairment because of its lack of executive function test, a first domain test of cognitive decline. However, the score results of Mini-Cog are significantly positive in correlation with the score results of MMSE Thai 2002. For all these reasons, Mini-Cog might be the preferred screening measure because it is practically less time-consuming, and because it assesses an early state of cognitive impairment or detects subtle deficits in the specific cognitive domains (short memory and executive function tests), associated with mild cognitive impairment in individuals with diabetes at primary care centres. However, the results of MMSE Thai 2002 in this study may have detected the group of moderate to severe cognitive impairment. Therefore, Mini-Cog might be used as a cognitive screening test to detect an early state of cognitive impairment, or to monitor cognitive function at primary care centres.

10.3.2 Implication for clinical and health care professionals

The clinical implications from these findings are as follows:

- Health care professionals should be trained according to the current knowledge of cognitive screening tests for an early recognition of cognitive impairment. Screening of cognitive impairment may help the health care professionals with further reference to diagnostic and treatment decisions. Effective screening allows health care staff to anticipate problems in self-care management of a diabetic patient.

- Routine screening or monitoring of cognitive impairment and depressive mood are recommended to prevent and delay the onset of cognitive impairment and depressive mood in the older people with type 2 diabetes. This is particularly important in patients with memory problems since memory problems are the first sign of cognitive impairment (Llorente and Malphurs 2007). More significantly, the patients with executive impairment may be at greatest risk for conversion to a diagnosis of dementia (Shulman and Feinstein, 2003, Petersen et al. 2004), highlighting the need to identify these individuals for early care and treatment when it might be most effective (Gauthier 2006). Moreover, based on this study, health care providers should be aware that a mild state of dementia might occur at younger old age groups (60-64 years). Early recognition of cognitive impairment allows health care professional to anticipate the problems that diabetic patients may have in understanding and adhering to self-care management. This information may also be useful for the patients' care-givers and their family members in helping to anticipate and plan for the future problems that may develop as a result of progressive cognitive impairment

- For the diabetic patients whose cognitive impairment is not suspected, health care clinicians should assess cognitive function whenever adherence or deterioration of self-care management is suspected. This should be based on direct observation or concerns raised by family members.

- This study finds the rate of undiagnosed cognitive impairment and undiagnosed depressive mood. This information shows that health care professionals may benefit from educational interventions aimed at improving the detection of cognitive impairment and depressive mood. They should be encouraged to refer the patients to specialist services for assessment.

- The effect of depression may be indirect, but result in cognitive impairment leading to poor self-care management or vice versa (Lustman 2002). Although the link between depression and diabetes may be understandable, it is not inevitable. Depression may indirectly affect self-care behaviour in diabetic older people patients by resulting in poor self-care behaviours, such as overeating, drinking alcohol, not exercising, skipping medication or failing to keep medical appointments. Therefore, efforts to identify and treat depression in the diabetic older people should been encouraged and strongly recommended (Trief 2007).

- It is important for health care providers to review the diabetic patients with a poor depression score, to rule out other possible reversible causes of cognitive impairment. This is because the initial poor screening score of the cognitive test may have been due to transient diagnoses such as depression (Mohs 2000).

- In order to minimise or delay the development of risk factors that might predispose to cognitive impairment or depressive mood, health care professionals should promote a healthy and active lifestyle to every patients.

- An early detection of cognitive impairment can improve the quality of care and life and reduce care expenditures for the diabetic patients and their families (American Diabetes Association 2009).

- More importantly, this study shows that even the participants in the group with HbA1c were likely to be healthier than the group without HbA1c in which cognitive impairment and depressive mood were found. Thus, health care professionals should be seriously concerned about the cognitive function and mood observed in the group without HbA1c as well. Due to the poor health condition and uncontrolled blood sugar in the group without HbA1c, there may be a high possibility of having cognitive impairment and depressive mood. Thus, a routine screening of these symptoms is recommended in the diabetic patients in clinical setting.

- The results of this study, particularly when associated with the clinical characteristics of cognitive impairment and depressive mood, could be generalised to older diabetic patients in Thailand because more than half of diabetic patients (64%) in San-sai district was the same age group (60-69) as the diabetic adults who were found to have a highest prevalence rate (16.7%) in Thai national health survey (Akeplakorn et al. 2011). Particularly, in rural areas where all primary care centres in Thailand have the same policy under the Universal Healthcare Coverage Scheme, chronic diseases (e.g. diabetes, hypertension and heart disease) are a major problem of non-communicable diseases (NCD) in ageing population (National Statistical Office of Thailand 2011). Since subtle changes in cognition, especially executive function, are difficult to detect during a short visit at a primary care centre, the screening tools such as Mini-Cog might be used to identify vulnerable individuals with cognitive decline quickly. This study shows that some clinical variables such as BMI and HDL may strongly associate with cognitive impairment. Hence, this information might be useful for the health care staff to screen and monitor cognitive function in patients with high BMI and a low level of HDL in each visit. It could be possible that a better control of these potential factors might modulate and improve cognitive function of individuals. Likewise, health care staff should be aware of microvascular complications such as retinopathy which may potentially trigger depressive mood in diabetic patients at primary care centres. As mentioned in Chapter 1, diabetes self-care and management could be indirectly affected by depression. This problem will also increase

healthcare use and expenditures in primary care centres. In summary, the results of this study suggest that in order to support an effective diabetes care, older patients at primary care centres in rural areas may need to be checked for cognition and mood. In particular, the health care staff should raise awareness in the group of patients with high BMI, low level of HDL and retinopathy, which are found as the potential factors of cognitive impairment and depressive mood in this study.

10.4 Implication for future research

- The present study is just an initial step towards exploring factors that are associated with the use of a brief cognitive screening test. There is necessary for similar or larger scale studies to consolidate the much-needed empirical evidence on factors that have an impact on the use of brief cognitive screening tests. Further studies may focus on Mini-Cog in other chronic diseases such as hypertension and heart disease affecting cognitive functions. This tool can also be studied in diabetes in other communities and regions of Thailand to see any differences in the results.

- In order to see whether age groups and the level of education in Thai older people influence the results of Mini-Cog, a further study of Mini-Cog is required in order to test the Thai older people living in urban areas where the heterogeneous nature of individual age groups and the level of education could provide a clearer trend of these factors.

- A further longitudinal study such as a prospective cohort study will be carried on a group of older people with type 2 diabetes with a 6+ years of follow-up. As this illness duration has been found an association with cognitive impairment in type 2 diabetes (Gregg et al. 2000, Cosway et al. 2001, Asimakopoulou and Hampson, 2002, Awad et al. 2004). Baseline of cognitive function will be assessed in all participants at the beginning of the study. In order to investigate the association between cognitive impairment and potential risk factors (demographic and clinical characteristics), the follow up data of the subjects with and without cognitive impairment will

be compared. Linear regression models will be used to estimate the mean change in cognitive outcomes over the follow-up period according to explanatory variables such as sociodemographic factors (age, sex, education), clinical variables (BMI, Cholesterol, HbA1c, use of diabetes medications, duration of diabetes, diabetic complications, medical conditions such as vascular diseases and depression; and life style such as alcohol intake and smoking history. Confounding variables such as age and education between the first two assessments will also be adjusted in the model.

- Limited research has been conducted into the prevalence and potential factors strongly associated with cognitive impairment and depressive mood in this target population. Thus, conducting further on the psychometric properties of Mini-Cog would expand the efficiency of the test and sharpen its accuracy in identifying of cognitive impairment in Thai population.

10.5 Summary

This study contributes to the estimated rate of cognitive impairment and depressive mood in Thai older people with type 2 diabetes in a primary care setting. Since cognitive function is one of the crucial factors in self-care management in diabetes, an early detection becomes more clinically relevant. This leads to the use of screening tools to help the early detection and these tools gain importance. This study focused on simulating the real world situation in a primary care setting with the well-known restraints of time and resources. Mini-Cog test, a cognitive screening test designed for use in primary care settings, was applied in order to promote the detection of suspected cognitive impairment in the older people with type 2 diabetes. Nevertheless, this study did not aim to compare the efficiency of Mini-Cog or MMSE Thai 2002 in detecting cognitive impairment against a 'gold standard' that would require a battery of neuropsychological tests.

Depression can cause an reversible cognitive impairment. This study showed that depression is also detected in diabetic patients. These results can enhance the understanding of how providing the optimal approaches to the diabetic patients

with cognitive impairment or depressive mood enhance the abilities of patients in performing diabetes self-management. It also provides useful information for family members to support patients in self-care management.

Type 2 diabetes is a major and complex public health problem accompanied with several complications and co-morbidities. Depression and cognitive decline are common, but often overlooked (Biessels et al. 2007).This study is important because findings show that older Thai people with type 2 diabetes in the community are found to have undiagnosed cognitive impairment and depressive mood. A possibility of individual characteristics at an increased risk for developing cognitive impairment and developing depressive mood are pointed out. This study stimulates the health care providers' awareness and understanding of the link between type 2 diabetes and cognitive function as well as the link between type 2 diabetes and depressive mood. A need for a routine assessment and monitoring of cognitive function with Mini-Cog Thai version can ultimately lead to improvements in the long-term outcomes of self care diabetes. Mini-Cog Thai version is a new reliable and simple tool fitting in 5 minutes and is practical to use in primary care centres.

A further longitudinal study is required to fully determine whether the associated variables are risk factors for cognitive impairment. In order to fulfil the development of Mini-Cog Thai version, the measures of psychometric properties compared with a neurological instrument such as Cambridge Cognitive Assessment (CAMCOG), a standardised neurological screening test (Ruth et al. 1986, Kwa et al. 1986), to establish a diagnosis of dementia are recommended for a new ideal dementia screening test.

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APPENDICES

Appendices	Topics
Appendix A	Ethical approval and the permission document A1: ethical approval, UEA A2: ethical approval, MOPH, Thailand A3: permission of the translation of the Mini-Cog from
Appendix B	Translation of Mini-Cog B1: Forward translation B1.1: forward translator 1 B1.2: forward translator 2 B2: Synthesis of forward translation B3: Backward translation B3.1: backward translator 1 B3.2: backward translator 1
Appendix C	Information Sheet and consent forms C1:Information Sheet and consent forms in English C2: Information Sheet and consent forms in Thai
Appendix D	Instruments of the study D1:Mini-Cog(English and Thai) D2: MMSE D3: TGDS
Appendix E	E1: Participant recording form E2: Codes of variables
Appendix F	F1: Normality test of data F2: Multicollinearity test of variables

Appendix A: Ethical approval and the permission document
Appendix A1: Ethical approval, UEA

Faculty of Health

University of East Anglia

Miss Supaporn Trongsakul
55 City Road
Norwich
NR1 3AS

Research Office, Room 1.04
Chancellors Drive Annex
University of East Anglia
Norwich NR4 7TJ
United Kingdom

Email:Jane.Carter@uea.ac.uk
Tel: +44 (0) 1603 591023
Fax: +44 (0) 1603 591132

Web:www.uea.ac.uk
Web: http://www.uea.ac.uk

7 December 2009

Dear Supaporn,

The prevalence of cognitive impairment or depressive mood in over 60's with type 2 Diabetes Mellitus in a Thai community – 2009/10-007

The submission of your above proposal has now been considered by the FOH Ethics Chair and we can now confirm that your proposal has been approved.

Please could you ensure that you have the relevant approvals for the project in Thailand.

Please could you ensure that any amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the committee. Please could you also arrange to send us a report once your project is completed.

The committee would like to wish you good luck with your project.

Yours sincerely,

Jane Carter

Jane Carter

Appendix A1: Ethical approval, UEA

Faculty of Health Research Ethics Committee

University of East Anglia

Miss Supaporn Trongsakul
55 City Road
Norwich
NR1 3AS

Faculty of Health Research Office
Elizabeth Fry Building, Room 2.30
University of East Anglia
Norwich NR4 7TJ

Email: margaret.rhodes@uea.ac.uk
Direct Dial: +44 (0) 1603 59 7190
Research: +44 (0) 1603 59 1720
Fax: +44 (0) 1603 59 1132

Web: http://www.uea.ac.uk

9th December 2010

Dear Supaporn

The prevalence of cognitive impairment or depressive mood in over 60's with type 2 Diabetes Mellitus in a Thai community – Reference 2009/10-007

The amendments to your above proposal have been considered by the Chair of the FOH Research Ethics Committee and we can now confirm that your proposal has been approved.

Please could you ensure that any further amendments to either the protocol or documents submitted are notified to us in advance and also that any adverse events which occur during your project are reported to the Committee. Please could you also arrange to send us a report once your project is completed.

