COST-EFFECTIVENESS ANALYSIS OF DIABETIC RETINOPATHY SCREENING IN TYPE 2 DIABETES MELLITUS

SUPAPORN PORNPINATEPONG

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.....

Ms. Supaporn Pornpinatepong
Candidate

.....

Ms. Montarat Thavorncharoensap,
Ph.D. (Social and Administrative Pharmacy)
Major-Advisor

.....

Assist. Prof. Nathorn Chaiyakunapruk,
Ph.D. (Pharmaceutical Outcomes Research and Policy Program)
Co-Advisor

.....

Assoc. Prof. Rassmidara Hoonsawat,
Ph.D.
Dean
Faculty of Graduate Studies

.....

Prof. Ampol Mitrevej,
Ph.D. (Pharmaceutics)
Chair
Master of Science in Pharmacy
Programme in Pharmacy Administration
Faculty of Pharmacy

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Entitled

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on
18 January, 2005

.....
Ms. Supaporn Pornpinatepong
Candidate

.....
Ms. Montarat Thavorncharoensap,
Ph.D. (Social and Administrative Pharmacy)
Chair

.....
Assist. Prof. Nathorn Chaiyakunapruk,
Ph.D. (Pharmaceutical Outcomes Research
and Policy Program)
Member

.....
Prof. Boonsong Ongphiphadhanakul,
M.D. (Certificate of fellowship in
Endocrinology and Metabolism)
Member

.....
Assoc. Prof. Rassmidara Hoonsawat,
Ph.D.
Dean
Faculty of Graduate Studies
Mahidol University

.....
Prof. Ampol Mitrevej,
Ph.D. (Pharmaceutics)
Dean
Faculty of Pharmacy
Mahidol University

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COST-EFFECTIVENESS ANALYSIS OF DIABETIC RETINOPATHY SCREENING IN TYPE 2 DIABETES MELLITUS

SUPAPORN PORNPINATEPONG 4536845 PYPA/M

M.Sc. in Pharm. (PHARMACY ADMINISTRATION)

THESIS ADVISORS: MONTARAT THAVORNCHAROENSAP, Ph.D. (SOCIAL AND ADMINISTRATIVE PHARMACY), NATHORN CHAIYAKUNAPRUK, Ph.D. (PHARMACEUTICAL OUTCOMES RESEARCH AND POLICY PROGRAM)

ABSTRACT

Diabetic retinopathy (DR), the leading cause of visual impairment, is preventable by early detection and appropriate laser treatment. The purpose of this study is to assess the cost-effectiveness of various screening intervals using indirect ophthalmoscopy performed by ophthalmologists for detecting DR among type 2 diabetic patients in hospital perspective.

The structure of the DR model consisted of six health states: NDR (no DR), BDR (background DR), PDR (proliferative DR), ME (clinically significant macular edema), Blindness, and Death. Transition probabilities were derived from published literature and expert opinions. Cost data were obtained from Ramathibodi hospital.

In base-case analysis, a Markov model was used for simulating a cohort of 10,000 newly diagnosed type 2 diabetic patients, who were followed from 40 years of age until the age of 75 years or death, whichever occurred first. The incremental cost-effectiveness ratio (ICER) comparing the group being screened every 4 years with the unscreened group found that it cost about 85,976.89 Baht to prevent blindness per eye. The ICER of increased screening frequency from every 4 years to every 3 years was 62,806.34 Baht to prevent blindness per eye. The ICER of increased screening frequency from every 3 years to biannual was 70,553.97 Baht to prevent blindness per eye. Finally, the ICER of increased screening frequency from biannual to annual was 95,865.04 Baht to prevent blindness per eye.

For sensitivity analysis, if the cost of eye screening, cost of laser treatment, probability of medical treatment seeking among unscreened, probability of screened patients being treated with vitrectomy, and annual mortality rate were increased, the ICER would be increased. If the progression of disease, effectiveness of treatment, the BDR risk at diagnosis of DM, discount rate, probability of unscreened patients being treated with vitrectomy, sensitivity of screening, and specificity of screening were increased, the ICER would be decreased. In addition, if the level of glycemic control among screened patients was incorporated in the model, the cost-effectiveness of screening would be increased dramatically. Additional analysis in societal perspective demonstrated that all screening intervals resulted cost-savings.

KEY WORDS: DIABETIC RETINOPATHY / DIABETES MELLITUS / MARKOV MODEL / COST-EFFECTIVENESS ANALYSIS / SCREENING

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การวิเคราะห์ต้นทุน-ประสิทธิผลของการตรวจคัดกรองพยาธิสภาพจอประสาทตาจากโรคเบาหวานในผู้ป่วยเบาหวานชนิดที่ 2 (COST-EFFECTIVENESS ANALYSIS OF DIABETIC RETINOPATHY SCREENING IN TYPE 2 DIABETES MELLITUS)

สุภาพร พรพิเนตพงศ์ 4536845 PYPA/M

ภ.ม. (บริหารเภสัชกิจ)

คณะกรรมการควบคุมวิทยานิพนธ์: มนทรัตม์ ถาวรเจริญทรัพย์, Ph.D. (Social and Administrative Pharmacy), ณธร ชัยญาคุณาพฤกษ์, Ph.D. (Pharmaceutical Outcomes Research and Policy Program)

บทคัดย่อ

พยาธิสภาพจอประสาทตาจากโรคเบาหวานซึ่งเป็นสาเหตุทำให้เกิดความผิดปกติทางสายตาจนถึงขั้นตาบอดได้นั้นสามารถป้องกันได้ถ้าได้รับการตรวจพบและรักษาด้วยการฉายแสงเลเซอร์ตั้งแต่ระยะแรก วัตถุประสงค์ของการศึกษาเพื่อประเมินต้นทุน-ประสิทธิผลของความถี่ของการตรวจคัดกรองพยาธิสภาพจอประสาทตาผู้ป่วยเบาหวานชนิดที่ 2 ด้วยเครื่องมือ Indirect ophthalmoscopy โดยจักษุแพทย์ ในมุมมองของโรงพยาบาล

โครงสร้างแบบจำลองโรคของการศึกษาประกอบด้วย 6 สถานะสุขภาพ: NDR (ไม่มีพยาธิสภาพจอประสาทตา), BDR, PDR, ME, ตาบอด, และเสียชีวิต ค่าความน่าจะเป็นในการเปลี่ยนจากสถานะสุขภาพหนึ่งไปสู่สถานะสุขภาพหนึ่งได้จากการทบทวนวรรณกรรมและผู้เชี่ยวชาญ สำหรับข้อมูลต้นทุนได้รับจากโรงพยาบาลรามาธิบดี

การวิเคราะห์กรณีหลักทำโดยใช้แบบจำลองมาร์คอฟ (Markov model) โดยทำการจำลองสถานการณ์ในผู้ป่วยเบาหวานชนิดที่ 2 ที่ได้รับการวินิจฉัยเป็นครั้งแรก จำนวน 10,000 คน อายุ 40 ปี ทำการจำลองสถานการณ์ที่เกิดขึ้นในผู้ป่วยเหล่านั้น จนถึงอายุ 75 ปีหรือเสียชีวิต ผลการศึกษาพบว่าอัตราส่วนต้นทุนที่เพิ่มขึ้นต่อหน่วยประสิทธิผลในกลุ่มผู้ป่วยที่ได้รับการตรวจคัดกรองทุก 4 ปีเปรียบเทียบกับกลุ่มผู้ป่วยที่ไม่ได้รับการตรวจคัดกรองมีค่าเท่ากับ 85,976.89 บาทต่อการป้องกันตาบอดได้หนึ่งตา อัตราส่วนต้นทุนที่เพิ่มขึ้นต่อหน่วยประสิทธิผลในกลุ่มผู้ป่วยที่ได้รับการตรวจคัดกรองทุก 3 ปีเปรียบเทียบกับกลุ่มผู้ป่วยที่ได้รับการตรวจคัดกรองทุก 4 ปี, ทุก 2 ปีเปรียบเทียบกับทุก 3 ปี และทุกปีเปรียบเทียบกับทุก 2 ปี มีค่าเท่ากับ 62,806.34 บาทต่อการป้องกันตาบอดได้หนึ่งตา, 70,553.97 บาทต่อการป้องกันตาบอดได้หนึ่งตาม และ 95,865.04 บาทต่อการป้องกันตาบอดได้หนึ่งตา ตามลำดับ

ผลการวิเคราะห์ความไวพบว่า ถ้าต้นทุนของการตรวจคัดกรอง, ต้นทุนของการรักษาด้วยแสงเลเซอร์, โอกาสที่ผู้ไม่ได้รับการตรวจคัดกรองจะมาพบแพทย์ด้วยตนเอง, โอกาสที่ผู้ได้รับการตรวจคัดกรองจะได้รับการรักษาด้วยการผ่าตัดจอประสาทตา และอัตราการตายเพิ่มขึ้น จะทำให้อัตราส่วนต้นทุนที่เพิ่มขึ้นต่อหน่วยประสิทธิผลเพิ่มขึ้น ถ้าการดำเนินโรค, ประสิทธิภาพของการรักษา, ความเสี่ยงของการเกิด BDR เมื่อแรกเริ่มวินิจฉัยโรคเบาหวาน, อัตราการปรับลด, โอกาสที่ผู้ไม่ได้รับการตรวจคัดกรองจะได้รับการรักษาด้วยการผ่าตัดจอประสาทตา, ความไวและความจำเพาะของการตรวจคัดกรองเพิ่มขึ้น จะทำให้อัตราส่วนต้นทุนที่เพิ่มขึ้นต่อหน่วยประสิทธิผลลดลง นอกจากนี้ยังพบว่าถ้าระดับน้ำตาลในผู้ป่วยที่ได้รับการตรวจคัดกรองลดลง จะส่งผลให้อัตราส่วนต้นทุนที่เพิ่มขึ้นต่อหน่วยประสิทธิผลลดลงอย่างมาก เมื่อวิเคราะห์ในมุมมองทางสังคม พบว่าการได้รับการตรวจคัดกรองจอประสาทตานั้นมีต้นทุนที่ต่ำกว่าและสามารถป้องกันตาบอดได้มากกว่าเมื่อเปรียบเทียบกับการไม่ได้รับการตรวจคัดกรอง

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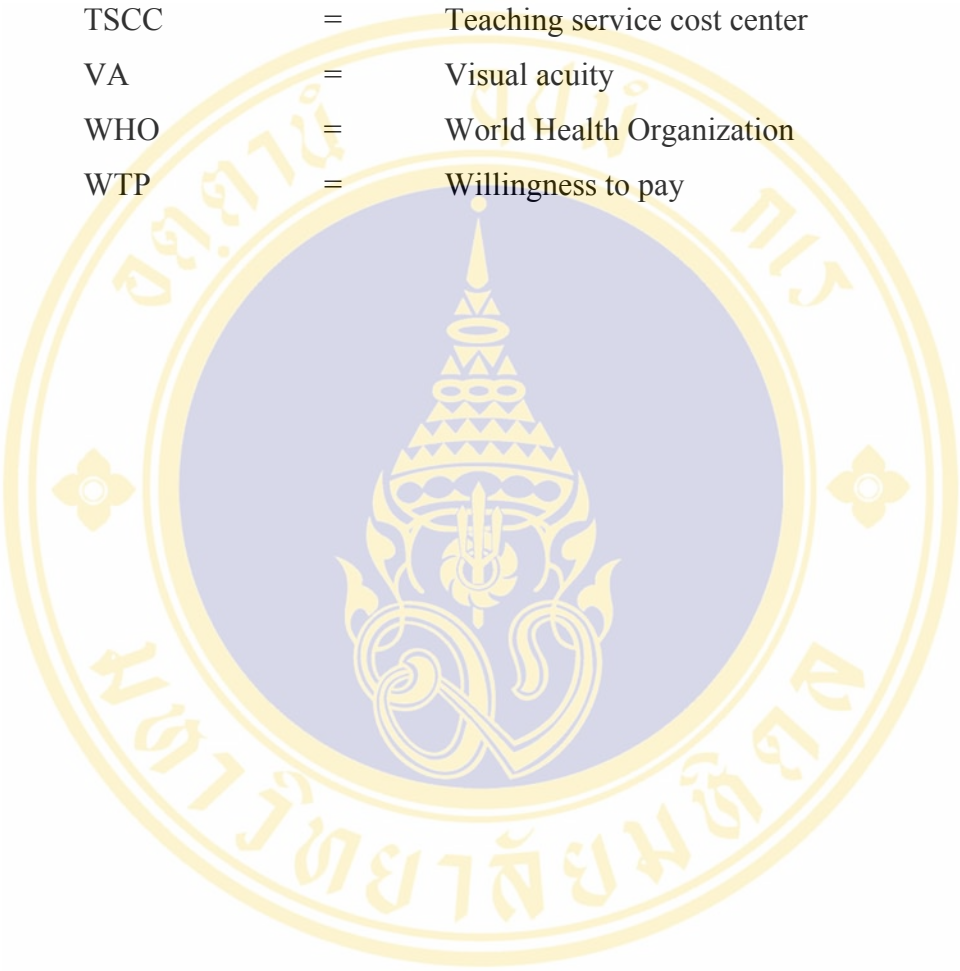
LIST OF ABBREVIATIONS

A/S	=	Anterior segment
ABC	=	Activity based costing
ADA	=	American Diabetes Association
BDR	=	Background diabetic retinopathy
CDC	=	Centers for Disease Control and Prevention Diabetes Cost-Effectiveness Study
CEA	=	Cost-effectiveness analysis
CSME	=	Clinically significant macular edema
DM	=	Diabetes mellitus
DR	=	Diabetic retinopathy
DRS	=	Diabetic Retinopathy Study
ETDRS	=	Early Treatment Diabetic Retinopathy Study
FBS	=	Fasting blood sugar
GDM	=	Global Diabetes Model
GDP	=	Gross Domestic Product
ICER	=	Incremental cost-effectiveness ratio
IOP	=	Intraocular pressure
IRMA	=	Intraretinal microvascular abnormality
NDR	=	No diabetic retinopathy
NPDR	=	Nonproliferative diabetic retinopathy
NRPCC	=	Non revenue producing cost center
PDR	=	Proliferative diabetic retinopathy
PPV	=	Pars plana vitrectomy
PROPHET	=	Prospective Population Health Event Tabulation
PSCC	=	Patient service cost center
QALY	=	Quality-adjusted life-year
RAS	=	Renin-angiotensin system
RPCC	=	Revenue producing cost center

LIST OF ABBREVIATIONS (continued)

RSCC	=	Research service cost center
SI	=	System International
TSCC	=	Teaching service cost center
VA	=	Visual acuity
WHO	=	World Health Organization
WTP	=	Willingness to pay



CHAPTER I
INTRODUCTION

Diabetes mellitus (DM) remains a profound health problem worldwide (1). The World Health Organization (WHO) estimates that there are currently 150 million people with diabetes and this number will double by the year 2025 (1). The most common type of DM in Thailand is type 2 DM, with the prevalence of 4-6 percent (2). It is estimated that about 2-3 million Thai people are diabetes (2). These patients are at increased risk of developing macrovascular complications and microvascular complications, such as diabetic neuropathy, nephropathy and retinopathy (3).

Diabetic retinopathy (DR) is a microvascular complication of diabetes and the leading cause of visual impairment all over the world (4). DR complicates both type 1 DM and type 2 DM. The cumulative risk of retinopathy is substantial in type 1 DM, reaching up to 60 percent for sight-threatening disease over 20 years. The overall burden of preventable blindness secondary to type 2 DM, however, is greater due to a higher prevalence of type 2 DM (5). Indeed, 20 percent of type 2 diabetic patients have retinopathy at diagnosis, whereas those with type 1 diabetes can expect to be free of clinically significant retinopathy for the first 5 years of diagnosis (6).

Disease duration and severity of baseline retinopathy are the prime determinants of both the onset and progression rate of DR (7). The prevalence of DR varied from 12 percent in patients who had diabetes less than 5 years to 44.4 percent in patients who had diabetes for 15 or more years (8). In addition, poor glucose control is associated with retinopathy (7). Patients with fasting blood sugar (FBS) ≥ 200 mg/dl had increased risk of DR 1.7 times of patients with FBS < 140 mg/dl (9).

Blindness caused by diabetes is preventable by early detection of retinopathy, good timely laser treatment, and glycemic control (4). Therefore, screening is vital for prevention of visual loss from DR (10). According to the

previous study, early detection and timely laser treatment for eye disease in type 2 DM could save 247 million US dollars per year (11). In addition, the laser photocoagulation treatment of DR is the most efficacious when started before any vision is lost (12). Timely laser photocoagulation treatment can prevent visual loss in patients with proliferative diabetic retinopathy and/or macular edema. (13, 14). Every diabetic patient should be routinely screened for retinopathy, even in the absence of any visual symptoms (12). From epidemiological data, patients are usually symptom-free at threshold levels of retinopathy. Therefore, retinopathy may be well advanced before visual deterioration is noticed (13). American Diabetes Association (ADA) guideline recommend that patients with type 1 DM should have an initial dilation and comprehensive eye examination within 3-5 years after the onset of diabetes (14). For patients with type 2 DM, retinal examination at time of diabetes diagnosis and annually examination by an ophthalmologist is recommended (14). However, adherence to the guidelines for annual ophthalmic examination is poor, ranging only from 34 to 65 percent (15, 16). Even among diabetic patients at high risk for vision loss because of pre-existent DR or long duration of diabetes, the rates of adherence were only 61 and 57 percent, respectively (15).

Annual screening for DR in all patients with type 1 diabetes is cost-effective, when the economic impact of a person's blindness is balanced against the health costs incurred by treatment and screening (17). The economic argument for the annual screening of all patients with type 2 diabetes might have been more persuasive if these costs had been taken into consideration (17). Several models were used to investigate the effects of different screening intervals for DR in type 2 DM patients. Javitt et al (11) concluded that changing the frequency of screening for patients with no or mild background retinopathy from one to two years has no effect on years of sight saved while screening costs is somewhat reducing. Vijan et al (10) provided additional analyses suggesting that annual screening for some patients without retinopathy may not be cost-effectiveness and that consideration should be given to prolonging the screening interval. Incremental cost-effectiveness study indicated that retinal screening annually vs. biannually costs $ 107,510 per QALY (Quality-adjusted life-year) gained, while screening biannually vs. every 3 years costs $ 49,760 per QALY

gained. Liu et al (18) suggested that a 4-year inter-screening interval is justified for patients without DR.

In Thailand, the prevalence of DR was 17.2-37.5 percent among DM patients (8, 9, 19-22). The prevalence of background or non-proliferative diabetic retinopathy and proliferative diabetic retinopathy varied from 12 to 28 percent and 1.9 to 8.6 percent, respectively (8, 9, 19-22). In Phramongkutklao hospital, cost of focal-grid laser photocoagulation was approximately 2,000 Baht per eye, while cost of panretinal laser photocoagulation, and vitrectomy was about 4,000 Baht per eye, and 10,000-40,000 Baht per eye, respectively (22). In addition, the prevalence of DR in Thailand is found to be increasing due to the increase of DM prevalence. Delayed diagnosis of DR could be more common in Thailand due to the inadequacy screening among DM patients. Besides the limited resources, inadequacy amount of ophthalmologists is the important reason for inadequacy screening. In Thailand, most ophthalmologists are available only in the secondary and tertiary hospitals. Many referrals to ophthalmologists occurred when the patients are already in the severe stage of DR. Although guidelines for eye examinations are recommended, most of DM patients have hardly screened for retinopathy by ophthalmologists before visual loss.

Although annual screening for DR is worthwhile, the insufficient amount of ophthalmologists makes it difficult to the patients to access to eye examinations. Moreover, an increasing frequency of DR screening was found to be associated with increasing costs. Therefore, several cost-effectiveness studies comparing several screening intervals were conducted. However, no such study was conducted in Thailand before.

In the case of DR screening, modeling technique would be appropriate since randomized controlled trial is unethical and is associated with high cost and very long duration. Disease modeling is a method to generate long-term health economic data in the absence of empirical data, based on the extrapolation of existing data (23). To determine the importance of retinopathy screening, modeling is a potential method to predict or estimate long-term health outcomes (24). The benefits of the model

application are that researchers are able to incorporate efficacy, safety, and cost data in order to estimate the effects of long-term treatment or treatment processes (24). The aim of this study is to assess the cost-effectiveness of various screening intervals to prevent blindness in type 2 diabetic patients in Thailand, using Markov model. This study is conducted from the hospital prospective. The results of this study could be used as the useful information for policy makers, practitioners, and providers in making rational policy, guidelines, and recommendation concerning the optimal eye-screening interval for type 2 DM patients. For ophthalmologists, it can also assist in the process of follow-up patients with mild to moderate DR. In addition, it can be used as a tool for disease management and public health planning. Moreover, it will be the basis for further study of other diabetes complications in Thailand.

Objectives

General Objective

To assess the cost-effectiveness of various screening intervals using indirect ophthalmoscopy performed by ophthalmologists for detecting diabetic retinopathy among type 2 diabetic patients from hospital perspective.

Specific Objectives

The specific objectives of this research are;

1. To construct a diabetic retinopathy model for evaluating the cost-effectiveness of diabetic retinopathy screening among patients with type 2 Diabetes Mellitus.
2. To determine costs of screening and treatment for diabetic retinopathy patients.
3. To evaluate the incremental cost-effectiveness ratio (ICER) of the screening intervals: annual, biannual, every 3 years, every 4 years, and no screening, as compared to the preceding screening frequency.

Expected Outcomes and Benefits

1. The results of this study could be used as the useful information for policy makers, practitioners, and providers in making rational policy, guidelines, and recommendation concerning the optimal DR screening interval for patients with type 2 DM. For ophthalmologists, it can also assist in the process of follow-up patients with mild to moderate DR. In addition, this study could be used as a tool for disease management and public health planning.

2. It will be the basis for further study of other diabetes complications in Thailand.

Definition of Terms

Diabetic retinopathy: Progressive damage to the eye's retina caused by long-term diabetes and abnormality of retinal vascular permeability, microaneurysm formation, capillary and arteriolar closure, neovascularization and associated hemorrhage, scarring, and tractional retinal distortion and detachment.

Background diabetic retinopathy or Nonproliferative diabetic retinopathy: It is characterized by microaneurysms, dot and blot hemorrhages, edema, hard exudates and capillary occlusions, cotton wool spots, intraretinal microvascular abnormalities (IRMA), venous changes, arterial charges, and dark blot hemorrhages.

Proliferative diabetic retinopathy: It is characterized by the growth of new vessels from the optic nerve head, or from elsewhere, which may lead to progressive visual impairment caused by scarring and bleeding

Clinically significant macular edema: The presence of any one of the following: thickening of the retinal located 500 μm or less from center of the macula; hard exudates with thickening of the adjacent retina 500 μm or less from the center of the macula; or a zone of retinal thickening one disc area or larger in size, located 1 disc diameter or less from the center of the macula.

Blindness: Visual acuity worse than 20/100 in better eye.

Diabetic retinopathy screening: The presumptive identification of unrecognized DR by the application of tests, examinations or other procedures which can be applied rapidly to sort out those who probably have DR. Eye screening examination used in the model consists of visual acuity, eye dilatation, anterior segment examination, intraocular pressure, and fundoscopic examination. The visual acuity and eye dilatation were performed by the nurses. Anterior segment examination, intraocular pressure, and fundoscopic examination (indirect ophthalmoscopy) were performed by the ophthalmologists.

Cost-effectiveness analysis: Cost-effectiveness analysis (CEA) is an approach used for identifying, measuring, and comparing the significant costs and consequences of alternative intervention. In CEA, costs are always measured in terms of monetary unit, but consequences of treatment are measured in non-monetary, natural unit such as life-year gained. The basic framework of CEA involves the comparison of costs of an intervention with its effectiveness. This is expressed as the ratio of costs and effectiveness, cost is a numerator, and effectiveness is a denominator.

Indirect ophthalmoscopy: Indirect ophthalmoscopy is a technique used to detect DR. It is generally done by ophthalmologists. Indirect ophthalmoscopy has the advantage of allowing the doctor to see the entire retina. When indirect ophthalmoscopy was performed, the patient either lie or sit in a semi-reclining position. The examiner wears an instrument on the head resembling a miner's light, while holding the eye open, and using a hand-held instrument, the examiner shines a very bright light into the eye. Some pressure may be applied to the eyeball using a small, blunt instrument, and the patient will be asked to look in various directions. This examination takes between 5 and 10 minutes.

Visual acuity: Visual acuity is the eye's ability to detect fine details and is the quantitative measure of the eye's ability to see an in-focus image at a certain distance. The standard definition of normal visual acuity (20/20 or 6/6 vision) is the ability to resolve a spatial pattern separated by a visual angle of one minute of arc. In

countries where the matrix system is used, acuity is expressed relative to 20/20. In countries that use System International (SI) units, visual acuity is expressed relative to 6/6 (where the 6 is measured in metres). For all intents and purposes, 6/6 vision is equivalent to 20/20. A visual acuity of 20/20 means that if you and a "normal" person with good eyesight both stand 20 feet away from an object, you would see the same thing. If you have a visual acuity of 20/40 (6/12), then if you stood 20 feet away from an object and the "normal" person stood 40 feet away, you would both see the same thing: this suggests that you have worse eyesight than normal.

CHAPTER II
LITERATURE REVIEW

1. An overview of diabetic retinopathy

1.1 The natural history of diabetic retinopathy

Diabetic retinopathy (DR) is progressive damage to the eye's retina caused by long-term diabetes (7). DR is characterized by the abnormality of retinal vascular permeability, microaneurysm formation, capillary and arteriolar closure, neovascularization and associated hemorrhage, scarring, and tractional retinal distortion and detachment (7) (Figure1).

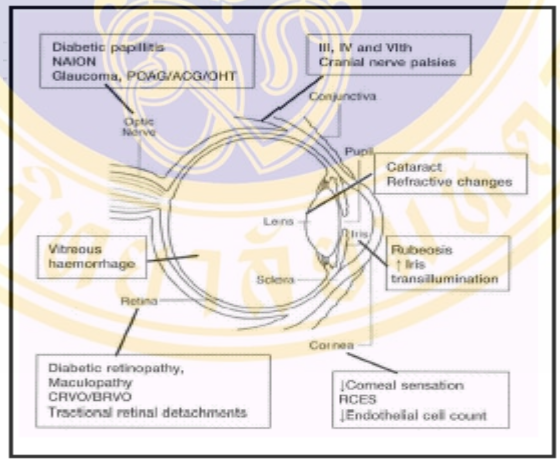


Figure 1. Common eye abnormalities in Diabetes Mellitus (6)

1.2 Pathogenesis of diabetic retinopathy

Hyperglycemia has been established as the primary pathogenesis factor in the development of DR (25). Several biochemical pathways may be activated

in the presence of hyperglycemia as shown in Figure 2 (25). These pathways do not operate in isolation and those extensive interactions occur between them. The combined effect of the mechanisms is a change in the production and interaction of vasoactive factors, leading to further cellular, functional, and structural changes. Several mutually interactive abnormal events, such as activation of the polyol pathway, protein kinase Cβ (PKCβ) activation, nonenzymatic glycation, and oxidative damage, may be promoted by sustained hyperglycemia in diabetic patients. Hyperglycemia activates the renin-angiotensin system (RAS) and these factors and/or their interactions aid the pathogenesis of DR including increased vascular permeability, vascular occlusion, and neovascularization.

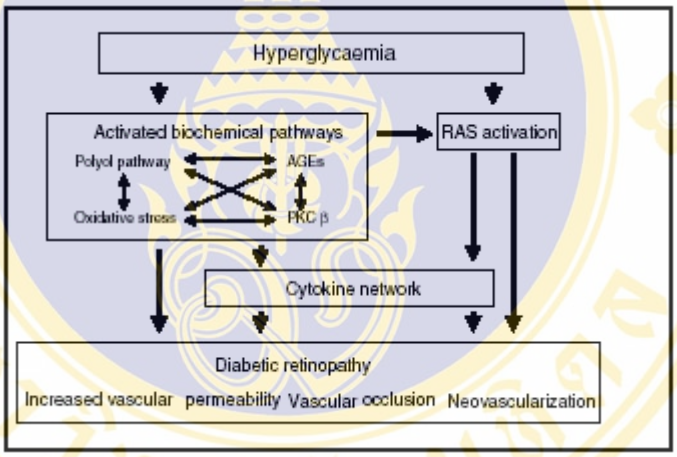


Figure 2. Pathogenesis of diabetic retinopathy (25)

1.3 Classification of diabetic retinopathy

Diabetic retinopathy: based on pathology and prognosis of disease, DR can be classified into nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR) (26).

1.3.1 NPDR or BDR (Nonproliferative diabetic retinopathy or Background diabetic retinopathy)

NPDR is the abnormality within the retina. NPDR is characterized by microaneurysms, dot and blot hemorrhages, edema, hard exudates and capillary

occlusions, cotton wool spots, intraretinal microvascular abnormalities (IRMA), venous changes, arterial changes, and dark blot hemorrhages (14).

1.3.2 PDR (Proliferative diabetic retinopathy)

PDR is characterized by the growth of new vessels from the optic nerve head, or from elsewhere, which may lead to progressive visual impairment caused by scarring and bleeding (14, 26).

1.4 Diabetic maculopathy

Diabetic maculopathy is a leading cause of visual impairment in diabetic patients, particularly among those with type 2 diabetes (27, 28). Diabetic maculopathy can be classified into non-clinically significant macular edema and clinically significant macular edema (CSME). The followings are characteristics of CSME (26);

- Retinal edema within 500 μm of the center of the fovea
- Hard exudates within 500 μm of the center of the fovea, if associated with adjacent retinal thickening (which may be outside the 500 μm limit)
- Retinal edema one disc area (1500 μm) or larger, any part of which is within one disc diameter of the center of the fovea.

DR progresses from mild nonproliferative abnormalities, which is characterized by an increase of vascular permeability to moderate and severe NPDR or BDR, which is characterized by vascular closure (14). Then it progresses to PDR, which is characterized by the growth of new blood vessels on the retina and posterior surface of the vitreous. Macular edema (ME), which is characterized by retinal thickening from leaky blood vessels, can occur in every stages of retinopathy (Figure 3) (14).

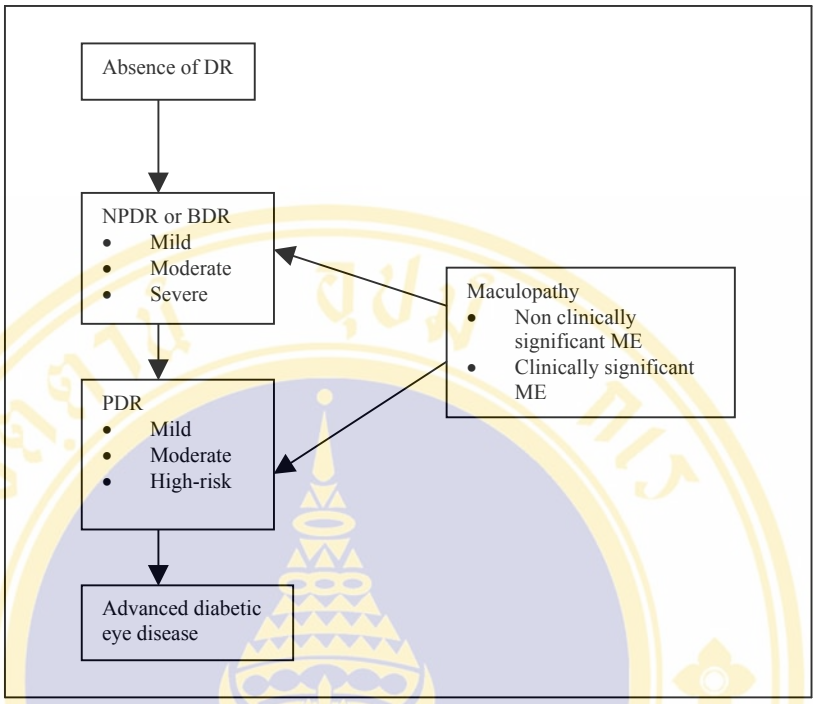


Figure 3. Classification of diabetic retinopathy (26)

Visual loss due to DR is the result from several mechanisms (14). First, central vision may be impaired by macular edema or capillary nonperfusion. Second, the new blood vessels of PDR and contraction of the accompanying fibrous tissue can distort the retina and lead to tractional retinal detachment, producing severe and often irreversible vision loss. Third, the new blood vessels may bleed, adding the further complication of pre-retinal or vitreous hemorrhage.

1.5 Detection of diabetic retinopathy

Every diabetic patient at risk should be routinely screened for retinopathy, even in the absence of any visual symptoms (14, 29). Various techniques can be used to detect DR (7). These include direct ophthalmoscopy (30), indirect ophthalmoscopy (31, 32), fluorescein angiography, stereoscopic fundus photography (through pupils) (7), and nonmydriatic photographic techniques (7).

1.6 Treatment of diabetic retinopathy

Laser photocoagulation has been shown to be effective in reducing vision loss and preventing blindness (14, 29). The treatment consists of applying 1,000 to 2,000 laser burns to the peripheral retina over several treatment sessions. Patients with mild or moderate NPDR require no treatment (14). Severe NPDR should be watched closely and treatment by photocoagulation should be considered. PDR is usually treated with panretinal or scatter photocoagulation, while focal laser coagulation may be more useful in treating CSME. In some cases of severe PDR and extensive vitreous hemorrhage or retinal detachment, an intraocular vitrectomy is needed (14).

1.7 Evaluation of diabetic retinopathy

Visual-threatening retinopathy is rare in type 1 diabetic patients in the first 3-5 years of diabetes or before puberty (14). Up to 20 percent of patients with type 2 diabetes have retinopathy at the time of first diagnosis of diabetes. Guidelines for the frequency of dilated eye examinations have been based on the severity of the retinopathy. American Diabetes Association (ADA) guidelines recommend that patients with type 1 DM should have an initial dilation and comprehensive eye examination within 3-5 years after the onset of diabetes (14). For patients with type 2 DM, retinal examination at time of diabetes diagnosis and annually examination by an ophthalmologist is recommended (14). However, some guidelines recommend that patients with well-controlled or low risk DM may require retinal examinations as biannual (33). Recommendations for DR evaluation in diabetic patients are shown in table 1.

