ต้นทุน และประสิทธิผล ของวิธีการคัดกรองภาวะน้ำตาลผิดปกติ และโรคเบาหวานชนิดที่ 2 ที่ยังไม่ได้รับการวินิจฉัย

นางสาวนิพา ศรีช้าง

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตร์มหาบัณฑิต
สาขาวิชาวิจัยเพื่อการพัฒนาสุขภาพ(สหสาขาวิชา)
บัณฑิตวิทยาลัย จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2551

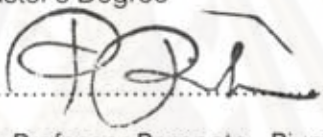
COST AND EFFECTIVENESS OF SCREENING METHODS FOR ABNORMAL FASTING PLASMA GLUGOSE AND UNDIAGNOSED TYPE 2 DIABETES

Ms. Nipa Srichang

A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science Program in Research for Health Development
(Interdisciplinary Program)
Graduate School
Chulalongkorn University
Academic Year 2008

Thesis Title	Cost and Effectiveness of Screening Methods for Abnormal Fasting Plasma Glucose and Undiagnosed Type 2 Diabetes
By	Ms. Nipa Srichang
Field of Study	Research for Health Development
Thesis Advisor	Assistant Professor Wiroj Jiamjarasrangsi, M.D., Ph.D.
Thesis Co-advisor	Associate Professor Wichai Aekplakorn, M.D., Ph.D.
	Associate Professor Siripen Supakankunti, Ph.D.

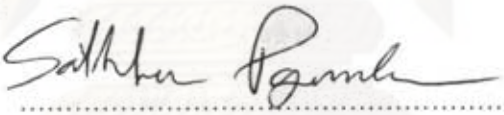
Accepted by the Graduate School, Chulalongkorn University in Partial Fulfillment of the Requirements for the Master's Degree



..... Dean of the Graduate School

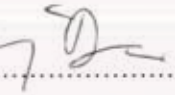
(Associate Professor Pornpote Piumsomboon, Ph.D.)

THESIS COMMITTEE



.....Chairman

(Associate Professor Sathirakorn Pongpanich, Ph.D.)

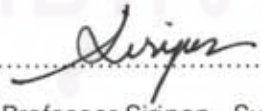


.....Thesis Advisor

(Assistant Professor Wiroj Jiamjarasrangsi, M.D., Ph.D.)

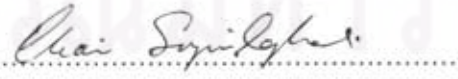
.....Thesis Co-advisor

(Associate Professor Wichai Aekplakorn, M.D., Ph.D.)



.....Thesis Co-advisor

(Associate Professor Siripen Supakankunti, Ph.D.)



.....External Examiner

(Chaisri Supornsilaphachai, M.D., M.P.H.)

นิพา ศรีช้าง : ต้นทุน และประสิทธิผล ของวิธีการคัดกรองภาวะน้ำตาลผิดปกติ และโรคเบาหวานชนิดที่ 2 ที่ยังไม่ได้รับการวินิจฉัย. (COST AND EFFECTIVENESS OF SCREENING METHODS FOR ABNORMAL FASTING PLASMA GLUGOSE AND UNDIAGNOSED TYPE 2 DIABETES) อ. ที่ปรึกษาวิทยานิพนธ์หลัก: ผศ.นพ.วิโรจน์ เจียมจรัสรังษี, อ.ที่ปรึกษาวิทยานิพนธ์ร่วม: รศ.นพ.วิชัย เอกพลากร, รศ.ดร.ศิริเพ็ญ ศุภกาญจนกันติ, 83 หน้า

เนื่องจากยังไม่มีข้อมูลเกี่ยวกับต้นทุน-ประสิทธิผล การคัดกรองโรคเบาหวานชนิดที่ 2 ที่ยังไม่ได้รับการวินิจฉัย ในคนที่ยังไม่มีอาการ และนโยบายในเรื่องนี้ยังมีความขัดแย้งกันอยู่ ในประเทศไทยการคัดกรองโรคเบาหวานชนิดที่ 2 ได้ขยายไปทั่วประเทศโดยคำแนะนำของกระทรวงสาธารณสุข แต่รูปแบบการคัดกรองโรคเบาหวานยังไม่ได้มีการประเมินที่สมบูรณ์ ดังนั้น การศึกษานี้จึงมีวัตถุประสงค์เพื่อเปรียบเทียบสมรรถนะ ต้นทุน ประสิทธิผล และต้นทุน-ประสิทธิผลของวิธีการตรวจคัดกรอง 4 แบบ ในการค้นหาบุคคลที่มีภาวะน้ำตาลผิดปกติ และโรคเบาหวาน

การวิจัยครั้งนี้เป็นการศึกษาในคนอายุ 35-60 ปี ที่ไม่ทราบว่ามีภาวะก่อนเบาหวานและโรคเบาหวานมาก่อน อาสาสมัครทุกคนตอบแบบสอบถามการตรวจคัดกรองทุกแบบ และตามด้วยการตรวจน้ำตาลในเลือด สำหรับผู้ที่ให้ผลบวกจากแบบสอบถาม โดยใช้การตรวจน้ำตาลในเลือดทุกคนเป็นวิธีการอ้างอิงเพื่อเปรียบเทียบวิธีการตรวจคัดกรองทุกแบบ การวิเคราะห์ต้นทุนและสมรรถนะ ในการตรวจคัดกรองเพียงรอบเดียว ทั้งมุมมองของสังคม และ มุมมองของหน่วยบริการสุขภาพ

ผลการศึกษาพบว่า วิธีการตรวจคัดกรองทุกแบบมีความไวสูงถึงสูงมาก (71-92% และ 65-97% ตามลำดับ สำหรับ ภาวะน้ำตาลผิดปกติ และโรคเบาหวาน) ขณะที่มีความจำเพาะต่ำถึงปานกลาง (31-57% และ 29-54% ตามลำดับ สำหรับการตรวจคัดกรองทั้ง 2 กรณี) ต้นทุนรวมของวิธีการตรวจคัดกรองที่มีประสิทธิผลสูงที่สุด (ซึ่งแนะนำโดยวิชัย เอกพลากร และคณะ) สำหรับภาวะน้ำตาลผิดปกติ และโรคเบาหวาน คือ 165,766 และ 166,477 บาท ตามลำดับ สัดส่วนต้นทุน-ประสิทธิผล คือ 2,047 – 2,381 และ 18,497 – 23,179 บาท ต่อรายใหม่ที่ตรวจพบ ในมุมมองของสังคม และ 933 – 1,185 และ 8,309-11,876 บาท ต่อรายใหม่ที่ตรวจพบ ในมุมมองของหน่วยบริการสุขภาพ ดังนั้น วิธีการตรวจคัดกรองที่แนะนำโดยวิชัย เอกพลากร และคณะ มีประสิทธิผล และต้นทุน-ประสิทธิผลสูงที่สุด สำหรับการค้นหาภาวะน้ำตาลผิดปกติ และโรคเบาหวานรายใหม่ ในประชากรไทย

สาขาวิชา วิจัยเพื่อการพัฒนาสุขภาพ ลายมือชื่อนิสิต Nipa Srichang

ปีการศึกษา 2551 ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์หลัก

ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์ร่วม

ลายมือชื่ออาจารย์ที่ปรึกษาวิทยานิพนธ์ร่วม

4989434420 : MAJOR RESEARCH FOR HEALTH DEVELOPMENT

KEYWORDS: TYPE 2 DIABETES / SCREENING / RISK ASSESSMENT QUESTIONNAIRE / FASTING PLASMA GLUCOSE / COST

NIPA SRICHANG: COST AND EFFECTIVENESS OF SCREENING METHODS FOR ABNORMAL FASTING PLASMA GLUCOSE AND UNDIAGNODES TYPE 2 DIABETES. THESIS ADVISOR: ASST. PROF. WIROJ JIAMJARASRANGSI THESIS COADVISOR: ASSOC.PROF. WICHAI AEKPLAKORN, ASSOC. PROF. SIRIPEN SUPAKANKUNTI, 83 pp.

Cost-effectiveness in whether or not screening for undiagnosed type 2 diabetes in asymptomatic individuals is unknown, and policy statements on this topic are controversial. In Thailand, type 2 diabetes was implementing at national level by the Ministry of Public Health (MOPH) recommendation but screening methods have not been fully evaluated. Thus, the aims were to compare the performance, cost, and cost-effectiveness of four screening methods in identifying individuals with abnormal fasting plasma glucose and type 2 diabetes.

This study was conducted among people ages 35 - 60 years old with no known type 2 diabetes and pre-diabetes (2,977 people). All subjects completed a set of screening questionnaires and followed by fasting plasma glucose (FPG) testing for those with positive result. Universal FPG testing was conducted and used as the reference for all other screening methods to compare with. One-time screening performance and costs were analyzed from both single-payer and societal perspectives.

The results show that sensitivities of all screening methods were high to very high (71-92% and 65-97% respectively for abnormal fasting plasma glucose and type 2 diabetes), while the specificities were low to moderate (31-57% and 29-54% respectively for the screening of both conditions). The total cost of the most effective screening method (which was proposed by Aekplakorn et al) for abnormal fasting plasma glucose and type 2 diabetes were 165,766 and 166,477 bahts respectively. Their corresponding cost-effectiveness was 2,047 to 2,381 and 18,497 to 23,179 bahts per newly detected case from societal perspective, and 933 to 1,185 and 8,309 to 11,876 baht per newly detected case from a single-payer perspective. Thus, screening method proposed by Aekplakorn et al was the most effective and highest cost-effectiveness to identify newly detected abnormal fasting plasma glucose and type 2 diabetes cases among Thai adults.

Field of study Research for Health Development Student's signature Nipa Srichang

Academic year 2008 Advisor's signature

Co-advisor's signature

Co-advisor's signature

ACKNOWLEDGEMENTS

Sincere appreciation and warmest thanks are extended to the many individuals who in their own ways have contributed to the completion of this study.

First, I sincerely acknowledge and thank my advisor, Dr. Wiroj Jiamjarasrangsi, who truly advised and strongly encouraged me to overcome an ordeal during the study.

I wish to acknowledge my co-advisor, Dr. Wichai Aekplakorn and Dr. Siripen Supakankunti , who kindly fulfilled my professional knowledge.

In addition, a special thank you and acknowledgement goes to Dr. Chaisri Supornsilaphachai, Dr. Ratana Somrongtong, and Dr. Sathirakorn Pongpanich who were thoughtful and gave me valuable advice.

I would also like to thank the head nurse and all staff of the preventive medicine clinic for greatly cooperating me in collecting data.

I wish to acknowledge Dr. Unchalee Siripitayakunkit and Ms. Sukalaya Kongsawat for all conveniences throughout the study.

To all my friends, thank for sharing emotions and sincere support.

Lastly, my acknowledgment of gratitude goes to my family for their understanding and encouraging my efforts toward the success.

CONTENTS

Page

Page

Page

LIST OF TABLES

Table **Page**

Table Page

LIST OF FIGURES

LIST OF ABBREVIATIONS

DM	Diabetes Mellitus
GDM	Gestational Diabetes Mellitus
FPG	Fasting Plasma Glucose
OGTT	Oral Glucose Tolerance Test
IFG	Impair Fasting Glucose
IGT	Impair Glucose Tolerance
PPV	Positive Predictive Value
NPV	Negative Predictive Value
ROC	Receiver Operating Characteristic Curve
AUC	Area under the ROC curve
CC	Capital Cost
MC	Material Cost
LC	Labor Cost
DC	Direct Cost
IDC	Indirect Cost
TC	Total Cost
NMC	Non medical Cost
CER	Cost Effectiveness Ratio
BMI	Body Mass Index
SRQ	Symptom Risk Questionnaire
ADA	American Diabetes Association
DRS	Diabetes Risk Score
NHES	National Health Examination Survey
MOPH	Ministry of Public Health
HDL-C	High Density Lipoprotein Cholesterol
BP	Blood Pressure

CHAPTER I

INTRODUCTION

1.1 Background and Significant of the Problem

Chronic degenerative diseases represent the major challenge to public health in the 21st century. Having largely conquered epidemic infectious diseases, we face a future in which non-communicable diseases such as diabetes and cardiovascular disease, and their underlying risk factors predominate. Non-communicable diseases already cause 70 percent of deaths worldwide[1]. The early stages of chronic degenerative disease and the risk factors that presage these diseases are often clinically silent and would go undetected without screening. On the other hand, infectious disease, which generally cause acute symptoms do not require screening.

Diabetes mellitus is a disease characterized by elevated blood glucose levels. It is the result of defective insulin secretion or action, or both. The resulting chronic hyperglycaemia is associated with damage to and subsequent dysfunction of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels[2].

The classification of diabetes mellitus is based on aetiological types. These include: (a) ***Type 1 diabetes*** which indicates the processes of beta-cell destruction that may ultimately lead to diabetes in which insulin is required for survival; **(b)** ***Type 2 diabetes*** which is characterized by disorders of insulin action and/or insulin secretion. Type 2 diabetes, the most prevalent 90-95% of the disease, is often asymptomatic in its early stage and can remain undiagnosed for many years; (c) ***Other specific types of diabetes*** which include diabetes cause by a specific and identified underlying defect, such as genetic defects or disease of the exocrine pancreas, and; ***Gestational diabetes mellitus (GDM)*** which is

defined as any degree of glucose intolerance with onset or first recognition during pregnancy.

Type 2 diabetes represents the archetype of a chronic degenerative disease. It has become epidemic, with fewer than 50 million cases worldwide in 1985 and more than 170 million cases today[3]. Diabetes is associated with substantial morbidity and mortality because it damages the eyes, kidneys, and nerves and accelerates disease of the cardiovascular system[4]. Approximately 20 percent of patients with newly diagnosed type 2 diabetes had already developed the above complications at the time of diagnosis[5]. In addition, cardiovascular disease, which is the cause of death in 75 percent of the diabetic population[6], begins to develop during the “pre-diabetic phase”[7]. Moreover, the onset of type 2 diabetes is often insidious, without symptoms that would alert the patient or clinician. One of the studies indicated the estimated 9 to12 years delay in diagnosis[8] is a particular concern because patients lose the opportunity to control hyperglycemia, dyslipidemia, and hypertension, which would increase the complications of diabetes[9]. Currently, diabetes screening is not standard practice in worldwide, these asymptomatic at-risk individuals cannot benefit from intensified treatment of blood pressure and dyslipidemia until symptoms or other circumstances lead to a diagnosis of diabetes[10]. Thus, the large population remains as undiagnosed type 2diabetes, half of this population and the failure to identify pre-diabetic persons are increasing with the pernicious effects of hyperglycemia and associated condition.

Cost-effectiveness in whether or not screening for undiagnosed type 2 diabetes in asymptomatic individuals is unknown, and policy statements on this topic are controversial. To some it is self-evident that screening should be commenced, given the rapidly increasing prevalence of type 2 diabetes, up to 50 percent of individuals with type 2 diabetes are undiagnosed[11], that 20-30 percent have complications at clinical diagnosis, and that individuals with type 2 diabetes have a two- to four-fold increased risk of dying from cardiovascular disease[1]. To others the evidence that screening is an appropriate public

policy is less clear because those recommendations only focus on screening high-risk groups rather than the whole population[12].

In Thailand, type 2 diabetes is also a serious public health problem. According to the "Burden of Disease and Injuries in Thailand, 2002" published by Bureau of Policy and Strategy, disability-adjusted life years (DALYs) lost due to diabetes ranked 3rd and 5th in Thai women and men respectively[13]. In 2004, the prevalence of diabetes and impair fasting glucose were 6.7 and 12.5 percents respectively for both genders. Half of diabetes patients are undiagnosed[14]. Moreover, the disease incidence rates increased with age and BMI[15, 16].

However, recent analysis pointed out that screening for type 2 diabetes and abnormal fasting plasma glucose is cost-effective. Nonetheless, appropriate screening method seemed to varied from country to country, depending on factors such as the disease prevalence, its risk factors, effectiveness of the treatment, and the type of most available screening test(s).

1.2 Research Questions

1. What are the performance, cost, and effectiveness of different screening methods for detecting abnormal fasting plasma glucose and undiagnosed type 2 diabetes among the 35-60 years old people who participate in the annual check-up at a university hospital in Bangkok, Thailand?

2. Which methods is the most effective in identifying individuals with abnormal fasting plasma glucose and undiagnosed type 2 diabetes?

1.3 Research Objective

To determine the performance, cost, and effectiveness of four screening methods (which were proposed by (1) The Royal college of physician of Thailand, (2) Thailand Ministry of Public Health, (3) Aekplakorn et al, and (4) Keesukphan et al) in identifying individuals with abnormal fasting plasma glucose and undiagnosed type 2 diabetes among the 35-60 years old people who participate in the annual check-up at a university hospital in Bangkok, Thailand.

1.4 Specific Research Objectives

1. To determine sensitivity, specificity, false positivity and false negativity of 4 screening methods in identifying individual with abnormal fasting plasma glucose and undiagnosed type 2 diabetes based on a one time screening.
2. To assess the total costs and cost-effectiveness of 4 screening methods in identifying individual with abnormal fasting plasma glucose and undiagnosed type 2 diabetes based on a one time screening from both provider's and societal views.
3. To compare the cost-effectiveness of 4 screening methods in identifying individual with abnormal fasting plasma glucose and undiagnosed type 2 diabetes based on a one time screening.

1.5 Research Hypothesis

No difference in performances and cost – effectiveness among four screening methods in identifying individuals with abnormal fasting plasma glucose and undiagnosed type 2 diabetes based on a one time screening among the 35-60 years old people who participate in the annual check-up at an university hospital.