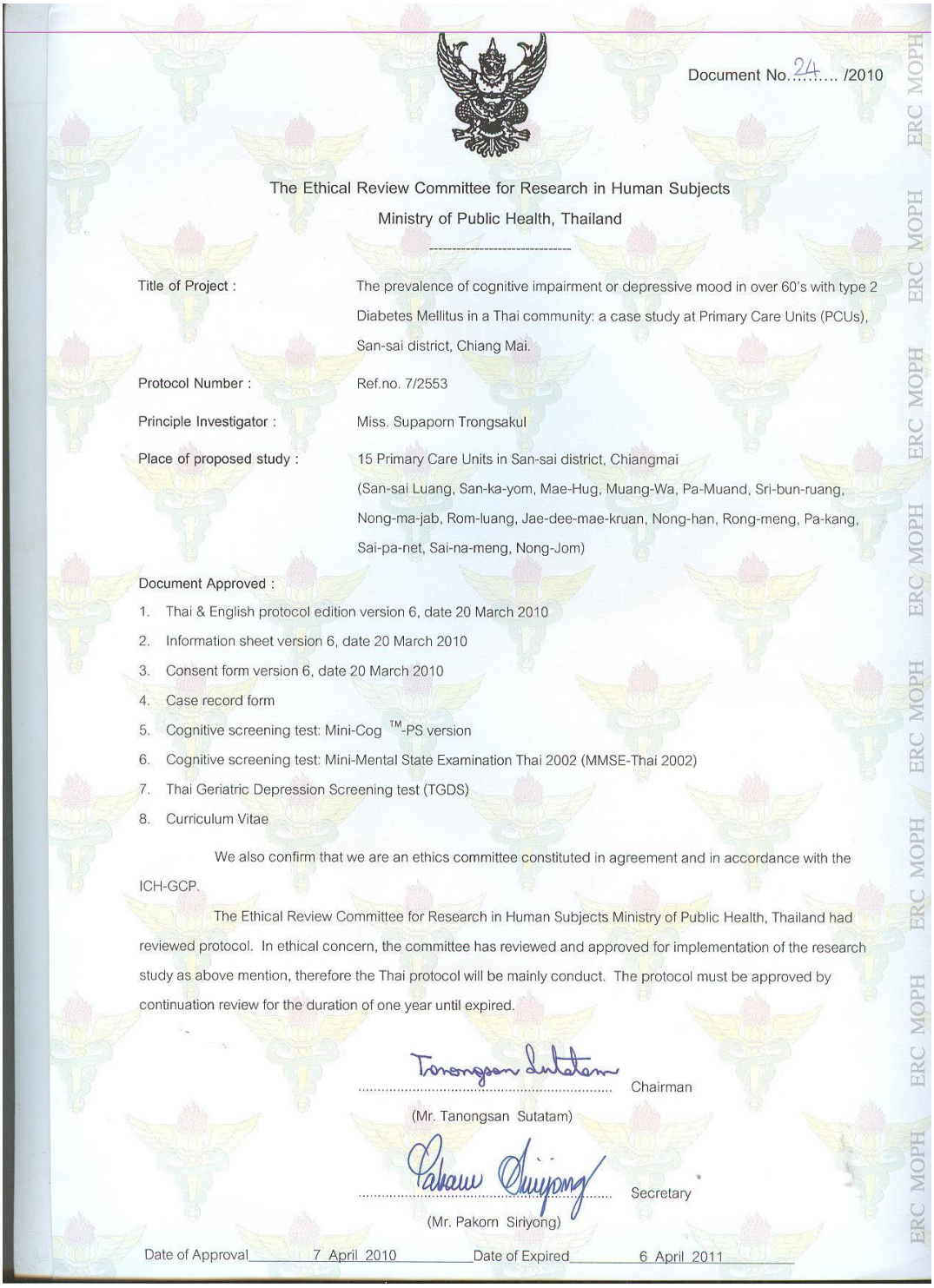
The Chair would like to wish you good luck with your project.

Yours sincerely

Maggie Rhodes
Research Administrator

Cc Dr Jane Cross, Supervisor

Appendix A2: Ethical approval, MOPH, Thailand



Document No. 24 /2010

The Ethical Review Committee for Research in Human Subjects
Ministry of Public Health, Thailand

Title of Project : The prevalence of cognitive impairment or depressive mood in over 60's with type 2 Diabetes Mellitus in a Thai community: a case study at Primary Care Units (PCUs), San-sai district, Chiang Mai.

Protocol Number : Ref.no. 7/2553

Principle Investigator : Miss. Supaporn Trongsakul

Place of proposed study : 15 Primary Care Units in San-sai district, Chiangmai (San-sai Luang, San-ka-yom, Mae-Hug, Muang-Wa, Pa-Muand, Sri-bun-ruang, Nong-ma-jab, Rom-luang, Jae-dee-mae-kruan, Nong-han, Rong-meng, Pa-kang, Sai-pa-net, Sai-na-meng, Nong-Jom)

Document Approved :

1. Thai & English protocol edition version 6, date 20 March 2010
2. Information sheet version 6, date 20 March 2010
3. Consent form version 6, date 20 March 2010
4. Case record form
5. Cognitive screening test: Mini-Cog ™-PS version
6. Cognitive screening test: Mini-Mental State Examination Thai 2002 (MMSE-Thai 2002)
7. Thai Geriatric Depression Screening test (TGDS)
8. Curriculum Vitae

We also confirm that we are an ethics committee constituted in agreement and in accordance with the ICH-GCP.

The Ethical Review Committee for Research in Human Subjects Ministry of Public Health, Thailand had reviewed protocol. In ethical concern, the committee has reviewed and approved for implementation of the research study as above mention, therefore the Thai protocol will be mainly conduct. The protocol must be approved by continuation review for the duration of one year until expired.

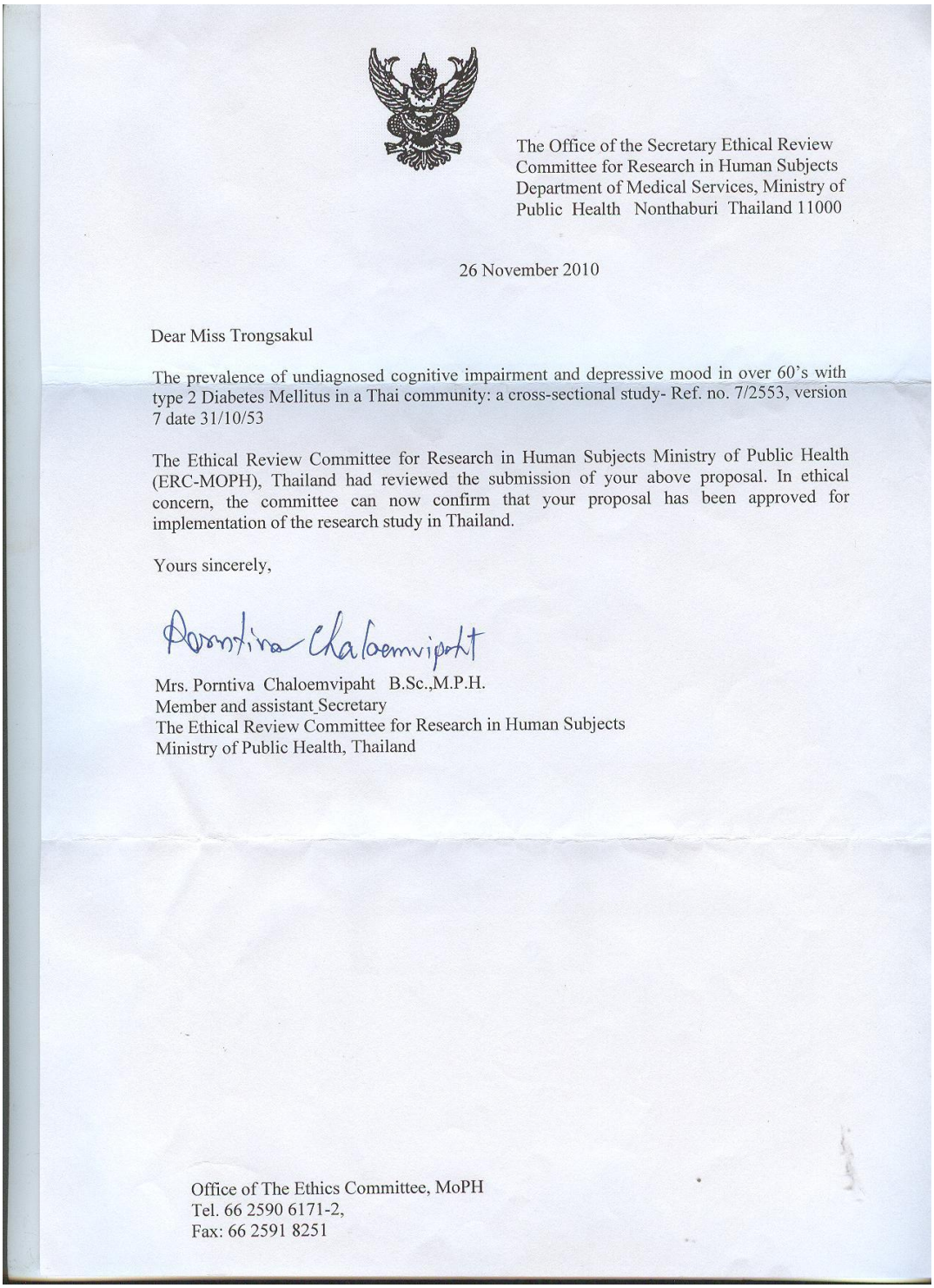
Tanongsan Sutatam
..... Chairman
(Mr. Tanongsan Sutatam)

Pakorn Siriyong
..... Secretary
(Mr. Pakorn Siriyong)

Date of Approval 7 April 2010 Date of Expired 6 April 2011

ERC MOPH ERC MOPH ERC MOPH ERC MOPH ERC MOPH ERC MOPH ERC MOPH

Appendix A2: Ethical approval, MOPH, Thailand



The Office of the Secretary Ethical Review
Committee for Research in Human Subjects
Department of Medical Services, Ministry of
Public Health Nonthaburi Thailand 11000

26 November 2010

Dear Miss Trongsakul

The prevalence of undiagnosed cognitive impairment and depressive mood in over 60's with type 2 Diabetes Mellitus in a Thai community: a cross-sectional study- Ref. no. 7/2553, version 7 date 31/10/53

The Ethical Review Committee for Research in Human Subjects Ministry of Public Health (ERC-MOPH), Thailand had reviewed the submission of your above proposal. In ethical concern, the committee can now confirm that your proposal has been approved for implementation of the research study in Thailand.

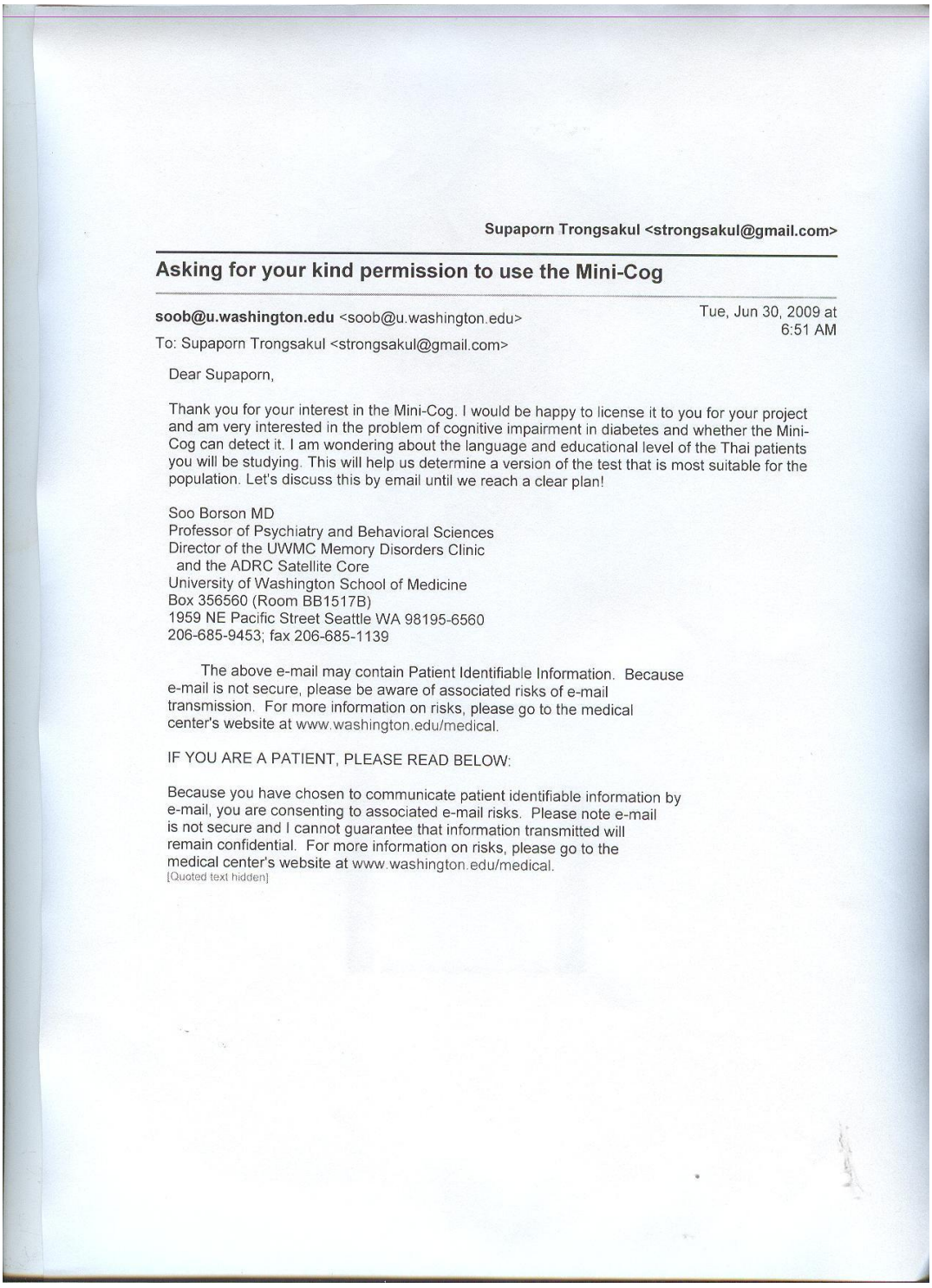
Yours sincerely,

Porntiva Chaloemvipaht

Mrs. Porntiva Chaloemvipaht B.Sc.,M.P.H.
Member and assistant Secretary
The Ethical Review Committee for Research in Human Subjects
Ministry of Public Health, Thailand

Office of The Ethics Committee, MoPH
Tel. 66 2590 6171-2,
Fax: 66 2591 8251

Appendix A3: Permission of the translation of the Mini-Cog



Supaporn Trongsakul <strongsakul@gmail.com>

Asking for your kind permission to use the Mini-Cog

soob@u.washington.edu <soob@u.washington.edu> Tue, Jun 30, 2009 at 6:51 AM

To: Supaporn Trongsakul <strongsakul@gmail.com>

Dear Supaporn,

Thank you for your interest in the Mini-Cog. I would be happy to license it to you for your project and am very interested in the problem of cognitive impairment in diabetes and whether the Mini-Cog can detect it. I am wondering about the language and educational level of the Thai patients you will be studying. This will help us determine a version of the test that is most suitable for the population. Let's discuss this by email until we reach a clear plan!