Table 1. Recommendations for periodic vision evaluation in type 2 Diabetes Mellitus (33)

Organization	Document title, Most Recent Update	Population	Frequency
American Association of Clinical Endrocrinologists / American College of Endocrinology (34)	Diabetes Guideline, 2002	Patients with DM	At diagnosis, then annually
American Diabetes Association (35)	Clinical Practice Recommendations, 2002	Patients with DM diagnosed after 30 year	At diagnosis, then annually
American Academy of Ophthalmology (36)	Preferred Practice Patterns: Diabetic Retinopathy, 2003	Patients with DM	At diagnosis, then annually
American Optometric Association (37)	Care of the Patient With Diabetes Mellitus, 2002	Patients with DM	At diagnosis, then at least annually
The National Committee for Quality Assurance, American Medical Association, and the Joint Commission on Accreditation of Healthcare Organizations (38)	Common Measures for Diabetes Care Consensus Statements: Diabetes Quality Improvement Project Initial Measure Set (final version), 2001	Low-risk patients with DM* High-risk patients with DM	Biannually At diagnosis, then annually
Veterans Administration (39)	The Management of Diabetes Mellitus in the Primary Care Setting, 1999	Low-risk patients with DM+ Patients with DM	Biannually Annually
International Diabetes Center (40)	Type 2 Diabetes Practice Guideline, 2001	Patients with type 2 DM	Annually

* Low-risk patients are defined as meeting any two of the following three conditions: the patient is not taking insulin, the patient has an HbA_{1C} of less than 8.0% (the most recent test result within the reporting period will be used), and the patient did not have any evidence of retinopathy on the previous year's examination.
+ Low-risk patients are defined as having type 2 DM with HbA_{1C} of less than 8.0% and treated with oral agents.

1.8 Risk factors of diabetic retinopathy

Disease duration and severity of baseline retinopathy are the prime determinants of both the onset and progression of DR (7). In addition, poor glucose control is associated with retinopathy (14). Proteinuria also seems to be a marker of risk for retinopathy (7). Pregnancy appears to pose an additional risk (14).

2. Epidemiology of diabetic retinopathy

Prevalence of diabetic retinopathy

In Thailand, the prevalence of DR reported from several centers (8, 9, 19-22) are shown in table 2 .

Table 2. Prevalence of diabetic retinopathy in Thailand (8, 9, 19-22)

Province/ Hospital	Chiang-Mai (8)	Chonburi (9)	Khon Kaen (19)	Nakornrat-chasima (20)	Trang (21)	Lampang (21)	Phramong-kutklao (22)
Year of study	1990	1991	1992	1994	1996	1999	2002
Type of DM	2	2	2	1, 2	2	1, 2	2
Number of examined DM	233	198	207	842	988	3049	201
Source of data collection	University Hospital Eye clinic	Regional Hospital Eye clinic	University Hospital Diabetic clinic	District Hospital	Provincial Hospital Eye clinic	District Hospitals	Hospital Eye clinic
Overall DR	17.2%	31.8%	25.1%	21.8%	20.6%	21.87	37.50%
BDR	12.0%	27.3%	21.2%	19.2%	18.7%	18.89%	28.91%
PDR	5.2%	4.5%	3.9%	2.6%	1.9%	2.98%	8.59%
ME	-	-	-	-	-	-	6%

According to the WHO (World Health Organization) study, the prevalence of DR in Thailand did not differ from those other Asian countries (41). According to table 3, prevalence of DR in Thailand was 32.1 percent while prevalence in other Asian countries ranged between 26.0-38.0 percent (41).

Table 3. Prevalence of diabetic retinopathy in Asian populations (41)

Country/ population	Age range (years)	Sample size	Study year	All retinopathy (%)
Thailand [b]	24-88	2060	-	32.1
India [a]	All ages	6792	-	34.1
Pakistan [a,b]	All ages	3000	-	26.0
Sri Lanka [a]	All ages	1003	-	31.3
Japan [a]	All ages	976	1960	33.0
South Korea [a]	30-75	631	1993	35.2
China [a]	All ages	114	1995	33.0
Hong Kong [a]	35-54	422	1975	32.5
Singapore [a]	All ages	300	-	38.0
Taiwan [a]	≥ 40	527	1985	34.9

[a] Direct and/ or indirect ophthalmoscopy with mydriasis
[b] Fundus photography

3. Decision analytic model

Mathematical modeling is widely used in economic evaluations of pharmaceuticals and other health care technologies (42). Economic evaluation of health care interventions based on decision analytic model can generate valuable information for health policy decision-makers (43).

Models synthesize evidence on health consequences and costs from many different sources, including data from clinical trials, observational studies, public health statistics, and surveys (42). However, the usefulness of the results obtained depends on the quality of the data input into the model. In other words, the accuracy of the result obtained from the model highly depends on the accuracy of the estimates for the costs, effectiveness, and transition probabilities between the different health states of the model.

The steps approach to decision-making analysis consist of the followings (43);

- Define the problem
- Reframe from multiple perspective
- Focus on the objective
- Consider all relevant alternative
- Model the consequences and estimate the chance
- Identify and estimate the value trade-off
- Integrate the evidence and values
- Optimize expected value
- Explore the assumptions and evaluate uncertainty

The commonly used models in health outcome research are classified into decision-tree model, Markov model, and simulation model (43).

3.1 Decision-tree model

Decision-tree model presents a sequence of decisions and chance events over time (44). Each chance event is assigned a probability. Alternative decision strategies are evaluated by calculating their average consequences. A limitation of decision-tree models is that the probability of each chance event is static. In chronic diseases, the probability of chance events changes with age, health status, and time. For this reason, decision-tree models are not often used for modeling chronic diseases such as diabetes.

3.2 Markov model

Markov model is state-transition model, allocates and reallocates subjects into health states defined according to population characteristics such as age, disease stage, and treatment (44). Age, clinical history, and treatment are included in the model by incorporating them into the definition of the health states or into the specification of the transition probability. Transitions occur from one health state to another at defined time intervals (usually one year) according to the transition probabilities. In Markov models, the proportion of subjects in each health state each year is treated as certain and the transition probabilities depend on the current state. Through simulation, the number of subjects in the population passing through each state at each point in time can be estimated.

3.3 Simulation model

3.3.1 Monte Carlo simulation

In Monte Carlo model, each possible chance event is simulated for each individual in the cohort. Summary statistics are computed by accumulating counts of these events over the simulated time span for the modeled population (44).

3.3.2 Discrete event simulation

A discrete-event simulation model is defined as one in which the state variables change only at those discrete points in time at which events occur (44). The

model building requires special training and analysis can be time consuming and expensive.

Comparison advantage and disadvantage of decision analytic models commonly used in health outcome research was presented in table 4.

Table 4. Comparison decision analytic model used in health outcome research (43)

Type of model	Advantage	Disadvantage
Decision-tree model	Simple and suitable for acute or short-term disease.	Poor for complex diseases that progress through multiple stages over long time frames.
Markov model	Suitable for complex or chronic disease. Allows probabilities to vary over time.	Markovian assumption: current probabilities of transition do not depend on patient history, thus future health is not affected by history.
Simulation model	Track history of every event that occurs to each patient.	Requires extensive data sources and computer programming.

4. Markov model process

Markov model is most useful when a decision problem involves risk over time, when the timing of events is important, and when events may happen more than once (45). The model assumes that the patient is always in one of a finite number of states of health referred to as Markov states. All events of interest are modeled as transitions from one state to another. Each state is assigned a utility, and the contribution of this utility to the overall prognosis depends on the length of time spent in the state.

Figure 4 shows a representation of Markov processes, called a state-transition diagram, in which each state is represented by a circle. Only certain transitions are allowed. For example, a person in the *well* state may make a transition to the *ill* state, but a transition from *ill* to *well* is not allowed. A person in either the *well* state or the *ill* state may die and thus make a transition to the *dead* state.

However, a person who is in the *dead* state, obviously, cannot make a transition to any other state. Therefore, a single arrow emanates from the *dead* state, leading back to itself. It assumed that a patient in a given state could make only a single state transition during a cycle. The probability of making a transition from one state to another during a single cycle is called a transition probability. For example, the probability that the *well* state to the *ill* state is 0.2. Hence the sum of probabilities over all arrows leading out of every state must equal 1.0.

The transition probabilities (tp) in Markov model are the movement of the patients from one state to another (46). The length of each Markov cycle was set equal to one year. To obtain the yearly transition probabilities, the following formula was used;

$$tp_1 = 1-(1-tp_t)^{1/t} \qquad \text{[equation 1]}$$

Where tp_1 is the yearly transition probability and tp_t is the overall probability over the time period of t.

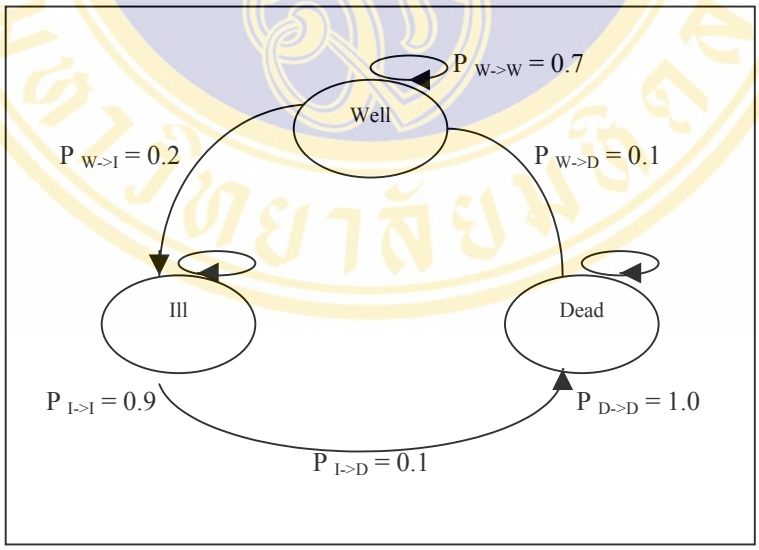


Figure 4. Markov state-transition diagram

Markov processes are categorized according to two types (43).

- Markov chain: the transition probabilities are constant over time.
- Markov process: the transition probabilities may change over time.

In general, the probabilities change over the time because the probabilities of transition to *dead* state tend to increase with age. Therefore, the assumption of Markov chain is seldom used.

Defining a Markov process requires several steps: define the health states, determine the cycle length, consider possible transitions among states, assess transition probabilities, and assess outcomes (43, 47). There are three basic methods to evaluate a Markov process (43, 45);

1. Fundamental matrix solution

The fundamental matrix solution can be used only for Markov chains, when the transition probabilities are constant over time. It requires some basic knowledge of matrix algebra.

2. Cohort simulation

Cohort simulation is a very intuitive representation of a Markov process. The simulation considers a hypothetical cohort of patients who are distributed among the possible states and follows their transition among the states from cycle to cycle based on the transition probabilities.

3. Monte Carlo simulation

In Monte Carlo simulation, individual patients are simulated going from cycle to cycle one at time, based on their transition probabilities. The transition probabilities that govern each individual transition during each cycle are realized as a random event through computer-generated random numbers between 0 and 1.

5. Diabetic retinopathy model studies

Disease modeling is a method to generate long-term health economic data in the absence of empirical data, based on the extrapolation of existing data (23). It is used to assist in complex decision making, especially chronic diseases (24). There have been several diabetic retinopathy models published in the literature (5, 10-11,

18, 48-60). Based on literature review, there are some differences and similarities in model structures. According to table 5, models numbered 1-7 (23, 49-53, 56) are retinopathy sub models of diabetes models while models numbered 8-13 (5, 10-11, 18, 57-60) were diabetic retinopathy models, themselves.

Table 5. Characteristics of diabetic retinopathy model published in previous literatures

	Study	Type of model	Type of DM	Health states of DR
1	Eastman et al (48, 49)	Monte Carlo simulation	2	NDR, BDR, PDR, CSME, and blindness
2	CDC (50)	Monte Carlo simulation	2	NDR, BDR, PDR, CSME, and blindness
3	GDM (51)	Monte Carlo simulation	2	NDR, BDR, PDR, CSME, and blindness
4	DCCT (52)	Monte Carlo simulation	1	NDR, BDR, PDR, CSME, and blindness
5	IMIB (23, 53)	Markov model	1, 2	NDR, BDR, PDR, CSME, and blindness
6	Bagust et al (55)	Markov model	2	NDR, BDR, ME, ME with blindness one eye, PDR, PDR with blindness one eye, ME and PDR, ME and PDR with blindness one eye, and blindness
7	Australia (56)	Simulation	1, 2	NDR, early stage, end stage
8	Javitt et al (11, 57)	Monte Carlo	1, 2	NDR, BDR, PDR, CSME, and blindness
9	Taiwan (18)	Markov model	2	NDR, BDR, PPDR, PDR, and blindness
10	Vijan et al (10)	Markov model	2	NDR, Retinopathy state 1,2,3, PDR, ME, blindness, and death
11	Davies et al (5, 58)	Simulation	1, 2	NDR, BDR, DME, PDR, CSME, loss of central acuity, severe visual loss, and death
12	Brailsford et al (59)	Simulation	2	NDR, BDR, BDR and ME, ME, PDR, PDR and ME, CSME, BDR and CSME, PDR and CSME, and blindness
13	Harper et al (60)	Simulation	2	NDR, BDR, PDR, CSME, vitreous hemorrhage, and blindness

- CDC= Centers for Disease Control and Prevention Diabetes Cost-Effectiveness Study, GDM= Global Diabetes Model, DCCT= Diabetes Control and Complications Trial, IMIB= Institute for Medical Informatics and Biostatistics
- NDR= no diabetic retinopathy, BDR= background diabetic retinopathy or nonproliferative diabetic retinopathy, PPDR= preproliferative diabetic retinopathy, PDR= proliferative diabetic retinopathy, DME= diabetic macular edema, ME= macular edema, CSME= clinically significant macular edema

6. The studies of cost-effectiveness analysis of screening for diabetic retinopathy

In the absence of primary research studies concerning the effectiveness of DR screening, the literature search was extended to include modeling studies. Models, that investigated the effect of different screening intervals and interventions were intensively reviewed in this study.

Javitt et al (1991) analyzed the effect of current recommendations for DR screening on a hypothetical cohort with type 1 diabetes (17). The analysis used Monte Carlo simulation to model the progression of DR, the development of visual loss, and survival for each member of the inception cohort of type 1 DM estimated to arise each year in the United States. The study was constructed the model reflecting to the federal government. The model was based on the assumption that PDR and ME would be treated in the year in which they were discovered. Five different screening strategies were compared in the model: 1) dilated ophthalmoscopic examination every 2 years; 2) dilated ophthalmoscopic examination every year; 3) dilated ophthalmoscopic examination every year plus additional 6-month examinations for those with any retinopathy; 4) dilated ophthalmoscopic examination every year plus fundus photography every year; and 5) dilated ophthalmoscopic examination every year plus fundus photography every year with 6-month examinations for patients with retinopathy. Incidence was estimated from Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) data. The benefits were estimated from the Diabetic Retinopathy Study (DRS) and the Early Treatment Diabetic Retinopathy Study (ETDRS) data. The costs were estimated from Medicare charges and costs for government expenditures per year of blindness were also factored into the model. The result found that all five strategies were cost saving. Examination every year was actually more cost-saving than examinations every other year.

Javitt et al (1994) described a computer simulation model of type 2 diabetic patients (11). The model was conducted in governmental perspective. The population was an estimated incident cohort of diabetic patients for the North American population, giving 576,136 cases in one single year. They used the

PROPHET (Prospective Population Health Event Tabulation) model as combing the features of decision trees, Markov process, and Monte Carlo simulation. It was used to model events and costs for each patient as a separate individual over the predicted lifetime of the cohort. Cost data included costs of a year of blindness for a working-age American. In estimating the effects of the interval for screening they concluded that a one or two-year interval had no detrimental effect on years of sight saved for patients with no or mild retinopathy, but for those with moderate nonproliferative or more advanced retinopathy would be saved by a one-year program over the lifetime of the cohort.

Davies et al (1996) described a computer simulation model examining the years of sight saved to a cohort of 1,000 insulin dependent diabetics, starting from initial diagnosis (58). The input data was derived from a range of sources and the program tested for validity of outcome against WESDR and other data. The program considered benefits over the lifetime of the cohort. Screening and treatment were considered to occur throughout this time. The simulation used a range of sensitivities and specificities and considered two different screening intervals. Screening took place annually or biennially until BDR developed and then patients were examined six-monthly or more frequently. The results showed that reducing the screening interval for those with no DR from two years to one year made little difference to the years of sight saved. Annual screening was normally desirable, biannual screening could be considered where patient compliance and screening sensitivities were both high.

Vijan et al (2000) constructed Markov model to examine the marginal cost-effectiveness of various screening intervals for eye disease in patients with type 2 diabetes, stratified by age and level of glycemic control (10). The study was conducted in third-party payer perspective, while government and societal perspective were explored in sensitivity analyses. Cost data did not include direct costs were attributed to blindness, however, the impact of attributing medical and societal costs to blindness was explored in sensitivity analyses. The rates of such progression were taken from DRS and ETDRS. The marginal cost-effectiveness of screening annually vs. biannually also varied; patients in the high-risk group (aged 45 years; average

HbA_{1C}, 11%) cost an additional $ 40,530 per QALY gained, while those in the low-risk group (aged 75 years; HbA_{1C}, 7%) cost an additional $ 211,570 per QALY gained. In the U.S. population, retinal screening annually vs. biannually for patients with type 2 diabetes costs $ 107,510 per QALY gained, while screening biannually vs. every 3 years costs $ 49,760 per QALY gained.

Liu et al (2003) assessed the progression and efficacy of treatment for DR following the proliferative pathway to blindness (18). According to the study, data from a retrospective cohort in a Taiwanese population were used in two Markov models. The pathway of maculopathy was excluded in the model. Simulated results showed that an annual screening program, a biannual screening regime, and a 4-yearly screening regime can lead to 54%, 51%, and 46% reductions in blindness, respectively. In this study, it was suggested that screening for DR was worthwhile and that a 4-year inter-screening interval for patients as yet without DR may be justified.

Comparison ICER (incremental cost-effectiveness ratio) of cost-effectiveness studies for DR screening type 2 DM is presented in table 6.

Table 6. Comparison ICER of cost-effectiveness studies: type 2 Diabetes Mellitus

Year	Study / country	Inter-screening	ICER	Reference
1996	Javitt et al / USA	Annual for NDR and every 6 months for DR	$ 3,190 per QALY	(57)
2000	Vijan et al / USA*	Every 5 years Every 3 years Biannual Annual	$ 16,790 per QALY $ 30,160 per QALY $ 49,760 per QALY $ 107,510 per QALY	(10)

* Marginal cost-effectiveness vs. the preceding screening frequency; e.g., annual compared with every other year screening.

7. Cost-effectiveness analysis (CEA)

Cost-effectiveness analysis (CEA) is an approach used for identifying, measuring, and comparing the significant costs and consequences of alternative

intervention (61). In CEA, costs are always measured in terms of monetary unit, but consequences of treatment are measured in non-monetary, natural unit such as life-year gained. The basic framework of CEA involves the comparison of costs of an intervention with its effectiveness. This is expressed as the ratio of costs and effectiveness, cost is a numerator, and effectiveness is a denominator.

7.1 Evaluation cost

Cost is the monetary value of the resource consumed by a provider in providing a particular service (62). Economic evaluations can include several types of costs including the following;

7.1.1 Direct costs

Direct costs include actual resources attributed to the delivery of medical care for detecting, preventing, and treating the disease. They are categorized as follows (62);

- Direct medical costs, such as payments for hospital or other medical services.
- Direct non-medical costs, such as transportation to hospital for treatment.

Costs most commonly included in economic analyses are direct medical costs, for the following reasons (62);

- They are the easiest costs to measure.
- They are the costs best understood by most health care decision-makers.
- They have a direct financial impact on health care organizations.

The calculation of direct medical cost or cost of treatment in hospital consisted of macro and micro cost calculation (63). The department costs are the total costs of each revenue or patient care cost center after receiving assigned costs from the non-revenue or non-patient care cost centers (64). These costs are derived to the individual units of service provided. There are many methods for allocation of

department costs to unit of service as the following (63, 64): the weighted procedure method, the hourly rate method, the surcharge method, cost to charge ratios, per diem method, activity based costing (ABC), and micro-costing method.

7.1.1.1 The weighted procedure method

The weighted procedure method or relative value unit (RVU) costing is useful for routine job (65). This method is the expense of performing the necessary observations of each service and then converting the various components into units suitable for assessing RUV.

7.1.1.2 The hourly rate method

This method using time of each service as a measure of the amount of service provided (65). The total costs for each department will be divided by that time. This approach is appropriate if all patients tend to use the same resource.

7.1.1.3 The surcharge method

This method commonly used by pass-through department such as central supply or pharmacy (65). The main in these departments is for the supplies that they purchase, stock, and pass-through to the patients.

7.1.1.4 Cost to charge ratios

The ratio of costs to charges is computed based on historical records (65, 66). It is used to estimate cost of each service from the relevant charge information obtained from patient's bills.

7.1.1.5 Per diem method

This method is used for some cost centers, e.g. housekeeping, nursing cost center (65). The total costs of these cost centers are divided by total patient-days to determine a cost per patient-day, or a per diem cost.

7.1.1.6 Activity based costing (ABC)

Activity based costing (ABC) is an alternative to the traditional way of accounting. ABC is a costing model that identifies the cost pools, or activity centers, in an organization and assigns costs to product and services (cost drivers) based on the

number of events or transactions involved in the process of providing a product or service (67).

7.1.1.7 Micro-costing method

Micro-costing method is suitable for unit cost calculation in department providing various different services (65, 68). However, this method requires more data collection than the other methods. The concept of this method is the attempt to determine direct cost of each service. Indirect cost of services is allocated to each service by average method or according to the proportion of direct cost of each service.

CTC = CDC + CDL + CDM + CDEPT [equation 2]

CTC = total cost for unit of service
CDC = total direct capital cost for unit of service
CDL = total direct labor cost for unit of service
CDM = total direct material cost for unit of service
CDEPT = total indirect cost from allocation of department costs to unit of service

7.1.2 Indirect costs

Indirect costs are costs valued as real money that are not directly paid for the treatment of a disease (62). These costs as the value of productivity losses caused by absence from work, disability, or death associated with a disease and its treatment. There are two forms of indirect costs: morbidity and mortality costs. Morbidity costs include the value of production losses of those who are sick-absent or unemployed or restricted from working due to illness. Mortality costs are calculated as the present value of lost production due to premature death caused by illness.

The methods for estimating these costs are human capital cost method, willingness to pay method, friction-cost method etc.

7.1.2.1 Human capital cost approach

Human capital cost approach is used the most in estimating the indirect costs (69, 70). This approach is based on the concept of potentially lost production as

a result of disease. This method is assumed that a vacant position will never be filled and that society will continue lose the production of those patients until retirement. In this case, the total productive value from the specific age of permanent disablement or premature death to the age of retirement is counted as indirect costs. And they are accounted to be full productivity. The market wage rates or per capita GDP (Gross Domestic Product) is usually used in calculation. Furthermore, the earnings in the future are discounted at a constant annual rate. This means that the labor markets are in equilibrium with or without unemployment.

So, there is comment that the real production loss can be much smaller than the potential loss because the workers who are sick can be replaced at a little amount of payment.

7.1.2.2 Willingness to pay (WTP)

Willingness to pay (WTP) relies on the view of individuals who are asked hypothetical questions regarding how much they would be prepared to pay to reduce their probability of death or morbidity (64). However, this approach is used less frequency because it difficult to apply and it is affected by earning. The lower income earners tend to be willing to pay less than higher income earners.

7.1.2.3 Friction cost approach

The basic idea of this approach is that the patients on short-term absence from their work can make up for the loss of production when they return, or can be taken care of by internal labor resources, or that non-urgent work may be canceled or postponed. For long-term work absence, patients can be permanently replaced by someone who are unemployed (70). The actual productivity loss from the work continues only during the period of time required for worker replacement. This period is called “Friction period”. They assume that workers who are on sick absence will be replaced after completion of the friction period. However, there are many information used in this information used in this method which are not available to access. Thus it is not popular for estimating indirect costs.

7.1.3 Intangible costs

Intangible costs represent non-financial outcomes of disease and medical care, such as emotional pain and suffering (62).

7.2 Evaluation of effectiveness

Effectiveness is the outcome of an intervention in a real situation. Measurement of effectiveness is different from disease to disease (61). Health care provider usually uses a reliable clinical indicator for measuring effectiveness.

7.3 Evaluation of cost-effectiveness

There are six steps in analysis (61):

- Define the problem
- Identify the alternative strategy
- Describe production relationships between inputs and outcomes
- Identify and measure outcomes of the alternative interventions
- Value costs and effectiveness
- Interpret and present result.

CHAPTER III
METHODOLOGY

This study consisted of three parts;

Part I: Diabetic retinopathy model development

Part II: Determination and calculation of cost incurred in the model

Part III: Cost-effectiveness analysis

- Base-case analysis
- Sensitivity analysis

Part I: Diabetic retinopathy model development

Study design

In this study, Markov model was used to evaluate the incremental cost-effectiveness ratio of screening intervals for diabetic retinopathy performed by ophthalmologists in type 2 diabetic patients.

Research tool

A computer program, Microsoft Excel spreadsheet version 97, was used as the study instrument for diabetic retinopathy model development.

Model assumptions

1. Hypothetical patients in the study are 10,000 patients with 40 years of age, who are newly diagnosed with type 2 DM. These hypothetical patients were followed until the age of 75 years or death, whichever occurred first.

2. In each "cycle" of the model, patients may progress to the next health state or to death, based on a specific transition probability (tp). Transition probability to the next health state was irreversible. For example, if patients with BDR had good glycemic control, they would not return to no DR state.

3. The transition probability of developing DR varied by duration of diabetes.

4. For all screening strategies, each diabetic patient was firstly screened at diagnosis of DM.

5. In this model screening for DR was performed by ophthalmologists using indirect ophthalmoscopy technique.

6. Every patient diagnosed with PDR or ME either from eye screening examination or from any other ways was assumed to be treated. Although treatment would lead to the reduction of blindness, these patients would receive only one course of laser treatment or one time of vitrectomy per person per lifetime.

7. Patients diagnosed with BDR from eye screening examination were remained untreated. However, they were assigned to a follow-up screening program by the ophthalmologist twice per year.

8. For unscreened diabetic patients, 20 percent of PDR patients and 50 percent of ME patients may seek medical care treatment by themselves.

9. It was assumed that 92.5 percent of PDR patients in the screened groups were treated with laser photocoagulation, while 7.5 percent of them were treated with vitrectomy.

10. It was assumed that 60 percent of PDR patients in the unscreened groups were treated with laser photocoagulation, while 40 percent of them were treated with vitrectomy.

11. Patients in the group being unscreened were required for eye examination before receiving treatment.

12. Only direct medical costs were used in the model. These costs consisted of eye screening examination cost, treatment cost, and follow-up cost.

13. Eye screening examination consisted of visual acuity examination, eye dilatation, anterior segment examination, intraocular pressure examination, and fundoscopic eye examination (with indirect ophthalmoscopy).

14. Cost of laser photocoagulation consisted of costs of visual acuity examination, eye dilatation, and laser photocoagulation.

15. Times per course of laser photocoagulation for PDR and ME were four times and twice, respectively.

16. After receiving laser photocoagulation or vitrectomy, patients were followed twice per year.

17. Costs per year of follow-up for PDR and ME were calculated by multiplying the number of time per course of follow-up with the eye examination cost.

18. Duration of admission for vitrectomy was assumed to be three days.

19. Cost for false positive (misdiagnosis cost) was incorporated into the model. Cost of false positive for patient with NDR, who was misdiagnosed as BDR was equal to eye screening examination cost. Misdiagnosis cost for false positive if the patient with NDR or BDR was misdiagnosed as PDR or the patient without ME was misdiagnosed as ME was equal to the summation of visual acuity cost, eye dilatation cost, and fundoscopic eye examination cost (with laser).

20. Cost incurred if the patient with PDR was misdiagnosed as BDR included eye screening examination cost (misdiagnosis cost), panretinal photocogulation cost and follow-up cost.

21. Costs and blindness were discounted at 3 percent per year.

22. Compliance to the screening, treatment procedure, and follow-up was assumed to be 100 percent.

Study Procedures:

1. Determination of screening strategies.

This study constructed five different strategies of screening as the following;

Strategy 1: no screening

Strategy 2: annual screening for all patients by ophthalmologist

Strategy 3: biannual screening for all patients by ophthalmologist

Strategy 4: every 3 years screening for all patients by ophthalmologist

Strategy 5: every 4 years screening for all patients by ophthalmologist

For all screening strategies, the first screening began at time of diagnosis of DM. The model assumed that all individuals with treatable retinopathy who were detected by screening would receive timely and appropriate treatment. The patients diagnosed with BDR were remained untreated, however, they were assigned to a follow-up screening program by the ophthalmologist. The patients diagnosed with PDR or CSME were treated with laser photocoagulation or vitrectomy. As the result of treatment, risk of blindness was reduced in treated patients. Then, these patients were assigned to a follow-up for twice per year. For the unscreened patients, some of them may also seek medical service without being diagnosed by screening strategy.

Sensitivity and specificity of the screening in detecting DR or diabetic maculopathy were shown in table 7. In this study, the features of the screening were presented in a different way as compared to the traditional description. In stead of directly incorporated sensitivity and specificity in the model, we adopt a concept of

categorizing the feature of screening as correct or incorrect diagnosis (10). For example, those patients with BDR can be misdiagnosed as either NDR or PDR. In this case, screening result could be 1) correct diagnosis as BDR 2) BDR called NDR and 3) BDR called PDR, as shown in table 7.

In the model, if screening failed to detect DR (false negative), the patients would remain at risk for all complications of DR, but would not be eligible for treatment until disease was detected. If the screen result was a false positive, the cost associated with the false positive during screening was incorporated into the model. For example, if patient with PDR was misdiagnosed as BDR, they were assigned to a follow-up screening by the ophthalmologists in next year. Thus, cost for misdiagnosis incurred. After that the patient would receive laser treatment. The figure 5 illustrates the screening process and shows where costs were incurred.

Table 7. Screening sensitivity and specificity in detecting diabetic retinopathy and maculopathy (10)

Screening sensitivity and specificity	Base-case analysis	Reference
NDR called BDR	0.05	(71)
NDR called PDR	0.003	(71)
BDR called NDR	0.22	(71)
BDR called PDR	0.02	(71)
PDR called NDR	0.02	(71)
PDR called BDR	0.03	(71)
Sensitivity for ME	0.82	(28)
Specificity for ME	0.79	(28)

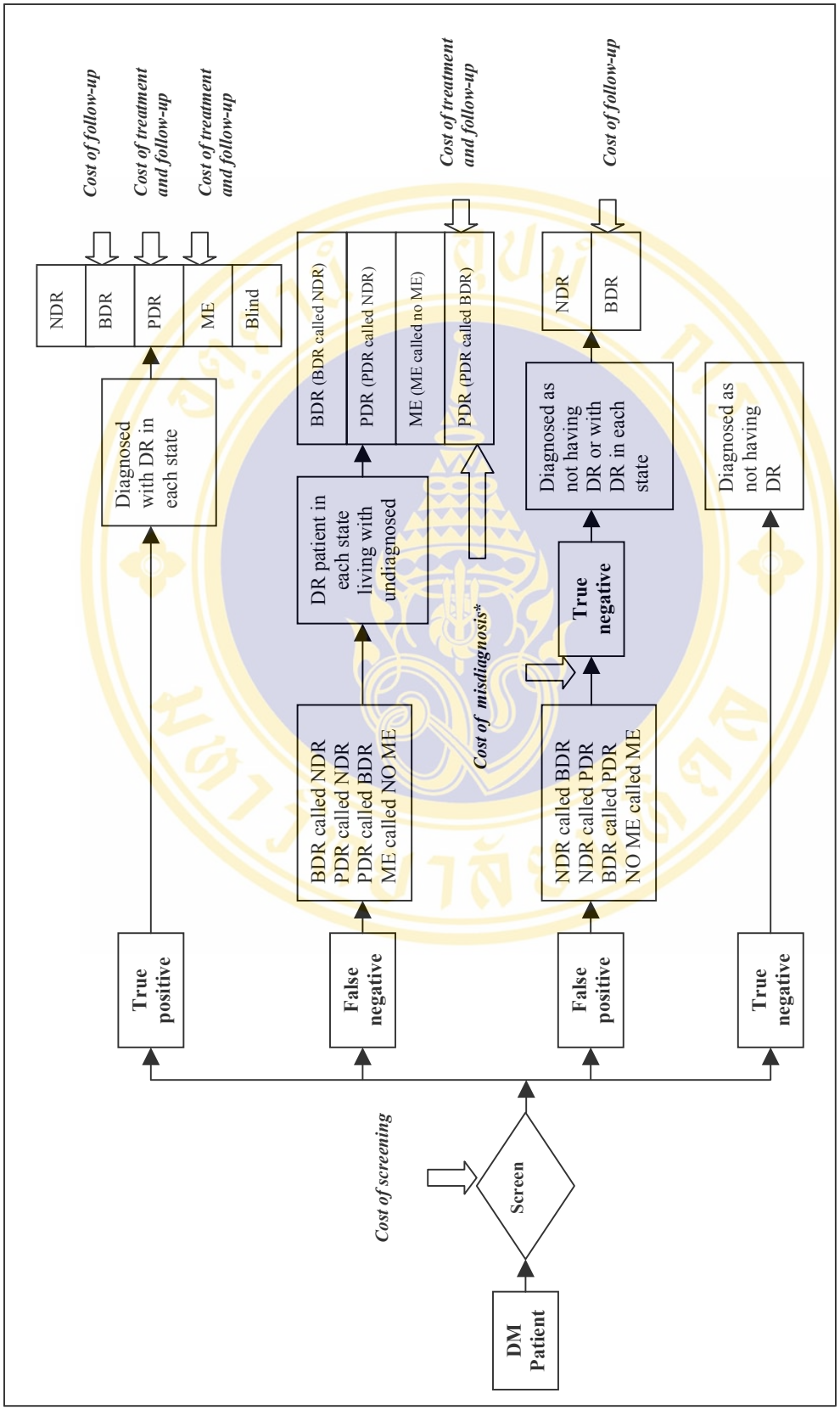


Figure 5. Screening process and costs incurred

* The misdiagnosis cost for misdiagnosed NDR or PDR as BDR was equal to eye screening cost. The misdiagnosis costs for misdiagnosed NDR or BDR as PDR, and no ME as ME were equal misdiagnosis cost for false positive.