1.6 Scope of the Research

1. Individuals at 35-60 years of age who are not known to have diabetes.

2. Study area is the out patient clinic at the university hospital

3. One time screening costs were evaluated from both direct medical and non-medical cost. The non-medical costs such as transportation cost and patient's time were include in the calculations

1.7 Operational Definition

Type 2 diabetes is defined as "a disease characterized by elevated blood glucose levels. It is the result of insulin resistance or relative insulin deficiency"[2]. In this study, type 2 diabetes cases are the study subjects with the FPG $\geq$ 126 mg/dl 2 times repeated at least 1 week apart.

Screening is the procedure to identify the subjects who are either at high risk for asymptomatic disease or have a risk factor that will probably develop type 2 diabetes.

Risk assessment questionnaire refers to diabetes risk score and diabetes risk factors used in assessing all participants before blood glucose levels was measure

Fasting plasma glucose refers to plasma glucose level at no consumption of food or beverage other than water for at least 8 hours before testing.

Undiagnosed diabetes is defined as individuals with an FPG $\geq$ 126 mg/dl (7.0 mmol/l) and no previous diabetes

Pre-diabetes is defined as individuals with an FPG $\geq$ 100 mg/dl (5.6 mmol/l) but <126 mg/dl (7 mmol/l) who are considered to have IFG[2]. People with IFG are now referred to as having "pre-diabetes" indicating the relatively high risk for developing diabetes in these people.

Abnormal fasting plasma glucose is defined as individuals with an FPG $\geq$ 100 mg/dl (5.6 mmol/l) and no previous diabetes or pre-diabetes.

Performance of screening test refers to sensitivity, specificity and receiver operating characteristic (ROC) curves of four screening methods to identified abnormal fasting plasma glucose and undiagnosed type 2 diabetes.

Cost of screening test refers to cost of risk assessment questionnaire and fasting plasma glucose testing to identify people with abnormal fasting plasma glucose and undiagnosed type 2 diabetes. This study evaluated the cost from both perspectives: a single – payer health care system and a societal perspective, which included only direct medical and non-medical costs.

Effectiveness of screening test is defined as the proportion of abnormal fasting plasma glucose and undiagnosed type 2 diabetes cases identified.

Cost- effectiveness refers to the cost of identifying one case for abnormal fasting plasma glucose and undiagnosed type 2 diabetes of screening methods. The cost-effectiveness was evaluated from both direct medical and non-medical costs.

1.8 Benefit of the Study

This study will provide critical information for policy makers and health care providers to make appropriate decision regarding screening policy for type 2 diabetes and abnormal fasting plasma glucose.

1.9 Conceptual Framework of the Research

Literature review revealed that the high prevalence of type 2 diabetes in Thailand was found in middle age group (45-64 years old) while the prevalence of pre-diabetes was frequently found in the younger to middle age group[14]. Furthermore, there was the delay in diabetes diagnosis for approximately 9 to12 years. This study therefore focused on the population of 35-60 years old.

Conceptual framework of the research

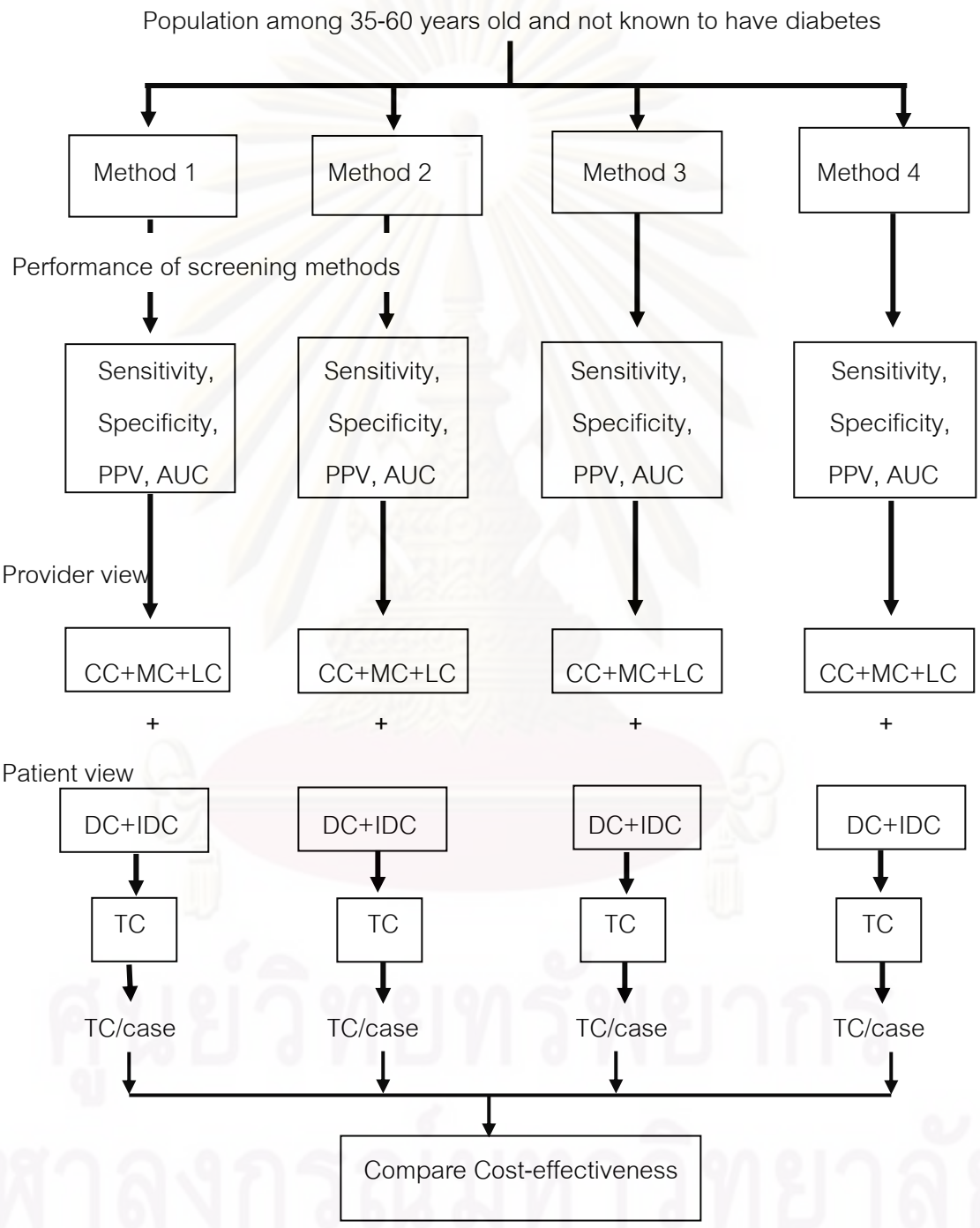


Figure 1: Conceptual Framework

Screening process could be done in two-stage, starting with the selection of people aged among 35-60 years and not known to have diabetes. The first stage was to administering risk assessment questionnaire to all target people. The second stage was to performing fasting plasma glucose measurement among people with positive assessment result or with risk score of higher than a pre-defined cut-off-point from the first stage assessment. The researcher was examining four screening methods are as follow:

Method 1 includes risk assessment questionnaire recommended by the Royal college of physician of Thailand, followed by FPG if a patient is over 40 years old and has one or more of risk factor [17].

Method 2 includes risk assessment questionnaire recommended by MOPH in 2007, followed by FPG if the patient is $\geq$35 years old and has one or more of risk factor [18].

Method 3 includes diabetes risk score assessment recommended by Aekplakorn et al, then followed by FPG if risk score $\geq$ 6[15].

Method 4 includes diabetes risk score assessment recommended by Keesukphan et al, then followed by FPG if risk score $\geq$ 240[19].

The gold standard of diabetes diagnosis is based on FPG $\geq$ 126 mg/dl 2 times repeated at least 1 week after the first test.

CHAPTER II

LITERATURE REVIEW

This section covers topics about 1) epidemiology of type 2 diabetes in Thailand and worldwide 2) existing type 2 diabetes screening measures and 3) economic evaluation of diabetes screening programs.

2.1 Epidemiology of Type 2 Diabetes in Thailand and Worldwide

The prevalence of type 2 diabetes is increasing rapidly worldwide, and currently affects for all age group. Wile et al reported in 2004 that the prevalence of diabetes was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030. Overall, diabetes prevalence is higher in men, but there are more women with diabetes than men[20]. In developing countries, the majority of people with diabetes are in the 45-64 years age range. In contrast, the majority of people with diabetes in developed countries are over 64 years of age. By 2030, it is estimated that the number of people who are 64+ years old with diabetes will be more than 82 millions in developing countries and more than 48 millions in developed countries[20].

In Thailand, according to the National Health Examination Survey (NHES) the prevalence of diabetes (fasting plasma glucose $\geq$ 126 mg%) among people aged 15-59 years were 4.4% in 1996[21] and 6.7 % in 2004[14]. However, several studies reported that the prevalence of diabetes ranged between 0.8%-13.9%[22-25], depending on the diagnostic criteria and target population. The prevalence of impaired fasting glucose (IFG) in $\geq$35 years old Thais was 5.4% in 2000 and 12.5% in 2004. On the other hand, type 2 diabetes prevalence in high risk population (those with at least one risk factor) was reported to be 26.8%--that is much higher than general population [23].

Diabetes prevalence in men was lower than that in women, whereas the IFG prevalence was higher in men than in women. Moreover, the incidence rates increased with age and BMI[15, 16]. Diabetes was more common in urban than in rural men but was similar in urban and rural women. However, Bangkok had the highest prevalence of diabetes [14].

2.2 Existing type 2 diabetes screening measures [26]

The main reasons for the current interest in type 2 diabetes screening are:

- There is a long, latent, asymptomatic period in which the condition can be detect.
- A substantial proportion of people with type 2 diabetes (up to 50% of individuals) are undiagnosed.
- A substantial proportion of newly referred cases of type 2 diabetes already have evidence of the micro-vascular complications of diabetes.
- The rising prevalence of type 2 diabetes world-wide.
- The seriousness of the immediate effects and long term complications of type 2 diabetes.
- Evidence supporting the efficacy of intensive controls of blood glucose, blood pressure control, and blood lipid in type 2 diabetes
- Accumulating evidence that treatment of hypertension, dyslipidaemia can prevent cardiovascular disease in people with type 2 diabetes.

There are several potential approaches to screening for diabetes [26]:

- Screening the entire population (never actually suggested).
- Selective or targeted screening performed in subgroup of subjects who have already been identified as being at relatively high risk in relation to age, body weight, ethnic origin etc.
- Opportunistic screening carried out at a time when people are seen by health care professionals for a reason other than the disorder in question.

Selective or targeted screening and opportunistic screening are not mutually exclusive since screening may be limited to those at highest risk. In opportunistic screening, the decision to initiate the health care encounter is made by the individual, albeit for reasons not related to the condition for which screening is offered[26].

Screening could be two-stage, starting with the selection of people at high risk, and the second-stage being testing of glucose level.

Stage 1: Selection by risk factors

Testing only people who are at higher than average risk means that a higher proportion of those who will be tested for glucose will be positive and the whole will be more cost-effective. Risk factors used for screening included age, BMI, co-morbidities (hypertension, hyperlipidaemia, peripheral vascular disease), family history of disease (diabetes, hypertension, premature vascular disease), ethnicity and drug treatments (hypertension, corticosteroids).

There are two methods in which such selection criteria could be applied including questionnaires and computer systems in general practice record. A number of questionnaires have been developed and used, with varying sensitivity and specificity as described in Table 1.

Some studies pointed out that high risk screening or diabetes risk assessment will not increase cost-effectiveness, but it can reduce the total cost of screening program.

Stage 2: Glucose testing

Screening tests for glucose include urine glucose and blood glucose testing such as glycated haemoglobin measurements, 1, 5-anhydroglucitol and fructosamine determinations, or the combinations of these tests. Because screening tests mentioned above have different performance to identify diabetes and pre-diabetes, oral glucose tolerance test is then used as the gold standard for the diabetes diagnosis.

The most widely used screening tests include the fasting plasma glucose (FPG) test and the oral glucose tolerance test (OGTT). However, the measurement of both OGTT and FPG require patients to fast overnight for at least 8 hour and confirmation of diagnosis using FPG requires the test to be repeated at least twice. Instead, testing random capillary blood sugar and glycated hemoglobin do not require fasting, so more people would be tested and diagnosed. Although, OGTT is gold standard test, it is also costly, time-consuming and labor intensive. It can be inconvenient and has weak reproducibility, thus an appropriate strategy should be selected depending on situation.

The FPG and OGTT are equally useful for assessing the risk of micro-vascular complications such as retinopathy, but OGTT level is better for assessing macro-vascular risk, because of the difference in heart disease risk between IFG and IGT. HbA1c has advantages in terms of convenience and reproducibility compared with the OGTT. FPG is also more reproducible than the OGTT. In practice, HbA1c may be the best test, but costs morn than FPG, although less than OGTT.

Table 1 Questionnaires Used for Pre-diabetes and Type 2 Diabetes Screening

Questionnaire	Variables	Score	Diabetes		Pre-diabetes		Remark
			sensitivity	specificity	sensitivity	specificity	
Symptom Risk Questionnaire (SRG)							
Ruige et al, 1997 [27]	Frequent thirst, pain on walking, shortness of breath, age, BMI, obesity, family history of diabetes, use of hypertensive drugs and cycling	34 cutoff point > 5	72 %	56 %			AUC 69 %
Baan et al, 1999 [28]	Model 1 age, sex, use of hypertensive drugs, obesity Model 2 add BMI, family history of diabetes and physical inactivity Model 3 add BP and waist-to-hip circumference ratio	cutoff point Model 1≥ 6 Model2≥ 36	78 %	55 %			AUC Model1 68% Model2 74%
ADA Questionnaire							
Rolka et al, 2001 [29]	Previous delivery of large infant(≥9lb), family or siblings history of diabetes, BMI, age, physical inactivity	27 cutoff point ≥10	72-78 %	50-51 %	69-72 %	51-54 %	

Table 1 Questionnaires Used for Pre-diabetes and Type 2 Diabetes Screening (cont')

Questionnaire	Variables	Score	Diabetes		Pre-diabetes		Remark
			sensitivity	specificity	sensitivity	specificity	
Diabetes Risk Score (DRS)							
Griffin, 2000 (population-basedsample)[30]	age, gender, BMI, steroid and antihypertensive medication, family and smoking history		77%	72%			AUC 80%
Lindstrom and Tuomilehto, 2003 (Finland-based study) [31]	age, BMI, waist circumference, history of antihypertensive drug use and high blood glucose, physical activity <4 h/wk and daily consumption of vegetables, fruits, or berries	20 cutoff point ≥ 9	77 %	66 %			AUC 80%
Glumer et al, 2004 (Inter 99 study) [32]	age, sex, BMI, known hypertension, physical activity at leisure time, and family history of diabetes	60 cutoff point ≥ 31	76 %	72 %			AUC 80%

Table 1 Questionnaires Used for Pre-diabetes and Type 2 Diabetes Screening (cont')

Questionnaire	Variables	Score	Diabetes		Pre-diabetes		Remark
			sensitivity	specificity	sensitivity	specificity	
Diabetes Risk Score (DRS)							
Ramachandran et al 2005 [33]	age, BMI, waist circumference, family history of diabetes and physical inactivity	42 cutoff point > 21	76.6	59.9			AUC 73.2%
Schulze et al, 2007 [34]	age, waist circumference, height, history of hypertension, physical activity, smoking, and consumption of red meat, whole-grain bread, coffee, and alcohol	983 cutoff point ≥500	94.4%	66.7%			AUC 84%
Simmons et al, 2007 [35]	age, sex, BMI, family history of diabetes, antihypertensive medication, recreational physical activity, consumption of green leafy vegetables, fresh fruit, and whole-meal/brown bread						AUC76.2%

Table 1 Questionnaires Used for Pre-diabetes and Type 2 Diabetes Screening (cont')

Questionnaire	Variables	Score	Diabetes		Pre-diabetes		Remark
			sensitivity	specificity	sensitivity	specificity	
Diabetes Risk Score (DRS)							
Al-Lawati and Tuomilehto, 2007 [36]	age, waist circumference, BMI, family history having diabetes, hypertension	34 cutoff point >10	78.6%	73.4%			AUC 83%
Cabrera de Leon A et al, 2007 [37]	Men: age, waist/height ratio, familial antecedents of diabetes, and systolic blood pressure Women: add GDM history	cutoff point >100	Men 94% Women 97%	Men 51% Women 48%			AUC men 83.7% women 87.4%

Table 2 Questionnaire/Tools for Type 2 Diabetes Screening in Thailand

Questionnaire	Variables	Score	Diabetes		Pre-diabetes		Remark
			sensitivity	specificity	sensitivity	specificity	
Risk Assessment Questionnaire							
The Royal college of physician of Thailand [17]	age, BMI, family history of diabetes, previous delivery of large infant (≥4000 gm) or GDM history, hypertension, history of HDL-C ≤ 35 mg/dl or triglyceride ≥ 250 mg/dl and IFG(110-125 mg/dl) or IGT						
MOPH 2007 [18]	age, BMI, family history of diabetes, previous delivery of large infant (≥4000 gm) or GDM history, hypertension, history of HDL-C ≤ 35 mg/dl or triglyceride ≥ 250 mg/dl and history of IFG or IGT						

Table 2 Questionnaire/Tools for Type 2 Diabetes Screening in Thailand (Cont')

Questionnaire	Variables	score	Diabetes		Pre-diabetes		Remark
			sensitivity	specificity	sensitivity	specificity	
Diabetes Risk Score (DRS)							
Aekplakorn et al 2006 [15]	age, sex, BMI, waist circumference, hypertension, history of diabetes in parent or sibling	22 cutoff point $\geq$6	77%	60%			AUC 74%
Keesukphan et al 2007 [19]	age, sex, BMI, history of hypertension	cutoff point $\geq$ 240	96.8%	24%			AUC 74%

2.3 Economic Evaluation of Diabetes Screening Programs

In 2007, Waugh et al[38] reviewed related studies and published evidence concentrated on economic modeling of screening up to the end of June 2005. They concluded that screening for pre-diabetes such as impaired glucose tolerance (IGT) was effective because early treatment may reduce the burden of diabetes and its complication. Recent clinical trials[39-41] indicated that lifestyle modification or medications can prevent and delay the onset of type 2 diabetes.