Soo Borson MD
Professor of Psychiatry and Behavioral Sciences
Director of the UWMC Memory Disorders Clinic
and the ADRC Satellite Core
University of Washington School of Medicine
Box 356560 (Room BB1517B)
1959 NE Pacific Street Seattle WA 98195-6560
206-685-9453; fax 206-685-1139

The above e-mail may contain Patient Identifiable Information. Because e-mail is not secure, please be aware of associated risks of e-mail transmission. For more information on risks, please go to the medical center's website at www.washington.edu/medical.

IF YOU ARE A PATIENT, PLEASE READ BELOW:

Because you have chosen to communicate patient identifiable information by e-mail, you are consenting to associated e-mail risks. Please note e-mail is not secure and I cannot guarantee that information transmitted will remain confidential. For more information on risks, please go to the medical center's website at www.washington.edu/medical.
[Quoted text hidden]

Appendix B: Translation of Mini-Cog
Appendix B1: Step 1: Forward translation
Appendix B1.1 forward translator 1

MINI-COG-PS Version

1) ให้ผู้ป่วยตั้งใจฟัง จากนั้นพูดว่า “ฉันจะพูดคำ 3 คำให้จำตอนนี้และภายหลัง คำเหล่านั้นได้แก่

บ้าน แมว สีเขียว

บอกฉันตอนนี้ว่ามีคำอะไรบ้าง” (ให้ผู้ป่วยตอบได้ 3 ครั้ง ถ้าผู้ป่วยไม่สามารถตอบได้หลังจาก 3 ครั้งไปแล้ว ให้ไปที่หัวข้อถัดไป)
(พับกระดาษตามเส้นประ 2 เส้นข้างล่างเพื่อให้เป็นพื้นที่ว่างและเพื่อปกปิดคำที่ให้จำ ยื่นดินสอ/ปากกาให้ผู้ป่วย)

2) พูดประโยคต่อไปนี้ตามลำดับ: “วาดรูปนาฬิกาในพื้นที่ว่างข้างล่างนี้ เริ่มวาดวงกลมใหญ่ก่อน” (หลังจากผู้ป่วยวาดวงกลมเสร็จ พูดว่า) “ใส่เลขทั้งหมดในวงกลม” (เมื่อผู้ป่วยวาดเสร็จ พูดว่า) “เอาล่ะ ใส่เข็มนาฬิกาบอกเวลา 11:10 (สิบเอ็ดนาฬิกาสิบนาที)” ถ้าผู้ป่วยไม่สามารถวาดนาฬิกาเสร็จใน 3 นาที ให้หยุดทำและถามหัวข้อความจำ

---

3) พูดว่า: “คำ 3 คำที่ให้จำมีอะไรบ้าง?”

_____ _____ _____ (ให้ 1 คะแนนในแต่ละหัวข้อ) คะแนนความจำ 3 หัวข้อ □

คะแนนวาดนาฬิกา (ดูการให้คะแนนในอีกหน้า): นาฬิกาปกติ 2
คะแนนนาฬิกาผิดปกติ 0 คะแนนนาฬิกา □

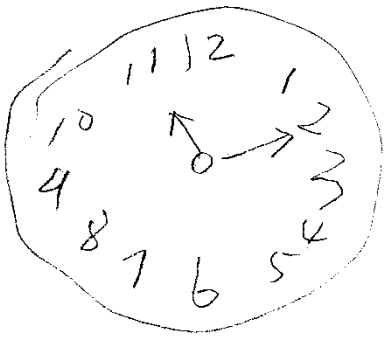
คะแนนรวม = คะแนนความจำ 3 หัวข้อบวกคะแนนนาฬิกา □
0, 1, หรือ 2 อาจมีความบกพร่อง; 3, 4, หรือ 5 ไม่มีความบกพร่อง

การให้คะแนนนาฬิกา

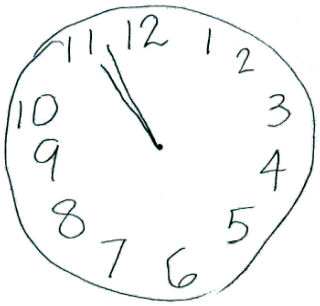
นาฬิกาปกติต้องมีส่วนต่าง ๆ ต่อไปนี้ครบถ้วน

มีเลข 1-12 ครบ, มีเลขแต่ละตัวเพียง 1 ตัว, เลขทุกตัวเรียงตามลำดับและมีทิศทางที่ถูกต้อง (ตามเข็มนาฬิกา) ภายในวงกลม

มีเข็มสั้นและยาวโดยเข็มสั้นชี้ที่เลข 11 เข็มยาวชี้ที่เลข 2



รูปนาฬิกาใด ๆ ที่มีส่วนต่าง ๆ ดังกล่าวไม่ครบถือว่าเป็นนาฬิกาผิดปกติ ผู้ป่วยที่ไม่ยอมวาดให้ถือว่าเป็นนาฬิกาผิดปกติ



วางเข็มไม่ถูก

ตัวเลขนาฬิกาไม่ครบ

Appendix B1.2 forward translator 2

MINI-COG ™ - PS Version

1) **ให้ผู้ป่วยตั้งใจฟัง บอกผู้ป่วยว่า** "**ฉัน (ผม) จะบอกคำ** 3 **คำขอให้คุณ .....จำไว้ในตอนนี้และจะถามอีกครั้งในเวลาต่อมา**"

   คำ 3 **คำนั้นได้แก่** คำว่า"**บ้าน**" "**แมว**" "**สีเขียว**"

   ขอให้คุณ.....ช่วยบอกฉัน (ผม)ว่าคำ3 **คำนั้นคือคำว่าอะไร**บ้าง (ผู้ป่วยพยายามตอบได้ 3 **ครั้งหากไม่สามาร**ถ **ตอบได้ถูกต้องหลังจากพยายาม** 3ครั้งแล้ว ให้ทดสอบในหัวข้อต่อไป)

   พับกระดาษไปด้านหลังตามรอยปรุ 2แถวด้านล่าง ให้เหลือกระดาษเป็นพื้นที่ว่างและไม่ให้เห็นส่วนของคำที่ใช้ทดสอบความจำ ส่งปากกาหรือดินสอให้คนไข้

2) พูดวลีต่อไปนี้โดยเรียงตามลำดับ:" ให้คุณ ....วาดนาฬิกาในพื้นที่ว่างบนกระดาษ เริ่มจากวาดวงกลมวงใหญ่ๆ" เมื่อผู้ป่วยทำเสร็จแล้ว บอกผู้ป่วยว่า "ใส่ตัวเลขในวงกลมให้ครบถ้วน" เมื่อผู้ป่วยทำเสร็จ บอกผู้ป่วย "ให้วาดเข็มนาฬิกาชี้ไปที่เวลา 11:10 น. (สิบเอ็ดโมงสิบนาที) หากผู้ป่วยไม่สามารถวาดนาฬิกาได้เสร็จเรียบร้อยภายใน 3 นาที ให้หยุดการทดสอบ จากนั้นกลับมาถามผู้ป่วยซ้ำถึงคำ3 คำที่บอกให้ผู้ป่วยจำในช่วงแรก

---

3) พูดกับผู้ป่วยว่า " คำ 3 คำที่ดิฉัน (ผม)ให้คุณ ....จำไว้มีคำว่าอะไรบ้าง"

   _____ _____ _____

   _____ (ให้1 คะแนนต่อ 1 คำ) คะแนนการระลึกคำ 3 คำ

   คะแนนวาดรูปนาฬิกา (ดูคำแนะนำการให้คะแนนในหน้าถัดไป):

   วาดนาฬิกาถูกต้อง 2 คะแนน

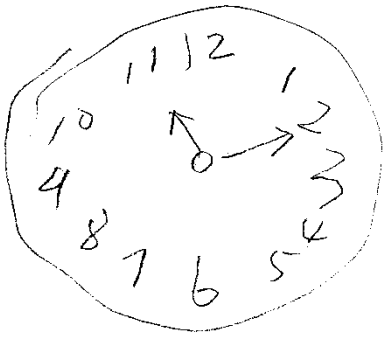
   คะแนนวาดรูปนาฬิกา วาดนาฬิกาไม่ถูกต้อง 0 คะแนน

รวม = คะแนนการระลึกคำ3 คำรวมกับคะแนนวาดรูปนาฬิกาคะแนน ☐

คะแนน0, 1, หรือ 2 น่าจะมีความบกพร่อง; 3, 4, หรือ 5 ไม่มีความบกพร่อง

การให้คะแนนการวาดรูปนาฬิกา

นาฬิกาปกติ (วาดถูกต้อง)

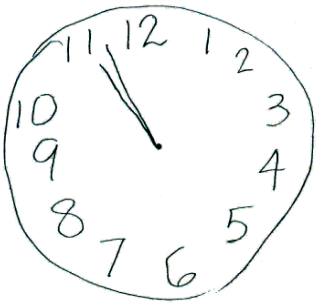


นาฬิกาปกติ (วาดถูกต้อง) ต้องมีองค์ประกอบดังต่อไปนี้ครบถ้วน:

- ในวงกลมมีตัวเลข 1-12 โดยตัวเลขแต่ละตัวปรากฏเพียงครั้งเดียว เรียงลำดับและทิศทาง (ตามเข็มนาฬิกา) ถูกต้อง
- มีเข็มนาฬิกา 2 อัน เข็มหนึ่งชี้ไปที่เลข 11 ส่วนอีกเข็มชี้ไปที่เลข 2

หากนาฬิการูปใดขาดองค์ประกอบข้อใดข้อหนึ่งข้างต้นให้คะแนนเป็นนาฬิกาที่วาดไม่ถูกต้อง และหากผู้ป่วยปฏิเสธการวาดรูปนาฬิกาให้ให้คะแนนเป็นวาดไม่ถูกต้อง

ตัวอย่างนาฬิกาที่ผิดปกติ (วาดไม่ถูกต้อง)



วางตำแหน่งเข็มนาฬิกาไม่ถูกต้อง

ตัวเลขขาดหายไป

Appendix B2: Synthesis of forward translation

MINI-COG ™ - PS Version

1) ให้ผู้ป่วยตั้งใจฟังแล้วบอกผู้ป่วยว่า "ดิฉัน (ผม) จะบอกคำ 3 คำซึ่งอยากให้คุณ (ชื่อ ป้า ลุง ยาย ตา) จำตอนนี้แล้วก็จำไว้ต่อไปนะคะ (นะครับ) คำเหล่านี้ได้แก่

บ้าน แมว สีเขียว

ไหนลองพูดออกมาให้ฟังสิคะ (ครับ)" (ให้โอกาสผู้ป่วยลองทำ 3 ครั้ง หากไม่สามารถทำได้หลังจากพยายาม 3 ครั้ง ให้ทำข้อต่อไป)

พับหน้านี้ไปทางด้านหลังตามรอยประ 2 แถวด้านล่างเพื่อให้เกิดพื้นที่ว่างและบังคำที่ให้จำไว้ ส่งดินสอ/ปากกาให้ผู้ป่วย

2) พูดวลีต่อไปนี้ตามลำดับ:" ช่วยวาดรูปนาฬิกาลงบนที่ว่างด้านล่างนี้หน่อยนะคะ (ครับ) เริ่มจากวาดวงกลมวงใหญ่ๆ ค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ใส่ตัวเลขลงไปในวงกลมให้ครบเลยค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ทีนี้ให้ตั้งเวลา โดยให้เข็มนาฬิกาชี้บอกเวลา 11:10 น. (สิบเอ็ดนาฬิกาสิบนาที) ค่ะ (ครับ)" หากผู้ป่วยไม่สามารถวาดนาฬิกาได้เสร็จภายใน 3 นาที ให้หยุดทำแล้วไปถามคำที่ให้จำไว้

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3) พูดว่า: "คำ 3 คำที่ดิฉัน (ผม)ให้คุณ (ชื่อ ป้า ลุง ยาย ตา)จำไว้มีอะไรบ้างคะ (ครับ)"

_____ _____ _____

_____ (ให้1 คะแนนต่อ 1 คำ) คะแนนการระลึกคำ 3 คำ

ให้คะแนนรูปนาฬิกา (ดูคำแนะนำอีกหน้าหนึ่ง):

คะแนนรูปนาฬิกาปกติ	2 คะแนน
คะแนนรูปนาฬิกาผิดปกติ	0 คะแนน

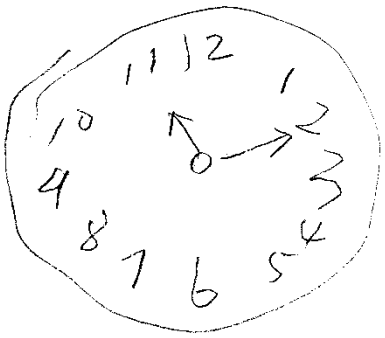
☐

คะแนนรวม = คะแนนการระลึกคำ 3 คำรวมกับคะแนนรูปนาฬิกา

คะแนน0, 1, หรือ 2 น่าจะมีความบกพร่อง; 3, 4, หรือ 5 ไม่มีความบกพร่อง

การให้คะแนนรูปนาฬิกา

นาฬิกาปกติ



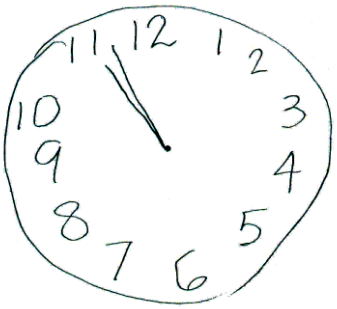
นาฬิกาปกติจะมีองค์ประกอบดังต่อไปนี้ครบถ้วน:

ตัวเลขครบ1-12 ไม่ซ้ำกัน อยู่อย่างถูกลำดับและทิศทาง (ตามเข็มนาฬิกา) ภายในวงกลม

เข็มนาฬิกามี2 อัน อันหนึ่งชี้ที่เลข 11 และอันหนึ่งชี้ที่เลข 2

รูปนาฬิกาที่ขาดองค์ประกอบข้อใดข้อหนึ่งเหล่านี้ให้ถือว่าผิดปกติ การปฏิเสธที่จะวาดรูปนาฬิกาให้ถือว่าผิดปกติ

ตัวอย่างของนาฬิกาที่ผิดปกติ



เข็มนาฬิกาผิดปกติ

ตัวเลขไม่ครบ

Appendix B3: Backward translation
Appendix B3.1 : Back translator 1

MINI-COG ™ - PS Version

1) ให้ผู้ป่วยตั้งใจฟังแล้วบอกผู้ป่วยว่า "ดิฉัน (ผม) จะบอกคำ 3 คำซึ่งอยากให้คุณ (ชื่อ ป้า ลุง ยาย ตา) จำตอนนี้แล้วก็จำไว้ต่อไปนะคะ (นะครับ) คำเหล่านี้ได้แก่

บ้าน แมว สีเขียว

ไหนลองพูดออกมาให้ฟังสิคะ (ครับ)" (ให้โอกาสผู้ป่วยลองทำ3 **ครั้งหากไม่สามาร**ถทำได้**หลังจากพยายาม** 3 ครั้ง ให้ทำข้อต่อไป)

พับหน้านี้ไปทางด้านหลังตามรอยประ2แถวด้านล่างเพื่อให้เกิดพื้นที่ว่างและปิดคำที่ให้จำไว้ ส่งดินสอ/ปากกาให้ผู้ป่วย

2) พูดวลีต่อไปนี้ตามลำดับ:" ช่วยวาดรูปนาฬิกาลงบนที่ว่างด้านล่างนี้หน่อยนะคะ (ครับ) เริ่มจากวาดวงกลมวงใหญ่ๆ ค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ใส่ตัวเลขลงไปในวงกลมให้ครบเลยค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ทีนี้ให้ตั้งเวลา โดยให้เข็มนาฬิกาชี้บอกเวลา 11:10 น. (สิบเอ็ดนาฬิกาสิบนาที) ค่ะ (ครับ)" หากผู้ป่วยไม่สามารถวาดนาฬิกาได้เสร็จภายใน 3 นาที ให้หยุดทำแล้วไปถามคำที่ให้จำไว้

1. Make sure that the patient is paying attention, then tell him/her that "I will tell you 3 words and I would like you to memorize them". These words are HOUSE, CAT, GREEN.

Let them try to say these words. (Give the patient at least 3 attempts and if he/she can not do it after trying three times, then continue onto the next step.

Fold this page to the back, following the 2 rows of ---------below to make a space and cover the three words. Pass a pen/ pencil to the patient.

2. Say these phrases in order: " Please draw a clock on the space below, begin by draw a big circle". When he/ she has finished, tell them "please put numbers around the circle". When they have finished, say " Can you set the time at 11.10am?" If the patient cannot draw a correct clock within three minutes, let him/her stop and ask questions.

---

3) พูดว่า: "คำ 3 คำที่ดิฉัน (ผม)ให้คุณ (ชื่อ ป้า ลุง ยาย ตา)จำไว้มีอะไรบ้างคะ (ครับ)"

_____ _____ _____

(ให้1 คะแนนต่อ 1 คำ)

คะแนนการระลึกคำ 3 คำ 

ให้คะแนนรูปนาฬิกา (ดูคำแนะนำอีกหน้าหนึ่ง): รูปนาฬิกาปกติ 2 คะแนน

รูปนาฬิกาผิดปกติ 0 คะแนน

คะแนนรวม = คะแนนการระลึกคำ 3 คำรวมกับคะแนนรูปนาฬิกา

คะแนน0, 1, หรือ 2 อาจจะมีความบกพร่อง; 3, 4, หรือ 5 ไม่มีความบกพร่อง

3) Say “What are those words that I asked you to remember”

(1 mark per word) 3 marks for all the words

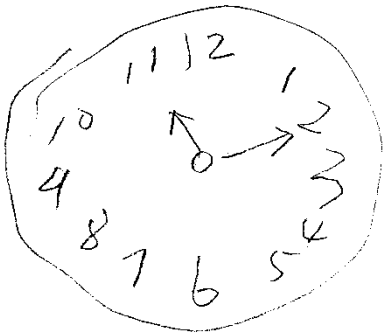
Give marks for clock drawing (see recommendation on the other side): a normal clock = 2 marks, not normal clock = 0

Total marks = mark from remembering the 3 words and marks from the clock picture.

0,1 or 2 marks may reflect on some disability, whereas 3,4 or 5 marks is normal.

การให้คะแนนรูปนาฬิกา how to mark clock picture

นาฬิกาปกติ normal clock



นาฬิกาปกติจะมีองค์ประกอบดังต่อไปนี้ครบถ้วน:

ตัวเลขครบ1-12 ไม่ซ้ำกัน อยู่อย่างถูกลำดับและทิศทาง (ตามเข็มนาฬิกา) ภายในวงกลม

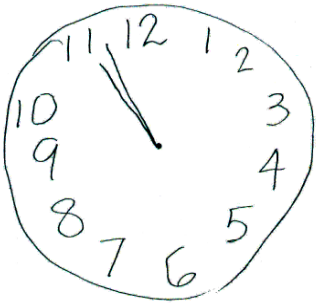
เข็มนาฬิกามี2 อัน อันหนึ่งชี้ที่เลข 11 และอันหนึ่งชี้ที่เลข 2

รูปนาฬิกาที่ขาดองค์ประกอบข้อใดข้อหนึ่งเหล่านี้ให้ถือว่าผิดปกติ การปฏิเสธที่จะวาดรูปนาฬิกาให้ถือว่าผิดปกติ

A normal clock should have the following:
Numbers running from 1-12, without any repetition and in order (following the clock hand) within the circle.There are two clock hands one is at number 11 and the other is at number 2.

Any clock pictures that don't have the requirement above are considered as not normal. Refusal to draw a clock picture is also considered as not normal.

ตัวอย่างของนาฬิกาที่ผิดปกติExample of a not normal clock



เข็มนาฬิกาผิดปกติ Hand is not correct

ตัวเลขไม่ครบ numbers are incomplete.

Appendix B3.2: Back translator 2

MINI-COG ™ - PS Version

1) ให้ผู้ป่วยตั้งใจฟังแล้วบอกผู้ป่วยว่า "ดิฉัน (ผม) จะบอกคำ 3 คำซึ่งอยากให้คุณ (ชื่อ ป้า ลุง ยาย ตา) จำตอนนี้แล้วก็จำไว้ต่อไปนะคะ (นะครับ) คำเหล่านี้ได้แก่

บ้าน แมว สีเขียว

ไหนลองพูดออกมาให้ฟังสิคะ (ครับ)" (ให้โอกาสผู้ป่วยลองทำ 3 ครั้งหากไม่สามารถทำได้หลังจากพยายาม 3 ครั้ง ให้ทำข้อต่อไป) พับหน้านี้ไปทางด้านหลังตามรอยประ 2 แถวด้านล่างเพื่อให้เกิดพื้นที่ว่างและปิดคำที่ให้จำไว้ ส่งดินสอ/ปากกาให้ผู้ป่วย

2) พูดวลีต่อไปนี้ตามลำดับ:" ช่วยวาดรูปนาฬิกาลงบนที่ว่างด้านล่างนี้หน่อยนะคะ (ครับ) เริ่มจากวาดวงกลมวงใหญ่ๆ ค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ใส่ตัวเลขลงไปในวงกลมให้ครบเลยค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ทีนี้ให้ตั้งเวลา โดยให้เข็มนาฬิกาชี้บอกเวลา 11:10 น. (สิบเอ็ดนาฬิกาสิบนาที) ค่ะ (ครับ)" หากผู้ป่วยไม่สามารถวาดนาฬิกาได้เสร็จภายใน 3 นาที ให้หยุดทำแล้วไปถามคำที่ให้จำไว้

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1) Ask the patient to listen as you say "I will tell you 3 words in which I would like you (name of aunt/uncle/grandparent) to memorize. The words are as follow: House Cat Green
Please repeat the words to me (Allow the patient 3 attempts at this. If after 3 attempts this cannot be achieved, move on to the next question).
Fold this page along the 2 dotted lines below to create a blank area and to hide the words to be memorized. Pass the pencil/pen to the patient.

2) Say the following sentence in this order: "Please draw a picture of a clock in the blank area below. Start from drawing a large circle" (Once completed, say) "Please place all the numbers into the circle" (Once completed, say) "Now set the time by showing the clock hands at 11.10 (ten minutes past eleven)"
If the patient is not able to draw a clock within 3 minutes, discontinue with the task and ask them to recall the words they were asked to memorize.

3) พูดว่า: "คำ 3 คำที่ดิฉัน (ผม)ให้คุณ (ชื่อ ป้า ลุง ยาย ตา)จำไว้มีอะไรบ้างคะ (ครับ)"

_____ _____ _____

_____ (ให้1 คะแนนต่อ 1 คำ) คะแนนการระลึกคำ 3 คำ

ให้คะแนนรูปนาฬิกา (ดูคำแนะนำอีกหน้าหนึ่ง): รูปนาฬิกาปกติ 2 คะแนน

รูปนาฬิกาผิดปกติ 0 คะแนน

คะแนนรวม = คะแนนการระลึกคำ 3 คำรวมกับคะแนนรูปนาฬิกา

คะแนน0, 1, หรือ 2 อาจจะมีความบกพร่อง; 3, 4, หรือ 5 ไม่มีความบกพร่อง

3) Say: “What are the 3 words I asked you (name of aunt/uncle/grandparent) to memorize?”

(1 mark per 1 word) Mark for memorizing the 3 words

Mark for the picture of the clock (see introduction on another page): Normal picture of a clock. Abnormal picture of a clock.

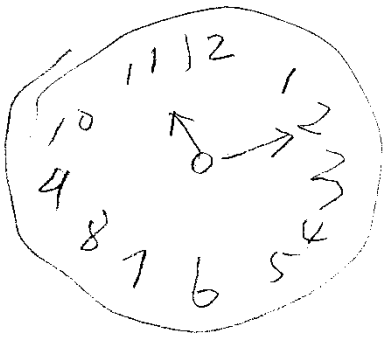
Mark for picture of the clock.

Total mark = mark for memorizing the 3 words plus mark for picture of the clock.

A mark of 0,1or 2 may suggest defective; 3, 4 or 5 suggesting no abnormality

การให้คะแนนรูปนาฬิกา How to mark the picture of the clock

นาฬิกาปกติ normal clock



นาฬิกาปกติจะมีองค์ประกอบดังต่อไปนี้ครบถ้วน:

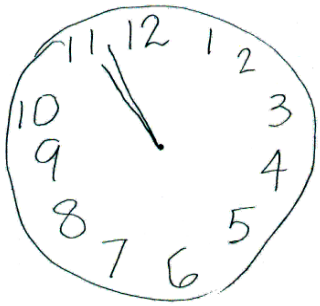
ตัวเลขครบ1-12 ไม่ซ้ำกัน อยู่อย่างถูกลำดับและทิศทาง (ตามเข็มนาฬิกา) ภายในวงกลม

เข็มนาฬิกามี2 อัน อันหนึ่งชี้ที่เลข 11 และอันหนึ่งชี้ที่เลข 2

รูปนาฬิกาที่ขาดองค์ประกอบข้อใดข้อหนึ่งเหล่านี้ให้ถือว่าผิดปกติ การปฏิเสธที่จะวาดรูปนาฬิกาให้ถือว่าผิดปกติ

A normal clock will have all of the following features:
Complete set of numbers of 1-12, without repetition, in the correct order and position (clockwise) within the circle.
Two clock hands, one pointing at the number 11 and the other at number 2
A picture of a clock without any of these features is held to be abnormal.
A refusal to draw a clock is held to be abnormal.

ตัวอย่างของนาฬิกาที่ผิดปกติ An example of an abnormal clock



เข็มนาฬิกาผิดปกติ abnormal clock hands

ตัวเลขไม่ครบ incomplete set of numbers

Appendix C: Information Sheets and consent forms
Appendix C1: Information Sheets and consent forms in English

Participant Information Sheet

Research title: The prevalence of undiagnosed cognitive impairment and undiagnosed depressive mood in over 60's with type 2 diabetes in a Thai community: a cross-sectional study.

Researcher: Miss Supaporn Trongsakul, a post-graduate research student at the School of Allied Health Professions, Faculty of Health, University of East Anglia, United Kingdom
Workplace address (in Thailand): School of Health Science, Mae Fah Luang University, 333 M.1 Tasud, Muang, Chaing Rai, Thailand 57000
Workplace address (in the United Kingdom): School of Allied Health Professions, Faculty of Health, University of East Anglia, United Kingdom, NR4 7TJ
Mobile phone number (in Thailand) 087-5585312
Home phone number (in Thailand) 053-890238 extension 5403
Mobile phone number (in the United Kingdom) +44-07-791541214

What is the study rationale?

Type 2 Diabetes Mellitus (DM) diabetes is one of the long-term (chronic) diseases which cause a health problem in Thai older people. The important self-care activities to ensure healthy lifestyle in diabetic patients are control of blood sugar level, regularly exercise, and keep taking medicine and properly diet e.g. low in fat, sugar and salt with plenty of fruit and vegetables. However, these activities may not succeed if the patients have poor memory or depressive mood. Therefore, screening of memory function and depressive mood in the Thai older people with type 2 DM will provide the information for the further suitable care.

What is the purpose of the study?