2. Determination of Markov model

Based on literature review, there have been several diabetes models (72). This DR model is a Markov model used to describe disease progression and to estimate the cost effectiveness of each screening interval. In this study a Markov model was used to describe disease progression and to estimate the cost-effectiveness of each screening interval. The reasons for choosing the Markov model were that it was the most useful when the decision problem involved risk over time, when the timing of events was important, and when events may happen more than once. The Markov model was particularly suited to model chronic diseases such as DM. In DR, the probabilities changed over the time because the probabilities of transition tended to change with duration of DM and age, therefore, the Markov model is appropriate.

3. Construction of diabetic retinopathy model

Model of progression of DR and macular edema were derived from the review of medical literatures and expert opinions.

4. Determination of transition probability data

The values of transition probability used in the model were derived from the review of medical literatures and expert opinions. The transition probabilities will be shown as part of the results.

Part II: Determination and calculation of cost incurred in the model

Study design

This part was a retrospective descriptive research. It was a cost analysis of medical services.

Study location

Ramathibodi hospital (University hospital)

Study period

Costs of medical services were calculated based on resources consumption in the fiscal year 2003, starting from October 2002 to September 2003.

Study procedures:

1. Identification of medical services associated with screening and treatment

In the model, medical services consisted of eye screening examination, treatment, and follow-up.

1.1 Eye screening examination

Activities performed during eye screening examination for DR consisted of the followings;

- Measurement of visual acuity using ETDRS charts,
- Eye dilatation using 1% tropicamide eye drop and 10% phenylephrine HCl eye drop,
- Anterior segment (A/S) examination using a slit lamp biomicroscope,
- Intraocular pressure examination (IOP) using a Goldmann Applanation Tonometry, and
- Fundoscopic examination for DR detection using indirect binocular ophthalmoscope and condensing lens 78 or 90D.

1.2 Treatment

Treatment for DR varied by states as follows;

- PDR: Panretinal laser photocoagulation

- CSME: Focal or Grid laser photocoagulation
- Severe PDR and extensive vitreous hemorrhage or retinal detachment: Vitrectomy

1.3 Follow-up

Follow-up occurred after the following situation;

- Patients were diagnosed with BDR from screening
- Patients with PDR, ME, severe PDR and extensive vitreous hemorrhage or retinal detachment were treated.

2. Determination of costs associated with each medical service

2.1 Cost center identification and grouping

First, organizational structure of Ramathibodi hospital was examined in order to identify cost centers. Cost center was classified into 5 groups.

- Non revenue producing cost center (NRPCC): accounting department, administration department
- Revenue producing center (RPCC): pharmacy department
- Patient service cost center (PSCC): emergency room, out patient department (OPD)
- Teaching service cost center (TSCC)
- Research service cost center (RSCC)

2.2 Direct cost determination

Direct costs of each medical service were calculated from the summation of capital (C), material (M), and labor (L) costs of each cost center.

2.2.1 Capital cost

Information on capital resources, i.e. acquisition costs of buildings and durable goods, useful life of buildings and durable goods were collected from the

ophthalmology department and the policy and planning division, Ramathibodi hospital. Depreciation cost was calculated as the following;

Depreciation cost = [(cost of purchasing / useful life (year) / month / day / hour / minute)] x time of each spent service (minute) [equation 3]

= [(cost of purchasing / useful life (year) / 12 / 20 / 8 / 60)] x time of each spent service (minute)

2.2.2 Material cost

Material costs consumed by medical services were determined using the following formula;

Material cost = unit price x quantity [equation 4]

Information on unit price of drugs and medical supplies was collected from the pharmacy department and the policy and planning division, Ramathibodi hospital.

2.2.3 Labor cost

Labor costs were collected from the policy and planning division.

Labor cost = [(average salaries and wages) x month (per year) / day (per year) / hour (per day) / minute (per hour)] x time of each spent service (minute) [equation 5]

= [(average salaries and wages x 12) / 237 / 6.3 / 60] x time of each spent service (minute)

2.3 Indirect cost allocation

Direct cost of NRPCC and RPCC were allocated to be indirect costs of PSCC.

Indirect cost = (NRPCC + RPCC) x allocation rate [equation 6]

Allocation rate = total time of each spent service (minute) / total time of all labors in department (per year) [equation 7]

= total time of each spent service (minute) / (all labors in department x 237 x 6.3 x 60)

2.4 Total cost determination

Total costs of each medical service were calculated as the summation of direct costs and indirect costs from the allocation.

Total cost = direct cost + indirect cost

CTC = CDC + CDL + CDM + CDEPT [equation 2]

Cost data were used in the model, were discounted to its present value at a rate of 3 percent per year.

Part III: Cost effectiveness analysis

Base-case analysis

Incremental cost-effectiveness (ICE) was assessed as the ratio of the net increase in health care costs to the net improvement in health outcome. The lower the value of this ratio, the higher the priority of the program in terms of maximizing the benefit achieved from a given health expenditure. Thus, the incremental cost-effectiveness ratio (ICER) was calculated from the following formula:

$$ICER = \frac{C_S - C_N}{E_S - E_N} = \frac{\Delta C}{\Delta E} \quad \text{[equation 8]}$$

Where; C_S= cost of every 4 years screening, every 3 years screening, biannual screening, and annual screening

E_S= the number of patients prevented from blindness for every 4 years screening, every 3 years screening, biannual screening, and annual screening

C_N= cost of no screening, every 4 years screening, every 3 years screening, and biannual screening

E_N= the number of patients prevented from blindness for no screening, every 4 years screening, every 3 years screening, and biannual screening

Sensitivity analysis

In this study, sensitivity analysis was used to test the effect of varying the assumptions used in the model on the ICER. One-way sensitivity and best-worst case analysis were performed.

1.One-way sensitivity

One-way sensitivity analysis was used to test the effect of varying a single assumption of the model, while holding all other assumptions constant. The value of parameters used in sensitivity analysis derived from literature reviews. If only single literature was available, the value of parameter was varied at 25 percent from base-case analysis. For cost data, minimum cost and maximum cost used in sensitivity analysis were obtained from Ramathibodi Hospital database and expert opinions. Finally, the ranges of the probability of medical treatment seeking among unscreened patient and the probability of being treated with vitrectomy were derived from expert opinions.

One way sensitivity analysis was performed on the following main variable;

- Transition probability
- Annual mortality rate
- Effectiveness of treatment
- Effect of glycemic control on the rate of progression

- Cost of eye screening, laser treatment, and vitrectomy
- Discount rate
- Indirect cost
- Probability of medical treatment seeking among unscreened patients
- Probability of being treated with vitrectomy
- Sensitivity and specificity

2. Best-worst case analysis

For best case analysis, the assumptions that would result in the lowest value of ICER were assumed in the model. Then the ICER was calculated based on those assumptions. On the other hand, the assumptions that would result in the highest value of ICER were assumed. The ICER for worst case was, then, calculated based on those assumptions.

CHAPTER IV
RESULTS

Results of the study were presented in four parts, as follows;

Part I: Diabetic retinopathy model development

- Diabetic retinopathy model structure
- Transition probability determination

Part II: Costs analysis of medical services

Part III: Base-case analysis

Part IV: Sensitivity analysis

Part I: Diabetic retinopathy model development

Diabetic retinopathy model structure

The structure of the model was derived from intensive reviews of related literatures (Eastman et al (48, 49), Javitt et al (11), CDC (Centers for Disease Control and Prevention Diabetes Cost-Effectiveness Study) (50), GDM (Global Diabetes Model) (51)), and expert opinions. The model was outlined in figure 6 and the health states for each DR were shown in table 8.

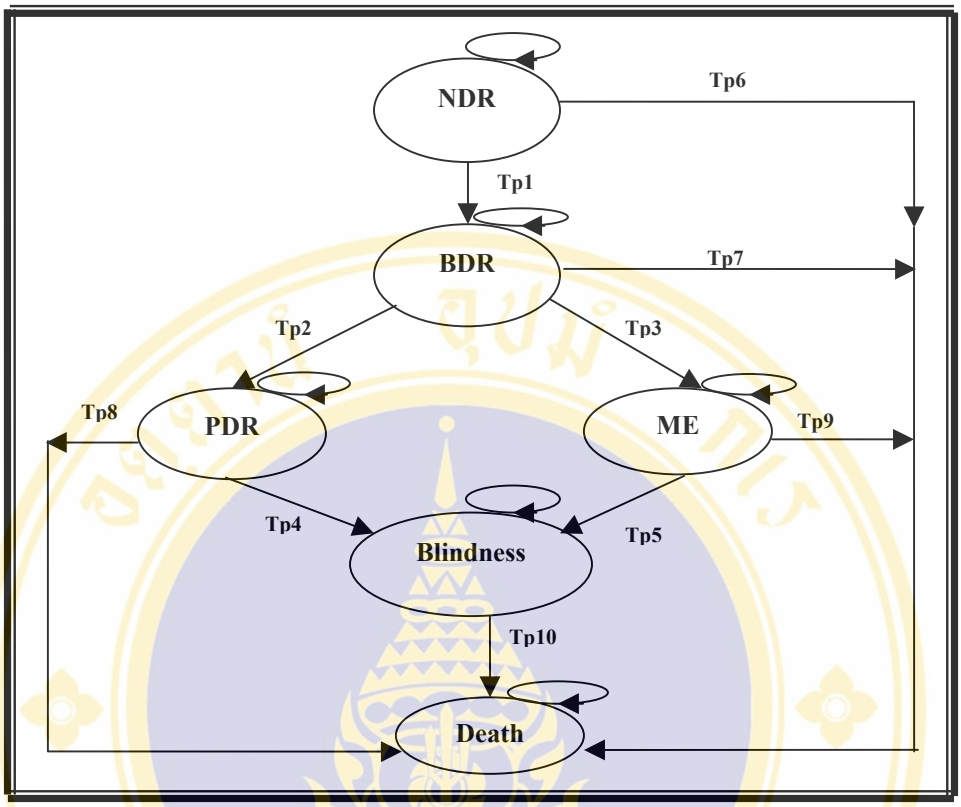


Figure 6. Diagram of the simulation model of diabetic retinopathy

For each "cycle" of the model, patients may progress to the next health state or to death, based on a specific transition probability (tp). To simulate the typical screening interval, this study used a cycle length of one year. The model was assumed that retinopathy did not regress and that progression was sequential (that was, no states were skipped). However, patients may make the transition to death at any time.

Table 8. Clinical definitions of the health states in the model

Health state	Clinical definition
NDR	No diabetic retinopathy
BDR	Background diabetic retinopathy or nonproliferative diabetic retinopathy
PDR	Proliferative diabetic retinopathy
ME	Clinically significant macular edema
Blindness	Visual acuity worse than 20/100 in better eye
Death	-

Transition probability determination

The values of transition probability used in the model were derived from Eastman et al (49), Javitt et al (11, 17, 57), and WESDR (Wisconsin Epidemiologic Study of Diabetic Retinopathy) (73). Based on Eastman et al (49), the transition probabilities of Asian-Americans were assumed to be equal to the probabilities of non-Hispanic whites used in the Eastman's study. In addition, these transition probabilities remained constant over time.

Based on Eastman et al (49, 74), risk of BDR was estimated to be about 20 percent at diagnosis of type 2 DM. In addition, after the review of the studies by Eastman et al (49) and Javitt et al (11), the transition probabilities (tp1, tp2, and tp3) used in their study were based on the cumulative incidences from four-year incidence of WESDR study (75). It was found that to calculate one-year risk, the probabilities from the WESDR study were equally divided by the number of observation years. However, the rates of progression were found to be related to the duration of DM. Since the transition probabilities were not linear then the cumulative incidences risks used in this study would be converted to one-year risk using equation 1.

$$tp_1 = 1-(1-tp_t)^{1/t} \qquad \text{[equation 1]}$$

The transition probabilities (tp1, tp2, and tp3) used in this study were based on the cumulative incidences from ten-year incidence of WESDR study (73), then the probabilities would be corrected by equation 1. Table 9 presents the comparison of annual disease progression rate used in this study and the studies by Eastman et al (49) and Javitt et al (11). In the WESDR study (73), cumulative incidences of DR were derived from the average of the rates of patients taking insulin and not taking insulin. The incidence and progression of DR in ten-year WESDR study assessed in a large population of people with diabetes living in southern Wisconsin, diagnosed at age 30 years or older. Average HbA_{1C} level of patients was approximately 10%.

Table 9. The comparison of annual disease progression rate used in this study and the studies by Eastman et al (49) and Javitt et al (11).

Probability for health state	Duration of DM (years)	Annual disease progression rate	
		Eastman et al (49) and Javitt et al (11)*	This study**
NDR to BDR (tp1)	1-4	0.073	0.1479
	5-9	0.129	0.1596
	10-14	0.116	0.1241
	15+	0.113	0.0785
BDR to PDR (tp2)	1-4	0.0025	0.0123
	5-9	0.009	0.0149
	10-14	0.0095	0.0204
	15+	0.026	0.0257
BDR to ME (tp3)_	1-4	0.047	0.0945
	5-9	0.095	0.1154
	10-14	0.092	0.1112
	15+	0.08	0.0840

* Based on the cumulative incidences from four-year incidence of WESDR study (75) and calculated one-year risk were equally divided by the number of observation years.
**Based on the cumulative incidences from ten-year incidence of WESDR study (73), then the transition probabilities would be converted to one-year risk using equation, $tp_1 = 1-(1-tp_t)^{1/t}$.

Tp4 and tp5 were derived from Javitt et al (11), and Eastman et al (49). As shown in table 9, the rate of progression to blindness from PDR and the rate of progression to blindness from PDR after panretinal photocoagulation were 0.088 and 0.0148, respectively. The rate of progression to blindness from CSME and the rate of progression to blindness from CSME after focal photocoagulation were 0.05 and 0.033, respectively.

The annual mortality risks (tp6, tp7, tp8, tp9, and tp10) were derived from Javitt et al (11, 17), WESDR (76), and expert opinions. According to Javitt et al (11, 17), annual mortality rate was calculated based on the annual mortality risk in type 2 DM with DR and the age-specific mortality in type 2 DM, as shown in equation 9.

Annual mortality rate = [(annual mortality risk in type 2 DM with DR (%) + (multiplication factor)x(age specific mortality)]/2 [equation 9]

According to table 10, the mortality risks among type 2 diabetic patients with different states of DR ranged from 6.2 percent per year to 19.9 percent per year (76). The mortality risks of each state of DR among type 2 diabetic patients were derived from WESDR (76), except the state of ME, which was derived from expert

opinions. Based on the age-specific mortality, the multiplication factors of each states of DR were derived from Javitt et al (11), except the state of blindness, which was derived from expert opinions. The age-specific mortality data in Thailand was obtained from the Bureau of Health Policy and Strategy Ministry of Public Health, as shown in the table 11.

In order to ensure the accuracy of the input, all of the transition probabilities used in the model were evaluated by the experts.

Table 10. Annual mortality rate for diabetic retinopathy in the model*

Health state	Absolute annual mortality risk in type 2 DM with DR (%)	Multiplication factor of age-specific mortality**	Data source
NDR (tp6)	6.2	2	WESDR and Javitt (11, 76)
BDR (tp7)	9.1	2	WESDR and Javitt (11, 76)
PDR (tp8)	11.5	5	WESDR and Javitt (11, 76)
ME (tp9)	9.3	2	WESDR, Javitt, and expert opinions (11, 76)
Blindness (tp10)	19.9	5	WESDR, Javitt, and expert opinions (11, 76)

* Annual mortality rate = [(annual mortality risk in type 2 DM with DR (%) + (multiplication factor)x(age-specific mortality)]/2

** Age specific mortality was derived from the Bureau of Health Policy and Strategy, Ministry of Public Health, Thailand.

Table 11. Age-specific death rate per 1,000-population, 2002, Thailand (77)

Age (year)	Death rate of population (per year)
0-4	2.0
5-9	0.6
10-14	0.4
15-19	0.6
20-24	1.0
25-29	2.1
30-34	2.2
35-39	2.1
40-44	2.5
45-49	3.5
50-54	5.1
55-59	7.6
60-64	10.5
65-69	16.2
70+	48.2

Source: Bureau of Health Policy and Strategy, Ministry of Public Health, Thailand

Annual mortality rate for each state of DR used in the model was presented in table 12. It was calculated from annual mortality risk for diabetic retinopathy (table 10) and age-specific death rate per 1,000-population, Thailand, 2002 (table 11), by using equation 9.

Table 12. Annual mortality rate in each state of diabetic retinopathy used in the model

Age	Annual mortality rate				
(year)	NDR	BDR	PDR	ME	Blindness
40-44	0.0335	0.0480	0.0638	0.0490	0.1058
45-49	0.0345	0.0490	0.0663	0.0500	0.1083
50-54	0.0361	0.0506	0.0703	0.0516	0.1123
55-59	0.0386	0.0531	0.0765	0.0541	0.1185
60-64	0.0415	0.0560	0.0838	0.0570	0.1258
65-69	0.0472	0.0617	0.0980	0.0627	0.1400
70-75	0.0792	0.0937	0.1780	0.0947	0.2200

Part II: Cost analysis of medical services

In base-case analysis, costs were determined from hospital perspective. Types of medical service incurred in each state of DR were shown in table13. Based on Ramathibodi hospital, all costs were adjusted to be equal to their values in the year 2003. Table 14 presents the summary of cost of each medical service used in the model. The cost of these medical services included cost of eye screening examination, cost of treatment in the group being screened and unscreened, cost of follow-up, and cost of misdiagnosis (false positive). The calculation of each medical service cost was shown in table 15-20. Details of the calculation of labor costs, material costs, capital costs, indirect costs, resources utilization, and data sources of each medical service were shown in appendix C.

According to table 14, costs of eye screening examination, which consisted of cost of visual acuity examination (VA), cost of eye dilatation, cost of anterior segment (A/S) examination and intraocular pressure, and cost of fundoscopic examination, were 113.79 Baht. Costs of laser photocogulation for PDR or ME in the group being screened were 2,333.41 Baht per course and 931.08 Baht per course, respectively. Costs of laser photocogulation for PDR and ME in the group being unscreened were 2,447.19 Baht per course and 1,044.87 Baht per course, respectively. Total costs of vitrectomy in the group being screened and unscreened were 20,825.61 Baht and 20,939.40 Baht

Follow-up costs of BDR, PDR, and ME were 227.57 Baht per year. Misdiagnosis cost for misdiagnosed NDR or PDR as BDR was 113.79 Baht, the misdiagnosis cost for misdiagnosed NDR or BDR as PDR was 98.03 Baht, and the misdiagnosis cost for misdiagnosed no ME as ME was 98.03 Baht.

Table 13. Types of medical service incurred in each state of diabetic retinopathy

Types of medical services	Health states of diabetic retinopathy			
	NDR	BDR	PDR	ME
Treatment				
Panretinal photocoagulation	NO	NO	YES*	NO
Focal or grid photocoagulation	NO	NO	NO	YES*
Vitrectomy	NO	NO	YES	NO
Follow-up	NO	YES+	YES+	YES+

* Times per course of laser photocoagulation: PDR = 4 times / course, ME = twice / course
+ Times per year of follow-up for BDR, PDR, ME were twice / year

Table 14. Summary cost of each medical service in diabetic retinopathy model

Type of cost	Cost (Baht)
Eye screening examination	113.79
Visual acuity examination	14.22
Eye dilatation	24.91
A/S examination and intraocular pressure	31.28
Fundoscopic examination with indirect ophthalmoscopy	43.38
Treatment: in the group being screened (per course)	
Panretinal photocoagulation: PDR	2,333.41
Focal/ Grid photocoagulation: ME	931.08
Vitrectomy	20,825.61
Treatment: in the group being unscreened (per course)	
Panretinal photocoagulation: PDR	2,447.19
Focal/ Grid photocoagulation: ME	1,044.87
Vitrectomy	20,939.40
Follow-up cost+ (per year)	
BDR	227.57
PDR	227.57
ME	227.57
Misdiagnosis cost	
NDR or PDR called BDR	113.79
NDR or BDR called PDR	98.03
No ME called ME	98.03

+ Follow-up cost = (times per year of follow-up) x (cost of eye screening examination)

Table 15 shows cost of eye screening examination. Eye screening examination consisted of visual acuity (VA) examination, eye dilatation, anterior segment (A/S) examination, intraocular pressure examination, and fundoscopic examination. According to table 15, cost of visual acuity examination was 14.22

Baht. Of this amount, 4.70 Baht was labor cost, 0.05 Baht was capital cost, and 9.47 Baht was indirect cost. Cost of eye dilatation with 1% tropicamide eye drop and 10% phenylephrine HCl eye drop was 24.91 Baht. Of this amount, 6.28 Baht was labor cost, 6.01 Baht was material cost, and 12.62 Baht was indirect cost. Cost of anterior segment and intraocular pressure examination were 31.28 Baht. Of this amount, 15.84 Baht was labor cost, 2.82 Baht was capital cost, and 12.62 Baht was indirect cost. Finally, cost of fundoscopic examination with indirect ophthalmoscopy was 43.38 Baht. Of this amount, 23.76 Baht was labor cost, 0.68 Baht was capital cost, and 18.93 Baht was indirect cost. Thus total cost of eye screening examination was equal to 113.79 Baht.

Table 15. Cost of eye screening examination

Procedure	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
1. Visual acuity examination+	4.70	0.05	0.00	9.47	14.22
2. Eye dilatation+	6.28	0.00	6.01	12.62	24.91
3. A/S examination and intraocular pressure+	15.84	2.82	0.00	12.62	31.28
4. Fundoscopic examination (with indirect ophthalmoscopy)+	23.76	0.68	0.00	18.93	43.38
Total cost of eye screening examination*			**113.79**		

* Cost of eye screening examination consisted of cost of visual acuity examination, cost of eye dilatation, cost of A/S (anterior segment) examination and intraocular pressure, and cost of fundoscopic examination (with indirect ophthalmoscopy).
+ See details and source of data in appendix C.

Costs of laser photocoagulation for PDR and ME were 544.22 Baht per time and 426.41 Baht per time, as shown in table 16. In base-case analysis, times per course of laser for PDR and ME were four times and twice, respectively. Total cost of laser photocoagulation was calculated from the summation of cost of visual acuity examination (VA), cost of eye dilatation, and cost of laser photocoagulation treatment. For patients in the group being unscreened who sought medical services by themselves because of the symptom, eye examination was required before receiving treatment. Thus, total cost for patients in the group being unscreened was greater than that of patients in the group being screened. According to table 17, total costs of laser

for PDR and ME in the group being screened were 2,333.41 Baht per course and 931.08 Baht per course, respectively. Total costs of laser for PDR and ME in the group being unscreened were 2,447.20 Baht per course and 1,044.87 Baht per course, respectively.

Table 16. Cost of laser photocoagulation (per person per time)

Procedure	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
Panretinal laser photcoagulation: PDR+	118.79	139.97	190.79	94.67	**544.22**
Focal/ Grid laser photocoagulation: ME+	79.19	93.32	190.79	63.11	**426.41**

+ See details of calculation and source of data in appendix C.

Table 17. Total cost of laser photocoagulation for patients with DR (per person per course)

Cost of each procedure	Times per course of treatment	Types of cost (Baht)				Total cost (Baht)
		Visual acuity	Eye dilatation	Laser treatment	Eye examination	
Laser for PDR in group being screened*	4	56.88	99.65	2,176.88	-	**2,333.41**
Laser for PDR in group being unscreened**	4	56.88	99.65	2,176.88	113.79	**2,447.20**
Laser for ME in group being screened*	2	28.44	49.82	852.82	-	**931.08**
Laser for ME in group being unscreened**	2	28.44	49.82	852.82	113.79	**1,044.87**

* Cost of laser in group being screened = (visual acuity exam. cost + eye dilatation cost + laser photocoagulation cost) x times per course of laser
**Cost of laser in group being unscreened = [(visual acuity exam. cost + eye dilatation cost + laser photocoagulation cost) x times per course of laser] + cost of eye examination

In this study, vitrectomy cost was an average cost of Pars Plana Vitrectomy (PPV) with endolaser, PPV with prefluoron, PPV with silicone oil injection, and PPV with DK line, as shown in table 18. Table 19 presents the total cost of vitrectomy for patients with DR. Cost of vitrectomy and laboratory, except cost of medication and room service, was calculated by the policy and planning division, Ramathibodi

hospital in 1997. These costs were adjusted to be their present values in the year 2003 by using consumer price index (see appendix E). From table 18, the average cost of vitrectomy after adjusted with consumer price index (CPI) was 14,542.26 Baht. Total cost of vitrectomy consisted of cost of vitrectomy, cost of medication, cost of laboratory and X-ray, and cost of room service. According table 19, cost of medication was 949.15 Baht. Cost of laboratory and X-ray after adjusted with CPI was 675.56 Baht. Cost of room service per one day was 1,552.88 Baht. In base-case analysis, admission for vitrectomy was assumed three days. Therefore, total cost of room service for vitrectomy was 4,658.64 Baht. Thus, total cost of vitrectomy for patients in the group being screened was 20,825.61 Baht per person per time. Patients in the group being unscreened were required for eye examination before receiving vitrectomy, so total cost among these patients was greater than screened group.

Table 18. Cost of vitrectomy (per person per time)

Type of vitrectomy	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
PPV with endolaser+	1,789.03	2,106.86	3,324.44	296.69	7,517.02
PPV with prefluoron+	1,841.20	932.38	8,483.44	304.63	11,561.65
PPV with silicone oil injection+	1,893.36	932.38	8,627.62	312.56	11,765.92
PPV with DK line+	1,841.20	932.38	14,833.44	304.63	17,911.65
Average cost of vitrectomy			12,189.06		
Average cost of vitrectomy (adjusted by CPI)++			**14,542.26**		

+ Cost data of each operation of vitectomy was received from the policy and planning division, Ramathibodi hospital and was calculated in 1997. See details of calculation and source of data in appendix C.
++Adjusted cost data in 1997 to 2003 with CPI (Consumer Price Index) = (cost in 1997x110)/92.2. See CPI in appendix E.

Table 19. Total cost of vitrectomy for patients with DR (per person per time)

Cost of each procedure	Types of cost (Baht)					Total cost (Baht)
	Vitrectomy	Medication+	Lab & X-ray+	Room service+	Eye examination	
Vitrectomy in the group being screened	14,542.26++	949.15	675.56++	4,658.64	-	**20,825.61**
Vitrectomy in the group being unscreened	14,542.26++	949.15	675.56++	4,658.64	113.79	**20,939.40**

+ See details and source of data in appendix C.
++Adjusted cost data in 1997 to 2003 with CPI = (cost in 1997x110)/92.2, see CPI in appendix E.

If the screening result was a false positive, the cost associated with false positive during screening was incorporated into the model, as shown in table 20. Misdiagnosis cost for false positive of the patient with NDR or BDR misdiagnosed as having PDR or the patient without ME misdiagnosed as having ME was equal to the summation of visual acuity cost, eye dilatation cost, and fundoscopic eye examination cost with laser. So, total cost of misdiagnosis the patient with NDR or BDR misdiagnosed as having PDR or the patient without ME misdiagnosed as having ME was 98.03 Baht. Misdiagnosis cost of patient with NDR misdiagnosed as having BDR and the patient with PDR misdiagnosed as having BDR were equal to eye screening examination cost. Thus, total cost of the patient with NDR or PDR misdiagnosed as having BDR was 113.79 Baht.

Table 20. Cost of misdiagnosis (false positive)*

Procedure	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
1. Visual acuity examination+	4.71	0.05	0.00	9.47	14.23
2. Eye dilatation+	6.28	0.00	6.00	12.62	24.90
3. Fundoscopic examination (with laser)+	19.80	23.32	0.00	15.78	58.90
Total cost of misdiagnosis*			**98.03**		

* Cost of misdiagnosis for NDR or BDR called PDR, or no ME called ME consisted of visual acuity examination cost, eye dilatation cost, and fundoscopic examination cost (with laser).
+ See details and data source in appendix C.

Part III: Base-case analysis

Parameters and assumptions used in base-case analysis were shown in table 21.

Table 21. Base-case parameters and assumptions used in the model

Parameters	Base-case analysis	Data source
Annual disease progression rates		
Progression from NDR to BDR (tp1)		
BDR risk present at diagnosis DM	20%	Eastman (49, 74)
1-4 year	0.1479	WESDR (73)
5-9 year	0.1596	WESDR (73)
10-14 year	0.1241	WESDR (73)
15+ year	0.0785	WESDR (73)
Progression from BDR to PDR (tp2)		
1-4 year	0.0123	WESDR (73)
5-9 year	0.0149	WESDR (73)
10-14 year	0.0204	WESDR (73)
15+ year	0.0257	WESDR (73)
Progression from BDR to ME (tp3)		
1-4 year	0.0945	WESDR (73)
5-9 year	0.1154	WESDR (73)
10-14 year	0.1112	WESDR (73)
15+ year	0.0840	WESDR (73)
Progression from PDR to Blindness (tp4)	0.088	Javitt (11), Eastman (49)
Progression from PDR to Blindness after treatment (tp4)	0.0148	Javitt (11), Eastman (49)
Progression from ME to Blindness (tp5)	0.050	Javitt (11), Eastman (49)
Progression from ME to Blindness after treatment (tp5)	0.033	Javitt (11), Eastman (49)
Annual mortality rate		
NDR (tp6)	[6.2%+(2 x age-specific mortality)]/2	Javitt (11)
BDR (tp7)	[9.1%+(2 x age-specific mortality)]/2	Javitt (11)
PDR (tp8)	[11.5%+(5 x age-specific mortality)]/2	Javitt (11)
ME (tp9)	[9.3%+(2 x age-specific mortality)]/2	Javitt (11), and expert
Blindness (tp10)	[19.9%+(5 x age-specific mortality)]/2	Javitt (11), and expert
Screening Test		
NDR called BDR	0.05	(10, 71)
NDR called PDR	0.003	(10, 71)
BDR called NDR	0.22	(10, 71)
BDR called PDR	0.02	(10, 71)
PDR called NDR	0.02	(10, 71)
PDR called BDR	0.03	(10, 71)

Table 21. Base-case parameters and assumptions used in the model (continued)

Parameters	Base-case analysis	Data source
Screening Test		
Sensitivity for ME	0.82	(10, 28)
Specificity for ME	0.79	(10, 28)
Costs (Baht)		
Eye screening examination	113.79	Ramathibodi Hospital
Panretinal photocoagulation (in group being screened)	2,333.41	Ramathibodi Hospital
Panretinal photocoagulation (in group being unscreened)	2,447.20	Ramathibodi Hospital
Focal /grid photocoagulation (in group being screened)	931.08	Ramathibodi Hospital
Focal /grid photocoagulation (in group being unscreened)	1,044.87	Ramathibodi Hospital
Vitrectomy (in group being screened)	20,825.61	Ramathibodi Hospital
Vitrectomy (in group being unscreened)	20,939.40	Ramathibodi Hospital
Follow-up for BDR	227.57	Ramathibodi Hospital
Follow-up for PDR	227.57	Ramathibodi Hospital
Follow-up for ME	227.57	Ramathibodi Hospital
Misdiagnosis of NDR or PDR called BDR	113.79	Ramathibodi Hospital
Misdiagnosis of NDR or BDR called PDR, and no ME called ME	98.03	Ramathibodi Hospital
Discount rate for present value analysis (per year)	3%	-
Others		
Probability of medical treatment seeking among unscreened PDR	20%	Expert opinions
Probability of medical treatment seeking among unscreened ME	50%	Expert opinions
Probability of unscreened patients were treated with vitrectomy	40%	Expert opinions
Probability of screened patients were treated with vitrectomy	7.5%	Expert opinions

Figure 7 displays the cumulative incidence of blindness among different screening interval groups. For a cohort of 10,000 patients age 40 years, newly diagnosed with type 2 DM, the model predicted that the cumulative incidence of blindness among no screening, annual screening, biannual screening, every 3 years screening, and every 4 years screening were 1,977 persons, 1,810 persons, 1,847 persons, 1,871 persons, and 1,889 persons, respectively. The discounted cumulative incidence of blindness among no screening, annual screening, biannual screening, every 3 years screening, every 4 years screening were 1,920 persons, 1,757 persons, 1,793 persons, 1,816 persons, and 1,834 persons, respectively.