Zhang and colleagues[42] assessed the costs and short-term outcomes of different screening strategies using different screening tests. This study considered the costs that would be incurred and the numbers identified by different tests, or different cut-offs.

The modeling exercise concluded that a significant cost-effectiveness was found in DM screening by age group of 40 - 70 years old. Furthermore, the cost-effectiveness was more significant in this group with hypertension and obesity. This is because the costs of long term treatment will be decreased.

The cost-effectiveness of screening is determined as much by, if not more than, assumptions about the degree of control of blood glucose and future treatment protocols than by assumptions relating to the screening program. The very low cost now of statins is an important factor.

However, results from one country cannot be applied to other countries [43]. In Thailand also no studies were completed to evaluate the effectiveness and cost of type 2 diabetes screening methods. Thus, this study was determined the performance of 4 published screening methods which were recommended for the 35-60 years old people in Thailand[8].

CHAPTER III

RESEARCH METHODOLOGY

3.1 Research Design

A cross-sectional design was utilized in examining the performance, cost, and effectiveness of four screening methods for detecting abnormal fasting plasma glucose and undiagnosed type 2 diabetes among the 35-60 years old people who participate in the annual check-up at the King Chulalongkorn Memorial Hospital in Bangkok, Thailand

3.2 Study Population and Sample

Individuals at 35 - 60 years of age with no known diabetes or pre-diabetes who participate in the annual health examination provided by the Preventive Medicine Clinic of the King Chulalongkorn Memorial hospital during July-December 2008

3.2.1 Exclusion criteria of the sample are as follows:

1. preexisting diseases of the exocrine pancreas
2. Being pregnant

3.3 Sample Size Calculation

The sample size was determined by the formula for sample size estimation in diagnostic study for categorical data as followed[44]:

$$n = \frac{Z^2 * P(1-P)}{\square^2}$$

When n = number of disease cases

Z = value for selected alpha level of .025 in each tail, which is 1.96

P = sensitivity from previous studies (sensitivity for method 3 is 0.77 [15]; method 4 is 0.96 [19]); methods 1 and 2 are assumed to be 0.80)

Δ = desired error rate, in this case = .05

$$N = \frac{n}{\text{Prevalence}}$$

When N = sample size

Prevalence = 10 % from previous study[24].

From these equations, the sample sizes of four screening methods were 2,461, 2,461, 2,731, and 481 respectively. The largest number of 2,731 was then selected to furnish adequate statistical power for all methods. Furthermore, in order to secure sufficient number of subjects in case of missing data, the final numbers of 3,000 subjects were recruited.

3.4 Sampling Technique and Sample Selection

All eligible individuals without sampling who were willing to participate in the study were recruited until the numbers of 3,000 subjects were reached.

3.5 Research Instruments

The research instrument was composed of 3 types:

1. Screening questionnaire (see in appendix A)
2. Laboratory measurements of fasting plasma glucose
3. Cost information from direct medical and non-medical cost ; worksheet for cost information in appendix B and C respectively

3.5.1 Screening questionnaire

Details on the development and validation of the screening methods 3 and 4 have been published elsewhere [15], [19], whereas screening methods 1 and 2 were proposed and published by professionals organization and Thailand Ministry of Public Health[17, 18]. The screening questionnaire composed of 2 parts as follows:

Part 1 Anthropometric measurements

This part include: - weight, height, body mass index (BMI), waist circumference and blood pressure. Weight and height were measured with the participants wearing indoor clothes and no shoes. Waist circumference was measured midway between the lower rib margin and iliac crest. BMI was calculated by dividing the weight by height squared (kilograms per meters squared). Blood pressure was measured in a sitting position in the right arm after 5 minutes of rest with a sphygmomanometer.

Part 2 Risk factors

This part include: -age, sex, history of hypertension, family history of diabetes, previous delivery of large infant($\geq$4000 gm) or previous diagnosed with GDM, history of HDL-C $\leq$ 35 mg/dl or history of triglyceride $\geq$ 250 mg/dl and history of high blood glucose. These data were obtained by a total of 15 questions with categorical answers. The total score is a simple sum of the weights of individual questions, and values shows in Table 3. The draft screening questionnaire was pre-tested with 15 subjects of similar characteristics to the study population. It was then modified, as suggested by the pre-test result, to be the final version and used in this study.

3.5.2 Laboratory measurements of fasting plasma glucose

Venous blood samples were obtained after an overnight fast. All subjects with a positive assessment result or with risk score of higher than a cutoff – point from screening questionnaire.

Table 3 Score the screening questionnaire

Risk factors	Score			
	Method 1	Method 2	Method 3	Method 4
Age				
≤ 40	0			
> 40	1			
35-39 years		1	0	
40-44 years		1	0	3 X age
45-49 years		1	1	
≥ 50 years		1	2	
Sex				
Female			0	
Male			2	
BMI				
≤ 27 kg/m^2	0			
> 27 kg/m^2	1			
< 25 kg/m^2		0		
≥ 25 kg/m^2		1		5 X BMI
<23 kg/m²			0	
23-<27.5 kg/m²			3	
≥ 27.5 kg/m²			5	
Waist circumference				
<90cm in men, <80 cm in women			0	
≥90cm in men, ≥80 cm in women			2	
Hypertension				
No	0	0	0	0
Yes (BP ≥140/90)	1			

Table 3 Score the screening questionnaire (cont')

Risk factors	Score			
	Method 1	Method 2	Method 3	Method 4
Hypertension				
Yes (BP ≥140/90, history of hypertension)		1	2	
Yes (history of hypertension)				50
History of diabetes in parent or sibling				
No	0	0	0	
yes	1	1	4	
Previous delivery of large infant (≥4000 gm) or Previous diagnosed with GDM				
No	0	0		
Yes	1	1		
History of HDL-C ≤ 35 mg/dl or History of triglyceride ≥ 250 mg/dl				
No	0	0		
Yes	1	1		
History of IFG or History of IGT				
No	0	0		
Yes	1	1		
Total score	6	6	17	
Cutoff- point	≥ 2[1]	≥ 2[2]	≥ 6	≥ 240

[1]1 point must be derived from age >40, [2]1 point must be derived from age ≥ 35

3.5.3. Cost

Direct medical costs include: - physician time, nurse time, secretary time, laboratory test, and other material cost (screening questionnaire and mailing).

Non- medical costs include: - transportation cost and patients' time.

The cost of each resource was the product of the following three components: number of physical unit used to screening one person, the unit value of the resource, and the number of individuals screened.

The cost of a Laboratory test was based on previous study [45]. The cost of physician, nurse, and secretary time was calculated from total salaries including welfare expenditure. Transportation costs to an university hospital were obtained from the literature [46]. Patients' time was obtained from the Ministry of Labor [47]. All costs were expressed in Thai Baht for the year 2008.

Thus, the full cost of screening method was calculated from the sum of total direct medical cost and total non medical cost. The cost-effectiveness was calculated as the total cost of a screening method divided by the total number of case identified.

3.6 Data Collection

1. Permission for conducting the study in Chulalongkorn Memorial Hospital was acquired from the hospital director and relevant departmental heads.
2. Research assistants were trained in the data collection procedure.
3. Upon consent, each eligible subject was asked to fill in the screening questionnaire
4. Blood sample was drawn from the cubital vein of each subject after an overnight fast.
5. Blood samples were then transferred to the biomedical laboratory of Chulalongkorn Memorial Hospital for fasting plasma glucose (FPG) analysis. The

analysis method is the hexokinase. The FPG level was reported as milligram per deciliter (mg/dl).

6. Four screening methods were then simulated by using the collected questionnaire data and the measured FPG results.
7. Cost data was collected as followed:
   - Health care system perspective: costs regarding the cost of personnel time and other material, while laboratory cost was gathered using previous studied as the reference sources[45].
   - Patient perspective: costs of transport for clinical examination were gathered using transportation fee by Department of Land Transport. Patients' time were gathered using minimum wage in Bangkok (2008) from the Ministry of Labor

3.7 Data Analysis

The data was analyzed by SPSS computer program, and the analytical procedures were as follows

1. Effectiveness of screening methods

Sensitivity and specificity of four screening methods were determined at different cut-off points of each method. The receiver operator characteristic (ROC) curves were then constructed by sensitivity plots against 1-specificity for each cut-off value and analyzed area under the curve (AUC) to compare the impact of screening[48].

2. Cost of screening methods

Outcome

The outcomes of screening methods are the proportion of cases identified for abnormal fasting plasma glucose and undiagnosed type 2 diabetes is equal to sensitivity of the screening method.

Cost

Both direct medical and non-medical costs of each method were calculated. Medical costs include laboratory tests, personnel time, other material costs. Non-medical costs include patients' time and money spent for transportation to the hospital for clinical examinations. The total direct cost for screening method was calculated as a sum of the cost associate with various resources used. The cost of each resource is the product of the following three components: number of physical units used to screen one person, the unit value of the resource, and the number of individuals screened. The cost-effectiveness (cost of identifying one case) was calculated from the following formula:

$$\text{Cost-effectiveness} = \frac{\text{total cost of a screening method}}{\text{total number of cases identified}}$$

The cost-effectiveness was evaluated from both direct medical and non-medical costs.

3. Sensitivity analysis

Sensitivity analysis was performed in several factors that may have important effects on study outcomes. These factors include; - changes in the prevalence rate of abnormal fasting plasma glucose and type 2 diabetes, laboratory cost, patients' and personnel time and transportation cost. This was due to the prevalence of abnormal fasting plasma glucose and type 2 diabetes in this study differs from previous research [24]. In this procedure, only a single item was changed from baseline value, while other parameters were fixed[49].

3.8 Ethical Considerations

At the beginning, the volunteer subjects were informed about the purpose of the study and the right to withdraw from the study at any time. Then, the consent forms were signed voluntarily by the subjects. All their personal information was regarded as strictly confidential and used for the research propose only. The protocols were approved by the ethics committees of Faculty of Medicine, Chulalongkorn University.

3.9 Variables and Measurement Methods

The measurement methods for the variables of interest are as follows.

Table 4 Variables and measurement methods

Data Collection Instrument	Operational Variables	Measurement (scale)	Value
Questionnaire			
Part 1	Weight	Ratio	In kilograms
	Height	Ratio	In metes
	BMI[weight(kg)/ height(m)^2]	Ratio	In kg/m^2
	Waist circumference	Ratio	In cm
	Blood Pressure	Ratio	In mmHg
Part 2	Gender	Nominal	1. Male, 2.Female
	Age	Ratio	In years
	History of diabetes in parent or sibling	Nominal	1. Yes, 2. No
	History of hypertension	Nominal	1. Yes, 2. No
	Previous delivery of large infant($\geq$4000 gm)	Nominal	1. Yes, 2. No
	Previous diagnosed with GDM	Nominal	1. Yes, 2. No
	History of HDL-C $\leq$ 35 mg/dl	Nominal	1. No, 2.Yes
	History of triglyceride $\geq$250 mg/dl	Nominal	1. No, 2.Yes
	History of IFG 110 – 125 mg/dl	Nominal	1. No, 2.Yes
	History of IGT 140 -199 mg/dl	Nominal	1. No, 2.Yes

Table 4 Variables and measurement methods (cont')

Data Collection Instrument	Operational Variables	Measurement (scale)	Value
Laboratory test	Blood sample (FPG)	Ratio	mg%
Cost information	Direct medical cost	Ratio	baht
	- personnel time		
	- laboratory tests		
	- screening questionnaire		
	- mail costs		
	Non-medical cost	Ratio	baht
	- transportation cost		
	- patients' time		

CHAPTER IV

RESEARCH RESULTS

This descriptive study aimed at examining the performance, cost, effectiveness, and compare cost-effectiveness of four screening methods for abnormal fasting plasma glucose and undiagnosed type 2 diabetes. The study subjects were 3,000 people (35 - 60 years old) who had participate in the annual check-up at an university hospital in Bangkok, Thailand. The results of the study were presented as follow:

1. Characteristics of the study population
2. Performance (sensitivity and specificity) of each variable in detecting the individuals with abnormal fasting plasma glucose and type 2 diabetes
3. Performance of screening methods in detecting the individuals with abnormal fasting plasma glucose and type 2 diabetes
4. Resources used and their unit values for abnormal fasting plasma glucose and type 2 diabetes screening per 1000 persons
5. Cost of screening methods for abnormal fasting plasma glucose and type 2 diabetes
6. Sensitivity analysis

4.1 Characteristics of the Study Population

A total of 2,977 respondents ages 35 through 60 years with no known diabetes or pre-diabetes were interviewed with screening questionnaire in Preventive medicine clinic at a university hospital. The majority of the respondents (73%) were women, with mean age of 46 years of both sexes. Age-group compositions of male and female respondents were

slightly different, except for the ≥50 years age group--of which the proportions were similar for both genders (29%) (Table 5).

The average values of BMI for men and women were 25 and 23.kg/m², while the average waist circumferences were 85.34 ±9.15 and 74.95 ±9.98 cm. respectively for both sexes. The proportions of over-weighted participants were 53.4 and 35.7% respectively for men and women.

Prevalence rates of high blood pressure were11.5 % for men and 5.6 % for women, while the proportions of those with personal history of hypertension were 15.6 and 10.6 % respectively. Frequencies of history of diabetes in parent or siblings were 37.3% among women and 31.8% among men.

Thirteen men (1.6% of men) and 18 women (0.9% of women) were diagnosed as diabetes, while 126 men (15.7%) and 163 women (7.5%) were diagnosed as IFG (Table 5).

Table 5 Baseline characteristics of the study population, according to gender

Characteristics	Men		Women	
Number of subject	803	(27)	2174	(73)
Age (years)	45.99	±6.69	45.61	±6.83
Age group				
35-39	153	(19.1)	526	(24.2)
40-44	204	(25.4)	499	(23.0)
45-49	209	(26.0)	512	(23.6)
≥50	237	(29.5)	637	(29.3)
BMI (kg/m^2)	25.09	±3.65	23.81	±3.93
BMI group				
< 23 kg/ m^2	204	(25.4)	1039	(47.8)
23-27.49 kg/m^2	429	(53.4)	776	(35.7)
≥ 27.5 kg/m^2	170	(21.2)	359	(16.5)
Waist circumference (cm)	85.34	±9.15	74.95	±9.98
Waist circumference	239	(29.8)	658	(30.3)
≥ 90 cm in men,				
≥ 80 cm in women				
Systolic BP (mmHg)	123.22	±15.00	115.15	±15.06
Diastolic BP (mmHg)	79.57	±10.53	73.61	±10.08
BP ≥ 140/90 mmHg	92	(11.5)	122	(5.6)
History of hypertension	125	(15.6)	231	(10.6)
History of diabetes in parent or sibling	255	(31.8)	810	(37.3)
Previous delivery of large infant			66	(5.2)
(≥4000 gm)				
Previous diagnosed with GDM			44	(3.4)

Data are means± SD or number (%)

Table 5 Baseline characteristics of the study population, according to gender (cont')

Characteristics	Men		Women	
History of HDL-C $\leq$ 35 mg/dl	157	(26.8)	226	(14.1)
History of triglyceride $\geq$ 250 mg/dl	197	(31.0)	262	(15.1)
History of IFG 110 -125 mg/dl	55	(8.9)	65	(3.8)
History of IGT 140-199 mg/dl	6	(8.3)	10	(6.6)
FBS, mg%	91.67	±14.63	87.43	±12.79
DM	13	(1.6)	18	(0.8)
IFG	126	(15.7)	163	(7.5)

Data are means± SD or number (%)

In the first stage assessment, the proportions of participants with positive screening test result among men were 70, 72.1, 76.7, and 79.3% for Methods 1, 3, 2 and 4, whereas those proportions among women were 42.1, 61.4, 66.6 and 68.3 % for Methods 3, 1, 2, and 4 respectively (Table 6)

Table 6 Characteristics of four screening methods, according to gender

Characteristics	Men		Women	
Method 1 value	1.13	±1.02	0.92	±0.93
Method 1, score $\geq$ 2	424	(70.0)	946	(61.4)
Method 2 value	1.38	±1.10	1.07	±1.01
Method 2, score $\geq$ 2	616	76.7	1448	(66.6)
Method 3 value	7.8	±3.46	5.08	±3.73
Method 3, score $\geq$ 6	579	72.1	916	(42.1)
Method 4 value	271.2	±37.05	261.23	±38.12
Method 4, score $\geq$ 240	637	79.3	1485	(68.3)

Data are means± SD or number (%)

4.2 Sensitivity and specificity of each variable in identifying abnormal fasting plasma glucose and type 2 diabetes cases

The ability of each variable in identifying abnormal fasting plasma glucose (FPG$\geq$ 100 mg/dl) and type 2 diabetes (FPG $\geq$126 mg/dl) cases was shown in Table 7. Overall, the sensitivity ranged between 6 to 86 and 0 to 94 % for abnormal fasting plasma glucose and type 2 diabetes respectively, while the specificity ranged between 29 to 97% and 27 to 97 % respectively for both conditions.