The purpose of this study is to investigate whether patients with type 2 Diabetes Mellitus (DM), aged 60 years old or more have difficulty with memory and/or mood changes such as depression. This is important because these may be linked to control of blood glucose and good management of their diabetes

Why have I been chosen?

You have been chosen because you are in the group of Thai people who are aged 60 and over, and who have registered as a patient with type 2 DM at a Primary Care Unit in the San-sai district at the time of the study. You are therefore eligible to be considered for the study

What will happen to me if I take part?

If you decide you would like to take part in the study I, the researcher, will ask the nurse some questions about you such as whether you have any problems in hearing or seeing. After this, I will meet you in the Diabetic Clinic you normally attend. I will ask you about your mood and memory. The assessment will take about 30 minutes

What is the possible benefit of taking part?

The information from this study may help the staff at Primary Care Units to provide more targeted care and without delay for the person who has been identified with cognitive impairment and depressive mood at the early state.

Are there any potential benefits to your community?

The results from this study may give information to the heath care services in your community for future planning to provide early advice, management and support for older people with type 2 DM who have early stage poor memory and depressive mood.

What is the possible risk of taking part?

There is no physical risk to you but you may feel uncomfortable answering some questions or you may feel weary from the tests during the study.

How to prevent the possible risk?

You do not have to answer any questions that you feel uncomfortable about and you can have a break during the study tests if you feel tired. If an emerging mental or health problems are identified during the study by the researcher, the researcher will, with the consent of the patient, notify a clinical member of staff within the Primary Care Unit to enable appropriate care to be provided. If necessary, any interview will be terminated.

Will my taking part in this study be kept confidential?

All information, which is collected about you, will be treated as strictly confidential in a locked cupboard in each primary care unit (this has already been negotiated with each of the primary care units) to which only the researcher has access or password protected on the researcher's computer. Nobody will see it except the researcher, the researcher's supervisors and a supervisory panel of academics. No individual will be identifiable from any report resulting from this research. All the information I collect about you will be destroyed 5 years after the study has finished.

Will I be paid for being in the study?

You will not be paid for participating in this study but I will give you a small refreshment (one bottle of soya milk) as a "thank you'' for your participation.

Are there any costs to being in the study?

There are no costs to you for any activities in this study but you have to spend an extra 30 minutes at DM clinic on your regular basis to participate in the study.

Do I have to take part?

No, it is entirely up to you whether you wish to take part or not. If you decide to take part you are still free to withdraw at anytime without giving a reason. Withdrawal will not affect your care in anyway and you have the right to not answer any question that you do not wish to answer.

Contact details of the field mentor

If you should have any question regarding this study, please contact Dr. Nahathai Wongpakaran, a geriatric psychiatrist and the field mentor who has the role to monitor and ensure that the research method does not present any undue risks to the participants.

For any concerns with your participation in this study, please contact:

Nahathai Wongpakaran, MD
Assistant Professor
Geriatric Psychiatry Unit
Department of Psychiatry, Faculty of Medicine

Chiang Mai University, 110 Intawaroros Rd., Sripoom, A. Muang, Chiang Mai,50200.
Telephone number: 053-945422 and Fax number: 053-945426 (working hours)
Mobile phone number: 08-66702400 (Non-working hours)

Who can answer my questions about the study?

For questions about your rights while taking part in this study,
The Office of the Secretary,
Ethical Review Committee for Research in Human Subjects,
Department of Medical Services,
3th floor of the Building No.2, Ministry of Public Health
Tiwanond Road, Nonthaburi 11000
Telephone number 02-590-6171-2 (working hours)

Research title:The prevalence of undiagnosed cognitive impairment and undiagnosed depressive mood in over 60's with type 2 diabetes in a Thai community: a cross-sectional study.

Consent date.....

Before signing the consent, the study's purpose, procedures, risks and possible benefits have been clearly explained to me by the researcher and I understand them.

The researcher has agreed to answer completely and honestly all questions to my satisfaction.

I am free to withdraw my consent and terminate my participation at any time without my medical care or legal rights being affected.

The researcher has guaranteed that all information I give will remain confidential and only shared amongst the research study team

The researcher has confirmed that I will not receive any compensation for the possible risks or disabilities that may happen to me during the study but I will be received the universal health care. I can contact Miss Supaporn Trongsakul at No 52 Soi 12 Sukkasem, Muang, Chaing Mai 503000, Mobile phone number 087-5585312 (24 hours)or Dr. Nahathai Wongpakaran, the field mentor of this research study, at Department of Psychiatry, Faculty of Medicine, ChiangMaiUniversity, 110 Inthravarorot, Sripoom, Chiang Mai,50200, Mobile phone number: 08-66702400 (24 hours)

The person who takes responsibility for this research isMiss Supaporn Trongsakul with the contact details at No 52 Soi 12 Sukkasem, Muang, Chaing Mai 50300, Mobile phone number 087-5585312 (24 hours)

I have read the information, or it has been read to me. I clearly understand what is involved and consent voluntarily to participate in this research.

Signature

/Thumbprint.....Participant

Full name……

(Date……month.....year.....)

Signature.....

Researcher

Full name……

(Date……month.....year.....)

Signature.....Witness

Full name……

(Date……month.....year.....)

Signature..... Witness

Full name……

(Date……month.....year.....)

Appendix C2: Information Sheets and consent forms in Thai

เอกสารแนะนำสำหรับอาสาสมัคร

โครงการวิจัยเรื่อง"อัตราชุกของภาวะพุทธิปัญญาบกพร่องหรือภาวะซึมเศร้าในผู้ป่วยเบาหวานชนิดที่สอง: กรณีศึกษาเฉพาะหน่วยปฐมภูมิ อำเภอสันทราย จังหวัดเชียงใหม่"

นางสาวสุภาพร ตรงสกุล นักศึกษาปริญญาเอก มหาวิทยาลัยอีสแอนเกลีย ประเทศอังกฤษ ผู้วิจัยหลัก สถานที่ปฏิบัติงานสำนักวิชาวิทยาศาสตร์สุขภาพ มหาวิทยาลัยแม่ฟ้าหลวงเลขที่ 333 หมู่ 1 ตำบลท่าสุด อำเภอเมืองจ.เชียงราย 57000

หมายเลขโทรศัพท์เคลื่อนที่087-5585312 (24 ชั่วโมง)

หมายเลขโทรศัพท์ที่บ้าน 053-890238 ต่อ 5403 (24 ชั่วโมง)

เหตุผลและความจำเป็นที่ต้องทำการวิจัย

โรคเบาหวานชนิดที่ 2 เป็นหนึ่งในโรคเรื้อรังที่เป็นปัญหาทางสุขภาพที่พบได้มากในผู้สูงอายุไทย การควบคุมระดับน้ำตาลในเลือดให้เหมาะสมอยู่เสมอร่วมกับการรับประทานยาอย่างต่อเนื่อง รวมทั้งการรับประทานอาหารและออกกำลังกายอย่างถูกต้อง เป็นสิ่งที่จำเป็นอย่างยิ่งต่อการดูแลรักษาตนเองของผู้ป่วยโรคเบาหวานทั้งนี้หากผู้ป่วยเบาหวานมีภาวะความจำบกพร่องหรือมีภาวะซึมเศร้าก็จะทำให้ไม่สามารถควบคุมระดับน้ำตาลในเลือดและดูแลรักษาตนเองได้อย่างถูกต้องเหมาะสม ดังนั้นการรู้ถึงภาวะทางความจำและภาวะซึมเศร้าในผู้สูงอายุที่ป่วยเป็นโรคเบาหวานชนิดที่2 จึงมีความจำเป็นเพื่อส่งเสริมให้มีการรักษาดูแลสุขภาพให้เหมาะสมต่อไป

วัตถุประสงค์ของการศึกษาวิจัย

การศึกษานี้มีวัตถุประสงค์เพื่อสำรวจดูว่าผู้ป่วยเบาหวานชนิดที่ 2 อายุตั้งแต่ 60 ปีขึ้นไป จะมีภาวะบกพร่องทางความจำหรือภาวะซึมเศร้าหรือไม่ ซึ่งภาวะดังกล่าวมีความสำคัญและมีส่วนเกี่ยวข้องต่อการควบคุมระดับน้ำตาลในเลือดและการดูแลรักษาตนเองต่อโรคเบาหวาน

ทำไมท่านจึงถูกเลือก

เนื่องจากท่านอยู่ในกลุ่มผู้ป่วยเบาหวานชนิดที่ 2 ที่มีอายุตั้งแต่ 60 ปีขึ้นไป ที่ได้มารับการดูแลรักษาที่สถานีอนามัย ในเขตพื้นที่ อำเภอ สันทราย จังหวัดเชียงใหม่ ซึ่งเป็นเขตพื้นที่ที่ทำการศึกษาวิจัย

วิธีการศึกษาวิจัย

หากท่านตัดสินใจเข้าร่วมงานวิจัย ผู้วิจัยก็จะถามพยาบาลหรือบุคลากรทางการแพทย์ที่ดูแลรักษาท่านเล็กน้อยเกี่ยวกับตัวท่าน เช่น ท่านมีปัญหาทางด้านการฟังหรือการมองเห็นหรือไม่ หลังจากนั้นผู้วิจัยก็จะไปพบท่าน ในวันที่ท่านมารับการตรวจดูแลรักษาโรคเบาหวาน ที่คลินิกเบาหวานของสถานีอนามัย โดยผู้วิจัยจะเป็นผู้ใช้แบบประเมินสอบถามท่านเกี่ยวกับภาวะความจำและภาวะซึมเศร้าของท่านเป็นเวลาโดยประมาณ 30 นาที

ประโยชน์ที่ท่านอาจจะได้รับต่อการเข้าร่วมงานวิจัย

ข้อมูลที่ได้จากงานวิจัยนี้อาจช่วยให้บุคลากรทางการแพทย์ในสถานีอนามัยที่ดูแลท่านนำข้อมูลไปปรับใช้เพื่อให้การดูและรักษาที่เหมาะสมและส่งเสริมให้ท่านสามารถดูแลรักษาตนเองต่อโรคเบาหวานให้ดียิ่งขึ้นและหากท่านมีความกังวลใจในเรื่องความจำและภาวะซึมเศร้า การเข้าร่วมการวิจัยนี้อาจช่วยให้ท่านลดความสงสัยและกังวลใจในภาวะดังกล่าว

ประโยชน์ที่ชุมชนของท่านจะได้รับจากงานวิจัยนี้

ผลการวิจัยที่ได้จะเป็นประโยชน์ต่อการวางแผนเพื่อให้บริการทางด้านสุขภาพในชุมชนของท่านต่อการให้คำแนะนำ ดูแลและจัดการ กลุ่มผู้ป่วยเบาหวานสูงอายุที่ป่วยเป็นโรคเบาหวานชนิดที่ 2 ที่เริ่มจะมีภาวะความจำบกพร่องและภาวะซึมเศร้าได้แต่เนิ่นๆ

ความเสี่ยงที่คาดว่าจะเกิดขึ้นกับอาสาสมัครในการเข้าร่วมการศึกษา

ท่านจะไม่ได้รับความเสี่ยงจากการใช้เครื่องมือทางการแพทย์หรือการให้ยาที่เป็นอันตรายต่อร่างกาย แต่การสัมภาษณ์เป็นระยะนานๆ อาจทำให้ท่านเบื่อหน่ายหรือเหนื่อยล้าได้ บางข้อคำถามอาจเป็นความรู้สึกส่วนตัว ท่านอาจรู้สึกอึดอัด ไม่สบายใจ

การป้องกันความเสี่ยง และการแก้ไขกรณีเกิดปัญหา

หากท่านเกิดความเหนื่อยล้าจากการตอบแบบสอบถาม ผู้วิจัยจะไม่เร่ง และจะให้ท่านพักระหว่างการตอบแบบสอบถาม หากท่านลำบากใจต่อข้อคำถามใดๆ ท่านไม่จำเป็นต้องตอบในข้อคำถามนั้น

ขอบเขตการดูแลรักษาความลับของข้อมูลต่างๆของอาสาสมัคร

ข้อมูลทุกอย่างของท่านจะถูกเก็บรวบรวมเป็นความลับอย่างเคร่งครัด จะมีเพียง ผู้วิจัย อาจารย์ที่ปรึกษาวิทยานิพนธ์ และกรรมการที่ปรึกษาวิทยานิพนธ์ เพียงเท่านั้นที่จะได้เห็นข้อมูลงานวิจัย โดยในรายงานผลการวิจัยจะไม่มีการระบุชื่อหรือข้อมูลส่วนตัวของผู้เข้าร่วมงานวิจัย

การตอบแทนแก่อาสาสมัคร

ท่านจะไม่ได้รับค่าตอบแทนในการเข้าร่วมงานวิจัยนี้ แต่ท่านจะได้รับ อาหารว่าง (นมถั่วเหลือง 1 กล่อง) เป็นการแสดงความขอบคุณต่อการเข้าร่วมการศึกษาวิจัยนี้

ค่าใช้จ่ายของท่านในการเข้าร่วมการวิจัย

ท่านไม่ต้องเสียค่าใช้จ่ายใดๆทั้งสิ้นในการเข้าร่วมงานวิจัยนี้

ท่านจำเป็นต้องเข้าร่วมงานวิจัยหรือไม่

ท่านไม่จำเป็นต้องเข้าร่วมการวิจัยครั้งนี้หากท่านไม่สมัครใจ และหากท่านเข้าร่วมงานวิจัย ท่านมีสิทธิที่จะถอนตัวหรือยกเลิกการเข้าร่วมการศึกษาวิจัยได้ทุกเมื่อ โดยไม่จำเป็นต้องบอกเหตุผล และ การถอนตัวจากการศึกษาจะไม่มีผลกระทบใดๆต่อการรักษาไม่ว่าในกรณีใดๆทั้งสิ้น อีกทั้งท่านมีสิทธิอย่างเต็มที่ในการไม่ตอบคำถามข้อใดก็ได้ที่ท่านไม่ต้องการที่จะตอบ

