การศึกษาค่าอรรถประโยชน์ในผู้ป่วยภาวะแทรกซ้อนจากเบาหวานทางตา

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Utilities value in Diabetic Retinopathy

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วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรดุษฎีบัณฑิต
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การใช้ค่าอรรถประโยชน์ประกอบกับการคำนวนปีสุขภาวะเป็นตัวชี้วัดหนึ่งที่ใช้ในการวิเคราะห์และประเมินเทคโนโลยีทางสุขภาพ สำหรับค่าอรรถประโยชน์ในโรคเบาหวานทางตา และโรคตานั้นยังมีการศึกษาไม่มากในพื้นที่ของประเทศเอเชียใต้ ดังนั้นการศึกษานี้จึงมีวัตถุประสงค์เพื่อที่จะศึกษาค่าอรรถประโยชน์ในผู้ป่วยที่เป็นโรคเบาหวานขึ้นตา (DR) ต้อกระจก (Cataract) และ จอตาเสื่อมในผู้สูงอายุชนิดมีเส้นเลือดงอกผิดปกติ (wet AMD) โดยเปรียบเทียบการวัดโดยเครื่องมือการวัดทางตรงแบบ Time trade-off โดยจำแนกเป็น tTTO และ cTTO เครื่องมือแบบสอบถามได้แก่ EQ-VAS, EQ-5D-5L และ HUI3 และดูความสัมพันธ์กับคุณภาพชีวิตทางตาโดยการวัดโดยแบบสอบถาม NEI VFQ-25. การศึกษานี้เป็นการศึกษาแบบพหุสถาบัน โดยสัมภาษณ์และเก็บข้อมูลผู้ป่วย 309 ราย ในคลินิกจักษุวิทยา (DR=141 ราย , wet AMD=90 ราย และ Cataract=78 ราย) โดยใช้วิธีการสัมภาษณ์แบบ face-to-face. สำหรับตัวแปรทางคลินิกหลักคือ ระดับค่าสายตาที่วัดด้วย Early Treatment Diabetic Retinopathy chart. จากการศึกษาพบควา ค่าอรรถประโยชน์จาก cTTO, EQ-VAS, EQ-5D-5L และ HUI3 เท่ากับ 0.84 ±0.25, 0.73 ±0.15, 0.70 ±0.19, and 0.68 ±0.26, ตามลำดับ ค่าคะแนนคุณภาพชีวิตวัดโดยเฉลี่ย คือ 70.71 ±17.76 โดยระดับค่าสายตาในตาข้างดี (Better-seeing-eye, BSE) พบมีความสัมพันธ์แบบเชิงลบกับค่าอรรถประโยชน์จากเครื่องมือ cTTO สำหรับค่าสายตาในตาข้างที่แย่ (Worse-seeing-eye) พบว่ามีความสัมพันธ์เชิงลบกับค่าอรรถประโยชน์จากcTTO, EQ-5D-5L และ HUI3 เมื่อแบ่งระดับการมองเห็นตามระดับความรุนแรงของสายตาเลือนรางพบว่า ค่าอรรถประโยชน์จาก cTTO , HUI3 และ EQ-5D-5L มีการลดลงอย่างมีนัยสำคัญในกลุ่มที่มีความรุนแรงระดับมาก cTTO สามารถพบความแตกต่างของคุณภาพชีวิตในผู้ป่วยที่มีสายตาเลือนรางระดับปานกลางขึ้นได้ โดย HUI3 และ EQ-5D-5L พบมีความสัมพันธ์กับค่าการเปลี่ยนแปลงของคุณภาพชีวิตในเชิงบวกในระดับ ($r=0.54$, $p<0.01$,$r=0.43$, $p<0.01$) โดยวิธี cTTO มีความสัมพันธ์กับการเปลี่ยนแปลงคุณภาพชีวิตที่น้อยว่า ($r=0.21$) เมื่อศึกษาค่าอรรถประโยชน์เปรียบเทียบกลุ่ม DR wet AMD และ Cataract พบว่าไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติโดยเมื่อปรับค่าตัวแปรกวนที่เกี่ยวข้อง ปัจจัยที่มีผลต่อการไม่ยินดีแลกชีวิตในการวิเคราะห์แบบ tTTO ได้แก่ผู้ป่วยที่อายุมาก , ภูมิลำเนา, ศาสนาพุธ และ การมีค่าสายตาที่ดีอยู่ จากการศึกษานี้สรุปว่า ระดับการมองเห็นเป็นปัจจัยหลักที่กระทบต่อค่าอรรถประโยชน์ในกลุ่มผู้ป่วยทางจักษุวิทยา โดยผู้ป่วยที่มีการมองเห็นแย่จะมีระดับค่าอรรถประโยชน์ที่แย่กว่าผู้ป่วยที่มองเห็นได้ดี โดยปัจจัยทางชนิดของตัวโรคไม่มีผลต่อการลดลงของค่าอรรถประโยชน์ในกลุ่มที่มีระดับการมองเห็นที่เท่ากัน แบบสอบถามวัดค่าอรรถประโยชน์ และ การวัดทางตรงแบบ cTTO และ แบบสอบถามอรรถประโยชน์พหุลักษ์ HUI3 และ EQ-5D-5L สามารถใช้ประเมินค่าอรรถประโยชน์ในผู้ป่วยทางจักษุวิทยาที่เป็นโรค DR, wet AMD และ Cataract ได้

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Health utilities has been used as weighted for a quality adjusted life year in health technology assessment. There are limited data on the utilites value in diabetic retinopathy and retina diseases in the South Asian region. The aim of this project are to estimate the visual health utility (HU) in patients with diabetic retinopathy (DR), age-related macular degeneration (AMD), and cataract. Moreover, we intended to evaluate an appropriate health utility instrument among a direct choice-based, traditional time trade-off (tTTO) and composite time trade-off (cTTO), and multiple attribute utility instrument (MAUI) (EQ-VAS, European Quality of Life (QoL) Five Dimension (EQ-5D-5L), and Health Utility Index 3 (HUI3) in patients, along with its association to a vision specific QoL measured by the National Eye Institute visual function questionnaire 25 (NEI VFQ-25). In this multicenter cross-sectional survey a total 309 patients from tertiary eye centers (DR=141, wet AMD=90, and cataract=78) were interviewed.We used the cTTO, EQ-5D-5L, HUI3, and NEI VFQ-25 for face-to-face interviews. We collected demographic data and Early Treatment Diabetic Retinopathy Study visual acuity from the participant during particular ophthalmic visits with the interview. The main outcome meaures are health utility and visual acuity.The overall mean utility value from the lead time cTTO, EQ-VAS, EQ-5D-5L, and HUI3 was 0.84 ±0.25, 0.73 ±0.15, 0.70 ±0.19, and 0.68 ±0.26, respectively. The mean NEI VFQ-25 score was 70.71 ±17.76. VA in the best-seeing eye was significantly associated with a negative change in the HU score in cTTO. By contrast, VA in worse-seeing-eyes was associated with the HU in cTTO, EQ-5D-5L and HUI3. HU from cTTO and HUI3 displayed a significant response to severe visual impairment status or worse. HU from HUI3 ($r=0.54$, $p<0.01$) and EQ-5D-5L ($r=0.43$, $p<0.01$) displayed a moderate correlation with the NEI VFQ-25 score. cTTO shows lower correlation ($r=0.21$). There were no significant differences in HU among DR , wet AMD, and cataract, upon adjusting for the VA and demographics. Moreover, there was no significant difference in the HU between DR with and with out macular edema. Factors associated with non-trader in tTTO were old age, demographic region, Buddhist religion, and good VA. Thie project conclude that the VA level exerted a higher impact on the patient's QoL than the type of eye disease. The Low VA resulted in poor QoL and HU. MAUI instruments and cTTO are suitable in HU measurement in DR, wet AMD, and cataract. cTTO, EQ-5D-5L and HUI3 are feasible and responses to the impact of vision in Thai's ophthalmic patients.

Field of Study: Clinical Sciences Student's Signature .....

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Chapter 1

Introduction

Background

Health technology assessment and cost-effectiveness analysis study within the decision-making in health care have been increasingly implemented worldwide to find the best relevant clinical practice, including treatment in a limited resources circumstance. Quality-adjusted life year (QALYs) has been developed to measure the effect of health intervention in cost-effectiveness analysis or cost-utility analysis. The QALYs are a combination of quality of life and length in a specific health state.(Fortney, Pyne, & Burgess, 2014) To calculate the QALYs, a weighted value of health state utility value (HU) represented a Health- related quality of life (HRQoL) which has been used in a combination of a duration of life in specific health states.(Sassi, 2006) Utilities are measured by an interval scale of 0 – 1, where 0 indicates the health state of death and 1 indicates the full health status. The negative value may indicate a state worse than death.

The World health organization (WHO) defines health as “a state of completed physical, mental, and social wellbeing and not merely the absence of disease or infirmity. It is an individual’s perception of their position in life in the context of the culture and value systems in which they live and concerning their goals, expectations, standards, and concern”. (Organization, 1997) HRQoL has been widely used in patient-reported outcome measurement (PRO). The concept included the evaluation of physical function, social function, and mental health status.

The conceptual model of HRQOL has resulted in multiple aspects such as functional status, symptom status, health perception, and quality of life, including biological and social variability(Wilson & Cleary, 1995). The different cultures and geographic may give rise to different perceptual of individual health states. In ophthalmology, the disease or treatment will affect on vision but not a person’s life which is measured by visual acuity. A better vision is related to good quality of life to the patient.(G. C. Brown, 1999) The change in visual acuity levels are associated with

utility value changes, and it is an important parameter in modeling to see the effect of treatment or any intervention of the disease/condition.(T. H. Tung et al., 2005)

Visual impairment (VI) and blindness are global concerns that affect about 293 million and 43 million people worldwide, respectively. The prevalence of these two conditions have been doubling in the past ten years. The World Health Organization (WHO) classifies VI based on the *International Classification of Diseases* 11 (2018) into distance VI and near VI. The severity of distance VI is defined as mild, Snellen visual acuity (VA) worse than 20/40 to 20/70; moderate, VA worse than 20/70 to 20/200; severe, VA worse than 20/200 to 20/400; and blindness in the Snellen visual acuity worse than 20/400.("World report on vision,") Among retina diseases, age-related macular degeneration and diabetic retinopathy are the top significant causes of VI.

Diabetes retinopathy (DR) is one of the most common leading causes of vision loss and results from complicated vascular disease.(Duh, Sun, & Stitt; Robinson & Spencer, 2006; Ting, Cheung, & Wong, 2016) Wild et al. predicted the prevalence of diabetes in 2030 to reach 4.4% of the population worldwide, that indicates the number of diabetes will rise from 171 million in 2000 to 366 million in 2030.(Wild, Roglic, Green, Sicree, & King, 2004) Visual deterioration from diabetes retinopathy can result from diabetic macular edema (DME) , Neovascularization complication, Tractional retinal detachment, and macular ischemia.(Tarr, Kaul, Wolanska, Kohner, & Chibber, 2012) Currently, Risk factor controls and routine screening play an important role in preventing the development of the visual deterioration of DR.(Duh et al.; Kollias & Ulbig, 2010). Moreover, A treatment of DR complications included pan retinal photocoagulation , focal/grid laser photocoagulation, vitreoretinal surgery, intravitreal steroid injection and Anti-vascular endothelial growth factor injection has been continuous growing in the last few decades.(Cai & Bressler, 2017; Cantrill, 1984; Lally, Shah, & Heier, 2016; Sullivan & Laidlaw, 2004) Cost effectiveness analysis (CEA) with in decision making in DR screening and treatment options has increasingly worldwide to find the best relevance in a limited resource circumstance. Visual acuity level has been common used as a primary outcome in clinical research in ophthalmology field. The vision loss from DR could reflect in a reduction in health

utility.(M. M. Brown, Brown, Sharma, & Shah, 1999) Wet-age related macular degeneration (wet AMD), is a common retina condition in elderly, causes vision loss in an elderly population, results damage by exudative and choroidal neovascularization (CNV).(Seddon & Chen, 2004) Unlike a complication of systemic changes in DR, the primary cause of vision loss in wet AMD is mainly in the macular area and contributes to irreversible damage. Regular treatment with anti-vascular endothelial growth factor (anti-VEGF) helps reduce the incidence of severe vision loss.(Chew et al., 2014) When comparing DR and wet AMD, the HRQoL seems to be influenced by the amount of vision loss rather than the cause of it.(Melissa M Brown, Gary C Brown, Sanjay Sharma, Jennifer Landy, & Jeff Bakal, 2002). Cataracts, unlike DR and wet AMD which presented in a chronic fashion, is also one of the common causes of vision loss in the elderly but most regain their vision through lens removal surgery with artificial lens implantation. Visual acuity level in cataract patients is associated with health utility and quality of life.(J. Lee, Fos, Zuniga, Kastl, & Sung, 2000).

The vision level contributes mainly to the HRQoL, but nevertheless, the level differs among eye diseases.(B. S. Lee et al., 2008). Furthermore, the level of HRQoL or HU are various cross-culturally.(J. E. Lee, Fos, Zuniga, Kastl, & Sung, 2003) A QALY weights data for retina disease are still limited in South East Asian region.(Au Eong et al., 2012; Wagle, Lim, Yap, Neelam, & Eong, 2011; บรรณ, 2019). The conceptual model of HRQOL results in multiple aspects, as shown in *Figure 1*. The different culture and geographic may give rise to different perceptual of individual health state. Up to now, CEA analysis in Thailand in ophthalmology aspect are using the utilities value to calculate QALYs obtained from western publications.

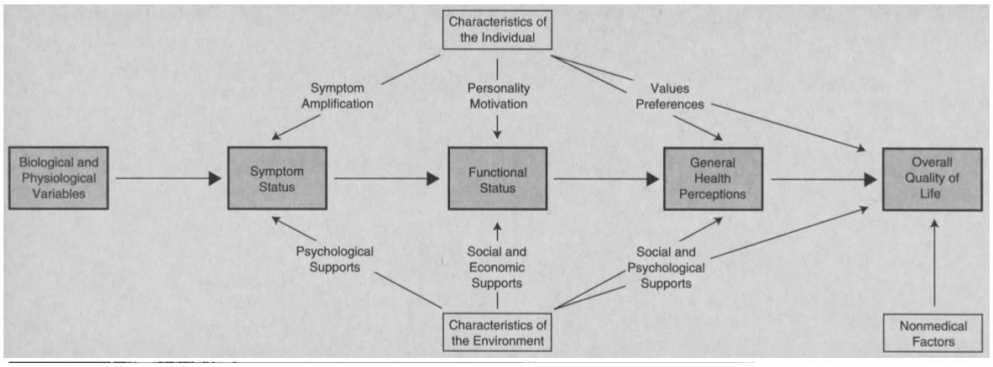


Figure 1: Relationships among measures of patient outcome in health-related quality of life conceptual model

(Ira B. Wilson et al. JAMA,1995)(Wilson & Cleary, 1995)

Study questions

1. What is the health utility level in eye patients in the Thai population?
2. What instruments can measure the impact of visual acuity on HRQoL in an ophthalmic patient in the Thai population?
3. What is the impact of diabetic retinopathy and its complication on health utility?
4. Are there any differences between diabetic retinopathy and other retina diseases: wet AMD, and cataract?

Study objectives

1. **Primary Objectives**
   - To evaluate a health utility in response to the change of visual acuity
   - To compare health utility by using direct preference methods and multi-attribute utility instruments (EQ-5D-5L and HUI3) in ophthalmic patients

2 **Secondary Objectives**
   - To evaluate the feasibility of using TTO, EQ-5D-5L, HUI3, and NEI VFQ-25 in Thai elderly
   - To evaluate the impact of religion on death-related questions of TTO
   - To assess the response of health utility to an impaired visual status

- To determine the correlation between health-related quality of life and disease-specific quality of life
- To evaluate the impact of eye diseases on HRQoL
- To evaluate the impact of diabetic macular edema on HRQoL

Significances of the study

The finding of this study will give references to the health utility of patient who has diabetic retinopathy, wet AMD, Cataract, or other related conditions in a context similar to Thailand. Moreover, this study evaluates the response of health utility among the level of visual acuity obtained by different methods. It helps in a selection of suitable health utility instruments to be used in the patient with visual disability and vision-related diseases population, which claims to be less responsive to the change of visual acuity in some methods, especially without integration of vision function concept in a utility valuation process. Moreover, visual impairment remains a public health burden, and an evaluation of health utility and quality of life, including factors associated with it, could be used in policy planning. This study also focuses on a diabetes-related eye condition, one of the most common causes of visual loss worldwide. Understanding how this condition impacts the quality of life, both vision-specific and health-related, helps to expand the capability to support patients with this condition and emphasizes how to prevent its burden.

Hypotheses

The main hypothesis of this study are;

There is an association between visual acuity on health utility.

H_0 There is no association between visual acuity and health utility.

H_A There is an association between visual acuity and health utility.

The health utility measuring by Time trade-off, EQ-5D-5L, and HUI3 are different.

H_0 There is no difference in health utility among instruments.

H_A There are different health utilities among instruments.

Keywords and abbreviations

Age-related macular degeneration (AMD)

Composite TTO (cTTO)

Diabetic retinopathy (DR)

Early Treatment Diabetic Retinopathy Study (ETDRS)

European QoL five dimensions (EQ-5D)

Finger counting (FC)

Hand movement (HM)

Health technology assessment (HTA)

Health utility (HU)

Health Utility Index 3 (HUI3)

Health-related quality of life (HRQoL)

Intraclass correlation (ICC)

Light perception (LP)

Linear mixed model (LMM)

Multi-attribute utility instrument (MAUI)

National Eye Institute Visual Function Questionnaire (NEI VFQ-25)

Quality-adjusted life years (QALYs)

Time trade-off (TTO)

Tractional retinal detachment (TRD)

Traditional TTO (tTTO)

Visual acuity (VA)

Visual analog scale (VAS)

Chapter 2

Literature review

Health utility instruments

The measurement of HU represents an exhibit of the perception of individual health conditions as resulting in a humanistic outcome.

1. Direct preference methods

1.1 A visual analog scale (VAS) or rating scale method is the patient is asked to estimate their own health on a range scale from 0 to 100, with 0 representing the worst imaginable health state and 100 being the best.("EuroQol - a new facility for the measurement of health-related quality of life," 1990) The level that the patient feels will point on the scale and be interpreted as health utility value. VAS is the easiest way to understand the question but lacks theoretical basis.

1.2 Standard gamble (SG) has been proposed since 1944 by von Neumann and Morgenstern(Von Neumann & Morgenstern, 2007) to allow the quantification of uncertainty, and later in 1977, Weinstein and Stassen developed this theory to be applied in health care. (Weinstein & Stason, 1977) The SG method is determined by comparing a specific number of years in one health state (A) for a specific time or gamble the offering treatment of receiving full health for the same number of time and immediate death. The probability of full health state gain is varied until the individual respondent feels similar to these two alternatives is the utility value of a specific health state. (Bleichrodt & Johannesson, 1997)

1.3 The time trade-off (TTO) theory was developed as a model of economic evaluation in health care in 1992 by Torrence W. et al.(Torrance, Thomas, & Sackett, 1972). The method is based on how many years in the current health state an individual with that health condition would give up in exchange for the number of years to gain in perfect health. The number of years respondents need to trade for a full health state varies. The

utility evaluates at the point when respondents feel no difference between the alternative way.

1.3.1 Traditional TTO (tTTO), a calculation of utility value, is the number of years expected life – Number of years that respondent trade-off and divided by the number of years expected life.(Torrance et al., 1972) A modified uncomplicated technique has been used in ophthalmology reported by Brown et al.(M. M. Brown et al., 1999) The patient will be asked with a trade-off question which related to an estimation of time of their remaining life expectancy. Afterward, the hypothetical situation where patients could return to their normal vision with special treatment would decrease their life expectancy. Then the patient will be asked to quantify the maximum number of years that they accept to trade to return to normal vision.

The utility value will be calculated as utility value = (No of years expected life – No of years trade-off)/No of years expected.

1.3.2 Composite TTO , is a technique developed in 1993 called MVH protocol by adopting the conventional TTO using the fixed time horizon of t=10 years. The EQ-VT protocol is another technique adopted from MVH protocol by starting with a comparison to 10 years in full health with immediate death and current health state to separate the better than death (BTD) and worse than death (WTD).Then for BTD states, life A is living in full health for x years followed by death while life B is living in the impaired state for 10 years followed by death . The titration is 1 year, or 6 months increments and corrections of 6 months whenever preference reversal occurs until reaching the state of indifference. For WTD stage, composite TTO as mentioned above, is used. (Oppe, Rand-Hendriksen,

Shah, Ramos-Goñi, & Luo, 2016) Even though EQ-VT has been widely used with standard protocol; however, computer software is needed to complete the full techniques in an original protocol. In the valuation of EQ-5D , cTTO was used .(Oppe et al., 2016) were used for BTD stage and if the respondents report WTD, lead-time TTO is used. The respondents will be asked between 2 hypothetical lives in which the first option involves x years of healthy life then, followed by death (alternative1). The downside of cTTO is worse than WTD stage, which gives a negative value, and sometimes creates an extremely negative one, especially the original TTO from Torrance et al. (Torrance, 1976). Later, there was subsequently transformed to varying arbitrary rules to a scale with a minimum of -1.(B. M. Janssen, Oppe, Versteegh, & Stolk, 2013) The new concept for TTO approach, which are "lead-time" and "lag-time," TTO was invented to provide more trading time in order to draw out the problematic prefer to the dead state of conventional TTO by adding trading time in full health to the state of being valued. Hence, when valuing the WTD health state, the respondents have more time to trade for the same health state with the same duration. If the additional time is placed before the health state being valued, that is called "lead time TTO" and vice versa for "lag-time TTO". The technique of cTTO has been described and widely used. The cTTO give rise to a more consistent approach of negative values adjustment and have high validity in a face-to-face interview setting.(B. M. Janssen et al., 2013) Furthermore, instead of Full health stage and death as alternative, this technique defined the best health state by EQ-5D-3L (health state "11111") and immediate death.

2. Indirect preference methods

Health state utilities can also measure from a multi-attribute utility instrument (MAUI) (Richardson, Khan, Iezzi, & Maxwell, 2015; Torrance, 1987) in the form of a questionnaire. An MAUI (Multi-attribute utility instrument) is an alternative method for evaluating utilities and measuring HRQoL. Each life domain of MAUI might be affected by health state, and a scoring algorithm based on population is applied.(Fenwick, Pesudovs, et al., 2012) The benefits of PROs include providing a sufficient and necessary set of questions to measure the outcome in a logical order and the response and clear instruction scoring of the instrument, all of which are feasible for outcome measurement by an investigator[10].

2.1 EQ-5D is a widely use instrument worldwide to measure generic health status which has been validated and weighted in Thai by Tongsiri S et al.(Tongsiri & Cairns, 2011) The studied patients were randomly selected from 76 provinces of Thailand and had face-to-face interviews. The health state gives into 3 stages (EQ-5D-3L): mild, moderate, and severe health stage. The Dolan(Dolan, 1997) and Dolan et al.(Dolan & Roberts, 2002) models were estimated and compared with Shaw et al.(Shaw, Johnson, & Coons, 2005) model. The Dolan 1997 model was preferred for using in the Thai algorithm with better in logical consistency, parsimony, and predictive performance when compared to other methods. Eighty-six health states were valued in the study and the highly consistent respondents tend to give a higher score for mild states and a lower score for the severe states when compared to the highly inconsistent respondent. The EuroQoL EQ-5D, an MAUI, is recommended by the National Institute for Health and Clinical Excellence (NICE) for HU measurement in economic evaluation.(Kay & Ferreira, 2014) In Thailand, EQ-5D also recommended to use in HTA.(Pattanaphesaj et al., 2018) But EQ-5D-3L is not included visual function as in the health status. This technique might not be the best suitable to evaluate current health state of ophthalmologic disease.