Variables with high sensitivity ($\geq$75%) were age >40 years, BMI > 23 kg/m^2, and BMI $\geq$ 25 kg/m^2 respectively, while those variables with low sensitivity (<25%) were previous diagnosed with GDM or previous delivery of large infant ($\geq$4000 gm), history of IFG or IGT, BP $\geq$ 140/90 mmHg, and history of hypertension respectively. In general, trend of specificity was opposite to that for sensitivity.

4.3 Performance of screening methods in detecting the individuals with abnormal fasting plasma glucose and type 2 diabetes

Sensitivity, specificity, positive and negative predictive values, and AUC curves for four screening methods were shown in Table 8. The overall performance of screening methods in identifying type 2 diabetes and abnormal fasting plasma glucose --as assessed by area under the ROC curves--was higher for methods 3, 4, and 2 respectively, and lowest for method 1.

In type 2 diabetes identification, Methods 4 and 2 had high sensitivity and low specificity (sensitivity=94 and 97% and specificity=29 and 31% respectively). Method 3 had relatively high sensitivity and moderate specificity (sensitivity and specificity =87 and 50% respectively), while Method 1 had moderate sensitivity and specificity (sensitivity and specificity =65 and 54% respectively).

For abnormal fasting plasma glucose identification, Methods 4 and 2 had high sensitivity and low specificity (sensitivity=92 and 89% and specificity=31 and 33% respectively). Method 3 had relatively high sensitivity and moderate specificity (sensitivity and specificity =83 and 53% respectively), while Method 1 had moderate sensitivity and specificity (sensitivity and specificity =71 and 57% respectively).

While the actual numbers of abnormal fasting plasma glucose and type 2 diabetes cases were 97 and 10 per 1,000 persons, the numbers cases identified by the screening methods ranged from 69 to 89 and 7 to 10 per 1,000 persons respectively for both conditions.

For abnormal fasting plasma glucose, the numbers of missed cases were higher for Methods 1 and 3 and lower for Methods 2 and 4. The numbers of missed cases were 28, 16, 11, and 8 out of totally 97 cases per 1,000 persons respectively for Methods 1, 3, 2, and 4 respectively. Concerning type 2 diabetes, the numbers of missed cases were 3, 1, and 1 out of totally 10 cases per 1,000 persons respectively for Methods 1, 3, and 4 respectively. However, percentage of the persons requiring laboratory testing was relatively high for Methods 4 and 2, and relatively low for Methods 3 and 1 (704, 683, 493, and 453 per 1,000 persons screened respectively for Methods 4, 2, 3, and 1).

Table 7 Sensitivity and specificity of each variable in identifying abnormal fasting plasma glucose and type 2 diabetes cases

Variables	Method 1	Method 2	Method 3	Method 4	Sensitivity		Specificity	
					Ab-FPG	Diabetes	Ab-FPG	Diabetes
Age (years)				/				
≥35		/						
> 40	/				86 (0.82-0.90)	77 (0.63-0.92)	29 (0.28-0.31)	28 (0.26-0.30)
≥45			/		72 (0.66-0.77)	52 (0.34-0.69)	48 (0.46-0.50)	46 (0.45-0.48)
≥50			/		50 (0.44-0.56)	36 (0.19-0.52)	73 (0.71-0.75)	71 (0.69-0.72)
Sex								
Male			/		44 (0.38-0.49)	42 (0.25-0.59)	75 (0.73-0.76)	73 (0.72-0.75)
Female			/		56 (0.51-0.62)	58 (0.41-0.75)	25 (0.24-0.27)	27(0.25-0.28)
BMI (kg/m^2)				/				
> 23 kg/m^2			/		80 (0.75-0.85)	94 (0.85-1.00)	46 (0.44-0.48)	44 (0.42-0.45)
≥ 25 kg/m^2		/			61 (0.55-0.67)	81 (0.67-0.95)	66 (0.64-0.68)	64 (0.62-0.66)
> 27 kg/m^2	/				40 (0.35-0.46)	55 (0.37-0.72	82 (0.81-0.83)	80 (0.79-0.82)
≥ 27.5 kg/m^2			/		36 (0.30-0.42)	45 (0.28-0.63)	84 (0.83-0.86)	83 (0.81-0.84)

Data are percentage (95%CI), Abbreviation: Ab-FPG, abnormal fasting plasma glucose

Table 7 Sensitivity and specificity of each variable in identifying abnormal fasting plasma glucose and type 2 diabetes cases (cont')

Variables	Method 1	Method 2	Method 3	Method 4	Sensitivity		Specificity	
					Ab-FPG	Diabetes	Ab-FPG	Diabetes
Waist circumference ≥ 90cm in men, ≥ 80cm in women			/		51 (0.45-0.56)	61 (0.44-0.78)	72 (0.70-0.74)	70 (0.69-0.72)
History of hypertension				/	24 (0.19-0.29)	26 (0.10-0.41)	89 (0.88-0.90)	88 (0.87-0.89)
BP≥140/90mmHg	/				19 (0.14-0.23)	26 (0.10-0.41)	94 (0.93-0.95)	93 (0.92-0.94)
BP≥140/90mmHg or history of hypertension		/	/		34 (0.29-0.40)	42 (0.25-0.59)	86 (0.85-0.87)	84 (0.83-0.86)
History of diabetes in parent or sibling	/	/	/		42 (0.36-0.48)	45 (0.28-0.63)	65 (0.63-0.67)	64 (0.63-0.66)
Previous delivery of large infant (≥4000 gm)	/	/			12 (0.05-0.18)	0	95 (0.94-0.97)	95 (0.94-0.96)

Data are percentage (95%CI), Abbreviation: Ab-FPG, abnormal fasting plasma glucose

Table 7 Sensitivity and specificity of each variable in identifying abnormal fasting plasma glucose and type 2 diabetes cases (cont')

Variables	Method 1	Method 2	Method 3	Method 4	Sensitivity		Specificity	
					Ab-FPG	Diabetes	Ab-FPG	Diabetes
GDM history	/	/			6(0.01-0.10)	7(0.00-0.19)	97(0.96-0.98)	97(0.96-0.98)
History of HDL-C ≤ 35 mg/dl	/	/			29 (0.23-0.36)	26 (0.07-0.46)	84 (0.82-0.85)	83 (0.81-0.84)
History of triglyceride ≥ 250 mg/dl	/	/			32 (0.26-0.38)	25 (0.06-0.44)	82 (0.80-0.84)	81 (0.79-0.82)
History of IFG 110 – 125 mg/dl	/	/			20 (0.15-0.25)	23 (0.05-0.40)	96 (0.96-0.97)	95 (0.94-0.96)
History of IGT 140 – 199 mg/dl	/	/			21 (0.05-0.37)	50 (0.00-1.00)	95 (0.91-0.98)	94 (0.90-0.97)

Data are percentage (95%CI), Abbreviation: Ab-FPG, abnormal fasting plasma glucose

Table 8 Performance of screening methods for screen-detected abnormal fasting plasma glucose and type 2 diabetes

Method	Sensitivity (%,95CI)	Specificity (%,95CI)	PPV (%)	NPV (%)	AUC (%,95CI)	Outcome per 1000 persons*		
						True positive	False positive	False negative
Abnormal fasting plasma glucose								
Method 1	71 (0.66-0.76)	57 (0.55-0.59)	14.96	94.77	68 (0.64-0.71)	69	391	28
Method 2	89 (0.85-0.93)	33 (0.31-0.35)	12.45	96.49	69 (0.66-0.72)	86	607	11
Method 3	83 (0.78-0.87)	53 (0.51-0.55)	15.98	96.63	73 (0.69-0.75)	81	421	16
Method 4	92 (0.89-0.95)	31 (0.29-0.33)	12.58	97.42	72 (0.69-0.75)	89	624	8
Universal FPG testing						97	-	-
Type 2 Diabetes								
Method 1	65 (0.48-0.81)	54 (0.52-0.56)	1.46	99.31	63 (0.52-0.73)	7	453	3
Method 2	97 (0.91-1.00)	31 (0.29-0.33)	1.45	99.89	72 (0.64-0.80)	10	683	-
Method 3	87 (0.75-0.99)	50 (0.48-0.52)	1.80	99.73	75 (0.67-0.83)	9	493	1
Method 4	94 (0.85-1.00)	29 (0.27-0.31)	1.37	99.76	73 (0.64-0.81)	9	704	1
Universal FPG testing						10	-	-

* Data are number

4.4 Resources used and unit values for abnormal fasting plasma glucose and type 2 diabetes screening per 1000 persons

The resources used for abnormal fasting plasma glucose and type 2 diabetes include: - direct medical cost and non-medical cost. Medical cost included personnel time, laboratory test, and other material cost. Non-medical cost included transportation to the hospital and patients' time.

The highest costs for abnormal fasting plasma glucose and type 2 diabetes screening per 1,000 persons were patients' and personnel's times, which ranged from 73,000 to 100,000 baht and from 64,200 to 102,000 baht. Laboratory and other medical costs were lower and ranged from 3,680 to 8,000 baht and from 3300 to 5,000 baht respectively.

The proportions of resources used for abnormal fasting plasma glucose and type 2 diabetes as the followings:

Patients' time : personnel time = 43 - 46% : 40 - 44%

Transportation cost : laboratory cost : other medical cost = 7 - 10% : 2 - 3% : 2%

The proportion of total medical cost and non-medical cost for abnormal fasting plasma glucose and type 2 diabetes = 71,180 - 115,130 baht : 89,000 - 116,660 baht

= 44 - 50% : 50 - 56%

Universal blood testing had the highest cost, followed by testing Methods 4, and 2 respectively (Table 9, 10). Methods 1 and 3 had the lowest cost respectively.

Table 9 Resources used and unit values for abnormal fasting plasma glucose screening per 1000 persons

Cost categories	Resources uses					Unit cost
	Method 1	Method 2	Method 3	Method 4	Universal FPG testing	
Direct medical cost						
• Screening questionnaire	1,000 X 1	1,000 X 1	1,000 X 1	1,000 X 1	0	฿1/test
• Physician time (¼ h) *	460 X 70	693 x 70	502 x 70	713 x 70	1,000 X 70	฿284/h
• Nurse time (1/6 h)	1,000 X 28	1,000 X 28	1,000 X 28	1,000 X 28	1,000 X 28	฿170/h
• Secretary time (1/12 h)	1,000 X 4	1,000 X 4	1,000 X 4	1,000 X 4	1,000 X 4	฿45/h
• Laboratory test *	460 X 8	693 X 8	502 X 8	713 X 8	1,000 X 8	฿8/test
• Other direct costs (1 mail) *	460 X 5	693 X 5	502 X 5	713 X 5	1,000 X 5	฿5/mail
Non-medical cost						
• Patients' time						฿25/h
- high score persons (4h) *	460 X 100	693 X 100	502 X 100	713 X 100	1000 X 100	
- low score persons (2h)	540 X 50	307 X 50	498 X 50	287 X 50	0	
• Transportation cost (1 trip)	1000 x 1	1000 x 1	1000 x 1	1000 x 1	1000 x 1	(฿16/trip)
Total cost (baht)	**160,180**	**191,169**	**165,766**	**193,829**	**231,000**	
Case identified (number)	69	86	81	89	97	
Cost-effectiveness (baht/case)	**2,321.45**	**2,222.90**	**2,046.49**	**2,177.85**	**2,381.44**	

* Number of subjects who test positive score

Table 10 Resources used and unit values for type 2 diabetes screening per 1000 persons

Cost categories	Resources uses					Unit cost
	Method 1	Method 2	Method 3	Method 4	Universal FPG testing	
Direct medical cost						
• Screening questionnaire	1,000 X 1	1,000 X 1	1,000 X 1	1,000 X 1	0	฿1/test
• Physician time (1/4h) *	460 X 70	693 X 70	502 X 70	713 X 70	1,000 X 70	฿284/h
• Nurse time (1/6 h)	1,000 X 28	1,000 X 28	1,000 X 28	1,000 X 28	1,000 X 28	฿170/h
• Secretary time (1/12 h)	1,000 X 4	1,000 X 4	1,000 X 4	1,000 X 4	1,000 X 4	฿45/h
• Lab test						฿8/test
- high score persons *	460 X 8	693 X 8	502 X 8	713 X 8	1,000 X 8	
- high blood glucose (repeat)	7 X 8	10 X 8	9 X 8	9 X 8	10 X 8	
• Other direct costs (mail)						฿5/mail
- high score persons *	460 X 5	693 X 5	502 X 5	713 X 5	1,000 X 5	
- high blood glucose persons (result repeat lab)	7 X 5	10 X 5	9 X 5	9 X 5	10 X 5	

* Number of subjects who test positive score

Table 10 Resources used and unit values for type 2 diabetes screening per 1000 persons (cont')

Cost categories	Resources uses					Unit cost
	Method 1	Method 2	Method 3	Method 4	Universal FPG testing	
Non-medical cost						
• Patients' time						฿25/h
- high score persons (4h) *	460 X 100	693 X 100	502 X 100	713 X 100	1,000 X 100	
- low score persons (2h)	540 X 50	307 X 50	498 X 50	287 X 50	0	
- high blood glucose persons (repeat lab)	7 X 50	10 X 50	9 X 50	9 X 50	10 X 50	
• Transportation cost						(฿16/trip)
- all persons (first time)	1,000 X 16	1,000 X 16	1,000 X 16	1,000 X 16	1,000 X 16	
- high blood glucose persons (repeat lab)	7 X 16	10 X 16	9 X 16	9 X 16	10 X 16	
Total cost (baht)	**160,733**	**191,959**	**166,477**	**194,540**	**231,790**	
Case identified (number)	7	10	9	9	10	
Cost-effectiveness (baht/case)	**22,961.86**	**19,195.90**	**18,497.44**	**21,615.56**	**23,179.00**	

* Number of subjects who test positive score

Table 11 Total cost and cost-effectiveness of screening methods for abnormal fasting plasma glucose and type 2 diabetes per 1000 persons from societal perspective

Case detection methods	Cases identified (number)		Societal perspective			
			Total direct medical and non-medical cost (baht)		Cost-effectiveness (baht/case)	
	Ab-FPG	Diabetes	Ab-FPG	Diabetes	Ab-FPG	Diabetes
Method 1	69	7	160,180	160,733	2,321.45	22,962.86
Method 2	86	10	191,169	191,959	2,222.90	19,195.90
Method 3	82	9	165,766	166,477	2046.49	18,497.44
Method 4	89	9	193,829	194,540	2177.85	21,615.56
Universal FPG Testing	97	10	231,000	231,790	2,381.44	23,179.00

Abbreviation: Ab-FPG, abnormal fasting plasma glucose

Table 12 Total cost and cost-effectiveness of screening methods for abnormal fasting plasma glucose and type 2 diabetes per 1000 persons from single payer perspective

Case detection methods	Cases identified (number)		Single payer perspective			
			Total direct medical cost(baht)		Cost-effectiveness (baht/case)	
	Ab- FPG	Diabetes	Ab- FPG	Diabetes	Ab- FPG	Diabetes
Method 1	69	7	71,180	71,258	1,031.59	11,876.33
Method 2	86	10	90,519	90,649	1,052.55	9,064.90
Method 3	82	9	74,666	74,783	933.33	8,309.22
Method 4	89	9	92,179	92,296	1.024.21	10,255.11
Universal FPG Testing	97	10	115,000	115,130	1,185.57	11,513.00

Abbreviation: Ab-FPG, abnormal fasting plasma glucose

4.5 Cost of screening methods for abnormal fasting plasma glucose and type 2 diabetes

The total costs (direct medical and non medical costs) for abnormal fasting plasma glucose and type 2 diabetes per 1000 persons screened ranged from 160,180 - 231,000 and 160,733 - 231,790 baht respectively (Table 9). Universal blood testing had the highest cost, followed by testing Methods 4, and 2 respectively (Table 10). Methods 1 and 3 had the lowest cost respectively.

From a societal perspective, the cost-effectiveness ranged from ฿2,047 to ฿2,381 for abnormal fasting plasma glucose and ฿18,497 to ฿23,179 for type 2 diabetes (Table 11). For abnormal fasting plasma glucose screening, Methods 3 and 4 had the highest cost-effectiveness (฿2,046 to 2,178 per one detected case), while universal FPG testing and Methods 1 and 2 had the lowest cost-effectiveness (฿2,223 to 2,381 per one detected case). Concerning type 2 diabetes screening, Methods 2 and 3 had the highest cost-effectiveness (฿18,497 to 19,196 per one detected case), while universal FPG testing and Methods 1 and 4 had the lowest cost-effectiveness (฿21,616 to 22,962 per one detected case).

From a single payer perspective, the cost-effectiveness ranged from ฿933 to ฿ 1,186 for abnormal fasting plasma glucose and ฿8,309 to ฿11,876 for type 2 diabetes (Table 12). Detailed results showed similar pattern to that for societal perspective For abnormal fasting plasma glucose screening, Methods 3 and 4 had the highest cost-effectiveness (฿933 to 1,024 per one detected case), while universal FPG testing and Methods 1 and 2 had the lowest cost-effectiveness (฿1,032 to 1,053 and 1,186 per one detected case). Concerning type 2 diabetes screening, Methods 2 and 3 had the lowest cost-effectiveness (฿8,309 to 9,065 per one detected case), while universal FPG testing and Methods 1 and 4 had the lowest cost-effectiveness (฿10,255 to 11,876 for per one detected case).