ชื่อ ที่อยู่ เบอร์โทรศัพท์ของแพทย์ สามารถติดต่อได้สะดวก ทั้งในและนอกเวลาราชการ กรณีมีเหตุจำเป็นหรือฉุกเฉิน

งานวิจัยนี้มี ผู้ช่วยศาสตราจารย์แพทย์หญิง ณหทัย วงศ์ปการันย์ จิตแพทย์ผู้เชี่ยวชาญด้านจิตเวชศาสตร์ผู้สูงอายุ เป็นที่ปรึกษาการเก็บข้อมูลพื้นที่วิจัยและเป็นนักวิจัยพี่เลี้ยง โดยทำหน้าที่กำกับดูแลการเก็บ

ข้อมูลงานวิจัยในประเทศไทย ให้ดำเนินการตามวิธีการและหลักการของคุณภาพงานวิจัยที่ดี ดังนั้น หากท่านมีคำถามหรือข้อสงสัยเกี่ยวกับการเข้าร่วมงานวิจัยนี้ ท่านสามารถติอต่อ

ผู้ช่วยศาสตราจารย์แพทย์หญิง ณหทัย วงศ์ปการันย์

ที่อยู่ ภาควิชาจิตเวชศาสตร์ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่

หมายเลขโทรศัพท์ 053-945422 และหมายเลขโทรสาร 053-945426 (ในเวลาราชการ (

โทรศัพท์เคลื่อนที่ 086-6702400 (นอกเวลาราชการ)

<u>ชื่อที่อยู่เบอร์โทรศัพท์ติดต่อเรื่องการสอบถามข้อมูลหรือสิทธิและผลประโยชน์ของผู้เข้าร่วมการวิจัยนี้</u>

ท่านสามารถสอบถามข้อมูลหรือสิทธิและผลประโยชน์ของการข้าร่วมวิจัยนี้ได้ที่

สำนักงานเลขานุการคณะกรรมการพิจารณาการศึกษาวิจัยในคน กระทรวงสาธารณสุข อาคาร 2 ชั้น 3 ตึกกรมการแพทย์ ถนนติวานนท์ อำเภอเมือง จังหวัดนนทบุรี 11000

หมายเลขโทรศัพท์ 02-590-6171-2 (ในเวลาราชการ)

ใบยินยอมด้วยความสมัครใจ

การวิจัยเรื่องอัตราชุกของภาวะพุทธิปัญญาบกพร่องหรือภาวะซึมเศร้าของผู้ป่วยสูงอายุเบาหวานชนิดที่สองในชุมชน: กรณีศึกษาเฉพาะหน่วยปฐมภูมิ อำเภอสันทราย จังหวัดเชียงใหม่

วันที่ให้คำยินยอม วันที่.....เดือน.....พ.ศ.....

ก่อนที่จะลงนามในใบยินยอมให้ทำการวิจัยนี้ข้าพเจ้าได้รับการอธิบายจากผู้วิจัยถึงวัตถุประสงค์ของการวิจัย วิธีการวิจัย อันตรายหรืออาการที่อาจเกิดขึ้นจากการวิจัยหรือจากยาที่ใช้ รวมทั้งประโยชน์ที่จะเกิดขึ้นจากการวิจัยอย่างละเอียด และมีความเข้าใจดีแล้ว

ผู้วิจัยรับรองว่าจะตอบคำถามต่างๆที่ข้าพเจ้าสงสัยด้วยความเต็มใจ ไม่ปิดบัง ซ่อนเร้น จนข้าพเจ้าพอใจ

ข้าพเจ้ามีสิทธิที่จะบอกเลิกการเข้าร่วมในโครงการวิจัยเมื่อใดก็ได้และเข้าร่วมโครงการวิจัยนี้โดยสมัครใจและการบอกเลิกการเข้าร่วมการวิจัยนี้ จะไม่มีผลต่อการรักษาโรคที่ข้าพเจ้าจะได้รับต่อไป

ผู้วิจัยรับรองว่าจะเก็บข้อมูลเฉพาะเกี่ยวกับตัวข้าพจ้าเป็นความลับและจะเปิดเผยได้เฉพาะสรุปผลการวิจัยหรือการเปิดเผยข้อมูลต่อผู้มีหน้าที่ที่เกี่ยวข้องกับการสนับสนุนและกำกับดูแลการวิจัยเท่านั้น

ข้าพเจ้าได้อ่านข้อความข้างต้นแล้ว และมีความเข้าใจดี

ลงนาม.....ผู้ยินยอม
ตัวบรรจง……..
วันที่.....เดือน.....พ.ศ.……

ลงนาม .....ผู้วิจัย
ตัวบรรจง…….
วันที่.....เดือน.....พ.ศ.……

ลงนาม .....พยาน

ตัวบรรจง…….

วันที่.....เดือน.....พ.ศ……

ลงนาม .....พยาน

ตัวบรรจง…….

วันที่.....เดือน.....พ.ศ……

Appendix D: Instruments of the study (English and Thai)
Appendix D1:Mini-Cog -Thai version

MINI-COG ™ - PS Version

2) **ให้ผู้ป่วยตั้งใจฟังแล้วบอกผู้ป่วยว่า "ดิฉัน (ผม) จะบอกคำ 3 คำซึ่งอยากให้คุณ (ชื่อ ป้า ลุง ยาย ตา) จำตอนนี้แล้วก็จำไว้ต่อไปนะคะ (นะครับ) คำเหล่านี้ได้แก่**

บ้าน แมว สีเขียว

ไหนลองพูดออกมาให้ฟังสิคะ (ครับ)" (ให้โอกาสผู้ป่วยลองทำ3 **ครั้งหากไม่สามาร**ถทำได้**หลังจากพยายาม**3ครั้งให้ทำข้อต่อไป)

พับหน้านี้ไปทางด้านหลังตามรอยประ2แถวด้านล่างเพื่อให้เกิดพื้นที่ว่างและปิดคำที่ให้จำไว้ส่งดินสอ/ปากกาให้ผู้ป่วย

3) พูดวลีต่อไปนี้ตามลำดับ:" ช่วยวาดรูปนาฬิกาลงบนที่ว่างด้านล่างนี้หน่อยนะคะ (ครับ) เริ่มจากวาดวงกลมวงใหญ่ๆค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ใส่ตัวเลขลงไปในวงกลมให้ครบเลยค่ะ (ครับ)" (เมื่อเสร็จแล้วให้บอกว่า) "ทีนี้ให้ตั้งเวลาโดยให้เข็มนาฬิกาชี้บอกเวลา11:10 น. (สิบเอ็ดนาฬิกาสิบนาที) ค่ะ (ครับ)" หากผู้ป่วยไม่สามารถวาดนาฬิกาได้เสร็จภายใน3 นาทีให้หยุดทำแล้วไปถามคำที่ให้จำไว้

4) พูดว่า: "คำ 3 คำที่ดิฉัน (ผม)ให้คุณ (ชื่อป้าลุงยายตา)จำไว้มีอะไรบ้างคะ (ครับ)"

_____ _____ _____

_____ (ให้1 คะแนนต่อ1 คำ)

คะแนนการระลึกคำ3 คำ

ให้คะแนนรูปนาฬิกา (ดูคำแนะนำอีกหน้าหนึ่ง): รูปนาฬิกาปกติ

2 คะแนน

รูปนาฬิกาผิดปกติ

0 คะแนน

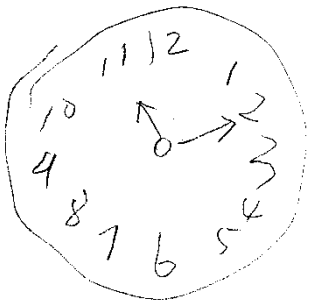
คะแนนรูปนาฬิกา 

คะแนนรวม = 

คะแนนการระลึกคำ 3 คำ รวมกับคะแนนรูปนาฬิกา

คะแนน 0, 1, หรือ 2 อาจจะมีความบกพร่อง; 3, 4, หรือ 5 ไม่มีความบกพร่อง

การให้คะแนนรูปนาฬิกา



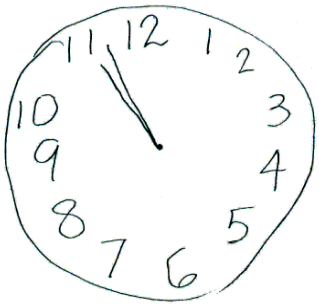
นาฬิกาปกติ

นาฬิกาปกติจะมีองค์ประกอบดังต่อไปนี้ครบถ้วน:

ตัวเลขครบ1-12ไม่ซ้ำกันอยู่อย่างถูกลำดับและทิศทาง (ตามเข็มนาฬิกา) ภายในวงกลม

เข็มนาฬิกามี2 อันอันหนึ่งชี้ที่เลข11 และอันหนึ่งชี้ที่เลข2

ตัวอย่างของนาฬิกาที่ผิดปกติ



เข็มนาฬิกาผิดปกติ

ตัวเลขไม่ครบ

รูปนาฬิกาที่ขาดองค์ประกอบข้อใดข้อหนึ่งเหล่านี้ให้ถือว่าผิดปกติ การปฏิเสธที่จะวาดรูปนาฬิกาให้ถือว่าผิดปกติ

Mini-Cog™ลิขสิทธิ์ S Borson. Mini-Cog PS ออกแบบมาเพื่อใช้กับผู้ใหญ่ที่จบการศึกษาระดับประถมศึกษาพิมพ์ซ้ำโดยได้รับอนุญาตจากเจ้าของเพื่อใช้ในงานวิจัยของสุภาพรตรงสกุล (School of Allied Health Professions, University of East Anglia, UK) ในงานวิจัยเกี่ยวกับความบกพร่องด้านพุทธิปัญญาของผู้ป่วยเบาหวานชาวไทยไม่อนุญาตให้ปรับปรุงหรือใช้ในวัตถุประสงค์อื่นเว้นแต่ได้รับอนุญาตจากเจ้าของ (soob@u.washington.edu). สงวนลิขสิทธิ์

Appendix D1:Mini-Cog -English version

MINI-COG ™ - PS Version

1) **GET THE PATIENT'S ATTENTION, THEN SAY: "I am going to say three words that I want you to remember now and later. The words are**

House Cat Green.

Please say them for me now." (Give the patient 3 tries to repeat the words. If unable after 3 tries, go to next item.)
(Fold this page back at the TWO dotted lines BELOW to make a blank space and cover the memory words. Hand the patient a pencil/pen).

1) **SAY ALL THE FOLLOWING PHRASES IN THE ORDER INDICATED**: **"Please draw a clock in the space below. Start by drawing a large circle."** (When this is done, say) **"Put all the numbers in the circle."** (When done, say) **"Now set the hands to show 11:10 (10 past 11)."** If subject has not finished clock drawing in 3 minutes, discontinue and ask for recall items.

---

2) SAY: "What were the three words I asked you to remember?"

_____ _____ _____

Score 1 point for each) 3-Item Recall Score ☐

Score the clock (see other side for instructions):
Normal clock 2 points

Abnormal clock 0 point

Clock Score ☐

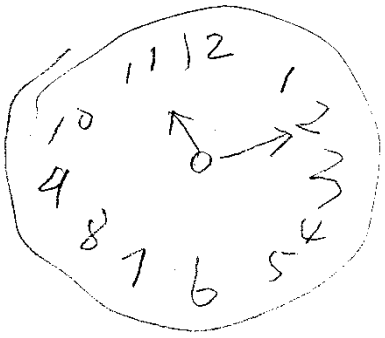
Total Score = 3-item recall plus clock score ☐

0, 1, or 2 possible impairment;

3, 4, or 5 suggests no impairment

CLOCK SCORING

NORMAL CLOCK



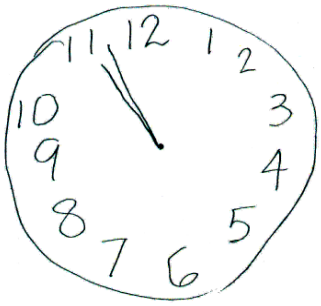
A NORMAL CLOCK HAS ALL OF THE FOLLOWING ELEMENTS:

All numbers 1-12, each only once, are present in the correct order and direction (clockwise) inside the circle.

Two hands are present, one pointing to 11 and one pointing to 2.