2.2 SF-36 item short-form survey (SF-6) is a generic questionnaire to measure patient quality of life and has been used worldwide. The 8 dimensions in SF36 included 1) Limitation of physical activity due to health state 2)limitation in physical activities 3)limitation in usual role activities 4) body pain 5) general mental health, which is psychological distress and well-being 6)limitation in usual role activities because of emotional problem 7) vitality (energy and fatigue(and 8) general health perception(Ware Jr & Sherbourne, 1992).

2.3 The Health utility index3 (HUI3) consists of 41 questions that include a question concerning how individuals perceive their own quality of life in the dimensions of hearing, speech, ambulation, dexterity, emotion, cognition, pain and vision. (Heintz, Wiréhn, Peebo, Rosenqvist, & Levin, 2012) The translation of HUI3 has been reported in Saiguay W and Sakthong P.(Saiguay & Sakthong, 2013) validated in ischemic heart disease patients. The overall test-retest reliability is 0.90, and specific in vision dimension is 0.52. However, it has not been evaluated in Thai ophthalmic patients.

2.4 The visual function Questionnaire-utility index (VFQ-UI) was estimated from the response from, a vision-specific QoL, NEI VFQ-25 in macular edema following a retinal vein occlusion, macular edema related to diabetes, uveitis, glaucoma and central vision loss related eye diseases. The health state classification includes 6 questions of Near vision, Social vision, Distance vision, Role difficulty and vision dependency and mental health.(Kowalski et al., 2012) Usage of VFQ-UI has still limited.(Goh, Fenwick, & Skalicky, 2016; Rentz et al., 2014)

Disease-specific quality of life instruments

1. The National Eye Institute Visual Function Questionnaire 25 (NEI VFQ-25)

Vision-specific patient-reported outcomes are also proposed for evaluating patient health states and determining vision status and its impact on individual quality of life. The National Eye Institute's Visual Function Questionnaire (NEI VFQ) is

widely used in the ophthalmic evaluation.(A. Lloyd et al., 2008; Payakachat et al., 2009; Tosh, Brazier, Evans, & Longworth, 2012) The instrument was designed to reduce the patient's burden as from an original consisted of 51 items and 3 subscales which were reduced to NEI VFQ-39 and then NEI VFQ-25.(Marella et al., 2010) The questionnaire is composed of 6 dimensions in visual function (near vision activities, distance vision activities, vision-specific social functioning, role difficulties, dependency, and mental health).NEI VFQ-25 has been widely used to evaluate patient QoL in dry eye, chronic ocular disease, glaucoma, macular disease, cataract, and visual impairment.(Lešin Gaćina et al., 2021) Moreover, it has been used as a secondary outcome in a clinical trial and validated in the different countries worldwide, such as Norway, USA, Sweden, Thailand, Greece, China, Denmark, Turkey , Germany Brazil, Japan, Italy and Serbia.(Assi et al., 2021; Jelin, Wisløff, Moe, & Heiberg, 2019) The test-retest reliability has been show as moderately to high (0.6-0.7).(Kovac et al., 2015; Simão, Lana-Peixoto, Araújo, Moreira, & Teixeira, 2008) In Thai version, Thai NEI VFQ-25 showed a Cronbach's alpha coefficient of 0.8 with total content validity of 0.8. The correlation of Thai-NEI VFQ-25 and Thai-SF 36 general health quality of life questionnaire was 0.6.(Setthawatcharawanich, Aui-aree, Sathirapanya, Phabphal, & Limapichat, 2009). Even though it has been widely used but some limitations were issued, including construct validity, clinical validity, and interpretability.(Petrillo, Bressler, Lamoureux, Ferreira, & Cano, 2017) New proposal of a revision called VFQ-28R seems to demonstrate the performance of response threshold and reduced ceiling effect. However, still limited in usage and acceptable in the ophthalmology field.(Petrillo et al., 2017) Unlike, other vision specific quality of life questionnaires, NEI VFQ-25 has shown responsive information on general health status. (Brémond-Gignac, Tixier, Missotten, Laroche, & Beresniak, 2002)

2. The Impact of vision impairment (IVI)

The impact of vision impairment questionnaire (IVI) was designed to use for daily living quality of life evaluation in visual impairment in the low vision rehabilitation population.(Weih, Hassell, & Keeffe, 2002) IVI shows the high psychometric quality and good content validity, including reproducibility, good discriminative ability, and

reliability.(De Boer et al., 2004; Lamoureux et al., 2007) IVI comprises 32 items which require 6 levels of scale responses. It captured a vision-specific profile of restriction and participation but not a clinical symptom of a disease and specific physical performance.(Weih et al., 2002) The development of IVI is based on a short version of SF-36, an SF-12 general health questionnaire.(Weih et al., 2002) IVI has been evaluated in low vision and rehabilitation patients (Lamoureux, Hassell, & Keeffe, 2004a), diabetic retinopathy(Lamoureux, Hassell, & Keeffe, 2004b), age-related macular degeneration and glaucomatous patient.(Noe, Ferraro, Lamoureux, Rait, & Keeffe, 2003) Thai version of IVI validated by Ratanasukon et al. (Ratanasukon, Tongsomboon, Bhurayanontachai, & Jirarattanasopa, 2016) the Cronbach's alpha range from 0.7 to 0.8 with test-retest reliability intraclass correlation of 0.96. However, IVI are still lacking of construct validity, interpretability including reproducibility.(De Boer et al., 2004)

3. The Visual Function Index (VF-14) Questionnaire

VF-14 questionnaire aims to evaluate the dependent activities of the patient in everyday life. The questionnaire was developed for usage in patients who are affected by cataract conditions (43) and has been widely used in cataract and refractive surgery since then.(Lamoureux, Fenwick, Pesudovs, & Tan, 2011; Lawrence, Fedorowicz, & van Zuuren, 2015) Further usage in other diseases has been reported, including glaucoma(Altangerel, Spaeth, & Rhee, 2003) AMD(Riusala, Sarna, & Immonen, 2003) corneal disease(Prem Senthil, Chakraborty, & Lim, 2022), strabismus(Sabri, Knapp, Thompson, & Gottlob, 2006) and other retina diseases (Linder et al., 1999). VF-14 is a self-administered questionnaire which gave a scoring of 0 to 100. The questionnaire focus on five dimensions, includes near-sight acuity, long-sight acuity, unclear sight, and driving during the day and night time. VF-14 also demonstrates a good responsiveness when assessing an outcome of eye surgery.(Sabri et al., 2006) With the lack of general health aspect, VF-14 has been used in conjunction with SF-36 to capture a general quality of life aspect. (Mylona, Aletras, Ziakas, & Tsinopoulos, 2021)A shortened version of VF-14 to VF-10 was also proposed(Pesudovs & Elliott, 2006)

Health utility measurement in diabetic retinopathy and eye conditions

TTO and SG in retinal patients demonstrate strong validity with the visual acuity in the best-seeing eye in retina patients. The disadvantage of these techniques is the difficulty to understand by respondents, especially older patients.(Sharma et al., 2002) Brown M. et al. used TTO to evaluate the patient with bilateral good visual acuity and unilateral good visual acuity. The study reported good bilateral VA had the highest utility value. From the patient reference-based point of view, the individual ocular disease affected QoL and TTO valued correlated with the visual loss in the better-seeing eye.(M. M. Brown, Brown, Sharma, Busbee, & Brown, 2001) Regarding to the report of Chinchongju W and Amornnopparattanakul studied in 36 Thai samples by using VAS, TTO and SG. The study results found that TTO and SG values were no large different and seem to be higher than VAS. The difficult to understand rankings from lower to the most difficult were VAS, SG and TTO. The general belief, horoscope, basic family status, household income, and age of heritage were concerned from sample when answering the questions. When asking SG questions, study samples need more explanation in payment, treatment detail, and risk of death from treatment.(Shingsongju W) TTO is one of the most common used direct methods to obtain the utility status of diabetic retinopathy patients as shown in **Table 1.**

Brown G. et al.(Gary C Brown, Brown, et al., 2000) studied 292 diabetic patients and utility by TTO method was measured. The study found that factors associated with the decrease in diabetic-associated QoL are the requirement of insulin, presence of depression, presence of diabetic retinopathy, and presence of co-morbidities. Huang E et al. (Huang, Brown, Ewigman, Foley, & Meltzer, 2007) interviewed 701 adults patient with diabetes in Chicago, USA to evaluate the impact of utility and co-morbidity of DM. TTO methods were used in this study. Blindness, end-stage renal disease, and Major stroke gave the lower mean utility. Diabetic retinopathy also had a mean utility of 0.53. The TTO and SG in eye patients demonstrate strong validity with the visual acuity in the best-seeing eye. The

disadvantage of these techniques is the difficulty of understanding by respondents, especially older patients.(Sharma et al., 2002)

The EQ5-D index score in Thai diabetes patients were published by Sakthong P. et al.(Sakthong, Shabunthom, & Charoenvisuthiwongs, 2008) A cross-sectional of 303 type 2 diabetics outpatient had face-to-face interviews, including EQ-5D and VAS questionnaires. In that study group, 64 patients were randomly selected for test-retest reliability. UK, US, and Japan preference weights for EQ-5D was evaluated. The results of this study shown US weights had the highest EQ-5D score. From the test-retest reliability results, Japan's weight had an excellent agreement by ICC while both derived from UK and US had a good agreement. The Japan's weight also gave the best discriminant validity. The Japan weight scheme was recommended to use in Thai diabetic type2 populations. The new version of EQ-5D has been developed by increasing the levels of response from 3 levels to 5 levels (EQ-5D-5L) to reduce the ceiling effect.(Herdman et al., 2011; M. F. Janssen, Birnie, Haagsma, & Bonsel, 2008) The measurement properties of EQ5D-5L compared to EQ-5D-3L was reported by Pattanaphesaj J. and Thavorncharoensap M.(Pattanaphesaj & Thavorncharoensap, 2015) who studied in 117 diabetes patient. The self-completion questionnaire of 3L and 5 L response scale, EQ-VAS and SF-36 generic questionnaire were evaluated. The 5L shows more power of discrimination and lower ceiling effect when compared to 3L. However, test-retest reliability showed higher weighted kappa coefficient in 3L but Intraclass correlation in 3L and 5L were 0.64 and 0.07 which indicated excellent reproducibility for both treatments. EQ-5D-5L is suggested to use over 3L. The Thai version of EQ-5D-5L is available at http://www.hitap.net/documents/24389. However, EQ-5D, similar to other generic instruments, lacks a direct question to vision-specific items. These resulted in a controversy about its responses to the change in visual level.(Macedo et al., 2022; Macedo et al., 2017) .

The visual acuity and relationship in diabetes patients has been evaluated by Clarke P M. et al(Clarke, Simon, Cull, & Holman, 2006) which studied in a large population of diabetes in the UK. There were a negative association of SF-36 domain utility score with declining visual acuity. The Thai version of SF-36 was validated in 2000 (Leurmarnkul & Meetam, 2000) and has been used in Thailand.(Kongsakon,

Silpakit, & Udomsubpayakul, 2007) The scoring of SF-36 has been estimated and generated to a utility value by a special derived version of SF-36 (the "SF-6D") to be more convenient for survey process and take shorter questionnaire time (Brazier, Roberts, & Deverill, 2002). SF-6D utility is associated with the change of visual acuity in retina disease.(Reeves et al., 2009; Visser, Amarakoon, Missotten, Timman, & Busschbach, 2017) Because of the lack of specific visual detention, SF-6D is less sensitive to visual acuity changes when compared to the TTO direct method.(Bozzani, Alavi, Jofre-Bonet, & Kuper, 2012) The comparison of EQ-5D-5L and SF-6D of chronic disease in Thai found that EQ-5D-5L was more related to physical aspect while SF-6D related to the mental aspect. The EQ-5D was more sensitive than SF-6D in discriminating patient with chronic diseases at different levels.(Sakthong & Munpan, 2017)

According to the systematic review conducted by Edith Poku et al. in 2013(Poku, Brazier, Carlton, & Ferreira, 2013a) , the study reviews health state utilities in patient with diabetic retinopathy , diabetic macular edema and age-related macular degeneration . From 17 studied reviews shown no relevant study specific for diabetic macular edema patient. The study reclassify visual acuity from included study to "Brown" visual acuity(M. M. Brown, G. C. Brown, S. Sharma, J. Landy, & J. Bakal, 2002) grouping which is Good reading vision (20/20 – 20/25), Legal driving vision (20/30 – 20/40), Moderate visual loss (20/50 – 20/100) and Legal blindness (equal or worse than 20/200) . The relationship between Health state utility value (HSUV) and visual acuity were analyzed. The generic instrument EQ-5D was found to be unresponsive to the changes in VA levels, while TTO and SG showed the consistent utility changes correlated with VA changes. SG seems to have a higher utility value than TTO. TTO shows decreasing of utility associated with a reduction of VA in best-seeing eye (BSE). HUI3 and EQ-5D showed estimates for a good reading vision for VA corresponding to counting fingers or worse ranged. A Significant relationship between VA in BSE and TTO values by regression analysis. Another systematic review of generic preference-based measures of HRQoL in visual disorder(Tosh et al., 2012) shows poor performance of EQ-5D in different VA ranges in DR and AMD. HUI-3 instrument was found to perform best in differentiation between

severity groups in glaucoma, AMD, DR, and cataracts. However, the small sample size was a limitation(A. Lloyd et al., 2008) Similar results were found in a systematic review of utility weight in wet AMD. TTO and HUI3 methods were sensitive to the change of VA, while EQ-5D and SF-6D had a poor impact on visual changes related to QoL.(I. Pearson, C. Rycroft, A. Irving, C. Ainsworth, & K. Wittrup-Jensen, 2013) Furthermore, SF-6D were shown to differentiate between patient with AMD. SG method was not common used for diabetic retinopathy patients due to the difficulty for imagination and patient demographic such as age, education level and religious belief might interfere the results. TTO is more simple and is preference-based for ophthalmology.(Alinia, Mohammadi, Lashay, & Rashidian, 2017)

Szabo S. et a(Szabo et al., 2010)l use NEI VFQ to compare TTO in measurement impact of DR patients. The development and progression of DR are associated with decreasing of health state in NEI VFQ preferences, but no association found with sex, age, VFQ quartile or status of better/worse seeing eye. Retnz et al. also created an algorithm to convert NEI VFQ in to a visual function health state (the Visual Functioning Questionnaire-Utility Index)(Rentz et al., 2014) and validated in diabetic macular edema and other retinal diseases.(Khadka, McAlinden, & Pesudovs, 2012; Lloyd, Loftus, Turner, Lai, & Pleil, 2013; Suner et al., 2009) Brazier J. et al(Brazier et al., 2017) evaluated the relationship between visual acuity and utility by using EQ-5D and VFQ-UI from the large aflibercept DME trail, VIVID, and VISTA study.(D. M. Brown et al., 2015) The responsive of VFQ-25 in RISE and RIDE study which collected data in DME shows a correlation with change of visual acuity during treatment follow-up.(Suñer et al., 2017) The new utility data were generated and shows more sensitivity than EQ-5D for measuring the impact of VA in BSE and worse-seeing eye (WSE). The study also supports the impact of utility-related to BSE. The poor visual acuity would give a large variation in the utility value, but different types of retina disease might not give significant differences in utility value.(Hornberger, Shewade, Doberne, Kowalski, & Nguyen, 2008)

Table 1 Review publications for utilities value in diabetic retinopathy

Sample	Region	Method of	Data gained	Results	Authors	Notes

		utility measurement				
Diabetic retinopathy (n=122) Type 1 or Type 2 diabetes (n = 49) General public UK (n = 150)	UK (5 clinical sites for patients and general public advertisement for the public)	Visual analog scale SG EQ-5D HUI-3 VFQ-25	Telephone and interview	Overall by SG 6/6 – 6/9 :0.814 6/12-6/18:0.728 6/24 – 6/36: 0.674 6/60 – 6/120 : 0.629 CF-HM: 0.570	Lloyd et al.(A. Lloyd et al., 2008) 2008	- SG utility score is not significantly different between the three HRQoL - Declining vision in DR is associated with declining in utility.
Age>40 years Total n=249 No DR (n=30) NPDR (n=73) Sight threatening DR (n=114) Blind from DR VA less than <6/60 (n=32) DR staging by international classification system	India (Chennai and Tamil - speaking)	TTO EQ5D	2 trained Interviewer	- 2 people refused and 1 unable to finish TTO - Utility by TTO - 6/6 – 6/9 :0.78 6/12-6+/18 :0.72 6/24-6/60: 0.63	Polack S et al.(Polack, Alavi, Rachapalle Reddi, Kulothungan, & Kuper, 2015) (2015)	- TTO decreased when DR increased (p<0.001) - Blindness from DR gives lower utility value in EQ-5D than TTO
Age>30 year, Type2 diabetes No DR(n=289) NPDR (n=87) PDR (n=21) Legal blindness (n=9)	Taiwan (Kinmen) Community-based cross-sectional study from 1991 – 1993)	TTO	One-to one interview	- mean utility value: 0.92 +/- 0.12 - Utility by TTO No DR: 0.94 NPDR: 0.87 PDR: 0.83 Legal blindness: 0.81	Tung T et al. (T. H. Tung et al., 2005)(2005)	- Half of the patient have 1.0 health state - Factors associated with utility value are age, DR status
DR patient VA<20/40 N=95 Diabetic retinopathy	USA (Retina Vascular Unit, Wills Eye hospital)	TTO SG	Interview	64 from 95 willing for TTO 47 patients from 64 TTO having SG	Brown M. et al.(M. M. Brown et al., 1999) 1999	

20/20 – 20/25 (n=15) 20/30 – 20/50 (n= 48 20/60 – 20/100 (n=21) 20/200 – 20/400 (n=7) CF – HM (n=4)				- Utility from TTO 20/20 – 20/25:0.84 20/30 – 20/50:0.78 20/60 – 20/100:0.78 20/200 – 20/400:0.64 CF to HM :0.59 - Utility from SG 20/20 – 20/25:0.90 20/30 – 20/50:0.92 20/60 – 20/100:0.84 20/200 – 20/400:0.71 CF to HM :0.70		
DR and AMD patients N= 617 DR(n=333) AMD (n= 246)	USA (Wills Eye hospital)	TTO	Interview	- Utility value from TTO in DR 20/20 – 20/25: 0.86 20/30 – 20/40:0.80 20/50 – 20/100:0.77 Less than or equal to 20/200: 0.60 - Utility value from TTO in AMD 20/20 – 20/25: 0.84 20/30 – 20/40: 0.80 20/50 – 20/100: 0.71 Less than or	Brown M.et al.(M. M. Brown et al., 2002) 2002	- No difference between utility value in DR and AMD - Visual acuity in better-seeing eye was significantly associated with utility value

				equal to 20/200: 0.59		
DR with VA<20/30 N= 186	Canada	TTO	Interview	Visual acuity better seeing eye by TTO 6/7.5 or better : 0.881 6/9 – 6/15: 0.786 6/18 -6/30: 0.728 6/60 – 6/120: 0.730 CF to NPL 0.478	Sharma S.(Sharma et al., 2003) 2002	- Utility cross border compares with Brown M. et al 1999 shows no statistical different
DM type 1,2 (N=129) No DR (n=35) BR (n=37) PDR (n=26) DME (n=31) Legal blindness (n=23)	Sweden (Lingkoping university hospital)	TTO EQ-VAS EQ-5D HUI-3 VFQ-25	Telephone interview	BSE utility value (adjusted) - HUI3 No DR: 0.88 DR0.86 PDR0.57 DME0.83 Blindness0.48 - EQ-5D No DR:0.82 DR:0.78 PDR:0.84 DME:0.86 Blindness:0.69 -TTO No DR:0.87 DR:0.78 PDR:0.81 DME:0.89 Blindness:0.62 EQ-VAS No DR: 80.59 DR:74.67 PDR:76.70 DME" 76.94 Blindness:60.08	Heintz E. et al.(Heintz et al., 2012) 2012	- HUI3 and EQ-VAS detected significant differences between different vision and pathological progression in the worse eye. HUI3 shows a high correlation to VFQ 25 (r=0.54)

DM or AMD VA<20/40 (N=150) DR (n=88) AMD (n =48)	USA	TTO	Interview	TTO utility (DM and AMD), 20/20 – 20/40:0.88 20/50 – 20/100:0.90 20/200 to no light :0.76perception	Shah V. et al.(V. A. Shah, Gupta, Shah, Vinjamaram, & Chalam, 2004) 2004	- No effect on utility score on age, education level and prior to ocular surgery - Significant decrease in utility score found in the poor visual acuity group
DM age > 22 years old (N=150) No DR to moderate NPDR without DME (n-37) Severe NPDR without DME (n=29) PDR without DME (n=22) No DR to moderate NPDR with DME (21) Severe NPDR with DME (n=23) PDR with DME (n=18)	Iranian	VAT SG TTO	Face-to-face interview	SG utility (vision health scale) No DR to moderate NPDR without DME:1.0 Severe NPDR without DME:0.97 PDR without DME 0.92 No DR to moderate NPDR with DME:1.0 Severe NPDR with DME :0.94 PDR with DME :0.87 TTO No DR to moderate NPDR without DME: 0.98 Severe NPDR without DME :0.90 PDR without DME 0.81 No DR to moderate NPDR with	Alinia C. et al.(Alinia et al., 2017) 2017	- Factors that affected utility were gender, smoking status, diabetic comorbidity - Macular edema was influencing utility value

				DME:0.95 Severe NPDR with DME :0.85 PDR with DME :0.72 VAT No DR to moderate NPDR without DME:0.97 Severe NPDR without DME :0.92 PDR without DME 0.75 No DR to moderate NPDR with DME:0.90 Severe NPDR with DME :0.79 PDR with DME :0.68		
	Australia (Melbourne)				Fenwick E. et al.(Fenwick, Xie, Pesudovs, et al., 2012) 2012	
DR age>18 years (N=98) Bilateral (n=82) DME (n=27)	Canada (Ontario and Vancouver)	TTO NEI VFQ	Interview	TTO utility in BSE and preference value 20/20-20/40:0.81 to 0.98 20/50 – 20/80:0.76 to 0.91 20/100 – 20/160: 0.70 20/200 :0.67	Szabo S. et al.(Szabo et al., 2010) 2010	- 6 health stats were identified by VFQ response and visual acuity - Preference weight declined with increasing bilateral disparity
DM (N=2213) include DR	USA (Kaiser Permanente	EQ5D	Self-complete	EQ-5D utility 20/20: 0.82	Smith D. H. et al.(Smith	

and DME	Northwest diabetes registry)		questionnaire	20/40: 0.75 Less than 20/80 :0.71	et al., 2008) 2008	

VAT=visual analogue thermometer, DM= Diabetes mellitus, DR=Diabetic retinopathy, DME-Diabetic macular edema, TTO=time-trade off, SG=Standard gamble, VFQ=Visual function questionnaire

Effect of cultural and beliefs on health state utility

1. Cultural and religious effect on health state utility

Cultural and religious can effect on the response of health state interview. In the study of Elbarazi et al., explored the relationship of religious and health perception in Muslim population, about 80% of the participant feel their health state influenced by spiritual or religious belief.(Elbarazi et al., 2017) Papadimitropoulos et al. also studied in Arab emirates , found that respondents had been reluctant to accept the state of worse than dead situation.(Papadimitropoulos et al., 2015) Health state preferences are a combination of results from demographic factors such as sex, age, personality, religion, occupation, and individual illness. Religions are known to affect the perception of death. Spiritual well-being and religion can reduce the anxiety related to death and mediate the depth perception.(Jeon, Kim, & Yoon, 2015) In the TTO question, imaginary death status is required to express the degree of individual health perception and mediate optimism, self-esteem, and life satisfaction.(Masel, Schur, & Watzke, 2012) No previous studies have demonstrated the association between religious belief and death-related health preference questions.