4.6 Sensitivity analysis

Sensitivity analysis was examined in five scenarios as the following.

4.6.1 Sensitivity analysis for different prevalence rates

Changes in prevalence rates of abnormal fasting plasma glucose and type 2 diabetes could affect both the effectiveness and cost-effectiveness of each method. Sensitivity analysis was performed for changes in prevalence rates of type 2 diabetes from 1% to 5 and 10%, and of abnormal fasting plasma glucose from 9.7% to 15 and 20%. The results were shown in Figures 2. When the prevalence rate increased, the cost-effectiveness ratio of all methods decreased. However, Cost-effectiveness of Method 3 remained highest both for abnormal fasting plasma glucose and type 2 diabetes.

Abnormal fasting plasma glucose

Type 2 diabetes

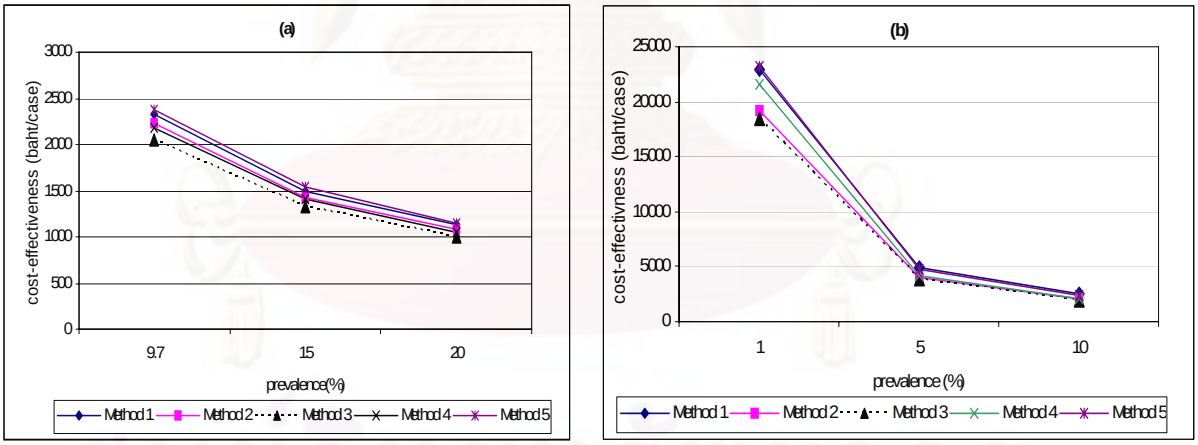


Figure 2 Sensitivity analytical results for abnormal fasting plasma glucose (graph a) and type 2 diabetes (graph b) screenings by varying levels of disease prevalence rates

4.6.2 Sensitivity analysis for changes of laboratory cost

Sensitivity analysis was performed for changes in the charges of laboratory FPG test from ฿8 in this study to ฿16 and ฿40 for abnormal fasting plasma glucose and type 2 diabetes. The findings were shown in Figures 3, graph (a) and graph (b) for abnormal fasting plasma glucose and type 2 diabetes respectively. Changes in cost-effectiveness for both abnormal fasting plasma glucose and type 2 diabetes screenings were small. Cost-effectiveness of Method 3 remained highest for both conditions.

Abnormal fasting plasma glucose

Type 2 diabetes

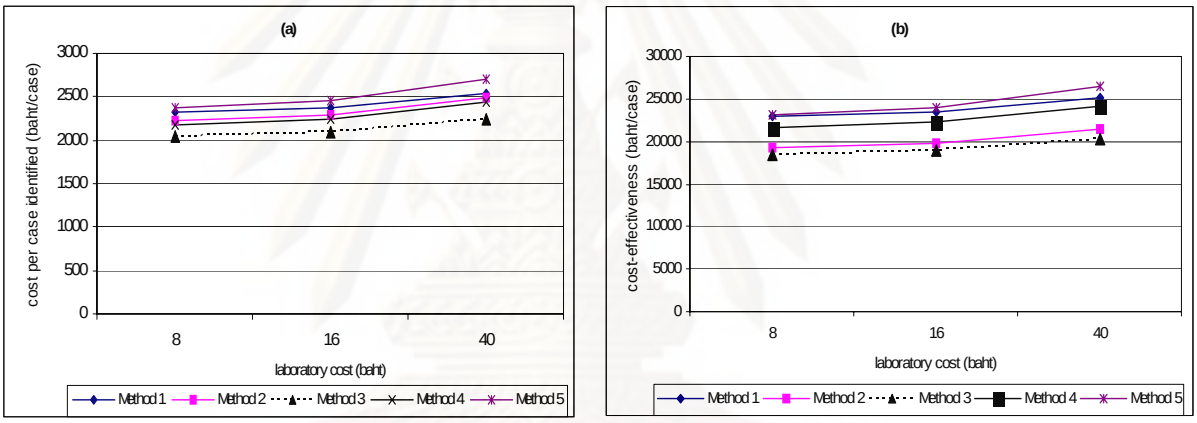


Figure 3 Sensitivity analytical results for abnormal fasting plasma glucose and type 2 diabetes screenings by varying levels of charges of FPG test

4.6.3 Sensitivity analysis for different wage rates of patient

Sensitivity analysis results by increasing the costs of wage rates of patient from 200 to 400 and 1,000 baht/day were shown in Figures 4, graph (a) and graph (b) for abnormal fasting plasma glucose and type 2 diabetes respectively. Changes the costs of wage rates could affect the cost-effectiveness ratios of each method. However, cost-effectiveness of Method 3 remained highest for both conditions.

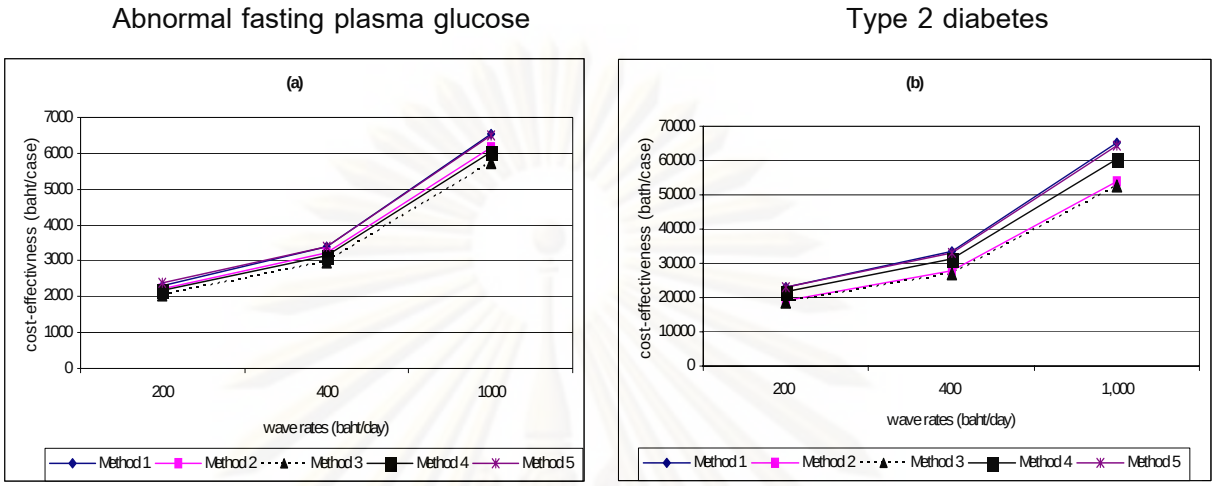


Figure 4 Sensitivity analytical results for abnormal fasting plasma glucose and type 2 diabetes screenings by varying levels of wage rates

4.6.4 Sensitivity analysis for changes of total salaries of personnel

Sensitivity analysis results by varying of the total salaries of physician, nurse, and secretary from total salaries to decreased 10% and increased 10% were shown in Figures 5, graph (a) and graph (b) for abnormal fasting plasma glucose and type 2 diabetes respectively. Changes in total salaries for 10% resulted in only minimal changes of cost-effectiveness ratio of screening methods.

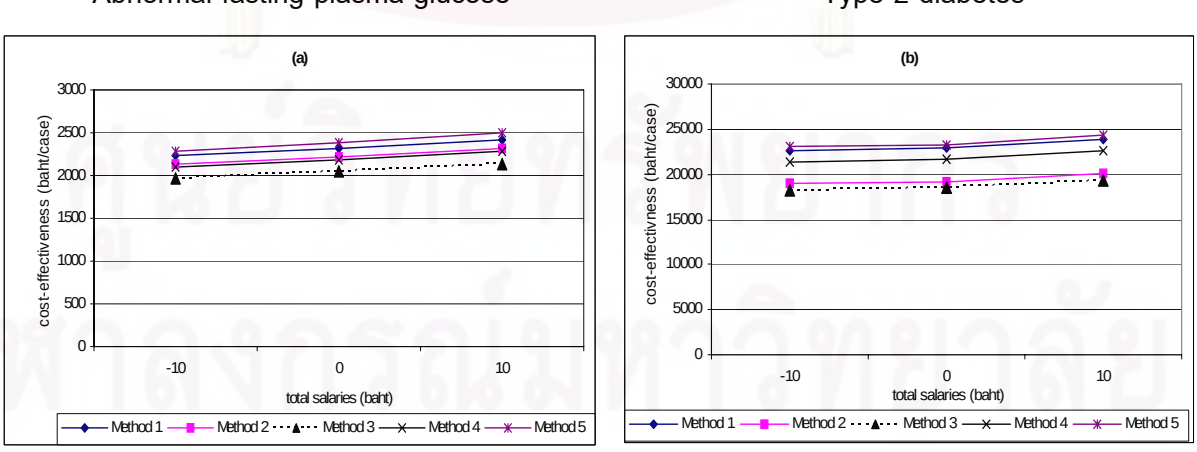


Figure 5 Sensitivity analytical results for abnormal fasting plasma glucose and type 2 diabetes screenings by varying levels of total salaries of personnel

4.6.5 Sensitivity analysis for different transportation rates

Sensitivity analysis results by increasing the costs of transportation from 16 to 32 and 70 baht/trip was shown in Figures 6, graph (a) and graph (b) for abnormal fasting plasma glucose and type 2 diabetes respectively. Changes in rates of transportation cost slightly affected cost-effectiveness ratio of each method. Cost-effectiveness of Method 3 remained highest both for abnormal fasting plasma glucose and type 2 diabetes.

Abnormal fasting plasma glucose

Type 2 diabetes

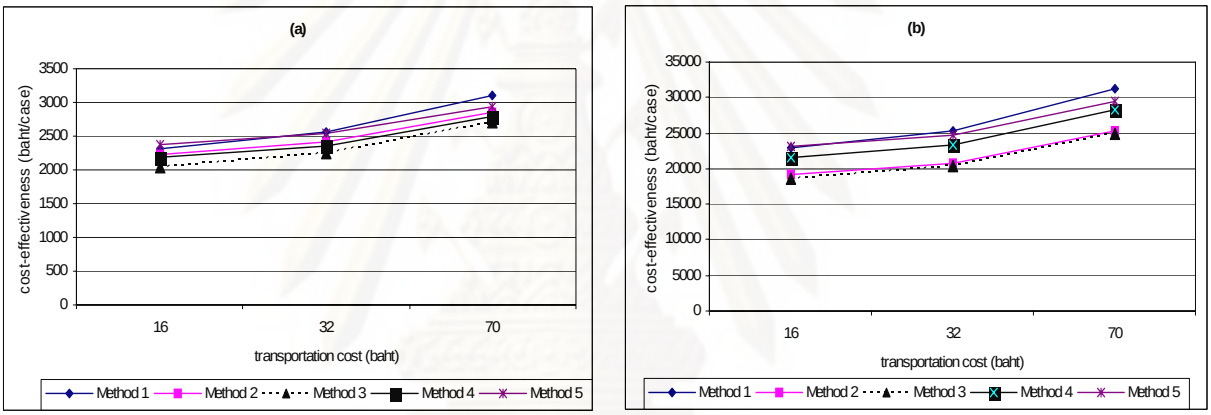


Figure 6 Sensitivity analytical results for abnormal fasting plasma glucose and type 2 diabetes screening by varying levels of transportation cost

CHAPTER V

CONCLUSION AND DISCUSSION

The aim of this research was to evaluate the performance, cost, effectiveness of four screening methods (which were proposed by (1) The Royal college of physician of Thailand, (2) Thailand Ministry of Public Health, (3) Aekplakorn et al, and (4) Keesukphan et al) in identifying individuals with abnormal fasting plasma glucose and undiagnosed type 2 diabetes. The specific research objectives were: ***(a)*** to determine sensitivity, specificity, false positivity, and false negativity; ***(b)*** to assess the total cost; and ***(c)*** to compare cost-effectiveness of the 4 screening methods based on a one time screening. Subjects were 2,977 people ages 35 through 60 years and no known diabetes who had participated in the annual check-up at an university hospital in Bangkok, Thailand.

The summary finding of this study, were presented as follows:

1. Performances of four screening methods

The overall sensitivities of all screening methods were high to very high and ranged between 65-97% and 71-92% respectively for type 2 diabetes and abnormal fasting plasma glucose screenings, while the overall specificities were low to moderate and ranged between 29-54% and 31-57% respectively for the screening of both conditions.

Methods 4 (Keesukphan et al's) and 2 (MOPH's) had highest sensitivity (94 and 97% respectively) but lowest specificity (29 and 31% respectively) in type 2 diabetes screening. These two methods also had highest sensitivity (89 and 92 % respectively for Methods 2 and 4) but lowest specificity (33 and 31 % respectively) in abnormal fasting plasma glucose screening. On the other hand, Method 1 (The Royal college of physician of Thailand's) had the lowest sensitivity (65 and 71 % respectively for type 2 diabetes and abnormal fasting

plasma glucose screenings) but highest specificity (54 and 57 % respectively) for both type 2 diabetes and abnormal fasting plasma glucose screenings.

However, when the performance of screening methods was assessed by area under the ROC curves, Method 3 (Aekplakorn et al's) performed the best in both type 2 diabetes and abnormal fasting plasma glucose screenings. This was due to its high sensitivity (87 and 83 % respectively for type 2 diabetes and abnormal fasting plasma glucose screenings) and moderate specificity (50 and 53 % respectively) as compared to the other methods.

The proportions of abnormal fasting plasma glucose and type 2 diabetes cases identified by different screening methods ranged from 71 to 92% and from 65 to 95% respectively. The numbers of abnormal fasting plasma glucose and type 2 diabetes detected by screening methods per 1,000 people screened ranged from 69 to 89 and 7 to10 respectively, while the actual numbers of abnormal fasting plasma glucose and type 2 diabetes cases were 97 and 10 per 1,000 persons screened.

For abnormal fasting plasma glucose, Method 4 (Keesukphan et al's) was able to identify the highest proportion of cases, followed by Methods 2 (MOPH's) and 3 (Aekplakorn et al's). Concerning type 2 diabetes, Method 2 (MOPH's) detected the highest proportion of cases, followed by Methods 3 (Aekplakorn et al's) and 4 (Keesukphan et al's).

The proportion of case missed ranged between 1 - 3 and 11 - 28 respectively for type 2 diabetes and abnormal fasting plasma glucose. Method 1 (Royal college of physician of Thailand's) missed highest numbers of cases of both conditions.

2. Cost of screening methods

The total costs for abnormal fasting plasma glucose and type 2 diabetes per 1000 persons screened ranged from 160,180 to 231,000 bahts and 160,733 to 231,790 bahts respectively from the societal perspective. Patients' and personnel's times contributed

highest to the total cost, and ranged from 73,000 to 100,000 and 64,200 to 102,000 bahts. Laboratory and other medical costs contributed less to the total costs and ranged from 3,680 to 8,000 and 3300 to 5,000 bahts respectively for abnormal fasting plasma glucose and type 2 diabetes screenings.

The percentage of the persons requiring laboratory testing was high in Methods 4 and 2 (713 and 693 persons per 1,000 persons screened) and low in Methods 3 and 1 respectively (502 and 460 persons per 1,000 persons screened).

From single payer perspective, the total costs for abnormal fasting plasma glucose and type 2 diabetes per 1000 persons screened range from 71,180 to 115,000 baht and from 71,258 to 115,130 baht. The total costs of screening for abnormal fasting plasma glucose were lower compare with type 2 diabetes.

Methods 3 and 1 had the lowest total costs for abnormal fasting plasma glucose and type 2 diabetes screening, while universal FPG testing had the highest cost followed by Methods 4 and 2 respectively.

3. Comparisons cost-effectiveness of screening methods

The cost-effectiveness for abnormal fasting plasma glucose and type 2 diabetes identified varied by screening method. From a societal perspective and a single payer perspective, cost-effectiveness was 2,046 - 2,381 and 933 - 1,186 baht/case for abnormal fasting plasma glucose, and 18,497 - 23,179 and 8,309-11,876 baht/case for type 2 diabetes respectively. The cost-effectiveness for abnormal fasting plasma glucose screening was highest compared with type 2 diabetes screening.

Method 3 (Aekplakorn's) had the highest cost-effectiveness for abnormal fasting plasma glucose and type 2 diabetes. Further, universal FPG testing had the lowest cost-effectiveness.

Sensitivity analysis by varying the disease prevalence rates, charge values of laboratory test, change values of patients' time and total salaries of personnel, and transportation rates did not alter the previous conclusion about the relative cost-effectiveness among different screening methods.