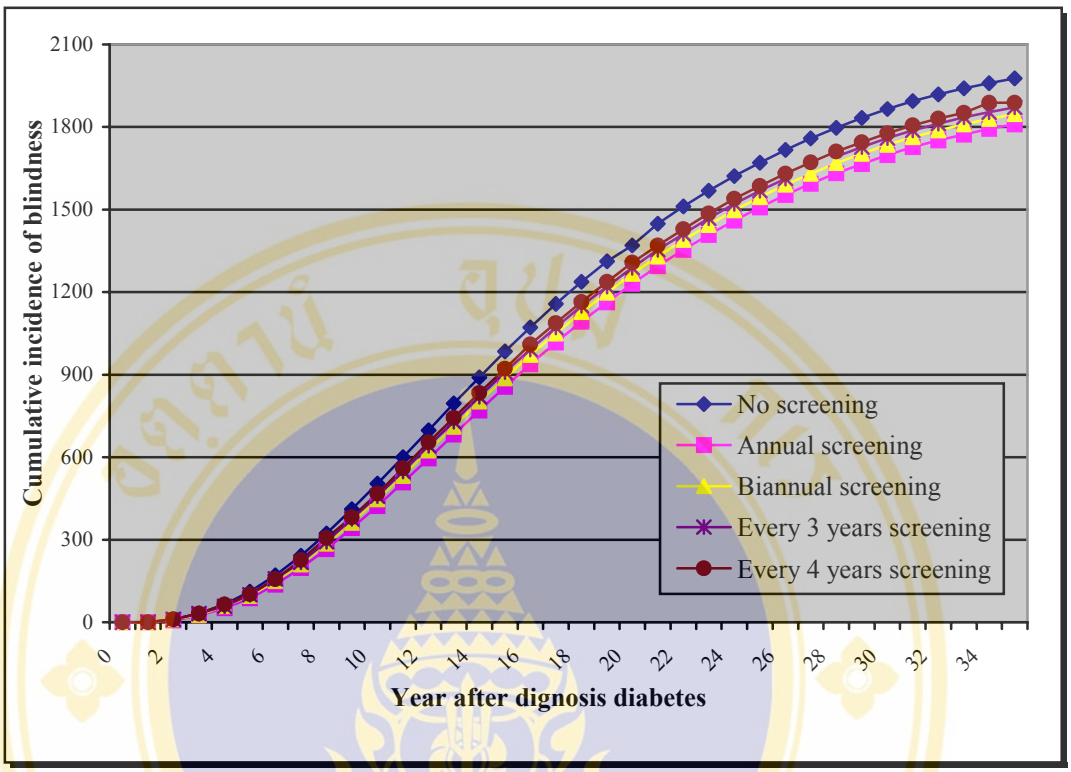


Figure 7. Cumulative incidence of blindness among different screening interval groups

As shown in table 22, the model predicted that the discounted total cost was 13,425,046.29 Baht among the group being unscreened. It was found that screening every 4 years, every 3 years, biannual, and annual increased cost to 20,824,736.62 Baht, 21,919,089.29 Baht, 23,569,641.06 Baht, and 26,997,752.90 Baht, respectively. Incremental cost effectiveness analysis was shown in table 22. Incremental cost-effectiveness ratio (ICER) comparing the group being screened every 4 years to the group being unscreened found that it cost about 85,976.89 Baht per additional blindness prevented. The ICER of increasing screening frequency from every 4 years to every 3 years was 62,806.34 Baht per additional blindness prevented. The ICER of increasing screening frequency from every 3 years to biannual was 70,553.97 Baht additional blindness prevented. Finally, the ICER of increasing screening frequency from biannual to annual was 95,865.04 Baht additional blindness prevented.

Table 22. Incremental cost-effectiveness ratio of increased screening frequency in Thailand [@]

Screening frequency*	Total cost [+] (Baht)	Total blindness [+] (person)	Incremental cost-effectiveness ratio[++] (Baht/additional blindness prevented)
None	13,425,046.29	1,920	-
Every 4 years	20,824,736.62	1,834	85,976.89
Every 3 years	21,919,089.29	1,816	62,806.34
Biannual	23,569,641.06	1,793	70,553.97
Annual	26,997,752.90	1,757	95,865.04

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Base-case analysis.).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+ Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

Part IV: Sensitivity analysis

One-way sensitivity analysis and best-worst case analysis were conducted to examine the impacts of several factors on the estimation of cost-effectiveness analysis.

One-way sensitivity analysis

For one-way sensitivity analysis, several factors such as transition probability, effectiveness of the treatment, cost of screening, cost of treatment, sensitivity, and specificity, etc. were varied to examine theirs impacts on the estimation of cost-effectiveness analysis. Table 23 displays the values of parameters used in one-way sensitivity analysis. In sensitivity analysis, values of BDR risk at diagnosis of DM, tp1, tp2, tp3, annual mortality rate, and effect glycemic control on the rate progression of DR were varied using information obtained from other studies. For other parameters, which their values could be found in only one study used for base-case analysis, their values were varied 25 percent from the base-case analysis for sensitivity analysis. These parameters included a transition probability from PDR or

ME to Blindness, annual mortality risk in type2 DM with DR, sensitivity, and specificity. For cost data used in sensitivity analysis, their values were derived from Ramathibodi Hospital database and expert opinions (see details of calculation in appendix C and D). Finally, the values of the probability of medical treatment seeking among unscreened patients and the probability of patients being treated with vitrectomy used in sensitivity analysis were derived from expert opinions.

Table 23. Parameters for one-way sensitivity analysis

Parameter	Base-case analysis	Sensitivity analysis
Annual disease progression rates		
BDR risk at diagnosis DM	20%	5-35% (8, 22)
Transition probability (tp): tp1-3	WESDR-10 year (See table 9)	WESDR-4 year (75) Taiwan-4 year (78) (See table 25, 27, 29)
Progression from PDR to Blindness (tp4)	0.088	0.0660-0.1100+
Progression from PDR to Blindness after treatment (tp4)	0.0148	0.0111-0.0185+
Progression from ME to Blindness (tp5)	0.050	0.0375-0.0625+
Progression from ME to Blindness after treatment (tp5)	0.033	0.0248-0.0413+
Effect glycemic control on the progression of DR	- -	Eastman (48) (See table 39) Vijan (10) (See topic 1.9.2)
Annual mortality rate	Javitt (See table 12)	Vijan (10) (See table 35)
Annual mortality risk in type 2 DM with DR		
NDR	6.2%	4.7-7.8%+
BDR	9.1%	6.8-11.4%+
PDR	11.5%	8.6-14.4%+
ME	9.3%	7.0-11.6%+
Blindness	19.9%	14.9-24.9%+
Screening Test		
NDR called BDR	0.05	0.04-0.06+
NDR called PDR	0.003	0.002-0.004+
BDR called NDR	0.22	0.17-0.28+
BDR called PDR	0.02	0.01-0.03+
PDR called NDR	0.02	0.01-0.03+
PDR called BDR	0.03	0.02-0.04+
Sensitivity for ME	0.82	0.62-0.99+
Specificity for ME	0.79	0.60-0.98+

+ The value in sensitivity analysis was varied 25 percent from the base-case analysis.

Table 23. Parameters for one-way sensitivity analysis (continued)

Parameter	Base-case analysis	Sensitivity analysis
Costs (Baht)		
Eye screening examination	113.79	50.75-260.71++
Panretinal photocoagulation	2,333.41	602.23-5,666.49++
Focal /grid photocoagulation	931.08	257.61-2,370.16++
Vitrectomy	20,825.61	14,849.81-34,797.25++
Add indirect cost (GDP per capita)	-	85,951.00*
Discount rate (per year)	3%	0-5%
Others		
Probability of medical treatment seeking among unscreened PDR	20%	10-30%+++
Probability of medical treatment seeking among unscreened ME	50%	25-75%+++
Probability of unscreened patients were treated with vitrectomy	40%	30-50%+++
Probability of screened patients were treated with vitrectomy	7.5%	5-10%+++

++ The value in sensitivity analysis was derived from Ramathibodi Hospital database and expert opinions.
* The value in sensitivity analysis was derived from the National Statistical Office, Thailand 2002.
+++ The value in sensitivity analysis was derived from expert opinions.

1. Transition probability

1.1 BDR risk at diagnosis

The onset of DR among type 2 DM patients may occur before clinical diagnosis. Moreover, epidemiological evidence indicates that complications may begin several years before clinical diagnosis. Ausayakhun et al. (8) and Chairungruang et al (22) examined the prevalence of DR in Maharaj Nakorn Chiang-Mai Hospital and Pramongkutklao Hospital, respectively. They found that 5-35 percent of BDR risk was found among patients age 40 years at diagnosis of type 2 DM. Table 24 presents the effect of BDR risk at diagnosis on ICER. As shown in table 24, by increasing BDR risk at diagnosis to 35 percent the total number of blindness and total cost would be increased. If BDR risk at diagnosis was 5 percent, the total number of blindness and total cost would be decreased.

Figure 8 presents the effect of BDR risk at diagnosis on ICER. By using 35 percent BDR risk at diagnosis, the ICER comparing annual screening vs. biannual

screening, biannual screening vs. every 3 years screening, and every 3 years screening vs. every 4 years screening were decreased about 15.98-16.82 percent from base-case analysis (20 percent BDR risk at diagnosis). However, the ICER comparing every 4 years vs. no screening was increased about 6.05 percent from the base-case analysis. On the other hand, by using 5 percent BDR risk at diagnosis, it was found that the ICER comparing annual screening vs. biannual screening, biannual screening vs. every 3 years screening, and every 3 years screening vs. every 4 years screening were increased about 7.72-33.29 percent from the base-case analysis. However, it was found that the ICER (5 percent BDR risk at diagnosis) comparing every 4 years screening vs. no screening was decreased about 6.07 percent from the base-case analysis.

Table 24. Effect of BDR risk at diagnosis on ICER[@]

Screening frequency*	**BDR risk at diagnosis of DM**		
	5% (8, 22)	**20% [Base-case]**	**35% (8, 22)**
Total cost (Baht)[+]			
None	12,619,800.15	13,425,046.29	14,230,292.43
Every 4 years	19,558,990.74	20,824,736.62	22,090,482.50
Every 3 years	20,827,577.05	21,919,089.29	23,010,601.53
Biannual	22,667,455.15	23,569,641.06	24,471,826.96
Annual	26,588,135.09	26,997,752.90	27,407370.71
Total blindness (person)[+]			
None	1,827	1,920	2,013
Every 4 years	1,741	1,834	1,927
Every 3 years	1,726	1,816	1,909
Biannual	1,701	1,793	1,884
Annual	1,667	1,757	1,848
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	80,755.09	85,976.89	91,182.08
Every 3 years	83,716.94	62,806.34	52,404.62
Biannual	75,998.43	70,553.97	59,282.63
Annual	112,965.42	95,865.04	79,742.82

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_BDR risk).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

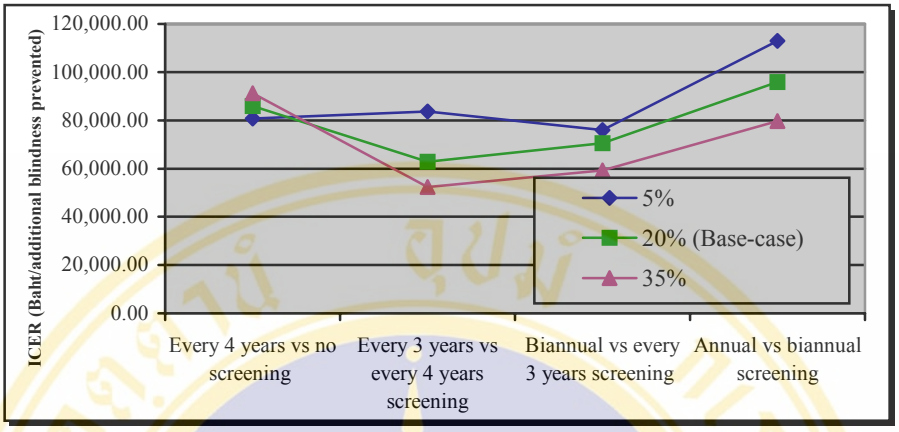


Figure 8. Effect of BDR risk at diagnosis on ICER

1.2 Transition probability from NDR to BDR (tp1)

1.2.1 Tp1 derived from WESDR 4-year incidence

From the review of the studies by Eastman et al (49) and Javitt et al (11), the transition probabilities including tp1 were derived from 4-year WESDR study (75), as shown in table 25. In base-case analysis, the probabilities from 10-year WESDR study (73) were used.

1.2.2 Tp1 derived from Taiwan 4-year incidence

Chen MS et al (78) assessed the incidence and progression of DR among patients diagnosed with type 2 DM aged ≥ 40 years in Taiwan. Average HbA_{1C} level of patients was 7.4 percent. Annual disease progression rate was presented in table 25.

Table 25. Annual disease progression rate from NDR to BDR (tp1)

Duration of DM (year)	Annual disease progression rate from NDR to BDR (tp1)		
	Base-case	WESDR 4-year (75)	Taiwan 4-year (78)*
1-4	0.1479	0.0823	1-3 year: 0.0398 4 year: 0.0889
5-9	0.1596	0.1789	0.0889
10-14	0.1241	0.1448	0.0889
15+	0.0785	0.1392	0.0889

* Annual disease progression rate of newly diagnosis for BDR of Taiwan was 0.0328.

The effect of transition probability (tp1) on ICER was shown in table 26 and figure 9. By using transition probabilities from WESDR 4-year study in sensitivity analysis, the ICER comparing every 4 years screening vs. no screening and biannual screening vs. every 3 years screening were decreased about 0.10-1.63 percent from base-case analysis. However, the ICER comparing every 3 years screening vs. every 4 years screening and annual screening vs. biannual screening were increased about 6.93-8.31 percent from the base-case analysis.

By using transition probabilities from Taiwan 4-year study, the ICER would be increased about 2.82-76.80 percent from the base-case analysis.

Table 26. Effect of transition probability from NDR to BDR (tp1) on ICER[@]

Screening frequency*	Transition probability from NDR to BDR (tp1)		
	Base-case	**WESDR-4 year (75)**	**Taiwan-4 year (78)**
Total cost (Baht)[+]			
None	13,425,046.29	12,824,559.39	9,405,381.62
Every 4 years	20,824,736.62	20,180,015.29	16,173,078.52
Every 3 years	21,919,089.29	21,337,514.10	17,418430.03
Biannual	23,569,641.06	23,011,760.43	19,682,514.97
Annual	26,997,752.90	26,731,726.19	24,944,435.72
Total blindness (person)[+]			
None	1,920	1,851	1,395
Every 4 years	1,834	1,764	1,318
Every 3 years	1,816	1,747	1,303
Biannual	1,793	1,723	1,283
Annual	1,757	1,687	1,252
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	85,976.89	84,573.47	88,401.18
Every 3 years	62,806.34	67,160.35	82,858.76
Biannual	70,553.97	70,486.44	111,509.67
Annual	95,865.04	103,828.52	169,488.06

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp1).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

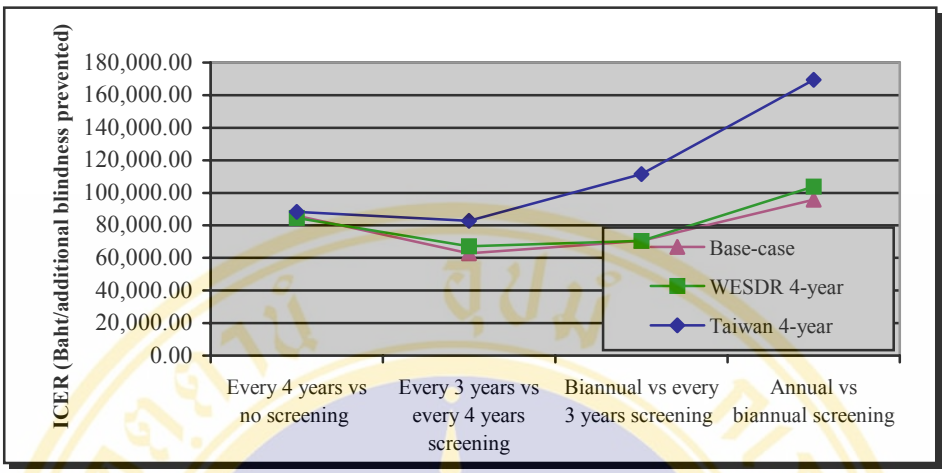


Figure 9. Effect of transition probability from NDR to BDR (tp1) on ICER

1.3 Transition probability from BDR to PDR (tp2)

1.3.1 Tp2 derived from WESDR 4-year incidence

From the review of the studies by Eastman et al (49) and Javitt et al (11), the transition probabilities including tp2 were derived from 4-year WESDR study (75), as shown in table 27. In base-case analysis, the probabilities from 10-year WESDR study (73) were used.

1.3.2 Tp2 derived from Taiwan 4-year incidence

Chen MS et al (78) assessed the incidence and progression of DR among patients diagnosed with type 2 DM aged ≥ 40 years in Taiwan. Average HbA_{1C} level of patients was 7.4 percent. Annual disease progression rate was presented in table 27.

Table 27. Annual disease progression rate from BDR to PDR (tp2)

Duration of DM (year)	Annual disease progression rate from BDR to PDR (tp2)		
	Base-case	WESDR 4-year (75)	Taiwan 4-year (78)
1-4	0.0123	0.0025	1-3 year: 0.0091 4 year: 0.0212
5-9	0.0149	0.0090	0.0212
10-14	0.0204	0.0070	0.0212
15+	0.0257	0.0221	0.0212

The effect of transition probability (tp2) on ICER was shown in table 28 and figure 10. By using transition probabilities from WESDR 4-year study in sensitivity analysis, the ICER would be increased about 32.13-64.18 percent from baseline. By using transition probabilities from Taiwan 4-year study, the ICER comparing every 4 years screening vs. no screening, biannual screening vs. every 3 years screening, and annual screening vs. biannual screening were decreased about 3.16-11.52 percent from the baseline. However, the ICER comparing every 3 years screening vs. every 4 years screening was increased about 6.01 percent from the baseline.

Table 28. Effect of transition probability from BDR to PDR (tp2) on ICER[@]

Screening frequency*	Transition probability from BDR to PDR (tp2)		
	Base-case	**WESDR-4 year (75)**	**Taiwan-4 year (78)**
Total cost (Baht)[+]			
None	13,425,046.29	11,887,674.40	13,780,075.34
Every 4 years	20,824,736.62	19,813,188.61	21,046,435.76
Every 3 years	21,919,089.29	20,958,322.16	22,143,501.81
Biannual	23,569,641.06	22,686,794.84	23,767,217.67
Annual	26,997,752.90	26,195,964.28	27,179,995.33
Total blindness (person)[+]			
None	1,920	1,885	1,924
Every 4 years	1,834	1,829	1,830
Every 3 years	1,816	1,816	1,814
Biannual	1,793	1,801	1,788
Annual	1,757	1,773	1,751
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	85,976.89	141,696.45	77,940.61
Every 3 years	62,806.34	85,737.32	66,583.30
Biannual	70,553.97	113,431.11	62,425.87
Annual	95,865.04	126,665.91	92,837.60

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp2).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

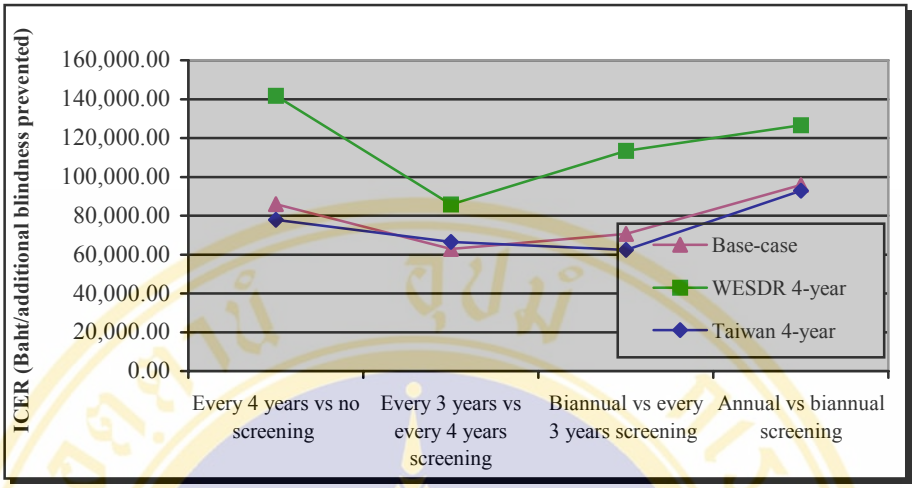


Figure 10. Effect of transition probability from BDR to PDR (tp2) on ICER

1.4 Transition probability from BDR to ME (tp3)

1.4.1 Tp3 derived from WESDR 4-year incidence

From the review of the studies by Eastman et al (49) and Javitt et al (11), the transition probabilities including tp3 were derived from 4-year WESDR study (75), as shown in table 29. In base-case analysis, the probabilities from 10-year WESDR study (73) were used.

1.4.2 Tp3 derived from Taiwan 4-year incidence

Chen MS et al (78) assessed the incidence and progression of DR among patients diagnosed with type 2 DM aged ≥ 40 years in Taiwan. Average HbA_{1C} level of patients was 7.4 percent. Annual disease progression rate was presented in table 29.

Table 29. Annual disease progression rate from BDR to ME (tp3)

Duration of DM (year)	Annual disease progression rate from BDR to ME (tp3)		
	Base-case	WESDR 4-year (75)	Taiwan 4-year (78)
1-4	0.0945	0.0500	1-3 year: 0.0666 4 year: 0.0963
5-9	0.1154	0.1153	0.0963
10-14	0.1112	0.1074	0.0963
15+	0.0840	0.0922	0.0963

The effect of transition probability (tp3) on ICER was shown in table 30 and figure 11. By using transition probabilities from WESDR 4-year study in sensitivity analysis, the ICER comparing every 3 years screening vs. every 4 years screening, biannual screening vs. every 3 years screening, and annual screening vs. biannual screening were decreased about 0.73-2.71 percent from baseline. However, the ICER comparing every 4 years screening vs. no screening was increased about 1.36 percent from the baseline. By using transition probabilities from Taiwan 4-year study, the ICER would be decreased about 0.23-4.06 percent from the baseline.

Table 30. Effect of transition probability from BDR to ME (tp3) on ICER[@]

Screening frequency*	Transition probability from BDR to ME (tp3)		
	Base-case	**WESDR-4 year (75)**	**Taiwan-4 year (78)**
Total cost (Baht)[+]			
None	13,425,046.29	13,078,309.39	13,065,910.10
Every 4 years	20,824,736.62	20,890,466.86	20,963,997.81
Every 3 years	21,919,089.29	22,034,619.16	22,061,583.78
Biannual	23,569,641.06	23,689,265.57	23,735,546.48
Annual	26,997,752.90	27,117,596.97	27,141,432.19
Total blindness (person)[+]			
None	1,920	1,854	1,839
Every 4 years	1,834	1,764	1,747
Every 3 years	1,816	1,746	1,730
Biannual	1,793	1,722	1,705
Annual	1,757	1,685	1,668
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	85,976.89	87,146.33	85,776.72
Every 3 years	62,806.34	61,487.64	62,609.76
Biannual	70,553.97	70,036.01	67,690.02
Annual	95,865.04	93,266.29	92,654.89

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp3).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

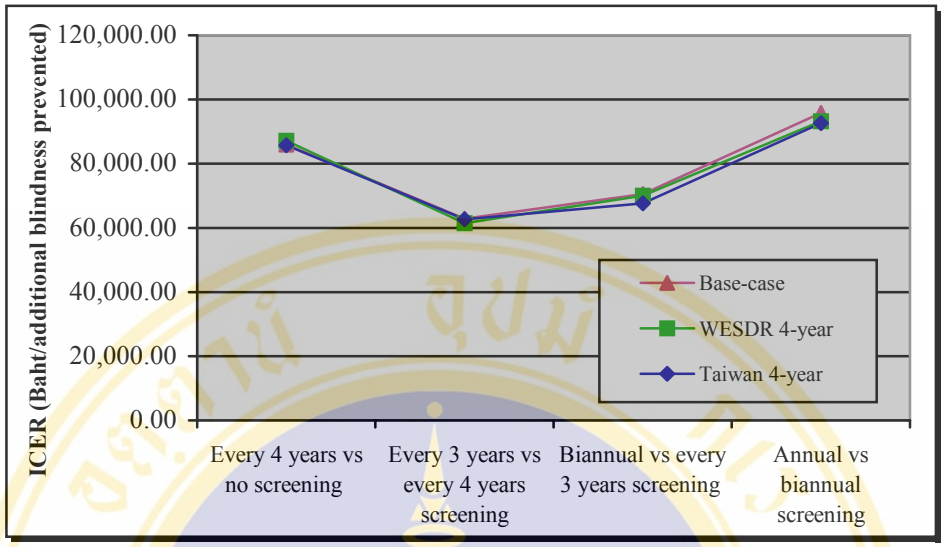


Figure 11. Effect of transition probability from BDR to ME (tp3) on ICER

1.5 Transition probability from PDR to Blindness (tp4): untreatment

Since only single study was available for information on tp4, then value of transition probability from PDR to Blindness was varied at 25 percent from base-case for sensitivity analysis. Table 31 and figure 12 present the effect of transition probability from PDR to Blindness among untreated patients on ICER. It was found that if transition probability from PDR to Blindness increased 25 percent (tp4 = 0.1100), the total number of blindness would be increased and the ICER would be decreased about 13.11-15.14 percent from base-case analysis. If transition probability from PDR to Blindness decreased 25 percent (tp4 = 0.0660), the total number of blindness would be decreased, the ICER would be increased about 21.73-23.70 percent from the base-case analysis.

Table 31. Effect of transition probability from PDR to Blindness (untreatment) on ICER[@]

Screening frequency*	Transition probability from PDR to Blindness (tp4): Untreatment		
	Tp4 = 0.0660	Tp4 = 0.0880 [Base-case]	Tp4 = 0.1100
Total cost (Baht)[+]			
None	13,630,104.74	13,425,046.29	13,238,528.49
Every 4 years	20,902,033.65	20,824,736.62	20,749,363.47
Every 3 years	21,976,086.45	21,919,089.29	21,862,939.71
Biannual	23,602,355.44	23,569,641.06	23,537,028.68
Annual	27,001,485.99	26,997,752.90	26,994,028.06
Total blindness (person)[+]			
None	1,887	1,920	1,950
Every 4 years	1,818	1,834	1,849
Every 3 years	1,804	1,816	1,828
Biannual	1,785	1,793	1,800
Annual	1,756	1,757	1,758
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	105,827.66	85,976.89	74,704.77
Every 3 years	77,691.24	62,806.34	53,546.84
Biannual	87,151.70	70,553.97	59,873.42
Annual	116,696.34	95,865.04	81,642.59

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp4_Untreatment).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

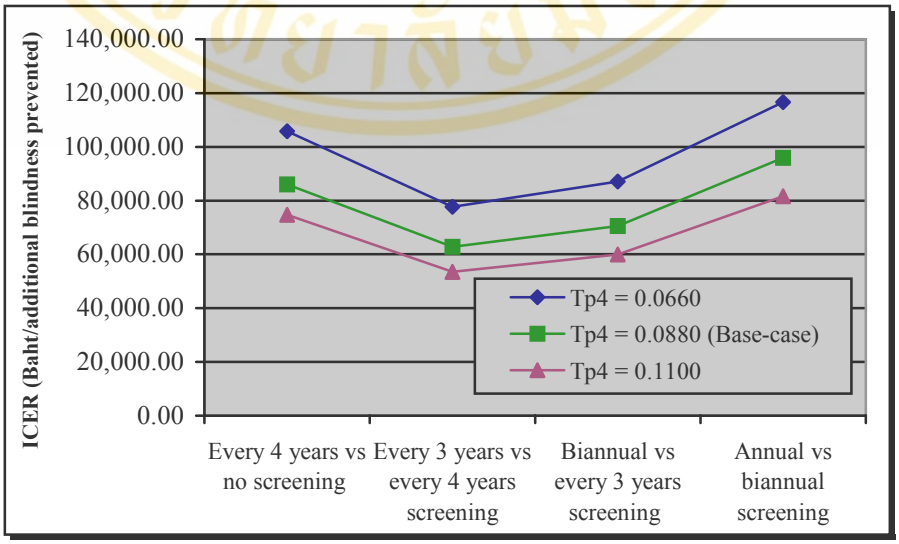


Figure 12. Effect of transition probability from PDR to Blindness (untreatment) on ICER

1.6 Transition probability from ME to Blindness (tp5): untreatment

Since only single study was available for information on tp5, then value of transition probability from ME to Blindness was varied at 25 percent from base-case for sensitivity analysis. Table 32 and figure 13 present the effect of transition probability from ME to Blindness among untreated patients on ICER. It was found that if transition probability from ME to Blindness increased 25 percent (tp5 = 0.0625), the total number of blindness would be increased and the ICER would be decreased about 9.79-20.81 percent from base-case analysis. If transition probability from ME to Blindness decreased 25 percent (tp5 = 0.0375), the total number of blindness would be decreased, the ICER would be increased about 12.88-37.14 percent from the base-case analysis.

Table 32. Effect of transition probability from ME to Blindness (untreatment) on ICER[@]

Screening frequency*	Transition probability from ME to Blindness (tp5): Untreatment		
	Tp5 = 0.0375	**Tp5 = 0.0500 [Base-case]**	**Tp5 = 0.0625**
Total cost (Baht)[+]			
None	13,525,332.94	13,425,046.29	13,326,858.19
Every 4 years	20,902,457.68	20,824,736.62	20,748,111.82
Every 3 years	21,988,248.07	21,919,089.29	21,850,761.40
Biannual	23,625,173.18	23,569,641.06	23,514,611.69
Annual	27,024,548.25	26,997,752.90	26,971,094.76
Total blindness (person)[+]			
None	1,883	1,920	1,956
Every 4 years	1,807	1,834	1,860
Every 3 years	1,793	1,816	1,840
Biannual	1,774	1,793	1,811
Annual	1,748	1,757	1,766
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	97,050.13	85,976.89	77,561.25
Every 3 years	76,900.27	62,806.34	53,455.15
Biannual	89,532.63	70,553.97	58,624.34
Annual	131,469.29	95,865.04	75,918.63

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp5_Untreatment).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

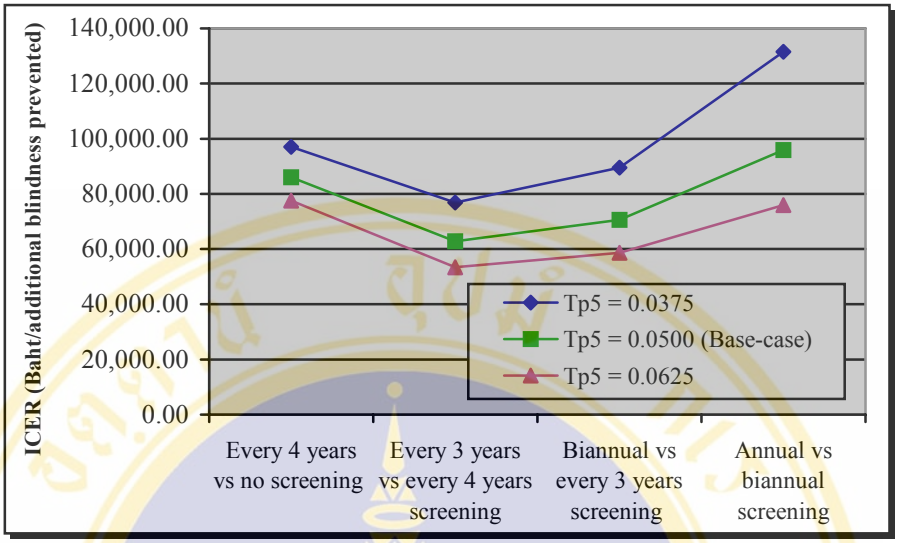


Figure 13. Effect of transition probability from ME to Blindness (untreatment) on ICER

1.7 Effectiveness of treatment

Since only single study was available for information on transition probability from PDR or ME to Blindness, then value of the transition probability was varied at 25 percent from base-case for sensitivity analysis.

1.7.1 Transition probability from PDR to Blindness (tp4): treatment

When transition probability from PDR to Blindness among treated patients was decreased, it indicated an increasing of effectiveness of treatment. Increasing the effectiveness of treatment was resulting in the reduction of blindness. It was found that if the transition probability decreased 25 percent (tp4 = 0.0111), the total number of blindness would be decreased, ICER would be reduced approximately 5.01-6.63 percent from base-case analysis (tp4 = 0.0148), as shown in table 33 and figure 14. On the other hand, if the probability increased 25 percent (tp4 = 0.0185), the total number of blindness would be increased, the ICER would be increased approximately 5.22-7.18 percent from the base-case analysis.

Table 33. Effect of effectiveness of treatment for PDR on ICER[@]

Screening frequency*	Transition probability from PDR to Blindness (tp4): Treatment		
	Tp4 = 0.0111	Tp4 = 0.0148 [Base-case]	Tp4 = 0.0185
Total cost (Baht)[+]			
None	13,440,499.86	13,425,046.29	13,410,218.24
Every 4 years	20,847,375.43	20,824,736.62	20,803,029.84
Every 3 years	21,943,208.34	21,919,089.29	21,895,969.12
Biannual	23,595,647.80	23,569,641.06	23,544,718.42
Annual	27,026,205.43	26,997,752.90	26,970,496.00
Total blindness (person)[+]			
None	1,905	1,920	1,934
Every 4 years	1,812	1,834	1,854
Every 3 years	1,794	1,816	1,838
Biannual	1,769	1,793	1,815
Annual	1,731	1,757	1,782
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	80,279.70	85,976.89	92,146.41
Every 3 years	59,042.50	62,806.34	66,811.58
Biannual	66,521.74	70,553.97	74,816.51
Annual	91,063.35	95,865.04	100,870.91

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp4_Treatment).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

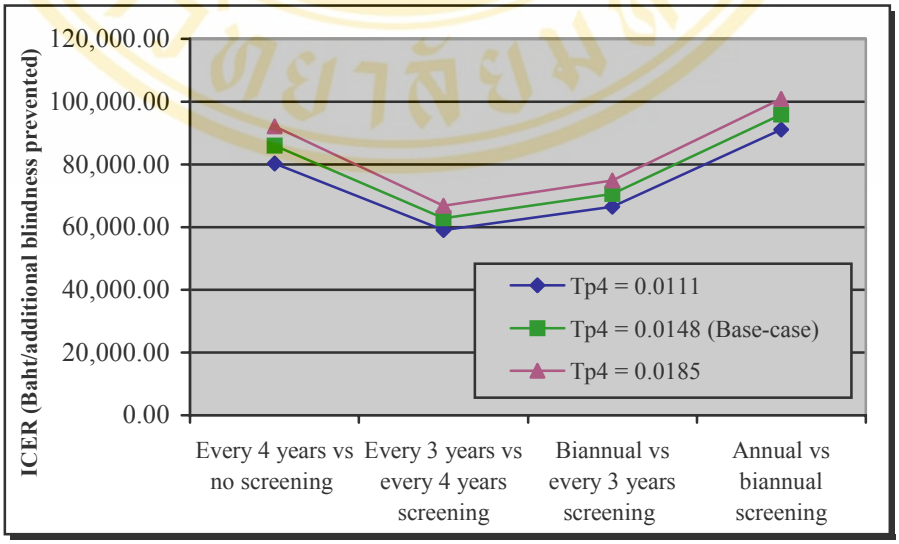


Figure 14. Effect of effectiveness of treatment for PDR on ICER

1.7.2 Transition probability from ME to blindness (tp5): treatment

Table 34 and figure 15 present the effect of effectiveness of treatment for ME on ICER. When transition probability from ME to Blindness among untreated patients was decreased, it indicated an increasing of effectiveness of treatment. It was found that if the transition probability decreased 25 percent (tp5 = 0.0248), the total number of blindness would be decreased, the ICER would be reduced approximately 8.83-18.66 percent, as compared to base-case analysis (tp5 = 0.0330). On the other hand, if the transition probability increased 25 percent (tp5 = 0.0413), the total number of blindness would be increased, the ICER would be increased approximately 9.06-24.53 percent, as compared to the base-case analysis.