2. Language effect on the response of health state utility

Language and understanding of health utility measurement can give rise to varied utility level, for example, Luo et al., using EQ5D and HUI2/3 studied in Hispanic population across three languages; Non-Hispanic surveyed in English (NHE), Hispanics surveyed in English(HE), and Hispanics surveyed in Spanish(HS). The study found that NHE reported more problems and disabilities in HUI2/3, while EQ5D showed no difference between languages.(Luo, Ko, Johnson, & Coons, 2009)

Factors effect to the TTO response

Factors associated with the TTO answer such as sex , age, marital status and education have been reported.(van Nooten, van Exel, Eriksson, & Brouwer, 2016) Furthermore, TTO responses related to the loss of life and attitudes on future life, including death, may play a role in the respondent's decision.(Rutten-van Mölken, Hoogendoorn, & Lamers, 2009) F.E. Van Nooten et al. studied the understanding in the beliefs on respondents regarding their future health and death, including the desire to witness certain life events. The studied survey on 3 TTO imperfect health states (own current health, perfect health and dead) using a 10 years timeframe, Health-Risk Attitude Scale (HRAS), the Expectations Regarding Aging (ERA) questionnaires, the importance of life events that take place in TTO time frame and more question about future health including death and after death life. The studied results have shown respondent's beliefs about future health, death, and desires to witness a life event significantly affected the year of TTO trade-off. (van Nooten et al., 2016) From the above mentioned, We know that different cultures, countries and ways of life can contribute to the response of TTO, which it should be explored in Thai population.

The mode of administration of TTO gave rise to a different levels of health states. Norman R et al. compare face-to-face interviews and remote electronic tools to obtain TTO health levels. The study showed a pattern of response different by mode of administration with a larger standard deviation and higher proportions of response from the electronic tool.(Norman et al., 2010) One to-one interviewer technique was more favorable than the group interview and self-complete. (K. K. Shah, Lloyd, Oppe, & Devlin, 2013) However, in some countries, computer-based was preferred.(Papadimitropoulos et al., 2015)

Diabetic retinopathy, wet AMD, and Cataract

DR is one of the most common retina diseases and a leading cause of vision loss resulting from complicated systemic vascular disease with increasing prevalence.(Duh et al.; Robinson & Spencer, 2006; Ting et al., 2016) The vision loss

from diabetic retinopathy is reflected in a reduction in health utility.(M. M. Brown et al., 1999)

Wet AMD, a common retina condition, causing vision loss in an elderly population, results in damage by exudative and choroidal neovascularization (CNV).(Seddon & Chen, 2004) Unlike a complication of systemic changes in DR, the primary cause of vision loss in wet AMD is mainly in the macular area and contributes to irreversible damage. Regular treatment with anti-vascular endothelial growth factor (anti-VEGF) helps to reduce the incidence of severe vision loss.(Chew et al., 2014) When comparing DR and wet AMD, the HRQoL seems to be influenced by the amount of vision loss rather than the cause of it.(Melissa M Brown, Gary C Brown, Sanjay Sharma, Jennifer Landy, et al., 2002)

Cataracts, unlike DR and wet AMD, which presented in a chronic fashioned, is also one of the common causes of vision loss in the elderly but most regain vision through the lens removal surgery with artificial lens implantation. Visual acuity level in cataract patients is associated with the level of health utility and quality of life.(J. Lee et al., 2000) The vision level contributes mainly to the HRQoL, but the level differs among eye diseases.(B. S. Lee et al., 2008) Furthermore, the level of HRQoL or HU are various cross-culturally.(J. E. Lee et al., 2003) A QALY weights data for retina disease are still limited in South East Asian region.(Au Eong et al., 2012; Wagle et al., 2011; บรรณ, 2019).

Chapter 3

Methods and Procedure

This project consists of 2 phases of study which are.

1. Phase I: Pilot study and feasibility evaluation of Time trade-off technique, EQ-5D-5L, HUI3 and NEI VFQ-25
2. Phase II: Multicenter Health states survey study in a patient with DR, wet AMD, and Cataract by using TTO, EQ-5D-5L, HUI3

Instruments and outcome measurements

1. Health utility Instruments

1.1. Traditional time-trade off (tTTO)

tTTO is a traditional TTO, the concept originally proposed by Torrance et al. (Torrance, 1987) and used in retina patients described by Sharma S et al. (Sharma et al., 2002). tTTO score calculated as

"Utility value= (Number of years expected life - number of years trade-off)/ Number of year expected life"

A questionnaire related to tTTO can be found in **Appendix.**

1.2. Composite time-trade off (cTTO)

The cTTO questionnaire was modified from EQ-VT protocol for TTO valuation in EuroQol protocol.(B. M. Janssen et al., 2013; Williams, 1995). A full health state defines as perfect vision in each eye. cTTO questions started with explaining an interview process and introducing the visual aid for comparison, then starting with one sample question. For a better than dead health state, participants were asked to choose between ten years of full health state (life A) and their vision condition health state for ten years (life B). If life B has been chosen, the participant was asked an explanation of the answer to determine the participant's cognitive and understanding of the question. If life A was selected or found to be equal to life B, participants would move to the next question to choose between life A in 0 year and life B in 10 years. If life A was chosen, a worse than the dead situation was

applied, and utility set as 0. If life B was preferred, the number of years in life A was started with x year with a healthy eye then followed by the dead. The x started with 0 and upward titration every 1 year until indifference or reversal occurred. The visual aid TTO board was used instead of a digital computer presentation as visual guide for respondents. Questionnaire related to cTTO can be found in **Appendix.**

1.3. EuroQoL EQ-5D-5L questionnaire (EQ-5D-5L)

The EQ-5D-5L interview started with EQ-VAS and was followed by five domains of questions as in EuroQoL protocol. The Thai version of EQ-5D-5L interview The Thai version of EQ-VT questionnaire.(Pattanaphesaj, 2014) started with EQ-VAS and was followed by five domains questions as in EuroQoL protocol. A hybrid model value set for Thai population was used to calculate the EQ-5D-5L utility score.(Pattanaphesaj et al., 2018) The domain of EQ-5D-5L includes mobility, self-care, pain/discomfort, usual activities and depression/anxiety. Each domain comprise 5 response question. The utility score from EQ-5D-5L range from 0 to 1.

1.4. Health utility index 3 questionnaires (HUI3)

The translated and validated Thai version of HUI3 was used in this study.(Saiguay & Sakthong, 2013) The interview and HU calculation were followed by instructions from HUI® (HUInc, Hamilton , Canada).(Feeny et al., 2002; Horsman, 2012) There are 8 dimentions in HUI3 questionnaires, including vision, hearing, speech, ambulation, dexterity, emotion, cognition, and pain. There are 41 questions on this questionnaire. However, a responder was not required to answer all of the items, the number of questions required to respond are related to an answer of the first question in each domain. The HUI3 result gives rise to a utility score range from -0.36 to 1.0

1.5. The National Eye Institute Visual Function Questionnaire (NEI VFQ-25)

The Thai version of NEI VFQ-25(Mangione et al., 2001; Setthawatcharawanich et al., 2009) comprises of 1 general health item, and 24 visual-related items, were used to evaluate the visual related QoL. All instruments had been authorized to use prior to the study. The NEI VFQ-25 score range from 0 to 100 , where a higher score indicates better visual function.

Measurement of visual acuity and visual impairment

The number Early treatment diabetic retinopathy study chart (ETDRS chart (Precision Vision, inc, IL, USA) were used to measure distant visual acuity. The visual acuity measure as presented distance visual acuity (Patient required to put their distant glasses on to read the chart) and pin-hole visual acuity were performed. When the patient couldn't read the charts, finger counting (FC), hand movement (HM), and light perception (LP) were tested. Converting to LogMar scale was applied to FC,HM,LP or complete blindness.(Schulze-Bonsel, Feltgen, Burau, Hansen, & Bach, 2006).

1. The ETDRS letter converting to LogMar visual acuity scale by using a formula(Holladay, 2004)

LogMAR = -0.02 (X) + 1.7 . where X = count of ETDRS letters

2. The Snellen visual acuity calculated by using a formula(Holladay, 2004)r

Snellen denominator = $20/10^{-X}$, where X- count of ETDRS letters

3. Visual impairment grading according to status according to WHO classification.(Pan, Wang, Wang, Xu, & Song, 2018). Level of visual impairment are indicated in **Table 2.**

Table 2 The levels of visual impairment

Level of VI	Distant snellen visual acuity in the best-seeing eye	Definition
0	20/20 to 20/40	No vision impairment
1	20/40 to 20/60	Mild vision impairment
2	20/60 to 20/200	Moderate vision impairment
3	20/200 to 20/400	Severe vision impairment
4	20/400 to 5/300	Blindness
5	Light perception	Blindness
6	No light perception	Blindness

Clinical diagnosis and terms

1. Diabetes mellitus defines according to an American diabetes association (ADA) guidelines(Association, 2020) which criteria are;
   1.1. Clinical symptom of hypoglycemia or hyperglycemia crisis with random plasma glucose≥ 200 mg/dl
   1.2. Fasting plasma glucose (8 hours fasting) ≥ 126 mg/dl
   1.3. 2- hour plasma glucose ≥ 200 mg/dl after oral intake of 75 grams of glucose solution in water
   1.4. Hemoglobin A_1C ≥ 6.5%
2. Diabetic retinopathy grading was followed the International classification of diabetic retinopathy (ICDR) (Wilkinson et al., 2003) and diabetic macular edema (Das et al., 2021), which detail are as in Table 3. However, a justification for disease diagnosis was referenced by retina specialist and ophthalmologist at a local study site.

Table 3 Classification of diabetic retinopathy and macular edema

Disease severity	Findings observable upon dilated ophthalmoscopy
Diabetic retinopathy (DR)	
No apparent DR	No abnormalities
Mild NPDR	Microaneurysms only
Moderate NPDR	More than just microaneurysms but less than Severe NPDR, (microaneurysms with other signs like intraretinal hemorrhages, hard exudates, cotton wool spots)
Severe NPDR	Any of the following: (4:2:1) 1. More than 20 intraretinal hemorrhages in each of 4 quadrants 2. Definite venous beading in 2+ quadrants 3. Prominent intraretinal microvascular abnormalities

	IRMA in 1+ quadrant (And no signs of PDR)
PDR	One or more of the following: 1. Neovascularization 2. Vitreous/preretinal hemorrhage
Diabetic macular edema (DME) by clinical appearance	
No apparent DME	No retinal thickening or hard exudates at macula
Mild DME	Some retinal thickening or hard exudates in posterior pole but distant from the center of the macula
Moderate DME	Retinal thickening or hard exudates approaching the center of the macula but not involving the center
Severe DME	Retinal thickening or hard exudates involving the center of the macula
DME classification by Center of macula involvement using Optical Coherence Tomography (OCT)	
Non-central involving DME	Retinal thickening in the macula that does not involve central subfield zone in OCT (1 mm diameter)
Center involving DME	Retina thickening in the macula that involves the central subfield zone in OCT (1 mm diameter)

3. Tractional retinal detachment (TRD) defines as fibrous traction on retina with elevation of retina tissue as a result from diabetic retinopathy. The diagnosis was based on a justification by retina specialist or ophthalmologist at local study site.

Non-medical expenses and income lost

1. Travel expense defines as an expense for transportation-related items for the doctor's visit, including gas, public transportation, and car rental.
2. Other non-medical expenses define as an expense which not related to medical treatment and transportation, including food and accommodation
3. Income losses

3.1. Patient income lost defines as an amount in monetary that patient lost from absence of work on the doctor's visit day

3.2. Caregiver income lost defines as an amount in monetary, that caregiver who brings the patient to hospital, losses on the doctor's visit day

Evaluation of systemic comorbidity

To evaluate the impact of systemic comorbidity on health utilities and quality of life. The Charlson comorbidity index (CCI) was used, it is a method for a prediction of mortality or use as weighting of comorbid conditions. It has been used to evaluate a burden of multiple systemic diseases. The comorbidity from the Charlson comorbidity included myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatologic disease, peptic ulcer disease, liver disease, diabetes with/ without chronic complication, hemiplegia or paraplegia, renal disease, malignancy including metastatic solid tumor and AIDS/HIV disease.(Charlson, Pompei, Ales, & MacKenzie, 1987) The CCI has been cited for more than 40,000 times and has been used widely in clinical practice including the data gathering from hospital chart.(Quan et al., 2011)

Methods for Pilot (Phase I) study

1. Study design

This study was a cross-sectional study that interviewed patients from an ophthalmic outpatient clinic at King Chulalongkorn Memorial Hospital from October 2019 to December 2019. We recruited consecutive patients attending the retina clinic and general eye clinic. Before the interview process, all patients were informed about the study and provided consent to be interviewed and for their clinical data records to be used. This study was approved by the local institutional review board committee and registered in the Thai clinical trial registry before data collection began (TCTR20190831002). Methods of this study has been published.(Pongsachareonnont, Sakthong, & Kulvichit, 2022)

2. Inclusion and exclusion criteria

The inclusion criteria were patients who were diagnosed of cataracts, wet-age-related macular degeneration (wet AMD) or diabetic retinopathy (DR). Patient who had mental impairment or non-native Thai speakers were excluded from the study.

3. Data collection

Participants were invited to the interview after their doctor visit by the principal investigator or research coordinator. None of the invited patients refused to join the study. Five trained interviewers with experience in health interviewing for at least 1 year conducted the face-to-face interviews. All interviews consisted of the same sequences of questionnaires. The licensed questionnaires were authorized before data collection was started. After completion of the QoL questionnaires, respondents and interviewers were asked their opinions about the feasibility of the interview, and their responses were recorded at the end of the interview. Snellen VA and clinical examination data were collected from the patient's chart of that visit. Interview started with demographic data and clinical data. The utility instruments started in a order with tTTO, cTTO, EQ-VAS, EQ-5D-5L and HUI3. After utility instruments were asked an NEI VFQ-25 was interviewed. An open-ended question was used to gather the interviewer's opinion about the understanding of the respondent, asking if the interviewer thought that there were important issues that might affect the accuracy of the respondent's answers during the interview. The respondent's understanding of the interview questions, based on the perception of the interviewer, was rated on a Likert-type scale ranging 0 to 4, where "0" means that the respondent understood 0%–25% of the questions, "1" means that the respondent understood 26%–50% of the questions, "2" means the respondent understood 51%–75% of the questions, "3" means the respondent understood 76%–99% of the questions, and "4" means the respondent understood fully or 100% of the interview questions.

An interviewer's low confidence in the accuracy of the answers was defined as a rating of less than 50%. Open-ended questions were asked at the end of each questionnaire, including "Are there any parts of this questionnaire interview that

make you feel discomfort, troubled, or inconvenienced? Please specify," and "Are there any parts that you dislike about this specific questionnaire?" The interview started by asking for general demographic health information, followed by tTTO, cTTO, EQ-VAS, EQ-5D-5L, HUI3, and NEI VFQ-25; and then closed with open-ended questions about the respondent's opinion of the questionnaires.

4. Feasibility assessment

The feasibility assessment of the questionnaires focused on the questionnaire interview time, the interviewer's rating of the respondent's understanding of the questionnaires, the open-ended problems of the difficulty in responding to each questionnaire, respondent feedback of the questions, respondent preferences, and the association between HU with the level of VI and vision-specific QoL score.

5. Statistical analysis

A prespecified sample size of 40 subjects was designated for this pilot and feasibility study. Continuous data were described as means and standard deviations. Proportions were described in percentages. Chi-square or Fisher's exact test was used to test the distribution of categorical data. We used Pearson correlation or Spearman correlation coefficients to explore the correlation between the HU and NEI VFQ-25 QoL scores. Analysis of covariance (ANOVA) were used to compare the mean HU among types of eye disease in from all questionnaire instruments. Multivariable linear regression analysis was used to explore the association between VI and HU. STATA/IC 15.1 (StataCorp LLC®, Texas, USA) was used for statistical analysis. A *p* value <0.05 indicated statistical significance. Complete case analysis was used.

Methods for Multicenter (Phase II) study

1. Study design

This cross-sectional survey was conducted in four study sites across Thailand from September 22, 2020 to April 02, 2021. The study protocol had been approved by the local ethics committee at each study site and adhered to the tenets of the Declaration of Helsinki. Clinical trial registration was submitted before commencing

the patient enrollment (TCTR20190831003). The participants were informed about the study by the research coordinators, and their consent was obtained prior to the interview. We requested all participants to partake in the survey following their doctor's visit. The participants were recruited from ophthalmic outpatient clinics across tertiary care centers in Bangkok province (Central region), Chiang Mai province (Northern region), Khon Kaen province (Northeastern region), and Songkhla province (Southern region).

2. Inclusion and exclusion criteria

The inclusion criteria were as follow: (1.) age ≥ 18 years diagnosed with either diabetic retinopathy (DR) or screened for diabetic retinopathy, visually affected cataract or wet AMD ; (2.) native Thai speaker; and (3.) no history of mental retardation or impaired cognitive function. Patients who were unwilling to response or trade-in any TTO question or had a dense cataract that substantially affected their vision following the diagnosis of wet AMD, DR or DR screening were excluded from the study.

3. Data collection

Participants were invited to the interview after their doctor visit by the principal investigator or research coordinator. The interview order commenced with general information and demographic data, followed by tTTO, cTTO. Following TTO questions, HUI3 or EQ-5D-5L was administered using a prespecified simple randomization sequences to offset the potential for sequence bias. Initially administered HUI-3 was administered, followed by EQ-5D-5L and vice versa. Eventually, we administered the National Eye Institute Visual function questionnaire (NEI VFQ-25). Face-to-face interviews were performed by trained local interviewers in similar fashion at all study sites. ETDRS visual acuity test was obtained before the pupil dilatation procedure. Charlson comorbidity index were calculated by using the interview and doctor records.

4. Statistical analysis

Data were entered and managed using REDCap® electronic data capture tools hosted at the Chulalongkorn University, Thailand. Data analysis was performed using STATA® version 15.1 (StataCorp.2017, StataCorp LLC, Tx, USA). Continuous data were summarized using means and standard deviations (SD), whereas categorical data were reported using percentages and counts. We performed the Student's t-test to compare two continuous means, and used the general linear model for more than two groups. We performed the Pearson chi-square test to compare the categorical variables. Pearson correlation coefficients were used for the correlation between HU score and NEI VFQ-25 score. Concordance correlation coefficient were used to determined the agreement of instrument to measure HU. We conducted a multivariable modeling of continuous outcomes using the linear mixed model (LMM) with study site as a fixed effect because it can account for any clustering effect, which many be an outcome of our multicenter design effect. Possible confounders to the relationship between VA and HU, including QoL score, were included in the model based on prior knowledge. For the relationship between predictor and confounder, variance inflation factors less than 10 as consider level of multicollinearity. A p-value ≤ 0.05 was considered statistically significant throughout all inferential analyses.

5. Sample size

The utility scores were the primary response outcomes. We calculated the sample size to detect a minimal clinical difference (effect size) of 0.15 utility score among any of the disease groups using an alpha of 0.05, power of 80%, and a cluster effect of intraclass correlation (ICC) = 0.1. Patients with DR displayed greater prevalence; thus, DR was oversampled at a proportion of 2:1. This yielded an overall sample size of at least 256 participants (128 participants with DR, 64 participants with wet AMD, and 64 participants with cataracts). The calculation of sample size calculated by STATA® . The testing methods and formulars can be found at https://www.stata.com/manuals/pss-2powertwomeanscluster.pdf.

Chapter 4

Results

The pilot study: results (Pongsachareonnont et al., 2022)

Forty respondents participated in this survey (1 missing demographic data). **Table 4** shows the respondents' demographics. All respondents had Buddhism religious beliefs, except for one person who was Christian. According to WHO VI criteria, about 43.59% of all respondents had mild VI, 25.64% had moderate VI, 23.08% had severe VI, and 7.69% were blind. None of participants were excluded after the recruitment.

Table 4 Demographics of 39 respondents in the pilot study among Diabetic retinopathy (DR), Cataract, and Wet-age-related macular degeneration (wet AMD) patients

Factors		DR N = 16	Cataract N = 15	Wet AMD N = 8	*P* value
Age [mean in year (SD)]		63.19 (9.63)	58.47(7.70)	72.00 (8.40)	>0.001
Sex [n(%)]	Male	6 (38)	10 (67)	2 (25)	0.12
Location [n(%)]	Bangkok	9 (60)	8 (53)	3 (38)	0.65
	Others	6 (40)	7 (47)	5 (62)	
Employment status [n(%)]	Unemployed or housewife	5 (31)	4 (27)	2 (25)	0.88
	Government worker	1 (6)	2 (13)	0 (0)	
	Daily employment	3 (19)	4 (27)	1 (12.5)	
	Employment/nongovernment	4 (25)	2 (13)	1 (12.5)	
	Retirement/monk	3 (19)	3 (20)	4 (50)	
Marital status [n(%)]	Single	3 (18.8)	2 (13)	2 (25)	0.22
	Married	7 (43.8)	12 (80)	5 (62.5)	
	Others/widow/divorce	6 (37.4)	1 (7)	1 (12.5)	
Education	Lower than grade 3 or none	4 (25)	3 (20)	1 (12.5)	0.19

[n(%)]					
	Grade 3 to grade 9	6 (37.5)	3 (20)	0 (0)	
	High school or technical school	4 (25)	6 (40)	2 (25)	
	Bachelor or above	2 (12.5)	3 (20)	5 (62.5)	
Average income per month [n(%)]	No direct income	5 (31.3)	3 (20)	1 (12.5)	0.64
	Less than 10,000 baht	6 (37.5)	4 (27)	1 (12.5)	
	10,000 to 25,000 baht	3 (18.7)	6 (40)	4 (50)	
	Above 25,000 baht	2 (12.5)	2 (13)	2 (25)	
Treatment coverage [n(%)]	No coverage/others	5 (31.3)	2 (13.3)	2 (25)	0.55
	Government reimbursement	3 (18.7)	3 (20)	3 (37.5)	
	Universal health coverage program (30 baht)	6 (37.5)	8 (53.3)	1 (12.5)	
	Social security insurance	2 (12.5)	2 (13.4)	2 (25)	
Caregivers accompany to hospital [n(%)]	None	4 (25)	5 (33)	2 (25)	0.83
	Family	11 (69)	10 (67)	5 (62.5)	
	Others	1 (6)	0 (0)	1 (12.5)	
History of alcohol drinking [n(%)]	No	9 (56)	6 (40)	4 (50)	0.65
	Yes	7 (44)	9 (60)	4 (50)	
History of smoking [n(%)]	No	12 (75)	11 (73)	6 (75)	1.00
	Yes	4 (25)	4 (27)	2 (25)	
Visual acuity in BSE** [n(%)]	20/20 to 20/40	6 (38)	7 (50)	3 (37.5)	0.99
	20/50 to 20/70	5 (31)	3 (21.5)	2 (25)	
	20/80 to 20/200	4 (25)	3 (21.5)	2 (25)	
	Less than 20/200	1 (6)	1 (7)	1 (12.5)	

Visual acuity in WSE*** [n(%)]	20/20 to 20/40	1 (6.3)	2 (14)	2 (25)	0.74
	20/50 to 20/70	2 (12.5)	3 (21)	1 (12.5)	
	20/80 to 20/200	9 (56.2)	4 (29)	3 (37.5)	
	less than 20/200	4 (25)	5 (36)	2 (25)	

* Categorical *P* value calculated by Fisher's exact test

** Best-seeing eye

*** Worse-seeing eye

Table 5 shows the mean utility score of the tTTO and cTTO, EQ-5D-5L, and HUI3 instruments. There were no statistically significant differences in all HU scores among DR, wet AMD and cataracts. Four of 40 respondents denied trading their life in tTTO because of the following reasons: satisfaction with vision status and personal beliefs. Off all non-traders for tTTO, two respondents had a visual acuity in a best-seeing eye (VABSE) of 20/20 to 20/40, with one subject diagnosed as DR (age 68 years) and another one had wet AMD (age 73 years); one respondent had VA 20/50 to 20/70 with a diagnosis of DR (age 65 years), and one respondent had VA 20/80 to 20/200 with a DR diagnosis (age 57 years). All respondents were Buddhist with a high school education level or lower. Among these non-traders for tTTO, three respondents had difficulty understanding the life-trading concept, and they all chose to answer the cTTO with the reason of easier to understand in concept. Meanwhile, one non-trader in the tTTO understood the concept of trading life but had an idea of acceptance in life and fatalism that caused a denial to trade for tTTO. All tTTO traders were able to respond to the cTTO instruments. Two patients with negative tTTO were willing to trade more years than their life span: one patient was diagnosed with cataract with a VABSE in the range of 20/80 to 20/200, and the other was diagnosed with wet AMD with a VABSE less than 20/200. The mean interview duration of the tTTO, cTTO, EQ5D-5L, HUI3, and NEI VFQ-25 were 2.89 minutes (SD 1.68, min–max: 0.3–7), 3.92 minutes (SD 2.43, min–max: 1–15.16), 3.07 minutes (SD 1.85, min–max: 1–12), 5.50 minutes (SD 2.10, min–max: 2–13), and 8.20 minutes (SD 2.87, min–max: 3—17),

respectively. The answers of one respondent received a rating of low confidence accuracy from the interviewer on the tTTO and cTTO. Two respondents on the tTTO questionnaire and one respondent on the cTTO questionnaire had difficulty understanding the concept of trading life for better health state, whereas none of the respondents to the EQ-5D-5L, HUI3, and NEI VFQ-25 showed nonunderstanding of the questions. For the effect of religion on the imagination of death and shortening of life, 87.5% reported some effect, 10% reported a moderate effect, and 2.5% reported a marked effect on the decision related to TTO questions. None of the respondents reported no effect of religion on the TTO decision, and none felt discomfort on all questions.