5.1 Discussion

The prevalence of pre-diabetes and type 2 diabetes vary among different populations. In this study, the proportions of pre-diabetes and type 2 diabetes were 8.7% and 1% respectively, which were lower than those in general population as previously reported by Aekplakorn and colleagues[24]. Men had two folds higher rates of type 2 diabetes and pre-diabetes than women (1.6 and 0.8% for type 2 diabetes, 15.7 and 7.5% for pre-diabetes).

The performance (sensitivity, specificity, and area under the ROC curve) of type 2 diabetes screening method 4 (Keesukphan et al's) reported in this study was similar to that reported in the original studies[15, 19], while our reported performance of Method 3 (Aekplakorn et al's) for type 2 diabetes screening was slightly different from the previous report (our versus originally reported sensitivity and specificity =87 vs. 77% and 50 vs. 60% respectively)[15]. This might be due to the originally reported performance of Method 3 was determined in a prospective setting while in this study we determined its performance in a cross-sectional setting.

With the optimal cut-off level, Method 3 ($\geq$ 6) identified 87% and 83% for type 2 diabetes and abnormal fasting plasma glucose cases respectively. For method 4 with cut-off point $\geq$ 240, it identified 94% and 92 % for type 2 diabetes and abnormal fasting plasma glucose cases respectively.

While the current cut-off points of $\geq$ 6 and $\geq$ 240 respectively for Methods 3 and 4 were for the identification of type 2 diabetes high risk persons, we also used the same cut-

off points for screening those at risk for abnormal fasting plasma glucose (FPG $\geq$ 100 mg/dl). The ability of Methods 3 and 4 to identify individuals with abnormal fasting plasma glucose were lower than that for type 2 diabetes. Therefore, the cut-off points should be modified when these two methods are used for the identification of individuals with abnormal fasting plasma glucose instead of type 2 diabetes.

5.1.1. Comparison among Thai diabetes screening methods

Although all screening methods shared many similar variables in the screening criteria, there were some differences among them. While age, BMI, and hypertension were utilized in all screening methods, different cut-off-points for these variables were applied. Pregnancy and delivery history, history of HDL-C $\leq$ 35 mg/dl or triglyceride $\geq$ 250 mg/dl, and history of high blood glucose, were included only in Methods 1 (The Royal college of physician of Thailand's) and 2 (MOPH's). Sex and waist circumference were utilized only in Method 3(Aekplakorn et al's). Furthermore, while different weights for each variable were applied in Methods 3 (Aekplakorn et al's) and 4 (Keesukphan et al's), equal weights were used in Methods 1 (The Royal college of physician of Thailand's) and 2 (MOPH's). The discrepancies in performance among these screening methods were attributed to these differences.

5.1.2. The implication of false negative and false positive of screening methods for abnormal fasting plasma glucose and type 2 diabetes

Two aspects of screening methods to be considered are false negative and false positive cases. False positivity results in higher percentage of the persons requiring laboratory testing, whereas false negativity causes some abnormal or diseased cases undetected and not receiving benefit from appropriate and timely treatment to reduce the risk for type 2 diabetes or disease complication.

The number of false negative cases in this finding ranged form 1 to 3 cases and from 8 to 28 cases per 1,000 persons screened for type 2 diabetes and abnormal fasting plasma glucose respectively. The problem of false negativity could be managed by continuing the periodic screening program that will detect false negative cases in the later period.

False negative cases may be quantified as number of cases or in monetary term. However, due to the scarcity of information for transforming false negative case into monetary term, they were therefore presented as the number of cases.

For abnormal fasting plasma glucose, the numbers of false negative cases were higher for Methods 1 and 3 and lower for Methods 2 and 4. Thus, Methods 2 and 3 should be selected for screening abnormal fasting plasma glucose and type 2 diabetes respectively based on the false negative cases.

For false positive cases, the number ranged from 453 to 704 cases and from 391 to 624 cases per 1000 person screened respectively for type 2 diabetes and abnormal fasting plasma glucose. Method 4 had highest number of false positive cases for both type 2 diabetes and abnormal fasting plasma glucose followed by Method 2. High number of false positivity should be managed by increase the specificity of screening method. Therefore, Method 3 should be selected for abnormal fasting plasma glucose and type 2 diabetes respectively based on moderate specificity and lower number of false positive cases.

5.1.3. Comparison with type 2 diabetes screening methods in other countries

When comparing with type 2 diabetes screening methods proposed in other countries, the performance of our studied screening methods were slightly inferior. The AUCs of Thai screening methods by Method 1 (AUC value=65%) was less than all studies in other countries, while Methods 2, 3 and 4 (AUC value= 72 - 75%) were comparable to those for Rotterdam[28] and Indian[33] studies (AUC value= 73-74%). They were higher than

those for the studies of Hoorn[27], and American Diabetes Association questionnaire[29] (AUC value = 69%) but less than those for the studies of Cambridge[30], Finnish[31], Danish[32], EPIC-Norfolk[35], Oman[36], and Spain[37] (AUCs value = 80-83%). The performance of German screening method [34] (AUC value = 84%) was very much higher than all Thai screening methods.

Detailed comparison showed that German, Cambridge, Finnish, and Danish screening methods differed from Thai screening methods in many aspects. Firstly, German diabetes risk score included height, physical activity, smoking, and consumption of red meat, whole-grain bread, coffee, and alcohol while these variables did not exist most in Thai screening methods. Secondly, Finnish diabetes risk score included history of antihypertensive drug use, physical activity < 4 h/wk and daily consumption of vegetables, fruits, or berries while these variables did not existed in Thai screening methods. Thirdly, Cambridge diabetes risk score included steroid and antihypertensive medication, smoking history while these variables did not existed in Thai screening methods. Lastly, Danish diabetes risk score included physical activity at leisure time while these variables did not existed in Thai screening methods. Applying some or all of these aspects into screening method might help improving future Thai type 2 diabetes screening methods. The aspects that might significantly improve the performance of the newly invented screening method are the inclusion of information about physical activity, consumption of vegetables, fruits and alcohol, and history of smoking.

Table 13 Variables of each screening method for type 2 diabetes

Variables	Method				References source										
					Lower performances				Higher performances						
	1	2	3	4	H[1]	R[2]	ADA[3]	I[4]	UK[5]	F[6]	D[7]	G[8]	E[9]	O[10]	S[11]
age	/	/	/	/	/	/	/	/	/	/	/	/	/	/	/
sex			/			/			/		/		/		
BMI	/	/	/	/	/	/	/	/	/	/	/		/	/	
Height												/			
waist circumference			/					/		/		/		/	
waist-to-hip circumference ratio						/									
waist-to-height ratio															/
Steroid medication									/						
Antihypertensive medication					/	/			/	/			/		
Hypertension	/	/	/	/		/					/	/		/	/
Family history of diabetes	/	/	/		/	/	/	/	/		/		/	/	/
Smoking history									/			/			
Alcohol consumption												/			
Physical activity						/	/	/		/	/	/	/		
cycling					/										

Table 13 Variables of each screening method for type 2 diabetes (cont')

Variables	Method				References source										
					Lower performances				Higher performances						
	1	2	3	4	H[1]	R[2]	ADA[3]	I[4]	UK[5]	F[6]	D[7]	G[8]	E[9]	O[10]	S[11]
Consumption of fruits, vegetables,										/		/	/		
berries, whole-grain bread															
Consumption of red meat												/			
Consumption coffee												/			
History of high blood glucose	/	/								/					
History GDM	/	/													/
Previous delivery of large infant	/	/					/								
(≥4000 kg)															
History of HDL-C ≤ 35 mg/dl	/	/													
or triglyceride ≥ 250															
Frequent thirst					/										
pain on walking, shortness of breath					/										
Performances															
- AUCs (%)	63	72	75	73	69	68-74		73	80	80	80	84	76	83	83-87

[1] = Hoorn study, [2]= Rotterdam study, [3]= ADA questionnaire, [4]= Indians risk score, [5]= Cambridge risk score, [6]= Finnish risk score,

[7]= Danish risk score, [8]= German risk score, [9]= EPIC-Norfolk study, [10]= Oman risk score, [11]= Spain risk score

5.1.4 Estimated implementation cost of type 2 diabetes screening program at the national level

Since there is evidence that early detection of pre-diabetes and type 2 diabetes can prevent or delay the disease development and progression, so the screening program might be implemented at the national level. We estimate the performance and cost of the national abnormal fasting plasma glucose and type 2 diabetes by basing on Method 3 (Aekplakorn et al's)--which was the most cost-effective screening method available nowadays for Thai population. We referred to previous study for the prevalence of abnormal fasting plasma glucose and type 2 diabetes [14] and to the results of population projections for Thailand 2005-2025 for the number of target population who are 35 years old and over in Thailand in 2008 [50]. It is estimated that the number of newly identified abnormal fasting plasma glucose among Thai adults who are 35 - 59 years or $\geq$ 35 years old would be 3,806,100 - 5,337,665 out of the total of 4,585,663 - 6,430,922 cases. In addition, the number of newly identified type 2 diabetes among these two age-ranges would be 904,021 - 1,287,633 out of the totally 1,039,105 - 1,480,038 cases. The number of missed abnormal fasting plasma glucose and type 2 diabetes cases would range from 779,563 to 1,093,257 (17%) and 135,084 to 192,405 (13%) among those aged 35 - 59 years and aged $\geq$ 35 years (Table 14).

From societal perspective, the total cost (in the first year) of the national abnormal fasting plasma glucose and type 2 diabetes screening program would range from 7,789,146,522 to 24,085,414,795 and from 10,923,478,578 to 34,305,793,848 bahts if the target population are those who were 35 - 59 years and $\geq$ 35 years old respectively.

Comparison with universal blood test, Method 3 would save screening cost around 3,131,334,248 to 4,391,376,310 bahts (29%) and 7,363,334,115 to 10,487,883,460 bahts (31%) for abnormal fasting plasma glucose and type 2 diabetes if the target populations are those who are 35-59 and $\geq$ 35 years old respectively.

However, as almost all cost data were obtained from secondary source, with some of them from university hospital setting which might be different from general or community hospital settings, our calculated total cost of national abnormal fasting plasma glucose and type 2 diabetes might be over- or underestimated[51].

Table 14 Estimated performances and cost of national abnormal fasting plasma glucose and type 2 diabetes screening program for Thai adults

Case detection methods	Cases identified * (number)		Total cost (Societal perspective) § (Thai ฿)	
	35-59 years	≥ 35 years	35-59 years	≥ 35 years
Abnormal fasting plasma glucose				
▪ Method 3	3,806,100	5,337,665	7,789,146,522	10,923,478,578
▪ Universal FPG testing	4,585,663	6,430,922	10,920,481,771	15,314,854,888
Type 2 Diabetes				
▪ Method 3	904,021	1,287,633	16,722,080,680	23,817,910,442
▪ Universal FPG testing	1,039,105	1,480,038	24,085,414,795	34,305,793,848

*Case identified = total number of people aged 35 years and over X prevalence of abnormal fasting plasma glucose and type 2 diabetes X sensitivity (Method 3 and Universal FPG testing)

§ Total cost = the total number of case identified X cost per case identified

Comparison the highest cost-effectiveness method (Aekplakorn et al's) with health care budget in 2008 [52], the total cost of the national abnormal fasting plasma glucose and type 2 diabetes screening would range from 7,789,146,522 to 10,923,478,578 bahts (5-8%) and from 16,722,080,680 to 23,817,910,442 bahts (12-17%) out of the totally 142,192,135,300 bahts by Method 3(Aekplakorn et al's), while range from 10,920,481,771 to 15,314,854,888 bahts (8-11%) and from 24,085,414,795 to 34,305,793,848 bahts (17-24%)

respectively for both conditions by universal FPG testing if the target populations are those who are 35-59 and ≥ 35 years old respectively. Thus, Method 3 would save screening cost for abnormal fasting plasma glucose and type 2 diabetes ranges from 3,131,335,249 to 4,391,376,310 bahts (2-3%) and from 7,363,334,115 to 10,487,883,406 bahts (5-7%) respectively (Table 15).

However, the cost of case identified is only a small part of the overall cost of implementing screening for abnormal fasting plasma glucose and type 2 diabetes programs. A more important of this part should include the benefit of preventing complication and delaying diabetes. Recent studies have documented that lifestyle intervention with high risk for diabetes is cost-saving for healthcare payer and highly cost-effectiveness for the societal [53].

Table 15 Comparison the highest cost-effectiveness method with health care budget in 2008 (142,192,135,300 baht)

Case detection methods	Cases identified (number)		Total cost (Societal perspective) (baht)	
	35-59 years	≥ 35 years	35-59 years	≥ 35 years
Abnormal fasting plasma glucose				
▪ Method 3	3,806,100	5,337,665	7,789,146,522 (5%)	10,923,478,578 (8%)
▪ Universal FPG testing	4,585,663	6,430,922	10,920,481,771 (8%)	15,314,854,888 (11%)
Type 2 Diabetes				
▪ Method 3	904,021	1,287,633	16,722,080,680 (12%)	23,817,910,442 (17%)
▪ Universal FPG testing	1,039,105	1,480,038	24,085,414,795 (17%)	34,305,793,848 (24%)

Currently, type 2 diabetes screening was implementing at the national level in Thailand by relying on Method 2 (MOPH's) [13, 18]. However, as Method 2 (MOPH's) had lower performance and cost-effectiveness than Method 3 (Aekplakorn et al's), the screening method of implementation should be altered to be more cost saving and being able to detecting higher proportions of individuals with type 2 diabetes and abnormal fasting plasma glucose.

5.1.5 Possible improvement in the performance of abnormal fasting plasma glucose and type 2 diabetes screening method for Thai adult population

Although the sensitivities of all available screening methods for Thai adults were quite satisfactory, their specificities were quite modest. One way to improve their cost-effectiveness is to implementing the screening program only among the high-risk sub-population. The other way is to improving the screening method by adding more determining variable(s) into the screening instrument and/or manipulating them by applying different weights on each included variable.

Table 16 Characteristics of behavior variables with type 2 diabetes and normal blood glucose subjects

Variables	Type 2 diabetes		Normal blood glucose	
	Men	Women	Men	Women
▪ Formal exercise	205.71±137.94	67.50±32.78	208.59±202.21	150.18±183.19
- Formal exercise ≥150 minutes/week	4(30.80)	0	261(33.00)	441(20.50)
▪ Consumption vegetable and fruit	3.73±1.86	4.00±2.40	3.57±1.95	3.68±1.98
- Consumption vegetable and fruit ≥5 saving/day	4(30.80)	4(22.20)	169(21.40)	546(25.30)
▪ Smoking history	3(23.10)	1(5.60)	153(19.40)	12(0.60)
▪ Alcohol consumption	6(46.20)	1(5.60)	326(41.30)	141(6.40)

Data are mean ± SD or number (%)

According to the result of this study, it indicated that the average values of exercise in type 2 diabetes by women and men were 67 and 205 minutes per week while150 and 208 respectively of both sexes in the cases of normal blood glucose (Table 16). The proportion of exercise ≥150 minute/week in type 2 diabetes (0% and 30% for women and men) was slightly lower than in the cases of normal blood glucose (20% and 33% respectively for both sexes).

In addition, the proportion of vegetable and fruit consumption ≥ 5 saving per day in type 2 diabetes women were slightly lower compare to the case of normal blood glucose (22% vs. 25%). Prevalence rate of smoking history in women and men were higher than normal blood glucose (5.6 and 23.1% vs. 0.6 and 19.4%) while the proportion of alcohol consumption in men was slightly higher than in cases without diabetes (46% vs. 41%).

Thus, variable(s) which should be utilized in future screening method included physical activity, consumption vegetable fruit and alcohol, smoking history, and particularly formal exercise.

5.2 Strength of this study

As the author evaluated the performance of four screening methods simultaneously within the same population, bias or confounding effects due to different study populations were thus automatically eliminated. Additionally, all blood tests, including FPG, were applied to the total population as the reference or gold standard method for all the target screening methods to compare with.

5.3 Limitations of this study

5.3.1 Two repeated FPG of ≥126 mg/dl was used as the gold standard in stead of the 75-g oral glucose tolerance test (OGTT). This might result in the underestimate of type 2 diabetes prevalence. However, the OGTT is not practical on large scale implementation. Furthermore, false negative cases, risk reduction, and treatment effectiveness were not being included in the cost analysis because of the scarcity of relevant information appropriate for the condition in Thailand.

5.3.2 The study subjects were the employees in public and private organizations. When the screening methods are applied to general population with poor reading literacy, performance of each screening methods might be lower than our reported performance.

5.3.3 This study used secondary data about laboratory cost, transportation cost and patients 'time, the total cost of screen detected for abnormal fasting plasma glucose and type 2 diabetes information might thus be inaccurate for a certain extent. Sensitivity analysis by varying all cost data showed that the conclusion of relative cost-effectiveness among the studied screening methods remains unchanged.

5.4 Policy recommendations

1. The screening program is the preventive program that can help in early detection of subjects at high risk for type 2 diabetes in high risk population. The highest cost-effectiveness method (Aekplakorn et al's) for abnormal fasting plasma glucose and type 2 diabetes could be cost saving than the universal FPG testing or the currently used screening method. Policy maker should consider incorporating this more effective and cost saving method into national type 2 diabetes screening program. Although, this study was conducted in the university hospital setting its result can also be applied into smaller hospital and community settings.

2. New cut off point for Method 3 (Aekplakorn et al's) is required in screen – detected individual at risk for abnormal fasting plasma glucose.

5.5 Recommendations for further research

1. Further study should develop the screening method based on a self-administered questionnaire, which high specificity and maintain high sensitivity for decrease the number of unnecessary screening and minimizing the costs associated with screening program.