ANY CLOCK MISSING ANY OF THESE ELEMENTS IS SCORED ABNORMAL. REFUSAL TO DRAW A CLOCK IS SCORED ABNORML

SOME EXAMPLES OF ABNORMAL CLOCKS



ABNORMAL HANDS

MISSING NUMBER

Appendix D2: MMSE Thai 2002 in Thai

แบบทดสอบ MMSE – Thai 2002*

Mini – Mental State Examination : Thai version (MMSE – Thai 2002)

1. Orientation for time(5 คะแนน)	บันทึกคำตอบไว้ทุกครั้ง	คะแนน
(ตอบถูกข้อละ 1 คะแนน)	(ทั้งคำตอบที่ถูกและผิด)	
1.1 วันนี้วันที่เท่าไร	……..	☐
1.2 วันนี้วันอะไร	……..	☐
1.3 เดือนนี้เดือนอะไร	……..	☐
1.4 ปีนี้ปีอะไร	……..	☐
1.5 ฤดูนี้ฤดูอะไร	……..	☐

2. Orientation for place (5 คะแนน)(ให้เลือกข้อใดข้อหนึ่ง)

(ตอบถูกข้อละ 1 คะแนน

2.1 กรณีอยู่ที่สถานพยาบาล

2.1.1 สถานที่ตรงนี้เรียกว่า อะไร <u>และ</u>.....ชื่อว่าอะไร	……..	☐
2.1.2 ขณะนี้ท่านอยู่ที่ชั้นที่เท่าไรของตัวอาคาร	……..	☐
2.1.3 ที่อยู่ในอำเภอ - เขตอะไร	……..	☐
2.1.4 ที่นี่จังหวัดอะไร	……..	☐
2.1.5 ที่นี่ภาคอะไร	……..	☐

2.2 กรณีที่อยู่ที่บ้านของผู้ถูกทดสอบ

2.2.1 สถานที่ตรงนี้เรียกว่าอะไร<u>และ</u>บ้านเลขที่อะไร	……..	☐
2.2.2 ที่นี่หมู่บ้าน หรือละแวก/คุ้ม/ย่าน/ถนนอะไร	……..	☐
2.2.3 ที่นี่อำเภอเขต / อะไร	……..	☐
2.2.4 ที่นี่จังหวัดอะไร	……..	☐
2.2.5 ที่นี่ภาคอะไร	……..	☐

3. Registraion (3 คะแนน)

ต่อไปนี้เป็นการทดสอบความจำ ดิฉันจำบอกชื่อของ 3 อย่าง คุณ (ตา , ยาย....) ตั้งใจฟังให้ดีนะเพราะจะบอกเพียงครั้งเดียว ไม่มีการบอกซ้ำอีก เมื่อ ผม (ดิฉัน) พูดจบ ให้ คุณ (ตา,ยาย....)**พูดทบทวนตามที่ได้ยิน ให้ครบ ทั้ง 3 ชื่อ** แล้วพยามจำไว้ให้ดี เดี๋ยวดิฉันจะถาม

ซ้ำ

∗ การบอกชื่อแต่ละคำให้ห่างกันประมาณหนึ่งวินาที ต้องไม่ช้าหรือเร็วเกินไป

(ตอบถูก 1 คำได้ 1 คะแนน)

〇ดอกไม้ 〇แม่น้ำ 〇รถไฟ …….. ☐

4. Attention/Calculation (5 คะแนน)(ให้เลือกข้อใดข้อหนึ่ง)

ข้อนี้เป็นการคิดเลขในใจเพื่อทดสอบสมาธิ คุณ (ตา,ยาย....) คิดเลขในใจเป็นไหม ?

ถ้าตอบคิดเป็นทำข้อ 4.1 ถ้าตอบคิดไม่เป็นหรือไม่ตอบให้ทำข้อ 4.2

4.1 “ข้อนี้คิดในใจเอา 100 ตั้ง ลบออกที่ละ 7

ไปเรื่อยๆ ได้ผลเท่าไรบอกมา …… …… …… …… …… …… …… …… ☐

บันทึกคำตอบตัวเลขไว้ทุกครั้ง (ทั้งคำตอบที่ถูกและผิด) ทำทั้งหมด 5ครั้ง

ถ้าลบได้ 1,2,หรือ3 แล้วตอบไม่ได้ ก็คิดคะแนนเท่าที่ทำได้ ไม่ต้องย้ายไปทำข้อ 4.2

4.2 “ผม (ดิฉัน) จะสะกดคำว่า มะนาว ให้คุณ (ตา , ยาย....) ฟังแล้วให้คุณ (ตา , ยาย ....) สะกดถอยหลังจากพยัญชนะตัวหลังไปตัวแรก คำว่ามะนาวสะกดว่า มอม้า-สระอะ-นอหนู-สระอา-วอแหนว ไหนคุณ(ตา,ยาย....)สะกอถอยหลัง ให้ฟังซิ

…… …… …… …… ……

วา น ะ ม

5. Recall (3 คะแนน)

เมื่อสักครู่ที่ให้จำของ 3 อย่างจำได้ไหมมีอะไรบ้าง” (ตอบถูก 1 คำได้ 1 คะแนน)

〇ดอกไม้ 〇แม่น้ำ 〇รถไฟ …….. ☐

6. Naming (2 คะแนน)

6.1 ยื่นดินสอให้ผู้ถูกทดสอบดูแล้วถามว่า

“ของสิ่งนี้เรียกว่าอะไร” …….. ☐

6.2 ชี้นาฬิกาข้อมือให้ผู้ถูกทดสอบดูแล้วถามว่า

“ของสิ่งนี้เรียกว่าอะไร” …….. ☐

7. Repetition (1 คะแนน)

(พูดตามได้ถูกต้องได้ 1 คะแนน)

ตั้งใจฟังผม (ดิฉัน) เมื่อผม (ดิฉัน) พูดข้อความนี้

แล้วให้คุณ (ตา,ยาย)พูดตาม ผม (ดิฉัน) จะบอกเพียงครั้งเดียว

“ใครใคร่ขายไก่ไข” …….. ☐

8. Verbal command (3 คะแนน)

ข้อนี้ฟังคำสั่ง “ฟังดีๆ นะเดี๋ยวผม (ดิฉัน)จะส่งกระดาษให้คุณ แล้วให้คุณ (ตา , ยาย....) รับด้วยมือขวา พับครึ่งกระดาษ แล้ววางไว้ที่.....”(พื้น,โต๊ะ,เตียง)

ผู้ทดสอบแสดงกระดาษเปล่าขนาดประมาณ เอ-4

ไม่มีรอยผับ ให้ผู้ถูกทดสอบ

○ รับด้วยมือขวา ○ พับครึ่ง ○ วางไว้ที่”(พื้น,โต๊ะ,เตียง) …….. ☐

9. Written command (1 คะแนน)

ต่อไปเป็นคำสั่งที่เขียนเป็นตัวหนังสือ ต้องการให้คุณ (ตา , ยาย....) อ่าน แล้วทำตาม (ตา , ยาย....) จะอ่านออกเสียงหรืออ่านในใจ

ผู้ทดสอบแสดงกระดาษที่เขียนว่า “หลับตาได้”○ หลับตาได้…..…….. ☐

หลับตา

10. Writing (1 คะแนน)

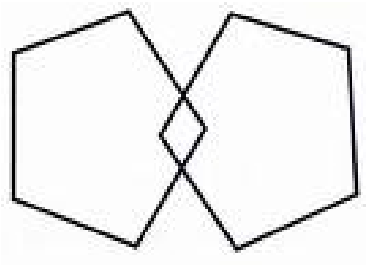
ข้อนี้จะเป็นคำสั่งให้ “คุณ (ตา , ยาย....) เขียนข้อความอะไรก็ก็ที่อ่านแล้วรู้เรื่อง หรือมีความหมายมา 1ประโยค” .....

○ ประโยคมีความหมาย …….. ☐

11. Visuoconstruction (1 คะแนน)

ข้อนี้เป็นคำสั่ง“จงวาดภาพให้เหมือนภาพตัวอย่าง”

(ในช่องว่างด้านขวาของภาพตัวอย่าง) …….. ☐

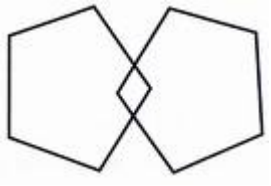


.....คะแนนเต็ม 30

ระดับการศึกษา	คะแนน	
	จุดตัด	เต็ม
ไม่ได้เรียนหนังสือ(อ่านหนังไม่ออก)	≤ 14	23
จบประถมศึกษา	≤ 17	30
สูงกว่าประถม	≤ 22	30

*สถาบันเวชศาสตร์ผู้สูงอายุกรมการแพทย์กระทรวงสาธารณสุข

Appendix D2: Translation of MMSE Thai 2002 from Thai to English
Mini - Mental State Examination Thai 2002 (MMSE Thai 2002) *

Questions	**Points**
1. What is the : Year? Season? Month? Day? Date?	5
2. Where are we : Province? Country? District? Hospital? Floor?	5
3. Name three objects (flower, river, train) taking one second to say each Then ask the patient to tell you the three. Repeat the answer until the patient learns all three words.	3
4. Attention/Calculation 4.1 Serial 7's. Subtract 7 from 100, then subtract 7 from that number, and then subtract 7 from that number, etc. Stop after five answers. 4.2 Alternative : Spell Ma-nao (lemon in Thai) backwards.	5
5. Ask for the names of the three objects learned in # 3.	3
6. Point to a pencil and a watch. Have the patient name them as you point.	2
7. Have the patient repeat "Kray-Krai-Kaii-Kai-Gai	1
8. Have the patient follow a three-stage command : "Take the paper in your right hand. Fold the paper in half. Put the paper on the floor"	3
9. Have the patient read and obey to following : "CLOSE YOUR EYES" (write it in large letters). **หลับตา**	1
10.Have the patient write a sentence of his or her own choice.	1
11. Have the patient copy the following design (overlapping pentagons). 	1

…….TOTAL points 30

Level of education	Point(s)	
	Cut-off score	Total score
Illiterate	≤ 14	23
Primary school	≤ 17	30
More than primary school	≤ 22	30

* Institute of Geriatric Medicine, Ministry of Public Health, Thailand

Appendix D3: TGDS in Thai

<u>แบบคัดกรองภาวะซึมเศร้าในผู้สูงอายุของไทย (Thai Geriatric Depression Scale –TGDS)*</u>

……1. คุณพอใจกับชีวิตความเป็นอยู่ตอนนี้

……...2. คุณไม่อยากทำในสิ่งที่เคยสนใจหรือเคยทำเป็นประจำ

……...3. คุณรู้สึกชีวิตของคุณช่วงนี้ว่างเปล่าไม่รู้จะทำอะไร

……4. คุณรู้สึกเบื่อหน่ายบ่อย ๆ

……5. คุณหวังว่าจะมีสิ่งที่ดีเกิดขึ้นในวันหน้า

……6. คุณมีเรื่องกังวลตลอดเวลา และเลิกคิดไม่ได้

……7.ส่วนใหญ่แล้วคุณรู้สึกอารมณ์ดี

……8. คุณรู้สึกกลัวว่าจะมีเรื่องไม่ดีเกิดขึ้นกับคุณ

……9. ส่วนใหญ่คุณรู้สึกมีความสุข

……10. บ่อยครั้งที่คุณรู้สึกไม่มีที่พึ่ง

……11. คุณรู้สึกกระวนกระวาย กระสับกระส่ายบ่อย ๆ

……..12. คุณชอบอยู่กับบ้านมากกว่าที่จะออกนอกบ้าน

……..13.บ่อยครั้งที่คุณรู้สึกวิตกกังวลเกี่ยวกับชีวิตข้างหน้า

……..14. คุณคิดว่าความจำของคุณดีไม่เท่าคนอื่น

……..15. การที่มีชีวิตอยู่ถึงปัจจุบันนี้เป็นเรื่องน่ายินดีหรือไม่

……..16. คุณรู้สึกหมดกำลังใจหรือเศร้าใจบ่อย ๆ

……..17. คุณรู้สึกว่าชีวิตคุณค่อนข้างไม่มีคุณค่า

……..18. คุณรู้สึกกังวลมากกับชีวิต ที่ผ่านมา

……..19. คุณรู้สึกว่าชีวิตนี้ยังมีเรื่องน่าสนุกอีกมาก

……..20. คุณรู้สึกลำบากที่จะเริ่มต้นทำอะไรใหม่ ๆ

……..21. คุณรู้สึกกระตือรือร้น

……..22. คุณรู้สึกสิ้นหวัง

……..23. คุณคิดว่าคนอื่นดีกว่าคุณ

……..24. คุณอารมณ์เสียง่ายกับเรื่องเล็ก ๆ น้อย ๆ อยู่เสมอ

……25. คุณรู้สึกอยากร้องไห้บ่อย

……26. คุณมีความตั้งใจในการทำสิ่งหนึ่งสิ่งใดได้ไม่นาน

……27. คุณรู้สึกสดชื่นในเวลาตื่นนอนตอนเช้า

……28. คุณไม่อยากพบปะพูดคุยกับคนอื่น

……29. คุณตัดสินใจอะไรได้เร็ว

……..30. คุณมีจิตใจสบาย แจ่มใสเหมือนก่อน

คะแนนรวม …….....

* กลุ่มฟื้นฟูสมรรถภาพสมอง (2537)

Appendix D3: Translation of TGDS from Thai to English

Thai Geriatric Depression Scale (TGDS)*

……1. Are you basically satisfied with your life?

……2. Have you dropped many of your activities and interests?

……3. Do you feel that your life is empty?

…....4. Do you often get bored?

……5. Are you hopeful about the future?

…….6. Are you bothered by thoughts you can t get out of your head?

…….7. Are you in good spirits most of the time?

…….8. Are you afraid that something bad is going to happen to you?

…….9. Do you feel happy most of the time?

…….10. Do you often feel helpless?

…….11. Do you often get restless and fidgety?

…….12. Do you prefer to stay at home, rather than going out and doing new things?

…….13. Do you frequently worry about the future?

…….14. Do you feel you have more problems with memory than most?

…….15 Do you think it is wonderful to be alive now?

…….16 Do you often feel downhearted and blue?

…….17 Do you feel pretty worthless the way you are now?

……18 Do you worry a lot about the past?

……19 Do you find life very exciting?

……20 Is it hard for you to get started on new projects?

……21 Do you feel full of energy?

……22 Do you feel that your situation is hopeless?

……23 Do you think that most people are better off than you are?

……24 Do you frequently get upset over little things?

……25 Do you frequently feel like crying?

……26 Do you have trouble concentrating?

……27 Do you enjoy getting up in the morning?

……28 Do you prefer to avoid social gatherings?

……29 Is it easy for you to make decisions?

……30 Is your mind as clear as it used to be?

Total score…….