Table 5 Utilities score and quality of life score

Instruments	n	Mean	SD	Min	Max
tTTO	36	0.50	0.50	-1.50	0.94
cTTO	40	0.49	0.48	-0.95	1.00
EQ-VAS	40	0.67	0.17	0.30	1.00
EQ-5D-5L	40	0.80	0.12	0.51	1.00
HUI3	39	0.61	0.30	-0.04	1.00
NEI VFQ-25	40	65.59	16.38	31.04	91.52

SD: standard deviation, Min: minimum, Max: maximum

Figure 2 shows the positive correlation between utility scores and visual-specific QoL questionnaire scores, demonstrating that utility scores from the EQ-VAS, EQ-5D-5L, and HUI3 are statistically significantly correlated with the VFQ-25 score. For the association of HU and VI status, a univariable analysis is shown in **Table 6**. When adjusting for baseline demographics, the utility scores obtained from HUI3 and EQ-5D-5L significantly decreased in mild and moderate to severe VI when compared with normal VI, as shown in **Table 7**.

Table 6 Univariable analysis of the association to utility by linear regression analysis (Pilot study)

	HUI3				EQ-5D-5L				EQ-VAS				tTTO				cTTO			
	β	p- value	95% CI		β	P-value	95% CI		β	p- value	95% CI		β	p- value	95% CI		β	p-value	95%CI	
Age	-0.01	0.16	-0.02	0.00	-0.01	0.16	-0.02	0.00	0.00	0.13	0.00	0.01	-0.01	0.13	-0.03	0.00	-0.01	0.22	-0.02	0.01
Female	-0.12	0.20	-0.32	0.07	-0.01	0.75	-0.09	0.07	0.04	0.43	-0.07	0.15	-0.01	0.94	-0.36	0.34	0.02	0.90	-0.29	0.33
History of smoking	-0.05	0.65	-0.28	0.17	-0.04	0.39	-0.13	0.05	-0.07	0.23	-0.20	0.05	0.13	0.53	-0.30	0.57	-0.18	0.31	-0.53	0.17
History of alcohol intake	0.02	0.85	-0.18	0.21	-0.03	0.49	0.11	0.05	-0.10	0.06	0.20	0.00	0.08	0.64	-0.26	0.42	0.00	0.99	-0.31	0.31
Employment status																				
Government worker	-0.05	0.80	-0.47	0.37	-0.09	0.26	-0.25	0.07	0.07	0.52	-0.15	0.30	0.44	0.18	-0.21	1.09	0.24	0.44	-0.39	0.87
Daily employment	-0.04	0.81	-0.34	0.27	-0.08	0.14	-0.20	0.03	-0.01	0.85	-0.18	0.15	0.42	0.08	-0.05	0.88	0.15	0.51	-0.30	0.60
/ non government	0.07	0.65	-0.23	0.37	-0.05	0.39	-0.16	0.06	0.10	0.22	-0.06	0.26	0.52	0.04	0.02	1.03	0.43	0.06	-0.02	0.88
Retirement/monk	-0.03	0.81	-0.32	0.25	0.02	0.68	-0.08	0.13	0.06	0.41	-0.09	0.21	0.45	0.05	0.00	0.90	0.19	0.38	-0.24	0.61
Marital status																				
Married	0.09	0.49	-0.17	0.35	-0.01	0.81	-0.12	0.09	0.00	1.00	-0.14	0.14	-0.07	0.77	-0.55	0.41	-0.01	0.98	-0.43	0.42
Other/widow/divorce	0.16	0.32	-0.16	0.48	0.02	0.76	-0.11	0.15	0.15	0.08	-0.02	0.32	-0.15	0.60	-0.73	0.43	-0.11	0.67	-0.62	0.40
Education level																				
Grade 4 to grade 9	0.07	0.66	-0.23	0.37	-0.03	0.59	-0.15	0.08	-0.15	0.08	-0.31	0.02	0.01	0.96	-0.51	0.53	-0.02	0.92	-0.51	0.46
High school or technical school	0.17	0.22	-0.11	0.45	0.08	0.11	-0.02	0.19	-0.09	0.24	-0.24	0.06	-0.14	0.55	-0.63	0.34	-0.14	0.53	-0.59	0.31
Bachelor or above	0.04	0.76	-0.25	0.34	0.00	0.94	-0.11	0.12	-0.12	0.13	-0.28	0.04	-0.41	0.10	-0.90	0.09	-0.07	0.78	-0.54	0.41
Average income per month																				
Less than 10,000 baht	0.06	0.14	-0.23	0.35	0.03	0.60	-0.08	0.14	0.09	0.27	-0.07	0.24	0.23	0.39	-0.30	0.75	0.00	0.99	-0.44	0.44
10,000 to 25,000 baht	0.10	0.14	-0.17	0.38	0.05	0.30	-0.05	0.16	0.06	0.40	-0.09	0.21	0.18	0.44	-0.29	0.65	0.25	0.22	-0.16	0.67
Above 25,000 baht	-0.01	0.17	-0.35	0.32	-0.03	0.70	-0.16	0.11	0.09	0.30	-0.09	0.28	0.18	0.52	-0.39	0.75	0.22	0.40	-0.30	0.73

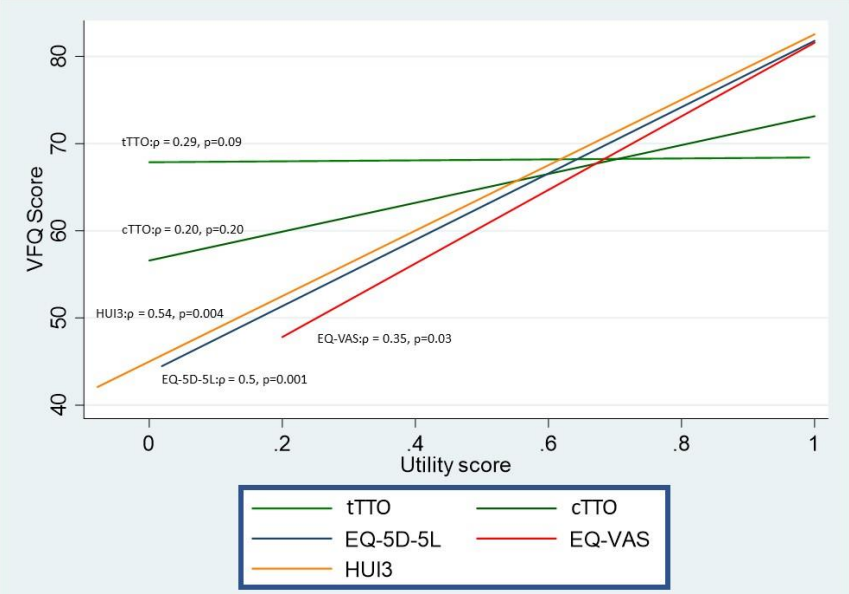
Treatment coverage																			
Government reimbursement	0.08	0.58	-0.21	0.38	0.10	0.08	-0.01	0.21	0.02	0.84	-0.18	0.15	-0.08	0.74	-0.59	0.42	0.08	0.72	-0.39	0.55
University health coverage (30 baht)	0.08	0.57	-0.19	0.34	-0.01	0.78	-0.11	0.09	-0.09	0.23	-0.23	0.06	-0.16	0.48	-0.61	0.29	0.05	0.81	-0.37	0.47
Social security insurance	0.05	0.77	-0.28	0.38	0.00	0.98	-0.12	0.12	-0.02	0.82	-0.19	0.15	0.16	0.56	-0.39	0.71	0.20	0.43	-0.30	0.70
Visual impairment status																				
Mild	-0.23	**0.02**	-0.42	-0.05	-0.09	**0.03**	-0.18	-0.01	0.05	0.39	-0.07	0.18	-0.02	0.94	-0.44	0.40	-0.19	0.26	-0.53	0.15
Moderate or above	-0.41	**<0.001**	-0.58	-0.23	-0.10	**0.02**	-0.18	-0.02	-0.07	0.24	-0.19	0.05	-0.40	0.05	-0.79	0.00	-0.20	0.22	-0.52	0.12

Table 7 Association between health utility (HU) and visual impairment status (VI) in the pilot study

VI	HUI3			EQ-5D-5L			EQ-VAS			tTTO			cTTO		
	β	p- value	95% CI	β	p- value	95% CI	β	p- value	95%CI	β	p- value	95% CI	β	p- value	95% CI
Normal		Ref.			Ref.			Ref.			Ref.			Ref.	
Mild	−0.38	**0.05**	−0.75 to −0.01	−0.16	**0.01**	−0.26 to −0.06	0.04	**0.68**	−0.15 to 0.22	0.33	**0.32**	−1.03 to 0.37	−0.34	**0.21**	−0.90 to 0.21
Moderate to severe	-0.50	**0.002**	−0.80 to −0.21	−0.09	**0.06**	−0.18 to 0.00	−0.05	**0.55**	−0.21 to 0.12	−0.38	**0.16**	−0.93 to 0.17	−0.27	**0.27**	−0.76 to 0.23

*Adjusted for age, sex, marital status, education level, income, health coverage, smoking status, and alcohol status

Figure 2 Correlation between the utility scores and the NEI VFQ-25 score in the pilot study



The multicenter study: results

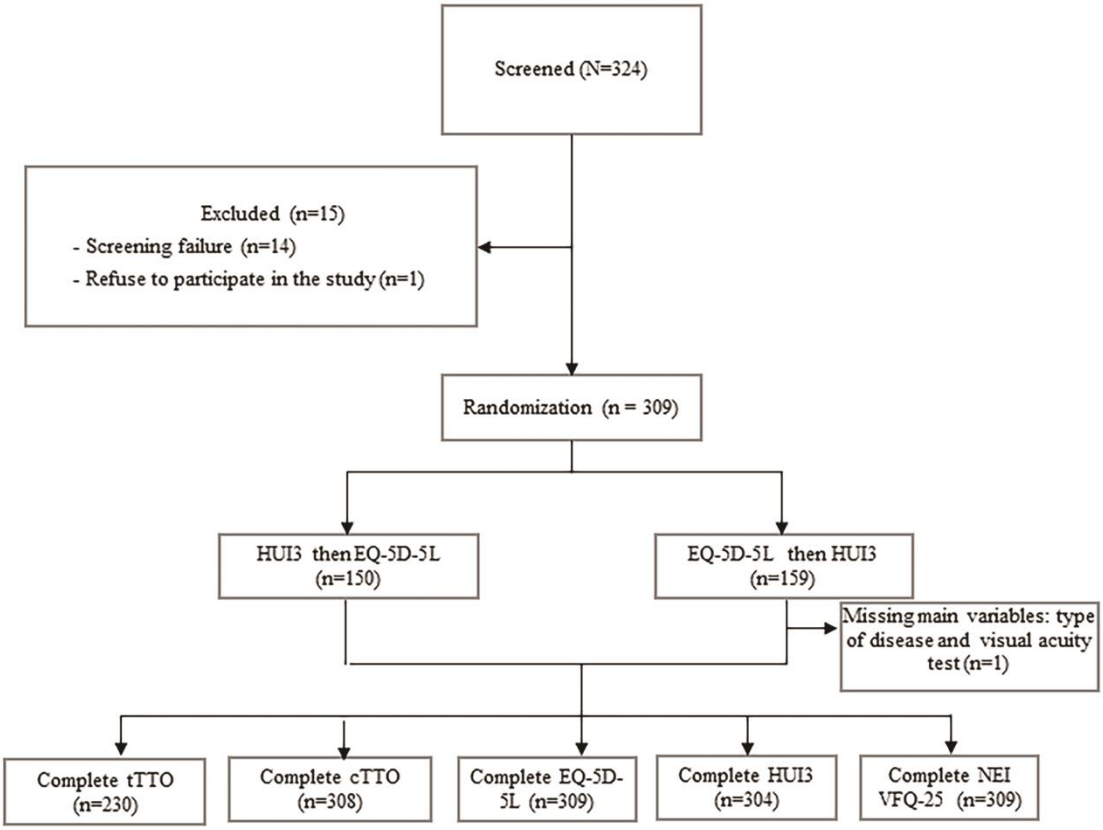
Utility scores and quality of life scores

1. Utility scores and vision specific quality of life score

We enrolled 324 patients for the study, and only 309 patients were eligible for the interviews **(Figure 3)**. From our sample, 79,68,78, and 84 participants were from the northern, northeastern, south, and central part of the country. There were 141, 78, and 90 patients in the DR, cataract and wet AMD groups, respectively. **Table 8** summarizes the demographic and baseline characteristics. There were statistically significant differences in the mean age group, the region of participants, marital status, the proportion of Buddhism follower, and types of healthcare coverage programs among the three diseases. The overall mean utility score obtained from tTTO, cTTO, EQ-VAS, EQ-5D-5L and HUI3 (mean ±SD) were 0.66 ±0.20, 0.84 ±0.25, 0.73 ±0.15, 0.70 ±0.19 and 0.68 ±0.26, respectively. The mean VFQ-25 score was

70.71 ±17.76. **Table 9** summarizes the mean utility score and VFQ-25 score among levels of visual impairment. Details of the utility score among types of eye diseases are provided in **Table 10**. In the paired comparison, the mean cTTO was higher than the HUI3 (mean difference ± SE: 0.16±0.02 , p<0.001) and EQ-5D-5L (mean difference ±SE: 0.14±0.02 , p<0.001). There was no difference between the HUI3 and EQ-5D-5L (mean difference ± SE: -0.02± 0.02 , p<0.23). **Table 11** summarizes an association of health utility scores across WHO visual impairment level. The NEI VFQ-25 score among visual impairment and association with visual impairment status are shown in **Table 12.** There were significant differences in all levels of visual impairment compared to normal vision from NEI VFQ score.

Figure 3 Patients enrollment workflow



2 Factors associated with the utilities and quality of life

The crude and adjusted for baselines patient-characteristic effect for HU from all measurements by using multivariable linear mixed model analysis are provided in the **Table 13 and 14.** Briefly, the VA in worse-seeing eyes was significantly associated with decreasing HU in EQ-5D-5L, HUI3 and cTTO. In better-seeing eyes, the HU from cTTO was significantly decreased along with the VA worsening. For adjusted factors, older age, marital status and non-smokers were significantly associated with HU increase in EQ-VAS. There were statistically significant differences in HU scores among the types of healthcare coverage in EQ-5D-5L, whereas HUI3 displayed potentially

different but statistically insignificant scores. The income level was significantly associated with increasing of HU in EQ-VAS, EQ-5D-5L and HUI3. There were no differences of HU among patients with DR, wet AMD and cataract when adjusted for VA levels and baseline characteristics. There were significantly reduce of the mean utility scores when the CCI increased in EQ-VAS, EQ-5D-5L and HUI3.

3 Utility and QoL among types of eye diseases

A one-way analysis of variance determined the mean HU among patients with DR, wet AMD and cataract in each utility instrument. There were no significant differences in the mean HU among these diseases. The NEI VFQ-25 score was insignificantly different between these diseases as well. Moreover, the linear mixed model adjustment did not demonstrate statistically different HU obtained from all techniques and the NEI VFQ-25 scores among the DR, wet AMD and cataract groups. In the DR group, the percentage of no DR, non-proliferative DR, proliferative DR and DR with tractional retinal detachment (TRD) was 8.4%, 27.3%, 51% and 13.3%, respectively. There were no differences in the HU between participants with and without diabetic macular edema (DME). However, the HU from cTTO score demonstrated that TRD patients had statistically significantly lower compared to no DR ($p = 0.041$, 95%CI of mean difference: -0.40 to -0.008)

4. Non-trader for tTTO

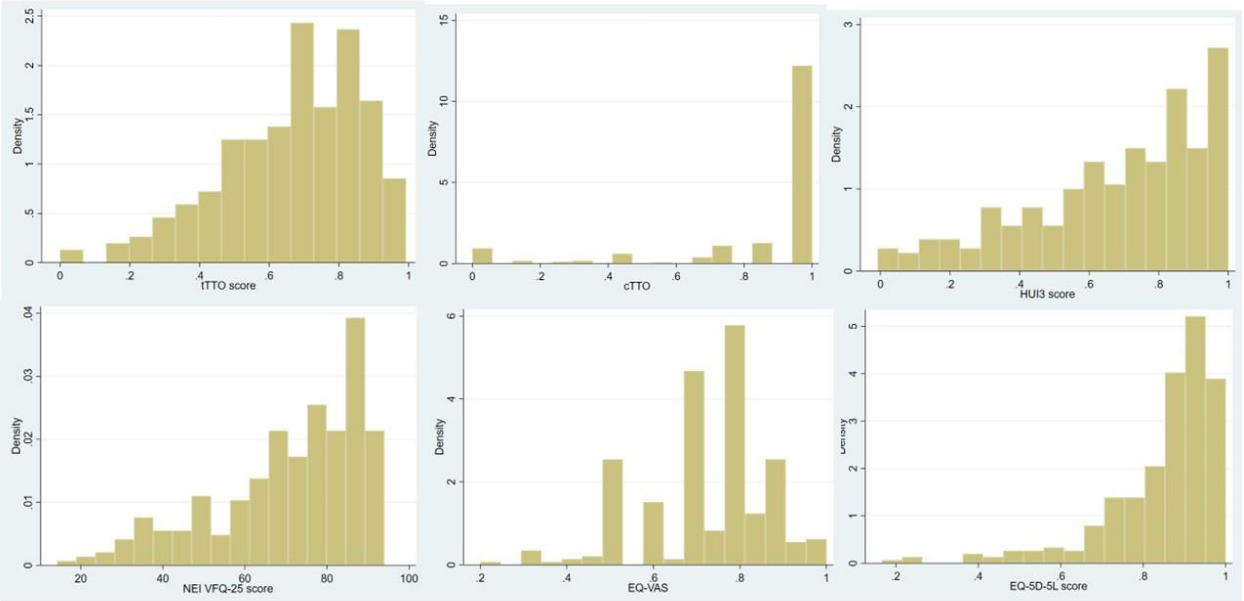
Of all 309 participants, only 230 patients were willing to trade their life to gain healthy vision in tTTO. The reasons for non-trader in the tTTO were that they considered their vision was in good condition (49.38%), accepted with their eye conditions/ or were happy with the impaired visual status (36.71%), not worthy of trading their life to gain healthy vision or could not accept the idea of a shortening of life (8.9%), and provided no reasons to be explanation (5%). For tTTO, participants in the non-trader group had higher age than those in the trader group (67.9% vs. 62.6%). The percentage of non-trader were higher than the traders in the central and

the Northern region (32.9% and 35.4%). The number of Buddhist participants was higher in the non-trader group than that in the trader group (97.5% vs. 90.0%). Moreover, the mean VA in worse-seeing eyes was lower in non-traders compared with traders (1.0 LogMar vs 1.2 LogMar). **Table 15**. Summarizes a detail of the comparison. Owing to the limitation of the willing to trade in tTTO, only cTTO was used to represent the visual utility of the direct method in the analysis.

Distribution of health utilities and NEI VFQ score and test of linearity assumption in the multicenter study

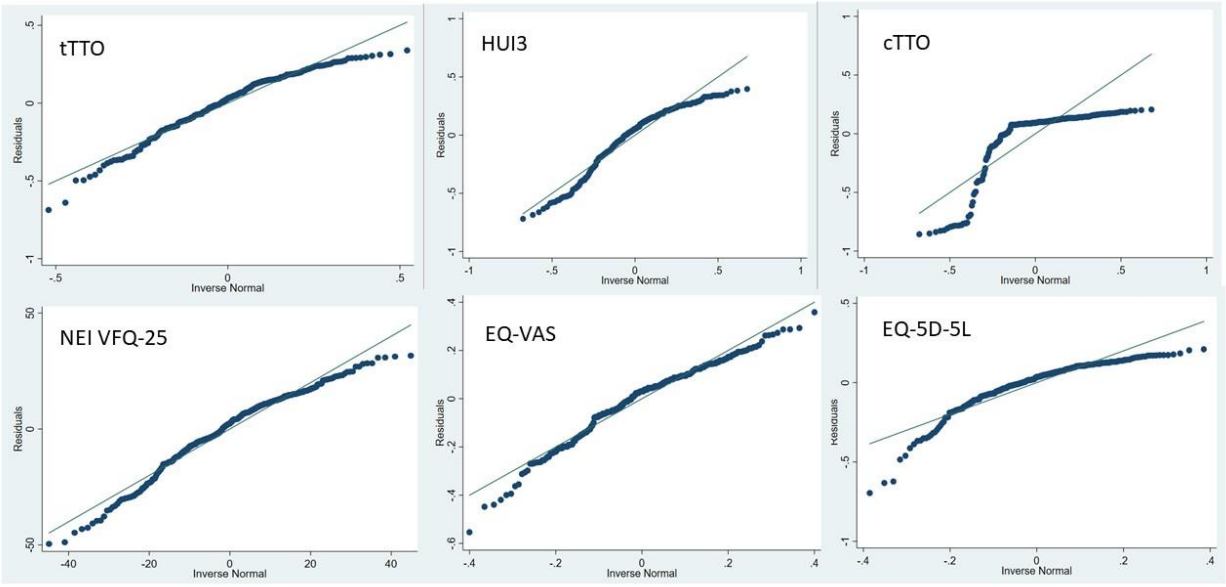
The distribution of utility score has shown left-skewed. cTTO has showed the most skewed of data. Figure X below shows histograms of the HU scores and QoL scores. Q-Q plot of the residual from regression function of the primary outcome (HU) and primary predictor (VA) is shown in Figure XX. The Q-Q plot has shown mild left skew distribution in tTTO, EQ-VAS, EQ-5D-5L, HUI3, and NEI VFQ-25, however, cTTO showed moderate left-skewed. None of the plots showed under/over disperse of the distribution. Although there were mild left skewed, but with the large samples (N=309), the central limit theorem was applied and linear regression analysis was acceptable for analysis. For the test of multicollinearity between adjusted variable for HU and VA in BSE, the variance inflation factors (VIF) was calculated. The VIF above 10 was considered as a high correlation and had significant multicollinearity. None of the results had shown a VIF score ≥ 5.