2. The study participants were the employees in public and private organizations. Their education level may be higher than general population. Further study should assess the performance of screening method in general population and poor reading literacy.

3. Further study should evaluate the total costs and benefits of screening programs, including the cost of both detection and risk reduction.

REFERENCES

[1] Narayan KMV, Zhang P, Kanaya AM, Williams DE, Engelgau MM, Imperatore G, et al. Diabetes: The Pandemic and Potential Solutions In: Dean T. Jamison JGB, Antrony R. Measham, George Alleyne, Marian Claeson, David B. Evans, ed., **Disease Control Priorities in Developing Countries**, 591-603. USA : Oxford University Press, 2006.

[2] Diagnosis and classification of diabetes mellitus. **Diabetes Care** 29, Suppl 1 (Jan 2006) : S43-S48.

[3] Zimmet P, Alberti KG, Shaw J. Global and societal implications of the diabetes epidemic. **Nature** 414, 6865 (Dec 2001) : 782-787.

[4] Nathan DM. Long-term complications of diabetes mellitus. **N Engl J Med** 328, 23 (Jun 1993) : 1676-1685.

[5] Davis TM, Stratton IM, Fox CJ, Holman RR, Turner RC. U.K. Prospective Diabetes Study 22. Effect of age at diagnosis on diabetic tissue damage during the first 6 years of NIDDM. **Diabetes Care** 20, 9 (Sep 1997) : 1435-1441.

[6] Panzram G. Mortality and survival in type 2 (non-insulin-dependent) diabetes mellitus. **Diabetologia** 30, 3 (Mar 1987) : 123-131.

[7] Haffner SM, Stern MP, Hazuda HP, Mitchell BD, Patterson JK. Cardiovascular risk factors in confirmed prediabetic individuals. Does the clock for coronary heart disease start ticking before the onset of clinical diabetes? **JAMA** 263 (1990) : 2893-2898.

[8] Harris MI, Klein R, Welborn TA, Knuiman MW. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. **Diabetes Care** 15, 7 (Jul 1992) : 815-819.

[9] The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. **N Engl J Med** 329, 14 (Sep 1993) : 977-986.

[10] Standards of medical care in diabetes. **Diabetes Care** Suppl 1 (Jan 2005) : S4-S36.

[11] King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence,

numerical estimates, and projections. **Diabetes Care** 21, 9 (Sep 1998) : 1414-1431.

[12] Wareham NJ, Griffin SJ. Should we screen for type 2 diabetes? Evaluation against National Screening Committee criteria. **Bmj** 322, 7292 (Apr 2001) : 986-988.

[13] Wibulpolprasert S, ed., **Thailand Health Profile 2001-2005**. Nonthaburi : Printing Press, Express Transportation Organization, 2005.

[14] Aekplakorn W, Abbott-Klafter J, Premgamone A, Dhanamun B, Chaikittiporn C, Chongsuvivatwong V, et al. Prevalence and management of diabetes and associated risk factors by regions of Thailand: Third National Health Examination Survey 2004. **Diabetes Care** 30, 8 (Aug 2007) : 2007-2012.

[15] Aekplakorn W, Bunnag P, Woodward M, Sritara P, Cheepudomwit S, Yamwong S, et al. A risk score for predicting incident diabetes in the Thai population. **Diabetes Care** 29, 8 (Aug 2006) : 1872-1877.

[16] Jiamjarasrangsi W, Aekplakorn W. Incidence and predictors of type 2 diabetes among professional and office workers in Bangkok, Thailand. **J Med Assoc Thai** 88, 12 (Dec 2005) : 1896-1904.

[17] Suthijumroon A. Diabetes Mellitus Screening In: Suntorntham S, ed., **Evidence-Based Clinical Practice Guideline Periodic Health Examination and Maintenance in Thailand**, 124-131. Bangkok : Mohchaoban press, 2001.

[18] Bureau of Non- communicable Disease. **Screening for Hypertension and Diabetes** Nonthaburi: Bureau of Non- communicable Disease, 2007. (Mimeographed)

[19] Keesukphan P, Chanprasertyothin S, Ongphiphadhanakul B, Puavilai G. The development and validation of a diabetes risk score for high-risk Thai adults. **J Med Assoc Thai** 90, 1 (Jan 2007) : 149-154.

[20] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. **Diabetes Care** 27, 5 (May 2004) : 1047-1053.

[21] Ministry of Public Health. **The Second National Health Examination Survey 1996-1997**.

Nonthaburi, 1998.

[22] Bhuripanyo K, Ruangratanaamporn O, Mahanonda N, Leowattana W, Sriratanasathaavorn C, Chotinaiwattarakul C, et al. Impaired fasting glucose, diabetes mellitus and coronary risk factors. **J Med Assoc Thai** 83 Suppl 2 (Nov 2000) : S146-S152.

[23] Puavilai G, Kheesukapan P, Chanprasertyotin S, Chantraraprasert S, Suwanvilaikorn S, Nitiyanant W, et al. Random capillary plasma glucose measurement in the screening of diabetes mellitus in high-risk subjects in Thailand. **Diabetes Res Clin Pract** 51, 2 (Feb 2001) : 125-131.

[24] Aekplakorn W, Stolk RP, Neal B, Suriyawongpaisal P, Chongsuvivatwong V, Cheepudomwit S, et al. The prevalence and management of diabetes in Thai adults: the international collaborative study of cardiovascular disease in Asia. **Diabetes Care** 26, 10 (Oct 2003) : 2758-2763.

[25] Vannasaeng S. Burden of Diabetes in Thailand. In: Nitiyanant W, Vannasaeng S, Deerochochanawong C, eds., **Diabetes Situation in Thailand 2007**, 1-16. Bangkok : Vivat press, 2007.

[26] World Health Organization. **Screening for Type 2 Diabetes: Report of a World Health Organization and International Diabetes Federation meeting** Geneva : WHO, 2003.

[27] Ruige JB, de Neeling JN, Kostense PJ, Bouter LM, Heine RJ. Performance of an NIDDM screening questionnaire based on symptoms and risk factors. **Diabetes Care** 20, 4 (Apr 1997) : 491-496.

[28] Baan CA, Ruige JB, Stolk RP, Witteman JC, Dekker JM, Heine RJ, et al. Performance of a predictive model to identify undiagnosed diabetes in a health care setting. **Diabetes Care** 22, 2 (Feb 1999) : 213-219.

[29] Rolka DB, Narayan KM, Thompson TJ, Goldman D, Lindenmayer J, Alich K, et al. Performance of recommended screening tests for undiagnosed diabetes and dysglycemia. **Diabetes Care** 24, 11 (Nov 2001) : 1899-1903.

[30] Griffin SJ, Little PS, Hales CN, Kinmonth AL, Wareham NJ. Diabetes risk score: towards earlier detection of type 2 diabetes in general practice. **Diabetes/metabolism research and reviews** 16, 3 (May-Jun 2000) : 164-171.

[31] Lindstrom J, Tuomilehto J. The diabetes risk score: a practical tool to predict type 2 diabetes risk. **Diabetes Care** 26, 3 (Mar 2003) : 725-731.

[32] Glumer C, Carstensen B, Sandbaek A, Lauritzen T, Jorgensen T, Borch-Johnsen K. A Danish diabetes risk score for targeted screening: the Inter99 study. **Diabetes Care** 27, 3 (Mar 2004) : 727-733.

[33] Ramachandran A, Snehalatha C, Vijay V, Wareham NJ, Colagiuri S. Derivation and validation of diabetes risk score for urban Asian Indians. **Diabetes Res Clin Pract** 70, 1 (Oct 2005) : 63-70.

[34] Schulze MB, Hoffmann K, Boeing H, Linseisen J, Rohrmann S, Mohlig M, et al. An accurate risk score based on anthropometric, dietary, and lifestyle factors to predict the development of type 2 diabetes. **Diabetes Care** 30, 3 (Mar 2007) : 510-515.

[35] Simmons RK, Harding AH, Wareham NJ, Griffin SJ. Do simple questions about diet and physical activity help to identify those at risk of Type 2 diabetes? **Diabet Med** 24, 8 (Aug 2007) : 830-835.

[36] Al-Lawati JA, Tuomilehto J. Diabetes risk score in Oman: a tool to identify prevalent type 2 diabetes among Arabs of the Middle East. **Diabetes Res Clin Pract** 77, 3 (Sep 2007) : 438-444.

[37] Cabrera de Leon A, Coello SD, Rodriguez Perez MD, Medina MB, Almeida Gonzalez D, Diaz BB, et al. A simple clinical score for type 2 diabetes mellitus screening in the Canary Islands. **Diabetes Res Clin Pract** Article in press (Dec 2007)

[38] Waugh N, Scotland G, McNamee P, Gillett M, Brennan A, Goyder E, et al. Screening for type 2 diabetes: literature review and economic modelling. **Health technol Assess** 11, 17 (May 2007) : iii-iv, ix-xi, 1-125.

[39] Pan XR, Li GW, Hu YH, Wang JX, Yang WY, An ZX, et al. Effects of diet and exercise in

preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. **Diabetes Care** 20, 4 (Apr 1997) : 537-544.

[40] Tuomilehto J, Lindstrom J, Eriksson JG, Valle TT, Hamalainen H, Ilanne-Parikka P, et al. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. **N Engl J Med** 344, 18 (May 2001) : 1343-1350.

[41] Kosaka K, Noda M, Kuzuya T. Prevention of type 2 diabetes by lifestyle intervention: a Japanese trial in IGT males. **Diabetes Res Clin Pract** 67, 2 (Feb 2005) : 152-162.

[42] Zhang P, Engelgau MM, Valdez R, Benjamin SM, Cadwell B, Narayan KM. Costs of screening for pre-diabetes among US adults: a comparison of different screening strategies. **Diabetes Care** 26, 9 (Sep 2003) : 2536-2542.

[43] Glumer C, Vistisen D, Borch-Johnsen K, Colagiuri S. Risk scores for type 2 diabetes can be applied in some populations but not all. **Diabetes Care** 29, 2 (Feb 2006) : 410-414.

[44] Jones SR, Carley S, Harrison M. An introduction to power and sample size estimation. **Emerg Med J** 20, 5 (Sep 2003) : 453-458.

[45] Charuruks N, Chamnanpai S, Seublinvog T. Cost analysis of laboratory tests: a study of the Central Laboratory of King Chulalongkorn Memorial Hospital. **J Med Assoc Thai** 87, 8 (Aug 2004) : 955-963.

[46] Department of Land Transport. **Transportation fee** [Online]. Available from: http:// www.dlt.go.th [6 March 2009].

[47] Ministry of Labour. **Minimum wage 2008** [Online]. Available from: http:// www.mol.go.th [6 March 2009].

[48] Fletcher R, Fletcher S, Wagner E. **Clinical epidemiology: the essential** Third edition ed. USA: Williams & Wilkins, 1996.

[49] Limwatananon S. Handling Uncertainty of Economic Evaluation Result: Sensitivity Analysis. **J Med Assoc Thai** 91, Suppl 2 (2008) : S59-S65.

[50] Institute for Population and Social Research. **Results of Population Projections for**

Thailand 2005-2025 [Online]. Available from: http://www.ipsr.mahidol.ac.th [26 March 2009].

[51] International Health Policy Program. **Unit cost for capitation** Nonthaburi: International Health Policy Program, 2009. (Unpublished Manuscript)

[52] Bureau of Policy and Strategy. **Budget of the Ministry of Public Health in 2008** [Online]. Available from: http://bps.ops.moph.go.th [29 March 2009].

[53] Lindgren P, Lindstrom J, Tuomilehto J, Uusitupa M, Peltonen M, Jonsson B, et al. Lifestyle intervention to prevent diabetes in men and women with impaired glucose tolerance is cost-effective. **International journal of technology assessment in health care** 23, 2 (2007) : 177-183.

APPENDICES

Appendix A: Screening questionnaires

ข้อมูลสำหรับผู้เข้าร่วมการวิจัย

ชื่อโครงการ ต้นทุน และประสิทธิผล ของวิธีการตรวจคัดกรอง ภาวะน้ำตาลในเลือดผิดปกติ และโรคเบาหวานชนิดที่ 2 ที่ยังไม่ได้รับการวินิจฉัย

เรียน ผู้เข้ารับการตรวจสุขภาพประจำปี ทุกท่าน ก่อนที่ท่านจะตกลงเข้าร่วมการศึกษาดังกล่าว ผู้วิจัยขอเรียนให้ท่านทราบถึงรายละเอียดเกี่ยวกับการศึกษาวิจัยครั้งนี้ ดังนี้

1) **ความเป็นมาและวัตถุประสงค์ของการศึกษาวิจัย**

ปัจจุบันโรคเบาหวาน กำลังเป็นปัญหาของประชากรทั่วโลก รวมทั้งในประเทศไทย ซึ่งในระยะแรกๆ จะไม่มีอาการและไม่สามารถทราบได้เลย หากไม่มีการตรวจคัดกรอง แต่การตรวจคัดกรองโดยการเจาะเลือดก็มีต้นทุนสูงหากนำไปใช้กับประชากรทั่วประเทศ

ดังนั้น ผู้วิจัย จึงมีความประสงค์ที่จะทำการศึกษา วิธีการตรวจคัดกรอง โรคเบาหวาน ที่มีประสิทธิภาพแต่ประหยัดและคุ้มค่าเพื่อนำไปใช้กับประชากรทั่วประเทศ

2) **วิธีการเก็บข้อมูล**

การเก็บข้อมูลในการศึกษานี้ คือ การตอบแบบสอบถาม(ร่วมกับการตรวจสุขภาพประจำปี) โดยใคร่ขอให้ผู้เข้าร่วมการวิจัยตอบแบบสอบถาม เกี่ยวกับประวัติส่วนตัวและพฤติกรรมสุขภาพ จำนวน 2 หน้า

ผู้วิจัยขอคัดลอกผลการตรวจน้ำตาลในเลือดจากเวชระเบียน และขอเก็บตัวอย่างเลือดส่งตรวจเพิ่มเติม อีก 1 ครั้ง ภายใน 2 อาทิตย์ หลังจากการตรวจสุขภาพครั้งแรก ในกรณีที่ผลการตรวจน้ำตาลในเลือดผิดปกติ เพื่อทำการตรวจสอบยืนยันความผิดปกติ โดยผู้ที่จะเข้าถึงตัวอย่างเลือดนี้ได้ คือ ผู้วิจัยและทีมงานวิจัยนี้เท่านั้น

3) ประโยชน์ที่จะได้รับจากการศึกษาวิจัย

ผู้เข้าร่วมการวิจัย จะได้ทราบสถานภาพความเสี่ยงต่อสุขภาพของตนเอง รวมทั้งได้รับประโยชน์จากการดำเนินการด้านการสร้างเสริมสุขภาพและป้องกันโรคที่เกี่ยวข้องโดยหน่วยงานของท่าน หลังจากทราบผลการตรวจสุขภาพครั้งนี้แล้ว

สำหรับผู้ให้บริการและผู้กำหนดนโยบาย คือได้ข้อมูลพื้นฐาน ในการกำหนดแนวทางการตรวจคัดกรองโรคเบาหวาน ในประชากรไทย

4) สิทธิของผู้ร่วมการวิจัย

การเข้าร่วมการศึกษาครั้งนี้ จะเป็นไปตามความสมัครใจ ท่านอาจจะปฏิเสธที่เข้าร่วมหรือถอนตัวจากการศึกษาได้ โดยไม่มีผลกระทบใดๆ ต่อการการปฏิบัติงานของท่าน ข้อมูลของท่านจะถูกเก็บเป็นความลับ และไม่มีการแพร่พรายสู่สาธารณชน และขอรับรองว่าจะไม่มีการเปิดเผยรายชื่อของท่านในที่ใดๆ

หากท่านมีปัญหาหรือข้อสงสัยประการใด ติดต่อสอบถามได้ที่ นางสาวนิพา ศรีช้าง นิสิตปริญญาโท สหสาขาวิชาวิจัยเพื่อการพัฒนาสุขภาพ โทร 081-3638810

ขอขอบคุณในความร่วมมือของท่านมา ณ ที่นี้

แบบสอบถาม

การวิจัย เรื่อง ต้นทุน และประสิทธิผลของวิธีการตรวจคัดกรอง ภาวะก่อนเบาหวาน และโรคเบาหวานชนิดที่ 2 ที่ยังไม่ได้รับการวินิจฉัย

คำชี้แจงในการตอบแบบสอบถาม

การวิจัยครั้งนี้เป็นการศึกษาทางวิชาการ ไม่มีผลใดๆทั้งทางตรงและทางอ้อมแก่ท่านผู้เข้าร่วมการศึกษา จึงขอความกรุณาให้ท่านตอบแบบสอบถามให้ตรงกับความเป็นจริงมากที่สุด

ส่วนที่ 1 สำหรับเจ้าหน้าที่ของโรงพยาบาลจะเป็นผู้ลงผลให้

ส่วนที่ 2 สำหรับผู้เข้ารับการตรวจคัดกรอง ขอให้ท่านเติมคำในช่องว่าง หรือ กาเครื่องหมาย x ลงในช่อง ○ ตามความเป็นจริง

ขอขอบคุณในความร่วมมือ
นิพา ศรีช้าง
(นางสาวนิพา ศรีช้าง)
นิสิตหลักสูตรวิทยาศาสตรมหาบัณฑิต
สหสาขาวิชาวิจัยเพื่อการพัฒนาสุขภาพ จุฬาลงกรณ์มหาวิทยาลัย

ลำดับในการตรวจ.....