Table 34. Effect of effectiveness of treatment for ME on ICER[@]

Screening frequency*	Transition probability from ME to Blindness (tp5): Treatment		
	Tp5 = 0.0248	**Tp5 = 0.0330 [Base-case]**	**Tp5 = 0.0413**
Total cost (Baht)[+]			
None	13,828,299.91	13,425,046.29	13,056,313.44
Every 4 years	21,243,725.20	20,824,736.62	20,441764.69
Every 3 years	22,343,575.08	21,919,089.29	21,531,155.73
Biannual	24,002,521.19	23,569,641.06	23,174,127.53
Annual	27,447,261.76	26,997,752.90	26,587,237.72
Total blindness (person)[+]			
None	1,635	1,920	2,169
Every 4 years	1,541	1,834	2,090
Every 3 years	1,520	1,816	2,075
Biannual	1,493	1,793	2,056
Annual	1,448	1,757	2,027
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	78,382.46	85,976.89	93,770.57
Every 3 years	54,344.10	62,806.34	72,504.61
Biannual	59,809.23	70,553.97	83,445.23
Annual	77,976.71	95,865.04	119,377.67

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Tp5_Treatment).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

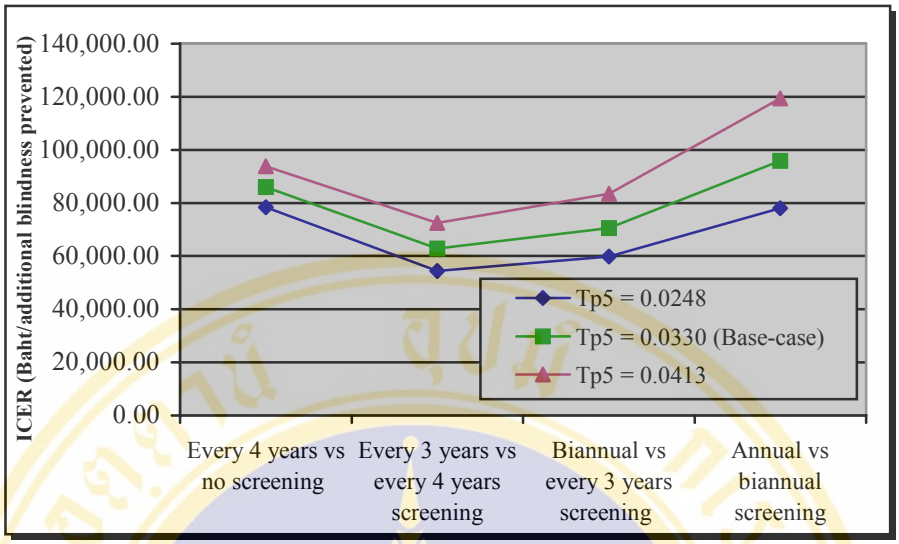


Figure 15. Effect of effectiveness of treatment for ME on ICER

1.8 Annual mortality rate

For base-case analysis, the annual mortality rate derived from Javitt et al (11) was calculated using equation 9.

Annual mortality rate = [(annual mortality risk in type 2 DM with DR (%) +
(multiplication factor)x(age specific mortality)]/2 [equation 9]

1.8.1 Annual mortality rate derived from Vijan study (10)

From the review of the study by Vijan et al (10), the annual mortality rate was derived from equation 10.

Annual mortality rate = (multiplication factor)x(age specific mortality) [equation 10]

The mortality multipliers for each state were derived from Vijan et al (10). Multiplication factors for DM, BDR, PDR, ME, and Blindness were 1.80, 1.49, 1.76, 1.76 and 2.34, respectively. According to equation 9 and 10, annual mortality rates used in the base-case analysis and annual mortality rate derived from Vijan et al (10) were shown in table 35.

Table 35 shows that annual mortality rates in each state of DR used in the base-case analysis were higher than the rate derived from Vijan et al (10). By using annual mortality rate derived from Vijan et al (10), total number of blindness

would be increased, and ICER would be decreased approximately 13.22-20.53 percent from the base-case analysis (table 36).

Table 35. Annual mortality rates in each state of diabetic retinopathy: Vijan et al (10)

Age (year)	Annual mortality rates									
	NDR		BDR		PDR		ME		Blindness	
	Base-Case	Vijan (10)	Base-Case	Vijan (10)	Base-Case	Vijan (10)	Base-Case	Vijan (10)	Base-Case	Vijan (10)
40-44	0.0335	0.0045	0.0480	0.0067	0.0638	0.0079	0.0490	0.0079	0.1058	0.0105
45-49	0.0345	0.0063	0.0490	0.0094	0.0663	0.0111	0.0500	0.0111	0.1083	0.0147
50-54	0.0361	0.0092	0.0506	0.0137	0.0703	0.0162	0.0516	0.0162	0.1123	0.0215
55-59	0.0386	0.0137	0.0531	0.0204	0.0765	0.0241	0.0541	0.0241	0.1185	0.0320
60-64	0.0415	0.0189	0.0560	0.0282	0.0838	0.0333	0.0570	0.0333	0.1258	0.0442
65-69	0.0472	0.0292	0.0617	0.0434	0.0980	0.0513	0.0627	0.0513	0.1400	0.0682
70-75	0.0792	0.0868	0.0937	0.1293	0.1780	0.1527	0.0947	0.1527	0.2200	0.2030

Table 36. Effect of annual mortality rate on ICER[@]

Screening* frequency	Base-case			Vijan et al (10)		
	Total cost [+] (Baht)	Total [+] blindness (person)	ICER [++] (Baht/additional blindness prevented)	Total cost [+] (Baht)	Total [+] blindness (person)	ICER [++] (Baht/additional blindness prevented)
None	13,425,046.29	1,920	-	21,656,349.31	3,307	-
Every 4 years	20,824,736.62	1,834	85,976.89	31,368,816.74	3,165	68,323.77
Every 3 years	21,919,089.29	1,816	62,806.34	32,679,517.36	3,140	53,096.97
Biannual	23,569,641.06	1,793	70,553.97	34,625,013.41	3,108	59,597.50
Annual	26,997,752.90	1,757	95,865.04	38,644,104.52	3,059	83,195.57

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Mortality / Sen_Mortality rate_Vijan).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

1.8.2 Annual mortality rate derived from Javitt et al (11)

In sensitivity analysis, the value of annual mortality risk in type 2 DM with DR was varied at 25 percent from base-case analysis (see table 23). Thus, annual mortality rates used in the sensitivity analysis were shown in table 37. Table 38 shows the effect of annual mortality rate in each state of DR on ICER. By decreasing the annual mortality risk 25 percent, total number of blindness would be

increased, and the ICER would be decreased about 3.96-6.11 percent from the base-case analysis. By increasing the annual mortality risk 25 percent, total number of blindness would be decreased, and the ICER would be increased about 4.06-6.51 percent from the base-case analysis.

Figure 16 indicates that if annual mortality risk decreased, the ICER would be decreased, as compared to the base-case analysis. If annual mortality risk increased, the ICER would be increased, as compared to the base-case analysis.

Table 37. Annual mortality rates in each state of diabetic retinopathy: Annual mortality risk

Age (year)	Annual mortality rates									
	NDR		BDR		PDR		ME		Blindness	
	Annual mortality risk in type 2 DM		Annual mortality risk in type 2 DM		Annual mortality risk in type 2 DM		Annual mortality risk in type 2 DM		Annual mortality risk in type 2 DM	
	4.7%	7.8%	6.8%	11.4%	8.6%	14.4%	7.0%	11.6%	14.9%	24.9%
40-44	0.0258	0.0413	0.0366	0.0594	0.0494	0.0781	0.0374	0.0606	0.0809	0.1306
45-49	0.0268	0.0423	0.0376	0.0604	0.0519	0.0806	0.0384	0.0616	0.0834	0.1331
50-54	0.0284	0.0439	0.0392	0.0620	0.0559	0.0846	0.0400	0.0632	0.0874	0.1371
55-59	0.0309	0.0464	0.0417	0.0645	0.0621	0.0909	0.0425	0.0657	0.0936	0.1434
60-64	0.0338	0.0493	0.0446	0.0674	0.0694	0.0981	0.0454	0.0686	0.1009	0.1506
65-69	0.0395	0.0550	0.0503	0.0731	0.0836	0.1124	0.0511	0.0743	0.1151	0.1649
70-75	0.0715	0.0870	0.0823	0.1051	0.1636	0.1924	0.0831	0.1063	0.2200	0.2200

Table 38. Effect of annual mortality risk in type 2 DM with DR on ICER[@]

Screening frequency*	Annual mortality risk		
	Base-case – 25%	Base-case	Base-case + 25%
Total cost (Baht)[+]			
None	15,514,222.70	13,425,046.29	11,699,291.87
Every 4 years	23,503,620.66	20,824,736.62	18,580,764.15
Every 3 years	24,653,996.81	21,919,089.29	19,622,948.90
Biannual	26,380,090.05	23,569,641.06	21,203,199.43
Annual	29,956,543.67	26,997,752.90	24,494,169.48
Total blindness (person)[+]			
None	2,291	1,920	1,622
Every 4 years	2,192	1,834	1,547
Every 3 years	2,172	1,816	1,531
Biannual	2,147	1,793	1,509
Annual	2,108	1,757	1,476
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	80,723.31	85,976.89	91,570.31
Every 3 years	59,878.29	62,806.34	65,753.80
Biannual	67,198.31	70,553.97	73,986.12
Annual	92,067.99	95,865.04	99,761.39

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Mortality / Sen_Mortality risk).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

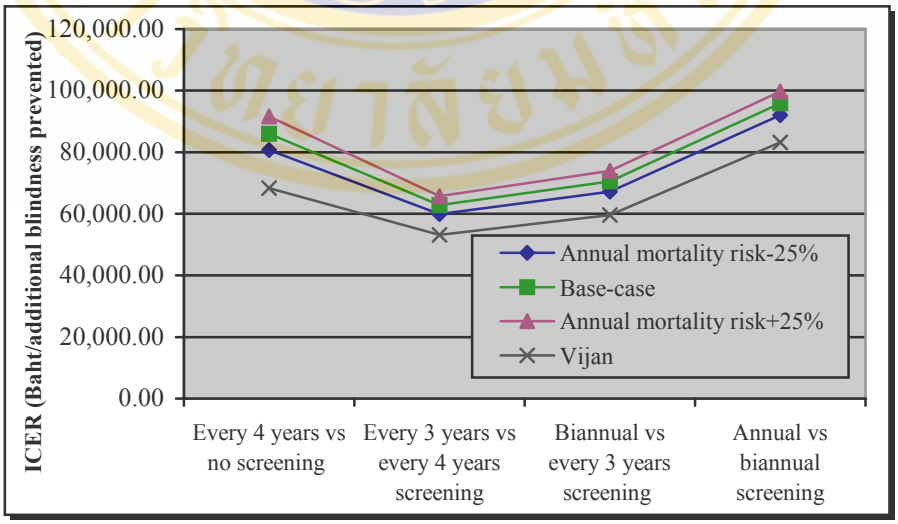


Figure 16. Effect of annual mortality risk in type 2 DM with DR on ICER

1.9 Effect of glycemic control on the rate of progression of DR

For sensitivity analysis, it was assumed that screening might improve glycemic control. Since the screened patients were informed of their status of DR then they might change their behaviors resulting in better glycemic control. As the result, the rate of progression to worsening DR will be retarded. In sensitivity analyses, the incidence of developing DR and progressing through the states of DR was assumed to be related to level of glycemic control. Adjustment for the incidence rates of DR as the result of screening was performed using two strategies derived from two different studies.

1.9.1 Eastman's study (48)

Eastman et al (48) proposed the adjustments of the incidence rates (hazard rate) for glycemic control. Hazard rate for intensive care was equal to the hazard rate (standard care) multiplied of an adjustment factor c^{β}. The equation was presented as follows,

Hazard rates (intensive care) = hazard rates (standard care) x c^{β} [equation 11]

Where, c was the ratio of HbA_{1C} under intensive care to HbA_{1C} under standard care, and β was a constant supplied by Eastman et al (48). The value of β for progression to BDR, ME, and PDR were 10.1, 1.20, and 6.30, respectively. In base-case analysis, it was assumed that HbA_{1C} level of patients were 10 percent. According to the calculation from equation 11, if the screening resulted in the decrease rate of DR progression via improving glycemic control from HbA_{1C} 10% to 9% or 7%, the annual disease progression rate would be decreased, as illustrated in table 39.

Table 39. Annual disease progression rates for each glycemic level: Eastman et al (48)

Transition probability	Duration of DM (years)	Annual disease progression rate		
		HbA_{1C}: 10% [Base-case]	**HbA_{1C}: 9%**	**HbA_{1C}: 7%**
NDR to BDR	1-4	0.1479	0.0510	0.0040
(tp1)	5-9	0.1596	0.0551	0.0044
	10-14	0.1241	0.0428	0.0034
	15+	0.0785	0.0271	0.0021
BDR to PDR	1-4	0.0.123	0.0063	0.0013
(tp2)	5-9	0.0149	0.0077	0.0016
	10-14	0.0204	0.0105	0.0022
	15+	0.0257	0.0132	0.0027
BDR to ME	1-4	0.0945	0.0833	0.0616
(tp3)	5-9	0.1154	0.1017	0.0752
	10-14	0.1112	0.0980	0.0725
	15+	0.0840	0.0740	0.0548

Table 40 shows the effects of glycemic control on the progression rate of DR on ICER. According to Eastman' s study (48), if the screening resulted in the decreased rate of DR progression via improving the glycemic control from HbA_{1C} 10% to HbA_{1C} 9%, total cost and the total number of blindness would be decreased. Then, the ICER would be decreased about 68.40-92.80 percent from base-case analysis, resulting in the increased of cost-effectiveness for screening. Moreover, if HbA_{1C} level was decreased to 7%, the ICER would be decreased about 83.83-98.45 percent from the base-case analysis.

Table 40. Effect of glycemic control on the rate progression of DR on ICER: Eastman et al (48)[@]

Screening frequency*	Glycemic control: Eastman's method (48)		
	HbA_{1C}: 10% [Base-case]	HbA_{1C}: 9%	HbA_{1C}: 7%
Total cost (Baht)[+]			
None	13,425,046.29	13,425,046.29	13,425,046.29
Every 4 years	20,824,736.62	19,474,209.53	18,422,091.77
Every 3 years	21,919,089.29	20,355,315.56	19,140,431.17
Biannual	23,569,641.06	21,519,356.47	19,893,615.47
Annual	26,997,752.90	24,041,900.80	20,974,338.68
Total blindness (person)[+]			
None	1,920	1,920	1,920
Every 4 years	1,834	1,645	1,397
Every 3 years	1,816	1,601	1,326
Biannual	1,793	1,501	1,166
Annual	1,757	1,135	439
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	85,976.89	22,008.45	9,560.37
Every 3 years	62,806.34	19,848.93	10,155.40
Biannual	70,553.97	11,704.83	4,685.28
Annual	95,865.04	6,897.92	1,487.39

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Glycemic control_Eastman).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

1.9.2 Vijan's study (10)

Vijan et al (10) presented that the incidence of developing and progressing through the states of BDR was related to the level of glycemic control. The annual progression rate from NDR to BDR (tp1) was 0.0406, 0.0761, 0.1425 and 0.2669 for 7% HbA_{1C}, 9% HbA_{1C}, 11% HbA_{1C}, and 13% HbA_{1C}, respectively. Progression beyond BDR to PDR (tp2), ME (tp3), and Blindness was assumed to be independent of level of glycemic control.

Table 41 illustrates the effects of glycemic control on the rate progression of DR on ICER. The ICER of HbA_{1C} 11% comparing every 4 years screening vs. no screening, every 3 years screening vs. every 4 years screening, biannual screening vs. every 3 years screening, and annual screening vs. biannual screening was 85,018.50 Baht, 61,482.22 Baht, 70,236.20 Baht, and 95,381.66 Baht,

respectively. If the screening resulted in the decrease rate of DR progression via improving the glycemic control from HbA_{1C} 11% to HbA_{1C} 9% and HbA_{1C} 7%, the probability was changed from 0.1425 to 0.0761 and 0.0406, respectively. If glycemic level was decreased from HbA_{1C} 11% to HbA_{1C} 9%, the ICER would be decreased about 48.71-85.06 percent from base-case analysis. Moreover, if HbA_{1C} level was decreased to 7%, the ICER would be decreased about 61.07-94.77 percent from the base-case analysis.

However, the ICER calculated from Eastman's method (48) was less than that of Vijan' s method (10). It might be the case that glycemic control from Eastman's method (48) had an impact on tp1,tp2, and tp3, while effect of glycemic control derived from Vijan's method (10) affected only tp1. As the result, the total cost, the total number of blindness, and the ICER were calculated from Eastman's method were lower than Vijan's method.

Table 41. Effect of glycemic control on the rate progression of DR on ICER: Vijan et al (10)[@]

Screening frequency*	Glycemic control: Vijan's method (10)			
	HbA_{1C}: 10% [Base-case]	HbA_{1C}: 11%	HbA_{1C}: 9%	HbA_{1C}: 7%
Total cost (Baht)[+]				
None	13,425,046.29	13,381,550.74	13,381,550.74	13,381,550.74
Every 4 years	20,824,736.62	20,802,882.35	20,346,927.54	20,077,272.33
Every 3 years	21,919,089.29	21,886,860.41	21,296,910.37	20,929,439.03
Biannual	23,569,641.06	23,549,656.82	22,709,018.71	22,120,374.21
Annual	26,997,752.90	27,003,661.09	25,748,720.32	24,327,835.03
Total blindness (person)[+]				
None	1,920	1,917	1,917	1,917
Every 4 years	1,834	1,829	1,759	1,717
Every 3 years	1,816	1,812	1,722	1,666
Biannual	1,793	1,788	1,656	1,564
Annual	1,757	1,752	1,444	1,123
ICER (Baht/additional blindness prevented)[++]				
None	-	-	-	-
Every 4 years	85,976.89	85,018.50	44,093.52	33,474.60
Every 3 years	62,806.34	61,482.22	25,926.96	16,765.22
Biannual	70,553.97	70,236.20	21,494.70	11,688.16
Annual	95,865.04	95,381.66	14,324.38	5,012.96

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Glycemic control_Vijan).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

2. Cost data

Based on base-case analysis, the cost was obtained from Ramathibodi hospital. For sensitivity analyses were examined the robustness of the results by changing staff salaries, prices of equipment, prices of drug, and resource utilization. Cost parameters for one-way sensitivity analysis were shown in table 23. Details of calculation and data sources were presented in appendix C and D.

2.1 Discount rate

In base-case analysis, costs and outcomes (blindness) were discounted at 3 percent per year. Table 42 and figure 17 show the effect of discount rate on ICER. For sensitivity analysis, by raising the discount rate from 3 percent to 5 percent, total costs and total number of blindness would be decreased. As the result, the ICER

would be reduced about 15.33-19.94 percent from baseline. If the discount rate was decreased to be 0 percent, the total cost would be increased resulting in the increase of the ICER about 30.59-39.73 percent from the baseline.

Table 42. Effect of discount rate on ICER[@]

Screening frequency*	Discount rate		
	0%	3% [Base-case]	5%
Total cost (Baht)			
None	17,476,488.88	13,425,046.29	11,803,263.75
Every 4 years	28,085,091.48	20,824,736.62	17,711,494.81
Every 3 years	29,660,052.17	21,919,089.29	18,570,895.36
Biannual	31,984,257.67	23,569,641.06	19,892,611.10
Annual	36,595,232.19	26,997,752.90	22,740,057.74
Total blindness (person)			
None	1,977	1,920	1,883
Every 4 years	1,889	1,834	1,799
Every 3 years	1,871	1,816	1,782
Biannual	1,847	1,793	1,759
Annual	1,810	1,757	1,724
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	119,671.07	85,976.89	69,980.61
Every 3 years	87,756.38	62,806.34	50,279.84
Biannual	96,456.08	70,553.97	57,594.69
Annual	125,187.44	95,865.04	81,173.25

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Discount rate).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

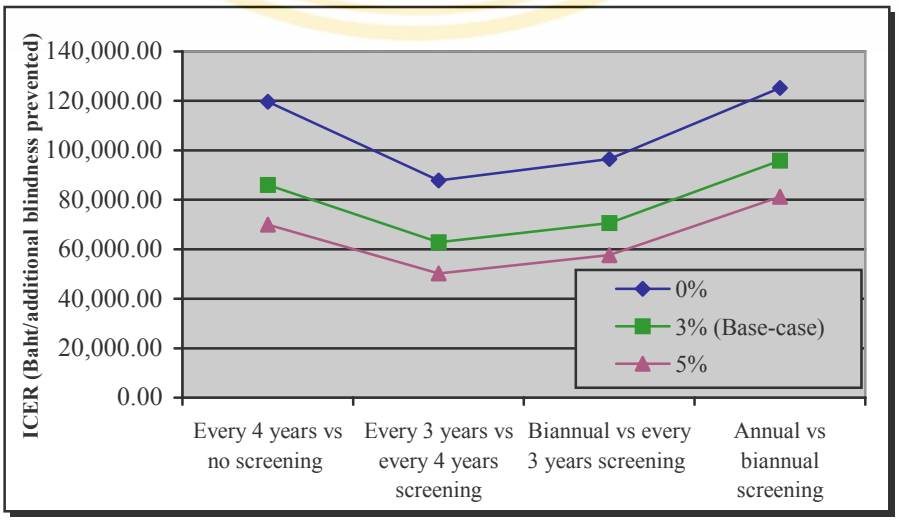


Figure 17. Effect of discount rate on ICER

2.2 Cost of eye screening examination

Cost of eye screening examination was one of the major costs in the study. Table 43 and figure 18 show the effect of eye screening examination cost on ICER. In sensitivity analysis, cost of eye screening examination was varied from 50.75 Baht (minimum) to 260.71 Baht (maximum). Details of cost calculation were shown in appendix C and D. It was found that if cost of eye screening examination decreased approximately 55.40 percent (50.75 Baht) from base-case analysis (113.79 Baht), the ICER would be decreased approximately 58.17-60.77 percent, resulting in the higher cost-effectiveness for screening. On the other hand, if cost of screening increased approximately 129.12 percent (260.71 Baht) from the base-case analysis, the ICER would be increased approximately 136.62-142.26 percent.

Table 43. Effect of eye screening examination cost on ICER[@]

Screening frequency*	**Eye screening cost (Baht)**		
	50.75	**113.79 [Base-case]**	**260.71**
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	34,274.80	85,976.89	206,938.48
Every 3 years	24,639.91	62,806.34	152,155.18
Biannual	28,311.74	70,553.97	169,556.60
Annual	40,095.78	95,865.04	226,836.74

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Cost_Screening).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening). Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

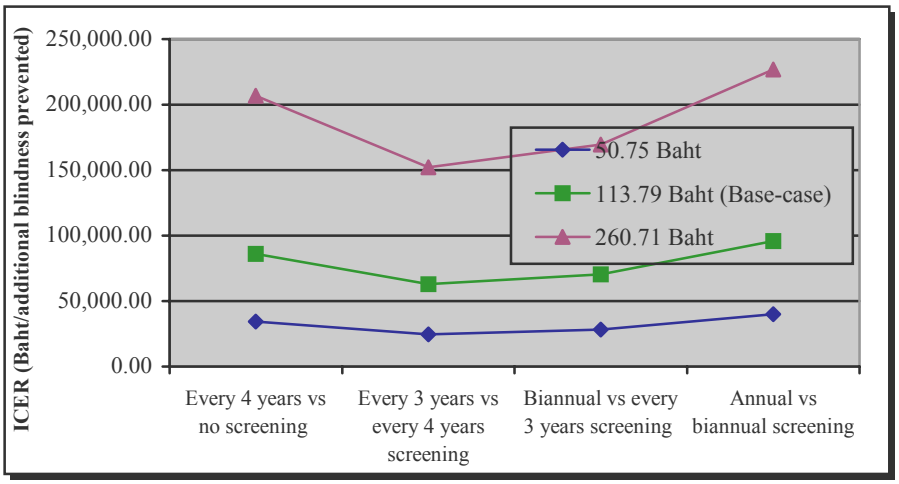


Figure 18. Effect of eye screening examination cost on ICER

2.3 Cost of laser treatment

Table 44 and figure 19 present the effect of laser photocoagulation cost on ICER. Cost of panretinal photocoagulation for PDR was varied from 602.23 Baht per course (minimum) to 5,666.49 Baht per course (maximum). Cost of focal or grid photocoagulation for ME was varied from 257.61 Baht per course (minimum) to 2,370.16 Baht per course (maximum). Details of cost calculation were shown in appendix C and D. It was found that if cost of laser photocoagulation decreased approximately 72.33-74.19 percent (602.23 Baht per course for PDR and 257.61 Baht per course for ME) from base-case analysis (2,333.41 Baht per course for PDR and 931.08 Baht per course for ME), the ICER would be decreased approximately 5.60-8.65 percent. On the other hand, if cost of laser photocoagulation increased approximately 142.84-154.56 percent (5,666.49 Baht per course for PDR and 2,370.16 Baht per course for ME) from the base-case analysis, the ICER would be increased approximately 11.28-17.18 percent.

Table 44. Effect of laser photocoagulation cost on ICER[@]

Screening frequency*	**Laser photocoagulation cost (Baht per course)**		
	PDR: 602.23 ME: 257.61	**PDR: 2,333.41 ME: 931.08 [Base-case]**	**PDR: 5,666.49 ME: 2,370.16**
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	80,956.14	85,976.89	95,834.69
Every 3 years	57,370.58	62,806.34	73,596.40
Biannual	65,097.58	70,553.97	81,429.97
Annual	90,497.08	95,865.04	106,677.30

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Cost_Laser).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening). Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

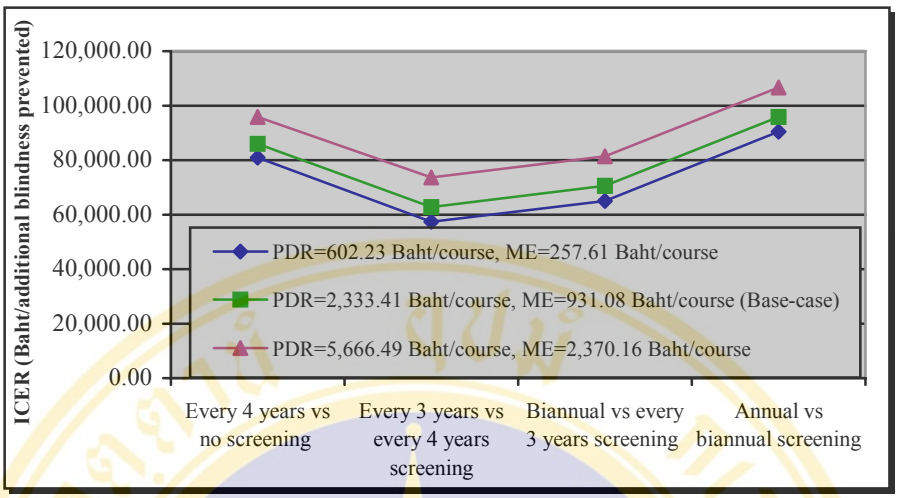


Figure 19. Effect of laser photocoagulation cost on ICER

2.4 Total cost of vitrectomy

Table 45 and figure 20 present the effect of total cost of vitrectomy on ICER. Total cost of vitrectomy was varied from 14,849.81 Baht (minimum) to 34,797.25 Baht (maximum). Details of cost calculation were shown in appendix C and D. It was found that if total cost of vitrectomy decreased approximately 28.69 percent (14,849.81 Baht) from base-case analysis (20,825.61 Baht), the ICER would be increased approximately 3.06-5.81 percent. On the other hand, if total cost of vitrectomy increased approximately 67.09 percent (34,797.25 Baht) from the base-case analysis, the ICER would be decreased approximately 7.16-13.59 percent, resulting in the higher cost-effectiveness for screening.

Table 45. Effect of total cost of vitrectomy on ICER[@]

Screening frequency*	**Total cost of vitrectomy (Baht)**		
	14,849.81	**20,825.61 [Base-case]**	**34,797.25**
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	89,786.74	85,976.89	77,069.33
Every 3 years	66,455.89	62,806.34	54,273.56
Biannual	74,017.11	70,553.97	62,457.02
Annual	98,800.75	95,865.04	89,001.22

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Cost_Vitrectomy).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening). Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

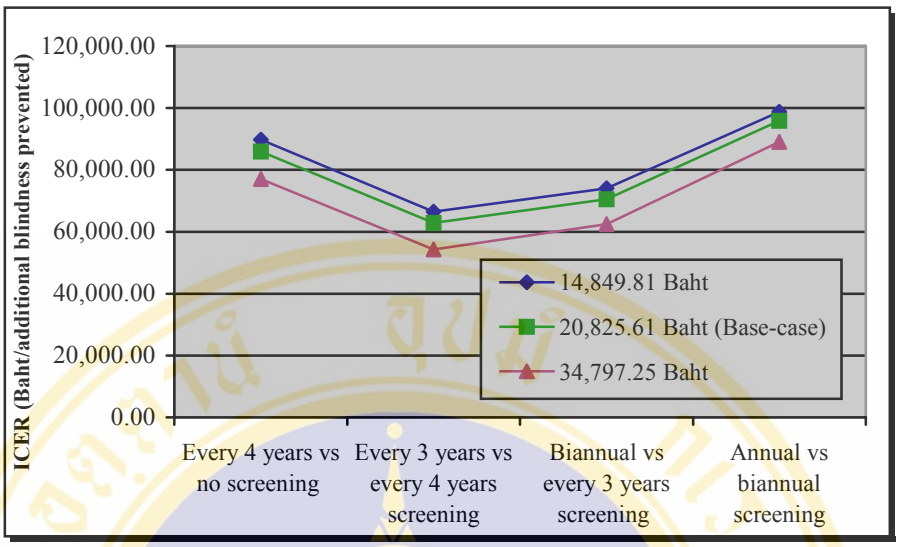


Figure 20. Effect of total cost of vitrectomy on ICER

2.5 Indirect cost

In base-case analysis, all direct medical costs associated with disease were considered. The impact of indirect cost was, further, examined in the sensitivity analysis. Indirect cost was calculated using human capital approach. Cost of morbidity was estimated by multiplying the total number of patient-days loss from work due to illness by the average earning per day (Gross Domestic Product (GDP) per capita divided by 365) of each patient. The patients who were blind from DR would be assumed as permanent disability. For blinded patients aged over 60 years old, indirect cost was not calculated since they were assumed to be retired. Mortality costs was assumed to be equal to the productivity losses from permanent disability. Costs of permanent disability and mortality were calculated from GDP per capita. According to the National Statistical Office, Thailand 2002, GDP per capita was 85,951.00 Baht. Details of analysis were shown in CD ROM (DR_Markov_Model / Sen_Indirect cost).

Table 46 shows that the inclusion of indirect cost in the model lead to the increase of the net benefit of screening. After the indirect cost was incorporated in the model, the discounted cost among unscreened patients was 426,673,744.84 Baht, which was higher than that of screened patients. Moreover, it was found that cost of

annual screening was the lowest, as compared to other frequency of screening interval.

Table 46. Effect of indirect cost on total cost [@]

Screening frequency*	Total cost (Baht)[+]	
	Base-case without indirect cost	Including indirect cost
None	13,425,046.29	436,977,739.75
Every 4 years	20,824,736.62	435,378,742.16
Every 3 years	21,919,089.29	432,501,235.52
Biannual	23,569,641.06	429,271,129.72
Annual	26,997,752.90	426,673,744.84

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Indirect cost).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

3. Probability of medical treatment seeking among unscreened patients

In base-case analysis, it was assumed that some patients in the group being unscreened might seek medical treatment, if they had PDR or ME. The probabilities were derived from expert opinions.

3.1 Probability of medical treatment seeking among unscreened PDR patients

Table 46 and figure 21 show the effect of the probability of medical treatment seeking among unscreened PDR patients. It was found that if the probability of medical treatment seeking among unscreened PDR patients was approximately 30 percent, ICER would be increased approximately 1.66-41.40 percent from base-case analysis (20 percent). On the other hand, if unscreened symptom patients hardly seek to the doctor (approximately 10 percent), the ICER would be decreased approximately 1.41-30.45 percent from the base-case analysis.