Figure 4 Histogram of the utility scores



Histogram of the utilities from tTTO, cTTO, EQ-VAS, EQ-5D-5L, HUI3 , and NEI VFQ-25 score

Figure 5 Q-Q plot of the residual (Health utility scores and Qol scores with the visual acuity in the best-seeing eye)



The Q-Q plot of the residual of the regression VABSE on the Utilities scores, and QoL score.

Table 8 Respondents demographics and baseline variables

		Total	DR	AMD	Cataract	p-value
		N=309	N=141	N=90	N=78	
Age, year (mean, SD)		63.9 (11.7)	57.9 (10.1)	71.0 (10.6)	66.5 (9.9)	**<0.001**
Region						**0.004**
	North	79 (25.6%)	33 (23.4%)	18 (20.0%)	28 (35.9%)	
	North east	68 (22.0%)	21 (14.9%)	24 (26.7%)	23 (29.5%)	
	South	78 (25.2%)	40 (28.4%)	26 (28.9%)	12 (15.4%)	
	Central	84 (27.2%)	47 (33.3%)	22 (24.4%)	15 (19.2%)	
Gender						
	Male	132 (42.7%)	59 (41.8%)	40 (44.4%)	33 (42.3%)	0.93
History of alcohol drinking	Yes	100 (32.4%)	42 (29.8%)	32 (35.6%)	26 (33.3%)	0.64
History of smoking	Yes	59 (19.1%)	20 (14.2%)	23 (25.6%)	16 (20.5%)	0.08
Having a caregiver						
	Yes	251 (81.2%)	115 (81.6%)	78 (86.7%)	58 (74.4%)	0.12
Marital status	Single	30 (9.7%)	19 (13.5%)	5 (5.6%)	6 (7.7%)	**0.03**
	Married	204 (66.0%)	97 (68.8%)	55 (61.1%)	52 (66.7%)	
	Separated	13 (4.2%)	2 (1.4%)	5 (5.6%)	6 (7.7%)	
	Divorce /Widow	60 (19.4%)	23 (16.3%)	24 (26.7%)	13 (16.7%)	

Religions				84	77	**0.006**
	Buddhism	284 (91.9%)	123 (87.2%)	(93.3%)	(98.7%)	
	Other	25 (8.1%)	18 (12.8%)	6 (6.7%)	1 (1.3%)	
Education level				57	43	
	Less than High school	173 (56.0%)	73 (51.8%)	(63.3%)	(55.1%)	0.54
	High-school and diploma degree	66 (21.4%)	34 (24.1%)	15 (16.7%)	17 (21.8%)	
	Bachelor's degree or higher	70 (22.7%)	34 (24.1%)	18 (20.0%)	18 (23.1%)	
Average income per month (1 USD = 35 THB)				54	41	
	Less than 10,000 THB	165 (53.4%)	70 (49.6%)	(60.0%)	(52.6%)	0.27
	10,000 to 25,000 THB	67 (21.7%)	32 (22.7%)	21 (23.3%)	14 (17.9%)	
	Above 25,000 THB	76 (24.6%)	39 (27.7%)	15 (16.7%)	22 (28.2%)	
	Missing	1 (0.3%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	
Health coverage program	Government or state enterprise officer reimbursement	156 (50.5%)	59 (41.8%)	47 (52.2%)	50 (64.1%)	**0.004**
	Universal health coverage program (30-Baht)	113 (36.6%)	60 (42.6%)	36 (40.0%)	17 (21.8%)	
	Social security scheme	20 (6.5%)	12 (8.5%)	1 (1.1%)	7 (9.0%)	
	Out of pocket, private insurance or others	20 (6.5%)	10 (7.1%)	6 (6.7%)	4 (5.1%)	
Charlson comorbidity index						**<0.001**
	0	61 (19.7)	0 (0)	31 (34.45)	30 (38.45)	
	1	111 (35.9)	57 (40.4)	31 (34.45)	23 (29.5)	
	2	105 (33.9)	64 (45.4)	22 (24.45)	19 (24.35)	

	3	14 (4.5)	7 (5)	4 (4.45)	3 (3.85)	
	4	18 (5.8)	13 (9.2)	2 (2.2)	3 (3.85)	
Worse eye visual impairment level*	Normal to mild	97 (31.4%)	48 (34.0%)	22 (24.4%)	27 (34.6%)	**0.09**
	Moderate	84 (27.2%)	42 (29.8%)	18 (20.0%)	24 (30.8%)	
	Severe	24 (7.8%)	9 (6.4%)	11 (12.2%)	4 (5.1%)	
	Blindness	104 (33.7%)	42 (29.8%)	39 (43.3%)	23 (29.5%)	
Best eye visual impairment level *	Normal to mild	192 (62.1%)	93 (66.0%)	55 (61.1%)	44 (56.4%)	0.33
	Moderate	81 (26.2%)	34 (24.1%)	24 (26.7%)	23 (29.5%)	
	Severe	15 (4.9%)	3 (2.1%)	7 (7.8%)	5 (6.4%)	
	Blindness	21 (6.8%)	11 (7.8%)	4 (4.4%)	6 (7.7%)	

Table 9 Cross tabulation of the visual utility scores and the NEI VFQ-25 scores

VI levels		Normal		Mild		Moderate		Severe		Blindness	
VA range		(20/20 to 20/30)		(20/40 to 20/70)		(20/80 to 20/200)		(20/250 to 20/400)		(Worse than 20/400)	
		Mean ± SE	Ceiling (Max, %)	Mean ± SE	Ceiling (Max, %)	Mean ± SE	Ceiling (Max, %)	Mean ± SE	Ceiling (Max, %)	Mean ± SE	Ceiling (Max, %)
tTTO	n=230	0.63±0.03	0.95 (1.9%)	0.67±0.02	0.99 (1.64%)	0.66±0.02	0.98 (1.41%)	0.67±0.05	0.98 (4.36%)	0.72±0.03	0.90 (9%)
cTTO	n=308	0.9±0.02	1.0 (2.7%)	0.82±0.03	1.0 (6.1%)	0.81±0.03	1.0 (7.3%)	0.84±0.05	1.0 (10%)	0.78±0.06	1.0 (3.9%)
EQ-VAS	n=309	0.78±0.01	1.0 (1.33%)	0.74±0.02	0.95(2.44%)	0.73±0.02	1.0 (5.21%)	0.66±0.03	0.95 (3.33%)	0.67±0.03	1.0 (3.85%)
EQ-5D-5L	n=309	0.76±0.02	1.0 (28%)	0.7±0.02	1.0 (19.51%)	0.7±0.02	1.0 (16.67%)	0.66±0.03	1.0 (13.33%)	0.62±0.03	1.0 (7.7%)
HUI 3	n=304	0.77±0.02	1.0 (9.33%)	0.66±0.03	1.0 (2.44%)	0.68±0.03	1.0 (4.26%)	0.61±0.05	1.0 (7.14%)	0.55±0.05	0.90 (8%)
NEI VFQ-25	n=309	79.58±1.39	92.5 (4%)	72.26±1.58	92.5 (2.44%)	67.75±1.9	93.96 (1.04%)	64.48±3.98	93.27 (3.33%)	58.37±4.14	91.73 (3.85%)

VI: Visual impairment, VA: Visual acuity

Table 10 Means of the health utility scores according to visual acuity levels in DR, wet AMD and Cataract in the multicenter study

Diabetic retinopathy											
VI levels		Normal		Mild		Moderate		Severe		Blindness	
VA range		(20/20 to 20/30)		(20/40 to 20/70)		(20/80 to 20/200)		(20/250 to 20/400)		(Worse than 20/400)	
		Mean ± SD		Mean ± SD		Mean ± SD		Mean ± SD		Mean ± SD	
tTTO	n=109	0.66	±0.05	0.69	±0.03	0.72	±0.04	0.61	±0.1	0.73	±0.06
cTTO	n=140	0.88	±0.03	0.84	±0.03	0.85	±0.04	0.75	±0.1	0.73	±0.11
EQ-VAS	n= 141	0.73	±0.03	0.73	±0.02	0.72	±0.03	0.67	±0.05	0.64	±0.06
EQ-5D-5L	n=141	0.73	±0.03	0.7	±0.03	0.7	±0.03	0.65	±0.05	0.6	±0.05
HUI3	n=140	0.75	±0.05	0.66	±0.04	0.65	±0.04	0.67	±0.08	0.51	±0.08
NEI VFQ-25	n=141	80.1	±2.11	73.73	±2.02	64.42	±3.1	64.97	±7.22	49.24	±6.28
Wet age-related macular degeneration											
tTTO	n=64	0.55	±0.06	0.65	±0.05	0.66	±0.03	0.67	±0.05	0.76	±0.06
cTTO	n=90	0.91	±0.03	0.8	±0.06	0.76	±0.07	0.92	±0.03	0.96	±0.01
EQ-VAS	n=90	0.82	±0.01	0.72	±0.03	0.74	±0.03	0.61	±0.04	0.69	±0.06

EQ-5D-5L	n=90	0.76	±0.03	0.68	±0.04	0.65	±0.03	0.66	±0.06	0.61	±0.08
HUI3	n=89	0.79	±0.03	0.62	±0.06	0.67	±0.04	0.6	±0.08	0.61	±0.08
NEI VFQ-25	n=90	77.73	±2.79	68.9	±3.07	67.8	±3.39	60.79	±5.79	74.83	±6.03
Cataract											
tTTO	n=57	0.71	±0.05	0.62	±0.08	0.57	±0.04	0.75	±0.06	0.69	±0.03
cTTO	n=78	0.92	±0.02	0.83	±0.06	0.8	±0.06	0.9	±0.04	0.69	±0.13
EQ-VAS	n=78	0.8	±0.03	0.8	±0.03	0.74	±0.03	0.69	±0.06	0.71	±0.05
EQ-5D-5L	n=78	0.8	±0.04	0.72	±0.04	0.72	±0.03	0.69	±0.1	0.65	±0.05
HUI3	n=75	0.79	±0.04	0.72	±0.08	0.74	±0.04	0.51	±0.1	0.56	±0.09
NEI VFQ-25	n=78	81.23	±2.28	72.61	±4.46	72.42	±3.23	67.83	±7.36	56.5	±6.59

VI: Visual impairment, VA: Visual acuity

Table 11 Association of visual impairment status and utility scores

		cTTO			EQ-VAS			EQ-5D-5L			HUI3		
VI levels	VA range	β	p-value	95%CI	β	p-value	95%CI	β	p-value	95%CI	β	p-value	95%CI
Normal	(20/20 to 20/30)	Ref.											
Mild	(20/40 to 20/70)	-0.06	0.13	-0.13 to 0.02	-0.04	0.06	-0.09 to 0.01	-0.01	0.70	-0.07 to 0.05	-0.07	0.07	-0.14 to 0.01
Moderate	(20/80 to 20/200)	-0.15	**<0.01**	-0.23 to -0.08	-0.01	0.53	-0.06 to 0.03	-0.03	0.30	-0.08 to 0.03	-0.06	0.11	-0.14 to 0.01
Severe	(20/250 to 20/400)	-0.20	**<0.01**	-0.31 to -0.09	-0.09	**0.01**	-0.15 to -0.02	-0.07	0.10	-0.15 to 0.01	-0.17	**0.004**	-0.28 to -0.05
Blindness	(worse than 20/400)	-0.26	**<0.01**	-0.37 to -0.14	-0.05	0.13	-0.12 to 0.02	-0.10	**0.02**	-0.19 to -0.02	-0.19	**0.001**	-0.31 to -0.08

VI: Visual impairment, VA: Visual acuity

*Linear mixed model regression analysis adjusted by age, sex, smoking, caregiver, alcohol, marital status, education level, income level, religious and health coverage program and Charlson comorbidity index scoring.

Table 12 Vision specific quality of life score and its association with visual impairment

VI levels	VA range	Mean score	SD	β*	p-value	95%CI
Normal	(20/20 to 20/30)	79.58	12.07	Ref.		
Mild	(20/40 to 20/70)	72.26	14.31	-5.70	**0.02**	-10.78 to -0.61
Moderate	(20/80 to 20/200)	67.75	18.59	-13.56	**<0.01**	-18.57 to -8.55
Severe	(20/250 to 20/400)	64.48	21.80	-21.20	**<0.01**	-28.71 to -13.69
Blindness	(worse than 20/400)	58.37	21.10	-24.29	**<0.01**	-32.08 to -16.51

VI: visual impairment, VA: visual acuity and SD: standard deviation

*Linear mixed model regression analysis adjusted by age, sex, smoking, caregiver, alcohol, marital status, education level, income level, religious and health coverage program and Charlson comorbidity index scoring.

Table 13 Univariable analysis of factor associated to the change of utility scores in the multicenter study (Univariable linear mixed model)

		EQ-VAS				EQ-5D-5L				HUI3				cTTO			
		β	p-value	95%CI Lower	95%CI Upper	β	p-value	95%CI Lower	95%CI Upper	β	p-value	95%CI Lower	95%CI Upper	β	p-value	95%CI Lower	95%CI Upper
Best- seeing eye visual acuity (LogMar)		-0.06	**0.002**	-0.10	-0.02	-0.09	**0.001**	-0.14	-0.04	-0.14	**<0.001**	-0.21	-0.07	-0.16	**<0.001**	-0.23	-0.09
Age, year		0.00	**0.004**	0.002	0.007	-0.001	0.10	-0.003	0.0003	-0.001	0.32	-0.004	0.001	-0.001	0.53	-0.003	0.002
Type of eye diseases																	
Cataract (Ref.)																	
DR		-0.05	**0.01**	-0.09	-0.01	-0.03	0.24	-0.08	0.02	-0.03	0.44	-0.10	0.04	0.02	0.62	-0.05	0.09
AMD		-0.02	0.35	-0.07	0.02	-0.03	0.25	-0.09	0.02	-0.01	0.88	-0.08	0.07	0.02	0.66	-0.06	0.09
Gender	Male	0.01	0.76	-0.03	0.04	0.06	**0.01**	0.01	0.10	0.06	0.05	0.0003	0.11	0.02	0.52	-0.04	0.07
History of alcohol drinking	Yes	0.01	0.47	-0.01	0.03	0.05	**0.001**	0.02	0.08	0.02	0.31	-0.02	0.06	0.03	0.18	-0.01	0.07
History of smoking	Yes	-0.03	**0.03**	-0.06	-0.003	0.02	0.20	-0.01	0.06	-0.01	0.82	-0.06	0.05	0.02	0.52	-0.03	0.07
Having a caregiver	Yes	-0.01	0.69	-0.05	0.03	-0.09	**<0.001**	-0.15	-0.04	-0.10	**0.01**	-0.18	-0.03	-0.01	0.74	-0.08	0.06
Marital status																	
Single (Ref.)																	

Married		0.02	0.40	-0.03	0.08	0.01	0.77	-0.06	0.08	-0.01	0.90	-0.10	0.09	0.05	0.28	-0.04	0.15
Separated		0.10	**0.03**	0.01	0.20	0.05	0.42	-0.07	0.17	-0.01	0.92	-0.17	0.15	-0.03	0.69	-0.19	0.13
Divorce /Widow		0.05	0.11	-0.01	0.12	-0.08	**0.049**	-0.16	-0.0003	-0.06	0.25	-0.17	0.04	0.04	0.43	-0.06	0.15
Religion: Buddhist		0.004	0.91	-0.06	0.07	0.02	0.59	-0.06	0.10	-0.03	0.65	-0.13	0.08	-0.05	0.35	-0.16	0.06
Education levels																	
Less than High school (Ref.)																	
High-school and diploma degree	0.01		0.71	-0.03	0.05	0.05	0.06	-0.003	0.10	0.06	0.08	-0.01	0.13	0.01	0.79	-0.06	0.08
Bachelor's degree or higher	0.02		0.24	-0.02	0.07	0.07	**0.01**	0.02	0.12	0.10	**0.01**	0.03	0.17	0.07	**0.04**	0.004	0.14
Average income per month (1 USD = 35 THB)																	
Less than 10,000 THB (Ref.)																	
10,000 to 25,000 THB	0.05		0.01	0.01	0.09	0.08	**0.003**	0.03	0.13	0.12	**<0.001**	0.05	0.19	0.03	0.37	-0.04	0.10
Above 25,000 THB	0.06		**0.002**	0.02	0.10	0.11	**<0.001**	0.06	0.16	0.13	**<0.001**	0.06	0.20	0.06	0.10	-0.01	0.12
Health coverage program																	
Out of pocket, private insurance or others (Ref.)																	
Government or state enterprise officer reimbursement	0.06		0.11	-0.01	0.12	0.10	0.02	0.01	0.19	0.11	0.07	-0.01	0.22	-0.05	0.43	-0.16	0.07

Universal health coverage program (30-Baht)	0.0003	0.99	-0.07	0.07	0.05	0.24	-0.03	0.14	0.03	0.61	-0.09	0.15	-0.09	0.14	-0.21	0.03
Social security scheme	0.01	0.87	-0.08	0.10	0.08	0.15	-0.03	0.20	0.07	0.35	-0.08	0.23	-0.22	**0.01**	-0.37	-0.07
Worse eye visual acuity (LogMar)	-0.04	**0.004**	-0.06	-0.01	-0.07	**<0.001**	-0.10	-0.04	-0.09	**<0.001**	-0.13	-0.05	-0.09	**<0.001**	-0.13	-0.05
Comorbidity (Charlson score)	-0.03	**<0.001**	-0.04	-0.01	-0.02	**0.02**	-0.04	0.00	-0.02	0.22	-0.04	0.01	-0.03	**0.03**	-0.06	0.00

DR: Diabetic retinopathy, AMD: Wet age-related macular degeneration

Table 14 Multivariable analysis for factor associated to the changes of utility scores in the multicenter study (Multivariable linear mixed model)

	EQ-VAS				EQ-5D-5L				HUI3				cTTO			
	β	p-value	95%CI		β	p-value	95%CI		β	p-value	95%CI		β	p-value	95%CI	
			Lower	Upper			Lower	Upper			Lower	Upper			Lower	Upper
Best- seeing eye visual acuity																
	-0.02	0.44	-0.06	0.03	-0.04	0.13	-0.09	0.01	-0.07	0.08	-0.14	0.01	-0.10	**0.01**	-0.18	-0.03
Age, year	0.00	**0.03**	0.00	0.00	0.00	0.11	0.00	0.00	0.00	0.09	-0.01	0.00	-0.02	0.29	0.00	0.00
Type of eye diseases																
Cataract (Ref.)																
DR	-0.01	0.58	-0.06	0.03	-0.03	0.33	-0.08	0.03	-0.05	0.19	-0.13	0.02	0.04	0.33	-0.04	0.11
AMD	-0.02	0.26	-0.07	0.02	-0.01	0.60	-0.07	0.04	0.02	0.65	-0.06	0.09	-0.02	0.96	-0.07	0.07
Gender	0.01	0.81	-0.04	0.05	0.02	0.46	-0.03	0.07	0.06	0.10	0.01	0.13	0.02	0	-	0
Male														.55	0.05	.09
History of alcohol drinking																
Yes																
	0.02	0.09	-0.004	0.05	0.03	0.13	-0.01	0.06	-0.01	0.77	-0.05	0.04	0.01	0.68	-0.04	0.05
History of smoking																
Yes	-0.04	0.01	-0.08	-0.01	-0.001	0.96	-0.04	0.04	-0.03	0.36	-0.08	0.03	0.04	0.20	-0.02	0.09
Having a caregiver																
Yes	-0.0001	1.00	-0.04	0.04	-0.05	0.07	-0.10	0.004	-0.06	0.13	-0.13	0.02	0.02	0.59	-0.05	0.09
Marital status																
Single (Ref.)																

Married	0.003	0.91	-0.05	0.06	0.01	0.68	-0.05	0.08	0.00	0.96	-0.09	0.10	0.07	0.13	-0.02	0.17
Separated	0.09	**0.04**	0.00	0.19	0.03	0.58	-0.08	0.14	-0.02	0.82	-0.17	0.14	-0.04	0.62	-0.19	0.11
Divorce /Widow	0.03	0.36	-0.03	0.10	-0.04	0.28	-0.12	0.04	-0.02	0.76	-0.13	0.09	0.09	0.11	-0.02	0.20
Religion: Buddhist	-0.02	0.50	-0.08	0.04	0.02	0.52	-0.05	0.09	-0.02	0.63	-0.13	0.08	-0.03	0.50	-0.14	0.07
Education levels																
Less than High school (Ref.)																
High-school and diploma degree	-0.005	0.82	-0.05	0.04	0.02	0.52	-0.04	0.07	0.03	0.41	-0.04	0.10	0.04	0.23	-0.03	0.12
Bachelor's degree or higher	-0.04	0.15	-0.09	0.01	-0.02	0.46	-0.09	0.04	0.00	0.98	-0.09	0.09	0.06	0.20	-0.03	0.15
Average income per month (1 USD = 35 THB)																
Less than 10,000 THB (Ref.)																
10,000 to 25,000 THB	0.05	**0.01**	0.01	0.10	0.06	**0.02**	0.01	0.11	0.09	0.02	0.01	0.16	-0.01	0.79	-0.08	0.06
Above 25,000 THB	0.07	**0.01**	0.02	0.13	0.07	**0.04**	0.00	0.13	0.07	0.14	-0.02	0.16	-0.03	0.46	-0.12	0.05
Health coverage program																
Out of pocket, private insurance or others (Ref.)																
Government or state enterprise officer reimbursement	0.06	0.08	-0.01	0.13	0.10	**0.01**	0.02	0.19	0.11	0.06	0.00	0.23	-0.04	0.52	-0.15	0.08

Universal health coverage program (30-Baht)	0.03	0.38	-0.04	0.10	0.08	0.06	0.00	0.16	0.06	0.32	-0.06	0.17	-0.06	0.30	-0.18	0.05
Social security scheme	0.04	0.35	-0.05	0.13	0.08	0.13	-0.02	0.19	0.08	0.29	-0.07	0.23	-0.21	0.01	-0.36	-0.06
Worse eye visual acuity	-0.02	0.11	-0.05	0.005	-0.06	**0.001**	-0.09	-0.02	-0.06	**0.02**	-0.10	-0.01	-0.06	**0.01**	-0.10	-0.01
Comorbidity (Charlson score)	-0.03	0.002	-0.04	-0.01	-0.02	**0.03**	-0.09	-0.02	-0.01	0.55	-0.04	0.02	-0.04	**0.004**	-0.07	-0.01

DR: Diabetic retinopathy, AMD: Wet age-related macular degeneration

Table 15 Compare factors between non-trader and trader for tTTO

	Non-trader	Trader	p-value
	N=79	N=230	
Age (mean, SD)	67.9 (9.7)	62.6 (12.0)	**<0.001**[a]
Region			**0.008**[b]
Central	26 (32.9%)	58 (25.2%)	
North	28 (35.4%)	51 (22.2%)	
Northeast	14 (17.7%)	54 (23.5%)	
South	11 (13.9%)	67 (29.1%)	
Male	39 (49.4%)	93 (40.4%)	0.19 [b]
Type of eye diseases			0.55 [b]
Cataract	21 (26.6%)	57 (24.8%)	
DR	32 (40.5%)	109 (47.4%)	
AMD	26 (32.9%)	64 (27.8%)	
History of alcohol drinking	29 (36.7%)	71 (30.9%)	0.4 [b]
History of smoking	21 (26.6%)	38 (16.5%)	0.07 [b]
Having caregiver	61 (77.2%)	190 (82.6%)	0.32 [b]
Marital status			0.91 [b]