*Train the Brain Forum Committee (1994)

Appendix E1: Participant record form

Participant recording form

PCU code	
ID number	
Part I: Demographic data	
Gender 0.male 1.female	Sex (…)
Age 0.60-64 1.65-69 2.70-74 3.75-79 4.80-84 5.over 85	Age (…) (…) Age group (…)
Education 0. uneducated 1. primary school (year(s) in school…..) 2. secondary school (year(s) in school…..) 3. high school (year(s) in school…..) 4. bachelor's degree and over	Edu (…) Yr in sch(…)
Ethnic 0.Thai 1. Hill tribe	Ethnic (…)
Marital status 0. single 1. married 2. separated 3. divorced 4. widow	Marital status (…)
Living arrangement 0.live alone☐no ☐ yes 1. spouse☐no ☐ yes 2. daughter/son☐no ☐ yes 3. grandchildren☐no ☐yes 4. parents☐no ☐ yes 5. relatives☐no ☐ yes 6.Others- specify.....	Liv. Status (…) Liv oth (……)
Income 0.none 1. pension 2. government support (500 baht) 3.saving 4. working 5. others-specify.....	Eco. Statuc (…) Eco oth (…..)
Health care service 0.health care coverage-30 baht scheme (national health insurance) 1.Social/Welfare health care 2.Self-funding	Health support (…) Heath oth (……)

3. Family support (specify who….) 4. Others-specify.....	
Health behaviour in present 1.alcohol drinking☐no ☐ yes 2.Smoking ☐no ☐yes 3. Exercise at least 30 minutes ☐no ☐yes	Health Behaviour Drinking 1. drinking (…) 2. Smoking (…) 3. exercise (…)
Part II: Medical record	
Height .....cms	H (…) (…) (…)
Weight…… kgs.	W (…) (…)
Body Mass Index (BMI)**.....**	BMI (…) (…)
Blood pressure mg/Hg Systolic (**....**) Diastolic (….)	BP S (**.....**) D (….)
Fasting Blood Sugar (FBS) mg/dl or mmol/l last visits; Date…….FBS……mg/dl or mmol/l	FBS (…) date (…)
HbA1C…….% (mmol/mol)	HbA1C (…)
HbA1c date..... HbA1c duration time from the study…….months	HbA1c date …… HbA1c dur time.....
Total Cholesterol ……..(mg/dl or mmol/l) Low density lipoprotein (LDL)…….. (mg/dl or mmol/l) High density lipoprotein (HDL)…… (mg/dl or mmol/l) Triglyceride……..(mg/dl or mmol/l)	Total Chol(…) LDL (…) HDL (…) Trigly (…)
DM treatment 1.No medicine/on diet 2.Medicine (oral) 3.Insulin injection 4.Combine treatment (Medication+Insuline injection)	DM treatment (…)
DM duration (year) 1.1-5 2. 6-10 3.11-15 4.15-20 5. over 20 years	DM duration (…)
Complications 1.Diabetic neuropathy ☐no ☐yes Yes How long……years and date…. 2.Diabetic retinopathy ☐no ☐yes Yes How long……years and date…. 3.Diabetic nephropathy ☐no ☐yes Yes How long……years and date…. 4. Others specify ……	Compli (.....)
History of Chronic disease 1.Heart disease Before DM ☐no ☐yes	Chronic disease (…) Before DM (…)

How long…..year (s) and date ……. 2.Hypertension Before DM ☐no ☐yes How long…..year (s) and date…….. 3.COPD Before DM ☐no ☐yes How long…..year (s) and date…….. 4. Osteoporosis Before DM ☐no ☐yes How long…..year (s) and date…….. 5. Arthritis Before DM ☐no ☐yes How long…..year (s) and date…….. 6.Others specify…… Before DM ☐no ☐yes How long…..year (s) and date……..	Time (….)
Part II: Score from questionnaire test	
MMSE …… /Cog result……. Mini-Cog…… /Cog result…….. TGDS…….	MMSE (…) CogMM……. Mini-Cog (…) CogMC……. TGDS (…)

Appendix E2:Codes of variables

Code of variables

Variables	Measurement	Type
Part I: Demographic data		
Gender	0 = male 1 = female	Categorical data
Age	Numeric	Continuous data
Age group	0 = 60-64 1 = 65-69 2 = 70-74 3 = 75-79 4 = 80-84 5 = 85+	Categorical data
Education	0 =uneducated 1= Primary school 2= Junior school 3= High school 4= Bachelor's degree and over	Categorical data
Years in school	Numeric	Continuous data
Ethnic	0 = Thai 1 = Hill tribe	Categorical data
Marital status	0 = single 1= married 2 = separated 3 = divorced 4 = widowed	Categorical data
Living arrangement	0 = living alone 1= not living alone	Categorical data
Income	0 = none 1 = pension 2 = government support (500 baht or £ 10)/ month) 3 = bank saving 4 = working	
Health care service	0 = health care coverage-30 baht scheme (national health insurance) 1 = Social/Welfare health care 2 = Self-funding 3 = Family support	Categorical data
Part I: Demographic data(continued)		
Current health behaviour		
drinking	0 = no	Categorical data

	1 = yes	
smoking	0 = no 1 = yes	Categorical data
exercise	0 = no 1 = yes	Categorical data
Part II: Medical record		
Height (centimetres)	Numeric	Continuous data
Weight (kilograms)	Numeric	Continuous data
Body Mass Index (kg/m^2)	Numeric	Continuous data
Body Mass Index (kg/m^2)	0 = < 23 1 = 23-25 2 = 25+	Categorical data
Systolic blood pressure (mg/Hg)	0 ≤ 130 1 > 130+	Continuous data
Diastolic blood pressure (mg/Hg)	0 ≤ 80 1 > 80+	Categorical data
Fasting Blood Sugar (mg/dl or mmol/l)	Numeric	Continuous data
Fasting Blood Sugar (mg/dl or mmol/l)	0 ≤ 140 (7.8) 1 > 140+ (7.8+)	Categorical data
HbA1C (%)	Numeric	Continuous data
HbA1C (% or mmol/mol)	0 ≤ 7 (53) 1 > 7+ (53+)	Categorical data
duration time of HbA1c before recruitment (months)	Numeric	Continuous data
Part II: Medical record (continued)		
Total Cholesterol (mg/dl or mmol/l)	Numeric	Continuous data
Total Cholesterol group (mg/dl or mmol/l)	0 ≤ 200 (11.1) 1 > 200+ (11.1+)	Categorical data
Low density lipoprotein (mg/dl or mmol/l)	Numeric	Continuous data
Low density lipoprotein group (mg/dl or mmol/l)	0 ≤ 100 (5.6) 1 > 100+ (5.6+)	Categorical data
High density lipoprotein (mg/dl or mmol/l)	Numeric	Continuous data
High density lipoprotein group (mg/dl or mmol/l)	0 ≤ 40 (2.2) 1 > 40+ (2.2+)	Categorical data
Triglyceride (mg/dl or mmol/l)	Numeric	Continuous data
Triglyceride group (mg/dl or mmol/l)	0 ≤ 150 (8.3) 1 > 150+ (8.3+)	Categorical data
DM treatment		
On diet alone	0 = no 1 = yes	Categorical data
Oral medication+ on diet	0 = no	Categorical data

	1 = yes	
Insulin injection + on diet	0 = no 1 = yes	Categorical data
Combine treatment (Medication+Insuline injection+on diet)	0 = no 1 = yes	Categorical data
DM duration (year)	Numeric	Continuous data
DM duration group (year)	0 = 1-4 1 = 5-8 2 = 8+	Categorical data
Part II: Medical record (continued)		
Diabetic complication		
Diabetic neuropathy	0 = no 1 = yes	Categorical data
Diabetic retinopathy	0 = no 1 = yes	Categorical data
Diabetic nephropathy	0 = no 1 = yes	Categorical data
Co-morbid disease		
Heart disease	0 = no 1 = yes	Categorical data
Hypertension	0 = no 1 = yes	Categorical data
Chronic Obstructive Pulmonary Disease (COPD)	0 = no 1 = yes	Categorical data
Gout	0 = no 1 = yes	Categorical data
Arthritis	0 = no 1 = yes	Categorical data
Dyslipidemia	0 = no 1 = yes	Categorical data
Asthma	0 = no 1 = yes	Categorical data
Others (specify)	character	Categorical data
Part III: score and result from screening tests		
Mini-Cog (scores)	Numeric	Continuous data
Result of Mini-Cog	0 = normal 1 = impair	Categorical data
MMSE Thai 2002 (scores)	Numeric	Continuous data
Result of MMSE Thai 2002	0 = normal 1 = impair	Categorical data
TGDS (scores)	Numeric	Continuous data
Result of TGDS	0 = normal 1 = impair	Categorical data

Appendix F1: Normality test of data

Test of normality (1)

	having HbA1c result	Kolmogorov-Smirnov[a]		
		Statistic	df	Sig.
gender	no	.436	273	.000
	yes	.411	283	.000
age	no	.156	273	.000
	yes	.159	283	.000
year in school	no	.424	273	.000
	yes	.430	283	.000
live alone	no	.537	273	.000
	yes	.540	283	.000
working	no	.395	273	.000
	yes	.418	283	.000
height	no	.063	273	.012
	yes	.094	283	.000
weight	no	.091	273	.000
	yes	.063	283	.009
body mass index	no	.070	273	.002
	yes	.060	283	.016
blood pressure_systolic	no	.084	273	.000
	yes	.072	283	.001
blood pressure_diastolic	no	.075	273	.001
	yes	.058	283	.024
fasting blood sugar 3	no	.098	273	.000
	yes	.104	283	.000
High density lipoprotein (mg/dl or mmol/l)	no	.133	273	.000
	yes	.091	283	.000
Triglyceride (mg/dl or mmol/l)	no	.137	273	.000
	yes	.159	283	.000

a. Lilliefors Significance Correction

Test of normality (2)

	having HbA1c result	Kolmogorov-Smirnov[a]		
		Statistic	df	Sig.
DM treatment_on diet (no medication)	no	.522	273	.000
	yes	.497	283	.000
DM treatment_oral medication	no	.515	273	.000
	yes	.500	283	.000
DM treatment_insulin injection	no	.540	273	.000
	yes	.539	283	.000
DM treatment_oral medication+insulin injection	no	.536	273	.000
	yes	.526	283	.000
years for DM duration	no	.187	273	.000
	yes	.162	283	.000
duration of year for having diabetic neuropathy	no	.518	273	.000
	yes	.521	283	.000
duration of year for having diabetic retinopathy	no	.464	273	.000
	yes	.465	283	.000
duration of year for having diabetic nephropathy	no	.508	273	.000
	yes	.485	283	.000
History of Chronic disease1_Heart disease	no	.541	273	.000
	yes	.538	283	.000

a. Lilliefors Significance Correction

Appendix F2: Table of Multicollinearity test

Coefficients[a]

Model	Collinearity Statistics	
	Tolerance	VIF
age	.687	1.456
year in school	.913	1.095
body mass index	.813	1.230
blood pressure_systolic	.730	1.371
blood pressure_diastolic	.710	1.408
fasting blood sugar	.650	1.537
HbA1c results	.669	1.495
total cholesterol (mg/dl or mmol/l)	.224	4.458
Low density lipoprotein (mg/dl or mmol/l)	.280	3.568
High density lipoprotein (mg/dl or mmol/l)	.641	1.560
Triglyceride (mg/dl or mmol/l)	.657	1.522
years for DM duration	.641	1.561
duration of year for having diabetic neuropathy	.896	1.116
duration of year for having diabetic retinopathy	.819	1.222
duration of year for having diabetic nephropathy	.860	1.163
duration of year for having heart disease	.982	1.018
duration of year for having hypertension	.589	1.698
duration of year for having COPD	.964	1.038
duration of year for having gout	.952	1.050
duration of year for having arthritis	.959	1.043
duration of year for having6 dyslipidemia	.905	1.105
duration of year for having7 asthma	.913	1.096
duration of year for having8 other	.962	1.040

a. Dependent Variable: Mini-Cog total score

Coefficients[a]

Model		Collinearity Statistics	
		Tolerance	VIF
1	age	.687	1.456
	year in school	.913	1.095
	body mass index	.813	1.230
	blood pressure_systolic	.730	1.371
	blood pressure_diastolic	.710	1.408
	fasting blood sugar	.650	1.537
	HbA1c results	.669	1.495
	total cholesterol (mg/dl or mmol/l)	.224	4.458
	Low density lipoprotein (mg/dl or mmol/l)	.280	3.568
	High density lipoprotein (mg/dl or mmol/l)	.641	1.560
	Triglyceride (mg/dl or mmol/l)	.657	1.522
	years for DM duration	.641	1.561
	duration of year for having diabetic neuropathy	.896	1.116
	duration of year for having diabetic retinopathy	.819	1.222
	duration of year for having diabetic nephropathy	.860	1.163
	duration of year for having heart disease	.982	1.018
	duration of year for having hypertension	.589	1.698
	duration of year for having COPD	.964	1.038
	duration of year for having gout	.952	1.050
	duration of year for having arthritis	.959	1.043
	duration of year for having6 dyslipidemia	.905	1.105
	duration of year for having7 asthma	.913	1.096
	duration of year for having8 other	.962	1.040

a. Dependent Variable: MMSE total score

Coefficients[a]

Model		Collinearity Statistics	
		Tolerance	VIF
1	age	.687	1.456
	year in school	.913	1.095
	body mass index	.813	1.230
	blood pressure_systolic	.730	1.371
	blood pressure_diastolic	.710	1.408
	fasting blood sugar	.650	1.537
	HbA1c results	.669	1.495
	total cholesterol (mg/dl or mmol/l)	.224	4.458
	Low density lipoprotein (mg/dl or mmol/l)	.280	3.568
	High density lipoprotein (mg/dl or mmol/l)	.641	1.560
	Triglyceride (mg/dl or mmol/l)	.657	1.522
	years for DM duration	.641	1.561
	duration of year for having diabetic neuropathy	.896	1.116
	duration of year for having diabetic retinopathy	.819	1.222
	duration of year for having diabetic nephropathy	.860	1.163
	duration of year for having heart disease	.982	1.018
	duration of year for having hypertension	.589	1.698
	duration of year for having COPD	.964	1.038
	duration of year for having gout	.952	1.050
	duration of year for having arthritis	.959	1.043
	duration of year for having6 dyslipidemia	.905	1.105
	duration of year for having7 asthma	.913	1.096
	duration of year for having8 other	.962	1.040

a. Dependent Variable: TGDS total score