Table 47. Effect of probability of medical treatment seeking among unscreened PDR patients on ICER[@]

Screening frequency*	Probability of treatment seeking among unscreened PDR		
	PDR: 10%	PDR: 20% [Base-case]	PDR: 30%
Total cost (Baht)[+]			
None	11,990,235.91	13,425,046.29	14,320,140.27
Every 4 years	20,257,033.75	20,824,736.62	21,325,545.59
Every 3 years	21,497,941.24	21,919,089.29	22,310,830.17
Biannual	23,330,046.58	23,569,641.06	23,807,639.23
Annual	26,997,752.90	26,997,752.90	26,997,752.90
Total blindness (person)[+]			
None	1,983	1,920	1,882
Every 4 years	1,844	1,834	1,824
Every 3 years	1,823	1,816	1,810
Biannual	1,796	1,793	1,790
Annual	1,757	1,757	1,757
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	59,798.81	85,976.89	121,574.35
Every 3 years	58,108.07	62,806.34	69,466.61
Biannual	67,559.80	70,553.97	74,627.11
Annual	94,510.90	95,865.04	97,456.28

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Unscreened patient seek doctor / Sen_PDR seek doctor).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

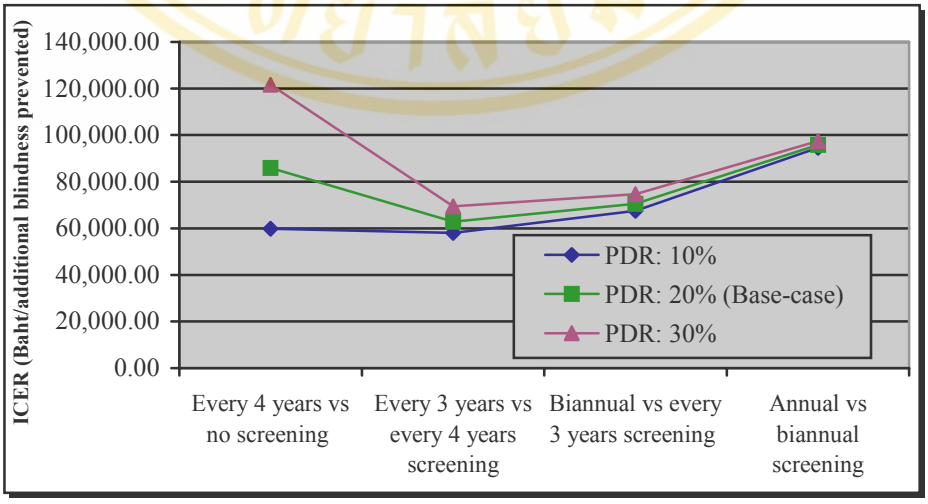


Figure 21. Effect of probability of medical treatment seeking among unscreened PDR patients on ICER

3.2 Probability of medical treatment seeking among unscreened ME patients

Table 48 and figure 22 show the effect of the probability of medical treatment seeking among unscreened ME patients on ICER. It was found that if the probability of medical treatment seeking among unscreened ME patients was 75 percent, then the ICER would be increased approximately 11.90-31.82 percent from base-case analysis (50 percent). On the other hand, if approximately 25 percent of unscreened symptom patients seek medical treatment, the ICER would be decreased approximately 18.31-26.48 percent from the base-case analysis.

Table 48. Effect of probability of medical treatment seeking among unscreened ME patients on ICER[@]

Screening frequency*	Probability of treatment seeking among unscreened ME		
	ME: 25%	ME: 50% [Base-case]	ME: 75%
Total cost (Baht)[+]			
None	11,618,229.51	13,425,046.29	14,226,263.99
Every 4 years	20,092,749.40	20,824,736.62	21,326,846.43
Every 3 years	21,399,088.10	21,919,089.29	22,321,965.21
Biannual	23,293,658.29	23,569,641.06	23,826,069.35
Annual	26,997,752.90	26,997,752.90	26,997,752.90
Total blindness (person)[+]			
None	1,998	1,920	1,887
Every 4 years	1,864	1,834	1,813
Every 3 years	1,838	1,816	1,800
Biannual	1,804	1,793	1,782
Annual	1,757	1,757	1,757
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	63,211.29	85,976.89	96,207.83
Every 3 years	49,792.81	62,806.34	73,744.79
Biannual	56,409.57	70,553.97	86,095.17
Annual	78,310.64	95,865.04	126,365.57

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Unscreened patient seek doctor / Sen_ME seek doctor).

* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.

+Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

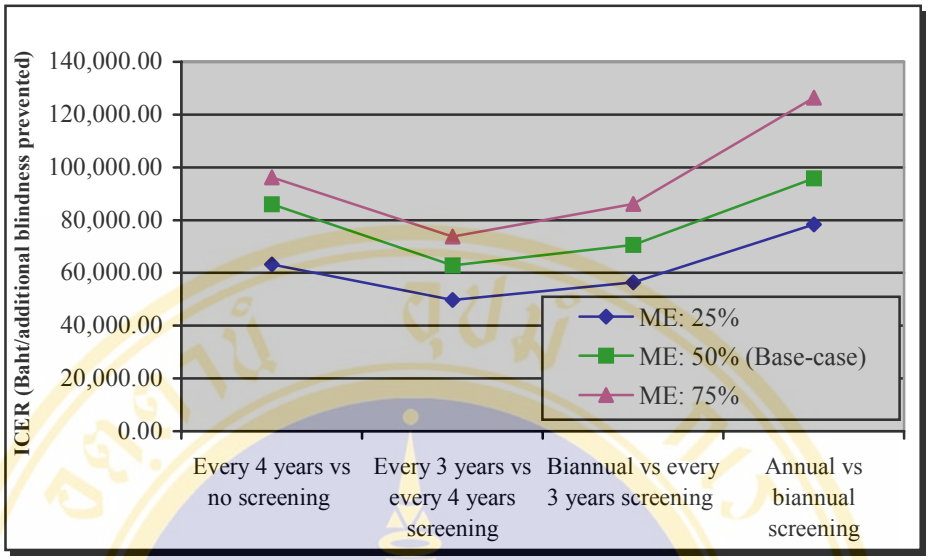


Figure 22. Effect of probability of medical treatment seeking among unscreened ME patients on ICER

4. Probability of being treated with vitrectomy

In base-case analysis, it was assumed that probabilities of being treated with vitrectomy among the unscreened and screened groups were different. The probabilities used in sensitivity analysis were obtained from expert opinions.

4.1 Probability of being treated with vitrectomy among unscreened patients

Table 49 and figure 23 show the effect of probability of being treated with vitrectomy among unscreened patients on ICER. For sensitivity analysis, if the probability of patient being unscreened treated with vitrectomy were approximately 50 percent, the ICER would be decreased approximately 3.66-6.58 percent as compared to base-case analysis (40 percent). On the other hand, if the probability decreased to be 30 percent, the ICER would be increased approximately 3.66-6.58 percent as compared to the base-case analysis.

Table 49. Effect of probability of being treated with vitrectomy among unscreened patients on ICER[@]

Screening frequency*	Probability of being treated with vitrectomy		
	30%	40% [Base-case]	50%
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	90,303.43	85,976.89	81,650.35
Every 3 years	66,940.92	62,806.34	58,671.76
Biannual	74,477.52	70,553.97	66,630.42
Annual	99,368.92	95,865.04	92,361.16

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Vitrectomy / Sen_Vitrectomy_Unscreen).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening). Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

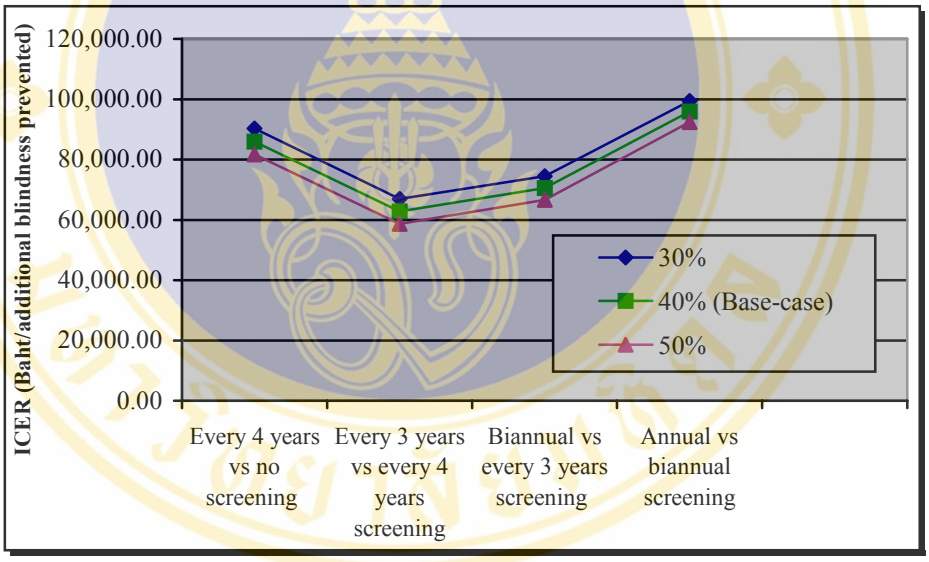


Figure 23. Effect of probability of being treated with vitrectomy among unscreened patients on ICER

4.2 Probability of being treated with vitrectomy among screened patients

Table 50 and figure 24 show the effect of probability of being treated with vitrectomy among screened patients on ICER. For sensitivity analysis, if the probability of patient being treated with vitrectomy among screened group increased to be 10 percent, the ICER would be increased approximately 1.71-2.78 percent as

compared to base-case analysis (7.5 percent). On the other hand, if the probability decreased to 5 percent, the ICER would be decreased approximately 1.71-2.78 percent as compared to the base-case analysis.

Table 50. Effect of probability of being treated with vitrectomy among screened patients on ICER[@]

Screening frequency*	**Probability of being treated with vitrectomy**		
	5%	**7.5% [Base-case]**	**10%**
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	84,138.05	85,976.89	87,815.74
Every 3 years	61,058.10	62,806.34	64,554.58
Biannual	68,894.81	70,553.97	72,213.12
Annual	94,221.41	95,865.04	97,508.67

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Vitrectomy / Sen_Vitrectomy_Screen).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening). Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.

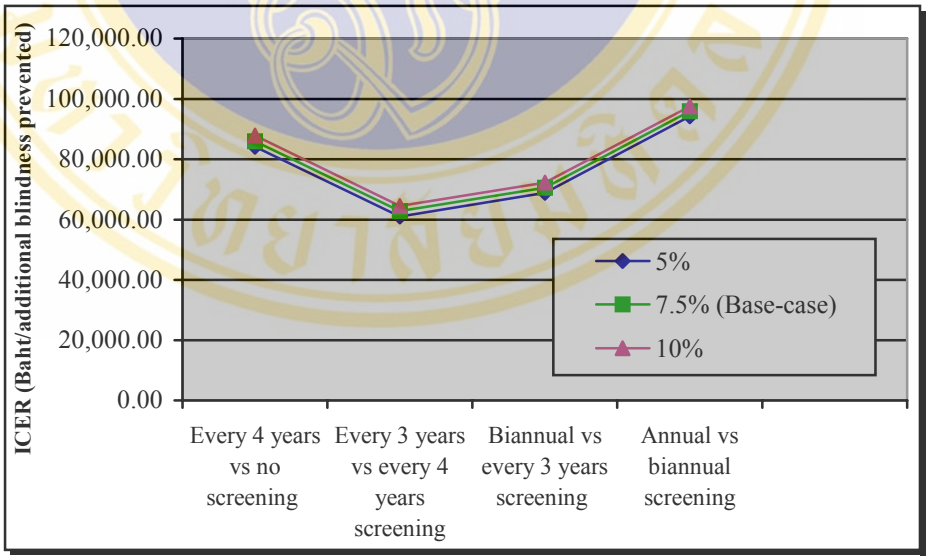


Figure 24. Effect of probability of being treated with vitrectomy among screened patients on ICER

5. Sensitivity and specificity

Sensitivity and specificity of DR screening were ranged 25 percent for one-way sensitivity analysis.

5.1 Sensitivity

Table 51 and figure 25 show the effect of sensitivity on ICER. It was found that if the sensitivity for DR detection was raised 25 percent from base-case analysis, the total number of blindness would be decreased, and the ICER would be decreased approximately 2.92-8.61 percent. On the other hand, if the sensitivity was reduced 25 percent from the base-case analysis, the total number of blindness would be increased, and the ICER would be increased approximately 6.98-18.27 percent.

Table 51. Effect of sensitivity on ICER[@]

Screening frequency*	**Sensitivity**		
	Low (Base-case – 25%)	**Base-case**	**High (Base-case + 25%)**
Total cost (Baht)[+]			
None	13,425,046.29	13,425,046.29	13,425,046.29
Every 4 years	20,440,121.39	20,824,736.62	21,136,289.69
Every 3 years	21,502,933.08	21,919,089.29	22,249,136.96
Biannual	23,133,770.08	23,569,641.06	23,895,233.43
Annual	26,588,293.07	26,997,752.90	27,246,524.03
Total blindness (person)[+]			
None	1,920	1,920	1,920
Every 4 years	1,844	1,834	1,825
Every 3 years	1,829	1,816	1,806
Biannual	1,809	1,793	1,781
Annual	1,779	1,757	1,745
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	91,976.42	85,976.89	81,725.38
Every 3 years	72,621.86	62,806.34	57,395.61
Biannual	83,444.10	70,553.97	64,778.85
Annual	112,184.10	95,865.04	93,064.41

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Sensitivity and Specificity / Sen_Sensitivity).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+ Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++ Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

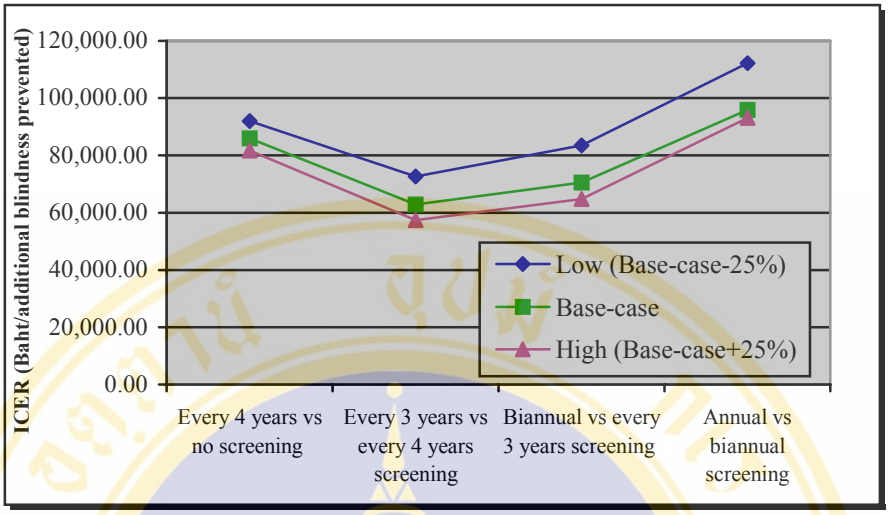


Figure 25. Effect of sensitivity on ICER

5.2 Specificity

Table 52 and figure 26 show the effect of specificity on ICER. It was found that if the specificity for DR detection was reduced 25 percent from baseline, cost associated with the false positive during screening would be increased, and the ICER would be increased approximately 5.37-9.61 percent. On the other hand, if the specificity raised 25 percent from the baseline, total cost would be decreased, and the ICER would be decreased approximately 5.37-9.61 percent.

Table 52. Effect of specificity on ICER[@]

Screening frequency*	Specificity		
	Low (Base-case – 25%)	Base-case	High (Base-case + 25%)
Total cost (Baht)[+]			
None	13,425,046.29	13,425,046.29	13,425,046.29
Every 4 years	21,221,930.90	20,824,736.62	20,427,542.33
Every 3 years	22,386,064.45	21,919,089.29	21,452,114.12
Biannual	24,167,805.22	23,569,641.06	22,971,476.90
Annual	27,925,195.48	26,997,752.90	26,070,310.32
Total blindness (person)[+]			
None	1,920	1,920	1,920
Every 4 years	1,834	1,834	1,834
Every 3 years	1,816	1,816	1,816
Biannual	1,793	1,793	1,793
Annual	1,757	1,757	1,757
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	90,591.89	85,976.89	81,361.90
Every 3 years	66,811.16	62,806.34	58,801.52
Biannual	76,161.73	70,553.97	64,946.20
Annual	105,073.11	95,865.04	86,656.97

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Sen_Sensitivity and Specificity / Sen_Specificity).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+ Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++ Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

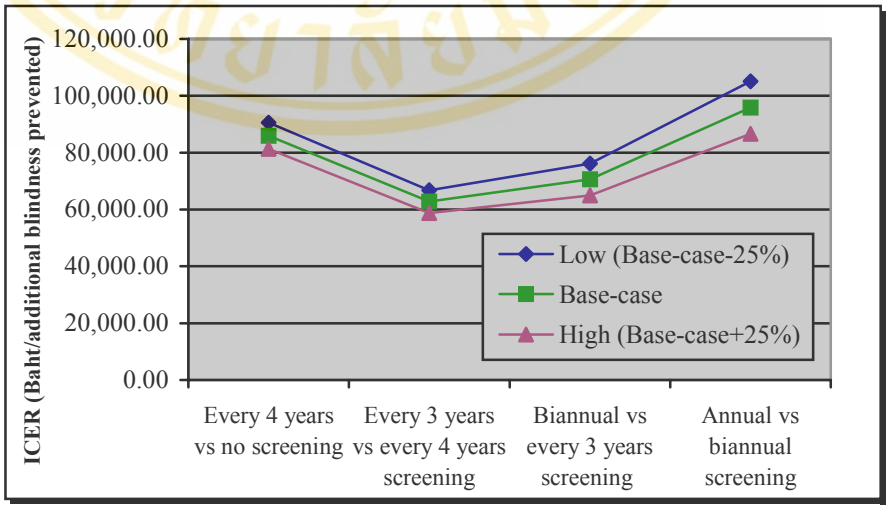


Figure 26. Effect of specificity on ICER

Table 53 displays the summary of result from one-way sensitivity analysis of increased screening frequency.

Table 53. One-way sensitivity analysis of incremental cost-effectiveness ratio of increased screening frequency in Thailand [@]

	Incremental cost-effectiveness ratio[++]			
	Every 4 years	**Every 3 years**	**Biannual**	**Annual**
Base-case analysis	85,976.89	62,806.34	70,553.97	95,865.04
Transition probability				
BDR risk at diagnosis (8, 22)				
5%	80,755.09	83,716.94	75,998.43	112,965.42
20% (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
35%	91,182.08	52,404.62	59,282.63	79,742.82
Transition probability (tp1)				
WESDR:10-year (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
WESDR: 4-year (75)	84,573.47	67,160.35	70,486.44	103,828.52
Taiwan: 4-year (78)	88,401.18	82,858.76	111,509.67	169,488.06
Transition probability (tp2)				
WESDR:10-year (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
WESDR: 4-year (75)	141,696.45	85,737.32	113,431.11	126,665.91
Taiwan: 4-year (78)	77,940.61	66,583.30	62,425.87	92,837.60
Transition probability (tp3)				
WESDR:10-year (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
WESDR: 4-year (75)	87,146.33	61,487.64	70,036.01	93,266.29
Taiwan: 4-year (78)	85,776.72	62,609.76	67,690.02	92,654.89
Transition probability (tp4): Untreatment				
Tp4 = 0.0660	105,827.66	77,691.24	87,151.70	116,696.34
Tp4 = 0.0880 (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
Tp4 = 0.1100	74,704.77	53,546.84	59,873.42	81,642.59
Transition probability (tp5): Untreatment				
Tp5 = 0.0375	97,050.13	76,900.27	89,532.63	131,469.29
Tp5 = 0.0500 (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
Tp5 = 0.0625	77,561.25	53,455.15	58,624.34	75,918.63
Transition probability (tp4): Treatment				
Tp4 = 0.0111	80,279.70	59,042.50	66,521.74	91,063.35
Tp4 = 0.0148 (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
Tp4 = 0.0185	92,146.41	66,811.58	74,816.51	100,870.91
Transition probability (tp5): Treatment				
Tp5 = 0.0248	78,382.46	54,344.10	59,809.23	77,976.71
Tp5 = 0.033 (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
Tp5 = 0.0413	93,770.57	72,504.61	83,445.23	119,377.67

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model). Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus. Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

Table 53. One-way sensitivity analysis of incremental cost-effectiveness ratio of increased screening frequency in Thailand [@] (continued)

	Incremental cost-effectiveness ratio[++]			
	Every 4 years	**Every 3 years**	**Biannual**	**Annual**
Glycemic control :Eastman (48)				
Base-case: HbA1c: 10%	85,976.89	62,806.34	70,553.97	95,865.04
HbA_{1C}: 9%	22,008.45	19,848.93	11,704.83	6,897.92
HbA_{1C}: 7%	9,560.37	10,155.40	4,685.28	1,487.39
Glycemic control: Vijan (10)				
Base-case: HbA_{1C}: 10%	85,976.89	62,806.34	70,553.97	95,865.04
Vijan: HbA_{1C}: 11%	85,018.50	61,482.22	70,236.20	95,381.66
HbA_{1C}: 9%	44,093.52	25,926.96	21,494.70	14,324.38
HbA_{1C}: 7%	33,474.60	16,765.22	11,688.16	5,012.96
Annual mortality				
Annual mortality risk -25%	80,723.31	59,878.29	67,198.31	92,067.99
Base-case	85,976.89	62,806.34	70,553.97	95,865.04
Annual mortality risk +25%	91,570.31	65,753.80	73,986.12	99,761.39
Annual mortality: Vijan (10)	68,323.77	53,096.97	59,597.50	83,195.57
Cost data				
Discount rate				
0%	119,671.07	87,756.38	96,456.08	125,187.44
3% (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
5%	69,980.61	50,279.84	57,594.69	81,173.25
Cost of eye screening				
50.75 Baht	34,274.80	24,639.91	28,311.74	40,095.78
113.79 Baht (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
260.71 Baht	206,938.48	152,155.18	169,556.60	226,836.74
Cost of laser treatment				
PDR: 602.23 Baht per course, ME: 257.61 Baht per course	80,956.14	57,370.58	65,097.58	90,497.08
PDR: 2,333.41 Baht per course, ME: 931.08 Baht per course (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
PDR: 5,666.49 Baht per course, ME: 2,370.16 Baht per course	95,834.69	73,596.40	81,429.97	106,677.30
Total cost of vitrectomy				
14,849.81 Baht	89,786.74	66,455.89	74,017.11	98,800.75
20,825.61 Baht (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
34,797.25 Baht	77,069.33	54,273.56	62,457.02	89,001.22
Indirect cost				
No indirect cost (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
Add indirect cost	-18,578.73	-165,143.90	-138,073.09	-72,634.27

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model). Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus. Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

Table 53. One-way sensitivity analysis of incremental cost-effectiveness ratio of increased screening frequency in Thailand [@] (continued)

	Incremental cost-effectiveness ratio[++]			
	Every 4 years	**Every 3 years**	**Biannual**	**Annual**
Probability of medical treatment seeking among unscreened patients				
PDR: 10%	59,798.81	58,108.07	67,559.80	94,510.90
PDR: 20% (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
PDR: 30%	121,574.35	69,466.61	74,627.11	97,456.28
ME: 25%	63,211.29	49,792.81	56,409.57	78,310.64
ME: 50% (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
ME: 75%	96,207.83	73,744.79	86,095.17	126,365.57
Probability of unscreened patients were treated with vitrectomy				
30%	90,303.43	66,940.92	74,477.52	99,368.92
40 % (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
50%	81,650.35	58,671.76	66,630.42	92,361.16
Probability of screened patients were treated with vitrectomy				
5%	84,138.05	61,058.10	68,894.81	94,221.41
7.5 % (Base-case)	85,976.89	62,806.34	70,553.97	95,865.04
10%	87,815.74	64,554.58	72,213.12	97,508.67
Sensitivity and specificity				
Base-case	85,976.89	62,806.34	70,553.97	95,865.04
Sensitivity: Low (-25%)	91,976.42	72,621.86	83,444.10	112,184.10
Sensitivity: High (+25%)	81,725.38	57,395.61	64,778.85	93,064.41
Specificity: Low (-25%)	90,591.89	66,811.16	76,161.73	105,073.11
Specificity: High (+25%)	81,361.90	58,801.52	64,946.20	86,656.97

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model). Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus. Total costs represents total costs associated with DR over 35 years after diagnosis; all costs and outcome (blindness) are discounted at 3%.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

Best-Worst case analysis

In best-worst analysis, the effects of all parameters affecting ICER were examined simultaneously. For best-case analysis, the values of each parameter that decreased the ICER the most were used. On the other hand, for worst-case analysis, the values of each parameter that increased the ICER the most were used. (Details were shown in appendix A: CD ROM / DR_Markov_Model / Best-Worst case analysis). Table 54 shows the values of each parameter used in best-case analysis and worst-case analysis.

Table 54. Values of each parameter for best-case analysis and worst-case analysis

Parameter	Best-case analysis	Worst-case analysis
Annual disease progression rates		
BDR risk present at diagnosis DM	35% (8, 22)	5% (8, 22)
Transition probability from NDR to BDR (tp1)	WESDR-10 year (73)	Taiwan-4 year (78)
Transition probability from BDR to PDR (tp2)	Taiwan-4 year (78)	WESDR-4 year (75)
Transition probability from BDR to ME (tp3)	Taiwan-4 year (78)	WESDR-10 year (73)
Progression from PDR to Blindness (tp4)	0.1100	0.0660
Progression from PDR to Blindness after treatment	0.0111	0.0185
Progression from ME to Blindness (tp5)	0.0625	0.0625
Progression from ME to Blindness after treatment	0.0248	0.0248
Effect glycemic control on the progression of DR	Decrease 1% Eastman (48)	-
Annual mortality risk in type 2 DM with DR		
NDR	4.7%	7.8%
BDR	6.8%	11.4%
PDR	8.6%	14.4%
ME	7.0%	11.6%
Blindness	14.9%	24.9%
Screening Test		
NDR called BDR	0.04	0.06
NDR called PDR	0.002	0.004
BDR called NDR	0.17	0.28
BDR called PDR	0.01	0.03
PDR called NDR	0.01	0.03
PDR called BDR	0.02	0.04
Sensitivity for ME	0.99	0.62
Specificity for ME	0.98	0.60
Costs (Baht)		
Eye screening examination	50.75	260.71
Panretinal photocoagulation	602.23	5,666.49
Focal /grid photocoagulation	257.61	2,370.16
Vitrectomy	34,797.25	14,849.81
Discount rate (per year)	5%	0%
Others		
Probability of medical treatment seeking among unscreened PDR	10%	30%
Probability of medical treatment seeking among unscreened ME	25%	75%
Probability of unscreened patients were treated with vitrectomy	50%	30%
Probability of screened patients were treated with vitrectomy	5%	10%

Table 55 shows the comparison among base-case analysis, best-case analysis, and worst-case analysis. It was found that, the ICER in best-case analysis for every-4 year screening compared no screen, every 3 years screening compared every 4 years screening, biannual screening compared every 3 years screening, and

annual screening compared biannual screening was reduced to 1,085.49 Baht per additional blindness prevented, 2,128.15 Baht per additional blindness prevented, 1,340.67 Baht per additional blindness prevented, and 1,144.55 Baht per additional blindness prevented, respectively. It was decreased approximately 96.61-98.81 percent, as compared to base-case analysis. On the other hand, the ICER in worst-case analysis for every-4 year screening compared no screening, every 3 years screening compared every 4 years screening, biannual screening compared every 3 years screening, and annual screening compared biannual screening was increased to 1,420,223.51 Baht per additional blindness prevented, 1,121,941.36 Baht per additional blindness prevented, 1,744,455.88 Baht per additional blindness prevented, and 2,081,962.99 Baht per additional blindness prevented, respectively. It was increased approximately 1,551.87-2,372.51 percent, as compared to the base-case analysis.

Table 55. Comparison of base-case analysis, best-case analysis, and worst-case analysis

Screening frequency*	Types of analysis		
	Best-case analysis	**Base-case analysis**	**Worst-case analysis**
Total cost (Baht)[+]			
None	8,373,287.42	13,425,046.29	22,187,935.91
Every 4 years	9,008,293.08	20,824,736.62	44,563,826.46
Every 3 years	9,156,534.17	21,919,089.29	48,717,263.95
Biannual	9,324,385.74	23,569,641.06	56,075,159.20
Annual	9,694,203.72	26,997,752.90	73,516,424.00
Total blindness (person)[+]			
None	2,289	1,920	1,300
Every 4 years	1,704	1,834	1,284
Every 3 years	1,634	1,816	1,281
Biannual	1,509	1,793	1,277
Annual	1,186	1,757	1,268
ICER (Baht/additional blindness prevented)[++]			
None	-	-	-
Every 4 years	1,085.49	85,976.89	1,420,223.51
Every 3 years	2,128.15	62,806.34	1,121,941.36
Biannual	1,340.67	70,553.97	1,744,455.88
Annual	1,144.55	95,865.04	2,081,962.99

[@] Data was derived from appendix A: CD ROM (DR_Markov_Model / Best-Worst case analysis).
* Population of homogeneous patients age 40 years, newly diagnosed as having type 2 diabetes mellitus.
+Total costs represent total costs associated with DR over 35 years after diagnosis.
++Incremental cost-effectiveness (compared with the preceding screening frequency; e.g. Annual screening compared with every other year screening).

CHAPTER V
DISCUSSION

The aim of this study is to assess the cost-effectiveness of various screening intervals for diabetic retinopathy among type 2 diabetic patients in Thailand, using Markov modeling technique. The results of this study revealed the incremental cost-effectiveness ratio (ICER) of annual screening, biannual screening, every 3 years screening, every 4 years screening, and no screening, as compared to the preceding screening frequency. As expected, it was found that, the discounted incidence rate of blindness among unscreened group was the highest, followed by the rates among every 4 years screening, every 3 years screening, biannual screening, and annual screening, respectively. On the other hand, the cost incurred among annual screening was the highest, followed by the costs among biannual screening, every 3 years screening, every 4 years, and no screening.

The ICER comparing the group being screened every 4 years to the group being unscreened found that it costs about 86,162.62 Baht per additional blindness prevented. The ICER comparing the group being screened every 3 years to the group being screened every 4 years found that it costs about 61,119.85 Baht per additional blindness prevented. The ICER comparing the group being screened biannually to the group being screened every 3 years found that it costs about 67,541.24 Baht per additional blindness prevented. Finally, the ICER comparing the group being screened annually to the group being screened biannually found that it costs about 98,749.59 Baht per additional blindness prevented. The result of this study was different from that of Vijan et al (10). Vijan et al (10) found that retinal screening annually vs. biannually for patients with type 2 diabetes costs $ 107,510 per QALY gained, while screening biannually vs. every 3 years costs $ 49,760 per QALY gained, every 3 years vs. every 5 years costs $ 30,160 per QALY gained,

effective and that consideration should be given to increasing the screening interval. While our findings indicated that an incremental cost incurred from increasing frequency intervals was less than 100,000 Baht, it cost at least $ 16,790 per QALY gained in Vijan et al. Besides the fact that Vijan et al (10), conducted cost utility analysis and their cost of treatment and screening were a lot higher than those used in our study, four differences between their assumptions and our assumptions should be discussed. First, rates of progression of Vijan et al (10) were stratified by age and level of glycemic control. Second, the unscreened patients in Vijan's study (10) did not seek medical treatment for PDR or ME. Thus the cost did not incurred among unscreened group. Third, hypothetical patients in Vijan et al (10) were based on the United States population of diabetic patients. Finally, cost of treatment in Vijan et al (10) was only cost of laser photocoagulation. No cost of vitrectomy was included in Vijan's model.

It was found that an incremental cost incurred from increasing frequency in all screening intervals was less than 100,000 Baht. In addition, all screening intervals were resulted in cost saving when indirect cost was taken into account. Annual screening can prevent the largest number of blindness. However, annual screening may lead to the large amount of budget and require a lot of ophthalmologists. Although annual screening seems to be cost-effective it may not be practical to screen for DR annually due to the limited resources both in terms of budget and the number of the ophthalmologists. Our study suggested that annual screening is the safest strategies for prevent blindness. However, for low risk groups (e.g., good glycemic control, no retinopathy on previous examination), biannual screening may be appropriated. The results from sensitivity analysis showed that the cost of the screening examination was an important parameter affecting the ICER. In addition, labor cost was found to be the highest proportion of the cost of screening. Based on the fact that labor cost for eye screening is the biggest part of cost of eye screening and that there was the inadequacy amount of ophthalmologists, training other health personnel for DR screening technique or use other techniques may be need in better managing DR during the time of inadequacy resources. For example, health officer and health volunteers should be trained in visual acuity measurement and provision of

health education about DR. Nurses, physicians at the distinct level should be trained particularly to measure visual acuity, and using ophthalmoscopy to screen for DR. Ophthalmic nurses and ophthalmologists in the provincial level should be trained to supervise and communicate with health care personnel in other levels. In addition, care of people with diabetes requires a multidisciplinary team with an active participation of the patients. The physicians and ophthalmologists should carefully advise the diabetic patients for the important of routine eye examination including good glycemic control to decrease the progression of DR.

Since the mortality in diabetic patients influence the development of complications. Cardiovascular diseases are the leading causes of mortality in type 2 DM (79). In addition, nephropathy complication was the underlying cause in death (79). In previous studies, Javitt et al (11, 17) assigned a person-years of sight saved for the outcome. While, Vijan et al (10) assessed the value of blindness in terms of quality-adjusted life-years (QALYs). Although presence of more severe retinopathy or visual impairment in diabetics patients is an indicator for increased risk of heart disease death (80), retinopathy, itself, had a small impact in increase mortality risk, as compared to other complications. Also, there is the absence of the utility value for each state of DR in Thailand. Thus, the ICER, assessed as the ratio of the net increase in health care costs to the net increase in blindness prevented in this study would be justified.

When looking at the assumptions used in the study, there are three main differences from the previous studies (10, 11, 49-51). First, the transition probabilities from NDR to BDR (tp1), BDR to PDR (tp2), and BDR to ME (tp3) used in this study were varied with the disease duration of diabetes while the probabilities used in the previous studies (11, 49-51) were assumed to be linear. Second, some of the unscreened patients in this study were assumed to seek medical treatment for PDR or ME by themselves, which is consistent with the real situation. Finally, the probability of patients being treated with laser photocoagulation and vitrectomy among screened patients and unscreened patients were incorporated in the model.

The benefits of screening can be explained by several reasons. Several potential mechanisms of benefits of screening can be explained. First, patients receiving screening will be diagnosed earlier and treated properly. As a result, those patients will have slower rate of progression to blindness (13, 14), as compared to those who are not screened. In this study, we have incorporated this fact into the model by using different probabilities of progression from PDR to blindness and from ME to blindness between unscreened patients and screened patients. In addition, the risks of blindness among patients with PDR or ME, who received treatment were assumed to be decreased (11, 49). The other benefits of screening that were not incorporated in base-case analysis are the benefit of screening on glycemic control and on other eye diseases.