Single	6 (7.6%)	24 (10.4%)	
Married	55 (69.6%)	149 (64.8%)	
Separated	3 (3.8%)	10 (4.3%)	
Divorce or widow	15 (19.0%)	45 (19.6%)	
Buddhism			**0.033** [b]
Yes	77 (97.5%)	207 (90.0%)	
Education level			0.14 [b]
Less than High-school	38 (48.1%)	135 (58.7%)	
High-school and diploma degree	17 (21.5%)	49 (21.3%)	
Bachelor degree or higher	24 (30.4%)	46 (20.0%)	
Average income per month			0.72 [b]
Less than 10,000 THB	40 (50.6%)	125 (54.3%)	
10,000 to 25,000 THB	17 (21.5%)	50 (21.7%)	
Above 25,000 THB	22 (27.8%)	54 (23.5%)	
Missing	0 (0.0%)	1 (0.4%)	
Health coverage program			0.28 [b]
Government or state enterprise officer	45 (57.0%)	111 (48.3%)	

reimbursement			
Universal health coverage program (30-Baht)	23 (29.1%)	90 (39.1%)	
Social security scheme	4 (5.1%)	16 (7.0%)	
Out of pocket, private insurance or others	7 (8.9%)	13 (5.7%)	
LogMar VA in best-seeing eye (mean, SD)	0.6 (0.4)	0.7 (0.5)	0.11 [a]
LogMar VA in worse-seeing eye (mean, SD)	1.0 (0.7)	1.2 (0.7)	**0.013** [a]

a : student's t-test, b: Pearson chi-square, DR: Diabetic retinopathy, AMD: wet age-related macular degeneration

Diabetic retinopathy and health utility scores

1. Utilities among DR levels

There were 141 respondents from total 309 participants categorized in DR group. In DR group, there were 10 participants (7.1 %) had DR screening but diagnosed as no DR, 39 participants (27.5%) diagnosed of NPDR , 73 participants (51.1%) diagnosed as PDR, and 19 participants (13.4%) diagnosed as TRD. There were 41 participants (29%) in DR group had no history of foveal involvement DME ,while 100 participants (71%) had no foveal involvement DME. The utility scores among DR levels shows in **Table 16.**

In the DR group, the percentage of no DR, non-proliferative DR, proliferative DR and DR with tractional retinal detachment (TRD) was 8.4%, 27.3%, 51%, and 13.3%, respectively. There were no statistically significant differences in the HU between participants with and without diabetic macular edema (DME) in all instruments when adjusted for confounder and baseline visual acuity level. The 95% CI of difference between DME compared with non DME from cTTO, EQ-5D-5L, HUI3 and NEI VFQ-25 were -0.03 to 0.15, -0.07 to 0.07, -0.05 to 0.13, and -2.6 to 8.3, respectively. However, the HU from cTTO score demonstrated that TRD patients had statistically significant lower comparing to no DR as shown in **Table 17.**

Table 16 Mean and SD of utility scores in levels of diabetic retinopathy

	tTTO		cTTO		EQ-5D-5L		HUI3	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
NO DR	0.63	0.19	0.93	0.04	0.67	0.16	0.73	0.19
NPDR	0.71	0.23	0.85	0.23	0.73	0.20	0.72	0.28
PDR	0.69	0.19	0.85	0.22	0.70	0.20	0.67	0.26

TRD	0.66	0.20	0.69	0.39	0.61	0.21	0.51	0.30

Table 17 The types of diabetic retinopathy and the changes of health utility scores

	cTTO			EQ-5D-5L			HUI3			NEI VFQ-25		
	β	Adjusted 95% CI		β	Adjusted 95% CI		β	Adjusted 95% CI		β	Adjusted 95% CI	
NPDR	-0.13	-0.29	0.04	0.02	-0.11	0.15	0.01	-0.16	0.18	9.12	-0.84	19.07
PDR	-0.12	-0.28	0.03	0.01	-0.12	0.13	-0.02	-0.19	0.14	1.61	-8.00	11.21
TRD	-0.25	**-0.44**	**-0.06**	-0.04	-0.20	0.11	-0.13	-0.34	0.07	-8.44	-20.28	3.41

* No DR as a reference level

** Linear mixed model regression analysis adjusted by age, sex, smoking, caregiver, alcohol, marital status, education level, income level, religious and health coverage program and visual acuity levels.

2. Utility scores between DME vs Non-DME

In an analysis of DME only subgroup, the level of visual acuity of BSE and WSE, along with a number of intravitreal injections indicated for DME is shown in **Table 18**. The mean visual acuity in WSE is better in patients who had a higher number of IVT treatments. Along with this, the increased number of DME Intravitreal treatments resulted in better HU and QoL scores when adjusted for visual acuity level and other possible confounders. The result is shown in **Table 19**.

Table 18 Level of visual acuity with number of intravitreal injection treatments for diabetic macular edema in the diabetic retinopathy

		BSE			WSE		
Number of injection	N	Mean visual acuity (LogMar)	Min	Max	Mean visual acuity (LogMar)	Min	Max
No DME	48	0.66	0	1.9	1.21	0.1	2.7
1 to 5	41	0.60	0.02	1.7	1.15	0.2	3
6 to 10	16	0.71	0.3	1.2	1.11	0.4	3
≥ 11	36	0.56	0	1.6	0.89	0	1.9

*BSE: Best-seeing eye, WSE: Worse-seeing eye

Table 19 Health utility scores and QoL associated to the number of DME intravitreal injection

Number of injection	cTTO			EQ-5D-5L			HUI3			NEI VFQ-25		
	β	Adjusted 95% CI		β	Adjusted 95% CI		β	Adjusted 95% CI		β	Adjusted 95% CI	
1 to 5												
6 to 10	0.17	**0.07**	**0.28**	0.07	-0.04	0.18	0.18	**0.31**	**0.18**	12.57	**5.64**	**19.49**
≥ 11	0.14	**0.05**	**0.22**	0.09	**0.01**	**0.18**	0.10	**0.21**	**0.18**	7.75	**2.10**	**13.40**

*Linear mixed model regression analysis adjusted by age, sex, smoking, caregiver, alcohol, marital status, education level, income level, religious and health coverage program and visual acuity levels.

Direct cost and indirect cost of treatment

Non-medical-related expenses and income lost for the doctor visited (same visit with the interview) are described in Thai Baht. Details are in **Table 20**.

Table 20 Non-medical expense and income lost (Thai Baht)

	Mean	SD	Median	N	Min	Max
Non-medical expense						
Travel expenses	567.94	518.63	500	305	0	4000
Non-travel expenses (eg. Food)	204.74	210.93	150	282	0	1500
Total non-medical expenses	756.91	623.02	600	305	10	4900
Income lost						
Patient	440.87	2297.42	0	196	0	30000
Caregiver(s)*	517.75	1456.44	0	173	0	14000
Total income lost/ family	720.05	2675.55	0	196	0	30450

*Maximum 2 persons

The average non-medical expenses and total family income lost categorized by study location is demonstrated in **Table 21**. There were 2 participants in Northeastern had extremely family income lost above than 10,000 baht while the remaining participants in all study site had the family income lost less than 10,000 baht. There were 18.6%, 45.9%, 56% and 80% from North, Northeast, South and central, respectively, reported no family income lost on the doctor visited day. None of participants reported no non-medical cost.

Table 21 Average income lost by study location (THB)

Study site	Total non-medical expenses						Total income lost/ family					
	n	Mean	SD	Median	Min.	Max	n	Mean	SD	Median	Min	Max
North	79	514.43	559.48	300	30	2600	43	642.09	591.65	500	0	2700
Northeast	67	944.63	777.57	800	70	4900	48	1611.46	5169.61	350	0	30450
South	77	857.27	474.87	700	100	2000	48	452.08	761.85	0	0	4000
Central	82	742.9	595.72	561	10	3400	57	253.86	882.75	0	0	6000

SD: standard deviation, Min: minimum, Max: maximum

Health utilities among instruments

1. Correlation of MAUI instruments with the direct method

The correlation between cTTO, EQ-5D-5L, HUI3 utilities and NEI VFQ-25 were calculated by the Pearson's correlation analysis. The correlation is shown in **Table 22.** HUI3 and EQ-5D-5L show a positive moderate correlation with the vision specific QoL, while cTTO shows mild correlate. The tTTO has no significant correlation to either NEI VFQ-25 score and health utility from MAUI, however, there was significant positive correlation to cTTO. In subgroup of 3 categories of VI : normal to mild VI ,moderate VI; and severe or worse VI, the correlation of MAUI instruments and NEI-VFQ-25 is shown in **Table 23**.

Table 22 Pearson's correlation coefficients of health utilities from tTTO, cTTO, EQ-5D-5L, HUI3 and the vision specific QoL score.

	tTTO	cTTO	EQ-5D	HUI3
tTTO	1			
cTTO	0.21*	1		
EQ-5D	0.09	0.16**	1	
HUI3	-0.007	0.12*	0.56**	1
NEI VFQ 25	-0.02	0.23**	0.43**	0.54**

* p-value <0.05

** p-value <0.01

Table 23 Pearson's correlation coefficients of MAUI instruments and disease specific quality of life score

	Normal to mild VI (n=157)	Moderate VI (n=94)	Severe VI or worse (n=53)
	r	r	r
cTTO	0.13	0.14	0.44
EQ-5D-5L	0.41	0.28	0.62
HUI3	0.53	0.54	0.51

r: Pearson's correlation coefficients

2. Agreement of cTTO and MAUI instruments

Concordance correlation coefficient is a method to evaluate an agreement on a continuous measure which gather by two person or methods.(Liao & Lewis, 2000) In this context, the utility score from each instrument were pair and evaluate for an agreement. The concordance correlation coefficient (Rho_c) of cTTO and EQ-5D-5L score, cTTO and HUI3 score; and HUI3score and EQ-5D-5L score are shown in **Table 24.** The HUI3 and EQ-5D-5L shown better agreement compare with the pair with cTTO.

Table 24 Concordance correlation coefficients among utility instruments

	Rho_C	SE	Obs	95% CI		p-value
cTTO - EQ-5D-5L	0.13	0.05	308	0.04	0.22	0.004
cTTO - HUI3	0.10	0.05	303	0.01	0.19	0.04
HUI3 - EQ-5D-5L	0.53	0.04	304	0.46	0.61	<0.001

Obs: number of observation , SE: standard error, 95%CI: 95% confidence interval

Bland-Altman plot of cTTO and EQ-5D-5L score is shown in **Figure 6**. We can see than there was more agreement when the utility score higher than 0.6 and the trend toward utility score of 1.0 from **Figure 6**. The Bland-Alman plot of cTTO and HUI3 utility score is shown in Figure 7. Similar pattern was found between **Figure 6 and Figure 7**. There were more agreement from MAUI instrument with cTTO for measuring utility when the utility level are high. Figure 8 demonstrates Bland-Altman plot between utility score from HUI3 and EQ-5D-5L. HUI3 and EQ-5D-5L utility score has better agreement when comparing to cTTO, with the Rho_c of 0.53. There was more agreement when the utility moves toward a full health state in **Figure 8**.

Figure 6 Bland-Altman plot of cTTO and EQ-5D-5L utility score

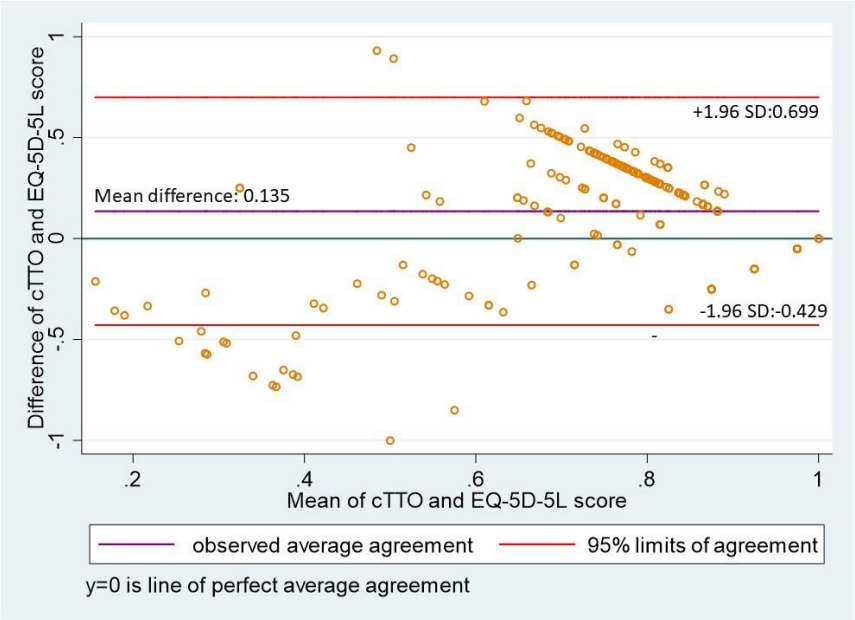


Figure 7 Bland-Altman plot of cTTO and HUI3 utility score

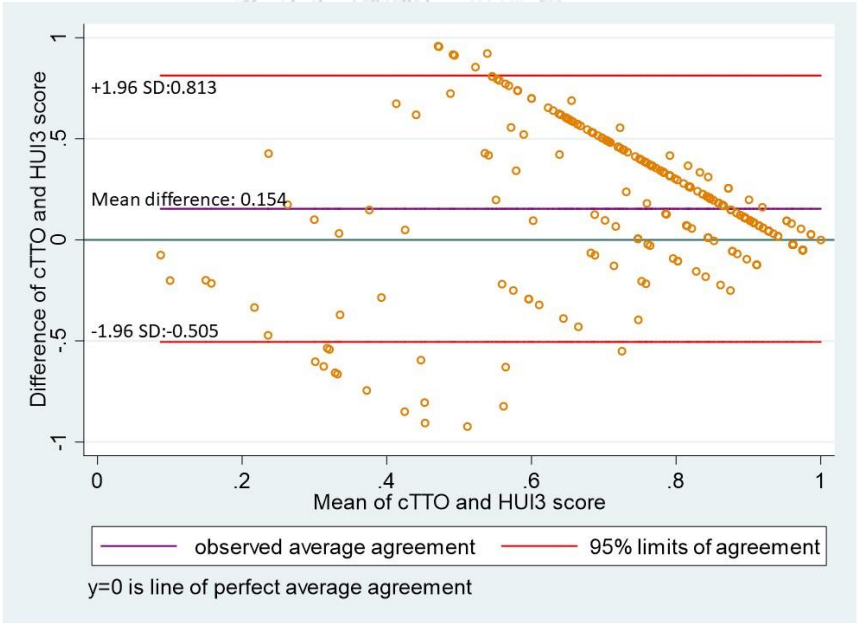
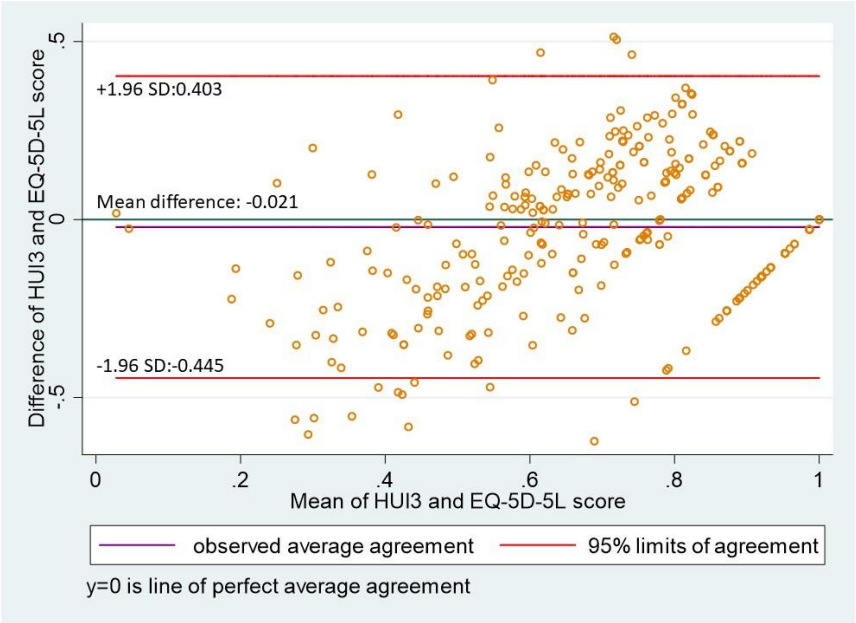


Figure 8 Bland-Altman plot of cTTO and EQ-5D-5L utility score



Chapter 5
Discussion

Health utility in diabetic retinopathy and other eye diseases

Despite the different nature of diseases in DR, AMD and cataract, our finding demonstrated that the HRQoL and vision-specific QoL were not different between similar VA levels. Several findings support this conclusion. (Melissa M Brown, Gary C Brown, Sanjay Sharma, Jennifer Landy, et al., 2002; B. S. Lee et al., 2008; V. A. Shah et al., 2004) The utility loss from DR substantially associated with the visual status over the DR severity(M. M. Brown et al., 1999) and the presentation of DME.(Fenwick et al., 2020; Fenwick, Xie, Ratcliffe, et al., 2012) Bilateral DR associated with a lower utility compared to no DR.(Pan et al., 2018)

In our study, there was no significant difference in the HU from DME presentation. TRD demonstrated a significant impact on lower HU; However, the worse visual acuity in TRD might take a primary role on the HU. T-H Tung et al. reported only 41% of the DR patients were willing to trade their life to be free from DR. The DR severities were substantially to HU when compared to no DR. Fenwick et al. reported on a novel instrument called Diabetic Retinopathy Utility Index (DRU-I), to estimate the utilities associated with vision-threatening in DR and visual impairment. This instrument demonstrated good validation.(Fenwick et al., 2020) However, there are limited data on this instrument. There were differences in HU when comparing DR in any stage to no DR. (T.-H. Tung et al., 2005) A shorter duration of age-related macular degeneration(AMD) diagnosis had a lower utility value compared with a diagnosis of >1 year, with a mean difference of 0.17.(Gary C Brown, Sharma, Brown, & Kistler, 2000)

Using time-trade-off method in ophthalmology

A value-based medicine reflects the quality of life that an individual perceives. This patient-reported outcome (PROs) is used in an outcome parameter of evidence-based trial and decision-making in economic evaluation. The standard methods in the direct utility analysis that were commonly used were the time trade-off technique and standard gambles technique, the former has been more frequently compared to the latter due to the easier to understand by old people and can be modified to evaluate the ocular utility values (Gary C Brown et al., 2004; M. M. Brown, Brown, Sharma, & Busbee, 2003; Heintz et al., 2012) . In general medicine, a perfect health state in time trade-off utility analysis is defined as a full health status without any systemic disease while, in ocular utility, analysis defines perfect health as a normal vision and perfect eye status. The TTO is a preference-based method for developing a health state and has been used to develop MAUI such as the EQ-5D, to determine the health state from TTO. It requires the respondents to trade their remaining lifetime for perfect health status. (Lugnér & Krabbe, 2020) Generally, perfect health represents a complete cure of the disease and regain of full general health function. However, normal vision represents a perfect health state in retina diseases and vision-related conditions. The TTO method necessitates respondents to understand the nature of health states and a the being dead concept. This concept is cognitively challenging and requires careful instruction during the interviews.(Lugnér & Krabbe, 2020) Some countries prefer direct choice-based methods from real conditions, such as TTO. However, the valuation of utility from the general public are widely accepted for cost-utility analyses.(Tavakoli, Davies, & Thomson, 2000) In the ophthalmic field , patient evaluation with TTO correlated with the commonly used vision-specific QoL such as the NEI VFQ-25 score. Researchers have criticized the visual utility to be overvalued than a general HU.(Kymes & Lee, 2007; B. S. Lee et al., 2008) There are some key differences between the TTO and MAUI instruments.

The impact of ocular utility can diminish the general utility analysis with the value of ±0.3.(M. M. Brown et al., 2003). Visual acuity are the factors that highly impact in ocular health utility. TTO reflects the impact from a patient perspective. TTO has been widely used in utility measurement in ophthalmology when compared to the Standard gamble technique. It has been shown good validity in visual impairment with long-term reproducibility and has high correlation to vision in better-seeing eye.(M. M. Brown, Brown, Sharma, Smith, & Landy, 2001; Hollands et al., 2001; Sharma et al., 2002)

The Multi-attribute utility instrument usage in the visual related conditions

An MAUI, EQ-5D-5L instrument is composed of items on five domains, including mobility, self-care, pain/discomfort, usual activities, and depression/anxiety domains, but no vision-specific domain. EQ-5D-5L health state derived from TTO valuation by describing various health states to the general healthy public person to get the utility values. This is different from a TTO visual utility value obtained from a patient perspective (Kind, Brooks, & Rabin, 2005)

The HUI3 contains eight dimensions (vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain) originally describing the health condition of the population in Canada and provides novel information and distinct dimension from the EQ-5D.(Furlong, Feeny, Torrance, & Barr, 2001) The slightly dissimilar nature of the origin of the visual utilities TTO and MAUI, could simplify our results regarding the higher mean visual utility from cTTO score compared with the EQ-5D-5L and the HUI3 scores. However, there were while no difference in both EQ-5D-5L and HUI3 utility scores. In our study, cTTO generated the most response in the reduction of visual impairment level, followed by HUI3 and EQ-5D-5L, whereas HU changes with VA levels were inconsistent with the EQ-VAS.

Previous publications demonstrated a better responses to the changes in vision-related conditions and retina disease in HUI3 comparing to EQ-5D-5L. Heintz et al. conducted telephonic interviewed with patients with DR and compared the HU between TTO, EQ-VAS, HUI-3 and EQ-5D scores. All instruments could identify the visual impairment level in better-seeing eyes, whereas only HUI3 displayed a significant response from the worse-seeing eyes and DR levels. Therefore, the EQ-5D did not differentiate between DR levels in both worse-seeing and better-seeing eyes. The HUI3 displayed the most relative efficiency compared to other measurements. However, no specific version of the EQ-5D nor the definition of full health was described in this study.(Heintz et al., 2012)

In Southeast Asia , Gandhi M. et al. reported on the HUI3 is the most sensitive to vision changes in patients with cataracts in Singapore, compared with the EQ-5D.(Luo et al., 2015) In age-related macular degeneration, the HUI3 contributed to a higher correlation with the change in VA followed by TTO. By contrast, results from the EQ-5D and SF-6D were controversial. However, the range of HU levels among VA levels was substantially different; nonetheless, we observed a significant trend toward increasing utility scores following VA improvement.(Espallargues et al., 2005; Isobel Pearson, Catherine Rycroft, Adam Irving, Claire Ainsworth, & Kim Wittrup-Jensen, 2013) The EQ-5D-5L comprises greater item response levels than the original EQ-5D-3L; nonetheless, increased response levels seldom affect the vision disorder and may introduce variability in responses.(Luo et al., 2015) The EQ-5D index displays a low predictive power while mapping with a disease-specific QoL instrument NEI VFQ-25.(Kay & Ferreira, 2014) With this limitation, a vision “bolt-on” had developed for the add-on to the EQ-5D-3L, in order to increase the sensitivity to use in vision-related aspects but data still limited.(Longworth et al., 2014; Luo et al., 2015)

Table 12 demonstrates the diminishing of vision specific quality of life score along with the worsening of visual impairment. HUI3 and EQ-5D-5L have shown a highest correlation to the NEI VFQ-25 score, while cTTO seems less correlate. With

the cTTO conceptual, the utility obtained from individual perception (holistic concept) which called “Visual health utility” while HUI3, EQ-5D-5L have a specific question related to specific activity domains aims to evaluate the general health, these domain concepts also implement in the disease specific quality of life NEI VFQ-25 questionnaire. The general health utility score and visual health utility score has been shown a slightly differ in number in the evaluation of cataract patient. (Perneger, Combescure, & Courvoisier, 2010)

The impact of visual impairment and health utilities

Visual impairment exert a major influence on the lower QoL and HU in ophthalmic conditions.(Gary C Brown, Sharma, et al., 2000; M. M. Brown et al., 1999; B. S. Lee et al., 2008) The good condition of VA in both eyes of an individual is necessary for binocular vision and provides stereopsis. The loss of vision in only one eye can impact driving ability and reduce the field of vision. Nonetheless, patient with monocular vision could maintain good general physical to live in society and mental health status.(Fenwick, Xie, Ratcliffe, et al., 2012) Poor VA played a higher effect on the change of HU than normal vision.(A Lloyd et al., 2008) Knauer et al. described an ophthalmic patient with a vision of 20/20 to 20/25 willing to pay only 11-15% of their remaining life time for the perfect vision while patient whose VA 22 to 28% of their remaining lifetime and patient whose VA 20/200 to 20/400 would like to exchange 39-48% of their remaining life, blind patient would like to trade 60% of their life to gain back the vision. Patients with AMD and low vision would even exchange more time of their life.(Knauer & Pfeiffer, 2008) The TTO value decrease in visual impaired person.(M. M. Brown et al., 2003; Knauer & Pfeiffer, 2008) In average, the mean TTO utility in eye diseases with VA 20/20 to 20/25 is 0.85 to 0.89 , VA 20/30 to 20/50 is 0.78 to 0.81, VA 20/60 to 20/100 is 0.57 to 0.72, VA 20/200 to 20/400 is 0.52 to 0.64 and CF to LP is 0.40 to 0.59.