บริษัท ..... **วันที่ตรวจ** .....

ส่วนที่ 1 สำหรับเจ้าหน้าที่

1. น้ำหนัก.....กก. ส่วนสูง.....ซม. BMI =.....kg/m^2
2. ความยาวรอบเอว..... ซม
3. ความดันโลหิต.....มม.ปรอท

ส่วนที่ 2 สำหรับผู้เข้ารับการตรวจคัดกรอง

4. เพศ	[1]○ ชาย [2]○ หญิง
5. วัน/เดือน/ปีเกิด	วันที่.....เดือน.....พ.ศ..... อายุ .....ปี
6. ท่านมีประวัติในครอบครัวเป็นโรคเบาหวานหรือไม่	[1]○ มี [2]○ ไม่มี [3]○ ไม่ทราบ } □ *ข้ามไปตอบข้อ 7*
→ 7. ผู้มีประวัติเป็นโรคเบาหวานในครอบครัวของท่าน คือใครบ้าง (ตอบได้มากกว่า 1 ข้อ)	[1]○พ่อ [2]○แม่ [3]○พี่ [4]○น้อง
8. ท่านเป็นโรคความดันโลหิตสูงหรือไม่	[1]○ เป็น [2]○ไม่เป็น [3]○ไม่ทราบ
9. สำหรับผู้หญิง ท่านเคยคลอดบุตรหรือไม่	[1]○ เคย [2]○ ไม่เคย □ *ข้ามไปตอบข้อ 12*
10. ท่านมีประวัติได้รับการวินิจฉัยว่าเป็นเบาหวานขณะตั้งครรภ์หรือไม่	[1]○ มี [2]○ ไม่มี
11. ท่านมีประวัติเคยคลอดบุตรตัวโต มากกว่าหรือเท่ากับ 4000 กรัม หรือไม่	[1]○ มี [2]○ ไม่มี

12. ท่านมีประวัติเคยตรวจระดับไขมันดี(HDL-C)ในเลือดหรือไม่ ในช่วงระยะเวลา 1 ปี	[1]○ เคย [2]○ ไม่เคย □ *ข้ามไปตอบข้อ 14*
13. ระดับไขมันดี(HDL-C)ในเลือดที่เคยตรวจผิดปกติหรือไม่	[1]○ ปกติ [2]○ ผิดปกติ
14. ท่านมีประวัติเคยตรวจไตรกลีเซอไรด์ หรือไม่ ในช่วงระยะเวลา 1 ปี	[1]○ เคย [2]○ ไม่เคย □ *ข้ามไปตอบข้อ* 16
15. ระดับไตรกลีเซอไรด์ที่เคยตรวจผิดปกติหรือไม่	[1]○ ปกติ [2]○ ผิดปกติ
16. ท่านเคยตรวจวัดระดับน้ำตาลในเลือด หลังอดอาหารอย่างน้อย 8 ชั่วโมง หรือไม่ ในช่วงระยะเวลา 1 ปี	[1]○ เคย [2]○ ไม่เคย □ *ข้ามไปตอบข้อ* 18
17. ท่านมีระดับน้ำตาลในเลือดเมื่ออดอาหารผิดปกติ แต่ยังไม่เป็นเบาหวานหรือไม่	[1]○ ปกติ [2]○ ผิดปกติ
18. ท่านเคยตรวจวัดระดับน้ำตาลกลูโคสหลังดื่มกลูโคส 75 กรัม หรือไม่ ในช่วงระยะเวลา 1 ปี	[1]○ เคย [2]○ ไม่เคย □ *ไปตอบข้อ 20*
19. ท่านมีระดับน้ำตาลในเลือดหลังดื่มกลูโคสผิดปกติ แต่ยังไม่เป็น เบาหวานหรือไม่	[1]○ ปกติ [2]○ ผิดปกติ
20. ในวันปกติของท่าน ท่านมีกิจกรรมที่ต้องออกแรงปานกลาง ทำให้หายใจแรงขึ้น เป็นเวลาตั้งแต่ 10 นาที ขึ้นไป ในแต่ละครั้ง เช่น การเดินไปมาในที่ทำงาน การเดินไปยังสถานที่ต่างๆ ทำงานบ้าน ทำครัว เป็นต้น เป็นเวลานานเท่าใด	.....ชั่วโมงต่อวัน .....วันต่อสัปดาห์
21. ท่านเล่นกีฬา ออกกำลังกาย หรือมีกิจกรรมอย่างปานกลาง เป็นเวลาตั้งแต่ 10 นาทีขึ้นไปในแต่ละครั้ง เช่น เดินเร็ว ขี่จักรยาน ว่ายน้ำ ในแต่ละครั้งเป็นเวลานานเท่าใด	.....ชั่วโมงต่อวัน .....วันต่อสัปดาห์

22. ท่านสูบบุหรี่หรือไม่	[1]○ ไม่สูบ [2]○ สูบ ระบุ.....มวน/วัน
23. ท่านดื่มสุราหรือไม่ โดยที่ 1 แก้วมาตรฐาน หมายถึง เหล้า ~ 2 ฝา (1 เป๊ก) หรือเบียร์ 1 กระป๋อง หรือไวน์ 1 แก้ว (140 ซีซี)	[1]○ไม่ดื่ม [2]○ ดื่ม< 6 แก้วมาตรฐาน/สัปดาห์ [3]○ ดื่ม> 6 แก้วมาตรฐาน/สัปดาห์
24. ท่านกินผัก กี่ส่วน/วัน โดยผัก 1 ส่วนมาตรฐาน เท่ากับ ผักใบ ปรุงสุกแล้ว 1 ทัพพี หรือ ผักใช้ผล/หัว/ราก เช่น มะเขือเทศ แครอท ฟักทอง ข้าวโพด กะหล่ำดอก ถั่วฝักยาว หอมหัวใหญ่ 1 ทัพพี หรือผักใบเขียวสด ไม่ผ่านการปรุงสุก 2 ทัพพี หรือ น้ำผัก ½ ถ้วยตวง	.....ส่วน/วัน (1 ส่วน = 1 ทัพพี)
25. ท่านกินผลไม้สด กี่ส่วน/วัน โดยผลไม้ 1 ส่วน มาตรฐาน เท่ากับ มะละกอ แตงโม หรือ สับปะรด 6-8 คำ หรือ กล้วยน้ำว้า 1 ผลเล็ก หรือกล้วยหอม ½ ผลกลาง หรือส้มเขียวหวาน 1 ผลใหญ่ หรือ 2 ผลกลาง หรือ เงาะ 4 ผล	.....ส่วน/วัน

Appendix B: Work sheets for direct medical cost calculation for abnormal fasting plasma glucose and type 2 diabetes

Item (1)	Unit (2)	Formula (3)	Unit cost of the item (4)	Hour or weight or volume or test or unit used for 1 person (5)	Sub total cost of the item (4X5)
Personnel time					
• Physicians time	1 h	1h =total income/22day/8 h	฿284 /h	¼ h	฿70
• Nurse time	1 h	1h =total income/22day/8 h	฿170 /h	1/6 h	฿28
• Secretary time	1 h	1h =total income/22day/8 h	฿45 /h	1/12 h	฿4
Laboratory cost					
• Fasting plasma glucose	1 test	1 test = 8 baht	฿8 /test	1 test	฿8 /test
Material cost					
• Screening questionnaire	1 test	1 test = 1 baht	฿1 /test	1 copy	฿1 /test
• Mail costs	1 mail	1 mail = 5 baht	฿5 /mail	1 mail	฿5 /mail
Total cost					$\sum x$

Appendix C: Work sheets for non-medical cost calculation for abnormal fasting plasma glucose and type 2 diabetes

Item(1)	Unit(2)	Formula(3)	Unit cost of the item(4)	Hour or weight or volume or test or unit used for 1 person(5)	Sub total cost of the item (4X5)
Transportation cost					
• Bangkok mass transportation cost	1 trip	1 trip = 16 baht	1trip	16 baht	฿16
Patient time	h	Bangkok Minimum wage = ฿200 /day	฿25/h		
• abnormal fasting plasma glucose					
- high score persons	4 h	1 h = 200 baht/8h	฿25/h	4 h	฿100
- low score persons	2 h	1 h = 200 baht/8h	฿25/h	2 h	฿50
• type 2 diabetes					
- high score persons	4 h	1 h = 200 baht/8h	฿25/h	4 h	฿100
- low score persons	2 h	1 h = 200 baht/8h	฿25/h	2 h	฿50
- high FPG persons	2 h	1 h = 200 baht/8h	฿25/h	2 h	฿50
Total cost					$\sum x$

Appendix D: Receiver operating characteristic (ROC) curves for abnormal fasting plasma glucose and type 2 diabetes

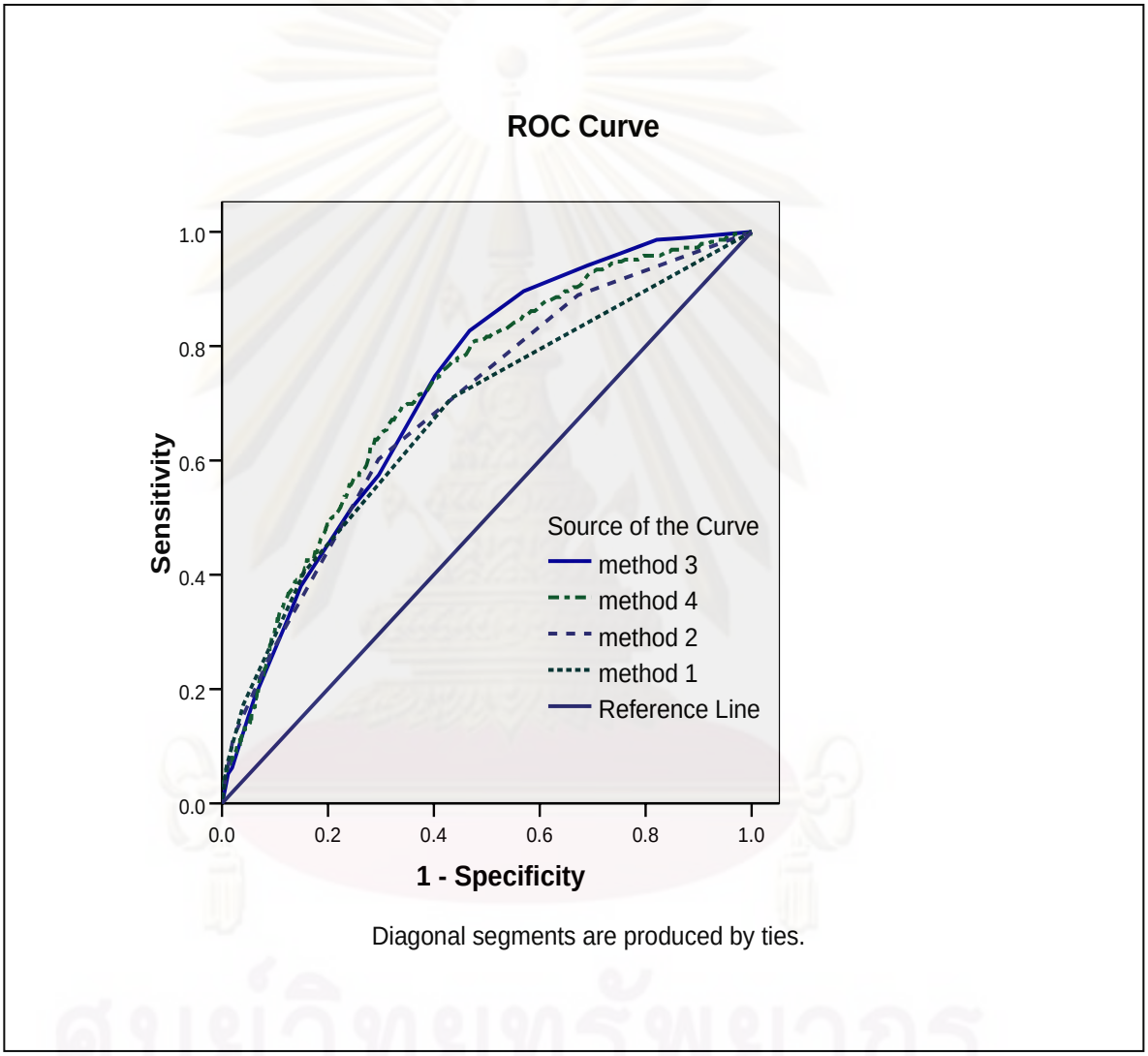


Figure 7 Receiver operating characteristics (ROC) curves for abnormal fasting plasma glucose of four screening methods

Figure shows the ROC curves for abnormal fasting plasma glucose. The areas under the curves were (73% [0.69-0.75]), (72% [0.69-0.75]), (69% [0.66-0.72]), (68% [0.64-0.71]), in screening methods 3, 4, 2 and 1 respectively.

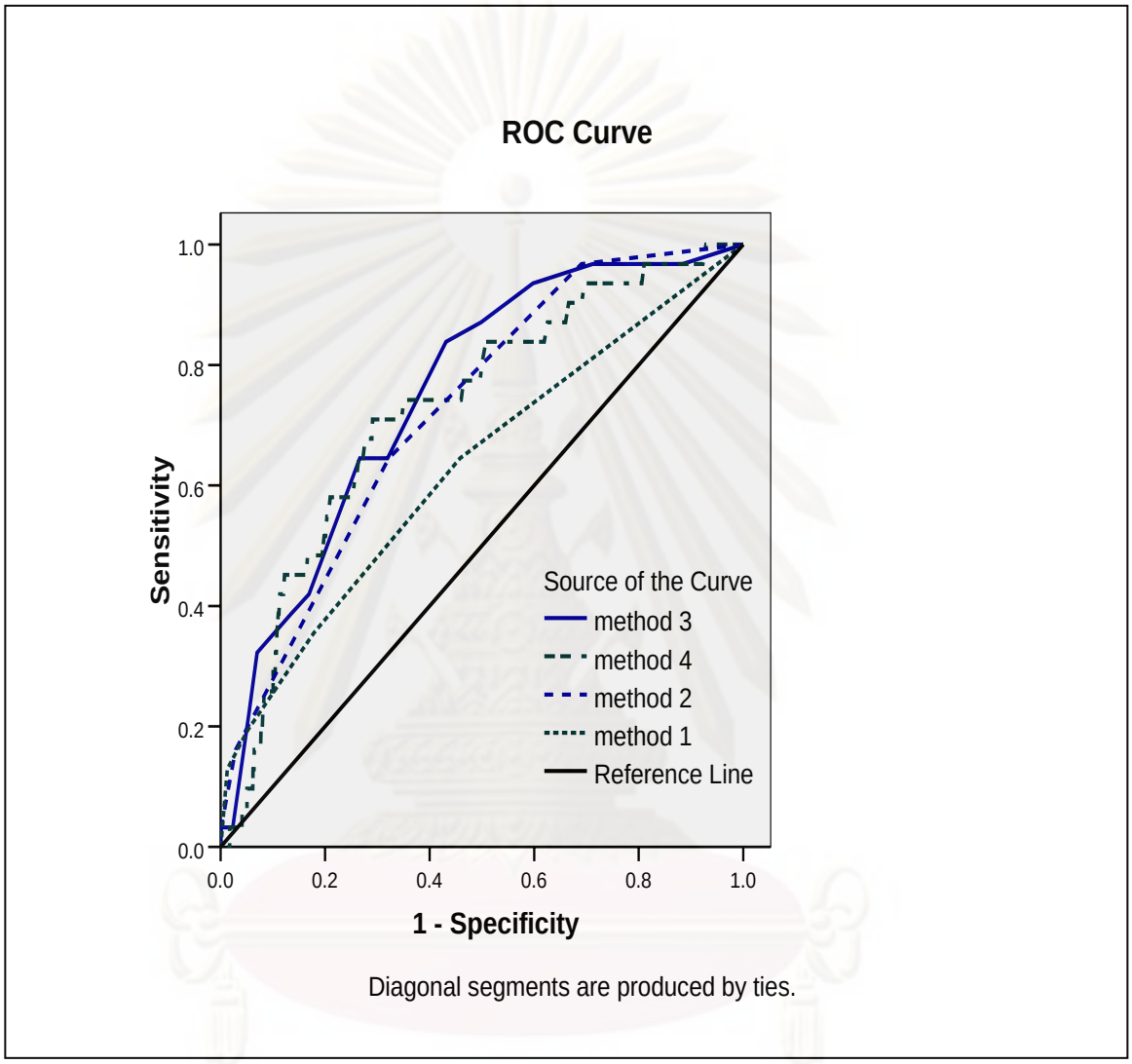


Figure 8 Receiver operating characteristic (ROC) curve for type 2 diabetes of four screening methods

Figure shows the ROC curves of the four screening methods for type 2 diabetes. The areas under the curve were (75% [0.67-0.83]), (73% [0.64-0.81]), (72% [0.64-0.80]), (63% [0.52-0.73]), in screening methods 3, 4, 2 and 1 respectively.

BIOGRAPHY

Name Nipa Srichang

Date of Birth March 6, 1968

Place of Birth Phatthalung, Thailand

Education

1986-1990 Bachelor of Science in Nursing, Mahidol University

1993-1994 Post graduate diploma on Occupational health nursing, Mahidol University

Work Experience

1990-1992 Ramathibodi Hospital

1992-1997 Thammasat Hospital

1997-2002 Medical Institute of Accident and Disaster, Department of Medical Service

2002-present Bureau of Non-communicable Disease, Department of Disease Control

Ministry of Public Health, Nonthaburi 11000, Thailand

Phone (66) 0259-03987-8

Email: srichang@health.moph.go.th