The screening may result in the increase awareness for glycemic control. Those who received screening may increase their effort to control their blood glucose to prevent DR. In addition, clinicians may use aggressive treatment in attempt for better blood glucose control when the eye examination results indicated the progression of DR. When the effect of glycemic control from screening was incorporated in the model, it was found that the ICER would be decreased dramatically from the base-case analysis. The benefit of glycemic control was derived from Eastman's method (48) was higher than that of Vijan' s method (10). It might be the case that glycemic control from Eastman's method (48) had an impact on tp1,tp2, and tp3, while effect of glycemic control derived from Vijan's method (10) affected only tp1. In addition, eye screening examination for DR would not only detect DR also detect several eye diseases. However, this benefit was not incorporated in the model.

Screening may also result in several disadvantages. First, it may cause anxiety among people who falsely classified as having disease. In addition, for those whose results were false negative, these people would still remain at risk for DR.

For sensitivity analysis, the impacts of each parameter were examined. As expected, if the cost of eye screening, or cost of laser treatment, or probability of medical treatment seeking among unscreened, or probability of screened patients

being treated with vitrectomy, or annual mortality rate were increased, the ICER would be increased. Consistent with the real situation, if the progression of disease, effectiveness of treatment, or the BDR risk at diagnosis of DM, or discount rate, or cost of vitrectomy, or probability of unscreened patients being treated with vitrectomy, or sensitivity of screening, or specificity of screening were increased, the ICER would be decreased. In addition, if the level of glycemic control among screened patients was incorporated in the model, the cost-effectiveness of screening would be increased dramatically. When the indirect cost was taken into account, all screening intervals would result in cost saving. The indirect cost used in sensitivity analysis, were calculated from GDP per capita. However, it can be calculated by other methods such as interviewing the patients or using information on minimum wage per day can also be calculated. In addition, for blinded patients aged over 60 years old, no indirect cost was calculated since they were assumed to be retired. However, these patients could have a job in the real situation.

The results from one-way sensitivity analysis also indicated that tp1, tp2, effect of glycemic control, cost of screening, had intense impact on the ICER. Therefore, the validity of these parameters should be examined carefully.

For best-worst analysis, the results from best-case analysis, ranging from 96.61-98.81 percent from the base-case analysis. On the other hand, the results from worst-case analysis, ranging from 1,551.87-2,372.51 percent from the base-case analysis. In the worst scenario, it might not be cost-effective for screening thus the ICER of screening was increased dramatically.

Several limitations of this study would be addressed. First, compliance rate of treatment, follow-up program, and screening were assumed to be 100 percent. In addition, all of the patients who were diagnosed with PDR or ME from screening were assumed to received treatment. This assumptions may not be true in the real situation. If the compliance and rate of treatment receiving among screened groups were decreased, the ICER would be increased from the base-case analysis.

Second, the benefits of screening may be underestimated since the DR screening may result in earlier detection of other eye diseases including cataract and

glaucoma. However, this benefit did not include in the model. If this benefit were incorporated in the model, the ICER would be decreased, resulting in the increase of cost-effectiveness of the screening.

Third, in this study, it was assumed that the progression to the next health state was irreversible. In the real situation, if the patients with BDR had good glycemic control, they would be regressed from BDR back to NDR (59). However, the benefit of good glycemic control resulting in the slower rate of DR progression was examined in the sensitivity analysis.

Forth, this study was conducted in the hospital perspective, therefore, the indirect cost was not included. From the societal perspective, when the indirect cost was included, the benefits of screening were outweigh its cost for all screening intervals, as shown in sensitivity analysis.

Fifth, this study did not include the state of having PDR and ME simultaneously in the model. Even though, this state may occur in the real situation it was not documented as a state in several previous studies (11, 49, 51, 52), resulting in the difficulty in obtaining the correct transition probabilities from PDR state or ME state to PDR and ME state, PDR and ME state to Blindness. Based on the reason, the structure of the model was not included state of PDR and ME, which is similar to the previous studies (11, 49, 51, 52). In addition, PDR and ME state were assumed to be the subset of PDR state in this study.

Sixth, the disease modeling in this study estimate the long-term benefit of screening based on the available data. In the absence of study and information in Thailand, the parameters used in the model were derived mostly from the studies conducted in the Western countries and from the expert opinions. However, these parameters were validated by the ophthalmologists in Thailand for their validity. In addition, information on cost including cost of treatment and screening were obtained from one university hospital in Bangkok. It may not be applied for other hospitals. However, in sensitivity analysis, the cost of treatment and screening were varied to determine its impact on ICER result. Also, cost of vitrectomy in this study was an average cost Pars Plana Vitrectomy (PPV) with endolaser, PPV with prefluoron, PPV

with silicone oil injection, and PPV with DK line. However, it should be calculated using the actual proportion of utilization of each method.

Seventh, patients who had PDR or ME were assumed to receive one course of laser photocoagulation or one time of vitrectomy. However, in the real situation, more than one course of laser photocoagulation or one time of vitrectomy may be required.

Finally, the hypothetical patients used in the model were 10,000 newly diagnosed with type 2 DM, age 40 years old with HbA_{1C} 10%. These patients were followed until the age of 75 years old or death, whichever, occurred first. Therefore, the generalizibility of this result to different group of patients should be made with caution.

CHAPTER VI
CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Diabetic retinopathy (DR) is the leading cause of visual impairment. However, it is preventable by early detection of retinopathy and appropriate laser treatment. Most guidelines (29, 34, 37) recommend annual retinal examinations for diabetic patients. Several cost-effectiveness studies comparing several screening intervals were conducted, but no such study was conducted in Thailand before. This study developed a Diabetic Retinopathy using Markov Modeling technique to assess the cost-effectiveness of various screening intervals (annual screening, biannual screening, every 3 years screening, every 4 years screening, and no screening) performed by ophthalmologists using indirect ophthalmoscopy technique for DR among type 2 diabetic patients in hospital perspective.

The structure of the model was derived from the intensive reviews of related literatures (11, 49-51) and expert opinions. The model consisted of six health states: NDR (no diabetic retinopathy), BDR (background diabetic retinopathy or nonproliferative diabetic retinopathy), PDR (proliferative diabetic retinopathy), ME (clinically significant macular edema), Blindness (visual acuity worse than 20/100 in better eye), and Death. The model simulated the progression from NDR to BDR, then either BDR to PDR or to ME, and finally PDR or ME to Blindness. In the model, it was assumed that retinopathy did not regress. Moreover, patients in all health states may be die at any time.

For each state of the model, the patient may progress to the next state including death based on the transition probabilities (tp). The transition probabilities from NDR to BDR (tp1), and BDR to PDR (tp2) or ME (tp3) were derived from the

ten-year of Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) study (73). The rates of progression were dependent on the duration of diabetes. At diagnosis of type 2 diabetes mellitus (DM), twenty percent of patients were assumed to be in the BDR state(49, 74). The rates of progression from PDR or ME to Blindness were derived from Javitt et al (11) and Eastman et al (49). Also, this progression rate was assumed to be decreased with laser treatment. Annual mortality rate for each state was calculated based on the annual mortality risk in type 2 DM with DR and the age-specific mortality in type 2 DM (11). The age-specific mortality data was derived from the Bureau of Health Policy and Strategy Ministry of Public Health, Thailand.

Cost data used in the model were determined from the hospital perspective. Based on Ramathibodi hospital, cost of eye screening examination with indirect ophthalmoscopy technique, which consisted of cost of visual acuity (VA), cost of eye dilatation, cost of anterior segment (A/S) examination, cost of intraocular pressure, and cost of fundoscopic examination, was 113.79 Baht.

Cost per course of laser photocogulation for PDR or ME in the group being screened was 2,333.41 Baht and 931.08 Baht, respectively. Cost per course of laser photocogulation for PDR and ME in the group being unscreened was 2,447.20 Baht and 1,044.87 Baht, respectively. Total cost of vitrectomy in the group being screened and unscreened was 20,825.61 Baht and 20,939.40 Baht, respectively. Follow-up cost of BDR, PDR, and ME was 227.57 Baht per year.

In addition, the model was incorporated the cost for a false positive (misdiagnosis) of the screening. The cost of the false positive for calling PDR or ME was 98.03 Baht. The misdiagnosis for calling BDR was 113.79 Baht.

In base-case analysis, the incremental cost-effectiveness ratio (ICER) of the screening intervals: annual screening, biannual screening, every 3 years screening, and every 4 years screening, as compared to the preceding screening frequency was examined. It was found that after follow a cohort of 10,000 patients, newly diagnosed

with type 2 DM age 40 years until they were 75 years old or death, the cumulative incidence of blindness among no screening, annual screening, biannual screening, every 3 years screening, and every 4 years screening were 1,977 persons, 1,810 persons, 1,847 persons, 1,871 persons, and 1,889 persons, respectively. The discounted cumulative incidence of blindness among no screening, annual screening, biannual screening, every 3 years screening, every 4 years screening were 1,920 persons, 1,757 persons, 1,793 persons, 1,816 persons, and 1,834 persons, respectively. The discounted total cost was 13,425,046.29 Baht among the group being unscreened. It was found that screening every 4 years, every 3 years, biannual, and annual increased the cost to 20,824,736.62 Baht, 21,919,089.29 Baht, 23,569,641.06 Baht, and 26,997,752.90 Baht, respectively. The ICER comparing the group being screened every 4 years to the group being unscreened found that it cost about 85,976.89 Baht per additional blindness prevented. The ICER of increasing screening frequency from every 4 years to every 3 years was 62,806.34 Baht per additional blindness prevented. The ICER of increasing screening frequency from every 3 years to biannual was 70,553.97 Baht per additional blindness prevented. Finally, the ICER of increasing screening frequency from biannual to annual was 95,865.04 Baht per additional blindness prevented.

In one-way sensitivity analysis, the impact of several factors on the estimation of cost-effectiveness analysis was examined, as follows;

- BDR risk at diagnosis

By increasing BDR risk at diagnosis, the total number of blindness and total cost would be increased, and the ICER would be decreased, as compared to the base-case analysis. On the other hand, if BDR risk at diagnosis was decreased, the total number of blindness and total cost would be decreased, and the ICER would be increased, as compared to the base-case analysis.

- Transition probability from NDR to BDR (tp1) and BDR to PDR (tp2) or BDR to ME (tp3)

If the transition probabilities were higher, the total number of blindness and total cost would be increased, and the ICER would be decreased, as compared to the base-case analysis. On the other hand, if the probabilities were lower, the total number of blindness and total cost would be decreased, and the ICER would be increased, as compared to the base-case analysis.

- Transition probability from PDR or ME to Blindness without treatment (tp4 and tp5)

If the transition probabilities from PDR or ME to Blindness without treatment were decreased, the total number of blindness would be decreased, total cost would be increased, and the ICER would be increased from the base-case analysis. If the probability was increased, the total number of blindness would be increased, total cost would be decreased, and the ICER would be decreased from the base-case analysis.

- Transition probability from PDR or ME to Blindness with treatment (tp4 and tp5)

By decreasing the transition probabilities from PDR or ME to Blindness with laser treatment, the effectiveness of treatment would be increased. If the probability from PDR or ME to Blindness with treatment was decreased, the total number of blindness would be decreased, total cost would be increased, and ICER would be decreased from the base-case analysis. If the probability was increased, the total number of blindness would be increased, total cost would be decreased, and the ICER would be increased from the base-case analysis.

- Annual mortality rate

By decreasing the annual mortality rate, the total number of death would be decreased, total number of blindness would be increased, and the ICER would be decreased from the base-case analysis. On the other hand, by increasing the annual mortality rate, total number of blindness would be decreased, and the ICER would be increased from the base-case analysis.

- The effect of glycemic control on the rate of progression

In sensitivity analysis, it was assumed that the screening might improve glycemic control. It was found that if the screening resulted in the decrease rate of DR progression via improving the glycemic control, the total number of blindness, total cost, and the ICER would be decreased.

- Discount rate

By raising the discount rate, total costs and total number of blindness would be decreased. As the result, the ICER was reduced. On the other hand, if the discount rate decreased, total cost and total blindness would be increased resulting in the increase of the ICER.

- Cost of eye screening examination

If cost of eye screening examination decreased, the ICER would be decreased. However, the higher cost of eye screening resulted in the increase of the ICER.

- Cost of laser treatment

As the result of decreasing the cost of laser treatment for PDR and ME, the ICER would be decreased. On the other hand, the increase of cost of laser treatment would lead to the increase of the ICER.

- Cost of vitrectomy

If cost of vitrectomy increased, the ICER would be decreased resulting in the higher cost-effectiveness for screening. On the other hand, if cost of vitrectomy decreased, the ICER would be increased.

- Indirect cost

When indirect cost was added in the sensitivity analysis, it was found that the total cost of no screening was the highest while the total cost of annual screening were the lowest. As the result, all screening intervals were cost-savings.

- Probability of medical treatment seeking among unscreened patients

In base-case analysis, it was assumed that some patients in the group being unscreened might seek medical treatment when they have PDR or ME. If unscreened symptom patients hardly seek to the doctor, the total number of blindness would be increased, total cost would be decreased, and the ICER would be decreased, as compared to the base-case analysis. While the probability of medical treatment seeking among unscreened patients was increased, the ICER would be increased, as compared to the base-case analysis.

- Probability of patients being treated with vitrectomy

If the probability of unscreened patients being treated with vitrectomy were higher, the ICER would be decreased, as compared to the base-case analysis. In addition, if the probability of screened patient being treated with vitrectomy were higher, the ICER would be increased. On the other hand, if the probability of unscreened patients being treated with vitrectomy decreased or the probability of screened patients being treated with vitrectomy increased, the ICER would be increased, as compared to the base-case analysis.

- Sensitivity and specificity

If the sensitivity for detection DR were higher, the total number of blindness and the ICER would be decreased, as compared to the baseline. If the sensitivity were lower, the total number of blindness and the ICER would be increased, as compared to the baseline.

If the specificity for detection DR were higher, the total cost and the ICER would be decreased, as compared to the baseline. If the specificity were lower, the total cost and the ICER would be increased, as compared to the baseline.

For best-worst case analysis, the ICER in the best case and the worse case were calculated by varying all parameters in the model. For the best-case analysis, it was found that the ICER was decreased approximately 96.61-98.81 percent, as compared to

the base-case analysis. On the other hand, the ICER in the worst-case analysis was increased approximately 1,551.87-2,372.51 percent, as compared to the base-case analysis.

Results from this study show that increasing frequency screening interval decreased the incidence rate of blindness. However, the total cost would be increased. The incidence rate of blindness among unscreened group was the highest. On the other hand, the cost incurred among annual screening was the highest. The results from one-way sensitivity analysis also indicated that tp1, tp2, effect of glycemic control, cost of screening, had intense impact on the ICER.

The result from this study would provide useful information for policy makers, practitioners, and providers in making rational policy, guidelines, and recommendation concerning the optimal eye-screening interval for type 2 DM patients. For ophthalmologists, it can also assist in the process of follow-up patients with mild to moderate DR. In addition, it can be used as a tool for disease management and public health planning. Moreover, it will be the basis for further study of other diabetes complications in Thailand.

Recommendations for the further study

1. Utility value should be incorporated in the further study for cost-utility analysis.

2. Further studies should incorporate the values of transitional probabilities and other parameters derived from information and epidemiological studies conducted in Thailand.

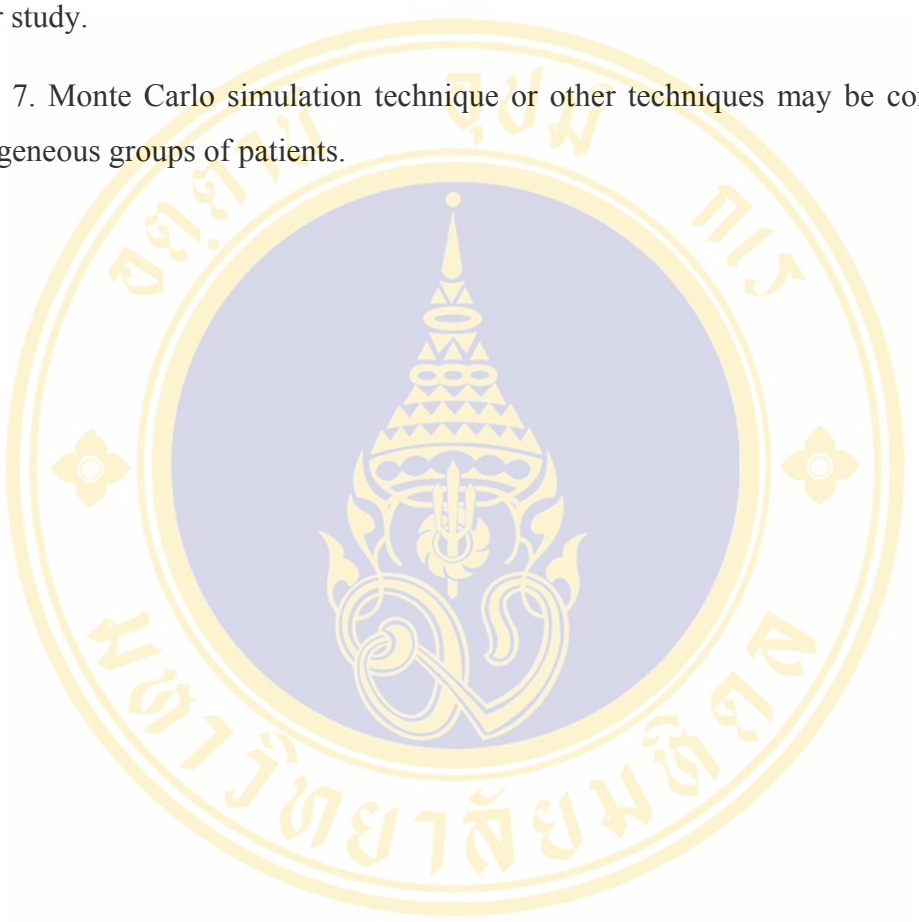
3. Similar study in societal perspective may be conducted.

4. Cost data from other settings may be incorporated in the further study.

5. Various screening techniques such as using digital fundus photography, would be examined.

6. Other risk factors for DR such as blood pressure may be incorporated in the further study.

7. Monte Carlo simulation technique or other techniques may be conducted for heterogeneous groups of patients.



REFERENCES

1. King H, Aubert RE, Herman WH. Global burden of diabetes, 1995-2025: prevalence, numerical estimates, and projections. Diabetes Care 1998; 21: 1414-1431.
2. Hanutsaha P. Strategies used in Thailand for early detection of diabetic retinopathy. Thai J PBI Hlth Ophthalmol 2001; 15(2): 167-172.
3. Ozmen B, Boyvada S. The relationship between self-monitoring of blood glucose control and glycosylated haemoglobin in patients with type 2 diabetes with and without diabetic retinopathy. J Diabetes Complications 2003; 17: 128-134.
4. Liu DP, Molyneaux L, Chua E, et al. Retinopathy in a Chinese population with type 2 diabetes: factors affecting the presence of this complication at diagnosis of diabetes. Diabetes Res Clin Pract 2002; 56: 125-131.
5. Davies R, Roderick P, Canning C, et al. The evaluation of screening policies for diabetic retinopathy using simulation. Diabet Med 2002; 19: 762-770.
6. Negi A, Vernon SA. An overview of the eye in diabetes. J R Soc Med 2003; 96: 266-272.
7. Singer DE, Nathan DM, Fogel HA, et al. Screening for diabetic retinopathy. Ann Intern Med 1992; 116: 660-671.
8. Ausayakhun S, Jiraratsatit J. Prevalence of diabetic retinopathy in non-insulin dependent diabetes mellitus patients. Thai J Opthalmol 1991; 5(2): 133-138.
9. Rasmidatta S, Khunsuk-mengrai K, Warunyuwong C. Risk factors of diabetic retinopathy in non-insulin dependent diabetes mellitus. J Med Assoc Thai 1998; 81(3): 169-174.
10. Vijan S, Hofer TP, Hayward RA. Cost-utility analysis of screening intervals for diabetic retinopathy in patients with type 2 diabetes mellitus. JAMA 2000; 283(7): 889-896.

11. Javitt JC, Aiello LP, Chiang Y, et al. Preventive eye care in people with diabetes is cost-saving to the federal government: Implications for health-care reform. Diabetes Care 1994; 17(8): 909-917.
12. Clark CM, Lee DA. Prevention and treatment of the complications of diabetes mellitus. NEJM 1995: 1210-1216.
13. Squirrell DM, Talbot JF. Screening for diabetic retinopathy. J R Soc Med 2003; 96: 273-276.
14. Fong DS, Aiello L, Gardner TW, et al. Diabetic retinopathy. Diabetes Care 2003; 26: S99-S102.
15. Brechner RJ, Cowie CC, Howie LJ, et al. Ophthalmic examination among adults with diagnosed diabetes mellitus. JAMA 1993; 270: 1714-1718.
16. Schoenfeld ER, Greene JM, Wu SY, et al. Patterns of adherence to diabetes vision care guidelines: baseline findings from the Diabetic Retinopathy Awareness Program. Ophthalmology 2001; 108: 563-571.
17. Javitt JC, Canner JK, Frank RG, et al. Detecting and treating retinopathy in patients with type I diabetes mellitus: A health policy model. Ophthalmology 1990; 97(4): 483-495.
18. Liu W-J, Lee L-T, Yent M-F, et al. Assessing progression and efficacy of treatment for diabetic retinopathy following the proliferative pathway to blindness: implication for diabetic retinopathy screening in Taiwan. Diabet Med 2003; 20: 727-733.
19. Bhuripanyo P, Suwanwatana C, Kiatsayompoo S, et al. Vascular complications in noninsulin dependent diabetes mellitus (NIDDM) in Srinagarind Hospital, Khon Kaen. J Med Assoc Thai 1992; 75(10): 570-577.
20. Nitipinyasakul A, Nitipinyasakul N. Risk factors of ophthalmic complications in diabetes. Thai J Opthalmol 1999; 13: 23-33.
21. Lertmeemongkolchai P, Samaiporn S, Chongwiriyanurak T, et al. Prevalence and risk of diabetic retinopathy in relation to duration of diabetes mellitus in Lampang. The Bulletin of Lampang Hospital. 2002; 23(3): 215-225.
22. Chairungruang A, Thanakitithum K, Ratanapojnard T, et al. The prevalence of diabetic retinopathy in type 2 diabetes mellitus in Phramongkutklao hospital. RTAMedJ 2002; 55: 85-98.

23. Palmer AJ, Weiss C, Sendi PP, et al. The cost-effectiveness of different management strategies for type I diabetes: a Swiss perspective. Diabetologia 2000; 43: 13-26.

24. Coyle D, Lee KM, O'Brien BJ. The role of models within economic analysis: focus on type 2 diabetes mellitus. Pharmacoeconomics 2002; 20(1): 11-19.

25. Funatsu H, Yamashita H. Pathogenesis of diabetic retinopathy and renin-angiotensin system. Ophthal Physiol Opt 2003; 23: 495-501.

26. Porta M, Bandello F. Diabetic retinopathy: A clinical update. Diabetologia 2002; 45: 1617-1634.

27. Ciulla T, Amador A, Zinman B. Diabetic retinopathy and diabetic macular edema: Pathophysiology, screening, and novel therapies. Diabetes Care 2003; 26: 2653-2664.

28. Kinyoun J, Barton F, Fisher M, et al. Detection of diabetic macular edema: Ophthalmoscopy Versus Photography-Early Treatment Diabetic Retinopathy Study Report Number 5. Ophthalmology 1989; 96: 746-751.

29. American Diabetes Association. Diabetic retinopathy. Diabetes Care 2002; 25: S90-S93.

30. Siu SC, Ko TC, Wong KW, et al. Effectiveness of non-mydriatic retinal photography and direct ophthalmoscopy in detecting diabetic retinopathy. HKMJ 1998; 4: 367-370.

31. Stefansson E, Bek T, Porta M, et al. Screening and prevention of diabetic blindness. Acta Opthalmol Scand 2000; 78: 374-385.

32. Hutchinson A, McIntosh A, Peters J, et al. Effectiveness of screening and monitoring tests for diabetic retinopathy-a systematic review. Diabet Med 2000; 17: 495-506.

33. Rowe S, MacLean CH, Shekelle PG. Preventing visual loss from chronic eye disease in primary care: scientific review. JAMA 2004; 291(12): 1487-1496.

34. American Association of Clinical Endocrinologists. Diabetes guidelines. Endocr Pract 2002; 8(1): 40-82.

35. The expert Committee on the Diagnosis and Classification of Diabetes Mellitus. American Diabetes Association: clinical practice recommendations 2002. Diabetes Care 2002; 25: S1-S147.

36. Preferred Practice Patterns: Diabetic Retinopathy. Sanfrancisco. Calif: American Academy of Ophthalmology. 1998.

37. American Optometric Association. Optometric Clinical Practice Guideline: care of the patient with diabetes mellitus: reference guide for clinicians, third revision. 2002.

38. National Committee for Quality Assurance. Diabetes quality improvement project initial measure set (final version). 2004.

39. National Guideline Clearinghouse. Guideline title: the management of diabetes mellitus in the primary care setting. 2004.

40. International Diabetes Center. Type 2 Diabetes Practice Guidelines. Minneapolis, Minn: International Diabetes Center; 2001.

41. Chang CJ, Lu FH, Yang YC, et al. Epidemiologic study of type 2 diabetes in Taiwan. Diabetes Res Clin Pract 2000; 50(2): S49-S59.

42. Weinstein MC, Brien BO, Hornberger J, et al. Principles of Good Practice for Decision Analysis Modeling in Health-Care Evaluation: Report of the ISPOR Task Force on Good Research Practices-Modeling Studies. Value in health 2003; 6(1): 9-17.

43. Hunink M, Glasziou P. Decision making in health and medicine: Integrating evidence and values: The press syndicate of the university of Cambridge; 2001.

44. Herman WH. Diabetes modeling. Diabetes Care 2003; 26(11): 3182-3183.

45. Sonnenberg FA, Beck JR. Markov Models in Medical Decision Making: A Practical Guide. Med Decis Making 1993; 13: 322-338.

46. Sakthong P, Tangphao O, Eiam-ong S, et al. Cost-effectiveness of using angiotensin-converting enzyme inhibitors to slow nephropathy in normotensive patients with diabetes type II and microalbuminuria. Nephrology 2001; 6: 71-77.

47. ฉัตรชัย พานิชศุภกรณ์, ธีรยุทธ รุจิเมธาภาส, ประทีป เปรมศรี. การวิเคราะห์ต้นทุน-ประสิทธิผลของการใช้แคลเซียมเสริมในคนไทยที่มีความเสี่ยงระดับปานกลางต่อการเกิดภาวะกระดูกพรุนที่ได้จากการคัดกรองโดยใช้เครื่องมือ OSTA. [วิทยานิพนธ์ปริญญาเภสัชศาสตรมหาบัณฑิต สาขาวิชาเภสัชกรรมชุมชน]. พิษณุโลก: มหาวิทยาลัยนเรศวร; 2546.

48. Eastman RC, Javitt JC, Herman WH, et al. Model of complications of NIDDM: II. Analysis of the health benefits and cost-effectiveness of treating NIDDM with the goal of normoglycemia. Diabetes Care 1997; 20(5): 735-744.

49. Eastman RC, Javitt JC, Herman WH, et al. Model of complications of NIDDM: I. Model construction and assumptions. Diabetes Care 1997; 20(5): 725-734.

50. CDC Diabetes Cost-Effectiveness Study Group. The cost-effectiveness of screening for type 2 Diabetes. JAMA 1998; 280(20): 1757-1763.

51. Brown JB, Russell A, Chan W, et al. The global diabetes model: user friendly version 3.0. Diabetes Res Clin Pract 2000; 50(3): S15-S46.

52. The Diabetes Control and Complications Trial Research Group. Lifetime benefits and costs of intensive therapy as practiced in the diabetes control and complications trial. JAMA 1996; 276(17): 1409-1416.

53. Palmer AJ, Brandt A, Gozzoli V, et al. Outline of a diabetes disease management model: principles and applications. Diabetes Res Clin Pract 2000; 50(3): S47-S56.

54. Palmer AJ, Sendi PP, Spinas GA. Applying some UK Prospective Diabetes Study results to Switzerland: the cost-effectiveness of intensive glycemic control with metformin versus conventional control in overweight patients with type 2 diabetes. Schweiz Med Wochenschr 2000; 130: 1034-1040.

55. Bagust A, Hopkinson PK, Maier W, et al. An economic model of the long-term health care burden of type II diabetes. Diabetologia 2001; 44: 2140-2155.

56. Walker A, Colagiuri S, McLennan M. Cost-benefit model of diabetes prevention and care, Australia: Model construction, assumptions and validation. In: The diabetes simulation modellers conference; San Francisco; 2002.

57. Javitt JC, Aiello LP. Cost-effectiveness of detecting and treating diabetic retinopathy. Ann Intern Med 1996; 124: 164-169.

58. Davies R, Sullivan P, Canning C. Simulation of diabetic eye disease to compare screening policies. Br J Ophthalmol 1996; 80: 945-950.

59. Brailsford SC, Davies R, Canning C, et al. Evaluating screening policies for the early detection of retinopathy in patients with non-insulin dependent diabetes. Health Care Manag Sci 1998; 1: 115-124.

60. Harper PR, Sayyad MG, Senna VD, et al. A systems modeling approach for the prevention and treatment of diabetic retinopathy. European Journal of Operational Research 2003; 150: 81-91.

61. Bootman J, Townsend R, McGhan WF. Principles of pharmacoeconomics. 2 ed. United States of America: Harvey Whitney books company; 1996.

62. Johnson NE, Nash DB. The role of pharmacoeconomics in outcomes management. USA: American Hospital Publishing; 1996.

63. Koopmanschap MA. Cost of illness studies: useful for health policy. Pharmacoeconomics 1998; 14(2): 143-8.

64. Koopmanschap MA, Rutten FFH. A practical guide for calculating indirect costs of disease. Pharmacoeconomics 2000; 17(6): 621-628.

65. Youngkong S. Costs of cerebral infarction from societal perspective: A case study at Prasat Neurological Institute. [M.S. Thesis in Pharmacy Administration] Bangkok: Faculty of Graduate Studies, Mahidol University; 2001.

66. Pornlertwadee P. Societal perspective on the cost of diabetes mellitus at Ampawa hospital, Samutsongkram province. [M.S. Thesis in Pharmacy Administration] Bangkok: Faculty of Graduate Studies, Mahidol University; 2002.

67. Surver JD, Cooper JC. Principles and methods of managerial cost-accounting systems. Am J Hosp Pharm 1988; 45: 145-152.

68. Finkler SA. The distinction between cost and charges. Ann Intern Med 1982; 96 (1): 102-109.

69. Baker JJ. Activity-based costing and activity-based management for health care. Dallas: An Aspen Publication; 1998.

70. Lerner WM, Wellman WL, Burik D. Pricing hospital unit of service using micro-costing techniques. Hospital and health service administration 1985:7-28.

71. Moss SE, Klein R, Kessler SD, et al. Comparison between ophthalmoscopy and fundus photography in determining severity of diabetic retinopathy. Ophthalmology 1985; 92: 62-67.

72. Brown JB, Palmer AJ, Bisgaard P, et al. The Mt. Hood challenge: cross-testing two diabetes simulation models. Diabetes Res Clin Pract 2000; 50(3): S57-S64.

73. Klein R, Klein BEK, Moss SE, et al. The Wisconsin Epidemiologic Study of Diabetic Retinopathy XIV: ten-year incidence and progression of diabetic retinopathy. Arch Ophthalmol 1994; 112: 1217-1228.

74. Harris MI, Klein R, Welborn TA, et al. Onset of NIDDM occurs at least 4-7 yr before clinical diagnosis. Diabetes Care 1992; 15(7): 815-819.

75. Klein R, Klein BEK, Moss SE, et al. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: X. Four year incidence and progression of diabetic retinopathy when age at diagnosis is 30 years or more. Arch Ophthalmol 1989; 107: 244-249.

76. Klein R, Moss SE, Klein BEK, et al. Relation of ocular ad systemic factors to survival in diabetes. Arch Intern Med 1989; 149: 266-272.

77. Ministry of Public Health. Public health statistics A.D.2002. Bangkok: Bureau of Health Policy and Strategy Ministry of Public Health; 2002.

78. Chen MS, Kao CS, Fu CC, et al. Incidence and progression of diabetic retinopathy among non-insulin-dependent diabetic subjects: a 4-year follow-up. Int J Epidemiol 1995; 24(4): 787-795.

79. Morrish NJ, Stevens LK, Head J, et al. A prospective study of mortality among middle-aged diabetic patients (the London cohort of the WHO Multinational Study of Vascular Disease in Diabetic) I: causes and death rates. Diabetologia 1990: 538-541.

80. Klein R, Klein BEK, Moss SE, et al. Association of ocular disease and mortality in a diabetic population. Arch Ophthalmol 1999; 117: 1487-1495.