In our study, only the cTTO was significantly correlated with the change in LogMar VA in the better-seeing eyes. However, the trend with HUI3 could not reach a statistically significant level. By contrast, the worse-seeing eyes were associated with HU changes in the EQ-5D-5L, HUI3 and cTTO. Brown M. et al. used the tTTO to evaluate patients with bilateral and unilateral good VA. From the patient reference-based point of view individual ocular disease affected QoL and TTO value correlated with the visual loss in the better-seeing eye and patient with bilateral good visual acuity had the highest utility value.(M. M. Brown, Brown, Sharma, Busbee, et al., 2001) Better-seeing eyes primarily accounted for the HU but worse-seeing eyes contributed to it as well.(Boye et al., 2014; Hahn & Krummenauer, 2017) In patients with AMD, poor VA levels displayed a high tendency to trade their remaining lifetime for perfect vision, compared with good VA in patients with the particular disease. In the Asia population, Eong K G Au et al. reported utility in AMD patients in Singapore and found weak association in only the worse-seeing eyes to HU from the TTO, while HU from EQ-5D was weakly correlated with both better-seeing eyes and worse-seeing eyes.(Au Eong et al., 2012) Our current results show minimal changes in VA and the variability in VA measurement have resulted in mild fluctuation in the association. Nevertheless, upon categorizing the better-seeing eye into an ordinal level of visual impairment status, HUI3 demonstrated effective responses to moderate or worse visual impairment. Moreover, the EQ-5D-5L utility score significantly reduced in blindness level. Furthermore, the HU displayed a decreasing trend with the reduction of vision in the cTTO, EQ-5D-5L and HUI3.

The NEI VFQ-25 is associated with visual impairment and VA reduction in retina disease, glaucoma, cataract and other eye conditions.(Deramo, Cox, Syed, Lee, & Fekrat, 2003; Mangione et al., 2001; Marella et al., 2010) Likewise, the NEI VFQ-25 score displayed a significantly negative correlation with an increase in the ETDRS VA LogMar in both better-seeing eyes and worse-seeing eyes. The HU from all

instruments were positively correlated with the NEI VFQ -25 score, but not to the tTTO score.

The response of health utility in good vision

There was a lack of response in HU from eye diseases when the vision reduced from normal to mild or moderate VI, unlike that when the vision altered to severe VI or blind.(V. A. Shah et al., 2004) Our study, the correlation of utility scores and vision specific quality of life score calculated among 3 levels of VI: normal to mild, moderate; and severe vi or worse . The severe VI or worse has shown a good correlation in both cTTO and MAUI instrument. HUI3 demonstrates good correlation in all VI levels, while EQ-5D-5L have fair correlation in moderate VI level. cTTO demonstrates good correlation to NEI VFQ-25 score only in severe VI level. These finding support the finding of Shah et al.(V. A. Shah et al., 2004) on the lack of response of the health utility in good or mild visual impairment. All instruments from our study show a good response in a worse VI level which impact on the lower quality of life.

Factors associated to health utilities

From previous data, factors associated with the HU include old age, the type of eye diseases, systemic conditions, diabetes-related microvascular complications, sex, VA in better-seeing eyes and worse-seeing eyes, and vision-specific QoL level .(A. Lloyd et al., 2008; Mok, Kwok, Ng, Leung, & Quan, 2021; Pan et al., 2018; Poku, Brazier, Carlton, & Ferreira, 2013b; T.-H. Tung et al., 2005; T. H. Tung et al., 2005) We demonstrated that age, history of smoking, marital status types of health care coverage program, and income levels were associated with HU levels: nonetheless, the significant effects were inconsistent among utility instruments. Higher income seems to give a better health utility. An education and income status indicated an

inequalities (Doorslaer & Koolman, 2004) which resulted on quality of life. Low socioeconomic status are related to the lower health utility value.(Roberge, Berthelot, & Wolfson, 1995)

The comorbidity were significant associate to health utility. Our study found that the higher number of Charlson comorbidity score were associated with the lower of health utility score, significant effect was found in EQ-VAS, EQ-5D-5L and cTTO. HUI3 has not shown a significant effect from the comorbidity condition, possible explanation is that the effect of comorbidity could diluted from the domain of the instrument. Health is a combination of multiple aspect of patient. However, some previous publication report non-significant effect of ocular utility from patient's systemic condition.(M. M. Brown, Brown, Sharma, Hollands, & Landy, 2002) The overall health utility are affecting from the major adversely condition of individual.(Real, Brown, Brown, & Brown, 2008)

Factors associated with the non-trader for TTO

Older age, demographic region, Buddhism religion and good VA were associated with the non-trader of tTTO. These findings supported that an emotional status was associated with the patient perception of vision loss and willing to trade part of their life.(Crewe et al., 2011) The TTO framework concept is related to a shortened life expectancy, which is shown to have an impact on religious beliefs. These beliefs, in turn, can affect the perception of life and is correlated with utility value in Christian(Jakubczyk, Golicki, & Niewada, 2016), Buddhist(Zeng et al., 2021), and Islamic respondents(Elbarazi et al., 2017). Studies in Europe also showed that religious beliefs have an effect on euthanasia and are prone to assigning a value worse than death for HU measurement by TTO. In the current study, about 87.5% of respondents reported a mild effect of religious belief on decision making in the TTO questions, and 2.5% reported a marked effect on their decision to shorten life,

whereas in their study conducted in an Islamic population(Elbarazi et al., 2017), Elbarazi et al reported that 81% of health states in TTO were influenced by respondents' religious beliefs and spirituality.(Zeng et al., 2021) However, some surveys have shown nonsignificant effects related to the decision of utility measurement.(Barry et al., 2018) In a small survey of Thai wet AMD patients reported 24%(บรรณ, 2019) of patients were non-trader from tTTO, which is no large differences from our study(34%). As Thailand is a Buddhism country, religious beliefs and culture could affect the concept of dying and life after dead in TTO.(Papadimitropoulos et al., 2015) It supports the evidence of cultural and region influence to the perception of life when measuring the QoL. Notely, that convenient sampling was used in the tertiary care outpatient clinic for the survey. The region effect might be a result of the selection bias.

Instrument for measuring the health utilities in Thailand

Feasibility of instruments

This novel study used TTO and HUI3 for the evaluate the HU of patients with retina disease and visual impairment in South East Asia.(Mok et al., 2021) In our study, The HU from all instruments were positively correlated with the NEI VFQ -25 score but not to the tTTO score. The HUI3 and EQ-5D-5L demonstrated a high correlation compared with others. This may be explained by the fact that the tTTO(Gary C Brown, Brown, et al., 2000; Sharma et al., 2002), which directly inquired the patients for the number willing to trade for their health, principally used in multiple utility measurements in eye disease in the North America may be unsuitable for our population. Moreover, a verbal explanation with an imagination of the dead may be difficult for the elderly. In our pilot study, 4 patients from 40 participants not willing to trade their life in tTTO open questions. The main factors associated with the willingness to trade are individual subjective life expectancy and the status of vision(Heintz et al., 2012; Van Nooten, Koolman, & Brouwer, 2009) The tTTO was

an open-end question that asked the patient to imagine their subjective life expectancy which can be a result from multifactorial from physical mental emotion and the perception of life, with these unstable question the 10 year lead time cTTO might be more appropriate and easy to understand for respondents and it will eliminate the variability life expectancy factor of each individual to 10 years. However, the 10 year-TTO concepts may affect the loss of a relatively expected life year and amount of the trade-off time compared to the TTO concept in tTTO.(Van Nooten et al., 2009)

Using EQ-5D-5L and HUI3 in Thailand

HTA guidelines in Thailand recommended EQ-5D for assessing a utility in Thai population.(Pattanaphesaj et al., 2018) Thailand also have a specific value set for their population.(Pattanaphesaj, 2014; Pattanaphesaj et al., 2018; Tongsiri & Cairns, 2011). To use in ophthalmic patient of Thai's population, both EQ-5D-5L and HUI3 shown responsive to the change of vision, especially in the severe level of visual impairment; and demonstrates higher correlation to the disease specific questionnaire score. These MAUI instruments and NEI VFQ-25 had shown a same level of correlation to the utility changes by cTTO. Both MAUI instruments could be feasible in used in the evaluation of HTA in an ophthalmic disease resulting to a poor VI status. The limitation of HUI3 in this context are the high number of question which required longer interview time; and the charge of using fees.

Using utility instrument as patient-reported outcome

For the interview time, TTO questions comprised of a short list of questions which require a short interview duration of about 2.89 minutes. This method might be suitable to obtained in-clinic visits for a clinician to evaluate their patient QoL.(Gary C Brown, Sharma, et al., 2000; M. M. Brown et al., 2003). The EQ-5D-5L also demonstrates a quick interview time about 3.07 minutes with less complex question

to TTO. Moreover, it has shown a response in the reduction to severe visual impairment level. The instrument could implement in an evaluation of general health quality of life in our population.

EQ-5D-5L has been introduced to routine collection of patient-reported outcome to measure a condition of patients. Devlin et al. applied EQ-5D in the NHS services and reported the different changes of EQ-5D score after surgical procedure.(N. J. Devlin, Parkin, & Browne, 2010) The instruments also applied in PROs in variety of diseases such as cancer, chronic disease, psychiatry and quality of life evaluation in clinical studies.(Åström et al., 2020; N. Devlin, Parkin, & Janssen, 2020; Jonsson, Orwelius, Dahlstrom, & Kristenson, 2020; Pickard, Jiang, Lin, Rosenbloom, & Cella, 2016; Revicki et al., 2009). The instruments could be applied in wide range of age group in worldwide. In ophthalmology, EQ-5D has been used as PROs in cataract surgery treatment. However, It might not highly correlates specific correlation to the mild changes of visual function.(Fung et al., 2016; Gandhi et al., 2019)

In our study, an EQ-5D-5L is feasible to measured the impact of vision loss in wet AMD , DR and cataract patient. The uncomplexity of EQ-5D-5L might suitable because these patients usually presented in elderly who might have problem in complex PROs question.

Strengths

The strength of our study was that we used a patient perspective individualized report, which could address the concerns of patients regarding their disease rather than an imaginary health stage that may not develop appropriately or represent the target population. The majority of HU data in ophthalmic diseases are obtained from the European region and North America; our study provided additional data for QALYs weighted as an outcome of clinical trials and decision-making policies in the Southeast Asia, thus representing the low and middle-income countries (LMIC).

Moreover, it demonstrated the HU score and vision utility score in common eye diseases from multiple centers across the country with a large sample population.

Limitations

Future research that expands the HU in other ophthalmic conditions could facilitate the generalization of data. Moreover, researchers should include a larger sample size in subtypes of DR or AMD to evaluate the HU in a specific group, such as the burden of intravitreal treatment on the QoL. The major limitation of this study was its cross-sectional design, which may not reflect the effect of time series on the change in the HU and VA. In addition, we included only the primary variables in ophthalmic conditions and demographics in an analysis model, whereas QoL was a combination of systemic diseases as well. For the survey method, the interviewer's assistance may have influenced the response of participants which lead to interviewer-dependent values. The respondents from our study were approached at an out-patient clinic, thus suggesting they were able to ambulate. We did not evaluate bed-ridden patients or those without transportability. Moreover, this study conducted in a tertiary care center, the characteristic of the patients might not fully represent a patient in general of the country. Thereby these resulting in a limitation for the generalization of our results.

Chapter 6
Conclusion

This study demonstrates the effect of visual acuity levels are more important than types of diseases. This novel study used TTO and HUI3 to evaluate the HU of patients with retina disease and visual impairment in South East Asia.(Mok et al., 2021) Importantly, The VA level exerted a higher impact on the patient's QoL than the type of eye disease. The Low VA resulted in poor QoL and HU. MAUI instruments and cTTO are suitable in HU measurement in DR, wet AMD, and cataract. With the good correlation to the vision-specific quality of life and changes of visual acuity level, HUI3 is recommended to evaluate HU in an ophthalmic patient in Thailand. The patient-reported outcome can be used to reflect on the patient's visual function. The types of diabetic retinopathy and other eye conditions have less influence on the HU compared to the level of visual acuity.

Although, It has been known that visual acuity has been the most common primary outcome in the measurement of ocular conditions in clinical trials and various research studies. Though, it represents the main ability of a person to visualize and function in daily living. Other visual functions such as contrast sensitivity and visual field also contribute to the capability of an individual to "see" and live, which affecting on the individual quality of life. This raises the question whether the visual acuity can truly represent the real-world effect of treatments or diseases on individual person. While a small change of VA had limited effect on the HU, but the visual specific QoL could be another way to report visual function from individual. The MAUI and TTO questions might not captures a small changes of vision function but the instruments might be helpful to evaluate the burden when there is a significant decrease in visual function.

Religion seems to have an effect on the dead-related question in TTO. tTTO, cTTO, EQ-5D-5L, HUI3, and NEI VFQ-25 are feasible to be used in Thai ophthalmic elderly patients. However, worse than the dead stage-related question is not preferred. With the prespecified questions and multiple-choice type of answer, indirect HU methods cause less confusion to respondents.

In Thailand, EQ-5D-5L which is recommended to use in HTA guidelines of the country, has been shown to be feasibly for using in ophthalmic patient in order to evaluate the burden of visual impairment. cTTO and HUI3 has shown an acceptable feasibility as well. Moreover, the instruments could be implemented as PROs so as to portray the impact of disease the patient's quality of life.

Future research that expands the HU in other ophthalmic conditions could facilitate data generalization. Moreover, researchers should include a larger sample size in subtypes of DR or AMD to evaluate the HU in a specific group, such as the burden of intravitreal treatment on the QoL.

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Appendices

Original questionnaires for the interview in this project

General information questionnaire

DATE __ __ /__ __ /__ __ (วัน/เดือน/พ.ศ.)

เวลาเริ่ม __ __ :__ __ น. (ชั่วโมง : นาที , ตัวอย่าง 13.05 น.)

รหัสผู้สัมภาษณ์ __ __ __

ส่วนที่ 1

ข้อมูลพื้นฐาน

กรุณา เลือกช่องที่ท่านต้องการโดยทำเครื่องหมาย ☑ และกรอกข้อมูลในช่องว่างที่เว้นไว้

1. เพศ 1.1☐ หญิง 1.2☐ ชาย
2. อายุ _____ ปี
3. ที่อยู่ปัจจุบันที่พำนักอยู่ 3.1 ☐ กรุงเทพฯ 3.2 ☐ อื่นๆ ระบุ _____
4. อาชีพ
   - 4.1 ☐ ข้าราชการ สังกัด ลักษณะงาน ระบุ.....
   - 4.2 ☐ ธุรกิจส่วนตัว ลักษณะธุรกิจ ระบุ.....
   - 4.3 ☐ รับจ้าง ลักษณะงาน ระบุ.....
   - 4.4 ☐ ลูกจ้างชั่วคราว ลักษณะงาน ระบุ.....
   - 4.5 ☐ แม่บ้าน ลักษณะงานระบุ.....
   - 4.6 ☐ พนักงานประจำ ลักษณะงาน ระบุ.....
   - 4.7 ☐ เกษียณอายุ ลักษณะงานก่อนเกษียณ ระบุ.....
   - 4.8 ☐ อื่นๆ ระบุ.....
5. นับถือศาสนาใด
   - 5.1 ☐ พุทธ
   - 5.2 ☐ คริสต์
   - 5.3 ☐ อิสลาม
   - 5.4☐ ไม่นับถือศาสนาใด
   - 5.5 ☐ อื่นๆ ระบุ.....
6. สถานภาพ
   - 6.1 ☐ โสด
   - 6.2 ☐ แต่งงาน อยู่ร่วมกัน
   - 6.3 ☐ แต่งงาน แยกกันอยู่

6.4 ☐ หย่าร้าง

6.5 ☐ หม้าย

6.6 ☐ อื่นๆ ระบุ .....

7. วุฒิการศึกษา

7.1 ☐ ประถมศึกษาตอนต้น

7.2 ☐ ประถมศึกษาตอนปลาย

7.3 ☐ มัธยมศึกษาตอนต้น

7.4 ☐ มัธยมศึกษาตอนปลาย

7.5 ☐ ปวช หรือเทียบเท่า ระบุสาขาหรือความชำนาญที่จบ .....

7.6 ☐ ปวส หรือเทียบเท่า ระบุสาขาหรือความชำนาญที่จบ .....

7.7 ☐ ปริญญาตรี หรือเทียบเท่า ระบุสาขาหรือความชำนาญที่จบ .....

7.8 ☐ ปริญญาโท หรือเทียบเท่า ระบุสาขาหรือความชำนาญที่จบ .....

7.9 ☐ ปริญญาเอก หรือเทียบเท่า ระบุสาขาหรือความชำนาญที่จบ .....

7.10 ☐ อื่นๆ ระบุ .....

8 กรุณาระบุรายได้เฉลี่ยต่อเดือนของท่าน

8.1 ☐ น้อยกว่า 10,000 บาท

8.2 ☐ 10000 – 25000 บาท/เดือน

8.3 ☐ 25000 – 50000 บาท/เดือน

8.4 ☐ 50000 – 100000 บาท/เดือน

8.5 ☐ มากกว่า 100000 บาท /เดือน

8.6 ☐ ไม่มีรายได้ ระบุผู้ดูแลค่าใช้จ่ายของท่าน .....

9 สิทธิในการรักษาพยาบาลในครั้งนี้ เลือกได้มากกว่า 1 ช่อง

9.1 ☐ เบิกจ่ายตรงกรมบัญชีกลาง (เบิกราชการ)

9.2 ☐ บัตรทอง บัตร 30 บาท

9.3 ☐ ประกันสังคม

9.4 ☐ ประกันสุขภาพกลุ่ม

9.5 ☐ ประกันสุขภาพส่วนตัว

9.6 ☐ ไม่มีสิทธิรักษาพยาบาลใดๆ , จ่ายเงินเอง

9.7 ☐ อื่นๆ ระบุ.....

ข้อมูลด้านสุขภาพ

รหัสผู้สัมภาษณ์ __ __ __

10 โรคประจำตัว

10.1 ☐ เบาหวาน ได้รับวินิจฉัยมา ..... ปี

10.1.1☐ ทานยา

10.1.2☐ ฉีดยา อินซูลิน

10.1.3☐ ทานยา ร่วมกับฉีดยา

10.2☐ ความดันโลหิตสูง ระดับความดันโลหิตล่าสุด ...../..... มม.ปรอท

10.2.1☐ คุมอาหารอย่างเดียว

10.2.2☐ ทานยา

10.3☐ ไขมันในเลือดสูง

10.3.1☐ คุมอาหารอย่างเดียว

10.3.2☐ ทานยา

10.4 ☐ เกาท์/ ยูริคในเลือดสูง ระบุค่ายูริค (ถ้าทราบ) .....มก/ดล

10.5 ☐ มะเร็ง ระบุ .....

10.6 ☐ โรคทางเดินหายใจ ระบุ .....

10.7 ☐ โรคไต ระบุ .....

10.8 ☐ อื่นๆ ระบุ .....

.....

11 ดื่มสุรา เบียร์ ไวน์ หรือเครื่องดื่ม แอลกอฮอล์

11.1☐ ไม่ดื่ม

11.2☐ เคยดื่ม หยุดแล้ว เป็นระยะเวลา ..... ปี

11.3☐ ดื่ม กรุณาเลือกความถี่

11.3.1☐ ทุกวัน หรือมากกว่า 3 ครั้งต่อสัปดาห์

11.3.2☐ สัปดาห์ละ 1-3 ครั้ง

11.3.3☐ น้อยกว่า สัปดาห์ละ 1 ครั้ง

12 สูบบุหรี่

12.1 ☐ ไม่สูบ

12.2 ☐ เคยสูบ หยุดสูบแล้วเป็นระยะเวลา ..... ปี

12.3 ☐ สูบ กรุณาระบุจำนวน ต่อสัปดาห์ ระบุ .....

13 เคยได้รับการผ่าตัด

13.1☐ ไม่เคย

13.2☐ เคย ระบุ.....

14 ประวัติทางด้านเบาหวาน (หากไม่ได้ป่วยเป็นโรคนี้ให้ข้ามไปข้อถัดไป)

14.1ระยะเวลาที่ป่วยเป็นเบาหวาน .....ปี

14.2 การคุมระดับน้ำตาลที่ผู้ป่วยเข้าใจ 14.2.1 ☐ ดี

14.2.2 ☐ คุมได้บ้าง

14.2.3 ☐ คุมไม่ดี

14.3 ระดับน้ำตาลครั้งล่าสุดเมื่ออดอาหาร ..... มก./ดล.

14.4 ระดับน้ำตาลสะสม HbA1c ล่าสุด ..... %

14.5รักษาเบาหวานด้วยการ

14.5.1☐ คุมอาหารอย่างเดียว

14.5.2☐ ทานยาคุมระดับน้ำตาลอย่างเดียว

14.5.3☐ ทานยาร่วมกับฉีดยา อินซูลิน

14.5.4☐ ฉีดยา อินซูลินอย่างเดียว

14.5.5☐ อื่นๆ

ระบุ.....

14.6 ภาวะแทรกซ้อนจากเบาหวาน

14.6.1 ☐ ยังไม่มีภาวะแทรกซ้อน

14.6.2 ☐ มีเบาหวานขึ้นตาแล้ว

14.6.3 ☐ มีเบาหวานลงไตแล้ว

14.6.4 ☐ มีเบาหวานที่ส่งผลต่อระบบประสาท เช่น มือชา เท้าชา

14.6.5 ☐ มีแผลเบาหวาน

14.6.6 ☐ อื่นๆ

ระบุ.....

15 มีโรคทางตาอื่นๆ ให้ ระบุชนิด/ ข้าง .....

16 ยาที่ใช้ในปัจจุบัน ยา .....

รับประทาน ระบุชนิด ขนาด .....

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17 ยาหยอดตาที่ใช้ในปัจจุบัน ระบุ .....

วิธีใช้ และ ชนิด .....

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18 ข้อมูลด้านสุขภาพอื่นๆ (ระบุชนิด และระยะเวลาที่เป็น)

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Expense and income lost questionnaire

ข้อมูลเชิงเศรษฐศาสตร์

รหัสผู้สัมภาษณ์/ ลงข้อมูล __ __ __

19 ผู้ป่วยมาโรงพยาบาลในครั้งนี้มีผู้ติดตาม/คนดูแลมาด้วยจำนวนเท่าไร และ มีความสัมพันธ์อย่างไรกับผู้ป่วย

19.1☐ ไม่มีผู้ติดตาม

19.2☐ มีผู้ติดตามจำนวน..... คน

☐ คนที่ 1 มีความสัมพันธ์เป็น .....

☐ คนที่ 2 มีความสัมพันธ์เป็น.....

☐ คนที่ 3 มีความสัมพันธ์เป็น.....

☐ คนที่ 4 มีความสัมพันธ์เป็น.....

20 ผู้ป่วยมาโรงพยาบาลในครั้งนี้ เสียค่าใช้จ่ายในการเดินทาง เป็นเงิน โดยประมาณ .....บาท (ค่าเดินทาง เช่น ค่าน้ำมัน ค่า taxi ค่าเหมารถ ค่ารถเมล์)

ผู้ป่วยมาโรงพยาบาลในครั้งนี้ เสียค่าใช้จ่ายที่ไม่ใช่การรักษาพยาบาล เป็นเงินจำนวนโดยประมาณ .....บาท (เช่น ค่าอาหาร ค่าที่พัก ฯลฯ ไม่รวมค่าเดินทาง)

ผู้ป่วยมาโรงพยาบาลในครั้งนี้ สูญเสียรายได้เป็นเงินจำนวน ประมาณ.....บาท (เช่น ค่าจ้างรายวัน ของผู้ป่วย)

ผู้ติดตามคนที่ 1 หรือผู้ดูแลที่พาท่านมาในโรงพยาบาลครั้งนี้ สูญเสียรายได้เป็นเงินจำนวน .....บาท เพื่อมาโรงพยาบาลกับผู้ป่วย

ผู้ติดตามคนที่ 2 หรือผู้ดูแลที่พาท่านมาในโรงพยาบาลครั้งนี้ สูญเสียรายได้เป็นเงินจำนวน .....บาท เพื่อมาโรงพยาบาลกับผู้ป่วย

ผู้ติดตามคนที่ 3 หรือผู้ดูแลที่พาท่านมาในโรงพยาบาลครั้งนี้ สูญเสียรายได้เป็นเงินจำนวน .....บาท เพื่อมาโรงพยาบาลกับผู้ป่วย

ผู้ติดตามคนที่ 4 หรือผู้ดูแลที่พาท่านมาในโรงพยาบาลครั้งนี้ สูญเสียรายได้เป็นเงินจำนวน .....บาท เพื่อมาโรงพยาบาลกับผู้ป่วย

ส่วนนี้สำหรับผู้สัมภาษณ์ตอบ

1. ท่านคิดว่าความน่าเชื่อถือของข้อมูลที่ได้จากการสัมภาษณ์ข้างต้นเป็นอย่างไร

☐เชื่อถือได้

☐เชื่อถือได้แค่บางส่วน ให้เหตุผล .....

☐เชื่อถือไม่ได้ ให้เหตุผล .....

2. ท่านคิดว่าการตอบคำถามของผู้ป่วย เป็นอย่างไร

☐ตอบตรงคำถาม คำตอบดูสมเหตุผล -→**ดำเนินการสัมภาษณ์ส่วนต่อไป**

☐ตอบไม่ตรงคำถาม ไม่สมเหตุสมผลในคำตอบ หรือผู้ป่วยอาจมีปัญหาทางจิตวิทยา ที่ส่งผลต่อผล การสัมภาษณ์แบบสอบถามต่อ → แนะนำหยุดสัมภาษณ์ **ปรึกษาผู้วิจัยหลัก**

3. ข้อเสนอแนะ หรือปัญหาที่พบจากการสัมภาษณ์นี้

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.....

ลงชื่อ ผู้บันทึก .....

เวลาสิ้นสุดการสัมภาษณ์แบบสอบถามนี้ เวลา __ __ :__ __ น. (ชั่วโมง : นาที , ตัวอย่าง 13.05 น.)

General health questionnaire

ส่วนที่ 2 ข้อมูลโรคของผู้ป่วย (สำหรับผู้ช่วยวิจัย หรือผู้สัมภาษณ์)

DATE __ __ /__ __ /__ __ (วัน/เดือน/พ.ศ.)

เวลาเริ่ม __ __ :__ __ น. (ชั่วโมง : นาที , ตัวอย่าง 13.05 น.)

รหัสผู้ลงข้อมูล __ __ __

แพทย์ผู้รักษา __ __ __

1. Visual acuity OD manifest

ETDRS	1.1 Manifestation	.....	Letters ☐ others.....
	1.2 Pinhole	.....	Letters ☐ others.....
	1.3 Corrected by auto refraction or BCVA	.....	Letters ☐ others.....
	1.4 With glass/ CL	1.4.1 ☐ Yes	..... Letters
		1.4.2 ☐ No	ข้ามไปข้อถัดไป

2. Visual acuity OS manifest

ETDRS	2.1 Manifestation	.....	Letters ☐ others.....
	2.2 Pinhole	.....	Letters ☐ others.....
	2.3 Corrected by auto refraction or BCVA	.....	Letters ☐ others.....
	2.4 With glass/ CL	2.4.1 ☐ Yes	..... Letters
		2.4.2 ☐ No	ข้ามไปข้อถัดไป

3. IOP 3.1OD..... mmHg By ☐ Air puff

3.2 OS.....mmHg

☐ Goldman Applanation
☐ I-care
☐ Tonopen

Current eye medication: .....

History of eye surgery /when/site/what

.....

Systemic underlying

☐ Hypertension ☐ Hypercholesterol/ Triglyceridemia ☐ Ischemic heart disease
☐ Renal failure /Renal dialysis ☐ Diabetic foot
☐ Autoimmune disease ระบุ..... ☐ Gout
☐ Stroke ระบุระยะเวลาที่เป็น .....เดือน/ ปี ☐ Asthma หรือ COPD
☐ อื่นๆ ระบุโรค และ ระยะเวลาที่เป็น

.....

.....

Note: ระบุรายละเอียดอื่นๆ เพิ่มเติมด้านพื้นฐานสุขภาพผู้ป่วย

.....

.....

.....

.....

Last lab

FBS ..... Mg/dl Date.....

HbA1C .....% Date.....

Creatinine ..... Mg/dl Date.....

Urine protein

Lab อื่นๆ ในช่วง 3 เดือนที่ผ่านมา โปรดระบุชนิด และผลการตรวจ (ถ้ามี)

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.....

.....

.....

ลงชื่อ ผู้บันทึก.....

Patient's clinical information form

ส่วนที่ 3 ข้อมูลโรคของผู้ป่วย (ให้แพทย์กรอก หรือ ลงจากประวัติการตรวจ)

DATE __ __ /__ __ /__ __ (วัน/เดือน/พ.ศ.)

รหัสผู้ลงข้อมูล __ __ __

รหัสแพทย์ผู้รักษา __ __ __

ผู้ป่วยเป็นโรคใด (กรุณาเลือกข้อที่ผู้ป่วยมี)

☐ Cataract

☐ OD Lens grading NS ระดับ .....

CC ระดับ .....

PSC ระดับ .....

☐ OS Lens grading NS ระดับ .....

CC ระดับ .....

PSC ระดับ .....

☐ Wet -AMD OD / OS/ OU

OD Treatment (กรุณาเลือก และวง รายการทุกข้อที่มี)

☐ VEGF Number of injection .....

1st treatment when.....

Last IVT injection .....

Type of med AV/RA/AF/Mixed

Regimen Fix/p.r.n./T&E/No regimen.....

Disease status today Active / quiet / conservative

☐ Laser PDT When .....

☐ Complication .....

OS Treatment

☐ VEGF Number of injection .....

1st treatment when.....

Last IVT injection .....

Type of med AV/RA/AF/Mixed

Regimen Fix/p.r.n./T&E/No regimen.....

Disease status today Active / quiet / conservative

☐ Laser PDT When .....

☐ Complication .....

☐ Diabetic retinopathy screening/treatment

OD

☐ No DR

☐ NPDR Mild/moderate/severe/very severe

☐ PDR/VH Quiet/ Active

☐ TRD Surgery ☐ No ☐ Yes

when.....

☐ PRP treatment

☐ No

☐ Yes when .....

☐ History of DME

☐ No

☐ Yes

☐ VEGF Number of injection .....

1st treatment when.....0

Last injection when .....

Type of med AV/RA/AF/Mixed

Regimen Fix/p.r.n./T&E/No regimen.....

Disease status Active / quiet or stable / conservative

☐ Focal/grid laser When

.....

.....

OS

☐ No DR

☐ NPDR Mild/moderate/severe/very severe

☐ PDR/VH Quiet/ Active

☐ TRD

☐ PRP treatment

☐ No

☐ Yes when .....

☐ History of DME

☐ No

☐ Yes

☐ VEGF Number of injection .....

1st treatment when.....
Last injection when .....
Type of med AV/RA/AF/Mixed
Regimen Fix/p.r.n./T&E/No regimen.....
Disease status Active / quiet or stable / conservative

☐ Focal/grid laser When .....
.....

History of angiography (FFA) when (last) .....
Result .....
OCT imaging Type of machine : HD, Cirrus, Optovue, others.....
OD: This visit date: ..... CST.....microns
☐ IRF ☐ SRF ☐ DRiLL ☐Loss IS/OS ☐ EMM ☐VMT
☐ MH ☐others.....
Previous visit: ..... CST.....microns
☐ IRF ☐ SRF ☐ DRiLL ☐Loss IS/OS ☐ EMM ☐VMT
☐ MH ☐others.....
OS: This visit date: ..... CST.....microns
☐ IRF ☐ SRF ☐ DRiLL ☐Loss IS/OS ☐ EMM ☐VMT
☐ MH ☐others.....
Previous visit: ..... CST.....microns
☐ IRF ☐ SRF ☐ DRiLL ☐Loss IS/OS ☐ EMM ☐VMT
☐ MH ☐others.....

General eye examination:

	OD		OS	
Lid	☐	Normal	☐	Normal
	☐	Abnormal	☐	Abnormal .....
Cornea	☐	Normal	☐	Normal
	☐	Abnormal	☐	Abnormal .....
AC	☐	Normal	☐	Normal
	☐	Abnormal	☐	Abnormal .....
Lens	☐	Pseudophakic	☐	Pseudophakic

	☐	Aphakic	☐	Aphakic
	☐	Phakic: cataract , no cataract	☐	Phakic: cataract , no cataract
Fundus	☐	Normal	☐	Normal
	☐	Can’t evaluate ระบุ	☐	Can’t evaluate ระบุ
		.....		.....
	☐	NVE	☐	NVE
	☐	NVD	☐	NVD
	☐	Dot blot	☐	Dot blot
	☐	CWS	☐	CWS
	☐	Others.....	☐	Others.....
Macular	☐	Normal	☐	Normal
	☐	New hemorrhage	☐	New hemorrhage
	☐	Old hemorrhage	☐	Old hemorrhage
	☐	Subretinal fibrosis	☐	Subretinal fibrosis
	☐	Edema	☐	Edema
	☐	RPE rip	☐	RPE rip
	☐	Disciform scar	☐	Disciform scar
	☐	Other.....	☐	Other.....
Optic nerve	☐	Cupping.....	☐	Cupping.....
	☐	Pale	☐	Pale
	☐	Edema	☐	Edema
	☐	Other.....	☐	Other.....
Other	☐	.....	☐	.....
		.....		.....

ลงชื่อ แพทย์ผู้ตรวจ ..... วันที่ ..... เดือน ..... พ.ศ. 25.....

tTTO question

เวลาเริ่ม __ __ . __ __ น. (เช่น 14.05 น.)

วันที่ __ __ เดือน __ __ ปี 25__ __

1. ***ปัจจุบันท่านมีอายุ*** ..... ปี
2. ***ท่านคิดว่าตัวท่านจะมีอายุยืนยาวถึงกี่ปี***

คำตอบ.....ปี

(หมายเหตุ: บอกจำนวนอายุที่มากกว่าจำนวนอายุปัจจุบัน)

☐ ไม่ตอบ เพราะ .....

(หากผู้ป่วยไม่ตอบคำถามนี้ ไม่ต้องไปข้อต่อไปถือว่าแบบสอบถามนี้ไม่สมบูรณ์)

3. ***ถ้ามีเครื่องมือและยาสมัยใหม่ที่จะทำให้ท่านกลับมามองเห็นได้เหมือนคนปกติทันที แต่จะทำให้อายุของท่าน สั้นลง***

ท่านคิดว่าท่านจะยอมอายุสั้นลงกี่ปีเพื่อแลกกับการมองเห็นที่เหมือนคนปกติ หรือเป็นปกติ โดยมีสุขภาพร่างกายอื่นๆ เหมือนที่เป็นอยู่ปัจจุบัน

คำตอบ.....ปี

เหตุใดจึงเลือกจำนวนนี้ ให้เหตุผล .....

(หมายเหตุ: เมื่อหักจำนวนที่ตอบจากข้อ 2 นี้ ออกจากข้อ 1 จะต้องมีจำนวนอายุเหลือมากกว่า หรือเท่ากับอายุปัจจุบัน)

☐ ไม่ยอมมีอายุสั้นลง เพราะ

.....

4. ***มีปัจจัยอะไรที่มีผลต่อการตัดสินใจ หรือ มีภาระ หรือมีห่วง ในการตัดสินเรื่องระยะเวลาที่จะยอมมีอายุสั้นลงดังในข้อ 3 หรือไม่*** **(**ตัวอย่างเช่น ลูก หลาน พ่อ แม่**)**

☐ ไม่มี **(**ข้ามไปข้อถัดไป **)**

☐ ลูก หลาน ☐ พ่อ แม่

☐ สามี ภรรยา ☐ ภาระหนี้สิน ☐ ภาระเลี้ยงดู

☐ อื่นๆ ระบุ**.....**

5. ***ถ้าไม่ต้องมีภาระความรับผิดชอบ หรือต้องกังวลเกี่ยวกับปัจจัยข้างต้น (ในข้อ 4) ท่านจะเลือกคำตอบตามเดิมอยู่หรือไม่***

☐ ใช่

☐ ไม่ใช่ ให้ระบุระยะเวลาที่ยอมเสียชีวิตเร็วขึ้นเ หรืออายุสั้นลง เพื่อแลกกับการให้สายตา หรือดวงตากลับมาเป็น ปกติ

เมื่อไม่มีปัจจัยอื่นๆ ระยะเวลาที่ยอมแลก เป็น .....ปี

เวลาสิ้นสุดแบบสอบถาม ___ ___ . ___ ___ น.

ลงชื่อผู้สัมภาษณ์ .....

cTTO question and visual guide

วันที่ __ __ เดือน __ __ ปี 25__ __

(ผู้สัมภาษณ์ เกริ่น) ***"ต่อไปนี้ จะมีสุขภาพ 2 แบบ ให้ท่านเลือก ขอให้ท่านคิดอย่างรอบคอบ แล้วเลือกสุขภาพที่ต้องการจะเป็น***

มากกว่า ถ้าท่านเห็นว่าทั้ง 2 แบบไม่แตกต่างกัน กรุณาบอกว่าไม่แตกต่างกัน"

(หมายเหตุ:

สุขภาพร่างกายคือสุขภาพที่ท่านเป็นอยู่ในระดับนี้ และได้รับการรักษาที่ท่านเป็นอยู่ยกเว้นแต่การรักษาทางตา)

(ระดับการมองเห็นที่ท่านเป็นอยู่ขณะนี้ คือ ระดับการมองเห็นโดยรวมของท่านทั้ง 2 ตา)

(ให้อ่าน สุขภาพแบบ ก และ สุขภาพ แบบ ข ให้ผู้ป่วยฟัง รวมถึงสามารถใช้ กร๊าฟแท่งที่แสดงแสดงให้ผู้ป่วยดูเพื่อเป็นการเปรียบเทียบ)

คำถามเพื่อซักซ้อมความเข้าใจ

สุขภาพแบบ ก	สุขภาพแบบ ข
● *มีสุขภาพร่างกายเหมือนในวันนี้* ● *ตามองเห็นเหมือนคนปกติ* ● *จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต*	● *มีสุขภาพร่างกายเหมือนในวันนี้* ● *ตามองเห็นได้เหมือนวันนี้ทั้งสองข้าง* ● *จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต*
คำถาม: ***ถ้าให้เลือกระหว่าง สุขภาพ ก กับ สุขภาพ แบบ ข ท่านจะเลือกสุขภาพแบบใด?*** ☐ สุขภาพแบบ ก ☐ สุขภาพแบบ ข (สอบถามเหตุผล) ☐ ไม่ต่างกัน (สอบถามเหตุผล)	
เหตุผล	
สำหรับผู้สัมภาษณ์ Note:	

เวลาเริ่ม __ __ . __ __ น. (เช่น 14.05 น.)

TTO – BTD

ข้อ 0

สุขภาพแบบ ก	สุขภาพแบบ ข
● เสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● **ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้**

	● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม : ***ถ้าให้เลือกระหว่าง ก. เสียชีวิตในตอนนี้เลย หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด?***

ท่านจะเลือกสุขภาพแบบใด

☐ สุขภาพแบบ ก (สอบถามเหตุผล และหยุด)

☐ สุขภาพแบบ ข (ทำข้อต่อไป)

☐ ไม่ต่างกัน (สอบถามเหตุผล และ หยุด)

เหตุผล .....

สำหรับผู้สัมภาษณ์ Note:

.....

.....

ข้อ 1

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **1** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม : ***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 1 ปีจากนั้นเสียชีวิต หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?***

ท่านจะเลือกสุขภาพแบบใด

☐ สุขภาพแบบ ก (หยุด)

☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)
เหตุผล .....
สำหรับผู้สัมภาษณ์ Note: ....

ข้อ 2

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นเหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **2** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม: ***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 2 ปีจากนั้นเสียชีวิต***

หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต

ท่านจะเลือกแบบใด ?

ท่านจะเลือกสุขภาพแบบใด ☐ สุขภาพแบบ ก (หยุด) ☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)
เหตุผล .....
สำหรับผู้สัมภาษณ์ Note: ....

ข้อ 3

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **3** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต
คำถาม:***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 3 ปีจากนั้นเสียชีวิต หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?***	
ท่านจะเลือกสุขภาพแบบใด ☐ สุขภาพแบบ ก (หยุด) ☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)	
เหตุผล	
สำหรับผู้สัมภาษณ์ Note:	

ข้อ 4

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **4** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม:ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 4 ปีจากนั้นเสียชีวิต หรือ ข. มีสุขภาพร่างกายและสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?

ท่านจะเลือกสุขภาพแบบใด

☐ สุขภาพแบบ ก (หยุด)

☐ สุขภาพแบบ ข (ทำข้อต่อไป)

☐ ไม่ต่างกัน (หยุด)

เหตุผล .....

สำหรับผู้สัมภาษณ์ Note:

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ข้อ 5

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **5** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม:ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 5 ปีจากนั้นเสียชีวิต หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?

ท่านจะเลือกสุขภาพแบบใด

☐ สุขภาพแบบ ก (หยุด)

☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)
เหตุผล .....
สำหรับผู้สัมภาษณ์ Note: ....

ข้อ 6

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **6** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม:***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 6 ปีจากนั้นเสียชีวิต***
หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?

ท่านจะเลือกสุขภาพแบบใด ☐ สุขภาพแบบ ก (หยุด) ☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)
เหตุผล .....
สำหรับผู้สัมภาษณ์ Note: ....

ข้อ 7

สุขภาพแบบ ก	สุขภาพแบบ ข
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **7** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม:***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 7 ปีจากนั้นเสียชีวิต***
หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?

ท่านจะเลือกสุขภาพแบบใด

☐ สุขภาพแบบ ก (หยุด)

☐ สุขภาพแบบ ข (ทำข้อต่อไป)

☐ ไม่ต่างกัน (หยุด)

เหตุผล .....

สำหรับผู้สัมภาษณ์ Note:

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ข้อ 8

สุขภาพแบบ ก	สุขภาพแบบ ข
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **8** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม:***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการ***

รักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 8 ปีจากนั้นเสียชีวิต ***หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?***
ท่านจะเลือกสุขภาพแบบใด ☐ สุขภาพแบบ ก (หยุด) ☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)
เหตุผล .....
สำหรับผู้สัมภาษณ์ Note: ....

ข้อ 9

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **9** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม: ***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 9 ปีจากนั้นเสียชีวิต*** ***หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?***
ท่านจะเลือกสุขภาพแบบใด ☐ สุขภาพแบบ ก (หยุด) ☐ สุขภาพแบบ ข (ทำข้อต่อไป) ☐ ไม่ต่างกัน (หยุด)
เหตุผล .....

สำหรับผู้สัมภาษณ์ Note: ....

ข้อ 10

สุขภาพแบบ ก	**สุขภาพแบบ ข**
● มีสุขภาพร่างกายเหมือนในวันนี้ ● มีดวงตาที่มองเห็นได้เหมือนคนปกติ ● จะมีชีวิตอยู่ต่อไปอีก **10** ปี แล้วเสียชีวิต	● มีสุขภาพร่างกายเหมือนในวันนี้ ● ระดับการมองเห็นที่ท่านเป็นอยู่ในขณะนี้ ● จะมีชีวิตอยู่ต่อไปอีก 10 ปี แล้วเสียชีวิต

คำถาม:***ถ้าให้เลือกระหว่าง ก. สายตาและโรคทางตากลับมาเป็นปกติ ไม่ต้องทำการรักษาใดๆ และมองเห็นได้ปกติ แต่มีชีวิตอยู่ไปได้ 10 ปีจากนั้นเสียชีวิต***
หรือ ข. มีสุขภาพร่างกาย และสายตาแบบที่ท่านเป็นอยู่ในระดับนี้ โดยมีชีวิตต่อไปอีก 10 จากนั้นเสียชีวิต ท่านจะเลือกแบบใด ?

ท่านจะเลือกสุขภาพแบบใด

☐ สุขภาพแบบ ก (หยุด)

☐ สุขภาพแบบ ข (หยุด)

☐ ไม่ต่างกัน (หยุด)

เหตุผล .....

สำหรับผู้สัมภาษณ์ Note:

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เวลาเริ่ม __ __ . __ __ น. (เช่น 14.05 น.)

ลงชื่อผู้สัมภาษณ์ .....

Interviewer form

ส่วนพิเศษ : สำหรับผู้สัมภาษณ์

คำถามนี้ ไม่ถูกนำไปวิเคราะห์ข้อมูล แต่หากเป็นการสื่อสารและการประเมินความเห็นของผู้สัมภาษณ์เกี่ยวกับการสัมภาษณ์ในครั้งนี้ กรุณาเลือกข้อที่ ตรงกับความคิดของท่าน

แบบสอบถาม EQ5D

ท่านคิดว่าความน่าเชื่อถือของคำตอบในการตอบสัมภาษณ์นี้เป็นอย่างไร	
☐	เชื่อถือได้
☐	ไม่น่าเชื่อถือ กรุณาระบุเหตุผล .....

แบบสอบถาม HUI 3

ท่านคิดว่าความน่าเชื่อถือของคำตอบในการตอบสัมภาษณ์นี้เป็นอย่างไร	
☐	เชื่อถือได้
☐	ไม่น่าเชื่อถือ กรุณาระบุเหตุผล .....

แบบสอบถาม VFQ-25

ท่านคิดว่าความน่าเชื่อถือของคำตอบในการตอบสัมภาษณ์นี้เป็นอย่างไร	
☐	เชื่อถือได้
☐	ไม่น่าเชื่อถือ กรุณาระบุเหตุผล .....

ท่านประสบปัญหาหรือข้อขัดข้องใดในการสัมภาษณ์ผู้ป่วยรายนี้หรือไม่ (เช่น ผู้ป่วยไม่ได้ยิน ผู้ป่วยไม่มีสมาธิในการตอบ ผู้ป่วย ไม่เข้าใจในคำถามต้องอ่านทวนหลายครั้ง เป็นต้น)

ท่านคิดว่าความน่าเชื่อถือของคำตอบในการตอบสัมภาษณ์นี้เป็นอย่างไร	
☐	ไม่มีปัญหา
☐	มีปัญหา แต่สามารถแก้ไขสถานการได้ กรุณาระบุ .....
☐	มีปัญหาอย่างมาก ไม่สามารถแก้ไขได้ กรุณาระบุรายละเอียด และ ส่วนที่กระทบต่อการสัมภาษณ์ครั้งนี้ .....

ข้อเสนอแนะอื่นๆ ที่อาจเกี่ยวข้องกับผลของการสัมภาษณ์ครั้งนี้ (ถ้ามี)

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ลงชื่อ .....

VITA

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