APPENDIX

APPENDIX A

Diabetic retinopathy Markov model

See Diabetic retinopathy Markov model in CD ROM:

I. Base-case analysis
:/DR_Markov_Model/Base-case analysis.

II. BDR risk at diagnosis
:/DR_Markov_Model/Sen_BDR risk

III. Transition probability from NDR to BDR (tp1)
:/DR_Markov_Model/Sen_Tp1

IV. Transition probability from BDR to PDR (tp2)
:/DR_Markov_Model/Sen_Tp2

V. Transition probability from BDR to ME (tp3)
:/DR_Markov_Model/Sen_Tp3

VI. Transition probability from PDR to Blindness (tp4): Untreatment
:/DR_Markov_Model/Sen_Tp4_Untreatment

VII. Transition probability from ME to Blindness (tp5): Untreatment
:/DR_Markov_Model/Sen_Tp5_Untreatment

VIII. Transition probability from PDR to Blindness (tp4): Treatment
:/DR_Markov_Model/Sen_Tp4_Treatment

IX. Transition probability from ME to Blindness (tp4): Treatment
:/DR_Markov_Model/Sen_Tp5_Treatment

X. Annual mortality rate of Vijan study
:/DR_Markov_Model/Sen_Mortality/Sen_Mortality rate_Vijan

XI. Annual mortality risk in type 2 DM with DR
:/DR_Markov_Model/Sen_Mortality/Sen_Mortality risk

XII. Effect of glycemic control on the rate progression of DR: Eastman study
:/DR_Markov_Model/Sen_Glycemic control_Eastman

Diabetic retinopathy Markov model (continued)

XIII. Effect of glycemic control on the rate progression of DR: Eastman study
:/DR_Markov_Model/Sen_Glycemic control_Vijan

XIV. Discount rate
:/DR_Markov_Model/Sen_Discount rate

XV. Cost of eye screening examination
:/DR_Markov_Model/Sen_Cost_Screening

XVI. Cost of laser treatment
:/DR_Markov_Model/Sen_Cost_Laser

XVII. Total cost of vitrectomy
:/DR_Markov_Model/Sen_Cost_Vitrectomy

XVIII. Indirect cost
:/DR_Markov_Model/Sen_Indirect cost

XIX. Probability of medical treatment seeking among unscreened PDR patients
:/DR_Markov_Model/Sen_Unscreened patient seek doctor/Sen_PDR seek doctor

XX. Probability of medical treatment seeking among unscreened ME patients
:/DR_Markov_Model/Sen_Unscreened patient seek doctor/Sen_ME seek doctor

XXI. Probability of being treated with vitrectomy among unscreened patients
:/DR_Markov_Model/Sen_Vitrectomy/Sen_Vitrectomy_Unscreen

XXII. Probability of being treated with vitrectomy among screened patients
:/DR_Markov_Model/Sen_Vitrectomy/Sen_Vitrectomy_Screen

XXIII. Sensitivity
:/DR_Markov_Model/Sen_Sensitivity and Specificity/Sen_Sensitivity

XXIV. Specificity
:/DR_Markov_Model/Sen_Sensitivity and Specificity/Sen_Specificity

XXV. Best-Worst case analysis
:/DR_Markov_Model/Sen_Best-Worst case analysis

Appendix B

Work load of Ramathibodi hospital

Detail	Time
One year: work	52 week
One week: work	5 day
Total time of work	260 day / year
Delete sick day	13 day / year
Delete vacation day	10 day / year
Real work-day in one year	**237 day / year**
One day: work	8 hour
Delete lunch time	1 hour
Delete relax time10 % of work time	0.7 hour
Real work-time in one day	**6.3 hour**

Appendix C

Cost analysis of medical services

Table C-1. Cost of visual acuity (VA) measurement

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Assistant Nurse	11,712.27 [5,740-18,500]	3 [2-10]	4.71 [1.54-24.78]	Policy and planning division, and observation
Capital cost				
Durable goods+	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
ETDRS Chart	15,000 [13,500-16,500]	3 [2-10]	0.05 [0.03-0.18]	Ophthalmology department
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
-	-	-	-	-
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.000000568	9.47 [5.68-31.87]	Policy and planning division
Total cost of visual acuity (Baht)			**14.22** [7.25-56.83]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Cost of purchasing of durable good and department allocation cost for sensitivity analysis were varied at 10 percent. Resource utilization for sensitivity analysis was obtained from expert opinions and observation.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours.

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-2. Cost of eye dilatation

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Assistant Nurse	11,712.27 [5,740-18,500]	4 [2-5]	6.28 [1.54-12.39]	Policy and planning division, and observation
Capital cost				
Durable goods+	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
-	-	-	-	-
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
10% phenylephrine HCl eye drop	385.00 [99.51-390]	1 drop [1-3]	3.85 [1-11.70]	Ophthalmology department and interview
1% tropicamide eye drop	202.23 [202.00-232.02]	3 drop [2-5]	2.02 [1.35-3.87]	
2% methylcellulose eye drop	27.00 [24.30-29.70]	1 drop [1-2]	0.14 [0.12-0.30]	
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.000000757	12.62 [5.68-15.94]	Policy and planning division
Total cost of eye dilatation (Baht)			**24.91** [9.68-44.19]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Material cost for sensitivity analysis was derived from Ministry of Public Health. Resource utilization for sensitivity analysis was obtained from expert opinions and observation.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours.

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-3. Cost of anterior segment (A/S) and intraocular pressure

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Doctor	29,561.23 [12,400.00-53,130.00]	4 [3-5]	15.84 [4.98-35.58]	Policy and planning division, and interview
Capital cost				
Durable goods+	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Slit lamp biomicroscope and Goldman Applanation Tonometry	650,000 [585,000-715,000]	4 [3-5]	2.82 [1.90-3.88]	Ophthalmology department
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
-	-	-	-	-
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.000000757	12.62 [8.52-15.94]	Policy and planning division
Total cost of A/S and intraocular pressure (Baht)			**31.28** [15.41-55.40]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Cost of purchasing of durable good and department allocation cost for sensitivity analysis were varied at 10 percent. Resource utilization for sensitivity analysis was obtained from expert opinions.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours.

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-4. Cost of fundoscopic examination with indirect ophthalmolscopy

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Doctor	29,561.23 [12,400.00-53,130.00]	6 [4-10]	23.76 [6.64-71.17]	Policy and planning division, and interview
Capital cost				
Durable goods+	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Indirect ophthalmoscopy and lens 78 or 90 D	105,000 [94,500-115,500]	6 [4-10]	0.68 [0.41-1.25]	Ophthalmology department
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
-	-	-	-	-
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.00000114	18.93 [11.36-31.87]	Policy and planning division
Total cost of fundoscopic examination with indirect ophthalmoscopy (Baht)			**43.38** [18.41-104.29]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Cost of purchasing of durable good and department allocation cost for sensitivity analysis were varied at 10 percent. Resource utilization for sensitivity analysis was obtained from expert opinions.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours.

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-5. Cost of panretinal laser photocogaulation (per time per person)

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Doctor	29,561.23 [12,400.00-53,130.00]	30 [20-40]	118.79 [33.22-284.67]	Policy and planning division, and interview
Capital cost				
Durable goods+	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Laser	4,300,000 [3,870,000-4,730,000]	30 [20-40]	139.79 [83.98-205.30]	Ophthalmology department
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
0.1% diclofenac sodium eye drop	189.39 [109.68-219.35]	1 bottle	189.39 [109.68-219.35]	Ophthalmology department and interview
Paracetamol 500 mg	0.07 [0.05-0.22]	20 tablet [10-30]	1.40 [0.50-6.60]	
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.00000568	94.67 [56.80-95.61]	Policy and planning division
Total cost of panretinal laser photocoagulation (Baht)			**544.22** [284.19-689.03]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Cost of purchasing of durable good and department allocation cost for sensitivity analysis were varied at 10 percent. Material cost for sensitivity analysis was derived from Ministry of Public Health. Resource utilization for sensitivity analysis was obtained from expert opinions.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours.

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-6. Cost of focal/ grid laser photocogaulation (per time per person)

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Doctor	29,561.23 [12,400.00-53,130.00]	20 [15-30]	79.19 [24.91-213.50]	Policy and planning division, and interview
Capital cost				
Durable goods	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Laser	4,300,000 [3,870,000-4,730,000]	20 [15-30]	93.32 [62.99-153.97]	Ophthalmology department
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
0.1% diclofenac sodium eye drop	189.39 [109.68-219.35]	1 bottle	189.39 [109.68-219.35]	Ophthalmology department and interview
Paracetamol 500 mg	0.07 [0.05-0.22]	20 tablet [10-30]	1.40 [0.50-6.60]	
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.00000568	63.11 [42.60-95.61]	Policy and planning division
Total cost of focal/ grid laser photocoagulation (Baht)			**426.41** [240.68-689.03]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Cost of purchasing of durable good and department allocation cost for sensitivity analysis were varied at 10 percent. Material cost for sensitivity analysis was derived from Ministry of Public Health. Resource utilization for sensitivity analysis was obtained from expert opinions.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours.

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-7. Cost of fundoscopic examination with laser (misdiagnosis)

Labor cost				
Labor	Average salaries (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Doctor	29,561.23 [12,400.00-53,130.00]	5 [2-10]	19.80 [3.32-71.17]	Policy and planning division, and interview
Capital cost				
Durable goods+	Cost of purchasing (Baht)	Time spent (minute)	Cost (Baht)	Data sources
Laser	4,300,000 [3,870,000-4,730,000]	5 [2-10]	23.33 [8.40-51.32]	Ophthalmology department
Material cost				
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)	Data sources
-	-	-	-	-
Indirect cost				
Department allocation (Baht)		Allocation rate*	Cost (Baht)	Data sources
16,679,387 [15,011,448.30-18,347,325.70]		0.00000568	15.78 [5.68-31.87]	Policy and planning division
Total cost of fundoscopic examination with laser (Baht)			**58.91** [17.40-154.36]	

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary for sensitivity analysis was obtained from the policy and planning division. Cost of purchasing of durable good and department allocation cost for sensitivity analysis were varied at 10 percent. Resource utilization for sensitivity analysis was obtained from expert opinions.

+ Useful life of durable good was 8 year, work time in one month was 20 day, and work time in one day was 8 hours

* Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-8. Cost of Par plana vitrectomy (PPV)*

Labor cost			
Labor	Numbers of personal	Average salaries (Baht)	Time spent (minute)
1.Staff	1	28,382.80 [12,400-48,500]	120 [105-135]
2.Doctor	1	9,002.50 [8,610-10,060]	150 [135-165]
3.Nurse	3	13,501.05 [7,210-25,110]	165 [150-180]
4.Nurse for admit-discharge	1	13,501.05 [7,210-25,110]	10 [5-15]
5.Nurse for prepare patient before operation	1	13,501.05 [7,210-25,110]	30 [20-45]
6.Assistant nurse for admit-discharge	1	6,776.36 [5,110-16,160]	10 [5-15]
7.Assistant nurse for prepare patient before operation	1	6,776.36 [5,110-16,160]	10 [5-15]
8.Aissistant nurse for clean tool	2	6,776.36 [5,110-16,160]	15 [10-20]
9.Receptionist for admit-discharge	1	5,605.00 [4,100-8,200]	15 [10-20]
10.Receptionist for prepare patient before operation	1	5,605.00 [4,100-8,200]	10 [5-15]
11.Person who clean operation room	1	7,918.33 [4,100-11,050]	15 [10-20]
Total labor cost (Baht)		**1,684.70** [823.11-3,326.21]	

Capital cost			
Durable goods+	Cost of purchasing (Baht)	Useful life (year)	Time spent (minute)
1.Opeartion bed	370,000 [333,000-407,000]	5	165 [150-180]
2.Retina operation set	170,000 [153,000-187,000]	10	165 [150-180]
3.Ceiling operation lamp	208,000 [187,200-228,800]	5	165 [150-180]
4.Operation lamp	490,000 [441,000-539,000]	5	165 [150-180]
5.Light bulb	3,500 [3,150-3,850]	0.5	165 [150-180]

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary and resource utilization for sensitivity analysis were obtained from the policy and planning division. Cost of purchasing of durable good for sensitivity analysis was varied at 10 percent.
+Work time in one month of durable good was 20 day, and work time in one day was 8 hours.

Cost analysis of medical services (continued)

Table C-8. Cost of Par plana vitrectomy (PPV)* (continued)

Capital cost			
Durable goods+	Cost of purchasing (Baht)	Useful life (year)	Time spent (minute)
6.Engine for vitrectomy	1,200,000 [1,080,000-1,320,000]	5	165 [150-180]
7.Vitrectomy set	60,000 [54,000-66,000]	3	165 [150-180]
8.Lens for vitrectomy	70,000 [63,000-77,000]	5	165 [150-180]
9.Microscope	586,667 [528,000-645,333]	0.25	165 [150-180]
10.Light bulb in microscope	650 [585-715]	5	165 [150-180]
11.Hiene	39,167 [35,250-43,083.33]	3	165 [150-180]
12.Len 20 D	6,810 [6,129-7,491]	5	165 [150-180]
13.Escalon	40,000 [36,000-44,000]	3	0.03 [0.02-0.05]
14.Semaster	1,850 [1,665-2,035]		
Total capital cost (Baht)	**932.38** [762.86-1,118.85]		

Material cost		
Materials	Price/ item (Baht)	Quantity used
1.Eye set	23.00 [20.70-25.30]	1 set [1-2]
2.Disposable glove	9.00 [8.10-9.90]	4 pairs [3-5]
3.Needle	1.00 [0.90-1.10]	3 pieces [3-5]
4.Syringe 5 cc	3.00 [2.70-3.30]	1 piece [1-2]
5.Syringe 2 cc	2.00 [1.80-2.20]	1 piece [1-2]
6.Gauze 4x4”	1.50 [1.35-1.65]	5 pieces [3-6]
7.Cotton bud 1x100	20.00 [18.00-22.00]	10 pieces [8-15]

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Cost of purchasing of durable good and material cost for sensitivity analysis were varied at 10 percent. Resource utilization for sensitivity analysis was obtained from the policy and planning division.
+Work time in one month of durable good was 20 day, and work time in one day was 8 hours.

Cost analysis of medical services (continued)

Table C-8. Cost of Par plana vitrectomy (PPV)* (continued)

Material cost		
Materials	Price/ item (Baht)	Quantity used
8.Cotton wool	0.05 [0.05-0.06]	3 pieces [2-5]
9.Eye pad	4.00 [3.60-4.40]	1 piece [1-2]
10.Opsite 15x28 cm	75.00 [67.50-82.50]	1 piece [1-2]
11.Weck cell (K-sponge)	0.76 [0.68-0.84]	3 pieces [2-5]
12.IV Set	10.00 [9.00-11.00]	2 sets [2-3]
13.Dexon No.5/0	298.00 [268.20-327.80]	½ pack [0.3-1.0]
14.Dexon No.7/0	329.00 [296.10-361.90]	1 pack [0.5-2.0]
15.Head of vitrectomy set	7,344.00 [6,609.60-8,078.40]	4 times/set [2-5]
16.Bullet shield	2,568.00 [2,311.20-2,824.80]	20 times/set [18-30]
17.Vitrectomy Set	7,000.00 [6,300-7,700]	40 times/set [20-50]
18.Fiber	22,000.00 [19,800-24,200]	200 times/set [160-240]
19.0.5% Betadine in NSS (120 ml)	60.00 [54.00-66.00]	30 ml [20-40]
20.0.5%Hibitane in alcohol (1000 ml)	100.00 [90.00-110.00]	5 ml [3-10]
21.70% alcohol (1000 ml)	80.00 [72.00-88.00]	5 ml [3-10]
22.NSS (1000 ml)	23.00 [20.70-25.30]	250 ml [200-300]
23.0.4% Oxybuprocain eye drop (10 ml)	113.00 [101.70-124.30]	0.5 ml [0.3-0.6]
24.Xanalin eye drop (10 ml)	23.00 [20.70-25.30]	0.2 ml [0.1-0.3]
25.Chloramphenicol eye ointment	16.00 [14.40-17.60]	0.1g [0.08-0.15]

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Material cost for sensitivity analysis was varied at 10 percent. Resource utilization for sensitivity analysis was obtained from the policy and planning division.

Cost analysis of medical services (continued)

Table C-8. Cost of Par plana vitrectomy (PPV)* (continued)

Material cost		
Materials	Price/ item (Baht)	Quantity used
26.2% Xylocain with adrenaline (50 ml)	123.00 [110.70-135.30]	3 ml [2-5]
27.0.5% Marcain with adrenaline (20 ml)	182.00 [163.80-200.20]	3 ml [2-5]
28.Wydase (1 ml)	700.000 [630.00-770.00]	0.1 ml [0.15-0.2]
29.Gentamycin (2 ml/vial)	15.00 [13.50-16.50]	0.5 ml [0.5-1.0]
30.Dexamethasone (1ml/amp)	39.00 [35.00-42.90]	1 amp/2 cases [1-2]
31.Adrenaline (1:1000) injection	10.00 [9.00-11.00]	0.5 ml [0.3-1.0]
32.1%Tropicamide eye drop (15 ml)	269.00 [242.10-295.90]	0.4 ml [0.3-0.5]
33.10%phenylephrine eye drop (5 ml)	491.00 [441.90-540.10]	0.2 ml [0.1-0.3]
34. Diclofenac eye drop (10 ml)	254.00 [228.60-279.40]	0.2 ml [0.1-0.3]
35.Steam cost for vitrectomy set	24.37 [21.93-26.81]	1
Total material cost (Baht)	**3,122.44** [2,166.99-6,374.83]	
Indirect cost		
Department allocation (Baht)	Allocation rate+	Cost (Baht)
2,485,765 [2,237,180.40-2,734,331.60]	0.00011	280.83 [218.47-350.80]
Total cost of PPV (Baht)	**6,020.35** [3,971.43-11,170.69]	

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Material cost for sensitivity analysis and department allocation cost were varied at 10 percent. Resource utilization for sensitivity analysis was obtained from the policy and planning division.

+Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-9. Cost of Par plana vitrectomy (PPV) with endolaser*

Labor cost of endolaser				
Labor	Numbers of personal	Average salaries (Baht)	Time spent (minute)	Cost (Baht)
1.Staff	1	28,382.80 [12,400-48,500]	10 [8-15]	38.02 [13.29-97.45]
2.Doctor	1	9,002.50 [8,610-10,060]	10 [8-15]	12.06 [9.23-20.21]
3.Nurse	3	13,501.05 [7,210-25,110]	10 [8-15]	54.25 [23.18-151.36]

Capital cost of endolaser				
Durable goods+	Cost of purchasing (Baht)	Useful life (year)	Time spent (minute)	Cost (Baht)
Diode laser	4,100,000 [3,690,000-4,510,000]	5	165 [150-180]	1,174.48 [960.94-1,409.38]

Material cost of endolaser			
Materials	Price/ item (Baht)	Quantity used	Cost (Baht)
Fiber laser	10,100 [9,090-11,110]	50 cases/fiber [40-60]	202.00 [151.50-277.75]

Indirect cost of endolaser			
	Department allocation (Baht)	Allocation rate++	Cost (Baht)
	2,485,765 [2,237,180.40-2,734,331.60]	0.00000638	15.87 [11.42-26.18]

Total cost of endolaser (Baht)	**1,496.68** [1,169.55-1,982.32]
Total cost of PPV (Baht)	**6,020.35** [3,971.43-11,170.69]
Total cost of PPV with endolaser (Baht)**	**7,517.03** [6,133.50-15,692.31]

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary and resource utilization for sensitivity analysis were obtained from the policy and planning division. Cost of purchasing of durable good, material cost, and department allocation cost for sensitivity analysis were varied at 10 percent.

** Total cost of PPV with endolaser = cost of PPV+ cost of endolaser

+Work time in one month of durable good was 20 day, and work time in one day was 8 hours.

++ Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-10. Cost of Par plana vitrectomy (PPV) with prefluoron*

Labor	Numbers of personal	Average salaries (Baht)	Time spent (minute)	Cost (Baht)
Labor cost of prefluoron				
1.Staff	1	28,382.80 [12,400-48,500]	15 [10-20]	57.03 [16.61-129.93]
2.Doctor	1	9,002.50 [8,610-10,060]	15 [10-20]	18.09 [11.53-26.95]
3.Nurse	3	13,501.05 [7,210-25,110]	15 [10-20]	81.38 [28.97-201.81]
Capital cost of prefluoron				
Durable goods+	Cost of purchasing (Baht)	Useful life (year)	Time spent (minute)	Cost (Baht)
-	-	-	-	-
Material cost of prefluoron				
Materials		Price/ item (Baht)	Quantity used	Cost (Baht)
1.Prefluoron (5 ml)		5,350.00 [4,815-5,885]	5 ml [5-10]	5,350.00 [4,815-11,770]
2.Syringe 10 ml		4.00 [3.60-4.40]	1 piece [1-2]	4.00 [3.60-8.80]
3.Extension tube 6"Fiber laser		7.00 [6.30-7.70]	1 piece [1-2]	7.00 [6.30-15.40]
Indirect cost of prefluoron				
Department allocation (Baht)			Allocation rate++	Cost (Baht)
2,485,765 [2,237,180.40-2,734,331.60]			0.00000638	23.80 [14.28-34.91]
Total cost of prefluoron (Baht)			**5,541.30** [4,896.30-12,187.80]	
Total cost of PPV (Baht)			**6,020.35** [3,971.43-11,170.69]	
Total cost of PPV with prefluron (Baht)**			**11,561.64** [10,579.72-27,868.04]	

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary and resource utilization for sensitivity analysis were obtained from the policy and planning division. Cost of purchasing of durable good, material cost, and department allocation cost for sensitivity analysis were varied at 10 percent

** Total cost of PPV with prefluoron = cost of PPV+ cost of prefluoron

+Work time in one month of durable good was 20 day, and work time in one day was 8 hours.

++ Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-11. Cost of Par plana vitrectomy (PPV) with silicone oil injection*

Labor cost of silicone oil injection				
Labor	Numbers of personal	Average salaries (Baht)	Time spent (minute)	Cost (Baht)
1.Staff	1	28,382.80 [12,400-48,500]	20 [15-30]	76.04 [24.91-194.90]
2.Doctor	1	9,002.50 [8,610-10,060]	20 [15-30]	24.12 [17.30-40.43]
3.Nurse	3	13,501.05 [7,210-25,110]	20 [15-30]	108.51 [43.46-302.71]
Capital cost of silicone oil injection				
Durable goods+	Cost of purchasing (Baht)	Useful life (year)	Time spent (minute)	Cost (Baht)
-	-	-	-	-
Material cost of silicone oil injection				
Materials		Price/ item (Baht)	Quantity used	Cost (Baht)
1.Silicone oil (10 ml)		9,100.00 [8,190-10,010]	6 ml [4-10]	5,460.00 [3,276-10,010]
2.Syringe 10 ml		4.00 [3.60-4.40]	1 piece [1-2]	4.00 [3.6-8.8]
3.T-way		16.00 [14.40-17.60]	1 piece [1-2]	16.00 [14.40-35.20]
4.Syringe insulin		4.00 [3.60-4.40]	1 piece [1-2]	4.00 [3.6-8.8]
5.Steam cost for silicone set		21.18 [19.06-23.30]	1	21.18 [19.06-23.30]
Indirect cost of silicone oil injection				
Department allocation (Baht)			Allocation rate++	Cost (Baht)
2,485,765 [2,237,180.40-2,734,331.60]			0.00000638	31.73 [21.42-52.36]
Total cost of silicone oil injection (Baht)			**5,745.57** [4,896.30-10,676.49]	
Total cost of PPV (Baht)			**6,020.35** [3,971.43-11,170.69]	
Total cost of PPV with silicone oil injection (Baht)**			**11,765.92** [8,822.89-26,064.97]	

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary and resource utilization for sensitivity analysis were obtained from the policy and planning division. Cost of purchasing of durable good, material cost, and department allocation cost for sensitivity analysis were varied at 10 percent

* Total cost of PPV with silicone oil injection = cost of PPV+ cost of silicone oil injection

+Work time in one month of durable good was 20 day, and work time in one day was 8 hours

++ Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-12. Cost of Par plana vitrectomy (PPV) with DK line*

Labor	Numbers of personal	Average salaries (Baht)	Time spent (minute)	Cost (Baht)
Labor cost of DK line				
1.Staff	1	28,382.80 [12,400-48,500]	15 [10-20]	57.03 [16.61-129.93]
2.Doctor	1	9,002.50 [8,610-10,060]	15 [10-20]	18.09 [11.53-26.95]
3.Nurse	3	13,501.05 [7,210-25,110]	15 [10-20]	81.38 [28.97-201.81]

Durable goods+	Cost of purchasing (Baht)	Useful life (year)	Time spent (minute)	Cost (Baht)
Capital cost of DK line				
-	-	-	-	-

Materials	Price/ item (Baht)	Quantity used	Cost (Baht)
Material cost of DK line			
1.DK line (7 ml)	11,700.00 [10,530.00-12,870.00]	7 ml	11,700.00 [10,530.00-12,870.00]
2.Syringe 10 ml	4.00 [3.60-4.40]	1 piece [1-2]	4.00 [3.6-8.8]
3.Extension 6”	7.00 [6.30-7.70]	1 piece [1-2]	7.00 [6.3-15.4]

Department allocation (Baht)	Allocation rate++	Cost (Baht)
Indirect cost of DK line		
2,485,765 [2,237,180.40-2,734,331.60]	0.00000638	23.80 [4.28-34.91]

Total cost of DK line (Baht)	**11,891.30**	[10,611.30-13,287.80]
Total cost of PPV (Baht)	**6,020.35**	[3,971.43-11,170.69]
Total cost of PPV with DK line (Baht)**	**17,911.64**	[17,398.05-29,180.40]

*Cost data were obtained from the policy and planning division and calculated in 1997. Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis. Average salary and resource utilization for sensitivity analysis were obtained from the policy and planning division. Cost of purchasing of durable good, material cost, and department allocation cost for sensitivity analysis were varied at 10 percent.
** Total cost of PPV with DK line = cost of PPV+ cost of DK line
+Work time in one month of durable good was 20 day, and work time in one day was 8 hours
++ Allocation rate = time spent of each service (min) / (all labors in department x 237 x 6.3 x 60) = time spent of each service (min) / (59 x 237 x 6.3 x 60).

Cost analysis of medical services (continued)

Table C-13. Medical, Laboratory, X-ray, and Room service for vitrectomy

Medication	Price / item (Baht)	Quantity used
Drugs*		
1.1% tropicamide eye drop (bottle)	202.23 [202.00-232.02]	1 [1]
2.0.4% oxybuprocain HCL eye drop (bottle)	84.32 [83.00-88.88]	1 [1]
3.0.3% tobramycin eye drop (bottle)	115.56 [83.57-121.72]	1 [1]
4.Poly-oph eye drop (bottle)	15.00 [11.60-25.00]	1 [0-1]
5.Spersadexoline eye drop (bottle)	109.78 [105.05-115.56]	1 [0-1]
6.Maxitol eye ointment (tube)	56.71 [43.87-103.26]	1 [1]
7.1%atropine eye drop (bottle)	98.12 [85.39-118.06]	1 [0-1]
8.0.5% Timolol maleate eye drop (bottle)	57.78 [53.00-62.49]	1 [0-1]
9.Lorazepam 0.5 mg (tablet)	0.30 [0.12-0.45]	10 [0-20]
10.Paracetamol 500 mg (tablet)	0.07 [0.05-0.22]	20 [10-30]
11.Cephalexin 250 mg (capsule)	1.98 [0.37-1.98]	40 [0-60]
12.Tramadol 50 mg (capsule)	9.10 [0.53-9.98]	10 [0-20]
13.Sodium chloride 100 ml (bottle)	13.50 [11.13-14.02]	1 [1-2]
Medical supply		
1.Cotton ball 50 ball (pack)	7.00 [6.00-10.00]	1 [1-2]
2.Eye pad (piece)	2.56 [2.50-3.00]	1 [1-2]
3.Micropore ½" x 10 yds (roll)	11.99 [11.00-13.00]	1 [1-2]
Total cost of medication (Baht)	**949.15** [452.70-1,281.03]	

Lab and X-ray**	Unit cost (Baht)	Times used in each services
CBC	90.63 [81.57-99.69]	1 [1-2]
UA	44.09 [39.68-48.50]	1 [1-2]
HIV	68.23 [61.41-75.05]	1 [1]
EKG	62.60 [56.34-68.86]	1 [1]
FBS	32.21 [28.99-35.43]	1 [1-2]
DTX	27.17 [24.45-29.89]	1 [0-2]
CXR	241.31 [217.18-265.44]	1 [1]
Total cost of laboratory and X-ray (Baht)	**675.56** [578.84-997.84]	

Room services per one day (Baht)	Numbers of day for admit
1,552.88 [1,542.37-1,563.39]	3 [2-5]
Total cost of room services for vitrectomy (Baht)	**4,658.64** [3,084.74-7,816.95]

Data in parenthesis [….] was sensitivity analysis range, used in one-way sensitivity analysis.
Resource utilization was obtained from expert opinions.
*Cost data were obtained from the pharmacy department. Drug and medical supply cost for sensitivity analysis was derived from Ministry of Public Health.
**Cost data were obtained from the policy and planning division and calculated in 1997. For sensitivity analysis was varied at 10 percent.
***Cost data were obtained from the policy and planning division. For sensitivity analysis was varied at 10 percent.

Appendix D

Cost for sensitivity analysis

Table D-1. Minimum and maximum cost of eye screening examination

Procedure	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
1. Visual acuity examination+	1.54-24.78	0.03-0.18	-	5.68-31.87	7.25-56.83
2. Eye dilatation+	1.54-12.39	-	2.46-15.86	5.68-15.94	9.68-44.19
3. A/S examination and intraocular pressure+	4.98-35.58	1.90-3.88	-	8.52-15.94	15.41-55.40
4. Fundoscopic examination with indirect ophthalmoscopy+	6.64-71.17	0.41-1.25	-	11.36-31.87	18.41-104.29
Total cost of eye screening examination (Baht)*			**50.75-260.71**		

* Cost of eye screening examination consisted of visual acuity examination, eye dilatation, A/S examination and intraocular pressure, and fundoscopic examination (with indirect ophthalmoscopy).

+ See details of calculation and source of data in appendix B.

Table D-2. Minimum and maximum cost of misdiagnosis for calling PDR or ME

Procedure	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
1. Visual acuity examination+	1.54-24.78	0.03-0.18	-	5.68-31.87	7.25-56.83
2. Eye dilatation+	1.54-12.39	-	2.46-15.86	5.68-15.94	9.68-44.19
3. Fundoscopic examination with laser+	3.32-71.17	8.40-51.32	-	5.68-31.87	17.40-154.36
Total cost of misdiagnosis (Baht)*			**34.33-255.38**		

* Cost of misdiagnosis for calling PDR or ME consisted of visual acuity examination cost, eye dilatation cost, and fundoscopic examination cost (with laser).

+ See details of calculation and data source in appendix B.

Cost for sensitivity analysis (continued)

Table D-3. Minimum and maximum cost of laser treatment (per time per person))

Procedure	Direct cost (Baht)			Indirect cost (Baht)	Total cost (Baht)
	Labor	Capital	Material		
Panretinal laser photcoagulation: PDR+	33.22-284.67	83.98-205.30	110.18-225.95	56.80-127.48	**284.19-843.40**
Focal/ Grid laser photocoagulation: ME+	24.91-213.50	62.99-153.97	110.18-225.95	42.60-95.61	**240.68-689.03**

+ See details of calculation and source of data in appendix B

Table D-4. Minimum and maximum total cost of laser photocoagulation (per course per person)

Cost of each procedure	Times per course of treatment	Types of cost (Baht)			Total cost (Baht)
		Visual acuity	Eye dilatation	Laser treatment	
Laser for PDR	2-6	14.50-340.98	19.35-265.14	568.38-5,060.37	**602.23-5,666.49**
Laser for ME	1-3	7.25-170.49	9.68-132.57	240.68-2,067.10	**257.61-2,370.16**

* Cost of laser = (visual acuity exam. cost + eye dilatation cost + laser photocoagulation cost) x times per course of laser

Table D-5. Minimum and Maximum total cost of vitrectomy (per time per person)

Types of cost (Baht)				Total cost (Baht)
Vitrectomy++	Medication+	Lab & X-ray++	Room service+	
10,733.54-24,701.43	452.70-1,281.03	578.84-997.84	3,084.74-7,816.95	14,849.81-34,797.25

+ See details of calculation and source of data in appendix B
++Adjusted cost data in 1997 to 2003 with CPI = (cost in 1997x110)/92.2, see CPI in appendix E.

Appendix E

General consumer price index of Bangkok metropolis (Non-food and beverages) 1994 –2004.

Year	Non-Food and Beverages		Apparel and Footwear		Housing and Furnishing		Medical and Personal Care		Transportation and Communication		Recreation and Education		Tobacco and Alcoholic Beverages	
	Index	Percentage Change	Index	Percentage Change	Index	Percentage Change	Index	Percentage Change	Index	Percentage Change	Index	Percentage Change	Index	Percentage Change
1994	82.8	4.0	83.5	6.6	85.2	3.5	84.7	6.1	87.6	1.1	76.9	3.4	66.3	10.3
1995	86.2	4.2	86.9	4.1	89.6	5.1	87.3	3.0	88.3	0.8	82.2	6.9	69.7	5.2
1996	89.2	3.4	89.0	2.4	92.6	3.3	88.9	1.9	89.2	1.0	89.5	8.8	73.2	5.0
1997	93.4	4.7	92.8	4.2	95.2	2.9	92.2	3.6	93.3	4.5	95.1	6.2	83.7	14.3
1998	100.0	7.1	100.0	7.8	100.0	5.0	100.0	8.6	100.0	7.1	100.0	5.2	100.0	19.5
1999	101.0	1.0	100.8	0.8	99.8	-0.2	103.0	3.0	101.8	1.8	99.8	-0.2	103.8	3.8
2000	104.1	3.0	101.9	1.2	101.5	1.7	105.5	2.4	110.6	8.5	99.2	-0.6	104.3	0.4
2001	106.5	2.3	103.1	1.1	103.1	1.7	107.8	2.2	114.0	3.2	100.2	1.1	110.4	5.8
2002	107.1	0.6	103.7	0.6	103.1	0.0	109.0	1.1	115.2	1.1	101.2	1.0	112.8	2.2
2003	107.7	0.6	103.7	0.0	102.3	-0.8	110.0	0.9	118.7	3.0	101.2	0.0	111.9	-0.8
2004 (Jan.-Jun.)	108.6	0.6	103.8	0.0	102.6	-0.1	111.6	1.9	121.1	1.9	101.8	0.4	111.0	-0.9

Base year: 1998 = 100

Reference from: Consumer price index. [Online]. Beureau of Trade and Economic Indices. Ministry of Commerce, Thailand; 2001. Available from: http//:www.indexpr.moc.go.th/econo-book/html/product.htm. [Accessed 2002 Aug 23]

BIOGRAPHY

NAME Ms. Supaporn Pornpinatepong

DATA OF BIRTH April 4, 1975

PLACE OF BIRTH Ranong, Thailand

INSTITUTIONS ATTENDED Silpakorn University, 1998:
Bachelor of Pharmacy
Mahidol University, 2005:
Master of Science in Pharmacy
(Pharmacy Administration)

POSITION & OFFICE Bangpa-in Hospital,
Pranakornsriayudthaya, Thailand
Position: Pharmacist
Tel. (035) 261173-4
E-mail: weaw_04@hotmail.com,
waew.supaporn@gmail.com